The Chemistry of Alkenes
Edited by Saul Patai

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The Hebrew University
Jerusalem, Israel

1964
INTERSCIENCE PUBLISHERS
a division of John Wiley & Sons
LONDON – NEW YORK – SYDNEY

Library of Congress Catalog Card Number 64–25218

ISBN 0 470 66930 6

Reprinted 1972

Printed in Great Britain by Unwin Brothers Limited
The Gresham Press, Old Woking, Surrey
A member of the Staples Printing Group

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Foreword

The aim of this book is to present an up-to-date dissertation on the chemistry of the carbon–carbon double bond in all its aspects. An encyclopaedic coverage of all known reactions, data, or measurements relating to the topics covered in the various chapters was not intended; indeed the authors were asked to refrain from doing so. Rather, the emphasis was put on comparative and critical discussion of the subjects, addressed to the advanced student and research chemist. It was attempted to include as far as possible all the relevant information on the recent advances regarding the theory and practice of the subject, stressing especially the theoretical, physical and mechanistical principles. In view of this it may possibly be argued that both directions of a reversible reaction, say addition and elimination, should have been discussed together in the same chapter. It was attempted to prepare such a plan for the contents of this book, but it soon became clear that it could not be carried out to its logical conclusion in a multi-authored treatise. The close interconnection of the various parts of the subject would make it possibly more suitable for unified treatment by a single author, if one could be found possessing the qualifications of encyclopaedical knowledge and unlimited time for writing. Therefore, while aware of the limitations of the present plan, this had to be adopted, giving each author the task of writing a more or less defined account of a single aspect of the chemistry of alkenes.

The treatment of the material was limited to the reactions in which the carbon–carbon double bond is either formed or is the site of reaction, and reactions occurring in parts of the molecule remote from the $C{=}C$ bond are discussed only if they are influenced by the latter. This puts the emphasis on the $C{=}C$ bond as a *functional group*. Again it may be argued that the treatment of a single functional group is not in accordance with the most modern principles, since mechanistic similarities unite the reactions of different functional groups, as for instance the nucleophilic reactions on an activated $C{=}C$ bond and on a carbonyl carbon atom. Still, organic chemistry is in most places taught according to functional groups and the mnemotechnic advantages of this division are so great that it will probably not be displaced for many decades yet to come. We hope that a series of advanced treatises on the chemistry of the functional groups will be a useful and valuable addition to the literature of organic chemistry, and the present volume is the first in this planned series.

There are two obvious gaps in the structure of the book. The chapters on 'Electrophilic Attacks on Alkenes' and on 'Biochemical Formation and Reactions of Alkenes' were promised but were not delivered. After several months waiting, what is believed by the editor and the publisher to be the lesser evil was chosen and it was decided to publish the book in its present form, with these chapters missing, as further delay would have rendered the text of the other chapters out of date.

I wish to thank Dr. Arnold Weissberger who encouraged me to undertake the task of editing this book, and who was always ready to help me with friendly advice and helpful suggestions. My thanks are also due to the staff of the publisher's editorial office in London, who took upon themselves additional work and trouble to overcome the difficulties of coping with an editor residing several thousand kilometers distant from their office. Finally, it is a pleasure to acknowledge the help given to me in many ways by my senior pupils and younger colleagues, especially by Dr. Z. Rappoport and by Mr. M. Michmann, who also undertook the arduous task of preparing the indexes.

Jerusalem, May 1964 SAUL PATAI

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CHAPTER 1

Wave mechanics and the alkene bond

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I. INTRODUCTION

There will be very few readers of this chapter who will not at first question the relevance of a great deal of the material in its earlier sections. It is not until section VIII that we venture to discuss an alkene molecule, and this may well seem excessively cautious at a time when all but the most sheltered students of elementary organic chemistry are introduced to terms like 'orbital,' 'hybridization', and 'overlap' almost as soon as they have learnt the structural formulae of the simplest hydrocarbons.

But of course a wave-mechanical description of bonding in organic molecules requires far more than just the assimilation of a little quantum-chemical terminology into the language of classical organic chemistry. We would do wrong not to make it clear at the outset that, from the wave-mechanical point of view, the σ–π systems with which this book is concerned are by no means as straightforward as is often suggested. Any worth-while study of the bonding in an alkene or polyene molecule (or, indeed, any polyatomic molecule) demands, quite inescapably, a prior understanding of the quantum chemistry of much simpler molecules. We have tried to provide a basis for this understanding in sections II to VII, our aim in these sections being to give an account which readers whose interests are in other fields of chemistry will find neither overtaxingly difficult nor unrewardingly elementary.

Because most other procedures lead to computational excesses, molecular wave functions are almost invariably compounded from atomic wave functions, which in turn are formulated by analogy with the wave functions for the one-electron series H, He^+, Li^{2+}, Be^{3+}, ... So in section II we discuss 'hydrogen-like' atomic wave functions and the energy levels to which they are related by the Schrödinger wave equation.

Wave functions for systems of more than one electron must always be approximate in some degree, and the analytical forms in which they are expressed can never be unique. It is mainly for this reason that the theoretical study of alkene molecules must be preceded by a study of much simpler systems, in which it is comparatively easy to demonstrate the nature and the quantitative importance of the approximations. In section III we outline some of the principles involved in obtaining approximate wave functions, and in section IV we apply these principles to the ground state of the hydrogen molecule, the wave functions for which have long been used as prototypes for the wave functions of almost all covalently bonded molecules.

In any wave function built up from two or more spatial orbitals it is necessary to take into account electron spin and the Pauli principle, which are extraneous to Schrödinger wave mechanics, and which have accordingly to be dealt with somewhat arbitrarily. Where results of wide applicability are required, the arbitrary procedure is most conveniently formulated in terms of angular momentum; but, to avoid embarking on an exposition which, though perfectly straightforward, is lengthy and not essential for our purposes, we give in section V an alternative formulation—admittedly restricted—in terms of electronic energy. In this we make use of the fairly detailed energy relations derived in section IV.

It is not always appreciated that, when the ground-state and the lower-excited-state wave functions for a molecule are built up from the same set of ground-state atomic orbitals, the molecular wave functions for the excited states are normally far less satisfactory than that for the ground state. This is an important point, so we have gone out of our way to emphasize it in section VI. In the same section we discuss linear variation functions, partly to illustrate the close resemblance between molecular-orbital and valence-bond wave functions, and partly to provide a background for the subsequent description of wave functions based on linear combinations of atomic orbitals.

In sections VII and VIII, after examining the restrictions on the linear combination of atomic orbitals which result from differences in symmetry or energy, we describe wave functions for the five molecules F_2, HF, C_2H_2, C_2H_4, CH_4 (taken in order of increasing geometrical complexity). In a monograph on the alkenes the preliminary study of the two diatomic molecules may seem an intrusion, but it enormously simplifies the later description of bonding in polyatomic organic molecules. In consequence of the development of electronic computing resources, much precise calculation on linear molecules, especially diatomic molecules, has been carried out in recent years. We have discussed this important work in some detail, partly because (so far as we know) no simple account of it has been given elsewhere, but mainly because most of the results are of quite general application and are by no means restricted to diatomic molecules, or even to linear molecules. In selecting F_2 and HF for detailed comparison with C_2H_2 our purpose has been to draw attention to some of the quantum-chemical resemblances between inorganic and organic molecules.

The remaining sections of the chapter are devoted to various aspects of the quantum chemistry of π-electron systems. In these sections we have tried to provide the background necessary for a perceptive study of the literature; we have made no attempt to review or catalogue the enormous amount of work published during the past thirty years. After a critical examination of the concept of π-electron energy in section IX, we explain the Hückel approximation in section

X, and show how this leads to greatly simplified procedures for describing the lower electronic transitions in an alkene molecule. Conjugation is dealt with in section X, and a miscellany of electronic spectral phenomena in section XI.

The general purpose of this chapter is to enable the reader without previous knowledge of quantum-chemical procedures* to appreciate the significance and also the limitations of wave-mechanical calculations, but not to enable him to perform such calculations himself or to encourage him to investigate subtle problems in valency theory. Even in the simplest cases these latter tasks call for considerable experience of wave-mechanical methods, and we strongly recommend that they be left to the specialist theoretician. The current fashion of providing an *ad hoc* theory for every new fact has led to endless confusion and misunderstanding, and it imposes a quite needless obligation on chemists who have no occasion to make a detailed study of wave mechanics.

It is idle to pretend that any but the most trivial features of organic quantum chemistry can be presented in non-mathematical terms. For our purposes, however, the mathematical analysis required is very straightforward and well within the repertoire of the average chemist. Although we have not tried to avoid any essential mathematics, we have assumed nothing more than a knowledge of the differentiation and integration of simple trigonometric and exponential functions[2], and we have explained other routine mathematical procedures wherever necessary[3].

We have arranged the contents of the chapter in order of increasing chemical complexity, stating quantum-mechanical postulates and principles piecemeal as required†. From the mathematical point of view this is a very untidy method, and it makes a rigorous exposition impossible, but we believe it is the method which will come nearest to meeting the requirements of the majority of organic chemists at the present time. We hope that some readers may be encouraged to embark on a far more systematic study of the principles of quantum mechanics. They will find these discussed at an appropriate level of sophistication in the well-known texts by Pauling and Wilson[4], Eyring, Walter and Kimball[5], Kauzmann[6], and Slater[7].

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* The reader who is already familiar with the elements of wave mechanics (at the level, say, of Coulson's[1] *Valence*) may omit sections II and III.

† We have not given literature references to work which is now firmly established as part of the standard subject matter of quantum chemistry. These are quoted in refs. 1 and 4–7.

II. HYDROGEN-LIKE WAVE FUNCTIONS

A. Energy Levels

It has long been known that the electronic energies* of bound states of atoms, molecules, and ions are 'quantized'; *i.e.* in any system of nuclei and electrons in which the composite particles are not undergoing a dissociation or recombination process the possible electronic energies are restricted to a discrete set. An atom, molecule, or ion can radiate or absorb energy only in 'quanta' whose magnitudes are determined by differences between pairs of energy 'levels': continuous variation in energy does not occur.

A chemical system is said to be in its ground state if its energy corresponds to the lowest of the permitted energy levels; otherwise it is said to be in an excited state. The spacing between successive energy levels decreases markedly with increase in energy, and thus, although in principle there are always an infinite number of excited states, only those relatively near to the ground state can be distinguished experimentally.

Corresponding to each of the permitted electronic energy levels there is a characteristic distribution of electronic charge around the nuclei. In general, the higher the electronic energy, the larger the effective volume which the electron 'clouds' occupy.

The main object of molecular quantum chemistry is to provide the means of calculating the possible electronic energies of any polyatomic system, together with quantities such as dipole moment and oscillator strength which depend upon the corresponding electronic charge distributions. Even with the computing resources now available, this can be done accurately only for very small molecules. For the relatively complex systems discussed in the later chapters of this book, purely theoretical calculations are too elaborate to be practicable, so the properties of an organic molecule have normally

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* In the sense in which we use the term in this chapter, the electronic energy of a chemical species is to be understood to be the sum of the following:

(*a*) the kinetic energy of the electrons;
(*b*) the potential energy of repulsion between the electrons;
(*c*) the potential energy of attraction between the nuclei and the electrons.

When considering the variation of electronic energy with internuclear distance, some authors find it convenient to include also

(*d*) the potential energy of repulsion between the nuclei,

although this last term is strictly non-electronic.

to be calculated from those of closely related atoms or molecules by interpolation or extrapolation procedures guided by the results of strict wave-mechanical calculations on much simpler molecules. These procedures cannot be applied to excited molecular states without considerable risk of error; but in the interpretation of ground-state phenomena they are often astonishingly successful.

Because the great majority of wave-mechanical studies of multiply bonded molecules have been carried out by analogy, and not *ab initio*, we cannot provide a basis for the later discussion in this chapter without first describing, at least in outline, something of the wave-mechanical treatment of very simple systems. Indeed, we can profitably carry the process of simplification to its extreme and begin with the hydrogen atom: this yields results which we shall find to have surprising relevance in organic quantum chemistry.

B. The Ground State of the Hydrogen Atom

Corresponding to each of the permitted electronic energies of a chemical species there is a wave function (or eigenfunction or eigenvector), conventionally represented by the symbol ψ. This is a function of the coordinates of the electrons, the origins of the coordinate axes being taken as the equilibrium positions of the nuclei. For the ground state of the hydrogen atom the wave function (in Cartesian coordinates and Hartree atomic units*) for the motion of the electron relative to the nucleus is

$$\psi = N \exp\left[-(x^2 + y^2 + z^2)^{\frac{1}{2}}\right], \tag{1}$$

which we can write more simply as

$$\psi = N \exp(-r), \tag{2}$$

where $r = (x^2 + y^2 + z^2)^{\frac{1}{2}}$ is the distance between the electron and the nucleus, and N is a numerical constant.

The wave function itself does not admit of any direct physical interpretation; but, if the electron is considered as a moving point charge, a quantity proportional to the probability of finding it in unit volume around the point (x, y, z) is obtained by substituting the

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* The Hartree atomic unit of length is the same as the first Bohr radius for the hydrogen atom. It is often represented by the symbol a_0, but we shall use instead the symbol B^8. $1\ \text{B} = 0{\cdot}529$ Å. Other atomic units are defined in section II.C.

values of x, y, and z in the expression for the square* of the wave function, *i.e.* by evaulating

$$\psi^2 = N^2 \exp\left[-2(x^2 + y^2 + z^2)^{\frac{1}{2}}\right] = N^2 \exp(-2r). \qquad (3)$$

To avoid the clumsiness of working with proportionalities instead of equalities, we can assign a convenient value to N, which is merely an arbitrary integration constant arising from the solution of the Schrödinger differential equation (section II.C). If we require $\psi^2 \mathrm{d}x\mathrm{d}y\mathrm{d}z$ to be *equal* to the probability that the electron is in the volume element $\mathrm{d}x\mathrm{d}y\mathrm{d}z$ around the point (x, y, z), then the probability that the electron is anywhere in the whole of the coordinate space is given directly by the integral

$$\int_{-\infty}^{\infty}\int_{-\infty}^{\infty}\int_{-\infty}^{\infty} \psi^2 \mathrm{d}x\mathrm{d}y\mathrm{d}z$$

$$= N^2 \int_{-\infty}^{\infty}\int_{-\infty}^{\infty}\int_{-\infty}^{\infty} \exp\left[-2(x^2 + y^2 + z^2)^{\frac{1}{2}}\right]\mathrm{d}x\mathrm{d}y\mathrm{d}z. \qquad (4)$$

By taking this probability to be unity we can evaluate N. We find that $N = \pi^{-\frac{1}{2}}$, and we say the wave function is normalized† when it is written as

$$\psi = \pi^{-\frac{1}{2}} \exp\left[-(x^2 + y^2 + z^2)^{\frac{1}{2}}\right]. \qquad (5)$$

The square of a normalized one-electron wave function measures not only the probability of finding the electron in unit volume around any specified point in the coordinate space, but also, equivalently, the electron density (effective charge per unit volume) around the point. Thus in the ground state of the hydrogen atom if we choose, for example, $x = 1$, $y = 2$, $z = 3$ (in Hartree atomic units), then

$$\psi^2 = \pi^{-1} \exp\left[-2(1^2 + 2^2 + 3^2)^{\frac{1}{2}}\right] = 0{\cdot}000179. \qquad (6)$$

---

* It is sometimes convenient, though not for the purposes of this chapter, to write ψ as a complex function of the electron coordinates (*i.e.* a function in which the factor $i = \sqrt{-1}$ appears). In this case ψ^2 must be replaced in any expression in which it occurs by $|\psi|^2 \equiv \psi^*\psi$, otherwise the probability would be represented by an imaginary number. ψ^* is called the complex conjugate of ψ, and is obtained from ψ by replacing i throughout by $-i$.

† A wave function is often written without the normalizing factor (here $\pi^{-\frac{1}{2}}$), and the same symbol may be used for both the normalized and the non-normalized forms. To test whether or not a wave function is normalized, it is necessary to evaluate an integral of the type (4); but it is usually fairly safe to assume that a wave function is normalized if it contains a numerical factor.

This means that the electron density at the point (1, 2, 3) is 0·000179 $e\,\text{B}^{-3}$ (= 0·00121 $e\,\text{Å}^{-3}$).

It is clear from the form of the wave function (5) that the electron density is finite wherever x, y, and z are finite: it has its maximum value in the immediate neighbourhood of the nucleus, and decreases to zero only when any of the coordinates x, y, z becomes infinite. This latter characteristic is common to the outermost regions* of all stationary distributions of electronic charge, and it follows that the volume occupied by the electrons associated with an atom or ion or molecule can never be specified or illustrated exactly. It is possible, however, to calculate the volume corresponding to any fraction of the total electronic charge: in a hydrogen atom in its ground state, for example, spheres of radii 1, 2, 3, 4, and 5 B, with the nucleus as centre, include 0·323, 0·762, 0·938, 0·986, and 0·997 of the total electronic charge.

C. The Schrödinger Energy Equation

We have now to consider the relation between the electronic energy (E) of a stationary state of a chemical species (a state whose energy does not change with time) and the corresponding charge distribution, ψ^2, or wave function, ψ. This is given by the Schrödinger energy equation, which, in its most general form, is simply

$$\mathbf{H}\psi = E\psi \tag{7}$$

or

$$(\mathbf{T} + V)\psi = E\psi. \tag{8}$$

The possible values of E are known as the eigenvalues of the equation.

Unlike ψ and E, the Hamiltonian operator, **H**, depends only upon the particles (nuclei and electrons) comprising the species, and not on the state of excitation. It consists of two terms, **T** and V. The first term is known as the kinetic-energy operator, and for a one-electron system it always has the form

$$\mathbf{T} = -\tfrac{1}{2}\left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}\right), \tag{9}$$

or, in abbreviated notation†,

$$\mathbf{T} = -\tfrac{1}{2}\nabla^2. \tag{10}$$

---

* Nearer the nuclei there may be surfaces (nodes) over which $\psi = \psi^2 = 0$ (see section II.G).

† ∇^2 is called the Laplacian operator. The symbol ∇ is usually pronounced 'del' in quantum mechanics.

The second term, V, is the electronic potential energy of the system, formulated, in contrast to the kinetic energy, exactly as in classical electrostatics. It is taken to be zero when the charged particles are infinitely far apart, and is thus necessarily negative for any bound state. For the hydrogen atom the potential energy is equal to the product of the electronic charge and the nuclear charge divided by the distance between them:

$$V = -\frac{1}{(x^2 + y^2 + z^2)^{\frac{1}{2}}} = -\frac{1}{r} \tag{11}$$

In equations (9) and (11) we have used Hartree atomic units; in conventional units the potential energy would have been $-e^2/r$. We have already seen* that the atomic unit of length (B) is equal to the first Bohr radius for the hydrogen atom (0·529 Å). The unit of charge is e (the absolute value of the charge of the electron), and the unit of mass is the reduced† mass of the electron in the system considered. The unit of energy, for which we use Shull and Hall's[8] symbol H, is then 27·2 ev.

It is important to note that, whereas ψ is a function of the electron coordinates, the eigenvalue E in the Schrödinger equation is a pure number. The kinetic energy and the potential energy are functions of position, but in a stationary state their sum, E, is constant.

By substituting (9) and (11) in (8) we obtain the Schrödinger energy equation for the hydrogen atom:

$$\left[-\frac{1}{2}\left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}\right) - \frac{1}{(x^2 + y^2 + z^2)^{\frac{1}{2}}}\right]\psi = E\psi. \tag{12}$$

Like any other Schrödinger energy equation, this has an infinite number of solutions, corresponding to an infinite set of eigenvalues. We may readily demonstrate that the ground-state wave function we have already quoted, $\psi = \exp[-(x^2 + y^2 + z^2)^{\frac{1}{2}}]$, satisfies this equation.

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* See first footnote in section II.B.

† The word 'reduced' may safely be ignored by readers unfamiliar with its dynamical significance. We have allowed for the slight error this may introduce in systems with light nuclei by quoting in the text only three digits in the conversion factors for the units of length and energy. For infinite nuclear mass 1 B = 0·52917 Å, 1 H = 27·209 ev (27·209 ev/atom = 2625·6 kJ/g atom). These conversion factors are appropriate to any organic molecule. Comprehensive tables of atomic units are given in refs. 6 and 9.

First we carry out the differentiation which the Laplacian operator requires:

$$\begin{aligned}\nabla^2\psi &= \left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}\right) \exp\left[-(x^2 + y^2 + z^2)^{\frac{1}{2}}\right] \\ &= \left[-2(x^2 + y^2 + z^2)^{-\frac{1}{2}} + 1\right] \exp\left[-(x^2 + y^2 + z^2)^{\frac{1}{2}}\right] \\ &= \left[-2(x^2 + y^2 + z^2)^{-\frac{1}{2}} + 1\right] \psi. \qquad (13)\end{aligned}$$

On substituting (13) in (12) we find, as required, that $\mathbf{H}\psi$ is equal to ψ multiplied by a pure number (the eigenvalue):

$$\begin{aligned}\mathbf{H}\psi &= \mathbf{T}\psi + V\psi \\ &= -\tfrac{1}{2}\left[-2(x^2 + y^2 + z^2)^{-\frac{1}{2}} + 1\right]\psi - (x^2 + y^2 + z^2)^{-\frac{1}{2}}\psi \\ &= -\tfrac{1}{2}\psi. \qquad (14)\end{aligned}$$

The eigenvalue is thus $-\frac{1}{2}$; *i.e.* the ground-state electronic energy of the hydrogen atom is $-\frac{1}{2}$ H = −13·6 ev, and the ionization energy (ionization 'potential') is 13·6 ev. It is clear from the form of equation (14) that multiplication of ψ by any numerical factor N would have no effect upon E.

D. Atomic Wave Functions

In fixing attention exclusively on the ground state of the hydrogen atom up to this point, our object has been to introduce the Schrödinger equation and some of the terminology of wave mechanics with the minimum of mathematical formalism. The atomic wave functions which we require in the study of organic molecules are, however, much more akin to those of the excited states of the hydrogen atom, which we must now consider.

But, before we can usefully define the excited-state wave functions in either algebraic or geometric form, we must abandon Cartesian coordinates, which are entirely unsuited to an essentially spherical system*, and which we have used in the foregoing pages merely because they are known universally. It is no more convenient to use rectangular coordinates for specifying the position of an electron in an atom than for specifying the position of a point on the surface of the earth: in each case we use spherical polar coordinates, because we wish to deal separately with radial and angular dependence.

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* The reader who has paused to check the integration (4) or the differentiation (13) will be in no doubt about this.

In these coordinates, as is shown in Figure 1, we locate a point by specifying (*i*) the length, r, of the line joining the point to the origin; (*ii*) the angle, θ, which this line makes with the z axis; and (*iii*) the angle, ϕ, between the xz plane and a plane including the z axis and the point. The angles θ and ϕ are thus analogous to co-latitude and longitude. The following relations between Cartesian and polar coordinates are apparent from Figure 1:

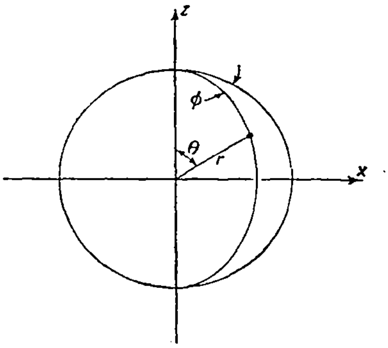

FIGURE 1. Spherical polar coordinates. The positive y axis points upwards from the plane of the paper.

$$x = r \sin\theta \cos\phi; \qquad y = r \sin\theta \sin\phi; \qquad z = r\cos\theta; \tag{15}$$

$$r = (x^2 + y^2 + z^2)^{\frac{1}{2}}. \tag{16}$$

The Laplacian operator, ∇^2, looks less simple in polar coordinates than rectangular coordinates:

$$\begin{aligned} \nabla^2\psi &= \frac{\partial^2\psi}{\partial x^2} + \frac{\partial^2\psi}{\partial y^2} + \frac{\partial^2\psi}{\partial z^2} \\ &= \frac{\partial^2\psi}{\partial r^2} + \frac{2}{r}\frac{\partial\psi}{\partial r} + \frac{1}{r^2 \sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta \frac{\partial\psi}{\partial\theta}\right) + \frac{1}{r^2 \sin^2\theta}\frac{\partial^2\psi}{\partial\phi^2}. \end{aligned} \tag{17}$$

So does the volume element in integration (usually abbreviated to $\mathrm{d}\tau$):

$$\mathrm{d}\tau = \mathrm{d}x\mathrm{d}y\mathrm{d}z = r^2 \sin\theta \,\mathrm{d}r\mathrm{d}\theta\mathrm{d}\phi. \tag{18}$$

Limits of integration over the whole of the coordinate space corresponding to

$$-\infty < x < \infty, \qquad -\infty < y < \infty, \qquad -\infty < z < \infty$$

are

$$0 \leqslant r < \infty, \qquad 0 \leqslant \theta \leqslant \pi, \qquad 0 \leqslant \phi \leqslant 2\pi. \tag{19}$$

TABLE 1. Hydrogen-like wave functions.

Spectroscopic symbol	Quantum numbers n	l	$\lvert m\rvert$	Energy (H)	$\psi = N R \Theta \Phi$ N	R	Θ	Φ	Nodal surfaces
$1s$	1	0	0	$-Z^2/2$	$(Z^3/\pi)^{\frac{1}{2}}$	$\exp(-Zr)$			
$2s$	2	0	0	$-Z^2/8$	$(Z^3/32\pi)^{\frac{1}{2}}$	$(Zr-2)\exp(-Zr/2)$			$Zr = 2$
$2p_z$	2	1	0	$-Z^2/8$	$(Z^5/32\pi)^{\frac{1}{2}}$	$r\exp(-Zr/2)$	$\cos\theta$		$\theta = \pi/2$
$2p_x$	2	1	1	$-Z^2/8$	$(Z^5/32\pi)^{\frac{1}{2}}$	$r\exp(-Zr/2)$	$\sin\theta$	$\cos\phi$	$\phi = \pi/2$
$2p_y$	2	1	1	$-Z^2/8$	$(Z^5/32\pi)^{\frac{1}{2}}$	$r\exp(-Zr/2)$	$\sin\theta$	$\sin\phi$	$\phi = 0$
$3s$	3	0	0	$-Z^2/18$	$(Z^3/19683\pi)^{\frac{1}{2}}$	$(2Z^2r^2 - 18Zr + 27)\exp(-Zr/3)$			$Zr = 4\frac{1}{2} \pm \frac{1}{2}\sqrt{27}$
$3p_z$	3	1	0	$-Z^2/18$	$(2Z^5/6561\pi)^{\frac{1}{2}}$	$(Zr^2 - 6r)\exp(-Zr/3)$	$\cos\theta$		$Zr = 6;\ \theta = \pi/2$
$3p_x$	3	1	1	$-Z^2/18$	$(2Z^5/6561\pi)^{\frac{1}{2}}$	$(Zr^2 - 6r)\exp(-Zr/3)$	$\sin\theta$	$\cos\phi$	$Zr = 6;\ \phi = \pi/2$
$3p_y$	3	1	1	$-Z^2/18$	$(2Z^5/6561\pi)^{\frac{1}{2}}$	$(Zr^2 - 6r)\exp(-Zr/3)$	$\sin\theta$	$\sin\phi$	$Zr = 6;\ \phi = 0$
$3d_{z^2}$	3	2	0	$-Z^2/18$	$(Z^7/39366\pi)^{\frac{1}{2}}$	$r^2\exp(-Zr/3)$	$3\cos^2\theta - 1$		$\theta = \arccos(\pm 3^{-\frac{1}{2}})$
$3d_{xz}$	3	2	1	$-Z^2/18$	$(2Z^7/6561\pi)^{\frac{1}{2}}$	$r^2\exp(-Zr/3)$	$\sin\theta\cos\theta$	$\cos\phi$	$\theta = \pi/2;\ \phi = \pi/2$
$3d_{yz}$	3	2	1	$-Z^2/18$	$(2Z^7/6561\pi)^{\frac{1}{2}}$	$r^2\exp(-Zr/3)$	$\sin\theta\cos\theta$	$\sin\phi$	$\theta = \pi/2;\ \phi = 0$
$3d_{x^2-y^2}$	3	2	2	$-Z^2/18$	$(Z^7/13122\pi)^{\frac{1}{2}}$	$r^2\exp(-Zr/3)$	$\sin^2\theta$	$\cos 2\phi$	$\phi = \pi/4;\ \phi = 3\pi/4$
$3d_{xy}$	3	2	2	$-Z^2/18$	$(Z^7/13122\pi)^{\frac{1}{2}}$	$r^3\exp(-Zr/3)$	$\sin^2\theta$	$\sin 2\phi$	$\phi = 0;\ \phi = \pi/2$

Wave Functions in Complex Form. In circumstances in which the sign of the magnetic quantum number m is important (notably in dealing with angular momentum), the trigonometric forms of Φ given in the table are inconvenient, and they are replaced by complex exponential forms. Any two orbitals differing only in their Φ factor ($\cos|m|\phi$ or $\sin|m|\phi$) may be transformed thus:

$$R\Theta\cos|m|\phi + iR\Theta\sin|m|\phi = R\Theta\exp(i|m|\phi); \qquad \text{(I)}$$

$$R\Theta\cos|m|\phi - iR\Theta\sin|m|\phi = R\Theta\exp(-i|m|\phi). \qquad \text{(II)}$$

For example, the following alternative set may replace the three $2p$ orbitals given in the table:

$$2p_0 = 2p_z \quad \psi = (Z^5/32\pi)^{\frac{1}{2}}\, r\exp(-Zr/2)\cos\theta; \qquad \text{(III)}$$

$$2p_{+1} \quad \psi = (Z^5/64\pi)^{\frac{1}{2}}\, r\exp(-Zr/2)\sin\theta\exp(i\phi); \qquad \text{(IV)}$$

$$2p_{-1} \quad \psi = (Z^5/64\pi)^{\frac{1}{2}}\, r\exp(-Zr/2)\sin\theta\exp(-i\phi). \qquad \text{(V)}$$

The members of the complex set, like those of the real set, are linearly independent and orthogonal. Unlike the $2p_x$ and $2p_y$ charge distributions, the $2p_{+1}$ and $2p_{-1}$ charge distributions are not dumb-bell-shaped and do not have symmetry axes at right angles to each other: in common with the $2p_0(= 2p_z)$ charge distribution, they are both symmetric about the z axis.

The real functions $2p_x$ and $2p_y$ may be regarded as representing stationary waves, and the equivalent complex functions as representing running waves; $2p_{+1}$ and $2p_{-1}$ then correspond to electronic currents travelling in opposite directions around the z axis.

For convenience, the signs of the magnetic quantum numbers are taken to be those of the exponents in (I) and (II). Thus $m = +1$ in (IV) and $m = -1$ in (V). This is indicated in the subscripts $+1$ and -1 in the symbols for the wave functions.

In Table 1 we list, in order of increasing energy, the first fourteen* hydrogen-like wave functions, *i.e.* wave functions for the hydrogen atom and the isoelectronic cations He$^+$, Li^{2+}, ... For these one-electron systems the Schrödinger equation† is

$$(-\tfrac{1}{2}\nabla^2 - Z/r)\psi = E\psi, \tag{20}$$

where Z is the atomic number ($Z = 1$ for the hydrogen atom itself).

Spherical polar coordinates are used in Table 1, but we also give below the equivalent expressions in Cartesian coordinates for the first five wave functions of the hydrogen atom.

$$\begin{aligned}
1s \quad \psi &= \pi^{-\frac{1}{2}} \exp[-(x^2 + y^2 + z^2)^{\frac{1}{2}}] \\
&= \pi^{-\frac{1}{2}} \exp(-r) \\
2s \quad \psi &= (32\pi)^{-\frac{1}{2}} [(x^2 + y^2 + z^2)^{\frac{1}{2}} - 2] \exp[-\tfrac{1}{2}(x^2 + y^2 + z^2)^{\frac{1}{2}}] \\
&= (32\pi)^{-\frac{1}{2}} (r - 2) \exp(-r/2) \\
2p_x \quad \psi &= (32\pi)^{-\frac{1}{2}} x \exp[-\tfrac{1}{2}(x^2 + y^2 + z^2)^{\frac{1}{2}}] \\
&= (32\pi)^{-\frac{1}{2}} r \exp(-r/2) \sin\theta \cos\phi \\
2p_y \quad \psi &= (32\pi)^{-\frac{1}{2}} y \exp[-\tfrac{1}{2}(x^2 + y^2 + z^2)^{\frac{1}{2}}] \\
&= (32\pi)^{-\frac{1}{2}} r \exp(-r/2) \sin\theta \sin\phi \\
2p_z \quad \psi &= (32\pi)^{-\frac{1}{2}} z \exp[-\tfrac{1}{2}(x^2 + y^2 + z^2)^{\frac{1}{2}}] \\
&= (32\pi)^{-\frac{1}{2}} r \exp(-r/2) \cos\theta.
\end{aligned} \tag{21}$$

These functions are obtained from those in Table 1 by using the relations (15) and (16). It is clear that the higher-energy wave functions could also be expressed in Cartesian form, but the results would be very unwieldy.

It must be emphasized, however, that the use of spherical polar coordinates is by no means merely a matter of convenience in notation or elegance in analysis. Whereas in these coordinates hydrogen-like wave functions can always be written in the form

$$\psi = NR\Theta\Phi, \tag{22}$$

---

* The sequence could be extended indefinitely, but we shall have no use for the higher members.

† By straightforward though sometimes rather tedious differentiation it can be verified, with the use of (17), that the functions listed in Table 1 are indeed eigenfunctions of equation (20), and that the eigenvalues are as specified. The normalizing factors may be checked by showing that

$$\int \psi^2 d\tau = \int_0^{2\pi} \int_0^{\pi} \int_0^{\infty} \psi^2 r^2 \sin\theta \, dr d\theta d\phi = 1.$$

where R, Θ, and Φ are functions of r only, θ only, and ϕ only, no such segregation of the three variables into separate factors is possible when Cartesian coordinates are used*. This is of the greatest importance in many-electron atomic systems, in which Θ and Φ, the angular factors of the composite one-electron wave functions, are exactly the same as for the hydrogen atom†. (The radial factors, R, are very different, and cannot even be expressed precisely as finite series.) In general, the angular factors determine the shape and the orientation of an electronic charge distribution, and the radial factor determines the size: the information we gain about the shapes and orientations of one-electron hydrogen-like charge distributions will thus serve equally well for many-electron atomic systems, and so also for the molecular systems with which this book is concerned.

E. Quantum Numbers

To save constant reference to the explicit analytical forms of the atomic orbitals, we shall often quote instead the corresponding quantum numbers n, l, and m. These are integers which arise automatically in the systematic solution of the Schrödinger equation (20) when restrictions are imposed on the forms of the wave functions to ensure that they are physically acceptable. We shall not be concerned here with the exact mathematical significance of the quantum numbers, which we shall generally use merely as labels, but we shall find it useful to note the following relations between the quantum numbers and the analytical forms of the wave functions:

(*a*) the highest power of r in the radial factor is $n - 1$, and the exponent is $-Zr/n$;

(*b*) if the highest powers of $\cos\theta$ and $\sin\theta$ are $\cos^a\theta$ and $\sin^b\theta$, then $l = a + b$;

(*c*) the factor Φ is $\cos|m|\phi$ or $\sin|m|\phi$.

Unlike (*b*) and (*c*), which hold for all atomic wave functions expressed in spherical polar coordinates, (*a*) is true only for solutions of equation (20).

The individual quantum numbers need not be given a precise

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* Note the surds in (21).

† This is strictly true only for spherically symmetrical systems, but it is assumed almost invariably, and the assumption appears to cause no significant error.

physical interpretation, but it is useful—and very nearly correct—to regard the principal quantum number, n, as defining the 'size' of an electronic charge distribution, and the quantum numbers l and m as defining the 'shape' and the orientation. In the first column of Table 1 we give the spectroscopic symbols corresponding to the quantum numbers l and m. The significance of the subscripts used to denote the orientation of orbitals with $l \geqslant 1$ (x, y, z in the case of p orbitals) is clear from the Cartesian forms (21).

In a one-electron atomic system the electronic energy depends only upon the principal quantum number ($E = -Z^2/2n^2$); in a many-electron system it depends not only upon n but (to a lesser extent) upon l.

F. Pictorial Representation of Atomic Orbitals

The pictorial representation of atomic and molecular orbitals* is a difficult problem, partly because ψ vanishes in the outer regions of an atom only as $r \rightarrow \infty$, but mainly because a two-dimensional diagram has, in general, to serve for three independent variables (r, θ, ϕ) as well as the dependent variable (ψ or ψ^2).

Although it is sometimes very useful, in non-quantitative work, to draw diagrams to attempt to illustrate the 'shapes' of atomic or molecular orbitals, it is obvious that a non-spherical charge distribution extending over the whole of space has no unique shape. It has, however, a characteristic symmetry, and when, for example, we conveniently describe a p orbital† as dumb-bell-shaped, we mean little more than that a p charge distribution has both an axis of symmetry and a plane of symmetry normal to the axis. (The charge distribution (ψ^2) is symmetric to reflexion in this plane; the wave function itself is antisymmetric.)

Dealing first with 'size' (Figures 2 and 3) and then with 'shape' or symmetry (Figures 4–7), we discuss below the uses and the limitations of some graphical methods of representing the atomic orbitals listed in Table 1. Our illustrations relate to the hydrogen atom, but the corresponding diagrams for other atoms (*e.g.* carbon) would either be identical (Figures 6 and 7) or would involve little more than changes in scale (Figures 2–4).

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* A *one*-electron wave function is often called an orbital (*e.g.* the functions (21) are known as the $1s$, $2s$, ... atomic orbitals).

† Strictly a $2p$ orbital: the higher p orbitals have radial nodes.

A straightforward two-dimensional plot of ψ or ψ^2 as a function of position (Figure 2) is of course possible only for spherically symmetrical (s) orbitals, which lack Θ and Φ factors, and are functions of r only.

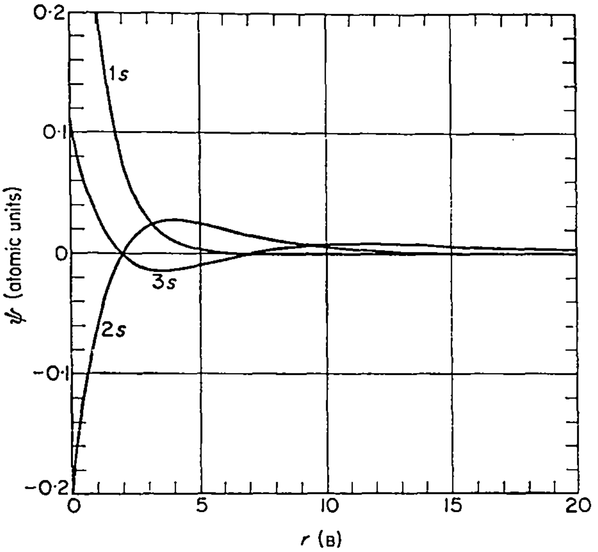

FIGURE 2. Electronic charge distribution in the hydrogen atom: ψ as a function of r.

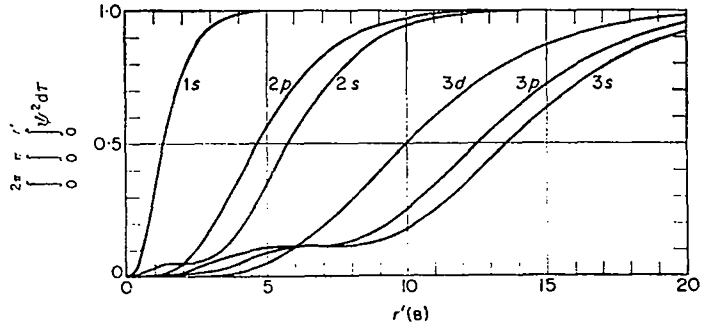

FIGURE 3. Electronic charge distribution in the hydrogen atom: proportion of total charge enclosed by a sphere of radius r'.

It is clear from Figure 2 that as the principal quantum number n increases there is a marked increase in orbital size, and hence a decrease in the mean electron density. Correspondingly, the mean potential energy becomes less negative (the mean value of $1/r$ decreases), and thus the total electronic energy increases*.

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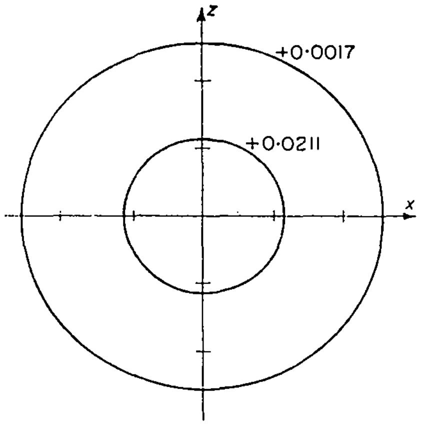
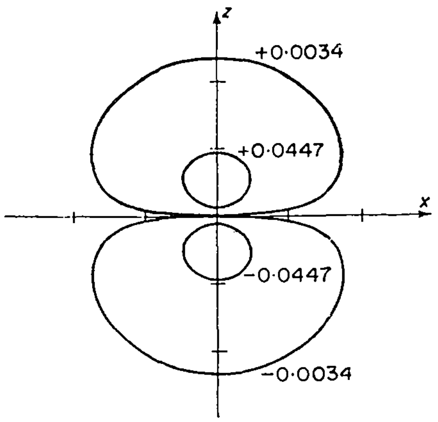
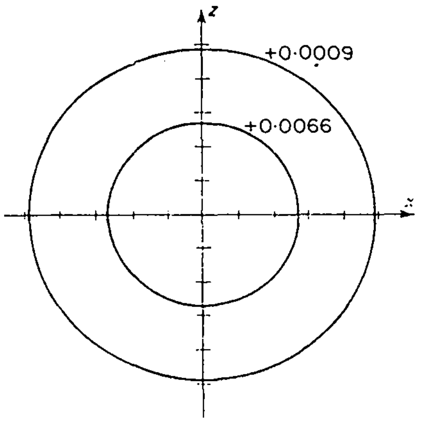
* Potential energy = $-2 \times$ kinetic energy (Virial theorem).



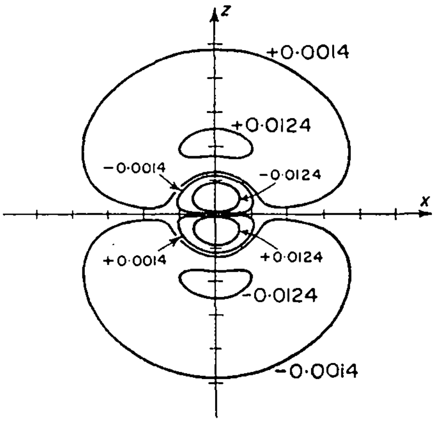
$2s$



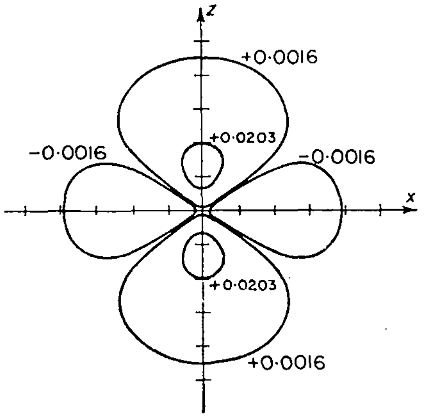
$2p_z$



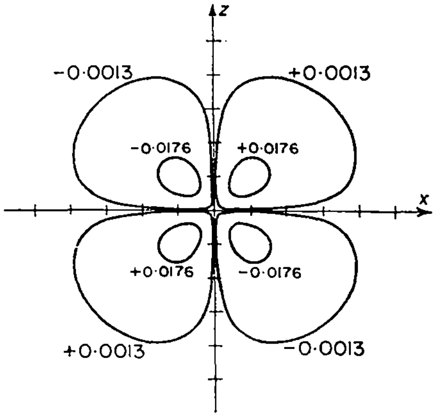
$3s$



$3p_z$



$3d_{z^2}$



$3d_{xz}$

It will be noted that there are finite values of r for which the $2s$ and the $3s$ wave functions vanish. In the case of the $2s$ wave function, $\psi = \psi^2 = 0$ at all points on a spherical surface having a radius of 2 B. Such a surface is called a node. For s wave functions the number of nodes is $n - 1$. Wave functions with angular dependence have angular nodes ($\Theta = 0$ or $\Phi = 0$) as well as radial nodes ($R = 0$); a brief account of these is given in section II.G.

Although Figure 2 gives a rough indication of the relative sizes of $1s$, $2s$, and $3s$ charge distributions, it provides no absolute measure of the effective sizes. In Figure 3, therefore, we have plotted the fraction of the total electronic charge enclosed by a sphere of given radius (r'), not only for the s states, but for all the states represented in Table 1. It is evident that, whereas an increase in the principal quantum number results in a striking increase in the effective size of the electronic charge distribution, an increase in the quantum number l has a slight effect in the opposite direction. The flat portions of the $2s$ and the $3s$ curves in Figure 3 are in the regions of the radial nodes.

The quantities plotted in Figure 3 are obtained by evaluating integrals of the type

$$\int_0^{2\pi}\int_0^{\pi}\int_0^{r'} \psi^2 r^2 \sin\theta \, dr d\theta d\phi, \tag{23}$$

where ψ is a normalized wave function. When the upper limit of r is infinity, (23) is just the normalization integral, and its value is unity.

Although it is not possible to provide a direct pictorial representation of the shape of an atomic orbital having angular dependence, a two-dimensional diagram can be used to convey a limited amount of quantitative information about the way in which ψ (or ψ^2) varies as a

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FIGURE 4. Contour diagrams for hydrogen wave functions (cross-sections in xz plane).

Apart from $3d_{xz}$, all the wave functions represented in the figure are symmetrical about the z axis: surfaces of constant $|\psi|$ would be obtained by rotating the contour lines about the z axis. In the case of $3d_{xz}$ the three-dimensional contour diagram would be obtained by rotating each 'lobe' about its own symmetry axis.

Except in orientation, p_x and p_y wave functions are identical with p_z wave functions, and d_{xy}, d_{yz}, and $d_{x^2-y^2}$ wave functions are identical with d_{xz} wave functions.

Values of ψ are given in atomic units; 5 B divisions are marked off on the x and the z axes. The diagrams for $n = 2$ are drawn on twice the scale of those for $n = 3$.

Two values of $|\psi|$ are represented in each diagram. These values have been chosen quite arbitrarily so that spheres enclosing the inner and the outer contour surfaces would contain respectively 50% and 99% of the total electronic charge.

function of r, θ, and ϕ. We reduce the number of independent variables from three to two by considering variation of ψ only within a suitable plane (normally a plane of symmetry) through the nucleus; *i.e.* we take a suitable cross-section. We then fall back upon the cartographical expedient of drawing a contour diagram: we assign both coordinates in a two-dimensional diagram to the independent variables and plot 'contours' of constant $|\psi|$ or ψ^2. These are surfaces in the three-dimensional wave function, but appear as lines in the cross-section.

In Figure 4 we give contour diagrams for a representative selection of wave functions for the hydrogen atom. We must make it clear that, while the information the diagrams convey is perfectly accurate, it is far too limited to be of any quantitative value. We could improve the diagrams by spacing the contour lines more closely and less arbitrarily, but this would be pointless, for the diagrams would still convey no quantitative information that could not be obtained much more simply from the analytical form of the wave function. The only merit of a contour diagram is that it reveals the symmetry and the orientation of an orbital in the most striking way, and this is the purpose for which we shall use contour diagrams in this chapter. Where it is desirable to represent an atomic or molecular orbital pictorially, we shall use a purely schematic contour diagram in which we shall sketch just one contour line (the shape of which is bound to be arbitrary, as it is evident from Figure 4 that the shape of a contour line varies considerably with the particular value of ψ selected). Thus, for example, we shall represent a p_z orbital as in Figure 5(*a*). We shall not, however, use the forms given in Figures 5(*b*) or 5(*c*). These are quite acceptable as means of indicating the symmetry of a p_z orbital, but they are inconsistent with the description we have just given. They are not contour diagrams but polar diagrams, in which r is the *dependent* variable. Polar diagrams give no information about radial dependence: Figure 5(*b*) is simply a graph of $r = |\cos\theta|$ in polar coordinates, and Figure 5(*c*) is a graph of $r = \cos^2\theta$.

Figures 6 and 7, which relate to all atomic orbitals, and not just to those of hydrogen, indicate the directional character of charge distributions with $l \geqslant 1$. In these figures we have plotted the angular analogues of the integral (23), *i.e.*

$$\underset{\text{(Figure 6)}}{\int_0^{\phi'}\int_0^{\pi}\int_0^{\infty} \psi^2 r^2 \sin\theta \, \mathrm{d}r\mathrm{d}\theta\mathrm{d}\phi} \quad \text{and} \quad \underset{\text{(Figure 7)}}{\int_0^{2\pi}\int_0^{\theta'}\int_0^{\infty} \psi^2 r^2 \sin\theta \, \mathrm{d}r\mathrm{d}\theta\mathrm{d}\phi}. \qquad (24)$$

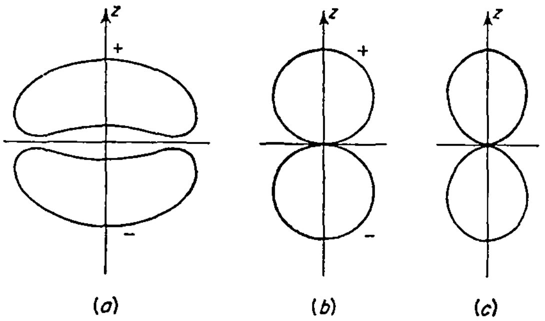

FIGURE 5. Schematic representations of a *p* orbital:
(*a*) contour diagram ($|\psi|$ or ψ^2);
(*b*) polar diagram ($|\psi|$);
(*c*) polar diagram (ψ^2).
All three diagrams reveal the symmetry of the charge distribution, but only (*a*) gives any indication of the 'shape'.

Figure 6 shows the fraction of the total electronic charge enclosed between the planes $\phi = 0$ and $\phi = \phi'$ (in the range $0 \leqslant \phi' \leqslant \pi/2$); Figure 7 shows the fraction enclosed within the infinite cone whose semi-vertical angle is $\theta = \theta'$ (in the range $0 \leqslant \theta' \leqslant \pi/2$). The flat portions of the curves correspond to the angular nodes. The *p* and the *d* orbitals represented in the figures have their maximum amplitudes along the *x* axis (Figure 6) or the *z* axis (Figure 7).

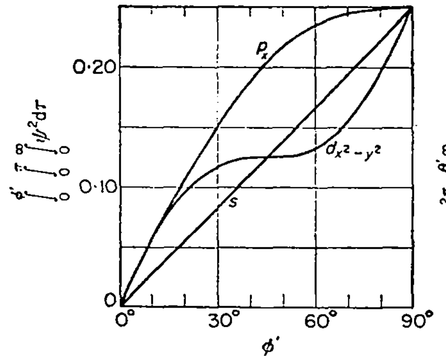

FIGURE 6. Angular distribution of electronic charge in a hydrogen-like atomic orbital: proportion of total charge enclosed between the planes $\phi = 0$ and $\phi = \phi'$.

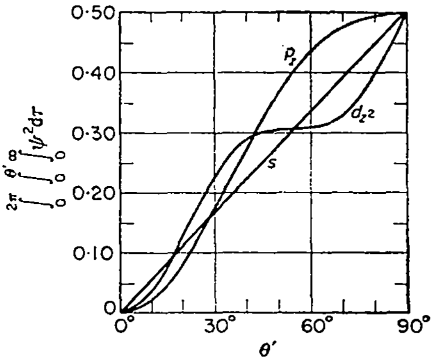

FIGURE 7. Angular distribution of electronic charge in a hydrogen-like atomic orbital: proportion of total charge included in an infinite cone of semivertical angle $\theta = \theta'$.

G. Nodes

An atomic wave function vanishes when $R = 0$ or $\Theta = 0$ or $\Phi = 0$. A *surface* over which $\psi = 0$ is called a node. For hydrogen-like wave functions as defined in Table 1, nodal surfaces may be spherical ($R = 0$), planar ($\Phi = 0$ or $\Theta = 0$, $\theta = \pi/2$), or conical ($\Theta = 0$, $\theta \neq \pi/2$; *e.g.* d_{z^2})*. Nodes are not usually of great physical importance; but, because they separate regions in which $\psi > 0$ from regions in which $\psi < 0$, they give information about the symmetries of wave functions.

The number of nodes associated with a wave function obviously depends upon its analytical form, and so do the values of n, l, and m. This suggests that there must be a relation between the number of nodes and the values of the quantum numbers: in fact the number of nodes is $n - 1$, and $n - l - 1$ of these are spherical nodes.

The relation just given may be used for specifying the principal quantum number in an orbital which is one of the constituents of a many-electron wave function: the radial factor in such an orbital cannot usually be expressed in a concise form from which the roots of $R = 0$ can be obtained by straightforward analysis, but the number and the positions of the radial nodes can still be determined graphically or numerically.

H. Degeneracy

An examination of Table 1 shows that there are three different $2p$ wave functions all corresponding to the same energy. In wave-mechanical terminology this is an example of degeneracy, and we say that the $2p$ energy level has threefold degeneracy, or that its degree of degeneracy is 3. Any other p energy level also has threefold degeneracy, and any d level has fivefold degeneracy; in general, the degree of degeneracy is $2l + 1$. This depends only upon the angular factors of the orbitals, so it applies to all atoms and not only to the hydrogen atom†.

If we use the symbol E_{2p} to represent the electronic energy of a $2p$ wave function (not necessarily of hydrogen), then we can write

$$\mathbf{H}\psi_x = E_{2p}\psi_x, \qquad \mathbf{H}\psi_y = E_{2p}\psi_y, \qquad \mathbf{H}\psi_z = E_{2p}\psi_z, \tag{25}$$

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* This classification does not necessarily apply if the degenerate wave functions in Table 1 are replaced by alternative linear combinations (section II.H).

† The degree of degeneracy is $2l + 1$ only when the electron is in a spherically symmetrical electrical field. In the less symmetrical fields found in molecules, the degeneracy is 'split', and the single energy level is replaced by two or more distinct levels with lower degrees of degeneracy.

or, equally well,

$$\mathbf{H}(a\psi_x) = E_{2p}(a\psi_x), \quad \mathbf{H}(b\psi_y) = E_{2p}(b\psi_y), \quad \mathbf{H}(c\psi_z) = E_{2p}(c\psi_z), \tag{26}$$

where a, b, and c are numerical constants (positive, negative, or zero), and $x = 2p_x$, $y = 2p_y$, and $z = 2p_z$. We can illustrate a very important feature of all degenerate wave functions simply by adding together the three Schrödinger equations (26):

$$\mathbf{H}(a\psi_x + b\psi_y + c\psi_z) = E_{2p}(a\psi_x + b\psi_y + c\psi_z). \tag{27}$$

The function

$$\psi = a\psi_x + b\psi_y + c\psi_z \tag{28}$$

is clearly another solution of the same Schrödinger equation, and it also corresponds to the $2p$ energy level. The coefficients a, b, and c may be chosen quite arbitrarily, so there are in fact infinitely many $2p$ wave functions.

This does not affect the statement above that the degree of degeneracy is 3, for the additional wave functions (28) are not independent, but are merely linear combinations of the functions given in Table 1. These three tabulated functions are themselves linearly independent: no non-zero coefficients a, b, c can be found such that

$$a\psi_x + b\psi_y + c\psi_z = 0. \tag{29}$$

In other words, none of the functions can be expressed as a linear combination of the other two.

There is nothing unique about the set of three orbitals given in Table 1. A set of linearly independent $2p$ wave functions may be chosen in an infinite number of ways, but it will always contain just three members. The three members we have chosen have, of course, the obvious merit of being very simply related to the coordinate axes.

For orbitals with $l \geqslant 2$, there is no such obvious criterion for choosing a set of $2l + 1$ linearly independent functions which will be generally convenient. We give one useful set of d orbitals in Table 1, but others may be chosen to meet the symmetry requirements of individual systems.

I. Orthogonality

Whatever the radial factors, sets of p or d orbitals having the angular factors given in Table 1 have the property of orthogonality, the convenience of which will later be readily apparent. If ψ_m and ψ_n are two solutions of the same Schrödinger equation, we say that they are orthogonal if

$$\int \psi_m \psi_n \mathrm{d}\tau = \int_0^{2\pi} \int_0^{\pi} \int_0^{\infty} \psi_m \psi_n r^2 \sin\theta \, \mathrm{d}r \mathrm{d}\theta \mathrm{d}\phi = 0. \tag{30}$$

It is not difficult to show that wave functions corresponding to different eigenvalues of the same Schrödinger equation are automatically orthogonal; degenerate wave functions corresponding to a single eigenvalue may always be made orthogonal by the formation of appropriate linear combinations.

In (30) ψ_m and ψ_n are supposed to be real: if they are complex, $\psi_m \psi_n$ in the integrand must be replaced by $\psi_m^* \psi_n$ or $\psi_m \psi_n^*$.

III. APPROXIMATE WAVE FUNCTIONS FOR MANY-ELECTRON SYSTEMS

A. Energies Corresponding to Approximate Wave Functions

The eigenvalues and the forms of the wave functions given in Table 1 are obtained at one and the same time by applying to the Schrödinger equation (20) the standard mathematical techniques for the solution of differential equations in several variables. We shall not examine these techniques, for, apart from requiring lengthy description, they are normally applicable to one-electron systems only, and are not at all typical of the methods used for determining the wave functions and the energies of many-electron systems. Although the wave functions for a many-electron system may, in principle, be calculated to any desired degree of accuracy, they cannot be expressed in the closed analytical form exemplified in Table 1, and, correspondingly, they cannot be obtained by the direct solution of a Schrödinger equation. We have accordingly to devise an alternative method for relating wave functions to energies.

First we consider any one-electron Schrödinger equation to which exact solutions are available:

$$\mathbf{H}\psi = E\psi. \tag{31}$$

If we premultiply* both sides of the equation by ψ and then integrate† we obtain

$$\int \psi \mathbf{H} \psi \mathrm{d}\tau = \int \psi E \psi \mathrm{d}\tau. \tag{32}$$

But as ψ is exact, E is not a function of the variables of integration, and so (32) may be rewritten

$$\int \psi E \psi \mathrm{d}\tau = E \int \psi^2 \mathrm{d}\tau. \tag{33}$$

Then, from (32) and (33),

$$E = \frac{\int \psi \mathbf{H} \psi \mathrm{d}\tau}{\int \psi^2 \mathrm{d}\tau}, \tag{34}$$

or, if ψ is normalized,

$$E = \int \psi \mathbf{H} \psi \mathrm{d}\tau. \tag{35}$$

These alternative expressions for E are of no value when ψ is exact, for E would then be obtained automatically on evaluating the $\mathbf{H}\psi$ factor in the integrand and there would be no point in carrying out the integration. They do, however, provide an indispensable analogue for calculations on approximate wave functions.

In a many-electron system (and even in a one-electron system if the wave function is only approximate), although we may write, purely formally,

$$\mathbf{H}\tilde{\psi} = \tilde{E}\tilde{\psi} \quad \text{or} \quad \tilde{E} = (\mathbf{H}\tilde{\psi})/\tilde{\psi}, \tag{36}$$

where the tildes denote approximate quantities, $\tilde{E}$ will not be a pure number, as an eigenvalue must be. It will be a function—usually complicated—of the electron coordinates, and will therefore vary in

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* Premultiplication of a by b gives ba; postmultiplication gives ab. The distinction between ab and ba is very important if a or b is an operator.

† For the remainder of this chapter, wherever integration in spherical polar coordinates is carried out over the whole of the coordinate space, we shall omit the limits of integration, write only one integral sign instead of three, and abbreviate the volume element to $\mathrm{d}\tau$.

An integral such as $\int \psi \mathbf{H} \psi \mathrm{d}\tau$ is evaluated in the following sequence of steps: first ψ is operated on by $\mathbf{H}$ to give $\mathbf{H}\psi$; then the resulting expression, no longer containing the differential operator, is multiplied by ψ; finally the integration is carried out. (If we wrote $\mathbf{H}\psi\psi$ instead of $\psi\mathbf{H}\psi$ it would not be clear whether $\mathbf{H}$ was to operate on ψ or ψ^2.)

value with the position(s) of the electron(s). It cannot thus be identified with the stationary energy. Whatever the form of ψ, however, the quotient of two definite integrals (34) is bound to be a pure number, so we *define* the mean energy $\tilde{E}$ associated with an approximate wave function $\tilde{\psi}$ to be

$$\tilde{E} = \frac{\int \tilde{\psi}\mathbf{H}\tilde{\psi}\,d\tau}{\int \tilde{\psi}^2\,d\tau}. \tag{37}$$

The step (33) is not valid for an approximate wave function, so (37) cannot be derived from (36) as (35) was from (31). However, the more nearly $\tilde{\psi}$ approaches the exact wave function, the more nearly $\tilde{E}$ approaches the exact energy*. [The tildes have now served their purpose, and we shall discard them. The remainder of this chapter will be devoted almost exclusively to approximate wave functions, so for simplicity we shall normally use the symbols ψ and E for approximate, as well as for accurate, wave functions and energies.]

A wave-mechanical calculation on a many-electron system is generally very much a matter of trial and error. The first step consists in deciding—rather arbitrarily—upon the form of a trial wave function. The choice of form is determined by (*a*) the symmetry of the system; (*b*) the need for keeping the amount of computation involved in evaluating integrals of the type (37) within reasonable bounds; (*c*) a knowledge of the wave functions which have been used successfully in similar or simpler systems (a molecular wave function being almost invariably constructed from the wave functions of the constituent atoms); (*d*) chemical intuition (as, for example, in covalent–ionic 'resonance'). Unfortunately it is very seldom that there is not a clash between (*b*) and (*c*), and a many-electron wave function normally represents a compromise between accuracy and computational convenience.

The trial wave function must, of course, be a function of the coordinates of all the electrons in the system. Although it may sometimes be completely inflexible (as with the Heitler–London wave function for the hydrogen molecule, which we describe shortly), it will normally contain at least one parameter which can be adjusted so as to provide the best possible wave function of the arbitrary form selected. In general, the greater the flexibility the better the wave function.

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* The converse is not always true.

B. The Variation Principle for Ground-state Wave Functions

There is a very straightforward criterion for determining the optimum values of the parameters, at least for ground-state wave functions. We invoke the wave-mechanical variation principle, which provides that, as long as no significant terms are omitted from the Hamiltonian operator, the energy of a system corresponding to an approximate wave function can never be lower than the lowest exact energy*. Thus the lower the value of the expression

$$E = \frac{\int \psi \mathbf{H} \psi \mathrm{d}\tau}{\int \psi^2 \mathrm{d}\tau},$$

the nearer the approximate energy is to the true ground-state energy, and the nearer the approximate wave function is to the true ground-state wave function†. Given an approximate wave function with adjustable parameters, we have thus merely to vary the parameters until E is minimized. If the arbitrary form of the wave function has been predetermined judiciously, and if there are sufficient parameters, we should then have a good approximation to the ground-state energy.

If the trial wave function gives a reasonably good energy, it may either be left as it is, or modified slightly, depending upon the purpose of the calculation and the accuracy required. If, however, it gives results in manifest disagreement with any experimental observation, it must be replaced by another trial function of different form. The relative (though not the absolute) merits of a set of trial wave functions may be assessed by the use of the variation principle without recourse to experimental results: the best trial function will be that which corresponds to the lowest energy.

C. The Hamiltonian Operator for the Hydrogen Molecule

The way in which approximate wave functions are used in the calculation of the energy levels of many-electron molecular systems is best illustrated in the first place by reference to the hydrogen molecule. Throughout the short history of wave mechanics no molecule has been studied more actively or more successfully. Interest in it arises

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* For a proof see, *e.g.*, ref. 4. Variational methods and the relation (37) are not peculiar to wave mechanics, but are firmly based in classical mechanics[6].

† The error in the wave function is of a higher order than the error in the energy; so unless the error in the energy is very small, the wave function will not be of much value for the accurate calculation of other physical quantities such as the dipole moment or the nuclear quadrupole coupling constant.

partly because new types of wave function are often best tried out on a two-electron system, and partly because many of the results obtained from work on the hydrogen molecule can be applied directly to much more complicated molecules.

The wave functions which have been used for the hydrogen molecule are of all degrees of accuracy and complexity. Ground-state wave functions giving energies correct to 0·00001 H have become available in recent years[10], but the simple wave functions which we shall use to illustrate some of the principles of molecular quantum chemistry date from the early years of wave mechanics, and have long served as models for the representation of covalent bonding in all types of molecules. We shall see, for example, that the π-electron system of ethylene may be described by approximate wave functions of exactly the same form as those used for the hydrogen molecule.

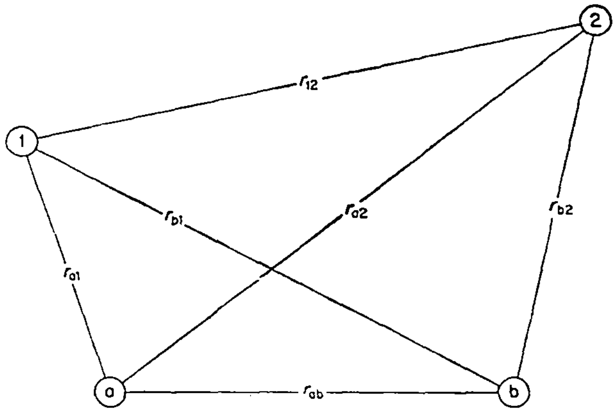

FIGURE 8. Coordinates for the hydrogen molecule. Letters denote nuclei; numerals denote electrons.

No new principles are involved in the formulation of the Hamiltonian operator for a many-electron system, except that, if there is more than one nucleus, we normally invoke the Born–Oppenheimer or fixed-nucleus approximation. Nuclei are much heavier than electrons, and therefore move much more slowly. In calculating the electronic energy of a molecule we can thus ignore the vibrational and rotational motion of the nuclei, and calculate the potential energy of the electrons as if the nuclei were in some fixed configuration (usually the observed equilibrium configuration in the ground state). This greatly reduces the complexity of molecular wave equations without introducing appreciable error.

The kinetic-energy operator in a many-electron system is always just the sum of the kinetic-energy operators for the individual electrons (*cf.* section II.C), and (as in a one-electron system) the potential-energy terms have the same form as in classical electrostatics. If, as in Figure 8, we label* the nuclei of the hydrogen molecule a and b, and the electrons 1 and 2, the Hamiltonian operator is thus, in atomic units,

$$\mathbf{H} = -\tfrac{1}{2}\nabla_1^2 - \tfrac{1}{2}\nabla_2^2 - 1/r_{a1} - 1/r_{a2} - 1/r_{b1} - 1/r_{b2} + 1/r_{12} + 1/r_{ab}. \tag{38}$$

Unlike the other potential-energy terms in the Hamiltonian operator, $1/r_{ab}$ is a constant. The integral $\int \psi \mathbf{H} \psi d\tau$ gives the sum of the electronic energy and the nuclear repulsion energy, the latter being of course just $1/r_{ab}$.

In the analysis which follows we shall find it convenient to write the Hamiltonian operator (38) in the slightly abbreviated form

$$\mathbf{H} = \mathbf{H}_{a1} + \mathbf{H}_{b2} - 1/r_{a2} - 1/r_{b1} + 1/r_{12} + 1/r_{ab}, \tag{39}$$

where

$$\mathbf{H}_{a1} = -\tfrac{1}{2}\nabla_1^2 - 1/r_{a1}, \tag{40}$$

$$\mathbf{H}_{b2} = -\tfrac{1}{2}\nabla_2^2 - 1/r_{b2}. \tag{41}$$

$\mathbf{H}_{a1}$ and $\mathbf{H}_{b2}$ may be regarded as the Hamiltonian operators for isolated hydrogen atoms: $\mathbf{H}_{a1}$ refers to an atom made up of nucleus a and electron 1, $\mathbf{H}_{b2}$ to an atom made up of nucleus b and electron 2.

D. Product Wave Functions

Before we consider approximate wave functions for the hydrogen molecule, it is useful to demonstrate that we already know the exact wave functions for a pair of *non*-interacting hydrogen atoms; *i.e.* we know the exact wave functions when r_{ab} is so large that the last four terms in (39) are negligible. The total energy is then the sum of the individual energies, and the two-electron wave function†, Ψ, is just the product of the individual wave functions‡:

$$\Psi = \psi_a(1)\psi_b(2). \tag{42}$$

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* Throughout this chapter we shall use lower-case Roman letters for labelling nuclei and numerals for labelling electrons.

† For the remainder of this chapter we shall use capital Greek letters for many-electron wave functions and lower-case Greek letters for one-electron wave functions.

‡ For the present we are ignoring the Pauli principle. Many-electron wave functions that satisfy the Schrödinger equation do not necessarily satisfy the Pauli principle, which imposes the additional requirement of 'antisymmetry' (section V.B).

The notation on the right-hand side of (42) is a standard abbreviated notation which we use whenever we wish to carry out mathematical analysis on a many-electron wave function without referring to the explicit forms of the constituent orbitals. If, for later convenience, we take the two hydrogen atoms to be in their ground states (*cf.* Table 1), then

$$\psi_a(1) = \pi^{-\frac{1}{2}} \exp(-r_{a1}) \quad \text{and} \quad \psi_b(2) = \pi^{-\frac{1}{2}} \exp(-r_{b2}). \tag{43}$$

The Hamiltonian operator for the two non-interacting hydrogen atoms is simply

$$\mathbf{H} = \mathbf{H}_{a1} + \mathbf{H}_{b2}, \tag{44}$$

and it is very easy to show that the corresponding Schrödinger equation is satisfied by the product wave function (42). The coordinates r_{a1} and r_{b2} in (43) are independent, so differentiation with respect to one of them will have no effect on a multiplying function of the other. Thus

$$\mathbf{H}_{a1}[\psi_a(1)\psi_b(2)] = \psi_b(2)\mathbf{H}_{a1}\psi_a(1), \tag{45}$$

$$\mathbf{H}_{b2}[\psi_a(1)\psi_b(2)] = \psi_a(1)\mathbf{H}_{b2}\psi_b(2). \tag{46}$$

From the Schrödinger equation for the hydrogen atom we have

$$\mathbf{H}_{a1}\psi_a(1) = E_H\psi_a(1), \tag{47}$$

$$\mathbf{H}_{b2}\psi_b(2) = E_H\psi_b(2), \tag{48}$$

where E_H is the ground-state energy if ψ_a and ψ_b are as in (43). To demonstrate that (42) satisfies the Schrödinger equation for the two non-interacting hydrogen atoms we have merely to substitute (47) in (45) and (48) in (46), and add the resulting equations:

$$\begin{aligned} \mathbf{H}[\psi_a(1)\psi_b(2)] &= (\mathbf{H}_{a1} + \mathbf{H}_{b2})[\psi_a(1)\psi_b(2)] \\ &= \psi_b(2)E_H\psi_a(1) + \psi_a(1)E_H\psi_b(2) \\ &= 2E_H[\psi_a(1)\psi_b(2)]. \end{aligned} \tag{49}$$

It will be noticed that in deriving (49) we have made no reference to the specific forms (43) of the two individual wave functions concerned, except in so far as the steps (45) and (46) require the coordinates of the two electrons to be independent. We have restricted our analysis to a system composed of two 1*s* hydrogen atoms only because we shall shortly be dealing with such a system: it is clear that the relation exemplified in (49) is capable of considerable extension and generalization. In fact the total wave function for any system consisting of a set of *non*-interacting and distinguishable sub-systems is just the product of the wave functions for the individual sub-systems, and in the absence of interaction the Hamiltonian operators and the energies are necessarily additive.

It is scarcely possible to overemphasize the importance of product wave functions, which are used (or implied) in almost every quantum-chemical calculation. The atomic, molecular, and ionic systems in which we are interested cannot of course be broken down into completely non-interacting sub-systems; but we shall see that product wave functions are nevertheless invaluable. Their importance lies in the fact that if we are considering a system which can be regarded as a set of *interacting* sub-systems, we may still use a product wave function as a trial function with reasonable hope of success as long as the energy of the system does not differ very much from that of a corresponding idealized system whose Hamiltonian operator is simply the sum of the operators for the component sub-systems. Formally this procedure may be justified by wave-mechanical perturbation theory*; in practice it must be justified by the results which it gives. It is not essential that exact wave functions for the sub-systems should be available. Where necessary the crude product wave function may be improved by the use of the variation principle.

By far the most widely used type of product wave function is that in which each electron is treated as a separate sub-system in the appropriate atomic or molecular field. In an N-electron system, if the exact or approximate wave functions for the individual electrons are $\psi_1, \psi_2, \ldots, \psi_N$, the approximate N-electron wave function is taken to be

$$\Psi = \psi_1(1)\psi_2(2)\cdots\psi_N(N). \tag{50}$$

Except in a two-electron system (and then only if ψ_1 and ψ_2 are identical) a wave function of the type (50) has to be suitably 'antisymmetrized' to meet the requirements of the general form of the Pauli principle, but this is a complication which we can ignore for the moment. We shall discuss the Pauli principle only after we have demonstrated the unhappy effects of contravening it.

Whether antisymmetrized or not, a wave function of the form (50) inevitably makes inadequate allowance for electron interaction, and cannot thus be an exact solution of the relevant Schrödinger equation. Even if the variation principle is used to determine the best possible forms of the orbitals $\psi_1, \psi_2, \ldots, \psi_N$ (in which case Ψ is described as a

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* See, *e.g.*, ref. 4.

self-consistent-field wave function and $\psi_1, \psi_2, \ldots, \psi_N$ as self-consistent-field orbitals), the integral $\int \Psi \mathbf{H} \Psi \mathrm{d}\tau$ gives a value for the energy* which is seldom less than 1% too high.

IV. THE GROUND STATE OF THE HYDROGEN MOLECULE

A. *Valence-bond Wave Functions*

The observed ground-state energy of the hydrogen molecule ($-1{\cdot}1744\,\mathrm{H} = -31{\cdot}95$ ev) is not markedly lower than that of two non-interacting hydrogen atoms in their ground states ($-1\,\mathrm{H} = -27{\cdot}21$ ev)†, so it would seem that we might reasonably expect some measure of success with the product wave function

$$\Psi_{\mathrm{na}} = \psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) = [\pi^{-\frac{1}{2}} \exp(-r_{\mathrm{a1}})][\pi^{-\frac{1}{2}} \exp(-r_{\mathrm{b2}})]. \qquad (51)$$

The subscript na (non-antisymmetrized) is merely a label to distinguish (51) from three other wave functions which we shall examine later.

Because the orbitals ψ_{a} and ψ_{b} are normalized, so is the molecular wave function Ψ_{na}:

$$\begin{aligned}\iint \Psi_{\mathrm{na}}^2 \mathrm{d}\tau_1 \mathrm{d}\tau_2 &= \iint [\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)]^2 \mathrm{d}\tau_1 \mathrm{d}\tau_2 \\ &= \int \psi_{\mathrm{a}}^2(1)\mathrm{d}\tau_1 \int \psi_{\mathrm{b}}^2(2)\mathrm{d}\tau_2 = 1 \times 1 = 1. \qquad (52)\end{aligned}$$

The energy corresponding to Ψ_{na} has thus the simple form (35):

$$E_{\mathrm{na}} = \iint \Psi_{\mathrm{na}} \mathbf{H} \Psi_{\mathrm{na}} \mathrm{d}\tau_1 \mathrm{d}\tau_2 = \iint \psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) \mathbf{H} \psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) \mathrm{d}\tau_1 \mathrm{d}\tau_2. \qquad (53)$$

With **H** as given in (39), the energy integral (53) breaks down into the sum of the six integrals listed in Table 2.

The first step in the simplification of the five integrals not involving the interelectronic distance r_{12} is to separate the factors in the integrands containing the coordinates of electron 1 from those containing the coordinates of electron 2. Each of the five integrals may then be

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* Where there is no indication to the contrary, we shall use the term energy (or molecular energy) to represent the sum of the electronic energy (as defined in section II.A) and the nuclear repulsion energy.

† Molecular energies are always much greater than dissociation energies because they include the energies of the dissociation products (atoms or groups of atoms).

TABLE 2. Expansion of the integral $\int\int \psi_a(1)\psi_b(2)H\psi_a(1)\psi_b(2)d\tau_1 d\tau_2$.

$$\begin{aligned}
&\int\int \psi_a(1)\psi_b(2)|H_{a1}|\psi_a(1)\psi_b(2)d\tau_1 d\tau_2\\
&\qquad = \int \psi_b(2)\psi_b(2)d\tau_2 \int \psi_a(1)|H_{a1}|\psi_a(1)d\tau_1\\
&\qquad = \int \psi_a(1)E_H\psi_a(1)d\tau_1 = E_H \qquad \text{(I)}
\end{aligned}$$

$$\begin{aligned}
&\int\int \psi_a(1)\psi_b(2)|H_{b2}|\psi_a(1)\psi_b(2)d\tau_1 d\tau_2\\
&\qquad = \int \psi_a(1)\psi_a(1)d\tau_1 \int \psi_b(2)|H_{b2}|\psi_b(2)d\tau_2\\
&\qquad = \int \psi_b(2)E_H\psi_b(2)d\tau_2 = E_H \qquad \text{(II)}
\end{aligned}$$

$$\begin{aligned}
&\int\int \psi_a(1)\psi_b(2)\left|-\frac{1}{r_{a2}}\right|\psi_a(1)\psi_b(2)d\tau_1 d\tau_2\\
&\qquad = \int \psi_a(1)\psi_a(1)d\tau_1 \int \psi_b(2)\left|-\frac{1}{r_{a2}}\right|\psi_b(2)d\tau_2\\
&\qquad = -\int \psi_b(2)\left|\frac{1}{r_{a2}}\right|\psi_b(2)d\tau_2 = -K \qquad \text{(III)}
\end{aligned}$$

$$\begin{aligned}
&\int\int \psi_a(1)\psi_b(2)\left|-\frac{1}{r_{b1}}\right|\psi_a(1)\psi_b(2)d\tau_1 d\tau_2\\
&\qquad = \int \psi_b(2)\psi_b(2)d\tau_2 \int \psi_a(1)\left|-\frac{1}{r_{b1}}\right|\psi_a(1)d\tau_1\\
&\qquad = -\int \psi_a(1)\left|\frac{1}{r_{b1}}\right|\psi_a(1)d\tau_1 = -K \qquad \text{(IV)}
\end{aligned}$$

$$\begin{aligned}
&\int\int \psi_a(1)\psi_b(2)\left|\frac{1}{r_{12}}\right|\psi_a(1)\psi_b(2)d\tau_1 d\tau_2\\
&\qquad = C \qquad \text{(V)}
\end{aligned}$$

$$\begin{aligned}
&\int\int \psi_a(1)\psi_b(2)\left|\frac{1}{r_{ab}}\right|\psi_a(1)\psi_b(2)d\tau_1 d\tau_2\\
&\qquad = \frac{1}{r_{ab}}\int \psi_a(1)\psi_a(1)d\tau_1 \int \psi_b(2)\psi_b(2)d\tau_2\\
&\qquad = \frac{1}{r_{ab}} \qquad \text{(VI)}
\end{aligned}$$

Note: The vertical rules in the integrands serve only to separate the operators from the wave functions: they have no mathematical function other than that of parentheses.

written as a product of two simpler integrals, and the fact that ψ_a and ψ_b are normalized brings about a further simplification:

$$\int \psi_a(1)\psi_a(1)d\tau_1 = \int \psi_b(2)\psi_b(2)d\tau_2 = 1.$$

The second step in the evaluation of the integrals (I) and (II) follows from the Schrödinger equations (45) and (46). The definite integrals (I) and (II) differ only in the 'names' of the variables of integration, and they are therefore identical in value*; so are (III) and (IV).

---

* *Cf.* $\int_a^b f(x)dx = \int_a^b f(y)dy.$

The energy integral (V) for which we have used the symbol C represents the purely electrostatic repulsion between the charge distributions ψ_a^2 and ψ_b^2, and it is accordingly called a Coulomb integral. The integral K represents the attraction of one nucleus for the electronic charge distribution whose centre is at the other nucleus*.

On adding together the integrals (I)–(VI) we find the energy E_{na} corresponding to the wave function Ψ_{na} to be

$$E_{na} = 2E_H - 2K + C + 1/r_{ab}. \tag{54}$$

K, C, and $1/r_{ab}$ are functions of the internuclear distance, and they all tend to zero as r_{ab} tends to infinity. We can assess the merits of the wave function Ψ_{na} by plotting E_{na} against r_{ab} and comparing the curve with the corresponding experimental curve obtained from spectroscopic measurements. It is immediately obvious from Figure 9 and Table 3 that Ψ_{na} is an exceedingly poor wave function. The calculated curve does indeed have a minimum, but this is far too shallow,

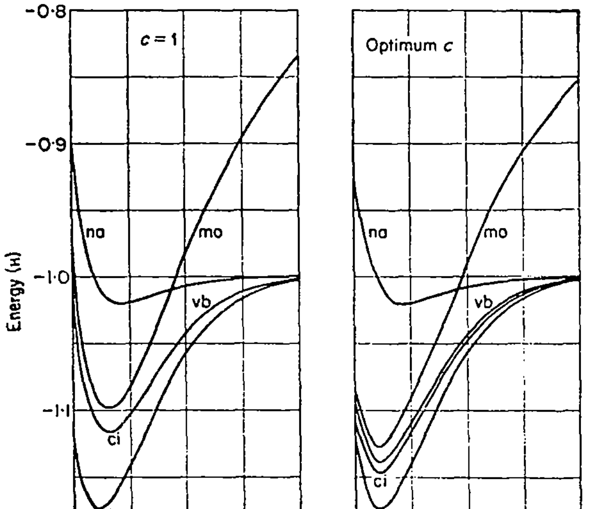

FIGURE 9. The ground-state energy of the hydrogen molecule calculated as a function of the internuclear distance.

With $c = 1$ the curves for E_{vb} and E_{ci} cannot be distinguished. Obs. = observed; other labels correspond to the subscripts used in the text.

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* There is unfortunately no generally accepted notation for the integrals used in quantum chemistry. The symbols which we have adopted here are those of Kopineck[11].

TABLE 3. Wave functions for the ground state of the hydrogen molecule. Equilibrium internuclear distance = 0·7413 Å = 1·4008 B

Wave function	$\psi = \pi^{-\frac{1}{2}} \exp(-r)$		$\psi = (c^3/\pi)^{\frac{1}{2}} \exp(-cr)$		
	Energy (H)	D_e (ev)	Optimum c	Energy (H)	D_e (ev)
Ψ_{na}	−1·0011	0·03	1·07	−1·0062	0·17
Ψ_{vb}	−1·1050	2·86	1·17	−1·1391	3·78
Ψ_{mo}	−1·0898	2·44	1·19	−1·1281	3·48
Ψ_{ci}	−1·1055	2·87	1·20	−1·1477	4·02

D_e is the dissociation energy ($2E_H - E$) at the observed equilibrium internuclear distance. Observed energy = −1·1744 H. Observed dissociation energy = 4·74 ev. (G. Herzberg, *Spectra of Diatomic Molecules*, Van Nostrand, 1950.)

and it occurs at rather too high a value of r_{ab}. At the equilibrium internuclear distance found experimentally (1·401 B = 0·7413 Å) the calculated molecular energy, instead of being stationary, is a rapidly changing function of r_{ab}, and the calculated dissociation energy ($2E_H - E_{na}$) is only just positive (0·03 ev instead of 4·74 ev). The wave function Ψ_{na} has indeed only its simplicity to commend it, and we have discussed it quantitatively only because the relatively straightforward analysis leading to the expression (54), which we shall soon require again, provides a valuable introduction to the methods used in calculating the energies of many-electron systems.

The poor results we have just described are due in part to the use at the observed internuclear distance of a wave function which is strictly valid only for infinite internuclear distance. But a much more fundamental shortcoming of the simple-product wave function Ψ_{na} is that it lacks the symmetry required by the Pauli principle. The earliest achievement in molecular quantum mechanics—and still perhaps the greatest—came from the recognition of this shortcoming by Heitler and London very soon after the discovery of the Schrödinger wave equation.

An account of electron spin and the Pauli principle at this stage would hold up our discussion of ground-state wave functions for the hydrogen molecule, so we give instead a much less formal interpretation of the inadequacy of the function Ψ_{na}. It is quite legitimate when $r_{ab} = \infty$ to associate electron 1 exclusively with nucleus a and electron 2 exclusively with nucleus b; but at internuclear distances at which there is appreciable interaction between the two hydrogen atoms, we could equally well associate electron 1 with nucleus b and electron 2 with nucleus a. In other words, the function

$$\psi_b(1)\psi_a(2) = [\pi^{-\frac{1}{2}} \exp(-r_{b1})][\pi^{-\frac{1}{2}} \exp(-r_{a2})] \tag{55}$$

has as much right to consideration as the function

$$\Psi_{na} = \psi_a(1)\psi_b(2) = [\pi^{-\frac{1}{2}} \exp(-r_{a1})][\pi^{-\frac{1}{2}} \exp(-r_{b2})]. \tag{56}$$

It is very reasonable to suppose that a wave function giving equal weight to the functions (55) and (56) would be more successful than either of these alone—and so it is. The Heitler–London wave function*

$$\Psi_{vb} = N_{vb}\{\psi_a(1)\psi_b(2) + \psi_b(1)\psi_a(2)\}, \tag{57}$$

sometimes called the Heitler–London wave function 'with exchange' to distinguish it from Ψ_{na}, gives a dissociation energy of 2·86 ev. This greatly improved value is still very much less than the observed dissociation energy (4·74 ev); but it must be remembered that we have not yet introduced any variational element into our calculations, and the variation principle provides by far the most powerful technique for refining wave functions.

It is instructive (though not essential for a general understanding of the later sections of this chapter) to see how the molecular integral

$$\begin{aligned} E_{vb} &= \iint \Psi_{vb}\mathbf{H}\Psi_{vb}\mathrm{d}\tau_1\mathrm{d}\tau_2 \\ &= N_{vb}^2 \iint [\psi_a(1)\psi_b(2) + \psi_b(1)\psi_a(2)]\mathbf{H}[\psi_a(1)\psi_b(2) \\ &\qquad + \psi_b(1)\psi_a(2)]\mathrm{d}\tau_1\mathrm{d}\tau_2 \end{aligned} \tag{58}$$

can be expanded as a sum of integrals over atomic orbitals. First we evaluate N_{vb} by integrating the square of the wave function:

$$\begin{aligned} N_{vb}^{-2} \iint \Psi_{vb}^2\mathrm{d}\tau_1\mathrm{d}\tau_2 &= \iint [\psi_a(1)\psi_b(2) + \psi_b(1)\psi_a(2)]^2\mathrm{d}\tau_1\mathrm{d}\tau_2 \\ &= \int \psi_a(1)\psi_a(1)\mathrm{d}\tau_1 \int \psi_b(2)\psi_b(2)\mathrm{d}\tau_2 \\ &\quad + \int \psi_b(1)\psi_b(1)\mathrm{d}\tau_1 \int \psi_a(2)\psi_a(2)\mathrm{d}\tau_2 \\ &\quad + \int \psi_a(1)\psi_b(1)\mathrm{d}\tau_1 \int \psi_b(2)\psi_a(2)\mathrm{d}\tau_2 \\ &\quad + \int \psi_b(1)\psi_a(1)\mathrm{d}\tau_1 \int \psi_a(2)\psi_b(2)\mathrm{d}\tau_2 \\ &= 2 + 2S^2 \quad [cf.\ \text{equation (52)}]. \end{aligned} \tag{59}$$

The integral $S = \int \psi_a\psi_b\mathrm{d}\tau$ is known as an 'overlap' integral, a name on which we comment later (section IV.B).

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* The significance of the subscript vb (valence bond) will be apparent later.

Expansion of the right-hand side of (58) gives a sum of four somewhat simpler integrals:

$$\begin{aligned} E_{\mathrm{vb}} = {} & N_{\mathrm{vb}}^2 \int\int \psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)|\mathbf{H}|\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2 \\ & + N_{\mathrm{vb}}^2 \int\int \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)|\mathbf{H}|\psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2 \\ & + N_{\mathrm{vb}}^2 \int\int \psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)|\mathbf{H}|\psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2 \\ & + N_{\mathrm{vb}}^2 \int\int \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)|\mathbf{H}|\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2. \qquad (60) \end{aligned}$$

The first and the second of these four definite integrals differ only in the 'names' of the variables of integration (represented by the numbers 1 and 2), and they are therefore equal in value. The third and the fourth of the integrals are likewise equal, so, for convenience in the next stage of the analysis, we may rewrite (60) as

$$\begin{aligned} E_{\mathrm{vb}} = {} & 2N_{\mathrm{vb}}^2 \int\int \psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)|\mathbf{H}|\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2 \\ & + 2N_{\mathrm{vb}}^2 \int\int \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)|\mathbf{H}|\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2. \qquad (61) \end{aligned}$$

In Table 2 we showed how the first of the two integrals in (61) may be broken down into a sum of basic integrals over atomic orbitals; in Table 4 we do the same for the second integral. From Table 2 we have

$$\begin{aligned} & \int\int \psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)|\mathbf{H}|\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2 \\ & \qquad = 2E_{\mathrm{H}} - 2K + C + 1/r_{\mathrm{ab}}, \qquad (62) \end{aligned}$$

and on adding together the basic integrals (VII)–(XII) in Table 4 we find

$$\begin{aligned} & \int\int \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)|\mathbf{H}|\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2 \\ & \qquad = 2S^2E_{\mathrm{H}} - 2SJ + A + S^2/r_{\mathrm{ab}}. \qquad (63) \end{aligned}$$

Substituting (59), (62), and (63) in (61) gives finally

$$\begin{aligned} E_{\mathrm{vb}} & \doteq \frac{2}{2+2S^2}[(2E_{\mathrm{H}} - 2K + C + 1/r_{\mathrm{ab}}) \\ & \qquad + (2S^2E_{\mathrm{H}} - 2SJ + A + S^2/r_{\mathrm{ab}})] \\ & = 2E_{\mathrm{H}} + \frac{1}{1+S^2}(-2K - 2SJ + C + A) + 1/r_{\mathrm{ab}}. \qquad (64) \end{aligned}$$

TABLE 4. Expansion of the integral $\int\int\psi_b(1)\psi_a(2)\mathbf{H}\psi_a(1)\psi_b(2)d\tau_1d\tau_2$.

$$\begin{aligned}&\int\int\psi_b(1)\psi_a(2)|\mathbf{H}_{a1}|\psi_a(1)\psi_b(2)d\tau_1d\tau_2\\&\qquad=\int\psi_a(2)\psi_b(2)d\tau_2\int\psi_b(1)|\mathbf{H}_{a1}|\psi_a(1)d\tau_1\\&\qquad=S\int\psi_b(1)E_H\psi_a(1)d\tau_1=S^2E_H\end{aligned}\tag{VII}$$

$$\begin{aligned}&\int\int\psi_b(1)\psi_a(2)|\mathbf{H}_{b2}|\psi_a(1)\psi_b(2)d\tau_1d\tau_2\\&\qquad=\int\psi_b(1)\psi_a(1)d\tau_1\int\psi_a(2)|\mathbf{H}_{b2}|\psi_b(2)d\tau_2\\&\qquad=S\int\psi_a(2)E_H\psi_b(2)d\tau_2=S^2E_H\end{aligned}\tag{VIII}$$

$$\begin{aligned}&\int\int\psi_b(1)\psi_a(2)\left|-\frac{1}{r_{a2}}\right|\psi_a(1)\psi_b(2)d\tau_1d\tau_2\\&\qquad=\int\psi_b(1)\psi_a(1)d\tau_1\int\psi_a(2)\left|-\frac{1}{r_{a2}}\right|\psi_b(2)d\tau_2\\&\qquad=-S\int\psi_a(2)\left|\frac{1}{r_{a2}}\right|\psi_b(2)d\tau_2=-SJ\end{aligned}\tag{IX}$$

$$\begin{aligned}&\int\int\psi_b(1)\psi_a(2)\left|-\frac{1}{r_{b1}}\right|\psi_a(1)\psi_b(2)d\tau_1d\tau_2\\&\qquad=\int\psi_a(2)\psi_b(2)d\tau_2\int\psi_b(1)\left|-\frac{1}{r_{b1}}\right|\psi_a(1)d\tau_1\\&\qquad=-S\int\psi_b(1)\left|\frac{1}{r_{b1}}\right|\psi_a(1)d\tau_1=-SJ\end{aligned}\tag{X}$$

$$\begin{aligned}&\int\int\psi_b(1)\psi_a(2)\left|\frac{1}{r_{12}}\right|\psi_a(1)\psi_b(2)d\tau_1d\tau_2\\&\qquad=A\end{aligned}\tag{XI}$$

$$\begin{aligned}&\int\int\psi_b(1)\psi_a(2)\left|\frac{1}{r_{ab}}\right|\psi_a(1)\psi_b(2)d\tau_1d\tau_2\\&\qquad=\frac{1}{r_{ab}}\int\psi_b(1)\psi_a(1)d\tau_1\int\psi_a(2)\psi_b(2)d\tau_2\\&\qquad=\frac{S^2}{r_{ab}}\end{aligned}\tag{XII}$$

B. The Overlap Integral

The expression (64) contains three integrals over atomic orbitals which were not represented in (54): these are S (the overlap integral), A (the exchange integral), and J. No purpose is served by trying to provide physical interpretations of A and J in isolation from the associated integrals C and K; but the integral S is so often used as a measure of bond strength (in other molecular systems) that it is worth examining its physical significance.

If ψ_a and ψ_b are 1s orbitals, the value of S decreases monotonically from a maximum at $r_{ab} = 0$ to zero at $r_{ab} = \infty$, the maximum value being unity if ψ_a and ψ_b are normalized (at zero internuclear distance

$\psi_a\psi_b \equiv \psi_a^2 \equiv \psi_b^2$). For $1s$ orbitals the integrand $\psi_a\psi_b$ is positive everywhere, and a high value of S is an indication that there is a substantial zone around the internuclear axis where *both* ψ_a and ψ_b have high amplitudes, *i.e.* where both r_{a1} and r_{b1} (or r_{a2} and r_{b2}) are relatively small:

$$\psi_a(1)\psi_b(1) = \pi^{-1} \exp(-r_{a1} - r_{b1}). \tag{65}$$

This condition is fulfilled in a hypothetical system of two non-interacting hydrogen atoms if the internuclear separation is small, and a high proportion of each charge cloud is concentrated near its own nucleus. It is only in this limited sense that S, a function of the coordinates of a *single* electron, may be taken to represent the 'overlap' between two electronic charge distributions.

As we are discussing wave functions for the hydrogen molecule less for their own sake than to provide a foundation for work on much more complex molecules, we must mention that the physical interpretation of S requires considerable care in any system in which ψ_a and ψ_b are not both $1s$ orbitals, for $\psi_a\psi_b$ is then positive in some regions of the coordinate space, and negative in others. There may well be little or no 'mathematical' overlap (S small or zero) when there is obviously substantial 'physical' overlap. Used with prudence, the overlap integral can be of considerable value in the discussion of chemical bonding[12], but we shall see that it need not be endowed with physical significance, and is probably best regarded as a purely mathematical quantity.

C. Molecular-orbital Wave Function

Discussions of covalent bonding in molecules of all types are almost invariably based on the use of trial wave functions of one of two forms, both having their origin in early work on the hydrogen molecule. The Heitler–London wave function leads to the valence-bond theory, and a wave function Ψ_{mo} which we shall now examine leads to the molecular-orbital theory.

If in a hydrogen atom in its ground state the internuclear distance could be reduced to zero, the resulting system would be identical, except in nuclear mass, with a helium atom, also in its ground state. The simplest wave function for the $1s^2$ state of helium—and one which gives quite a good value for the electronic energy—is the product

$$\Psi = \psi(1)\psi(2), \tag{66}$$

where ψ is the wave function each electron would have if the other were absent (*i.e.* ψ satisfies the Schrödinger equation for the ion He^+). Knowing that (66) is a reasonably satisfactory wave function for He $1s^2$, we may usefully enquire whether an analogous product function

$$\Psi_{mo} = \chi(1)\chi(2) \tag{67}$$

would serve for the hydrogen molecule, which can be supposed to be formed by the reversal of the hypothetical process described at the beginning of this paragraph. Unlike ψ, the one-electron function χ, which we shall call a molecular orbital, would naturally not be spherically symmetrical: it would correspond to a bicentric charge cloud produced by stretching the $1s$ charge cloud of helium in the direction of the internuclear axis (Figure 10).

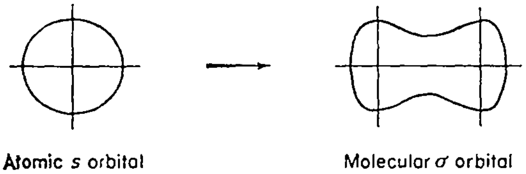

FIGURE 10. Hypothetical formation of a σ molecular orbital from an atomic *s* orbital.

If we accept the form (67), the problem of finding a wave function for the ground state of the hydrogen molecule reduces to that of obtaining a sufficiently accurate expression for the orbital χ. Our choice is guided by the following physical requirements: (*a*) the molecular charge distribution must be axially symmetrical; (*b*) it must also be symmetric to reflexion in a plane through the centre of the molecule perpendicular to the internuclear axis; (*c*) the general features of the electronic charge distribution around each nucleus should be much the same as in the uncombined atoms; and (*d*) as we shall see later, the formation of a bond between the two hydrogen atoms should result in some build-up of electronic charge between them. It is possible to devise an unlimited number of molecular orbitals which meet these requirements: of these the simplest is the linear combination

$$\chi = (2 + 2S)^{-\frac{1}{2}}(\psi_a + \psi_b), \tag{68}$$

where ψ_a and ψ_b are the atomic orbitals (43). It is convenient to normalize each molecular orbital χ; then the wave function Ψ_{mo} is normalized automatically. This has been done in (68). In expanded form Ψ_{mo} is as follows:

$$\begin{aligned}\Psi_{\mathrm{mo}} = \chi(1)\chi(2) &= (2+2S)^{-1}[(\psi_{\mathrm{a}}+\psi_{\mathrm{b}})(1)][(\psi_{\mathrm{a}}+\psi_{\mathrm{b}})(2)] \\ &= (2+2S)^{-1}[\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)+\psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2) \\ &\qquad + \psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2)+\psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)]. \qquad (69)\end{aligned}$$

It is worth noting that the function (69) embodies two distinct approximations: (*a*) the molecular wave function is taken to be a product of one-electron wave functions or molecular orbitals; (*b*) each molecular orbital is taken to be a linear combination of atomic orbitals—a far from optimum form. The first approximation is fundamental to molecular-orbital wave functions; the second is customary (for computational convenience), but not essential. If the error resulting from approximation (*b*) is removed completely, in which case (67) is described as a self-consistent-field wave function, the calculated dissociation energy is 3·63 ev[10, 13], still considerably lower than the experimental value (4·74 ev). Because of the elaborate computations which they necessitate, self-consistent-field wave functions are available for only a very small number of molecules.

By the same methods as those used in obtaining the expression (64), it can be verified without much difficulty that the energy corresponding to the wave function Ψ_{mo} is

$$\begin{aligned}E_{\mathrm{mo}} &= 2E_{\mathrm{H}} + 2(1+S)^{-1}(-K-J) \\ &\quad + (1+S)^{-2}(\tfrac{1}{2}C_0 + \tfrac{1}{2}C + A + 2L) + 1/r_{\mathrm{ab}}, \qquad (70)\end{aligned}$$

where

$$C_0 = \int \psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2)\left|\frac{1}{r_{12}}\right|\psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2, \qquad (71)$$

$$\begin{aligned}L &= \int \psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2)\left|\frac{1}{r_{12}}\right|\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2 \\ &= \int \psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)\left|\frac{1}{r_{12}}\right|\psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)\mathrm{d}\tau_1\mathrm{d}\tau_2. \qquad (72)\end{aligned}$$

It is apparent from Table 3 that the molecular-orbital wave function Ψ_{mo}, which gives a dissociation energy of 2·44 ev, is rather less successful than the Heitler–London wave function Ψ_{vb}. Furthermore, faulty asymptotic behaviour is revealed in Figure 9, and explained by equation (70): as r_{ab} tends to ∞, E_{mo} tends to $2E_{\mathrm{H}} + \frac{1}{2}C_0$ instead of $2E_{\mathrm{H}}$.

D. Configuration Interaction

A comparison of Ψ_{vb} and Ψ_{mo} as written in (57) and (69) suggests the formulation of a wave function which would avoid the defects of the molecular-orbital wave function, and might also be better than the Heitler–London wave function. Although Ψ_{vb} and Ψ_{mo} were obtained by quite different lines of argument, the only difference between them (apart from normalization) turns out to be that Ψ_{mo} contains the extra terms* $\psi_{\text{a}}(1)\psi_{\text{a}}(2)$ and $\psi_{\text{b}}(1)\psi_{\text{b}}(2)$: these terms must clearly account for the unsatisfactory features.

Ψ_{vb} and Ψ_{mo} may be regarded as special cases of a more general wave function†

$$\Psi_{\text{ci}} = N_{\text{ci}}[\{\psi_{\text{a}}(1)\psi_{\text{b}}(2) + \psi_{\text{b}}(1)\psi_{\text{a}}(2)\} + \lambda\{\psi_{\text{a}}(1)\psi_{\text{a}}(2) + \psi_{\text{b}}(1)\psi_{\text{b}}(2)\}]. \quad (73)$$

There was nothing rigorous about the reasoning which led to the formulation of Ψ_{vb} and Ψ_{mo}, there being indeed a considerable element of guesswork in each case, so instead of taking λ to be zero (as in Ψ_{vb}) or unity (as in Ψ_{mo}), we are at liberty to treat it as a parameter which can be varied to give the best energy: λ proves to be much less than unity at the equilibrium internuclear distance, and it decreases to zero as r_{ab} increases to infinity.

When the variation principle is applied in this way, the valence-bond and molecular-orbital wave functions lose their identities, and merge in the improved wave function Ψ_{ci}. A function of the type Ψ_{ci} is usually described either as a valence-bond wave function with ionic terms or (for reasons which will appear in section VI.F) as a molecular-orbital wave function with configuration interaction.

If wave functions analogous to Ψ_{ci} could be obtained easily for systems more complex than the hydrogen molecule, there would be little reason for the continued existence of distinct valence-bond and molecular-orbital procedures for the formulation of approximate wave functions; but unfortunately the variation process which seems so simple and so obvious in a two-electron system leads to analysis which rapidly becomes intractable as the number of electrons increases.

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* These two terms are often described as 'ionic' because either of them in isolation is an approximate wave function for the ion H^-; but the name should not be taken too seriously[14].

† The subscript ci (configuration interaction) is explained in section VI.F.

E. The Scale Parameter (Orbital Exponent)

Although Ψ_{ci} is the best of the wave functions we have so far considered for the hydrogen molecule, it gives a dissociation energy differing by nearly 2 ev from the observed value (Table 3). This is mainly because we have not yet used the variation principle in the most effective way. We have seen that

$$\begin{aligned}\Psi &= (2 + 2S^2)^{-\frac{1}{2}}[\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)] \\ &= (2 + 2S^2)^{-\frac{1}{2}}[(c^3/\pi)\exp(-cr_{\mathrm{a}1})\exp(-cr_{\mathrm{b}2}) \\ &\qquad + (c^3/\pi)\exp(-cr_{\mathrm{b}1})\exp(-cr_{\mathrm{a}2})],\end{aligned} \tag{74}$$

with $c = 1$, is an exact wave function for the hydrogen molecule when r_{ab} is very large. If r_{ab} is reduced to zero, $S = 1$ and $\psi_{\mathrm{a}} \equiv \psi_{\mathrm{b}}$ (*i.e.* $r_{\mathrm{a}1} = r_{\mathrm{b}1}$ and $r_{\mathrm{a}2} = r_{\mathrm{b}2}$), so (74) becomes

$$\Psi = (c^3/\pi)\exp(-cr_{\mathrm{a}1})\exp(-cr_{\mathrm{a}2}). \tag{75}$$

With $c = 2$, (75) is the simplest approximate wave function for a helium atom with its nucleus at a. It is reasonable to suppose that c increases smoothly when r_{ab} decreases from ∞ to 0, so the value $c = 1$ which we have used up to now in our wave functions for the hydrogen molecule is most unlikely to be the optimum value at the equilibrium internuclear distance. In each of these four wave functions we may replace the atomic-orbital function $\pi^{-\frac{1}{2}}\exp(-r)$ by the more flexible function $(c^3/\pi)^{\frac{1}{2}}\exp(-cr)$, and treat c as a variational parameter. As expected, we find that the best energy is obtained in each case with $c > 1$, the exact value of c depending upon the form of the wave function (Table 3).

The parameter c modifies the 'size' of the molecular charge cloud, and it is accordingly called a scale parameter: the higher the value of c (in any particular function) the smaller the average distance of the electrons from the nuclei, *i.e.* the smaller the effective size of the charge cloud.

Except in the case of Ψ_{na}, which is too unsatisfactory in form to admit of appreciable improvement, the effect of introducing the exponential scale parameter is very striking. Having also the linear variation parameter λ, Ψ_{ci} remains the best of the four wave functions, and it now gives a dissociation energy of 4·02 ev (Table 3). This is the best that can be done with a molecular wave function embodying atomic orbitals of only the 1*s* type. There remains the rather large discrepancy of 0·72 ev between the calculated and the observed dissociation energies. This discrepancy can be eliminated completely by the use of better wave functions, but these are far too elaborate to have any analogues in the quantum chemistry of the alkenes, and we do not consider them here.

F. Electron Density

We have not so far considered the distribution of electronic charge in the ground state of the hydrogen molecule. This involves extending our concept of the square of the wave function as a probability distribution (section II.B). If we use the symbol $\Psi(1,2)$ for a normalized two-electron wave function (such as any of our wave functions for H_2), then, according to the basic postulates of quantum mechanics, we can calculate the probability that electron 1 is in unit volume around a specified point and electron 2 simultaneously in unit volume around a second specified point by substituting the coordinates of the two points in the expression for the square of the wave function, $[\Psi(1,2)]^2$. This probability is not in itself a very useful quantity; but if we suppose electron 1 to be at a fixed point, then evaluate $[\Psi(1,2)]^2$ for all positions of electron 2, and sum all the probabilities so calculated, we obtain a quantity which measures the probability of finding electron 1 at its specified point irrespective of the position of electron 2. Of course we carry out the 'summation' by integrating $[\Psi(1,2)]^2$ over the coordinates of electron 2. For the molecular-orbital wave function (69) for the ground state of the hydrogen molecule the integration is trivial:

$$\begin{aligned}\int[\Psi(1,2)]^2 d\tau_2 = \int \Psi_{\text{mo}}^2 d\tau_2 &= \int[\chi(1)\chi(2)]^2 d\tau_2 \\ &= [\chi(1)]^2\int[\chi(2)]^2 d\tau_2 = [\chi(1)]^2. \qquad (76)\end{aligned}$$

As in section II.B, we can regard $[\chi(1)]^2$ as a measure of the electron density (effective charge per unit volume) due to electron 1. Exactly the same contribution is made by electron 2, so the total electron density as given by the molecular-orbital wave function for the ground state of hydrogen is

$$\begin{aligned}2\chi^2 &= \frac{2(\psi_a+\psi_b)(\psi_a+\psi_b)}{2(1+S)} \\ &= \frac{\psi_a^2+\psi_b^2+2\psi_a\psi_b}{1+S}. \qquad (77)\end{aligned}$$

(For economy in notation in (77) we have omitted the numerals identifying the electron coordinates.)

For the valence-bond wave function (57) the integration analogous to (76) over the positions of electron 2 is

$$\int[\Psi(1,2)]^2\mathrm{d}\tau_2 = \int\Psi_{\mathrm{vb}}^2\mathrm{d}\tau_2 = \frac{\int[\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)]^2\mathrm{d}\tau_2}{2+2S^2}$$

$$= \frac{[\psi_{\mathrm{a}}(1)]^2\int[\psi_{\mathrm{b}}(2)]^2\mathrm{d}\tau_2}{2+2S^2} + \frac{[\psi_{\mathrm{b}}(1)]^2\int[\psi_{\mathrm{a}}(2)]^2\mathrm{d}\tau_2}{2+2S^2}$$

$$+ \frac{2[\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(1)]\int[\psi_{\mathrm{a}}(2)\psi_{\mathrm{b}}(2)\mathrm{d}\tau_2}{2+2S^2}$$

$$= \frac{[\psi_{\mathrm{a}}(1)]^2 + [\psi_{\mathrm{b}}(1)]^2 + 2S[\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(1)]}{2+2S^2}. \tag{78}$$

The expression (78) represents the electron density due to electron 1, and an identical expression is obtained for electron 2, so the total electron density corresponding to Ψ_{vb} is

$$\frac{\psi_{\mathrm{a}}^2 + \psi_{\mathrm{b}}^2 + 2S\psi_{\mathrm{a}}\psi_{\mathrm{b}}}{1+S^2}. \tag{79}$$

It is useful to compare the charge distributions indicated by the functions (77) and (79) with that in a hypothetical system of two non-interacting hydrogen atoms having the same internuclear separation. The comparison may be made qualitatively by the rough method described later in section VII.D, or quantitatively by evaluating the functions (77) and (79), and also the function $\psi_{\mathrm{a}}^2 + \psi_{\mathrm{b}}^2$, at various points in the coordinate space. In either case we find that the molecular charge distributions correspond to a greater average electron density in the internuclear region than the sum $\psi_{\mathrm{a}}^2 + \psi_{\mathrm{b}}^2$. This is a perfectly general result: in its ground state a homonuclear diatomic molecule always has a greater proportion of its total electronic charge in the internuclear region than non-interacting atoms at the same internuclear distance*.

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* It is interesting to note that the non-antisymmetrized valence-bond wave function (51) for the ground state of the hydrogen molecule, $\Psi_{\mathrm{na}} = \psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)$, which proved to be very unsuccessful (section IV.A), indicates no change in electronic charge distribution on molecule formation. (This is readily demonstrated by the integration procedure described in the text.)

The analysis which we have given in this section for a two-electron system may be generalized without difficulty. The electron density corresponding to an N-electron wave function is obtained by integrating the square of the wave function over the coordinates of all the electrons but one, and multiplying the result by N. (Provided the wave function is properly antisymmetrized (section V.C), exactly the same one-electron density is obtained whichever electron is excluded from the integrations.)

V. ANTISYMMETRIZED WAVE FUNCTIONS

A. Electron Spin

Before we can discuss wave functions for many-electron systems, or even for the excited states of the hydrogen molecule, we must examine the influence of the Pauli principle on Schrödinger wave mechanics. We begin by drawing attention to a function which we previously suppressed in the interests of simplicity of analysis and conception. In section IV.A we obtained the Heitler–London wave function for the hydrogen molecule,

$$\Psi_{\mathrm{vb}} = (2 + 2S^2)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)\}, \tag{80}$$

by reasoning that an adequate wave function should associate the two electrons equally with the two nuclei. What we did not point out was that this requirement by itself was also met by the function

$$(2 - 2S^2)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) - \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)\}, \tag{81}$$

the square of which conforms with the molecular symmetry just as well as the square of (80). The function (81) cannot, however, be a ground-state wave function: the corresponding energy, which is readily shown to be

$$2E_{\mathrm{H}} + (1 - S^2)^{-1}(-2K - 2SJ + C - A) + 1/r_{\mathrm{ab}}, \tag{82}$$

is higher than E_{vb} for all values of r_{ab}, and, moreover, (81) can only be a wave function for a triplet state, whereas the ground state of the hydrogen molecule is of course a singlet state.

From the wave-mechanical principles we have enunciated up to now, it is by no means clear why (80) and (81), in which there is not even any reference to electron spin, should represent states of different multiplicity. Obviously we require some further basic principle, and we shall see that this is the Pauli principle, familiar in its most limited form as the exclusion principle.

In addition to the angular momentum which may result from the type of electronic motion about the nucleus which we have already considered, a single electron has a further angular momentum which can be explained in part by the assumption that it spins about an axis through its centre. The two types of angular momentum are known as 'orbital' angular momentum and 'spin' angular momentum. The spin angular momentum has the curious property that its scalar magnitude can have only the single value $(\frac{3}{4})^{\frac{1}{2}}(h/2\pi)$, and its component about an arbitrary axis (usually taken, for convenience, as the z axis), can have only the two values $\pm\frac{1}{2}h/2\pi$ (or, in atomic units, $\pm\frac{1}{2}$) associated with the *ad hoc* quantum numbers $m_s = \frac{1}{2}$ and $m_s = -\frac{1}{2}$.

Electron spin cannot be easily visualized, partly because it is almost certainly not a real rotation. Dirac showed in 1928 that the phenomena for which we have to invoke the postulate of electron spin are accounted for automatically without such a postulate when the Schrödinger equation is made relativistically invariant (a matter we cannot deal with here).

Schrödinger wave mechanics gives an exact account of orbital angular momentum in both one-electron and many-electron systems, but it is not able to provide an interpretation of the phenomenon of electron spin. In a formal treatment of spin it is customary to postulate artificial spin operators and equations of the Schrödinger type by analogy with the operators and equations for orbital angular momentum, and to impose arbitrary limitations on the eigenvalues so that they correspond with experimental observations as far as possible. This procedure is quite straightforward, but it requires rather lengthy explanation, so we give instead a set of rules which will suffice for the types of state in which organic chemists are normally interested, *i.e.* molecular states of low multiplicity which can be represented adequately by product wave functions. The rules suffice for distinguishing between functions of different multiplicities, and they involve little arbitrariness that is not also found in the more formal procedure. We illustrate the operation of the rules by reconsidering the familiar Heitler–London and molecular-orbital wave functions for the hydrogen molecule.

The first step involves replacing the atomic and molecular orbitals we have used up to now by spin-orbitals. A spin-orbital is obtained by multiplying the corresponding orbital by one of two possible spin factors: these are written as α (if $m_s = \frac{1}{2}$) and β (if $m_s = -\frac{1}{2}$). Thus the spin-orbitals derived from the atomic orbital ψ_a and the molecular orbital χ would be

$$\psi_a \rightarrow \psi_a\alpha \text{ and } \psi_a\beta; \qquad \chi \rightarrow \chi\alpha \text{ and } \chi\beta.$$

The factors α and β are fictitious in the sense that they have no known functional form. Surprisingly, however, this is not important, for all that our rules require of them is that they should survive unchanged as multiplying factors in differentiations or integrations involving the spatial coordinates of the electrons*, and that they should be orthonormal (orthogonal and normalized):

$$\int \alpha\beta \mathrm{d}\tau = 0; \qquad \int \alpha^2 \mathrm{d}\tau = 1; \qquad \int \beta^2 \mathrm{d}\tau = 1. \tag{83}$$

We do not enquire into the nature of either the integrands or the variables of integration†, but merely accept the relations (83) as part of a convenient and successful device for reproducing experimental results mathematically.

B. The Pauli Principle

Before we consider how the replacement of orbitals by spin-orbitals affects the form of a many-electron wave function, we must state the Pauli principle, which, although it preceded the Schrödinger wave equations, can conveniently be regarded in its most general form as one of the basic postulates of wave mechanics. If in a many-electron wave function the coordinates of any two electrons are interchanged, the Pauli principle requires that the wave function should change sign, but should be unchanged in absolute magnitude, at all points in the coordinate space. As we show later, a consequence of this requirement—the so-called exclusion principle—is that no two spin-orbitals can be identical in a many-electron system: if two (spatial) orbitals are the same, one of the related spin-orbitals must have the spin factor α and the other the spin factor β. In an atomic system this means that no two spin-orbitals can correspond to the same set of four quantum numbers n, l, m, and m_s. A wave function which conforms with the general form of the Pauli principle is said to be 'antisymmetrized'.

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* They are obviously not functions of the spatial coordinates: if they were, a spin-orbital would not satisfy the same Schrödinger equation as the parent orbital. In the interests of subsequent simplicity of notation, we have ignored the possibility in (83) that α and β may be complex functions.

† We shall continue to use the symbol dτ for the volume element in integration, whether the variables are spatial variables, or spin variables, or both.

(Pauli antisymmetry is quite distinct from the geometrical antisymmetry found in, say, a *p* orbital.)

To see how the Pauli principle operates in the simplest possible circumstances, it is convenient to examine $\Psi_{\mathrm{mo}} = \chi(1)\chi(2)$, the molecular-orbital wave function for the ground state of the hydrogen molecule (69). Only two spin-orbitals, $\chi\alpha$ and $\chi\beta$, can be formed from the single molecular orbital χ, so as the first step in modifying Ψ_{mo} we form the two possible products

$$\chi(1)\alpha(1)\chi(2)\beta(2) \quad \text{and} \quad \chi(1)\beta(1)\chi(2)\alpha(2),$$

which we shall find it more convenient to write as

$$\chi\alpha(1)\chi\beta(2) \quad \text{and} \quad \chi\beta(1)\chi\alpha(2)$$

when we are not concerned with operations (notably integration) in which it is necessary to separate the spin factors from the spatial factors. Although neither of these two products separately satisfies the Pauli principle, the linear combination

$$2^{-\frac{1}{2}}\{\chi\alpha(1)\chi\beta(2) - \chi\beta(1)\chi\alpha(2)\} \tag{84}$$

is indeed properly antisymmetrized, for if the electron coordinates (or the spin-orbitals) are interchanged, each of the terms in braces changes into the other, and the whole function thus changes sign. The normalizing factor $2^{-\frac{1}{2}}$ follows from the orthonormality of α and β: an integrand containing the factors $\alpha(1)\beta(1)$ or $\alpha(2)\beta(2)$ gives zero on integration, whereas an integrand containing the factors $\alpha(1)\alpha(1)$, $\beta(1)\beta(1)$, $\alpha(2)\alpha(2)$, or $\beta(2)\beta(2)$ gives the same result on integration as if these spin factors were absent.

By using the orthonormality relations (83) and the fact that α and β are not functions of the spatial coordinates of the electrons, it is easy to show that our original molecular-orbital wave function (69) and the antisymmetrized form (84) correspond to the same energy (70). This feature is peculiar to two-electron systems.

The antisymmetrization of a two-electron wave function requires more care when the two orbitals are different than in the simple case we have just described, but it yields more interesting results. It is informative to reconsider the function $\Psi_{\mathrm{na}} = \psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2)$, which we found to be an exceedingly poor wave function for the ground state of the hydrogen molecule. As the first step in the construction of a wave function satisfying the Pauli principle, we rewrite Ψ_{na} in terms of spin-orbitals. The atomic orbitals being different, there is no restriction on the choice of spin factors. If we assign the same spin factor to the two atomic orbitals, we obtain the spin-orbital products (85) and (86):

$$\psi_a\alpha(1)\psi_b\alpha(2); \tag{85}$$

$$\psi_a\beta(1)\psi_b\beta(2). \tag{86}$$

If we use different spin factors for the two orbitals we obtain (87) and (88):

$$\psi_a\alpha(1)\psi_b\beta(2); \tag{87}$$

$$\psi_a\beta(1)\psi_b\alpha(2). \tag{88}$$

These last two products represent equivalent ways of distributing the spin factors, so, using much the same reasoning as led us to replace $\psi_a(1)\psi_b(2)$ by $\psi_a(1)\psi_b(2) \pm \psi_b(1)\psi_a(2)$ in passing from (55) to (57), we replace (87) and (88) by the following linear combinations*:

$$2^{-\frac{1}{2}}[\psi_a\alpha(1)\psi_b\beta(2) + \psi_a\beta(1)\psi_b\alpha(2)]; \tag{89}$$

$$2^{-\frac{1}{2}}[\psi_a\alpha(1)\psi_b\beta(2) - \psi_a\beta(1)\psi_b\alpha(2)]. \tag{90}$$

The last stage in the formulation of antisymmetrized wave functions based on the orbital product $\psi_a(1)\psi_b(2)$ consists in subtracting from each term in the functions (85), (86), (89), and (90) the same term with the electron coordinates permuted. In this way we arrive at the following four wave functions, all satisfying the Pauli principle:

$$(2 - 2S^2)^{-\frac{1}{2}}\{\psi_a\alpha(1)\psi_b\alpha(2) - \psi_b\alpha(1)\psi_a\alpha(2)\}; \tag{91}$$

$$(2 - 2S^2)^{-\frac{1}{2}}\{\psi_a\beta(1)\psi_b\beta(2) - \psi_b\beta(1)\psi_a\beta(2)\}; \tag{92}$$

$$\begin{aligned}2^{-\frac{1}{2}}(2 - 2S^2)^{-\frac{1}{2}}[\{\psi_a\alpha(1)\psi_b\beta(2) - \psi_b\beta(1)\psi_a\alpha(2)\}\\ + \{\psi_a\beta(1)\psi_b\alpha(2) - \psi_b\alpha(1)\psi_a\beta(2)\}];\end{aligned} \tag{93}$$

$$\begin{aligned}2^{-\frac{1}{2}}(2 + 2S^2)^{-\frac{1}{2}}[\{\psi_a\alpha(1)\psi_b\beta(2) - \psi_b\beta(1)\psi_a\alpha(2)\}\\ - \{\psi_a\beta(1)\psi_b\alpha(2) - \psi_b\alpha(1)\psi_a\beta(2)\}].\end{aligned} \tag{94}$$

By using the orthonormality of α and β, it is readily verified that the normalizing factors are correct as given above, that the three distinct wave functions (91)–(93) all give the same energy (82), and that (94) gives the Heitler–London energy (64). As we show in the

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[*] Whether the linear combinations are formed at this stage or after the antisymmetrization has been carried out is a matter of convenience. If the functions (87) and (88) are antisymmetrized as they stand, and then combined to form linear variation functions as described later in section VI.E, the final wave functions are (93) and (94), exactly as in the present procedure.

next paragraph, the function (94) is simply the Heitler–London wave function written in terms of spin-orbitals, whereas the functions (91)–(93) represent the three components of an excited triplet state. The threefold degeneracy is 'split' to a very slight extent by interactions between spin and orbital motion for which there is no provision in our Hamiltonian operator (38).

It is useful to rewrite the functions (93) and (94) to clarify their relationship with the earlier functions (81) and (80) built up from atomic orbitals without spin factors:

$$\begin{aligned}
&2^{-\frac{1}{2}}(2 \mp 2S^2)^{-\frac{1}{2}}[\{\psi_a(1)\alpha(1)\psi_b(2)\beta(2) - \psi_b(1)\beta(1)\psi_a(2)\alpha(2)\} \\
&\qquad \pm \{\psi_a(1)\beta(1)\psi_b(2)\alpha(2) - \psi_b(1)\alpha(1)\psi_a(2)\beta(2)\}] \\
&\quad = [(2 \mp 2S^2)^{-\frac{1}{2}}\{\psi_a(1)\psi_b(2) \mp \psi_b(1)\psi_a(2)\}] \\
&\qquad\qquad [2^{-\frac{1}{2}}\{\alpha(1)\beta(2) \pm \beta(1)\alpha(2)\}]. \qquad (95)
\end{aligned}$$

The lower signs in (95) refer to the singlet state, the upper signs to the component of the triplet state. Because of the orthonormality of α and β, the factors $2^{-\frac{1}{2}}\{\alpha(1)\beta(2) \pm \beta(1)\alpha(2)\}$ in (95) have no effect when the wave functions are used for the calculation of physical quantities. This simplifying feature is not found in systems of more than two electrons: it is impossible in such systems to write a properly antisymmetrized total wave function as a product of two factors, one a function of spatial coordinates only, and the other a function of spin coordinates only.

It will be noticed that not only in the singlet function (94), but also in the triplet function (93), each of the four product terms incorporates both possible spin factors α and β, corresponding to $m_s = \frac{1}{2}$ and $m_s = -\frac{1}{2}$. Clearly the terms 'parallel' and 'antiparallel' used in the conventional description of triplet and singlet states must be treated with some caution.

C. Determinantal Wave Functions

We have seen that the antisymmetrization of a two-electron wave function increases the number of product terms by a factor of 2. In a three-electron system the factor would be 6; in a four-electron system it would be 24; and in an N-electron system it would be $N!$, where

$$N! = N \times (N-1) \times (N-2) \times \cdots \times 2 \times 1$$

is the number of ways of associating N electrons with N spin-orbitals.

If $U_1, U_2, \ldots, U_N$ are N spin-orbitals from which an N-electron atomic or molecular wave function (or one of the terms in such a wave function) is built up, the product $U_1(1)U_2(2)\ldots U_N(N)$ will yield on antisymmetrization a linear combination of $N!$ terms obtained by permuting either the spin-orbitals or the electrons. The $N!$ coefficients will all have the same absolute magnitude (determined by normalization), but some will be positive and some negative, the signs being determined by the Pauli principle. If we arrange that terms in the linear combination differing by an odd number of interchanges of electron coordinates differ in sign, whereas those differing by an even number of interchanges have the same sign, we shall satisfy the Pauli principle. For example, in the simple case of a three-electron wave function built up from three orthonormal spin-orbitals U_1, U_2, and U_3, antisymmetrization would give

$$\begin{aligned}(3!)^{-\frac{1}{2}}\{&U_1(1)U_2(2)U_3(3) - U_2(1)U_1(2)U_3(3)\\ &- U_3(1)U_2(2)U_1(3) - U_1(1)U_3(2)U_2(3) + U_2(1)U_3(2)U_1(3)\\ &+ U_3(1)U_1(2)U_2(3)\}.\end{aligned} \tag{96}$$

It is a trivial matter to show that (96) conforms with the Pauli principle: if we interchange the coordinates of, say, electrons 1 and 2, the first term changes into the second and *vice versa*, the third into the fifth, and the fourth into the sixth; *i.e.* the antisymmetrized function changes sign.

To avoid the handling of expansions of excessive length, antisymmetrized wave functions are normally written as determinants. In determinantal notation (96) becomes

$$(3!)^{-\frac{1}{2}}\begin{vmatrix} U_1(1) & U_1(2) & U_1(3)\\ U_2(1) & U_2(2) & U_2(3)\\ U_3(1) & U_3(2) & U_3(3)\end{vmatrix}$$

and this in turn can be abbreviated to

$$(3!)^{-\frac{1}{2}}\det\{U_1(1)U_2(2)U_3(3)\}, \tag{97}$$

n which only the diagonal term of the determinant is specified. A function like (97) is sometimes written in the equivalent non-determinantal form

$$(3!)^{-\frac{1}{2}}\mathbf{A}\{U_1(1)U_2(2)U_3(3)\},$$

where **A** is an 'antisymmetrization operator' which generates the required permutations.

In the same way a product of N orthonormal spin-orbitals would yield the antisymmetrized function

$$(N!)^{-\frac{1}{2}}\begin{vmatrix} U_1(1) & U_1(2) & \cdots & U_1(N) \\ U_2(1) & U_2(2) & \cdots & U_2(N) \\ \cdots & \cdots & \cdots & \cdots \\ U_N(1) & U_N(2) & \cdots & U_N(N) \end{vmatrix}$$

$$= (N!)^{-\frac{1}{2}} \det \{U_1(1)U_2(2)\ldots U_N(N)\}. \quad (98)$$

Readers who are not familiar with determinants need note only that (98) is a shorthand notation for a linear combination of $N!$ terms, all of the same form as the expression in braces on the right-hand side, but differing in the order of the spin-orbitals; the coefficients in the linear combination all have the absolute value $(N!)^{-\frac{1}{2}}$, and their signs are determined in the way already described. We shall be concerned with only the most obvious of the mathematical properties of determinants.

The Pauli exclusion principle follows automatically from the form of (98): a determinant is identically equal to zero if it has two identical rows or two identical columns, so no two of the N spin-orbitals in (98) may be the same. In the particular case of the three-electron system which we have considered, the operation of the exclusion principle may be demonstrated by reference to the expanded form of the wave function (96), which obviously vanishes if $U_1 = U_2$ or $U_1 = U_3$ or $U_2 = U_3$.

D. Spin States

It will be clear from the examples we have discussed that the formulation of a wave function of the antisymmetrized-product type for an N-electron system may, for our purposes, be regarded as a three-stage process.

(1) The first stage is by far the most difficult, and consists in deciding upon the trial forms of the atomic or molecular orbitals which are to be used in the construction of the N-electron wave function. The set of orbitals (some used twice) is called a configuration*. The exclusion principle requires that the configuration should contain at

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* It is not always possible to build up a satisfactory wave function from a single configuration, and superposition of configurations (configuration 'interaction') has then to be taken into account. We ignore this complication for the time being.

least $N/2$ distinct orbitals if N is even, and at least $(N + 1)/2$ if N is odd. We shall see that molecular-orbital wave functions for the ground states (though not the excited states) of organic molecules generally embody no more than this minimum number of orthogonal orbitals.

(2) In the second stage the possible spin-orbitals (twice as many as there are orbitals) are grouped into linear combinations appropriate to states of definite multiplicity (singlet, triplet, . . . if N is even; doublet, quartet, . . . if N is odd).

(3) Finally the trial wave functions are antisymmetrized: each term in the linear combinations formulated in stage (2) is replaced by an Nth-order determinant.

To illustrate the three stages we may once again trace the systematic development of the Heitler–London wave function for the ground state of the hydrogen molecule ($N = 2$):

Stage (1) $\psi_a(1)\psi_b(2)$.

Stage (2) $$2^{-\frac{1}{2}}\{\psi_a\alpha(1)\psi_b\beta(2) - \psi_a\beta(1)\psi_b\alpha(2)\} = \psi_a(1)\psi_b(2)[2^{-\frac{1}{2}}\{\alpha(1)\beta(2) - \beta(1)\alpha(2)\}].$$

Stage (3) $$2^{-\frac{1}{2}}(2 + 2S^2)^{-\frac{1}{2}} \left\{ \begin{vmatrix} \psi_a\alpha(1) & \psi_a\alpha(2) \\ \psi_b\beta(1) & \psi_b\beta(2) \end{vmatrix} - \begin{vmatrix} \psi_a\beta(1) & \psi_a\beta(2) \\ \psi_b\alpha(1) & \psi_b\alpha(2) \end{vmatrix} \right\}$$

As in (95), this last expression simplifies to

$$[(2 + 2S^2)^{-\frac{1}{2}}\{\psi_a(1)\psi_b(2) + \psi_b(1)\psi_a(2)\}] \times [2^{-\frac{1}{2}}\{\alpha(1)\beta(2) - \beta(1)\alpha(2)\}].$$

It is only the second stage in the formulation of an N-electron wave function that we need to examine further at this point: the first stage we shall consider when discussing specific molecules, and the third stage is merely an automatic routine.

The way in which the spin-orbitals derived from a single configuration of orbitals are combined linearly to give wave functions of various multiplicities is usually determined by the use of the artificially defined operators for spin angular momentum to which we referred earlier. This is an elegant but rather elaborate procedure. We shall not follow it here, because we can obtain the particular results we require by the methods we have already described, *i.e.* by calculating energies rather than angular momenta.

We saw in the case of the hydrogen molecule that four antisymmetrized wave functions could be produced from the orbital configuration $\psi_a(1)\psi_b(2)$. Three of these could be shown by direct calculation to correspond to the same energy, and they therefore represented the components of a triplet state. Only one function remained: it was thus necessarily a singlet function, and it corresponded to a different energy. The singlet function and one of the triplet functions were linear combinations of the same two determinants; the other two triplet functions were single determinants. Results of exactly the same form would be obtained with any two-electron system having a wave function embodying two different orbitals.

Our problem now is to determine the form of the antisymmetrized wave functions for systems of more than two electrons. There is an important simplifying feature which we may note at the outset: it can be demonstrated without difficulty that, in consequence of the orthogonality of α and β, a linear combination of products of spin-orbitals can be formed only if in each term there are the same numbers of α factors and β factors as in every other term. For example, the terms in (89) or (90) can combine because each term has one α factor and one β factor; but there is no combination between (85), which has two α factors and no β factor, and (86), which has two β factors and no α factor.

We shall be concerned mainly with molecular-orbital wave functions for the remainder of this chapter, and these very fortunately do not provide opportunity for a great variety of distributions of spin factors within a single orbital configuration. Molecular-orbital ground-state wave functions normally incorporate as few distinct molecular orbitals as the exclusion principle permits: if the molecular orbitals available for the construction of an N-electron molecular wave function are, in order of increasing energy (*cf.* section VII.C), $\chi_1, \chi_2, \chi_3, \ldots, \chi_N$, then, unless electron-repulsion effects are more than usually important, the lowest-energy wave function will be that based on the configuration

$$\chi_1(1)\chi_1(2)\chi_2(3)\chi_2(4)\chi_3(5)\chi_3(6)\ldots,$$

in which the higher-energy orbitals are ignored and the fullest possible use is made of the lower-energy orbitals (each of which can be used twice, once with α spin and once with β spin). If N is even, there can then be only one possible set of spin-orbitals, comprising $N/2$ orthogonal orbitals with the spin factor α plus the same $N/2$ orbitals with the factor β. There is only one antisymmetrized wave function; it must be a singlet; and it consists of just one determinant:

$$(N!)^{-\frac{1}{2}} \det \{\chi_1\alpha(1)\chi_1\beta(2)\chi_2\alpha(3)\chi_2\beta(4)\ldots\chi_{N/2}\alpha(N-1)\chi_{N/2}\beta(N)\} \tag{99}$$

If N is odd and the ground-state configuration embodies $(N+1)/2$ orthogonal molecular orbitals, $(N-1)/2$ of which are necessarily used twice, there will be two possible distributions of spin factors (differing in the factor assigned to the orbital which is used once only). These give two single-determinant wave functions, (100) and (101); they have the same energy; and they are the components of a doublet state:

$$(N!)^{-\frac{1}{2}} \det \{\chi_1\alpha(1)\chi_1\beta(2)\ldots \times \chi_{(N-1)/2}\alpha(N-2)\chi_{(N-1)/2}\beta(N-1)\chi_{(N+1)/2}\alpha(N)\}; \tag{100}$$

$$(N!)^{-\frac{1}{2}} \det \{\chi_1\alpha(1)\chi_1\beta(2)\ldots \times \chi_{(N-1)/2}\alpha(N-2)\chi_{(N-1)/2}\beta(N-1)\chi_{(N+1)/2}\beta(N)\}. \tag{101}$$

The only other case we need consider is that in which the N-electron wave function is constructed from $(N/2+1)$ orthogonal molecular orbitals, N being necessarily even. Two of the orbitals, which we call χ_q and χ_r, are each used once only; they are of higher energy than the orbitals used twice. There are four ways of distributing the spin factors, and the four antisymmetrized wave functions so produced, (102)–(105), are entirely analogous to (91)–(94).

$$(N!)^{-\frac{1}{2}} \det \{\chi_1\alpha(1)\chi_1\beta(2)\ldots\chi_q\alpha(N-1)\chi_r\alpha(N)\}; \tag{102}$$

$$(N!)^{-\frac{1}{2}} \det \{\chi_1\alpha(1)\chi_1\beta(2)\ldots\chi_q\beta(N-1)\chi_r\beta(N)\}; \tag{103}$$

$$2^{-\frac{1}{2}}(N!)^{-\frac{1}{2}}[\det \{\chi_1\alpha(1)\chi_1\beta(2)\ldots\chi_q\alpha(N-1)\chi_r\beta(N)\} + \det \{\chi_1\alpha(1)\chi_1\beta(2)\ldots\chi_q\beta(N-1)\chi_r\alpha(N)\}]; \tag{104}$$

$$2^{-\frac{1}{2}}(N!)^{-\frac{1}{2}}[\det \{\chi_1\alpha(1)\chi_1\beta(2)\ldots\chi_q\alpha(N-1)\chi_r\beta(N)\} - \det \{\chi_1\alpha(1)\chi_1\beta(2)\ldots\chi_q\alpha(N-1)\chi_r\beta(N)\}]. \tag{105}$$

The first three of these functions are the components of a triplet state, whereas the fourth is a singlet function.

As we shall show later for hydrogen (section VI.B), ethylene (section X) and butadiene (section X), functions of the type (102)–(105) generally represent the lowest excited states of a molecule[*]

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[*] Or an atom if the molecular orbitals are replaced by atomic orbitals.

having an even number of electrons. In this case $q = N/2$ and $r = N/2 + 1$. The configuration on which the wave functions are based,

$$\chi_1(1)\chi_1(2)\ldots\chi_{N/2}(N-1)\chi_{N/2+1}(N),$$

is formed from the corresponding ground-state configuration [*cf.* (99)],

$$\chi_1(1)\chi_1(2)\ldots\chi_{N/2}(N-1)\chi_{N/2}(N),$$

by the excitation of one electron from the orbital $\chi_{N/2}$ to the orbital $\chi_{N/2+1}$ (next in order of energy).

VI. LOW-ENERGY STATES OF THE HYDROGEN MOLECULE

A. Atomic-orbital Bases

We must make it clear at the outset that the simple excited-state wave functions which we describe in this section are greatly inferior to the ground-state wave functions of section IV: the formulation of excited-state molecular wave functions giving energies correct to within a few percent is a very difficult problem, calling for techniques far more sophisticated than those which can be described in this introductory account.

We have seen that tolerably accurate wave functions for the ground state of the hydrogen molecule can be compounded in various ways from the ground-state orbitals of the constituent atoms, and the same is true for molecules with up to about twenty electrons*. But it is impossible to build up an accurate *excited*-state molecular wave function solely from *ground*-state atomic orbitals, and the most formidable problem in the quantitative wave-mechanical description of excited molecular states is the choice of sets of atomic orbitals which are effective without being unwieldy. A knowledge of the states of excitation of the atomic dissociation products is of less value than might be expected, for the composition of the predominant configuration often changes with internuclear distance. It is not at all surprising that there are as yet relatively few successful wave-mechanical calculations on excited molecular states.

This is a tantalizing situation, for, especially in alkene chemistry, there is an abundance of spectroscopic data on excitation energies which can be interpreted and coordinated only by wave-mechanical methods; yet accurate wave-mechanical calculations from first

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* This limit is not one of principle: it is determined by current computing techniques.

principles on the excited states of even the simplest alkene molecules are likely to be out of the question for many years to come.

For the present the only way out of the difficulty is to abandon all attempt at the absolute calculation of state energies or excitation energies, and—with discretion—to apply simple wave-mechanical techniques to very crude wave functions for the rough estimation of small changes in energy. These may be changes resulting from the introduction of substituents or from distortion of molecular shape, or changes in a characteristic transition energy in passing from one member to another in an alkene or polyene series.

The wave functions used in this way—excited-state wave functions as well as ground-state wave functions—are almost always constructed from the minimum number of *ground*-state atomic orbitals: no other procedure is consistent with simplicity, and there is no point in elaborating computations which can have only a very limited objective. This means that the excited-state wave functions are generally far too inaccurate to be used for the satisfactory calculation of quantities dependent on electronic charge distribution. They correctly define the symmetries of the states they represent, but would give quite useless results if used, say, for the calculation of oscillator strengths or dipole moments.

The parameters in excited-state wave functions are normally determined by the application of the variation principle, and, as we have seen (section III.B), this procedure gives wave functions which are more seriously in error than the corresponding energies. In alkene molecules there is the further difficulty that the almost universal use of the π-electron approximation (section X) makes direct comparison of calculated and observed energies impossible: we cannot compare state energies (which have variational significance), but only transition energies (which have not). In other words, we have no fundamental criterion for determining how good or bad a π-electron wave function may be.

The very marked difference in accuracy between ground-state and excited-state molecular wave functions based on the same set of atomic orbitals is sufficiently important to be worth demonstrating quantitatively. For reasons which will be readily appreciated later, alkene molecules cannot be used conveniently for purposes of illustration, so instead we again examine the application of the molecular-orbital and valence-bond procedures to the hydrogen molecule. The wave functions we are about to discuss are, however, the same in form as those for the π-electron system of ethylene.

B. Molecular-orbital Wave Functions

First we consider molecular-orbital wave functions. It can be shown that if we start with a 'basis' of N atomic orbitals, then, irrespective of the number of atoms involved, we can construct just N linearly independent molecular orbitals by linear combination of the atomic orbitals. In the case of the hydrogen molecule, two molecular orbitals can thus be formed from the two ground-state $1s$ atomic orbitals, ψ_a and ψ_b. The symmetry of the molecule requires that ψ_a and ψ_b should have the same 'weight' in the molecular wave functions, so the molecular orbitals must be

$$[\sigma_g] \quad \chi_1 = (2 + 2S)^{-\frac{1}{2}}(\psi_a + \psi_b); \tag{106}$$

$$[\sigma_u] \quad \chi_2 = (2 - 2S)^{-\frac{1}{2}}(\psi_a - \psi_b). \tag{107}$$

Along with the analytical forms of these two orbitals we give symbols which denote their symmetry. Being built up from $1s$ atomic orbitals, the molecular orbitals are necessarily symmetric about the internuclear axis: this is indicated by the symbol σ. The subscript g indicates that the molecular orbital is symmetric to inversion in the centre of the molecule, the subscript u that it is antisymmetric: if a straight line is drawn through the centre of the molecule in any direction, the value of the *gerade* function χ_1 at any point on the line will be the same as the value at the point equidistant from the centre on the opposite side; the two values for the *ungerade* function χ_2 will be the same in absolute magnitude but opposite in sign (Figure 11).

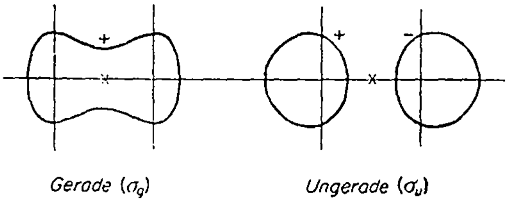

FIGURE 11. *Gerade* and *ungerade* molecular orbitals for the hydrogen molecule. The σ_g orbital is symmetric to reflexion in the midpoint of the molecule (marked by a cross); the σ_u orbital is antisymmetric.

From the two molecular orbitals χ_1 and χ_2 we can build up the three configurations $\chi_1(1)\chi_1(2)$, $\chi_1(1)\chi_2(2)$, and $\chi_2(1)\chi_2(2)$. The first and the third necessarily lead to singlet states (because of the exclusion principle), but the second can give either a singlet or a triplet state.

In antisymmetrized form the four possible wave functions are, in order of decreasing energy,

$$\Psi_{\mathrm{mo}}(^1\Sigma_g^*) = 2^{-\frac{1}{2}} \det \{\chi_2\alpha(1)\chi_2\beta(2)\}; \tag{108}$$

$$\Psi_{\mathrm{mo}}(^1\Sigma_u) = 2^{-1}[\det \{\chi_1\alpha(1)\chi_2\beta(2)\} - \det \{\chi_1\beta(1)\chi_2\alpha(2)\}]; \tag{109}$$

$$\Psi_{\mathrm{mo}}(^3\Sigma_u) = 2^{-1}[\det \{\chi_1\alpha(1)\chi_2\beta(2)\} + \det \{\chi_1\beta(1)\chi_2\alpha(2)\}]; \tag{110}$$

$$\Psi_{\mathrm{mo}}(^1\Sigma_g) = 2^{-\frac{1}{2}} \det \{\chi_1\alpha(1)\chi_1\beta(2)\}. \tag{111}$$

Because we are dealing with the special case of a two-electron system, it is possible, as we saw in section V.C, to write functions without spin factors which give the same energies as (108)–(111):

$$\Psi_{\mathrm{mo}}(^1\Sigma_g^*) = \chi_2(1)\chi_2(2); \tag{112}$$

$$\Psi_{\mathrm{mo}}(^1\Sigma_u) = 2^{-\frac{1}{2}}[\chi_1(1)\chi_2(2) + \chi_2(1)\chi_1(2)]; \tag{113}$$

$$\Psi_{\mathrm{mo}}(^3\Sigma_u) = 2^{-\frac{1}{2}}[\chi_1(1)\chi_2(2) - \chi_2(1)\chi_1(2)]; \tag{114}$$

$$\Psi_{\mathrm{mo}}(^1\Sigma_g) = \chi_1(1)\chi_1(2). \tag{115}$$

The multiplicities of the states for which these are approximate wave functions are indicated by the superscripts preceding the spectroscopic† symbol Σ; this symbol has the same significance as σ in the one-electron functions (106) and (107). We use an asterisk in (108) and (112) to distinguish the higher-energy $^1\Sigma_g$ wave function from the ground-state wave function. The functions (111) and (115) are, of course, the same as the function which we previously called just Ψ_{mo}.

The symbols g and u in (112)–(115) are simply related to the same symbols in (106) and (107). A wave function for a homonuclear diatomic molecule has u symmetry if it is based on a configuration containing an odd number of u orbitals; otherwise it has g symmetry.

The energies corresponding to the wave functions (112)–(115) may be calculated in the usual way for various values of r_{ab} and compared with energies determined spectroscopically. The function $\Psi_{\mathrm{mo}}(^1\Sigma_g^*)$ cannot be associated with any spectroscopically observed state of the hydrogen molecule, but $\Psi_{\mathrm{mo}}(^1\Sigma_u)$ and $\Psi_{\mathrm{mo}}(^3\Sigma_u)$ may be taken to be approximations to the functions for the lowest excited singlet and triplet states. In Table 5 the calculated energies are compared with the observed energies for internuclear distances of 1·401 B and 2·443 B.

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† In describing these Σ states spectroscopists usually add a redundant superscript plus sign.

These are the equilibrium internuclear distances for the ground state and the $^1\Sigma_u$ state; the triplet state is unstable and does not have an energy minimum (except in the region of the van der Waals dispersion forces).

Our reason for quoting the excited-state energies for $r_{ab} = 1{\cdot}401$ B is that calculations on alkene molecules, for which the present calculations serve as a model, normally give only vertical excitation energies. The term 'vertical' arises from the well-known graphical representation of the energies of a sequence of molecular states as functions of the internuclear coordinates. A vertical transition from the ground state, normally corresponding to the maximum in an absorption peak, is one in which the electronic configuration in the excited state is established before the relatively slow-moving nuclei have time to change their ground-state configurations appreciably. In Table 6 we give the vertical excitation energies corresponding to the state energies listed in Tables 3 and 5.

TABLE 5. Energies of the lowest excited states of the hydrogen molecule.

State	$r_{ab} = 1{\cdot}401$ B			$r_{ab} = 2{\cdot}443$ B		
	c	$\tilde{E}$ (H)	E (H)	c	$\tilde{E}$ (H)	E (H)
$^1\Sigma_u$	1	−0·35	−0·71	1	−0·60	−0·76
	0·80*	−0·40		0·79*	−0·64	
$^3\Sigma_u$	1	−0·63	−0·79	1	−0·92	−0·94
	0·93*	−0·64		0·99*	−0·92	

$\tilde{E}$ = energy calculated from functions (113) and (114); E = observed energy (G. Herzberg, *Spectra of Diatomic Molecules*, Van Nostrand, 1950).

The exponential scale parameter c is defined in the same way as in Table 3. The asterisked values are those obtained by applying the variation principle (*i.e.* those for which $\partial\tilde{E}/\partial c = 0$).

TABLE 6. Lowest vertical excitation energies of the hydrogen molecule.

		Excitation energy (ev) for $r_{ab} = 1{\cdot}401$ B		
Transition	Scale parameters	Molecular orbital	Valence bond	Observed
$^1\Sigma_g$–$^1\Sigma_u$	$c = 1$	20·1	20·5	12·7
	optimum	19·9	20·2	
$^1\Sigma_g$–$^3\Sigma_u$	$c = 1$	12·5	12·9	10·6
	optimum	13·4	13·7	

It is clear from Table 5 that the singlet wave function $\Psi_{\mathrm{mo}}({}^1\Sigma_u)$ greatly overestimates the energy, even at the larger of the two internuclear distances, and for the calculation of the vertical excitation energy it is worthless. At $r_{\mathrm{ab}} = 2{\cdot}443$ B the triplet wave function gives as good an energy as the ground-state wave functions of sections IV.A to IV.C, although it also is badly in error at $r_{\mathrm{ab}} = 1{\cdot}401$ B. The comparative success of the triplet wave function is due to the fact that it becomes exact when $r_{\mathrm{ab}} \rightarrow \infty$; this will become clear when we examine the equivalent valence-bond representation (117).

It would be wrong to attach too much importance to the breakdown of the approximate calculation of the vertical excitation energies, for this is due to some extent to the abnormally small internuclear distance in the ground state of the hydrogen molecule: much more significant is the inadequacy of the function $\Psi_{\mathrm{mo}}({}^1\Sigma_u)$ even at the larger internuclear distance. It is clear that $\Psi_{\mathrm{mo}}({}^1\Sigma_u)$ could not be used for the calculation of physical quantities dependent upon electronic charge distribution.

It will be noted that the excitation energies listed in Table 6 are all too high: this is because the excited-state wave functions are much less accurate than the ground-state wave functions.

C. *The Variation Principle for Excited-state Wave Functions*

The variation principle, which we applied only to ground-state wave functions in section VII.B, can be extended to excited-state wave functions. We shall now make use of the following more general statement of the principle: the exact energy of the lowest-energy state of any given symmetry and multiplicity is always lower than that calculated by the formula $E = \int \Psi \mathbf{H} \Psi d\tau / \int \Psi^2 d\tau$ from an approximate wave function of the same symmetry and multiplicity. This means that if we introduce the scale parameter c (*cf.* section IV.E) into the functions $\Psi_{\mathrm{mo}}({}^1\Sigma_u)$ and $\Psi_{\mathrm{mo}}({}^3\Sigma_u)$, and vary it so that the energy is minimized in each case, the state energies will necessarily be better than in the absence of the scale parameter. This is clear from Table 5.

It is interesting to note that the scale parameter is lower—*i.e.* the electron cloud is more diffuse—in the excited states than in the ground state (*cf.* section II.A).

A curious, but unfortunately very common, result of applying the variation principle to inflexible excited-state wave functions is seen in Table 6. If $\Psi_{\mathrm{mo}}({}^1\Sigma_g)$ and $\Psi_{\mathrm{mo}}({}^3\Sigma_u)$ are both improved by proper scaling, the calculated excitation energy is worsened, not improved: this is because scaling improves the ground-state wave function more effectively than the triplet function. In the same way, if the molecular-orbital ground-state wave function were improved, as, for example, in (73), the calculated excitation energies would become even higher for both the singlet and the triplet states.

D. Valence-bond Wave Functions

To provide a link with the valence-bond wave functions which we are about to discuss, it is useful to rewrite the functions $\Psi_{\mathrm{mo}}(^1\Sigma_u)$ and $\Psi_{\mathrm{mo}}(^3\Sigma_u)$, as formulated in (113) and (114), in terms of products of atomic orbitals. In the case of the singlet function we find

$$\begin{aligned}\Psi_{\mathrm{mo}}(^1\Sigma_{\mathrm{u}}) &= 2^{-\frac{1}{2}}[\chi_1(1)\chi_2(2) + \chi_2(1)\chi_1(2)]\\ &= 2^{-\frac{1}{2}}[(2+2S)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(1)+\psi_{\mathrm{b}}(1)\}(2-2S)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(2)-\psi_{\mathrm{b}}(2)\}\\ &\quad + (2-2S)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(1)-\psi_{\mathrm{b}}(1)\}(2+2S)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(2)+\psi_{\mathrm{b}}(2)\}]\\ &= (2-2S^2)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2)-\psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)\}. \end{aligned} \tag{116}$$

Likewise, for the triplet function,

$$\Psi_{\mathrm{mo}}(^3\Sigma_{\mathrm{u}}) = (2 - 2S^2)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) - \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)\}. \tag{117}$$

It is clear from (117), which is the same as (81), that, provided both are based on 1*s* orbitals only, the molecular-orbital and valence-bond procedures give identical wave functions for the lowest triplet state of the hydrogen molecule.

It happens that the same is true for the lowest excited singlet state, though this is by no means so obvious. We have seen that the valence-bond formalism is based on the expectation that a wave function which is accurate when the internuclear distance is infinite may be a reasonable approximation at the equilibrium internuclear distance. The only valence-bond wave functions that can be constructed from the 1*s* orbitals of two infinitely separated hydrogen atoms are the two we have already considered,

$$\Psi_{\mathrm{vb}}(^1\Sigma_g) = (2 + 2S^2)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)\}, \tag{118}$$

$$\Psi_{\mathrm{vb}}(^3\Sigma_{\mathrm{u}}) = (2 - 2S^2)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) - \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)\}, \tag{119}$$

yet the molecular-orbital method gives four wave functions, (112)–(115), from the same two atomic orbitals. We need two more valence-bond functions, and the only way to obtain them is to consider an artificial process of dissociation into the ions $\mathrm{H}_{\mathrm{a}}^{+} + \mathrm{H}_{\mathrm{b}}^{-}$ or $\mathrm{H}_{\mathrm{a}}^{-} + \mathrm{H}_{\mathrm{b}}^{+}$. This leads, by the same type of argument as in section

IV.A, to the additional valence-bond functions (120) and (121), having, as is indicated in parentheses, the same overall symmetries as the molecular-orbital functions (112) and (113):

$$\Psi_{\mathrm{vb}}({}^1\Sigma_g^*) = (2 + 2S^2)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)\}; \tag{120}$$

$$\Psi_{\mathrm{vb}}({}^1\Sigma_u) = (2 - 2S^2)^{-\frac{1}{2}}\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2) - \psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)\}. \tag{121}$$

The atomic-orbital products $\psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2)$ and $\psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)$ are approximate wave functions for the ions $\mathrm{H}_{\mathrm{a}}^-$ and $\mathrm{H}_{\mathrm{b}}^-$. The valence-bond function (121) is, of course, the same as the molecular-orbital function (116).

The valence-bond excitation energies quoted in Table 6 are a little worse than the molecular-orbital excitation energies which we have already examined. This is because the valence-bond ground-state wave function is a little *better* than the molecular-orbital ground-state wave function: the two methods give the same energies for the excited states considered.

E. Linear Variation Functions

Like the molecular-orbital function (115), the valence-bond function (120) cannot be used directly to describe any observed molecular state. Before we can find a use for these two wave functions we must interpolate a brief discussion of linear variation functions.

We consider a set of *approximate* solutions to a many-electron Schrödinger equation obtained by some arbitrary method (*e.g.* the molecular-orbital method or the valence-bond method), and we use the symbol Ψ_1 for the lowest-energy function of a given symmetry and multiplicity. The principle involved in the method of linear variation functions is very straightforward: if the set includes other functions $\Psi_2, \Psi_3, \ldots$ of the same symmetry and multiplicity as Ψ_1, then the linear combination

$$\Psi = c_1\Psi_1 + c_2\Psi_2 + c_3\Psi_3 + \cdots, \tag{122}$$

where the coefficients are chosen to minimize the energy

$$E = \frac{\int \Psi \mathrm{H} \Psi \mathrm{d}\tau}{\int \Psi^2 \mathrm{d}\tau},$$

is necessarily a better wave function than Ψ_1 (unless the minimization condition happens to give $c_2 = c_3 = \ldots = 0$, in which case $\Psi = \Psi_1$).

The determination of the coefficients in an expansion such as (122) is the commonest of all the algebraic operations carried out in quantum-mechanical calculations. We illustrate the procedure for the simple case of a linear combination of two terms,

$$\Psi = c_1\Psi_1 + c_2\Psi_2. \tag{123}$$

The energy to be minimized is

$$\begin{aligned} E &= \frac{\int (c_1\Psi_1 + c_2\Psi_2)\mathbf{H}(c_1\Psi_1 + c_2\Psi_2)\mathrm{d}\tau}{\int (c_1\Psi_1 + c_2\Psi_2)(c_1\Psi_1 + c_2\Psi_2)\mathrm{d}\tau} \\ &= \frac{c_1^2H_{11} + c_1c_2H_{12} + c_1c_2H_{21} + c_2^2H_{22}}{c_1^2M_{11} + c_1c_2M_{12} + c_1c_2M_{21} + c_2^2M_{22}}. \end{aligned} \tag{124}$$

In (124) we have used the abbreviated notation

$$H_{12} = \int \Psi_1\mathbf{H}\Psi_2\mathrm{d}\tau; \qquad H_{21} = \int \Psi_2\mathbf{H}\Psi_1\mathrm{d}\tau;$$
$$M_{12} = \int \Psi_1\Psi_2\mathrm{d}\tau; \qquad M_{21} = \int \Psi_2\Psi_1\mathrm{d}\tau.$$

M_{12} is obviously equal to M_{21}; and for all the functions with which we shall be concerned it may be shown, either by substitution of the explicit forms of Ψ_1, Ψ_2, and $\mathbf{H}$, or from the fundamental principles of quantum mechanics, that $H_{12} = H_{21}$. (This is because all ordinary Hamiltonian operators are Hermitean.) Accordingly we may slightly simplify the expression for the energy:

$$E = \frac{c_1^2H_{11} + 2c_1c_2H_{12} + c_2^2H_{22}}{c_1^2M_{11} + 2c_1c_2M_{12} + c_2^2M_{22}}. \tag{125}$$

We obtain the partial differential coefficients of E with respect to c_1 and c_2 with the aid of the well known rule for differentiating the quotient of two functions:

$$\frac{\partial E}{\partial c_1} = \frac{(2c_1H_{11} + 2c_2H_{22}) - E(2c_1M_{11} + 2c_2M_{12})}{c_1^2M_{11} + 2c_1c_2M_{12} + c_2^2M_{22}};$$
$$\frac{\partial E}{\partial c_2} = \frac{(2c_1H_{12} + 2c_2H_{22}) - E(2c_1M_{12} + 2c_2M_{22})}{c_1^2M_{11} + 2c_1c_2M_{12} + c_2^2M_{22}}.$$

On putting $\partial E/\partial c_1 = 0$ and $\partial E/\partial c_2 = 0$ to find the minimum value of E, we obtain the simultaneous equations

$$c_1(H_{11} - EM_{11}) + c_2(H_{12} - EM_{12}) = 0, \tag{126}$$

$$c_1(H_{12} - EM_{12}) + c_2(H_{22} - EM_{22}) = 0. \tag{127}$$

Ignoring the valueless solution $c_1 = c_2 = 0$, we eliminate c_1 and c_2 from (126) and (127) as follows. From (126),

$$\frac{c_1}{c_2} = -\frac{H_{12} - EM_{12}}{H_{11} - EM_{11}}, \tag{128}$$

and from (127),

$$\frac{c_1}{c_2} = -\frac{H_{22} - EM_{22}}{H_{12} - EM_{12}}. \tag{129}$$

From (128) and (129) we obtain a quadratic equation in E:

$$(H_{11} - EM_{11})(H_{22} - EM_{22}) - (H_{12} - EM_{12})^2 = 0. \tag{130}$$

The lower root (the more negative root) gives the minimum energy we require, the upper root corresponding to a maximum with respect to c_1 and c_2. We find the ratio c_1/c_2 for which E is minimized by substituting the value of the lower root in (128) or (129). The individual values of c_1 and c_2 are then obtained from the normalization requirement

$$c_1^2M_{11} + 2c_1c_2M_{12} + c_2^2M_{22} = 1,$$

and substituted in (123) to give the optimum linear combination.

The simultaneous equations (126) and (127) are known as secular equations, a name borrowed from classical mechanics. The equation (130) resulting from the elimination of c_1 and c_2 from the secular equations is usually written in the determinantal form

$$\begin{vmatrix} H_{11} - EM_{11} & H_{12} - EM_{12} \\ H_{21} - EM_{21} & H_{22} - EM_{22} \end{vmatrix} = 0, \tag{131}$$

the left-hand side of the equation being known as the secular determinant. The secular equations are simplified if Ψ_1 and Ψ_2 are normalized ($M_{11} = M_{22} = 1$) or orthogonal ($M_{12} = 0$).

It sometimes happens that H_{12} and M_{12} are both zero (this is always the case if Ψ_1 and Ψ_2 differ in symmetry or multiplicity), and the roots of (130) or (131) are then just $E = H_{11}/M_{11}$ (lower) and $E = H_{22}/M_{22}$ (upper). On substitution in (128) or (129) the lower root gives $c_2 = 0$ and the upper root gives $c_1 = 0$; *i.e.* there is no combination between Ψ_1 and Ψ_2*.

* This holds quite generally for any number of component functions. If a trial linear combination of the type (122) includes a function differing in symmetry or multiplicity from the rest, the result of applying the variation principle is that either its coefficient is zero, or otherwise all the other coefficients are zero. The inclusion of such a function does not affect the accuracy of a calculation, but it can lead to a lot of unnecessary algebra.

The analysis we have given here can be extended without difficulty to cover a combination of any number of functions, $\Psi_1, \Psi_2, \ldots, \Psi_N$. On putting $\partial E/\partial c_1 = \partial E/\partial c_2 = \cdots = \partial E/\partial c_N = 0$, we obtain a set of N simultaneous equations:

$$\begin{aligned}
c_1(H_{11} - EM_{11}) + c_2(H_{12} - EM_{12}) + \ldots + c_N(H_{1N} - EM_{1N}) &= 0;\\
c_1(H_{21} - EM_{21}) + c_2(H_{22} - EM_{22}) + \ldots + c_N(H_{2N} - EM_{2N}) &= 0;\\
\ldots \qquad\qquad \ldots \qquad\qquad \ldots \qquad\qquad \ldots &\\
c_1(H_{N1} - EM_{N1}) + c_2(H_{N2} - EM_{N2}) + \ldots + c_N(H_{NN} - EM_{NN}) &= 0.
\end{aligned} \tag{132}$$

These give an Nth-order secular determinant when the coefficients are eliminated. In expanded form this is an Nth-order polynomial in E, which can be shown to have only real roots. On substitution in the equations (132) the lowest of the N real roots gives the set of coefficients corresponding to the optimum linear combination of the original functions $\Psi_1, \Psi_2, \ldots, \Psi_N$.

If $\Psi_1, \Psi_2, \ldots, \Psi_N$ represent configurations in the sense in which we used the word in section V.D, the process of combining the configurations to form improved wave functions is known as superposition of configurations or, more conveniently but less accurately, as configuration interaction. The latter term originated in atomic spectroscopy; it is harmless as long as it is appreciated that the 'interaction' is purely mathematical, and not physical.

To provide the analysis required in section VI.G, our discussion of linear variation functions has been illustrated by reference to the case where the component functions are approximate solutions of a many-electron Schrödinger equation. But we shall meet many other types of linear variation function to which exactly the same analysis would apply. The most important of these are functions of the type

$$\chi = c_a\psi_a + c_b\psi_b + \ldots + c_n\psi_n,$$

where χ is one of a set of molecular orbitals, and $\psi_a, \psi_b, \ldots, \psi_n$ are the atomic orbitals from which the set is constructed. In this case integrals of the kind we have called M are just overlap integrals.

F. Configuration Interaction in the Ground State

We may now apply the linear combination principle we have just developed to our wave functions for the hydrogen molecule. The results we obtain may subsequently be used with scarcely any modification for the π-electron system of ethylene.

We have seen that, whichever method of approximation we adopt, whether molecular-orbital or valence-bond, we obtain four linearly independent wave functions for the hydrogen molecule from the two 1*s* atomic orbitals: if we use the molecular-orbital method, the molecular wave functions are (112)–(115); and if we use the valence-bond method, they are (118)–(121). In either case there are two functions of ${}^1\Sigma_g$ symmetry, one of ${}^1\Sigma_u$ symmetry, and one of ${}^3\Sigma_u$ symmetry. Without enlarging the atomic-orbital basis we can do nothing to improve the ${}^1\Sigma_u$ or ${}^3\Sigma_u$ functions; but, because there are two of them, we can improve the ${}^1\Sigma_g$ functions by the formation of optimum linear combinations.

First we consider the valence-bond wave functions $\Psi_{\mathrm{vb}}({}^1\Sigma_g)$ and $\Psi_{\mathrm{vb}}({}^1\Sigma_g^*)$. If we determine the coefficients by applying the variation principle, a linear combination of these two functions will give a better ground-state energy than $\Psi_{\mathrm{vb}}({}^1\Sigma_g)$ alone. We can write the linear combination as

$$\Psi = c_1\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)\} \\ + c_2\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)\}. \tag{133}$$

The terms in braces are obtained from (118) and (120) by omitting the normalizing factors, which can conveniently be included in the coefficients c_1 and c_2.

Dealing in the same way with the molecular-orbital wave functions $\Psi_{\mathrm{mo}}({}^1\Sigma_g)$ and $\Psi_{\mathrm{mo}}({}^1\Sigma_g^*)$, we obtain the important result that the improved molecular-orbital ground-state wave function is identical with the improved valence-bond ground-state wave function (133). We start by substituting (106) and (107) in (112) and (115):

$$\begin{aligned}\Psi_{\mathrm{mo}}({}^1\Sigma_g) &= \chi_1(1)\chi_1(2) \\ &= (2+2S)^{-1}\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2) \\ &\qquad + \psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)\};\end{aligned} \tag{134}$$

$$\begin{aligned}\Psi_{\mathrm{mo}}({}^1\Sigma_g^*) &= \chi_2(1)\chi_2(2) \\ &= (2-2S)^{-1}\{-\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) - \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2) \\ &\qquad + \psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)\}.\end{aligned} \tag{135}$$

If we again include the normalizing factors in the coefficients, the linear combination to which we are to apply the variation principle is

$$\begin{aligned}\Psi &= C_1\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2) + \psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)\} \\ &\quad + C_2\{-\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) - \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2) \\ &\qquad + \psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)\}\end{aligned} \tag{136}$$

$$\begin{aligned}&= (C_1 - C_2)\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{b}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{a}}(2)\} \\ &\qquad + (C_1 + C_2)\{\psi_{\mathrm{a}}(1)\psi_{\mathrm{a}}(2) + \psi_{\mathrm{b}}(1)\psi_{\mathrm{b}}(2)\}.\end{aligned} \tag{137}$$

The functions in braces are the same in (137) as in (133), so varying C_1 and C_2 to obtain the minimum energy is bound to give the same result as varying c_1 and c_2. In fact

$$c_1 = C_1 - C_2; \qquad c_2 = C_1 + C_2.$$

In other words, if the coefficients are determined by the variation principle in each case, the functions (133) and (137) are identical: they are in fact the same as the function Ψ_{ci} which we obtained by a less systematic procedure in section IV.D. The complete equivalence of molecular-orbital and valence-bond wave functions based on the same set of atomic orbitals, where both types of function are refined by configuration interaction, is perfectly general, and is not confined to the simple case of a homonuclear two-electron system which we have chosen for convenience in analysis.

Unfortunately, however, this equivalence is not of great practical value, for in all but the smallest molecules computational difficulties still make it impossible to take into account all relevant superpositions of configurations based on a given set of atomic orbitals. Indeed, the wave functions used for organic molecules are almost always molecular-orbital or valence-bond functions of the simplest possible type.

VII. MOLECULAR-ORBITAL WAVE FUNCTIONS FOR DIATOMIC MOLECULES

A. Orbital Energies and 'One-electron' Hamiltonian Operators

In this section we explain the terms orbital energy (ε) and 'one-electron' Hamiltonian operator ($\mathscr{H}$), which are frequently used in approximate wave-mechanical descriptions of many-electron systems. We consider an N-electron atomic or molecular wave function Ψ which can be written as a single* determinant built up from N orthonormal spin-orbitals† $U_1, U_2, \ldots, U_N$. If Ψ is normalized, the corresponding energy is

$$E = \int \Psi \mathbf{H} \Psi \mathrm{d}\tau_1 \mathrm{d}\tau_2 \cdots \mathrm{d}\tau_N. \tag{138}$$

In (138), as in the previous sections of this chapter, **H** is the complete Hamiltonian operator. If internuclear-repulsion terms are omitted,

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* Some spin states require linear combinations of determinants (section V.D). This is a complication which affects only the exchange energy, and we ignore it in this section.

† The N spin orbitals require at least $N/2$ spatial orbitals; these must be orthogonal.

it has the general form

$$\mathbf{H} = \sum_{i=1}^{N} (-\tfrac{1}{2}\nabla_i^2) + \sum_{i=1}^{N} V_i + \sum_{\substack{i=1 \\ i<j}}^{N-1} \sum_{j=2}^{N} \frac{1}{r_{ij}}. \tag{139}$$

V_i is the total potential energy of attraction of all the nuclei for electron i; the other terms have their usual significance*. It is important to distinguish between the complete Hamiltonian operator ($\mathbf{H}$) and the 'one-electron' Hamiltonian operator ($\mathscr{H}$).

Ψ is a linear combination of $N!$ terms (section V.C), so E in (138) may be expanded as a linear combination of $(N!)^2$ integrals†. If we omit the normalizing factor $(1/N!)$, the leading term in the linear combination of integrals is

$$\int U_1(1)U_2(2)\cdots U_N(N)|\mathbf{H}|U_1(1)U_2(2)\cdots U_N(N)\mathrm{d}\tau_1\mathrm{d}\tau_2\cdots\mathrm{d}\tau_N, \tag{140}$$

and the following may be chosen as another typical term:

$$-\int U_1(1)U_2(2)\cdots U_N(N)|\mathbf{H}|U_2(1)U_1(2)\cdots U_N(N)\mathrm{d}\tau_1\mathrm{d}\tau_2\cdots\mathrm{d}\tau_N. \tag{141}$$

(Because of spin orthogonality the integral (141) is different from zero only if U_1 and U_2 have the same spin factor.) Each integral of the type (140) or (141) may be broken down into as many simpler integrals as there are terms in the Hamiltonian operator (139). Fortunately, most of these simpler integrals have the value zero, as can easily be seen if we substitute in (140) or (141) any term in the operator (139). If, for example, we select the first term (*i.e.* $-\frac{1}{2}\nabla_1^2$), we obtain integrals which, after factorization, give respectively

$$\int U_1(1)|-\tfrac{1}{2}\nabla_1^2|U_1(1)\mathrm{d}\tau_1 \int U_2(2)U_2(2)\mathrm{d}\tau_2\cdots\int U_N(N)U_N(N)\mathrm{d}\tau_N, \tag{142}$$

$$-\int U_1(1)|-\tfrac{1}{2}\nabla_1^2|U_2(1)\mathrm{d}\tau_1 \int U_2(2)U_1(2)\mathrm{d}\tau_2\cdots\int U_N(N)U_N(N)\mathrm{d}\tau_N. \tag{143}$$

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* The meaning of the double summation is best illustrated by reference to a specific system, say a four-electron atom or molecule. In this case the third term in (139) would give on expansion

$$1/r_{12} + 1/r_{13} + 1/r_{14} + 1/r_{23} + 1/r_{24} + 1/r_{34}.$$

† The $(N!)^2$ integrals have only $N!$ distinct values, and, because of orthogonality (space or spin), many of these are zero.

Because of orthonormality all factors other than the first in (142) have the value unity, and the integral may be written simply

$$\int U_1(1)|-\tfrac{1}{2}\nabla_1^2|U_1(1)\mathrm{d}\tau_1 \quad \text{or} \quad \int U_1|-\tfrac{1}{2}\nabla^2|U_1\mathrm{d}\tau; \tag{144}$$

on the other hand (143) has the value zero because the second factor vanishes*.

When the integral $\int \Psi\mathbf{H}\Psi\mathrm{d}\tau$ is broken down as far as possible in the way just described, and the non-vanishing terms collected together, the resulting expression is a sum of energy integrals of four types†:

$$\int U_i(1)|-\tfrac{1}{2}\nabla_1^2|U_i(1)\mathrm{d}\tau_1 \qquad \text{(kinetic)}; \tag{145}$$

$$\int U_i(1)|V_1|U_i(1)\mathrm{d}\tau_1 \qquad \text{(nuclear attraction)}; \tag{146}$$

$$\int U_i(1)U_j(2)\left|\frac{1}{r_{12}}\right|U_i(1)U_j(2)\mathrm{d}\tau_1\mathrm{d}\tau_2 \qquad \text{(Coulomb)}; \tag{147}$$

$$\int U_i(1)U_j(2)\left|\frac{1}{r_{12}}\right|U_j(1)U_i(2)\mathrm{d}\tau_1\mathrm{d}\tau_2 \qquad \text{(exchange)}. \tag{148}$$

It is not difficult to show that there are N kinetic-energy integrals of the type (145), one for each spin-orbital (or each electron); the same is true for the nuclear-attraction integrals, type (146). There are $\tfrac{1}{2}N(N-1)$ Coulomb integrals (as many as there are $1/r_{ij}$ terms in the Hamiltonian operator), and there is an exchange integral corresponding to each Coulomb integral in which the spin factor is the same for U_i as for U_j. After the spin factors have been removed by integration over the spin coordinates, the integrals (145)–(147) all have the coefficient $+1$ if Ψ is properly normalized, whereas the exchange integrals all have the coefficient -1. The antisymmetrization of the wave functions affects the energy only by introducing the exchange integrals (148): integrals of the other three types (145)–(147) have exactly the same coefficients when the total wave function is written as a determinant as when it is written as any one of the $N!$ terms of the determinant.

In applying the variation principle to the total wave function it is sometimes convenient to deal separately with each of the spin-orbitals

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* So usually does the first, but we do not need to use this fact.

† The numerals 1 and 2 (in parentheses and as subscripts) are dummies representing pairs of members of the set 1, 2, . . ., N. The numbering of the electron coordinates is arbitrary in an antisymmetrized wave function, and irrelevant once the many-electron integrals have been factorized.

$U_1, U_2, \ldots, U_N$, and to define quantities known as orbital energies (ε). The energy ε_i of the spin-orbital U_i is obtained by extracting from E all the integrals of the type (145)–(148) in which U_i appears*:

$$\begin{aligned}\varepsilon_i = &\int U_i(1)|-\tfrac{1}{2}\nabla_1^2|U_i(1)\mathrm{d}\tau_1 + \int U_i(1)|V_1|U_i(1)\mathrm{d}\tau_1 \\ &+ \sum_{\substack{j=1\\ j\neq i}}^{N} \int U_i(1)U_j(2)\left|\frac{1}{r_{12}}\right| U_i(1)U_j(2)\mathrm{d}\tau_1\mathrm{d}\tau_2 \\ &- \sum_{\substack{j=1\\ j\neq i}}^{N} \int U_i(1)U_j(2)\left|\frac{1}{r_{12}}\right| U_j(1)U_i(2)\mathrm{d}\tau_1\mathrm{d}\tau_2. \end{aligned} \tag{149}$$

Unless all N spin-orbitals have the same spin factor, some of the terms in the second of the two summations in (149) vanish when integration is carried out over the spin coordinates. In any case the total exchange energy is always much smaller than the total Coulomb energy.

The presence of the exchange integrals in (149) makes it impossible to give a precise physical interpretation of the term 'orbital energy'. We may say however that, if a single spin orbital U_i completely described the motion of one of the N electrons, the corresponding orbital energy would comprise:

(*a*) the kinetic energy of the electron;

(*b*) the potential energy of attraction between the electron and all the nuclei;

(*c*) the potential energy of repulsion between the electron considered and the other $N - 1$ electrons.

The contributions (*a*) and (*b*) are not affected by antisymmetrization.

It is important to note that the total electronic energy in a many-electron system is not equal to the sum of the individual orbital energies:

$$E < \varepsilon_1 + \varepsilon_2 + \ldots + \varepsilon_N. \tag{150}$$

Each electron-repulsion term is counted once on the left-hand side of (150), but twice on the right-hand side. For example, a Coulomb or exchange integral in which U_1 and U_2 appear would be included in ε_1 and also in ε_2. It is a very crude approximation to treat the inequality (150) as an equality.

Orbital energy is not an observable quantity, but it can sometimes be formally related to ionization energy. If, as a result of ionization, the spin-orbital U_i is removed from the set of N spin-orbitals from

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* See previous footnote.

which the total wave function is constructed, the terms correspondingly removed from E can easily be shown to be those on the right-hand side of (149), provided (in the case of the exchange integrals) that the ionic configuration of $N - 1$ spin-orbitals leads to only one spin state. If ionization does not affect the optimum forms of the $N - 1$ surviving orbitals*, the absolute value of the orbital energy ε_i may thus be identified with the calculated ionization energy. This observation, originally stated in rather different terms, is usually known as Koopmans' theorem[15].

If c_i is a variational parameter appearing in the spin-orbital U_i, but not in any of the other $N - 1$ spin orbitals, then

$$\frac{\partial \varepsilon_i}{\partial c_i} = \frac{\partial E}{\partial c_i}, \tag{151}$$

and thus exactly the same value of c_i is obtained by minimizing ε_i as by minimizing E. The relation (151) is often used in an iterative process for determining the optimum values of the adjustable parameters in a many-electron wave function. Approximate parameters are assigned initially to the spatial factors of the spin-orbitals U_2, $U_3, \ldots, U_N$, and ε_i is minimized. The parameters thus found for U_1 are used along with the approximate parameters for $U_3, U_4, \ldots, U_N$ to minimize ε_2. The process is continued until all N spin-orbitals have been dealt with. The whole cycle is then repeated as often as may be necessary until self-consistency is attained, *i.e.* until no further changes occur in the orbital energies or the orbital parameters†.

When a variational calculation is based on orbital energies, the complete Hamiltonian operator **H**, which we have used up to now, is generally replaced by a set of so-called 'one-electron' Hamiltonian operators $\mathscr{H}$. We shall not be concerned with the explicit forms of these operators, and need merely note that the one-electron operator $\mathscr{H}_i$ corresponding to the spin-orbital U_i is defined so that‡

$$\varepsilon_i = \int U_i(1)\mathscr{H}_{i1}U_i(1)\mathrm{d}\tau_1. \tag{152}$$

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* This is an unlikely situation, but, because of a cancellation of errors which is not properly understood, ionization energies and orbital energies are often very similar in absolute value, at least in atomic systems.

† If there are enough adjustable parameters in each orbital—strictly, an infinite number of parameters—to ensure that determining the optimum values of the parameters is equivalent to determining the optimum forms of the orbitals, the latter may be described as self-consistent orbitals or Hartree–Fock orbitals.

‡ The numeral 1 is arbitrary.

Comparison with (149) shows that the first two terms in $\mathscr{H}_{l1}$ are simply $-\frac{1}{2}\nabla_1^2$ and V_1; but the electron-repulsion terms are much more complicated in that they incorporate the orbitals of the other electrons. Unlike the genuine Hamiltonian operator **H**, the one-electron operator depends upon the form of the wave function, and thus varies somewhat from one step to the next in an iterative procedure. We shall see later (section IX) that this variation in $\mathscr{H}$ is ignored in certain simple calculations.

B. Linear Combinations of Atomic Orbitals (LCAO)

The results described in sections VI.A to VI.D showed that, when simple wave functions without configuration interaction are used, the valence-bond method provides a slightly better description of the ground state of the hydrogen molecule than the molecular-orbital method. This is true also for many alkene and polyene molecules. To save uninformative duplication, we must choose one of the two methods as the basis of the analysis in the remainder of this chapter, and it might seem that our choice should fall upon the valence-bond method because of its slight superiority in describing molecular ground states. Unfortunately, however, this advantage is more than offset by the relative unwieldiness of valence-bond wave functions (especially excited-state wave functions) for alkene molecules with more than a few carbon atoms. So, now that we have illustrated the close resemblance between the molecular-orbital and the valence-bond methods when both are based on the same set of atomic orbitals, we shall confine our attention almost exclusively to molecular-orbital procedures.

Before we can formulate wave functions for molecules more complicated than hydrogen, we must decide which atomic orbitals can be combined effectively in the construction of the component molecular orbitals. It follows from the discussion of linear variation functions in section VI.E that, if two atomic orbitals ψ_a and ψ_b combine to form a pair of bicentric molecular orbitals*, the orbital energies (section VII.A) and hence the optimum values of the coefficients of the atomic orbitals are obtained from the secular determinant

$$\begin{vmatrix} H_{aa} - S_{aa}\varepsilon & H_{ab} - S_{ab}\varepsilon \\ H_{ab} - S_{ab}\varepsilon & H_{bb} - S_{bb}\varepsilon \end{vmatrix} = 0, \tag{153}$$

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* The arguments given in this section may be generalized to cover the case where ψ_a and ψ_b combine to form not a bicentric orbital but part of a polycentric orbital.

that is,

$$(H_{aa} - S_{aa}\varepsilon)(H_{bb} - S_{bb}\varepsilon) - (H_{ab} - S_{ab}\varepsilon)^2 = 0. \tag{154}$$

The extent to which the atomic orbitals 'interact' is determined by the values of the integrals

$$S_{ab} = \int \psi_a \psi_b d\tau = \int \psi_b \psi_a d\tau = S_{ba},$$

$$H_{ab} = \int \psi_a \mathscr{H} \psi_b d\tau = \int \psi_b \mathscr{H} \psi_a d\tau = H_{ba},$$

and on the energy difference $|H_{aa} - H_{bb}|$, where

$$H_{aa} = \int \psi_a \mathscr{H} \psi_a d\tau \quad \text{and} \quad H_{bb} = \int \psi_b \mathscr{H} \psi_b d\tau.$$

$\mathscr{H}$ is the 'one-electron' molecular Hamiltonian operator (section VII.A). If, as we shall always suppose to be the case, the atomic orbitals are normalized, $S_{aa} = 1$ and $S_{bb} = 1$.

An examination of the equation (153) or (154) is greatly simplified by the fact that $|H_{ab}|$ depends in much the same way as $|S_{ab}|$ upon the nature of the atomic orbitals and upon the internuclear distance. In particular, it is almost always true that $H_{ab} = 0$ when $S_{ab} = 0$. The two integrals have relatively large values only when there is considerable 'overlap' between ψ_a and ψ_b.

Irrespective of the relative values of H_{aa} and H_{bb}, there is no effective combination between ψ_a and ψ_b unless S_{ab} and H_{ab} are appreciably different from zero. If S_{ab} and H_{ab} are exactly equal to zero, there is no combination at all. If S_{ab} and H_{ab} are very small, or if H_{aa} is very different from H_{bb}, the molecular orbitals

$$\chi = c_a \psi_a + c_b \psi_b \tag{155}$$

are not significantly different from the parent atomic orbitals in charge distribution or in energy ($\varepsilon \sim H_{aa}$ or $\varepsilon \sim H_{bb}$).

S_{ab} and H_{ab} are exactly zero whenever the two atomic orbitals ψ_a and ψ_b have different symmetries with respect to the internuclear axis, for regions in the coordinate space in which the integrands are positive are then exactly balanced by regions in which they are negative. Even when the symmetry requirement is fulfilled, S_{ab} and H_{ab} are still very small if the nuclei a and b are far apart, or if ψ_a and ψ_b correspond to markedly different distributions of electronic charge (in which case H_{aa} and H_{bb} are also markedly different).

Provided $H_{aa} \neq H_{bb}$, the absolute value of the ratio c_a/c_b in (155) is a measure of the effectiveness of the combination between ψ_a and ψ_b. If the ratio is either very high or very low (either ∞ or 0 in the extreme case where $S_{ab} = 0$ and $H_{ab} = 0$), combination is negligible. If ψ_a and ψ_b are normalized, a ratio of about unity signifies maximal 'interaction'. When $H_{aa} = H_{bb}$, however, as in a homonuclear diatomic molecule, the ratio c_a/c_b is independent of S_{ab} and H_{ab}, and (provided degeneracy does not permit the formation of arbitrary combinations of *molecular* orbitals) its value is always ± 1.

All permitted combinations of *s*, *p*, and *d* orbitals are listed in Table 7. Contour diagrams (constant $|\chi|$ or χ^2) depicting combinations of *s* and *p* orbitals in a heteronuclear diatomic molecule are given in Figure 12. The internuclear axis is the *z* axis, and the two positive *z* directions point towards each other. The diagrams are drawn on the assumption that S_{ab} and H_{ab} are significantly different from zero; if they are not, contours of $|\chi|$ are inappreciably different in shape from those of the individual atomic orbitals, although the signs are as in Figure 12.

TABLE 7. Linear combinations of atomic orbitals allowed by symmetry.

	s	p_z	p_x	p_y	d_{z^2}	d_{xz}	d_{yz}	$d_{x^2-y^2}$	d_{xy}
s	✓	✓			✓				
p_z	✓	✓			✓				
p_x			✓			✓			
p_y				✓			✓		
d_{z^2}	✓	✓			✓				
d_{xz}			✓			✓			
d_{yz}				✓			✓		
$d_{x^2-y^2}$								✓	
d_{xy}									✓

The *z* axis is the internuclear axis.

With axes chosen as in Figure 12, molecular orbitals built up from *s* and p_z atomic orbitals have complete axial symmetry, and are described as σ orbitals. Molecular orbitals built up from p_x (or p_y) atomic orbitals, however, are antisymmetric to reflexion in the *yz* (or *xz*) plane, *i.e.* the same plane as the parent atomic orbitals; they are called π_x (or π_y) orbitals.

Strictly, the symbols σ and π should be used only for linear molecules (they are defined fundamentally in terms of angular momentum about the internuclear axis), but we shall follow the convenient practice of

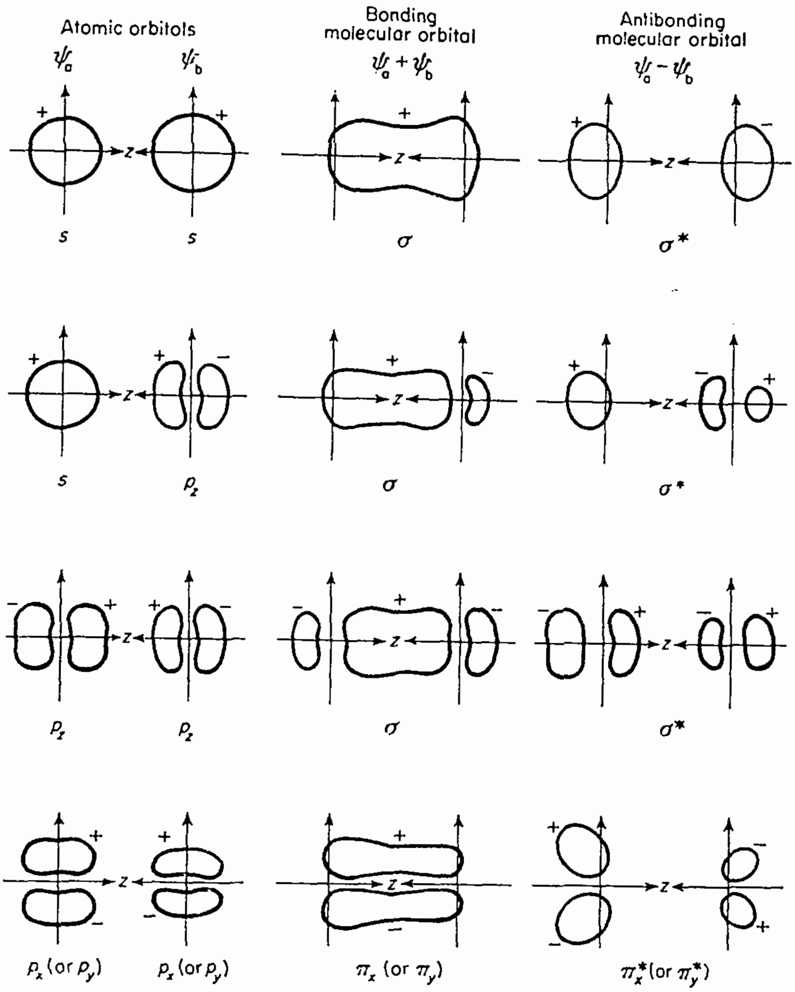

FIGURE 12. Linear combinations of atomic orbitals in a heteronuclear diatomic molecule.

The diagrams are intended to show symmetry only: the contours have been chosen quite arbitrarily, and no attempt has been made at numerical accuracy or consistency of scale.

The internuclear axis is the *z* axis, and the positive *z* directions point towards each other.

The plane in which the contours of the σ orbitals are drawn may be taken to be any plane which includes the internuclear axis. In the case of the π orbitals, however, the plane must be the *xz* plane if p_x atomic orbitals are used, and the *yz* plane if p_y atomic orbitals are used.

Contour lines in either of the *xy* planes (the planes through the nuclei perpendicular to the plane of the paper) would be of the same form for the molecular orbitals as for the atomic orbitals.

using them for planar molecules, the π orbitals being those having nodal planes coincident with the molecular planes.

With z axes directed as in Figure 12, the orbitals $\psi_a + \psi_b$ are often described as 'bonding', and the orbitals $\psi_a - \psi_b$ as 'antibonding'. These are useful terms, but they do not admit of simple and unambiguous definition (especially in polyatomic systems), and they cannot always be taken at their face value. In general the formation of a bonding molecular orbital from the orbitals of the free atoms results in an increase in electronic charge in the internuclear zone, whereas the formation of an antibonding orbital results in a decrease. Also, a bonding molecular orbital has a lower energy (in the sense of section VII.A) than the corresponding antibonding molecular orbital formed from the *same* atomic orbitals.

As in the labels in Figure 12, an asterisk is often used to distinguish an antibonding orbital from the related bonding orbital. (In a homonuclear diatomic molecule the symmetry symbols g and u serve the same purpose: σ_g and π_u are bonding, whereas σ_u and π_g are antibonding.)

Although the nuclei in Figure 12 are those of a diatomic molecule, the general features of the distribution of electronic charge between them would be very much the same if they were adjacent nuclei in a polyatomic molecule.

C. Diatomic Molecules

In formulating molecular-orbital wave functions for organic molecules we encounter two new complications: the molecular orbitals are polycentric*, and, as in almost all non-linear molecules, the bond angles do not correspond with the apparent orientations of the basic atomic orbitals.

Before dealing with these problems we discuss two diatomic molecules, one homonuclear and one heteronuclear. These are F_2 and HF, and between them they bring out many of the wave-mechanical features of covalent bonding which it would be needlessly perplexing to illustrate at this stage by direct reference to alkene or other organic molecules. Once we have examined F_2 and HF, we shall find little difficulty in describing the bonding in acetylene, ethylene, and methane.

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* With the object of preserving the classical concept of a chemical bond, a polyatomic molecular wave function is often written in terms of two-centre molecular orbitals. This almost always involves some loss of accuracy.

We shall be concerned only with the ground states of F_2 and HF ($^1\Sigma_g$ and $^1\Sigma$ respectively). The wave functions which we shall quote for these states are not the best now available, but they are the best that can helpfully be used as models for alkene wave functions. We suppose that satisfactory molecular orbitals can be formed from linear combinations of 1*s*, 2*s*, and 2*p* orbitals only, and that in each case the molecular wave functions can be built up (as indicated towards the end of section V.D) from a single configuration containing the minimum number of molecular orbitals consistent with the Pauli principle. Even with these seemingly severe approximations, the error in the calculated molecular energy is less than 1%.

The atomic orbitals have the same angular factors as the hydrogen-like orbitals in Table 1. The radial factors are taken to be as in Table 8, those of the 1*s* and 2*p* orbitals being hydrogen-like in form. As in the case of the hydrogen molecule, the exponential parameters are varied so as to minimize the total molecular energy. The parameters listed in Table 8 and all other numerical values which we quote for F_2 and HF have been obtained from Ransil's[16] comprehensive set of calculations on simple diatomic molecules*.

TABLE 8. Atomic orbitals used in wave functions for $F_2(^1\Sigma_g)$ and $HF(^1\Sigma)$.

Atomic orbital	Radial factor for F_2	Radial factor for HF
$1s_F$	$\exp(-8{\cdot}65r)$	$\exp(-8{\cdot}65r)$
$2s_F$	$r\exp(-2{\cdot}58r) - A\exp(-8{\cdot}65r)$	$r\exp(-2{\cdot}56r) - B\exp(-8{\cdot}65r)$
$2p_{zF}$	$r\exp(-2{\cdot}49r)$	$r\exp(-2{\cdot}67r)$
$2p_{xF}$ or $2p_{yF}$	$r\exp(-2{\cdot}57r)$	$r\exp(-2{\cdot}50r)$
$1s_H$		$\exp(-1{\cdot}32r)$

A and *B* are numerical constants chosen so that the 1*s* and 2*s* orbitals of the fluorine atoms are orthogonal. (The same orbital energies and total energies are obtained with $A = 0$ and $B = 0$, but the molecular orbitals are most easily interpreted when written in terms of 'orthogonalized' 2*s* orbitals.)

For typographical convenience we shall omit our usual symbol ψ in referring to the atomic orbitals. For example, we shall write the atomic orbitals from which the HF wave function is built up as

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* The computational procedures are not adequately defined in the condensed account which follows; details should be sought in the original papers.

$1s_H$, $1s_F$, $2s_F$, $2p_{zF}$, $2p_{xF}$, $2p_{yF}$, enclosing the symbols in parentheses where confusion might otherwise arise. In the case of F_2 we shall use the customary subscripts a and b to distinguish the two nuclei, and omit the subscript F.

D. Fluorine

The arbitrary basis we have chosen for the construction of the eighteen-electron wave function for the fluorine molecule comprises ten atomic orbitals (five from each atom), so it is possible to construct ten linearly independent and orthonormal molecular orbitals. Nine of these, which we temporarily label $\chi_1, \chi_2, \ldots, \chi_9$ in order of increasing energy, are required in a ground-state wave function of the type we have prescribed; the orbital of highest energy, χ_{10}, is discarded.

The minimization of the energy integral $\int \Psi \mathbf{H} \Psi d\tau$, where

$$\Psi = (18!)^{-\frac{1}{2}} \det \{\chi_1\alpha(1)\chi_1\beta(2) \cdots \chi_9\alpha(17)\chi_9\beta(18)\}, \qquad (156)$$

is a twofold problem involving variation of the atomic-orbital exponential parameters as well as the coefficients of the atomic orbitals in the molecular orbitals. The coefficients are determined by an extension of the linear variation procedure outlined in section VI.E*. The optimum values of the exponential parameters are given in Table 8, and those of the coefficients in Table 9. The total energy obtained in this way is −197·88 H; the observed energy is −199·67 H.

The numerals preceding the symmetry symbols in the first column of Table 9 are *not* quantum numbers, but merely serial numbers† used to grade the orbitals of each symmetry type in order of increasing orbital energy (section VII.A).

The most obvious feature of Table 9 is one which we shall subsequently find to be of the greatest importance: the six σ orbitals and the four π orbitals form entirely distinct groups. Were it not for this sharp distinction between σ and π orbitals, it would be quite impossible to deal in any simple way with the quantum chemistry of alkene molecules.

Of the five orbitals which each atom contributes to the F_2 wave function two ($2p_x$ and $2p_y$) have symmetry axes oriented at right angles to the internuclear axis and to each other. Because of the symmetry

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* Details for a simpler four-electron system are given in section X.

† Because of the absence of *g–u* symmetry, twice as many of these serial numbers are required for a heteronuclear diatomic molecule as for a homonuclear diatomic molecule with the same number of molecular orbitals.

TABLE 9. Molecular-orbital wave function for the ground state of fluorine[18].

Configuration: $1\sigma_g^2 1\sigma_u^2 2\sigma_g^2 2\sigma_u^2 1\pi_{xu}^2 1\pi_{yu}^2 3\sigma_g^2 1\pi_{xg}^2 1\pi_{yg}^2$ $(^1\Sigma_g)$ Equilibrium internuclear distance = 1·418 Å = 2·680 B

Molecular orbital	Coefficients of orbitals of atom a					Coefficients of orbitals of atom b					Orbital energy ε(H)
	1*s*	2*s*	$2p_z$	$2p_x$	$2p_y$	1*s*	2*s*	$2p_z$	$2p_x$	$2p_y$	
$1\sigma_g[=\chi_1]$	0·7070	0·0071	−0·0001			0·7070	0·0071	−0·0001			−26·36
$1\sigma_u[=\chi_2]$	0·7071	0·0085	0·0014			−0·7071	−0·0085	−0·0014			−26·36
$2\sigma_g[=\chi_3]$	−0·0121	0·6505	0·0835			−0·0121	0·6505	0·0835			−1·63
$2\sigma_u[=\chi_4]$	−0·0041	0·7376	−0·0724			0·0041	−0·7376	0·0724			−1·36
$3\sigma_g[=\chi_5]$	−0·0050	−0·1784	0·6477			−0·0050	−0·1784	0·6477			−0·55
$3\sigma_u[=\chi_{10}]$	0·0082	0·2143	0·8000			−0·0082	−0·2143	−0·8000			0·34
$1\pi_{xu}[=\chi_6]$				0·6902					0·6902		−0·61
$1\pi_{yu}[=\chi_7]$					0·6902					0·6902	−0·61
$1\pi_{xg}[=\chi_8]$				0·7254					−0·7254		−0·47
$1\pi_{yg}[=\chi_9]$					0·7254					−0·7254	−0·47

Total energy: −197·88 H (calculated); −199·67 H (observed).

The coefficients of the 1*s* and the 2*s* orbitals have been recalculated from the original paper[18] so as to correspond to an 'orthogonalized' 2*s* orbital. (See footnote to Table 8.)

restriction mentioned in section VII.B, $2p_{x\mathrm{a}}$ can combine only with $2p_{x\mathrm{b}}$, and likewise $2p_{y\mathrm{a}}$ can combine only with $2p_{y\mathrm{b}}$. In this way, as Table 9 shows, we obtain the following (normalized) π orbitals, much simpler than the associated σ orbitals:

$$\begin{aligned}
\chi_6 &= 1\pi_{xu} = 0{\cdot}6902(2p_{x\mathrm{a}} + 2p_{x\mathrm{b}});\\
\chi_7 &= 1\pi_{yu} = 0{\cdot}6902(2p_{y\mathrm{a}} + 2p_{y\mathrm{b}});\\
\chi_8 &= 1\pi_{xg} = 0{\cdot}7254(2p_{x\mathrm{a}} - 2p_{x\mathrm{b}});\\
\chi_9 &= 1\pi_{yg} = 0{\cdot}7254(2p_{y\mathrm{a}} - 2p_{y\mathrm{b}}).
\end{aligned}$$

The molecular orbitals π_{xu} and π_{yu} differ only in their orientation with respect to the internuclear axis, and are therefore degenerate; so, of course, are π_{xg} and π_{yg}.

The form of the orbitals $1\sigma_g$ and $1\sigma_u$ shows that they are almost independent of the higher-energy σ orbitals, and that they make no contribution to the bonding between the fluorine atoms. Atomic orbitals differing widely in energy cannot combine to any significant extent (section VII.B), and this is shown by the negligibly small coefficients of $2s$ and $2p_z$. The orbitals $1\sigma_g$ and $1\sigma_u$ are in fact essentially

$$\begin{aligned}
\chi_1 &= 1\sigma_g = (2 + 2S)^{-\frac{1}{2}}(1s_\mathrm{a} + 1s_\mathrm{b});\\
\chi_2 &= 1\sigma_u = (2 - 2S)^{-\frac{1}{2}}(1s_\mathrm{a} - 1s_\mathrm{b}).\\
&[S = \int 1s_\mathrm{a}1s_\mathrm{b}\mathrm{d}\tau].
\end{aligned}$$

Furthermore, the coefficients of the $1s$ atomic orbitals in these molecular orbitals are almost precisely $2^{-\frac{1}{2}}$ ($= 0{\cdot}7071$), an indication that S is exceedingly small. In other words, there is no appreciable combination between $1s_\mathrm{a}$ and $1s_\mathrm{b}$. This is also shown by the fact that the molecular orbitals $1\sigma_g$ and $1\sigma_u$ have the same energy, from which it follows that H_{ab} must be negligible:

$$\int[2^{-\frac{1}{2}}(1s_\mathrm{a} \pm 1s_\mathrm{b})]\mathscr{H}[2^{-\frac{1}{2}}(1s_\mathrm{a} \pm 1s_\mathrm{b})]\mathrm{d}\tau = \tfrac{1}{2}H_{\mathrm{aa}} + \tfrac{1}{2}H_{\mathrm{bb}} \pm H_{\mathrm{ab}}.$$

The reason for the absence of 'interaction' between the two $1s$ atomic orbitals (despite their degeneracy) is that each is so highly concentrated about its own nucleus (because of the relatively high nuclear charge) that there is no effective overlap*. Very fortunately,

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* 99% of the $1s$ charge 'cloud' of each atom is within 0·484 B of the nucleus, and 99·999% within 0·925 B (*cf.* equation 23). The internuclear distance, however, is 2·680 B.

this characteristic of the F—F bond is found also in all C—C bonds (but, in so far as $1s_H$ is concerned, not in C—H bonds).

Unlike the π orbitals and the 1σ orbitals, the higher σ orbitals cannot be regarded as being formed from atomic orbitals of just one type: in the 2σ and 3σ molecular orbitals $2s$ and $2p_z$ are mixed inextricably, although it is certainly the case that $2s$ predominates in the 2σ orbital and $2p_z$ in the 3σ orbital*. It is important to appreciate, as a matter of principle, that the clear-cut quantum distinctions which exist between atomic orbitals in atomic wave functions are very largely lost when the same orbitals are used as the basis of a molecular wave function. This is because molecules lack the spherical symmetry which determines the *s*, *p*, *d*, . . . character of atomic orbitals. Many linear combinations of atomic orbitals which are forbidden in atomic wave functions occur perfectly generally in molecular wave functions. These linear combinations are often described (especially when they are formulated rather more restrictively than in Tables 9–11) as hybrid atomic orbitals† (see section VIII.C).

The relative order of σ and π molecular-orbital energies (ε_i) given in Table 9 for F_2 is found also in C_2, O_2, and N_2. This order is

$$\begin{aligned}1\sigma_g \sim 1\sigma_u \ll 2\sigma_g < 2\sigma_u < 1\pi_{xu}&\\ = 1\pi_{yu} < 3\sigma_g < 1\pi_{xg} = 1\pi_{yg} < 3\sigma_u.&\end{aligned}$$

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* There is little to be gained by unduly emphasizing this predominance. Before relatively accurate wave functions for homonuclear diatomic molecules became available, it was customary to describe the first six σ orbitals as follows (in non-normalized form):

$$1s_a \pm 1s_b; \qquad 2s_a \pm 2s_b; \qquad 2p_{za} \pm 2p_{zb}.$$

This is now seen to be an oversimplification. Contrary to what might appear at first sight, recognition of the more correct forms involves no additional complication: in a quantitative variational calculation there is no escaping the proper linear combinations (which are in any case obtained automatically); and in a qualitative description of a molecular wave function based on a given set of atomic orbitals one needs to know the number of molecular orbitals of each symmetry type, and whether any are degenerate, rather than the precise details of their make-up.

† We must emphasize at this earliest opportunity that hybridization occurs in *all* LCAO wave functions with optimum coefficients, except where it is deliberately suppressed by the use of a severely truncated atomic-orbital basis (as in our wave functions for H_2, where the basis included only $1s_a$ and $1s_b$). Hybridization is by no means confined—as is so often suggested—to atoms or molecules of particular electronic or geometrical configurations.

The configuration on which our ground-state wave function for F_2 is based is

$$1\sigma_g^2 1\sigma_u^2 2\sigma_g^2 2\sigma_u^2 1\pi_{xu}^2 1\pi_{yu}^2 3\sigma_g^2 1\pi_{xg}^2 1\pi_{yg}^2, \tag{157}$$

where (157) is an alternative (and more directly informative) way of writing the expression in braces in (156). We have still to show that this configuration has Σ symmetry, *i.e.* that the four π orbitals taken together have Σ symmetry. In non-normalized form the electron-density distributions (section IV.F) corresponding to the molecular orbitals $1\pi_x$ and $1\pi_y$ are

$$(2p_{x\mathrm{a}} \pm 2p_{x\mathrm{b}})^2 = (2p_{x\mathrm{a}})^2 + (2p_{x\mathrm{b}})^2 \pm 2(2p_{x\mathrm{a}})(2p_{x\mathrm{b}}); \tag{158}$$

$$(2p_{y\mathrm{a}} \pm 2p_{y\mathrm{b}})^2 = (2p_{y\mathrm{a}})^2 + (2p_{y\mathrm{b}})^2 \pm 2(2p_{y\mathrm{a}})(2p_{y\mathrm{b}}). \tag{159}$$

The upper signs refer to the *ungerade* orbitals, and the lower signs to the *gerade* orbitals. The sum ($u + u$ or $g + g$) of the two distributions (158) and (159) may be written

$$\begin{aligned}&\{(2p_{x\mathrm{a}})^2 + (2p_{y\mathrm{a}})^2\} + \{(2p_{x\mathrm{b}})^2 + (2p_{y\mathrm{b}})^2\}\\ &\qquad \pm 2\{(2p_{x\mathrm{a}})(2p_{x\mathrm{b}}) + (2p_{y\mathrm{a}})(2p_{y\mathrm{b}})\}.\end{aligned} \tag{160}$$

In spherical polar coordinates (Table 1) the first of the three terms in braces in (160) is

$$\begin{aligned}(2p_{x\mathrm{a}})^2 + (2p_{y\mathrm{a}})^2 &= (NR\sin\theta_\mathrm{a}\cos\phi_\mathrm{a})^2 + (NR\sin\theta_\mathrm{a}\sin\phi_\mathrm{a})^2\\ &= N^2R^2\sin^2\theta_\mathrm{a}\,(\cos^2\phi_\mathrm{a} + \sin^2\phi_\mathrm{a})\\ &= N^2R^2\sin^2\theta_\mathrm{a}.\end{aligned} \tag{161}$$

N is the normalizing factor and R the radial factor of the $2p$ orbital of fluorine; the explicit forms of these factors are not relevant to the present argument. Reference to Figure 1 shows that the function (161), *i.e.* the first term in (160), is symmetrical about the z axis, and it is easy to demonstrate that the same is true for the second and the third* terms in (160). So the function (160) as a whole clearly has axial symmetry. It follows that a molecular-orbital configuration will have Σ symmetry if it is constructed from σ orbitals plus any of the following combinations of π orbitals:

$$1\pi_{xu}1\pi_{yu}; \qquad 1\pi_{xu}^2 1\pi_{yu}^2; \qquad 1\pi_{xg}1\pi_{yg}; \qquad 1\pi_{xg}^2 1\pi_{yg}^2. \tag{162}$$

In each of these π sub-configurations the two members of a pair of degenerate molecular orbitals are used together.

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* Note that $\phi_\mathrm{a} = \phi_\mathrm{b}$.

E. Bond Order

In classical terms the bond in a halogen molecule is supposed to concern only two of the eighteen electrons, and it is accordingly described as a single bond or as a bond of order 1. Before we leave the F_2 wave function for the present, we must consider whether it provides any justification for the classical description of the bond.

The wave function is antisymmetrized to satisfy the Pauli principle, each of the eighteen electrons being associated equally with each of the eighteen spin-orbitals, so for the most fundamental reasons we cannot describe two particular electrons as the bonding electrons. This is a trivial difficulty, however, for we may equally well enquire whether there are just two spin-orbitals which we can reasonably describe as the bonding spin-orbitals*.

We shall find that there are not, but this does not mean that we require eighteen spin-orbitals to describe what the chemist is content to call a single bond. We have already seen, in fact, that four of the spin-orbitals—those built up from the $1s$ atomic orbitals—take no part in the bonding: it does not matter whether we write the molecular configuration as $1\sigma_g^2 1\sigma_u^2 \ldots$ or as $1s_a^2 1s_b^2 \ldots$.

We next show, by calculating the corresponding charge distributions, that the eight π spin-orbitals make no contribution to the bonding between the fluorine atoms. The 'bonding' orbital $1\pi_{xu}$ occurs twice in the molecular configuration, and the corresponding charge distribution is

$$\begin{aligned}&2[0{\cdot}6902(2p_{xa}) + 0{\cdot}6902(2p_{xb})]^2\\ &\qquad = 0{\cdot}9526(2p_{xa})^2 + 0{\cdot}9526(2p_{xb})^2 + 1{\cdot}9052(2p_{xa})(2p_{xb}). \qquad (163)\end{aligned}$$

If we subtract from (163) the charge distributions corresponding to the $2p_x$ orbitals in the uncombined atoms, we obtain the following expression for the change in charge distribution brought about by molecule formation $(2p_{xa}2p_{xb} \rightarrow 1\pi_{xu}^2)$:

$$-0{\cdot}0474(2p_{xa})^2 - 0{\cdot}0474(2p_{xb})^2 + 1{\cdot}9052(2p_{xa})(2p_{xb}). \qquad (164)$$

By substituting in (164) the values of $2p_{xa}$ and $2p_{xb}$ at various points in the coordinate space, we could obtain a detailed description of the movement of electronic charge brought about by interaction between the two atoms. For our present purposes, however, it will suffice to

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* We commonly speak of s, p, σ, π, . . . electrons, but we mean, of course, s, p, σ, π, . . . orbitals.

consider the change in charge density in a plane through the midpoint of the molecule perpendicular to the internuclear axis. At all points in this mid-plane $2p_{xa} = 2p_{xb}$, so the expression (164) is positive or zero. Molecule formation clearly increases the charge density in a zone around the mid-plane (and, correspondingly, reduces it in the zones beyond the nuclei).

For the 'antibonding' $1\pi_{xg}$ orbital the expression analogous to (164) for the change in configuration $2p_{xa}2p_{xb} \rightarrow 1\pi_{xg}^2$ is

$$0{\cdot}0524(2p_{xa})^2 + 0{\cdot}0524(2p_{xb})^2 - 2{\cdot}1048(2p_{xa})(2p_{xb}). \qquad (165)$$

This represents a decrease in charge density in the region between the nuclei. The total change in charge density corresponding to the configurational change $2p_{xa}^2 2p_{xb}^2 \rightarrow 1\pi_{xu}^2 1\pi_{xg}^2$ is given by the sum of (164) and (165):

$$0{\cdot}0050(2p_{xa})^2 + 0{\cdot}0050(2p_{xb})^2 - 0{\cdot}1996(2p_{xa})(2p_{xb}). \qquad (166)$$

The expression (166) indicates a decrease in charge density in the internuclear region, but the effect is only a slight one: the coefficients of $2p_{xa}$ and $2p_{xb}$ are very small, and the product $2p_{xa}2p_{xb}$ is not large anywhere in the coordinate space*. (This product, which is always positive, is the integrand in the overlap integral between the two $2p_x$ orbitals; the value of the integral is only 0·0497.)

The simple analysis we have just given for the $1\pi_x$ orbitals applies equally to the $1\pi_y$ orbitals. In all, the eight spin-orbitals corresponding to the configuration $1\pi_{xu}^2 1\pi_{yu}^2 1\pi_{xg}^2 1\pi_{yg}^2$ make no contribution to the bonding in the fluorine molecule; their effect is indeed very slightly 'antibonding'.

Having shown that twelve of the eighteen spin-orbitals make no appreciable contribution to the F—F bond, we have carried the process of simplification by elimination as far as we can. Of the surviving molecular orbitals, the $2\sigma_g$ and the $3\sigma_g$ orbitals can be shown to be 'bonding' in character, and the $2\sigma_u$ orbital 'antibonding'. If the effects of the $2\sigma_g$ and the $2\sigma_u$ orbitals cancelled exactly, we could ascribe the bonding exclusively to the two $3\sigma_g$ spin-orbitals, and so confirm the chemist's description of the bond as a single bond; but it

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* In general, if χ_1 and χ_2 are bonding and antibonding diatomic molecular orbitals formed from two atomic orbitals ψ_a and ψ_b, the electron density distributions corresponding to the configurations $\chi_1\chi_2$ or $\chi_1^2\chi_2^2$ are very much the same as those corresponding to the uncombined atomic orbitals. What little difference does exist is in the 'antibonding' direction.

happens that the configuration $2\sigma_g^2 2\sigma_u^2$ has a net 'antibonding' character that is too large to be ignored. It is quite generally true that no strict wave-mechanical calculation ever provides a quantity which can be identified with the chemist's integral bond order. This is simply because the classical description of a bond as single, double or triple involves little more than counting up the 'valency' electrons, whereas even a crude wave-mechanical description is concerned with charge distributions and orbital energies. In other words the wave-mechanical description begins where the classical description leaves off.

F. Hydrogen Fluoride

Having discussed the molecular orbitals of F_2 in some detail, we need say very little about those of HF: Table 10 now almost explains itself. The arbitrary atomic-orbital basis consists of one hydrogen orbital ($1s$) and five fluorine orbitals ($1s$, $2s$, $2p_z$, $2p_x$, $2p_y$). There would be no symmetry restriction on the use of five hydrogen orbitals to match the five fluorine orbitals, but this would not improve the molecular wave function to a significant extent: because of the relatively high energy of the $2s_{\mathrm{H}}$ and $2p_{\mathrm{H}}$ orbitals (0·375 H or 10·2 ev higher than that of $1s_{\mathrm{H}}$ in a free hydrogen atom), these would not combine effectively with any other of the basis orbitals.

From the six atomic orbitals which it is thus profitable to use as a basis six linearly independent molecular orbitals (twelve molecular spin-orbitals) can be constructed. Only five of the six molecular orbitals are required for the ten-electron ground-state wave function.

Three of the orbitals of the fluorine atom are not significantly affected by molecule formation: these are $2p_{x\mathrm{F}}$ and $2p_{y\mathrm{F}}$ (because they lack axial symmetry) and $1s_{\mathrm{F}}$ (because it has a much lower energy than any of the other atomic orbitals). So we may formulate the configuration on which the molecular wave function is based in any of the following ways:

$$1\sigma^2 2\sigma^2 3\sigma^2 1\pi_x^2 1\pi_y^2 = 1\sigma^2 2\sigma^2 3\sigma^2 2p_{x\mathrm{F}}^2 2p_{y\mathrm{F}}^2 \sim 1s_{\mathrm{F}}^2 2\sigma^2 3\sigma^2 2p_{x\mathrm{F}}^2 2p_{y\mathrm{F}}^2.$$

Like the F—F bond (and indeed almost every other covalent bond), the H—F bond cannot be described in terms of two spin-orbitals only: it is clear from Table 10 that all four spin-orbitals of the sub-configuration $2\sigma^2 3\sigma^2$ are concerned in the bonding.

Combination of $2s$ and $2p$ atomic orbitals within a single molecular orbital, which we have found in F_2 and HF, is perfectly general, and is by no means peculiar to the fluorine atom. It occurs in all accurate molecular wave functions built up from LCAO molecular orbitals*. Of special interest in alkene chemistry is the inevitable mixing of the 2*s* and the 2*p* orbitals of carbon.

VIII. MOLECULAR-ORBITAL WAVE FUNCTIONS FOR SIMPLE ORGANIC MOLECULES

A. Acetylene

Being linear, the tetratomic acetylene molecule provides a useful link, for wave-mechanical purposes, between alkene molecules and the simple diatomic molecules we have just studied.

In describing the ground state of acetylene we use an atomic-orbital basis of exactly the same type as for fluorine and hydrogen fluoride. We suppose that each carbon atom contributes five orbitals ($1s$, $2s$, $2p_z$, $2p_x$, $2p_y$) and each hydrogen atom one orbital ($1s$). To distinguish the four atoms from each other we use the subscripts a, b, c, d ($H_aC_bC_cH_d$).

Twelve linearly independent molecular orbitals can be constructed from this arbitrary atomic-orbital basis, but in a single-configuration ground-state wave function only seven of these are required (to provide fourteen spin-orbitals for the fourteen electrons). The optimum forms of the molecular orbitals have been determined by McLean[17], whose results we quote in Table 11.

An examination of McLean's wave function reveals several features which our study of F_2 and HF would have led us to expect. The $1s$ orbitals of the carbon atoms, like those of the fluorine atoms in F_2 and HF, take no part in the bonding. The $1\sigma_g$ and $1\sigma_u$ molecular orbitals have very nearly equal energies, and in charge distribution they are almost identical with each other and with the parent $1s$ atomic orbitals. Again, as in F_2 and HF, the π orbitals are simpler than the σ orbitals and constitute a distinct sub-configuration; this as a whole has axial symmetry.

However, while the π orbitals make no contribution to the bonding in F_2 and HF, they are of overwhelming importance in C_2H_2. This difference is easily explained: in the π sub-configuration in C_2H_2 there are no antibonding orbitals to offset the effect of the bonding orbitals

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* See, for example, Ransil's[16] collection of wave functions for simple diatomic molecules from which we have transcribed the molecular orbitals quoted in Tables 9 and 10.

TABLE 10. Molecular-orbital wave function for the ground state of hydrogen fluoride[16].

Configuration: $1\sigma^2 2\sigma^2 3\sigma^2 1\pi_x^2 1\pi_y^2\ (^1\Sigma)$ Equilibrium internuclear distance = 0·917 Å = 1·733 B

Molecular orbital	Coefficients of atomic orbitals						Orbital energy
	$1s_H$	$1s_F$	$2s_F$	$2p_{zF}$	$2p_{xF}$	$2p_{yF}$	ε(H)
1σ	−0·0033	1·0001	0·0124	0·0021			−26·27
2σ	0·1537	−0·0180	0·9140	0·0904			−1·49
3σ	0·5161	−0·0228	−0·4106	0·7115			−0·61
4σ	−1·0744	0·0489	0·5244	0·8046			0·67
$1\pi_x$					1		−0·47
$1\pi_y$						1	−0·47

Total energy: −99·54 H (calculated); −100·53 H (observed).

The coefficients of the $1s_F$ and the $2s_F$ orbitals have been recalculated so as to correspond to an 'orthogonalized' $2s_F$ orbital. (See footnote to Table 8.)

TABLE 11. Molecular-orbital wave function for the ground state of acetylene[17] ($H_aC_bC_cH_d$).

Configuration: $1\sigma_g^2 1\sigma_u^2 2\sigma_g^2 2\sigma_u^2 3\sigma_g^2 1\pi_{xu}^2 1\pi_{yu}^2 (^1\Sigma_g)$ R_e(C—C) = 1·207 Å = 2·281 B; R_e(C—H) = 1·060 Å = 2·002 B

Molecular orbital	Coefficients of orbitals of H_a and C_b						Coefficients of orbitals of H_d and C_c						Orbital energy ε (H)
	$1s_H$	$1s_C$[a]	$2s_C$[a]	$2p_{z}C$[b]	$2p_{x}C$	$2p_{y}C$	$1s_H$	$1s_C$[a]	$2s_C$[a]	$2p_{z}C$[b]	$2p_{x}C$	$2p_{y}C$	
$1\sigma_g$	−0·0033	0·7067	0·0098	−0·0007			−0·0033	0·7067	0·0098	−0·0007			−11·400
$1\sigma_u$	−0·0031	0·7091	0·0188	0·0042			0·0031	−0·7091	−0·0188	−0·0042			−11·397
$2\sigma_g$	0·1033	−0·0702	0·4557	0·1850			0·1033	−0·0702	0·4557	0·1850			−1·041
$2\sigma_u$	0·2957	−0·0411	0·3159	−0·3139			−0·2957	0·0411	−0·3159	0·3139			−0·776
$3\sigma_g$	−0·3109	−0·0202	−0·0942	0·4761			−0·3109	−0·0202	−0·0942	0·4761			−0·683
$3\sigma_u$	−0·9259	0·1220	1·1522	−0·1334			0·9259	−0·1220	−1·1522	0·1334			0·353
$4\sigma_g$	1·0594	−0·1157	−0·8057	0·7016			1·0594	−0·1157	−0·8057	0·7016			0·484
$4\sigma_u$	0·5989	0·2309	1·2970	1·6753			−0·5989	−0·2309	−1·2970	−1·6753			1·195
$1\pi_{xu}$					0·6071						0·6071		−0·441
$1\pi_{yu}$						0·6071						0·6071	−0·441
$1\pi_{xg}$					0·8814						−0·8814		0·251
$1\pi_{yg}$						0·8814						−0·8814	0·251

Total energy: −76·54 H (calculated); −77·39 H (observed[c]).

[a] The coefficients in the columns headed $1s_C$ and $2s_C$ (A. D. McLean, personal communication) relate to a $2s_C$ orbital of the form $r \exp(-1{\cdot}6082\,r) - C \exp(-5{\cdot}6726\,r)$, where the positive number C is chosen so that $2s_C$ is orthogonal to $1s_C$; in the original paper $C = 0$. The 'orthogonalization' of the $2s_C$ atomic orbital has no effect upon the molecular orbitals or their energies; it merely alters the grouping of two of the terms in the LCAO expansions.

[b] The z axis is the internuclear axis. The positive z axes of the atomic orbitals all point toward the midpoint of the molecule.

[c] Quoted by L. Burnelle, *J. Chem. Phys.*, **35**, 311 (1961).

($1\pi_{xu}^2 1\pi_{yu}^2$), whereas in F_2 there are equal numbers of bonding and antibonding orbitals ($1\pi_{xu}^2 1\pi_{yu}^2 1\pi_{xg}^2 1\pi_{yg}^2$), and in HF there are only non-bonding orbitals ($1\pi_x^2 1\pi_y^2 = 2p_x^2 2p_y^2$).

Because the four π spin-orbitals in acetylene are all bonding, and because they do not concern the hydrogen atoms, we can say, in semi-classical language, that there is a double π bond, or a π bond of order 2, between the carbon atoms. We can regard a double π bond as a superposition of two single π bonds with mutually perpendicular symmetry planes.

There is also, of course, a σ bond resulting from the net effect of six σ spin-orbitals ($2\sigma_g^2 2\sigma_u^2 3\sigma_g^2$); but the forms of the orbitals in Table 11 give us no grounds for assigning the same σ order to the C—H bonds as to the C—C bond, or for taking either of the two σ bond orders to be unity. As we saw at the end of section VII.E, σ bonding is more difficult to describe in quantitative wave-mechanical terms than π bonding, and it is fortunate that we shall be concerned primarily with π bonding in the remaining sections of this chapter.

B. Bond Orbitals

Although it is certainly an oversimplification, the classical concept of a chemical bond as a distribution of electronic charge associated exclusively with two adjacent atoms is still of considerable value for some purposes. The four-centre σ orbitals in the acetylene sub-configuration $2\sigma_g^2 2\sigma_u^2 3\sigma_g^2$ obviously violate this concept, so we now describe an alternative formulation of the σ bonding, which, although it involves a deliberate sacrifice of accuracy, is often very useful.

In the alternative formulation we replace the molecular orbitals by bond orbitals. A bond orbital is a *two*-centre orbital constructed from the atomic orbitals of a pair of adjacent atoms; thus, for example, a bond orbital formed by linear combination of orbitals of H_a and C_b will not have any contribution from the orbitals of C_c or H_d.

The π molecular orbitals are unchanged, and the 1σ molecular orbitals virtually unchanged, by the transformation from molecular orbitals to bond orbitals. These unchanged orbitals account for eight of the fourteen spin-orbitals required for the ground-state wave function, so we require three new bond orbitals to provide the remaining six spin-orbitals. In classical terms, we also require three σ bonds apart from the two π bonds. So the new bond orbitals must be the 'bonding' (*i.e.* lowest-energy) linear combinations of the axially symmetric orbitals of each of the three pairs of atoms C_b and

C_c, C_b and H_a, C_c and H_d. If we use the symbols $\sigma(C_bC_c)$, $\sigma(C_bH_a)$, $\sigma(C_cH_d)$ to represent these bond orbitals, the new molecular wave function is obtained by replacing the molecular-orbital sub-configuration $2\sigma_g^2 2\sigma_u^2 3\sigma_g^2$ (see Table 11) by the bond-orbital sub-configuration

$$\sigma(C_bC_c)^2\sigma(C_bH_a)^2\sigma(C_cH_d)^2$$

and antisymmetrizing the resulting product of fourteen factors in the usual way.

Although less accurate than the molecular-orbital wave function, this bond-orbital wave function has the advantage of providing some justification for the electron-counting process which results in the C—C bond being described as triple, and the C—H bond as single. This is because, apart from the lowest-energy σ orbitals (which are essentially non-bonding $1s_C$ atomic orbitals), the ground-state configuration comprises five bond orbitals (or ten bond spin-orbitals), all 'bonding' in character.

If we ignore the negligible contribution from $1s_C$, the new bond orbitals may be written as follows:

$$\sigma(C_bC_c) = \{\alpha(2s_b) + \beta(2p_{zb})\} + \{\alpha(2s_c) + \beta(2p_{zc})\}; \tag{167}$$

$$\sigma(C_bH_a) = \{\kappa(2s_b) - \lambda(2p_{zb})\} + \xi(1s_a); \tag{168}$$

$$\sigma(C_cH_d) = \{\kappa(2s_c) - \lambda(2p_{zc})\} + \xi(1s_d). \tag{169}$$

The subscripts b and c denote carbon orbitals, and the subscripts a and d hydrogen orbitals. The Greek letters represent positive coefficients. The variation process by which the optimum values of the coefficients in the bond orbitals are obtained is less flexible than that based on four-centre molecular orbitals, and it thus gives poorer results*.

In equations (167)–(169) it will be noted that whereas the carbon $2p_z$ orbitals ($2p_{zb}$, $2p_{zc}$) have positive coefficients in the C—C bond orbitals, they have negative coefficients in the C—H bond orbitals. The negative coefficients have no 'antibonding' significance, being determined simply by the way in which the z axes are directed. The positive lobe of the $2p_z$ orbital of each carbon atom points toward the other carbon atom, so the negative lobe necessarily points toward the adjacent hydrogen atom. If the coefficients of adjacent $2p_{zC}$ and $1s_H$ orbitals were not of opposite sign, the C—H bond orbital would

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* Unfortunately there are no published bond-orbital calculations suitable for direct comparison with the results quoted in Table 11.

thus have a nodal surface between the carbon and the hydrogen nuclei (indicating a lack of 'bonding' character).

C. Hybridization

Although unnecessary, it is sometimes convenient to formulate bond orbitals as two-term functions in which each term is a linear combination of all the orbitals contributed by one of the two atoms. Written in this way, the bond orbitals (167)–(169) become

$$\sigma(\mathrm{C_bC_c}) = \alpha h_{1\mathrm{b}} + \alpha h_{1\mathrm{c}}, \qquad (170)$$

$$\sigma(\mathrm{C_bH_a}) = \kappa h_{2\mathrm{b}} + \xi(1s_{\mathrm{a}}), \qquad (171)$$

$$\sigma(\mathrm{C_cH_d}) = \kappa h_{2\mathrm{c}} + \xi(1s_{\mathrm{d}}), \qquad (172)$$

where

$$h_1 = 2s + \frac{\beta}{\alpha}(2p_z), \qquad (173)$$

$$h_2 = 2s - \frac{\lambda}{\kappa}(2p_z). \qquad (174)$$

The functions h_1 and h_2, each a linear combination of $2s_{\mathrm{C}}$ and $2p_{z\mathrm{C}}$, are known as digonal hybrid orbitals. The word hybrid serves as a reminder that no linear combination of $2s_{\mathrm{C}}$ and $2p_{z\mathrm{C}}$ is possible in a free carbon atom. The symmetry axes of the two hybrid orbitals are collinear, and this is indicated by describing the hybrids as digonal.

As long as the coefficients β/α and λ/κ in (173) and (174) are treated as independent variational parameters, the same total energy and the same orbital energies are bound to be obtained when the forms (170)–(172) are used in the molecular wave function as when the forms (167)–(169) are used. Frequently, however, the condition that h_1 and h_2 shall be orthogonal is imposed. This reduces the flexibility of the variation process unnecessarily by requiring that $\beta/\alpha = \kappa/\lambda$:

$$\begin{aligned}\int h_1 h_2 \mathrm{d}\tau &= \int [(2s) + \frac{\beta}{\alpha}(2p_z)][(2s) - \frac{\lambda}{\kappa}(2p_z)]\,\mathrm{d}\tau \\ &= \int (2s)^2 \mathrm{d}\tau - \frac{\beta\lambda}{\alpha\kappa}\int (2p_z)^2 \mathrm{d}\tau + \left(\frac{\beta}{\alpha} - \frac{\lambda}{\kappa}\right)\int (2s)(2p_z)\mathrm{d}\tau \\ &= 1 - \frac{\beta\lambda}{\alpha\kappa} + 0.\end{aligned}$$

Although in a many-electron system only the total electronic charge distribution is of physical significance, it is occasionally useful to be able to visualize—however roughly—the charge distribution

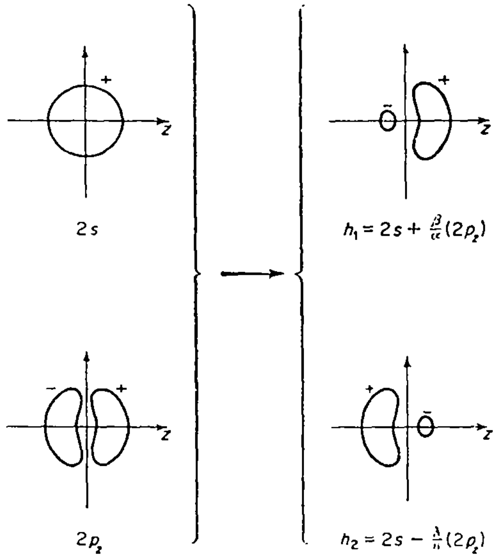

FIGURE 13. Digonal hybrid orbitals in acetylene.

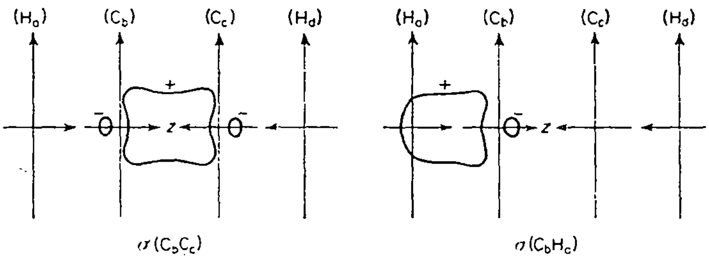

FIGURE 14. Bond orbitals in acetylene.

corresponding to a component one-electron wave function. So we have sketched contour diagrams for the digonal hybrids (173) and (174) and their parent orbitals in Figure 13, and for the bond orbitals (170) and (171) in Figure 14*.

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* It must be remembered that contour diagrams are not superposable. Only in exceptional cases do contour lines for a many-electron system look anything like a superposition of the contour lines for the individual orbitals.

D. Ethylene

Wave functions for ethylene exactly analogous to those given in Table 11 for acetylene are not available at the time of writing, so in this section we merely draw attention to some of the wave-mechanical principles involved in the formulation of molecular-orbital and bond-orbital ground-state wave functions. We reserve a semi-quantitative discussion of the π-electron system for section X.

The ethylene molecule is well known to be planar, with bond angles (like those in aromatic molecules) of about 120°. As in Figure 15, we refer the angularly dependent carbon orbitals to the usual Cartesian axes, taking the molecular plane to be the yz plane, and the central internuclear axis to be the z axis.

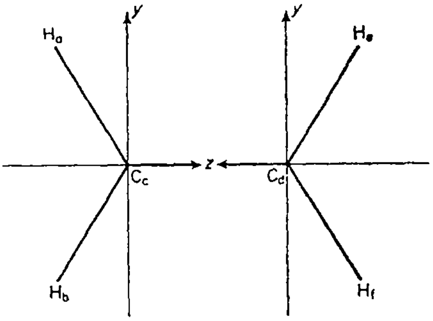

FIGURE 15. Cartesian axes for ethylene.

As in the case of the acetylene molecule, we use the same arbitrary atomic-orbital basis for the molecular-orbital wave function as for the bond-orbital wave function. This comprises five orbitals from each carbon atom ($1s$, $2s$, $2p_z$, $2p_x$, $2p_y$), and one orbital from each hydrogen atom ($1s$). From this basis we can construct fourteen linearly independent molecular orbitals, of which eight are required for the sixteen-electron single-configuration ground-state wave function.

The ethylene molecule has a number of elements of symmetry, so we can classify the molecular orbitals in various ways. For our purposes it will be sufficient to consider whether the orbitals are symmetric ($\mathscr{s}$) or antisymmetric ($\mathscr{a}$) to reflexion in the molecular plane.

The $2p_{xC}$ orbitals are the only atomic orbitals which are antisymmetric in this sense, so they give rise to a quite distinct pair of antisymmetric molecular orbitals, which, in non-normalized form, may be written

$$1a = 2p_{xc} + 2p_{xd}, \tag{175}$$

$$2a = 2p_{xc} - 2p_{xd}. \tag{176}$$

In a bond-orbital wave function, in which the component orbitals are classified according to their symmetry with respect to an individual bond axis (and not with respect to the whole molecule), the orbitals $1a$ and $2a$ could be described strictly as π orbitals, and, by an extension of usage which is now universal, they are also so described even when they occur in a molecular-orbital wave function ($1a = 1\pi$; $2a = 2\pi$).

The twelve remaining atomic orbitals are all symmetric to reflexion in the molecular plane, so they give twelve s molecular orbitals. Two of these (those of lowest energy) are the now very familiar non-bonding combinations which in non-normalized form are essentially

$$1s = 1s_{\mathrm{c}} + 1s_{\mathrm{d}}, \tag{177}$$

$$2s = 1s_{\mathrm{c}} - 1s_{\mathrm{d}}. \tag{178}$$

In the acetylene molecule (Table 11) the highest-energy molecular orbitals to be utilized in the ground-state wave function are the degenerate π orbitals $1\pi_{xu}$ and $1\pi_{yu}$. For the ethylene molecule the corresponding molecular orbital is (175), so we may write the ground-state configuration as

$$1s^2 2s^2 3s^2 4s^2 5s^2 6s^2 7s^2 1a^2,$$

where

$$1s^2 2s^2 \sim 1s_{\mathrm{c}}^2 1s_{\mathrm{d}}^2 \quad \text{and} \quad 1a^2 = 1\pi^2.$$

When we change from a molecular-orbital to a bond-orbital description, we consider only one pair of atoms at a time, so we can revert to our earlier σ–π classification of orbitals. We have already seen that the π bond orbitals are identical with the π (or a) molecular orbitals, and the lowest-energy σ bond orbitals (built up almost exclusively from $1s_{\mathrm{C}}$) are very nearly identical with the molecular orbitals $1s^2 2s^2$. The bonding π orbital and the two non-bonding σ orbitals provide six spin-orbitals, so five new σ bond orbitals are required to provide the remaining ten spin-orbitals. These will consist of a C—C bond orbital and four degenerate* C—H bond

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[*] The C—H bond orbitals are degenerate because of the symmetry of the molecule. Degeneracy is almost always associated with symmetry.

orbitals, each orbital being the lowest-energy linear combination available from the orbitals ($1s_C$ excluded) of the respective atoms.

On the bond-orbital basis we can describe the C—H bonds as single σ bonds, and the C—C 'double' bond as a superposition of a σ bond and a π bond.

The σ C—C bond orbital in ethylene is of the same form as the corresponding orbital in acetylene [*cf.* (167)], although of course the coefficients α and β are slightly different:

$$\sigma(C_cC_d) = \{\alpha(2s_c) + \beta(2p_{zc})\} + \{\alpha(2s_d) + \beta(2p_{zd})\}. \tag{179}$$

In formulating the C—H bond orbitals, however, we meet a new feature. In acetylene $1s_H$ combines with $2p_{zC}$ but not with $2p_{xC}$ or $2p_{yC}$; this is because the symmetry axis of $2p_{zC}$ is collinear with the C—H bond axis, whereas the symmetry axes of $2p_{xC}$ and $2p_{yC}$ are at right angles to the bond axis. In ethylene the $2p_{xC}$ symmetry axis makes an angle of 90° with the bond axis, but the $2p_{yC}$ and $2p_{zC}$ symmetry axes make angles of approximately 30° or 60°. If we regard the atomic orbitals as vectors, we can say that $2p_{yC}$ and $2p_{zC}$ both have non-zero components in the C—H direction. It follows that

$$\int(1s_H)\mathscr{H}(2p_{yC})d\tau \neq 0 \quad \text{and} \quad \int(1s_H)\mathscr{H}(2p_{zC})d\tau \neq 0,$$

so $1s_H$ can enter into linear combinations with $2p_{yC}$ and $2p_{zC}$.

Using Greek letters as before (section VIII.B) to represent positive coefficients, we can write the C—H bond orbitals as follows:

$$\sigma(C_cH_a) = \{\kappa(2s_c) - \lambda(2p_{zc}) + \mu(2p_{yc})\} + \xi(1s_a); \tag{180}$$

$$\sigma(C_cH_b) = \{\kappa(2s_c) - \lambda(2p_{zc}) - \mu(2p_{yc})\} + \xi(1s_b). \tag{181}$$

There are analogous expressions, of course, for $\sigma(C_dH_e)$ and $\sigma(C_dH_f)$. The orbitals (180) and (181) have coefficients with the same absolute values because the xz plane is a molecular symmetry plane.

The bond orbitals (179)–(181) are all symmetric about their respective bond axes, and are very similar in 'shape' to the corresponding bond orbitals in acetylene (Figure 14).

The coefficients κ, λ, μ, and ξ in the C—H bond orbitals are determined, like all the other atomic-orbital coefficients in the complete molecular wave function, by minimizing the total molecular energy. With a slight sacrifice of flexibility we can, however, determine the ratio λ/μ by purely geometrical means. If we assume that the radial factors of $2p_{zC}$ and $2p_{yC}$ are identical in the ethylene molecule (as they must be in a free carbon atom), we can treat the two orbitals as if they were vectors of equal length, and resolve them in directions parallel (‖) and perpendicular (⊥) to, say, the C_c—H_a bond axis. If, for trigonometrical simplicity, we take the bond angles to be exactly 120°, we may then write

$$2p_{zc} = (-\cos 60°)2p_{\parallel c} + (\cos 30°)2p_{\perp c}, \tag{182}$$

$$2p_{yc} = (\cos 30°)2p_{\parallel c} + (\cos 60°)2p_{\perp c}, \tag{183}$$

where $2p_{\parallel c}$ and $2p_{\perp c}$ are orthogonal $2p$ orbitals. Because of the usual symmetry restriction (section VII.B), $1s_a$ cannot combine with $2p_{\perp c}$, so the coefficient of $2p_{\perp c}$ in the function obtained by substituting (182) and (183) in (180) must be zero. This is the case if

$$\frac{\lambda}{\mu} = \frac{\cos 60°}{\cos 30°} = \frac{1}{\sqrt{3}}.$$

Like the corresponding bond orbitals in acetylene (section VIII.C), the bond orbitals (179)–(181) are often written in the abbreviated form

$$\sigma(C_cC_d) = \alpha h_{1c} + \alpha h_{1d},$$
$$\sigma(C_cH_a) = \kappa h_{2c} + \xi(1s_a),$$
$$\sigma(C_cH_b) = \kappa h_{3c} + \xi(1s_b),$$

where

$$h_1 = 2s + \frac{\beta}{\alpha}(2p_z),$$

$$h_2 = 2s - \frac{\lambda}{\kappa}(2p_z) + \frac{\mu}{\kappa}(2p_y),$$

$$h_3 = 2s - \frac{\lambda}{\kappa}(2p_z) - \frac{\mu}{\kappa}(2p_y).$$

The functions h_1, h_2, and h_3 are known as trigonal hybrid orbitals. Contour diagrams for a set of trigonal hybrids are given in Figure 16.

E. Bent-bond Orbitals

The classification of the C—C bond orbitals in ethylene as two σ spin-orbitals and two π spin-orbitals is by far the most convenient classification for almost all purposes, and the only one which we shall need to consider later in this chapter. By introducing a further approximation, however, we can obtain an infinite number of distinct but equivalent representations of the bonding. We shall examine one of these, partly because it introduces a type of transformation we have not yet described, partly because it illustrates the danger of attaching too much significance to the 'shapes' of individual orbitals in a many-electron wave function, and partly because it provides an interesting link with the pre-wave-mechanical 'bent-bond' description of multiple bonds.

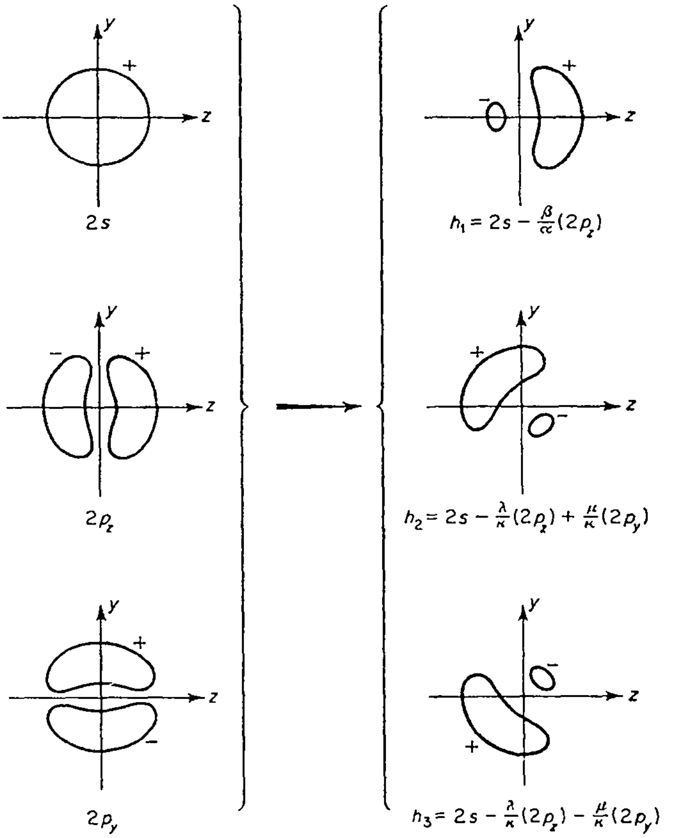

FIGURE 16. Trigonal hybrid orbitals in ethylene.

The sixteen-electron antisymmetrized ground-state wave function for ethylene can be written as a 16 × 16 determinant. The approximation we require to obtain the bent-bond representation of the C—C bonding involves neglecting a considerable number of small terms in the determinantal wave function. We replace the 16 × 16 determinant by a product of a 12 × 12 determinant and a 4 × 4 determinant, the latter being constructed from the four C—C spin-orbitals derived from the π orbital and the σ orbital (179). In other words, we suppose that the four C—C spin-orbitals can be antisymmetrized independently of the other twelve spin-orbitals.

If we use the symbols σ and π for the C—C bond orbitals, the sub-configuration $\sigma^2\pi^2$ gives on antisymmetrization the following determinant (section V.C), multiplied by a suitable normalizing factor:

$$\begin{vmatrix} \sigma\alpha(1) & \sigma\alpha(2) & \sigma\alpha(3) & \sigma\alpha(4) \\ \sigma\beta(1) & \sigma\beta(2) & \sigma\beta(3) & \sigma\beta(4) \\ \pi\alpha(1) & \pi\alpha(2) & \pi\alpha(3) & \pi\alpha(4) \\ \pi\beta(1) & \pi\beta(2) & \pi\beta(3) & \pi\beta(4) \end{vmatrix} = \det\{\sigma\alpha(1) \quad \sigma\beta(2) \quad \pi\alpha(3) \quad \pi\beta(4)\}. \tag{184}$$

Except in appearance, a determinant is unchanged if the elements of one row (or column), all multiplied by the same numerical factor, are added to the corresponding elements of another row (or column). We can thus form an infinite number of determinants, all identical with (184), merely by forming linear combinations of the bond orbitals σ and π. One such determinant is (185).

$$\frac{1}{4}\begin{vmatrix} (\sigma + \pi)\alpha(1) & (\sigma + \pi)\alpha(2) & (\sigma + \pi)\alpha(3) & (\sigma + \pi)\alpha(4) \\ (\sigma + \pi)\beta(1) & (\sigma + \pi)\beta(2) & (\sigma + \pi)\beta(3) & (\sigma + \pi)\beta(4) \\ (\sigma - \pi)\alpha(1) & (\sigma - \pi)\alpha(2) & (\sigma - \pi)\alpha(3) & (\sigma - \pi)\alpha(4) \\ (\sigma - \pi)\beta(1) & (\sigma - \pi)\beta(2) & (\sigma - \pi)\beta(3) & (\sigma - \pi)\beta(4) \end{vmatrix} \tag{185}$$

The determinantal wave functions (184) and (185) may be shown to be identical by the following additions and subtractions of rows:

$$\begin{aligned} &\tfrac{1}{4}\det\{[(\sigma + \pi)\alpha(1)][(\sigma + \pi)\beta(2)][(\sigma - \pi)\alpha(3)][(\sigma - \pi)\beta(4)]\} \\ &\quad = \tfrac{1}{4}\det\{[2\sigma\alpha(1)][(2\sigma\beta(2)][(\sigma - \pi)\alpha(3)][(\sigma - \pi)\beta(4)]\} && (186) \\ &\quad = \tfrac{1}{4}\det\{[2\sigma\alpha(1)][2\sigma\beta(2)][-\pi\alpha(3)][-\pi\beta(4)]\} && (187) \\ &\quad = \det\{\sigma\alpha(1) \quad \sigma\beta(2) \quad \pi\alpha(3) \quad \pi\beta(4)\}. \end{aligned}$$

In (186) the third row of (185) has been added to the first row, and the fourth row to the second row. In (187), which is the same as (184), half the first row of (186) has been subtracted from the third row, and half the second row from the fourth row.

The determinant (185) is built up from the normalized bent-bond orbitals

$$2^{-1/2}(\sigma + \pi) \quad \text{and} \quad 2^{-1/2}(\sigma - \pi), \tag{188}$$

and corresponds to the sub-configuration $[2^{-1/2}(\sigma + \pi)]^2[2^{-1/2}(\sigma - \pi)]^2$. Contour diagrams for the orbitals (188) are given in Figure 17 for comparison with those of the original σ and π orbitals. Contours are drawn both in the *xz* plane and in the *xy* plane through one of the carbon nuclei. The origin of the name 'bent bond' is obvious from the *xz* contours.

It is important to note that when all four spin-orbitals are taken together the right half of Figure 17 represents the same distribution of electronic charge as the left half. This shows again how very misleading the 'shape' of a one-electron charge distribution can be in a many-electron system.

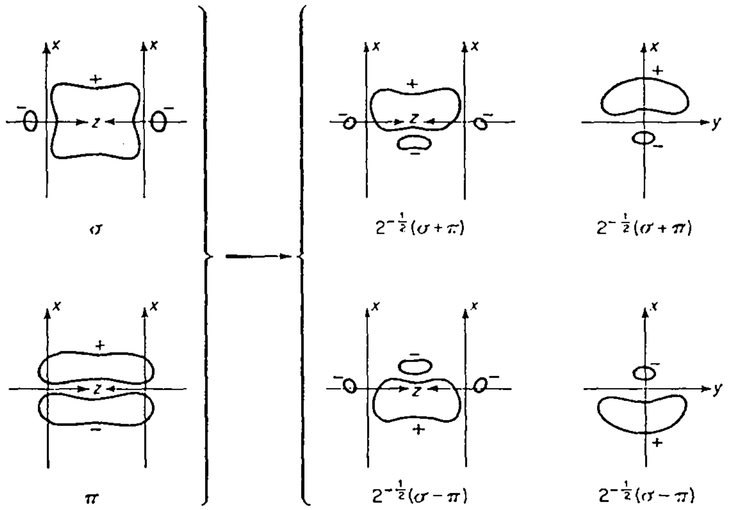

FIGURE 17. Bent-bond orbitals in ethylene. The coordinate axes are chosen as in Figure 16.

The right halves of Figures 13 and 17 should be compared. Seen end-on, the bent-bond orbitals in ethylene look similar to digonal atomic-orbital hybrids.

The C—C bond orbitals in acetylene can be transformed in much the same way as those of ethylene[18]. A suitable choice of coefficients gives three equivalent bent-bond orbitals. In a plane normal to the internuclear axis these have contours reminiscent of those of trigonal atomic-orbital hybrids (*cf.* Figure 16). The three bent-bond orbitals are transformed into each other by rotations of 120° about the internuclear axis.

Whether they are σ and π bond orbitals or bent-bond orbitals, the six C—C spin-orbitals in acetylene correspond in all to an axially symmetrical distribution of electronic charge.

F. Methane

Because of its high symmetry, which considerably reduces the number of independent parameters to be evaluated in a variational calculation, the methane molecule has been the subject of far more sophisticated quantum-mechanical calculations than the two organic molecules we have already considered. Here, however, we shall need to examine only the forms of the LCAO bond orbitals.

The four bonds in methane are entirely equivalent, and we may define the bond angles by saying that the bonds are directed from the centre to the corners of a regular tetrahedron, or (to use a more familiar geometrical figure) from the centre to the alternate corners of a cube (Figure 18).

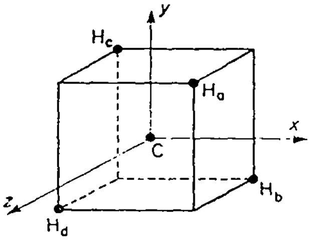

FIGURE 18. Cartesian axes for methane.

We build up the ten-electron molecular wave function from the usual five carbon orbitals and the $1s$ orbitals of the four hydrogen atoms. The $1s_C$ orbital provides two non-bonding spin-orbitals, leaving eight spin-orbitals to be accounted for by the four C—H bond orbitals. Because of the symmetry of the molecule (*i.e.* because of the equivalence of the four C—H bonds), the C—H bond orbitals are degenerate.

The $1s_H$ and the $2s_C$ orbitals are symmetric about the C—H bond axes, but the $2p_C$ orbitals have symmetry axes which are neither collinear with the bond axes nor orthogonal (perpendicular) to them. This means that each of the bond orbitals will be a linear combination of $1s_H$, $2s_C$, and all three $2p_C$ orbitals*.

Though the five coefficients in each bond orbital can be determined by minimizing the total molecular energy, only three need be so determined. As in the case of ethylene (section VIII.D), but now

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* The orientation of the Cartesian axes in Figure 18 is arbitrary. We could simplify the form of *one* of the bond orbitals by taking one of the Cartesian axes to be collinear with one of the C—H bond axes, but this would merely obscure the equivalence of the four bonds.

without any approximation*, the ratios in which the $2p_C$ orbitals combine amongst themselves in the methane molecule can be determined from the molecular geometry without recourse to the variation principle.

There are various methods of utilizing the molecular geometry for this purpose. For the sake of variety we shall describe one which differs slightly in principle from that which we used for ethylene.

The three $2p_C$ orbitals are degenerate, so, as we showed in section II.H, any linear combination of them must satisfy the Schrödinger energy equation for a free carbon atom. If the combination coefficients are all the same in absolute magnitude, differing only in sign, any normalized combination of $2p_C$ orbitals differs only in orientation from the individual $2p_C$ orbitals. Thus the combination $2^{-\frac{1}{2}}(2p_{xC} + 2p_{yC})$ is exactly the same in 'shape' as $2p_{xC}$ or $2p_{yC}$, but its symmetry axis bisects the angle between the x and the y axes. Likewise, in the notation of Figure 18, the symmetry axis of the combination $3^{-\frac{1}{2}}(2p_{xC} + 2p_{yC} + 2p_{zC})$ is collinear with the C—H$_a$ bond axis. The degeneracy of the $2p_C$ orbitals clearly enables us to form linear combinations with σ symmetry about the four bond axes in methane. The normalized linear combinations, with coefficients whose signs are obvious from Figure 18, are listed below, together with the bond axes about which they are symmetrical:

$$\begin{array}{ll} \text{C—H}_a & 3^{-\frac{1}{2}}(2p_{xC} + 2p_{yC} + 2p_{zC}); \\ \text{C—H}_b & 3^{-\frac{1}{2}}(2p_{xC} - 2p_{yC} - 2p_{zC}); \\ \text{C—H}_c & 3^{-\frac{1}{2}}(-2p_{xC} + 2p_{yC} - 2p_{zC}); \\ \text{C—H}_d & 3^{-\frac{1}{2}}(-2p_{xC} - 2p_{yC} + 2p_{zC}). \end{array} \tag{189}$$

The four lowest-energy bond orbitals in methane are then as follows†:

$$\begin{aligned} \sigma(\text{CH}_a) &= \{\kappa(2s_C) + \lambda(2p_{xC} + 2p_{yC} + 2p_{zC})\} + \xi(1s_a); \\ \sigma(\text{CH}_b) &= \{\kappa(2s_C) + \lambda(2p_{xC} - 2p_{yC} - 2p_{zC})\} + \xi(1s_b); \\ \sigma(\text{CH}_c) &= \{\kappa(2s_C) + \lambda(-2p_{xC} + 2p_{yC} - 2p_{zC})\} + \xi(1s_c); \\ \sigma(\text{CH}_d) &= \{\kappa(2s_C) + \lambda(-2p_{xC} - 2p_{yC} + 2p_{zC})\} + \xi(1s_d). \end{aligned} \tag{190}$$

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* Because of the high symmetry the radial factors of the three $2p_C$ orbitals are necessarily identical in the molecular wave function. This is not the case in the less symmetrical ethylene molecule.

† It might seem, because of the tetrahedral orientation of the combinations (189), that each $1s_H$ orbital would combine with all four of these $2p_C$ combinations, and not just the combination having σ symmetry about the corresponding bond axis. This is true, but the bond orbitals would not be altered, for the $2p_C$ combinations (189) are not linearly independent (section II.H), each one being minus the sum of the other three.

The variation problem is reduced to determining the optimum values of κ, λ, and ξ. The normalizing factor $3^{-\frac{1}{2}}$ in (189) is absorbed into the variational parameter λ in (190).

The bond orbitals (190) may of course be formulated in terms of hybridized carbon orbitals h_1, h_2, h_3, h_4, where

$$\begin{aligned}
h_1 &= 2s + \frac{\lambda}{\kappa}(2p_{x\mathrm{C}} + 2p_{y\mathrm{C}} + 2p_{z\mathrm{C}});\\
h_2 &= 2s + \frac{\lambda}{\kappa}(2p_{x\mathrm{C}} - 2p_{y\mathrm{C}} - 2p_{z\mathrm{C}});\\
h_3 &= 2s + \frac{\lambda}{\kappa}(-2p_{x\mathrm{C}} + 2p_{y\mathrm{C}} - 2p_{z\mathrm{C}});\\
h_4 &= 2s + \frac{\lambda}{\kappa}(-2p_{x\mathrm{C}} - 2p_{y\mathrm{C}} + 2p_{z\mathrm{C}}).
\end{aligned} \tag{191}$$

The hybrids are described as tetrahedral*.

G. Atomic Orbitals in Molecular Wave Functions

The final topic which we discuss in this section is one which, oddly enough, has very little relevance to the wave functions we have been considering, but one which we cannot omit without the risk of causing confusion.

The quasi-wave-mechanical approach to the teaching of organic chemistry has become so popular in recent years that there will be few readers of this book who have not encountered the statement, made without qualification, that wave functions for organic molecules are derived from an excited-state configuration of the carbon atom, $1s^2 2s 2p^3$, rather than the ground-state configuration, $1s^2 2s^2 2p^2$. The statement is true for *valence-bond* wave functions of the simplest possible type (*i.e.* those based on a *single* electronic configuration of each atom), but for LCAO molecular-orbital or bond-orbital functions it lacks precise meaning. To appreciate this point it is sufficient to consider even so simple a wave function as the molecular-orbital wave function for the hydrogen molecule (section IV.C), with or without configuration interaction (section IV.D). If, omitting the

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* Hybrid orbitals having the relative orientations we have described as digonal, trigonal, and tetrahedral are sometimes represented by the symbols *di*, *tr*, and *te*; *e.g.* the hybrids h_1, h_2, h_3, h_4 in (191) might be written te_1, te_2, te_3, te_4. We have avoided these two-letter symbols because they are generally understood to refer to hybrid orbitals in which the balance between $2s$ and $2p$ contributions is determined by arbitrary non-variational procedures.

normalizing factor, we write this function as

$$\{1s_a(1)1s_b(2) + 1s_b(1)1s_a(2)\} + \lambda\{1s_a(1)1s_a(2) + 1s_b(1)1s_b(2)\},$$

it is apparent that it embodies not only the $1s$ configuration of H, but also the $1s^2$ configuration of H^-. An LCAO molecular-orbital wave function may always be expanded as a linear combination of valence-bond wave functions, and the terms in the expansion represent in general several different electronic configurations of each of the constituent atoms. The concept of a unique atomic configuration within a molecular wave function is thus unrealistically oversimplified.

At first sight there certainly does seem to be a configurational distinction between the use of the $2p_x$, $2p_y$, and $2p_z$ orbitals of fluorine in our LCAO wave functions for F_2 and HF and the use of the same set of carbon $2p$ orbitals in wave functions for organic molecules. Whereas all three $2p_F$ orbitals are used in the ground-state wave function for the fluorine atom, only two of the three $2p_C$ orbitals appear to be used in the ground-state wave function for the carbon atom—if we take the lowest-energy configuration of the carbon atom to be *either* $1s^22s^22p_x2p_y$ *or* $1s^22s^22p_x2p_z$ *or* $1s^22s^22p_y2p_z$. But of course any linear combination of these degenerate configurations is equally acceptable in an isolated atom, so the apparent difficulty is easily resolved.

There remains the question of the relative 'weights' of $2s_C$ and $2p_C$ orbitals in wave functions for organic molecules; but this is a question that really ought not to be asked, for, as we have shown repeatedly, the distinction which exists between $2s$ and $2p$ orbitals in a free atom vanishes when the same orbitals are used in molecular linear combinations*. In a free carbon atom in its ground state we can say that, on average, two electrons 'occupy' $1s$ orbitals, two 'occupy' $2s$ orbitals, and two 'occupy' $2p$ orbitals; but we can make no corresponding statement for *atomic* orbitals in an LCAO wave function. We know that the variation principle gives the optimum $2s$:$2p$ ratio, but we cannot say what the ratio is†.

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* For this reason we have avoided using the customary symbols sp, sp^2, and sp^3 in describing digonal, trigonal, and tetrahedral hybrid orbitals. They are quite appropriate to the simple valence-bond functions for which they were originally intended, but they have a configurational implication which is out of place in LCAO wave functions.

† We can calculate the coefficients of the arbitrarily formulated $2s$ and $2p$ atomic orbitals in each individual molecular orbital; but assessing the contribution of $2s$ and $2p$ atomic orbitals to the molecular wave function *as a whole* is a very different problem. The difficulties involved in analysing atomic-orbital 'populations' in molecular wave functions have been discussed by Mulliken[19].

IX. THE π-ELECTRON HYPOTHESIS

A. π-*Electron Energy*

For the past thirty years research work in organic quantum chemistry has been concerned predominantly with the energetics of multiply bonded molecules, especially conjugated molecules. It is a very curious feature of most of this work that, although it has been remarkably successful in providing a semiquantitative interpretation of a wealth of experimental data, it is based on an assumption that is often no more than a convenient fiction. This is the assumption that the 'π' electrons (*i.e.* 'π' orbitals*) in a multiply bonded molecule can be treated independently of the 'σ' electrons, or, more explicitly, that the electronic energy of a multiply bonded molecule includes a quantity which we can call the π-electron energy, and that there exist chemical changes and spectral transitions in which this π-electron energy is altered while the rest of the electronic energy remains constant. The assumption carries with it the implication that although π-electron energy is not an observable quantity, changes in π-electron energy admit of direct experimental measurement. We shall see, however, that π-electron energy is a purely theoretical quantity which can be defined only for certain types of approximate wave function (notably those constructed from products of orbitals).

We begin our examination of the π-electron hypothesis by considering an N-electron multiply bonded molecule in a state which can be represented by a wave function Ψ consisting of a single† determinant built up from M orthonormal π spin-orbitals ($U_1, U_2, \ldots, U_M$) and N–M orthonormal σ spin-orbitals ($U_{M+1}, U_{M+2}, \ldots, U_N$):

$$\Psi = (N!)^{-\frac{1}{2}} \det \{U_1 U_2 \ldots U_M U_{M+1} U_{M+2} \ldots U_N\}. \tag{192}$$

The spin-orbitals U may be derived from either bond orbitals or molecular orbitals. The energy corresponding to the wave function (192) is $E = \int \Psi \mathbf{H} \Psi \mathrm{d}\tau$, where $\mathbf{H}$ is the complete Hamiltonian operator. When the determinant is expanded and the orthonormality relations

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* For the remainder of this chapter we shall use the symmetry labels 'σ' and 'π' (without the cautionary quotation marks), for both molecular orbitals and bond orbitals, in the loose sense mentioned in section VII.B.

† A linear combination of determinants is required for certain spin states (section V.D), and in cases where configuration interaction is taken into account. This complication does not affect the general argument given in this section.

used as described in section VII.A, the resulting energy expression has the form indicated in Table 12*.

TABLE 12. Composition of electronic energy in a σ–π system (Single-determinant orbital wave function).

	Number of integrals[a] containing		
	π orbitals only (*a*)	σ orbitals only (*b*)	σ and π orbitals (*c*)
(1) Kinetic energy	M	$N - M$	0
(2) Nuclear-attraction energy	M	$N - M$	0
(3) Coulomb energy	$\frac{1}{2}M(M - 1)$	$\frac{1}{2}(N - M)(N - M - 1)$	$M(N - M)$
(4) Exchange energy[b]	$\leqslant \frac{1}{2}M(M - 1)$	$\leqslant \frac{1}{2}(N - M)(N - M - 1)$	$\leqslant M(N - M)$

[a] If the molecular wave function is normalized and the spatial orbitals are orthonormal, the integrals (1), (2), and (3) all have the coefficient +1, whereas the integrals (4) have the coefficient −1.

[b] Unless all the spin orbitals concerned have the same spin factor (which is possible only if there are N distinct spatial factors), there are fewer exchange integrals than Coulomb integrals.

The π-electron energy, E_π, associated with the wave function (192) is obtained by extracting from E all the integrals in which a π orbital appears†; these are the integrals in columns (*a*) and (*c*) of Table 12. It is very important to note that E_π is a mathematical quantity associated with an approximate wave function, and not a physical quantity associated with the molecule itself. The concept of π-electron energy is entirely dependent upon the use of a molecular wave function which contains no σ–π interelectronic coordinates (being based, in the present case, on products of *one*-electron functions only); such a wave function is necessarily approximate. The concept of π-electron energy is often exceedingly useful, but it can never be precise.

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* For the sake of readers who may care to verify the information given, we have listed the numbers of integrals of each type in Table 12; but only the nature of the integrals is important at this stage.

† E_σ may be defined correspondingly. Clearly $E_\sigma + E_\pi \neq E$, for both E_σ and E_π include the σ–π integrals listed in column (*c*) of Table 12.

B. π-Electron Wave Functions

Even for the smallest alkene or alkyne molecule, a wave function of the type (192) is so unwieldy that there would be little point in dealing with π-electron energy instead of total electronic energy if the wave function could not itself be simplified. This is, however, possible: in calculations in which the total electronic energy is not required, the complete wave function (192) may be replaced by an artificial π-electron wave function

$$\Psi_\pi = (M!)^{-\frac{1}{2}} \det \{U_1 U_2 \cdots U_M\}, \tag{193}$$

provided that the complete Hamiltonian operator is correspondingly replaced by an *ad hoc* π-electron Hamiltonian operator $\mathbf{H}_\pi$ defined expressly so that

$$E_\pi = \int \Psi_\pi \mathbf{H}_\pi \Psi_\pi \mathrm{d}\tau; \tag{194}$$

i.e. so that the right-hand side of (194) generates the integrals listed in columns (*a*) and (*c*) of Table 12. For ethylene Ψ_π is a two-electron wave function exactly analogous to the molecular-orbital wave function for hydrogen (sections IV.C and D); for acetylene Ψ_π is a four-electron wave function. We shall not require the explicit form of $\mathbf{H}_\pi$ (which is very seldom used*): it is sufficient to note that $\mathbf{H}_\pi$ provides for the kinetic energy of the π electrons, the energy of attraction of the nuclei for the π electrons, the Coulomb and exchange π–π repulsion energy, and the Coulomb and exchange σ–π repulsion energy.

Having introduced π-electron wave functions, we must investigate the uses to which they can be put; *i.e.* we must enquire in what circumstances it may be supposed that a π sub-configuration changes while the associated σ sub-configuration remains unaltered. This enquiry will occupy most of the remainder of this chapter, but, before we embark on it, we must explain the term 'empirical', which is frequently applied to calculations on π-electron systems. A calculation is described as non-empirical if the energy integrals are all evaluated mathematically ('*ab initio*'), and as empirical or semi-empirical if all or some of the integrals are evaluated by reference to experimental data (usually transition energies or changes in enthalpy). The calculations we have described up to now have been exclusively

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* In almost all calculations carried out up to now the LCAO σ molecular orbitals or bond orbitals which contribute to the potential field in which the π electrons move have been replaced by the simple atomic orbitals from which they are constructed[20].

non-empirical (*i.e.* based on strict wave-mechanical principles), whereas those we shall describe in sections X and XI will all have an empirical element.

Although π-electron wave functions are invaluable—or, at least, inescapable—in empirical and semi-empirical calculations, they are of scarcely any use in non-empirical calculations. The reason for this is worth investigating, and we may note for a start that a calculation of the π-electron energy of a single state of a single molecule is not likely to be of much interest, however thoroughly it may be carried out, for, as π-electron energy is not an observable quantity, there is nothing with which to compare the calculated result.

At first sight this difficulty might not seem to apply to the non-empirical calculation of transition energies. In a molecular-orbital or bond-orbital formulation, some (though not all[21]) of the low-energy transitions observed in the ultraviolet absorption spectrum of an alkene molecule may be described as transitions in which one of the π orbitals used in the ground-state wave function is replaced by another π orbital of higher energy. (In the vernacular the transitions would be described as those in which a π electron is excited from a π orbital 'occupied' in the ground state to a 'vacant' π orbital.) These descriptions imply that the change in the π orbitals is not accompanied by any change in the σ orbitals. This obviously cannot be true except for 'vertical' transitions (section VI.B), for a change in the molecular dimensions cannot but affect the σ orbitals, and hence the σ-electron energy. Even in a vertical transition it is possible that a change within the π sub-configuration may bring about a change in the optimum forms of some of the σ orbitals*.

Superimposed on these difficulties is the problem we encountered in attempting to calculate transition energies in the hydrogen molecule on an inadequate atomic-orbital basis (section VI): in general, an *excited* molecular state cannot be described with any accuracy by a wave function built up from only the *ground*-state orbitals of the constituent atoms. In ethylene, for example, $2p_C$ orbitals suffice for the construction of reasonably accurate π orbitals in the ground state, but not in the excited states; as in the hydrogen molecule the calculated transition energies are thus very much exaggerated[22]. An enlargement of the atomic-orbital basis might give significantly improved results, but not without considerable computational difficulty.

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* No calculations are yet available to settle this point.

We may summarize the discussion given in this section by saying that the only molecular processes that can be represented with any degree of accuracy as changes involving π-electron energy exclusively are those in which there is no change in molecular dimensions. In such processes the initial and final states may reasonably be represented by π-electron wave functions; but in the case of an excited state it is usually impossible to determine the optimum form of the wave function without very elaborate computation. The impracticability of carrying out non-empirical calculations on π-electron systems forces us to adopt empirical methods. The best known of these is the Hückel[23] method, which we describe in section X.

X. THE HÜCKEL APPROXIMATION

A. Ethylene

Although the immediate results will prove to be of little value in themselves, it is convenient to introduce the Hückel approximation by reference to the ethylene molecule.

If we suppose the molecular-orbital or bond-orbital wave function for ethylene to be built up from the same atomic-orbital basis as in section VIII.D, the normalized π orbitals are

$$\chi_1 = (2 + 2S)^{-\frac{1}{2}}(\psi_a + \psi_b), \tag{195}$$

$$\chi_2 = (2 - 2S)^{-\frac{1}{2}}(\psi_a - \psi_b), \tag{196}$$

where the carbon atoms are labelled a and b, and ψ_a and ψ_b are normalized $2p_C$ orbitals having symmetry axes perpendicular to the molecular plane*. S is the overlap integral between the two orbitals:

$$S = \int \psi_a \psi_b \mathrm{d}\tau.$$

As in section VI.B, three two-electron configurations can be constructed from the orbitals χ_1 and χ_2. Written in the usual abbreviated

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* Except as far as symmetry is concerned, this conventional definition of ψ_a and ψ_b is unnecessarily restrictive, and we have given it only because of its simplicity. The explicit form of ψ is never used in a Hückel calculation, and it may be imagined to be whatever gives the best energy when the variation principle is applied to the molecular wave function, at least in the ground state. (In the excited states, where the charge 'clouds' are rather more diffuse, the optimum forms of ψ are not the same as in the ground state. It is impossible to allow for these differences in the simple Hückel theory.)

notation (*i.e.* without the numerals which represent the electron coordinates) they are χ_1^2, $\chi_1\chi_2$, and χ_2^2. In conformity with the exclusion principle, the first and the third of these configurations each gives only a singlet state, but the second gives both a singlet state and a triplet state. The antisymmetrized wave functions for the four states may be written as in (108)–(111) or, because we are dealing with the special case of a *quasi*-two-electron system, as in (112)–(115). In the Hückel approximation, however, the general form of the Pauli principle is ignored, the distinction between different spin states of the same configuration is obliterated, and the π-electron wave functions of ethylene are taken to be the three simple products (197)–(199) instead of the four antisymmetrized products just mentioned:

$$\Psi_\pi(^1A_{1g}^*) = \chi_2(1)\chi_2(2); \tag{197}$$

$$\Psi_\pi(B_{1u}) = \chi_1(1)\chi_2(2); \tag{198}$$

$$\Psi_\pi(^1A_{1g}) = \chi_1(1)\chi_1(2). \tag{199}$$

The functions (197)–(199) are listed in order of decreasing energy, the asterisk in (197) indicating that this is an excited state of the same symmetry as (199). No definite spin state is represented by the function (198), the corresponding energy lying between that of the $^1B_{1u}$ and the $^3B_{1u}$ states. [A_{1g} and B_{1u} are symmetry symbols, which we are using merely as labels. The symbols Σ_g and Σ_u associated with the functions (108)–(115) do not, of course, apply to ethylene.]

In principle, the use of orbitals rather than spin-orbitals in Hückel wave functions is a very serious limitation indeed, especially in the description of excited states; in practice, the limitation can be overcome to a surprising extent by discretion in the choice of experimental data for the evaluation of energy integrals. In any case, however undesirable it may be to use wave functions which are not properly antisymmetrized, in work on really large π-electron systems it is almost unavoidable.

In calculating the energies corresponding to the functions (197)–(199), we shall use the π-electron Hamiltonian operator introduced in section IX.B. Excluding internuclear-repulsion terms, this operator for the ethylene molecule is

$$\mathbf{H}_\pi = -\tfrac{1}{2}\nabla_1^2 - \tfrac{1}{2}\nabla_2^2 + V_1 + V_2 + 1/r_{12}, \tag{200}$$

where the π electrons are numbered 1 and 2. V_1 and V_2 are omnibus terms, V_1 for example representing the attraction between electron 1 and the nuclei as well as the repulsion between electron 1 and all the σ electrons. The term $1/r_{12}$ concerns the π electrons only. The operator (200) may be written more concisely as

$$\mathbf{H}_\pi = \mathbf{H}_1 + \mathbf{H}_2 + 1/r_{12}, \tag{201}$$

where $\mathbf{H}_1$ includes all the terms involving electron 1 only, and $\mathbf{H}_2$ those involving electron 2 only*; *i.e.*

$$\mathbf{H}_1 = -\tfrac{1}{2}\nabla_1^2 + V_1; \qquad \mathbf{H}_2 = -\tfrac{1}{2}\nabla_2^2 + V_2. \tag{202}$$

To show how π-electron energies are calculated by the Hückel method we shall consider the function (198), and then write down the analogous results for (197) and (199). $\Psi_\pi(B_{1u})$ is already normalized, so the energy is

$$\begin{aligned} E_\pi(B_{1u}) &= \int \chi_1(1)\chi_2(2)\mathbf{H}_\pi\chi_1(1)\chi_2(2)\, d\tau_1 d\tau_2 \\ &= \int \chi_1(1)\chi_2(2) \left| \mathbf{H}_1 + \mathbf{H}_2 + \frac{1}{r_{12}} \right| \chi_1(1)\chi_2(2) d\tau_1 d\tau_2 \\ &= \int \chi_2(2)\chi_2(2) d\tau_2 \int \chi_1(1)\mathbf{H}_1\chi_1(1) d\tau_1 \\ &\quad + \int \chi_1(1)\chi_1(1) d\tau_1 \int \chi_2(2)\mathbf{H}_2\chi_2(2) d\tau_2 \\ &\quad + \int \chi_1(1)\chi_2(2) \frac{1}{r_{12}} \chi_1(1)\chi_2(2) d\tau_1 d\tau_2. \end{aligned} \tag{203}$$

In the first two terms of the expansion (203) the first factor is unity in each case, so we may write the π-electron energy more simply as

$$E_\pi(B_{1u}) = \int \chi_1(1)\mathbf{H}_1\chi_1(1) d\tau_1 + \int \chi_2(2)\mathbf{H}_2\chi_2(2) d\tau_2 + C_{12}, \tag{204}$$

where

$$C_{12} = \int \chi_1(1)\chi_2(2) \frac{1}{r_{12}} \chi_1(1)\chi_2(2) d\tau_1 d\tau_2, \tag{205}$$

the subscripts in C_{12} denoting the *molecular* orbitals concerned in the Coulomb repulsion integral. [It is worth noting that in (204) and (205) the subscripts 1 and 2 associated with χ identify orbitals, whereas the same subscripts associated with $\mathbf{H}$, r, and τ identify electrons. Like the numerals in parentheses, the latter subscripts are irrelevant in (204), and we have inserted them temporarily merely to clarify the transition from (203).]

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* The partitioning of the Hamiltonian operator in (201) is not analogous to that in (39).

From this point onwards we shall generally find it convenient to work in terms of individual orbital energies rather than total π energies. As in section VII.A, the energy ε_i of the molecular orbital χ_i is obtained by extracting from either the total electronic energy or the π energy all the integrals in which χ_i appears*. Thus

$$\varepsilon_1 = \int \chi_1(1)\mathbf{H}_1\chi_1(1)\mathrm{d}\tau_1 + C_{12}; \tag{206}$$

$$\varepsilon_2 = \int \chi_2(2)\mathbf{H}_2\chi_2(2)\mathrm{d}\tau_2 + C_{12}. \tag{207}$$

If we use the *ad hoc* 'one-electron' Hamiltonian operator $\mathscr{H}$ introduced in section VII.A, (206) and (207) may be written in the outwardly simpler forms

$$\varepsilon_1 = \int \chi_1\mathscr{H}\chi_1\mathrm{d}\tau; \tag{208}$$

$$\varepsilon_2 = \int \chi_2\mathscr{H}\chi_2\mathrm{d}\tau. \tag{209}$$

In (208) and (209) we have discarded the numerals identifying the electron coordinates, and also those identifying $\mathscr{H}$. As we pointed out towards the end of section VII.A, $\mathscr{H}$ is not exactly the same in (208) as in (209), but this is a nicety which is dwarfed by the more gross simplifications of the Hückel theory.

The integrals in equations (203)–(209) have all been integrals over molecular orbitals; in the next step these integrals are replaced by integrals over atomic orbitals. To keep the algebraic operations as simple as possible, it is customary (though by no means essential) to take the factor $(1 \pm S)^{-\frac{1}{2}}$ in (195) and (196) to be equal to unity†.

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* There are, of course, no exchange integrals, because the wave function is not antisymmetrized.

† For $2p_C$ orbitals separated by the usual double-bond length, $S \sim 0{\cdot}25$, so putting $S = 0$ may seem to be a very crude approximation. There is little reason, however, why we should not evade the problem of the non-orthogonality of the atomic orbitals by using the artifice of rewriting the (non-normalized) molecular orbitals as $\psi_a' \pm \psi_b'$, where $\psi_a' = \psi_a + \lambda\psi_b$ and $\psi_b' = \lambda\psi_a + \psi_b$. The coefficient λ can be chosen so that $S' = \int \psi_a'\psi_b'\mathrm{d}\tau = 0$. The functions ψ' cannot, of course, be regarded as atomic orbitals; indeed they differ from molecule to molecule.

Alternatively, we may replace the approximation $S = 0$ by the less severe approximation $S \propto \beta$. It can be shown[24] that this affects the optimum molecular orbitals only by changing their normalizing factors; but an orbital energy $\alpha + k\beta$ becomes $\alpha + k(\beta - \alpha S)/(1 + kS)$.

The molecular orbitals then become $2^{-\frac{1}{2}}(\psi_a \pm \psi_b)$, and the orbital energy ε_1 may be written as

$$\begin{aligned}\varepsilon_1 &= \int \chi_1 \mathscr{H} \chi_1 \mathrm{d}\tau \\ &\sim \tfrac{1}{2}\int (\psi_a + \psi_b)\mathscr{H}(\psi_a + \psi_b)\mathrm{d}\tau \\ &= \tfrac{1}{2}\int \psi_a \mathscr{H} \psi_a \mathrm{d}\tau + \tfrac{1}{2}\int \psi_b \mathscr{H} \psi_b \mathrm{d}\tau + \tfrac{1}{2}\int \psi_a \mathscr{H} \psi_b \mathrm{d}\tau + \tfrac{1}{2}\int \psi_b \mathscr{H} \psi_a \mathrm{d}\tau.\end{aligned} \tag{210}$$

Because of the symmetry of the molecule, the first and the second integrals in (210), which we shall call α, are equal; so are the third and the fourth integrals, which we shall call β. Hence

$$\varepsilon_1 = \alpha + \beta, \tag{211}$$

and, likewise,

$$\varepsilon_2 = \alpha - \beta. \tag{212}$$

In α and β nuclear-attraction terms predominate over kinetic terms and electron-repulsion terms, so the integrals are both negative.

The definitions of α and β depend on the definitions of $\mathscr{H}$ and ε. In this section, as in section VII.A, we have defined the 'one-electron' operator and the orbital energy in conformity with current usage in 'self-consistent' molecular-orbital calculations; α and β thus include π–π electron-repulsion terms. It should be noted, however, that, especially in the older literature, α and β are often defined in such a way as to imply the exclusion of π–π repulsion energies. This is equivalent to omitting $1/r_{12}$ from $\mathbf{H}_\pi$ in (200) or (201), and there is then no distinction in energy between antisymmetrized and non-antisymmetrized wave functions based on the same configuration (*i.e.* all multiplet splittings are calculated to be zero).

If we apply the same analysis to the ${}^1A_{1g}$ wave functions as to the B_{1u} wave function, we obtain, without any difficulty, the following expressions for the energies of the three Hückel π-electron states of the ethylene molecule:

$$E_\pi({}^1A_{1g}^*) = \varepsilon_2 + \varepsilon_2 - C_{22} = 2\alpha - 2\beta - C_{22}; \tag{213}$$

$$E_\pi(B_{1u}) = \varepsilon_1 + \varepsilon_2 - C_{12} = 2\alpha \qquad - C_{12}; \tag{214}$$

$$E_\pi({}^1A_{1g}) = \varepsilon_1 + \varepsilon_1 - C_{11} = 2\alpha + 2\beta - C_{11}. \tag{215}$$

The electron-repulsion integrals C have to be subtracted in equations (213)–(215), otherwise they would be counted twice over [compare (206) and (207) with (204)]. The total π-electron energy of any state is not simply the sum of the individual orbital energies. However, the three integrals C_{22}, C_{12}, and C_{11} in ethylene are similar in magnitude (as are usually the corresponding integrals in other π-electron systems), and, as a further approximation, they are taken to be equal.

In (213)–(215), and in the analogous equations for other π-electron systems, the coefficient of α is the same for all the π-electron states; it is simply equal to the number of π orbitals. Vertical† transition energies can thus be expressed approximately in terms of β only.

It might seem that the two energies of excitation from the ground state corresponding to the relations (213)–(215) would provide an obvious means of testing the approximations we have introduced in the foregoing analysis, for one excitation energy should be twice the other:

$$E_\pi(^1A^*_{1g}) - E_\pi(^1A_{1g}) = (2\alpha - 2\beta) - (2\alpha + 2\beta) = -4\beta; \quad (216)$$

$$E_\pi(B_{1u}) - E_\pi(^1A_{1g}) = 2\alpha \quad - (2\alpha + 2\beta) = -2\beta. \quad (217)$$

However, in seeking spectroscopic confirmation of the calculated transition energies we encounter considerable difficulty, which we mention here as a warning that the results of a Hückel calculation are usually vastly easier to obtain than to interpret.

In the first place, the energy $E_\pi(B_{1u})$ does not correspond to that of any spectroscopic state, for, as we have seen, the Hückel procedure does not distinguish between singlet and triplet states of the same configuration. We can say only that the calculated transition energy -2β corresponds to an observed energy lying somewhere between 7·6 ev and 4·6 ev, these being the now generally accepted[21] excitation energies for the $^1B_{1u}$ and the $^3B_{1u}$ states‡. A second difficulty is that the transition $^1A_{1g} \leftrightarrow {}^1A^*_{1g}$ is spectroscopically 'forbidden' (because it involves no change in symmetry), and is indeed unknown. Lastly, whatever functions we may suppose the symbols ψ_a and ψ_b to represent, the optimum forms of these functions, and hence the values of α and β, vary from one state of excitation to another: as the π-electron energy increases, so the π-electron charge distribution becomes more diffuse. We shall see, in dealing with molecules more complex than ethylene, that the uses of the relations (213)–(215) are not the obvious ones suggested by (216) and (217).

The energy parameters α and β occur in all Hückel calculations,

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† As shown in section IX.B, transitions involving changes in internuclear distances cannot be treated as changes in π-electron energy.

‡ In fact, if all the foregoing approximations are accepted, -2β corresponds to the average of the two values 7·6 ev and 4·6 ev.

and it is important that their significance should be properly appreciated. A great deal of confusion has been caused by over-simplified interpretations[25]. The parameters should be regarded as essentially mathematical quantities which do not admit of straightforward physical interpretations. Contrary to what is so often suggested, the integral α does not correspond to the energy (ε_{2p}) of a $2p$ orbital in an isolated carbon atom, for the operator $\mathscr{H}$ in (210) is a molecular Hamiltonian operator which incorporates a considerable number of interactions not included in the atomic Hamiltonian operator. It is true, however, that under the influence of certain perturbations the value of α varies in much the same way as that of ε_{2p}, and this is why arguments based on a false interpretation of α often lead to the correct results. As α includes a substantial kinetic-energy contribution, the name Coulomb integral or Coulomb term which is often applied to it is misleading.

The parameter β, known as the bond integral, because it involves orbitals of adjacent atoms, or (less desirably but more frequently) as the resonance integral, is no easier to interpret than α. To save confusion, however, we may at least mention two quantities with which β may not be identified; β is not 'the energy of interaction of two atomic orbitals'[26] (in a thermodynamic sense*), nor, assuredly, is it 'the energy of an electron in the field of both nuclei'[27].

B. Buta-1,3-diene

Although we shall have ultimately to leave the reader to decide the question for himself, it is interesting to enquire whether the simple Hückel model, despite all its limitations, can provide an interpretation of the marked difference between the chemical behaviour of buta-1,3-diene and that of dienes or polyenes with non-conjugated double bonds. Like all other chemical reactions, the reactions of the alkenes involve changes in molecular dimensions, so the reacting species can never be described adequately by π-electron wave functions (section IX.B). This means that, although a Hückel calculation for butadiene is well worth examining as an illustration of the techniques and approximations involved, the analysis of the results is bound not to be straightforward.

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* In the jargon of quantum chemistry the term 'interaction energy' is often used to describe a quantity represented by an energy integral appearing in an off-diagonal element of a secular determinant (section VI.E). The quantity need have no relation to ΔH or ΔU for a thermodynamically definable process.

The butadiene molecule is planar, and has the dimensions[28] shown in Figure 19. If we use the customary atomic-orbital basis ($1s_H$, $1s_C$, $2s_C$, $2p_{zC}$, $2p_{xC}$, $2p_{yC}$), all but the $2p_{xC}$ atomic orbitals are concerned with the σ bonding. Each of the four carbon atoms contributes a $2p_x$ orbital to the molecular wave function, so we can construct four linearly independent π orbitals (only two of which are required in the ground-state wave function). If we label the carbon atoms a, b, c, d, and write the normalized $2p_{xC}$ orbitals as ψ_a, ψ_b, ψ_c, ψ_d, each π orbital will be of the form

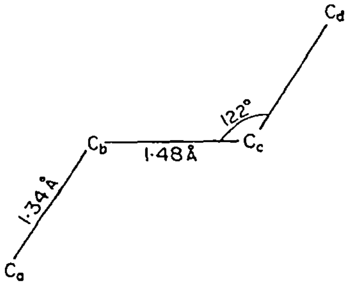

FIGURE 19. The carbon skeleton of buta-1,3-diene.

$$\chi = c_a\psi_a + c_b\psi_b + c_c\psi_c + c_d\psi_d. \tag{218}$$

In the ethylene molecule the coefficients of the atomic orbitals in the LCAO expansions (195) and (196) were determined purely by symmetry, but, because the butadiene molecule is less symmetrical, we have to invoke the variation principle for the evaluation of the coefficients in (218). We use the linear variation method described in section VI.E, minimizing the orbital energy

$$\varepsilon = \frac{\int \chi \mathscr{H} \chi \, d\tau}{\int \chi^2 d\tau} \tag{219}$$

with respect to variations in the coefficients*. If we use the symbols α and β as defined in section X.A, but for the moment with subscripts

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* Varying the orbital energy (as defined here) gives the same linear combinations as varying the total π energy.

to identify the orbitals, we obtain the following expansion on substituting (218) in the numerator of (219):

$$\begin{aligned}\int \chi\mathscr{H}\chi \mathrm{d}\tau = {} & c_\mathrm{a}^2\alpha_\mathrm{aa} + c_\mathrm{b}^2\alpha_\mathrm{bb} + c_\mathrm{c}^2\alpha_\mathrm{cc} + c_\mathrm{d}^2\alpha_\mathrm{dd} \\ & + 2c_\mathrm{a}c_\mathrm{b}\beta_\mathrm{ab} + 2c_\mathrm{a}c_\mathrm{c}\beta_\mathrm{ac} + 2c_\mathrm{a}c_\mathrm{d}\beta_\mathrm{ad} \\ & + 2c_\mathrm{b}c_\mathrm{c}\beta_\mathrm{bc} + 2c_\mathrm{b}c_\mathrm{d}\beta_\mathrm{bd} + 2c_\mathrm{c}c_\mathrm{d}\beta_\mathrm{cd}. \end{aligned} \tag{220}$$

At this stage we introduce two approximations which were not applicable when we were dealing with the ethylene molecule. We suppose that all the so-called 'Coulomb' terms have the same value* α, and that all bond integrals involving adjacent atomic orbitals have the same value† β, whereas bond integrals involving more distant orbitals may be neglected‡.

With these approximations (220) is considerably simplified:

$$\int \chi\mathscr{H}\chi \mathrm{d}\tau \sim (c_\mathrm{a}^2 + c_\mathrm{b}^2 + c_\mathrm{c}^2 + c_\mathrm{d}^2)\alpha + (2c_\mathrm{a}c_\mathrm{b} + 2c_\mathrm{b}c_\mathrm{c} + 2c_\mathrm{c}c_\mathrm{d})\beta. \tag{221}$$

If, in accordance with the approximation we used in section X.A, we take all the overlap integrals over atomic orbitals to be zero, the denominator in (219) is

$$\int \chi^2 \mathrm{d}\tau \sim c_\mathrm{a}^2 + c_\mathrm{b}^2 + c_\mathrm{c}^2 + c_\mathrm{d}^2. \tag{222}$$

Substituting (221) and (222) in (219) gives

$$\varepsilon = \frac{\int \chi\mathscr{H}\chi \mathrm{d}\tau}{\int \chi^2 \mathrm{d}\tau} \sim \alpha + \frac{(2c_\mathrm{a}c_\mathrm{b} + 2c_\mathrm{b}c_\mathrm{c} + 2c_\mathrm{c}c_\mathrm{d})\beta}{c_\mathrm{a}^2 + c_\mathrm{b}^2 + c_\mathrm{c}^2 + c_\mathrm{d}^2}. \tag{223}$$

---

[*] From the symmetry of the molecule, $\alpha_\mathrm{aa} = \alpha_\mathrm{dd}$ and $\alpha_\mathrm{bb} = \alpha_\mathrm{cc}$, but the potential field due to the nuclei and the σ electrons is not the same at a as at b, so $\alpha_\mathrm{aa} \neq \alpha_\mathrm{bb}$. The discrepancy may be quite large[29].

[†] By symmetry, $\beta_\mathrm{ab} = \beta_\mathrm{cd}$, but, because the middle C—C bond is significantly longer than the terminal C—C bonds, $|\beta_\mathrm{bc}| < |\beta_\mathrm{ab}|$. Inequalities of this type are unfortunately much more important in alkene molecules than in aromatic molecules, where the bond lengths are more uniform.

[‡] Ignoring bond integrals except between adjacent atomic orbitals is equivalent to ignoring the molecular geometry. The simple Hückel method takes no account of interactions between atoms which are not bonded in the ordinary chemical sense. Thus it does not distinguish, for example, between the *cis* and the *trans* forms of buta-1,3-diene.

To obtain the minimum value of ε with respect to variations in c_a, c_b, c_c, c_d we must put

$$\frac{\partial\varepsilon}{\partial c_a} = \frac{\partial\varepsilon}{\partial c_b} = \frac{\partial\varepsilon}{\partial c_c} = \frac{\partial\varepsilon}{\partial c_d} = 0. \tag{224}$$

To illustrate the procedure, we need evaluate only one of these partial differential coefficients, say $\partial\varepsilon/\partial c_a$. From (223),

$$\begin{aligned}\frac{\partial\varepsilon}{\partial c_a} &= \frac{2c_b\beta}{c_a^2 + c_b^2 + c_c^2 + c_d^2} - \frac{2c_a(2c_ac_b + 2c_bc_c + 2c_cc_d)\beta}{(c_a^2 + c_b^2 + c_c^2 + c_d^2)^2}\\ &= \frac{2c_b\beta}{c_a^2 + c_b^2 + c_c^2 + c_d^2} + \frac{2c_a(\alpha - \varepsilon)}{c_a^2 + c_b^2 + c_c^2 + c_d^2}.\end{aligned}$$

Analogous expressions are obtained for the other partial differential coefficients. Equating all four of these in turn to zero gives the four simultaneous equations (225)–(228).

$$c_a(\alpha - \varepsilon) + c_b\beta = 0 \tag{225}$$

$$c_a\beta + c_b(\alpha - \varepsilon) + c_c\beta = 0 \tag{226}$$

$$c_b\beta + c_c(\alpha - \varepsilon) + c_d\beta = 0 \tag{227}$$

$$c_c\beta + c_d(\alpha - \varepsilon) = 0 \tag{228}$$

The standard procedure for solving the secular equations (225)–(228) was mentioned in section VI.E. Elimination of the coefficients gives the determinantal equation (229):

$$\begin{vmatrix} \alpha - \varepsilon & \beta & 0 & 0 \\ \beta & \alpha - \varepsilon & \beta & 0 \\ 0 & \beta & \alpha - \varepsilon & \beta \\ 0 & 0 & \beta & \alpha - \varepsilon \end{vmatrix} = 0. \tag{229}$$

On expansion this gives a quartic equation in ε. There are four real roots, and each of these when substituted in the equations (225)–(228) gives a relation between the coefficients c_a, c_b, c_c, c_d corresponding to a stationary value of the orbital energy. We obtain the normalized values of the coefficients by equating the right-hand side of (222) to unity. The four molecular orbitals obtained by substituting the four sets of coefficients in (218) are listed in Table 13 in order of increasing energy.

Table 13. Hückel molecular orbitals for buta-1,3-diene.

Bonding orbitals

$$\chi_1 = 0{\cdot}372\psi_a + 0{\cdot}601\psi_b + 0{\cdot}601\psi_c + 0{\cdot}372\psi_d \qquad \varepsilon_1 = \alpha + 1{\cdot}618\beta$$
$$\chi_2 = 0{\cdot}601\psi_a + 0{\cdot}372\psi_b - 0{\cdot}372\psi_c - 0{\cdot}601\psi_d \qquad \varepsilon_2 = \alpha + 0{\cdot}618\beta$$

Antibonding orbitals

$$\chi_3 = 0{\cdot}601\psi_a - 0{\cdot}372\psi_b - 0{\cdot}372\psi_c + 0{\cdot}601\psi_d \qquad \varepsilon_3 = \alpha - 0{\cdot}618\beta$$
$$\chi_4 = 0{\cdot}372\psi_a - 0{\cdot}601\psi_b + 0{\cdot}601\psi_c - 0{\cdot}372\psi_d \qquad \varepsilon_4 = \alpha - 1{\cdot}618\beta$$

The coefficients in χ_1 and χ_3 are symmetric about the midpoint of the molecule; those in χ_2 and χ_4 are antisymmetric.

It will be noted that the energy of the orbitals increases with the number of alternations of sign (*i.e.* with the number of orbital 'nodes'). In the terminology of the Hückel theory a molecular orbital is described as 'bonding' if the coefficient of β in the orbital energy is positive, 'non-bonding' if the coefficient is zero, and 'antibonding' if the coefficient is negative*.

The orbitals χ_2, χ_3, and χ_4 call for some comment. We began this analysis by seeking the lowest-energy orbital of the type (218), as required by the variation principle† in the form in which we stated it earlier in this chapter. However, the differentiations (224) have given us not just one orbital but four. The orbital χ_2 presents no difficulty, for, as shown below, it is the lowest-energy orbital of its symmetry type (section VI.C); but the status of χ_3 and χ_4 may not be immediately obvious, for, like all 'antibonding' Hückel orbitals, they represent maxima with respect to variation of the coefficients. The reader may readily verify, however, that the orbitals χ_1, χ_2, χ_3, and χ_4 are linearly independent and orthogonal‡ (as solutions of a Schrödinger equation corresponding to different eigenvalues must always be), and that no other set fulfils this requirement once χ_1 and χ_2 are fixed: if the only orbitals of π symmetry included in the atomic-orbital basis are $2p_{x\mathrm{C}}$ orbitals, there is no escaping χ_3 and χ_4. Of course, only χ_1 and χ_2

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* The terms 'bonding' and 'antibonding' are used in different ways in different branches of quantum chemistry (and sometimes in different ways in one and the same branch by different authors).

† Because the Hamiltonian operator is not properly defined, and because the energy expression is simplified, the use of the variation principle in this section is not strictly legitimate. But the coefficients obtained in Hückel calculations are generally remarkably similar to those obtained in far more precise calculations.

‡ Provided that all overlap integrals are taken to be zero.

are required in the ground-state wave function, which is taken to be the non-antisymmetrized product

$$\Psi_\pi = \chi_1(1)\chi_1(2)\chi_2(3)\chi_2(4). \tag{230}$$

In indicating a little earlier that the solution of the secular equations (225)–(228) involved finding the roots of a quartic equation, we were stating a general rule and ignoring a simplification which results from the symmetry of the butadiene molecule. The quartic equation can be replaced by a pair of quadratic equations, and, because this simplification draws attention to the importance of orbital symmetry, it is useful to see how it is effected.

The molecule has a centre of symmetry (Figure 19), and the electron density distribution must, of course, be symmetrical about this centre. This is the case if the molecular orbitals are either symmetric or antisymmetric about the centre, for the π-electron density is determined by the sum of the squares of the 'occupied' π orbitals (section IV.F). So, for the symmetric orbitals

$$c_a = c_d \quad \text{and} \quad c_b = c_c, \tag{231}$$

whereas for the antisymmetric orbitals

$$c_a = -c_d \quad \text{and} \quad c_b = -c_c. \tag{232}$$

First we consider the symmetric orbitals. By substituting (231) in (228) we obtain (233), which is identical with (225); by substituting (231) in (226) or (227) we obtain (234):

$$c_a(\alpha - \varepsilon) + c_b\beta = 0; \tag{233}$$

$$c_a\beta + c_b(\alpha - \varepsilon + \beta) = 0. \tag{234}$$

Elimination of the coefficients c_a and c_b from (233) and (234) gives the quadratic equation

$$\begin{vmatrix} \alpha - \varepsilon & \beta \\ \beta & \alpha - \varepsilon + \beta \end{vmatrix} = (\alpha - \varepsilon)^2 + \beta(\alpha - \varepsilon) - \beta^2 = 0,$$

whence

$$\varepsilon = \alpha + 1{\cdot}618\beta \quad \text{or} \quad \varepsilon = \alpha - 0{\cdot}618\beta.$$

These two values of ε were labelled ε_1 and ε_3 in Table 13. Substituting $\varepsilon_1 = \alpha + 1{\cdot}618\beta$ in (233) or (234) gives the ratio $c_a/c_b = 1/1{\cdot}618$, and hence, after normalization, the coefficients in χ_1; substituting $\varepsilon_3 = \alpha - 0{\cdot}618\beta$ in the same equations gives the ratio $c_a/c_b = -1/0{\cdot}618$, and hence the coefficients in χ_3.

Proceeding in exactly the same way with the antisymmetric orbitals, we obtain the determinantal equation

$$\begin{vmatrix} \alpha - \varepsilon & \beta \\ \beta & \alpha - \varepsilon - \beta \end{vmatrix} = (\alpha - \varepsilon)^2 - \beta(\alpha - \varepsilon) - \beta^2 = 0,$$

whence

$$\varepsilon = \alpha + 0{\cdot}618\beta \quad \text{or} \quad \varepsilon = \alpha - 1{\cdot}618\beta.$$

These two roots are the same as those labelled ε_2 and ε_4 in Table 13, and they correspond to the orbitals χ_2 and χ_4.

C. Higher Polyenes

Hückel orbitals and their energies may be determined in exactly the same way for the higher polyenes as for butadiene. The results for planar acyclic polyenes may be represented by very simple general formulae[30]. If in the polyene molecule each of N consecutive carbon atoms contributes one $2p$ orbital to the π-electron wave function, there will be N linearly independent π molecular orbitals. If, in order of increasing energy, the π orbitals are labelled $\chi_1, \chi_2, \ldots, \chi_N$, the energy of χ_j is

$$\varepsilon_j = \alpha + 2\beta \cos\left(\frac{180^\circ j}{N+1}\right).$$

If the carbon atoms associated with the π orbitals are numbered consecutively $C_{(1)}, C_{(2)}, \ldots, C_{(N)}$, then the coefficient of the $2p$ orbital contributed by $C_{(r)}$ to χ_j is

$$c_{jr} = \left(\frac{2}{N+1}\right)^{\frac{1}{2}} \sin\left(\frac{180^\circ jr}{N+1}\right).$$

In a polyene molecule (or, indeed, any other molecule) there is an obvious interrelation between the bond lengths, the molecular energy, and the molecular wave function (*i.e.* the σ and π orbitals). In so far as Hückel π orbitals are concerned, the effect of bond length is shown in the LCAO coefficients. The relation between bond lengths and atomic-orbital coefficients (*via* bond orders[1]) has aroused considerable interest from the early days of the Hückel theory, and this is an appropriate point for a passing reference to an old problem in the quantum chemistry of conjugated polyenes which has recently been re-examined. It is well known that in small conjugated polyene molecules there is a marked difference in length between bonds that would be written as single in a classical chemical formula and those that would be written as double. The problem, first studied by Lennard-Jones[31] and by Coulson[32], is to investigate by purely theoretical methods whether the alternation in bond lengths persists as the number of carbon atoms increases to infinity in a polyene series, or whether the difference between 'single' and 'double' bonds dwindles away. By comparing the energy* of a model of a very long polyene chain having just two distinct C—C bond lengths† with that of one having uniform C—C bond lengths, Longuet-Higgins and Salem[33] have come to the conclusion that the model with alternating bond lengths is the more stable‡.

D. Delocalization Energy

Having shown how the π-orbital energies of polyene molecules are calculated in the Hückel approximation, we now face the far more difficult problem of interpreting the results we have obtained. We shall confine the discussion to butadiene. The chemical behaviour of this molecule suggests that it is rather more stable than a diene with non-conjugated double bonds, and, in so far as the difference is thermochemical in origin, it is conventionally attributed to a difference in π-electron energy.

So we commence this section by calculating the Hückel π-electron energy of a planar non-conjugated diene, for comparison with the results obtained in section X.B. Because the Hückel procedure takes no account of molecular dimensions, it does not matter what the non-conjugated diene is, and, to preserve the notation of section X.B, we may take it to be a hypothetical butadiene molecule with two non-interacting π bonds. We must suppose that the σ orbitals are the same for the hypothetical molecule as for the real molecule; this implies that there are no differences in the molecular dimensions or in α or β.

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* It does not, of course, suffice to calculate the π-electron energy: provision must be made for the variation of σ-electron energy with bond length.

† In a real molecule the number of distinct C—C bond lengths would be restricted only by symmetry.

‡ The use of the Hückel theory for determining which of two nuclear configurations of a large molecule is the more stable requires careful consideration. Even with the full use of the computing resources now available, this is a type of calculation which can be carried out on a strict wave-mechanical basis for only the very smallest molecules.

In section X.B the only integral involving atomic orbitals from both halves of the butadiene molecule which survived the Hückel approximations was β_{bc}. In the hypothetical molecule we are now considering, in which it is supposed that π orbitals from one half of the molecule do not interact with π orbitals from the other half, β_{bc} must also vanish. The secular equations analogous to (225)–(228) are thus (235)–(238).

$$c_a'(\alpha - \varepsilon) + c_b'\beta = 0 \tag{235}$$

$$c_a'\beta + c_b'(\alpha - \varepsilon) = 0 \tag{236}$$

$$c_c'(\alpha - \varepsilon) + c_d'\beta = 0 \tag{237}$$

$$c_c'\beta + c_d'(\alpha - \varepsilon) = 0 \tag{238}$$

From (235) and (236) we obtain the roots $\varepsilon' = \alpha \pm \beta$ and the relations $c_a' = \pm c_b'$; from (237) and (238) we obtain the same roots and the relations $c_c' = \pm c_d'$. The secular equations do not indicate how c_a' and c_b' are related to c_c' and c_d', but, as we noted in section X.B, the symmetry of the molecule requires that $c_a' = \pm c_d'$ and $c_b' = \pm c_c'$. Using all these relations between the four coefficients, we arrive at the (normalized) molecular orbitals listed in Table 14.

TABLE 14. Hückel molecular orbitals for a non-conjugated diene.

Bonding orbitals	
$\chi_1' = \frac{1}{2}\psi_a + \frac{1}{2}\psi_b + \frac{1}{2}\psi_c + \frac{1}{2}\psi_d$	$\varepsilon_1' = \alpha + \beta$
$\chi_2' = \frac{1}{2}\psi_a + \frac{1}{2}\psi_b - \frac{1}{2}\psi_c - \frac{1}{2}\psi_d$	$\varepsilon_2' = \alpha + \beta$
Antibonding orbitals	
$\chi_3' = \frac{1}{2}\psi_a - \frac{1}{2}\psi_b - \frac{1}{2}\psi_c + \frac{1}{2}\psi_d$	$\varepsilon_3' = \alpha - \beta$
$\chi_4' = \frac{1}{2}\psi_a - \frac{1}{2}\psi_b + \frac{1}{2}\psi_c - \frac{1}{2}\psi_d$	$\varepsilon_4' = \alpha - \beta$

Because of their degeneracy, the orbitals χ_1' and χ_2' are not unique: any linear combination of them would correspond to the same orbital energy $\alpha + \beta$. Likewise, any linear combination of χ_3' and χ_4' would correspond to the energy $\alpha - \beta$. One interesting transformation is shown in equations (239)–(242).

$$2^{-\frac{1}{2}}(\chi_1' + \chi_2') = 2^{-\frac{1}{2}}(\psi_a + \psi_b) \tag{239}$$

$$2^{-\frac{1}{2}}(\chi_1' - \chi_2') = 2^{-\frac{1}{2}}(\psi_d + \psi_c) \tag{240}$$

$$2^{-\frac{1}{2}}(\chi_3' + \chi_4') = 2^{-\frac{1}{2}}(\psi_a - \psi_b) \tag{241}$$

$$2^{-\frac{1}{2}}(\chi_3' - \chi_4') = 2^{-\frac{1}{2}}(\psi_d - \psi_c) \tag{242}$$

These transformed orbitals (239)-(242) are the (normalized) π orbitals we should obtain in the LCAO bond-orbital description of a non-conjugated diene if we adopted the Hückel approximations. The bond orbitals and their energies have the same form as for ethylene (section X.A), though the values of α and β are somewhat different.

We can now compare the π-electron energies of butadiene and the hypothetical diene in their ground states. If we take the wave functions to be the simple products

$$\Psi_\pi = \chi_1(1)\chi_1(2)\chi_2(3)\chi_2(4),$$
$$\Psi_\pi' = \chi_1'(1)\chi_1'(2)\chi_2'(3)\chi_2'(4),$$

then from the orbital energies listed in Tables 13 and 14 we find

$$E_\pi = 2\varepsilon_1 + 2\varepsilon_2 - C_\pi = 4\alpha + 4{\cdot}472\beta - C_\pi; \tag{243}$$

$$E_\pi' = 2\varepsilon_1' + 2\varepsilon_2' - C_\pi' = 4\alpha + 4\beta \quad - C_\pi'. \tag{244}$$

C_π and C_π' are the total π electron-repulsion energies (sums of integrals over π molecular orbitals or bond orbitals), which would be counted twice over if they were not subtracted in (243) and (244). If we suppose that the difference between C_π and C_π' is small enough to be neglected, we obtain from (243) and (244)

$$E_\pi' - E_\pi \sim -0{\cdot}472\beta. \tag{245}$$

The parameter β is negative*, so our calculation suggests that a conjugated diene has a markedly lower π-electron energy than a non-conjugated diene. The energy difference $-0{\cdot}472\beta$ is usually known as the delocalization energy.

Whether or not the calculations we have just described can be regarded as offering a satisfactory interpretation of some of the features

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* In the study of delocalization energies, the absolute value of β is usually taken to be rather less than 1 ev in calculations in which overlap integrals are neglected. A considerably larger value is required if the overlap integrals are taken into account.

of the chemical reactivity of butadiene is very much a matter of personal judgement. There is an appreciable energy difference in the desired direction; but it would be misleading not to point out that this difference is probably considerably overestimated. The difference between the two calculations is produced solely by putting $\beta_{bc} = 0$ in the calculation on the hypothetical diene. But there is no doubt that $|\beta_{bc}|$ is much too large in the calculation on butadiene. We have put β_{bc} equal to β_{ab} and β_{cd}, but $|\beta_{bc}|$ should certainly be reduced to allow for the length of the central C—C bond relative to that of the terminal C—C bonds. This would raise the calculated π-electron energy of butadiene, and so reduce the delocalization energy.

Furthermore it is clear from the fairly low symmetry of the butadiene molecule that the wave functions listed in Table 14 or equations (239)–(242) cannot be quite correct: the coefficients of ψ_a and ψ_d should not be identical in absolute magnitude with those of ψ_b and ψ_c. That they are so is the result of using a single value of α and a single value of β. The wave function for the hypothetical reference molecule is thus of non-optimum form, and the calculated energy presumably too high.

It is evident that a substantial part of the quantity which we have called the delocalization energy may be nothing more than an error resulting from the excessively approximate character of the Hückel calculation. For the purposes of this book it is most unfortunate that the Hückel method is at its worst when applied to acyclic π-electron systems. The difficulties we have just outlined are not usually very important in aromatic molecules, and in the highly symmetrical benzene molecule they are not found at all. (In benzene there is genuinely only one value of α, and, if interactions between non-neighbouring orbitals are neglected, only one value of β.)

From the discussion given in section IX, it will be obvious that delocalization energy, unlike resonance energy, is a purely theoretical quantity which cannot be measured experimentally. Resonance energies are usually estimated by comparing enthalpies of hydrogenation of conjugated compounds with those of non-conjugated reference compounds; and, as hydrogenation involves changes in bond lengths and bond angles, a resonance energy is a difference between two total electronic energies (including internuclear-repulsion energies), not between two π-electron energies. In aromatic systems there is usually a remarkably close parallel between measured resonance energies and calculated delocalization energies[1], but, as a recent compilation[34] of enthalpies of hydrogenation shows only too clearly, this good fortune does not extend to acyclic systems.

E. Antisymmetrized Wave Functions

Despite the many limitations to which we have been careful to draw attention, the Hückel theory is often of considerable value in the semi-quantitative study of ground-state energies in σ–π systems. It can even be used very successfully, as we show in section XI, in the interpretation of a limited range of low-energy spectral transitions, provided that care is taken not to apply it in circumstances in which its shortcomings are emphasized, and provided that some blurring of the distinction between differences in π energy and differences in total electronic energy is not exceptionable. In the study of excited states in general, however, the failure of the Hückel theory to distinguish between different multiplets of the same configuration can lead to serious difficulties, and it is then essential to replace the Hückel simple-product wave functions by new wave functions which meet the requirements of the general form of the Pauli principle.

Fortunately the use of properly antisymmetrized wave functions need not in itself involve the sacrifice of all the computational simplicity of the Hückel theory. Pople[35], Pariser and Parr[36], and others have shown that it is not difficult to estimate the electron-repulsion terms that are ignored in the simple Hückel procedure. We now describe the essential features of Pariser and Parr's modification of the simple Hückel method; but details should be sought in the original papers, where various applications are described. Other modifications of Hückel's method are discussed by Longuet-Higgins[37].

Three kinds of energy integral have to be considered in a modified Hückel calculation: there are the 'Coulomb' integrals (α), the bond integrals or 'resonance' integrals (β), and the electron-repulsion integrals. In the original Hückel method the electron-repulsion integrals are not considered explicitly; in fact they are in many ways ignored altogether.

We have seen that when a simple-product wave function is replaced by a determinantal (*i.e.* antisymmetrized) wave function, only the electron-repulsion terms are affected: the terms in α and β are unchanged. When the values of the α terms are required in Pariser and Parr's method, they are taken to be the negatives of the ionization energies* of the atoms concerned, modified to some extent to allow for

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* According to Koopmans' theorem (section VII.A), the absolute value of an orbital energy (as defined in this chapter) may be identified with the corresponding ionization energy. (It should be noted that Pariser and Parr's α and β do not include π–π electron-repulsion terms.)

the change in potential energy in passing from an atomic to a molecular environment (the change in kinetic energy is ignored). The integrals β are evaluated empirically by reference to spectral data, much as in the original Hückel method, integrals involving non-neighbouring atoms being neglected.

Were it not for a most useful approximation (the 'zero differential overlap' approximation) introduced by Pople[35] and by Pariser and Parr[36], the electron-repulsion integrals would cause considerable computational difficulty. Even in a small π-electron system, when the electron-repulsion integrals over molecular orbitals are expanded a great many distinct integrals over atomic orbitals are produced (*e.g.* 28 in the case of butadiene). Their presence in the energy expression which has to be minimized when the variation principle is applied adds enormously to the difficulty of finding the optimum values of the atomic-orbital coefficients in the molecular orbitals. This is, of course, one reason why electron-repulsion energy is not considered explicitly in the simple Hückel method.

In the zero-differential-overlap approximation any overlap or electron-repulsion integral over atomic orbitals in which the integrand includes a factor* $\psi_i(1)\psi_j(1)$, where ψ is a $2p\pi$ orbital, is taken to be zero if i and j denote different nuclei. This removes all 'ionic' and exchange† electron-repulsion integrals (the types we labelled L and A in section IV), leaving only a comparatively small number of Coulomb‡ integrals ($i = j$), which are easily evaluated§. Applied separately to the overlap integrals or the electron-repulsion integrals, the approximation would be very crude, but applied to the two types jointly it produces astonishingly little error.

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* The numeral 1 is arbitrary. It is inserted to emphasize that the orbitals ψ_i and ψ_j are functions of the coordinates of the *same* electron.

† It is important to note that the exchange integrals removed are integrals over atomic orbitals, not integrals over molecular orbitals. Without the latter there would, of course, be no distinction in energy between different multiplets of the same configuration.

‡ It is unfortunate that the name Coulomb is applied not only to electron-repulsion integrals (type C in section IV.A), but also, misleadingly, to the Hückel α terms.

§ The calculated value of the one-centre Coulomb integral, *i.e.* the $2p_C$ analogue of the $1s_H$ integral which we called C_0 in (71), is about 17 ev. This value is perfectly satisfactory in strict wave-mechanical calculations (see, *e.g.*, reference 17), but in Pariser and Parr's method it has to be reduced empirically to about 11 ev to obtain satisfactory agreement between theory and experiment. The reduction is justified by an argument involving the ionization energy and the electron affinity of a carbon atom in a *quasi*-molecular environment.

In a calculation of the type we are now considering, the atomic-orbital coefficients may (for simplicity) be determined exactly as in the original Hückel method, and the electron-repulsion energy introduced explicitly only in the subsequent evaluation of the energy integral

$$E_\pi = \int \Psi_\pi \mathbf{H}_\pi \Psi_\pi \mathrm{d}\tau.$$

Alternatively, the electron-repulsion integrals can be included before the energy is minimized, and the resulting orbitals are then often described (rather generously) as 'self-consistent'. It is possible, though by no means certain, that the latter procedure represents a more legitimate application of the variation principle than the former: there is bound to be some uncertainty in a variational calculation based on an incomplete Hamiltonian operator, especially when part of the energy is evaluated empirically. In molecules of sufficiently high symmetry to have only one C—C bond length (*e.g.* ethylene or benzene), the two methods give identical coefficients.

The ways in which Pariser and Parr's modification of Hückel's procedure can be used in the study of 'π-electron' spectra are described fully in the original papers, so in section XI we shall confine our discussion to the simple Hückel method. We have already made it very clear that the only outstanding merit of the Hückel theory is its simplicity, and we can offer no rigour in the arguments we shall have to present in the remainder of this chapter. We do not suggest that our analysis be accepted unquestioningly, but we do point out that, in the present state of knowledge, the only alternative to an incomplete or oversimplified interpretation of a complex spectral phenomenon is usually no interpretation at all. The more closely the reader feels inclined to examine our reasoning in section XI, the better the earlier sections will have served their purpose.

XI. SPECTRA

A. *Ethylene and the Higher Polyenes*

In this section we shall be concerned with electronic spectra. First we consider ethylene and the higher polyenes, and then we discuss how the ultraviolet spectrum of ethylene is modified by rotation of one CH_2 group relative to the other. Finally we investigate the influence of substitution, particularly by alkyl groups or halogens, on the ultraviolet absorption and on ionization potentials.

In section X.C we showed that in a long polyene molecule with N consecutive carbon atoms, there would be N molecular orbitals χ_j and associated energies ε_j, available for π electrons. In order of increasing energy

$$\varepsilon_j = \alpha + 2\beta \cos\left(\frac{j\pi}{N+1}\right) \qquad (j = 1, 2, \ldots, N) \tag{246}$$

Figure 20 shows how these energies are located, for various even values of N. The particular cases of ethylene, where $N = 2$, and of butadiene, where $N = 4$, have already been dealt with in section X.

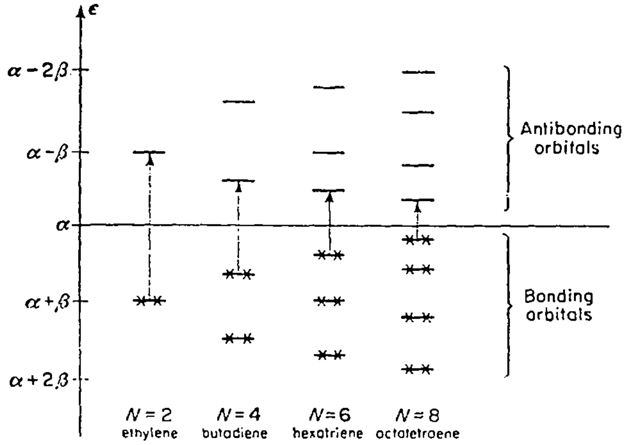

FIGURE 20. Orbital energies (246) for the π electrons in polyene chains. Crosses denote electrons in the ground state. The $N \rightarrow V_1$ transition corresponds to the electron jumps shown by arrows.

We may allot our given number of π electrons to these orbitals χ_j. Each such allocation defines a *configuration*. When supplemented by statements about the spins of the electrons, this gives us approximate descriptions of the actual electronic states of the molecule. The Pauli principle suggests that we obtain the lowest-energy configuration by putting the maximum number (two) of electrons in the lowest molecular orbitals and so filling up the χ_j from the lowest energy upwards. In this way the ground state of ethylene is χ_1^2 and of butadiene $\chi_1^2\chi_2^2$. No ambiguities arise in regard to the spin, since when two electrons occupy the same space orbital, their spins must be opposed.

It will be noticed from Figure 20 that in the ground state of all these molecules all the bonding orbitals ($j = 1, 2, \ldots, N/2$) are each doubly 'occupied', and all the antibonding orbitals ($j = N/2 + 1, \ldots, N$) are 'empty'. Further in the Hückel approximation used, there is complete mirror symmetry between a bonding orbital energy ε_j and its complementary antibonding orbital energy ε_{N-j+1}. (However, if we had included the overlap integral between neighbouring atomic orbitals, this exact mirror symmetry would have been slightly modified. We shall not consider such situations in this section.)

The lowest configuration is shown in the figure. In the general polyene it could be written [*cf.* equation (99)]

$$\chi_1^2\chi_2^2 \cdots \chi_{N/2}^2. \tag{247}$$

Its energy (if electron-repulsion terms are ignored) would be

$$2\sum_{j=1}^{\frac{1}{2}N} \varepsilon_j. \tag{248}$$

If we are interested in electronic spectra we shall need to consider excited states. Figure 21 shows four of these, corresponding to excitations represented by

$$\begin{aligned}&(a)\ \chi_{N/2} \to \chi_{N/2+1},\\ &(b)\ \chi_{N/2} \to \chi_{N/2+2}, \qquad (c)\ \chi_{N/2-1} \to \chi_{N/2+1},\\ &(d)\ \chi_{N/2-1} \to \chi_{N/2+2}.\end{aligned} \tag{249}$$

In general there will, of course, be many more excited levels, but it will be seen from the diagram that the transitions shown appear to correspond to a smaller excitation energy than all others. Let us for the moment disregard any question of spin multiplicity, such as that dealt with in section V; then we see that the energy of the excited state (*a*) is

$$2\sum_{j=1}^{N/2-1} \varepsilon_j + \varepsilon_{N/2} + \varepsilon_{N/2+1}.$$

Thus the excitation energy in the transition of an electron from $\chi_{N/2}$ to $\chi_{N/2+1}$ will be $\varepsilon_{N/2+1} - \varepsilon_{N/2}$. If we use (246) this gives $4|\beta| \cos \frac{\frac{1}{2}N\pi}{N+1}$, *i.e.*

$$4|\beta| \sin \frac{\pi}{2(N+1)}. \tag{250}$$

In the same way the energies of the two excited configurations (*b*) and (*c*) are identical, with excitation energy

$$2\beta \cos \frac{(N+4)\pi}{2(N+1)} - 2\beta \cos \frac{N\pi}{2(N+1)}$$

i.e.

$$2|\beta|\left\{\sin \frac{3\pi}{2(N+1)} + \sin \frac{\pi}{2(N+1)}\right\}. \tag{251}$$

Similarly the transition to configuration (*d*) involves an energy

$$4|\beta| \sin \frac{3\pi}{2(N+1)} \tag{252}$$

The energies represented by (250)–(252) are in increasing order of magnitude.

If we use the symbol N to denote the ground state, taking care to distinguish this use of N from the symbol denoting the number of carbon atoms in the chain, and if we call the excited states V_1, V_2, $V_3, \ldots$, in ascending order of energy, the lowest transition would be written $N \rightarrow V_1$, as in (249*a*), and with energy (250). The two transitions $N \rightarrow V_2$, $N \rightarrow V_3$ would be associated with the excited configurations (*b*) and (*c*), and the next higher transition would be $N \rightarrow V_4$, as in (249*d*), and with energy (252). The situation with the two configurations (*b*) and (*c*) is a little more complicated. As (251) shows, they are degenerate. A careful investigation of their symmetry, similar to that for butadiene in section X.B, shows that these two configurations have the same symmetry. They will therefore mix together, and form two new states. Such mixing is merely another example of the configuration interaction discussed in section IV.D. A precise calculation of the mixing coefficients would be very complex, due to the presence of many other higher-energy configurations of the same symmetry which, presumably, should also be included. But if, on grounds of simplicity, and energy considerations, we neglect all these other configurations, then it may be shown that the two configurations mix in equal proportions. The corresponding normalized wave functions are then

$$\sqrt{\tfrac{1}{2}}\{\psi_{N/2}^{N/2+2} \pm \psi_{N/2-1}^{N/2+1}\}, \tag{253}$$

where, *e.g.*, the symbol $\psi_{N/2}^{N/2+2}$ denotes a wave function obtained from the ground state function (247) by promoting an electron from the molecular orbital $\chi_{N/2}$ to the molecular orbital $\chi_{N/2+2}$.

The mixing represented by (253) will split the otherwise degenerate levels, pushing one energy up and the other down. The corresponding transitions are now represented by

$$N \rightarrow V_2 \text{ (choosing the } - \text{ sign in (253))}$$
$$N \rightarrow V_3 \text{ (choosing the } + \text{ sign in (253))}$$

In this way we obtain descriptions, sometimes called characterizations, of the lower excited states and of the energies of the corresponding transitions.

It may be interesting to add that a precisely similar description applies to the energy levels of aromatic and polynuclear molecules. Sometimes, as in naphthalene, the configuration interaction shown in (253) depresses the $N \rightarrow V_2$ transition below the $N \rightarrow V_1$ transition. More often, however, as in the polyenes, this does not occur, and the sequence of increasing energy is

$$N \rightarrow V_1, N \rightarrow V_2, N \rightarrow V_3, N \rightarrow V_4, \ldots,$$

The transition $N \rightarrow V_1$ is allowed. It is also a strong transition. Let us consider it a little more carefully. Figure 20 suggests that as the length of the polyene chain increases, the energy difference should tend to zero. Equation (250) suggests just the same. An homologous series such as this where the energy of excitation tends to zero, is called a divergent series, since the wavelength of the transition tends to infinity. In fact, if (250) were correct, we could say that in the $N \rightarrow V_1$ transition

$$h\nu = 4|\beta| \sin \frac{\pi}{2(N+1)} \approx \frac{2|\beta|\pi}{N+1} \tag{254}$$

since for large N, $\pi/2(N + 1)$ is small, and for small angles $\sin \theta$ may be replaced by θ. This would mean that

$$\lambda = \frac{c}{\nu} \approx (N+1) \times \frac{ch}{2|\beta|\pi} \tag{255}$$

This formula indicates clearly the divergent nature of the series. Experimentally, however, this series is convergent, *i.e.* λ tends to a finite value as the chain increases in length. Table 15 shows some experimental values for this $N \rightarrow V_1$ transition. It is clear from this table that although λ increases with length of chain, its increase is far from linear, as required by (255) and the series does in fact show signs of converging.

There are two reasons for this. First, the formula (255) and Figure 20 are both based on the assumption that the resonance integrals β are the same for all pairs of neighbour carbon atoms. This would be reasonable if all the bond lengths were identical. This seems not to be the case, both experimentally and theoretically. For these polyenes* a degree of bond alternation survives even with long chains. It may be shown that if the resonance integrals are alternately β_1 and β_2 (where $|\beta_1| > |\beta_2|$), then the group of bonding levels in Figure 20 is pushed down, and the group of antibonding ones is pushed up. The $N \rightarrow V_1$ transition will then decrease in energy as the chain length increases, but will tend to a finite value. This can be shown to be $2|\beta_1 - \beta_2|$. Convergence of the series would then be expected.

The second reason for the failure of (255) is neglect of spin. The excited configuration (*a*) of (249) leads to a singlet and a triplet (compare section V.D), and at best our calculations should give the mean of these. It is difficult to calculate the singlet–triplet separation, but we can state that (1) the triplet lies below the singlet, and (2) the separation will decrease as the chain increases, and probably tends to zero for large chains. The values quoted in Table 15 refer, of course to the allowed $N \rightarrow V_1$ singlet transition; the $N \rightarrow V_1$ triplet transition is spin-forbidden. It occurs (see following paragraphs) at about 2500 Å in ethylene, but is very weak.

TABLE 15. $N \rightarrow V_1$ transitions observed in polyene chains.

Molecule	Number of carbon atoms in polyene chain	λ (Å)
Ethylene	2	~ 1630
Butadiene	4	2100
Hexatriene	6	2400
—	12	3700
—	20	4610
—	30	5040

The absorption bands are rather diffuse, and the positions of the maxima are not well defined. There are also displacements due to solution effects. Most of the values in this table are taken from a compilation due to Preuss[38].

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* But not for odd-numbered chains, as in the cyanine dyes, where a formula similar to (255) often fits very well.

B. Ethylene: Rotation Around the Double Bond

We must now return to a rather more detailed study of ethylene. We shall want to know how the energies of the lower states of the molecule depend upon the geometrical shape, more especially the angle of twist of one half of the molecule relative to the other, around the C=C bond. It is probable that racemization of unsymmetrically substituted ethylenes may occur by a mechanism involving one or other of these excited states.

There are two π-electron molecular orbitals built from atomic $2p\pi$ orbitals. They are [see (195), (196)]

$$\begin{aligned} \chi_1 &= (2 + 2S)^{-\frac{1}{2}}(\psi_a + \psi_b), \\ \chi_2 &= (2 - 2S)^{-\frac{1}{2}}(\psi_a - \psi_b). \end{aligned} \tag{256}$$

From these we can build four configurations, of which three are singlets, and one is a triplet. The discussion in section X.A shows that these are:

$$\begin{array}{lllll} N: & \Psi_\pi(^1A_{1g}) & \chi_1^2 = \pi^2 & \text{singlet} & (0) \\ T: & \Psi_\pi(^3B_{1u}) & \chi_1\chi_2 = \pi\pi^* & \text{triplet} & 4{\cdot}6 \\ V: & \Psi_\pi(^1B_{1u}) & \chi_1\chi_2 = \pi\pi^* & \text{singlet} & 7{\cdot}6 \\ Z: & \Psi_\pi(^1A_{1g}) & \chi_2^2 = \pi^{*2} & \text{singlet} & \text{not observed} \end{array} \tag{257}$$

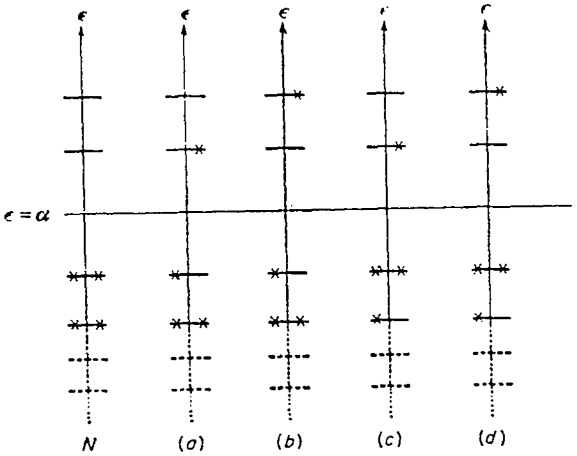

FIGURE 21. Orbital energies for the polyene C_NH_{N+2} (N even) and various ground and excited configurations, according to (249).
The transition $N \rightarrow V_1$ is from N to (a)
The transitions $N \rightarrow V_2$, $N \rightarrow V_3$ are from N to combinations of (b) and (c)
The transition $N \rightarrow V_4$ is from N to (d)

The symbols N, T, V, Z on the left represent a labelling introduced by Mulliken. The second column gives the group-theoretical description, the third column shows the configuration, the fourth column denotes singlet or triplet character, and the final column gives the observed[21] energy of excitation (in ev) relative to the ground state N.

When the molecule is planar, the order of these energies is $N < T < V < Z$; this is the sequence shown in (257). The two B_{1u} levels here labelled T and V correspond to the first excited transition $N \rightarrow V_1$ of section XI.A. The singlet–triplet separation is seen to be 3·0 ev, approximately one-half of the mean excitation energy $\frac{1}{2}(4{\cdot}6 + 7{\cdot}6) = 6{\cdot}1$ ev.

Configuration interaction will somewhat modify the simple descriptions given in the third column of (257), but without doubt the configurations listed are the dominant ones. Atomic $3p\pi$ orbitals, for example, are known[39] to play a part in these electron states, but for the levels shown this is not large.

It is important to realize that in addition to the states listed in (257) there will be more excited levels, called Rydberg levels, arising from the excitation of one of the χ_1 electrons into a higher orbital. If the principal quantum number of the atomic orbitals from which the excited molecular orbital is built up is larger than 2, then the excited orbital will lie outside most of the rest of the molecule, and the orbital itself will closely resemble an excited hydrogen-like orbital. We could therefore describe these excited orbitals as orbitals of a hydrogen-like atom at the centre of the molecule, but slightly perturbed by the $C_2H_4^+$ ion that forms the pseudo-nucleus. Thus there will be transitions in which

$$\begin{aligned} &\pi \rightarrow 3s, 4s, 5s, \ldots \\ &\pi \rightarrow 3d, 4d, 5d, \ldots \end{aligned} \tag{258}$$

as well as others, corresponding to forbidden (or near-forbidden) transitions. The lowest of the excited states described by (258) is the configuration $\chi_1, 3s$ (or simply $\pi, 3s$) resulting from the excitation $\pi \rightarrow 3s$. This configuration will give rise to a singlet and triplet state, according as the two spins are 'antiparallel' or 'parallel'. These are believed to be at energies 7·1 and 6·4 ev respectively above the ground state N. These are the beginnings of Rydberg series, and, in the symbolism of (257) may be labelled R and T_R respectively. The final allocation of energies, when the molecule is planar, is as shown in Figure 22.

This interpolation of the Rydberg-type 3*s* orbital among the familiar excited π-type molecular orbitals has only recently been recognized. Its presence shows how careful one must be, even in an apparently straightforward situation, in characterizing excited states.

It is important to know how the energies of the various states of Figure 22 are influenced by a rotation of one CH_2 group relative to the other. Accurate calculations are not yet available, and so we must proceed somewhat tentatively. A first assumption may be that in such a rotation all the σ bonds remain substantially unaffected, and only the π bond is modified. If this is so, each carbon atom preserves its trigonal hybridization, and we are concerned with only a two-electron problem. The symmetry[40] of the molecule is reduced by the distortion from D_{2h} to D_2, but this does not affect the forms of the allowed molecular orbitals χ_1 and χ_2 in (256). However, the overlap integral S between ψ_a and ψ_b diminishes as the angle of twist θ increases, and is approximately given by

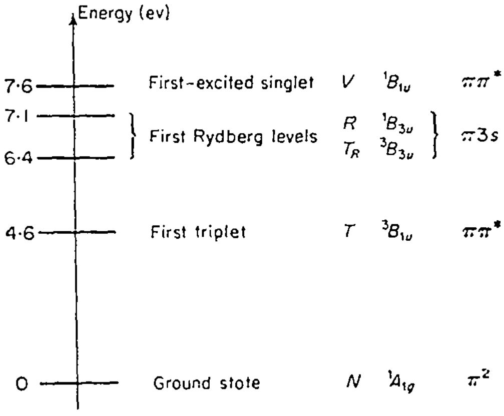

FIGURE 22. Energy levels in planar ethylene.

$$S(\theta) = S(0) \cos \theta. \tag{259}$$

When $\theta = 90°$, so that the planes of the two CH_2 groups are at right angles, $S = 0$.

Just as S varies with θ, so also will the resonance integral β [see equations (211)–(215)], and thus the energies ε_1 and ε_2. We can see that since $|\beta|$ will decrease, probably like S in (259), the energies ε_1 and ε_2 will both tend steadily to the value α as θ increases from 0° to 90°.

The total molecular energies will change in a manner whose general character follows from the changes in ε_1 and ε_2. Thus the ground state N, with representation χ_1^2, will certainly find its energy increasing with θ, in an approximately cosine law. Similarly the state Z, with representation χ_2^2, will drop in energy, since both π electrons will become less antibonding. A more careful analysis is needed, in order to see what happens to the other states. Since $3s$ in (258) will not be expected to change much with θ, the energies of R and T_R will vary similarly to ε_1; they will therefore rise as θ increases. As for T and V, it appears[41] that when all the relevant Coulomb and exchange terms are taken care of, the total energies decrease. Thus the general appearance of the energies as a function of θ is as shown in Figure 23.

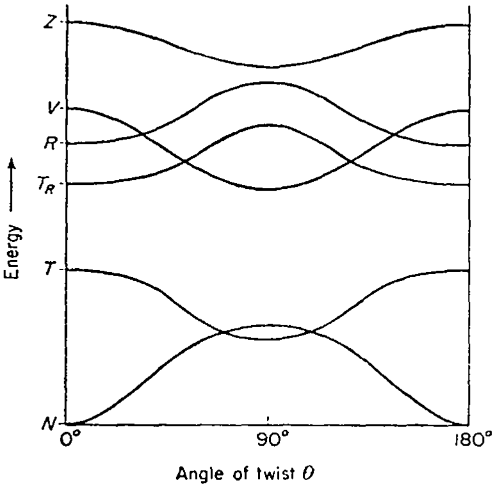

FIGURE 23. Variation of energy levels of ethylene with angle of twist θ around C=C.

It must not be supposed that the detailed energy values implied in Figure 23 are exactly correct. For they are not. But the fact that the N state increases in energy as θ increases, whereas the other π electron states T, V, Z decrease, and R, T_R probably increase, is almost certainly correct. It is also likely that at $\theta = 90°$ ('perpendicular' ethylene) the lowest state is the triplet T state. This may explain how certain racemizations are believed to occur by a triplet mechanism.

Figure 23 provides the basis for any discussion of the influence of substituents in changing the barrier height for rotation around the double bond. We can also see how, if the molecule is in state V, a collision with a mercury atom in the ^3P state could lead to a transition in which spin is interchanged, and the ethylene itself goes into the triplet state T. This represents one of the ways in which fluorescence of an excited molecule may be quenched by metastable Hg atoms.

C. Alkylation of Ethylene: Substituted Alkenes

Let us now consider what happens to the important transition $\pi^2 \rightarrow \pi\pi^*$ (*i.e.* $N \rightarrow V_1$ of the preceding paragraphs) when one of the hydrogen atoms in ethylene is replaced by some other atom (*e.g.* a halogen), or group of atoms (*e.g.* an alkyl group). It will be simplest to begin the discussion by supposing that the substituent is a single atom, such as F, Cl, Br, ... Conventional chemical theory distinguishes two effects, (a) inductive, and (b) mesomeric, or conjugative. Each of these may be translated into the wave-mechanical framework that we have been developing in this chapter, even though detailed calculations are still too complex to be made. This latter limitation means that any theory we propose must inevitably be at best semi-empirical. But we may nevertheless hope to gain considerable insight into the effects of substitution from even simple types of argument. Let us therefore first deal with the inductive effect.

We fix attention on the difference between the two groups H—C═C and X—C═C. The bond X—C will be of σ type, and its polarity will be different from that of H—C. If X is a halogen such as fluorine, the two σ electrons in the X—C bond will be drawn towards the X atom. This will leave the carbon atom more 'bare' of electrons. Any other electrons will therefore be attracted more strongly to it. We should expect this to increase the energy difference between the states N and V, and so lead to a blue (*i.e.* shortwave) shift in the absorption.

An explanation of this blue shift, in the spirit of sections X.A and X.B, is as follows. The enhanced electron-attracting power of the carbon adjacent to the substituent X, may be described by saying that the Coulomb term of this atom is changed from its previous value α to some new value $\alpha - \delta$, where δ is positive. (Note that α is negative, so that $|\alpha - \delta| > |\alpha|$, and we have therefore increased the apparent electronegativity of this atom.) We have thus to consider the energy levels for two π electrons, moving around the two carbon atoms, when the Coulomb terms are $\alpha - \delta$, α and the resonance integral is β. Comparison with equation (229) shows that the energies of the two molecular orbitals are given by the roots of the determinantal equation

$$\begin{vmatrix} \alpha - \delta - \varepsilon & \beta \\ \beta & \alpha - \varepsilon \end{vmatrix} = 0. \tag{260}$$

The roots of this equation are

$$\varepsilon_{\pm} = \alpha - \tfrac{1}{2}\delta \pm \sqrt{(\beta^2 + \tfrac{1}{4}\delta^2)}. \tag{261}$$

If δ is small, we may expand the square root by the binomial theorem. Then

$$\varepsilon_{\pm} = \alpha - \tfrac{1}{2}\delta \pm \left(\beta + \frac{\delta^2}{8\beta} + \dots\right). \tag{262}$$

Putting $\delta = 0$ reduces (262) to the familiar forms (211) and (212)

$$\varepsilon_{\pm} = \alpha \pm \beta. \tag{263}$$

The difference between (262) and (263) is most conveniently illustrated by a diagram. Figure 24 shows how the term $-\tfrac{1}{2}\delta$ in (262) lowers both ε_+ and ε_- by the same amount. Then the term $\delta^2/8\beta$ lowers ε_+ a little further, and similarly raises ε_-. As a result the difference between ε_+ and ε_- becomes increased. In fact

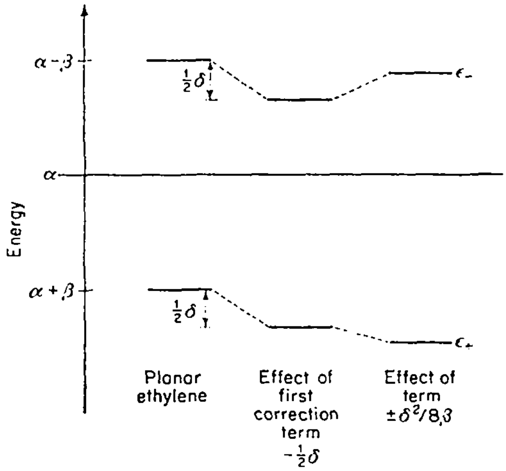

FIGURE 24. Influence of induction parameter δ on orbital energies $\varepsilon_{\pm}$ in ethylene.

$$\varepsilon_- - \varepsilon_+ = 2\sqrt{(\beta^2 + \tfrac{1}{4}\delta^2)} = 2|\beta| + \frac{\delta^2}{4|\beta|} + \text{terms in } \delta^4. \tag{264}$$

This shows that insofar as the difference $\varepsilon_- - \varepsilon_+$ really represents the excitation $N \rightarrow V$, the inductive effect will lead to a shift to higher energies. Further, this shift is proportional to δ^2, so that it should be much more significant for fluorine than for chlorine or bromine.

We now turn to the mesomeric, or conjugative, effect. Here we take into account the possibility that π electrons from the double bond should be able to migrate onto the substituent X, and π electrons from X should migrate into the C═C region. In molecular orbital language we are now interested in the allowed molecular orbitals for the three-centre system X—C═C instead of the old two-centre system C═C.

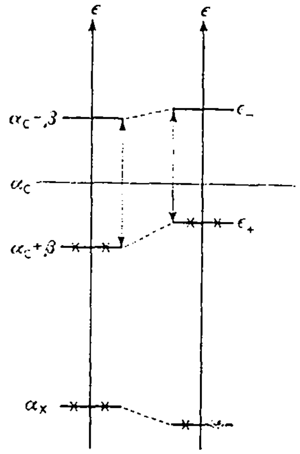

FIGURE 25. Influence of delocalization on ethylene π electron energies. On the left we have the non-conjugated system, and on the right the conjugated one. Crosses denote electrons in the ground state of the system. The arrows describe the $N \rightarrow V_1$ transition.

A full $2p\pi$-electron calculation would now proceed by setting up the determinantal equation of three rows and columns, very much as in equation (229), except that the Coulomb term α_X for the substituent atom will differ from that for a carbon atom α_C. We have seen that in a rough sort of way $|\alpha|$ measures the ionization potential of an atom. So, at any rate for fluorine and chlorine, $|\alpha_X| > |\alpha_C|$. Fortunately, however, we can get a qualitative account of the molecular orbital energies without direct solution of this determinantal equation. Figure 25 shows the situation. First, on the left, we show the energies when we put $\beta_{XC} = 0$. Physically this means that no delocalization of the electrons in the substituent on the double bond is being allowed. Since $|\alpha_X| > |\alpha_C|$, the energy of the X-atom orbitals lies below that of the double bond. (Strictly, of course, we require that $|\alpha_X| > |\alpha_C + \beta|$, rather than $|\alpha_X| > |\alpha_C|$. But this inequality almost certainly holds also.) Now, on the right, we show what happens when we allow delocalization, and effectively mix together the orbitals on the left. A general rule[42] is that when mixing in this way, the energies behaved as if they repelled each other on an energy diagram. This means that the C=C energy ε_+ is pushed upwards by the X energy α_X. This will now lead to a smaller upward movement of ε_-. The result, however, is that the energy difference $\varepsilon_- - \varepsilon_+$ is reduced. There is therefore a shift of absorption towards the red, *i.e.* longwave, region.

It thus appears that the delocalization, or mesomeric, effect causes a shift to the red, but the inductive effect causes a shift to the blue. The resultant shift will depend upon their relative magnitudes. However, we can expect that with fluorine the blue inductive shift will be large. We shall also expect that the red mesomeric shift will be small, since the mutual 'repulsion' of energies involved in Figure 25 decreases markedly when the difference in energies α_X and $\alpha_C + \beta$ is large. It is quite understandable, therefore, that in fluoroethylene the net result is a blue shift, but in chloroethylene, where the inductive shift is smaller and the mesomeric shift is larger, there is a displacement to the red.

Accurate calculations of this type of phenomenon are not worth making at this stage. But it is clear that the analysis of the preceding pages does give insight into the changes in the $N \rightarrow V$ transition as a result of substitution.

To a first approximation additional substitutions should give additive shifts; but inevitably with increasing substitution, a degree of saturation sets in. If required, all this may be demonstrated along the lines of our discussion of the monosubstituted molecule.

There is one other kind of substitution about which more must be said. This is the case of alkyl substitution, already mentioned at the beginning of the present subsection (XI.C). Let us therefore suppose that our previous substituent X is not a halogen atom, but a methyl group. This means that we are discussing propylene $CH_3—CH=CH_2$.

In considering the ultraviolet absorption due to the $N \rightarrow V$ transition, we shall expect to find both the inductive and mesomeric effects just discussed for halogen substitution. Thus a variety of chemical evidence, particularly from a study of the reactions of toluene and other methylated benzenes, suggests that a methyl group appears to push electrons towards the benzene ring. In our previous terminology it exerts an inductive effect opposite in sign to that of the lighter halogens. This, by itself, should lead to a blue shift. But this shift will not be large, because the quantity δ in (260) will be small. Its sign, however, is now negative and not positive.

But there is also a mesomeric effect, due to the fact, first stressed by Mulliken[43], that the $—CH_3$ group can behave as if it were a diatomic radical in which the H_3 group was represented as a single pseudo-atom Y. Then propylene would be

$$Y\equiv C—CH=CH_2 \qquad (265)$$

In (265) we have represented the three H—C bonds of the methyl group as if they were the triple bond, of type $\sigma^2\pi^4$, found in $—C\equiv C—$ or $—C\equiv N$. In the representation (265) we shall have π orbitals associated both with the two carbon atoms of the double bond, and also with the pseudo-atom Y and the methyl carbon. Schematic diagrams of these pseudo π orbitals are given in reference 1, page 362, and need not be reproduced here. All that is needed is that, from this point of view, there are π orbitals in the $Y\equiv C—$ region that can conjugate with the π orbitals of $—CH=CH_2$. There is a close analogy between the bond diagram (265) and the situation in butadiene $H_2C=CH—CH=CH_2$. As a result there will be a delocalization, *i.e.* mesomeric, effect. The magnitude of this effect will depend upon two factors. One is the closeness of the pseudo π electron energy levels of the substituent $Y\equiv C$ to those of the $C=C$ double bond. The other is the magnitude of the resonance integral for the bond joining the two groups. The first factor is probably quite favourable, since the H_3 group in CH_3 is not very different in electronegative character from a single carbon atom. Unfortunately no one knows how serious the second factor is. There is considerable evidence (summarized by Dewar in the book listed in reference 43) to suggest that the length of this bond shows only a little shortening—or even no shortening at all—below that for a pure single bond. This would imply a small numerical value for the important resonance integral, and consequently a small conjugative effect.

The situation may therefore be summarized by saying that methyl substitution leads to (*a*) a small blue inductive shift, and (*b*) a small red conjugative shift. It seems that the conjugative shift is the larger, for methylation of ethylene changes the $N \rightarrow V$ transition from 7·6 to 7·1 ev. The last row of Table 16 shows that increasing the number of methyl substituents leads to progressive reduction in the excitation energy, though a saturation effect is also noticeable.

TABLE 16[a]. Ionization potentials in ev of methyl-substituted ethylenes ($C_2H_{4-n}Me_n$).

Number of methyl groups (n)	0	1	2[b]	3	4
Ionization potential:					
ground state	10·51	9·73	9·13	8·68	8·30
excited state	2·9	2·6	2·2	1·9	1·7
Difference ($N \rightarrow V$ energy)	7·6	7·1	6·9	6·8	6·6

[a] Quoted, by permission, from ref. 1, p. 358.

[b] These figures refer to the *cis*-butene.

The next point concerns ionization potentials. We have already seen that—subject to many qualifications and approximations—the energy value ε_+ is a measure of the ionization potential for a π electron in the orbital χ_1. This value will be influenced by both the inductive and conjugative effects. Formula (262) shows that the inductive effect changes the ionization potential from

$$|\alpha + \beta| \text{ to } \left|\alpha + \beta - \tfrac{1}{2}\delta + \frac{\delta^2}{8\beta}\right|.$$

For methyl substitution, α, β, and δ are all negative, so that the ionization potential is reduced by an amount

$$-\tfrac{1}{2}\delta + \frac{\delta^2}{8\beta}. \tag{266}$$

The mesomeric influence is less easy to formulate. But it follows from Figure 25 that the ionization potential is reduced further because of it. The experimental values are shown in Table 16, and fit very nicely with this general argument.

Our discussion above has been concerned with ionization potentials, and their change due to substitution. We have not been concerned with total molecular energies. Indeed a moment's reflection back to some of the difficulties discussed earlier in this chapter will soon convince us that there is at present no reasonable hope of significant *ab initio* calculations of total energies. But if we use the symbol ΔI.P. to denote the change in ionization potential resulting from substitution of the parent ethylene, then we may write

$$\Delta\text{I.P.} = S^* - S, \tag{267}$$

TABLE 17[a]. Stabilization energies S and S^* for substituted ethylenes.

Substituents	S (kcal/mole)	S^* (kcal/mole)
Methyl	2·67	20·6
Ethyl	2·28	23·7
Propyl	2·59	25·8
n-Pentyl	2·60	26·8
1,1-Dimethyl	5·51	35·1
cis-1,2-Dimethyl	4·0	35·9
trans-1,2-Dimethyl	5·1	37·0
Trimethyl	7·9	50·2
Tetramethyl	8·7	59·8

[a] Largely the work of W. C. Price and his colleagues, as summarized by D. W. Turner[44].

where S and S^* represent the stabilization energies conferred on the molecule and ion respectively by the substitution. Values of S and S^* are shown in Table 17. Both S and S^* increase with increasing substitution, and both show a saturation effect. The stabilization of the ion is very much greater than that of the parent molecule, a situation related to the well-known fact that hyperconjugation is far more effective in cations than in neutral molecules. There are certain features in this table, such as the differences between the three isomeric dimethyl ethylenes, which clearly depend upon long-range effects. But the qualitative features are all very understandable in terms of the ideas developed earlier.

This is the place at which to stop the theoretical account of this chapter. Subsequent chapters will show how individual features of our survey are extended and applied in particular aspects of the chemistry of the alkenes. The characteristic features of this group of molecules are the result of their having two electrons (the π electrons) in orbitals less tightly bound than most molecular electrons, whose shape is characteristically different from the more usual σ electrons, whose charge-cloud is more easily polarized by an attacking charge or dipole to form $\overset{\delta+}{\mathrm{C}}\text{—}\overset{\delta-}{\mathrm{C}}$, and whose directional power to hold the double-bond region coplanar allows all sorts of chemical situations to arise and be understood. Here surely quantum chemistry has made a highly significant contribution to our total chemical insight.

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 2

Elimination reactions in solution

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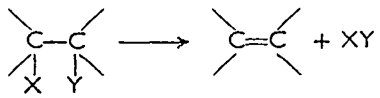
I. INTRODUCTION

Nearly all olefin-forming elimination reactions of any theoretical or synthetic importance are β-eliminations, in which two groups are lost from adjacent carbon atoms (equation 1). One of these groups is usually a hydrogen. Although eliminations from 1,2-dihalides and related compounds may be brought about by a metal or by

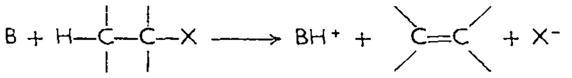


(1)

iodide ion, they are of little practical interest, as the dihalide is almost always obtained by addition of a halogen to an olefin. The present review will concentrate on the mechanisms of β-elimination of HX and the various factors influencing reactivity, though some attention will be given to synthetic applications. The same general area has been treated in recent years by a number of authors[1–5]. Ideas and references furnished by them have been very useful in the present effort to provide an up-to-date account.

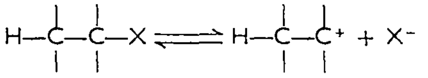
At least half a dozen mechanisms for olefin-forming eliminations have some current credibility, and all of these will be discussed in later sections. By far the larger number of elimination reactions appear to involve either of two of these mechanisms, the *E*1 and the *E*2. Both the terminology and much of our fundamental knowledge of these reactions are due to Hughes, Ingold, and their collaborators.

*E*2 means 'elimination, bimolecular', and is so called because it involves a single-step reaction of a molecule of base with a molecule of substrate (equation 2). The example is given for the case where the base B and the leaving group X are neutral, though the base may be negatively charged and/or the leaving group positively charged as well. The reaction is normally first order in substrate and first order in base.

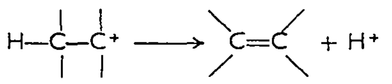


$$\mathrm{B + H{-}C{-}C{-}X \longrightarrow BH^+ + {>}C{=}C{<} + X^-} \qquad (2)$$

*E*1 means 'elimination, unimolecular', and occurs when certain substrates are placed in ionizing solvents (equations 3–4). Here the reaction occurs in two stages, and no added base is necessary.



$$\mathrm{H{-}C{-}C{-}X \rightleftharpoons H{-}C{-}C^+ + X^-} \qquad (3)$$



$$\mathrm{H{-}C{-}C^+ \longrightarrow {>}C{=}C{<} + H^+} \qquad (4)$$

Synthetically useful elimination reactions are found in both categories. Particularly prominent are the *E*2 reactions of alkyl halides and tetraalkylammonium salts, and the acid-catalyzed *E*1 dehydration of alcohols. More is to be gained by covering general principles rather than specific procedures, so most of the chapter will be devoted to the various mechanisms and their areas of applicability.

II. MECHANISMS AND STEREOCHEMISTRY

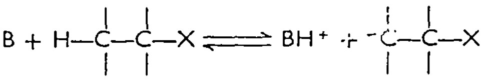
A. The E2 Mechanism

This mechanism was first suggested by Hanhart and Ingold[6] for the Hofmann decomposition of quaternary ammonium hydroxides to olefins and tertiary amines. The reaction was shown to be second order, first order in the tetraalkylammonium ion and first order in hydroxide ion[7]. The wide applicability of the reaction has been demonstrated kinetically, and an even wider range of qualitative examples is available.

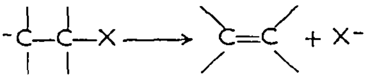
The bases usually employed are hydroxide or alkoxide ions, though others of different charge types and of a wide range of strengths have been tried in some instances. A popular synthetic procedure calls for the action of ethanolic potassium hydroxide on an alkyl halide. More recently, higher alkoxides have been used increasingly[8], and have some advantage with compounds, such as tertiary alkyl halides, that are prone to react by the *E*1 mechanism in ethanol or water.

The positively charged leaving groups may be trialkylammonium[6,7], trialkylphosphonium[9–11] (though phosphonium hydroxides usually give a saturated hydrocarbon and a phosphine oxide rather than an olefin and a phosphine), or dialkylsulfonium[12]. The numerous uncharged leaving groups include bromide[13], chloride[14], iodide[15], fluoride[16,17], arylsulfonate[18,19], sulfone[20], and hindered carboxylate[21]. Ethers are inert to normal *E*2 conditions, but may be cleaved by the action of some organometallic compounds[22]. Isolated examples of still more leaving groups may be found in the literature.

The description of the *E*2 reaction in the Introduction states that it is a single-stage process, but no evidence given so far compels this conclusion. The mechanism of equations (5) and (6) predict the same kinetic dependence upon substrate and base. Ingold has called this the *E*lcB mechanism (elimination, unimolecular, from the conjugate base of the substrate).



$$\mathrm{B} + \mathrm{H}-\overset{|}{\underset{|}{\mathrm{C}}}-\overset{|}{\underset{|}{\mathrm{C}}}-\mathrm{X} \rightleftharpoons \mathrm{BH}^{+} + {}^{-}\overset{|}{\underset{|}{\mathrm{C}}}-\overset{|}{\underset{|}{\mathrm{C}}}-\mathrm{X} \qquad (5)$$



$$ {}^{-}\overset{|}{\underset{|}{\mathrm{C}}}-\overset{|}{\underset{|}{\mathrm{C}}}-\mathrm{X} \longrightarrow {>}\mathrm{C}{=}\mathrm{C}{<} + \mathrm{X}^{-} \qquad (6)$$

A reliable distinction between the *E*2 and *E*lcB mechanisms is possible if the reversal of reaction (5) occurs at a rate comparable to or greater than that of reaction (6). Under this circumstance some carbanion reverts to starting material, and the starting material exchanges its β-hydrogen with the solvent. Such exchange can be detected by labeling either the starting material or the solvent with deuterium or tritium, followed by examination of the remaining starting material after part of it has reacted. Skell and Hauser[23] demonstrated that 2-phenylethyl bromide reacted with ethoxide in deuteroethanol with no uptake of deuterium by the halide. Since then, the exchange criterion has been applied to a number of typical *E*2 reactions, including other alkyl halides[24], sulfonium salts[25], and ammonium salts[26]. No exchange was noted in any of these examples.

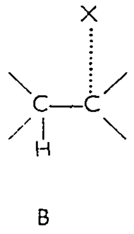
This method cannot detect a carbanion which goes on to products much more rapidly than it reverts to starting material. Other methods of distinguishing the *E*1cB from the true *E*2 mechanism depend upon indirect arguments and are notably less trustworthy. One might, for example, attempt to decide whether the reaction was faster than could be reasonably expected for simple proton removal without any driving force from C—X cleavage. This point will be discussed more thoroughly in connection with the stereochemistry of the reaction (section II.5).

Some possible examples of the *E*1cB mechanism have been subjected to exchange experiments. Cristol and Fix[27] found a very small amount of exchange in the dehydrohalogenation of the β-stereoisomer of benzene hexachloride, where a normal *trans* elimination is impossible. Much more extensive exchange is found in dehydrohalogenation of 2,2-dihalo-1,1,1-trifluoroethanes[28]. Unsaturated halides appear to be rather prone to the *E*1cB reaction[29]. Recently the decomposition of Michael adducts was shown to proceed *via* carbanion intermediates[30]. These examples suggest that the *E*1cB mechanism will operate only when the *E*2 reaction is hindered by factors such as a poor leaving group or unfavorable stereochemistry.

Even when no discrete intermediates occur, there is still room for considerable variation within the scope of the *E*2 reaction. During the reaction a C—X bond breaks, a C—H bond breaks, a double bond forms, and a base-hydrogen bond forms. Until recently these processes were generally considered to be synchronous. The original paper of Hanhart and Ingold[6] implies that this is not necessarily so, and other suggestions of a variable transition state for

*E*2 reactions have been made[31]. Only recently, however, has specific experimental evidence been adduced for this viewpoint.

While the *E*2 reaction may be completely synchronous in many instances, with a transition state like **2**, transition states in which C—X or C—H bond breaking has taken precedence may also be envisioned. These latter two cases are represented by **1** and **3**, respectively. One thus has a spectrum of possible transition states,



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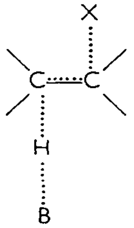

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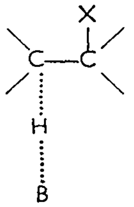
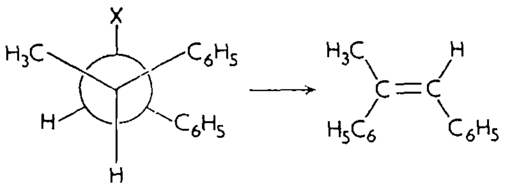


(3)

ranging from one similar to that of the *E*1 reaction (**1**) all the way to one similar to that of the *E*1cB reaction (**3**). A transition state like **1** will have carbonium-ion character at the α-carbon, and one like **3** will have carbanion character at the β-carbon. In addition, different amounts of double-bond character may occur in different examples of **2**, depending upon how far the synchronous breaking of the C—H and C—X bonds has progressed. Obviously the stereochemical and electronic character of the transition state will, in this picture, be subject to considerable variation.

Clear evidence that the geometry of the transition state is not constant was provided by studies of eclipsing effects[32]. The *threo* and *erythro* isomers of the 1,2-diphenyl-1-propyl-X system were used. In a normal *trans* elimination these would give the *trans* (equation 7) and *cis* (equation 8) isomers of α-methylstilbene, respectively. The *threo* and *erythro* compounds differ little in stability, while the *trans* olefin is at least fifty times more stable than the *cis*. Consequently, a reaction in which the transition state resembles olefin **2** should proceed up to about 50 times faster with the *threo* isomer than with the *erythro*. There should be little difference in rate between the diastereomers for a reaction in which the geometry of the transition state is closer to that of the reactant. Transition states **1** and **3** both should resemble reactant in geometry.



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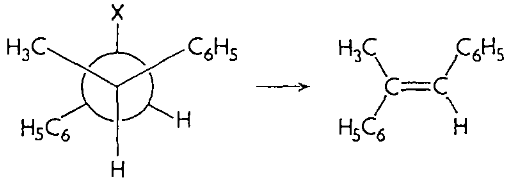


(8)

The bromide and the chloride with ethoxide ion in ethanol both show $k_{threo}/k_{erythro}$ ratios near one, and it was concluded that the transition state resembles **1**. Changing the leaving group to $N(CH_3)_3$ raises the ratio to 57, which was interpreted as increased eclipsing and hence a transition state like **2**. Changing the solvent to *t*-butanol and the base to *t*-butoxide increases the ratio to 5·4 for the bromide and 15 for the chloride. A more eclipsed transition state is again indicated, but whether the change of base or of solvent is primarily responsible is not entirely clear. This point will be discussed more extensively in section III.F.

Another way of detecting a variable transition state is a study of electronic effects of substituents, which should change as the electron distribution in the transition state changes. Qualitative examples of this behavior could be adduced, but it is best illustrated in the 2-phenylethyl system. Here electronic effects can be varied without steric complications by placing *meta* and *para* substituents on the phenyl group. The reactions of *m*- and *p*-substituted benzene derivatives can often be correlated by the Hammett equation (equation 9)[33,34], where k is the rate or equilibrium constant for the substituted, and k_0 the rate or equilibrium constant for the

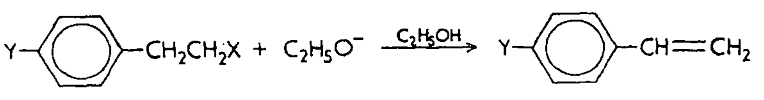
$$\log (k/k_0) = \rho\sigma \tag{9}$$

unsubstituted compound. The substituent constant, σ, is characteristic of the substituent only and the reaction constant, ρ, of the reaction only. Since σ is defined as positive for electron-withdrawing and negative for electron-repelling substituents, ρ will be positive if the reaction is favored by electron withdrawal. Further, electron-withdrawing substituents should favor reactions in which there is an increase in electron density at the reaction site in the transition state, and hinder reactions for which the converse is true. In the 2-phenylethyl system, the sign and magnitude of ρ therefore should measure the electron density at the β-carbon in the transition state relative to the ground state.

Values of ρ for reaction (10) have been determined as a function of the leaving group X and are given in Table 1. The increasingly positive values of ρ suggest that the poorer the leaving group, the greater the carbanion character of the transition state. The β-phenyl group alone will provide considerable stabilization of a carbanion-like β-carbon. Thus, though the order of the leaving groups should remain constant, a shift to less carbanion character is expected for simple alkyl derivatives. Even in the 2-phenylethyl system a discrete carbanion intermediate is shown to be improbable by the absence of deuterium exchange[25]. An uncertainty in interpreting these ρ values is that we are not sure of the value to be

TABLE 1. Hammett-reaction constants for the reaction for 2-arylethyl derivatives with sodium ethoxide in ethanol at 30°c.

Leaving group, X	ρ	Reference
I	+2·07	15
Br	2·14	15
Br	2·15	35
OTs	2·27	19
Cl	2·61	16
$S(CH_3)_2$	2·64	35
$S(CH_3)_2$	2·75	15
F	3·12	16
$N(CH_3)_3$	3·77	36



(10)

expected for a completely concerted reaction. Though no change in charge occurs at the β-carbon in such a case, a change in electron affinity does accompany the change from sp^3 to sp^2 hybridization[37]. The effect of changing the base and the solvent in the reactions of 2-phenylethyl derivatives has also been studied, but the interpretation of the results is more complex and will be discussed later (section III.6).

The methods described so far give an overall picture of the transition state. Thus, Cram's approach indicates the degree of eclipsing, and substituent effects the amount of disparity between C—X and C—H bond breaking. Isotope effects provide us with a means of fixing our attention on individual bonds in the transition state. With deuterium or tritium isotope effects the C—H bond can be examined, and with other isotope effects (such as sulfur or nitrogen) the C—X bond is accessible.

The presence of a substantial deuterium isotope effect in the reaction of isopropyl-d_6 bromide with ethoxide ion in ethanol was demonstrated by Shiner[38]. Later investigations have considered the variation of isotope effect with changes in structure and reaction conditions. Before these are discussed, the qualitative theory of isotope effects in proton transfers will be outlined. For purposes of this discussion, the $E2$ reaction may be treated as a simple proton transfer (equation 11). For this model, the motion along the reaction coordinate is represented by an asymmetric stretching vibration. This leaves the transition state with one real symmetric stretching vibration. If H is equally bonded to A and B, it will not move appreciably in the symmetric vibration. Hence, replacing the H by D will not alter the zero-point energy of this vibration.

$$\mathrm{B + HA \longrightarrow \underset{\text{Transition state}}{[B\cdots\cdots H\cdots\cdots A]} \longrightarrow BH + A} \tag{11}$$

$$\underset{\text{Asymmetric stretch}}{\overset{\rightarrow}{\mathrm{B}}\cdots\cdots\overset{\leftarrow}{\mathrm{H}}\cdots\cdots\overset{\rightarrow}{\mathrm{A}}} \qquad\qquad \underset{\text{Symmetric stretch}}{\overset{\leftarrow}{\mathrm{B}}\cdots\cdots\mathrm{H}\cdots\cdots\overset{\rightarrow}{\mathrm{A}}}$$

The isotope effect then will be essentially that predicted for complete loss of the H—A stretching vibration of the reactant (k_H/k_D around 7 at room temperature). If H is more tightly bound to A than to

B, or to B than to A, the difference in zero-point energy of the isotopic transition states will partly cancel the corresponding difference for the isotopic reactants, and a *lower* isotope effect will result[39]. Alterations in bending vibrations between reactant and transition state might complicate the picture, but are probably not of great importance. Even though the H—A bond is loosened in the transition state, the bonding of H to both A and B probably constrains lateral motion about as much as a full A—H bond.

Isotope effects for a number of elimination reactions in the 2-phenylethyl system (equation 12) are recorded in Table 2[25]. The order of k_H/k_D with respect to leaving group is Br > OTs > $S(CH_3)_2$ > $N(CH_3)_3$. This might represent a case in which the H

$$C_6H_5CD_2CH_2X + OR^- \xrightarrow{ROH} C_6H_5CD{=}CH_2 + X^- + ROD \qquad (12)$$

is less than half transferred in the transition state and the extent of C—H stretching becoming progressively less along the series, but more probably the hydrogen transfer is past the half-way point and most nearly complete for trimethylammonium. This latter interpretation accords better with the order of ρ values (see above), which suggests increasing advantage of C—H over C—X bond cleavage along the same series. The *E*2 reaction of benzyldi-

TABLE 2. Isotope effects in the elimination reactions of 2-phenylethyl derivatives at 30°c.

Leaving group, X	Solvent[a]	k_H/k_D
Br	Ethanol	7·1
Br	*t*-Butanol	7·9
OTs	Ethanol	5·7
OTs	*t*-Butanol	8·0
$S(CH_3)_2$	Ethanol	5·1
$S(CH_3)_2$	Water	5·9[b]
$N(CH_3)_3$	Ethanol	3·0[c]
$N(CH_3)_3$	50% Ethanol/water	3·0[c]

[a] The base was always the conjugate base of the solvent.
[b] Extrapolated from data at 60, 70, and 80°.
[c] Determined at 50°. Value at 30° expected to be *ca.* 3·5.

methylcarbinyl chloride with sodium methoxide probably is an example of a proton transfer that has not yet reached the half-way point[40]. The deuterium isotope effect in elimination toward the benzyl carbon is only 2·6, and the tertiary α-carbon should favor a transition state with much C—Cl stretching (structure **1**).

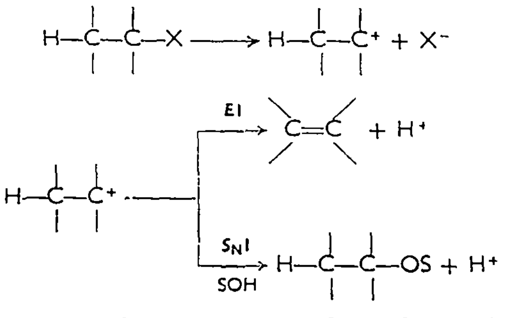
The isotope effect on C—X bond cleavage has been examined in a few cases. The $^{32}S/^{34}S$ isotope effect was found to be very small (0·15% slower for the heavier isotope) in the reaction of 2-phenylethyldimethylsulfonium ion with hydroxide ion at 60°c[41]. This was much smaller than the 1·8% effect observed in the hydrolysis of *t*-butyldimethylsulfonium ion at 60°c, an S_N1 reaction in which C—S cleavage is certainly far advanced in the transition state. The small effect in the *E*2 reaction is consistent with a high degree of carbanion character for the transition state. More recently, the solvolysis of *t*-butyldimethylsulfonium ion in ethanol at 40°c gave a 1·0% sulfur isotope effect, while the *E*2 reaction of the same substance with ethoxide ion (the solvolysis can be rendered negligible at high base concentrations) has a sulfur isotope effect of 0·7%[42]. One would expect more C—S cleavage with a tertiary than with a primary α-carbon, and also more C—S cleavage with a solvolytic than with an *E*2 reaction of the same substrate. The only surprising feature is the considerable difference between the solvolytic reaction in water and in ethanol. The theory of isotope effects predicts an effect of about 1·5% for complete loss of a C—S stretching vibration. No new bonds to sulfur are formed, so this simple model should correspond to the maximum sulfur isotope effect.

These changes in sulfur isotope effect with changes in reactants and conditions provides further evidence for the variable transition state. Later (sections II.E and III.A) data on nitrogen isotope effects, which also support the general picture, will be discussed.

The main problems with the variable transition state now are associated with predicting the effect of a given structural change and correlating the various criteria of transition-state structure. As will be seen, different experimental approaches occasionally give results that appear mutually contradictory, or that disagree with theoretical expectations. Another uncertain area is the range of application of steric effects and the manner in which they operate. While these ambiguities indicate the need for more work, they do not detract from the general validity of the variable transition state.

B. The E1 Mechanism

This mechanism was first proposed by Hughes[43]. It is not an independent mechanism in the same sense as the *E*2 reaction, since it shares its rate-determining step with the S_N1 reaction:



(13)

(14)

(15)

Here SOH represents solvent, though the substitution may also be by other nucleophiles present. No effort will be made to cover unimolecular solvolyses, except as they relate directly to eliminations, for the general field is much too large and complex.

The types of compounds that will undergo *E*1 reaction are broadly similar to those that undergo the *E*2. In some cases the same compound can be made to react by either mechanism, depending upon conditions. A discussion of the influence of structure and environment will be given later. For the present, it will suffice to say that circumstances promoting carbonium-ion formation favor the *E*1 reaction. Among compounds that react by the *E*1 mechanism are alkyl halides[44], trialkylsulfonium salts[45], and sulfonate esters[46]. Recently, some tetraalkylammonium salts[47] have been found to be capable of undergoing *E*1 reactions.

Much less information on details of mechanism is available in the *E*1 than in the *E*2 reaction. The role of ion pairs in solvolytic reactions has been studied intensively in recent years[48]. Evidence that the intermediacy of ion pairs noticeably affects the course of *E*1 reactions has just been found. The elimination–substitution ratio in solvolysis of alkyl halides is much higher in glacial acetic acid and in absolute ethanol (solvents favoring ion pairs) than in water. In water the olefin yield is independent of the nature of the leaving group (Cl, Br, I, and $S(CH_3)_2$), but in acetic acid and ethanol varies widely (from 12% for $S(CH_3)_2$ to 73% for Cl in acetic acid)[48b]. No such variation had been noted in earlier work in ethanol–water mixtures[49–51]. Ion pairs seem to be involved only in less ionizing solvents.

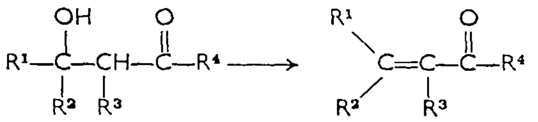
Another possible complication lies in the nature of the carbonium ion itself. Usually we assume that elimination occurs from a normal classical carbonium ion, but examples of bridged, 'non-classical' carbonium ions are now known. The mode of formation of olefinic product in the solvolysis of 3-phenyl-2-butyl *p*-toluenesulfonate, where the substitution products seem to come from bridged ions, has been discussed by Cram. He suggests that the olefin arises from classical ions[52] (see section II.E). Sufficient evidence for useful generalizations is not available.

Since the intermediate in *E*1 reactions is a carbonium ion, the possibility that rearrangements will occur must always be kept in mind. This is a part of the much larger field of carbonium-ion rearrangements, which has been the subject of recent reviews[53-57]. In general, a carbonium ion that can give a substantially more stable isomeric carbonium ion by a 1,2-shift will often do so. The opportunity for rearrangement is greatly increased if the reaction is a reversible one such as the acid-catalyzed dehydration of alcohols. For these reasons, *E*1 reactions are usually not suitable preparative procedures when highly pure product of unequivocal structure is desired.

One might expect the deuterium isotope effect to give useful information on the behavior of the carbon–hydrogen bond, just as it does in the *E*2 reaction. Some loosening of this bond occurs in the ionization step, since each β-deuterium atom diminishes solvolysis rates by about 10–30%[58,59]. The bond loosening is usually considered to arise from interaction of the carbon–hydrogen bonding electrons with the vacant *p* orbital of the carbonium ion, but the exact nature of this interaction has been the subject of some dispute. In the product-forming step, k_H/k_D ratios of up to 3·1 have been noted with *t*-amyl derivatives[60]. These relatively low ratios probably indicate a transition state in which transfer of the proton to a solvent molecule has not reached the half-way point. A transition state close to reactant is expected if the reactant is a high-energy species such as a carbonium ion[61].

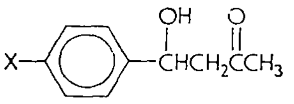
Carbonium ions from non-solvolytic sources may, of course, also decompose to olefin. The acid-catalyzed dehydration of alcohols appears to involve carbonium-ion intermediates, though some aspects of the mechanism are not thoroughly understood. Taft and his coworkers have made extensive mechanistic studies of the dehydration and its reverse, the hydration of olefins[62]. The dehydration of secondary alcohols likewise appears to involve carbonium ions[63]. The carbonium ion is undoubtedly produced from a protonated alcohol molecule ROH_2^+, but how free the ion is and the role played by solvent in the elimination are not clear.

The second stage of condensation reactions frequently involves dehydration of an alcohol β to a carbonyl group:



$$R^1\text{—}\underset{R^2}{\overset{OH}{C}}\text{—}\underset{R^3}{CH}\text{—}\overset{O}{\overset{\|}{C}}\text{—}R^4 \longrightarrow (R^1)(R^2)C{=}\underset{R^3}{C}\text{—}\overset{O}{\overset{\|}{C}}\text{—}R^4 \qquad (16)$$

The dehydration of β-aryl-β-hydroxy acids appears to proceed *via* a carbonium ion[64,65]. The isotope effect on proton loss, k_H/k_D, is 2·8, similar to those found in simple *E*1 reactions[66]. The carbonium-ion mechanism applies to β-hydroxy ketones only when a particularly stable carbonium ion is involved. More often, the dehydration proceeds *via* the enol. For example, **4** gives a carbonium ion when X is methoxyl, but not when it is hydrogen or nitro[67].



(4)

The deamination of aliphatic amines by nitrous acid also leads in part to olefin, presumably *via* the diazonium ion RN_2^+ and/or a carbonium ion[68]. The product proportions are often different from those produced by solvolytically generated carbonium ions, and in some cases cyclopropanes as well as olefins result[69,70]. An apparently related reaction is the interesting 'deoxideation' of alcohols by treatment with a haloform and base[71].

Another *E*1 reaction of some mechanistic and practical interest is the action of thionyl chloride on alcohols. The initial stage of this reaction is formation of an alkyl chlorosulfite which then decomposes to olefin and alkyl chloride (equations 17–19).

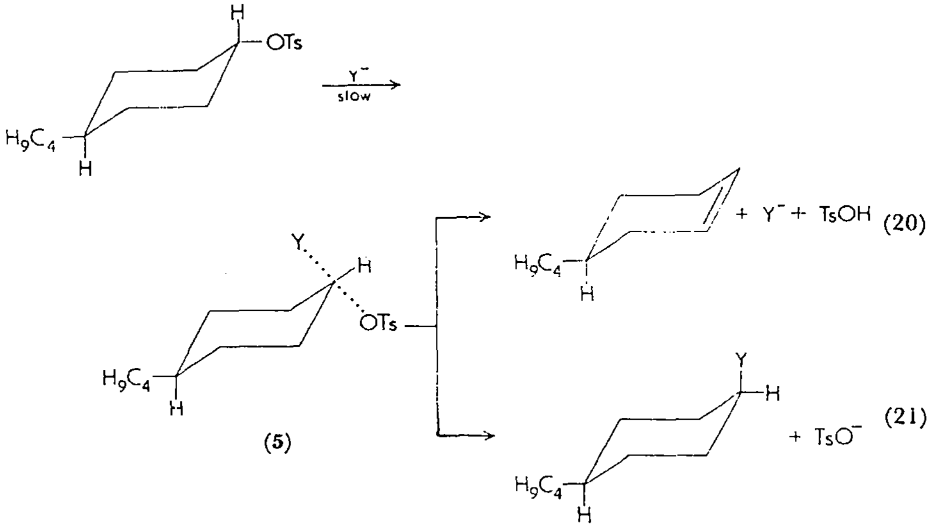
$$ROH + SOCl_2 \text{ ——— } ROSOCl + HCl \qquad (17)$$

$$ROSOCl \text{ ——} \begin{cases} \longrightarrow \text{olefin} + HCl + SO_2 & (18) \\ \longrightarrow RCl + SO_2 & (19) \end{cases}$$

The decomposition appears to go *via* a carbonium ion or an ion pair[72,73].

C. Mechanisms on the E1–E2 Borderline

The transition state for an *E*2 reaction usually will be shifted in the *E*1 direction (more C—X cleavage, less C—H cleavage) by change to a better leaving group, a weaker base, a more ionizing solvent, or a more highly substituted α-carbon. Eventually a point will be reached at which C—X cleavage no longer requires the driving force of concomitant C—H cleavage, and then the reaction goes over to the *E*1 mechanism. There will thus be a region of mixed-order kinetics, in which some individual molecules decompose with the aid of base, and others without. In this region the *E*2 reactions will show a dependence very similar to the *E*1 reactions on structural and environmental factors. Conversely, one can imagine reactions which appear kinetically to belong to the *E*1 category, but are mechanistically *E*2 with solvent molecules functioning as bases. There has been little systematic investigation of this intermediate area.



(5)

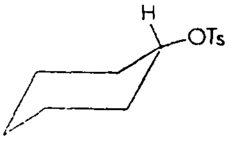
(20)

(21)

A suggestion that still another mechanism may operate has been advanced by Winstein[74]. The reaction of *cis*- and *trans*-4-*t*-butylcyclohexyl *p*-toluenesulfonate with halide ions in acetone was studied. The reactions were kinetically second order, and substantial proportions of elimination were observed with both isomers. Since the bulky *t*-butyl group constrains the leaving group to an equatorial position in the *trans* isomer and an axial position in the *cis* isomer, one would expect the stereochemistry to be far more favorable for an $E2$ reaction in the latter case (see section II.E). In addition, there was no correlation of elimination rate with basicity of the anion.

These facts led Winstein to suggest a 'merged' mechanism in which substitution and elimination occur from a common intermediate (equations 20 and 21). Here the intermediate **5** is viewed as being very much like the carbonium ion of the $E1$ mechanism, except it is 'solvated' by Y^- and TsO^- rather than by a solvent molecule and TsO^-, or by two solvent molecules. Thus, one would expect the elimination/substitution ratio to depend primarily on the nucleophilicity rather than the basicity of the anion.

This mechanism was adopted by Eliel and Ro[75,76] to explain their results on the reaction of thiophenoxide ion with **6** and **7**. Both react at nearly the same rate, but **6** gives 45% of olefin while **7** gives entirely substitution product. They suggested that the rates were



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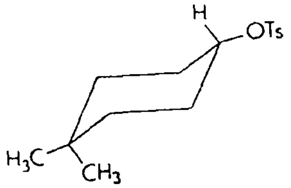


(7)

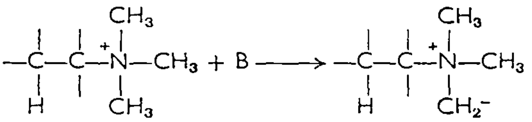
similar because of a common rate-determining step, but in **7** the subsequent attack on a β-proton was hindered by the methyl groups. The results of de la Mare and Vernon[77], who found that *t*-butyl chloride gave isobutylene ten times faster with thiophenoxide than with ethoxide ion, were also considered explicable by the merged mechanism. Though thiophenoxide is less basic than ethoxide it is more nucleophilic, so the result is just as expected for a rate-determining nucleophilic attack. A merged mechanism has also been suggested for the elimination reactions that occur when α-haloketones are treated with amines or bromide ion in non-hydroxylic solvents[78].

Up to the present, no really conclusive evidence for the merged mechanism is available. Certain observations are better accommodated by it than by more conventional means, but they do not require it. Bunnett[5] argues that a key piece of evidence, the unusual effectiveness of weak bases in promoting reaction, is unconvincing because kinetic basicity need not parallel equilibrium basicity, and that little is known about basicities in the non-polar solvents used for many presumed examples of the merged mechanism. In view of these objections, the applicability of the merged mechanism must be regarded as uncertain.

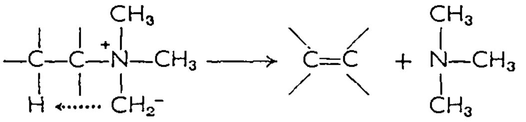
D. Miscellaneous Mechanisms

In addition to the major mechanisms already outlined, other mechanisms have been suggested to apply to elimination reactions in special circumstances. So far there is no evidence that these mechanisms are of general occurrence, but they are certainly worth mention.

The α'–β mechanism for 'onium salts, first suggested by Wittig[79], involves the abstraction of an α-proton (equation 22) to give an ylide, which then attacks a β-proton of another alkyl group (equation 23) to complete the reaction.

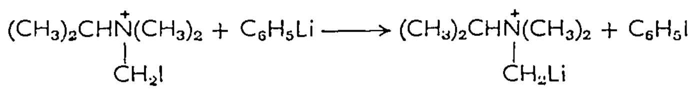


$$-\overset{|}{\underset{\mathrm{H}}{\underset{|}{\mathrm{C}}}}-\overset{|}{\underset{|}{\mathrm{C}}}-\overset{\mathrm{CH_3}}{\underset{\mathrm{CH_3}}{\overset{+}{\mathrm{N}}}}-\mathrm{CH_3} + \mathrm{B} \longrightarrow -\overset{|}{\underset{\mathrm{H}}{\underset{|}{\mathrm{C}}}}-\overset{|}{\underset{|}{\mathrm{C}}}-\overset{\mathrm{CH_3}}{\underset{\mathrm{CH_2^-}}{\overset{+}{\mathrm{N}}}}-\mathrm{CH_3} \qquad (22)$$

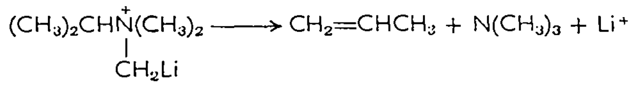


(23)

The basis of this suggestion was the observation that an ylide can be made by metallation (equation 24) as evidenced by the presence of iodobenzene among the final products. The other products, propylene and trimethylamine, were presumed to have been formed *via* an α'–β elimination (equation 25).



$$(\mathrm{CH_3})_2\mathrm{CH}\underset{\mathrm{CH_2I}}{\overset{+}{\mathrm{N}}}(\mathrm{CH_3})_2 + \mathrm{C_6H_5Li} \longrightarrow (\mathrm{CH_3})_2\mathrm{CH}\underset{\mathrm{CH_2Li}}{\overset{+}{\mathrm{N}}}(\mathrm{CH_3})_2 + \mathrm{C_6H_5I} \qquad (24)$$

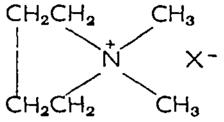


$$(\mathrm{CH_3})_2\mathrm{CH}\underset{\mathrm{CH_2Li}}{\overset{+}{\mathrm{N}}}(\mathrm{CH_3})_2 \longrightarrow \mathrm{CH_2{=}CHCH_3} + \mathrm{N(CH_3)_3} + \mathrm{Li^+} \qquad (25)$$

A normal $E2$ reaction with phenyllithium functioning as base can be excluded, as this would have produced benzene rather than iodobenzene. Attack of phenyllithium on isopropyltrimethylammonium iodide also gave elimination, and by analogy was suggested to involve initial removal of an α-proton, again followed by reaction (25).

Further examples of eliminations induced by organometallic compounds have been presented in subsequent papers[80-82]. Butyllithium and potassium amide have been tried as bases, though the latter gives results more like those of a normal Hofmann reaction with hydroxide. For example, cyclooctyltrimethylammonium ion gives more *trans*- than *cis*-cyclooctene with hydroxide or amide, but *cis*-cyclooctene is favored 9:1 when phenyllithium is the base. Action of methyllithium on cyclooctyldimethyl(bromomethyl)-ammonium ion presumably follows the route of equations (24) and (25), and also favors *cis*-cyclooctene by 9:1.

Further evidence was provided by studying the compounds **8** and **9**. Both undergo normal Hofmann reactions to give 4-dimethylamino-1-butene and 4-dimethylamino-1-pentene, respectively. Both form ylides on treatment with butyllithium, but these ylides are stable and regenerate starting material on hydrolysis. Only at elevated temperatures do the ylides decompose, and then the product mixtures are distinctly different from those obtained in the normal Hofmann reaction.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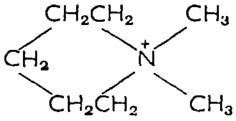
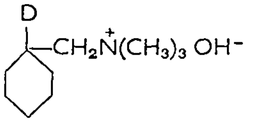

(9)

The above results imply that the α'–β mechanism does not operate under the usual conditions for the Hofmann reaction. Recently more positive evidence on this point has resulted from tracer studies[26,83]. Thermal decomposition of **10** and **11** gave trimethylamine that contained no deuterium, while the α'–β mechanism would require one deuterium per molecule of trimethylamine.

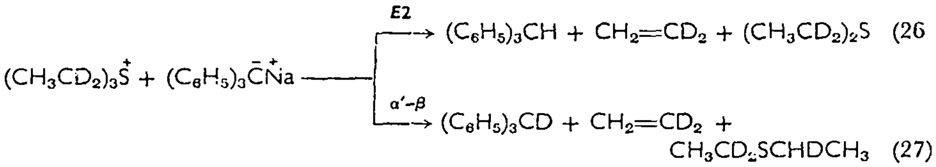

(10)

$CD_3CH_2\overset{+}{N}(CH_3)_3\ OH^-$

(11)

(Actually, amine obtained in the later stages of the reaction contained some deuterium, presumably because the water becomes partially deuterated as the $E2$ reaction progresses, and exchanges this deuterium with remaining quaternary ammonium ion. The initially formed amine, however, was deuterium-free.) Even the *cis* Hofmann elimination from *trans*-2d-2-phenylcyclohexyltrimethylammonium ion with ethanolic potassium hydroxide does not proceed *via* the α'–β mechanism, as the trimethylamine produced is free of deuterium[84].

The behavior of sulfonium salts seems similar. The action of tritylsodium on tri(ethyl-1,1-d_2)-sulfonium ion was studied by Franzen[85]. The triphenylmethane resulting should be labeled for the α'–β mechanism but not for the *E*2 mechanism (equations 26 and 27).



$$(CH_3CD_2)_3\overset{+}{S} + (C_6H_5)_3\overset{-}{C}\overset{+}{Na} \xrightarrow{E2} (C_6H_5)_3CH + CH_2{=}CD_2 + (CH_3CD_2)_2S \quad (26)$$

$$(CH_3CD_2)_3\overset{+}{S} + (C_6H_5)_3\overset{-}{C}\overset{+}{Na} \xrightarrow{\alpha'\text{-}\beta} (C_6H_5)_3CD + CH_2{=}CD_2 + CH_3CD_2SCHDCH_3 \quad (27)$$

Though the α'–β mechanism was clearly favored it did not occur exclusively, since 25% of the triphenylmethane was not deuterated. Again, the *E*2 reaction takes over completely in hydroxylic solvents, as shown by tracer experiments on deuterated 2-phenylethyldimethylsulfonium salts[86,87].

Obviously, the α'–β mechanism can be expected only in aprotic solvents. Under these circumstances not much can be said about the details of the process, since we know little about the state of aggregation of ions and ylides in média of low dielectric constant. It is even possible that some presumed α'–β reactions may actually involve an ylide functioning as base in an *E*2 attack on the β-proton of an onium ion. The pattern of Wittig's results—for example, the relative inertness of the piperidinium and pyrrolidinium ions—makes this less likely, but it cannot be entirely excluded.

Another variant of the usual base-promoted elimination is the α-elimination followed by hydrogen migration (equations 28 and 29).

$$RCH_2CH_2X + B \xrightarrow{\text{slow}} RCH_2\ddot{C}H \qquad (28)$$

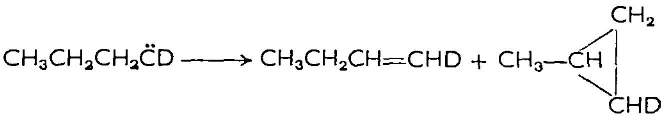
$$RCH_2\ddot{C}H \xrightarrow{\text{fast}} R\ddot{C}H{=}CH_2 \qquad (29)$$

There is strong evidence for unstable carbene intermediates in a number of organic reactions[88,89].

The α-elimination mechanism can be distinguished by the use of deuterium tracers, and seems by this criterion to be unimportant under normal conditions for base-promoted elimination[26,90].

Another piece of evidence for the α-elimination would be the presence of products typical of carbene reactions but not of normal β-elimination. For example, carbenes can undergo insertion reactions with carbon–hydrogen bonds. Recently, an α-elimination mechanism was confirmed for the action of phenylsodium on deuterated butyl chloride (equations 30 and 31)[91]. Both product and tracer criteria

$$CH_3CH_2CH_2CD_2Cl \xrightarrow{C_6H_5Na} CH_3CH_2CH_2\ddot{C}D \qquad (30)$$

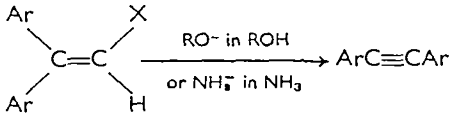


(31)

were used. Only 6% of dideuterated butene, the expected product of β-elimination, was obtained.

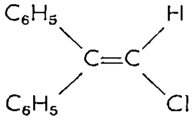
Similar results are reported for the action of sodium and potassium on isobutyl chloride[92]. The methylcyclopropane undoubtedly arises from insertion of the carbene in one of the methyl C—H bonds, and this provides convincing evidence for a discrete carbene (rather than migration of a β-hydrogen simultaneous with departure of halogen). A probable case of formation of a carbene from a sulfonium salt has been provided by Franzen[93], who found both isobutylene and methylcyclopropane among the products from the action of tritylsodium on isobutyldiphenylsulfonium fluoborate. Just like the α'–β mechanism, the α-elimination seems important only under aprotic conditions and with organometallic bases.

When a normal β-elimination is impossible because of the absence of β-hydrogens, an α-elimination with rearrangement may occur (equation 32). Offhand, a carbene would seem an eminently



(32)

reasonable intermediate for this reaction, but Bothner-By[94] has shown that migration of the aryl group *trans* to the halogen is preferred by about 10:1. This suggests that departure of the halogen is accompanied by, rather than followed by, aryl migration. Curtin[95] obtained similar results using butyllithium as the base. In a particularly interesting study, Cristol and Bly[96] determined rates of elimination reactions of compounds **12** to **14**. With phenyllithium as base, the α-elimination (with rearrangement) of **12** was faster than either the *cis*-β-elimination of **13** or the *trans*-β-elimination of **14**.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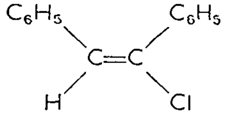
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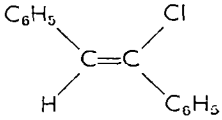

(14)

With sodium hydroxide, however, **12** was by far the slowest of the three to react.

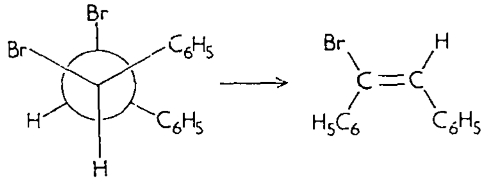
In addition to the mechanisms already discussed, there is an important class of intramolecular *cis* eliminations in which the leaving group takes with it a *cis*-β-hydrogen. Included in this class are pyrolyses of esters, xanthate esters, alkyl halides, and amine oxides. Since many of these reactions occur in the gas phase, and all are related mechanistically, they will be discussed in the chapter on gas-phase elimination (Chapter 3) in the present volume. Finally, no effort has been made to cover elimination reactions yielding substances other than olefins as the major products, such as the 'γ-eliminations' to produce cyclopropanes[97].

E. *Stereochemistry*

In the *E*2 reaction, an electron pair produced by removal of the β-hydrogen occupies in the product a π orbital covering both the α- and β-carbons. One can visualize the process schematically as: (*a*) removal of the β-hydrogen, (*b*) removal of the leaving group X, (*c*) rehybridization of the α- and β-carbons from sp^3 to sp^2, producing a *p* orbital on the β-carbon containing two electrons and a vacant *p* orbital on the α-carbon, and (*d*) overlap of these two *p* orbitals to give a π orbital containing its normal complement of two electrons. Because the *p* orbitals must be parallel for effective overlap, the original C—H and C—X bonds obviously must also be parallel if the steps (*a*)–(*d*) are to blend smoothly into a single-stage process. Whether they should be *trans* or *cis* to each other is not determined by this reasoning, though analogy to the S_N2 reaction has led to a preference for the *trans* orientation. The electrons released by removal of the β-hydrogen are regarded as 'displacing' the leaving group X.

Before the experimental results are discussed, two points should be emphasized. First, the absence of rigorous stereoelectronic arguments for *trans* elimination leads one to seek an explanation in other factors. A probable factor is eclipsing. A completely eclipsed transition state is required for *cis* elimination. The transition state for *trans* elimination lacks eclipsing of C—H and C—X bonds. Except when double bond character is high, there will also be some staggering of other groups attached to the α- and β-carbons. Eclipsing may not be the only contribution, but it is easy to imagine it producing a factor as high as 10^2 or 10^3 in favor of *trans* elimination. Second, reactions having transition states close to either extreme of the spectrum (near *E*1 or near *E*1cB) should show lowered stereochemical preference. Double-bond character is so slight in these transition states that there should be little energetic advantage to a transition state oriented for maximum orbital overlap.

In fact, most *E*2 reactions show a rather strong preference for *trans* elimination. Among early examples was the demonstration that the action of ethanolic potassium hydroxide on *meso*-stilbene dibromide gave *cis*-bromostilbene (equation 33), while the *dl*-dibromide gave the *trans* olefin (equation 34)[98]. Examination of perspective drawings shows that the hydrogen eliminated must have been *trans* to the bromine in each case for this stereochemical result. A modern example of the same approach has already been described



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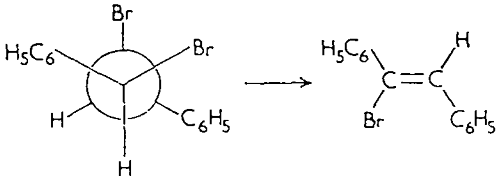
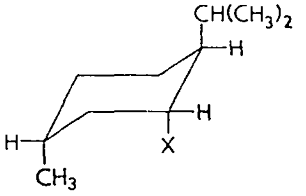


(34)

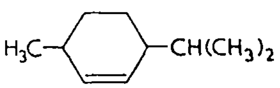
(section II.A, ref. 32) in another connection. The *threo* and *erythro* isomers of 1,2-diphenyl-1-propyl derivatives reacted in a stereospecific *trans* fashion, whether the leaving group was halogen or trimethylammonium. Since the steric course of the reaction is independent of the charge on the leaving group, electrostatic repulsion between the base and the leaving group cannot be an important factor.

The preference for *trans* elimination seems to extend to the conversion of vinylic halides to acetylenes. Chlorofumaric acid is dehydrohalogenated fifty times faster than chloromaleic acid[99], and *trans*-dichloroethylene reacts with base twenty times faster than the *cis* isomer[100]. Other early examples of the steric course of *E*2 reactions have been summarized by Frankland[101].

The preference for *trans* elimination may be very substantial. The β-isomer of benzene hexachloride, which has adjacent chlorine and hydrogen atoms all *cis* to each other, is dehydrohalogenated 7000 times more slowly than the least reactive of the other isomers[102–104]. This figure represents a lower limit to the specificity of the *E*2 reaction in this system, since the *cis* elimination may be proceeding by the *E*1cB mechanism[27]. Similar specificity is observed in studies on other substituted cyclohexanes. Menthyl derivatives (**15**), for example, often yield under *E*2 conditions only 2-menthene (**16**), the product of *trans* elimination[105–107]. In such competition experiments, the ability of the analytical method to detect small quantities of the minor product decides how stringently the stereospecificity is established. A few percent of 3-menthene could probably be found, so a lower limit of about 50:1 can be set on the ratio of *trans* to *cis* elimination for these reactions.



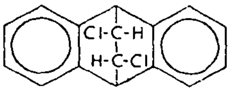
(**15**)



(**16**)

Though *trans* elimination is the general rule for *E*2 reactions, there are notable exceptions. These occur mainly when the C—X and C—H bonds are unable to adopt a *trans* coplanar conformation, or when the *cis* hydrogen is strongly activated by an electron-withdrawing substituent. Whether the resulting *cis* eliminations are genuine *E*2 reactions has been a subject of much controversy.

In the first category are found a number of bridged-ring compounds in which conformation is rigidly fixed by the bridging. The alkaline dehydrochlorination of the isomers of 11,12-dichloro-9,10-dihydro-9,10-ethanoanthracene (**17** and **18**) actually proceeds faster with the *trans* isomer (*cis* elimination of H and Cl) than with



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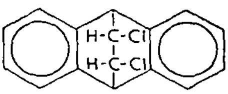
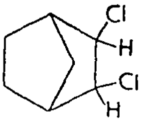


(18)

the *cis*[108]. Both isomers react much more slowly than ordinary non-bridged chlorocyclohexanes. Similar results were obtained with the 2,3-dichloronorbornane isomers (**19**)[109], but the 1,2-dichloroacenaphthenes (**20**) apparently are flexible enough to permit



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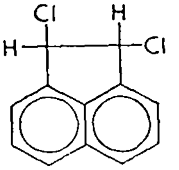
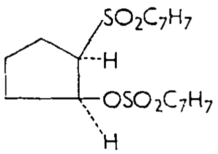


(20)

a relatively normal *trans* elimination, since the *cis* isomer reacts about 750 times faster than the *trans*[110].

Among violations of the rule of *trans* elimination arising from activation of the β-hydrogen, perhaps the best known is the production of 1-phenylcyclohexene in the thermal degradation of *trans*-2-phenylcyclohexyltrimethylammonium hydroxide[111]. Originally it appeared likely that 3-phenylcyclohexene was formed and then isomerized. Later work has proved that 1-phenylcyclohexene must be formed directly[112,113]. A kinetic study has shown that the *cis*-2-phenyl isomer (*trans* elimination) reacts 133 times faster than the *trans*-2-phenyl isomer, and that both give 1-phenylcyclohexene[114]. Therefore the phenyl-activated *trans* is faster than the phenyl-activated *cis* elimination, but the unactivated *trans* elimination (to give 3-phenylcyclohexene) is slower than either. Finally, the *trans* elimination shows a 1·2% $^{14}N/^{15}N$ isotope effect, but the effect in the *cis* elimination is only 0·2%[115]. The results so far permit the *cis* elimination to be either an *E*1cB reaction, or an *E*2 reaction close to the *E*1cB end of the scale. The α'–β mechanism is excluded by tracer experiments (section II.D, ref. 84).

Further examples of abrogation of the *trans* elimination rule by a strongly electron-withdrawing β-substituent are found in the 2-(*p*-tolylsulfonyl)cyclopentyl *p*-toluenesulfonates (**21** and **22**)[116]. Both *cis* and *trans* isomers in each case give the same product, **23**. Thus



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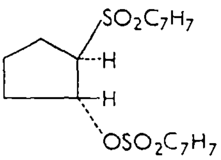

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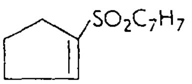


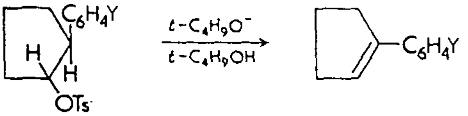
(23)

the activated *cis* elimination is faster than the unactivated *trans* elimination. When one considers only the activated elimination by comparing rates of reaction of the *cis* and *trans* isomers, the *trans* rule still holds, though less strictly than in unactivated systems. Elimination of the *trans* hydrogen is favored over the *cis* by a factor of 20 in the cyclopentane and 435 in the cyclohexane series. The stereospecificity is reduced still further if trimethylamine or triethylamine is used as the base[117]. All of these cyclic compounds react more slowly than the open-chain analogue, 1-(*p*-tolylsulfonyl)-2-propyl *p*-toluenesulfonate.

Arguments were advanced that both the *cis* and *trans* eliminations described above are single-stage *E*2 processes. They show general base catalysis, which means that the rate depends on the nature and the concentration of the base present. If a carbanion were formed reversibly in the first step, its concentration, and hence the rate, would depend solely on the pH of the solution and not on the nature of the base employed. A short-lived carbanion cannot be excluded, but an upper limit of 10^{-9} seconds to its mean lifetime was estimated.

In a later paper, deuterium exchange of cycloalkyl *p*-tolyl sulfones was reported[118]. The observed rates were used to estimate the rates to be expected if the elimination reactions involved rate-determining carbanion formation. The estimates ran 10^3 to 10^5 less than the actual rates of elimination, so the elimination was considered to be assisted by C—X bond cleavage and hence to be *E*2. Recently this claim has been disputed by Hine[119], who uses a different method of estimation to conclude that a simple proton removal could be as fast as the elimination. Obviously these reactions are very close to the *E*2–*E*1cB borderline, and a meaningful distinction between the two mechanisms may not be possible.

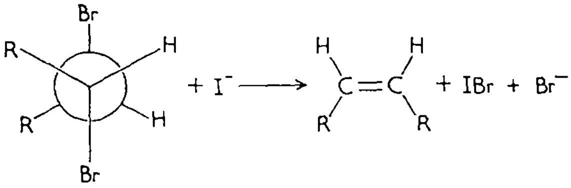
A very interesting recent development in this area arises from a study of the reaction between *t*-butoxide ion and a series of *trans*-2-arylcyclopentyl *p*-toluenesulfonates (**24**)[120]. Here the product is exclusively **25**, and again the activated *cis* elimination is preferred over the unactivated *trans* elimination. *cis*-2-Phenylcyclopentyl *p*-toluenesulfonate (*trans* elimination) reacts only 14 times faster than



(24) (25)

the *trans* isomer. The corresponding ratio in the cyclohexane system is greater than 10^4. Furthermore, the reactions of the *trans*-2-arylcyclopentyl *p*-toluenesulfonates fit the Hammett equation with a ρ of $+2{\cdot}34$ under conditions where the 2-arylethyl *p*-toluenesulfonates give a ρ of $+3{\cdot}39$. From these results, DePuy concludes that the *cis* elimination is a true *E*2 reaction, since it shows even less carbanion character than the (presumably *trans*) open-chain reaction. He further suggests that the most important stereochemical factor governing *E*2 reactions is coplanarity, and that either a *trans* or *cis* coplanar will be much preferred to a non-coplanar transition state. This contention is certainly not unreasonable, though the results could arise from other factors, such as a variation of the substituent effect with the angle between the substituent and the reaction site due to a varying field effect.

Finally, brief mention should be made of some reactions of 1,2-dihalides and related compounds. The action of iodide ion in acetone on 1,2-dibromides results in *trans* elimination of the two bromine atoms (equation 35)[121]. A mechanism entirely analogous

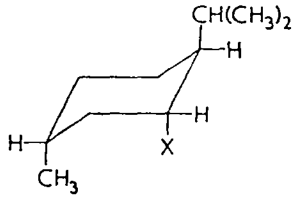


(35)

to the *E*2 mechanism seems to be involved. The reaction of zinc with dibromides also seems to prefer a *trans* course, though the selectivity is distinctly lower[108,122–124]. The reaction of iodide ion with 2-bromocyclohexyl nitrates and arenesulfonates shows very little stereoselectivity. These results were explained by assuming that the rate-determining step was not the elimination, but a displacement by iodide ion to give a 1-iodo-2-bromo compound which then rapidly eliminated[125].

Turning now to the *E*1 reaction, we find that generalizations on stereochemical behavior are more difficult to make. In principle, a planar carbonium ion should lose a β-proton from either side of the plane with equal facility, and there should thus be no stereoselectivity at all. Several factors work to upset this simple picture. First, the leaving group may still be close enough to the carbonium ion to exert some influence (*i.e.* the ion might not be symmetrically solvated when it begins to lose a proton), and hence the two sides of the plane would not be equivalent. Similarly, a β-hydrogen may be so situated as to offer neighboring group participation in the ionization. If this weakened C—H bond is subsequently broken in the second stage, the elimination clearly should be *trans*. Some neighboring groups other than hydrogen may give bridged intermediates. The stereochemistry of proton loss from such intermediates is difficult to predict.

Most of the stereochemical studies of the *E*1 reaction have been performed with substituted cyclohexyl derivatives. Qualitatively, the *cis*-2-alkylcyclohexanols dehydrate more rapidly than the *trans* isomers[126,127]. The *cis* isomers of their sulfonate esters also solvolyze more rapidly, yielding both elimination and substitution products[128].



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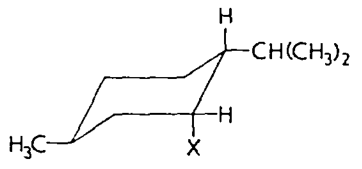

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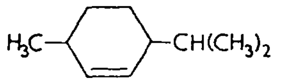

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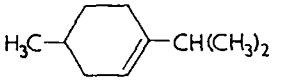
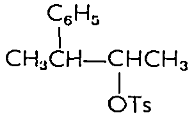


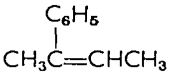
(29)

Studies of product distribution in solvolyses of halides and sulfonate esters were carried out by Hückel[105], and extended by later workers, who also carried out kinetic studies[106,129]. The general pattern in the menthyl–neomenthyl series was that the menthyl derivative **26** gave both 2-menthene (**28**) and 3-menthene (**29**) with the latter predominating. The neomenthyl derivative (**27**) reacts at a considerably greater rate (about 170 times faster than **26** in acetolysis of the *p*-toluenesulfonate), and yields almost exclusively **29**. This did not arise mainly from 1,2-hydrogen shift to give a tertiary carbonium ion which then lost a proton, since the **29** obtained was only partially racemized, and thus could not have come entirely from a symmetrical intermediate. These results indicate a lack of much stereoselectivity in the *E*1 reaction except when a tertiary hydrogen is located *trans* to the leaving group. In this case, the tertiary hydrogen seems to aid the ionization and to be lost much more easily than other hydrogens. The same strong preference for *trans* elimination of a tertiary hydrogen is found in ethanolysis of 2-phenylcyclohexyl *p*-toluenesulfonate and 2-phenylcyclohexyldimethylsulfonium ion. The *trans* isomers give mixtures of 1- and 3-phenylcyclohexene, the latter in larger amount, while the *cis* isomers give almost entirely 1-phenylcyclohexene[114].

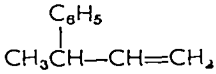
The deuterium isotope effect provides confirmation of the weakening of a tertiary C—H bond in the β-position during solvolysis. Substitution of deuterium for hydrogen slows the ionization by factors of 1·5 to 2·3[130,131]. These effects are considerably larger than those normally observed in solvolysis of β-deuterated substances (section II.B), and suggest that the hydrogen is participating in the ionization. Possibly a hydrogen-bridged intermediate is formed, and loses the proton in a subsequent fast step.


$CH_3\overset{C_6H_5}{CH}-\underset{OTs}{CHCH_3}$

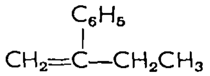
(30)


$CH_3\overset{C_6H_5}{C}=CHCH_3$

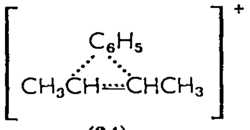
(31)


$CH_3\overset{C_6H_5}{CH}-CH=CH_2$

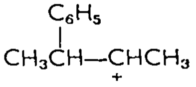
(32)


$CH_2=\overset{C_6H_5}{C}-CH_2CH_3$

(33)

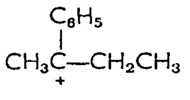

$\left[\overset{C_6H_5}{CH_3CH\cdots CHCH_3}\right]^+$

(34)


$CH_3\overset{C_6H_5}{CH}-\underset{+}{CHCH_3}$

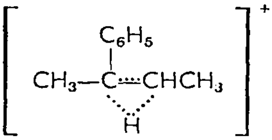
(35)

Not much information is available on the stereochemistry of the *E*1 reaction in open-chain systems, but what there is suggests a pattern similar to that already outlined. Cram[52] has examined carefully the olefinic products in solvolysis of the *threo*- and *erythro*-3-phenyl-2-butyl *p*-toluenesulfonates (**30**). These yield *cis*- and *trans*-**31**, along with **32** and **33**. The bridged ion **34** appeared to be the major intermediate in acetate ester formation, but the evidence suggested that it was *not* an intermediate in olefin formation. The olefin fraction from the *threo* isomer still possessed some optical activity (**34** has a plane of symmetry), and such racemization as did occur could be explained by prior racemization of the starting material. Part of the olefin resulted from a non-stereospecific loss of hydrogen, probably from the classical ions **35** and **36**, and the remainder from a stereospecific *trans* loss of the hydrogen on $C_{(3)}$. Cram suggests that this may come from the hydrogen-bridged ion **37**.



$\mathrm{CH_3}\underset{+}{\overset{\overset{\mathrm{C_6H_5}}{|}}{\mathrm{C}}}\mathrm{-CH_2CH_3}$

(36)



$\left[\mathrm{CH_3-}\overset{\overset{\mathrm{C_6H_5}}{|}}{\mathrm{C}}\underset{\mathrm{H}}{\overset{\cdots}{=}}\mathrm{CHCH_3}\right]^+$

(37)

Relatively little is known about stereochemistry in the remaining mechanistic categories. Reactions on the *E*1–*E*2 borderline, insofar as they consist of simultaneous *E*1 and *E*2 processes, would be expected to show partial *trans* specificity. Reactions proceeding by Winstein's merged mechanism might be stereochemically similar to the *E*1 reaction. Since the intermediate is an *asymmetrically* solvated carbonium ion, the specificity could be greater than for a genuine *E*1 process.

The Wittig α'–β mechanism, since it involves a cyclic intermediate, should be favored when the leaving group and the β-hydrogen are *cis*. Evidence that the stereochemical course is different from that of the *E*2 reaction (and presumably *cis*) is furnished by results on cyclooctyltrimethylammonium ion (section II.D). Here *trans*-cyclooctene is favored under Hofmann conditions, but *cis*-cyclooctene is favored with phenyllithium as base. Neither reaction affords cleanly one isomer, though, so one or both may not be entirely stereospecific. (This is not compelling evidence, as the cyclooctane ring may be flexible enough for either β-hydrogen to attain the proper conformation for *trans* or, as the case may be, *cis* elimination.)

Finally, there is no evidence on the stereochemistry of α-eliminations, though a discrete carbene intermediate would lead to a completely non-specific process. If hydrogen migration is concerted with departure of the leaving group (as is phenyl migration in the cases studied by Bothner-By[94] and Curtin[95]), by analogy the *trans* hydrogen would migrate preferentially. This would probably be detectable only with a vinylic halide, as the α-carbanion from a saturated halide should not be stereochemically stable.

III. EFFECTS OF STRUCTURE AND CONDITIONS ON REACTIVITY

A. Some Basic Ideas

A statement concerning relative reactivity in elimination reactions should always make clear the nature of the comparison involved. For instance, elimination reactions are usually accompanied by substitution reactions, and to say that a low yield of olefin indicates low reactivity may be incorrect. The elimination reaction may be quite normal compared to other eliminations, but be 'drowned out' by an unusually fast substitution reaction. Obviously it is not legitimate to interpret substitution/elimination ratios solely in terms of the reactivity toward elimination.

Though the rate-determining and product-determining steps are the same in the $E2$ reaction, they are not in the $E1$ reaction. The rate of an $E1$ reaction tells us nothing about the elimination *per se*. The substitution/elimination ratio does, subject to the limitation mentioned in the preceding paragraph. Orientation studies (for example, of the 1-butene/2-butene ratio from solvolysis of a 2-butyl derivative) will give relative rates of the two $E1$ processes involved. The Winstein merged mechanism, and probably the α and α'–β mechanisms as well, would also be expected to have separate product- and rate-determining steps.

Even when we are comparing two $E2$ reactions, it is necessary to decide whether the structural difference between the two affects primarily their ground states or their transition states. In the special case of orientation studies the ground states are the same, and the isomer ratios in the products are determined solely by the relative energies of the transition states. This simplifies but by no means solves our theoretical problem, as it is far more difficult to gain information about transition states than about ground states.

To appreciate this problem, we must remember that the transition state is by definition too unstable to observe or measure in any way, so we must be content with indirect methods of studying its properties. These indirect methods all give information about *differences* between the ground state and the transition state. They involve studies of the effects on reaction rate of such factors as isotopic substitution, variation in electronic and steric properties of substituents, and variation in medium. The review by Bunnett[5] presents systematically the anticipated results of structural and environmental changes on the $E2$ transition state. A remarkably good correlation with experimental fact is obtained, but some ambiguities still exist. Difficulties in reconciling the results of different experiments sometimes occur, as not all approaches measure the same properties of the transition state.

The problem is complicated further by cases of seemingly contradictory experimental results from different laboratories. The $^{32}S/^{34}S$ isotope effect in reaction of hydroxide with 2-phenylethyldimethylsulfonium ion is only 0·15%[41], or about one-tenth of the theoretical maximum. The 2-phenylethyltrimethylammonium ion with ethoxide ion in ethanol gives an $^{14}N/^{15}N$ isotope effect of 0·94%[132a]. Though the theoretical maximum here is 3–4%, there is clearly greater weakening of the C—N than of the C—S bond in the transition state. Doubt is cast on the generality of this conclusion by the 0·14% $^{14}N/^{15}N$ isotope effect reported for reaction of the 2-phenylethyltrimethylammonium ion with hydroxide ion in water[132b]. This is a surprisingly large solvent effect. Only part of the difference can be attributed to the higher temperature (100°) used by Asperger.

If the C—N bond is weaker than the C—S bond in the transition states of the reactions with ethoxide in ethanol, difficulty in reconciling isotope effects with substituent effects arises. Substituted 2-phenylethyltrimethylammonium salts have a Hammett ρ value of $+3{\cdot}8$ under conditions where ρ for the sulfonium salts is only $+2{\cdot}7$ (see Table 1, section II.A). The clearly greater carbanion character in the transition state for the ammonium salt implies less, rather than more, C—N than C—S stretching. If the carbanion character of the transition state is primarily a consequence of the extent of C—H stretching, a consistent interpretation becomes possible. This conclusion is not *a priori* obvious, but it can be rationalized if we remember that the C—H bond is in both cases much more stretched than the C—X bond. The 'looser' C—H bond might be expected to respond more than the C—X bond to a change in structure or environment. Even so, the picture would be more satisfying if the influence of C—H bond stretching on carbanion character did not have to overcome an effect of C—X stretching that worked in the opposite direction. More data on the effect of solvent and structure on nitrogen and sulfur isotope effects are needed to clarify this troublesome point.

The relationship between nitrogen and sulfur isotope effects to be expected on theoretical grounds is not entirely settled. Recently Swain and Thornton[133] have suggested a rule for predicting the effect of structural changes on transition-state bonds. According to this rule, the more electron-rich bond should be longer in the transition state. Since $(CH_3)_3N$ is more basic than $(CH_3)_2S$, and also since the valence electrons of nitrogen are closer to the nucleus and less diffused than those of sulfur, the electron density should be greater in the C—N than in the C—S bond. Another way of viewing this situation is that the stronger C—N bond must be stretched farther before its binding energy is overcome and the *energy maximum* that is the transition state reached.

As was emphasized by the authors, the Swain–Thornton rule deals with the behavior of individual bonds. Effects on rates or activation energies are much more difficult to predict, especially in elimination reactions, as they are determined by the balance and timing of a number of bond-making and bond-breaking processes, and by environmental effects as well. More information on the interaction of these processes would be desirable.

The Swain–Thornton hypothesis may prove to be very useful in working out these details. Isotope effects are the ideal experimental data for testing the hypothesis, but not enough examples of deuterium *and* leaving-group isotope effects on the same compound are available. Until this deficiency is remedied, certain aspects of the hypothesis must remain uncertain. Swain and Thornton suggest that the basicity of the leaving group be taken as a measure of its ability to supply electrons, but this is arguable. The rule takes no explicit account of charge type or solvation phenomena. Even the definition of a 'reacting orbital' is not entirely obvious once one gets beyond the bond that is the immediate site of substitution (for example, when one is trying to decide the effect of changing X on the C—H bond, or the effect of changing base on the C—X bond). More data may make it possible to devise simple rules for applying the hypothesis so that it unambiguously predicts the correct experimental result, but this is clearly not the case so far. The basic idea that electron supply lengthens a reacting bond in the transition state certainly seems sound and reasonable.

In broader terms, one must be prepared to face the prospect that the mechanical properties of a bond, as measured by the isotope effect, and the electron distribution, as measured by the substituent effect, may not always parallel each other. Knowledge of both is desirable for a complete mechanistic picture, but substituent effects alone are a good basis for predicting and correlating various influences on reactivity. Even where a complete picture of the transition state is not available, many useful generalizations can be formulated.

B. Substitution versus Elimination

The yield of elimination product relative to substitution product depends upon reactivity in both reactions. Since relative reactivities in elimination reactions will be discussed in detail later, only a few of the more general conclusions will be presented here.

In the case of $E2$ *vs.* S_N2, we are concerned with two competing bimolecular reactions, so that the product ratio should remain constant throughout the reaction. If it does not, the products are unstable to the reaction conditions, or else a part of the product mixture is produced by a reaction of different (probably first) order. Frequently reactions near the $E1$–$E2$ borderline will give elimination product by an $E2$ mechanism but substitution product by an S_N1 mechanism. Attempts to interpret such a mixed situation on either basis alone would obviously founder.

Staying within the bimolecular category, the rate of elimination generally increases, and the rate of substitution decreases, with increasing α-substitution. An overall rapid increase in olefin yield is thus to be expected. For example, in a reaction with sodium ethoxide in ethanol at 55°, ethyl bromide gives only 1% of olefin, while isopropyl bromide gives 79%[38] (this figure may be slightly high), and *t*-butyl bromide gives a practically quantitative yield of olefin[13]. A similar progression is noted with sulfonium salts. For a series of alkyldimethylsulfonium salts with sodium ethoxide in ethanol at 45°, the results are: ethyl, 12% olefin; isopropyl, 61% olefin; and *t*-butyl, 97–100% olefin[134]. Somewhat surprisingly, the variation in this case seems to result almost entirely from sharp increases in the rate of elimination.

Results of other changes are not so easy to predict. Substitution on the β-carbon almost invariably slows the S_N2 reaction, presumably *via* steric interference with displacement, but may either aid (with halides) or hinder (with 'onium salts) the $E2$ reaction. This point is discussed more fully in section III.C. The electronic effects of substituents other than alkyl again depend upon the nature of the reaction. Substituents, such as aryl groups, which can conjugate with either a developing double bond, or with developing p orbitals on the α- or β-carbons, appear to exert a uniformly favorable effect on $E2$ reactions. A change in solvent generally has a greater effect on the $E2$ than on the S_N2 reaction, probably because charge is more dispersed in the $E2$ transition state. The usual effect is to favor the elimination reaction in less polar solvents[135]. Finally, an increase in temperature increases the $E2$ rate faster than the S_N2 rate, and thus increases the olefin proportion[136].

In the $E1$ reaction the rate-determining step precedes the product-determining step, so there is no necessary relation at all between rates and product proportions. The overall rate merely decides whether a bimolecular or unimolecular path will predominate. As conditions become more and more favorable for unimolecular mechanisms, the S_N2–S_N1 border is generally reached before the $E2$–$E1$ border. The practical result of this phenomenon is generally a decrease in olefin proportion in this region. Whether or not the Winstein merged mechanism operates near the borderline should not change the overall picture, since it probably will behave in a manner similar to the S_N1–$E1$ reaction.

In the unimolecular region, the olefin yield is determined by the relative rates at which the intermediate carbonium ion loses a proton or combines with a solvent molecule. Olefin formation should be accelerated by structural changes leading to a more stable olefin (see section III.C), and by structural changes that hinder the formation of substitution product. Before discussing the explanations that have been advanced, we should first consider the facts.

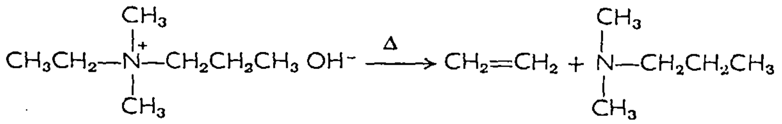
In general, olefin proportions seem much lower in unimolecular than in bimolecular reactions. Solvolysis of isopropyl bromide in 60% aqueous ethanol yields only 5% of olefin[137]. Similarly, *t*-butyl and *t*-amyl bromides solvolyze in ethanol to give 19 and 36%[138], respectively, of olefin, instead of the almost quantitative yields they afford in the $E2$ reaction. The solvolysis in 80% ethanol of an extensive series of alkyl chlorides shows a general, though not entirely regular, increase in olefin yield with increasing size and complexity of the alkyl group[139]. As has been noted previously (section II.B), the olefin yield is approximately independent of the nature of the leaving group.

Though the facts are clear enough, their interpretation has been a matter of considerable dispute. Ingold believes the major factor is that the transition states leading to the more highly branched olefins are more stable, and has presented semiquantitative arguments in his favor[140]. Brown, on the other hand, claims that a decreased rate of substitution due to steric effects in the more complex carbonium ions is decisive[141]. In turn, he has criticized the approach of Ingold[142,143]. Because neither the elimination nor substitution rates can be measured separately, an unequivocal solution to this controversy does not appear close. One would consider steric influences most likely to play a role in reactions of the most highly branched halides, particularly those that show a pronounced rate acceleration in solvolysis[144]. If the carbonium ion is formed more readily because of internal steric repulsions in the halide, there is certainly every reason to believe it reluctant to form a substitution product in which those repulsions would be restored. On the other hand, few of the compounds show rate increases unambiguously attributable to steric effects. Since product stability is known to play a part in deciding orientation in *E*1 reactions (see section III.C), it certainly must influence the overall rate of elimination as well. In the less-branched compounds, at least, it may well be the controlling factor in olefin yield.

C. Orientation Rules

Long before anything was known about the kinetics or mechanisms of eliminations, certain regularities in relative reactivities had been observed. These were summarized in the Hofmann rule[145], which dealt with orientation in eliminations from quaternary ammonium hydroxides, and the Saytzeff rule[146], which dealt with eliminations from alkyl halides.

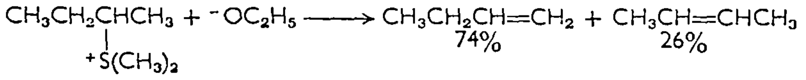
The Hofmann rule, as originally stated, pointed out that a quaternary ammonium hydroxide containing two or more different alkyl groups would lose an ethyl group (as ethylene) in preference to a larger alkyl group. Thus, **38** gives almost exclusively ethylene. A more general statement of the rule requires loss of that alkyl group



$$\mathrm{CH_3CH_2{-}\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{\overset{+}{N}}}{-}CH_2CH_2CH_3\ OH^-} \xrightarrow{\Delta} \mathrm{CH_2{=}CH_2 + \overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{N}}{-}CH_2CH_2CH_3}$$

(38)

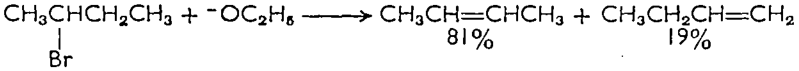
which will give the olefin with the least substituted double bond. Numerous examples of this behavior have been provided by Ingold and his collaborators, who showed that sulfonium as well as ammonium salts obey the rule[6,12]. Further confirmation and new examples have resulted from more recent work using modern analytical tools[147,148]. The rule also applies to eliminations in different branches of the same alkyl group. Thus, **39** gives the monsubstituted olefin 1-butene in preference to the disubstituted 2-butene[149].



$$\underset{\displaystyle {}^{+}S(CH_3)_2}{CH_3CH_2CHCH_3} + {}^{-}OC_2H_5 \longrightarrow \underset{74\%}{CH_3CH_2CH{=}CH_2} + \underset{26\%}{CH_3CH{=}CHCH_3}$$

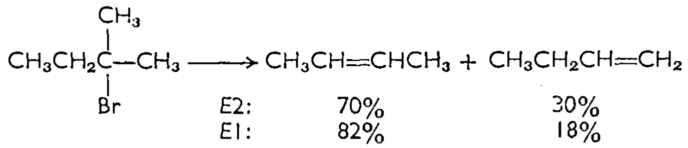
(39)

The Saytzeff rule was originally proposed to apply to elimination reactions of secondary and tertiary alkyl halides. The preferred olefin, in cases where elimination in either of two different branches of an alkyl group is possible, will be the one bearing the greater number of alkyl groups on the double bond. For example, the major product from the action of ethoxide ion in ethanol on 2-bromobutane (equation 36) is 2-butene, in contrast to the result with the sulfonium salt[137,150].



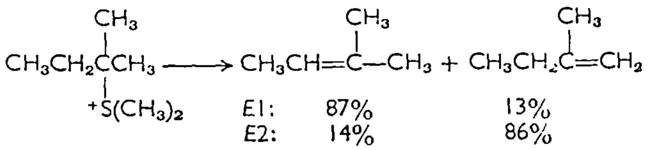
$$\underset{\displaystyle Br}{CH_3CHCH_2CH_3} + {}^{-}OC_2H_5 \longrightarrow \underset{81\%}{CH_3CH{=}CHCH_3} + \underset{19\%}{CH_3CH_2CH{=}CH_2} \qquad (36)$$

The mechanisms of the reactions were, of course, unknown when the Hofmann and Saytzeff rules were formulated. The work of Hughes and Ingold and their coworkers defined the mechanistic areas of applicability of the two rules[151,152]. With a few exceptions that will be considered later, their classifications still hold. They found that the Hofmann rule applies to $E2$ reactions of 'onium ions. The Saytzeff rule applies to $E2$ reactions of halides and to all $E1$ reactions, regardless of the charge type of the leaving group. For example, t-pentyl bromide follows the Saytzeff rule in both the $E2$ reaction with ethoxide in ethanol and the $E1$ solvolysis in ethanol (equation 37)[138,141,153]. In contrast, t-pentyldimethylsulfonium



$$\begin{array}{llll} CH_3CH_2\overset{\displaystyle CH_3}{\underset{\displaystyle Br}{C}}{-}CH_3 \longrightarrow & CH_3CH{=}CHCH_3 & + & CH_3CH_2CH{=}CH_2 \\ \quad E2: & 70\% & & 30\% \\ \quad E1: & 82\% & & 18\% \end{array} \qquad (37)$$

ion gives entirely different results under the two sets of conditions (equation 38). Note also that the Saytzeff-rule product is obtained in larger proportion in the $E1$ than in the $E2$ reaction even with the bromide (equation 37). This phenomenon appears to be general.



$$\begin{array}{llll} CH_3CH_2\overset{\displaystyle CH_3}{\underset{\displaystyle {}^{+}S(CH_3)_2}{C}}CH_3 \longrightarrow & CH_3CH{=}\overset{\displaystyle CH_3}{C}{-}CH_3 & + & CH_3CH_2\overset{\displaystyle CH_3}{C}{=}CH_2 \\ \quad E1: & 87\% & & 13\% \\ \quad E2: & 14\% & & 86\% \end{array} \qquad (38)$$

Exceptions to the rules fall into several categories, which will only be mentioned here and discussed later (sections III.D–F). First, the charge type of the leaving group does not always control the orientation in *E*2 reactions. Some neutral groups such as SO_2CH_3 give Hofmann-rule products[20,154], and by use of tertiary alkoxide bases in the corresponding tertiary alcohol as reagent, even alkyl halides can be made to follow the Hofmann rule[155]. A case of Hofmann-rule orientation in *E*1 reactions, those of the highly branched 2,4,4-trimethyl-1-pentyl halides, is known[156]. Finally, many cyclic ammonium salts appear to obey the Saytzeff rather than the Hofmann rule in their *E*2 reactions[47,157,158]. A reasonable explanation is that the $N(CH_3)_3$ group must be axial for a *trans* coplanar transition state (section II.E), and that forcing such a bulky group into an axial conformation is energetically feasible only when the C—N bond is considerably stretched. There is thus much more double-bond character in these transition states than is usual in *E*2 reactions of quaternary ammonium salts.

Discussion of the reasons behind the orientation rules is best postponed until section III.E, where the effect of the leaving group will be considered. A point to keep in mind is that the Saytzeff-rule products are generally also the more thermodynamically stable products. The transition states leading to these products therefore should possess considerable double-bond character, as they are stabilized by the same factors that stabilize the olefins. Hofmann-rule products are usually *not* the more thermodynamically stable ones, which suggests transition states in which double-bond character is either slight or else overshadowed by other effects. In fact, this distinction based on thermodynamic stability of the products offers an attractive redefinition of the Hofmann and Saytzeff rules. The original meanings have already been altered by usage, and mechanistic criteria are certainly more desirable than purely empirical ones.

A further point to keep in mind is that the effects we are dealing with in the orientation rules usually correspond to quite small energy differences. A change from a 1:2 to a 2:1 product ratio, for example, requires a change of only about 0·8 kcal in relative activation energies if the reactions occur at or near room temperature. That such subtle effects sometimes present difficulties in interpretation is to be expected, and the only surprising aspect is that they should be as regular and predictable as they are.

D. Variations in the Alkyl Group

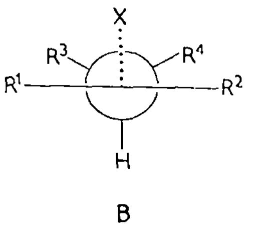
This section will deal with one of the most important aspects of reactivity in eliminations, the effect of changing the alkyl group into which the elimination occurs. The causes of different rates of elimination into different branches of the same molecule, *i.e.* the orientation rules, will also be discussed. First the theoretical possibilities will be presented, then the experimental facts and their probable interpretations.

The concept of the variable transition state for $E2$ reactions, presented in section II.A and discussed further in section III.A, means that a given structural change may have quite different effects on different reactants. The Hofmann–Saytzeff dichotomy is, of course, a prime example. The factors affecting reactivity fall into two main categories: polar and steric effects. These may each be subdivided further according to the mode of operation of the effect.

The simplest polar effect is the inductive effect. Electron withdrawal should aid a reaction in which electron density at the site of substitution is greater in the transition state than in the ground state, and hinder a reaction for which the reverse is true. Thus, an electron-withdrawing β-substituent should strongly aid a reaction with a near-$E1$cB transition state. The same substituent in the α-position should strongly hinder a reaction with a near-$E1$ transition state. The effect of either situation on a completely synchronous $E2$ reaction is difficult to predict, except that the transition-state structure will probably shift so as to benefit from any possible stabilization. For example, the electron-withdrawing β-substituent should shift a synchronous $E2$ reaction toward the $E1$cB end of the scale.

Groups capable of exerting a conjugative or hyperconjugative influence may have similar effects. The carbonyl group attached to the β-carbon will greatly stabilize a near-$E1$cB transition state, and α-alkyl or -aryl substitution will favor a near-$E1$ transition state. Still another effect enters, however, as these groups are also capable of stabilizing double bonds and hence will help reactions in which the transition state possesses double-bond character. This stabilization can operate from either the α- or β-position. Whether the stabilizing effect of alkyl substitution on double bonds is the result of hyperconjugation has been the subject of much controversy. In a recent symposium on hyperconjugation a number of papers discussed this point[159-162]. Whatever the cause, the more highly alkylated olefins are, with few exceptions, more stable. Furthermore, as will be seen shortly, there are many examples of correlation between olefin stability and rate of elimination. These facts are in no way dependent upon the respectability of hyperconjugation as a rationalization for them.

The steric effects of substituents will again depend upon the nature of the transition state. The structures **40** to **42** are Newman projections of **1** to **3** in section II.A. The high double-bond character of **41** offers the greatest opportunity for R^1–R^3 and R^2–R^4 interferences (eclipsing effects). In **40** the β-carbon is still tetrahedral, so less eclipsing is expected. Eclipsing should be least in **42**, since the α-carbon is still tetrahedral, and the carbanion-like β-carbon is probably pyramidal rather than planar. (By analogy to the isoelectric amines, carbanions should be pyramidal, except in species such as enolate ions where a planar structure allows resonance stabilization.) The *E*1 reaction should be subject to eclipsing effects, too. While eclipsing is the only steric effect involving the alkyl group alone, other possible effects are interference of R^1 and R^2 with X, R^3 and R^4 with X, or of any of the alkyl groups with B. Most of the discussion of these other effects will be postponed to later sections, as they are more relevant to discussions of the leaving group and the base than to our present topic.



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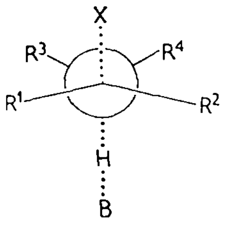

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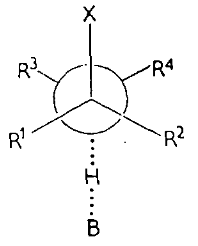


(42)

The existence of pure polar effects in *E*2 reactions is shown by experiments on *m*- and *p*-substituted 2-phenylethyl derivatives (see section II.A) in which electron-withdrawing groups aided and electron-repelling groups hindered reaction. The large effect of the *p*-nitro group provided evidence for conjugative stabilization of negative charge on the β-carbon[35]. When the structural variation occurs close to the reacting system, as in replacement of a hydrogen by an alkyl group on the α- or β-carbon, the possibility of a steric effect enters. Unless clearly different trends are predicted for polar and steric effects, deciding between them may be a difficult matter.

In such cases, appeal may be made to quantitative arguments, or to more subtle qualitative differences, but the conclusions will be less reliable. Where both steric and polar effects predict identical trends, the choice between them is little more than a matter of taste or, at most, which fits better into the overall picture of organic theory.

The *E*2 reactions of 'onium salts are generally slowed by β-alkyl substitution. For example, rates of attack of ethoxide on alkyldimethylsulfonium ions run in the order:

ethyl > n-propyl > n-butyl > isobutyl[12b].

Many similar cases are afforded by orientation studies (see section III.C). Ingold originally ascribed this pattern to an unfavorable inductive effect of the alkyl group on the acidity of the β-hydrogen[6]. He has held to this explanation, though recently he has modified it to take explicit account of the variable transition state. Thus, a transition state with carbanion character will be destabilized by β-alkyl substitution[163].

Brown, following a suggestion made by Schramm, argues that steric interference of the bulky leaving group with the β-alkyl groups is the controlling factor[154,164]. This point will be discussed more fully in section III.E.

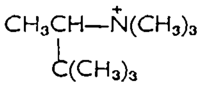
Eclipsing effects seem of relatively little importance in Hofmann-rule reactions. The *trans/cis* ratio for 2-pentene in eliminations from 2-pentyl derivatives decreases steadily along the series

bromide > tosylate > dimethylsulfonium > trimethylammonium[154]

as expected for decreasing double-bond character in the transition state. If either the α- or β-carbon bears *two* alkyl groups, then any eclipsing should decrease the overall rate of elimination rather than just shift the product ratio. In fact, on treatment with ethoxide ion **43** eliminates 42 times faster than **44**, and **45** eliminates 22 times

$CH_3CH_2\overset{+}{N}(CH_3)_3$

(43)

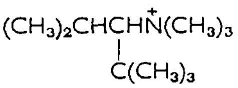


$CH_3CH(C(CH_3)_3)\overset{+}{N}(CH_3)_3$

(45)

$(CH_3)_2CHCH_2\overset{+}{N}(CH_3)_3$

(44)



$(CH_3)_2CHCH(C(CH_3)_3)\overset{+}{N}(CH_3)_3$

(46)

faster than **46**. If eclipsing between methyl and *t*-butyl were important, the **45**/**46** ratio should be *larger* than the **43**/**44** ratio where only methyl–hydrogen eclipsing can occur.

Groups other than alkyl seem to exert effects in accord with expectations of their ability to stabilize negative charge. Thus, a β-phenyl group greatly increases the rate of elimination from sulfonium and ammonium salts[7,12b]. If its major effect were steric hindrance, the phenyl group would be expected to change the rate in the same direction as a methyl group and probably to a greater extent.

Alkyl substitution on the α-position of sulfonium salts causes an increase rather than a decrease in rate. The rate of reaction with ethoxide of alkyldimethylsulfonium ions increases sharply in the order

ethyl < isopropyl < *t*-butyl[12b,134,149].

A few available comparisons suggest that the same holds true for ammonium salts[163]. An α-phenyl group greatly increases the rate of elimination of sulfonium salts[163]. This accelerating influence of a α-substitution is reflected in orientation studies as well, since $R^1R^2(CH_3)_2N^+OH^-$ loses isopropyl and *t*-butyl more readily than ethyl[148]. Clearly, α-substituents are not exerting just an inductive effect on proton loss, and it appears that they are shifting the transition state away from the carbanion-like end of the scale. Evidence that α-substitution increases the extent of C—S cleavage in the transition state for *E*2 reactions of sulfonium salts is afforded by the greater sulfur isotope effect with the *t*-butyldimethylsulfonium ion than with the 2-phenylethyldimethylsulfonium ion (section II.A)[41,42].

In most *E*2 reactions of compounds having uncharged leaving groups (only the halides and the *p*-toluenesulfonates have been studied extensively), and in all *E*1 reactions, either α- or β-alkyl substitution produces acceleration. The effect of a β-alkyl substituent is moderate, and usually larger for methyl than for other alkyl groups. Reaction rates for a series of primary bromides with ethoxide in ethanol at 55°C are: ethyl, 1·6; n-propyl, 5·3; n-butyl, 4·3; isobutyl, 8·6[13,165]. The effect per methyl group is a factor of 2–3, and this order of magnitude is in accord with the intramolecular effects represented by Saytzeff orientation (section III.C).

An α-alkyl substituent exerts a rather more pronounced effect. Again for *E*2 reactions of the alkyl bromides, the rate per branch goes from ethyl, 1·0, to isopropyl, 3·2, and *t*-butyl, 14. Increasing α-substitution probably tends to aid C—X heterolysis and shift the transition state toward the near-*E*1 direction, as well as leading to a more stable product. Phenyl substitution, on the other hand, works more strongly from the β-position than from the α-position[13]. In both α- and β-positions it can stabilize, by conjugation, a transition state with double-bond character, and in the α-position should encourage C—X heterolysis. The additional effect in the β-position is undoubtedly its ability to stabilize increased electron density, and probably to shift the transition state toward the near-*E*1cB end of the scale. The Hammett ρ of $+2{\cdot}15$ for *p*-substituted 2-phenylethyl bromides also attests the favorable effect of electron withdrawal from the β-position. Even so, the transition state still seems to possess some double-bond character. A secondary isotope effect of 17% is noted with 2-phenylethyl-1,1-d_2 bromide[166], and it is difficult to see how such a large effect could arise unless the change in hybridization of the α-carbon from sp^3 to sp^2 is fairly well advanced[167]. The inductive effect of β-substituents thus may persist into a region where there is still considerable double-bond character. Perhaps the small stabilizing effect of a β-alkyl group is in part a balance between an unfavorable inductive effect and a stronger favorable effect on the developing double bond.

Most of what has been said about the stabilizing effect of alkyl substituents applies to *E*1 reactions as well, though here we cannot measure the rate of the elimination step directly. Judging from the orientation results (section III.C), alkyl substitution exerts a stronger directive effect here than in *E*2 reactions. While this might not have been predicted, it is reasonable. Since the *p* orbital on the α-carbon is not occupied in bonding at all, the amount of double-bond character in the transition state is limited only by the extent of C—H bond breakage. In the *E*2 reaction, the amount of double-bond character is limited by the less-weakened of the two bonds (C—H and C—X). Aryl substituents should also favor double-bond character, but here the situation is complicated by effects on the stability of the carbonium ion.

As mentioned earlier, eclipsing effects are often significant with Saytzeff-rule leaving groups. Thus, 2-pentyl *p*-toluenesulfonate, bromide and iodide give a *trans*/*cis* ratio for 2-pentene of 2–3[154]. Interestingly, the *trans*/*cis* ratio is smaller (1·4) in the *E*1 acetolysis of 2-pentyl *p*-toluenesulfonate[156], while results cited in the preceding paragraph suggest greater double-bond character in *E*1 reactions.

Perhaps the enhanced effect of alkyl substitution on the *E*1 transition state arises from its electron deficiency, rather than from unusually large double-bond character.

Eclipsing effects can also operate to affect orientation, as the less substituted olefin will have fewer interferences between α- and β-substituents. It is not easy to disentangle this effect from the hyperconjugative effect on olefin stability, as the larger alkyl groups that should give increased eclipsing also usually have fewer α-hydrogens for hyperconjugation. The significant point again is that the orientation results parallel olefin stability. In the more highly branched compounds, at least, eclipsing undoubtedly is important.

$$(CH_3)_3CCH_2\underset{X}{C}(CH_3)_2 \longrightarrow (CH_3)_3CCH_2\underset{CH_3}{C}{=}CH_2 + (CH_3)_3CCH{=}C(CH_3)_2$$

(47) **(48)** **(49)**

The halides of **47** give at least 80% of **48** and less than 20% of **49** in both *E*1 and *E*2 reactions[153,156].

E. The Nature of the Leaving Group

Perhaps the single most important factor determining reactivity in elimination reactions is the nature of the leaving group. Among the common leaving groups, bromides are about 10 times as reactive as *p*-toluenesulfonates, and dimethylsulfonium salts are about 50 times more reactive than trimethylammonium salts[25,36]. Comparison of charged and uncharged leaving groups is more difficult, because solvent effects can be very pronounced with the charged leaving groups. A change from ethoxide in ethanol to hydroxide in water lowers the *E*2 rate for sulfonium salt by a factor of more than 10^3[168]. All of these figures are for the 2-phenylethyl series, though qualitatively similar behavior is found with other alkyl groups. Among the least reactive of all compounds undergoing the *E*2 reaction are the alkyl fluorides, which react about 5×10^3 times slower than the bromides[16,17].

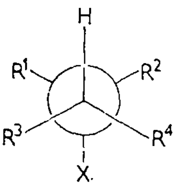
Similar variations in overall reactivity are noted in *E*1 reactions, though here the leaving group usually has little or no effect on the product-determining stage (section II.B). Some reversals of order of reactivity has been observed. *p*-Toluenesulfonates, for example, are more reactive than bromides in solvolytic reactions[169]. Tetraalkylammonium salts seem especially reluctant to undergo *E*1 reactions. Only recently have examples of this mechanism been observed, and then with cyclic systems where steric facilitation of ionization may be important[47,157].

More interesting than the overall effect of the leaving group on reactivity is its effect on relative reactivities. The variation in orientation between 'onium salts (Hofmann rule) and halides (Saytzeff rule) has already been mentioned (section III.C). Compounds whose reactions follow the Saytzeff rule generally give the more thermodynamically stable product. This is easily explicable by a transition state possessing double-bond character. Obviously, some other factor is of greater importance with Hofmann-rule leaving groups. The nature of this other factor has been the subject of recent controversy (see below).

The sensitivity of $E2$ reactions to the inductive effects of substituents has been demonstrated conclusively in the 2-phenylethyl system. Figures given in Table 1, section II.A, show that the response to inductive effects increases in the order of Br < OTs < $S(CH_3)_2$ < $N(CH_3)_3$ and, for the halogens, I < Br < Cl < F. In simple alkyl derivatives, β-alkyl substitution exerts an unfavorable effect on eliminations from sulfonium and ammonium salts, but a favorable effect on bromides and tosylates. That this is the result of the greater response of the 'onium salts to the electron-repelling inductive effect of the β-alkyl groups was first suggested by Hanhart and Ingold[6]. In present terminology, one would say that the 'onium salts have transition states with relatively high carbanion character, and the halides transition states with relatively high double-bond character[163].

Few cases of transition states that are either purely carbanionic or purely concerted will exist and, consequently, some inductive influences may operate in Saytzeff-rule reactions and some olefin-stability effects in Hofmann-rule reactions. This interplay of effects has been discussed at some length by Ingold[1,152]. He also presents the arguments in favor of hyperconjugation as the major factor in stabilizing the developing double bond in Saytzeff-rule reactions.

Ingold's overall picture of the effect of the leaving group on orientation and relative reactivities has been widely accepted, but recently his explanation of the Hofmann rule has been challenged. The suggestion that the steric effect of the leaving group is the important factor has been vigorously prosecuted by Brown[154,164]. He pictures the effect as operating *via* the interference between the leaving group and the β-substituent, introduced by the necessity of making H and X *trans* and coplanar in the transition state. In **50**, interferences between X and the β-substituents, R^3 and R^4, should increase with the bulk of X. Hence, elimination into a branch where R^3 and R^4 are hydrogens rather than alkyl groups should be favored with a bulky X. This explanation is predicated upon the assumption that the transition state is *geometrically* similar to reactants (**50**). Qualitatively, the tendency toward elimination in the less-substituted alkyl group or branch does increase with the steric bulk of the group. The order is halogen < OTs < $S(CH_3)_2$ < SO_2CH_3 < $N(CH_3)_3$.



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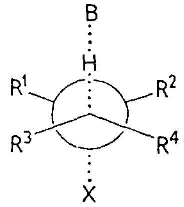

(51)

Ingold has argued against this effect as a general explanation of the Hofmann rule, though he considers that it may enter with very large β-substituents[163]. He suggests that the sharp decrease in rate of elimination observed with a β-*t*-butyl group is ascribable to this cause. He points out that an increase in double-bond character of the transition state should lessen the interference[154] between X and a β-alkyl group by flattening out the system and lengthening the C—X bond as in **51**. An α-phenyl group, which should encourage double-bond character, does indeed cancel the retarding effect of a β-*t*-butyl group.

The argument for a steric effect of the leaving group is further weakened by the fact that it explains little or nothing which electronic effects cannot also explain. The order of increasing bulk of X, cited by Brown as evidence, is the same as the order of increasing carbanion character to the transition state. An increasing sensitivity to inductive effects of β-alkyl substituents is therefore also to be expected.

A case where the two explanations do not run parallel is that of the halogens, where carbanion character increases in the order I < Br < Cl < F[16] and steric requirements were expected to increase in the order F < Cl < Br < I. Brown and Wheeler found no significant difference in the proportions of 1-pentene from 2-pentyl bromide and iodide. From this they argued that the larger steric requirement of iodine was counterbalanced by a larger covalent radius, which placed it farther from the site of interference.

A more extensive investigation has in fact revealed an order in accord with that expected from increasing carbanion character[170a]. With ethoxide ion in ethanol, the 2-pentyl halides gave proportions of 1-pentene which ran: chloride, 37%; bromide, 25%; iodide, 20%. Similarly, the 2-methyl-2-butyl halides gave 43% 2-methyl-1-butene from the chloride and 34% from the bromide. The value of these results as evidence *against* the steric explanation is lessened by recent data indicating that the equatorial/axial equilibrium in halocyclohexanes is little affected by changes in the halogen[170b]. The apparent steric requirements by this criterion actually run $Cl > Br > I$. The free-energy differences seem too small to account for the changes in orientation in *E*2 reactions, but the belief that the alkyl halides constitute a clear case of opposing steric and electronic effects is apparently incorrect.

A recent study varied the electronic effect of the leaving group while keeping its steric effect constant. A series of *p*-substituted 2-pentyl benzenesulfonates reacted with ethoxide ion to give a product mixture in which the proportion of 2-pentene showed a small but regular increase as the *p*-substituent became more electron withdrawing[171]. Again, the better leaving groups seem to give transition states with more double-bond character.

At present, the weight of evidence seems in favor of the electronic explanation of the effect of the leaving group in *E*2 reactions. Steric effects can be demonstrated in certain special cases and may play a role in others, but do not account for the overall orientation pattern as well as electronic effects can.

F. Variations in Base and Solvent

These two influences are considered at the same time because the base is often the conjugate base of the solvent, such as hydroxide ion in water or ethoxide ion in ethanol. Any change in one thus requires a change in the other, and this fact creates certain difficulties. The first is that of determining relative basicities, which can be done rigorously only when bases are compared in the same solvent. The second is that of deciding whether observed changes in a given elimination reaction are the consequence of difference in base strength, difference in solvation, or both. Even if equilibrium basicities are known, these may not always parallel rates of elimination because of the incursion of steric effects.

In some cases, interpretation of the results may be simplified if a base other than the conjugate base of a hydroxylic solvent is used, but this must be done with care. If the pure base is used as solvent, there is no guarantee that one is not observing an *E*1 solvolysis rather than an *E*2 reaction. If the base is added to a hydroxylic solvent, the reacting base might again be the conjugate base of the solvent, formed in the equilibrium of equation (39). This point can

$$\mathrm{ROH} + \mathrm{B} \rightleftharpoons \mathrm{RO^-} + \mathrm{BH^+} \tag{39}$$

be tested by adding different amounts of the same buffer in order to vary the concentrations of B and BH^+ while keeping their ratio constant. If both are doubled, the rate of an *E*2 reaction involving B should be doubled, but the concentration of RO^- is unaffected and a reaction depending upon RO^- should show at most a salt effect.

Returning to the first difficulty, some data are available on relative basicities on the conjugate bases of solvents commonly used in elimination reactions. Hine and Hine[172] have studied the ionization of water and various alcohols in isopropanol solution. They conclude that hydroxide ion is a stronger base than methoxide ion and similar in strength to ethoxide ion. The strongest base of all was *t*-butoxide ion. Whether this order would still apply when referring each base to its own conjugate acid as solvent cannot be decided readily. Very probably the advantage of *t*-butoxide would be maintained, but the others are too close to each other for reliable prediction. A common medium for *E*2 reactions is ethanol containing a few percent of water, either present at the outset or produced by dissolving potassium hydroxide in absolute ethanol. A study by Caldin and Long[173] suggests that the base in such solutions is present mainly as ethoxide ion. Additional data on ionization of common alcohols have been obtained by Ballinger and Long[174].

The experimental results on change of base in *E*2 reactions present a somewhat mixed picture. In the 2-phenylethyl system, the Hammett ρ for the *p*-toluenesulfonates increases sharply from $+2{\cdot}60$ to $+3{\cdot}39$ on going from ethoxide in ethanol to *t*-butoxide in *t*-butanol, while the bromides and iodides show no significant change (if anything, a slight decrease)[19].

A study of orientation in *E*2 reactions of alkyl bromides has revealed an increasing tendency toward formation of the less-substituted olefin along the series

ethoxide < *t*-butoxide < *t*-pentyloxide < triethylcarbinyloxide

(each in its conjugate acid as solvent). For example *t*-pentyl bromide yields only 30% of 2-methyl-1-butene with ethoxide, but 72·5% with *t*-butoxide and 88·5% with triethylcarbinyloxide. Brown ascribes this result to the increasing steric requirements of the base, which should favor attack at the more exposed β-hydrogens. He notes that the order is also the same as the expected order of increasing basicity, but reports a similar, though less marked, trend along the series pyridine, 2-picoline and 2,6-lutidine.[175] He argues that the base strength cannot be important, as 2-picoline gives an increase in the yield of less-substituted olefin while 4-picoline, of about the same strength, does not. Unfortunately, the pyridine bases were used as solvents and all of the bromides were tertiary. Under these circumstances the possibility of a solvolytic (*E*1) rather than an *E*2 reaction must be considered.

The phenomenon noted by Brown seems to persist in cyclic systems, since *cis*-2-methylcyclohexyl *p*-toluenesulfonate gives 76% 1-methylcyclohexene with ethoxide, but only 40% with *t*-butoxide[157]. Evidence that it also is found when the leaving group is positively charged is given by the work of Banthorpe, Hughes and Ingold[163]. They report, for example, that the decrease in rate from ethyl to n-propyl in $RS(CH_3)_2^+$ and $RN(CH_3)_3^+$ is greater when *t*-butoxide is the base than when ethoxide is the base. The reactions with *t*-butoxide were run at lower temperatures, but the differences appear too large to be attributed solely to temperature. Another example is provided by *t*-pentyl chloride and bromide, where the change from ethoxide to the weaker thiophenoxide (both in ethanol) produced a decrease in 2-methyl-1-butene[176]. This may be a case of the 'merged' mechanism (section II.C) rather than a normal *E*2 reaction.

In terms of the variable transition state, a change from ethoxide in ethanol to higher alkoxides in the corresponding alcohol seems usually to result in increased carbanion character. This might be the consequence either of a base-strength effect or a solvation effect.

The base-strength effect presents problems. In the 2-phenylethyl series, both the *p*-toluenesulfonate and the bromide give larger deuterium isotope effects with *t*-butoxide in *t*-butyl alcohol than with ethoxide in ethyl alcohol[25]. If the proton is past the midway point (see section II.A), this represents a more symmetrical transition state; *i.e.* a longer base–hydrogen bond. This is predicted by the Swain–Thornton rule[133], which also predicts that the carbon–hydrogen bond in the transition state will become *shorter*. This is difficult to reconcile with the apparent increase in carbanion character. Only if *both* the carbon–hydrogen and base–hydrogen bonds are longer in transition states with stronger bases can the base-strength explanation accommodate all the facts.

The solvation effects offer a more straightforward explanation, provided one assumes that the main function of solvation is to aid the departure of the leaving group X. Ethanol is better than the higher alcohols at solvating anions, and hence transition states with more C—X cleavage, and less carbanion character, are expected in ethanol. That the effect seems to persist with $S(CH_3)_2$ and $N(CH_3)_3$ as leaving groups (see above) is unexpected, as these should be less sensitive to solvation. A solvation effect which considers only overall charge distribution fails, as the less polar solvents should favor greater dispersal of charge in the transition state, and this would correspond to less carbanion character.

In summary, there appears to be a regular trend toward Hofmann-rule behavior with larger and more branched alkoxides. The possible sources of this trend are base strength, solvation and steric effects. Definitive evidence for the predominance of any one of these effects is lacking, and neither can any of them be entirely excluded.

Little evidence is available on the effect of solvent on product proportions in *E*1 reactions. Some data on solvolyses of 2-butyl bromide and *p*-toluenesulfonate in various solvents are given by Smith and Watson[177]. All product ratios obey the Saytzeff rule, and the *trans*/*cis* ratio for 2-butene is near unity. Differences in the 1-butene/2-butene ratio occur, but there is no obvious regularity to them. The greatest change is with 2-butyl bromide, which yields 5% 1-butene with silver nitrate in water, and 24% 1-butene with silver nitrate in *t*-butanol.

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 3

Olefin-forming eliminations in the gas phase

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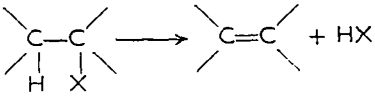
I. GENERAL INTRODUCTION

Olefin-forming eliminations can be represented in general by equation (1), where X = Cl, Br, I, RCO_2, $CH_2{=}CHO$, OCS_2CH_3, OH, NH_2 and $ClCO_2$. Interest in these reactions lies in two areas, first



(1)

in their synthetic applications and secondly insofar as they belong to a class of molecular reactions which can be studied from a physico-chemical point of view. The synthetic importance derives from those cases where more than one olefin can be formed in the reaction (equation 2) and where, by choice of X, either **1** or **2** may predominate.

$$\mathrm{CH_3CHXCH_2CH_3} \longrightarrow \underset{(1)}{\mathrm{CH_3CH{=}CHCH_3}} + \underset{(2)}{\mathrm{CH_2{=}CHCH_2CH_3}} + \mathrm{HX} \qquad (2)$$

Thus in the case of *s*-butyl chloride[1], the percentage of **1** is about 40%, whereas for the acetate[2] it is about 60%. The behaviour is even more marked in the case of the *t*-amyl compounds. Eliminations are said to follow the Saytzeff rule if the olefin produced has the greatest number of alkyl groups adjacent to the double bond, and to follow the Hofmann rule if the opposite obtains. In view of the fact that olefins isomerize in the presence of hydrogen halides[3], the tendency is to approach the equilibrium proportions in eliminations from alkyl halides, whereas, with the esters, an olefin composition far from the equilibrium one is produced. The effect is most marked with the iodide[1], since iodine produced in the pyrolysis also appears capable of bringing about an approach to equilibrium. From the physico-chemical point of view, the primary problem is the assignment of a mechanism to these reactions. Also, because of their clean stoichiometry, they provide a useful area for testing theories of unimolecular reactions.

When studied in clean glass or metal vessels, the majority of alkyl halides decompose by a heterogeneous mechanism, which is also observed when halide salts are present. This is particularly marked with the *t*-butyl compounds; thus *t*-butyl chloride equilibrates with hydrogen chloride and isobutene[4] on a glass wool surface at temperatures as low as 90°c, whereas the convenient temperature range for studying the homogeneous reaction[5] is 270–350°c. Again, *t*-butyl iodide appears to decompose heterogeneously to hydrogen iodide and isobutene under all conditions under which it has been studied[6].

There is a third possibility, namely a chain mode of decomposition, which has been observed for primary alkyl bromides[7], for primary esters[8] and for certain polychlorides[9]. The mechanism of these reactions is by no means clear; in particular, the question whether chain initiation and termination are homogeneous or heterogeneous

An excellent review of olefin-forming eliminations in the gas phase has been given by DePuy and King, *Chem. Rev.*, **60,** 431 (1960).

has not been unambiguously settled. For the polychlorides, two main initiating steps have been postulated (equations 3 or 4), while for the

$$\left.\begin{array}{l} CH_2ClCH_2Cl \longrightarrow CH_2{=}CH_2 + Cl_2 \\ Cl_2 + M \longrightarrow 2\,Cl\cdot + M \end{array}\right\} \quad (3)$$

$$CH_2ClCH_2Cl \longrightarrow CH_2ClCH_2 + Cl\cdot \quad (4)$$

bromides the steps (5) or (6) have been suggested. For the iodides

$$C_2H_5Br \longrightarrow C_2H_5 + Br\cdot \quad (5)$$

$$\left.\begin{array}{l} C_2H_5Br + HBr \longrightarrow C_2H_6 + Br_2 \\ Br_2 + M \longrightarrow 2\,Br\cdot + M \end{array}\right\} \quad (6)$$

(for which the stoichiometric reaction is given in equation (7),

$$C_nH_{2n+1}I \longrightarrow C_nH_{2n} + C_nH_{2n+2} + I_2 \quad (7)$$

except for *t*-butyl iodide), no reasonable chain scheme can be written to account for the observed products. No detailed discussion has been given of the chain mechanisms observed with the primary esters. The propagation steps in the case of the halides are widely accepted as depicted in equation (8), where X = Cl or Br. Various chain-termination steps have been postulated to explain the observed kinetic results[7] (first or 1·5 order). To sum up, there still exists a considerable area of doubt as to the exact nature of the elementary reactions in the chain mode of pyrolysis.

$$\left.\begin{array}{l} X\cdot + C_nH_{2n+1}X \longrightarrow C_nH_{2n}X + HX \\ C_nH_{2n}X \longrightarrow C_nH_{2n} + X\cdot \end{array}\right\} \quad (8)$$

There are two types of equilibria of importance in these pyrolytic reactions, namely the dissociative equilibrium (9) and the isomeric equilibrium (10) between olefins. Study of the former[4] leads to rates of homogeneous addition by use of equation (11), where k_2 is the rate constant for addition and K the equilibrium constant. In most cases K is very large over the temperature range in which k_1

$$C_nH_{2n+1}X \underset{k_2}{\overset{k_1}{\rightleftharpoons}} C_nH_{2n} + HX \quad (9)$$

$$C_nH_{2n} \rightleftharpoons (C_nH_{2n})' \quad (10)$$

$$k_2 = \frac{k_1}{K} \quad \text{with} \quad K = \frac{p_{HX}\,p_{C_nH_{2n}}}{p_{C_nH_{2n+1}X}} \quad (11)$$

can be conveniently measured and so the back reaction does not complicate the kinetics. This also implies that the homogeneous back reaction will be too slow to measure in the temperature range when the equilibrium is favourable. This is illustrated in the case of ethyl chloride investigated by Howlett[10].

The purpose of the present chapter is to review the evidence regarding homogeneous olefin molecular elimination from (a) hydrocarbons, (b) chlorides, bromides and iodides, (c) esters and vinyl ethers, (d) xanthates, (e) alcohols and amines, and (f) chloroformates. This will be followed by a short section on catalysis of the elimination reaction, both homogeneous and heterogeneous, and on the relevant equilibria. Finally, the various theories of the gas-phase elimination reaction will be discussed.

II. HOMOGENEOUS ELIMINATIONS[11]

These reactions have been widely studied, in general by pressure measurements, since in the course of the reaction the pressure increases. It is usual to work with seasoned vessels, that is vessels that have been covered by a thin carbonaceous film by prolonged contact with the products, or more rapidly produced by pyrolysing allyl bromide. Homogeneity may be verified by using vessels packed with glass tubes and a convenient method is to use rigidly held concentric glass cylinders. The stoichiometry of the reaction may be checked by analysis for HX, and olefin composition is most conveniently determined by vapour-phase chromatography. In the case of the molecular eliminations, the kinetic order is unity, and when two molecules of product are produced, the total pressure P obeys equation (12),

$$k_1t = \ln \frac{p_0}{2p_0 - P} \tag{12}$$

where p_0 is the initial pressure and k_1 the first-order rate constant. Thus a plot of $\log (2p_0 - P)$ against t is a straight line of slope $-k_1/2{\cdot}303$. The variation of the rate coefficient with temperature is given by equation (13), A being the preexponential term and E the

$$\log k_1 = \log A - \frac{E}{2{\cdot}303\,RT} \tag{13}$$

activation energy. In those cases where reaction chains are suspected, use of an inhibitor (propene, cyclohexene, *etc.*) will decide the issue. An underlying molecular mechanism in a mixed chain and molecular mode of decomposition may often be isolated by studying the elimination under conditions of maximal inhibition.

The effect of substitution upon the rate of a given class of reaction may be expressed either by a discussion of the rates of a series of compounds relative to that of a given basic compound, or by a comparison of the Arrhenius parameters for the series. In the latter case, if the frequency factor A is constant over the series, the variation in rate may be discussed in terms of the activation energy. For unimolecular gas-phase reactions, log A is usually taken to be of the order of magnitude of 13 (A in $\sec^{-1}$). A distribution curve of the number of reactions with logarithms of the frequency factors in the range log A to log A + 0·5 is shown in Figure 1 for the reactions listed in Tables 2, 3 and 4. It will be seen that the values are in fact distributed about the value 13·25, and further that the distribution

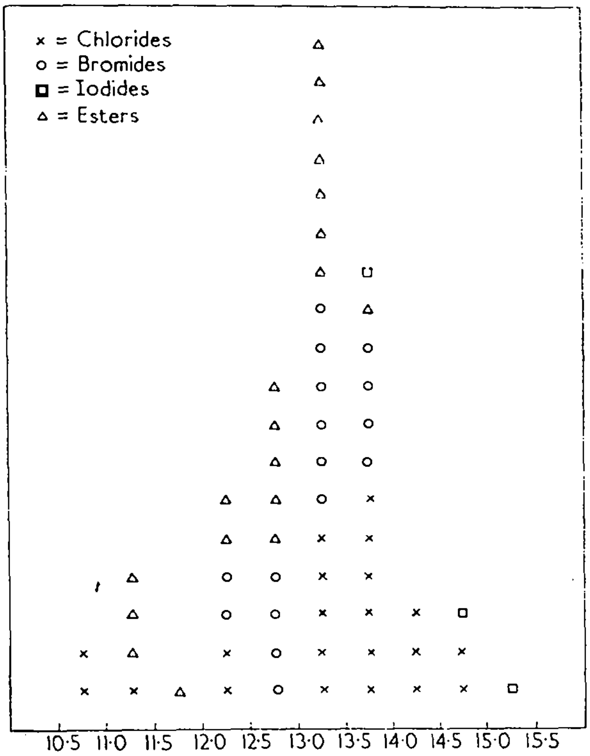
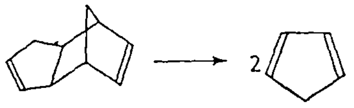


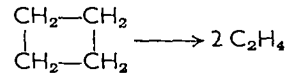
FIGURE 1. The number of elimination reactions with frequency factors in the range log A to log A + 0·5 for the reactions listed in Tables 2, 3 and 4.

is approximately normal. In what follows, then, variations in rate will be discussed either in terms of relative rates or activation energies, the latter quantity being regarded as the major factor influencing the rate.

A. Hydrocarbons

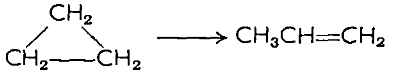
Aliphatic hydrocarbons decompose by a complex chain route, leading to a variety of products. One reaction which may be a simple molecular one is the pyrolysis of neopentane, which yields isobutene and methane predominantly, and for which the kinetics have been variously reported as first order or of order 1·5. However, the most widely studied and best understood class of reaction is the reverse Diels–Alder reaction, yielding di- or monoolefinic products (*e.g.* reaction 14). A related reaction is the pyrolysis of cyclobutane and its derivatives (equation 15). Cyclopropane, on the other hand, undergoes isomerization to propylene (equation 16). Similarly cyclobutene isomerizes to butadiene (equation 17). The Arrhenius parameters for the above reactions are shown in Table 1. It may be


(14)



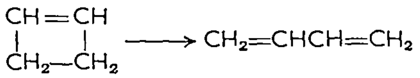
$$\begin{array}{l} CH_2{-}CH_2 \\ |\qquad\;\; | \\ CH_2{-}CH_2 \end{array} \longrightarrow 2\,C_2H_4$$

(15)



$$\begin{array}{c} CH_2 \\ /\quad\;\; \backslash \\ CH_2{-\!-}CH_2 \end{array} \longrightarrow CH_3CH{=}CH_2$$

(16)



$$\begin{array}{l} CH{=}CH \\ |\qquad\;\; | \\ CH_2{-}CH_2 \end{array} \longrightarrow CH_2{=}CHCH{=}CH_2$$

(17)

TABLE 1.

Reaction	Log A	E (kcal/mole)	Reference
Cyclohexane decomposition	13·0	57·5	12
Dicyclopentadiene decomposition	13·1	35	13
Cyclobutane decomposition	15·6	62·5	14
Ethylcyclobutane decomposition	15·6	62·0	15
Cyclopropane isomerization	15·7	65·0	16
Cyclobutene isomerization	13·1	32·5	17

noted in passing that the effect of alkyl substitution on the rate of reaction is small. Thus ethylcyclobutane pyrolyses at a rate only about 1·3 times faster than cyclobutane itself.

B. *Halides*

All the reactions discussed in this section have been shown to be homogeneous, first order and molecular in nature. The chlorides and bromides decompose according to equation (18). The chlorides

$$C_nH_{2n+1}X \longrightarrow C_nH_{2n} + HX \tag{18}$$

and bromides have been widely investigated, the iodides to a lesser extent. The decomposition of the iodides is not of so much interest from a preparative point of view, since the product is usually an equimolar mixture of an alkane with an alkene. In all cases, the alkenes may be a mixture of isomers. One difficulty inherent in the isolation of molecular reactions in the case of the iodides is that the energy for homolytic splitting of the carbon–iodine bond is close to that for elimination. Thus radical and molecular processes may proceed simultaneously, as has possibly been observed in the case of ethyl iodide[18].

There is no positive evidence for the molecular reaction (19) in the

$$CH_3X \longrightarrow :CH_2 + HX \tag{19}$$

case of the methyl halides. For methyl bromide in the temperature range 480–500°c, Meissner and Schumacher[19] showed that, in a static system, the products were carbon, hydrogen bromide and methane, the latter products being in the ratio of 2 : 1. Whittingham[20] has suggested the mechanism (20) to account for the observed products.

$$\left.\begin{array}{r}2\,CH_3Br \longrightarrow 2\,:CH_2 + 2\,HBr\\ CH_2: + CH_2: \longrightarrow :C: + CH_4\end{array}\right\} \quad (20)$$

Sehon and Szwarc[21] have used the toluene-flow technique to investigate the pyrolysis of methyl bromide. Again, the reaction is complex and first-order rate coefficients are pressure dependent, but the results were considered consistent with an activation energy of 67·5 kcal/mole. In the case of methyl chloride, Shilov and Sabirova[22], using a flow system, showed that at 844 and 874°c, the main products were hydrogen chloride, methane and acetylene in the approximate ratio 3 : 1 : 0·5. The rate equation was $k_1 = 10^{15} \exp(-85{,}000/RT)$ sec^{-1}, the first-order rate coefficients showing an increase with pressure. This would be expected, as the methyl chloride molecule contains too few atoms to decompose by a unimolecular route at the pressures used in the investigation. The activation energy suggests that carbon–chlorine bond breaking is rate controlling and the authors suggest Scheme 1 as the probable mechanism. The greatly enhanced tem-

$$\begin{aligned} CH_3Cl &\longrightarrow CH_3\cdot + Cl\cdot \\ Cl\cdot + CH_3Cl &\longrightarrow HCl + CH_2Cl\cdot \\ CH_3\cdot + CH_3Cl &\longrightarrow CH_4 + CH_2Cl\cdot \\ CH_2Cl\cdot + CH_2Cl\cdot &\longrightarrow C_2H_4Cl_2 \\ C_2H_4Cl_2 &\longrightarrow C_2H_2 + 2\,HCl \end{aligned}$$

SCHEME 1.

TABLE 2. The Arrhenius parameters and temperature ranges for chloride pyrolyses.

Molecule	Log *A*	*E* (kcal/mole)	Temp. range (°c)	Reference
Ethyl chloride	14·60	60·8	400–490	25
	13·63	56·9	420–500	26
n-Propyl chloride	13·45	55·0	420–478	27
n-Butyl chloride	14·00	57·0	430–470	27
	14·50	57·9	391–458	28
Neopentyl chloride	—	57	444–470	29
Isobutyl chloride	14·02	56·9	417–474	30
s-Propyl chloride	13·40	50·5	367–406	31
s-Butyl chloride	13·75	50·1	339–390	32
	14·00	50·6	316–393	33
Cyclopentyl chloride	13·39	48·1	309–376	34
Cyclohexyl chloride	13·17	50·0	318–385	35
t-Butyl chloride	12·40	41·4	290–341	36
	13·90	45·0	274–372	37
	13·73	45·0	290–330	38
	14·41	46·6	271–346	39
	13·70	44·9	284–309	40
t-Amyl chloride	13·82	44·2	280–320	38
2-Chloro-2,3-dimethylbutane	13·38	42·3	270–311	38
2-Chloro-2,3,3-trimethyl-butane	13·80	41·9	250–295	38
(−)-Menthyl chloride	12·60	45·0	320–440	41
	11·60	41·8	300–350	42
Neomenthyl chloride	10·65	40·1	300–350	42
Bornyl chloride	13·78	50·6	320–390	43
Isobornyl chloride	14·78	49·7	310–350	43
1,1-Dichloroethane	12·08	49·5	356–453	25
1,1,1-Trichloroethane	14·0	54·0	363–434	44
1,2-Dichloropropane	13·8	54·9	416–452	31
α-Phenylethyl chloride	10·78	39·3	310–365	45
α-Methoxyethyl chloride	11·46	33·3	180–250	46

peratures for the methyl halides as compared with other primary halides ($\sim$420°c for the chlorides and $\sim$380°c for the bromides) strongly suggests than an entirely different reaction path is being followed in those compounds possessing a β-carbon–hydrogen bond. In his studies of the reaction between methyl iodide and hydrogen iodide, Ogg[23] suggested that the activation energy for reaction (21)

$$\mathrm{CH_3I} \longrightarrow \mathrm{CH_3}\cdot + \mathrm{I}\cdot \qquad (21)$$

was about 43 kcal/mole, but this value now seems to be too low[24]. Thus it would appear likely that the initial step in the pyrolysis of the methyl halides is (22) and that this is followed by various subsequent steps.

$$\mathrm{CH_3X} \longrightarrow \mathrm{CH_3}\cdot + \mathrm{X}\cdot \qquad (22)$$

Dealing now with those halide decompositions which have been shown to be unimolecular, Tables 2, 3 and 4 show the Arrhenius

TABLE 3. The Arrhenius parameters and temperature ranges for bromide pyrolyses.

Molecule	Log *A*	*E* (kcal/mole)	Temp. range (°c)	Reference
Ethyl bromide	13·45	53·9	380–430	47
	12·86	52·3	527–626	48
n-Propyl bromide	12·80	50·7	350–390	49
	13·00	50·7	500–600	48
n-Butyl bromide	13·18	50·9	370–420	49
Isobutyl bromide	13·06	50·4	360–420	50
n-Pentyl bromide	13·09	50·5	370–420	51
n-Hexyl bromide	13·13	50·5	370–420	51
Isopropyl bromide	12·62	47·8	310–350	52
	12·60	47·7	500–600	48
s-Butyl bromide	12·63	43·8	300–350	53
	13·04	45·5	326–398	54
	13·53	46·5	299–354	55
Cyclopentyl bromide	12·84	43·7	300–360	56
	11·90	41·4	300–360	57
Cyclohexyl bromide	13·51	46·1	300–350	58
4-Bromo-1-pentene	12·94	44·7	300–350	47
α-Phenylethyl bromide	12·18	38·8	255–285	45
t-Butyl bromide	14·00	42·0	230–280	59
	13·30	40·5	235–290	4a
	13·23	41·0	276–326	54
t-Amyl bromide	13·60	40·5	220–270	60
2-Bromo-2,3-dimethylbutane	13·54	39·0	210–260	61
1,1-Dibromoethane	12·91	49·5	350–430	62

TABLE 4. The Arrhenius parameters and temperature ranges for iodide pyrolyses.

Molecule	Log A	E (kcal/mole)	Temp. range (°c)	Reference
Ethyl iodide	13·53	49·3	325–380	18a
	13·66	50·0	330–392	18b
s-Propyl iodide	14·79	48·0	290–357	63
	13·20	42·9	292–336	64
s-Butyl iodide	15·20	57·9	290–330	63

parameters and the temperature ranges studied in the case of the chlorides, bromides and iodides respectively.

In each of the series shown, the trends are the same. This is shown for the case of α- and β-methylation in Table 5. For each temperature, the rate coefficient of the ethyl compound is taken as unity, and the value quoted gives the ratio of the rate of the given compound to that of the ethyl halide. In all cases, the effect of α-methylation is large, while that of β-methylation is small, but still significant. The results for the α-series may be interpreted in terms of the effect of α-methylation upon the carbon–halogen bond; for the β-series, the question arises whether the effect is a first-order effect upon the α-carbon–halogen bond. The answer is suggested by the following tertiary series (Table 6) investigated by Wong[38]. In this series a β-carbon–

TABLE 5. The effects of α- and β-methylation.

R	Isopropyl	*t*-Butyl	*n*-Propyl	Isobutyl
	Temp. 361°c		Temp. 457°c	
X = Cl	223	41,000	3·9	3·9
	Temp. 320°c		Temp. 404°c	
Br	280	78,000	3·3	5·9
	Temp. 285°c		Temp. 327°c	
I	80	—	2·70[a]	—

[a] This value is the ratio of the rates for *s*-butyl and isopropyl iodides

TABLE 6. The effect of β-methylation at 290°c.

Compound	$(CH_3)_3CCl$	$C_2H_5(CH_3)_2CCl$	iso$C_3H_7(CH_3)_2CCl$
Relative rate	1	2·0	4·5
Compound	t-$C_4H_9(CH_3)_2CCl$		
Relative rate	16·0		

hydrogen bond changes from primary to secondary to tertiary and then back to primary, while the rate of elimination smoothly increases. Again, the close similarity in rate between *s*-butyl bromide and 4-bromo-1-pentene (relative rate 1·05:1 at 380°c) has been taken by Thomas[47] to suggest the importance of the carbon–halogen centre; for the β-hydrogen atom in this case is an allylic one (and hence homolytically weakened), so an enhancement of rate would be expected if the homolytic bond dissociation energy of the β-carbon–hydrogen bond were of importance in the transition state. From these pieces of evidence, it may be concluded that the effect of β-substitution is a second-order effect on the α-carbon–halogen bond.

The effects of α- and β-halogen substitutions are also of significance. Although 1,2-dichloro- and 1,2-dibromoethane decompose predominantly by a chain mechanism, inhibition studies have been made at 437° and 416°c respectively, which enable the rates of molecular dehydrohalogenation to be estimated. The rates relative to the ethyl halide are shown in Table 7. For both series α-halogen substitution increases the rate of elimination, while β-halogen substitution decreases it. This latter result is also consistent with the effect of β-substitution being a second-order effect on the α-carbon–halogen bond.

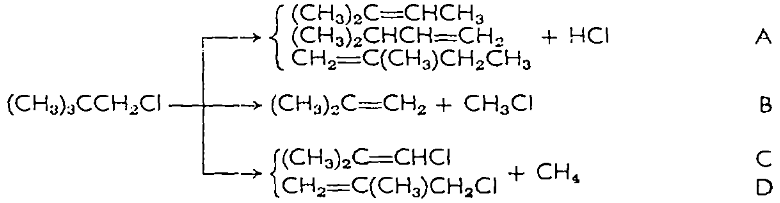
TABLE 7. The effect of α- and β-halogen substitution[65].

Temperature (°c)	CH_3CX_3	CH_3CHX_2	CH_3CH_2X	CH_2XCH_2X
416 (X = Br)	—	9·6	1	0·25
437 (X = Cl)	32	8·2	1	0·55

Stephenson[45] has studied the α- and β-phenylethyl chlorides and bromides. In the case of the α-phenyl compounds, the Arrhenius parameters given in Tables 2 and 3 may be used to show that these compounds decompose at about the same rate as the corresponding *t*-butyl halides. For the β-phenyl compounds, a chain mechanism predominated, but it was possible to measure the inhibited molecular rate at one temperature in each case. The values were, for the chloride, $10^4k = 3{\cdot}0\ \text{sec}^{-1}$ at 425·5°c, and, for the bromide, $10^4k = 0{\cdot}85\ \text{sec}^{-1}$ at 385·5°c. The values for the n-propyl halides calculated from the Arrhenius parameters of Tables 2 and 3 are 1·8 and 0·96 respectively. Thus the β-phenylethyl halides decompose unimolecularly at a rate almost identical with the rate of decomposition of the corresponding n-propyl halides. Thus in the α-position, a phenyl group is about equivalent to two methyl groups; in the β-position, to one.

An exciting investigation of the pyrolysis of α-methoxyethyl chloride was made by Thomas[46]. Methoxy substitution reduces the activation energy by some 25 kcal/mole (Table 2) compared with ethyl chloride. The rate relative to that of ethyl chloride at 330° is 7,000,000, and so the accelerating effect of the α-methoxy group is most strikingly portrayed.

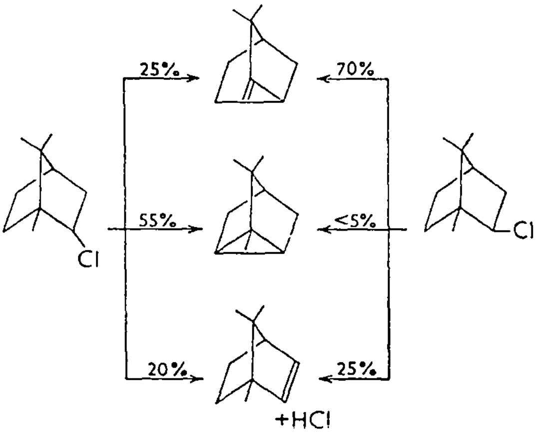
The case of neopentyl chloride[29] is of great significance, since it represented the first observation of a gas-phase Wagner–Meerwein rearrangement. Since this compound contains no β-carbon–hydrogen bond, migration of a methyl group from the β-position must occur (if pentenes are to be produced). At 444°c, the decomposition could be interpreted in terms of four simultaneous reactions, as follows: reaction A (75%), formation of hydrogen chloride and an equilibrium mixture of methylbutenes (2-methyl-2-butene, 2-methyl-1-butene and 3-methyl-1-butene in the ratio of 60:35:5); reaction B (10%), formation of methyl chloride and isobutene; reaction C (7%) formation of methane and 1-chloro-2-methyl-1-propene; reaction D (7%), formation of methane and 3-chloro-2-methyl-1-propene, with subsequent rapid decomposition of the latter compound. Reaction A was shown to be homogeneous and unimolecular: reactions B, C and D were in part heterogeneous. Reactions B, C and D may conveniently be grouped together and the total rate is very close to the rate of elimination of methane from neopentane. The reactions are shown in Scheme 2.



Scheme 2.

The case of bornyl[43] and isobornyl chlorides provides a further example of a Wagner–Meerwein-type rearrangement. From each of these compounds, a mixture of camphene, bornylene and tricyclene is obtained, together with hydrogen chloride, as shown in Scheme 3. The bornylene undergoes a reverse Diels–Alder reaction at the temperatures involved. It is also worth noting that isobornyl chloride decomposes more rapidly than bornyl chloride.

The first evidence as to stereospecificity of the elimination reaction came from the study of (−)-menthyl chloride by Barton and colleagues[41]. These authors showed that Δ^2-methene and Δ^3-menthene were produced in the ratio of 1:3 from this compound. This work was extended by Bamkole[42] who showed that for neomenthyl chloride, the proportions were 6:1. Thus it would appear that the *cis* orientation of the halogen and the β-hydrogen atom is energetically favoured.



SCHEME 3.

The effect of deuteration upon the reaction was first studied by Good[62], who showed that deuteration decreased the rate of elimination of hydrogen bromide from isopropyl bromide, although it was difficult to say definitely whether the effect was in the activation energy or the preexponential term of the Arrhenius equation. Blades[66], using a flow technique, was able to obtain the Arrhenius equation $k = 2{\cdot}1 \times 10^{13} \exp(-54{,}840/RT)\ \text{sec}^{-1}$ for ethyl bromide-d_5, to be compared with $k = 8{\cdot}5 \times 10^{12} \exp(-52{,}200/RT)\ \text{sec}^{-1}$ obtained from a study of ethyl bromide. The effect appears to be largely in the activation energy. Blades[66,67] has extended this work by determining the relative rates of deuterium bromide and hydrogen bromide elimination from partially deuterated ethyl halides. Again, the difference seems largely to reside in the activation energy.

Relative rates of elimination of the hydrogen halides from the ethyl and isopropyl series may be calculated from Tables 2, 3 and 4. The results are shown in Table 8. In both cases the order is clearly chloride < bromide < iodide.

TABLE 8. The relative rates of elimination from RCl, RBr, RI.

X	Chloride	Bromide	Iodide
R = Ethyl (442°c)	1	8·3	173
R = Isopropyl (361°c)	1	14·1	185

The direction of elimination has been investigated in relatively few cases. For the *s*-butyl halides, Stone[32] has given the following (Table 9) product proportions. Because of the possibility of isomerization brought about by the hydrogen halide, the analysis was also made for runs carried out in the presence of ammonia, which would reduce the partial pressure of the hydrogen halide. The values thus obtained are shown in parentheses. Again, Harden[60] investigated the pyrolysis products of *t*-amyl bromide in a heated infrared cell, because of the possibility of back addition if condensation were allowed to take place, and concluded that 2-methyl-2-butene was the major product. Stimson (private communication referred to in ref. 29) has suggested that the methylbutenes rapidly isomerize at 400° in the presence of hydrogen halides. What evidence there is thus suggests that the Saytzeff rule is obeyed in elimination from alkyl halides.

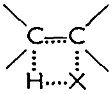
TABLE 9. Product composition from *s*-butyl halides.

Olefin	Chloride	Bromide	Iodide
2-Butene (*cis–trans*)	60 (59)	77 (66)	84
1-Butene	40 (41)	23 (34)	16

(a) $(CH_3)_3CX \gg (CH_3)_2CHX \gg CH_3CH_2X$ $(X = Cl, Br)$
(b) $(CH_3)_2CHCH_2X > CH_3CH_2CH_2X > CH_3CH_2X$ $(X = Br)$
$(CH_3)_3CC(CH_3)_2X > (CH_3)_2CHC(CH_3)_2X >$
$CH_3CH_2C(CH_3)_2X > (CH_3)_3X$ $(X = Cl)$
(c) $CH_3CX_3 > CH_3CHX_2 > CH_3CH_2 > CH_2XCH_2X$ $(X = Cl, Br)$
(d) $PhCH_2CH_2X \sim CH_3CH_2CH_2X$ $(X = Cl, Br)$
$PhCHXCH_3 \sim (CH_3)_3CX$ $(X = Cl, Br)$
(e) $CH_2{=}CH(CH_3)CHBrCH_3 \sim CH_3CH_2CHBrCH_3$
(f) $CH_2OCHClCH_3 \ggg CH_3CH_2Cl$
(g) $C_nH_{2n+1-x}D_xX < C_nH_{2n+1}X$ $(X = Cl, Br)$

SCHEME 4.

On the basis of some of the results given in Tables 2, 3, and 4, Maccoll and Thomas[68] were led to suggest an analogy between the rate of gas-phase elimination by the S_N1 or $E1$ mechanism in a polar solvent. The evidence[65] was drawn from the rate sequences given in Scheme 4. These have been drawn up on the basis of studies of gas-phase elimination; they are identical with those found for unimolecular solvolysis in a polar solvent. The evidence for this has previously been reviewed[65], and suggests that the convention representation of the transition state as a four-centred one (**3**) needs modification. In addition, the Wagner–Meerwein rearrangements described earlier are in very good agreement with those observed in solvolytic reaction[69]. The analogy may be taken as verified; its interpretation will be dealt with in a later section.



(**3**)

C. Esters

Ester pyrolysis has been studied from two points of view, first for gaining information as to the behaviour of unimolecular gas-phase reactions and secondly as a useful synthetic route. This latter aspect has been very fully reviewed by DePuy and King[70]. The Arrhenius parameters for unimolecular elimination from the systems studied are given in Table 10.

Using the Arrhenius parameters shown in Table 10, relative rates may be calculated. The effect of α-methylation is shown in Table 11. The effect of β-methylation can be seen by comparing the rates of *s*-butyl and isopropyl, *t*-amyl and *t*-butyl acetates. The values are 0·96 (308°) and 1·50 (237°c). Thus as in the case of the halogen compounds, α-methylation has a large effect, while β-methylation has only a small effect. The scale is, however, greatly reduced as compared with the halides.

The small effect of homolytic weakening of the β-carbon–hydrogen bond is shown by comparing the rates of pyrolysis of vinylisopropyl and *s*-butyl acetates[77]. The rate ratio at 360°c is 2:1, but only 34% of the terminal olefin is formed from the former whereas 60% is formed from the latter. Thus, whereas the rate is scarcely affected, the direction of elimination is reversed. A more striking effect is found with acetoisopropyl acetate, which decomposes at 260°c

TABLE 10. The Arrhenius parameters and temperature ranges in unimolecular ester pyrolyses.

Ester	Log A	E (kcal/mole)	Temp. range (°C)	Reference
Ethyl formate	11·33	44·1	540–650	71
Ethyl acetate	12·49	47·8	510–610	71
Ethyl propionate	12·72	48·5	—	72
Di-(2-ethylhexyl) sebacate	12·43	47·1	260–310	73
Acetic anhydride	12·10	34·5	280–650	74
Isopropyl formate	12·58	44·0	450–540	71
	12·43	44·2	310–340	75
Isopropyl acetate	13·00	45·0	440–530	71
	13·42	46·3	310–360	76
s-Butyl acetate	13·30	46·6	300–360	76
Vinylisopropyl acetate	13·00	44·4	290–360	77
Acetoisopropyl acetate	11·88	37·4	250–300	77
Cholesteryl acetate	13·70	44·1	280–330	78
Menthyl benzoate	11·00	38·1	300–400	79
α-Phenylethyl acetate	12·81	43·7	320–370	80
1,2-Diphenylethyl acetate	13·05	43·3	315–360	81
t-Butyl formate	11·11	34·6	230–300	82
t-Butyl acetate	13·34	40·5	240–290	76
	13·15	40·0	240–300	83
t-Butyl propionate	12·80	39·2	240–300	84
t-Amyl acetate	13·43	40·3	230–300	76
t-Butyl chloroacetate	13·09	38·1	215–265	85
t-Butyl dichloro-acetate	12·77	36·1	215–250	85

TABLE 11. The effect of α-methylation in ester pyrolysis at 400°C.

XCO_2R	Ethyl	Isopropyl	*t*-Butyl
X = H (formate)	1	20	720
X = CH_3 (acetate)	1	26	1660

at a rate 120 times that of *s*-butyl acetate[77]. The direction of elimination is such as to lead almost entirely to the conjugated olefin. The direction of elimination has been widely discussed by DePuy and King[70], and it is found that, except where special structural features exist, this factor is governed by the Hofmann rule. Thus 60% of the terminal olefin is produced from *s*-butyl acetate; 75% from *t*-amyl acetate[76].

The effect of acid strength has been investigated qualitatively by Smith and Wetzel[86], who showed that the stronger the acid, the greater the rate of elimination. Emovon[85] has studied *t*-butyl mono- and dichloroacetates and gives the relative rates and values of pK_a for the acids (Table 12). This clearly supports the views of Smith and Wetzel.

TABLE 12. Rates of *t*-butyl ester pyrolysis as a function of acid strength.

Ester	Acetate	Formate	Chloroacetate	Dichloracetate
pK_a	4·75	3·75	2·85	1·3
Relative rate (250°)	1·6	1·0	5·5	18·6

The effect of α- and β-phenyl substitution can be calculated from Table 10. The results (Table 13) show that a phenyl group in the α-position has a relatively large effect, whereas a second phenyl group in the β-position has only a rather small effect. This type of behaviour is also shown by the halides though the magnitude of the effect in that case is much greater.

TABLE 13. The effect of α- and β-phenyl substitution.

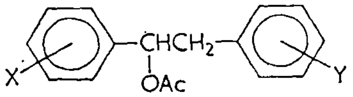
Compound	CH_3CH_2OAc	$CH_3CH(OAc)Ph$	$PhCH_2CH(OAc)Ph$
Relative rate (400°)	1	45	130

DePuy, King and Froemsdorf[87] have observed a considerable deuterium isotope effect in 1-methylcyclohexyl-2,2,6,6,-d_4 acetate. Blades and Gilderson carried out kinetic studies of ethyl-1,1,2,2-d_4 acetate[88] and of ethyl acetate and ethyl-d_5 acetate[89]. In the latter paper, these authors measured the relative rate of production of ethylene and ethylene-d_4 from a mixture of the acetates at two temperatures and arrived at the expression (23). These authors also

$$\frac{k_H}{k_D} = 0{\cdot}8 \exp (1513/RT) \tag{23}$$

observe that the rate of pyrolysis of ethyl-d_3 acetate was almost identical with that of the normal acetate.

Smith, Bagley and Taylor[81] have measured the rate of gas-phase pyrolysis of esters of the type **4** where X and Y may be hydrogen, methyl, chlorine or methoxyl. As might be expected, since the substitutions are far from the seat of reaction, the effect is small, the total range in rate relative to α,β-diphenylethyl acetate at 600°K from α-4-methoxyphenyl-β-4-chlorophenylethyl acetate to a α-3-chlorophenyl-β-phenylethyl acetate being from 3·20 to 0·582. With X in the 4-position, the sequence


(4)

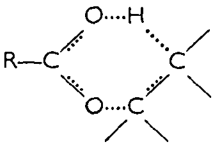
$$X = CH_3O > CH_3 > H > Cl$$

is established, while with Y in the 4-position the sequence

$$Y = Cl > H > CH_3 > CH_3O$$

is obtained. Furthermore, for both the α-aryl-β-phenylethyl acetates and the α-phenyl-β-arylethyl acetates, a good correlation is found between the relative rate and the Hammett σ function. Taylor[80] has taken this work further, and used the method to deduce the electrophilic reactivity of pyridine from a study of the pyrolysis of the α-arylethyl acetates.

The transition state in ester pyrolysis has been widely accepted as six centred (**5**), a representation first suggested by Hurd and Blunck[90].


(5)

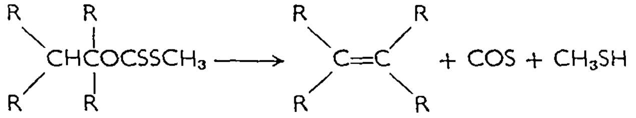
Further discussion of this point will be given in section V.

One point worthy of mention is that the rates of pyrolysis of esters would appear to be the same whether studied in the pure liquid state or in the gas phase. Thus the Arrhenius parameters for di-2-ethylhexyl sebacate (Table 10) are almost the same as those for a simple primary ester, while those for cholesteryl acetate are very close to those of a simple secondary ester.

The only alkyl vinyl ethers that have been investigated are the ethyl[91] and isopropyl[92] compounds. The Arrhenius parameters are E, 43·6, 43·6 and $\log A$, 11·43, 12·58 respectively. These are very close to those observed for the esters (Table 10) and give at 400° a relative rate of isopropyl to ethyl of 17 : 1. The mechanism is unimolecular and analogous to that of ester pyrolysis.

D. Xanthates

The pyrolysis of xanthates, commonly called the Chugaev reaction, has been widely used for preparative purposes. The overall stoichiometry is given in equation (24), the reaction leading to carbonyl sulphide and methyl mercaptan. No quantitative kinetic studies have so far been made of this reaction in the gas phase, and very few have been made of the reaction in the liquid phase. However, in view of what was noted above regarding the near-identity of gas- and condensed-phase ester pyrolysis, it is worth while including a discussion of the liquid-phase xanthate pyrolyses in this chapter. O'Connor and Nace[78,93] have compared the behaviour of 3β-cholesteryl acetate and 3β-cholesteryl-*S*-methyl xanthate (Table 14). The xanthates decompose with an activation energy some 10 kcal/mole less than that of the corresponding esters. This would give a relative rate at 200° of some 5000. Electron-withdrawing groups attached to the xanthate increase the rate of pyrolysis and there is a good correlation between the rate of pyrolysis and the strength of the corresponding carboxylic acid, and with Hammett σ values[78].



(24)

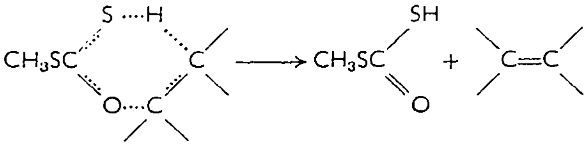
TABLE 14. A comparison of ester and xanthate pyrolyses.

Molecule	Log *A* (kcal/mole)	*E*	Reference
Cholesteryl acetate	12·71	44·1	78
Cholesteryl xanthate	12·38	32·9	93
Cholestanyl xanthate	12·30	33·8	93

Extensive studies[e.g. 70] have shown that except where special factors operate, elimination from xanthates leads to the olefin with the least number of alkyl groups attached to the double bond, that is the elimination is essentially Hofmann.

Recently, some confusion has been caused by an observation of Nace and coworkers[94] that the so-called 'stable' form of the xanthates[95] is really the normal form from which peroxides have been removed. Nearly identical products have been reported for the pyrolysis of both the normal and the stable forms. The role of peroxide is not at present understood.

Two possible six-centred transition states have been proposed for xanthate pyrolysis. Bourns and Bader[96] by a study of the S- and



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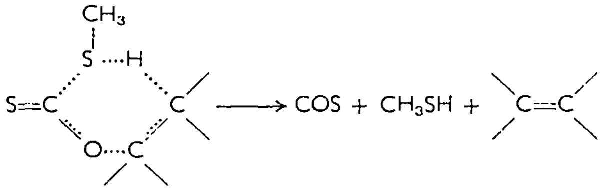


(26)

C-isotope effects have demonstrated that equation (25) is in fact correct.

E. Alcohols and Amines

The pyrolysis of alcohols is complicated in the first instance by the fact that there is no unambiguous route of decomposition, since either water or hydrogen may be eliminated, as shown for the case of isopropyl alcohol (equation 27). In addition, apart from the tertiary

$$CH_3CHOHCH_3 \longrightarrow \begin{cases} CH_3CH{=}CH_2 + H_2O \\ CH_3COCH_3 + H_2 \end{cases} \tag{27}$$

alcohols, chain mechanisms appear to predominate. Kistiakowsky and Schultz[97] investigated the elimination of water from *t*-butyl and *t*-amyl alcohols and obtained the Arrhenius equations (28) and (29),

$$t\text{-butyl:}\quad k_1 = 4{\cdot}8 \times 10^{14} \exp(-65{,}500/RT)\ \text{sec}^{-1} \tag{28}$$

$$t\text{-amyl:}\quad k_1 = 3{\cdot}3 \times 10^{13} \exp(-60{,}000/RT)\ \text{sec}^{-1} \tag{29}$$

the temperature ranges being 487–555°c. Barnard[98] has repeated the study of *t*-butanol and obtained the Arrhenius equation (30) over

$$k = 3{\cdot}24 \times 10^{11} \exp(-54{,}500/RT)\ \text{sec}^{-1} \tag{30}$$

the temperature range 487–620°c. As nitric oxide had no effect on the rate of the reaction, this author concluded that the elimination of water was unimolecular. This author also studied isopropanol[99], which decomposed mainly by a chain mechanism. However, a maximally inhibited rate in the presence of nitric oxide might correspond to one or other or both of the processes shown above. The Arrhenius equation of the maximally inhibited rate was (31) for the

$$k = 1{\cdot}26 \times 10^{15} \exp(-62{,}400/RT)\ \text{sec}^{-1} \tag{31}$$

temperature range 524–615° c. The Arrhenius parameters would be consistent with this type of mechanism.

In an examination of *t*-butylamine, Pritchard, Sowden and Trotman-Dickenson[100] have isolated a unimolecular reaction, the Arrhenius equation being (32). A concurrent unimolecular reaction yielding

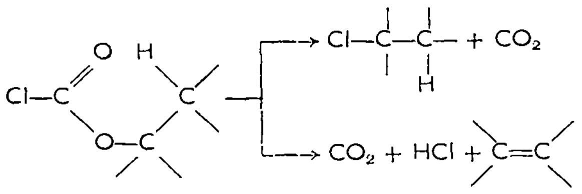
$$k = 1{\cdot}7 \times 10^{14} \exp(-67{,}000/RT)\ \text{sec}^{-1} \tag{32}$$

methane and an unidentified nitrogenous product was also observed.

As can be seen either from the temperature ranges over which the reactions have been studied, or from the Arrhenius equations, these reactions are very much slower than the eliminations discussed earlier in this chapter. This implies that they are not of great importance synthetically, since the higher temperatures cause secondary reactions to occur.

F. Chloroformates

The pyrolysis of a number of chloroformates has been studied systematically by Lewis and coworkers[101,102,103] and a number of difficulties in earlier work in this field cleared up. Two distinct reactions occur: (33a) internal substitution with CO_2 elimination; and (33b) elimination of both CO_2 and HCl in the case of those



(33a)

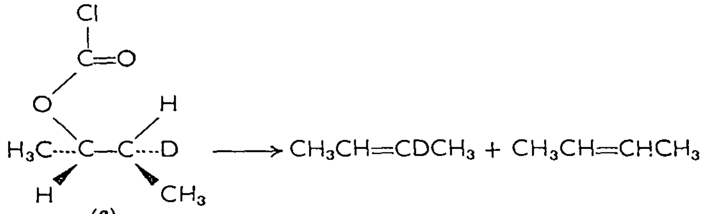
(33b)

TABLE 15. The pyrolysis of chloroformates.

R	E_s (kcal/mole)	E_e (kcal/mole)	10^5k_s	10^5k_1	10^5k_c	10^5k_t
				(sec^{-1} at 240°c)		
CH_3	—	—	0·53	—	—	—
C_2H_5	36·7	—	1·17	—	—	—
isoC_3H_7	26·2	37·2	12·0	112	—	—
s-C_4H_9	27·8	35·9	343	64	48	46

molecules possessing a β-hydrogen atom. In addition, in certain cases the olefin, *e.g.* from *s*-butyl chloroformate, may be any one of a number of isomers. The Arrhenius parameters for both reactions (33a) and (33b) are shown in Table 15, together with the rate constants at 240°c. In Table 15, k_s is the value for substitution, k_1, k_c and k_t being the values for elimination to give the 1-olefin and the *cis* and *trans* form of the 2-olefin respectively. The elimination reaction does not, of course, exist for methyl chloroformate; for the ethyl compound it was not found, although the results would not be inconsistent with a very slow reaction[104].

Use of an optically active 2-butanol to prepare *s*-butyl chloroformate enabled a study of the stereochemical course of the reaction to be made[102]. It was found that the substitution reaction produced *s*-butyl chloride with retention of configuration. In addition, pyrolysis of the *erythro* and *threo* form of 2-butyl-3-d$_1$ chloroformate (**6** and **7** respectively) gave 1-butene containing 1 atom of deuterium, but the *trans*-2-butene from the *erythro* and *threo* forms contained 1 and 0 atoms of deuterium, whereas the *cis*-2-butene from the same two forms contained 0 and 1 atoms of deuterium.



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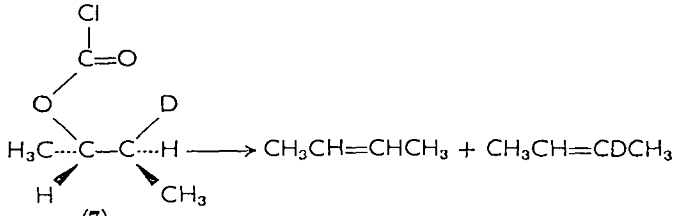
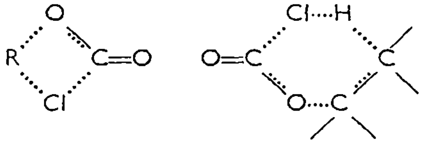


(7)

Neopentyl chloroformate[103] has been shown to produce neopentyl chloride and a mixture of isomeric methylbutanes and hydrogen chloride. The possibility of the formation of the methylbutenes through a carbene intermediate (equation 34) was ruled out by

$$\left.\begin{aligned}(CH_3)_3CH_2OCOCl &\longrightarrow CO_2 + HCl + (CH_3)_3CCH\colon\\ (CH_3)_3CCH\colon &\longrightarrow (CH_3)_2C{=}CHCH_3\end{aligned}\right\} \quad (34)$$

studies with deuterated species. Also, reaction through a 1,1-dimethylcyclopropane was excluded. The rate of the substitution reaction to give neopentyl chloride at 240°c ($1{\cdot}8 \times 10^{-5}$ sec^{-1}) was very close to the rate observed for ethyl chloroformate at this temperature ($1{\cdot}2 \times 10^{-5}$ sec^{-1}). The transition state suggested for substitution and elimination are respectively four- and six-centred:



III. THE CATALYSIS OF GAS-PHASE ELIMINATION

A. Homogeneous

No evidence exists in the literature for homogeneous catalysis of elimination from halides. In fact, Failes and Stimson[40] have shown that the rate of pyrolysis of *t*-butyl chloride in the gas phase is unchanged in the presence of sulphur hexafluoride, a substance known to produce acceleration of certain decompositions[105-108].

Following the discovery of a catalysis of the elimination of water from *t*-butanol by hydrogen bromide[109,110], Stimson and coworkers have made a systematic study of this field. The reactions (35) are

$$C_nH_{2n+1}OH + HX \longrightarrow C_nH_{2n} + H_2O + HX \qquad (35)$$

all homogeneous and are first order with respect to both alcohol and hydrogen halide. The hydrogen halide is not used up, and the temperature range over which the reaction may be studied is about 150° lower than that at which the uncatalysed reaction can be followed. This is mainly due to a lowering of the activation energy by some 20 kcal/mole. The *A* factors are all normal, implying no restrictive spatial requirements of the reaction. The Arrhenius parameters are shown in Table 16. Use of hydrogen iodide as a catalyst is complicated by the production of iodine. However, with *t*-butanol at 320°c, the relative rates of catalysis[110] by hydrogen chloride,

TABLE 16. The Arrhenius parameters for the catalytic dehydration of alcohols.

Molecule	Catalyst	$10^{-12}A$ (cm³/mole sec)	E (kcal/mole)	Temp. range (°c)	Reference
isoC_3H_7OH	HBr	1·0	33·2	369–520	111
s-C_4H_9OH	HBr	5·8	34·9	387–510	112
t-C_4H_9OH	HBr	9·2	30·4	315–422	110
t-$C_5H_{11}OH$	HBr	1·0	27·1	308–415	113
t-$C_4H_9OCH_3$	HBr	0·67	25·6	258–371	114
t-C_4H_9OH	HCl	2·0	32·7	328–454	115
t-$C_5H_{11}OH$	HCl	6·7	34·0	370–503	116

hydrogen bromide and hydrogen iodide were as shown in Table 17[117]. The values are reasonably constant, independent of the substrate.

Cyclohexene and propene, which are well known to be inhibitors of the chain mechanism, had no effect on the rate of reaction. Neither were induction periods ever observed. These facts taken together with the observed Arrhenius parameters strongly suggest a bimolecular mechanism. This is consistent with the observation that, with mixtures of hydrogen bromide and hydrogen chloride, the catalytic effect is additive.

TABLE 17. Relative rates with HX.

Molecule	Temp. (°c)	HCl	HBr	HI
t-$C_5H_{11}OH$	410	1	27	—
t-C_4H_9OH	320	1	27	180
isoC_3H_7OH	420	1	25	130
t-$C_4H_9OCH_3$	371	1	23	—

Relative rates in the α- and β-methylated series are shown in Table 18. As with the halides, esters and chloroformates, the effect of α-methylation is large, where that of β-methylation is small.

B. Heterogeneous

Heterogeneous catalysis of dehydrochlorination and dehydration, while being of great importance as a preparative method, is very much more difficult to account for theoretically, since many new factors are introduced over and above those obtaining in homogeneous catalysis. The overall rate will be determined by the nature of the

TABLE 18. The effect of α- and β-methylation on catalysed dehydration.

		α-Methylated series	
Temp. (°c)	C_2H_5OH	isoC_3H_7OH	t-C_4H_9OH
440	1	25	1600

		β-Methylated series	
Temp. (°c)	isoC_3H_7OH	s-C_4H_9OH	$(CH_3)_2CHCH(OH)CH_3$
446	1	2·0	2·1
	t-C_4H_9OH	t-$C_5H_{11}OH$	$(CH_3)_2CHC(OH)(CH_3)_2$
361	1	1·7	1·7

catalyst surface, by the nature of the molecules undergoing reaction, and may be determined by either the rate of adsorption of the reactants, rate of reaction of the adsorbed molecules or rate of desorption of the products of reaction. The simplest case to discuss will be that for which adsorption and desorption are rapid, and the rate-controlling process is reaction on the surface. In this case, the effect of both the nature of the catalyst and the nature of the reactant can with profit be investigated. For a heterogeneous reaction, $k_{\text{obs.}}$, the observed

$$k_{\text{obs.}} = k_0 S \tag{36}$$

rate constant, is given by equation (36), where k_0 is the value per unit area and S is the surface area of the catalyst. So in order to obtain absolute rate coefficients, it is necessary to know the surface area of the catalyst under investigation.

In the case of the dehydrochlorination of ethyl chloride, an intensive study has been made of the nature of the catalyst by Schwab, Noller[118,119,120] and coworkers in the case of metals, oxides, nitrides, carbides and salts. Some of the results are shown in Table 19. A difficulty arises in the interpretation of the catalysis by platinum, since metal wires were used and the temperature and extent of the reaction zone cannot be precisely defined. The rates, and also those for the silica surface, would appear small compared with the rates of the homogeneous reaction. Young and Swinbourne[121] have found

TABLE 19. The effect of the catalyst on dehydrochlorination.

Catalyst	Pt	SiO_2	γ-Al_2O_3	LiCl	$CaCl_2$
Temp. range (°c)	700–780	520–600	370–420	420–440	360–400
E(kcal/mole)	43	24·5	13·2	24	11·4

an activation energy of 24–25 kcal/mole for the pyrolysis of ethyl chloride in clean vessels in the temperature range 400–450°c. The effect of different alkali halide surfaces on the pyrolysis of cyclohexyl chloride is shown in Table 20.

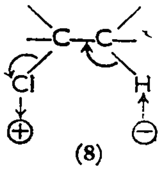
Table 20. The effect of surface on the pyrolysis cyclohexyl chloride.

Catalyst	LiCl	NaCl	KCl	RbCl
Temp. range (°c)	240–250	230–270	310–350	320–360
E (kcal/mole)	11	13	17	25

The effect of varying the alkyl chloride on a titanium carbide surface is shown in Table 21. On the basis of these and other results, Noller and colleagues relate the case of catalysis to the interatomic spacing and charge structure of the catalyst. The transition state is 8[119,122],

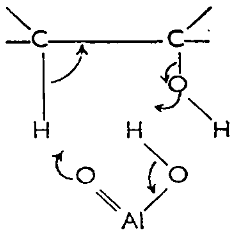
Table 21. The effect of titanium carbide on different halides.

Halide	n-C_3H_7Cl	n-C_4H_9Cl	isoC_3H_7Cl	*s*-C_4H_9Cl	*t*-C_4H_9Cl
Temp. range (°c)	410–440	—	280–310	230–250	150–190
E (kcal/mole)	34	34	30	22	12

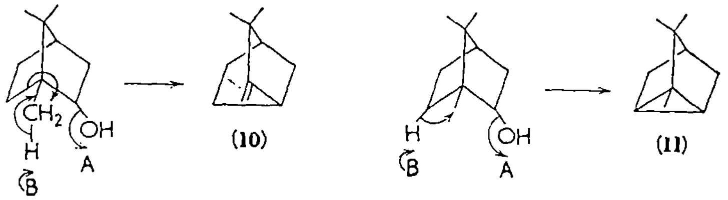


(8)

and is thus synchronous and heterolytic in nature. A similar type of transition state (**9**) is also suggested for the dehydration of alcohols on an alumina surface, where reaction occurs at a site containing a hydrogen atom.



Some very interesting dehydration studies have been made using modified alumina. Thus Pines and Pillai[123] have used alumina treated with ammonia, and were able to obtain very clean reactions in the case of borneol, neopentanol, menthol and neomenthol. In the case of borneol, a yield of 77% camphene (**10**) and 23% of tricyclene (**11**) was obtained, the suggested mechanism being synchronous as shown; sites A and B are respectively acidic and basic. Again, neopentanol yielded 70% of 2-methyl-1-butene and 30% of 2-methyl-2-butene, while menthol gave 91% of 2-menthene and neomenthol gave 75% of 3-menthene and 25% of 2-menthene. These results are explained on the basis of the suppression of the carbonium-ion character[124] of the dehydration. Kochloefl and colleagues[125] have also invoked a cyclic mechanism for the dehydration of *cis*-alkylcyclohexanols on alumina modified by pyridine.



(10) (11)

IV. EQUILIBRIA IN ELIMINATION REACTIONS

A. Isomeric Equilibria

The N.B.S. compilation of the thermodynamic properties of the hydrocarbons[126] enables the isomeric composition at equilibrium to be estimated from the relevant free energies. For the butenes, the

TABLE 22. Calculated equilibrium mixtures of butenes.

Temp. (°K)	% 1-butene	% *trans*-2-butene	% *cis*-2-butene
550	12·6	55·2	32·2
575	13·8	54·1	32·2
600	14·9	52·8	32·2
625	16·0	52·0	32·1
650	17·3	50·8	32·0
675	18·3	49·7	31·8

data shown in Table 22 may be derived. When the olefins are produced from alkyl halides, the hydrogen halide may catalyse the isomerization. Thus Maccoll and Stone[1] have made a preliminary investigation of this phenomenon by decomposing the appropriate isopropyl halide in the presence of 1-butene and measuring the degree of isomerization. The results are shown in Table 23. The catalytic activity is in the order iodine > hydrogen bromide > hydrogen chloride. An unpublished investigation by Ross[127] of the catalysis by hydrogen bromide of the reaction (37) has yielded a value of the activation energy for the homogeneous bimolecular reaction of about 27 kcal/mole. This is to be compared with the hydrogen bromide catalysed isomerization of cyclopropane to propylene[128], for which the activation energy is 38·8 kcal/mole.

TABLE 23. The effect of catalysts on the isomerization of 1-butene.

	Catalyst: hydrogen chloride *Temp.:* 342·8°c				
Reaction time (hours)	4	4	18	16	
Molar ratio[a] acid : butene	0	0·30	0·75	2·00	
Isomerization (%)	2	2	33	70	
	Catalyst: hydrogen bromide *Temp.:* 342·8°c				
Reaction time (hours)	2	1·5	18		
Molar ratio[a] acid : butene	0·5	2·0	2·0		
Isomerization (%)	16	70	82 (equil.)		
	Catalyst: iodine *Temp.:* 353·8°c				
Reaction time (hours)	1	1	1	0·67	0·50
Molar ratio[a] iodine : butene	0·9	1·1	1·3	1·4	3·7
Isomerization (%)	69	75	79	63	69

[a] Obtained at the moment of sampling

$$\text{1-Butene} \rightleftharpoons \text{2-Butene} \qquad (37)$$

B. Dissociative Equilibria

The equilibria (38) have usually been studied in clean glass vessels

$$C_nH_{2n+1}X \rightleftharpoons C_nH_{2n} + HX \qquad (38)$$

packed with glass wool. The equilibrium constant, as given by equation (39), may be calculated if the total pressure of the reaction

$$K_p = \frac{p_{\mathrm{HX}} p_{\mathrm{C}_n\mathrm{H}_{2n}}}{p_{\mathrm{C}_n\mathrm{H}_{2n+1}\mathrm{X}}} \tag{39}$$

mixture is known at a given temperature. The values obtained are shown in Table 24, where $\log K_p(\mathrm{mm}) = \Delta H/2{\cdot}303RT - \log A$.

TABLE 24. Dissociative equilibria.

Reaction	ΔH (kcal/mole)	log A	Reference
$C_2H_5Cl \rightleftharpoons C_2H_4 + HCl$	17·44	6·858	129
	18·27	7·355	130
$C_2H_5Br \rightleftharpoons C_2H_4 + HBr$	20·10	7·274	130
$C_2H_5I \rightleftharpoons C_2H_4 + HI$	22·20	6·990	18b
$\mathrm{iso}C_3H_7Cl \rightleftharpoons C_3H_6 + HCl$	17·54	7·563	129
$\mathrm{iso}C_3H_7I \rightleftharpoons C_3H_8 + HI$	20·94	7·640	131
$t\text{-}C_4H_9Cl \rightleftharpoons C_4H_8 + HCl$	17·10	7·89	4a
	17·70	8·27	4b
$t\text{-}C_4H_9Br \rightleftharpoons C_4H_8 + HBr$	18·90	8·12	4a
$t\text{-}C_4H_9I \rightleftharpoons C_4H_8 + HI$	19·15	7·952	6a
	19·46	8·083	6b

In the case of the iodides, care has to be taken in using the tabulated values at elevated temperatures, since the reaction (40) may tend to

$$C_nH_{2n} + 2\,HI \rightleftharpoons C_nH_{2n+2} + I_2 \tag{40}$$

occur. Green[132] has published computed values of the thermodynamic properties of some n-alkyl bromides, which can be used in conjunction with the published data for the olefins and for hydrogen bromide to estimate the equilibrium constant by use of equation (41).

$$\Delta G^0 = -2{\cdot}303RT \log K_p \tag{41}$$

This same method may be used to estimate the position of equilibrium for the reaction (42) using the data of Green[133]. Some values

$$C_2H_5OH \rightleftharpoons C_2H_4 + H_2O \tag{42}$$

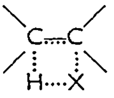
are shown in Table 25. Dehydration is thus effectively complete above 500°K.

TABLE 25. K_p for the dehydration of ethanol.

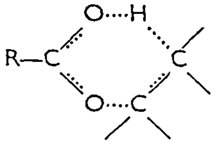
Temp. (°K)	298	400	500	600	700
K_p (atm)	$3{\cdot}9 \times 10^{-2}$	4·5	74	$4{\cdot}8 \times 10^{2}$	$1{\cdot}8 \times 10^{3}$

V. THEORIES OF THE GAS-PHASE ELIMINATION REACTIONS

These reactions used to be discussed in terms of a four-centred transition state for the alkyl halides (**12**), and a six-centred transition state for the esters (**13**). This formulation, however, does not provide an explanation of the effects of substitution on the rate of reaction. The effects which are common to both classes of reaction are: (1) the large increase in rate on α-methylation; (2) the small effect of β-methylation; (3) the small effect of β-vinylation; (4) the relatively large increase in rate on α-phenylation and the small effect of β-phenylation; and (5) the very large increase (in the case of the halides) on α-methoxy substitution. This is paralleled on a greatly reduced scale by the small rate increase in going from α,β-diphenylethyl acetate to α,4-methoxyphenyl-β-phenylethyl acetate. In addition, both series show a reduction in rate on deuteration, while for the halides there is an enhancement of rate on α-halogen substitution and a decrease in rate on β-halogen substitution. Also, for the ester series, heterolytic weakening of the β-carbon–hydrogen bond, *e.g.* in acetoisopropyl acetate, leads to an increase in rate.



(12)



(13)

It was pointed out some years ago[134] that the major factor controlling the rate of elimination from alkyl halides was the environment of the carbon–halogen bond. This view was developed when the analogy between gas-phase elimination and the S_N1 or $E1$ reactions in a polar solvent was drawn[68]. It was later suggested that those gas-phase reactions which show similar effects of substitution upon the rate as do unimolecular solvolytic reactions proceeding through a carbonium-ion transition state should be called 'quasi-heterolytic'[65]. The evidence for this point of view will now be examined.

The most direct means of investigating the energetics of carbonium-ion formation is by use of the mass spectrometer to determine the appearance potential A_{R^+}, which is defined as the energy of the process (43). This in turn may be regarded as occurring in two steps, *viz.*

$$RX + e \rightarrow R^+ + X + 2e, \quad -A_{R^+} \tag{43}$$

(44a) and (44b), when D_{R-X} and I_R are the homolytic bond dissociation

$$RX \rightarrow R + X, \quad -D_{R-X} \tag{44a}$$

$$R \rightarrow R^+ + e, \quad -I_R \tag{44b}$$

energy and radical ionization potential respectively. Finally, the heterolytic bond dissociation energy may be defined by equation (45), and since (46) is true, where $-I_{X^-}$ is the electron affinity of X,

$$RX \rightarrow R^+ + X^-, \quad -D_{R^+X^-} \tag{45}$$

$$X^- \rightarrow X - e, \quad -I_{X^-} \tag{46}$$

the two relationships (47a) and (47b) hold. These are illustrated in Figure 2.

$$D_{R^+X^-} = A_{R^+} - I_{X^-} \tag{47a}$$

$$= D_{R-X} + I_R - I_{X^-} \tag{47b}$$

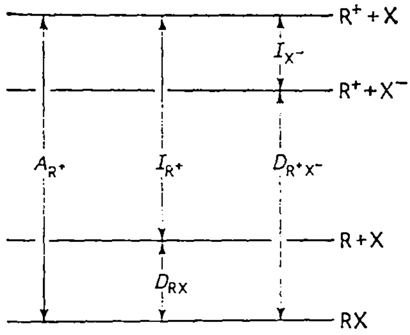


FIGURE 2. The energetics of ionization

Where the appearance potentials of an ion from a molecule are known, $D_{R^+X^-}$ may be obtained directly; if, on the other hand, I_R is known, then assuming D_{R-X} constant, variations in $D_{R^+X^-}$ may be taken to follow variations in I_R. The effect of α-methylation on $D_{R^+X^-}$ is shown in Table 26.

TABLE 26. α-Methylation and $D_{R^+X^-}$ (kcal/mole).

R	CH_3[135]	C_2H_5[136]	isoC_3H_7[137]	t-C_4H_9
X = Cl	224	194	168	149[138]
Br	221	180	158	(138)[139]
I	212	180	151	—

As contrasted with the big drop in $D_{R^+X^-}$ on progressive α-methylation, the effect of β-methylation on the radical ionization potential is relatively small. Thus for ethyl, n-propyl and isobutyl radicals, the ionization potentials are 8·78[136], 8·69[140], 8·35[140] ev. Thus the effects of α- and β-methylation upon the heterolytic bond dissociation energy and upon the activation energy for eliminations follow the same pattern. The same is true for the variation of the halogen from chlorine to iodine.

Chlorination of the α-carbon atom causes a reduction in ionization potential as is seen for the series CH_3, CH_2Cl, $CHCl_2$, CCl_3 for which the ionization potentials are 9·95[141], 9·32, 9·30[142] and 8·75[143] ev respectively. The decrease in ionization potential is thus paralleled by the increased rate of elimination (Table 7). Again, the ionization potential of α-methoxybenzyl is 0·94 ev lower than the ionization potential of benzyl, while there is a lowering in the activation energy for elimination from α-methoxyethyl chloride as compared with ethyl chloride[46]. In all cases so far, where it is possible to compare $D_{R^+X^-}$ or I_R with activation energies or rates of elimination, factors which decrease the first also decrease the second and increase the third. To this extent the elimination reaction may be regarded as quasi-heterolytic.

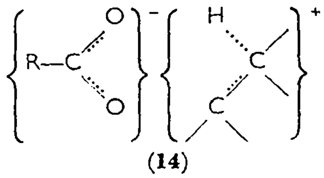
The transition state for elimination from halides may thus be pictured as having an elongated carbon–halogen bond, polarized in the $C^{\delta+}-X^{\delta-}$ direction. Alternatively, it may be looked upon as a polarized ion pair R^+X^-. In this way, both the analogy with unimolecular solvolytic reactions, and the relation between heterolytic bond dissociation energies and activation energies for elimination may be understood. The α- and β-methylated series may be interpreted in terms of the resonance structures of the carbonium ions as tabulated below, where the number in brackets after a formula gives the number of structures of that type. Going down the columns in either case increases the stability of the structures because of the increasing stability of the olefin, but whereas in the α-series, the

α-Series	β-Series
$CH_3CH_2^+$ $H^+CH_2{=}CH_2$ (3)	
$CH_3CHCH_3^+$ $H^+CH_2{=}CHCH_3$ (6)	$CH_3CH_2CH_2^+$ $CH_3CH(H^+){=}CH_2$ (2)
$CH_3C(CH_3)_2^+$ $H^+CH_2{=}C(CH_3)_2$ (9)	$(CH_3)_2CHCH_2^+$ $(CH_3)_2C(H^+){=}CH_2$ (1)

number of structures increases, in the β-series it decreases. This provides an explanation of the different effects of α- and β-methylation.

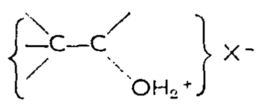
It is not necessary to assume nearly complete cleavage of the β-carbon–hydrogen bond to explain the reduction of rate in the deuterated molecules; for it is quite conceivable the $D_{\mathrm{R}^+\mathrm{X}^-}$ for C_2D_5X is greater than the corresponding quantity for C_2H_5X, which would explain the observed effects, and also for the partially deuterated compounds $C_2H_xD_{5-x}X$, the structures $C_2H_{x-1}(H^+)D_{5-x}$ and $C_2H_xD_{4-x}(D^+)$ would not necessarily make the same contribution to the carbonium ion, thus explaining the greater rate of elimination of HX as compared with DX. The chloroformate decompositions can be discussed in the same terms as those of the halides.

In the case of the esters and vinyl ethers, it would seem from the effect of substitution, that the same ideas apply, although the scale involved is greatly reduced. This would imply that structures of the type **14** play an important role in the transition state. A similar type of mechanism presumably holds in the case of xanthate pyrolysis.



(**14**)

The transition state for the catalysed elimination of water from alcohols and methanol from methyl *t*-butyl ether can be represented by the formula **15**, namely a polarized ion pair produced by the addi-



(**15**)

tion of a proton to the alcohol. In this way the effects upon the rate of varying the structure of the alcohol can be understood.

The transition state pictured above cannot be ruled out on energetic grounds, since the coulombic energy of the ion pair has to be taken into account. Thus from Table 26, the energy to dissociate ethyl bromide into an ethyl carbonium ion and a bromide ion is 180 kcal/mole. If now the ions are allowed to approach so that the carbon–halogen distance is the mean of the covalent and ionic distances, then the system is stabilized by about 120 kcal/mole. The energy required, neglecting polarization stabilization, is thus about 60 kcal/mole, which is not too far removed from the observed activation energy (53 kcal/mole).

The conclusion to be drawn from the above discussion is that there is a class of gas-phase elimination reactions which are essentially heterolytic in character, in which the effects of substitution on the rates can be discussed in terms of effects in the heterolytic bond dissociation energies. This formulation stresses the analogies between the various types of gas-phase elimination reactions and elimination occurring by the unimolecular mechanism in a polar solvent. The major factor controlling the rate is the stability of the carbonium ion R^+ in RX. The dependence of rate upon the stability of the carbonium ion is greatest for the halides and chloroformates, less for esters and vinyl ethers, and has almost disappeared in the hydrocarbons (*cf.* cyclobutane and methyl cyclobutane).

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 4

Alkene-forming condensation reactions

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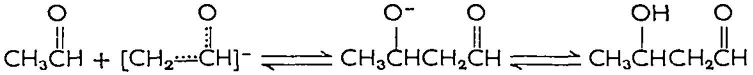
I. EXAMPLES AND GENERAL FEATURES OF MECHANISM

The condensation reactions important in alkene production are the result of an attack by a nucleophilic carbon atom, typically a carbanion, upon the more electrophilic carbon in a carbonyl group. Dehydration is then often favored by the structural features which created the nucleophilic center.

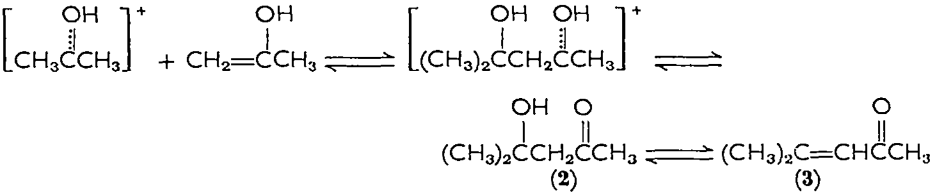
A. Aldol Condensations

The aldol condensation is catalyzed by bases and by acids. In the base-catalyzed reaction, the nucleophile is the ambident enolate anion, reaction with an unionized acetaldehyde molecule giving the conjugate base of aldol (**1**). Acid catalysis serves to increase both the rate of enol formation and the concentration of protonated carbonyl compound. It is probable that these two species participate in the reaction, as in the acid-catalyzed condensation of acetone.



$$CH_3\overset{O}{\overset{\|}{C}}H + [CH_2{\cdots}\overset{O}{\overset{\vdots}{C}}H]^- \rightleftharpoons CH_3\overset{O^-}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}H \rightleftharpoons CH_3\overset{OH}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}H$$

(**1**)



$$\left[CH_3\overset{OH}{\overset{\vdots}{C}}CH_3\right]^+ + CH_2{=}\overset{OH}{\overset{|}{C}}CH_3 \rightleftharpoons \left[(CH_3)_2\overset{OH}{\overset{|}{C}}CH_2\overset{OH}{\overset{\vdots}{C}}CH_3\right]^+ \rightleftharpoons$$

$$(CH_3)_2\overset{OH}{\overset{|}{C}}CH_2\overset{O}{\overset{\|}{C}}CH_3 \rightleftharpoons (CH_3)_2C{=}CH\overset{O}{\overset{\|}{C}}CH_3$$

(**2**) (**3**)

Dehydration of aldols such as **1** and **2** to the corresponding unsaturated compounds—crotonaldehyde and mesityl oxide (**3**) in the examples—proceeds more readily in acid solution. However, in some cases, especially the aldol-type condensation of an aromatic aldehyde with a ketone, the unsaturated ketone is obtained directly even under alkaline conditions. In others, it is advantageous to use special dehydration methods, for example, pyrolysis of the benzoate of the aldol.

$$C_6H_5CHO + CH_3COCH_3 \xrightarrow[\text{or NaOH}]{\text{HCl}} C_6H_5CH{=}CHCOCH_3$$

(**4**)

$$C_6H_5FeC_6H_4CHO + CH_3COC_6H_5 \xrightarrow{\text{NaOH}} C_6H_5FeC_6H_4CH{=}CHCOC_6H_5$$

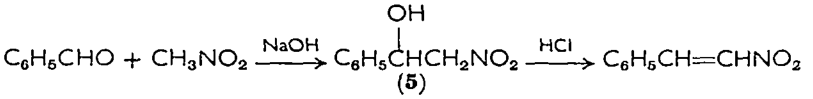
Formylferrocene (ref. 1)

Condensation of the methyl group of benzalacetone (**4**) with a second molecule of benzaldehyde produces $C_6H_5CH{=}CHCOCH{=}CHC_6H_5$ in good yield. Another type of diolefin-forming condensation is the vinylog of the simple aldol type.

$$C_6H_5CHO + CH_3CH{=}CHCHO \longrightarrow C_6H_5CH{=}CHCH{=}CHCHO$$

B. Knoevenagel Condensations

Many compounds containing an acidic methylene group will condense with aldehydes and ketones in the presence of bases. Nitromethanes react to form β-nitroalcohols which are dehydrated to nitroolefins. Benzaldehyde yields β-nitrostyrene (equation 1).



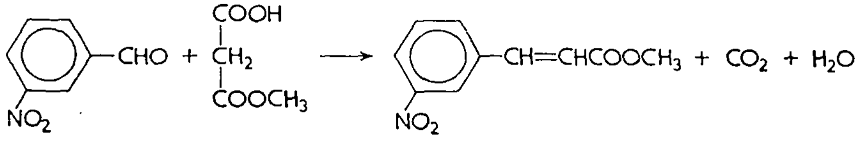
$$C_6H_5CHO + CH_3NO_2 \xrightarrow{NaOH} \underset{(\mathbf{5})}{C_6H_5\overset{\overset{\displaystyle OH}{|}}{C}HCH_2NO_2} \xrightarrow{HCl} C_6H_5CH{=}CHNO_2 \qquad (1)$$

The condensation of malonic acid is catalyzed by ammonia or amines (equation 2) while its nitrile will undergo condensations

$$CH_3CHO + CH_2(COOH)_2 \xrightarrow{Piperidine} CH_3CH{=}C(COOH)_2 \longrightarrow$$
$$CH_3CH{=}CHCOOH + CO_2 \qquad (2)$$

without a catalyst (equation 3). The use of alkyl hydrogen malonates affords a route to unsaturated esters (equation 4).

$$CH_2(CN)_2 + C_6H_5CHO \longrightarrow C_6H_5CH{=}C(CN)_2 \qquad (3)$$



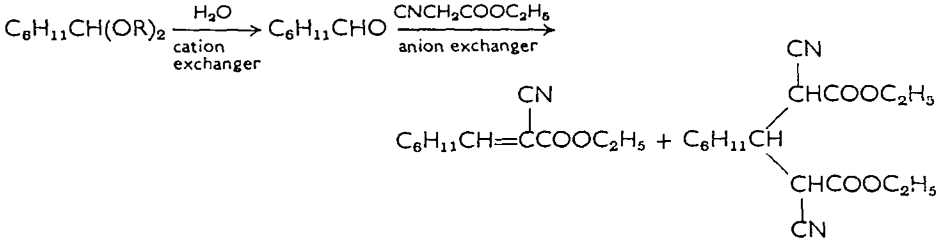
(4)

The mechanism of each of the reactions in the preceding paragraph has been investigated and will be discussed in section II.C. All four are examples of Knoevenagel reactions, so-called because of the extensive development of this kind of condensation, especially as catalyzed by amines, by E. Knoevenagel at the end of the nineteenth century*. Additional examples can be found in treatises on synthetic organic chemistry[3].

No less interesting than the variety of aldol, Knoevenagel and related condensations is the number of catalysts which have been used. The base-catalyzed aldol condensation of a simple aliphatic aldehyde proceeds in aqueous or alcoholic solution if the pH is raised by carbonates or hydroxides. Tertiary amines in the aldol condensation[4] and Group I fluorides in Knoevenagel condensations[5] also serve as basic catalysts. Ammonia, piperidine and pyridine are very frequently used; their function is discussed in section II.C.

The unfavorable equilibrium between acetone and its aldol ('diacetone alcohol') led to the synthetic method in which refluxing acetone flows over solid barium, calcium or ferric[6] hydroxide or a strongly basic anion-exchange resin[7]. Catalysis by ion-exchange resins is currently ascribed to the action of the exchanging counterions within the confines of the resin[8,9]. Hydroxyl ions, for example, can be placed as counterions in a resin having positively charged quaternary ammonium groups in its lattice. Acetone diffusing into the resin is then acted upon by these hydroxyl ions. The products diffuse out but the ions, in the absence of other anions to take their place, cannot. If the diacetone alcohol is formed in the thimble of a Soxhlet extractor, it can be dehydrated to mesityl oxide by an acidic cation-exchange resin in the boiling liquid below.

The aldol condensation of aldehydes is, like some Knoevenagel condensations[8], best catalyzed by a weak-base resin: one bearing amino groups which, as in homogeneous solution, can give rise to only a much smaller hydroxyl-ion concentration than the quaternary ions. A strong-base resin is rapidly neutralized and deactivated by acidic components of the reaction mixture.



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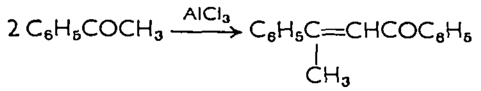
* A wealth of references to the original writings on many topics is to be found in ref. 2.

Intimately mixed cation and anion exchangers make possible the condensation of an acetal with ethyl cyanoacetate[10].

The use of various acids to catalyze alkene-forming condensations is illustrated by reactions (5), (6)[11] and (7)[12].

$$CH_3COCH_3 + CH_2(COOC_2H_5)_2 \xrightarrow[Ac_2O]{ZnCl_2} (CH_3)_2C{=}C(COOC_2H_5)_2 \qquad (5)$$

$$C_6H_5CHO + CH_3COC_6H_5 \xrightarrow{BF_3} C_6H_5CH{=}CHCOC_6H_5 \qquad (6)$$



$$2\,C_6H_5COCH_3 \xrightarrow{AlCl_3} \underset{\displaystyle CH_3}{\underset{|}{C_6H_5C}}{=}CHCOC_6H_5 \qquad (7)$$

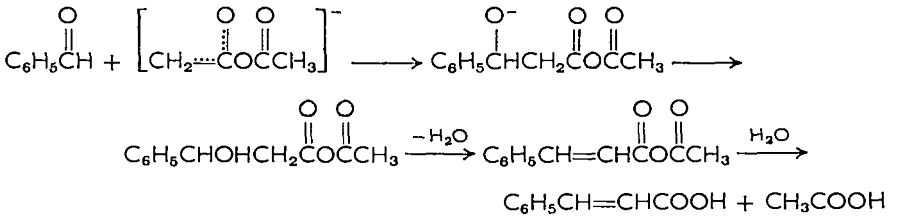
Aldol and related condensations have been carried out in the gas phase over solid catalysts[13].

$$CH_3CN + HCHO \xrightarrow[288^\circ]{SiO_2} \underset{32\%}{CH_2{=}CHCN}$$

C. Related Condensations

In the Reformatsky reaction, the negative carbon atom is that linked to zinc in the organometallic compound produced by the attack of zinc on an α-halo ester. Although the intermediate β-hydroxy ester is usually isolated, under some conditions the olefin is formed directly[14].

The Perkin reaction is the base-catalyzed condensation of an anhydride with an aromatic aldehyde (equation 8).



$$C_6H_5\overset{\overset{\displaystyle O}{\|}}{C}H + \left[CH_2{\cdots}\overset{\overset{\displaystyle O}{\vdots}}{C}O\overset{\overset{\displaystyle O}{\|}}{C}CH_3\right]^- \longrightarrow C_6H_5\overset{\overset{\displaystyle O^-}{|}}{C}HCH_2\overset{\overset{\displaystyle O}{\|}}{C}O\overset{\overset{\displaystyle O}{\|}}{C}CH_3 \longrightarrow$$

$$C_6H_5CHOHCH_2\overset{\overset{\displaystyle O}{\|}}{C}O\overset{\overset{\displaystyle O}{\|}}{C}CH_3 \xrightarrow{-H_2O} C_6H_5CH{=}CH\overset{\overset{\displaystyle O}{\|}}{C}O\overset{\overset{\displaystyle O}{\|}}{C}CH_3 \xrightarrow{H_2O}$$

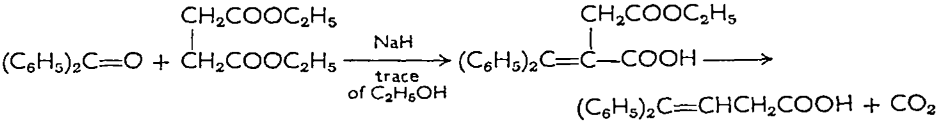
$$C_6H_5CH{=}CHCOOH + CH_3COOH \qquad (8)$$

The base which promotes ionization of the anhydride may be the sodium salt of the corresponding acid, potassium carbonate or an amine. A highly conjugated olefin can be made by reaction (9)[15].

$$C_6H_5CH_2COOH + C_6H_5CH{=}CHCHO \xrightarrow[(CH_3CO)_2O]{PbO}$$

$$C_6H_5CH{=}CHCH{=}CHC_6H_5 + CO_2 + H_2O \qquad (9)$$

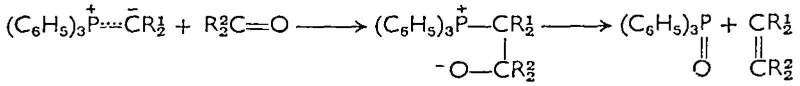
The Stobbe condensation of diethyl succinate with ketones, when applied to aromatic ketones, is similar in the first step to the reactions of diethyl malonate. Acid-catalyzed hydrolysis and decarboxylation gives the product which would be formed if the ketone could condense with propionic acid at the β-position[16].



$$(C_6H_5)_2C{=}O + \begin{matrix} CH_2COOC_2H_5 \\ | \\ CH_2COOC_2H_5 \end{matrix} \xrightarrow[\text{trace of } C_2H_5OH]{\text{NaH}} (C_6H_5)_2C{=}\begin{matrix} CH_2COOC_2H_5 \\ | \\ C{-}COOH \end{matrix} \longrightarrow (C_6H_5)_2C{=}CHCH_2COOH + CO_2$$

D. The Wittig Reaction

The Wittig reaction[17-20] is a more recently developed olefin synthesis. Wittig and Schöllkopf[21] showed that methylene triphenylphosphorane and its homologs react with aldehydes and ketones to give zwitterions which dissociate into olefins and triphenylphosphine oxide (equation 10). In this condensation the

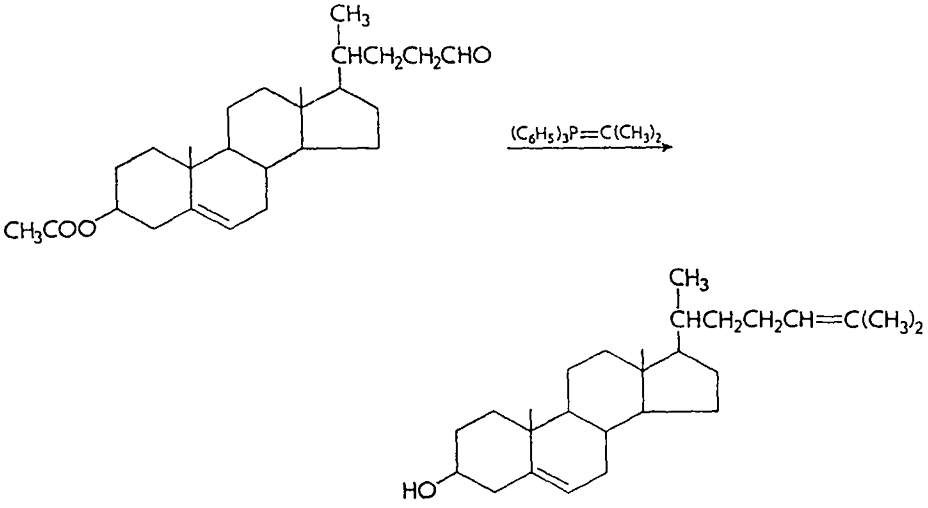


$$(C_6H_5)_3\overset{+}{P}{\cdots}\overset{-}{C}R^1_2 + R^2_2C{=}O \longrightarrow (C_6H_5)_3\overset{+}{P}{-}\begin{matrix} CR^1_2 \\ | \\ {}^{-}O{-}CR^2_2 \end{matrix} \longrightarrow \begin{matrix} (C_6H_5)_3P \\ \| \\ O \end{matrix} + \begin{matrix} CR^1_2 \\ \| \\ CR^2_2 \end{matrix} \qquad (10)$$

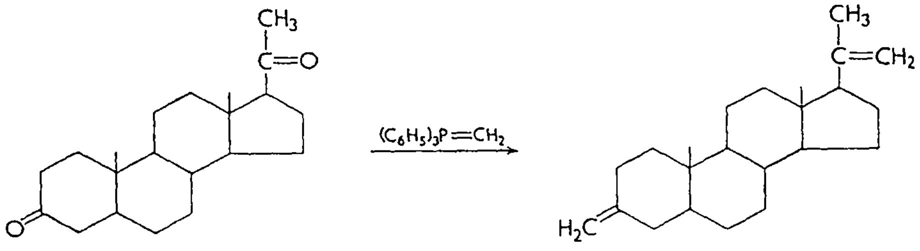
alkylene phosphorane, an ylide[22,23], functions both as nucleophile and as oxygen acceptor. Since there is no separate dehydration step, the position of the double bond, between the carbonyl and the ylide carbons, is uniquely determined. The ylide is generally formed by the action of base on the phosphonium salt made from triphenylphosphine and an alkyl halide[20].

A number of interesting examples have appeared to show the generality of the method. A substituted methylene group can in the absence of side-reactions replace a carbonyl group in any molecule. 24-Dehydrocholesterol (**6**), isolated from barnacles, was synthesized[24] from 3β-acetoxycholenaldehyde by the Wittig reaction. The method has proved especially useful in the vitamin D and carotenoid fields[20].

Bifunctional carbonyl compounds can react at both sites as in the preparation[25] of 3,20-dimethyleneallopregnane (**7**). The diketone **8**, however, in the presence of six equivalents of $(C_6H_5)_3P{=}CH_2$ gave 55% of **9** and only 10% of **10**. This differentiation between the keto groups was probably caused by low solubility of the intermediate complex[25]. Further treatment of **9** with $(C_6H_5)_3P{=}CH_2$ gave a 76% yield of **10**.



(6)



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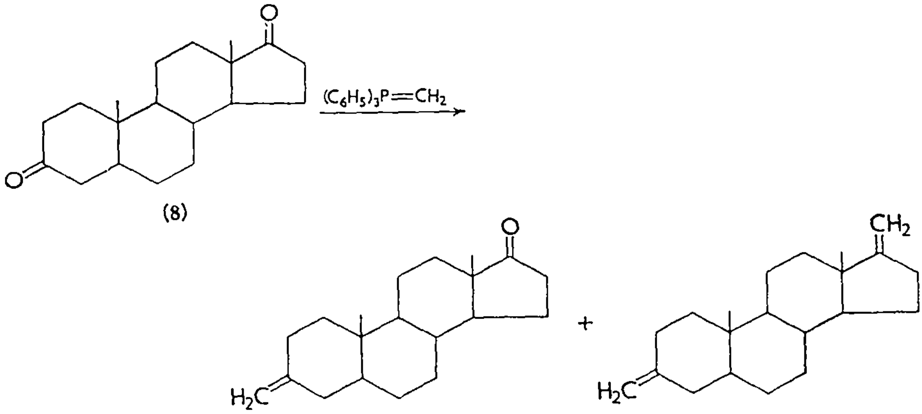
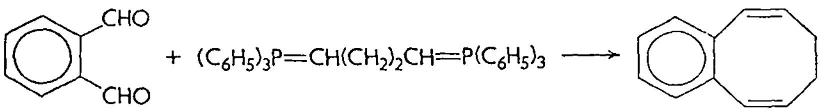


(8)

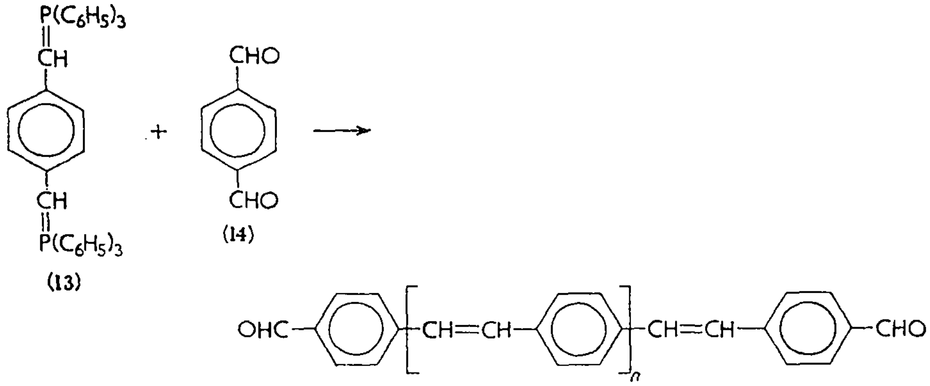
(9)

(10)

The reaction of the bifunctional ylide **11** with phthalaldehyde formed the cyclic product **12**[26], whereas the reactants **13** and **14** undergo polymerization[27].

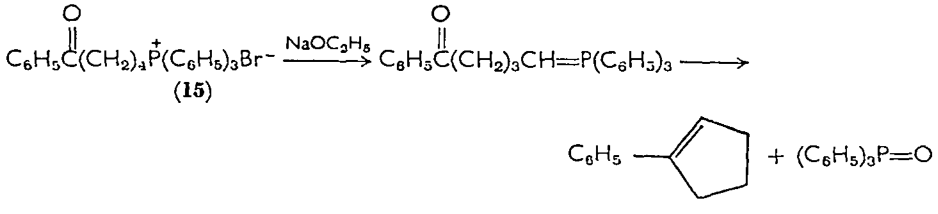


(11) (12)



(13) (14)

The phosphonium salt **15**, when treated with base, reacts to form the hydrocarbon **16** by an internal Wittig synthesis[28].



$$C_6H_5\overset{O}{\overset{\|}{C}}(CH_2)_4\overset{+}{P}(C_6H_5)_3Br^- \xrightarrow{NaOC_2H_5} C_6H_5\overset{O}{\overset{\|}{C}}(CH_2)_3CH{=}P(C_6H_5)_3 \longrightarrow$$

(15)

(16)

I. Changes in structure of the ylide

The alkylidene group of the ylide in the Wittig reaction can carry a variety of substituents besides hydrocarbon residues. Vinyl ethers and thioethers (**17**) are prepared from corresponding ylides[29].

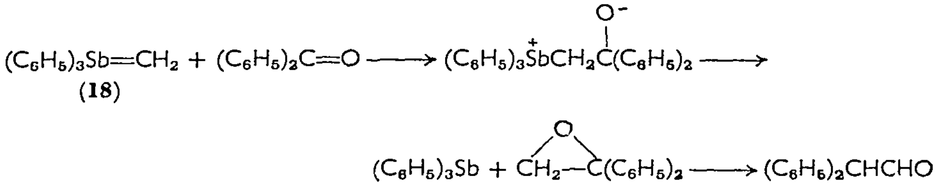
$$(C_6H_5)_3P{=}CHSCH_3 + (C_6H_5)_2C{=}O \longrightarrow \underset{(17)}{(C_6H_5)_2C{=}CHSCH_3}$$

Similar preparation of a vinyl ether followed by acid-catalyzed hydrolysis was suggested as an aldehyde synthesis[30].

$$(C_6H_5)_3P{=}CHOCH_3 + R_2CO \longrightarrow R_2C{=}CHOCH_3 \xrightarrow{H^+} R_2CHCHO$$

Contrary to early reports, it has been found[31] that methylene trimethylphosphoranes will undergo the complete Wittig reaction as in fact will phosphoranes of the type $(C_6H_5)_n(CH_3)_{3-n}P{=}CH_2$ where $n = 0, 1, 2$ or 3.

When the Wittig reaction is attempted with arsenic or antimony ylides (**18**) and benzophenone, the zwitterion is formed but an internal displacement reaction causes the metal–carbon bond to break with formation of diphenylacetaldehyde[32].



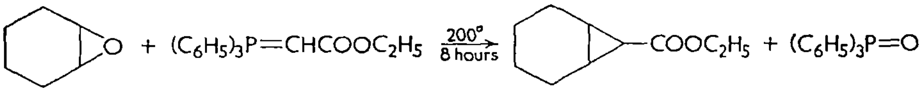
$$(C_6H_5)_3Sb{=}CH_2 + (C_6H_5)_2C{=}O \longrightarrow (C_6H_5)_3\overset{+}{Sb}CH_2\overset{O^-}{\overset{|}{C}}(C_6H_5)_2 \longrightarrow$$

$$(C_6H_5)_3Sb + CH_2\overset{O}{-}C(C_6H_5)_2 \longrightarrow (C_6H_5)_2CHCHO$$

(18)

2. Other substrates in the Wittig reaction

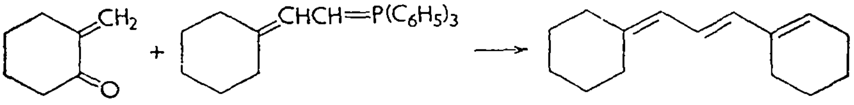
The use of an epoxide furnishes a new synthesis of cyclopropane carboxylic esters[33].



Schiff bases can be prepared from nitroso compounds in analogy with the formation of alkenes from aldehydes[34].

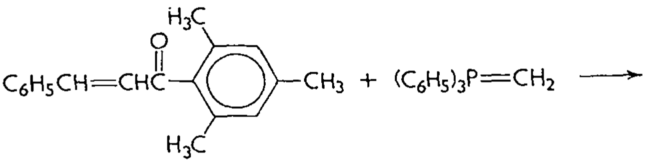
$$ArNO + (C_6H_5)_3P{=}CR_2 \longrightarrow ArN{=}CR_2 + (C_6H_5)_3P{=}O$$

1,4-Addition to α,β-unsaturated ketones is known in the formation of **21** from **19** and **20**[35]. The reaction of methylene triphenylphosphine

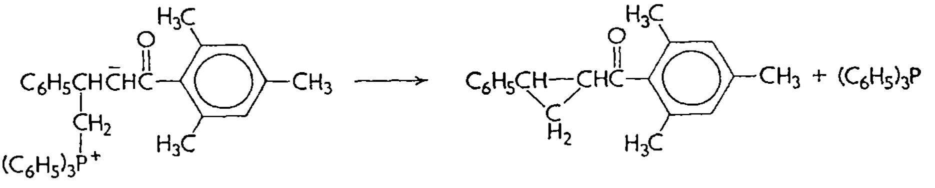


(19) (20) (21)

with the chalcone analog **22** leads, however, to cyclopropane formation[36] without oxygen transfer.

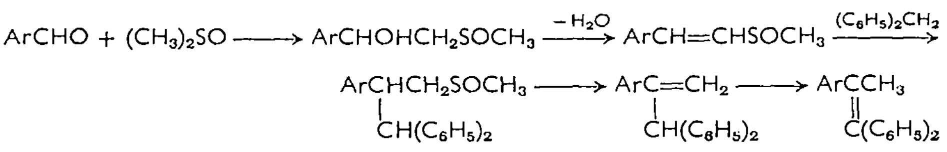


(22)



E. Miscellaneous Olefin-forming Condensations

When an aromatic aldehyde, an active methylene compound such as diphenylmethane, and dimethylsulfoxide are condensed by base, a series of reactions takes place[37] which yields the Knoevenagel condensation product with an extra methyl group on the aldehydic carbon atom.



$$\mathrm{ArCHO + (CH_3)_2SO \longrightarrow ArCHOHCH_2SOCH_3 \xrightarrow{-H_2O} ArCH{=}CHSOCH_3 \xrightarrow{(C_6H_5)_2CH_2} \underset{\underset{CH(C_6H_5)_2}{|}}{ArCHCH_2SOCH_3} \longrightarrow \underset{\underset{CH(C_6H_5)_2}{|}}{ArC{=}CH_2} \longrightarrow \underset{\underset{C(C_6H_5)_2}{\|}}{ArCCH_3}}$$

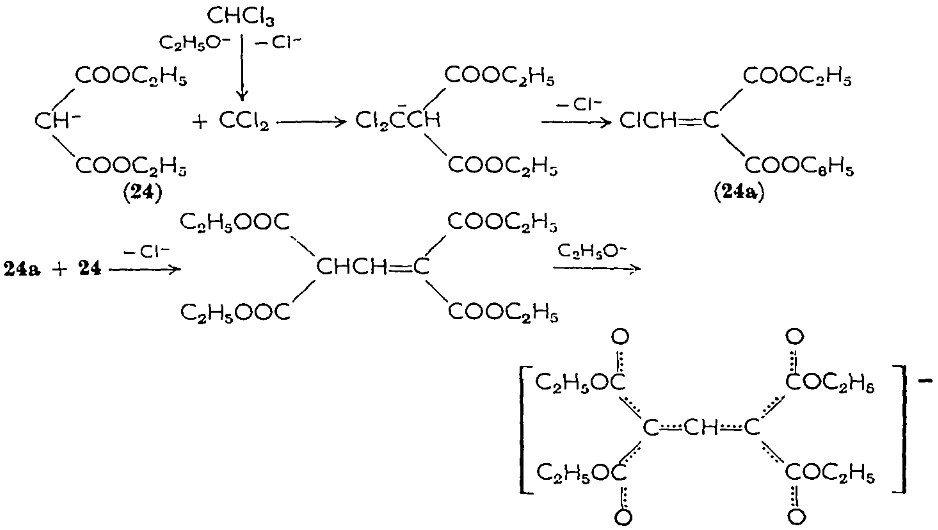
The coupling of two methylenes would form an alkene molecule. This is a possible final step for the dimerizations in reactions (11) and (12)[38,39]. However, a displacement by the carbanion **23** on

$$\mathrm{C_6H_5CH_2Cl \xrightarrow{Base} \underset{(\mathbf{23})}{C_6H_5\bar{C}HCl} \xrightarrow{-Cl^-} C_6H_5CH \longrightarrow C_6H_5CH{=}CHC_6H_5} \qquad (11)$$

$$\mathrm{(C_6H_5)_2CN_2 \xrightarrow{h\nu} (C_6H_5)_2C \longrightarrow (C_6H_5)_2C{=}C(C_6H_5)_2} \qquad (12)$$

benzyl chloride followed by dehydrohalogenation was indicated for the first example[40] by the isolation of $C_6H_5CHClCH_2C_6H_5$. The methylene is undoubtedly the reactant in the second example, but displacement of nitrogen from the undissociated diphenyldiazomethane is not ruled out. Methylenes are also believed to be intermediates in the formation of compounds of the type $(RS)_2C{=}C(SR)_2$ from the action of potassium amide on trialkylorthothioformates[41].

A novel reaction involving carbanions and methylenes is the base-catalyzed condensation of diethylmalonate with chloroform[42].



The condensation or polymerization of polyolefins to form new carbon–carbon double bonds will arbitrarily not be considered here, nor will reactions which are alkene syntheses only by virtue of functional groups not involved in the condensation.

II. MORE DETAILED STUDIES OF MECHANISM

A. The Kinetics of Consecutive Reactions

All but the very simplest chemical reactions proceed in several steps. The kinetics is consequently complex in principle at least, although in practice the rapidity of certain steps always results in some simplification, often to the point of straight first-, second- or third-order kinetics. The ultimate goal of a thorough kinetic study of a reaction is, however, to define the steps (mechanism) of the reaction and to evaluate the rate coefficient for every step. Too often it is believed that the task is merely to find a rate-controlling step.

Three arbitrary types of kinetics will be briefly discussed, differing in the relative rates of formation and disappearance of the intermediates. For simplicity, the case of one intermediate and first-order kinetics will be considered.

$$A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \xrightarrow{k_2} C \qquad (13)$$

1. The general case

The differential equations for any system of consecutive first-order reactions can be integrated exactly[43]. The solution for the scheme (13) is given in equation (14), where m and n are functions of

$$[\mathrm{A}] = [\mathrm{A}]_0\left[\frac{k_1(m - k_2)}{m(m - n)}\,\mathrm{e}^{-mt} + \frac{k_1(k_2 - n)}{n(m - n)}\,\mathrm{e}^{-nt}\right] \tag{14}$$

k_1, k_{-1} and k_2. It is characterized by an induction period in product formation, a rise and fall in the concentration of B and the lack of a simple kinetic order in A.

Equation (14) must be used if the concentrations of A, B and C are all appreciable at any time. Several approximate methods as well as machine computation are available for the evaluation of these concentrations from given rate coefficients.

2. The steady-state method

If the concentration of the intermediate B is small throughout the reaction, its time derivative may be set equal to zero in the very useful steady-state approximation.

$$\frac{\mathrm{d}[\mathrm{B}]}{\mathrm{d}t} = k_1[\mathrm{A}] - (k_{-1} + k_2)[\mathrm{B}] = 0$$

Solving for [B],

$$[\mathrm{B}] = \frac{k_1[\mathrm{A}]}{k_{-1} + k_2}$$

The rate of product formation is

$$\frac{-\mathrm{d}[\mathrm{A}]}{\mathrm{d}t} = \frac{\mathrm{d}[\mathrm{C}]}{\mathrm{d}t} = k_2[\mathrm{B}] = \frac{k_1k_2[\mathrm{A}]}{k_{-1} + k_2} = \frac{k_1[\mathrm{A}]}{(k_{-1}/k_2) + 1} \tag{15}$$

Thus the reaction follows a first-order course with rate coefficient equal to $k_1/[(k_{-1}/k_2) + 1]$. The last expression shows that when the steady-state approximation is used, only the ratio of the rate coefficients for reaction and reversion of the intermediate is needed or, conversely, can be obtained from the data.

Many reactions can be run with all reagents except a single substrate in excess, so that the separate steps and, as shown above, the overall reactions are pseudo first order. (A self-condensation such as the simple aldol condensation would not fall in this category, however.) The great usefulness of the steady-state method is found when the concentrations which affect k_1, k_{-1} and k_2 are changed and the observed effects on k are compared with those predicted for the possible mechanisms. A number of special cases encountered in acid–base catalyzed reactions have been described[44].

3. The limiting cases

The most familiar rate equations for consecutive reactions are those which are valid when there is a rate-controlling step. When $k_2 \gg k_1$, the formation of B is rate-controlling and simple first-order kinetics result with $k = k_1$. When $k_1 \gg k_2$, there is rapidly established equilibrium between A and B with the second step rate-controlling. In the latter case if $k_{-1} \gg k_1$, the concentration of B is low and $k = k_1k_2/k_{-1}$. However, if $k_1 \gg k_{-1}$ practically all of A is transformed to B before the second step has time to take place. Product formation will then be first order in B, with a starting concentration equal to that of A, and a rate coefficient $k = k_2$.

B. *Aldol Condensations*

1. Acetaldehyde and acetone in aqueous solution[44–46]

Including the catalyzing base B and its conjugate acid BH^+ which must catalyze the reversal of the first step, the mechanism of the formation of aldol (PH) from acetaldehyde (SH) may be written[47]:

$$\mathrm{SH} + \mathrm{B} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{S}^- + \mathrm{BH}^+$$

$$\mathrm{S}^- + \mathrm{SH} \xrightarrow{k_2} \mathrm{P}^-$$

$$\mathrm{P}^- + \mathrm{BH}^+ \xrightarrow{k_3} \mathrm{PH} + \mathrm{B}$$

The rate coefficient k_3 for oxygen protonation is large and does not appear in the rate equations. The amount of enolate ion S^- is always small, allowing the steady-state approximation to be applied:

$$\frac{d[S^-]}{dt} = k_1[B][SH] - k_{-1}[BH^+][S^-] - k_2[S^-][SH] = 0$$

$$[S^-] = \frac{k_1[B][SH]}{k_{-1}[BH^+] + k_2[SH]}$$

$$\frac{-d[SH]}{dt} = 2k_2[S^-][SH] = \frac{2k_1k_2[SH]^2[B]}{k_{-1}[BH^+] + k_2[SH]}$$

$$\frac{-2}{d[SH]/dt} = \frac{1}{k_1[SH][B]} + \frac{k_{-1}[BH^+]}{k_1k_2[SH]^2[B]}$$

A thermodynamic relationship exists between k_{-1}, k_1, K_{BH^+} and K_{SH}[48]; in other words, the ratio of forward and reverse rates of a base-catalyzed ionization is determined by the dissociation constants of the two acidic species. At equilibrium,

$$k_1[B][SH] = k_{-1}[BH^+][S^-]$$

$$\frac{k_{-1}}{k_1} = \frac{[B][SH]}{[BH^+][S^-]} = \frac{K_{BH^+}}{K_{SH}}$$

and since this last expression contains only constants, it holds whether there is equilibrium or not.

The catalyzing species B and BH^+ are, unlike S and S^-, certain to be at equilibrium unless they are a very sluggish acid–base system. Therefore

$$\frac{[BH^+]}{[B]} = \frac{[H^+]}{K_{BH^+}} = \frac{K_w}{[OH^-]K_{BH^+}}$$

and the final rate equation for the aldol condensation is[49]

$$\frac{2^*}{d[SH]/dt} = \frac{1}{[SH](k_0 + k_{OH}[OH^-] + k_B[B])} + \frac{K_w}{[SH]^2 k_2 K_{SH}[OH^-]} \qquad (16)$$

In equation (16), the term $k_1[B]$ has been separated into the three terms which would correspond to catalysis by H_2O, OH^- and B in an aqueous solution of a buffer $B\text{–}BH^+$.

The experimental data for the aldol condensation seem consistent with equation (16), although quantitative proof is prevented by several complications, notably the formation of acetaldehyde hydrate, which ionizes as a weak acid, changing the hydroxyl-ion and acetaldehyde concentrations and furnishing a new catalytic species. The unionized hydrate, though present in large quantities, is in rapid equilibrium with acetaldehyde and should not affect the kinetics.

The observation of Broche and Gibert[50] that the reaction order in aldehyde varies between first and second is explained by equation (16); the second term is the more important[49]. Also to be expected

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* Bell and McTigue[49] use 3 in their rate equation on the assumption that aldol reacts with a third molecule of acetaldehyde to form 6-hydroxy-2,4-dimethyl-1,3-dioxane.

is the existence of a general base catalysis which is less effective the lower the pH value[49], the second term becoming large as the hydroxyl-ion concentration decreases, choking off any acceleration due to the term $k_B[B]$.

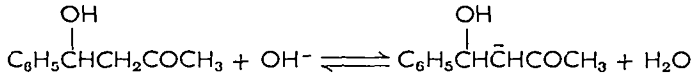
Deuterium-exchange experiments[48] support the kinetic work. In heavy water, deuterium is introduced into the unchanged acetaldehyde at low concentrations but only negligibly at high aldehyde concentrations[51], where the reaction of S^- with SH is faster than with BH^+.

The same mechanism can be applied to the condensation of acetone, which has been studied mainly as the cleavage[45]. Rapid exchange[47] and the absence of general base catalysis[52] suggest that $k_{-1} \gg k_2$.

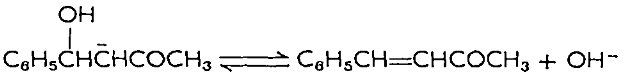
2. Aromatic aldehydes

The base-catalyzed reaction of benzaldehyde with acetone[53,54] or with acetophenone[55] shows a first-order dependence upon each reactant and, when water or ethanol is the solvent, upon the hydroxide- or ethoxide-ion concentration.

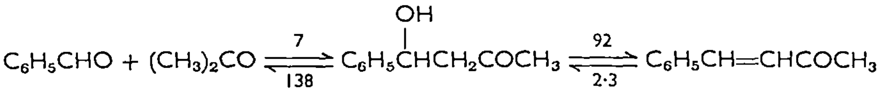
The mechanism of the condensation is similar to those already discussed; that of the ensuing base-catalyzed dehydration is given in equations (17) and (17a). The kinetic role of the intermediate has been carefully established[53]. The rate coefficients in equation (18) (expressed as $sec^{-1} \times 10^5$ for 0·1 N NaOH) show that the dehydration step is more rapid than the condensation when the acetone concentration is 0·0119 M.



$$C_6H_5\overset{OH}{\overset{|}{C}}HCH_2COCH_3 + OH^- \rightleftharpoons C_6H_5\overset{OH}{\overset{|}{C}}H\bar{C}HCOCH_3 + H_2O \quad (17)$$

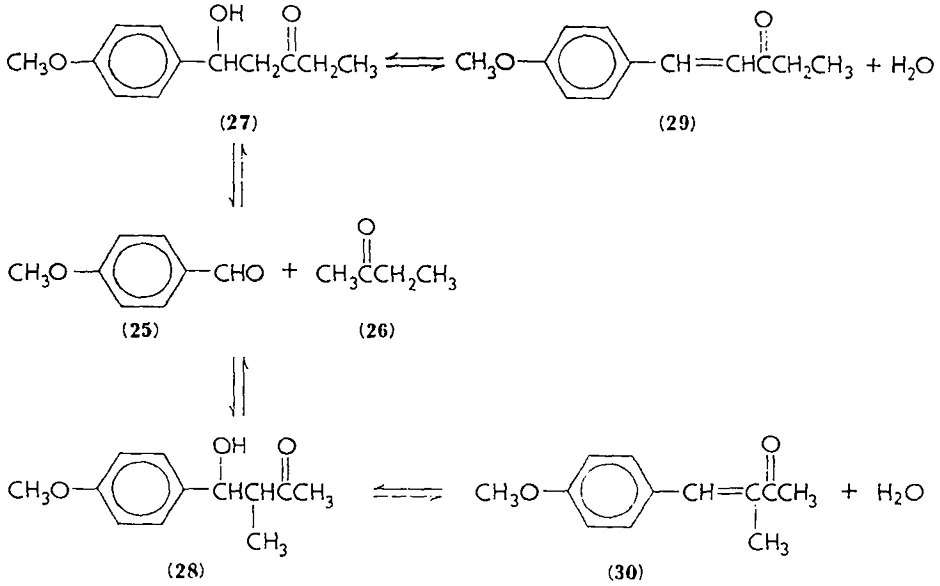


$$C_6H_5\overset{OH}{\overset{|}{C}}H\bar{C}HCOCH_3 \rightleftharpoons C_6H_5CH{=}CHCOCH_3 + OH^- \quad (17a)$$



$$C_6H_5CHO + (CH_3)_2CO \underset{138}{\overset{7}{\rightleftharpoons}} C_6H_5\overset{OH}{\overset{|}{C}}HCH_2COCH_3 \underset{2\cdot3}{\overset{92}{\rightleftharpoons}} C_6H_5CH{=}CHCOCH_3 \quad (18)$$

The ketol is therefore a transient intermediate. Moreover, the product first produced in the alkaline condensation of an unsymmetrical ketone with benzaldehyde is determined by the relative rates of dehydration of the two possible ketols to the corresponding unsaturated ketones. The product of the reaction of *p*-methoxybenzaldehyde with methyl ethyl ketone is **29**. Noyce and coworkers observed that if ketol **28** is treated with base, it does not dehydrate but reverts to **25** and **26** eight times as rapidly as **27**. Entirely similar results were obtained by Stiles, Wolf and Hudson[56], who showed also that the two types of ketol both yield only the straight-chain unsaturated ketone in base. The competitive, product-determining dehydration generally leads to the compound resulting from condensation at the methyl rather than the more highly substituted carbon.

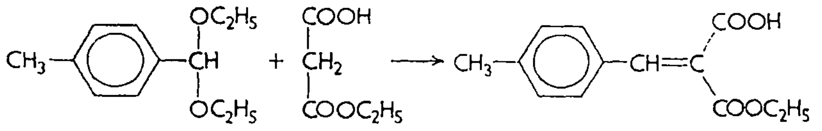


On the other hand, in acid-catalyzed condensations of the compounds shown[57], the product is determined by selectivity in the condensation step of the reaction: the ketols are rapidly dehydrated in strong acid and the relative rates of reaction of benzaldehyde at the two points of attack in methyl ethyl ketone determines the ratio of unsaturated ketones formed. It turns out that the product is **30** is spite of the fact that, in acid solution also, **27** is more rapidly dehydrated than **28**. The striking difference in the products of acid- and base-catalyzed aldol-type condensation reactions seems explained by the foregoing considerations.

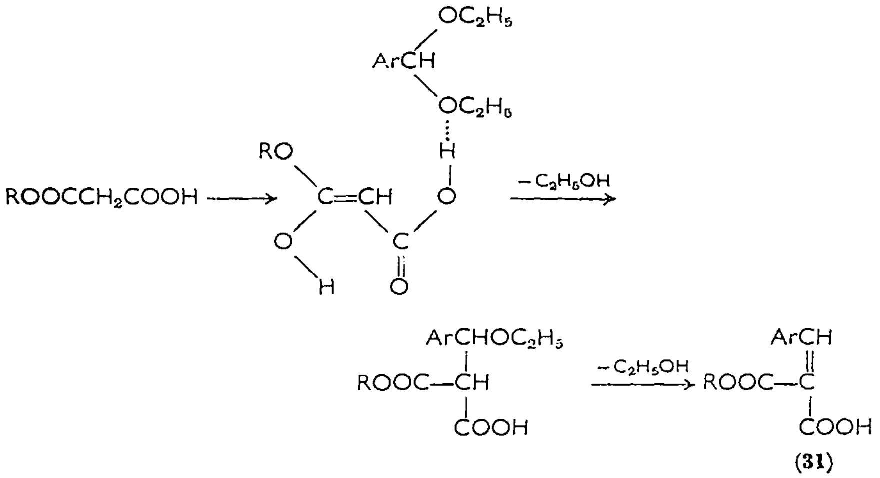
C. Knoevenagel Condensations

Base-catalyzed Knoevenagel condensations, like the aldol types, presumably involve the carbanion formed by ionization of the acidic reactant. In support of this fundamental premise, it is known that the more acidic the reactant the less basic the conditions required[58,59]. Inhibition by hydrogen ion and a positive salt effect have been observed[58].

An interesting internal catalysis is seen in the reaction of ethyl hydrogen malonate with aromatic acetals (equation 19)[60]. Diethyl


(19)

malonate does not react under the conditions used, and substitution of the free aldehyde for the acetal reduces the yield to 5%. The proposed intermediate is a hydrogen-bonded complex of enol and acetal (equation 20). The product **31** can be decarboxylated to $ArCH{=}CHCOOC_2H_5$ with pyridine.


(20)

(31)

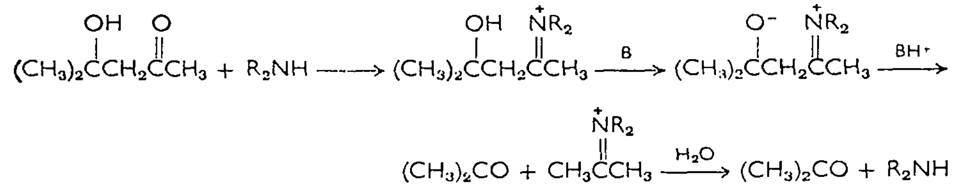
In the similar series of reactions (21), the decarboxylation step, measured by CO_2 evolution, is faster than the condensation[61].

$$ArCHO + CH_2(COOH)_2 \xrightarrow{\text{Pyridine}} ArCH{=}C(COOH)_2 \xrightarrow{-CO_2} ArCH{=}CHCOOH \quad (21)$$

The efficiency of ammonia and amines as catalysts is demonstrated by the success of a great many synthetic procedures and by several kinetic studies. Although they could serve merely as bases in the ionization steps of condensation mechanisms[62] (and a weak base would have the advantage of coexisting with acids necessary in the protonation steps[63]), primary amines and piperidine especially among secondary amines seem to have a catalytic effect larger than expected from their basicity[64].

The catalysis of carbonyl reactions by addition of an amine and its subsequent replacement by the attacking reagent was suggested long ago[65], and the possible intermediates have been formulated[66]. Nucleophilic catalysis of ester hydrolysis and related processes has been extensively studied, largely because of its biochemical importance, and is the subject of a comprehensive review by Bender[67].

Westheimer and Cohen[52] in 1938 concluded that the specific effect of amines on the cleavage of diacetone alcohol[68] is to form a ketimine which undergoes rapid dissociation and hydrolysis.



$$(CH_3)_2\overset{\overset{OH}{|}}{C}CH_2\overset{\overset{O}{\|}}{C}CH_3 + R_2NH \longrightarrow (CH_3)_2\overset{\overset{OH}{|}}{C}CH_2\overset{\overset{\overset{+}{N}R_2}{\|}}{C}CH_3 \xrightarrow{B} (CH_3)_2\overset{\overset{O^-}{|}}{C}CH_2\overset{\overset{\overset{+}{N}R_2}{\|}}{C}CH_3 \xrightarrow{BH^+}$$

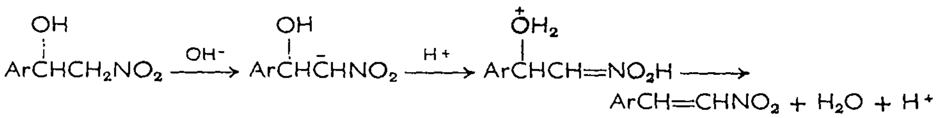
$$(CH_3)_2CO + CH_3\overset{\overset{\overset{+}{N}R_2}{\|}}{C}CH_3 \xrightarrow{H_2O} (CH_3)_2CO + R_2NH$$

The condensation of nitromethane with aromatic aldehydes to form nitroalcohols (equation 1) is catalyzed by amines[69]. The kinetics of the reaction catalyzed by ammonia[70] or n-butylamine[71] and an equivalent quantity of acetic acid in methanol shows an induction period in aldehyde disappearance. The aldehyde reacts rapidly with n-butylamine to form the Schiff base, which reacts more slowly with nitromethane, yielding the nitrostyrene (equation 22).

$$ArCHO + C_4H_9NH_2 \longrightarrow ArCH{=}NC_4H_9 \xrightarrow{CH_3NO_2} ArCH{=}CHNO_2 \qquad (22)$$

The course of the overall amine-catalyzed reaction, calculated from the measured rates of the two reactions, is in agreement with experiment.

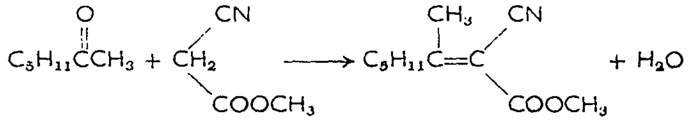
It is significant that amine catalysis seems to bypass the nitroalcohol stage (5) and yield the nitrostyrene at pH values where the nitroalcohol dehydrates only slowly[72]. In fact, the dehydration by acid recommended in nitrostyrene syntheses which use sodium hydroxide in the first step is carried out on the sodium salt of the nitroalcohol; possibly this dehydration proceeds *via* a rapid protonation of the alcohol oxygen followed by loss of water, the reverse of the mechanism



$$\mathrm{Ar\overset{OH}{\overset{|}{C}}HCH_2NO_2} \xrightarrow{OH^-} \mathrm{Ar\overset{OH}{\overset{|}{C}}H\bar{C}HNO_2} \xrightarrow{H^+} \mathrm{Ar\overset{\overset{+}{O}H_2}{\overset{|}{C}}HCH{=}NO_2H} \longrightarrow \mathrm{ArCH{=}CHNO_2 + H_2O + H^+}$$

proposed for base-catalyzed hydrolysis in acid solution[73]. The fact that the amine-catalyzed reaction requires no high acidity suggests that the nitroalcohol is not an intermediate.

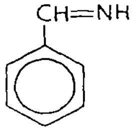
Glacial acetic acid is also a suitable medium for amine catalysis of the Knoevenagel condensation. Cope[63] found that acetamide and amines catalyze the reaction of cyanoacetic esters with ketones. It is noteworthy that acetamide would react with water to form



$$\mathrm{C_5H_{11}\overset{O}{\overset{\|}{C}}CH_3 + CH_2(CN)(COOCH_3) \longrightarrow C_5H_{11}\overset{CH_3}{\overset{|}{C}}{=}C(CN)(COOCH_3) + H_2O}$$

ammonia and acetic acid. In the nitrostyrene condensation under similar conditions, spectrophotometric observation of Schiff base formation is consistent with nucleophilic catalysis as is the suppression of the reaction by small amounts of water[74].

There are certain similarities between catalysis by amines in acetic acid solution and the anion-exchange resin catalysis of the condensation of diethyl malonate with acetaldehyde. Hydroxyl ion is not necessary: the condensation proceeds as well when the counterion is acetate[7]. Although nucleophilic catalysis by the resin amino groups has not been proved, it does seem to be a possibility in this case.



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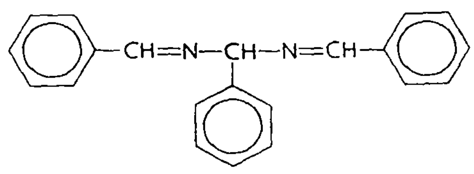

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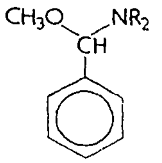

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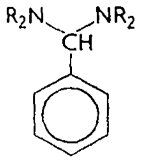


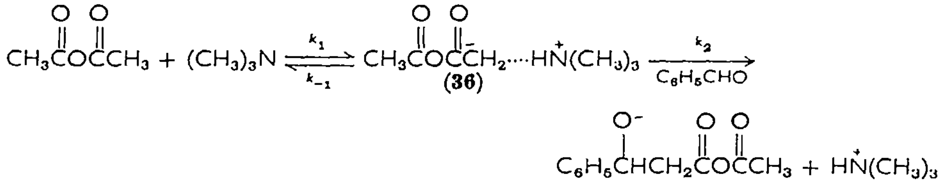
(35)

The ketimine and Schiff base types proposed as intermediates in condensation reactions are not the only species present in solutions of carbonyl compounds and amines. For example, ammonia with benzaldehyde produces the imine **32**[75] and hydrobenzamide **33**[76]. Secondary amines in methanol solutions are known to form **34**[77] and at higher amine concentrations **35**. Other tetrahedral intermediates such as $C_6H_5CH(OH)NH_2$ are not formed in high concentration from aromatic aldehydes but can, along with still other compounds, assume major importance with aliphatic aldehydes and ketones. The determination of the actual details of nucleophilic catalysis and the accompanying acid–base relations for condensation reactions is a challenging problem.

D. The Perkin Reaction

The discovery by Kalnin[78] that amines and other bases may be substituted for the sodium salt of an acid in the Perkin reaction proved that the carboxylate ion is a basic catalyst and the anhydride the substrate in this condensation[79]. Kinetic studies by Buckles and Bremer[80] seem consistent with the aldol-type condensation shown in equation (8). The intermediates expected in this type of mechanism have been isolated and shown to react to give the known products[79,81,82].

Ogata and Tsuchida[83] found the rate of the triethylamine-catalyzed reaction of benzaldehyde with acetic anhydride to be third order but independent of the concentration of amine or anhydride if in excess. Apparently this is an example of the kinetic type in which $k_1 \sim k_{-1} > k_2$. The proposed intermediate **36** is reasonable in the hydrocarbon solvent used.

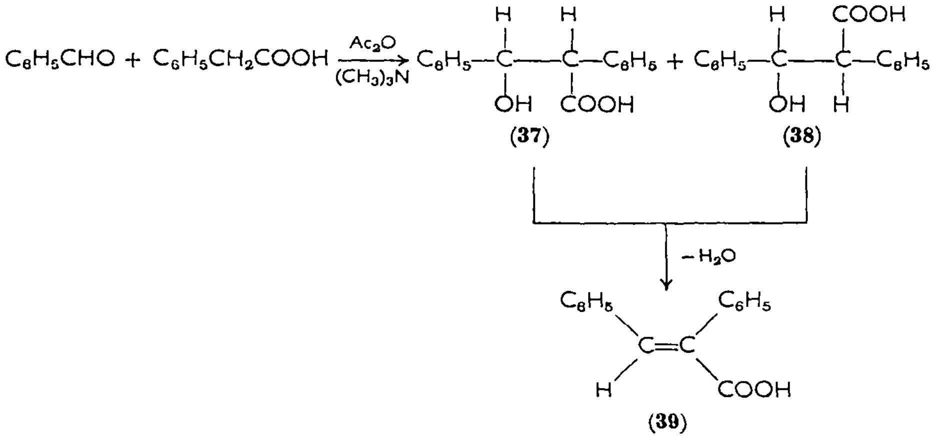


$$CH_3\overset{O}{\overset{\|}{C}}O\overset{O}{\overset{\|}{C}}CH_3 + (CH_3)_3N \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\mathbf{(36)}}{CH_3\overset{O}{\overset{\|}{C}}O\overset{O}{\overset{\|}{C}}\overset{-}{C}H_2\cdots H\overset{+}{N}(CH_3)_3} \xrightarrow[C_6H_5CHO]{k_2}$$

$$C_6H_5\overset{O^-}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}O\overset{O}{\overset{\|}{C}}CH_3 + H\overset{+}{N}(CH_3)_3$$

The stereochemistry of the Perkin reaction has provided valuable information concerning the mechanism[84]. Benzaldehyde and phenylacetic acid react to form α-phenyl-*trans*-cinnamic acid (**39**). This is the more stable isomer, the equilibrium constant for its formation from α-phenyl-*cis*-cinnamic acid having been reported as

6[85]. When the diastereoismeric 3-hydroxy-2,3-diphenylpropionic acids (**37** and **38**) were prepared and subjected to the conditions of the Perkin reaction, each yielded the same product (**39**) quantitatively[84]. The elimination reaction is therefore not stereospecific but highly stereoselective. Reversibility of the condensation step is ruled out by the lack of intervention of *m*-nitrobenzaldehyde or of phenylacetic acid-carboxyl-^{14}C. It follows that the intermediates eliminate much more rapidly than they revert to the starting materials and that the *cis* elimination in the *threo* isomer (**38**) competes with the *trans* to the complete exclusion of the latter. The rapid *cis* elimination results from more favorable orbital overlap in the transition state[84]; steric effects in the transition state for *trans* elimination would probably lead to poorer overlap, causing a higher activation energy.



E. *The Wittig Reaction*

1. Formation of the reagent

Staudinger's original triphenylphosphorane preparation was the thermal decomposition of **40**[22]; an analogous but more general

$$\underset{(\mathbf{40})}{(C_6H_5)_3P{=}N{-}N{=}C(C_6H_5)_2} \longrightarrow (C_6H_5)_3P{=}C(C_6H_5)_2 + N_2$$

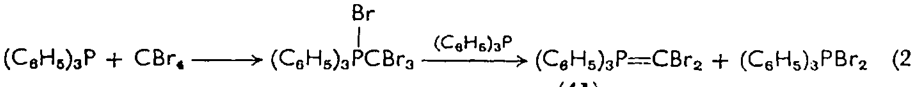
method is the cuprous-ion catalyzed decomposition of a diazo compound in the presence of triphenylphosphine[86].

$$(C_6H_5)_3P + CH_2N_2 \xrightarrow[\text{dioxane}]{Cu^+} (C_6H_5)_3P{=}CH_2 + N_2$$

The methylenes CHCl[87] and CCl_2[88] have been shown to react with triphenylphosphine to form the triphenylphosphoranes directly. The reaction of bromoform, in the absence of bases, is catalyzed by light or peroxides and seems to be a free-radical process with $CHBr_2$ as chain carrier (equation 23)[89]. Ramirez and coworkers formulate

$$(C_6H_5)_3P + \cdot CHBr_2 \longrightarrow (C_6H_5)_3\overset{\bullet}{P}CHBr_2 \xrightarrow{CHBr_3} (C_6H_5)_3\overset{+}{P}CHBr_2 + Br^- + \cdot CHBr_2 \qquad (23)$$

still another mechanism for the formation of the ylide **41** from carbon tetrabromide (equation 24)[90]. The decarboxylation of **42** takes place



$$(C_6H_5)_3P + CBr_4 \longrightarrow (C_6H_5)_3\overset{Br}{P}CBr_3 \xrightarrow{(C_6H_5)_3P} (C_6H_5)_3P{=}CBr_2 + (C_6H_5)_3PBr_2 \qquad (24)$$

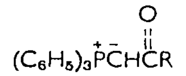
(41)

if $n = 1$ but not if higher homologs ($n = 2$ or 3) are used[91].

$$(C_6H_5)_3\overset{+}{P}(CH_2)_nCOO^- \longrightarrow (C_6H_5)_3P{=}CH_2 + CO_2 \ (n = 1)$$

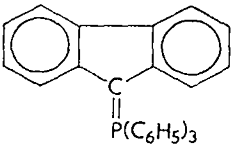
(42)

The standard method of preparing the Wittig reagent, however, is the reaction of the phosphonium salt $R_3\overset{+}{P}CHR_2X^-$ with base. The negative charge on carbon in the phosphorylides is compensated by the positive charge on the adjacent atoms as in the nitrogen ylide $(CH_3)_3\overset{+}{N}CH_2^-$. When the central element is phosphorus, however, greater stability can be attained by *d*-orbital resonance[92] (which is implied in the use of the form $Ar_3P{=}CH_2$ with considerable contribution of the form $Ar_3\overset{+}{P}CH_2^-$ understood). The negative charge can be further delocalized by neighboring unsaturated groups as in **43**[93] and **44**[31]. The charge distribution in such species as



$$(C_6H_5)_3\overset{+}{P}\overset{-}{C}H\overset{O}{\overset{\|}{C}}R$$

(**43a**, R = C_6H_5; **43b**, R = CH_3)



(**44**)

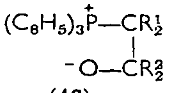
indicated by their dipole moments (5·45 D for **43a** and 5·54 D for **43b**)[93], the pK of their conjugate acids (8·0 for **44**) and other physical properties, is related to their activity in the Wittig reaction[94].

While the comparatively stable species **43** and **44** are formed without complications under moderately basic conditions, the very strong bases required to ionize simpler alkyltriarylphosphonium salts can attack the phosphorus atom[95]. A considerable quantity of benzene is produced when $[(C_6H_5)_3\overset{+}{P}CH_3]Br^-$ reacts with methyllithium, and tetraphenylphosphonium bromide (**45**) yields triphenylphosphonium methylide.

$$\underset{\textbf{(45)}}{(C_6H_5)_4\overset{+}{P}Br^-} + CH_3Li \longrightarrow (C_6H_5)_3P{=}CH_2 + C_6H_6 + LiBr$$

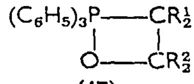
2. Reaction with the carbonyl compound

The zwitterion **46** differs from the presumed but undetected cyclic intermediate **47** in geometry and freedom of rotation. The former



$$\begin{array}{l}(C_6H_5)_3\overset{+}{P}-CR^1_2\\ \quad\;\, ^-O-CR^2_2\end{array}$$

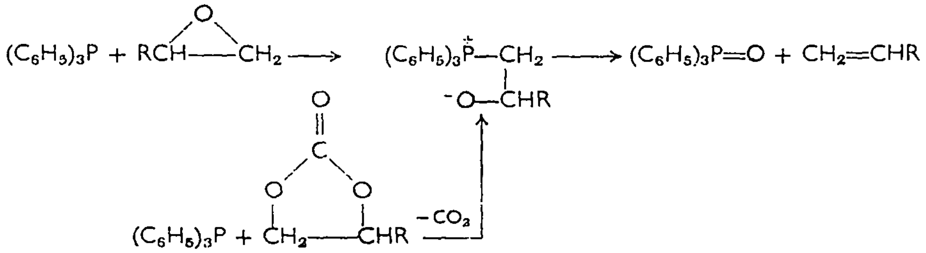
(46)



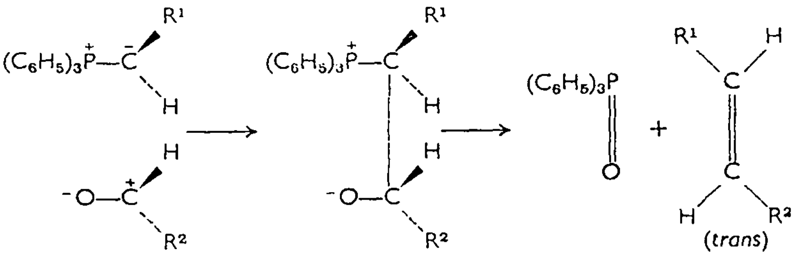
$$\begin{array}{l}(C_6H_5)_3P-CR^1_2\\ \qquad\;\;\, O-CR^2_2\end{array}$$

(47)

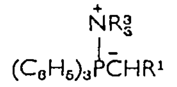
may also be formed as an intermediate when triphenylphosphine acts upon an epoxide[96] or a cyclic carbonate[97]; there are analogies for **47** in other cyclic compounds of pentacovalent phosphorus.



The Wittig reaction generally yields a mixture of the *cis* and *trans* isomers of the olefin. The product is determined when the C—C bond is formed between the ylide and the carbonyl compound. For minimum steric interaction, the *trans* isomer will result from the lower-energy dipole–dipole orientation as shown, and the *cis* from the higher. Shemyakin and coworkers[98] discovered that piperidine,



lithium iodide and other bases, by attachment to the phosphorus atom to form species such as **48**, decrease the possibility for dipole–

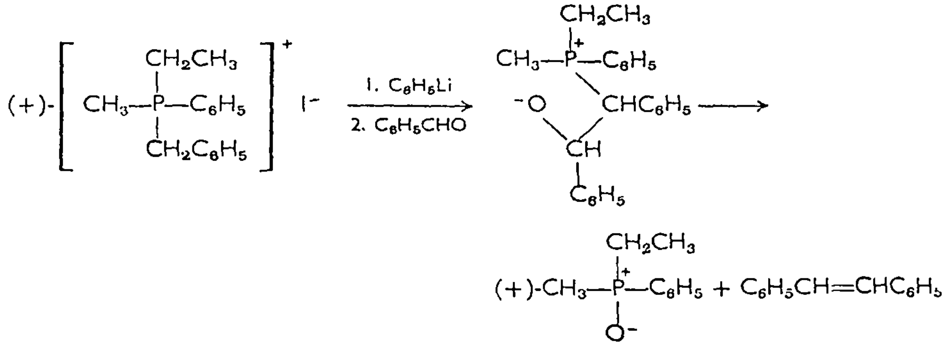


$(C_6H_5)_3\overset{\overset{+}{N}R_3^3}{P}\overset{-}{C}HR^1$

(48)

dipole orientation in many cases to the point where the reaction yields *cis* product exclusively.

The driving force of the last step of the Wittig reaction is the stability of triphenylphosphine oxide. This step proceeds with retention of configuration at the phosphorus atom[99].



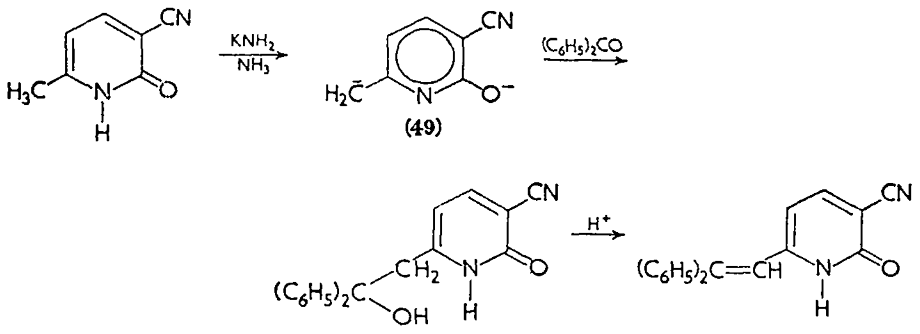
III. THE EFFECT OF STRUCTURE ON REACTIVITY

A. Reaction Rates

Structural changes in the reactants affect the rate of each step of a complex reaction and will be reflected in the overall rate according to the form of the rate equation. Until the reaction has been thoroughly investigated, the rate equation is not known and structural effects can only tentatively be attributed to a step or group of steps in the mechanism; they serve, however, as clues in its clarification.

For example, the Perkin reaction of aliphatic aldehydes is inhibited when the chain length is increased beyond five carbon atoms, and citral-a is more reactive than citral-b[100]. This influence can provisionally be ascribed to steric hindrance at the carbonyl group, which in turn can imply a steric effect on rate or equilibrium in attack by the anhydride anion, or on more obscure causes. Nevertheless these observations, apart from their intrinsic interest, prove that the ionization which precedes the condensation is not rate controlling.

The effect of changing the metallic ion associated with enolate ions is not well understood. It is customary to write sodium enolates as ions[101] but ion-pair formation can affect their reaction rates very markedly in non-aqueous solvents[102]. These effects would be magnified in condensation reactions involving dianions like the proposed intermediate **49**[103].



B. Correlations with the Hammett Equation

Although structural effects in alkene-forming condensation reactions have not been subjected to such a quantitative scrutiny as in semicarbazone formation and related reactions, some interesting variations of rate with aromatic substituents have been observed.

The more straightforward consequences of structural changes can, for a two-step reaction, be derived from equation (15), assuming that the rate coefficients all obey the Hammett equation in its usual form, *viz.*

$$\log \frac{k_1^X}{k_1^H} = \rho_1 \sigma_X$$

and similarly for k_{-1} and k_2. The two limiting cases then are

$$\log \frac{k^X}{k^H} = \rho_1 \sigma_X \tag{25}$$

when the first step is rate controlling and

$$\log \frac{k^X}{k^H} = (\rho_1 + \rho_2 - \rho_{-1}) \sigma_X \tag{26}$$

when the first step is a rapidly established equilibrium. If the steps are of comparable rate, and meet the requirements of the steady-state method, equation (15) may be put into the notation $k = k_1 r/(1 + r)$ where $r = k_2/k_{-1}$. It is also convenient to define $\rho_r = \rho_2 - \rho_{-1}$ so that the Hammett equation for r is $\log (r^{\mathrm{X}}/r^{\mathrm{H}}) = \rho_r \sigma_{\mathrm{X}}$. Equation (15) then becomes

$$\begin{aligned} \log k^{\mathrm{X}} &= \log k_1^{\mathrm{X}} + \log r^{\mathrm{X}} - \log (1 + r^{\mathrm{X}}) \\ &= \log k_1^{\mathrm{H}} + \rho_1 \sigma_{\mathrm{X}} + \log r^{\mathrm{H}} + \rho_r \sigma_{\mathrm{X}} - \log (1 + r^{\mathrm{X}}) \qquad (27) \\ &= \log k_1^{\mathrm{H}} r^{\mathrm{H}} + (\rho_1 + \rho_r)\sigma_{\mathrm{X}} - \log (1 + r^{\mathrm{X}}) \end{aligned}$$

If r is very large or very small, equation (27) approaches respectively equation (25) or (26). Generally, however, a plot of $\log (k^{\mathrm{X}}/k^{\mathrm{H}})$ *vs.* σ_{X} will not be linear and may even show a maximum (or minimum). The position of the maximum is found by differentiating equation (27) with respect to σ.

$$\begin{aligned} \frac{\mathrm{d} \log k}{\mathrm{d}\sigma} &= \rho_1 + \rho_r - \frac{0{\cdot}4343}{1 + r} \cdot \frac{\mathrm{d}r}{\mathrm{d}\sigma} \\ &= \rho_1 + \sigma_r - \frac{r\rho_r}{1 + r} \\ &= \rho_1 + \frac{\rho_r}{1 + r} = 0 \end{aligned}$$

$$\rho_1(1 + r) = -\rho_r \text{ when } k \text{ is maximum.}$$

It follows that there will be no maximum unless ρ_r is negative and larger in absolute value than ρ_1 which must be positive. The opposite condition will cause a minimum. Of course the maximum or minimum may be far outside the practical range of σ. Several cases are plotted in Figure 1. Many condensation reactions give a linear Hammett plot, implying that there is a rate-controlling step. Ogata[83] found the value 2·25 for ρ in the Perkin condensation. Noyce attributed the slight sensitivity of rate to substituent in the acid-catalyzed condensation of methyl ethyl ketone with benzaldehydes to opposite effects on the basicity of the aldehyde and the rate of attack of its protonated form on the enol[104]. The rate of piperidine-catalyzed condensation of diethyl malonate with benzaldehyde in kerosene or isopropanol is depressed by both positive and negative substituents, possibly according to equation (27)[105]. On the other hand, the maximum may be the result of non-linear Hammett plots[106] for several steps in the complex mechanism, even though there is a rate-controlling step.

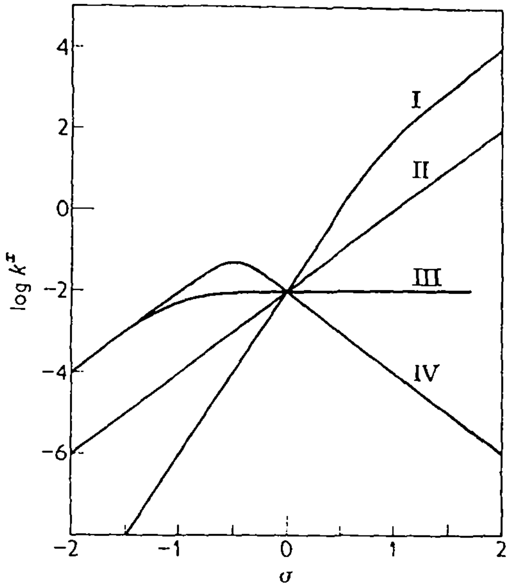
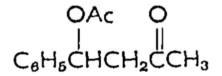


FIGURE 1. Calculated Hammett plots (equation 9) for a reaction $A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \xrightarrow{k_2} C$, where $k_1^H = 1$, $r^H = 10^{-2}$ and $\rho_1 = 2$. The value of ρ_r for each curve is as follows: I, 2; II, 0; III, −2; IV, −4. Validity of the steady-state method is assumed.

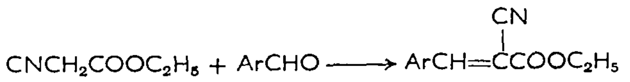
A warning against any premature interpretation of deviations from linearity in ρ–σ plots is to be found in the reason for non-linearity in acid-catalyzed condensations in acetic acid[107]. A reaction path through the ketol acetate **50** competes with the normal path in such a way as to cause a complex dependence of log k upon σ.



$$C_6H_5\overset{\overset{\large OAc}{|}}{C}HCH_2\overset{\overset{\large O}{\|}}{C}CH_3$$

(50)

A series of interesting experiments by Patai and coworkers indicates the effect of substituents on several different steps of the reaction of ethyl cyanoacetate (**51**) and cyanoacetamide with benzaldehydes[108].



$$CNCH_2COOC_2H_5 + ArCHO \longrightarrow ArCH{=}\overset{\overset{\large CN}{|}}{C}COOC_2H_5$$

(51)

A linear Hammett plot is obtained with $\rho = 1{\cdot}6$. However, while anisaldehyde shows second-order kinetics at the concentrations used, the more reactive *p*-chlorobenzaldehyde allows the ionization to be rate controlling so that the reaction is first order. At the much higher σ-value of *p*-nitrobenzaldehyde second-order kinetics returns, possibly because the dehydration step is rate controlling due to a ρ for this step which is negative though not sufficiently negative to cause a maximum.

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 5

Detection and determination of the alkenes

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I. INTRODUCTION

Various chemical and physical techniques are available for analyzing the alkenes. The techniques which are currently being used quite extensively are discussed in the following text. Approaches which have not been employed to a great extent in the analysis of the alkenes are also mentioned, but not dealt with to any great length. An effort is made to present chemical and physical methods which have been used for the solution of analytical problems encompassing assay, mixture analysis and trace amounts of an alkene.

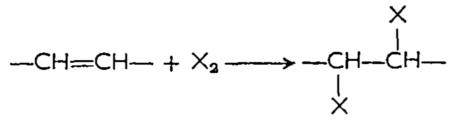
Usually, a particular analytical problem concerned with the alkenes might be solved by several of the techniques mentioned. In view of this, an attempt is made in the description of each technique to indicate the scope of each approach such that the proper choice can be made for the solution of a particular problem.

The literature references which are discussed were chosen on the basis of application to problems which may be generally encountered in alkene chemistry.

II. CHEMICAL METHODS

A. Quantitative Analysis

The reactivity of the double bond of the alkenes is the basis for practically all of the chemical methods used in the analysis of these compounds. Quantitative methods based on hydrogenation, halogenation, *etc.*, are of this type and usually involve the addition of an excess of the reagent to the sample (equation 1). The reagent



$$-CH{=}CH- + X_2 \longrightarrow -\underset{X}{CH}-\overset{X}{CH}- \qquad (1)$$

consumed is then taken as a measure of the alkenes. The data obtained in a hydrogenation can be expressed in several ways, *viz.* moles or grams of hydrogen reacted per 100 grams of sample or grams of sample reacting with one mole of hydrogen ('hydrogen number'). Halogenation data are usually expressed as bromine or iodine number, *i.e.* grams of bromine or iodine per 100 grams of sample.

The majority of the methods for determining the double bond involve halogenation, using bromine, iodine monobromide or iodine monochloride. Chlorine and iodine have not been used to any great extent: chlorine is too reactive, causing side-reactions such as extensive substitution and oxidation; iodine, on the other hand, does not add readily to the double bond.

The halogen procedures were developed originally for determining unsaturation in animal and vegetable fat and were generally modified when applied to materials such as the alkenes. The complexity of the reaction of the halogens with unsaturated compounds limits any particular halogen method from being used as a universal method for the double bond. As a result, many methods have evolved and generally are workable for only a limited range of compounds.

I. Halogenation

The halogen procedures which have been developed for the alkenes generally employ some form of bromine as the addition reagent. Various solvents, such as acetic acid, carbon tetrachloride, chloroform, methanol (saturated with sodium bromide), water, *etc.*, have been used.

Generally, bromine is very reactive with materials containing the double bond, and consequently side-reactions can also occur, depending upon the brominating reagent used and the sample under study. The side-reactions[1] that may occur can be grouped as follows: (*a*) substitution in a position removed from the double bond; (*b*) spontaneous elimination of hydrogen bromide from the addition product; (*c*) elimination of hydrogen bromide from the addition product under the influence of water; (*d*) reaction of the sample with the solvent; and (*e*) effect of peroxides in the sample.

If substitution occurs at other points in the molecule [effect (*a*)] and the addition to the double bond is quantitative, then a means of correcting for the amount of hydrogen bromide released should permit an accurate measure of the unsaturation. The method of McIlhiney[2], which employs bromine in carbon tetrachloride as reagent, provided for a substitution correction by the addition of potassium iodate, which reacts with hydrobromic acid to release iodine. The iodine is then titrated as a measure of substitution. However, subsequent data[3,4] obtained by using this correction factor was indicative of low corrected values, and in some cases negative values were obtained. The conclusions that could be arrived at are (*i*) complete addition did not take place or (*ii*) other side-reactions occurred, other than substitution, which produced hydrobromic acid. Side-effects (*b*), (*c*) and (*e*) would lead to low results.

Wilson[3] investigated the reactions which take place when a solution of halogen is added to an unsaturated compound. Data on straight-chain alkenes in which the Rosenmund and Kuhnhenn[5] solution was employed (pyridinium sulfate–dibromide) were indicative of good results even with reaction times of one hour; however, results obtained on branched-chain pentenes were abnormally high, suggesting substitution. The Kaufmann[6] reagent, which consists of bromine in absolute methanol saturated with sodium bromide, was used with slight modification by Wilson[3] for the analysis of the alkenes. The total bromine absorption values obtained on several alkenes were within several bromine number units of the theoretical value. However, examination of the reacted solutions after titration of the excess bromine revealed that acid was present, and thus it was concluded that reactions other than addition must be occurring. Even though side-reactions were evident, the total absorption of bromine was reproducible and near theoretical for the alkenes such as 1-octene, 1-hexene and 2,4,4-trimethyl-1-pentene. With 2,4,4-trimethyl-2-pentene, the results obtained were low and were stated to be probably due to dimerization of the alkene[3]. Wilson concluded from these data that addition and substitution in the same molecule are mutually exclusive and that substitution takes place at one of the double-bonded carbon atoms, since the relationship between the two processes could not exist if an atom remote from this position in the same molecule were involved. Therefore, the acidity produced should not be used as a correction for substitution in the Kaufmann method.

Lewis and Bradstreet[7,8] employed a solution of bromide–bromate in the presence of sulfuric acid as the brominating reagent for the determination of the alkenes. The aspect of side-reactions was also investigated[7] on alkenes such as di-, tri- and tetraisobutylene, pentene, hexenes and octene. The amount of reaction in which acidity was produced amounted to about 40% (depending upon the amount of excess reagent) for the polyisobutylenes and from 12–25% for the straight-chain alkenes. The bromine numbers obtained for the alkenes were near theoretical (especially the straight-chain compounds) even though the reaction is not all addition. These data and that obtained by Wilson[3] are indicative of the complexity of the bromination reaction with the double bond. In view of these data, it would appear that the substitution correction based on the acidity determination is not valid and may be applicable only with specific compounds.

Although the bromination of alkenes is a complex reaction, many methods are available which have been used to obtain reliable data. The methods are usually more applicable to the straight-chain alkenes, whereas the branched materials are generally difficult to analyze.

The stable potassium bromide–bromate reagent introduced into the English literature by Francis[9] will be discussed as a background to the procedure adopted as a standard method for determining the bromine number of petroleum products by the American Society for Testing Materials (ASTM).

The procedure, as indicated by Francis[9], involves the addition of an excess of the reagent to an acidified sample with subsequent iodometric titration of the excess. Trimethylethylene and hexene were analyzed satisfactorily with this method.

Bacon[10] modified the procedure by addition of a solvent, such as benzene, which allows the method to be workable in the presence of highly colored materials. Mulliken and Wakeman[11] altered the procedure by adding the reagent in two proportions and agitating the solution containing the excess reagent for 2 minutes. Generally, good results were obtained for the alkenes investigated. Thomas, Block and Hoekstra[12] cooled the reaction mixture in order to prevent any substitution. Lewis and Bradstreet[8] used n-heptane as a solvent for the sample and titrated in the presence of sulfuric acid saturated with potassium bromide. The potassium bromide–bromate titrant was added directly until a faint yellow color appeared and then 1 ml. excess was added. Two minutes were allowed for reaction and the excess reagent then determined iodometrically. The procedure was rapid, and theoretical values for 1-heptene, diisobutylene and trimethylethylene were obtained at 0°c or at room temperature.

Johnson and Clark[13] combined some of the modifications to the Francis method and that of Uhrig and Levin[14] into a method that was subsequently designated as a tentative ASTM method[15]. Acetic acid was used as the solvent, which permitted the reaction to take place rapidly in a single phase while retaining the stable bromide–bromate reagent. The results obtained with straight-chain alkenes were near theoretical; however, high results were obtained with some of the branched-chain alkenes.

DuBois and Skoog[16] utilized the potassium bromide–bromate titrant with mercuric chloride as a catalyst[17] and an electrometric end-point detection. The titration was run at a low temperature (0–5°c) so that substitution would be kept to a minimum. One advantage of this method is that no problems are encountered with colored solutions as with a visual method. Data obtained were satisfactory for the straight-chain alkenes investigated; however, high results were obtained with highly branched compounds. The method of DuBois and Skoog was adopted as the basis for the tentative ASTM electrometric method, D-1159.

Unger[18] studied the influence of structure of unsaturated compounds *versus* the bromine number obtained with the ASTM color and electrometric methods, and a modification of the ASTM electrometric method in which the mercuric chloride catalyst was omitted. The data were generally more accurate and reproducible with the modified electrometric method. This is essentially that adopted in 1961 as the standard ASTM method for bromine number of petroleum distillates (D1159–61).

These methods can also be used for the determination of gaseous alkenes. The method of Davis and colleagues[19] involves the transfer of a measured volume of gaseous sample into an evacuated flask which contains standard bromide–bromate solution. Bromine is released by the slow addition of acid into the system and the reaction is allowed to proceed. The results obtained with ethylene, propylene, 1-butene, 2-butene and isobutene were near the theoretical values.

The C_3–C_5 alkenes were determined in the presence of ethylene and paraffins by Stanerson and Levin[20]. The reagent employed was that of Uhrig and Levin[14] and consisted of bromine in glacial acetic acid. The gaseous sample was condensed in a suitable apparatus into chloroform and then titrated with the bromine solution. The absolute error ranged from 0·05–0·8 volume percent unsaturation when this method was used for the analysis of several alkenes in the presence of paraffins.

Miller and Pearman[21] employed a two-bulb arrangement in which ethylene was determined by reaction with bromine in acetic acid. The excess reagent was introduced through a tap into one compartment of the apparatus and subsequently transferred into the portion containing the gaseous sample. The reaction was performed at room temperature with shaking for 20 minutes. The excess reagent was then determined iodometrically. Mixtures investigated contained nitrogen as the major constituent with oxygen, carbon dioxide and ethylene as the minor components. The technique was also used to analyze ethylene in about 90% methane and in the presence of hydrogen, carbon monoxide and nitrogen, with very good precision. The authors claim an accuracy of ±0·02%.

The procedures described generally employ 0·1 N to 0·5 N bromine reagent; however, they can also be adapted to the analysis of micro amounts of unsaturated compounds. Reid and Beddard[22] utilized 0·01 N bromine in glacial acetic acid as the reagent for determining unsaturation as low as 0·0001 bromine number. Benson[23] analyzed micro amounts of *cis*-2-butene in cyclobutane with dilute reagent adapted from the Uhrig and Levin[14] procedure.

Trace amounts of alkenes (bromine numbers from 0·000 to 0·180) were determined by Leisey and Grutsch[24] with coulometrically generated bromine. The bromine was generated at very low concentration so that errors due to substitution were avoided. The excess bromine was detected amperometrically, and the results obtained were within 0·5% of the theoretical values.

Mixtures of alkenes have not been analyzed quantitatively for each component by any of the previously mentioned bromination methods with the exception of the method of Stanerson and Levin[20], in which the C_3, C_4 and C_5 alkenes are determined in the presence of ethylene. Recently, however, Siggia and coworkers[25] have employed differential reaction rate techniques to the analysis of mixtures of unsaturated compounds by bromination. Although alkenes were not specifically investigated, the procedure should be applicable to a two-component mixture of the non-volatile alkenes[26].

A particular bromination method cannot be recommended that would be universally applicable to all alkenes. However, the ASTM D1159-61 electrometric method has been used to analyze a number of straight- and branched-chain alkenes with reasonable accuracy (Table 1) and therefore the essential steps of this method are outlined[27].

Reagent. Potassium bromide–bromate, standard solution (0·500 N). Fifty-one (51·0) g of potassium bromide and 13·92 g of potassium bromate are dissolved in water and diluted to 1 liter. This solution is standardized as follows: 50 ml. of glacial acetic acid and 1 ml. of concentrated hydrochloric acid are placed in a 500 ml. iodine flask. The flask and contents are chilled in an ice bath for about 10 minutes. With constant swirling of the contents of the flask, 5 ± 0·01 ml. of the bromide–bromate solution are added at

TABLE 1. Bromine number data.

Compound	Purity[a] (%)	Bromine number (g/100 g) Theory	Found	Deviation
Straight-chain olefins				
1-Pentene	99·7	228·0	208	−20
trans-2-Pentene	99·91	228·0	235	+ 7
1-Hexene	—[b]	189·9	181	− 9
cis-2-Hexene	99·80	189·9	189	− 1
trans-2-Hexene	99·83	189·9	189	− 1
cis-3-Hexene	99·87	189·9	193	+ 3
trans-3-Hexene	99·94	189·9	191·4	+ 1·5
1-Heptene	99·8	162·8	136	−27
trans-2-Heptene	99·85	162·8	163	0
trans-3-Heptene	99·80	162·8	163	0
1-Octene	99·7	142·4	132	−10
2-Octene	—[b]	142·4	139	− 3
trans-4-Octene	99·84	142·4	149	+ 7
1-Decene	99·89	114·1	111·4	− 2·7
1-Dodecene	99·9	95·1	82·9	−12·2
1-Tridecene	99·8	87·7	81·4	− 6·3
1-Tetradecene	99·7	81·4	70·8	−10·6
1-Pentadecene	99·8	76·0	62·9	−13·1
1-Hexadecene	99·84	71·2	62·8	− 8·4
Branched-chain olefins				
2-Methyl-1-butene	99·90	228·0	231·8	+ 3·8
2-Methyl-2-butene	99·94	228·0	235	+ 7
2,3-Dimethyl-1-butene	99·86	189·9	194	+ 4
3,3-Dimethyl-1-butene	99·91	189·9	167	−23
2-Ethyl-1-butene	99·90	189·9	198	+ 8
2,3-Dimethyl-2-butene	99·90	189·9	191	+ 1
2-Methyl-1-pentene	99·92	189·9	182	− 8
3-Methyl-1-pentene	99·70	189·9	152	−38
4-Methyl-1-pentene	99·82	189·9	176	−14

(*Table continued*)

TABLE 1. Bromine number data (*continued*).

Compound	Purity[a] (%)	Bromine number (g/100 g)		
		Theory	Found	Deviation
2-Methyl-2-pentene	99·91	189·9	190	0
3-Methyl-*cis*-2-pentene	99·85	189·9	193·7	+ 3·8
3-Methyl-*trans*-2-pentene	99·86	189·9	191	+ 1
4-Methyl-*cis*-2-pentene	99·92	189·9	190	0
4-Methyl-*trans*-2-pentene	99·75	189·9	190	0
2,3,3-Trimethyl-1-butene	99·94	162·8	161	− 2
3-Methyl-2-ethyl-1-butene	99·8	162·8	165·4	+ 2·6
2,3-Dimethyl-1-pentene	99·80	162·8	158·5	− 4·3
2,4-Dimethyl-1-pentene	99·87	162·8	152·8	− 10·0
2,3-Dimethyl-2-pentene	99·6	162·8	162·3	− 0·5
4,4-Dimethyl-*cis*-2-pentene	99·79	162·8	159	− 4
4,4-Dimethyl-*trans*-2-pentene	99·91	162·8	158	− 5
3-Ethyl-1-pentene	99·85	162·8	173·1	+ 10·3
3-Ethyl-2-pentene	99·80	162·8	165	+ 2
2-Methyl-1-hexene	99·88	162·8	161	− 2
5-Methyl-1-hexene	99·80	162·8	154	− 9
3-Methyl-*cis*-2-hexene	99·8	162·8	163·6	+ 0·8
2-Methyl-*trans*-3-hexene	99·9	162·8	163·4	+ 0·6
2-Methyl-3-ethyl-1-pentene	99·81	142·4	139·8	− 2·6
2,4,4-Trimethyl-1-pentene	99·91	142·4	137·0	− 5·4
2,4,4-Trimethyl-2-pentene	99·92	142·4	141·2	− 1·2
Diisobutene	—[c]	142·4	139·8[c]	− 2·6
2-Ethyl-1-hexene	—[d]	142·4	140·2	− 2·2
2,3-Dimethyl-2-hexene	99·71	142·4	143	+ 1
2,5-Dimethyl-2-hexene	99·8	142·4	142·8	+ 0·4
2,2-Dimethyl-*trans*-3-hexene	99·80	142·4	139	− 3
Triisobutene	99·0[e]	95	57·5	− 37·5

[a] API Standard Samples, unless otherwise noted.

[b] Purity not stated.

[c] Average value obtained in September 1957 Cooperative Program on purified Eastman product.

[d] Dow Research Chemical.

[e] Synthesized (352°F boiling point fraction). Purity determined by gas chromatography impurities identified as diisobutenes.

the rate of 1 to 2 drops per second. The flask is then stoppered, contents swirled and placed in the ice bath and 5 ml. of potassium iodide (15% aqueous solution) are added to the lip of the flask and allowed to flow slowly into the flask. The contents of the flask are swirled vigorously, 100 ml. of water are added and the solution titrated to the starch end point with standard 0·1 N sodium thiosulfate.

Titration solvent. One liter of titration solvent is prepared by mixing 714 ml. of glacial acetic acid, 134 ml. of carbon tetrachloride, 134 ml. of methanol and 18 ml. of 6 N sulfuric acid.

Apparatus. Dead-Stop Electrometric Titration Apparatus. The method is based on the use of the electric-eye titrimeter described in D1159-61. Any other sensitive dead-stop apparatus may be used with approximately 0·5 v across the two platinum electrodes.

Procedure. The sample is weighed into a 50 ml. volumetric flask containing about 10 ml. of carbon tetrachloride and diluted to the mark. The amount of sample taken is dependent upon the bromine number (Table 2). A 5 ml. aliquot is then pipetted into the cooled (0–5°c) titration vessel containing 110 ± 10 ml. of the stirred titration solvent. The 'eye' of the electrometric titrator is adjusted to a very nearly closed position. The standard bromide–bromate solution is then added in small increments from a buret. The end point is indicated when two drops of reagent cause the 'eye' to remain open for at least 30 seconds. A blank is run on the solvents and is usually less than 0·1 ml. The bromine number is then calculated from equation (2), where A = milliliters of bromide–bromate solution for the sample; B = milliliters of bromide–bromate solution for the blank; N = normality of the bromide–bromate solution; and W = grams of sample represented by the aliquot used.

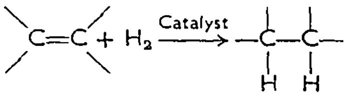
TABLE 2. Correlation of bromine number with sample size.

Bromine number	Sample size (g)
0 to 10	20 to 16
10 to 20	10 to 8
20 to 50	5 to 4
50 to 100	2 to 1·5
over 100	1 to 0·5

$$\text{Bromine number (g/100 g)} = \frac{(A - B)N \times 7{\cdot}99}{W} \qquad (2)$$

2. Hydrogenation

Hydrogenation as a means of determining unsaturation of the alkenes has distinct advantages over halogenation. Problems concerned with substitution, oxidation, *etc.*, are not encountered. The usual procedure for determining the double bond by hydrogenation involves reacting the unsaturated compound with excess hydrogen in a suitable solvent (if necessary) in the presence of a catalyst (equation 3). The amount of reacted hydrogen is determined manometrically or volumetrically by difference and is a measure of the unsaturation. The majority of the analytical hydrogenation procedures are usually run at atmospheric pressure, either in semimicro quantities of sample (5 to 50 ml. hydrogen reacted) or in micro quantities (1 to 5 ml. of hydrogen reacted).



(3)

Solvents that have been employed in analytical hydrogenations are acetic acid, ethers, alcohols, esters, saturated cyclic hydrocarbons and chloroform. Glacial acetic acid is the most common solvent, since the rate of hydrogenation[28] is more rapid in solvents which are capable of providing protons than in solvents which are proton acceptors, such as the ethers. The solvent chosen should be free from compounds which tend to inhibit catalyst activity. Sulfur compounds are generally 'poisons' for catalyst, whereas organic nitrogen and chlorine compounds specifically decrease the activity of Raney nickel catalyst[1]. A solvent is not absolutely necessary if the amount of sample for hydrogenation is sufficiently large and is a material of low viscosity such that good agitation can be achieved during the experiment.

Platinum, platinum oxide, palladium and nickel are generally used as catalysts, in a finely divided form as such, or on carriers of activated carbon or silica. The amount of catalyst used has an influence on the rate of reaction.

Electrolytic hydrogen delivered from a compressed gas cylinder or that from a Kipp generator is generally acceptable without purification. If necessary, the hydrogen can be purified by passing the gas through scrubbers of aqueous sodium plumbite, potassium permanganate, and concentrated sulfuric acid and finally through a drying tube. Alternatively, the gas can be purified by passage over a heated copper wire or platinum (or palladium) on asbestos[1].

The apparatuses that have been used for hydrogenation were based on (*i*) the measurement of a decrease in pressure at constant volume and (*ii*) volumetric measurement of the reacted hydrogen at constant pressure. The apparatuses based on the manometric procedures were modified from the original Warburg[29] manometers. The devices designed by Hyde and Scherp[30] and Kuhn and Möller[31] utilized this procedure to obtain accuracies of ±2 and ±0·5%, respectively. One of the first micro hydrogenation apparatuses which utilized the volumetric measurement was that by Smith[32].

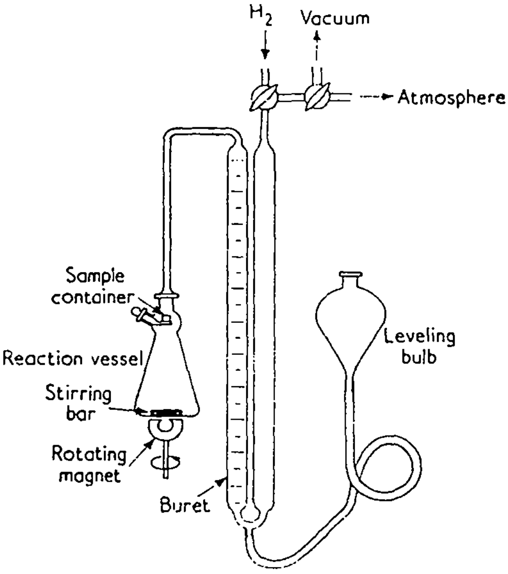


FIGURE 1. A simplified hydrogenation apparatus[1].

The volumetric techniques usually employ a gas buret for measuring the hydrogen consumed (by difference); however, the semimicro hydrogenation apparatus described by Miller and De Ford[33] is a modification of Manegold and Peters' method[34] in which electrically generated hydrogen replaces the conventional gas buret. The hydrogen uptake is then determined by the number of counts recorded on the coulometer.

Most apparatuses currently used for analytical hydrogenations employ the volumetric measurement and are usually of the simplified type as presented in Figure 1, although differing as to ease of operation, method of agitation, sample introduction, modifications for handling volatile samples, *etc.*[35-38]. The precision that can be expected with this type of apparatus is approximately 1–2%.

The procedure used for determining the amount of unsaturation in a compound with the equipment as illustrated in Figure 1 is as follows[1]:

The catalyst and solvent are introduced into the reaction vessel. A suitable portion of sample is weighed into the sample container, which is then placed in position isolated from the catalyst and solvent. Volatile samples should be sealed in a thin-walled tube, and provision made for breaking the container when desired. With the leveling liquid (usually mercury) lowered below the junction of the buret and leveling tube, the apparatus is filled with hydrogen by successively evacuating and admitting hydrogen five or six times. (In apparatus designed to permit direct flow-through of hydrogen, the apparatus is flushed with a stream of hydrogen for several minutes.) Before admission to the apparatus, the hydrogen should be bubbled through a scrubber containing the same solvent as used in the reaction flask in order to reduce the time necessary to saturate the atmosphere in the apparatus.

With the buret full of hydrogen, a small amount is carefully bled off to the vacuum such that, when the leveling liquid is raised, the pressure in the reactor side of the apparatus will be equal to atmospheric pressure. (In apparatus designed for direct hydrogen flow-through, the pressure can be equalized after raising the leveling liquid by briefly opening the outlet in the arm of the reaction vessel.) Subsequent readings are made with the leveling leg of the buret open to the atmosphere.

The solvent and catalyst are stirred until saturated, as indicated by no further decrease in hydrogen volume. The stirrer is stopped, and the system is allowed to come to thermal equilibrium. The buret reading, temperature, and atmospheric pressure are recorded.

The sample is then brought into contact with the solvent and catalyst, and the mixture is stirred until the consumption of hydrogen ceases. Buret reading, temperature, and atmospheric pressure are again recorded after thermal equilibrium is obtained. The hydrogenation value is then calculated from the volume of hydrogen consumed, corrected for the vapor pressure of the solvent at the temperature employed, and converted to standard temperature and pressure.

Analytical hydrogenation of the alkenes has not been employed as extensively as the halogenation reactions. This is probably due to the length of time required to run a single analysis and also the fact that many samples cannot be analyzed simultaneously without employing an apparatus for each sample.

A macro hydrogenation apparatus described by Waterman and coworkers[39] was used for the hydrogenation of alkenes such as 1-pentene through to octene, decene and hexadecene[40]. The results obtained were in good agreement with values obtained by bromination.

McMillan and colleagues[41] used a hydrogenation procedure to analyze gaseous olefins. A known volume of gaseous sample was mixed with a measured volume of hydrogen, and the subsequent mixture was then passed over a catalyst. The hydrogen thus consumed is a direct measure of the amount of olefin present. Synthetic mixtures of alkenes with paraffins were tested. The accuracy obtained at the 10 and 50% level for propylene in propane was usually ±0·1% absolute.

Robey and Morrell[42] employed an apparatus similar to that used by McMillan, and corrected for deviation of the gases from ideal gas behavior. With isobutene the results obtained were 100·2 and 99·8%. Shively and coworkers[43] modified the McMillan apparatus by providing a boiling water jacket over the catalyst in order to prevent adsorption of the gases being investigated. Complex C_5 fractions containing the pentenes were analyzed using this modification.

Corner and Pease[44] selectively hydrogenated propylene in a cyclopropane mixture over a nickel–kieselguhr catalyst partially poisoned with mercury. Hydrogenation over a non-poisoned catalyst allowed the cyclopropane to be hydrogenated.

Shepp and Kutschke[45] also employed a nickel–kieselguhr catalyst for the hydrogenation of ethylene in admixture with ethane. Ethylene, present to about 0·03 c.c. per 1·5 c.c. of sample, was analyzed with an accuracy of about 0·5%.

Mixtures of alkenes have not been analyzed for individual components by hydrogenation; however, the method of Siggia and coworkers[25], in which the differential reaction rate technique was employed to analyze two-component systems of unsaturated compounds by hydrogenation, should be applicable to a two-component mixture of alkenes[26]. Mixtures of an alkene and an aromatic compound can be resolved by selective hydrogenation, employing palladium on carbon[40].

The hydrogenation method can be adapted to the analysis of small amounts of alkenes (less than 1%) by modification for the introduction of larger samples.

3. Miscellaneous chemical methods

Chemical methods utilizing oxidizing reagents have been used for the quantitative determination of unsaturation. Perbenzoic acid has been employed for determining the double bond in rubber polymers[46], straight-chain, branched and cyclic olefins[47], and in dearomatized cracked petroleum products[48]. Boer and Kooyman[49] employed the reagent in a comparison study in which alkenes were investigated, and generally the accuracy obtained using perbenzoic acid was only fair.

Oxidation of impurities present in the sample, long and varied reaction times and the instability of the reagent, are disadvantages of the reagent for analytical use.

Ozone reacts readily with ethylenic bonds to form ozonides. This reaction has been used in qualitative studies for determining the location of the ethylenic bond. Early quantitative analytical methods were based on the analysis of the decomposition products formed by hydrolysis under conditions of oxidation or reduction.

Boer and Kooyman[49] introduced the use of ozone as a titrimetric reagent. The procedure involves a constant flow of ozone into a reaction vessel containing the ethylenic compound and a dye which serves as an indicator for excess ozone. Alternatively, the exit gas from the reaction vessel can be monitored for ozone and, by means of a plot of ozone equivalents *versus* time, the end-point can be determined. Since the flow of ozone produced by the generator employed by Boer and Kooyman[49] is constant, then the time from the beginning of ozone absorption to the end-point is a direct measure of the ethylenic compound, assuming, of course, that the reaction has gone to completion. A number of straight- and branched-chain alkenes were determined in chloroform at -40°c. No major discrepancies between the theoretical values and the experimental results were obtained.

Mercuric salts of organic acids, such as mercuric acetate, form addition compounds with certain olefinic materials and have been used in the quantitative analysis of these compounds[50-53]. The methods employing mercuric acetate are most applicable to the determination of compounds containing a terminal double bond or an internal double bond with *cis* configuration[54,55]. Johnson and Fletcher[53] employed this reagent for the assay of 4-methyl-1-pentene.

Other reagents used include nitrogen tetroxide, nitrogen trioxide, nitrosyl chloride, tetranitromethane and sulfuric acid. Sulfuric acid has been used *per se* or with solutions of metal salts such as silver and mercury[56,57] for selectively absorbing or extracting both gaseous and liquid alkenes. These reagents will only be mentioned here, since the majority of them have not found wide use or are currently being replaced by other methods. A very good discussion concerning these reagents can be found in *Organic Analysis*, Volume III, by Polgár and Jungnickel[1].

B. Qualitative Analysis

As indicated by Hendrickson and Hatch[58], it seems somewhat archaic to discuss qualitative detection of the alkenes by chemical methods in view of the present-day instrumentation, which can be used to positively identify an unknown compound without great difficulty. Nevertheless, a short discussion on chemical methods which can be used in the identification of an alkene does not seem entirely out of order.

The olefinic double bond can be qualitatively identified by a number of chemical reactions. The two most commonly used chemical tests employ a solution of bromine or of alkaline potassium permanganate. A positive test is indicated if the solutions are discolored when added to a compound containing the double bond. These reagents are not specific in that compounds which are easily oxidized or brominated, such as certain aldehydes and phenols, alkynes, *etc.*, respectively, will also give a positive test.

Sharefkin and Sulzberg[59] proposed a method for detecting the olefinic bond by forming the 2,4-dinitrophenylhydrazone derivatives of the methyl ketone formed in a Friedel–Crafts acetylation of the olefin. The hydrazone can then be used to characterize a given olefinic compound. A number of the gaseous and liquid alkenes were tested by this procedure, and the expected hydrazones were formed.

Peroxyacetic acid has been employed by Sharefkin and Shwerz[60] for the identification of a number of alkenes. The presence of the double bond is indicated by reaction with peroxyacetic acid to form an epoxide which is subsequently converted into a glycol monoacetate. The ester is then reacted with hydroxylamine in an alkaline methanol solution. The solution is acidified, and a positive test for the double bond is indicated when a wine-red or purple color is produced by addition of ferric ion to form ferric hydroxamate.

Characterization of a particular alkene was made by Sharefkin and Shwerz[60] by isomerization of the epoxide to a carbonyl compound with boron trifluoride etherate. The 2,4-dinitrophenylhydrazone derivative of the carbonyl was then prepared and the melting point determined as a means of identification.

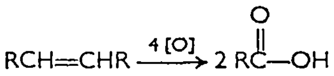
Several investigators have prepared solid derivatives of the alkenes which can be used for qualitative purposes. Kharasch and Buess[61] prepared solid derivatives of the gaseous and several liquid alkenes by reaction with 2,4-dinitrobenzenesulfenyl chloride. The melting points of the alkenes investigated were sufficiently different to permit use of these derivatives for identification.

Halperin and coworkers[62] treated alkenes with the silver salt of 3,5-dinitrobenzoic acid in the presence of iodine to form β-iodoalkyl-3,5-dinitrobenzoates. Solid derivatives were obtained for several of the alkenes from ethylene through to 1-heptene. The melting points of the derivatives, with few exceptions, were sufficiently different to permit the use of these solids in the identification of the common low molecular weight alkenes.

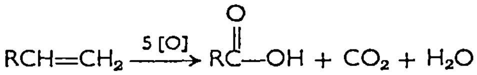
Hendrickson and Hatch[58] prepared solid *S*-alkylmercaptosuccinic acid derivatives of olefins which could be used to characterize these materials. Several straight- and branched-chain alkenes reacted, and acceptable derivatives were formed. The primary alkenes reacted to give good yields of pure derivative; however, the 2-alkenes gave mixtures of two products which melted over a range of 5–10° between the melting points of the 2-alkyl- and 3-alkylmercaptosuccinic acids. Several of the branched alkenes, such as 2,6-dimethyl-2-heptene and 2,4,4-trimethyl-2-pentene, did not form the derivative; 2-methyl-2-pentene and 3-ethyl-2-pentene, however, gave satisfactory yields. These derivatives are acids and thus can be titrated to obtain a neutralization equivalent which is additional evidence for confirmation of a particular alkene.

Ozone[63,64] adds to the double bond of an alkene to form an ozonide, which can be decomposed to produce ketones and aldehydes or ketones or acids, depending upon the reaction conditions. The products formed by decomposition can usually be identified chemically, such as derivatives of 2,4-dinitrophenylhydrazine[65,66], and thus related back to the unknown alkene. For example, a good indication of the presence of an alkene containing a terminal double bond can be obtained from the ozone reaction by hydrolyzing the ozonide under reducing conditions and subsequently confirming the presence of formaldehyde with a nearly specific reagent such as chromotropic acid (1,8-dihydroxynaphthalene-3,6-disulfonic acid)[67]. Knights and Waight[68] found that compounds of the type $R^1R^2C{=}CHCH_2OH$ (*e.g.* 3-methyl-2-buten-1-ol) and $RCH{=}CHCH_2OH$ (*e.g.* 2-butene-1-ol) also produce formaldehyde. However, it is generally expected that alkenes react normally with ozone and that this reaction should be a reliable means of locating the double bond in an alkene.

Exhaustive oxidation with either acidic permanganate or dichromate results in fission of the unsaturated compound between the unsaturated centers (equations 4 and 5), thus providing a method for locating these centers and hence possible identification of the unsaturated compound.

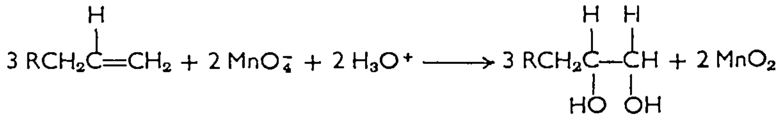


$$\mathrm{RCH{=}CHR \xrightarrow{4\,[O]} 2\,R\overset{\overset{O}{\|}}{C}{-}OH} \tag{4}$$

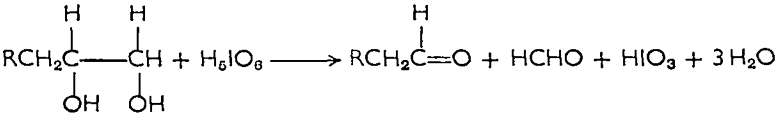


$$\mathrm{RCH{=}CH_2 \xrightarrow{5\,[O]} R\overset{\overset{O}{\|}}{C}{-}OH + CO_2 + H_2O} \tag{5}$$

Potassium permanganate can also be used in the qualitative identification of the alkenes *via* controlled oxidation to a glycol (equation 6) and subsequent cleavage of the glycol with periodic acid (equation 7).



$$\mathrm{3\,RCH_2\overset{H}{\overset{|}{C}}{=}CH_2 + 2\,MnO_4^- + 2\,H_3O^+ \longrightarrow 3\,RCH_2\underset{\underset{HO}{|}}{\overset{\overset{H}{|}}{C}}{-}\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}H + 2\,MnO_2} \tag{6}$$



$$\mathrm{RCH_2\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}{-}\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}H + H_5IO_6 \longrightarrow RCH_2\overset{\overset{H}{|}}{C}{=}O + HCHO + HIO_3 + 3\,H_2O} \tag{7}$$

Bricker and Roberts[69] utilized the above approach for determining end unsaturation in organic compounds. Periodic acid, *per se*, was employed by Chatterjee and Majumdar[70] for detecting ethylenic unsaturation.

III. PHYSICAL METHODS

A. Chromatography

Chromatography of various forms has extremely wide application in the field of analysis. Although there are many ways of employing the principles of chromatography, all of these techniques can be reduced to the following: (*i*) gas–liquid; (*ii*) gas–solid; (*iii*) liquid–liquid; (*iv*) liquid–solid; (*v*) solid–liquid, and (*vi*) solid–solid. Some of these techniques have been used in the analysis of the alkenes[71–79]; however, gas–liquid and gas–solid chromatography are presently being used more extensively and, therefore, the discussion will be concerned primarily with gas chromatography.

The extension of chromatography to include systems in which the mobile phase is a gas was first suggested by Martin and Synge in 1941[80]. Gas chromatography (GC) is subdivided according to the nature of the stationary phase; when this is a solid, the technique is referred to as gas–solid chromatography (GSC) and when a liquid, it is called gas–liquid chromatography (GLC).

Gas–solid chromatography is an absorption method in which the sample is adsorbed by the active material in the column. The separation of components or analysis can then be effected by one of several ways, *viz.*, elution, frontal analysis and displacement analysis. In the elution method, the band of each component is moved through the column by the carrier gas at a rate specific for that component under the conditions used. The resulting chromatogram is a series of peaks, usually having a sharp front and a trailing rear boundary. In frontal analysis, the sample is continuously carried at a constant concentration by the carrier gas into the column. The chromatogram obtained is a series of steps, each of which corresponds to an additional component as it emerges from the column. That is, with the exception of the first step, all subsequent steps contain additional components until the last component emerges in a mixture corresponding to the original sample composition. In most cases, frontal analysis can give information only about the number of components that have been separated in the column, but it is of little value as a separation procedure. In analysis by displacement, the carrier gas is saturated with the vapor of a strongly adsorbed material called the displacer. The displacer moves the components of the adsorbed sample along the column and the components in turn displace one another, depending upon their affinity for the column. The net result is a series of bands, corresponding to the number of components in the sample which move toward the outlet of the column at the same rate that the displacer is saturating the column. The chromatogram obtained is a series of steps which can be related to the amount of each component present in the mixture.

Gas–solid chromatography techniques are utilized predominantly in the analysis of low-boiling components such as CO, H_2, O_2, CH_4 and the rare gases. The disadvantages or unfavorable features of GSC include the tailing of peaks in elution analysis, variable activity and catalytic effect of the adsorbents, irreversible adsorption and excessive retention of polar materials[81].

Gas–liquid chromatography is a method in which a component is partitioned between a stationary liquid phase and a moving gas phase. This technique is currently more popular than GSC, since it is more versatile, highly reproducible and less subject to the difficulties encountered with GSC. Added advantages of this method are the large number of liquid phases which can be employed to perform necessary separations, unlike the limited range of available solid adsorbents for GSC.

Owing to the nature of the partitioning process, GLC nearly always employs the elution procedure. This subdivision of gas chromatography is used extensively in the analysis of the alkenes.

The apparatus used in gas chromatography consists of four basic components: (*a*) a carrier gas supply and control; (*b*) a sample inlet; (*c*) a column; and (*d*) a detector. A schematic diagram is presented in Figure 2. The carrier gas, as the term implies, carries the sample through the instrument and is usually supplied from a compressed source through a pressure-reducing valve, which controls the input pressure on the apparatus. The choice of a particular gas to be used as the carrier gas depends to a great extent upon the detector used and the resolution desired. Helium and hydrogen are usually used with GC instruments employing a thermal conductivity cell as a detector. This detector measures a difference in the thermal conductivity between pure carrier gas and carrier gas plus the sample components; therefore, hydrogen and

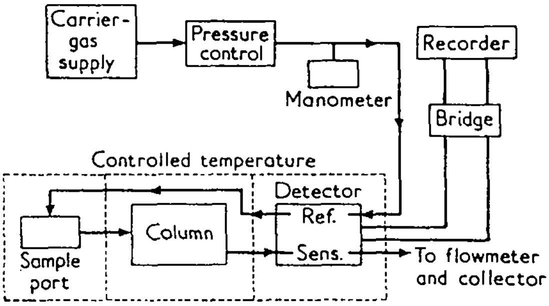


FIGURE 2. The essential components of a gas chromatogram[81].

helium are good choices because of their high thermal conductivity[82]. Although hydrogen has the greater thermal conductivity, helium is generally preferred owing to the explosive nature of hydrogen. Nitrogen, argon, carbon dioxide and air have also been used with the thermal conductivity cell, but give a lower sensitivity than that of hydrogen or helium. Argon is used as the gas in instruments employing the ionization detector; nitrogen is used with the flame and gas density balance detectors.

The flow rate of the carrier gas can be controlled adequately by means of a diaphragm-type, two-stage reducing valve connected in series with a precision needle valve. The flow rate must be kept constant during the sample runs if reproducible results are to be obtained.

The sample inlet or port is usually constructed of either metal or glass which can be heated to the desired temperature. Sample port designs are available[81] in which the sample is vaporized directly into the carrier gas stream and then through the column or into a separate chamber while the carrier gas flows through a by-pass to the column. A valve is then manipulated so that the carrier gas sweeps the sample from the chamber into the column. Stream splitters[83] are employed in ports in order to deliver small samples (1–10 μg) to capillary columns. Both liquid and gaseous samples are usually introduced to the column through a self-sealing septum in the port by means of a hypodermic syringe. The septums are usually constructed of rubber, neoprene or silicone, depending upon the temperature at which the port is operated.

The column is that part of the GC apparatus in which the sample is resolved into the individual components. Analytical columns are ordinarly prepared with 2–6 mm i.d. glass tubing or $\frac{1}{8}$–$\frac{3}{8}$ in. o.d. metal tubing of varying length. Capillary columns, which were first reported by Golay[84], are being employed in the separation of complex hydrocarbon mixtures[85,86].

The liquid phase is applied as a thin coating to a solid support such as Celite or firebrick in the case of conventional columns, whereas in capillary columns the liquid phase is applied as a film on the walls of the column. The particular liquid phase selected will depend upon the type samples which are to be resolved. Factors such as stability, low vapor pressure and viscosity at the temperature of operation, thickness of the liquid phase on the support, nonreactivity of the liquid phase with the components of the sample, must all be taken into consideration in selecting the liquid phase. Some experimentation is needed to find the best liquid phase for a particular sample system; however, the amount of experimentation can be greatly reduced by studying factors such as polarity, hydrogen bonding and chemical interaction of the sample system under investigation. The liquid phases which have found application in the analysis of the alkenes will be discussed under the qualitative and quantitative sections.

The column is maintained at a constant temperature as in isothermal chromatography (Figure 2), whereas, in programmed-temperature chromatography, the temperature of the entire column is varied with time in a linear or non-linear manner[87-90].

The columns are usually operated singly, although GC units can be modified to handle two columns. The dual column approach is useful in quantitative analysis, where two different columns are more readily adapted to obtain the necessary resolution and thus determination of all the components present.

The detector is that portion of the instrument which detects and measures the small amount of the components present in the carrier gas stream leaving the chromatographic column. The output signal from the detector is amplified and relayed to a strip-chart recorder. The resulting chromatogram which is recorded depends upon the detector used. When an integral detector is employed, the resulting chromatogram is a series of step heights which are a direct measure of the amount of material present. Examples of this type of detector are the nitrometer used by Janák[91] and the recording titration buret of James and Martin[92]. These types of detectors are generally very precise and accurate; however, they lack sensitivity and versatility.

The differential chromatogram is represented ideally by a straight base line with a series of peaks corresponding to the number and amount of components present. The most widely used differential detector is the sensitive and versatile thermal conductivity cell. This contains a heated metal filament or a thermistor as a resistance element for sensing changes in thermal conductivity. The detecting element and matching reference element are opposed in a suitable electrical bridge to obtain the differential signal.

Various other types of detectors are available, some of which are the hydrogen flame detector[93]; the gas density balance[94]; the time-of-flight mass spectrometer[95]; flame ionization[96,97]; β-ray ionization[98,99]; glow discharge[100]; thermionic emission[101] and radio-frequency discharge[102]. The last five detectors, owing to their high sensitivity, can be utilized with Golay capillary columns.

A differential and integral chromatogram for a single component or solute are illustrated in Figure 3.

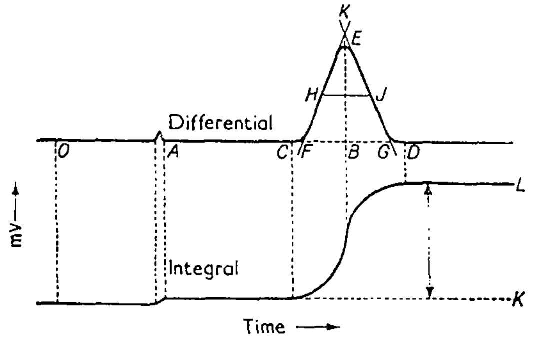


FIGURE 3. The chromatogram of a single solute. Differential and integral plots of detector response (mv) *versus* time[107]. (Reproduced, by permission, from *Chromatography* (Ed. E. Heftman), Reinhold Publishing Corp., New York, 1961, p. 165.)

In the illustrated chromatograms, the line *OAFG* is the base line and is the portion of the chromatogram which is produced when only the carrier gas emerges from the column. A peak is the portion of the differential chromatogram that records the detector response while the component emerges. The area enclosed within the peak and peak base *CD* is the peak area and *BE* is the peak height. The peak width is represented by the segment of peak base *FG*, while *HJ* is the peak width at half-height. The time corresponding with the distance *OB* is the elution or retention time of the component. The small step and peak *A* is often produced by the presence of small amounts of air in the sample and is referred to as the air peak. The distance from *L* to *K* in the integral plot is a quantitative measure of the component.

The references tabulated in Table 3 can be consulted for more extensive information concerning theory, detector types, programmed-temperature columns (capillary and conventional), application and instrumention of gas chromatography.

I. Quantitative analysis

Gas chromatography is readily adaptable to the quantitative analysis of the alkenes. Quantitative methods depend upon the detector system used and the nature of response to the components passing through in the carrier gas[123]. Two general types of detectors are available, *viz.* integral and differential.

TABLE 3[a]. Books, summaries and reviews.

	Language	Reference
Books		
Am. Chem. Soc. Symposium, 1957	English	103
Amsterdam Symposium, 1958	English	104
Bayer	German	105
Dal Nogare and Juvet	English	81
Edinburgh Symposium, 1960	English	106
Heftmann (editor)	English	107
Johns (editor)	English	108
Kaiser	German	109
Keulemans	English	110
London Symposium, 1956	English	111
Michigan State Symposium, 1957	English	112
Michigan State Symposium, 1959	English	113
Michigan State Symposium, 1961	English	114
New York Academy of Science Symposium, 1958	English	115
Pecsok (editor)	English	116
Phillips	English	117
Schay	German	118
Summaries and reviews		
Beerthuis	Dutch	119
Bennett *et al.*	English	120
Chovin	French	121
Dal Nogare and Safranski	English	122
Hardy and Pollard	English	123
Horn *et al.*	German	124
James	English	125
James and Martin	English	92
Janák	German	126
Keulemans and Rijnders	German	127
Knox	English	128
Leithe	German	129
Lotz and Willingham	English	130
Munch	English	131
Phillips	English	132
Ray	English	133
Röck	German	134

[a] From S. Dal Nogare and R. S. Juvet, Jr., *Gas–Liquid Chromatography* (ref. 81), p. 18 in part.

The step height recorded in the chromatogram obtained with an integral detector is a direct measure of the substance separated on the column in terms of volume or pressure of a gas, microequivalents of acid or base, *etc.*, and therefore no calibration is necessary. These detectors are highly accurate (±0·1% for the Janák type[123]); however, the sensitivity is limited in that difficulties are encountered in the measurement of very small volumes of gases, titers, *etc.*

The series of peaks obtained with a differential detector can be related to the quantity of compound by peak height or the area under the peak. These types of detectors are as a rule more versatile and sensitive than the integral type; however, they are usually not as accurate and often require calibration. The area under the peak can be measured by various means such as a planimeter, cutting out and weighing of the chart, by mechanical or electrical integrators[135], which can be attached directly to the recorder, and by multiplying peak height by the width at half-height[136].

The various methods which can be used for quantitative analysis by either peak height or peak area will depend to a large extent upon the sample to be analyzed. For instance, gaseous samples under pressure are most conveniently analyzed by peak-height measurements, using calibration curves prepared on a peak height *versus* millimeter pressure basis; whereas samples which require wide variations in instrument operating conditions for complete analysis are best handled by the peak-area method[108].

Quantitative analyses of hydrocarbons have been made with fair accuracy by the area-normalization method[137,138] if the carrier gas is either helium or hydrogen and the detector a thermal conductivity cell. In this method, the amount of each component (i) is determined from the ratio of the area under the respective peak (A_i) to the total area under all the peaks (equation 8). This approach is

$$\%i = [A_i/\Sigma(A_1 + A_2 + \cdots A_n)] \times 100 \tag{8}$$

based on the assumption that the thermal conductivities of all components in the sample are equal. However, this is rarely the case; therefore, in order to obtain fairly accurate data, the carrier gas used must have a thermal conductivity much greater than that of the components under investigation. Hydrogen or helium are the best choice, since the thermal conductivities of these gases are about ten times greater than most hydrocarbons.[82]

More accurate data may be obtained by the application of area-correction factors[139,140], which compensate for the differences in detector response for the compounds under study. Equation (8) then becomes equation (9), where f_i is the area factor (mg/cm^2)

$$\%i = [f_iA_i/\Sigma(f_1A_1 + f_2A_2 + \cdots f_nA_n)] \times 100 \tag{9}$$

and A_i is the measured peak area (cm^2) for component i.

The factors for each component are determined by chromatographing known quantities of the pure constituents. A known compound can be added as an internal standard[141] and then the factors for each component normalized to $f = 1{\cdot}00$ for the standard. The percentage of any individual component can then be calculated from equation (10), where R is the percent internal standard added

$$\%i = f_iA_iR/A_s \tag{10}$$

to the sample and A_s is the area of the internal standard peak[81].

Quantitative data by peak height and peak area can be obtained by direct comparison with calibration curves prepared from pure standards; however, precise control must be maintained on all detector and column variables[142,143]. Minor fluctuations of some of the above variables are difficult to control and therefore, for more accurate data, an internal standard must be employed in the calibration method. In this approach, a standard compound of known concentration is added to synthetic samples containing varying known amounts of the component which is to be studied. These synthetic mixtures are then chromatographed and a plot of percent component in the synthetic samples *versus* the ratio of the component/standard peak areas or heights is then made[144]. The standard is then added to the sample, the sample chromatographed, and a comparison of the component/standard peak height or area made. The component concentration is then determined from the calibration curve. Harvey and Chalkley[144] were able to obtain an accuracy of ±3% over the whole range from 0–100% component in the sample using this calibration method.

Quantitative gas chromatographic methods reported in the literature for the analysis of hydrocarbon gases and liquids containing alkenes are numerous.

Martin[145] described a procedure in which the C_3–C_6 olefinic naphthas are chromatographed and subsequently passed through a short absorber containing silica gel coated with sulfuric acid. The unsaturated hydrocarbons are retained and the saturated materials pass through to the detector. Another run is made without the absorber and the unsaturated compounds appearing in the same peak with the saturated materials are determined by difference. Synthetic blends in which several alkenes were present were analyzed by this approach, and the difference between the amount of constituents present and found averaged 1·3%.

Nelson and colleagues[146] have analyzed the C_6, C_7 and C_8 olefins according to their carbon structure. In this procedure, a hydrogenated and a non-hydrogenated portion of the sample are extracted with acid. The raffinates are then chromatographed and, from the two chromatograms, the various olefins having the same carbon structures are calculated. On the basis of synthetic blends, the accuracy of the determination for a group of olefins is of the order of ± 6% of the amount present.

Ray[143] reported the analysis of isobutene in the presence of hydrogen, isobutane and n-butane on a column of dinonyl phthalate.

Van de Craats[147] described various column substrates used in the analysis of the gaseous alkenes. Liquid paraffin is used for determining minor components in ethylene and also for determining high- and low-boiling components in propane and propene. Polar substrates such as dimethylsulfolane and dimethyl formamide were used successfully for the analysis of impurities in propene–propane and butane–butene mixtures.

Cope and coworkers[148] determined by gas chromatography the C_2–C_5 alkenes formed in the thermal decomposition of unsymmetrical amine oxides and structurally related quaternary ammonium hydroxides. Several columns were used to obtain the necessary separations; *viz.*, dimethyl formamide, carbethoxy dimethyl formamide and saturated silver nitrate in diethylene glycol.

Polgár and coworkers[85] have used coated glass capillary columns to analyze mixtures containing alkanes, cyclopentanes, cyclohexanes and the C_2–C_7 alkenes. Fifty-one of the 63 alkenes masterblended could be analyzed quantitatively using silicone oil as the capillary coating. The coated columns which were first introduced by Golay[84] possess great fractionating efficiencies and thus are adaptable to analysis of complex mixtures as above.

Fredericks and Brooks[149] have reported the analysis of gaseous hydrocarbons containing alkenes. These investigators used two columns in order to effect good separation of the olefins and paraffins. The gaseous alkenes investigated were resolved well from the paraffins and from their homologs on a 50 ft. column of dimethylsulfolane. The area-normalization technique was used for the calculations, and the results obtained on a 19-component mixture were indicative of good correlation of peak area and weight percent.

Knight[150] also used the dimethylsulfolane column in the analysis of the C_5 and C_6 olefins. Analysis of a known pentene blend containing five alkenes was indicative of a maximum error of 1·6% and an average error less than 1%. The substrate of 2,2′-oxydipropionitrile was also used in this investigation and proved to be a satisfactory material for the blends.

Gas chromatography is also a valuable tool for the analysis of trace components and has been employed for determining trace constituents in the alkenes. The limit of detection of trace compounds is dependent primarily upon the detector used and the system under investigation[81,151]. For instance, the flame and β-ray detector are sensitive to organic material and therefore are useful in determining traces of organics in water and air. If the sample is such that the minor component cannot be resolved chromatographically from the major component, then techniques of extraction[152,153], adsorption, low-temperature trapping[154,155], and precolumn removal[156,157,158] can be applied. Some of the above techniques have been used in the analyses of the alkenes for trace constituents. Ray[159] reported the determination of non-olefinic impurities (other than carbon dioxide) in ethylene by absorbing the ethylene on charcoal impregnated with bromine. Brenner and Ettre[156] determined acetylene down to 1 p.p.m. in ethylene by maintaining a column of polyethylene glycol at low temperature to retain the acetylene; purging to remove ethylene and subsequent volatilization and chromatography of the acetylene on dimethylsulfolane.

E. Bua and colleagues[160] utilized a silver nitrate–glycol column to determine propadiene down to 5 p.p.m. in propylene. The sensitivity of the method can be extended to less than 1 p.p.m. propadiene by cold-trapping techniques.

The method of Fredericks and Brooks[149] permits a quantitative measure of the gaseous alkenes in the presence of other hydrocarbon gases and likewise the method of Knight[150] is adaptable to a number of the C_5 and C_6 olefins. The instrumentation used in both investigations was conventional, with some modification for sample introduction. The carrier gas used was helium and the detector, a thermal conductivity cell. In their work to obtain the necessary separations, Frederick and Brooks utilized several different columns such as: (*i*) a dual column in which one is 6 ft. of diisodecylphthalate (DIDP) (40 g to 100 g of Celite 545) and the other a 16 ft. column of dimethylsulfolane (DMS) (40 g to 100 g of Celite 545) connected in series, and (*ii*) a 50 ft. column of DMS (40 g to 100 g of Johns–Manville C-22 firebrick). The columns were constructed of $\frac{3}{8}$ in. copper tubing, and the temperature was usually maintained either at 35 or 0°c. The gas flow rate for the DMS column was controlled at 100 ml./minute, whereas the other columns were run with a 45 ml./minute flow rate. The data obtained on several standard mixtures with these columns are tabulated (Table 4) and are in good agreement with the 'prepared' values. The calculations were done by peak area without the use of correction factors.

TABLE 4. Comparison of area distribution with known weight percent values[149].

	Phillips mixture 37			Phillips mixture 40		
Hydrocarbon	Phillips values	Analysis on DIDP–DMS column (35°c)	Analysis on DMS column (0°c)	Phillips values	Analysis on DIDP–DMS column (35°c)	Analysis on DMS column (0°c)
Ethane	—	—	—	2·4	2·4	2·2
Propane	—	—	—	13·7	13·0	13·4
Propylene	—	—	—	13·8	14·2	14·6
Isobutane	3·1	2·9	2·8	21·2	20·3	20·1
n-Butane	14·6	14·7	14·9	9·2	9·6	9·9
1-Butene	16·9	—	16·9	9·6	—	10·0
Isobutylene	7·0	—	7·0	15·3	—	15·3
trans-2-Butene	22·2	22·1	22·0	—	6·2	6·0
cis-2-Butene	19·0	19·7	19·6	—	6·5	6·4
1,3-Butadiene	17·3	17·2	16·6	—	—	—
Isopentane	—	—	—	1·4	1·6	0·8
1-Pentene	—	—	—	0·7	0·7	0·6
trans-2-Pentene	—	—	—	—	0·4	0·4
cis-2-Pentene	—	—	—	—	0·2	0·3

Knight utilized 50 ft. columns of 20% DMS and 40% 2,2′-oxydipropionitrile on C-22 firebrick in $\frac{1}{4}$ in. o.d. copper tubing; a helium flow rate of 30 ml./min and a column temperature of 25°c in the analysis of the hexenes and pentenes. The calculations were based on peak area measurements, and an analysis of a synthetic hexene blend on the two columns is tabulated in Tables 5 and 6. The compounds in brackets were not separated on the column used.

The published work of Polgár and coworkers[85], in which a coated capillary column was used in the determination of the C_2–C_7 alkenes, is probably the approach that will be taken to analyze the higher molecular weight alkenes.

TABLE 5. Analysis of known hexene blend[150].

Conditions: 40% 2,2′-oxydipropionitrile on 35- to 48-mesh C-22 firebrick, 50 ft. by ¼ in., at 25°C; helium flow, 30 ml./min at 10 lb./in.^{2} inlet pressure.

Compound	Composition (% weight)		
	Known	Found	Error
3,3-Dimethyl-1-butene	2·7	3·3	+0·6
4-Methyl-1-pentene 3-Methyl-1-pentene	11·4	12·9	+1·5
4-Methyl-2-pentene[a]	8·4	7·0	−1·4
2,3-Dimethyl-1-butene	5·8	5·8	0·0
1-Hexene *trans*-3-Hexene	8·9	10·4	+1·5
2-Methyl-1-pentene *cis*-2-Hexene	7·3	6·6	−0·7
cis-3-Hexene	5·8	6·4	+0·6
2-Methyl-2-pentene 2-Ethyl-1-butene	17·0	16·6	−0·4
trans-2-Hexene	1·5	1·3	−0·2
3-Methyl-*trans*-2-pentene	3·0	3·5	+0·5
3-Methyl-*cis*-2-pentene	8·7	8·2	−0·5
2,3-Dimethyl-2-butene	3·2	3·3	+0·1
1,5-Hexadiene	2·2	2·9	+0·7
2,3-Dimethyl-1,3-butadiene	8·0	7·5	−0·5
4-Methyl-1,3-pentadiene	5·2	4·2	−1·0
2-Methyl-1,3-pentadiene	0·9	trace	—

[a] *Cis–trans* ratio unknown.

2. Qualitative analysis

Gas chromatography can be used as an analytical tool for the qualitative identification of the alkenes by comparison of retention volume or retention time data. However, GC cannot be considered independently, such as one might consider infrared spectroscopy, as an exceptionally good qualitative tool.

The retention volume, V_R (uncorrected), is the volume of gas, measured at column outlet pressure and temperature, required to sweep the compound under consideration from the sample port to the detector. The retention time, t_R (uncorrected), is the time required from the start of the analysis (sample injection or admission to the column if this is delayed) to the maximum of the peak of the compound under consideration[161]. The two terms are related by $V_R = F_c t_R$, where F_c is the (volume) flow rate of the carrier gas at

TABLE 6. Analysis of known C_6 monoolefin blend[150].
Conditions: 20% dimethylsulfolane on 35- to 48-mesh C-22 firebrick, 50 ft. by ¼ in., at 25°c; helium flow, 30 ml./min at 10 lb./in.^{2} inlet pressure.

Compound	Composition (% weight)		
	Known	Found	Error
3,3-Dimethyl-1-butene	3·2	3·4	+0·2
4-Methyl-1-pentene	13·6	13·8	+0·2
3-Methyl-1-pentene			
4-Methyl-2-pentene[a]	10·0	12·1	+2·1
2,3-Dimethyl-1-butene	7·0	7·4	+0·4
1-Hexene	7·0	8·3	+1·3
2-Methyl-1-pentene	7·0	7·6	+0·6
trans-3-Hexene			
cis-2-Hexene	12·2	11·6	−0·6
cis-3-Hexene			
2-Ethyl-1-butene	10·2	9·9	−0·3
2-Methyl-2-butene			
trans-2-Hexene	12·0	10·3	−1·7
3-Methyl-*trans*-2-pentene	3·6	3·6	0·0
3-Methyl-*cis*-2-pentene	10·4	9·2	−1·2
2,3-Dimethyl-2-butene	3·8	2·6	−1·2

[a] *Cis–trans* ratio unknown.

the temperature of the column, measured at the outlet[161]. The retention volume and time are constant for a given compound on a given column provided the temperature and carrier gas flow rate are maintained constant[162]. Therefore, if the retention volume or time of an unknown alkene is compared to known alkenes on the same column and at the same temperature, and other conditions being constant, qualitative identification can be made. However, for positive identification in this manner, it is a necessity that a good history of the unknown sample be available.

Generally, it is more advantageous to compare relative retention values of compounds under investigation[92]. This is done by comparing corrected retention data, *i.e.* the uncorrected volume (V_R) corrected for the pressure drop in the column and equal to V_R^0 [161], compared with a standard material taken as 1·00 on the same column under identical conditions. The major advantage of relative retention data is that effects of operating conditions and column dimensions are eliminated, since these factors affect the standard compound and sample components in the same manner. The conditions which must be maintained are the same column temperature and substrate phase[162]. Data obtained in this manner are reasonably reproducible from laboratory to laboratory[162,163].

Generally, if a particular homologous series is being investigated, *e.g.* the n-alkenes, then it is convenient to plot the logarithm of the relative retention data of the known standard n-alkenes against some property such as the number of carbon atoms, boiling point, or the logarithm of the vapor pressure[162,163,164]. For identification of the unknown compound, the relative retention value is determined, and identification is then made from the plot as above.

Frequently, the unknown may be one of several compounds which have the same relative retention data on a given stationary phase, and thus positive identification cannot be made by the above technique. In these instances, a positive identification is sometimes possible by determining the relative retention data of the unknown on two different substrates and subsequent comparison with a plot of the logarithm of the relative retention data of the known homologous series on the one substrate *versus* another[162,163,165]. Although identification by this approach is generally adequate, it may fail in cases where there are a large number of compounds present. Under these conditions, it may be possible to identify the unknowns by using alternative detection methods. This may either take the form of employing detectors, such as the gas density balance and flame ionization, for which the compounds have different response factors[151,166] or of trapping[167,168,169] and then identifying the unknowns by infrared or mass spectrometry. The time-of-flight mass spectrometer has also been used as the detector in gas chromatography for qualitative identification[170]. This technique is readily adaptable to the identification of complex mixtures.

Relative retention data of a number of alkenes are reported in the literature. Hively[171] has established the relative retention times of a large number of alkenes and other hydrocarbons with methylal as standard compound on five different substrates.

James and Martin[162] have tabulated relative retention volumes of several alkenes relative to pentane on paraffin wax, Lubrol MO (ethylene oxide polyether) and benzyldiphenyl (Table 7). Desty and Whyman[163] have also investigated several of these same alkenes on benzyldiphenyl at the same operating temperature as that of James and Martin[162]. The data compare favorably, the majority of the data being within 5% of each other.

TABLE 7. Retention volumes of several alkenes relative to n-pentane[162].

Alkene	B.p. (°c)	Stationary phase at 78·6°c Paraffin wax	Lubrol	Benzyl-diphenyl
2-Methyl-3-butene	20·50	0·61	0·74	0·73
2-Methyl-1-butene	31·16	0·86	1·08	1·28
1-Pentene	31·0	0·87	1·05	1·27
2-Pentene	35·9	0·87	1·16	1·42
2-Methyl-2-butene	38·57	1·17	1·31	1·58
cis-4-Methyl-2-pentene	56·3	1·73	—	2·16
trans-4-Methyl-2-pentene	58·5	1·73	—	2·16
1-Hexene	61·5	2·13	2·32	3·07
1-Heptene	94·5	5·1	—	6·8
2,4,4-Trimethyl-1-pentene	101·44	6·23	—	6·4
2,4,4-Trimethyl-2-pentene	104·91	6·64	—	7·5
1-Octene	121·28	11·95	—	15·5

Scholly and Brenner[172] reported retention times of a large number of chemical types (among which are several alkenes) on eight substrate phases of different polarity.

Retention data for the gaseous alkenes are reported by Fredericks and Brooks[149]. The column substrate used was dimethylsulfolane for resolving the alkenes from each other and from several of the paraffins.

Smith and Ohlson[173] employed micro hydrogenation of trapped fractions of unsaturated hydrocarbons from a packed column, and subsequently chromatographed the hydrogenated fractions with a number of C_4, C_5 and C_6 alkenes.

Rowan[174] reported a procedure in which sequential class reactions and gas chromatography are applied for the identification of alkenes in admixture with other hydrocarbons. The reactions employed include absorption of the alkenes in sulfuric acid and hydrogenation. The operations are performed rapidly and conveniently in a closed system which is an integral part of the gas chromatographic apparatus.

Several investigators[147,164,171,175,176] have used saturated solutions of silver nitrate in ethylene glycol, triethylene glycol, glycerin and benzyl cyanide as a column substrate for the separation and identification of the alkenes. Bradford and colleagues[176] first introduced the substrate in the analysis of ethane as an impurity in ethylene. Tenney[164] has reported retention data for a number of normal and branched alkenes on silver nitrate–triethylene glycol substrate. Van der Craats[147] suggested the use of benzyl cyanide as the solvent in order to prevent interference due to water which may be present in the glycols. Bednas and Russell[175] have studied saturated solutions of silver nitrate in ethylene glycol, polyglycols and glycerin as column substrates, these being stable up to 65°c for long periods and up to 85°c for short periods. Their procedure is outlined below.

Apparatus. A commercial chromatographic unit was employed. The columns consisted of ¼ in. copper tubing wound into a coil 6 in. in diameter. Both the thermistor detector and the column are contained in the same air bath, which can be controlled at 50°, 65°, 85°, 100°, 120° and 140°c, or can also be used at the ambient temperature. The peaks are recorded on a conventional strip-chart recorder, fitted with a ball-and-disk integrator. Helium was the carrier gas used.

Preparation of columns. Approximately 30 g of finely pulverized silver nitrate was added slowly to 20 ml. glycerin (or glycol) in a beaker while stirring vigorously with a magnetic stirrer. In some cases, the beaker was placed in warm water to hasten the solution of the salt. Care was taken to keep the temperature below 50°c. After several minutes' stirring, the undissolved silver nitrate was separated by centrifuging for a few minutes.

Exactly 17 ml. of this saturated solution was then added to 39 g (100 ml.) 30–60 mesh firebrick to give a packing which contained about 40% solvent by weight. The usual care was taken to ensure a uniform mixture. The resulting material appeared to be quite dry and flowed readily.

Sufficient ¼ in. diameter copper tubing was degreased and filled with the prepared packing. Approximately 6 ml. of packing was required to fill 1 ft. of tubing. The tubing was carefully filled while it was suspended by one end, being shaken at intervals to produce a uniform bed. The ends were plugged with glass wool and the tubing was wound to form a coil of 6 in. diameter.

Retention data obtained by Bednas and Russell[175] are tabulated in Table 8.

B. Infrared Spectroscopy

Infrared spectroscopy is a powerful analytical technique which can be used for the rapid identification and measurement of organic compounds. The portion of the infrared spectrum most useful to

TABLE 8. Relative retention times for $AgNO_3$ – ethylene glycol column[175].
Conditions: 11 ft. column; 50°c; flow rate, 25 ml./min; corrected retention time for ethylene, 4·5 min.

Compound	Retention time (ethylene = 1·00)
n-Pentane (and lighter alkanes)	0 (not retained)
trans-2-Butene	0·56
trans-2-Pentene	0·89
Ethylene	1·00
Isobutene	1·19
Propylene	1·22
cis-2-Butene	2·00
1-Butene	2·35
1-Pentene	2·8
cis-2-Pentene	2·95
1-Hexene	4·2
1-Heptene	6·1
1-Octene	8·9

the chemist and most commonly employed in the analysis of the alkenes is the fundamental region 2–15 μ (5000 to 667 cm^{-1}). The spectrum of the fundamental region results principally from the stretching or deformation ('bending') vibrations of the atoms within the molecule, and the absorption bands recorded for a particular compound give information concerning the types of functional groups present, their relative concentration and the nature of the overall molecular configuration. These bands are unique to the compound and can be used as a qualitative and quantitative measure of that compound.

The absorption frequency most characteristic of the alkenes in general is due to the C=C stretching vibration which occurs in the vicinity of 6·0 to 6·1 μ. However, since infrared absorption depends upon changes in dipole moment, the C=C absorption band is strong only in the infrared spectrum of highly unsymmetrical alkenes such as 1-alkenes, being very weak for compounds that have approximately centrosymmetric structures about the C=C bond and completely absent for symmetrical compounds such as ethylene, *trans*-2-butene and tetramethylethylene[1].

Other infrared absorption bands characteristic of the alkenes can be used to determine these compounds. For all alkenes except the type $R^1R^2C{=}CR^3R^4$ where the R groups are not hydrogen, the vibrations of the hydrogen atoms attached to ethylenic carbon atoms can be employed for analysis. The C—H stretching vibrations in the 3·2 to 3·5 μ region are intense and characteristic and have been utilized[177] for the analysis of simple mixtures of alkenes and other CH-containing compounds. The out-of-plane 'bending' vibrations of C—H bond angles, which give bands in the 10–15 μ region, are very intense and highly specific for some types of alkenes. This region is frequently used for alkene-type analysis[178,179].

The infrared spectrophotometer consists essentially of three major sections: (*i*) source of radiation; (*ii*) dispersing device; and (*iii*) detection and recording system. The most common source of infrared radiation are the Globar (silicon carbide rod) and the Nernst Glower, a bonded mixture of rare-earth oxides in rod form.

Two methods of dispersing infrared energy are a diffraction grating and a refraction prism. Greater resolution of the radiation is obtained with the diffraction grating; however, a fore prism is usually required to eliminate higher orders of diffraction. Even though lower resolution is obtained with the refraction prism, it is more generally used because of its greater spectral range and simplicity. The most common prism material used for the 2–15 μ range is sodium chloride; however, for better resolution in the 1–5 μ and 1–8 μ range, lithium fluoride and calcium fluoride, respectively, can be used.

Detectors which are used for sensing infrared radiation are the thermocouple, bolometer, photoconductive cell, Golay cell and thermistor; of these, the most widely used is the thermocouple. The output signal from the detector is amplified to operate a recording potentiometer that is designed to produce a direct recording of the transmission of the sample *versus* wavelength.

Various types of cells are available for handling samples for infrared analysis. The windows of these cells are usually constructed of sodium chloride for the 2–15 μ range. The cells used for gases usually vary from 1–20 cm, whereas the optimum thickness of the cells employed for liquids is in the order of 0·01–1·0 mm. Solid materials can be handled in several ways. In the mull technique, the solid is dispersed in some viscous liquid such as mineral oil (Nujol) and/or Fluorolube. This suspension is then placed between two salt plates and the infrared spectrum scanned. In the potassium bromide method, a few milligrams of the sample are mixed intimately with about 1 g of potassium bromide and the mixture is then subjected to high pressure in a suitable die to form a clear, nearly transparent disk, which is subsequently placed in the path of the infrared radiation and the spectrum scanned.

Liquid and solid samples are also analyzed by dissolution in a solvent which is relatively transparent in the infrared. Solvents such as carbon disulfide and carbon tetrachloride are usable and are good solvents for the alkenes.

Two main types of infrared spectrophotometers are available, namely the single-beam and the double-beam instruments. The single-beam instruments measure the energy of the incoming beam as a function of wavelength, and the absorption spectrum obtained with this instrument is superimposed on the spectrum of source intensity and atmospheric absorption. Double-beam spectrophotometers compare the light energy passing through the sample with the energy passing through a reference cell. In this way, the atmospheric bands and the source changes are eliminated. The double-beam principle for obtaining infrared spectra is more rapid than the single-beam technique, besides having other advantages.

I. Quantitative analysis

Infrared techniques have extensive application in the quantitative analysis of various organic materials. As in other spectrophotometric methods of analysis, the Lambert–Beer equation, $A = abc$, is usually applicable, where $A = \log_{10}(I_0/I)$ and equal to absorbance; I and I_0 are the transmitted and incident radiation intensities, respectively; a = absorbance index; b = thickness of the cell and c = concentration of the compound. Therefore, a calibration curve can usually be constructed for a single component in a system (*e.g.* a two-component system) by measuring the absorbance of a series of solutions of the component at a suitable wavelength at which the other component does not absorb and plotting the absorbance versus concentration. If the same cell is used throughout, the equation reduces to $A = kc$, where k is a new constant incorporating the absorbance index and the cell thickness. Reliable data can be obtained in this manner so long as the conditions of sample temperature, cell thickness, slit width, wavelength settings, *etc.*, are kept constant. The calibration curves obtained in infrared should be checked frequently, since changes in the above-mentioned variables can occur.

The absorbance data used in the preparation of the calibration curves can be obtained by the convenient base-line method developed by Wright[180] or by determining the absorbance at the chosen wavelength and correcting for the cell and solvent absorbance at that wavelength.

If an assay of a particular alkene is required, a differential spectrophotometric technique may be employed which is capable of better precision and accuracy than conventional infrared spectroscopy. The technique involves a comparison of a known and an unknown sample simultaneously in a double-beam spectrophotometer. The calibration curve for this type of analysis is constructed by preparing a series of samples of known concentration and determining the absorbance values at a selected wavelength *versus* a sample of known purity. The differential absorbance data are then plotted against concentration. The absorbance of the unknown is then measured and the purity determined from the calibration curve. The differential technique is also applicable to the quantitative determination of minor components in that the absorption of the major absorber can usually be cancelled, thus permitting the minor component to be detected and accurately measured.

The data of Hammer and Roe[181] are indicative of an operating precision of ±0·1% absolute when using the Perkin–Elmer Model 21 double-beam spectrophotometer in the differential analysis of cyclohexane. Theoretical details of differential infrared spectrophotometry are discussed by Robinson[182]. Powell[183] has utilized the differential technique on several systems.

The conventional method of analyzing a multicomponent mixture for each component by infrared involves (*i*) knowledge of the number of components present, and (*ii*) infrared spectrum of each constituent to determine the suitable wavelength for measurement. The optimum wavelength would be that where the other components do not absorb; however, this is rarely the case in a multicomponent system, so that a suitable wavelength is chosen where only one component has intense absorption relative to the other components. Once the proper wavelengths have been selected, then the absorption coefficients are determined for each component at each wavelength. These absorption coefficients are then used to form simultaneous equations such as (11) and (12), where $A_{\lambda l}$ and $A_{\lambda n}$ are equal to the absorbance at wavelength l and n respectively; c is the concentration and k is equal to a constant incorporating

$$A_{\lambda l} = k_{1_{\lambda l}}c_1 + k_{2_{\lambda l}}c_2 + \cdots k_{n_{\lambda l}}c_n \tag{11}$$

$$A_{\lambda n} = k_{1_{\lambda n}}c_1 + k_{2_{\lambda n}}c_2 + \cdots k_{n_{\lambda n}}c_n \tag{12}$$

absorbance index and thickness of the cell. The absorbance values for the unknown mixture are determined and the equations solved for the concentration of each component by one of several ways, *e.g.* by using determinants (for $n \leqslant 3$), inverted matrix[184] or successive approximations[185]. A computer[186,187] can also be used for a more rapid solution of the equations.

If the concentrations of the components of a system do not vary over a wide range and the number of components is small (~ 3 to 4), it may be feasible to analyze the mixture by use of working graphs[188,189] instead of the usual simultaneous equations. Once the working graphs are constructed, this technique is very rapid and readily adaptable to control-type analysis.

Problems can arise in analyzing gases in that the absorption coefficients, for a given gas, may vary somewhat even at the same partial pressure, depending upon the other gases present. This phenomenon is attributable to the 'pressure broadening' of spectral lines caused by collision damping and seems to occur to a greater extent with the first member of each homologous series[190]. Even though a linear relationship is not obtained when the partial pressure of the gas is plotted against absorbance, a working curve can usually be obtained which can be used for a quantitative analysis.

Generally, infrared spectroscopy has not been applicable to trace analysis; however, recent advances in infrared equipment in the form of accessories, such as beam-condensing systems[191,192], microscope attachments[193,194] and scale expansion units have enabled identification of samples in the parts per million range[195].

Among the quantitative infrared methods which have been used in the analysis of hydrocarbons, there are a number concerned with the determination of the alkenes. Publications of 'handbook' infrared data are found in the journal *Analytical Chemistry*. These data were published in cooperation with the Coblentz Society[196]; however, this practice was discontinued with the December 1960 issue and has since started in the journal *Applied Spectroscopy* with volume **15**, 1961.

Handbook data[197] are available for 2-methylpropene, 1-butene, and *cis*- and *trans*-2-butene in mixtures with isobutane; 1-butene, *cis*- and *trans*-2-butene, isobutylene in mixtures with 1,3-butadiene[198]; and mixtures of ethylene, propylene, 2-methylpropylene, 1-butene, *cis*- and *trans*-2-butene[199].

The method of Saier and Coggeshall[177], in which a lithium fluoride prism is used for better resolution of the C—H absorption bands, has been used successfully to analyze a mixture of 2,4,4-trimethyl-1-pentene and 2,4,4-trimethyl-2-pentene. Octene and heptene have also been analyzed by this method in the presence of saturated aliphatic and some oxygenated compounds.

The base-line method developed by Wright[180] has been utilized by Seyfried and Hastings[190] for analyzing isobutylene in admixture with C_4 hydrocarbons.

Multicomponent mixtures of alkenes have been analyzed[178,200] using group-type analysis by infrared. The classes which have been analyzed are $RCH{=}CH_2$, $R^1R^2C{=}CH_2$, $R^1CH{=}CHR^2$ (*cis* and *trans*), and $R^1R^2C{=}CHR^3$. The data obtained on synthetic mixture by Saier and coworkers[178] (Table 9) are indicative of reasonable accuracy for all the classes with the exception of *cis*-$R^1CH{=}CHR^2$ and $R^1R^2C{=}CHR^3$.

TABLE 9. Analyses of synthetic blends[a] of pure olefins[178]. (Concentrations in mole per cent)

	$RCH{=}CH_2$		$R^1R^2C{=}CH_2$		$R^1R^2C{=}CHR^3$		*trans*-$R^1CH{=}CHR^2$		*cis*-$R^1CH{=}CHR^2$	
Sample[b]	Known	Calc.	Known	Calc.	Known	Calc.	Known	Calc.	Known	Calc.
1	18·6	19	34·3	34	10·8	8	14·5	12	21·8	27
2	17·2	18	28·9	31	20·3	16	11·2	12	22·4	24
3	27·2	31	19·1	22	16·9	23	12·3	14	24·5	10
4	23·2	26	16·3	18	29·0	34	10·6	13	20·9	9
5	17·1	20	28·8	30	20·4	19	11·2	14	22·5	17

[a] Each blend was prepared to contain several members of each class.

[b] Samples 1 and 2 were analyzed using a 1·5 mm cell and CS_2 as solvent. Samples 3, 4 and 5 were analyzed in a 0·15 mm cell with n-heptane as the solvent.

Methods published for the analysis of light hydrocarbons by the Butadiene Committee[201] include the detailed infrared analysis of C_2–C_4 alkenes in the presence of propane, carbon monoxide, methane, hydrogen, oxygen and nitrogen; and the analysis of 1-butene, *cis*-2-butene, *trans*-2-butene, isobutylene in the presence of n-butane, isobutane, 1,3-butadiene and 1,2-butadiene.

The method of Brattain and coworkers[202] was used to analyze mixtures containing 1-butene, *cis*-2-butene, *trans*-2-butene, isobutene, n-butane and isobutane. The work of Perry and Bain[203] involves a general differential infrared procedure for analyzing multicomponent mixtures utilizing wire screens which are used as convenient references against which samples can be matched in differential measurements of absorbance. The procedure is illustrated by the analysis of a mixture of 1-butene, isobutene, *trans*-2-butene, *cis*-2-butene, isobutane and n-butane. The data are indicative of greater precision than that obtained by conventional infrared analysis of an identical mixture.

The near-infrared[204] (1–3 μ) has also been used to determine quantitatively terminal methylene groups and *cis* double bonds. Mixtures such as 1-octene and *cis*-4-methyl-2-pentene were analyzed quantitatively. The method is capable of analyzing terminal methylene groups with a sensitivity within 0·01% $>C{=}CH_2$, and a precision and accuracy within ±1 to 2%. *Cis* double bonds may be determined with a sensitivity of about 1% $-CH{=}CH-$. The method can be used for trace work in that a few hundred parts per million of 3-chloro-2-chloromethyl-1-propene in 3,3-bis(chloromethyl)oxetane has been analyzed.

Quantitative techniques in infrared spectroscopy, both practical and theoretical, are reviewed in the literature. These[180,182,186,190,202,203,205–207] are but a few which can be referred to for specific details of the technique.

2. Qualitative analysis

Infrared spectroscopy has probably been used more than any other analytical technique in the qualitative identification of organic compounds. The majority of the alkenes have characteristic absorption bands in the infrared which are indicative of a particular type alkene. The following discussion is concerned with some of the different type alkenes and the approximate wavelength at which a characteristic band occurs[208].

Generally, the spectroscopist is able to recognize the presence and type of unsaturation in an unknown alkene, although this depends to some extent upon the amount of substitution at the double bond. Unsaturation is extremely difficult to detect in compounds of the type $R^1R^2C{=}CR^3R^4$, as the only remaining characteristic frequency is the C=C stretching mode, the intensity of which is considerably reduced by the symmetry around the bond.

The absorption peak of an alkene due to the C=C stretching normally occurs within the range of 6·0 to 6·1 μ and is strong only in compounds which are highly unsymmetrical. Alkenes such as $R^1R^2C{=}CH_2$ and $R^1R^2C{=}CHR^3$ can be differentiated in this region by means of the position and intensity of the absorption peak, as the terminal double bond gives a considerably more intense band than an internal double bond[209]. Absorptions very characteristic of certain alkenes also occur in the 10·0 to 12·5 μ region; *e.g.* absorptions in the 10·1 to 10·36 μ region are indicative of alkenes containing the structure $R^1CH{=}CHR^2$ (*trans*). The absorption band at 10·36 μ had been used by Anderson and Seyfried[200] for a quantitative measure of this group of alkenes.

Monosubstituted alkenes containing the vinyl-type double bond have two strong bands near 10·1 and 10·98 μ which are characteristic of this class. In addition, there is usually a band of medium intensity in the 5·4 to 5·56 μ region. Alkenes such as $R^1R^2C{=}CH_2$ have absorption bands at about 11·23 μ with a band usually present in the 5·56 to 5·72 μ region. The general frequency range for the trisubstituted alkenes ($R^1R^2C{=}CHR^3$) is 11·9 to 12·5 μ[208].

As an aid to the spectroscopist in the identification of unknowns, spectra of known alkenes are available in compilations of the American Petroleum Institute Research Project 44, National Bureau of Standards; Hydrocarbons Research Group Reports I to XI (1941–46); the ASTM–IBM index and the Sadtler Standard Spectra.

Most simple mixtures of organic materials can be identified by infrared, since the absorption spectrum of a mixture is essentially identical to a superposition of the spectra of the individual components, providing no reaction occurs between them. As the number of components in the mixture increases, these could first be partially resolved by fractional distillation or by gas chromatography, with subsequent infrared analysis of the separated fractions.

Qualitative identification of minor components is also possible by infrared. Application of differential spectrophotometry[182] has been made to qualitative analysis[210,211]. Bellamy[210] utilized a double-beam spectrophotometer to cancel out the major component and to detect a minor component which could not be detected by ordinary spectrophotometry.

General discussions concerning qualitative analysis by infrared as regards instrumentation[205,206], interpretation of spectra[208,212], type of cells[205], application[205,207], techniques[182,188], *etc.*, are abundant in the literature.

C. *Mass Spectrometry*

Analysis by the mass spectrometer consists of bombarding a compound in the gaseous phase with an electron beam to produce ions which are subsequently sorted according to their mass-to-charge ratio (m/e). The recorded mass spectrum of these ions can then be used as a quantitative and qualitative measure of the compound.

The instrument employed to obtain the mass spectrum is illustrated in the schematic drawing (Figure 4) of the Consolidated Electrodynamics Corp. Model 21–103 mass spectrometer. The compound under investigation is introduced into the inlet system *b*, which is usually constructed to accommodate gases and volatile liquids, but can be modified to analyze liquids or solids having very low vapor pressures. In the usual case of a gas, the pressure in the reservoir of the inlet system is maintained at about 10^{-2} mm. The sample is allowed to flow through a small orifice called a 'leak', *c*, into a section of the mass spectrometer designated the ionization chamber (Isatron, *d*). The pressure of the gas in the ionization chamber is maintained at about 10^{-5} to 10^{-7} mm by means of continuous evacuation. The sample is then bombarded by an electron beam under a potential of about 50–100 volts (conventional mass spectrometry) to produce positive and negative ions as well

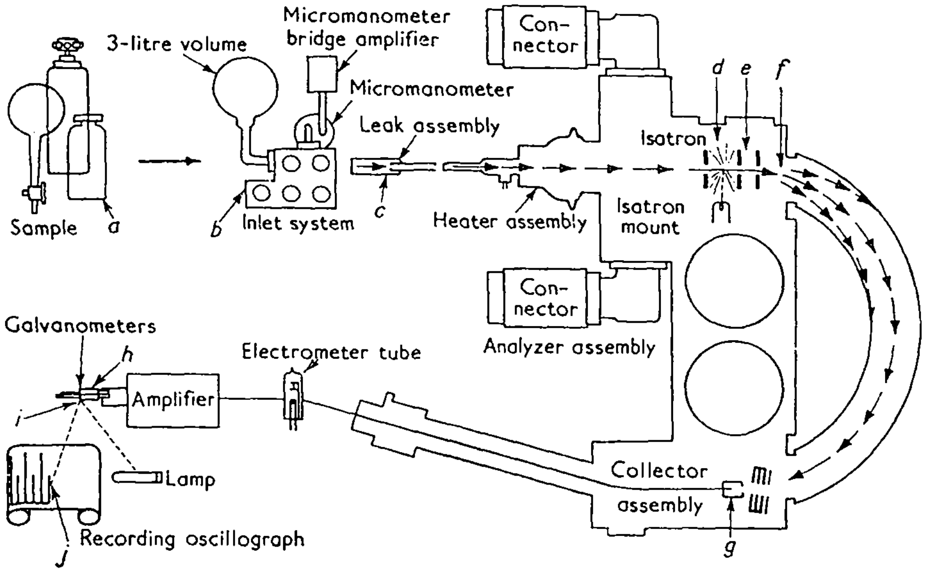


FIGURE 4. The schematic diagram of a 180° magnetic mass spectrometer. (Reproduced by courtesy of The Consolidated Electrodynamics Corp., Pasadena, California, U.S.A.)

as neutral fragments. The positive ions are then accelerated by means of an applied potential of several thousand volts through an entrance slit, *e*, into the mass spectrometer analyzer tube. The beams of ions are then bent by a magnetic field into a circular path, the radius of which depends upon the ratio of the mass of the ions to their charge. For a given accelerating voltage, V, and magnetic field H, this radius, R, is given by equation (13). Only those ions

$$R = \left(\frac{2mV}{eH^2}\right)^{\frac{1}{2}} \tag{13}$$

describing a certain radius R will pass through the exit slit and be recorded by the ion collector *g*. The remainder strike the analyzer tube and are grounded. The ions that impinge on the collector plate produce a current which is amplified and fed to a recording galvanometer, which records their abundance. By continuously changing either the magnetic field or the accelerating voltage in the course of a spectral recording, ions of different and known m/e value are focused on the exit slit in turn, and thus the mass spectrum is scanned[213]. The recorded spectrum is a series of peaks, called a 'pattern' which is characteristic of a given compound and is a plot of ion abundance *versus* m/e.

In conventional mass spectrometry, the ionization voltage is substantially higher than the minimum energy necessary for ionization to occur. Thus, there is sufficient energy available, not only to ionize the compound, but to produce multiply charged ions and to fragment molecular bonds as well. Consequently, the mass spectrum of most chemical compounds will consist of a number of peaks; for instance, a pure compound of molecular weight of about 100 atomic mass units (a.m.u.) may contain dozens of peaks[214].

The spectrum can be recorded photographically by a strip chart recorder or by digital readout equipment.

Most commercial mass spectrometers for chemical analysis employ magnetic deflection of the ion beams; however, other forms of ion beam separation are being used. Non-magnetic time-of-flight spectrometers[215–219] have been described in which the ion beam is pulsed and accelerated into a long drift tube. The ions arrive at the collector at short measured time intervals, depending upon their mass-to-charge ratios. The collector current is displayed on an oscilloscope whose sweep is synchronized with the production of ion pulses, thus exhibiting a complete mass spectrum for each ion pulse. This instrument has been used successfully as a detector in vapor phase chromatography[170]. In the 'radio-frequency'[220] mass spectrometer, the ion beam passes through a linear series of grids. Radio frequency potentials applied at each grid are timed to accelerate ions of one mass only as they arrive at the grid. A retarding potential in front of the collector then repels all ions except those possessing maximum energy. The mass spectrum is scanned by varying the frequency of the alternating voltage.

Crossed electric and magnetic fields are used in the cycloidal focusing mass spectrometer, which was first built by Bleakney and Hipple[221]. The spectrum is scanned when either of the crossed fields is varied. The omegatron described by Sommer, Thomas and Hipple[222,223] uses essentially the cyclotron principle for separation of ions with various mass-to-charge ratios. The electric field frequency is varied to scan the mass spectrum.

The mass spectrometer gained impetus as a versatile analytical tool during World War II when it was utilized quite extensively for rapid and accurate analysis of complex hydrocarbon mixtures. The rapidity with which an analysis can be made by mass spectrometry is a distinct advantage of the technique in process monitoring and plant control[224,225].

The instrument is well adapted to the analysis of gases and volatile liquids, and it has found wide application in the determination of alkenes. With the recent development of heated inlet systems[226–228], materials having very low vapor pressures can also be handled.

The high cost of the instrument is a drawback of the technique when compared to gas chromatography, which competes and has replaced the mass spectrometer as an analytical tool for the analysis of certain systems. Another disadvantage occurs in systems where the mass spectra of components of a mixture are too similar so that identification of the components cannot be made. In the analysis of such mixtures, a combination of gas chromatography and mass spectrometry has proved to be an excellent analytical approach. That is, the mixture is resolved by gas chromatography, and the subsequent constituents are then easily analyzed by mass spectrometry.

For more specific and detailed information concerning mass spectrometry, several literature references should prove to be helpful[214, 229–233].

1. Quantitative analysis

The mass spectrometer has been employed in the quantitative analysis of hydrocarbons for a number of years. The outstanding advantage of quantitative analysis by the mass spectrometer is that this technique can be applied to a large number of components in a mixture without previous extraction, distillation, *etc.*, and usually, where applicable, the analyses can be accomplished with rapidity and accuracy.

Quantitative analysis of a mixture by conventional mass spectrometry is based on the premises that the spectrum of a mixture is the sum total of the spectra of all the components comprising that mixture. In the analysis of a multicomponent system, a proportionality factor termed 'sensitivity' must be determined for each compound of the mixture. The sensitivity is calculated for each component for any desired peak by running the pure compound at definite operating parameters such as ionizing current, *etc.*, and inserting the proper data into the equation $H_n/p = S_n$, where H_n = peak height (scale divisions) at mass number n, p = pressure in microns, and S_n (divisions/μ) = the sensitivity at mass number n. The sensitivity can vary from instrument to instrument and also on the same instrument; therefore, this factor must be checked frequently. Daily calibration runs on known compounds such as n-butane can serve as a means of adjusting the sensitivities of the materials under investigation.

Once all the sensitivities and cracking patterns are obtained for a mixture, then the analysis of a system containing components $A \cdots N$ can be made by choosing n peaks from the spectrum of the mixture, measuring the peak heights and inserting the data into simultaneous equations (14), where $H_1 \ldots H_n$ = peak heights at the mass

$$\begin{array}{l} H_1 = S_1^A P^A + S_1^B P^B + \ldots S_1^N P^N \\ \cdot \quad \cdot \quad \cdot \quad \cdot \quad \cdot \quad \cdot \quad \cdot \\ H_n = S_n^A P^A + S_n^B P^B + \ldots S_n^N P^N \end{array} \tag{14}$$

number chosen, $P^A \cdots P^N$ are equal to the partial pressures of components $A \cdots N$, and S_1^A corresponds to the sensitivity of component A at the mass number of H_1 with similar meanings for S_1^N, *etc.* Solution of (14) gives values of $P^A \cdots P^N$; once the partial pressure of each component has been calculated, then the mole percent component can be obtained from equation (15).

$$\text{mole } \% \ A = \frac{100P^A}{p_{\text{total}}} \tag{15}$$

The peak chosen for each component is ideally that which has little or no contribution from the other components of the mixture. If a peak occurs in the spectrum of the mixture where only one component contributes, then the partial pressure of that component can be calculated directly from $P = H/S$ and its contribution subtracted from the total pressure, thus lessening the calculations. If more than about 3 or 4 simultaneous equations are involved in the mixture, short-cut calculation methods[234,235] or computer devices can be used for the solution of the equations[186,236-239].

A check on the accuracy of the analysis can be made by comparing the total of the partial pressures determined by calculation to the measured pressure at which the mixture was introduced. If the analysis accounted for all components present and the calculations were performed correctly, these two pressures should agree within 1 or 2%[240].

Simple binary mixtures can be analyzed as above[241] or by measurement of the ratio of ion currents, or peak height[242] at selected masses and then determination of the composition from a working calibration curve of the binary mixture. This approach avoids a pressure measurement and any changes in instrument sensitivity.

Complex mixtures containing a large number of isomers or other compounds which give very similar mass spectra can be analyzed by compound-type analysis[243]. By this method, classes of compounds such as alkenes, paraffins, acetylenes, *etc.*, are determined quantitatively as a group by applying the sums of mass peaks specific for each type.

Basic assumptions that are made in the analysis of mixtures are: (*i*) that the ionization behavior of compounds being considered is constant and known during the measurement of the mass spectrum; (*ii*) that the intensity of ions and fragments produced is a linear function of gas pressure; and (*iii*) that the intensity of ions and fragments is independent of the presence of other ions, fragments or molecules. If these conditions hold reasonably well, then calculations of mixture compositions can be made that are satisfactory for most analytical purposes.

Low voltage mass spectrometry[244,245] has also been employed in quantitative analysis. This technique involves the use of low energy electrons (~10 v for the n-alkenes[246]) to produce a mass spectrum consisting of molecular ions. That is, the ionizing voltage is adjusted to a value in excess of the appearance potential of the molecular ion, but less than the appearance potential of the fragment ions. The spectrum of a mixture by this technique consists of a series of peaks, each representing compounds of corresponding molecular weights.

One advantage of the low voltage technique is that it is possible to analyze a multicomponent mixture without resorting to tedious calculations[244]. The quantitative data obtained by Varsel and coworkers[245] with this technique were comparable with data by conventional mass spectrometry.

Analysis of trace quantities (p.p.m. range) of material in a mixture is usually accomplished by mass spectrometry by first concentrating the trace constituent by techniques such as condensation, distillation, adsorption, gas chromatography, *etc.* Shepard and coworkers[247] and Quiram and coworkers[248] employed low-temperature and adsorption techniques, respectively, for the analysis of trace components in air. The C_3, C_4 and C_5 hydrocarbons were detected in the p.p.m. range with these techniques.

Starr and Lane[249] reported on the accuracy and precision of the mass spectrometer analysis of synthetic light hydrocarbon mixtures which has been analyzed by a number of laboratories. The alkenes (C_3–C_4) were analyzed with a precision and accuracy less than 1·0 mole percent. Washburn[250] tabulated results of a synthetic mixture containing some of the lower alkenes. Isobutylene, 1-butene and 2-butene were determined ninety percent of the time within $\pm 0{\cdot}8$, $\pm 1{\cdot}4$ and $\pm 1{\cdot}2$ mole percent, respectively.

Brewer and Dibeler[234] outlined basic principles for the mass spectrometric analysis of hydrocarbon mixtures containing the C_2–C_5 alkenes.

Milsom and colleagues[251] utilized both the mass spectrometer and infrared to analyze mixtures of light hydrocarbons containing the butenes. The mass spectrometer was used for the non-isomer constituents, and infrared was used to analyze the isomeric materials. O'Neal[252] also employed the two instruments for the complete analysis of the C_1 to C_4 paraffin–monoalkene hydrocarbons in order to obtain a more accurate butene analysis. The data are indicative of better accuracy for all components (0·3–0·6%) when the combined instruments were used as compared with 0·4–1·1% by the mass spectrometer alone.

Techniques of absorption and reaction of components of mixtures containing alkenes were employed in order to analyze olefinic compounds in mixtures that could not be handled *per se.* Mikkelsen and coworkers[253] reacted a mixture containing olefins and cycloparaffins with benzenesulfenyl chloride to form a high-boiling product with the olefins such that only the cycloparaffins would be determined by the mass spectrometer. The olefins were then determined by difference on another aliquot of the sample. Melpolder and Brown[254] improved the accuracy of the determination of isobutene in the presence of other butenes by converting isobutene into *t*-butyl chloride before analysis.

Coulson[255] separated the olefins from cycloparaffins by adsorption of the olefins on firebrick containing mercuric perchlorate–perchloric acid. The cycloparaffins were then determined as a group. An untreated sample was run, and the olefin types were determined by difference.

Low-voltage techniques are also reported for quantitative analysis of the alkenes. Field and Hastings[244] used the technique to analyze unsaturates in petroleum naphthas. Results of synthetic blends of the methylbutenes alone and in the presence of paraffins were indicative of an accuracy within 2% of the butenes present.

Frisque and coworkers[256] analyzed hydrocarbon types containing monoolefins in naphthas by a combination of low-voltage and conventional mass spectrometry. The ratio of olefin to alkyl benzene was obtained by the low-voltage technique and the olefin content then calculated from the alkyl benzene content, which was determined accurately from the conventional spectrum.

Lumpkin[257] used the low-voltage technique in the compound-type analysis of C_{14}–C_{21} monoolefins from a fraction of polypropylene.

2. Qualitative analysis

The mass spectrometer has been utilized more extensively as a quantitative analytical tool than as a means for qualitative analysis. However, with the development of instruments with heated inlet systems[226–228] the technique has gained impetus in the qualitative identification and structure determination of unknown compounds.

Since the mass spectrum is unique for a given compound, the identification of pure materials can generally be made without great difficulty. Qualitative identification of some of the alkenes may not be readily accomplished owing to the similarity of spectra among the isomers, *e.g.* the C_4 and C_5 isomers[258,259].

Methods specific for the identification of the alkenes are not outlined; however, a general procedure as recommended by

McLafferty[260] for the identification of compounds by mass spectrometry is as follows:

(*a*) Before the mass spectrum is run, all other available information should be obtained, such as possible structures or types of functional groups present, thermal stability, vapor pressure, purity, *etc.*

(*b*) The mass spectrum is run and checked to determine if impurities, sample decomposition or insufficient vapor pressure are indicated. A check is also made to determine if the m/e scale is accurately identified. This is conveniently done by running a known compound (internal standard) while the sample is still in the mass spectrometer.

(*c*) The molecular ion is identified. This is usually the highest mass in the spectrum (excluding its heavy isotopes). If there is doubt concerning the identification of the molecular ion, it can be verified with '$M + 1$' pressure-sensitive peak[261], or by the rate of effusion, or by conversion to a more amenable chemical derivative. If it is suspected that the highest m/e is an impurity, the rate of effusion can be checked or the effect of lowering the ionizing voltage to near the appearance potential.

(*d*) The empirical formulas of the molecular ion and other prominent ions are determined by using isotopic abundances or exact mass determination.

(*e*) The prominent ions, beginning with the highest m/e, are tabulated along with the group lost to give these ions. In general, ions of lower m/e in a particular spectrum have the greater probability of rearrangement and thus are less useful for qualitative work.

(*f*) The larger peaks are compared (m/e) with known common ions encountered in mass spectra[262].

(*g*) Indications of a rearrangement process are noted by checking the ions formed, and especially the corresponding lost neutral fragments.

(*h*) All possible molecular structures are listed and, from available correlation data, an attempt is made to predict the mass spectral features of each structure and compare these features against the spectrum of the unknown.

(*i*) Reference spectra of the most promising candidate structures are obtained.

(*j*) The structure is proved by superimposing the sample and reference spectra.

The mass spectrometer can also be used to identify components in a multicomponent system, since the mass spectrum of such a system is a summation of the mass spectra of the individual components. Identification of a mixture can be relatively easy or difficult, depending upon the particular system under investigation. If the mass spectrum contains a number of overlapping peaks resulting from several components which have similar mass spectra, then the interpretation can be very difficult. The C_4 and C_5 alkene isomers are of this nature. If very few overlapping peaks are evident, interpretation of the spectrum is less difficult, and the experienced mass spectroscopist with the aid of a compilation of known mass spectral data such as that from the American Petroleum Institute, Project 44, can usually identify the individual components.

Complex mixtures which cannot be resolved by conventional mass spectroscopy may be analyzed by first separating several of the components by distillation, chromatography, *etc.*, and subsequently analyzing the separated fractions. A combination of gas chromatography for resolving the complex mixture and subsequent analysis of the resolved constituents by mass spectrometry has been used quite successfully for qualitative work[170].

Low-voltage mass spectrometry[244,245] can also be applied to the qualitative analysis of mixtures. That is, if conditions are favorable, the mixture may be resolved by applying an ionizing voltage such that only certain components of the mixture appear in the mass spectrum. This technique has been used by Field and Hastings[244] at ionizing voltages such that only the unsaturates in petroleum naphthas are ionized.

General qualitative techniques of mass spectrometry are discussed in the literature[259,263,264].

D. *Miscellaneous Physical Methods*

1. Nuclear magnetic resonance

Nuclear magnetic resonance (n.m.r.) techniques and instrumentation have been developed such that the n.m.r. spectrometer has become a very useful analytical tool. The technique depends upon the nucleus possessing a magnetic moment; that is to say a nucleus with no magnetic moment, *e.g.* ^{12}C or ^{16}O, will not have any nuclear magnetic resonance.

The n.m.r. spectrum which is observed for a particular compound is due to the energy transitions that occur whenever the nuclei are placed in an appropriate magnetic field and subjected to a rotating radio-frequency field. The spectrum is characteristic for each compound and therefore can be used in the identification of unknown materials.

Nuclear magnetic resonance spectrometry is usually divided into two categories—wide-line and high-resolution n.m.r. Wide-line spectra are those in which the observed width of the resonance line is as large or larger than the major resonance shifts caused by differences in the chemical environment of the nucleus under study. In high-resolution spectra, the widths of the observed resonance lines are smaller than the major resonance shifts caused by differences in the chemical environment of the nucleus, *i.e.* chemical shifts and spin–spin coupling are observed in the former case and can be analyzed. It is this area of n.m.r. spectrometry that is of greatest interest to the chemist. For instance, the high resolution n.m.r. spectrum of hydrogen can provide data concerning the chemical nature, spatial position and number of each type of hydrogen present in a particular compound. In a favorable case, this information would be sufficient to establish the identity of the compound, either from past experience with spectra of similar materials or by comparing chemical shift data of such a spectrum with data obtained on compounds containing various hydrogen groups. The chemical shift data obtained by Chamberlain[265] on olefinic protons are indicative of the possibility of distinguishing between terminal and non-terminal ethylenic hydrogens.

Quantitative analysis is also possible by high-resolution n.m.r. since the area under a peak is a measure of the nuclei being studied. The accuracy that can be obtained with careful work in n.m.r. is comparable to wet combustion methods, as evidenced by the data obtained on several different material (Table 10[266]).

The n.m.r. techniques possess certain advantages which are very desirable for analytical work, so that its application to problems concerning the alkenes and other compounds of a qualitative and quantitative nature should continue to increase at a rapid rate. Some of the advantages of the technique are: (*i*) speed of analysis; (*ii*) intensity calibrations for quantitative work are not necessary, as in other spectrometric methods; (*iii*) chemical shift calibration can be done indirectly; and (*iv*) the technique is usually insensitive to sample impurities, which is an advantage when the major constituent is of interest. The high cost of the equipment and maintenance detract from the instrument as an analytical tool. Other

TABLE 10. Total hydrogen analyses from nuclear magnetic resonance integrated intensities[266].

Compound	% H by wt.	% H (n.m.r.)
Ethylbenzene	9·48	9·48[a] ± 0·04[b]
Water	11·17	11·08 ± 0·04
Chloroform	0·843	0·83 ± 0·01
Toluene	8·75	8·76 ± 0·03
p-Dioxane	9·16	9·13 ± 0·09
17α-Hydroxyprogesterone (17·4 mg)	9·16	9·18 ± 0·04
3α-Acetoxypregnan-20-one (24·5 mg)	9·99	9·99 ± 0·06

[a] Reference compound. [b] Standard deviation.

features which are disadvantages are insensitivity to trace components and the necessity of the sample being in the liquid state before it can be analyzed by conventional high-resolution n.m.r.

Information on the basic principles, instrumentation and techniques of n.m.r. can be found in the *Annual Review of Physical Chemistry*, beginning with the 1954 edition, and also in several recent texts[267-269].

2. Ultraviolet and visible spectrophotometry

Ultraviolet spectroscopy has been used to determine alkenes according to types by means of their iodine complexes. Long and Neuzil[270] reported a procedure for distinguishing types of alkyl-substituted alkenes by means of the ultraviolet spectra of reversible complexes formed with iodine. The maximum absorption band for each type occurs at a characteristic wavelength (Table 11).

TABLE 11. Maximum absorption band for alkene types.

Compound	Maximum absorption (mμ)
$RCH{=}CH_2$	275
$R^1R^2C{=}CH_2$	290–295
$R^1CH{=}CHR^2$	295–300
$R^1R^2C{=}CHR^3$	317
$R^1R^2C{=}CR^3R^4$	337

The method was used to analyze a synthetic blend of the above five types and the data were indicative of a maximum absolute error of +1·8%, which was obtained for the $RCH{=}CH_2$ type.

The far, or vacuum, ultraviolet (170 to 230 mμ) spectra of unsaturated and aromatic hydrocarbons have been investigated by Jones and Taylor[271]. The spectra obtained of a large number of alkenes are indicative of the possibility of determining total alkene content in this region, although individual alkenes or types cannot be differentiated.

A spectrophotometric method was employed by MacPhee[272] for the determination of traces of olefinic-type material in air by reaction with acid molybdate solution and subsequent measurement of the absorbance of the color produced at 685 mμ as a measure of the olefin. The procedure was used to estimate the C_3 and heavier olefinic hydrocarbons.

Mader and coworkers[273] reported a method for detecting trace olefins (25–10,000 p.p.m. by volume in air) by a spectrophotometric titration. The olefins are absorbed in carbon tetrachloride and then titrated spectrophotometrically with bromate–bromide reagent by measuring the absorbance due to the tribromide ion in the ultraviolet region. The method is applicable to the C_4 and higher olefins.

Altshuller and colleagues[274] determined small quantities of olefins by reaction with concentrated sulfuric acid and subsequent measurement of the absorbance of the reaction products at 300–310 mμ. The procedure is insensitive to ethylene under all conditions and to propylene below 1500 p.p.m. The method appears usable between 100 and 10,000 p.p.m. of total four-carbon and higher molecular weight olefins. A spectrophotometric procedure reported by Altshuller and Sleva[275] involves reaction of an olefin with *p*-dimethylaminobenzaldehyde in concentrated sulfuric acid to form a colored product. The method was used to analyze the four-carbon and higher molecular weight olefins and is sensitive to at least 0·1 p.p.m. by volume of gaseous olefins and to a p.p.m. for the liquid olefins.

3. Raman spectroscopy

Raman spectroscopy has been employed in the analysis of alkenes[276–279]; it has not, however, attained very much practical importance.

The Raman effect is based on the fact that when a beam of light is passed through certain substances, part of the light is scattered with a wavelength different from that of the exciting radiation. This scattered light constitutes the Raman spectrum of the substance and is a series of lines of extremely low intensities on either side of the exciting line. The extent of the shift in position of the lines from that of the exciting source depends upon the molecular structure of the sample and the intensities of the lines depend upon the concentration of the molecular groups or linkages present.

Fenske and coworkers[276] and Braun and coworkers[277] reported Raman spectral data for a number of olefins and other hydrocarbons. In general the data are within 2% of the actual amount of the compounds present in synthetic mixtures.

Goubeau[280] recorded spectra of the olefins and made assignments of the wave-number shifts of 'characteristic bands' to the individual olefin types, on the basis of constancy of intensity and shift for a series of molecules of the same type. Rea[281] also correlated the Raman Spectra with molecular structures for a large number of the olefins.

Heigl and coworkers[279] employed the technique for the quantitative determination of total olefin content in hydrocarbon mixtures. That is, the area under the peak, characteristic of the olefins, was used as a measure of the olefin types. Based on molal scattering coefficients obtained on pure olefins (hexenes through decenes) a method was developed that could be used to obtain results within ± 10% of the correct value.

IV. ACKNOWLEDGMENT

The author wishes to express his appreciation to Dr. Sidney Siggia for the opportunity to do this work. He also wishes to thank his fellow members of Central Analytical for their constructive suggestions and help.

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 6

Alkene complexes of some transition metals

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I. INTRODUCTION

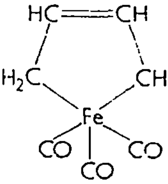
Little more than a decade ago, the generally prevalent view was that the transition metals were unable to form organic derivatives having a direct carbon-to-metal bond. The realization that this belief was erroneous and the recognition that transition metals can indeed be bonded directly to carbon atoms to form organometallic compounds represent one of the more fascinating recent developments in chemistry.

A good indication of this changed situation can best be found in the number of excellent reviews on this subject which have been published within the last few years[1–10].

The availability of these reviews has made much easier the task of writing this chapter and at the same time it has absolved this writer from the necessity of providing an overall survey of this already wide and rapidly expanding field. Consequently, reference will be made in this chapter to complexes of di- and oligoolefins with only some of the transition metals and in particular to those complexes arising from the reactions between alkenes and metal carbonyls.

II. METAL π-COMPLEXES OF BUTADIENE AND HOMOLOGOUS COMPOUNDS

The first reported compound of an unsaturated hydrocarbon with a metal appears to be $PtCl_2 \cdot C_2H_4$ described[11] as early as 1827, but the first compound of immediate interest to the present review was isolated in 1930 by Rheilen and coworkers[12] from the reaction of butadiene with iron pentacarbonyl. This compound, which gave the formula $C_4H_6Fe(CO)_3$ on analysis, appeared remarkable for its high thermal stability and very good solubility in organic solvents. Rheilen[12] suggested structure **1** for this compound, which remained a chemical curiosity until it was reinvestigated[13] by Hallam and Pauson in 1958.



(1)

The impetus for this reinvestigation was undoubtedly provided by the discovery in 1951 of another remarkably stable unsaturated hydrocarbon-iron derivative, namely dicyclopentadienyliron, or 'ferrocene', $C_5H_5 \cdot Fe \cdot C_5H_5$, from the reaction between cyclopentadiene and iron powder[14] and also from the reaction between cyclopentadienylmagnesium bromide and a ferrous salt[15]. The early recognition[16] of the π-bonding involved in the 'sandwich' structure of ferrocene has resulted in an unprecedented development of the chemistry of unsaturated hydrocarbon–metal compounds. The 'metallocenes', of which ferrocene is the prototype, have been amply reviewed[1,2,10] and will not be discussed here in any detail.

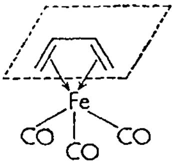
Hallam and Pauson[13] rejected the Rheilen structure **1** on the basis of the following evidence:

(*a*) Structure **1** would have only 34 electrons about the iron atom and would most probably be paramagnetic, whereas butadieneiron tricarbonyl is diamagnetic.

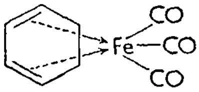
(*b*) Even a 'chelated' dialkyl derivative of iron would not be expected to be so remarkably stable as butadieneiron tricarbonyl, let alone a compound containing two C—Fe σ-bonds such as portrayed in structure **1**.

(*c*) No hydrogen was absorbed when a solution of butadieneiron tricarbonyl in ethanol was hydrogenated with Adams platinum oxide catalyst.

By analogy with the theory of carbon–metal bonding in ferrocene, Hallam and Pauson[13] suggested that the butadiene–metal bond resulted from overlap of a π-orbital of the conjugated diene with a suitable orbital of the metal. This would result in structure **2**, in which the hydrocarbon attains a planar (or nearly planar) configuration. The iron atom, lying outside the plane defined by the hydrocarbon portion, is roughly equidistant from the four carbon atoms of butadiene and it probably forms a tetrahedron with the three carbonyl groups. The suggestion for a *cis*-oid configuration for the butadiene moiety in **2** was supported by the isolation[13] of the analogous cyclohexadieneiron tricarbonyl (**3**).

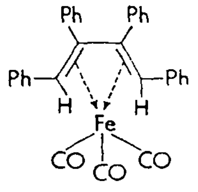


(**2**)

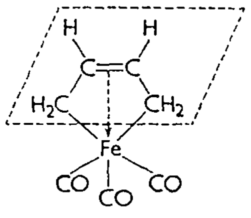


(**3**)

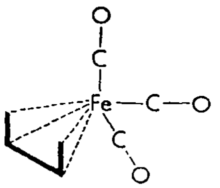
In a later study of the nuclear magnetic resonance spectrum of butadieneiron tricarbonyl, Green, Pratt and Wilkinson[17] observed three symmetrical complex bands, each of an intensity corresponding to two protons. Comparison of the spectra at 40 and 60 Mc/sec showed that the separations between the bands were chemical shifts. The low-field band at 5·28 p.p.m. (relative to tetramethylsilane) was assigned to the two equivalent protons on the central carbon atoms. The bands in the high-field region (1·68 p.p.m. and 0·22 p.p.m.) were assigned to the four protons on the terminal carbon atoms. On the basis of the symmetry of all the band patterns it was concluded that the terminal $=CH_2$ groups are equivalent but that the two protons of this group are not equivalent. Support for this assignment was derived from the nuclear magnetic resonance spectra of 1,2,3,4-tetraphenylbutadieneiron tricarbonyl (**4**) which showed a doublet band at low fields (6·92 and 7·66 p.p.m.) assigned to the protons on the phenyl groups, and an unresolved band at higher fields (2·38 p.p.m.) assigned to the two protons on the terminal carbon atoms. On the basis of these data (and in spite of the infrared spectrum of butadieneiron tricarbonyl which has a main strong peak at 3050 cm^{-1} assigned to the olefinic C—H stretching frequencies), Green, Pratt and Wilkinson[17] considered the feasibility of structure **5** for butadieneiron tricarbonyl.



(**4**)



(**5**)

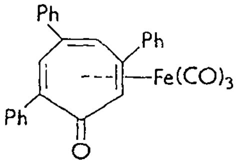


(**6**)

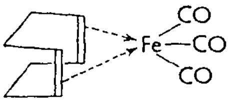
This structure **5** was rejected by Mills and Robinson[18], who have carried out an x-ray analysis of butadieneiron tricarbonyl and have put forward structure **6** for this complex. As described by Mills and Robinson, the butadiene moiety is *cis*-oid and accurately planar, but this plane is not parallel to that defined by the carbon or oxygen atoms of the $Fe(CO)_3$ group. The iron atom is roughly equidistant (2·1 Å) from the four carbon atoms of the butadiene and the angle $Fe\text{–}C_{(1)}\text{–}C_{(2)}$ is approximately 70°.

Complete delocalization of the π-electrons from the formal diene structure is suggested by the C—C distances ($\sim$1·45 Å) which are very nearly those expected (1·48 Å) for a single bond formed between two sp^2-hybridized carbon atoms and the 118° angle of $C_{(1)}\text{–}C_{(2)}\text{–}C_{(3)}$ is in full agreement with this assumption. The Fe—C(carbonyl) and C—O distances are normal for linear iron carbonyl groups. The three carbon atoms of the carbonyl groups and the two terminal carbons of butadiene occupy positions around the iron atom which correspond to square pyramidal coordination while the remaining two carbon atoms do not occupy regular coordination sites.

More recently[19], Smith and Dahl, in reporting their results of an x-ray study of 2,4,6-triphenyltroponeiron tricarbonyl (**7**, see below), have expressed preference for the Green, Pratt and Wilkinson description of bonding (**5**) which would lead to an approximately octahedrally coordinated iron atom.



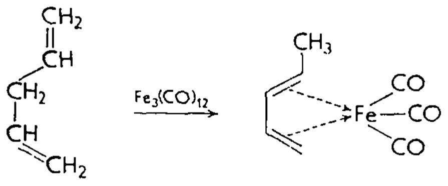
(7)



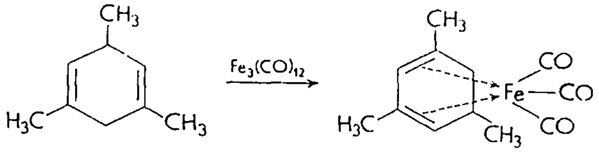
(8)

Stone and coworkers[20a], in a further reinvestigation of some of the results reported by Rheilen and coworkers[12], considered the importance of the conjugation of the double bonds to the formation and stability of the dieneiron tricarbonyl complex. Thus, these authors[20a] have found that although 1,5-cyclooctadieneiron tricarbonyl (**8**) could be obtained from the reaction between 1,5-cyclooctadiene and triiron dodecacarbonyl, the complex is very unstable, decomposing in a few hours at room temperature even when kept under nitrogen. The instability of **8** as compared with butadieneiron tricarbonyl implies that conjugation in a diene leads to greater stability of the iron complex. This inference seems to be further justified by the fact[20a] that when the non-conjugated dienes 1,4-pentadiene (**9**) and 1,4-dihydromesitylene (**10**) were reacted with triiron dodecacarbonyl, complexes of the expected stoichiometry were obtained, namely C_5H_8—$Fe(CO)_3$ and $(CH_3)_3$-C_6H_5—$Fe(CO)_3$ respectively. However, the stability of these complexes as well as infrared and nuclear magnetic resonance spectral data[20a] showed them to be the isomerized conjugated dieneiron tricarbonyl complexes **11** and **12** respectively. Indeed, when **11** was heated with triphenylphosphine it afforded pure *trans*-1,3-pentadiene.

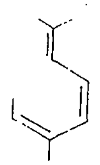
In an attempt to determine whether 1,3-dienes possessing functional groups in conjugation with the diene system would form iron dicarbonyl complexes with the iron bonded to the functional group as well as to the diene system, reactions were carried out[20a] between a series of butadiene derivatives of the general formula **13**, as well as with alloocimene (**14**). In all cases, complexes were obtained of



(9) (11)



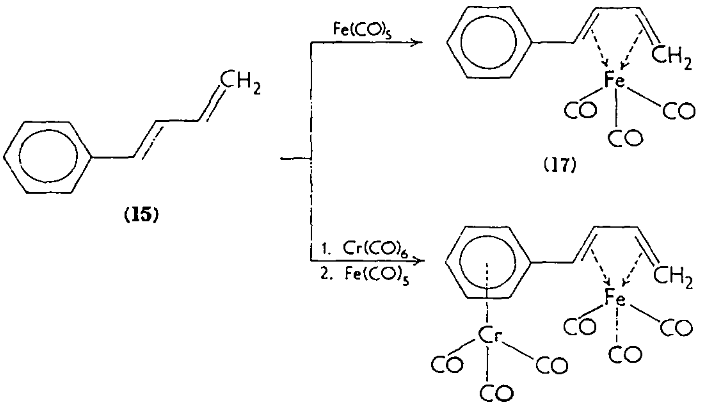
(10) (12)



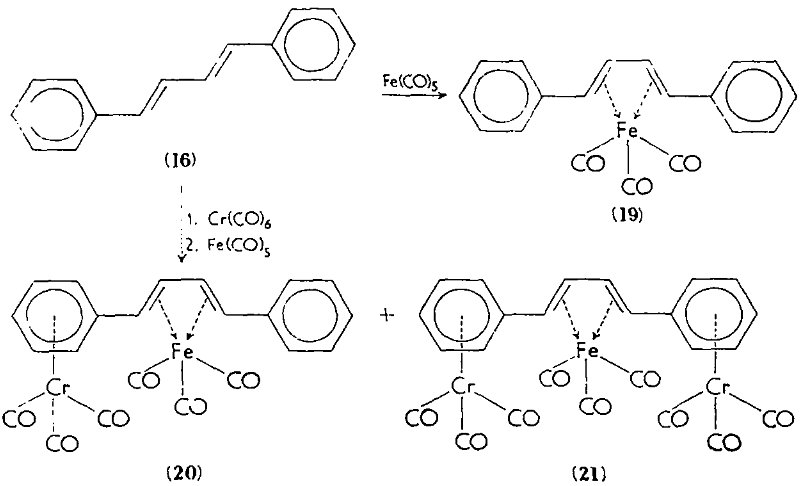
(13, R = $—CO_2C_2H_5$, $—CO_2H$, —CN, $—CONH_2$, $—COCH_3$, —CHO) (14)

composition L•Fe(CO)$_3$ where L represents the ligand taken for the reaction.

Similar results were obtained by Cais and Feldkimel[21,24] who studied the reaction between 1-phenyl-1,3-butadiene (**15**) and 1,4-diphenyl-1,3-butadiene (**16**) with iron pentacarbonyl. In both



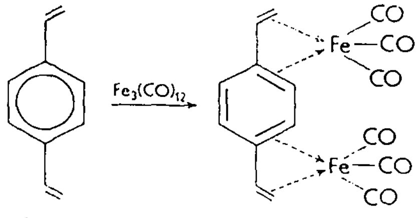
(15) (17) (18)



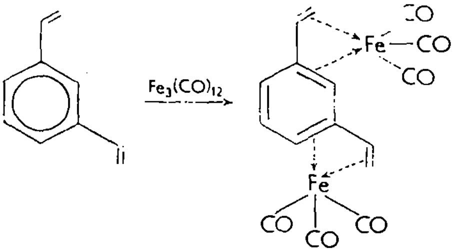
cases, these authors[21–24] obtained the compounds L•Fe(CO)$_3$, namely **17** and **19** respectively. Moreover, they have been able to show that the phenyl and diene parts of the ligand L can react independently of each other to form the metal carbonyl complexes **18**, **20** and **21**.

The ultraviolet spectra of these compounds show[23,24], in addition to the MC (metal–carbon) band[25], the expected absorptions of the substituted conjugated diene chromophores.

Stone and coworkers[26], who have independently prepared the complex **19** by reaction of 1,4-diphenylbutadiene (**16**) with triiron dodecacarbonyl, as well as the bimetal complex **20**, have concluded on the basis of nuclear magnetic resonance studies that in **19** the iron cannot be bonded to one of the benzene rings and that in **20** one of the benzene rings is bonded to a metal. Furthermore, these workers[26] could not isolate any π-complexes from the reaction between triiron dodecacarbonyl and alkylbenzenes, mesitylene, naphthalene, anthracene, styrene, 2,4-dimethylstyrene, vinyltoluene and 2,4,6-trimethylstyrene. However, *p*-divinylbenzene (**22**) as well as the *m*-isomer (**23**) reacted with triiron dodecacarbonyl to form the complexes *p*- and *m*-divinylbenzenediiron hexacarbonyl, **24** and **25** respectively. Both complexes are soluble in organic solvents and stable in air, the *m*-complex appearing to be more stable than the *p*-isomer as indicated by the results of competitive reactions between triiron dodecacarbonyl and excess of the two divinylbenzene isomers.



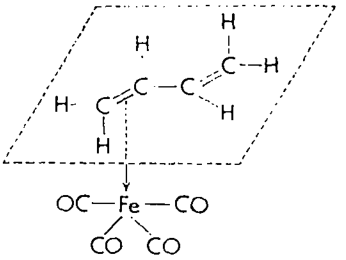
(22) **(24)**



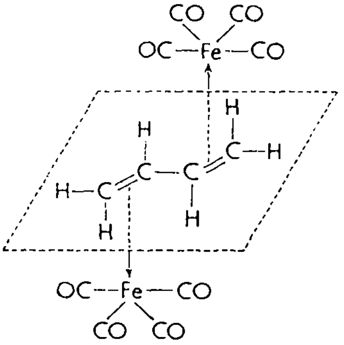
(23) **(25)**

Although the infrared spectra of both iron complexes lack the strong bands in the regions 990–1005 cm^{-1} and 905–920 cm^{-1}, characteristic of C—H deformation modes of a free vinyl group, the data available do not allow for any definite conclusions as to whether structures **24** and **25** are the correct ones, or whether one of the —Fe(CO)$_3$ moieties is linked to the six-membered ring leaving a free vinyl group not bonded to the metal.

The structure of the divinylbenzene metal complexes requires further investigation in particular in view of the recently reported[27] butadieneiron tetracarbonyl (**26**) and butadienediiron octacarbonyl (**27**). It is suggested[27] that in both of these compounds the iron tetracarbonyl moiety is coordinated to only one pair of π-electrons of the two pairs available for coordination. This is an interesting



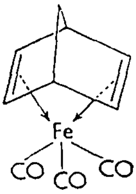
(26)



(27)

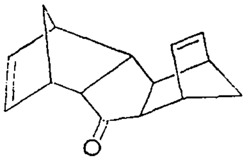
result if it is considered in connexion with the suggested[18] delocalization of the four π-electrons coordinated to the iron tricarbonyl moiety in butadieneiron tricarbonyl (**2**).

The requirement of conjugation of the double bonds for the formation of stable complexes with the —$Fe(CO)_3$ moiety is further exemplified by the properties of the isolated[28] bicyclo[2.2.1]heptadieneiron tricarbonyl (**28**). In bicyclo[2.2.1]heptadiene, the two double bonds are not in conjugation but still have a suitable spatial arrangement for possible interaction with the metal atomic orbitals. The iron complex **28**, an orange-red liquid at room temperature, is stable when stored under nitrogen but is oxidized slowly in air, with the deposition of iron oxide, as opposed to the excellent stability of butadieneiron tricarbonyl (**2**).



(**28**)

It is interesting to note that the formation of **28** following reflux of $Fe(CO)_5$ with excess bicyclo[2.2.1]heptadiene is accompanied[28] by the formation of considerable amounts of an unknown ketone (white needles, m.p. 82°). No formula is suggested[28] for this compound but a consideration of the elemental analysis results shows that $C_{15}H_{16}O$ could very well fit these analytical data. This could be a dimer of norbornadiene (C_7H_8) with the inclusion of a carbonyl group such as represented by **29**. This structure has indeed been proposed by Bird, Cookson and Hudec[29a], who also state that they have rigorously proved the *endo-trans-endo* configuration for this ketone. On the other hand, Green and Lucken have recently[29b] studied the nuclear magnetic resonance spectrum of this ketone and



(**29**)

by comparison with the spectra of five bicycloheptane derivatives of known structure, conclude that the configuration of the ketone **29** is *exo-trans-exo*.

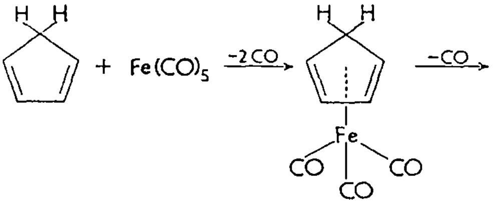
Several instances[30,31] are known where a ketonic carbonyl is introduced during the reaction of a conjugated diene; for example[30] bicyclohexenyl, or bicyclopentenyl, with iron pentacarbonyl. This reaction deserves further investigation since it may offer interesting possibilities in organic synthesis.

In addition to the already mentioned conjugated cyclic diene complex **3**, a variety of metal complex derivatives of five-, six-, seven- and eight-membered homocyclic conjugated dienes and polyenes have been reported. These have been competently reviewed[9] recently and only selected examples will be described here.

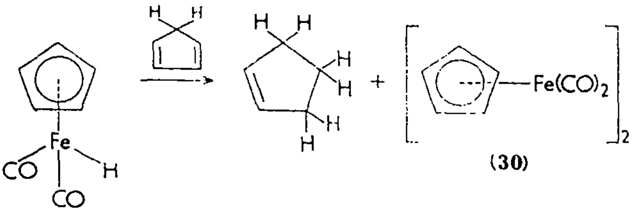
III. METAL π-COMPLEXES OF FIVE-MEMBERED HOMOCYCLIC COMPOUNDS

The metal complexes of cyclopentadiene are of particular interest in view of the ease with which cyclopentadiene tends to loose hydrogen in order to form the well known cyclopentadienyl compounds—the metallocenes and related compounds[1,2,10].

Thus the preparation of ferrocene directly from cyclopentadiene and iron carbonyl has been reported[32]. The same reaction has



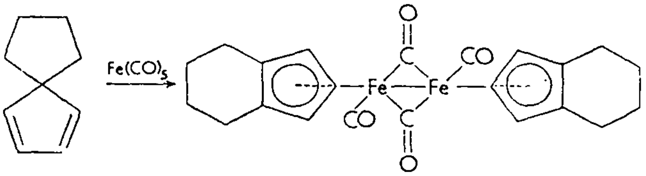
(31)



(30)

also been reported[33,34] to yield the binuclear compound $[C_5H_5Fe(CO)_2]_2$ (**30**) the production of which has been postulated[35] to proceed through the initial formation of the intermediate cyclopentadieneiron tricarbonyl (**31**). In the next steps, the hydrogen from the cyclopentadiene moiety of **31** is not evolved but is transferred to another molecule of unreacted cyclopentadiene to give cyclopentene, cyclopentane[31] and the binuclear complex **30**.

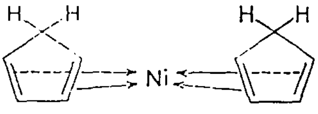
The tendency of cyclopentadiene to form cyclopentadienyl complexes is even more dramatically exemplified by the isolation of the rearranged binuclear derivative **33** from the reaction between the spirononadiene **32** and iron pentacarbonyl[36].



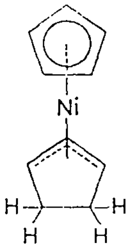
(**32**) (**33**)

On the other hand, several stable cyclopentadienemetal complexes have been reported recently[37,38,17]. The reaction between cyclopentadiene and nickel carbonyl yields a red, volatile, air-stable, low-melting (42°) and diamagnetic compound for which structure **34a** has been proposed[37a]. The metal is considered[37a] to have sp^3 hybridization with tetrahedral geometry in the coordinated complex.

The structure of this compound has been revised recently as a result of nuclear magnetic resonance studies and an alternative synthesis of $C_{10}H_{12}Ni$. Dubeck and Filbey[37b] have isolated a red complex $C_{10}H_{12}Ni$ of melting point 43° from the reaction of cyclopentadienyl and 3-cyclopentenyl anions with nickel bromide. The strongest signal in the n.m.r. spectrum of this complex consists of a



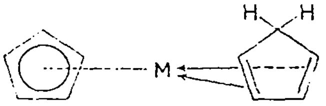
(**34a**)



(**34b**)

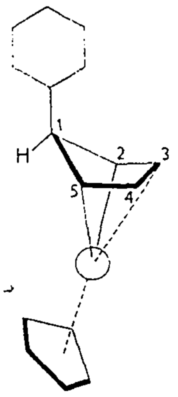
singlet with a chemical shift of 5·22 p.p.m. relative to tetramethylsilane and this is said[37b] to correspond exactly to the shift displayed by the protons of a cyclopentadienyl group bonded to nickel. On the basis of these data, Dubeck and Filbey suggest structure **34b** for $C_{10}H_{12}Ni$. In this structure the cyclopentenyl moiety behaves as a three π-electron donor and therefore it can be considered as an example of a π-allylmetal complex, the so-called 'enyl' structure[37c]. Several other groups[37c-37f] have suggested independently structure **34b** for the complex $C_{10}H_{12}Ni$.

Mixed cyclopentadiene–cyclopentadienyl derivatives of rhodium[38] (**35**) and iridium[38a] (**36**), as well as of cobalt[17] (**37a**), have been reported. The rhodium and iridium complexes are very easily oxidized[38a] by hydrogen peroxide in acidic solution to the corresponding cations $[Rh(C_5H_5)_2]^+$ (**38**) and $[Ir(C_5H_5)_2]^+$ (**39**), in which the metal changes its formal oxidation number from +1 to +3 and the cyclopentadiene looses a hydrogen atom to form the aromatic cyclopentadienyl ring. The same cations **38** and **39** are also formed when **35** and **36** respectively are allowed to stand in 2 N HCl solution.

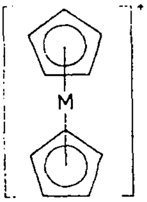


(**35**, M = Rh; **36**, M = Ir; **37a**, M = Co·)

A very recent[38b] x-ray analysis of π-cyclopentadienyl-1-phenylcyclopentadienecobalt (**37b**) indicates that the cyclopentadiene is bonded to the cobalt by one π- and two σ-bonds, as postulated by Wilkinson[17,53]. This is supported by the short bond length (1·38 Å) for the 3,4-bond in the cyclopentadiene ring, and the deviation (by 36° away from the cobalt atom) of $C_{(1)}$ from the plane of the ring. The cobalt–$C_{(1)}$ distance has been found to be 2·55 Å, compared with an average cobalt–carbon distance of 2·01 Å for the remaining four carbon atoms of this system. The average cobalt–carbon distance in the π-cyclopentadienyl ring is 2·06 Å, indicating that the bonding is slightly weaker than that for the cyclopentadiene to the metal. This result, together with the reported[19] x-ray analysis of a substituted troponeiron tricarbonyl derivative (*vide infra*), may necessitate the reformulation of other closely related conjugated diene–transition metal complexes.



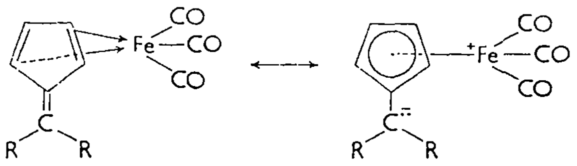
(37b)



(**38**, M = Rh; **39**, M = Ir)

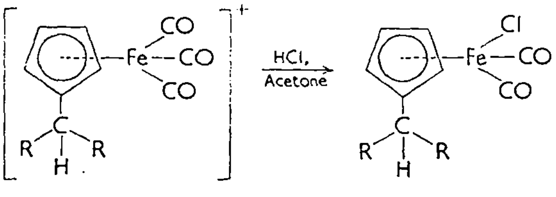
The presence of an additional exocyclic double bond attached to the cyclopentadiene ring, such as found in fulvenes or cyclopentadienones, appears to allow for the formation of stable metal complexes in which the cyclopentadiene moiety retains its conjugated diene character.

Although at temperatures of about 150° the reaction of fulvenes with metal carbonyls has been reported[39] to yield substituted cyclopentadienylmetal carbonyl derivatives, it has been shown more recently[40] that the use of milder conditions (reaction temperature of about 40°) in the reaction between fulvenes and diiron enneacarbonyl, $Fe_2(CO)_9$, allows for the isolation of fulveneiron tricarbonyl derivatives for which the resonating structure **40a**↔**40b** is suggested[40]. The results of dipole-moment measurements[40] tend



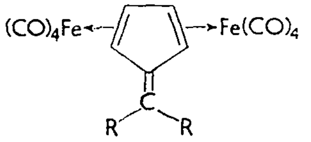
(40a) **(40b)**

to confirm this structure. The electronegative character of the ω-carbon atom is evident from the reaction of **40** with hydrogen chloride in benzene to form the cation **41**, isolated in the form of its tetraphenylborate or hexafluorophosphate salt. The cation **41** appears to react further with concentrated hydrochloric acid in acetone to form the stable complex **42**.

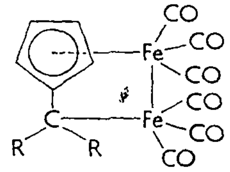


(41) **(42)**

In addition to the fulveneiron tricarbonyl compounds, Weiss and Hübel report[40] the isolation of fulvenediiron octacarbonyl and fulvenediiron hexacarbonyl for which structures **43** and **44** respectively are suggested.



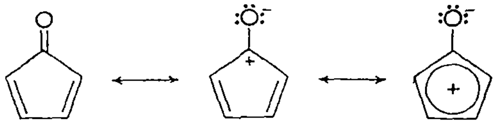
(43)



(44)

The structural relationship between **43** and **40** is evident from the thermal decomposition (between 60–70°) of **43** into **40** and iron pentacarbonyl as well as from the formation of **40** by treating **43** with excess of the appropriate uncomplexed fulvene derivative. This latter reaction deserves further investigation since the use of **43** may provide a method for the generation of the —Fe(CO)$_3$ moiety under relatively mild conditions.

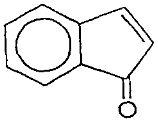
Of particular interest are the recently reported[9,41] metal complexes of cyclopentadienone, **45**. Until recently, cyclopentadienone



(45a) **(45b)** **(45c)**

had been unknown. Its oxime, prepared[44] from the condensation of cyclopentadiene with ethyl nitrite, exists as a dimer as does[42,43] cyclopentadienone itself. Allen and Van Allan[45], in summarizing the structural requirements for the existence of monomeric and dissociable dimeric cyclopentadienones, conclude that any cyclopentadienone having fewer than three substituents will exist only as a non-dissociating dimer. If there are three substituents, the dienones will exist as the non-dissociating dimer except when there are two aryl groups next to the carbonyl group. When all four positions of the dienones are substituted, a dissociable dimer results when the substituents in the 2- and 5-positions are methyl and an alkyl; otherwise the substance is a monomer.

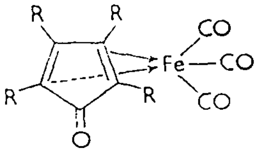
Indenone (**46**) has also been reported[46] to polymerize with great ease.



(46)

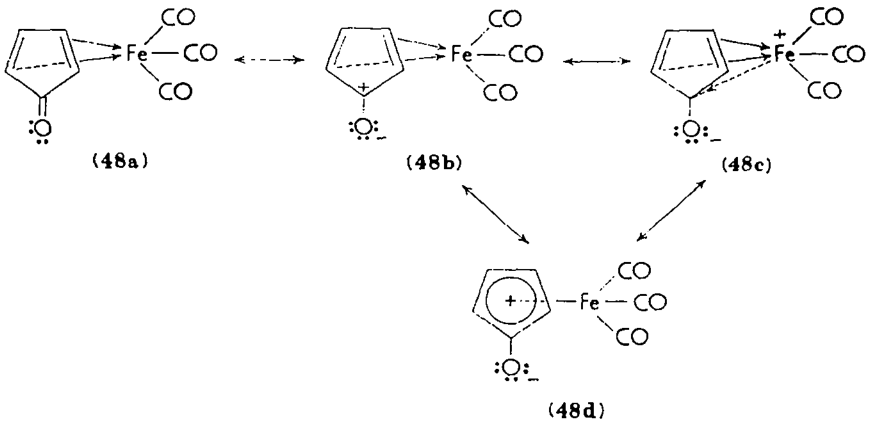
Molecular-orbital calculations[47] for cyclopentadienone confirm its easy dimerization. Streitwieser[48] associates the instability of cyclopentadienones with the relatively high energy of structures of the type **45b** and **45c** which cannot contribute effectively to the overall resonance hybrid.

Taking into account the above considerations, it is most remarkable that the reaction between acetylene, or substituted acetylenes, and iron pentacarbonyl $Fe(CO)_5$, or triiron dodecacarbonyl $Fe_3(CO)_{12}$, yields stable, crystalline cyclopentadienoneiron tricarbonyl derivatives[9,41,49], of the general structure **47**, which melt[49] (with decomposition) between 150–250° and absorb in the infrared (ketonic $>C{=}O$) between 1653–1605 cm^{-1}.



(47)

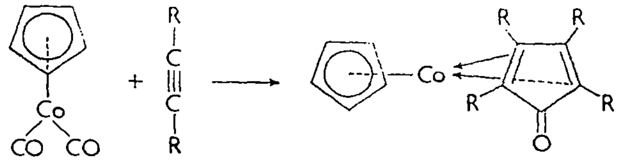
The parent compound of the series, cyclopentadienoneiron tricarbonyl (**48**), is a yellow crystalline compound (m.p. 114–116° dec.), diamagnetic, and with a dipole moment[41] of 4·45 D. The infrared absorption spectrum of the ketonic carbonyl at 1637 cm^{-1} together with the high dipole moment indicate the important contribution of such resonating forms as **48b**, **48c** and **48d**. The highly polar character of the ketonic carbonyl in **48** is further exemplified by



the unreactivity of **48** towards phenyl- or 2,4-dinitrophenylhydrazine and by the formation of 1:1 adducts between **48** and HX (X = Cl, Br, I)[41].

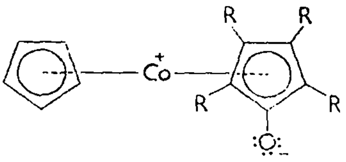
If one recalls that the instability of cyclopentadienones has been connected[48] with the polar structures **45b** and **45c** and one considers the fact that the cyclopentadienonemetal complexes nevertheless are relatively stable compounds, one can find in this series an excellent example of stabilization of a labile organic compound through metal complex formation.

Complexes of cyclopentadienones with Co, Mn, Mo and Ni have been described[49] and reviewed[9]. A related cyclopentadienone complex has been isolated recently[50]; this was prepared by exposing cyclopentadienylcobalt dicarbonyl (**49**) to sunlight for two weeks in excess 2-butyne or in diphenylacetylene. The orange crystals (m.p. 178–180°) obtained from the reaction with 2-butyne and the brick-red crystals (m.p. 327–329°) obtained from the reaction with diphenylacetylene (both in 80% yield) were shown[50] to have structure **50**. Both complexes showed an infrared absorption band at 1569 cm^{-1}, ascribed to the ketonic carbonyl. As for



(49) (50a, R = CH_3; 50b, R = C_6H_5.)

the previously described cyclopentadienonemetal complexes (*vide supra*), the low C—O stretching frequency of **50** is explained[50] by the meso-ionic structure **51**, in which cobalt is attached essentially to two cyclopentadienyl rings. Furthermore both **50a** and **50b** form stable monohydrochlorides, the former being hygroscopic and readily soluble in water.

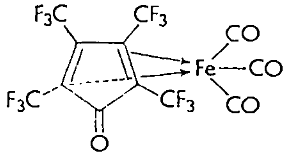


(51)

A recent x-ray study[51] of the tetramethylcyclopentadienone complex **50a** has confirmed the sandwich structure in which the cobalt lies between a cyclopentadienyl ring (at a distance of 1·67 Å) and a tetramethylcyclopentadienone ring (at a distance of 1·63 Å). The essentially equal distances between all the carbon atoms in the latter ring indicates complete delocalization of the four π-electrons and supports the meso-ionic structure **51**. Of particular interest is the finding[51] that, in contrast to the cyclopentadienyl ring which is planar, the cyclopentadienone ring is not planar; the carbonyl group is tilted at an angle of 9° out of the plane of the other atoms, away from the cobalt. The five carbon atoms of the two rings are eclipsed with respect to one another in contrast to the rings in ferrocene which are staggered. Brown has recently carried out a qualitative molecular-orbital analysis of this type of compound[52].

Recently an alternative possible structure for a cyclopentadienone-metal complex has been considered[53]. When a mixture of 2-hexafluorobutyne and iron pentacarbonyl was heated in a stainless-steel bomb at a temperature of about 110°, a single product was isolated, in contrast to the multiplicity of products isolated from the same reaction with acetylenic hydrocarbons[49]. The orange-yellow crystals analyzed as $C_9F_{12}OFe(CO)_3$ and the compound has good solubility in cold polar solvents. The infrared spectrum shows, in addition to the strong CF_3 group absorption in the region 1000–1300 cm^{-1} and the strong metal–carbonyl stretching frequencies at 2133, 2083 and 2040 cm^{-1}, two strong bands at 1742 and 1729 cm^{-1}. The presence of these bands in the ketonic carbonyl region is most remarkable in view of the fact that the previously described[49] cyclopentadienonemetal complexes show the ketonic carbonyl absorption in the 1600 cm^{-1} region and even as low[50] as 1570 cm^{-1}. Since in concentrated sulfuric acid which protonates the keto group, $C_9F_{12}OFe(CO)_3$ shows a single band (position not specified[53]) in the ketone stretching region, this band is assigned as a coordinated C=C stretching frequency. The solvent-dependency of the position of this band makes it impossible to decide which of the bands at 1742 and 1729 cm^{-1} is the ketone stretching frequency and which the coordinated C=C stretching frequency.

On the basis of the chemical properties, the infrared absorption data, and the nuclear magnetic resonance spectrum of $C_9F_{12}OFe(CO)_3$ (which appears to show two different types of CF_3 groups), Wilkinson and coworkers[53] suggest that, in addition to the cyclopentadienone structure **52**, the alternative formulation **53** is possible.



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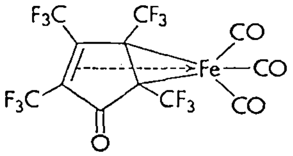
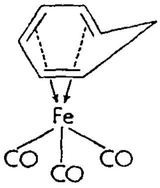


(53)

It is significant, however, that $C_9F_{12}OFe(CO)_2(PPh_3)$, obtained from the treatment of $C_9F_{12}OFe(CO)_3$ with triphenylphosphine, shows[53] a very strong absorption band at 1660 cm^{-1} in addition to a weak band at 1731 cm^{-1}.

IV. METAL π-COMPLEXES OF SIX-MEMBERED HOMOCYCLIC COMPOUNDS

The successful preparation of cyclohexadieneiron tricarbonyl (**3**) has already been mentioned[13]. The reported[13] ultraviolet absorption maxima at 207 mμ (log ε = 4·36) is most probably due to the high end-absorption of the metal tricarbonyl moiety as observed in



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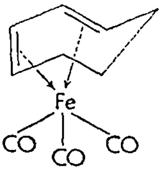

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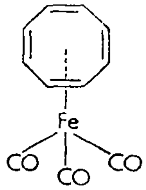


(56)

other similar compounds[25]. The nuclear magnetic resonance spectrum of **3** has been compared[54] with the spectra of cycloheptatrieneiron tricarbonyl (**54**), cyclohepta-1,3-dieneiron tricarbonyl (**55**), cyclooctatetraeneiron tricarbonyl (**56**) and butadieneiron tricarbonyl (**2**). The n.m.r. spectrum of **2**[17] has already been discussed. All four iron compounds show two bands which are attributed to the four protons of the conjugated diene group

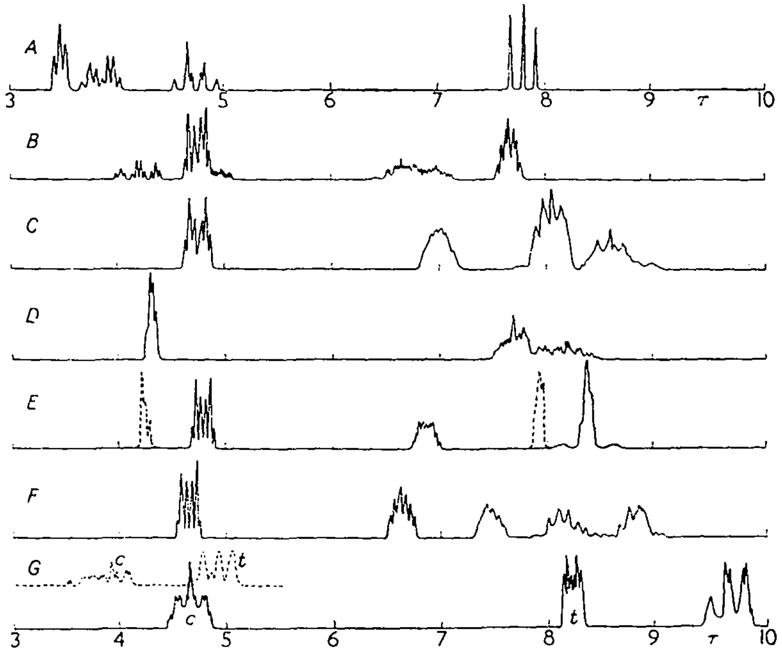
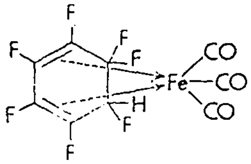


FIGURE 1. Proton resonance spectra of iron tricarbonyl derivatives of olefins at 56·45 Mc/sec. Magnetic field increasing from left to right. *A*, Cycloheptatriene; *B*, cycloheptatrieneiron tricarbonyl; *C*, cyclohepta-1,3-dieneiron tricarbonyl; *D*, cyclohepta-1,3-diene; *E*, (broken lines) cyclohexa-1,3-diene, (full lines) cyclohexa-1,3-dieneiron tricarbonyl; *F*, bicyclo[4.2.0]octa-2,4-dieneiron tricarbonyl; *G*, (broken lines) butadiene, (full lines) butadieneiron tricarbonyl (*c* = central protons, *t* = terminal protons). [Reprinted, by permission, from R. Burton, L. Pratt and G. Wilkinson, *J. Chem. Soc.*, 596 (1961).]

bound to the iron atom, in addition to the lines in the region 7·5–9·0 τ due to the aliphatic protons. Whereas in the olefins themselves, the olefinic proton resonances lie at low fields, one of the coordinated olefinic bands occurs at high fields (7·0–6·5 τ) and is assigned to the 'terminal' protons; the second olefinic band remains at low fields and is assigned to the 'central' protons of the diene grouping. The position of the high-field band changes from one compound to another more than does that of the low field band and this is thought to be so because the 'terminal' protons are more affected by the different groups attached to the coordinated conjugated diene system[54].

The preparation[20] of 5,6-dihydromesityleneiron tricarbonyl (**12**) has already been mentioned (page 339).

A recently reported iron complex of the cyclohexadiene structure is $C_6F_8Fe(CO)_3$, obtained from the reaction of either octafluorocyclohexa-1,3- or -1,4-diene with triiron dodecacarbonyl. On the basis of spectroscopic evidence, the colorless crystalline compound $C_6F_8Fe(CO)_3$ is assigned structure **57**, in which the iron atom is bound to a 1,3-diene. This must mean formation of **57** from the 1,4-diene involves migration of fluorine.



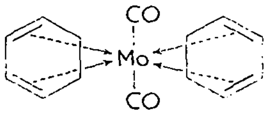
(**57**)

The infrared spectrum of **57** shows three strong carbonyl stretching frequencies at 2108, 2054 and 2018 cm^{-1}, which are displaced to higher wave numbers than in the hydrocarbon complex **3**, presumably due to the electronegativity of the fluorine atoms. In addition, there is a strong band at 1550 cm^{-1} which is assigned as a C═C stretching frequency associated with a conjugated double-bond system. It is interesting to note that octafluorocyclohexa-1,4-diene absorbs at 1740 cm^{-1} and the 1,3-diene at 1750 and 1710 cm^{-1}, the doublet of the latter arising from splittings due to conjugation[55,56]. The absence of these bands in the spectrum of **57** is taken to indicate[55] coordination of the conjugated diene to the metal atom. The fluorine nuclear magnetic resonance spectrum of $C_6F_8Fe(CO)_3$ is also considered[55] to be consistent with the depicted structure **57** although a similar structure with two Fe—C σ-bonds plus a coordinated double bond cannot be rigorously excluded. The mass spectrum analysis of **57** has been reported[55].

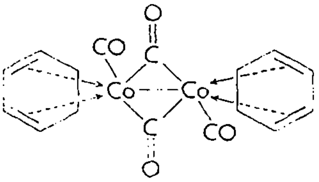
The reaction of cyclohexa-1,3-diene with molybdenum hexacarbonyl, $Mo(CO)_6$, results[57] in the formation of a disubstituted complex, $[1,3\text{-}C_6H_8]_2Mo(CO)_2$ (**58**), thought to have an octahedral configuration with both diene moieties occupying *cis* positions.

A similar disubstituted complex has been obtained[58] from the reaction of cyclohexa-1,3-diene with dicobalt octacarbonyl, $Co_2(CO)_8$.

The complex $Co_2(CO)_4\ (C_6H_8)_2$ is thought to have structure **59** in which the bridging carbonyl groups have been retained. The infrared spectra of both **58** and **59** do not show the C=C stretching frequencies in the 1600–1550 cm^{-1} region but instead they show bands[57,58] in the region 1470–1425 cm^{-1}.

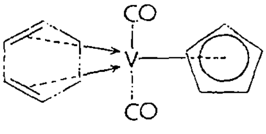


(**58**)



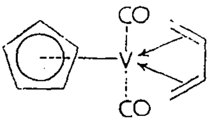
(**59**)

The ability of conjugated dienes to displace CO molecules from metal carbonyl compounds is further illustrated by the recently reported reaction[59] between cyclohexa-1,3-diene and cyclopentadienylvanadium tetracarbonyl, $C_5H_5V(CO)_4$, under the influence of ultraviolet irradiation. The resulting complex, cyclopentadienylvanadiumcyclohexadiene dicarbonyl, obtained in 28% yield as red crystals (m.p. 98–100°), is thought to have structure **60**.



(**60**)

This reaction has been extended[59] to give a series of diene complexes with metals of Group V, VI and VII as for example **61**, **62** and **64**.



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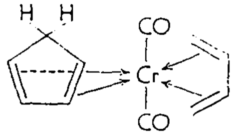

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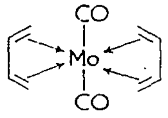

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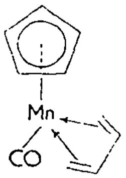
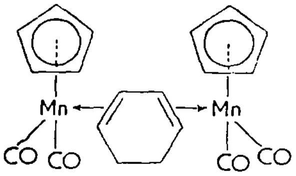


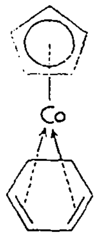
(64)

When cyclohexa-1,3-diene was reacted with cyclopentadienylmanganese tricarbonyl (**68**) under ultraviolet irradiation, the compound isolated was not the expected cyclopentadienylmanganesecyclohexadiene monocarbonyl, $C_5H_5MnC_6H_8CO$. Instead, two other compounds were isolated[60]: a small amount (2%) of cyclopentadienylmanganesecyclohexa-1,3-diene dicarbonyl, $C_5H_5MnC_6H_8(CO)_2$ and 19% of $C_6H_8[C_5H_5Mn(CO)_2]_2$ (**65**) in which the cyclohexadiene moiety is thought to serve as a bridge between the two cyclopentadienylmanganese dicarbonyl moieties. This appears to be the first reported example of a metal π-complex in which the cyclohexadiene molecule is incorporated as a bridge between two metal atoms. The infrared spectrum of **65** shows the terminal carbonyl absorption bands at 1972 and 1912 cm^{-1}, the coordinated double-bond absorption band at 1464 cm^{-1} and the $>CH_2$ absorption bands at 2933 and 2865 cm^{-1}. On the other hand, the reaction between cyclohexa-1,3-diene and cyclopentadienylcobalt dicarbonyl resulted[61] in the formation of the expected complex $C_5H_5CoC_6H_8$ (**66**).



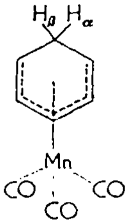
(65)

In contrast to the reactions mentioned above in which cyclohexadiene reacts with metal carbonyls in a manner similar to



(66)

butadiene, the reaction between cyclohexa-1,3-diene and manganese carbonyl proceeds[62] with the loss of a hydrogen atom to give cyclohexadienylmanganese tricarbonyl, $C_6H_7Mn(CO)_3$. The structure of this complex, as depicted in **67**, has the C_6H_7 group bound to the metal in a manner similar to the bonding in the iso-π-electronic derivative cyclopentadienylmanganese tricarbonyl (**68**).



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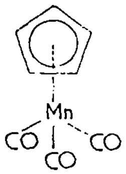


(68)

The infrared spectrum of **67** shows strong carbonyl bands at 2030 and 1937 cm^{-1} as well as C—H stretching bands at 3050, 2960 and 2800 cm^{-1}. The last band is assigned to the C—H_α (*endo*) stretching[17]. There is no absorption in the 1600–1500 cm^{-1} where the C=C stretching modes of aromatic hydrocarbons are found or where cyclohexadiene absorbs. The bands which appear in the region 1450–1400 cm^{-1} are assigned as the ring C—C stretching modes lowered by conjugation and bonding to the metal[62b]. The constitution of **67** is further confirmed through its preparation by the sodium borohydride reduction of the benzenemanganese tricarbonyl ion, $[C_6H_6Mn(CO)_3]^+$ in aqueous solution. This latter reaction provides a general method for the preparation of **67**, and substituted derivatives, in good yields[62b].

Arenemanganese tricarbonyl salts can be conveniently prepared[62b] by reacting an excess of the arene with manganese pentacarbonyl chloride in the presence of aluminum chloride. Hydrolysis of the reaction mixtures gives yellow aqueous solutions of the ions

$[\mathrm{ArH{\cdot}Mn(CO)_3}]^+$ which have been isolated as the perchlorates, polyiodides, tribromides and mercuric chlorides.

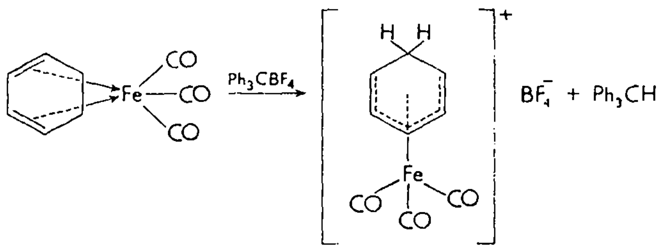
The arenemanganese tricarbonyl cations can be reduced directly in aqueous solution with sodium borohydride; or, more conveniently, an ether suspension of the anhydrous perchlorate is reduced with lithium aluminum hydride. The use of lithium tetradeuteroaluminate in the latter reaction allows for the preparation of the deuterium compound $(\mathrm{C_6H_6D})\mathrm{Mn(CO)_3}$.

The π-cyclohexadienyl compounds prepared by this method have been derived from benzene, toluene, mesitylene, hexamethylbenzene and naphthalene[62b]. All these complexes possess a reactive hydrogen atom considered to be the H_α atom of the $-\mathrm{CH_2}$ group formed in the reduction. This reactive hydrogen atom can be removed with hydride-abstracting reagents such as triphenylmethyl tetrafluoroborate, which shows the reversibility of such a reaction.

$$[\mathrm{ArH{\cdot}Mn(CO)_3}]^+ \underset{-\mathrm{H}^-}{\overset{+\mathrm{H}^-}{\rightleftharpoons}} (\mathrm{ArH_2})\mathrm{Mn(CO)_3}$$

The high-resolution nuclear magnetic resonance spectra of cyclohexadienylmanganese tricarbonyl and its substituted derivatives are thought[62b] to be in agreement with the proposed structure **67**.

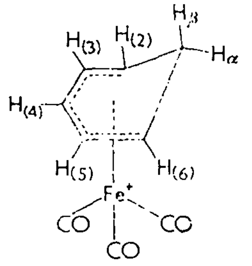
The iron complex cation **69**, isoelectronic with **67**, has been prepared[63] from cyclohexadieneiron tricarbonyl (**3**) by treating the latter with triphenylmethyl tetrafluoroborate. The salt **69** is a yellow, diamagnetic, air-stable compound, readily soluble in polar solvents such as water, dimethyl sulfoxide and dimethylformamide. With nucleophilic reagents, **69** reacts[3b] to regenerate the neutral compound **3**.



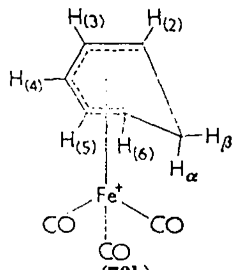
(**3**) (**69**)

The nuclear magnetic resonance spectrum of **69** shows[61] the cyclohexadienyl grouping bands more widely separated than the spectrum of π-$\mathrm{C_6H_7Mn(CO)_3}$(**67**). One of the protons of the $-\mathrm{CH_2}$

group in π-$C_6H_7Fe(CO)_3BF_4$ (**69**) gives two sharp bands at τ 7·85 and 8·11 and the other gives two 'triplets' at τ 7·09 and 6·86. This is taken to indicate that H_α and H_β are coupled in different ways to $H_{(2)}$ and $H_{(6)}$. Such different coupling could arise if the methylene carbon atom $C_{(1)}$ were bent out of the plane of the other carbon atoms of the π-C_6H_7 ring. As shown in **70a**, the —CH_2 group points away from the metal atom, whereas in **70b**, it points towards it. In **70b**, H_α will make a dihedral angle of about 90° with $H_{(2)}$ and $H_{(6)}$ and therefore there should be no coupling between them. On the other hand, H_β will make a dihedral angle of about 30° with



(70a)

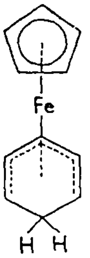


(70b)

$H_{(2)}$ and $H_{(6)}$ and these protons would be expected to couple. This is actually observed for π-$C_6H_7Fe(CO)_3BF_4$ and the coupling, 6·5 c/sec, is of the expected order[61].

An explanation is still needed for the absence of a strong band at about 2800 cm^{-1} in the solid-state infrared spectrum of the salt **69**; in similar compounds the presence of such a band has been taken[17, 62b, 67] as indication of the C—H_α stretch of the methylene group.

The synthesis of π-cyclohexadienyl complexes such as **67** has been recently extended to other transition metals and, in addition to iron derivatives, rhenium and ruthenium complexes have been reported[64]. Elucidation of the structure of the π-cyclohexadienyl-metal complexes, and the availability of nuclear magnetic resonance spectra for a relatively large number of such compounds, has led to a reformulation of the complex $C_{11}H_{12}Fe$ previously thought[65] to have structure $(C_6H_6)(C_5H_6)Fe(0)$. The complex $C_{11}H_{12}Fe$ was obtained[65,66] by reacting cyclopentadienyliron dichloride with benzene in the presence of aluminum chloride. The cation $[C_6H_6(\pi\text{-}C_5H_5)Fe]^+$ was isolated as the tribromide salt and reduction of the latter compound with lithium aluminum hydride gave a neutral compound $C_{11}H_{12}Fe$, formulated as $(C_6H_6)(C_5H_6)Fe$ on the basis of nuclear magnetic resonance spectrum taken at 40 Mc/sec. Reexamination of the nuclear magnetic resonance spectrum at 56·4 Mc/sec showed the presence of five π-cyclopentadienyl protons and consequently $C_{11}H_{12}Fe$ was reformulated[62b,64] as π-C_6H_7(π-C_5H_5)Fe (**71**).

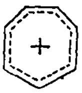


(71)

V. METAL π-COMPLEXES OF SEVEN-MEMBERED HOMOCYCLIC COMPOUNDS

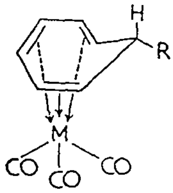
The knowledge acquired from the reactions of dienes with metal carbonyls as well as the advances made in the chemistry of metallocenes and arenemetal complexes has brought about very interesting developments in the chemistry of metal complexes of seven-membered ring systems.

Acting upon the premise that the tropylium (or tropenium) cation **72**, π-isoelectronic with the cyclopentadienyl anion as well as with the neutral benzene nucleus, should be able to form a



(72)

'sandwich' type bond with a transition metal, Wilkinson and coworkers[68] attempted the reaction of cycloheptatriene with metal carbonyls. It was hoped that such a reaction would lead to a hydrogen loss, of a type similar to that which occurs with cyclopentadiene, with the consequent formation of the expected π-tropyliummetal complex. However, when cycloheptatriene was refluxed with chromium and molybdenum hexacarbonyls, the complexes isolated were the cycloheptatrienechromium and -molybdenum tricarbonyls, $C_7H_8M(CO)_3$ (**73**) in which the hydrocarbon ligand remained intact, without the loss of hydrogen[68].

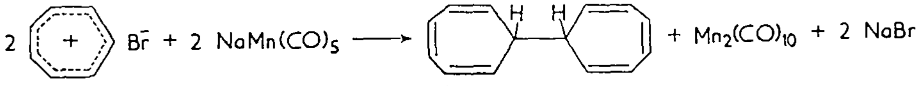


(**73a**, M = Cr, R = H; **73b**, M = Mo, R = H.)

The same type of structure as **73** was obtained[68] when the reaction was carried out with 1-substituted cycloheptatriene derivatives. It is claimed that even with 1-phenylcycloheptatriene, the seven-membered ring takes precedence as donor ligand over the six-membered ring, in spite of the ease of formation of (arene)M$(CO)_3$ compounds[8].

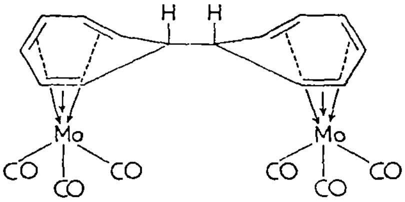
However, more recently, Munro and Pauson have reported[72] that chromatography of the reaction mixture produces a fraction whose infrared spectrum shows the presence of cycloheptatrienylbenzenechromium tricarbonyl. Moreover, these authors[72] have been able to displace cycloheptatriene from its tricarbonyl chromium complex with mesitylene.

The reaction between tropylium bromide and sodium manganese pentacarbonyl did not yield the expected tropyliummetal complex but instead, bicycloheptatrienyl (**74**) was formed in quantitative yield[68].



(**74**)

Reaction of bicycloheptatrienyl (**74**) with molybdenum produced, in addition to the monomolybdenum tricarbonyl complex (structure **73**, M = Mo, R = C_7H_7), a bismolybdenum tricarbonyl complex **75**, in which both rings are attached to molybdenum tricarbonyl moieties.



(**75**)

The structure of cycloheptatrienemolybdenum tricarbonyl (**73**, M = Mo, R = H) has been elucidated by x-ray analysis[69]. The molecule possesses an approximate symmetry plane passing through the Mo atom, the —CH_2 group of the ring and one of the CO groups. The six olefinic carbon atoms are virtually planar and the metal atom is on one side of the plane and almost equidistant (2·31 to 2·46 Å) from them. The —CH_2 group is bent out of this plane (0·67 Å) away from the metal atom and the three carbonyls (Mo—C, 1·95 to 1·99 Å; C—O, 1·13 to 1·18 Å) are situated on the opposite side of the metal atom to the ring. The observed C—C distances in the seven-membered ring show clearly alternation of single and double bonds and thus indicate the presence in the complex of three localized metal–olefin bonds formed by donation of an electron pair from each π-bond in the ring.

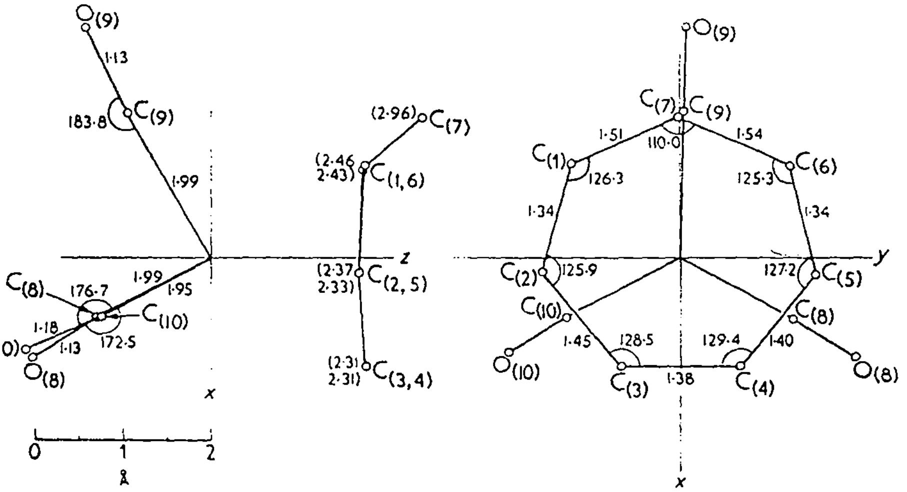
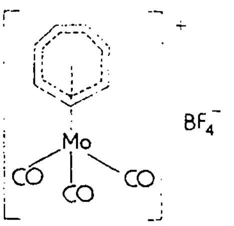


FIGURE 2. Cycloheptatrienemolybdenum tricarbonyl bond distances and angles as determined by x-ray analysis. [Reprinted, by permission, from J. D. Dunitz and P. Pauling, *Helv. Chim. Acta*, **43**, 2193 (1960).]

The nuclear magnetic resonance spectrum of cycloheptatrienemolybdenum tricarbonyl has been interpreted[70] to agree with the x-ray data and the proposed structure **73**.

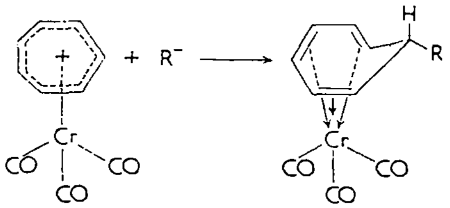
The successful synthesis of a π-metal complex of the tropenium ion (**72**) has been realized[81] by reacting cycloheptatrienemolybdenum tricarbonyl (**73**) with trityl fluoroborate. This reaction, which involves hydride-ion abstraction from the cycloheptatriene



(76)

moiety, produces a nearly quantitative yield of π-tropeniummolybdenum tricarbonyl fluoroborate (**76**). The single proton resonance band in the high resolution nuclear magnetic resonance spectrum of **76** is consistent with the formulation of a fully aromatic structure in which the metal atom is complexed with the cyclic π-molecular orbital encompassing all seven carbon atoms of the tropenium ion ligand[71].

The π-tropeniumchromium tricarbonyl cation (**77**) in the form of its perchlorate salt, has been shown[72] to react readily with a variety of anions, with the formation of the 1-substituted cycloheptatrienemetal complexes **78**. This result is taken to indicate[72] that the



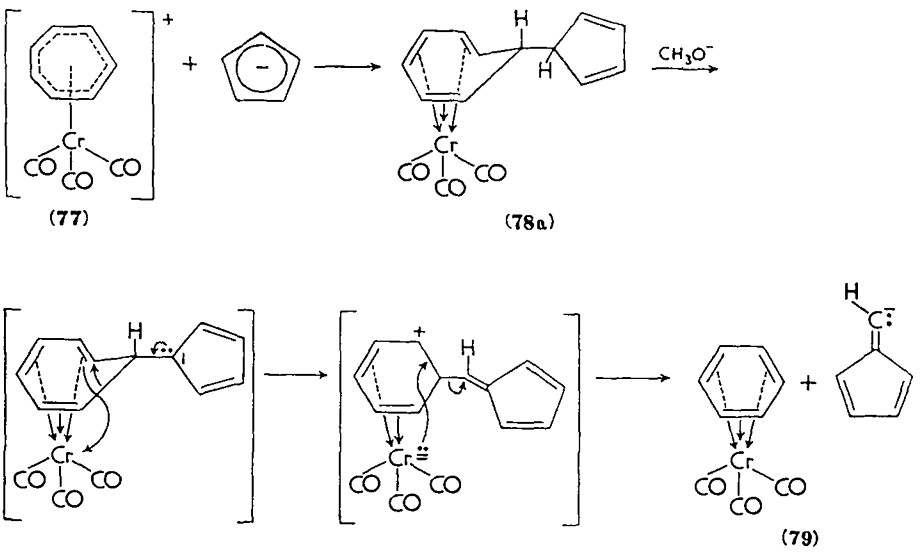
(77) (78)

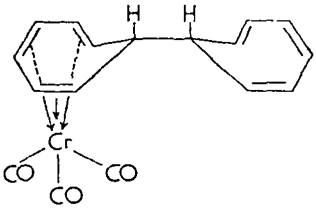
[R = H, OCH_3, SH, $C_6H_4C(CH_3)_3$, $CCH_3(CO_2C_2H_5)_2$]

positive charge resides largely on the seven-membered ring and the anions add to this ring as they do to the free tropylium ion.

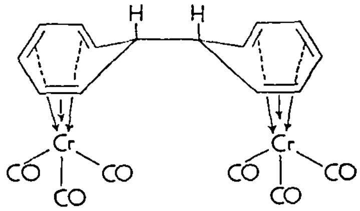
However, reaction of **77** with the cyclopentadienyl anion does not produce the cycloheptatriene complex **78a**; collapse of the seven-membered ring occurs with the formation[73] of benzenechromium tricarbonyl (**79**). This interesting reaction is thought[73] to take place by the mechanism shown.

A different result is obtained when the salt **77** is reacted with cyanide ion. In addition to a small amount of the expected derivative **78** (R = CN), the main products obtained from the reaction were shown[74] to have structures **80** and **81**. It has been suggested[74] that formation of **80** could be explained by postulating





(80)



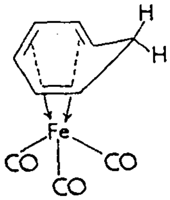
(81)

an initial attack by the anion on the metal atom followed by cleavage of the complex (prior to the coupling reaction which leads to the formation of **80** or **81**).

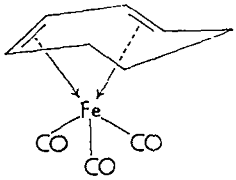
The reaction of cycloheptatriene with iron pentacarbonyl is even less straightforward than the reactions just described with the carbonyls of chromium and molybdenum. It was originally thought[75] that the complex isolated from the reaction between cycloheptatriene and iron pentacarbonyl had the expected structure $C_7H_8Fe(CO)_2$, by analogy with the molybdenum and chromium complexes. However, subsequent investigations[54,76] have shown that the expected dicarbonyl derivative is not formed in this reaction; instead, two major products are formed in amounts which vary with the reaction conditions. Heating equimolar amounts of cycloheptatriene and iron pentacarbonyl, under nitrogen, at 135° for one day yielded[77] a 19:1 ratio of $(C_7H_8)Fe(CO)_3$, **82**, and

$(C_7H_{10})Fe(CO)_3$, **83**. After five days, the same reaction conditions yielded[76] the complexes **82** and **83** in a ratio of 2:1. When the reaction was continued for seven days at 135–140°, a third complex ($C_{23}H_{16}Fe_3O_9$, **84**) was isolated[54] in addition to **82** and **83**.

On the basis of infrared and nuclear magnetic resonance spectra (see page 353), the cycloheptatriene complex $C_7H_8Fe(CO)_3$ has been assigned[54,76] structure **82** in which an —$Fe(CO)_3$ group is bound to two adjacent double bonds of the triene, leaving the third double bond uncoordinated. The complex $C_7H_{10}Fe(CO)_3$, on similar spectral evidence, was formulated as cyclohepta-1,3-dieneiron tricarbonyl (**83**) and is thought to be formed by hydrogen transfer to the coordinated triene system from excess of the triene under reaction conditions[54] or it may involve an iron carbonyl hydride intermediate[76]. The structure of the diene complex was confirmed[54,76] by direct preparation from cycloheptadiene and iron pentacarbonyl as well as by catalytic reduction of $C_7H_8Fe(CO)_3$, **82**.

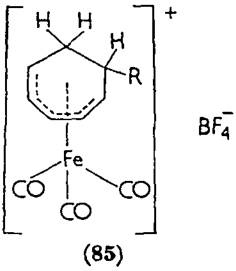


(82)



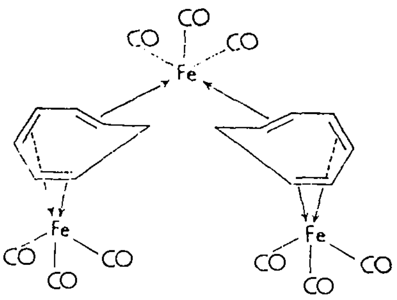
(83)

It is significant to note that the cycloheptatriene complex, **82**, reacts with triphenylmethyl fluoroborate to give a fluoroborate adduct which has been formulated[76] as **85** [R = —$C(C_6H_5)_3$].



(85)

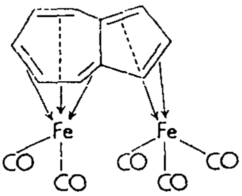
The same type of fluoroborate derivative, cycloheptadieniumiron tricarbonyl fluoroborate (**85**, R = H) is obtained[75] by hydride ion abstraction from the cycloheptadiene complex **83** or by the addition of fluoroboric acid, HBF_4 to the cycloheptatriene complex **82**.



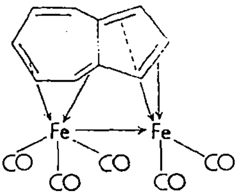
(84)

The crystalline trinuclear complex $C_{23}H_{16}Fe_3O_9$ has been speculatively formulated[54] as **84**.

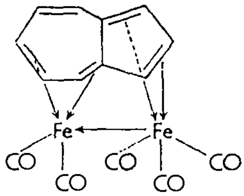
Azulene and substituted azulenes have been reacted[77] with iron penta- or dodecacarbonyl, with dimanganese decacarbonyl and with molybdenum hexacarbonyl. In order to interpret the structure of the complexes formed from the interaction between azulenes and metal carbonyls, the former may be regarded formally as consisting of cyclopentadiene and cycloheptatriene moieties. The complexes isolated in each case have been assigned[77] the structural formulae **86a–86c, 87** and **88a–88b**, respectively.



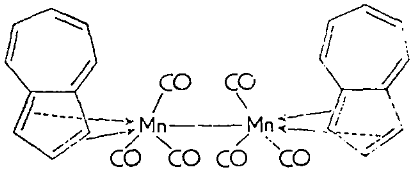
(86a)



(86b)



(86c)



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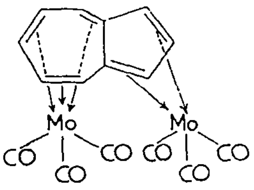
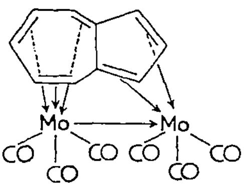


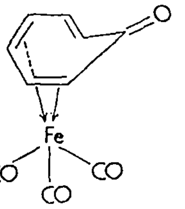
(88a)



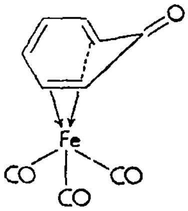
(88b)

It may be profitable to investigate further this interesting series of azulene complexes in order to obtain an unambiguous elucidation of their structure.

One of the compounds isolated from the reaction between acetylene and diiron enneacarbonyl, $Fe_2(CO)_9$, which analyzed into $C_7H_6OFe(CO)_3$ has been found[78] to be identical with the product obtained from the reaction between tropone (cycloheptatrienone) and triiron dodecacarbonyl, $Fe_3(CO)_{12}$. This complex was formulated as a troponeiron tricarbonyl derivative and at first it was envisaged[79] as a planar tropone ring with the iron bonding equally to all three double bonds of the ring. However, by analogy with the structure of cycloheptatrieneiron tricarbonyl, **82**, Weiss and Hübel[80] reformulated the tropone complex so as to have the iron atom bound to only two of the three double bonds. Such a structure could be represented by either formula **89** in which the two complexed double bonds remain in conjugation with one another or by formula **90** in which the two complexed double bonds are cross-conjugated through the ketonic carbonyl group.

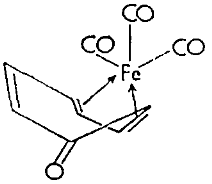


(89)



(90)

The infrared spectrum of the troponeiron tricarbonyl complex could be interpreted in favour of **89** rather than **90**. The ketonic carbonyl stretching frequency of the free tropone has been shown[81] to occur at 1582 cm^{-1}. By analogy with the cyclopentadienoneiron tricarbonyl complexes (see page 349), structure **90** may be expected to exhibit a lowering of this $\rangle C{=}O$ stretching frequency. However, the troponeiron tricarbonyl complex exhibits[80] the ketonic carbonyl absorption at 1637 cm^{-1}. This shift to a higher frequency may be ascribed to a change in the planarity of the molecule following the coordination of the *s*-butadiene moiety to the metal atom, thus leaving the α,β-unsaturated carbonyl group less conjugated to the complexed diene moiety. An exaggerated picture of this interpretation is depicted in **91**. A clearer picture of the structure of troponeiron tricarbonyl emerges from a recently



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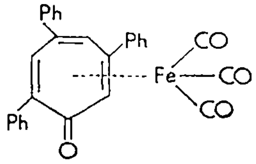


(92)

reported[19] x-ray structural analysis of a substituted tropone, 2,4,6-triphenylcycloheptatrienoneiron tricarbonyl[78] $[C_6H_3(C_6H_5)_3CO]$-$Fe(CO)_3$, **92.**

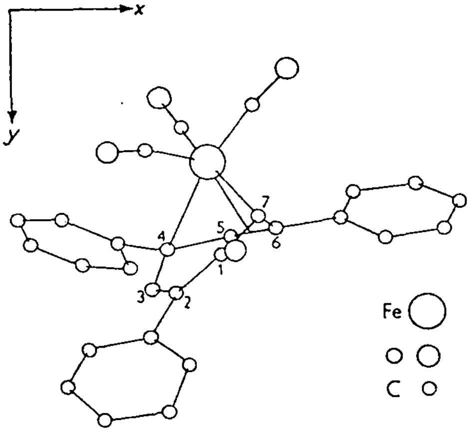
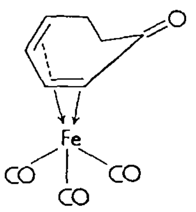


FIGURE 3. [001] Molecular projection of $[C_6H_3(C_6H_5)_3CO]Fe(CO)_3$. Bond distances for the tropone ring are 1·45 and 1·49 Å for $C_{(4)}$—$C_{(5)}$ and $C_{(6)}$—$C_{(7)}$ respectively; 1·38 Å for $C_{(5)}$—$C_{(6)}$, 1·34 Å for the normal double bond $C_{(2)}$—$C_{(3)}$, 1·44 Å (av.) for the other three bonds, and 1·26 Å for $C_{(1)}$—O (all with e.s.d. ±0·02 Å). Fe—C distances are 2·17, 2·00, 2·09 and 2·13 Å to carbon atoms $C_{(4)}, \ldots, C_{(7)}$ respectively; iron distances to the midpoints of $C_{(4)}$—$C_{(5)}$, $C_{(5)}$—$C_{(6)}$ and $C_{(6)}$—$C_{(7)}$ are 1·96, 1·93 and 1·98 Å respectively. Other non-bonding iron-tropone distances are Fe...$C_{(1)}$ = 2·97 Å, Fe...$C_{(2)}$ = 3·46 Å and Fe...$C_{(3)}$ = 3·12 Å. Fe—C (carbonyl) = 1·73 Å(av.), C—O = 1·18 Å (av.) (all with e.s.d. ±0·02). C—C bond lengths in phenyl rings range from 1·31 to 1·51 Å (e.s.d. ±0·03) with average length 1·40 Å. Bond angles are $(C_6H_5)\text{-}\hat{C}_{(4)}\text{-}C_{(5)}$ = 118·2°, $(C_6H_5)\text{-}\hat{C}_{(4)}\text{-}C_{(3)}$ = 112·2°, $C_{(3)}\text{-}\hat{C}_{(4)}\text{-}C_{(5)}$ = 122·4°, $C_{(4)}\text{-}\hat{C}_{(5)}\text{-}C_{(6)}$ = 124·3, $C_{(5)}\text{-}\hat{C}_{(6)}\text{-}C_{(7)}$ = 116·2, $(C_6H_5)\text{-}\hat{C}_{(6)}\text{-}C_{(5)}$ = 126·0, $(C_6H_5)\text{-}\hat{C}_{(6)}\text{-}C_{(7)}$ = 117·5°, $C_{(6)}\text{-}\hat{C}_{(7)}\text{-}C_{(1)}$ = 129·5°, $C_{(7)}\text{-}\hat{C}_{(1)}\text{-}C_{(2)}$ = 125·0°, $C_{(1)}\text{-}\hat{C}_{(2)}\text{-}C_{(3)}$ = 121·8°, $(C_6H_5)\text{-}\hat{C}_{(2)}\text{-}C_{(1)}$ = 117·3, $(C_6H_5)\text{-}\hat{C}_{(2)}\text{-}C_{(3)}$ = 119·9, $C_{(2)}\text{-}\hat{C}_{(3)}\text{-}C_{(4)}$ = 127·7° (all with e.s.d. ± 1·6°). The dihedral angle between the two planes in the tropone ring is 139°. [Reprinted, by permission, from D. L. Smith and L. F. Dahl, *J. Am. Chem. Soc.*, **48**, 1743 (1962).]

The intramolecular distances (see Figure 3) clearly indicate bonding of the —$Fe(CO)_3$ moiety with only two of the three double bonds of the ring. This causes a bending of the tropone ring at atoms $C_{(4)}$ and $C_{(7)}$ into two approximate planes: one plane contains the *s*-diene carbon atoms $C_{(4)}$, $C_{(5)}$, $C_{(6)}$ and $C_{(7)}$; the remaining ring atoms are contained in the other plane. Most surprising is the finding that the $C_{(4)}$ atom does *not* lie in the localized plane of its three bonded carbons, being located about 0·22 Å above this plane. The central diene atoms ($C_{(6)}$ and presumably $C_{(5)}$) are planar with their immediate neighbors. The distortion of the terminal $C_{(4)}$ (and presumably $C_{(7)}$) atoms towards sp^3 hybridization has prompted Smith and Dahl[19] to favor a representation based on a three point attachment of the *s*-diene moiety to the iron atom, *via* two σ-alkyl bonds and an additional bond to the central olefinic group, such as depicted by Wilkinson and coworkers[17] for butadieneiron tricarbonyl in **5** (page 338). The actual electron-density distribution, however, would involve contributions from both formal structures. The final decision on the interpretation of the x-ray analysis data will have to take into consideration the chemical evidence.

Weiss and Hübel[80], who favor structure **89** for troponeiron tricarbonyl have shown that catalytic hydrogenation of **89** in both polar and non-polar solvents (at 40–70°, under pressure), produces two isomeric cycloheptadienoneiron tricarbonyl derivatives, formulated as **93** (~60% yield) and **94** (~20% yield). Compound **93** shows a ketonic carbonyl stretching frequency at 1661 cm^{-1} (*i.e.* disappearance of the uncoordinated α,β-unsaturated bond). The second isomer was formulated as **94** because it showed a non-conjugated ketonic carbonyl absorption at 1712 cm^{-1}. The formation of **94** from **89** implies a rearrangement of the coordinated π-bonds during the hydrogenation reaction. It is also pertinent to add that all three complexes, **89**, **93** and **94** readily form 2,4-dinitrophenylhydrazone derivatives.



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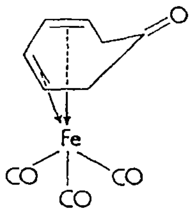
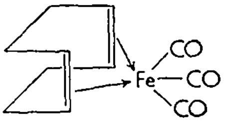


(94)

VI. METAL π-COMPLEXES OF EIGHT-MEMBERED HOMOCYCLIC COMPOUNDS

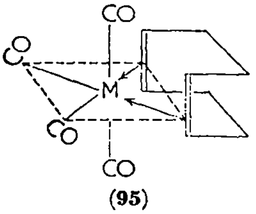
Eight-membered ring compounds discussed in this section are cyclooctadienes, cyclooctatrienes and cyclooctatetraene.

It has already been mentioned (page 339) that interaction between cycloocta-1,5-diene and iron pentacarbonyl produces[20a] the unstable complex cycloocta-1,5-dieneiron tricarbonyl, **8**. On the other hand it has been reported[20b] that heating equimolar quantities of cycloocta-1,5-diene and iron pentacarbonyl yields quantitatively cycloocta-1,3-diene. Subsequent work[20b] has further shown that even catalytic amounts of $Fe(CO)_5$ are sufficient to effect complete isomerization of the non-conjugated to the conjugated cyclooctadiene. It is significant to note that no cycloocta-1,3-dieneiron tricarbonyl has been isolated by these workers[20b] from this reaction, although in other cases of known isomerizations with iron carbonyls[20] the isomerized conjugated diene has been isolated in the form of a metal complex (page 339).



(8)

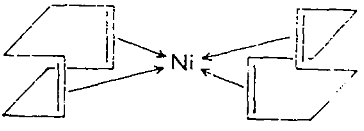
The interest in 1,5-cyclooctadiene as a ligand in metal complexes may be seen as due mainly to the fact that it can serve as a model of a non-conjugated cyclic diene and thus may offer the possibility of pertinent comparisons. Interaction of cycloocta-1,5-diene with carbonyls of Group VI metals results[82-84] in the formation of compounds of the general structure $C_8H_{12}M(CO)_4$ (**95**, M = Cr, Mo, W). The infrared spectra[82-84] of these compounds show three carbonyl stretching modes in the region 2050–1895 cm^{-1} and the nuclear magnetic resonance spectrum[83] shows two absorptions,



(95)

at 2·43 p.p.m. (—CH_2 protons) and 4·59 p.p.m. (=CH protons) on the low-field side relative to $Si(CH_3)_4$. The relatively slight changes in the n.m.r. spectrum of **95** as compared to the free diene (2·31 p.p.m. and 5·53 p.p.m.) indicate that the double bonds of the diene act independently of one another, *i.e.* there is very little or no delocalization between the double bonds, and they are not greatly changed by coordination.

The ability of cycloocta-1,5-diene to act as an olefinic ligand is further shown in the suggested structure **96** for the recently[85,86] reported bis(cycloocta-1,5-diene)nickel(0), as well as in the stable derivative[87] cycloocta-1,5-dienecyclopentadienylrhodium, C_8H_{12}-RhC_5H_5 (**97**).



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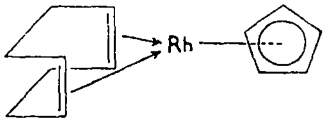
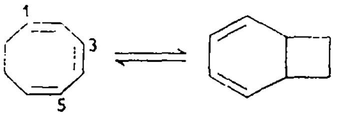
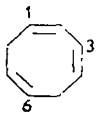


(97)

Two isomeric cyclooctatrienes, the 1,3,5-triene (**98**) and the 1,3,6-triene (**99**) have to be considered in discussing metal complexes of this eight-membered cyclic triene. Moreover, it has been established[88] that cycloocta-1,3,5-triene (**98a**) is found in mobile equilibrium with the valence tautomer bicyclo[4.2.0]octa-2,4-diene, **98b**. Since all three isomeric forms have conjugated diene structures, they may all be expected to form π-metal complexes.

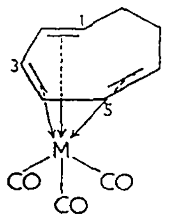


(98a) **(98b)**

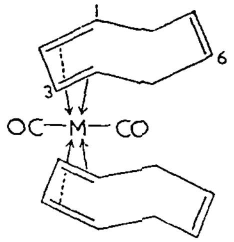


(99)

Interaction of a freshly prepared mixture of the cycloocta-1,3,5- and -1,3,6-triene isomers with the carbonyls of Group VI metals results in the formation of two compounds to which structures **100** and **101** have been assigned[89]. The correctness of structure **100** for 1,3,5-cyclooctatrienechromium tricarbonyl has been confirmed by a recent x-ray analysis of this compound[90]. This study shows that the structure of **100** with M = Cr resembles that found[69] for tropylidenemolybdenum tricarbonyl (**83**, M = Mo, R = H). The conjugated system of the hydrocarbon is approximately planar and



(**100**, M = Cr, Mo)



(**101**, M = Mo, W)

is situated on the opposite side of the metal atom to the carbonyl groups; the latter form an irregular pyramid. The methylene groups of the hydrocarbon are on the opposite side of the conjugated system to the metal atom.

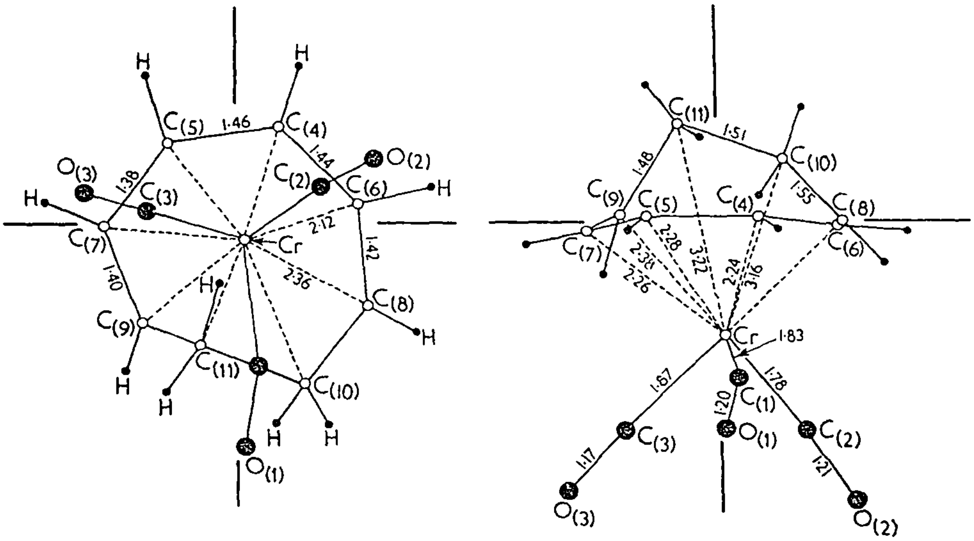
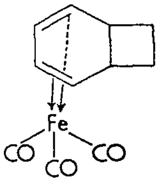


FIGURE 4. Tricarbonyltricyclooctatrienylchromium molecule projected onto the best plane through the six near-planar carbon atoms of the conjugate system, and a projection perpendicular to this plane. Some interatomic distances are given (in Å). [Reprinted, by permission, from V. S. Armstrong and C. K. Prout, *J. Chem. Soc.*, 3772 (1962).]

From the interaction of the same mixture of isomeric cyclooctatrienes with iron pentacarbonyl, a compound of composition $C_8H_{10}Fe(CO)_3$ has been isolated by two independent groups[89,91]. Fisher and coworkers[89] considered this complex to be cycloocta-1,3,6-trieneiron tricarbonyl on the basis of a comparison of its infrared spectrum with the spectra of compounds **100** and **101**.



(102)

Stone and coworkers[91,92], on the other hand, proposed structure **102** on the basis of thermal degradation of the compound, yield data and the failure of **102** to absorb hydrogen over platinum catalyst. Moreover, the latter workers have reported[92] that by treating cycloocta-1,3,5-triene with triiron dodecacarbonyl in refluxing benzene, it is possible to obtain two different iron complexes of composition $C_8H_{10}Fe(CO)_3$. The compound obtained in higher yield (24%) was identical with that obtained from the reaction with iron pentacarbonyl and to which structure **102** has been assigned. The second compound, obtained in a much lower yield (5%) is less stable in air than **102** and on heating with iron pentacarbonyl it is converted into **102**. If structure **102** is the correct one for the more stable isomer, the less stable one might be the iron tricarbonyl complex of either cycloocta-1,3,5-triene (**98a**) or of cycloocta-1,3,6-triene (**99**). However, preparation of both isomers from 94% pure cycloocta-1,3,5-triene might be construed to indicate that cycloocta-1,3,6-triene is not involved in the formation of the complexes. Further evidence is needed for final elucidation of these structures.

Cyclooctatetraene represents a specially interesting case. It is now generally accepted that the structure of cyclooctatetraene is best represented by the puckered tub (D_{2d}) formulation[93] **103**.

(103)

This structure, which is practically strainless, prevents appreciable interaction of the formally conjugated double bonds and forms instead a system of four 'isolated' double bonds.

An x-ray diffraction study[94] has shown that the D_{2d} tub structure is retained also in the cyclooctatetraene silver complex, $(C_8H_8Ag)NO_3$. The strongest bonding in the complex is between one Ag^+ and one C_8H_8 molecule, and these units $(C_8H_8)Ag^+$ are then joined more weakly into infinite chains along the *c* axis of the crystal.

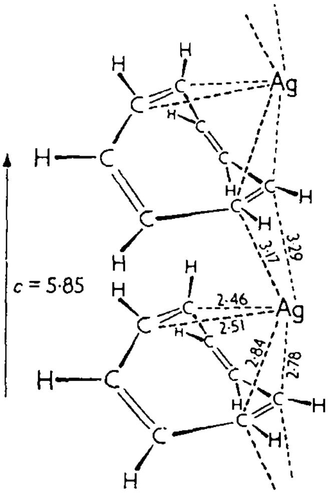
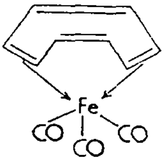


FIGURE 5. The structure of the $Ag^+ (C_8H_8)$ complex as determined by x-ray analysis. Distances are in Å. [Reprinted, by permission, from F. S. Mathews and W. N. Lipscomb, *J. Am. Chem. Soc.*, **80**, 4746 (1958).]

The reaction of cyclooctatetraene with iron pentacarbonyl has been investigated independently by several groups[95-99]. The reaction affords the isolation of two complexes, a monoiron complex $C_8H_8Fe(CO)_3$, **104**, and a diiron complex $C_8H_8Fe_2(CO)_6$, **105**. The main differences in the reports of the various research groups lie in the interpretation of the structure of the isolated complexes.

On the basis of ultraviolet and infrared spectroscopic data, Nakamura and Hagihara[95] proposed structures **106** and **107** for the monoiron and diiron complexes respectively.

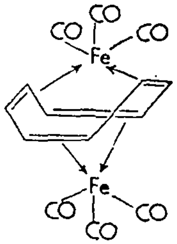
Manuel and Stone[98,99] report for the infrared spectrum of $C_8H_8Fe(CO)_3$ a single sharp strong absorption, in the carbon–hydrogen stretching region, at 3012 cm^{-1} (in CS_2) and a single



(106)

Ultraviolet[95] (95% C_2H_5OH):
$\lambda_{max} = 300$ mμ ($\log \varepsilon = 3{\cdot}99$)

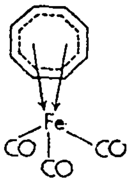
Infrared[95] (KBr): $\nu_{C\equiv O} = 2050, 1961\ cm^{-1}$
$\nu_{cis\text{-}C=C} = 720, 716, 699\ cm^{-1}$



(**107**)

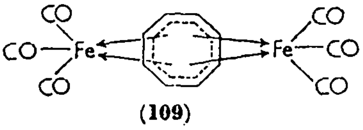
Ultraviolet[95] (95% C_2H_5OH):
$\lambda_{inf.}$ = 258 mμ (log ε = 3·15
Infrared[95] (KBr): $\nu_{C\equiv O}$ = 2035, 1972 cm^{-1}
(no bands in the 700 cm^{-1} region)

proton resonance in the nuclear magnetic resonance spectrum of this compound. A mixture of $C_8H_8Fe(CO)_3$ in glacial acetic acid and platinum catalyst did not absorb any hydrogen. They also suggested, on the basis of spectral evidence and chemical considerations a planar or nearly planar cyclooctatetraene ring in the structure of the two complexes, as may be depicted in **108** and **109**.



(**108**)

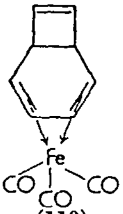
Ultraviolet[99] (C_6H_{12}):
λ_{max} = 304 mμ (ε = 11,500)
Infrared[99] (CS_2): $\nu_{C\equiv O}$ = 2051, 1992,
1978 cm^{-1}
$\nu_{C=C}$ = 1416 cm^{-1}



(**109**)

Ultraviolet[99] (C_8H_{12}): λ_{max} = 256 mμ
(ε = 22,700)
359 mμ
(ε = 5,320)
Infrared[99] (CS_2): $\nu_{C\equiv O}$ = 2047, 1984 cm^{-}
$\nu_{C=C}$ = 1414 cm^{-1}

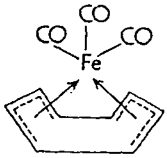
Rausch and Schrauzer[97], whose spectral data are in agreement with those of Manuel and Stone[99], exclude the possibility that the C_8H_8 moiety in $C_8H_8Fe(CO)_3$ is present as bicyclo[0.2.4]octa-2,4,7-triene, such as shown in **110**, on the basis of the single proton resonance of the compound, and these authors suggest that all four double bonds of the C_8H_8 moiety in $C_8H_8Fe(CO)_3$ are affected by π-complex formation.



(**110**)

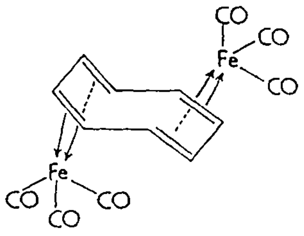
In a discussion of the structures of the two complexes $C_8H_8Fe(CO)_3$ and $C_8H_8Fe_2(CO)_6$ in terms of simple molecular-orbital theory, Cotton[100] states that the possibility of the C_8H_8 being planar in both compounds is consistent with effective metal-to-ring bonding of a delocalized 'sandwich' type.

A spectroscopic investigation, including infrared, ultraviolet and nuclear magnetic resonance, of eight cyclooctatetraene metal complexes including the iron carbonyl derivatives, has led Fritz and Keller[101] to suggest that in addition to the planar configuration of C_8H_8 in $C_8H_8Fe(CO)_3$ it is possible to consider a 'pseudo-dibutadiene' tub-like structure such as depicted in **111**.



(**111**)

It remained for x-ray analysis studies to settle this controversy and, as had happened so often in the past with x-ray studies, the answer when it arrived proved to be a complete surprise. In the first compound to be studied, $C_8H_8Fe_2(CO)_6$, Dickens and Lipscomb[102] have shown that the form of the cyclooctatetraene moiety is neither tub nor crown but an eight membered 'chair' form such as drawn in **112** (or better in Figure 6). Each set of four



(112)

carbons forms a planar, or nearly planar group, somewhat like butadiene, and with each such set there is associated an $Fe(CO)_3$ group. There seems to be little or no π–π interaction between the two halves of the cyclooctatetraene complex. There appears to be octahedral coordination around the Fe atoms since the three C—C bonds are staggered with respect to the three CO groups around each corresponding Fe atom.

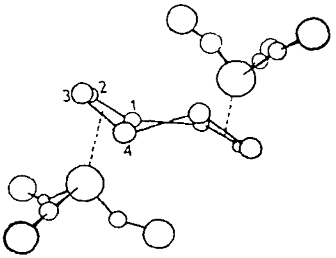


FIGURE 6. The $(OC)_3Fe(cyclooctatetraene)Fe(CO)_3$ molecule. Bond distances average to 1·39 Å for the two central bonds, and 1·44 Å for the other four C—C bonds, all ±0·03 Å. Fe...C distances are 2·06 Å to the end carbon atoms (bonded together) and 2·15 Å to the central four carbon atoms, to be compared with 2·05 Å for Fe...C in ferrocene. The average Fe—C and C≡O distances are 1·76 Å and 1·15 Å, respectively, in the Fe—C≡O groups. [Reprinted, by permission, from B. Dickens and W. N. Lipscomb, *J. Am. Chem. Soc.*, **83**, 4862 (1961).]

The surprise evoked by the proof of the unsuspected chair form for the geometry of C_8H_8 in $C_8H_8Fe_2(CO)_6$ was perhaps surpassed when yet another geometry, not considered by any of the other workers, was found[103] to occur for the cyclooctatetraene ring in $C_8H_8Fe(CO)_3$. Dickens and Lipscomb have shown that the $Fe(CO)_3$ group is attached to a butadiene part of the C_8H_8 ring in such a way that six of the eight atoms of the ring are very nearly coplanar, and this plane makes an angle of 41° with the plane of the 'butadiene' part which is complexed to the metal. This is best seen in Figure 7.

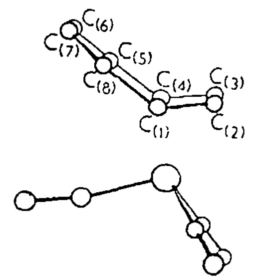


FIGURE 7. The structure of $C_8H_8Fe(CO)_3$. Bond distances are $C_{(1)}—C_{(2)} = C_{(3)}—C_{(4)} = 1{\cdot}42$ Å, $C_{(2)}—C_{(3)} = 1{\cdot}42$ Å, $C_{(4)}—C_{(5)} = C_{(1)}—C_{(8)} = 1{\cdot}45$ Å, $C_{(5)}—C_{(6)} = C_{(7)}—C_{(8)} = 1{\cdot}34$ Å, $C_{(6)}—C_{(7)} = 1{\cdot}49$ Å, Fe—C (carbonyl) = 1·80 Å (av.), C—O = 1·13 Å (av.), all ± about 0·02 Å. Bond angles are $C_{(1)}\text{–}\widehat{C}_{(2)}\text{–}C_{(3)} = C_{(2)}\text{–}\widehat{C}_{(3)}\text{–}C_{(4)} = 124{\cdot}6°$, $C_{(3)}\text{–}\widehat{C}_{(4)}\text{–}C_{(5)} = C_{(2)}\text{–}\widehat{C}_{(1)}\text{–}C_{(8)} = 132{\cdot}4°$, $C_{(4)}\text{–}\widehat{C}_{(5)}\text{–}C_{(6)} = C_{(1)}\text{–}\widehat{C}_{(8)}\text{–}C_{(7)} = 133{\cdot}2°$, $C_{(5)}\text{–}\widehat{C}_{(6)}\text{–}C_{(7)} = C_{(8)}\text{–}\widehat{C}_{(7)}\text{–}C_{(6)} = 131{\cdot}8$, all ± about 1°, and to be compared with 135° in the regular plane octagon. The angle between normals to the two planes in C_8H_8 is 41° in $C_8H_8Fe(CO)_3$. [Reprinted, by permission, from B. Dickens and W. N. Lipscomb, *J. Am. Chem. Soc.*, **83**, 4862 (1961).]

The two complexes, $C_8H_8Fe(CO)_3$ and $C_8H_8Fe_2(CO)_6$ have been used[104] as absorbers in a Mösbauer resonance experiment[105], and the results indicate[104] that the charge density of the delocalized π-electrons is essentially the same in the C_4 residues of $C_8H_8Fe(CO)_3$ as in the two C_4 residues in $C_8H_8Fe_2(CO)_6$ to which the iron atoms are bonded.

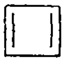
Still lacking is an explanation that will bring into accord the infrared and nuclear magnetic resonance spectral data with the structures which have emerged from the x-ray analysis studies.

VII. CONCLUSION

An attempt has been made in this chapter to present a bird's eye view of an exciting new field in the chemistry of olefins. The developments in the chemistry of hydrocarbon derivatives of transition metals are taking place at such a rapid pace that it is quite possible this review may have become obsolete by the time it reaches print. Furthermore, in view of the innumerable surprises which are constantly cropping up, it would be unwise to try to predict which is the most likely area of massive development in this branch of chemistry. Nevertheless, some comments can be ventured without running too much of a risk of being proved a false prophet.

There are good reasons to think that one of the more important lines for future development from the point of view of the organic chemist may consist in the use of the new organometallics as intermediates in organic synthesis. This may be applied either to the synthesis of known compounds by new methods or to the synthesis of new structural systems which may be incapable of existing in the free state but may be found to be capable of giving stable metallic complexes. To stress this latter aspect two such examples may be given, in addition to those already mentioned in the text (see *e.g.* cyclopentadienone).

The first example will refer to cyclobutadiene, **113**. As late as 1958, M. J. S. Dewar stated[106], 'Cyclobutadiene would have a negative resonance energy and I cannot encourage anyone to try to make it'. On the other hand, in 1956 Longuet-Higgins and Orgel predicted[107] that cyclobutadiene may be capable of existence in the form of a stable transition metal complex. This prediction was proved correct in 1959 when Criegee and Schroeder[108] reported the synthesis of tetramethylcyclobutadienenickel dichloride, by reacting 1,2-dichlorocyclobutene with nickel tetracarbonyl, and when Dunitz and coworkers in 1960 confirmed[109,110] the cyclobutadiene structure in the complex **114** by x-ray analysis. Several more derivatives of cyclobutadiene metal complexes have since been reported[3b,9].



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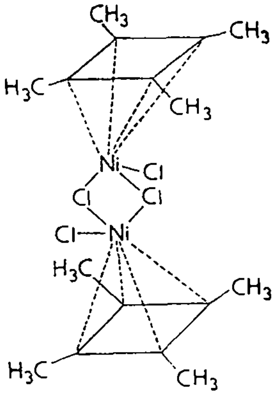
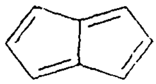
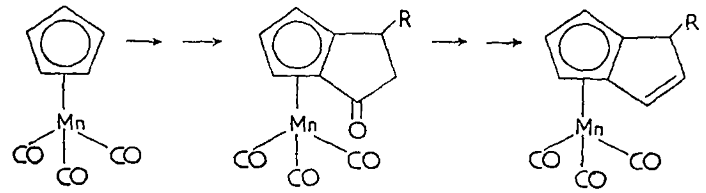


(114)

The second example refers to the case of pentalene, **115**. Attempts to synthesize this compound have been unsuccessful for


(115)

nearly forty years[111]. Using the Longuet-Higgins and Orgel prediction[107] for cyclobutadiene as a guide, Cais and coworkers began work in 1958 in an attempt to synthesize a metal complex derivative of the pentalene system. Starting with cyclopentadienylmanganese tricarbonyl (**68**), these workers prepared[112,113] the two dihydropentalenyl derivatives **117a** and **117b**. Then, using 2,3-



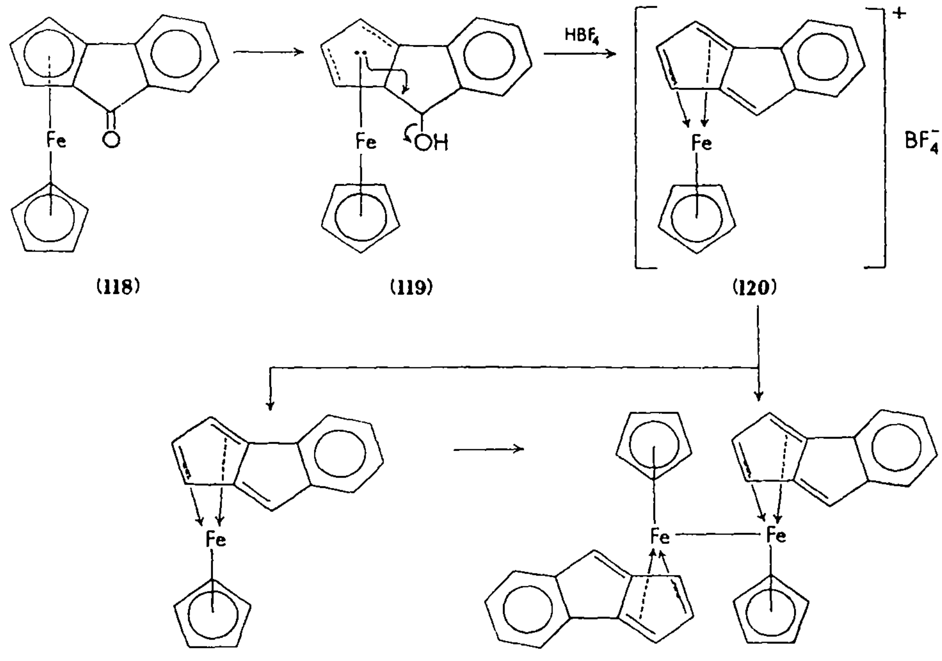
(**116a**, R = H; **116b**, R = CH_3.) (**117a**, R = H; **117b**, R = CH_3.)

ferrocoindenone[115] (**118**) as model compound for application to the problem in hand, Cais and coworkers[114] reduced the ketone **118** to the alcohol **119** and followed this by solvolysis in HBF_4[116] to obtain the benzpentalenylium salt **120**. The latter might, upon reduction, yield the not yet known benzpentalene structure **121** or **122**.

Using the same series of reactions starting with the ketone **116** and going through the intermediate unsaturated ketones **123**, it has been possible to prepare the two pentalenylium complexes **124a** and **124b**. The latter two might serve as starting materials for the synthesis of the two neutral compounds **125a** and **125b** (or the dimers analogous to **122**).

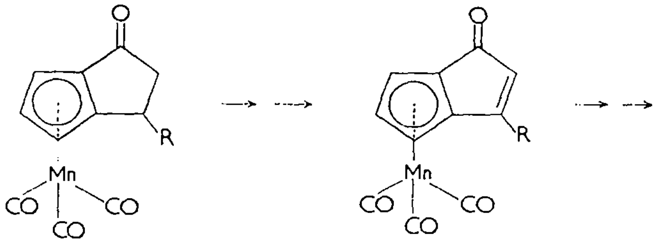
Preliminary reduction experiments[114] with **120** have yielded a compound which, on the basis of ultraviolet, infrared and n.m.r. spectroscopy as well as molecular weight determination, appears to have the structure depicted in **126**.

In addition to such possible applications to synthesis, one can say that the knowledge acquired from the structural elucidations of the



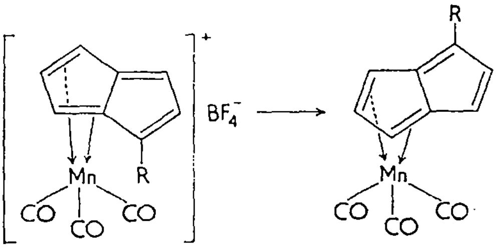
(118) (119) (120)

(121) (122)



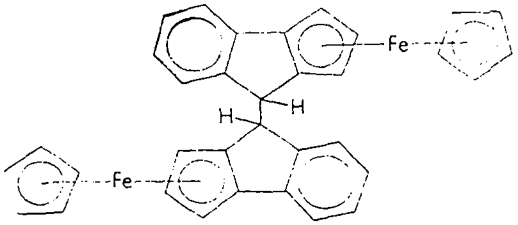
(116)

(123a, R = H;
123b, R = CH_3)



(124a, R = H;
124b, R = CH_3)

(125a, R = H;
125b, R = CH_3)



(126)

many new compounds described in the text cannot but have a very strong impact in future developments on the theory of chemical bonding.

The possible commercial uses of some of the new compounds *per se* have yet to be demonstrated. It may prove to be worthwhile investigating the properties of the new organometallics as potential semiconductors. There should not be much doubt that important commercial uses will eventually be found.

In the meanwhile there may be lots of fun for the chemists working in this exciting new field of hydrocarbon–metal complexes.

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 7

Alkene rearrangements

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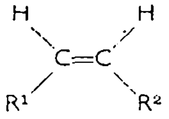
I. *CIS–TRANS* ISOMERISM

A. Introduction

Trigonally hybridized carbon is characteristic of ethylenic linkages; in this state it has three singly occupied sp^2 orbitals available for bonding whose axes lie in the same plane and at 120° to each other, whilst normal to this plane there is a singly occupied p_z orbital. Overlap between two coaxial hybrid orbitals of different carbon atoms generates a σ-bond, and in the position of minimum energy overlap of the two p_z orbitals of the adjacent carbon atoms is as complete as possible, constituting a π-bond. In each case the electron pairs constituting the bonds have their electron spins coupled, *i.e.* antiparallel. In order to maintain maximum π-orbital overlap, this situation requires that the remaining four hybrid bonds to end-groups shall as far as possible remain in the same plane. Rotation about the central σ-bond is therefore restricted, the origin of the barrier to rotation lying in the consequent reduction in π-orbital overlap. The possibility of stereoisomerism therefore arises, since rotation through 180° about the σ-bond gives a new stable planar array, as first deduced, although from rather different reasoning, by van't Hoff[1]. It follows that substituted ethylenes can exist in the isomeric forms generalized in the formulae **1** to **4**.



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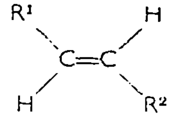

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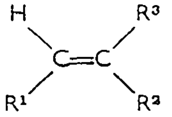

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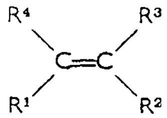


(4)

($R^2 \not\equiv R^3$ and $R^1 \not\equiv R^4$, but R^1 may be identical to R^2)

The position is essentially the same if the groups R^1, R^4, R^2, R^3 are fused into ring systems, as in the unsymmetrical fulvenes and fulvalenes. This account will, however, be mainly concerned with isomers of the types **1** and **2**, first designated as '*cis–trans*' isomers by Baeyer[2].

The interconversion of pure geometrical isomers to equilibrium mixtures containing both isomers (one of them sometimes preponderating) is a common experience in organic chemistry. Poutet observed such a change when he shook olive oil (largely the *cis*-olefin, triolein) with a reagent in which the active principle was nitrous acid, and obtained a solid product—the *trans* isomer[3]. Later, the stereomutation of maleic acid was observed to be catalysed by acids and salts[4], as were the isomerization of isocrotonic acid[5], isocinnamic acid[6] and citraconic acid[7]. Stereomutation was also realized by heating the pure isomers, and it is now known that the position of equilibrium between the two forms depends upon their relative thermodynamic stability. Mixtures resulting from the interconversion of isomers under the influence of radiation, however, often contain larger than usual proportions of the less stable isomer. This comes about because the photochemically excited molecules spend most of their time in phases of high potential, and, on returning to the ground state, that isomer predominates whose configuration corresponds most closely with that pertaining to the excited state[8]. Frequently, catalysts are employed for facilitating photochemical stereomutation; common ones include elements of high atomic number such as bromine and iodine.

The early work on the kinetics of thermal stereomutation of unsaturated esters and related compounds[9] revealed two distinct types of reaction with unimolecular rate coefficients expressed approximately as $k_1 = 10^{11} \times e^{-45,000/kT}$ and $10^4 \times e^{-25,000/kT}$. It is suggested that the latter group of reactions are most likely those which proceed by a non-adiabatic pathway[10], *i.e.* the molecules stereomutating must change from one potential to another with which the first interacts only in a second order of approximation; this corresponds to the low value of the preexponential factor. In the former class, the reactions are slower than most unimolecular processes (for which the preexponential factor is usually about 10^{13}) but are probably adiabatic.

In both cases, the transition state is reached when the two p_z orbitals constituting the original π-bond are perpendicular to each other. The simplest view of the excitation process which leads to stereomutation is that one of the electrons from the bonding π-orbital passes to the higher energy antibonding orbital formed by the alternative combination of atomic p_z orbitals. The molecular wave function, excluding spin, is now antisymmetric and, because of the Pauli exclusion principle, the spin function for the electrons must be symmetric. The ground state configuration is now unstable since the antibonding electron more than neutralizes the effect of the bonding electron so that the position of minimum energy is achieved by twisting the molecule through 90°, resulting in minimum overlap of the bonding and antibonding orbitals. During this process, the triplet level therefore becomes the more stable state, and it ought to be possible for molecules to pass from the singlet to the triplet level during rotation; but the chance of this happening is reduced because, at the crossing points of the potential curves, the energy states do not exactly correspond. Alternatively, linear combination of the bonding and antibonding π-orbitals can give a series of hybrid orbitals in pairs, the electrons occupying the lowest available level. In non-planar ethylene this means that one of the hybrid orbitals will have an energy lower than that of either of the simple π-orbitals, so that, as the rotation proceeds, the molecule passes through a succession of states into the excited orbital, which at the perpendicular configuration is more stable than the normal bonding orbital. The result of this type of hybridization is that the energy required to rotate the molecule through 90° is lower than would otherwise be required. In this process, the spins of the electrons remain coupled and the transition is from a lower to an upper singlet level, being associated with those reactions having a relatively large energy of activation and a preexponential factor of 10^{11}. Once the molecule reaches the excited singlet state, the electrons occupy separate orbitals and accordingly may uncouple their spins, giving rise to the triplet state; but for the reasons previously mentioned, the chance of this happening is small[11], and this process corresponds to those reactions having a low energy of activation and a frequency factor of 10^4. In both processes, the energy of activation depends upon the difference between the bonding and antibonding π-orbital energies.

It is clear from the nature of the ethylenic double bond and the mode of its stereomutation that a wide range of stability of isomers of types **1** and **2**, for example, would be expected, depending upon the electronic and steric nature of the substituents R^1 and R^2. The energy difference between the bonding and antibonding π-orbitals will determine the energy of activation for stereomutation, which will therefore be proportional to the energy of light absorption. Consequently, in conjugated systems, *cis–trans* isomerization will be facilitated. This becomes clearly apparent in the polyene compounds considered below. Generally speaking, the *trans* isomer is the more stable of a pair on account of steric and dipolar interactions in the *cis* form, but this is by no means always true, and some examples of cases where the *cis* isomer is actually the more stable of a pair will be discussed later.

B. Thermal and Photochemical Stereomutation

I. Alkylethylenes

The thermal isomerization of *cis*-2-butene was among the first stereoisomeric systems to be examined kinetically. Kistiakowsky and Smith[12] found an anomalous value for the activation energy, which has since been attributed to the method of product analysis[13]. The reaction has been examined more recently[13,14] and found to be a first-order process with essentially normal preexponential factor and activation energy typical of the singlet mechanism. The reaction is catalysed in the gas phase by additives which seem likely to activate the triplet process, *e.g.* nitric oxide[15], which reduces the activation energy by as much as 50%. In cases such as this, and where heavy-atom catalysts are employed, a probable explanation of their action is that the magnetic field round the catalytic species causes perturbation of the energy levels in the olefin, allowing singlet–triplet transitions to occur with greater frequency. In other cases, catalytic action involves chemical binding.

The thermal stereomutation of *cis*-ethylene-d_2, the simplest possible case, is also a homogeneous unimolecular process under specified pressure conditions with essentially singlet kinetic parameters[16]. Again, catalysis by nitric oxide and free radicals is observed.

Specific attempts to detect triplet states as intermediates in stereomutations have been made by a number of workers. For example, it has been suggested that the transition from singlet to triplet level might be catalysed by paramagnetic substances, which could act unequally on the magnetic dipoles of the π-bond by providing a non-homogeneous field[17]; or similarly by a catalyst in any other than a singlet state, which might then interact favourably with the substrate[18]. In experiments based on these suggestions, however, the effects observed have proved to be very small, *e.g.* when using rare earth halides as catalysts for the stereomutation of maleic acid[19]. Very recently, investigations into the effect of added inert gases on the isomerism of *cis*-2-butene have revealed that xenon is a very efficient catalyst which may in part be due to the heavy-atom effect[20], surprisingly absent in the presence of stable organic iodides in similar cases.

Greater success has attended investigation into photosensitized stereomutations. In the presence of certain carbonyl compounds such as acetophenone, benzil, *etc.*, irradiation of pure stereoisomers leads to *cis–trans* mixtures whose compositions vary with the sensitizer; for example, piperylene in the presence of benzophenone gives a mixture rich in *trans* isomer (*trans/cis* ratio 1·23) whilst in the absence of sensitizer the reaction is very slow and a much smaller *trans/cis* isomer ratio is observed (0·33). Under these conditions, the excited carbonyl compound in the triplet state transfers energy to the olefin which subsequently isomerizes[21]. A more decisive test for the participation of induced triplet molecules in stereomutations is to have another species present with which an exchange of multiplicity can occur (equation 1). If a triplet intermediate T_1 is involved in

$$T_1 + S_2 \rightleftharpoons S_1 + T_2 \qquad (1)$$

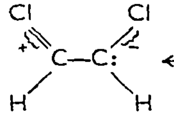
the stereomutation of an olefin, exchange of this kind should suppress the reaction if the triplet formed T_2 is relatively unreactive. By choosing the components correctly, it is possible to ensure that multiplicity exchange occurs at every collision. This kind of situation has been realized with the photochemical stereomutation of *cis*-dichloroethylene: the reaction is quenched by *cis*-2-butene, which does not absorb radiation itself at the wavelength used, but without isomerization of the butene. Isomerization does occur at lower pressures, however, and the high-pressure process corresponds to deactivation of excited singlet dichloroethylene molecules before transition to their triplet state can occur. Triplet butene molecules formed by multiplicity exchange in the low-pressure process may themselves isomerize, but do not isomerize or activate other butene molecules which suggests that they are readily deactivated to the vibrationally excited ground state by crossing of the potential curves. The photochemical decomposition of formic acid is also quenched by *cis*-butene and similar isomerization occurs[22]. Such techniques may well be extended to reactions in solution and a ready method for the detection and estimation of triplet intermediates evolved.

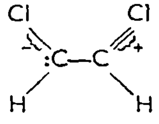
In the mercury-sensitized photoisomerization of *cis*-butene, all the features of the reaction can be explained by the production of vibrationally excited triplet intermediates resulting from transfer of energy from excited mercury atoms, and a similar process may be brought about in the presence of benzene, although in this case the experimental results do not allow a distinction between the singlet and triplet mechanisms[23]. Photochemical reactions of this kind are often complicated, however, by bond-fission reactions leading to the production of free radicals, these leading to further rearrangement products[24].

Few cases are known in which the isomerization of simple olefins presents difficulties. One such case recently encountered is the interconversion of *cis*- to *trans*-di-*t*-butylethylene, the *cis* compound being recovered unchanged after heating, or treatment with proton acid catalysts; isomerization is achieved, however, by heating the pure liquid with palladium on an alumina catalyst[25].

2. Dihalogenoethylenes

The electronic character of the halogens is such as to raise legitimate doubts regarding the normal order of stability of *cis–trans* isomers when applied to the dihalogenoethylenes. Early calculations which took account of dipole–dipole interactions, induction and dispersion forces indicated that the *cis* isomer of dichloroethylene was the more stable of the isomers by about 1 kcal/mole[11] and this order of stability was confirmed experimentally[27], the method of calculation not being without its critics[28]. Later workers have calculated thermodynamic functions for diiodo-[29], dibromo-[30] and dichloroethylene[31] respectively using infrared and Raman data: ΔH_0^0 for the series of isomers varies from 0·5 kcal/mole *endothermic* for the dichloro compound, through practically zero for the dibromo compound, to 2 kcal/mole *exothermic* for the diiodo compound. In order to explain these differences in stability, Pitzer and Hollenberg[31] suggest that canonical forms such as **5a** and **5b** may play a part in stabilizing the *cis* isomer of dichloroethylene for example.


(5a)


(5b)

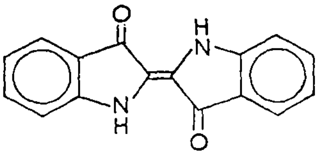
Since fluorine shows a greater tendency to participate in double-bond formation than does chlorine[32], difluoroethylene might be expected to be even more stable in the *cis* configuration than dichloroethylene, and measurement of ΔH^0 for the isomerization of difluoroethylene confirms the trend towards more stable *cis* isomers in this series[33]. Mixed halogenoethylenes having a stable *cis* configuration at equilibrium have also been discovered[34].

Recent work on the kinetics of thermal isomerization of *cis*-dichloroethylene shows that it is a normal first-order process with characteristic parameters of a singlet intermediate[35, *cf.* 36].

3. Ethylenic compounds with conjugated aromatic substituents

In their early work on the kinetics of *cis–trans* isomerism, Kistiakowsky and coworkers[9] suggested that the striking difference in the kinetic parameters for methyl maleate and methyl cinnamate lay in the fact that an aromatic conjugated system could provide electronic energy levels which would allow easy internal conversion of collision energy and thereby undergo internal predissociation, a process not open to maleic esters; similar values to those for methyl cinnamate were found for stilbene[37] and cyanostyrene[38]. Substituents in the aromatic rings of such conjugated molecules might also be expected to modify profoundly the course of stereomutation. Arguments from the point of view of the contribution of ionized canonical forms (*e.g.* **7**) to a mesomeric ground state in which the central double bond has reduced π-bond character have been advanced to explain the difficulty of isolating the highly labile second isomer of indigo[39,40], which rapidly reverts to the common form (**6**) on standing in air.

Similar arguments applied to *p*-amino-*p'*-nitrostilbene[41], where the contribution of canonical forms as shown would be expected to be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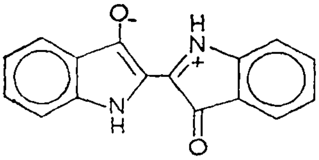
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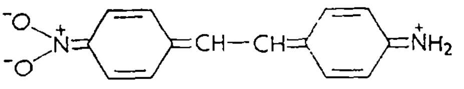
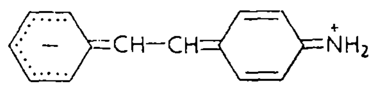
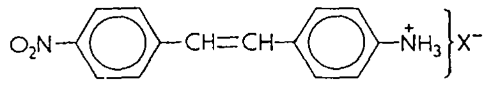
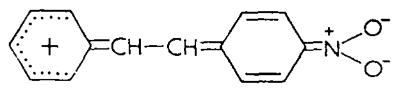








rather greater than the analogous ionized forms in *p*-amino- or *p*-nitrostilbene alone, suggest that it would be difficult to separate the isomers.

For salts of *p*-amino-*p*′-nitrostilbene, on the other hand, this kind of resonance is blocked; consequently the salts, as predicted, prove to be separable and readily come to equilibrium in acidic media. Nevertheless, the *cis* isomer of *p*-amino-*p*′-nitrostilbene has been isolated, enabling comparison to be made between it and other substituted stilbenes[42]. The transition from purely adiabatic singlet stereomutation in stilbene, through what probably represents mixed singlet–triplet kinetics in *p*-methoxystilbene and *p*-methyl-*p*′-nitrostilbene to the purely triplet process in *p*-amino-*p*′-nitrostilbene is clearly seen (Table 1).

TABLE 1. Kinetic parameters for *cis–trans* isomers of ethylenic compounds with aromatic substituents[a].

Compound	Preexponential factor, *A*	Energy of activation, *E* (kcal/mole)	Reference
Stilbene	$6{\cdot}0 \times 10^{12}$	42·8	37
Cyanostilbene	$1{\cdot}0 \times 10^{11{\cdot}6 \pm 0{\cdot}4}$	46·0 ± 1·0	38
Methyl cinnamate	$3{\cdot}5 \times 10^{10}$	41·6	9
p-Methoxystilbene	$1{\cdot}7 \times 10^{10}$	35·5 ± 1·0	42
p-Nitrostilbene	$1{\cdot}7 \times 10^{10}$	34·0 ± 1·5	42
p-Methoxy-*p*′-nitrostilbene	$1{\cdot}3 \times 10^{8}$	28·8 ± 1·5	42
p-Amino-*p*′-nitrostilbene	$1{\cdot}0 \times 10^{8}$	17·1 ± 2·5	42

[a] Where the singlet and triplet mechanisms operate together, plots of log *k vs.* $1/T$ should show slight curvature; apparently the effect is not observable with the present available data[46].

It is of interest in this connexion to compare the heats of hydrogenation of typical *cis–trans* isomeric compounds in this series, as a measure of the difference in energy between them (Table 2).

TABLE 2. Heats of hydrogenation and calculated heats of isomerization of substituted ethylenes.

Compound	$\Delta H_{\text{hydrog.}}$ (kcal/mole)	Calculated $\Delta H_{\text{isom.}}$ (kcal/mole)	Reference
trans-2-Butene	27·62	0·59	43
cis-2-Butene	28·57		43
Methyl *cis*-cinnamate	28·69^{a}	4·01	44
Methyl *trans*-cinnamate	24·68^{a}		44
Diethyl maleate	34·02^{a}	4·22	44
Diethyl fumarate	29·80^{a}		44
cis-Stilbene	26·30^{a}	5·70	44
trans-Stilbene	20·60^{a}		44

[a] Estimated values for the gaseous phase, corrected from the liquid phase by a factor of 0·5 kcal/mole.

The effect of conjugated substituents on stabilizing the *trans* isomers is clearly apparent; conjugation, and hence internal energy minima, will be favoured in those compounds which can remain planar as in the *trans* form where there can be no steric or polar interaction.

In the field of photochemically induced isomerization, the direct preparation of a number of *cis*-chlorocinnamic acids from the corresponding *trans* compounds is striking for the yields obtained (80–95%)[46]. The kinetics of isomerization are necessarily complicated, however, on account of the presence of differently absorbing species due to ionization[47]. Indirect stereomutation of stilbenes may also be achieved by dissolving the compounds in a suitable solvent which contains a fluorescent compound or scintillator emitting in the region where the olefin absorbs, without itself absorbing in the same region. Examples of fluorescent compounds used include terphenyl[48].

It is generally accepted that heavy-atom elements catalyse stereomutation, and this is also true in the presence of radiation, where iodine is the reagent of choice. Using this combination, in the case of the isomerization of stilbene, two processes have been discerned by working in the short and long wavelength regions of the visible spectrum[49]. In both these regions the rate law for the reaction takes the form given in equation (2), where $[C]$ is the con-

$$\frac{\mathrm{d}[C]}{\mathrm{d}t} = -k \,.\, I_0^{\frac{1}{2}} \,.\, [\mathrm{I}_2]^{\frac{1}{2}} \,.\, [C]^{\frac{1}{2}} \qquad (2)$$

centration of *cis*-stilbene, I_0 is the light intensity and $[I_2]$ is the concentration of molecular iodine. The quantum yields and energies of activation are, however, different in the two regions.

By considering the absorption curves of the components in solution together with the kinetics, it appears that in the short wavelength region, the primary process is the activation of a preformed complex between the olefin and molecular iodine (equation 3).

$$\mathrm{CI_2} + h\nu \longrightarrow \mathrm{CI_2^*} \tag{3}$$

Equations (4) and (5) give the secondary steps which then occur.

$$\mathrm{C} + \mathrm{CI_2^*} \longrightarrow 2\,\mathrm{CI} \tag{4}$$

$$\mathrm{CI} \longrightarrow \mathrm{TI} \longrightarrow \mathrm{T} + \mathrm{I}\cdot \qquad (\mathrm{T} = \text{trans-olefin}) \tag{5}$$

At longer wavelengths the photodissociation of iodine is the primary process, as in the thermal reaction[50], leading to stereomutation by the sequences (6) and (7). It seems likely that the

$$\mathrm{I_2} + h\nu \longrightarrow 2\,\mathrm{I}\cdot \tag{6}$$

$$\mathrm{C} + \mathrm{I}\cdot \longrightarrow \mathrm{CI}, \text{ then as equation (5) above.} \tag{7}$$

triplet state is involved in the step CI → TI, although the experiments as described do not prove this.

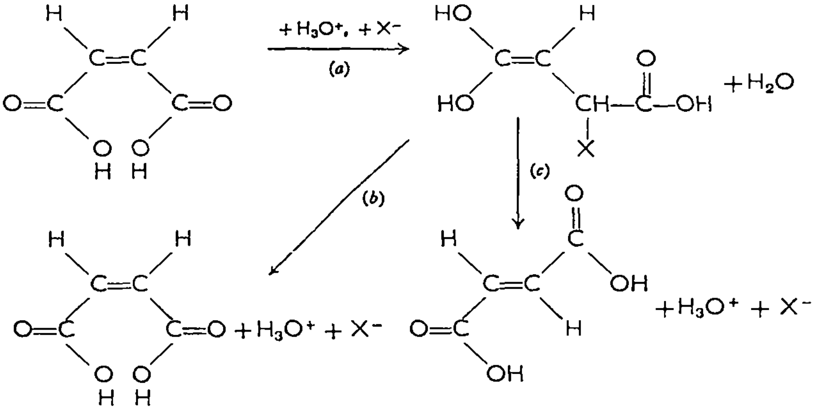
On the other hand, the rate of conversion of *trans*-stilbene to a mixture of the two isomers in the short wavelength region is the same as when no iodine is present; the *trans–cis* conversion is caused solely by the absorption of light and no conversion of *trans*-stilbene to the *cis* isomer occurs in the long wavelength region, where iodine strongly absorbs but stilbene is transparent.

The manner of isomerization of *trans*-stilbene induced by radiation appears to involve an excited state which loses its energy by several pathways, the main one being transition to the *cis* form which loses excess energy vibrationally. The triplet state once formed does not lose its configuration by free rotation; instead there is a small thermal barrier between the triplet states corresponding to the *cis* and *trans* isomers[51, 51a].

C. *Acid–Base Catalysis in the Stereomutation of Ethylenic Carbonyl Compounds*

I. Isomerization of maleic acid

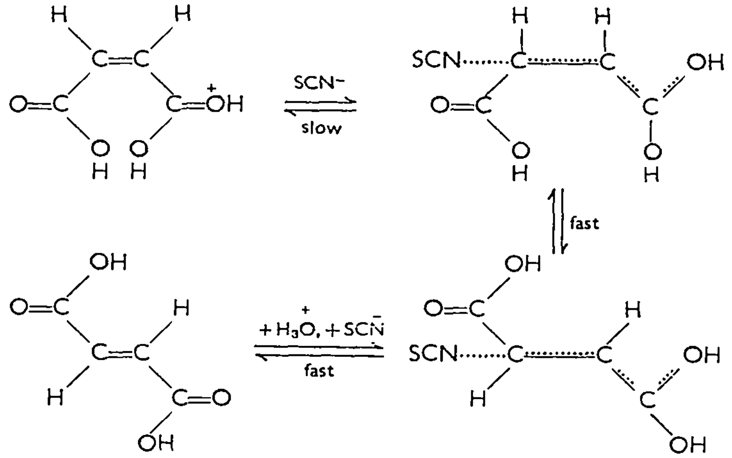
Catalysis by acids and salts in the conversion of maleic to fumaric acid is well known. The first suggestions relating to the mechanism considered that addition of a proton to the double bond followed by rotation and loss of the proton gave the more stable isomer. The advent of isotopic labelling techniques in the study of organic reactions prompted Horrex[52] to use deuterium chloride as catalyst in the maleic acid conversion, because consideration of the geometry of the expected intermediate showed that the added and ejected protons would be different. Since no deuterium was introduced into the fumaric acid formed, it left only the possibility that the carbonyl function was involved, as had previously been postulated[53]. Shortly afterwards, it was found that catalysis of the conversion by strong acids was dependent upon the nature of the acid used[54], and coupled with the fact of catalysis by certain salts, a scheme for isomerization in which the anion also played an important role was proposed (Scheme 1). In this scheme, the forward process at (*a*) is



SCHEME 1.

considered to be the rate-determining step, whilst (*b*) and (*c*) are very fast. In the presence of salts the proton is supplied by the maleic acid and the anion by the salt.

The kinetic isotope effect and its temperature dependence in the stereomutation of maleic acid-2,3-d_2 catalysed by thiocyanate ion has been examined more recently, enabling a more detailed description of the transition state to be given[55]. An inverse secondary α-deuterium isotope effect is expected since in going from the ground state to the transition complex the ethylenic C—H bonds in maleic acid are undergoing a change from the purely sp^2 hybridized condition to the partially sp^3 hybridized state[56]. The total net change in the frequency of the C—H deformation mode, calculated from the temperature dependence of the isotope effect, is a little more than half that expected assuming complete transition to the sp^3 condition in the transition state, which therefore lies a little more than half-way along the path between the trigonal and tetrahedral configuration. The mechanism for the reaction can be written as in Scheme 2.



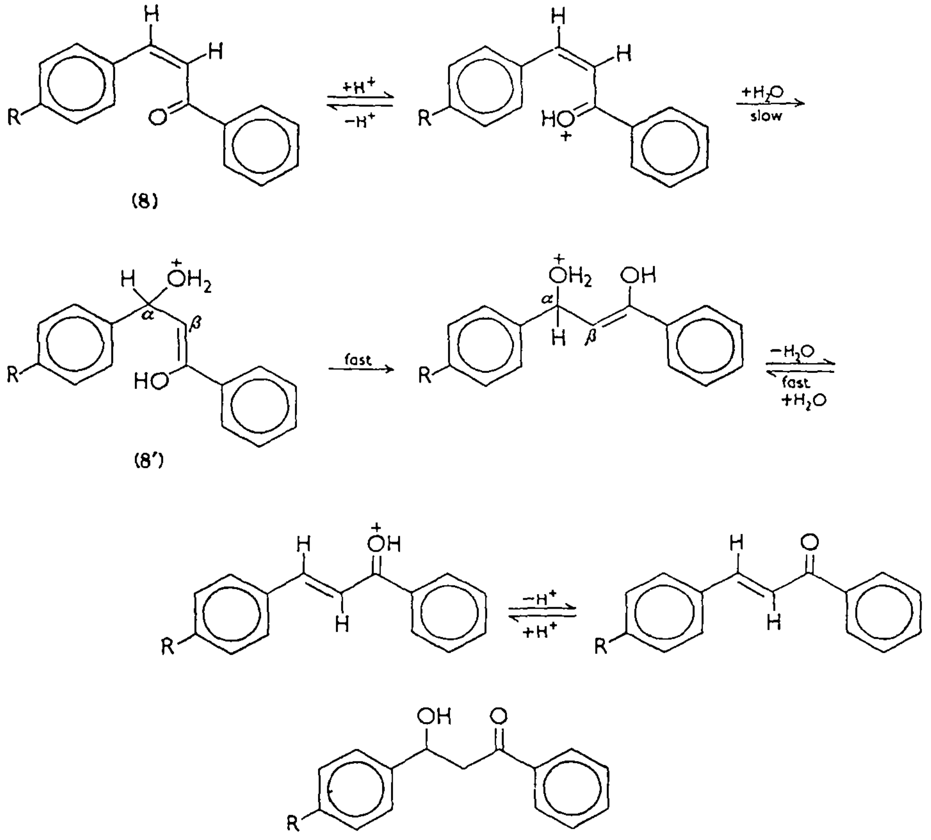
SCHEME 2.

An interesting variant of the acid-catalysed isomerization of maleic acid occurs when the pentamminocobaltic complex ion, with the hydrogen or methyl maleate ion as further ligand, is reduced by vanadous or chromous ion in acid solution; a mixture of maleic and fumaric acids (or half esters) can be isolated from the reaction mixture, and their ratio is found to depend linearly upon the hydrogen-ion concentration. *Electron transfer occurs at the carboxyl group remote from the metallic atom in the complex* and hydrolysis, when it occurs, takes place by alkyl–oxygen fission almost exclusively, as demonstrated by labelling techniques with ^{18}O. The formation of a bridge between the two metallic atoms concerned appears a necessary concomitant for the reaction to occur, but the mechanism of *cis–trans* isomerism which occurs is as yet unclear[57].

The use of acetylenic intermediates in the preparation of *cis*-olefins is by now firmly established, but certain limitations to the usefulness of the method are imposed by the fact that hydrolysis of 2,3-*cis*-olefinic acetals gives only the *trans*-aldehydes[58]. Here the mesomeric conjugate acid of the aldehyde is probably the intermediate involved in stereomutation. Remote *cis* linkages in similar molecules are unaffected. Similar considerations apply to the hydrolysis of the semicarbazones of 2,3-olefinic aldehydes which, although isolable from the corresponding acetylenic compounds, are hydrolysed to the *trans*-aldehydes[59].

2. Olefins with aromatic substituents

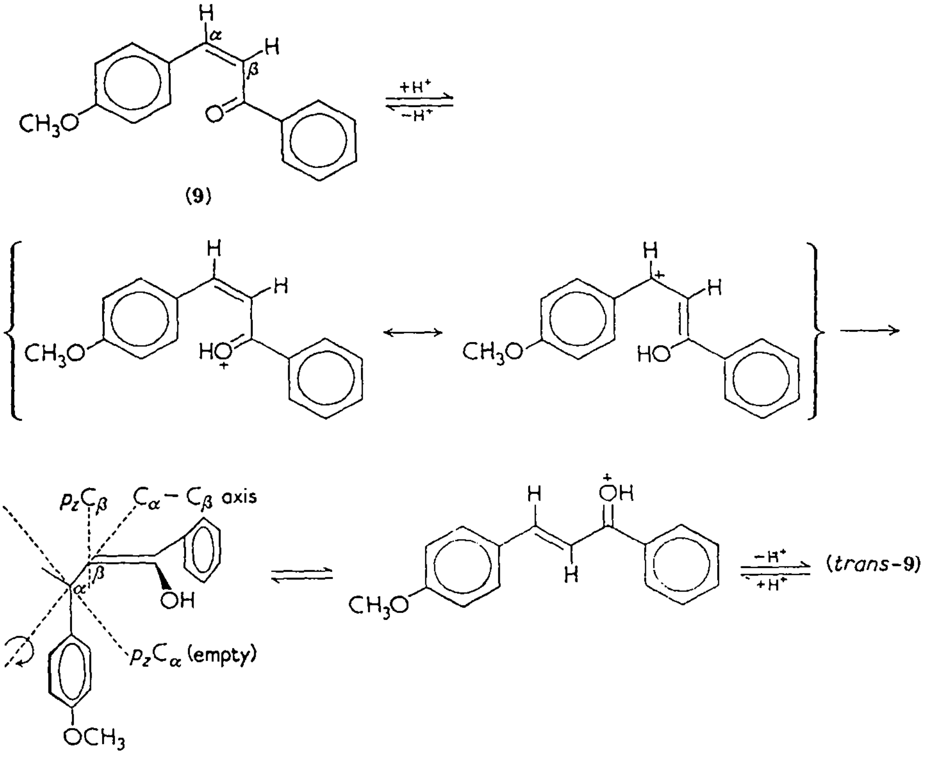
The acid-catalysed isomerization of *cis*-benzalacetophenone (**8**, R = H) and its derivatives (**9**, R = OCH_3; **10**, R = Cl; **11**, R = NO_2) provides a series of examples where the effect of conjugated substituents on the isomerization process can be studied in detail. In the case of chalcone, the mechanism proposed[60] involves the protonation of the carbonyl oxygen atom, as in maleic acid. The rate of reaction does not parallel the acidity function H_0 in either sulphuric or perchloric acid, and is faster than the acid-catalysed dehydration of a possible intermediate compound, *i.e.* β-hydroxy-β-phenylpropiophenone, so that the rate-determining step in the isomerization is the addition of water to the conjugate acid of **8** to produce the protonated enol of **12**, which loses water



(**12**, R = H)
Scheme 3.

rapidly before ketonization. The reaction is rapid in acidic aqueous dioxan, and even more rapid in dioxan containing deuterium oxide and deuterosulphuric acid; no isotope is incorporated into the product however, confirming the nature of the rate-determining step as the aquation of the oxonium salt of the ketone (Scheme 3).

The rate of reaction in the case of both the halogeno and nitro compounds **10** and **11** is slower than for the ketone **8**, but the rate *vs.* H_0 curves are all very similar. The behaviour of ketone **9** is anomalous and here a different mechanism supervenes involving rotation about the C_α—C_β bond in the oxonium salt of ketone **9** (Scheme 4).



(9)

(trans-9)

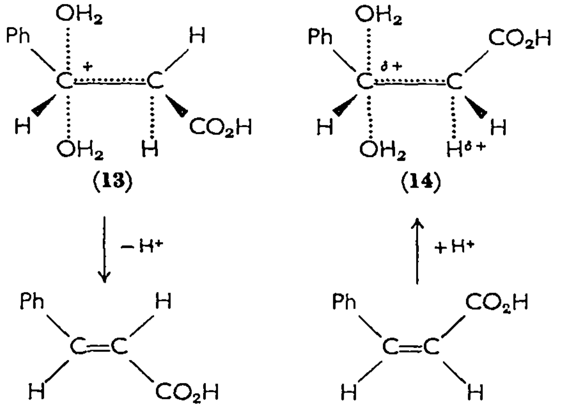
(9′)

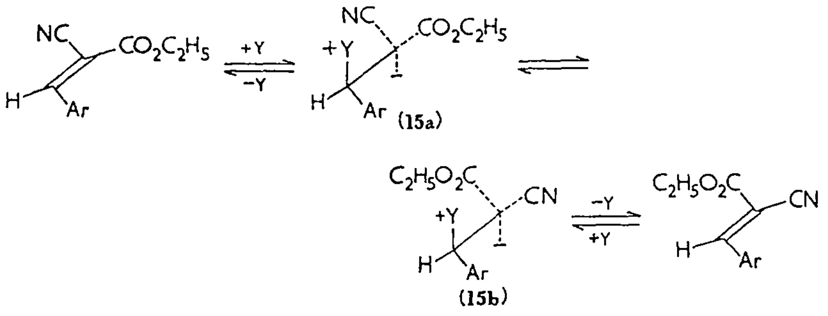
Scheme 4.

The rate of stereomutation of **9** is much faster than that of **8**, increasing rapidly with acid concentration, but again no deuterium is incorporated under appropriate conditions. In order to understand these differences in substituent effects, the detailed structure of the molecules and ions involved must be considered. In the ground state, all these ketones are distorted from the planar configuration by steric interaction; hence the effects of the *p*-substituents are somewhat reduced. In the oxonium salts of the ketones interaction through the conjugated system is increased but the effect of the substituents in the *para* position is to *increase* the energy of the intermediates in the order $OCH_3 < H < Cl < NO_2$ following the usual order for their effect on a carbonium ion. In the cases of **8**, **10** and **11** there is little or no interaction between the centre of positive charge in the hydroxyenol oxonium ion and the substituents, since there is no conjugation with either the double bond or the aromatic ring; resonance is similarly interrupted depending upon the extent to which the water molecule is bonded to the α-carbon (*e.g.* **8′**). Consequently the effect of the substituents is moderated, this being reflected in the general similarity of the rate *vs.* H_0 plots. The effect of substituents on the transition state for direct rotation about the C_α—C_β bond, however, will be enormous (*e.g.* **9′**) for here the *p* orbitals of the C_α and C_β atoms are orthogonal, and therefore the positive charge can only be located on the benzylic carbon atom or in the ring. Substituents other than electron-donating ones will therefore strongly destabilize this transition state, and the relative rates clearly show that it is a forbidden state for any other than the *p*-methoxy compound, unless there are steric effects precluding β-aquation, or the water activity is drastically reduced[60a].

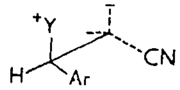
In the case of the acid-catalysed stereomutation of cinnamic acids, the kinetic data clearly support only a mechanism where there is a large deficiency of electronic charge on the benzylic carbon atom in the transition state. A very large isotope effect is observed in moderately concentrated sulphuric acid, and the rate is proportional to the acidity function H_0, with unit slope. Direct proton transfer is clearly involved here and the overall reaction involves an addition–elimination sequence with aryl-β-hydroxypropionic acids as intermediates[61]. The transition state for the elimination is regarded as having the structure **13** (cinnamic acid), for the isotope effect indicates that the proton being lost from the α-carbon has suffered some bond weakening in the transition state, whilst the large negative value of ρ in the Hammett σ–ρ relationship indicates that the β-carbon is electron deficient. In the addition of a proton to *cis*-cinnamic acid, the transition state therefore can be thought of as structure **14**, for although the reaction is not carried out under equilibrium conditions, as required by arguments involving the principle of microscopic reversibility, nevertheless the close similarity justifies the argument that protonation may well be the direct reverse of dehydration. Like **13**, **14** has pronounced carbonium-ion character at C_β and a partial C_α—H bond as required by the kinetic evidence. The structure **14** is rather exceptional, however, in that protonation of similar double bonds usually involves formation of π-bond complexes.

Only isolated instances of stereomutation induced by nucleophilic reagents have been recorded, but quite recently the isomerization of *cis*-α-cyano-β-*o*-methoxyphenyl acrylate under the influence of a variety of nucleophilic reagents has been studied[62]. This process is represented in equation (8), where Y is the nucleophile. The inversion of configuration must be very fast, for in the presence of acids the rate is unaffected and, of course, protons are known to react extremely rapidly with carbanions. Of the two possible conformations for the intermediate carbanion, **15a** is the favoured one on thermodynamic grounds, so that, in base-catalysed condensations leading to this type of structure, only the *trans* isomer is ever isolated, for even unchanged methylene compound or solvent may be sufficiently basic to react with the substrate, leading to





(8)



(**15c**)

the carbanion **15b**. It is also possible to explain the observations on the basis of the conformation **15c**, for although this would be of relatively high energy, probably not much more energy would be required to form **15c** than **15a** or **15b**, and furthermore if the nucleophile Y is neutral, attraction between the two opposite charges will favour **15c**. If the olefinic compound already bears a charged group such as carboxyl ion, inhibition of the approach of a nucleophile precludes isomerization by this mechanism.

D. Cis–Trans *Isomerism in Conjugated Polyenes*

1. Synthetic polyenes

In a molecule containing more than one double bond, the number of possible isomers is increased. If n is the number of double bonds, then the number of isomers N is given by equation (9a) if n is even, by (9b) if n is odd, or by (9c) in the case of an unsymmetrical polyene[63].

$$N = 2^{(n-1)} + 2^{(\frac{1}{2}n-1)} \tag{9a}$$

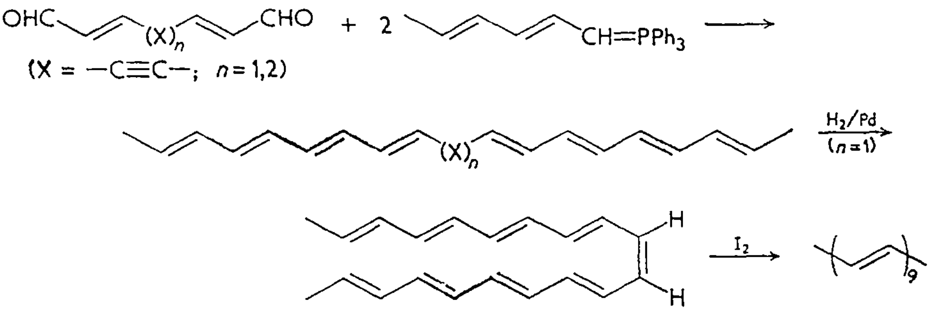
$$N = 2^{(n-1)} + 2^{(n-\frac{1}{2})} \tag{9b}$$

$$N = 2^{n} \tag{9c}$$

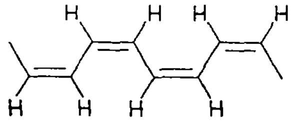
In a conjugated system the ease of rotation about the double bonds is greatly increased, and the synthesis of long-chain polyenes by the conventional methods almost invariably leads to the all-*trans* isomers. However, the availability of acetylenic intermediates and their stereospecific catalytic reduction to *cis*-olefins has facilitated the synthesis of polyenes with one or more *cis* double bonds. For example, using the Wittig procedure[64], conjugated polyenes containing as many as nine or ten double bonds have been prepared, the central one or two double bonds having the *cis* configuration, depending upon whether a mono- or diacetylene intermediate is chosen[65].

The resulting *cis*-olefins are readily isomerized to the all-*trans* compounds simply by heating in the presence of iodine.

Simple all-*cis*-polyenes are also known, and contrary to prediction on the basis of the Zechmeister rules[66] have longer wavelength



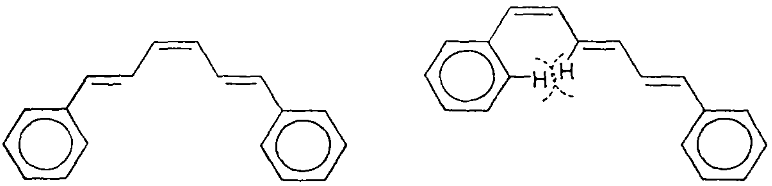
absorption maxima than the corresponding all-*trans* compounds, where, because of the coplanarity of the double bonds, greater overlap of adjacent *p* orbitals is expected with consequent reduction in photoexcitation energy. Those examples of all-*cis*-polyenes known however, *e.g.* all-*cis*-decatetraene[67], belong to the unbranched series, where steric effects are less important. The reversal of the Zechmeister rules in these cases applies only to the position of maxima, their intensity, as expected, being reduced; the decrease in the difference between energy levels is accompanied by decreased probability for the electronic transition.



all-*cis*-Decatetraene. Notice the compactness of the molecule.

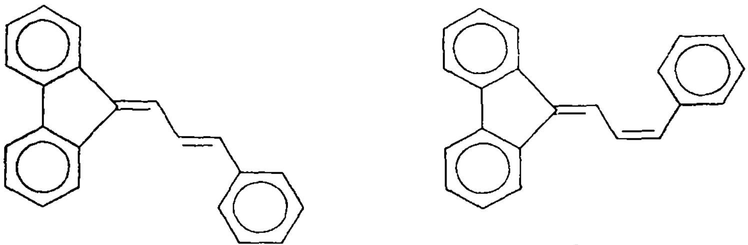
The α,ω-diarylpolyene series has received more attention from the point of view of isomer distribution in equilibrium mixtures obtained from pure stereoisomers under the influence of iodine, with irradiation or thermal treatment, than the simple polyenes so far. The components of diarylpolyene mixtures obtained in this way are readily separated by their differential adsorption on alumina columns, and distinguished by their fluorescence behaviour and general stability. They are usually designated '*Cis*-I', '*Cis*-II', *etc.*, in order of their increasing adsorption affinity, and they may be divided into two classes: (*i*) those in which there is no steric hindrance; and (*ii*) those where there is steric conflict between the *ortho*-hydrogen atoms of the aromatic ring and the $H_{(3)}$ of the polyene chain in the case of terminal *cis* isomers. This is illustrated below. The proportion of hindered *cis* isomers of this type is expected to be reduced in the mixture obtained by stereomutation. They may be expected to show different properties from other unhindered isomers[68].

As an example of the kind of work which has been carried through in this field, the various isomers separated from adsorption columns in the stereomutation of 1,6-diphenylhexatriene and 1,8-diphenyloctatetraene have been classified into mono- and di-*cis* types depending upon their light absorption and stability[69]. Similar studies have been made with biphenylenephenylbutadiene and dibiphenylenehexatriene, where observations tend, in general, to parallel those in the hexatrienes above, the *cis* forms (especially the hindered *cis* compounds) showing reduced adsorption affinity[70]. But there is need for caution here, for some more recent kinetic studies of the isomerization of diphenylhexatriene establish that a component, previously regarded as the 3-mono-*cis* isomer, is actually the 1-mono-*cis* compound[71].



3-mono-*cis* 1-mono-*cis* (hindered)

1,6-Diphenylhexatrienes



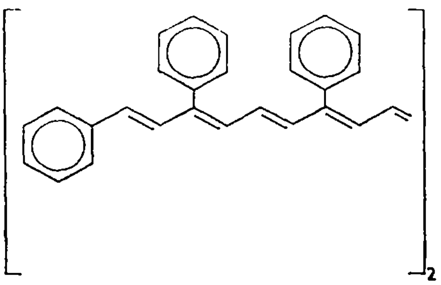
trans-form *cis*-form

Biphenylenephenylbutadiene

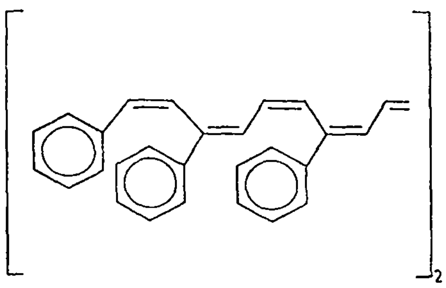
From the point of view of their relationship to the carotenoids, the hexaphenyloctadecanonaene and diphenyltetramethyloctadecanonaene series are known both in their all-*cis* and all-*trans* forms, and have been prepared using the much favoured acetylenic intermediate route[72, 73].

2. Carotenoids and related polyenes

It is surprising in retrospect that it was not until 1942 that a final decision in favour of a geometrical basis to account for the



all-*trans*

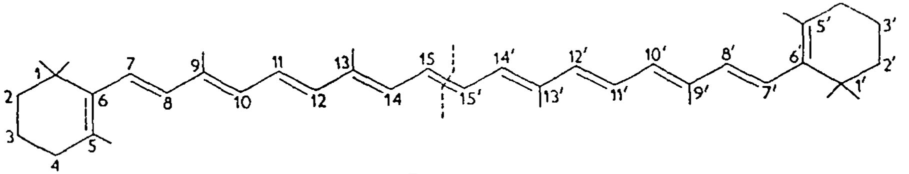


all-*cis*

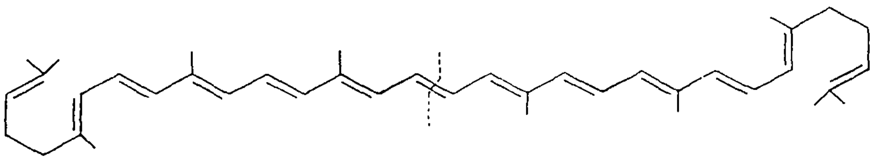
isomerization of carotenoid hydrocarbons was announced by Zechmeister[74], and even more surprising that this explanation was received with scepticism by Karrer[75] and other workers in this field, who have since achieved so much from the point of view of synthesis as to leave the issue beyond doubt.

Some years previously, it had been observed that chromatography of β-carotene on alumina or calcium hydroxide apparently isomerized the hydrocarbon, a second adsorption band appearing below the more firmly adsorbed β-carotene zone[76]. Later it was found that this isomerization was a spontaneous process both with regard to β-carotene and the closely related hydrocarbon lycopene[77,78]. It was the method of working with these compounds which had caused the observed heterogeneity and conditions were then discovered which led to rapid isomerization—such as the use of iodine as catalyst in the presence of light[79]; thermal treatment, with or without iodine; and also melting the crystals. At first it was considered that the phenomenon could have either a geometrical or tautomeric basis, since the isolated isomer of β-carotene had an absorption spectrum more like that of a compound containing ten rather than eleven double bonds, slight shift of the absorption maximum having occurred towards shorter wavelengths[76,80]. But isomers were also obtained even when the ends of the conjugated system were blocked with carbonyl groups,[81] precluding bond migration; consequently the isomerism could only have a geometrical basis and this received strong support from the fact that in the isomerization of α-carotene to neo-α-carotene, optical activity was retained[82]. Later the synthesis of β-carotene confirmed its structure as a conjugated C_{40} terpenic hydrocarbon, all the double bonds having the *trans* configuration[83].

Clearly there are enormous possibilities for stereoisomerism, but the molecule must be considered as a whole, since the *trans*-to-*cis*



β-Carotene



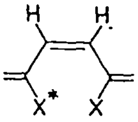
Lycopene

conversion of one of the double bonds affects the shape of the whole molecule.

Carotenoids can be divided into two classes depending upon whether or not the two halves of the molecule are identical[84]. If n is the number of sterically effective double bonds, the number of possible isomers N for the two classes of carotenoids can be calculated from equations (9a), (9b) or (9c) (section I.D.1).

Conversion of all-*trans*-carotenoids to quasi-equilibrium mixtures containing some *cis* isomers is quite simply achieved merely by exposing a solution of the polyene (usually in hexane) in the presence of iodine to daylight, or by heating a similar solution. The mixture can be separated into its constituents by chromatography and repetition of the process by re-equilibration of the remaining product can lead to quite high overall yields of the desired isomer. Usually the products of this type of reaction contain both mono- and di-*cis* forms, but no poly-*cis* forms can be detected in such mixtures by the combination of chromatographic and spectroscopic techniques, which have been shown to be very sensitive by using artificially prepared mixtures containing poly-*cis* isomers.

The *cis* isomers of carotenoids can be divided into those in which the *cis* double bond is hindered, and those in which it is unhindered[85]. If one of the groups X or X* is methyl, significant steric interaction



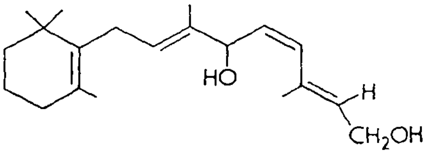
X, X* Limited in size for no steric repulsion.

will occur, and it will therefore be difficult to form a *cis*-olefin of this type by stereomutation of the all-*trans* compound. In its original form, this postulate—the Pauling 'rule'—was interpreted to mean that no hindered *cis* isomers could exist, but the whole question of polyenes containing hindered *cis* double bounds has been considered in detail, and their existence irrefutably demonstrated; but under equilibrium conditions, isomerization to the all-*trans* forms and unhindered *cis* forms is rapid[86].

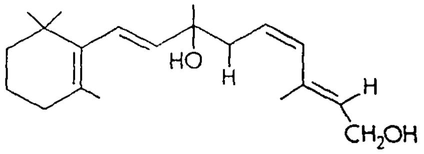
In their approach to the question of hindered *cis* isomers of methylated polyenes, Oroshnik and Mebane[86] synthesized a number of compounds containing a hindered double bond by partial hydrogenation of acetylenic intermediates. Examples of compounds in which the *cis* bond was part of a conjugated chain of increasing length were compared for stability and light absorption, steric effects in this series being known to result in profound changes in light absorption. In compounds of type **16a**, the characteristic diene absorption peak is missing, the spectral degradation corresponding to severe steric conflict between the $C_{(13)}$-methyl and $C_{(10)}$-hydroxyl groups. In a closely similar compound where the $C_{(10)}$-hydroxyl is replaced by hydrogen, similar spectral degradation is apparent (compound **16b**). Because the rest of the molecule also absorbs in the relevant region, it is necessary to compare **16a** with the *cis* isomer of occimene (**17**). Here, although pronounced spectral degradation indicates steric interaction, nevertheless there is a well defined band in the diene region (210–270 mμ), contrasting with the case of **16a** where the degradation appears to be complete, as might be expected on the basis of the size of the groups involved.

In spite of this obvious steric effect both compounds **16a** and **17** show unusual stability to heat and light and resemble in this respect *cis*-1,4-diphenylbutadiene and the *cis*-carotenoids prolycopene and pro-γ-carotene, both of which are recovered from boiling hexane unchanged, whereas under the same conditions the all-*trans* compounds readily steromutate[87].

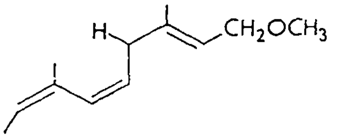
As the hindered *cis* double bond is introduced into a longer conjugated system as in the compound **18**, spectral degradation diminishes and is in fact confined to the difference in shape between the absorption peaks for the *cis* and *trans* isomers. Again, although the hindered forms are relatively stable in the absence of catalyst, rapid and complete stereomutation occurs in the presence of iodine. By way of contrast, spectral degradation in the conjugated pentaene (**19**) is comparable to that observed for *cis*-*retro*-vitamin A methyl



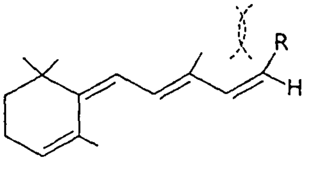
(16a)



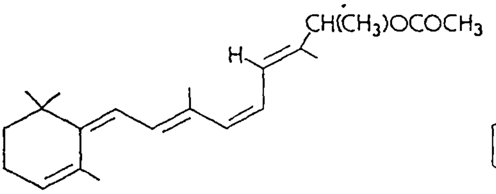
(16b)



(17)



(**18**, $-R = -CH_2CH_2CH_2CH_3$, $-CH_2C(CH_3)(OH)CH{=}CH_2$ or $-CH(OH)CH_2CH_2CH_3$)



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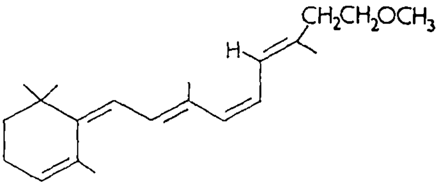


(20)

ether (**20**), which had been the first exception to the 'forbidden' hindered structures to be encountered.

Clearly the exact location of the hindered *cis* double bond is important in determining the stability and spectral characteristics of polyenes of the carotenoid and vitamin A type. The exclusion of such structures can only be assumed under true equilibrium conditions; the application of these ideas to quasi-equilibrium mixtures produced by light is questionable, however, in view of the isolation of hindered *cis* structures of the *retro*-vitamin A methyl ether type under photolytic conditions[88].

3. Relative stabilities of geometrical isomers in natural polyenes

Since there is almost perfect resonance in flat all-*trans*-polyenes they would be expected to be more stable than the *cis* isomers, but as has been indicated already the stability of the system depends not only on the presence of a *cis* double bond but also on its location, and the overall shape of the molecule. Initially, thermal stability decreases as the number of *cis* double bonds increases, the effect of the rigidity and compactness conferred by the introduction of *cis* bonds supervening only when a high proportion of them are present. On the other hand, sensitivity to light increases markedly with the presence of *cis* bonds, and compounds with a central *cis* bond are strongly photosensitive, owing to the overall bent shape of the molecule. Sterically hindered *cis*-carotenoids are surprisingly stable to heat, but, as might be expected, are isomerized more rapidly than the all-*trans* compounds or the unhindered *cis* isomers in the presence of light and iodine.

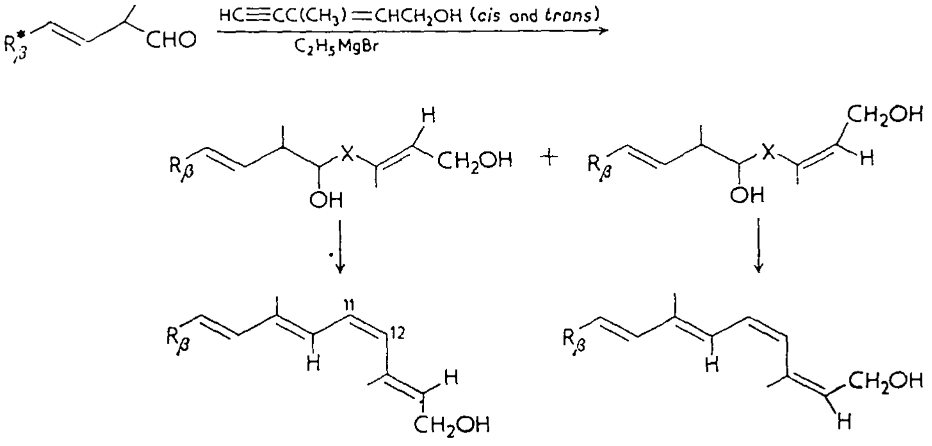
Like the α,ω-diarylpolyenes discussed above, the various carotenoid isomers have well defined adsorption affinities on chromatographic columns which facilitates their separation and estimation, often by spectrographic techniques.

Striking changes appear in the spectra of all-*trans*-carotenoids following stereomutation. A new absorption band appears in the 320–380 mμ range, hypsochromically displaced from the main *trans* band by an almost constant factor of 142 mμ. This new peak is often referred to as the '*cis* peak', and the effect has obvious diagnostic significance. It is of interest also that absorption in the '*cis* peak' region is held responsible for the phenomenon of photoconductivity observed with 'glass-like' carotene obtained by the melting and cooling of crystals of the natural isomer. It is believed that a triplet intermediate is involved in the process of conduction[89].

Although there are laboratory techniques for the preparation of mono- and di-*cis*-carotenoids from the all-*trans* compounds, poly-*cis* isomers are not encountered. They do, however, occur in nature, for both prolycopene[90] and pro-γ-carotene exhibit the poly-*cis* chromophore[91], their spectra consisting of a series of ill-defined bands in the visible region, which undergo a striking change on the addition of iodine, the well known equilibrium spectrum appearing. Prolycopene probably contains about six to seven *cis* bonds and pro-γ-carotene one or two fewer than this.

Isomers having the *cis* configuration appear to be more stable in the *retro*-dehydro-β-carotene series, probably as a result of the presence of the more stable cyclohexenylidene system. In this series there does not appear to be a *cis*-peak effect, although there is evidence that at least one of the isomers obtained by stereomutation of the all-*trans* compound is a hindered *cis* type, a degraded spectrum appearing[92].

Of the known isomers of vitamin A, only two have a hindered *cis* double bond, namely neo-c-vitamin A (11,13-di-*cis*) and the neo-b compound (11-*cis*), both of which have been synthesized from a common precursor, 3-methylpent-1-en-4-yn-3-ol, by anionotropic rearrangement and separation of the *cis* and *trans* isomers of 3-methylpent-2-en-4-ynol followed by their incorporation into trimethylcyclohexenylnonatetraene synthesis[93].

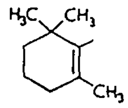


neo-b-Vitamin A

neo-c-Vitamin A

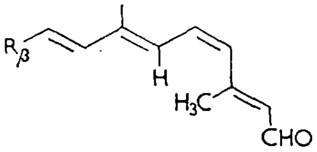
Spectrophotometric comparison of the stability of vitamin A isomers and isomers of retinene and retinene oxime in catalysed stereomutation, indicates, as expected, that the carbonyl group in retinene, with the possibility of contributing to the resonance of the conjugated chain in its polarized form, renders the aldehyde more labile; in the oxime this kind of resonance is blocked and consequently there is a resemblance to vitamin A in general stability of isomers[94]. In this connexion it is of interest that the 13-*cis* isomers of retinene and its oxime are probably closer to the 9-*cis* isomers in terms of free energy content than to the hindered 11-*cis* compounds which they

* Following the usual convention, the radical R_β in the following formulae refers to the trimethylcyclohexenyl group,

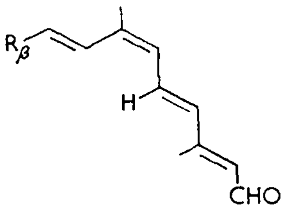


nevertheless more closely resemble in terms of kinetic behaviour, illustrating the general principle that the kinetic behaviour of a compound does not necessarily reflect its relative thermodynamic status.

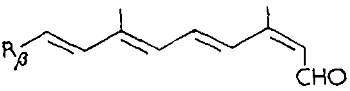
Resonance involving the carbonyl group may also be involved in the case of *cis*-11- and *cis*-13-vitamin A aldehyde, both of which show a higher biopotency than the corresponding alcohols, suggesting that stereomutation to the more active all-*trans* compound occurs[95].



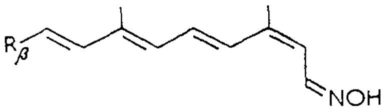
cis-11-Retinene (hindered)



cis-9-Retinene



cis-13-Retinene



cis-13-Retinene oxime

E. Cis–Trans *Isomerism in Unsaturated Fatty Acids*

Many naturally occurring unsaturated fatty acids have the *cis* configuration, but they are readily converted by a variety of catalysts* to their geometrical isomers. The transformation has been most fully studied in the case of oleic acid, the isomer being known as elaidic acid, and the process in general therefore as 'elaidinization'[97]. In the case of oleic acid the equilibrium mixture obtained consists of 67% *trans* and 33% *cis* isomers of octadec-9-enoic acid, and similar mixtures have been isolated from analogous monoethylenic acids, the components usually being readily separable on account of the reduced solubility and higher melting points of the *trans* isomers, whose configuration evidently allows closer packing in the crystal lattice.

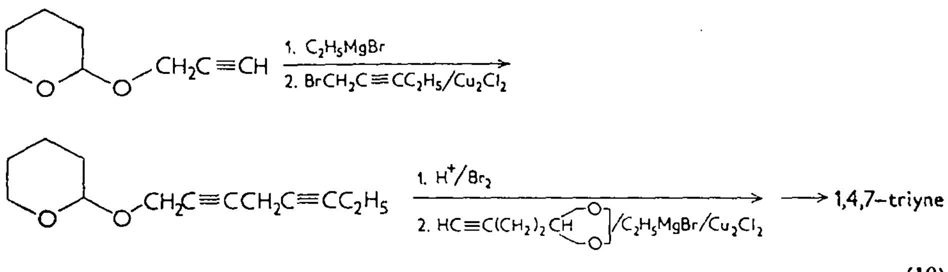
* Oxides of nitrogen, sulphur, selenium, phosphorus and the halogens are among the common catalysts which have been used for this purpose. A comprehensive list of reagents which have been used is given in a review[96].

The detailed mechanism of stereomutation of fatty acids has received little attention, most of the earlier work being concerned with establishing the reagents and optimum conditions required for elaidinization[3,97]. Special interest, therefore, attaches to the recent report that the high-temperature selenium-catalysed isomerization of oleic acid probably involves a π-complex with the catalyst, the rate of reaction initially being proportional to the concentration of selenium, which dissolves as the reaction proceeds, the high temperature being required to dissociate the molecules of catalyst. The reverse reaction is much slower, and the overall reaction is accompanied by an irreversible reaction with selenium. The formation of a π-complex here bears analogy with the well known tendency of olefins to form such complexes, for example with iodine and silver salts[98].

An important observation from the synthetical point of view is that stereomutation can also occur during the catalytic hydrogenation of olefinic esters, and kinetic studies indicate that the rearrangement involves the ester, the catalyst surface and hydrogen associated in a complex array which may break up to give alkanoic ester, starting material or stereochemically rearranged product[99].

Numerous polyene natural fatty acids are also known, and of course there are many possibilities for stereoisomerism. Where the double bonds are non-conjugated, stereomutation is almost always to the all-*trans* form[100], but rearrangement is less readily achieved than with the conjugated structures under similar conditions, where rotation about the several double bonds is a concerted rather than a stepwise process[101].

The synthesis of positional and configurational isomers of known structure in the lipid field presents an interesting challenge, which has been systematically approached only comparatively recently. Again, acetylenic compounds are the key intermediates, enabling the introduction of *cis*-olefinic linkages to be made, usually by coupling of the sodioacetylene with an α,ω-iodochloroalkane, which can then be converted to a carboxylic acid through the cyanide, followed by stereospecific reduction of the acetylene. In this way multifarious configurational and positional isomers of oleic acid have been prepared[102]. A rather different technique is used for the introduction of methylene-interrupted olefinic links as in linolenic acid. Here an acetylenic Grignard reagent is coupled with a propargyl halide in the presence of a copper catalyst introducing a 1,4-diyne system, and if the Grignard reagent is suitably chosen (*e.g.* from



(10)

propargyl alcohol tetrahydropyranyl ether) the sequence can be repeated giving a 1,4,7-triyne, and hence an all-*cis* triene system[103] (equation 10).

Further syntheses employing acetylenes are those of ricinoleic acid[104], and the eloeostearic acids and punicic acid[105], the latter employing a normal propargyl Grignard reaction with an α-acetylene aldehyde (equation 11) as a route to the *cis-trans-cis* conjugated triene system, by dehydration of the initial product and semi-hydrogenation of the resulting enediyne.

$$-C\equiv CCHO \xrightarrow{XMgH_2CC\equiv C-} -C\equiv CCH(OH)CH_2C\equiv C \xrightarrow{-H_2O} \underset{trans}{-C\equiv CCH=CHC\equiv C-} \qquad (11)$$

The acetylenic Grignard–propargyl halide coupling reaction has been thoroughly investigated, and a flexible method for the introduction of the methylene-interrupted polyyne function worked out. The polyyne alcohols so obtained can then be brominated, and condensed with ω-acetylenic acids *via* their Grignard complexes; acids containing up to five methylene-separated triple bonds have been obtained by this method[106]. Stereospecific syntheses of isomers of linoleic acid with *polymethylene*-separated double bonds and related compounds have also been made[107] and problems arising in the field of lipid isobutylamides have been approached from the same angle[108].

$$CH_3(CH_2)_4C\equiv CCH_2Br + BrMgC\equiv CCH_2OH \xrightarrow{Cu_2Cl_2} CH_3(CH_2)_4(C\equiv CCH_2)_2OH$$

$$\longrightarrow CH_3(CH_2)_4(C\equiv CCH_2)_2Br$$

sequence repeated twice

$$\longrightarrow CH_3(CH_2)_4(C\equiv CCH_2)_4Br$$

$$CH_3(CH_2)_4(C\equiv CCH_2)_4Br + HC\equiv C(CH_2)_{(y+1)}CO_2H \xrightarrow{C_2H_5MgBr} CH_3(CH_2)_4(C\equiv CCH_2)_5(CH_2)_yCO_2H$$

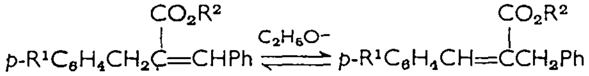
II. PROTOTROPIC REARRANGEMENTS

A. Introduction

The removal of hydrogen ions from saturated carbon compounds is achieved only with extreme difficulty. This is not the case, however, with compounds where the resulting carbanion can be stabilized by resonance, either by spreading of the negative charge over an unsaturated system, or involving heteroatoms as in carbonyl compounds, or halogen atoms in polyhalogeno compounds. Where this type of situation arises, the formation of carbanions can be significant and has interesting consequences.

It is not within the scope of this discussion to consider in detail the numerous and well known kinds of prototropic tautomerism found in 1,3-dicarbonyl compounds, methyleneazomethines and diazoamino compounds*; instead only rearrangements involving shifts of carbon–carbon double bonds are documented.

Early investigations of prototropic mobility and equilibria and the effect of structural variations were hampered by the lack of suitable systems for detailed study. Those compounds, which were known to be active in undergoing alkali-catalysed isomerization, whether by metal uptake or in the actual presence of bases, either isomerized too rapidly or else represented too one-sided equilibria, *e.g.* the propenylbenzenes or propenylammonium salts[110, 111]. Substitution of a further aryl group into the 3-position of propenylbenzenes, however, restored the equilibrium, and 1,3-diarylpropenes were among the first compounds to be examined quantitatively for mobility of the double bond and the position of equilibrium under the influence of alkoxide-ion catalyst[112]. It was during this period that theories concerning the electrical basis of bond formation and disruption were being formulated, and it was therefore but a short step to the proposal that base-catalysed isomerizations of this type were brought about by transfer of hydrogen ions. Significant effects on the mobility and position of equilibrium could therefore be expected by substitution of the benzene rings in diarylpropenes with groupings of different electronic character.



$$p\text{-}R^1C_6H_4CH_2\overset{\overset{\displaystyle CO_2R^2}{|}}{C}{=}CHPh \xrightleftharpoons{C_2H_5O^-} p\text{-}R^1C_6H_4CH{=}\overset{\overset{\displaystyle CO_2R^2}{|}}{C}CH_2Ph$$

($R^1 = (CH_3)_2N$, CH_3O, I, Br or Cl; R^2 = H or C_2H_5)

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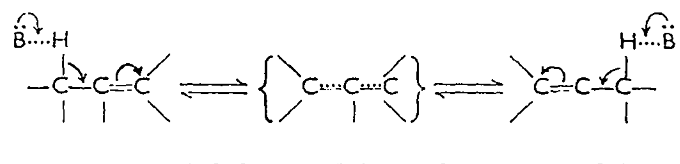
* An unrivalled account of these phenomena is to be found elsewhere[109].

The fact that electron-withdrawing groups accelerated, whilst electron-donating groups retarded interconversions in carbalkoxydiarylpropenes[113] lent strong support to the view that rearrangment involves loss of a proton from the reactive centre giving a mesomeric carbanion which is subsequently protonated with rearrangement. This mechanism, the unimolecular mechanism of base-catalysed prototropy, or $B\text{–}S_E1'$ as it has since become designated (*i.e.* base-catalysed unimolecular electrophilic substitution with rearrangement), can be generalized by equation (12)[114].

$B\text{–}S_E1'$



(12)

Here the base catalyst is left out of the molecularity of the reaction, partly because it is convenient to consider the process as analogous to the unimolecular mechanism of anionotropy (to be discussed later), but also because the precise nature of the base may be indeterminate—it could, for example, be an aggregate of molecules, especially if the catalyst were a hydrogen-bonded solvent such as water.

In those cases where the solvent provides the catalyst, the mobility of the system is necessarily very high, but if the effect of an added base can be measured in a particular instance, it is found that all bases catalyse the reaction. Catalysis by acids is also known, but in these cases it is the conjugate acid of the substrate which undergoes rearrangement in the subsequent deprotonation step and not the neutral substance itself. It is clear that a carbonium ion generated will have higher mobility than the parent compound.

The presence of a positively charged heteroatom may also confer mobility, as in the di-quaternary ammonium salts (equation 13),

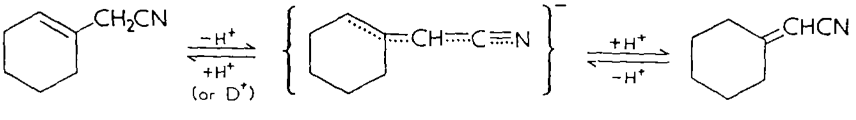
$$X_2^-\{(CH_3)_3\overset{+}{N}CH_2\text{—}CH{=}CH\overset{+}{N}(CH_3)_2C_2H_5\} \rightleftharpoons \{(CH_3)_3\overset{+}{N}CH{=}CH\text{—}CH_2\overset{+}{N}(CH_3)_2C_2H_5\}X_2^- \quad (13)$$

where both isomers have been isolated, unlike the propenylammonium compounds where the equilibrium is too one-sided, or else is disturbed by further reaction[115].

The examples of prototropic systems so far mentioned have involved only three carbon atoms, but multiple double bond shifts may also occur giving rise to pentad, heptad and even higher orders of rearrangement, and examples of these types will be discussed later.

Substituents on an unsaturated carbon chain will of course modify both the direction and speed of rearrangement; consideration of these kinds of effects will be included in the more specific discussion below, but, in general, conjugating or hyperconjugating groups will stabilize double bonds, much as in the case of β-elimination reactions and anionotropic shifts. The electronic effects will, however, be the opposite of those pertaining to anionotropic rearrangements, for electron-withdrawing groups will facilitate proton loss.

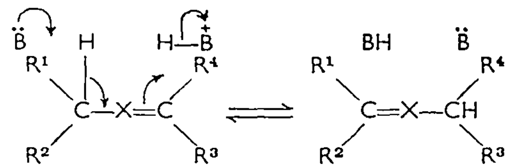
It is possible to demonstrate the participation of carbanions in the unimolecular process of prototropy by conducting the rearrangement in a labelled solvent (*e.g.* deuteroethanol) in the presence of a suitable catalyst. If the reaction is stopped in its early phase, considerable amounts of deuterium may have become incorporated into the unchanged starting material, demonstrating the reversibility of the initial process and its relative speed compared to that of the subsequent rearrangement. This kind of experiment has been carried out, for example, with cyclohexenylacetonitrile, confirming the unimolecular mechanism[116].



There is also the possibility that the removal of a proton and the addition of a proton to the other end of the rearranging system can be concerted processes: this, the bimolecular mechanism of prototropy (or electrophilic substitution with rearrangement B–S_E2'), has also been discerned[117].

Rearrangement of a propene or methyleneazomethine system which contains an asymmetric carbon atom must result in racemization of the optically pure substrate during the early phase of the reaction. If prototropic shift occurs by the bimolecular mechanism, the rate of rearrangement and change of optical activity must of necessity be the same during the initial stages, since there is no possibility of loss of optical activity by way of an intermediate carbanion; only those molecules which rearrange are the ones which lose the original asymmetric centre. Similar considerations also

B–S$_E$2′

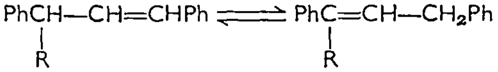


(X may be CH or N; R^1, R^2, R^3, R^4 are aryl or alkyl groups)

apply to the rates of isomerization and deuterium exchange, again the concerted mechanism implying that they should be equal.

The first systematic experiments based on these principles concerned the methyleneazomethines[118], where observations of rate of loss of optical activity, deuterium exchange and rearrangement were all found to be essentially equal, confirming the bimolecular mechanism[119, 120]. Later studies with the diarylpropenes and their derivatives have shown that the bimolecular mechanism applies here also.

It is interesting that, in the case of the 1-alkyl-1,3-diphenylpropenes, the mobility (which is extremely low in the diphenylpropene case) is enhanced by release of steric strain in the transition state, rather than by any decisive conjugative or inductive effect of the alkyl substituents in the carbon chain[121].



$$\underset{\displaystyle R}{\mathrm{PhCH}}\text{—CH=CHPh} \rightleftharpoons \underset{\displaystyle R}{\mathrm{PhC}}\text{=CH—CH}_2\text{Ph}$$

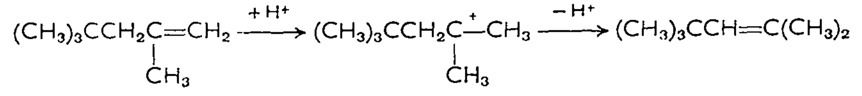
($R = CH_3$ or C_2H_5)

Further work in this field with labelled propenes promises to be interesting, especially in view of the recent report that 2-methyl-1,3-diphenylpropene-1-^{14}C exhibits very high mobility, the equilibrium in basic media appearing to lie in favour of the 1-^{14}C compound, 60–70% of the radioactivity remaining in the ethylenic group[122].

B. *Prototropic Rearrangements of Simple Olefins*

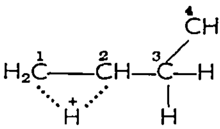
1. Alkylethylenes

Rearrangements of olefins induced by acids of the type encountered by Butlerow with diisobutylene, which are rationalized on the basis of a classical carbonium-ion intermediate, have been known for many years[123].



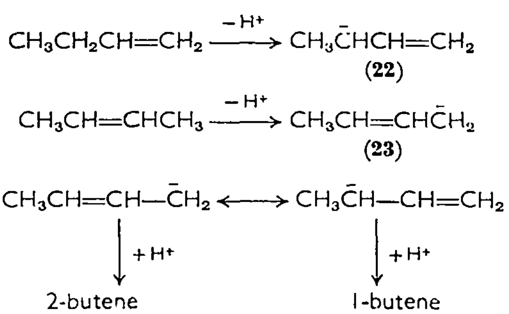
$$(CH_3)_3CCH_2\underset{\displaystyle CH_3}{C}{=}CH_2 \xrightarrow{+H^+} (CH_3)_3CCH_2\underset{\displaystyle CH_3}{\overset{+}{C}}{-}CH_3 \xrightarrow{-H^+} (CH_3)_3CCH{=}C(CH_3)_2$$

More recently closer attention to stereochemical detail in studies of prototropic rearrangements involving carbonium ions has revealed some of the more subtle features in transformations of this kind. For example, in the rearrangement of 1-butene to 2-butene over a silica–alumina catalyst, the reaction proceeds markedly in favour of the thermodynamically less stable *cis* isomer, by kinetic control of the product whose precursor is therefore the stabilized non-classical carbonium ion **21**, in which deformation about the $C_{(1)}$—$C_{(2)}$ bond is prevented so that $C_{(1)}$ is unable to assume the *trans* configuration relative to $C_{(4)}$ without internal energy increase. Consequently, the initial product is largely the *cis* compound, which equilibrates, however, to a mixture rich in *trans* isomer[124].



(21)

In view of the extremely low mobility of diarylpropenes, where at least potential intermediate carbanions can be stabilized by resonance involving the aromatic rings, it is hardly surprising that rearrangements of simple olefins catalysed by strong bases have only recently been discovered and studied in detail. Here, powerful nucleophilic reagents are required, and a typical case is the conversion of 1-butene to 2-butene in the presence of promoters such as sodium anthracene and sodium in the presence of *o*-chlorotoluene[125]. The proportions of allylic carbanions formed here as determined by carbonation to pentenoic acids* appear to be roughly constant regardless of the starting hydrocarbon, an indication of the relative ease of rearrangement of the relevant carbanions, **22** and **23**.



$$CH_3CH_2CH{=}CH_2 \xrightarrow{-H^+} CH_3\bar{C}HCH{=}CH_2$$

(22)

$$CH_3CH{=}CHCH_3 \xrightarrow{-H^+} CH_3CH{=}CH\bar{C}H_2$$

(23)

$$\begin{tikzcd} CH_3CH{=}CH{-}\bar{C}H_2 \arrow[r, leftrightarrow] \arrow[d, "+H^+"] & CH_3\bar{C}H{-}CH{=}CH_2 \arrow[d, "+H^+"] \\ \text{2-butene} & \text{1-butene} \end{tikzcd}$$

---

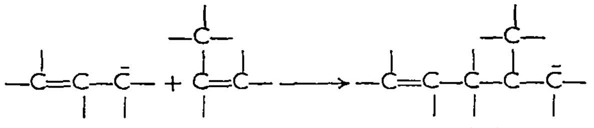
* Allowance must be made for the possible formation of dianions, *e.g.* from structure **23**, which give dicarboxylic acids.

Similarly, metalation of 1-hexene with n-amylsodium followed by carbonation indicates rearrangement of the initially formed carbanion, high yields of 3-heptenoic acid and 2-propyl-3-butenoic acid appearing in the product[126].

Analysis of the products in the reactions of olefins and olefin mixtures in the presence of organosodium compounds, where condensations involving carbanions and olefins may occur, can throw light on the question of relative carbanion stability. Those carbanions which are most stable are likely to be more selective in their reactions with an unsymmetrical substrate; unstable dimeric carbanions, *e.g.* of type **25**, will abstract a proton from the olefin, if this is present in excess, leading to dimeric hydrocarbon, whose skeletal structure will remain unchanged even though the molecule may suffer further prototropic rearrangement. The second product in this type of reaction will be a further chain-carrying carbanion. The proportions of products in reactions of this kind show that the relative stability of carbanions lies in the order:

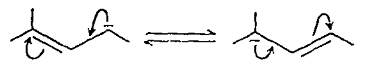
primary > secondary > tertiary

which is precisely the opposite of the stability relationships among the corresponding carbonium ions, and also among the free radicals formed in thermal reactions of olefins in the absence of alkali metal catalysts[127].



(24) **(25)**

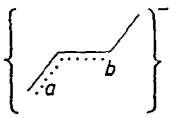
Essentially the same conclusion has been reached from observations of rearrangement of 2-methyl-1-pentene and the isomeric methyl-2-pentene under the influence of potassium *t*-butoxide, especially in the presence of dimethyl sulphoxide which acts as a 'cation scavenger'. Chromatographic examination of the products shows that the rates of isomerization past a tertiary carbon–hydrogen bond (equation 14a) is much slower than past a similar primary or secondary bond[128] (equation 14b). The detailed nature of the proton transfer step in this type of reaction is indicated by the relative rates of double-bond shift and deuterium exchange of perdeutero-1-pentene with unlabelled 2-methyl-1-pentene and solvent: isomerization is faster than exchange and therefore proton transfer is intramolecular. Rearrangement of 3-phenyl-1-propene in labelled solvent points to a similar conclusion[128a] and an ion pair is postulated, but the actual intermediate in individual cases may depend upon the type of base employed.



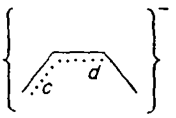
(14a)

(14b)

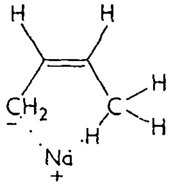
It is significant that solutions of lithium in ethylenediamine are more effective than sodio compounds in bringing about rearrangement of terminal to internal olefins, where once again carbanion intermediates are involved, proton abstraction by the ethylenediamine anion being the essential step[129]. The effectiveness of the reagent compared with sodioanthracene and n-amylsodium suggests that the cation is also involved, but its role is not yet clear. The nature of this role may, however, be reflected in the results obtained in the isomerization of *trans*-2-butene, where stereomutation occurs at a faster rate than double-bond shift, whilst the reverse is true of the *cis* isomer[130]. The observed stereoselectivity *may* be explained on the grounds of kinetic control of the final products by attack at various positions in the allylic carbanion intermediate, for which two distinct configurations are possible, separated by an appreciable energy barrier to rotation about the partial double bond.



trans



cis



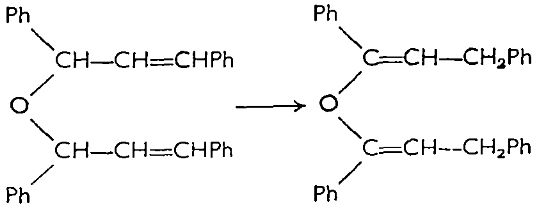
(26)

Propagation of the reaction by proton abstraction from butene molecules attacking the carbanions at either *a* or *c* produces *trans*- or *cis*-2-butene respectively, whereas attack at either *b* or *d* produces 1-butene. The rate data for these reactions show that protonation at *c* occurs four times more frequently than at *a*, and it seems more likely that this is due to the *cis* carbanion being present in larger concentration than the *trans* ion, rather than to any intrinsic difference in reactivity between the two ions. The *cis* carbanion derives additional resonance stabilization compared with the *trans* ion as a result of favourable interaction between the positive ion and the methyl hydrogens, as shown in **26**. In this connexion, it is significant that the butenyl Grignard reagent and sodiobutene have similar infrared spectra, although the Grignard reagent is covalent, and therefore not strictly comparable.

The theory is as yet incomplete, however, for in the isomerization of the series of compounds 1-butene, 1-pentene, 4-methyl-1-pentene and 4,4-dimethyl-1-pentene with potassium *t*-butoxide in dimethyl sulphoxide solution, the large initial *cis*/*trans* ratio of the 2-alkenes produced (which varies from 47·4 to 0·25 as estimated by extrapolation of the data to zero time) decreases rapidly with increasing methylation at the 4-position. At equilibrium, as expected, the stereoisomer ratio is very small (0·25–$<$0·001) favouring the *trans* isomers, but similarly decreases with 4-methylation. Here the unfavourable geometry of the methylated pentenes and the lack of suitable methyl hydrogen atoms for metal or oxygen bonding appears to preclude the kind of carbanion stabilization referred to above, and initial isomer ratios much closer to equilibrium values would be expected. The fact that this is clearly not the case indicates that other factors also operate, and the reaction mechanism may include base, solvent and olefins as proposed in the case of the 2-methylpentenes[131]. Conformational energy differences could also be invoked (see section I.B.3 below).

2. Alkene ethers and thioethers

Discussion as to whether rearrangement of α-arylated allylic alcohols to ketones under the influence of strong bases was an example of triad prototropy or pinacolic electron displacement led Shoppee



to examine the properties of unsaturated ethers in which there can be no ionization of the alkoxy group to drive the reaction in the direction of ketone. The compound chosen was bis-(α,γ-diphenylallyl) ether which isomerized readily under the influence of ethoxide ion, demonstrating true triad prototropic rearrangement[132].

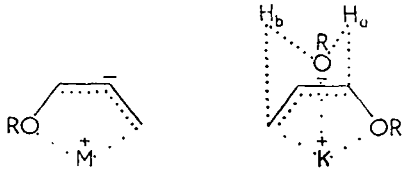
Since the time of this experiment, only isolated examples of this type of rearrangement have been discovered, *e.g.* sodamide in liquid ammonia converts vinylallyl ether into propenylvinyl ether[133], and 3-butoxy-3-methylpropene into 1-butoxy-2-methylpropene[134]. A more interesting recent result is that mono- and polyfunctional allyl ethers rearrange stereospecifically under strongly basic conditions giving almost entirely *cis*-propenyl ethers[135]. In the case of these allyl ethers, the oxygen atom does not initially appear to be involved in stabilizing intermediate carbanions, since no prototropic shifts occur under conditions where corresponding allyl sulphides are readily isomerized to their propenyl analogues. The difference in behaviour between the oxygen and sulphur compounds arises on account of the ability of the sulphur to expand its outer electron shell to a decet, thereby participating in stabilization of the carbanion intermediate[136].

Among the allylic compounds rearranged in high yields to preponderantly *cis*-propenyl ethers are 1,4-diallyloxybutane, 1,5-diallyloxypentane and their analogues, 4-allyloxybutanol and allyl ethers of pentaerythritol (the tri- and tetraethers, since the mono- and diallylethers rearrange to carbonyl compounds unless protected as isopropylidene ketals). The stereospecificity observed in these reactions is rationalized on the basis of a cation-stabilized mesomeric carbanion intermediate similar to that proposed for the 1-butene to *cis*-2-butene transformation, *but involving the oxygen atom.* Regardless of the mechanism, the reaction appears to require a *cis* configuration in the transition state, for where this cannot be achieved no isomerization occurs under the conditions employed.

The postulate of a resonance-stabilized cyclic transition state in prototropic shifts in allyloxyalkanes receives further support from the observation that catalysis by potassium *t*-butoxide is markedly enhanced in the presence of dimethylsulphoxide (by a factor of 10^3!) and the products are again *cis* isomers (99%). The dimethyl sulphoxide acts as a cation scavenger, effectively activating the alkoxide anion by removing the environment of potassium ions. Addition of alcohol reduces the rate, partly by solvation of the anion, and partly by precipitation of the alkoxide as its molar complex with the alcohol. These effects suggest a ternary transition state of the type shown in **27**[137].

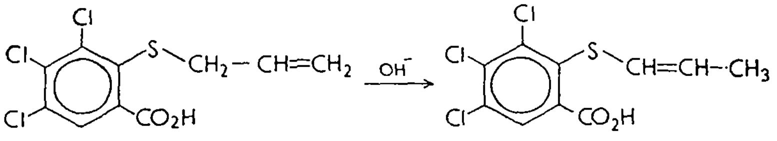
Here it is visualized that H_a is labilized by approach of alkoxide ion. Simply by movement of hydrogen only, a complex with this atom at H_b results.

The facility with which the isomerization of aryl allyl thioethers to propenyl analogues can be achieved was discovered during investigations into the Claisen rearrangement. Similar prototropic shifts of sulphur compounds had, however, been encountered earlier, for example with the sulphones, where the powerful electronegative character of the sulphone group is responsible for the observed mobility, and doubtless such reactions involve the familiar pattern of removal of the proton from the α-carbon and re-entry at the γ-carbon of the chain[138]. The mobility of the thiosalicylate allyl ethers involves the formation of a resonance-stabilized carbanion, in which contributions to the resonance hybrid of canonical forms involving sulphur in a decet of electrons are possible, unlike the corresponding oxygen compounds, which are therefore unaffected under similar conditions. The effect is relatively pronounced in thiosalicylic acids on account of the fact that they exist as anions in solution, which nevertheless lose a further proton resulting in prototropic shift[136].



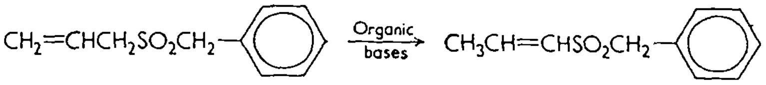
(27)

Similar mobility is observed with allyl n-alkyl sulphides, and, if isomerization is carried out in deuteroethanol, considerable quantities of mono- and dideuteroalkylpropenyl sulphides are isolable, showing that the intermediate carbanion exchanges with the solvent quite easily, thereby eliminating the possibility of a concerted mechanism, where a maximum of only one deuterium atom per molecule of product could be incorporated. The alkylpropenyl sulphides formed occur in both stereoisomeric forms. Double prototropic shifts are also known, for example diallyl sulphide can be converted to dipropenyl sulphide under basic conditions, but some decomposition also occurs.

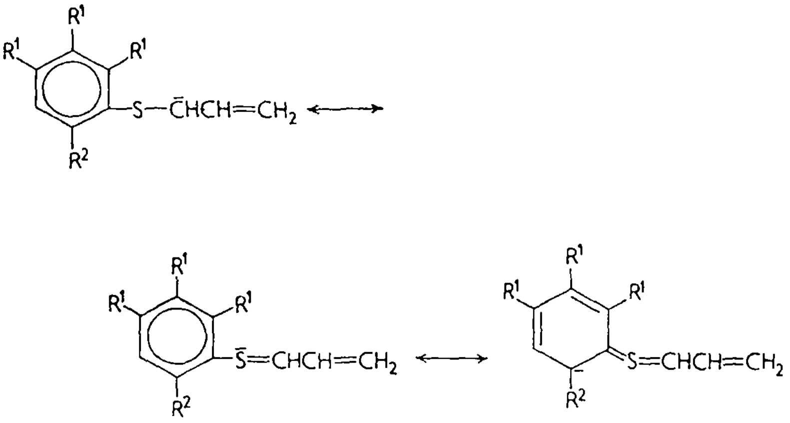


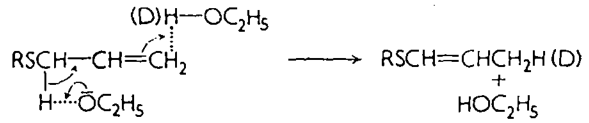
(*cis–trans* mixture)

(28) **(29)**



(30) (31)





3. Allylamine rearrangements

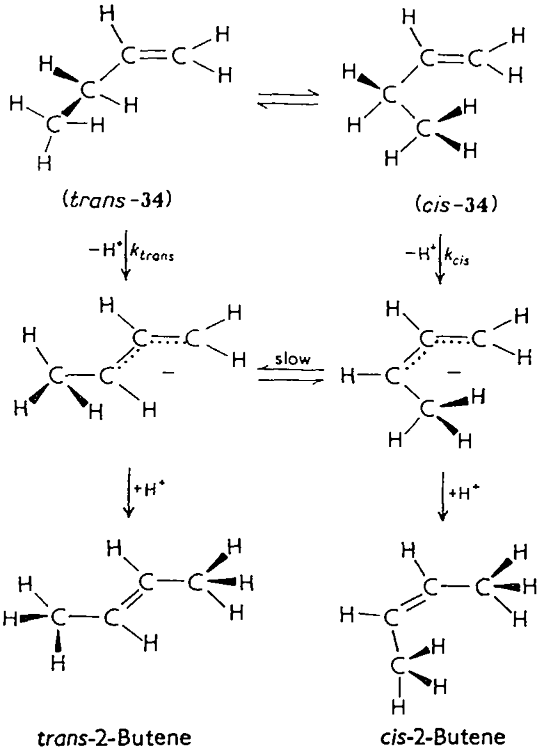
Unlike the stereoselective *cis* isomerization of n-alkenes and allylic ethers, prototropic shifts in allylamines under essentially similar conditions leads on the whole to predominantly *trans*-propenylamines with formation of less than one per cent of *cis* product[139].

$$CH_2{=}CH{-}CH_2NR^1R^2 \xrightarrow[(CH_3)_2SO]{t\text{-}C_4H_9OK} CH_3{-}CH{=}CHNR^1R^2$$

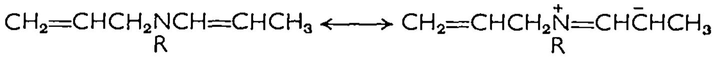
(32) **(33)**

(**a**, $R^1 = R^2 = CH_3$; **b**, R^1 = allyl, $R^2 = CH_3$; **c**, R^1 = allyl, R^2 = propenyl)

However, for the case where R^1 is allyl and R^2 is propenyl (**32c**), rearrangement of the allyl group is predominantly to *cis*-propenyl. These differences in steric course for the prototropic shift may be explained by making certain assumptions regarding the detailed conformations of 1-butene, and the various allylamines involved, principally that the energy difference between the conformations *cis*-**34** and *trans*-**34**, which, although probably no larger than a kilocalorie or so owing to favourable interaction between the methyl hydrogens and the double-bond system, will nevertheless exert a decisive effect. Under these conditions, the rate coefficients for the isomerizations k_{cis} and k_{trans} will be very nearly equal, but yet there will be a preference for *cis*-butene. The stereomutation of the intermediate carbanions would be slow owing to the partial double-bond character of the $C_{(2)}$—$C_{(3)}$ bond which would restrict rotation.



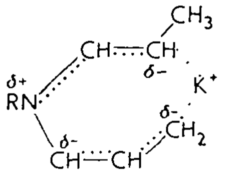
If on the other hand the methyl group is replaced by the dimethylamino group, strong repulsion between the π-bond system and the nitrogen lone-pair electrons would arise, and the *trans* conformation would therefore be strongly favoured, a larger value for k_{trans} leading to predominantly *trans* product. However, if a propenyl group is also present on the nitrogen atom, as in the allylpropenylamine **35b**, diminished electron availability on nitrogen caused by resonance



$$\mathrm{CH_2{=}CHCH_2\underset{R}{N}CH{=}CHCH_3 \longleftrightarrow CH_2{=}CHCH_2\underset{R}{\overset{+}{N}}{=}CH\overset{-}{C}HCH_3}$$

(35a) **(35b)**

effects reduces repulsion and also provides an alternative reaction path involving a cyclic transition state which would enhance k_{cis} compared to k_{trans} and therefore circumvent unfavourable stereochemical features. As in the case of the base-catalysed stereomutation of *trans*-2-butene, the cyclic transition state is stabilized by the cation, **36**.



(36)

4. Olefinic acids and other carbonyl compounds

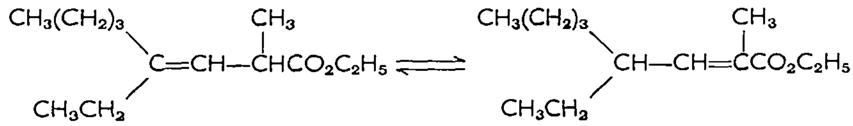
Prototropic rearrangements involving olefinic acids induced by aqueous alkali are well known and have received detailed study along with corresponding esters, ketones and nitriles which, although actually pentad systems, are more conveniently regarded as triad, the functional group being regarded as the activating moiety[140].

$$\mathrm{RCH_2{-}CH{=}CHX \rightleftharpoons RCH{=}CH{-}CH_2X}$$

(R = alkyl or aryl; X = CO_2^-, $CO_2C_2H_5$, CN, $COCH_3$, etc.)

In simple unsaturated compounds of this type, the carbonyl- or cyano-conjugated forms predominate at equilibrium, unless there are unsaturated substituents in the γ-position, under which conditions the equilibrium may be shifted in favour of the γ-conjugated isomer, *e.g.* γ-phenylbutenoic acid exists largely in the but-3-enoic acid form. Substituents in the α-position generally favour the α,β-unsaturated isomers, as the conjugated or hyperconjugated groups disturb the conjugation between the double bond and the activating group only to a small extent. The importance of hyperconjugation may be seen in the case of γ-methyl compounds where the equilibrium is shifted towards the β,γ-isomer, and, as might be expected, conjugative shift is almost complete in the case of the γ-arylated compounds. The position becomes rather complicated when the γ-position is substituted with larger alkyl groups, and all that can be said in general is that the effect is less marked than with the simple methyl compounds. Methyl and higher alkyl substituents in the β-position also appear to have a small but inconsistent effect.

In highly substituted unsaturated carbonyl compounds, the position of equilibrium may also be determined by steric effects. The equilibrium between the isomers **37** and **38** for example favours **38** by a factor of two to one; substitution of the smaller terminal group with other alkyl groups has little effect on the equilibrium unless the ethyl group is replaced by methyl, and then the proportion of non-conjugated isomer increases. This effect can be thought of as either due to increased hyperconjugative stabilization of the form **37** or else as due to reduced steric strain about the double bond. If the ethyl group is replaced by a larger more branched group such as isopropyl or *t*-butyl, the proportion of the non-conjugated isomer decreases and this must surely be due to increased steric strain. A similar effect is observed with 3-substituted 1-arylpropenes where the proportion of conjugated isomer at equilibrium increases markedly[141].

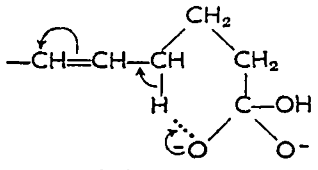


$$(CH_3(CH_2)_3)(CH_3CH_2)C{=}CH{-}CH(CH_3)CO_2C_2H_5 \rightleftharpoons (CH_3(CH_2)_3)(CH_3CH_2)CH{-}CH{=}C(CH_3)CO_2C_2H_5$$

(**37**) (**38**)

It has not always been appreciated that similar prototropic shifts occur when olefinic acids are fused with alkali. Under these conditions, cleavage can occur to give a saturated acid and acetic acid (the Varrentrapp reaction[142]). Clearly, if the reaction is used to diagnose the position of a double bond without consideration of the possibility of isomerization, confusion can arise. For example, oleic acid (which gives palmitic acid, acetic acid and hydrogen on fusion with alkali) was long considered to be octadec-2-enoic acid, until reliable oxidative techniques established the true structure as octadec-9-enoic acid[143]. Similar alkaline degradations have been carried out with other natural olefinic fatty acids, double-bond shift frequently being observed, and the mechanism of the Varrentrapp reaction has been the subject of much discussion. Most authors take the view that the double bond first shifts to the 2,3-position before fission occurs, since no normal Varrentrapp reaction can be realized with unsaturated acids where the 3-position is effectively blocked as in 3,3-dimethylnon-8-enoic acid, whilst, on the other hand, many 2,3-unsaturated carboxylic acids readily undergo fission in fused alkali with loss of two carbon atoms, *e.g.* octadec-2-enoic acid, oct-2-enoic and hex-2-enoic acids, in each case the proportions of alkanoic and acetic acids formed being roughly equal[144,145]. The same product ratio appears in fission of long-chain olefinic acids in which the double bond is remote from the carboxyl group.

The concept of a prototropic mechanism for migration of the double bond in Varrentrapp reactions has been advanced only comparatively recently and is supported by the general developments in this field[146,147,148,149]. The overall process can be visualized as a sequence of 1,3-prototropic rearrangements in which proton removal and return may be either concerted, or a consecutive series of reactions. Such a process might be expected to lead to an equilibrium mixture, but fission of 2,3-unsaturated acid continually disturbs the equilibrium. The carboxyl group has no directive effect, since, in reactions which are prematurely terminated by quenching, ozonolysis of the product gives dicarboxylic acids in proportion to the amounts of double-bond isomers present, and the results in fact correspond to migration of the double bond in both directions along the chain. With oleic acid, for example, all octadecenoic acids from the 6- to the 11-enoic acid isomers can be detected in this way, but no large amounts of the octadec-2-, 3-, 4- or 5-enoic acids, suggesting that the rate of rearrangement accelerates in approaching the carboxyl group. In direct confirmation of this, comparison of the rates of rearrangement of octadec-6-enoic acid (petroselenic acid) and oleic acid under identical conditions of time and temperature shows that the rate of reaction is increased in the former case, and that although migration takes place in both directions there is more migration towards the carboxyl group than away from it. In order to explain this proximity effect of the carboxyl



(39)

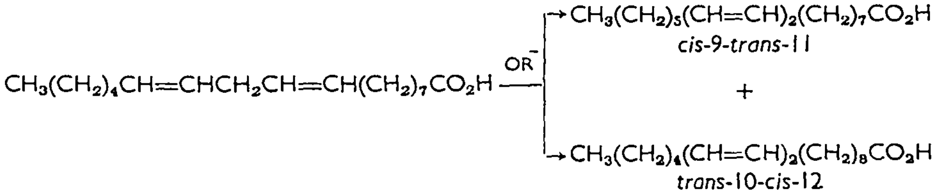
group, an intramolecular process must be postulated, and structures such as **39** may be important.

In view of this, it is not surprising that olefinic acids of shorter chain length are correspondingly more reactive in the Varrentrapp reaction. Very brief exposure of non-2-enoic acid to fused alkali affords as much as 20% non-3-enoic acid. Under the conditions of these reactions, stereomutation of geometrical isomers often occurs, and, with the octadecenoic acids, the proportion of residual olefinic acids with the *trans* configuration approaches an equilibrium figure of 65%, that pertaining to the well known oleic–elaidic acid transformation.

C. Prototropic Rearrangements in Polyenes

1. Fatty acids

The study of prototropic rearrangements in polyene fatty acids has grown from observations of rearrangement during the saponification of natural drying oils[150], and has found application in the analytical field where conjugated chromophores introduced by comparatively mild alkaline treatment are readily estimated by absorption spectroscopy[151]. Perhaps the most common example is that of linoleic acid, which is isomerized by mild alkaline treatment to a mixture of octadec-*cis*-9-*trans*-11-dienoic and octadec-*trans*-10-*cis*-12-dienoic acid, both of which can be elaidinized by iodine to the all-*trans* forms.



$$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H \xrightarrow{OR^-} \begin{cases} CH_3(CH_2)_5(CH{=}CH)_2(CH_2)_7CO_2H \quad \textit{cis-9-trans-11} \\ + \\ CH_3(CH_2)_4(CH{=}CH)_2(CH_2)_8CO_2H \quad \textit{trans-10-cis-12} \end{cases}$$

Similarly, octadec-10,12,14-trienoic acid (a solid acid which may be the all-*trans* isomer) can be obtained from linseed oil, which consists largely of linolenic acid[152], whilst arachidonic acid (eicosa-5,8,11,14-tetraenoic acid) gives a conjugated tetraenoic acid under similar conditions[153].

In these shifts, the static double bond normally retains its geometrical configuration, but the one which migrates, if originally *cis* becomes predominantly *trans*, but if originally *trans* appears to form both *cis* and *trans* isomers equally easily. For example, the all-*trans*-3,5-dienoic acids are obtained from the 2-*cis*-5-*trans* series of acids by mild alkaline treatment, and other *retro* transformations are also known in this series[154].

$$\underset{trans}{\mathrm{RCH_2CH{=}CHCH_2}}\underset{cis}{\mathrm{CH{=}CHCO_2H}} \longrightarrow \mathrm{RCH_2}\underset{trans}{\mathrm{CH{=}CH}}\underset{trans}{\mathrm{CH{=}CH}}\mathrm{CH_2CO_2H}$$

Normally these types of conjugative isomerization require mild heating, but the same kind of shifts can be brought about at room temperature by using mixtures of *t*-butanol and *t*-butoxide ion together with dimethylformamide, dimethyl sulphoxide or tetramethylurea. The enhanced activity of the base is ascribed to the ability of the additives to form strong hydrogen bonds with the alcohol, as well as their ability to solvate the metallic ions effectively, hence removing them from the reaction site[155]. (Enhanced rates in the reaction of alkyl halides with sodiomalonic ester are also observed in the presence of these types of additives, whose specific cation solvation effect must therefore be considerable[156].) Complete conjugation of the unsaturated system in linolenic and arachidonic acids can, however, be brought about by butoxide ion alone (in butanol), although higher temperatures and sealed tubes are required; under similar conditions other natural polyene fatty acids are conjugated to a greater extent than with the more usual reagents[157].

Under the even more drastic conditions of alkali fusion, conjugated polyolefinic acids produced can react further by fission, and ozonolysis[158] of the products obtained from linoleic acid under these conditions gives not only a series of monocarboxylic acids (C_6–C_{16}) but also a range of dicarboxylic acids (C_3–C_{11}) showing that the double-bond system is capable of migrating along the chain in both directions, the carboxyl group exerting no directive effect. Moreover, unconjugated isomers can also be formed, as seen in the isolation of octadeca-8,12-dienoic acid (**40a**) and octadeca-9,13-dienoic acids (**40b**), the double bonds migrating independently of each other: removal of the protons from the less reactive $C_{(8)}$ and $C_{(14)}$ positions becomes feasible under the more vigorous conditions used[159]. Unconjugated isomers are not usually formed under mild conditions[160].

$$\mathrm{CH_3(CH_2)_4CH{=}CH(CH_2)_2CH{=}CH(CH_2)_6CO_2H}$$

(40a)

$$\mathrm{CH_3(CH_2)_3CH{=}CH(CH_2)_2CH{=}CH(CH_2)_7CO_2H}$$

(40b)

Discussion of prototropic rearrangements of polyene acids would be incomplete without reference to the most interesting work with certain unconjugated enynoic acids such as **41** (*cf.* **42**), which under-

$$\underset{(41)}{\mathrm{HO_2CC{\equiv}C(CH_2)_2CH{=}CHCO_2H}} \xrightarrow{t\text{-}\mathrm{C_4H_9O^-}} \mathrm{HO_2C(CH{=}CH)_3CO_2H}$$

$$\underset{(42)}{\mathrm{HO_2CC{\equiv}C(CH_2)_2C{\equiv}CCO_2H}} \xrightarrow{t\text{-}\mathrm{C_4H_9O^-}} \mathrm{HO_2C(CH{=}CH)_2C{\equiv}CCO_2H}$$

$$\left.\begin{array}{l} \underset{(43)}{\mathrm{[\text{-}C{\equiv}C(CH_2)_2CH{=}CHCO_2H]_2}} \\ \underset{(44)}{\mathrm{[\text{-}C{\equiv}CCH{=}CH(CH_2)_2CO_2H]_2}} \end{array}\right] \xrightarrow[\mathrm{C_2H_5O^-}]{\mathrm{C_2H_5O^-}} \underset{(45)}{\mathrm{HO_2C(CH{=}CH)_6CO_2H}}$$

go prototropic shift in alkaline media to give the straight through conjugated dicarboxylic acids[161]. The synthesis of the highly unsaturated crystalline naturally occurring tetradecahexaendioic acid corticrocin (**45**) relies upon similar transformations of the penultimate diacids in the synthetic chain, namely **43** and **44**, which form golden-yellow plates of the acid in the presence of alcoholic alkali[162,163].

Similar rearrangements have been realized with the parent hydrocarbons and their higher homologues, *e.g.* *trans*-5-decaene-1,9-diyne is converted in 9% yield to the mainly all-*trans*-decapentaene and *trans-trans*-5,15-eicosadiene-1,9,11,19-tetrayne to the mainly all-*trans*-eicosadecaene, but there is spectrographic evidence for the

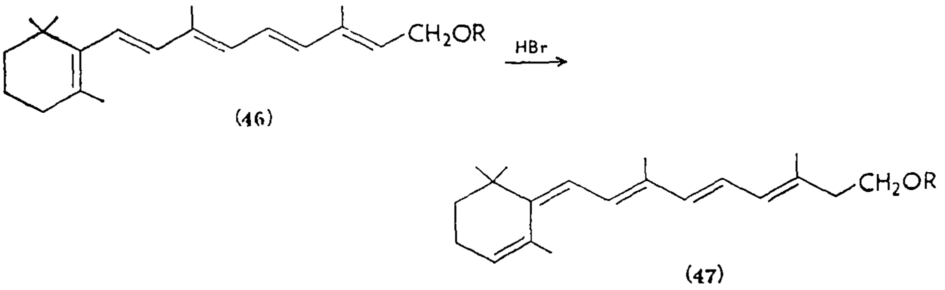
$$\mathrm{HC{\equiv}C(CH_2)_2CH{=}CH(CH_2)_2C{\equiv}CH} \xrightarrow[t\text{-}\mathrm{C_4H_9OH}]{t\text{-}\mathrm{C_4H_9O^-}} \mathrm{H(CH{=}CH)_5H}$$

$$\mathrm{[HC{\equiv}C(CH_2)_2CH{=}CH(CH_2)_2C{\equiv}C\text{-}]_2} \longrightarrow \mathrm{H(CH{=}CH)_{10}H}$$

presence of some *cis* isomers in chromatographic fractions obtained from the crude products of these reactions, especially in the case of the decaene, and also in the similarly prepared hexaene and octaene[164].

2. Prototropy in polyenes of the vitamin A type

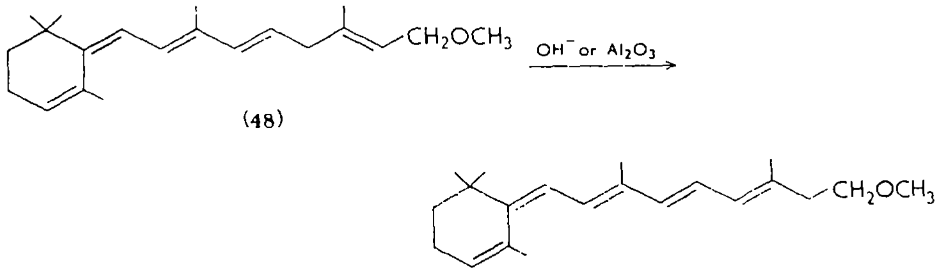
Both acid- and base-catalysed double-bond shifts are known in the vitamin A series of polyenes and related compounds. Perhaps the most interesting rearrangements are those which relate the cyclohexenylnonatetraene structures with the isomeric cyclohexenylidene types (the '*retro*' structures) illustrated for vitamin A acetate and *retro*-vitamin A acetate (**46** and **47**, R = $\mathrm{COCH_3}$).



(46)

(47)

The molecule of vitamin A exhibits considerable steric interaction between the methyl groups on the ring and the side chain, absent in the *retro* isomer, so that the latter type of compound is thermodynamically more stable. It is not surprising then that the *retro* series of compounds is directly accessible merely on treating the normal isomer with hydrobromic acid, displacement of all five double bonds taking place, probably through a mesomeric carbonium ion—a reasonable postulate in view of the well known proton acceptor properties of polyenes; certainly no evidence has been found that extended rearrangements of this type occur by a consecutive series of double-bond shifts. Partial shifts are, however, known among synthetic intermediates, such as **48** and **49** which both rearrange



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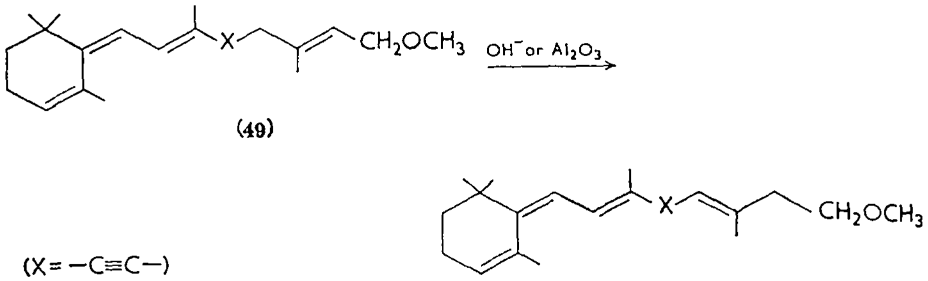
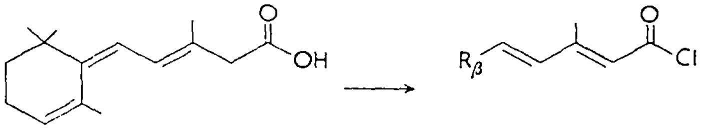


(49)

(X= —C≡C—)

conjugatively under the influence of both acid and basic catalysts such as alkali or alumina. Where there are *cis* double bonds in intermediates of this type, both *cis* and *trans* isomers are found in the products, as might be anticipated if mesomeric ions are involved[165].

The reverse transformation, *retro* to normal polyene, has not been realized with the isomers of vitamin A, where the geometrical features of the molecule appear to control the final products in isomerization media. That it should be, and in fact is, possible to realize the *retro* to normal transformation by suitable variation in electronic makeup in molecules of this type has been elegantly demonstrated in the case of the acids **50** and **51**. Conversion of these acids to their chlorides takes place with prototropic shift, the 'normal' structures resulting, probably because of the increased lability of the hydrogens on the adjacent methylene on account of the tautomeric effect of the COCl function[166].



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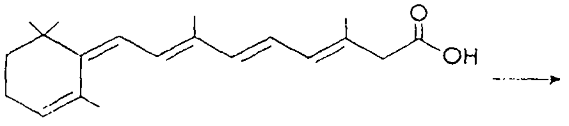

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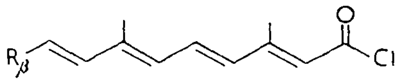
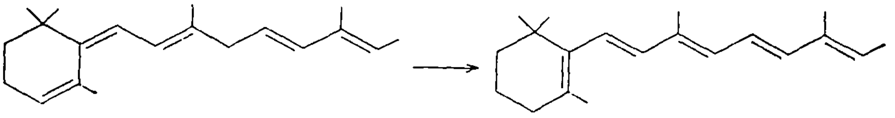
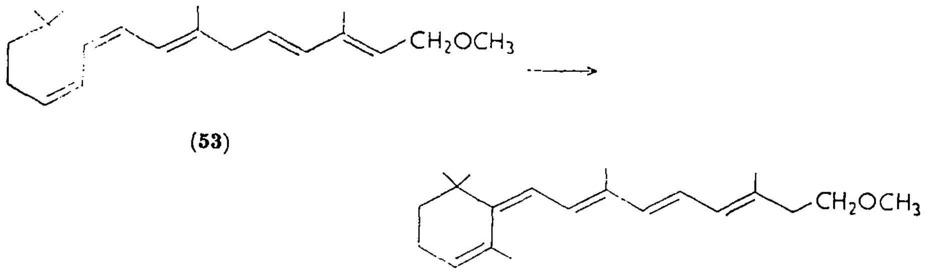


A similar *retro* to normal transformation is known with the hydrocarbon **52** which under basic conditions affords the conjugated normal structure, in contrast with the case of **53** which, although conjugated, gives the *retro* compound[167]. It is clear from these



(52)



(53)

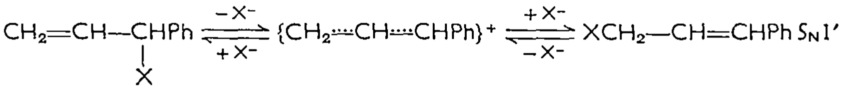
examples that the relationship between the cyclohexenyl- and cyclohexenylidene compounds is one of delicate balance between electronic and steric factors in the intermediate carbonium ions or carbanions, and prediction is therefore difficult or impossible unless closely similar structures in a given instance have received prior examination, in the manner which Oroshnik and his collaborators have brought to bear on this and other problems referred to previously in the polyene field.

III. ANIONOTROPIC REARRANGEMENTS

A. Introduction

The rearrangement of unsaturated compounds which involves the shift of a double bond, or a series of double bonds, with simultaneous migration of an electronegative atom or group of atoms together with the electrons which originally bound it to the carbon chain, is classified under the general term *anionotropy*, which in its wider sense also includes rearrangements of saturated compounds, and compounds where a heteroatom is joined to carbon by a double bond, such as the Beckmann transformation of oximes. The simplest types of olefins undergoing anionotropic rearrangements are the allylic compounds[168], which are the subject of a later chapter in this book (Chapter 10). It is relevant here, however, to give a brief account of the development and the present position regarding the theory and experimental observation of anionotropic transformations between isomers in both simple and substituted allylic compounds for the conclusions have obvious relevance to more complex molecules.

The possibility of transfer of a nucleophile or anionic fragment in an allylic compound was first clearly stated by Burton and Ingold[169] who studied the rearrangement of phenylallyl esters and other compounds and based their views on the fact that in general the tendency of the migrating group to form an anion paralleled the ease of rearrangement which was also facilitated by electron-donating substituents in the molecule. Further, the rearrangement was diverted to substitution in the presence of foreign anions pointing to the involvement of free mesomeric carbonium-ion intermediates. The facts seemed best explained by heterolysis of the molecule into a free carbonium ion and an anion, which then had the opportunity of reuniting to give an isomeric rearranged product, as in Scheme 5.



$$CH_2{=}CH{-}\underset{\underset{X}{|}}{C}HPh \underset{+X^-}{\overset{-X^-}{\rightleftharpoons}} \{CH_2{\cdots}CH{\cdots}CHPh\}^+ \underset{-X^-}{\overset{+X^-}{\rightleftharpoons}} XCH_2{-}CH{=}CHPh \quad S_N1'$$

SCHEME 5.

Reactions of this kind were also investigated by Meisenheimer, who found them to be kinetically of the first order and catalysed by neutral ionic salts in relatively non-polar solvents, in accord with elementary theory[170].

The rearrangement of allylic esters can occur spontaneously, but more often rearrangements are brought about by acid catalysis, this being particularly the case for allylic alcohols, whose transformation is often referred to specifically as *oxotropy*. Alkylated allyl chlorides have also been found to isomerize slowly at elevated temperatures in polar solvents with or without inorganic halides as catalysts[171], whilst the more labile 1- and 3-phenylallyl chlorides are interconverted at a rate which is proportional to the acidic strength of the acid catalyst used[172]. By way of contrast, the analogous rearrangement of simple alkylallylic bromides is spontaneous, rapid at the boiling point, and catalysed by traces of peroxides suggesting a free-radical mechanism[173,174]. These few examples illustrate the diversity of mobility encountered among relatively simple and closely related structures, which is to be expected, however, on account of the wide possibilities for combination of alkenyl ions and migrating nucleophiles, both of which contribute to the overall reactivity of a given molecule.

In all these isomerizations a *unimolecular* reaction pathway like that of Scheme 5 can be visualized, but it has become apparent from later work that the simple idea of the allylic compound dissociating into nucleophile and carbonium ion—which separate, become kinetically free and then reunite—must be modified to take account of catalysis when it occurs, and the participation of intimate and solvent-separated ion pairs, in the dissociation step, especially in solvents of low dielectric constant. The solvent therefore plays a more decisive role in determining the separation, reactivity and fate of the fragments than previously realized[175]. The consequences of ion-pair formation will become apparent in examples of rearrangement to be discussed later.

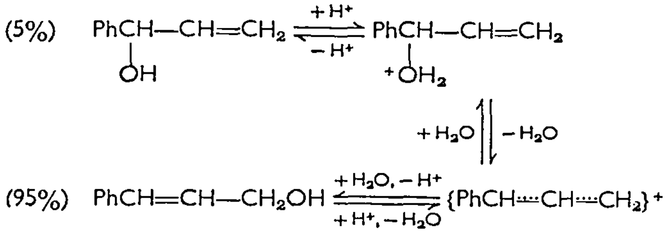
Nevertheless, the basic idea implied in Scheme 5 is very useful, especially from the immediate practical point of view, for in general the heterolytic mechanism for anionotropic rearrangement will be facilitated by solvents of high dielectric constant and by electron-donating substituents in the unsaturated compound, which will stabilize the carbonium ion formed. Numerous studies have established the essential correctness of these principles, and will be described in detail below, particularly in connexion with oxotropy.

An alternative unimolecular reaction pathway is available for rearrangement which involves a cyclic transition state (the S_Ni' process). Here the geometrical configuration of the molecule may determine whether or not synchronous shift of bonds can occur, but it is not a necessary condition, because the transition-state assembly appears to be capable of assuming spatially extended dipolar character to a considerable degree—certainly to the extent that solvent effects can be discerned, and of course rearrangement will be facilitated by suitable substituents in the molecule. In these cases no actual separation of fragments occurs. The detection of the intramolecular S_Ni' pathway in rearrangements where it makes a significant contribution to the overall process affords a stimulating illustration of the degree of sophistication achieved in the technique of studying reaction mechanisms.

B. Catalysis and Mechanism of Anionotropic Transformations

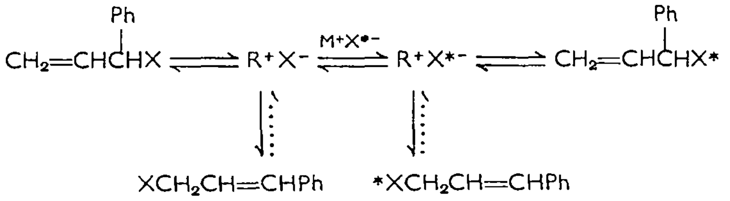
1. The unimolecular mechanism, S_N1'

A number of instances of acid-catalysed rearrangement of allylic compounds have been investigated in detail, particularly the oxotropy of 1-phenylallyl alcohol in aqueous mineral acids. The earlier proposals for the mechanism of isomerization to 3-phenylallyl alcohol represented something of a departure from the traditional concepts, for it was suggested that the reaction involved a concerted cyclic process, in which the function of the catalyst is to protonate the hydroxyl group facilitating stretching and eventual cleavage of the $C_{(1)}$—OH bond, with a simultaneous double-bond shift and the formation of a new bond to $C_{(3)}$[176]. However, later evidence based on the labelling of the aqueous solvent with ^{18}O points in fact to the true S_N1' pathway, the catalyst functioning as previously suggested, but the protonated species losing a water molecule to give a carbonium ion which appears to become free before reaction with the solvent ensues giving original and rearranged product[177] (Scheme 6).



SCHEME 6.

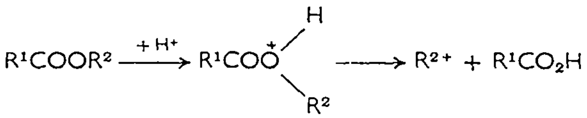
As mentioned earlier, in reactions of the S_N1' type, the scheme for the reaction pathway should be expanded to take account of ion-pair formation which has an important effect in aprotic solvents or media of low dielectric constant. Under these conditions a considerable degree of C—X (X = nucleophile) bond heterolysis can occur without the result that the ion X^- becomes kinetically free, the reactions resembling those of the S_Ni' type, for the carbonium ion in the ion pair recaptures the original anion, and rearrangement may occur. Cases of this type which have been studied include the isomerization of 1-phenylallylbenzoate and *p*-nitrobenzoate, which have been examined in detail, using chlorobenzene as aprotic solvent. In the absence of acids, the reactions are unimolecular and there is slight catalysis by added neutral salts[178,179]. Tracer experiments with added common labelled anion indicate that there is some incorporation of the labelled anion into both rearranged and unrearranged material, whilst the acyl oxygen of the starting material becomes largely the alkyl oxygen of the product of rearrangement. Further, rearrangement is more rapid than exchange in the 3-position. Scheme 7 accommodates these results.



SCHEME 7.

The precise nature of the ion pairs R^+X^- and R^+X^{*-} is not specified. However, although it is true that the reactions are carried out at a higher temperature than comparable reactions which are known to produce the phenylallyl cation, nevertheless it is surprising that a preponderance of the thermodynamically stable rearranged product is obtained, contrary to the usual experience that the more reactive less stable unrearranged classical ion reacts fastest, producing larger amounts of the less stable product by *kinetic* control[180]. Reactions of this type should be formally included with the S_Ni' class of reactions, but are extreme cases on account of the considerable dipolar character developed in the transition state[181].

The earlier view that acid catalysis is necessary for these types of ester rearrangement is now known to be incorrect, although it can occur. This is hardly surprising in view of the nature of the ester function, which is easily protonated at the alkyl oxygen with subsequent bond fission, giving the carbonium ion of the alcohol (equation 15); it has been shown, for example, that the rearrangement of phenylallyl *p*-nitrobenzoate is catalysed by *p*-nitrobenzoic acid in chlorobenzene[178].

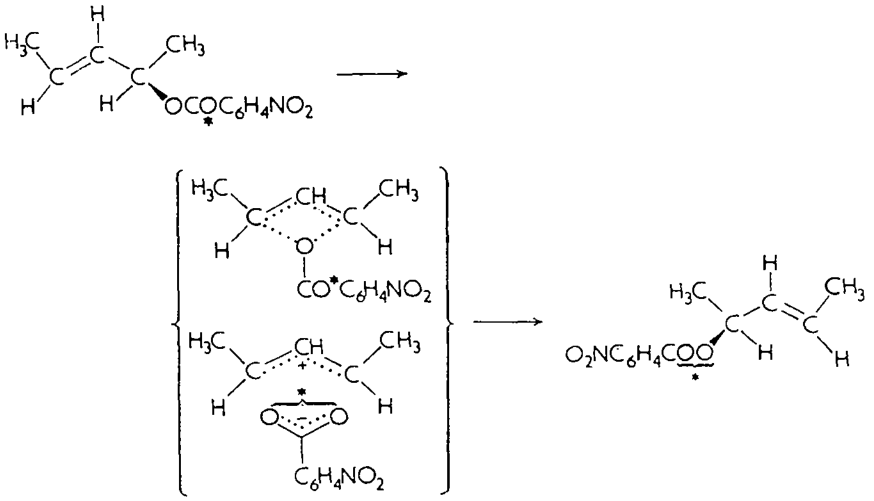


$$R^1COOR^2 \xrightarrow{+H^+} R^1CO\overset{+}{O}\begin{matrix}H\\R^2\end{matrix} \longrightarrow R^{2+} + R^1CO_2H \qquad (15)$$

On the other hand, evidence also exists for the carbonium-ion S_N1' mechanism in ester rearrangements. In the transformation of (−)-1-phenylallyl ^{14}C-acetate in acetic acid catalysed by perchloric acid, the rates for exchange with the solvent, racemization and rearrangement are all proportional to the acidity function H_0[182]. Here the rate of dilution of the tracer in the ester mixture is the same as the rate of racemization but is slightly higher than the rate of rearrangement. The 3-phenylallyl acetate isolated after the rearrangement is free of tracer and the directly measured rate of exchange is found to be slower than the rate of rearrangement. The simplest explanation is that both racemization and symmetrical exchange proceed through what may be a free carbonium ion which reacts with the acetic acid at either available position to give some unrearranged material, this being also racemized. The nature of the charged species is governed by the low dielectric constant of the solvent, which may, however, contribute to the ionization process by hydrogen bonding.

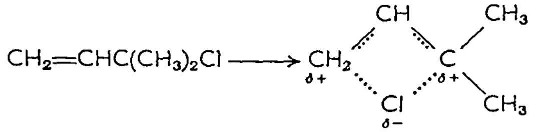
2. The intramolecular mechanism, S_Ni'

Evidence for the intramolecular mechanism of anionotropic rearrangement has been detected in a number of cases, notably in the solvolysis of (+)-*trans*-1,3-dimethylallyl *p*-nitrobenzoate, where it accompanies the unimolecular solvolysis process[183]. The relative positions of the ester oxygen atoms in the reactant and product were established using ^{18}O-labelled ester as the starting material (label in the carbonyl group). Observation of the rate of equilibration of the labelled oxygen atom between the acyl and alkyl positions suggest that the mechanism could be presented as in equation (16). Clearly, the labelled oxygen remains in the carbonyl group in the cyclic-intramolecular process, but in the ion pair it can obviously have the possibility of becoming the acyl oxygen. The results show that the intermediate is a tightly bound ion pair with some internal flexibility, the rate of racemization being about three times that of oxygen interchange, increased solvent polarity having only a small effect on their ratio[183a].



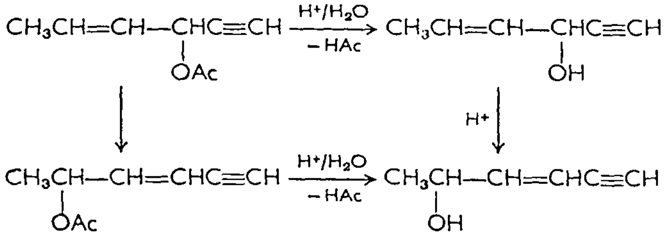
(16)

A further reaction in which the cyclic-intramolecular mechanism for rearrangement has been detected is in the acetolysis of 1,1-dimethylallyl chloride, concomitant rearrangement of the chloride accompanying the substitution reaction, since the kinetics of liberation of hydrogen chloride do not accord with the simple unimolecular solvolysis process[184]. The transition state is pictured as synchronous transfer of chlorine and double-bond shift. Competition of the cyclic-intramolecular pathway is not as important in *less* ionizing media, but is catalysed by added labelled chloride anion, incorporation of the labelled anion into both rearranged and unrearranged material indicating the heterolytic component of the total reaction pathway.



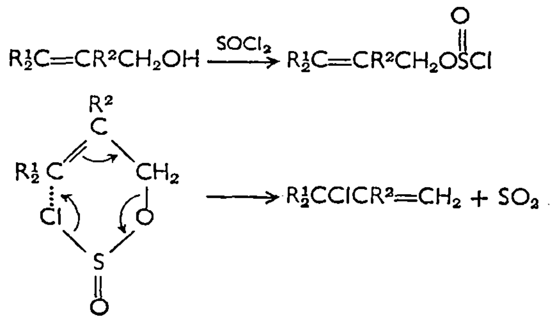
The relative rates of solvolysis are not completely in accord with the sequence of ionizing power of the media, however, but again the polar character of the cyclic-intramolecular transition state is evident from their effect, more polar media favouring its participation[185].

Few mechanistic studies have been made on extended allylic systems, for which numerous kinds of anionotropic rearrangement are known. One exception is the hydrolytic rearrangement of hex-4-en-1-yn-3-ol acetate, which has been examined with the interesting result that the activation energy is greater for rearrangement than for hydrolysis. Rearrangement is almost certainly intramolecular in part, and here it also seems likely that the anion is trapped by the developing carbonium ion before it becomes free[186].



Little systematic study of higher vinylogues of three-carbon anionotropic systems has been made, but it is clear that factors favouring the S_Ni' process will in general be absent in these compounds[187,188].

An allylic rearrangement in which the cyclic-intramolecular pathway is the predominant one occurs in the chlorination of alcohols with thionyl chloride, in which a chlorosulphite is first formed and then decomposes either by the unimolecular routes or by a bimolecular process involving attack by halide ion[189]. For allylic halides formed in this process, S_Ni' replacement is strongly favoured over cyclic-intramolecular replacement without rearrangement which would involve a four-centre transition state of higher energy. Preparatively the method is used for obtaining rearranged products from primary allylic alcohols, where the chloride is very labile. An interesting and important feature of the reaction is that optically active 1,3-dimethylallyl alcohol under these conditions gives chloride with maintained optical activity, but of course inversion of absolute configuration. Again, experiments with labelled (^{14}C) chlorosulphite support the view that the S_Ni' transition state has considerable polar character.



$$R^1_2C{=}CR^2CH_2OH \xrightarrow{SOCl_2} R^1_2C{=}CR^2CH_2O\overset{O}{\overset{\|}{S}}Cl$$

$$\longrightarrow R^1_2CClCR^2{=}CH_2 + SO_2$$

C. *The Effect of Substituents on Anionotropic Mobility and Equilibria*

1. Alkyl groups

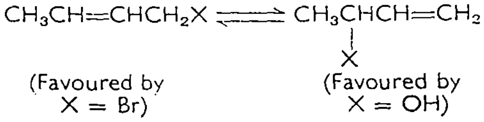
As has already emerged from the previous discussion, wide variations in reactivity are encountered amongst allylic compounds. Kinetic control in the initial phases of isomerization can lead to mixtures containing a higher than normal proportion of thermodynamically less stable product. The position of the final equilibrium will, of course, be affected by the position of substituents in the molecule, and the most extensive investigations of structural effects have been conducted with allylic alcohols.

For allylic alcohols containing one alkyl substituent, oxotropic mobility is very low, but the distribution of isomers in the equilibrium mixture is determined by the position of the alkyl group. For example in allylic alcohols of the type **54**, substitution of an alkyl

$$\overset{3}{C}R^1R^2{=}\overset{2}{C}R^3{-}\overset{1}{C}R^4R^5X$$

(**54**, X = potential nucleophile)

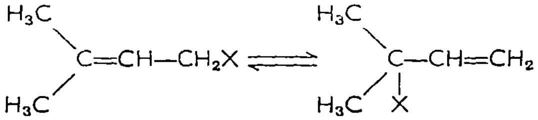
group in the 2-position has little effect on the equilibrium for it hyperconjugates with the double bond in both positions to about the same extent. On the other hand, substitution into the 1- or 3-positions might be expected to lead to preferential stabilization of one of the isomers, again by hyperconjugation, but this is not always observed in practice. For the methylallyl bromides and alcohols, the secondary isomer is favoured in the case of the alcohol, contrary to expectation, which is, however, realized in the case of the bromide, a higher proportion of *trans*-crotyl bromide appearing in equilibrium mixtures.



$$CH_3CH{=}CHCH_2X \rightleftharpoons \underset{\displaystyle X}{CH_3\underset{|}{C}HCH{=}CH_2}$$

(Favoured by X = Br) (Favoured by X = OH)

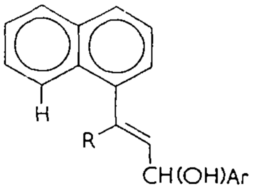
Two alkyl groups are much more effective than one in promoting mobility, but frequently the equilibrium set up favours one of the isomers almost entirely, as in the case of the dimethylallyl chlorides, the proportion of tertiary chloride at equilibrium being very small[190] in contrast to the corresponding alcohols, where the equilibrium mixture contains nearly equal proportions of both isomers[191].



2. Aryl substituents

It is immediately clear that aryl groups will stabilize the double bond by direct conjugation, but the degree of stabilization is often greater than expected on the grounds of resonance alone. In the phenylallyl–cinnamyl systems, the cinnamyl compounds are favoured almost exclusively[192]. In those systems where the phenyl and methyl groups are in competition, the phenyl conjugated compound is favoured by a factor of about 10:1. Substitution in the aryl group does not normally have a spectacular effect, the rates of attainment of equilibrium covering a range of not greater than 6×10^2 in the *p*-halogeno-, *p*-methyl- and *p*-methoxyphenylmethylallyl alcohols[193]. As might be expected, if the methyl group in these compounds is replaced by an aryl group, approximate equipartition of isomers is restored but in those cases where one of the aryl groups is 1- or 2-naphthyl or *p*-nitrophenyl, the equilibrium lies somewhat in favour of the naphthyl or nitrophenyl conjugated isomer, presumably in virtue of the more extended conjugated system.

Special effects need to be considered in assessing the factors which decide the final position of equilibrium; for example, steric hindrance in the conjugated naphthyl compound **55** (where the grouping R interferes with the nuclear hydrogen at the 8-position) favours the alternative isomer. The total hyperconjugative effect of the CH(OH)Ar group may also influence the equilibrium.



(55)

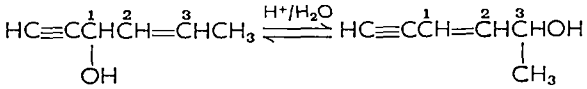
Effects of this kind probably explain the preponderance of cinnamyl compounds in equilibria involving phenylallyl compounds.

Addition of a further aromatic substituent to the diarylallyl system causes a large shift of the equilibrium, the diarylvinyl isomers being favoured[194].

$$\mathrm{PhCH{=}CHC(Ph)_2OH \xrightleftharpoons{H^+/H_2O} Ph_2C{=}CHCH(Ph)OH}$$

3. Ethynyl and vinyl substituents

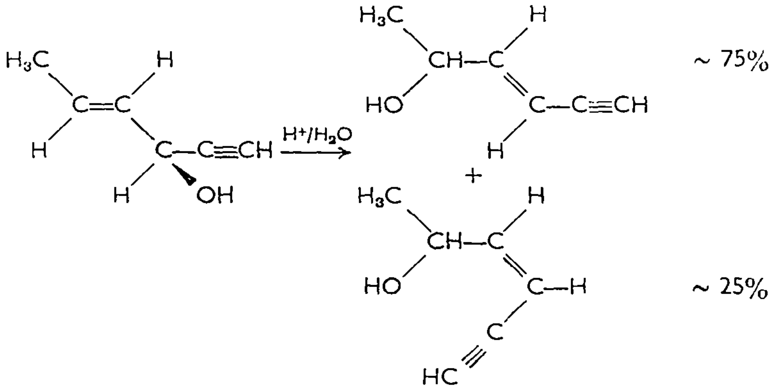
In the oxotropy of ethynylallyl alcohols, the equilibria lie far on the side of the conjugated isomers, but the mobility of these systems is very much less than for the corresponding diolefinic compounds[195,196]. This result is to be anticipated from the electron-withdrawing effect of the ethynyl group.



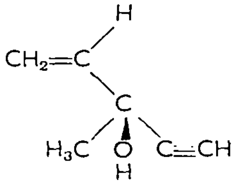
$$\mathrm{HC{\equiv}C\underset{\displaystyle OH}{\overset{1}{C}}H\overset{2}{C}H{=}\overset{3}{C}HCH_3 \xrightleftharpoons{H^+/H_2O} HC{\equiv}C\overset{1}{C}H{=}\overset{2}{C}H\underset{\displaystyle CH_3}{\overset{3}{C}}HOH}$$

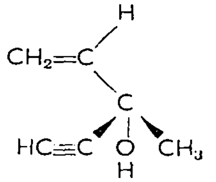
Alkyl substituents in these systems exert a marked but regular effect on their mobility, the extent of which depends upon the exact position of the alkyl group. The difference in reactivity for the three isomeric methyl ethynylvinyl carbinols, for example, can be clearly seen in the ratios of their rate coefficients for the rearrangement, these being ~ 10^3, 10^2, and 10 for the methyl group on the 3-, 1- and 2-position respectively. These differences correspond to the operation of the inductive effect, which falls off with distance, and the hyperconjugative effect which can operate through the double-bond system[193], these effects facilitating the carbon–oxygen bond cleavage.

Recently, it has been discovered that anionotropic rearrangement of *trans*-propenylethynyl carbinol gives not only *trans*-hex-3-en-5-yn-2-ol, the major product, but also some of the *cis* compound, which had previously been discarded in the lower boiling fractions of the reaction product as unchanged starting material[197]. Here, kinetic rather than thermodynamic control governs the composition of the product, for heating of the *cis* compound with *p*-toluenesulphonic acid results in recovery of starting material in high yield[198].

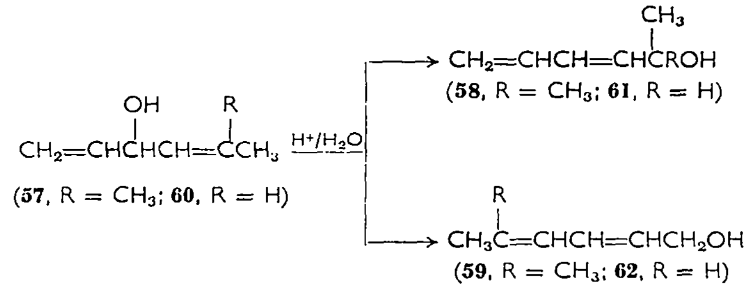


A similar effect is observed with the lower homologue, 3-methylpent-1-en-4-yn-3-ol, which rearranges, however, to a mixture containing approximately equal proportions of *cis* and *trans* isomers, the result being ascribed to the comparable stability of the conformers (**56a** and **56b**) which are involved in the isomerization[199]. In fact, there is a slight preponderance of the *cis* isomer.


(56a)


(56b)

Although pent-1-en-4-yn-3-ol is recovered apparently unchanged after treatment with hot sulphuric acid, so low is the mobility, the derived pentadienol is rapidly isomerized by the reagent. In fact, the rate factor is of the order of 10^4, this great difference in reactivity being associated with the replacement of the electron-withdrawing ethynyl group with the electron-donating vinyl group. Isomerization of these polyethylenic carbinols is often complete, and in alkylated unsymmetrical systems where the migrating hydroxyl group has the possibility of giving more than one product, it is found that migration to the carbon atom bearing the largest number of substituents takes place preferentially but slow equilibration usually gives a substantial amount of the other possible isomer as well. In the case of methylhexadienol (**57**), the equilibrium mixture contains approximately equal proportions of the two isomers[200] **58** and **59**, but the initial *exclusive* formation of **58** reported is now suspect since the alcohol **60** rearranges to give the carbinols **61** and **62** under similar conditions to those used earlier and reported to give exclusively **61**. It seems likely that the methods of product analysis used were insufficiently sensitive to detect the relatively small amounts of alternative isomers. Furthermore the carbinol **61** is not the precursor of **62**, because the latter carbinol is formed much more rapidly from **60** than it is from **61**[201]; consequently, earlier arguments[193] rationalizing the *initial products* on the basis of the differences of inductive and conjugative effects of methyl groups in the 1- and 3-positions of an allylic system (p. 445) cannot apply.



$$CH_2{=}CH\overset{OH}{\overset{|}{C}}HCH{=}\overset{R}{\overset{|}{C}}CH_3 \xrightarrow{H^+/H_2O} CH_2{=}CHCH{=}CH\overset{CH_3}{\overset{|}{C}}ROH$$

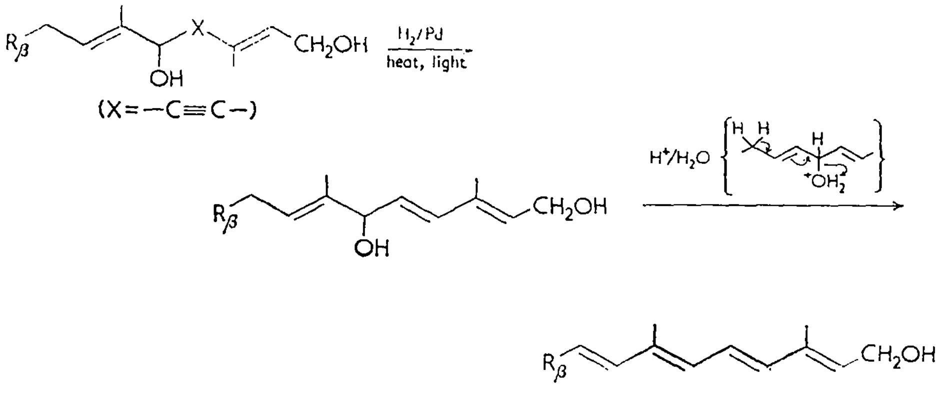
(**57**, R = CH_3; **60**, R = H) → (**58**, R = CH_3; **61**, R = H)

$$\xrightarrow{H^+/H_2O} CH_3\overset{R}{\overset{|}{C}}{=}CHCH{=}CHCH_2OH$$

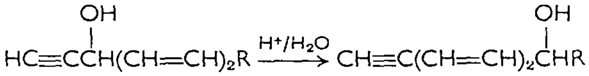
(**59**, R = CH_3; **62**, R = H)

In compounds where there is the possibility of pentad as well as triad anionotropy, the latter process takes place preferentially, and this effect has found application in vitamin A synthesis, where a key step is often the addition of an acetylenic Grignard reagent to a cyclohexenylmethylbutenal followed by semi-hydrogenation and an anionotropic rearrangement-dehydration of the resulting doubly-allylic alcohol (loss of a proton from the carbonium-ion intermediate)[202].

Pentad oxotropy is known, however[203], and if alkyl groups are present in the system, the stability difference between isomers depends upon the relatively small hyperconjugative effects. The rearrangements, as in the triad oxotropic isomerizations, are reversible.



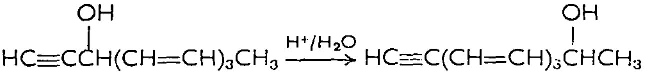
In the presence of unsaturated groups, the equilibrium is shifted to favour the triply conjugated compound, as might be expected. The octadienynol **63**, for example, is converted to its isomer **64**[204].



$$\mathrm{HC{\equiv}C\overset{OH}{\overset{|}{C}}H(CH{=}CH)_2R \xrightarrow{H^+/H_2O} CH{\equiv}C(CH{=}CH)_2\overset{OH}{\overset{|}{C}}HR}$$

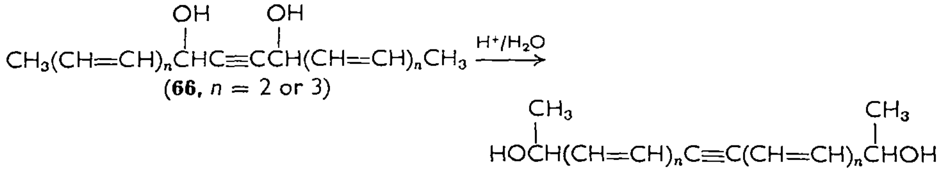
(**63**, R = CH_3) (**64**)

Analogous rearrangements are known for other pentadienylic ethynyl carbinols[205], and for phenylbutadienyl and pentadienyl carbinols[206]. Higher oxotropic systems are also known, for example the rearrangement of the decatrienynol **65**[207], and the double shifts in the compounds represented by **66**[208]. Further examples of multiple double-bond shifts of these types will be discussed in the next section.



$$\mathrm{HC{\equiv}C\overset{OH}{\overset{|}{C}}H(CH{=}CH)_3CH_3 \xrightarrow{H^+/H_2O} HC{\equiv}C(CH{=}CH)_3\overset{OH}{\overset{|}{C}}HCH_3}$$

(**65**)

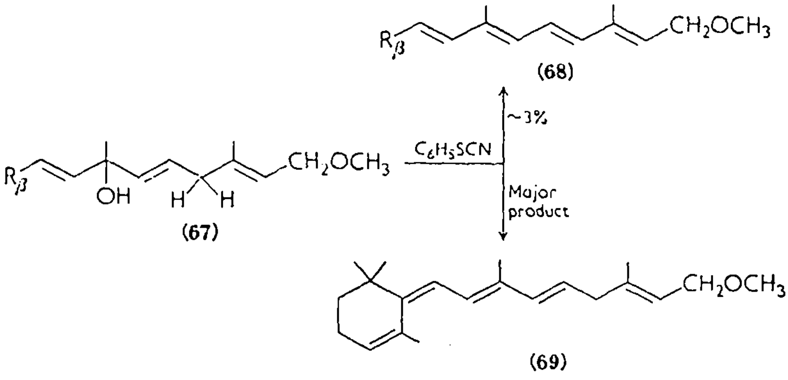


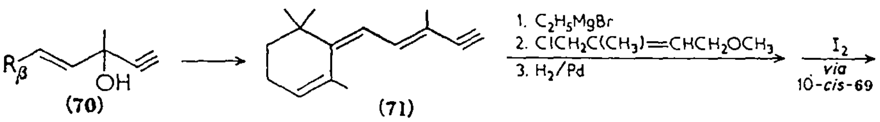
$$\mathrm{CH_3(CH{=}CH)_n\overset{OH}{\overset{|}{C}}HC{\equiv}C\overset{OH}{\overset{|}{C}}H(CH{=}CH)_nCH_3 \xrightarrow{H^+/H_2O} HO\overset{CH_3}{\overset{|}{C}}H(CH{=}CH)_nC{\equiv}C(CH{=}CH)_n\overset{CH_3}{\overset{|}{C}}HOH}$$

(**66**, n = 2 or 3)

D. Anionotropic Rearrangements of Polyene Natural Products, Their Synthetic Precursors and Analogues

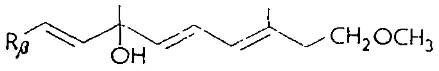
The field of natural product synthesis is rich in interesting examples of anionotropy. As previously mentioned, syntheses of vitamin A frequently include an anionotropic rearrangement–dehydration step, so that a logical route might seem to be the application of this method to the compound **67**. Surprisingly, only small yields of vitamin A methyl ether are obtained, the major product being the *retro* compound **69** when phenyl thiocyanate is used as dehydrating agent; on the other hand, in acetic acid, or by using phosphorous oxychloride, some 10-*cis*-**69** can also be obtained. Similar considerations apply to the compound **70**, the precursor of **67**; further operations lead eventually to 10-*cis*-**69** confirming its structure independently[209].



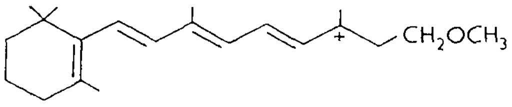


Rearrangements of this type almost certainly proceed through mesomeric carbonium-ion intermediates, and the final *retro* structures reflect the greater stability of the tertiary ion site at $C_{(5)}$ of the ring, with a larger contribution of this canonical form to the resonance hybrid. A further consequence of the involvement of mesomeric ions in these types of reaction, is revealed in the dehydration of 10-*cis*-**67**, some stereomutation of the *cis* double bond taking place, whilst the ratio of 10-*cis*-/10-*trans*-**69** remains constant. Preference for the *trans* configuration at $C_{(10)}$ is clearly the result of considerable steric interaction in the *cis* form.

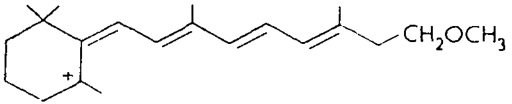
If there is more than one tertiary carbonium-ion site available, as with the isomers of **67** (*e.g.* **72**) then, irrespective of the stereochemical features about the $C_{(10)}$ position, the major product after anionotropic rearrangement–dehydration is again the *retro*-ionylidene compound.



(72)



(72a)

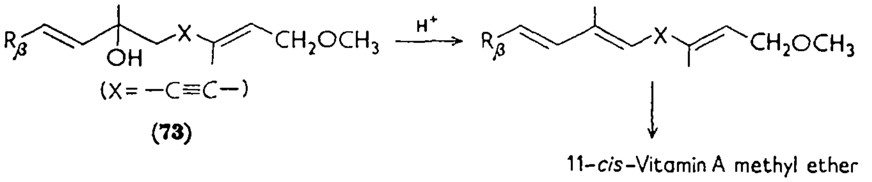


(72b)

In this case, the two major contributing forms to the resonance hybrid are **72a** and **72b**, of which the former ion is the less stable owing to steric interactions betwen the side chain and the three ring-methyl groups which restrict coplanarity with the ring*. Thermodynamic control of the product thereby leads to the formation of the *retro*-ionylidene compound.

Cases of forward as opposed to *retro* dehydration are known, however, in this series of compounds. For example, the synthetic intermediate **73** dehydrates in the forward sense without anionotropic shift, and this is due not only to the destabilizing effect of the triple bond on the intermediate carbonium ion, but also to the labilizing effect on the adjacent methylene group[209, 211].

Remarkable extended anionotropic shifts have also been observed with carotenoid compounds. The alcohol **74** dehydrates with rearrangement in acidic chloroform[212], presumably through the protonated species shown.



(73)

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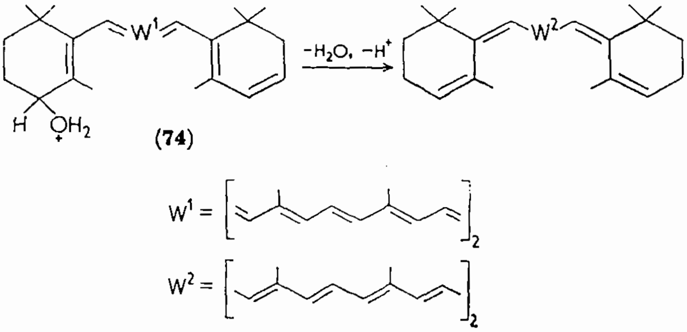
* The *retro*-ionylidene structures are therefore the most stable, and should be regarded as 'normal' from the point of view of ultraviolet light absorption[210].

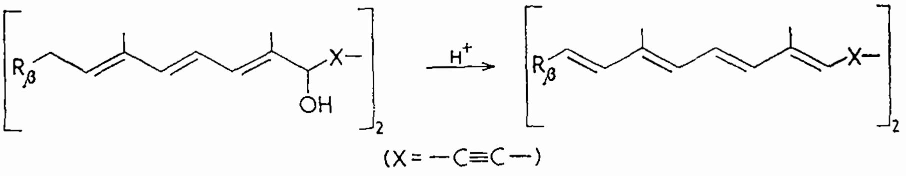
A number of double anionotropic shifts are also known, leading to elegant syntheses of carotenoid hydrocarbons, *e.g.* from the diacetylenediol **75**, which gives the hydrocarbon **76**.

It is of interest that semi-hydrogenation of the diacetylene **76** gives the rather unstable di-*cis*-olefin, which stereomutates on melting, first to give the mono-*cis*- and then the all-*trans*-carotenoid[213]. Very similar double anionotropic shifts form the basis for the industrial preparation of β-carotene[214], and the synthesis of iso-zeaxanthin by reversion of the *retro* structure **77**[215].



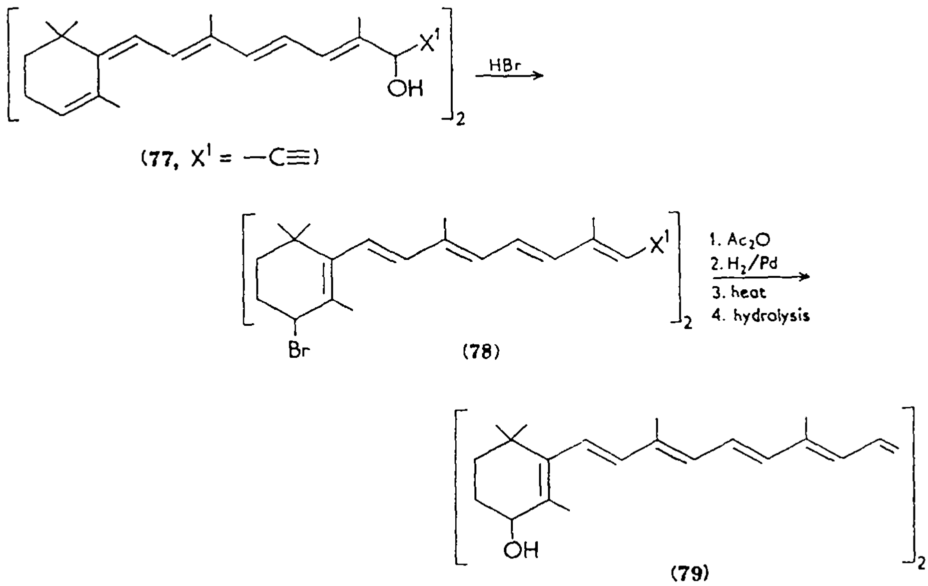
(74)

The reverse of the above process is observed in the dehydration of isocryptoxanthin (**80**), or its methyl ether with acidic chloroform[216] and in the vitamin A field with the isomer of vitamin A (**81**)[217].



(75) **(76)**

The reaction of polyenes with Lewis acids has long been known to result in the development of striking colours in the reaction mixture, varying from deep blue to green[218]. Cleavage of the resulting product with water results in the formation of alcohols, in carotenoids only one ring usually being affected if more than one is present, and the ring being the preferred site of reaction if the compound is

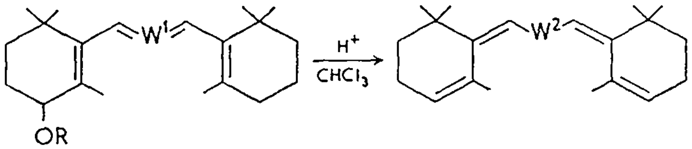


(77, X¹ = —C≡)

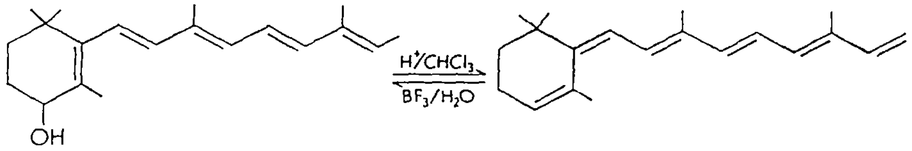
(78)

(79)

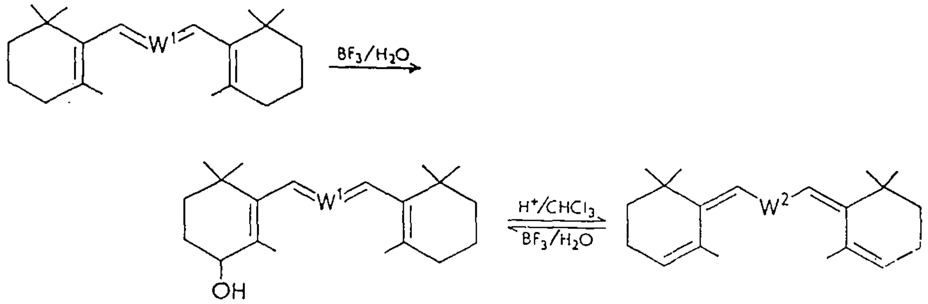
monocyclic. Treatment of β-carotene with boron trifluoride and then water, for example, gives the cyclic alcohol isocryptoxanthin (**80**), but if instead of water, ammonia gas is used to decompose the complex, *retro*-dehydro-β-carotene (**83**) results. The latter is also produced if isocryptoxanthin is treated with acidic chloroform, anionotropic rearrangement dehydration occurring. The detailed nature of the boron trifluoride complexes and their reactions have been discussed recently[219].



(**80**, R = H or CH_3)



(**81**) (**82**)

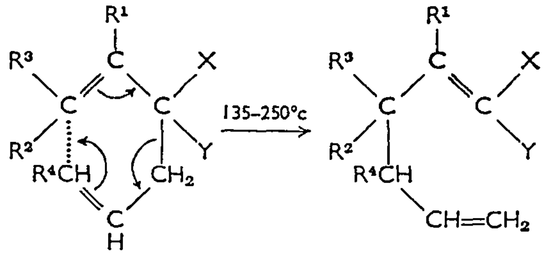


(83)

IV. MISCELLANEOUS ALKENE REARRANGEMENTS

A. The Cope Rearrangement of 1,5-Hexadienes

The thermal rearrangement of vinyl allyl cyanoacetic esters was discovered by Cope and coworkers in 1940[220]. It is now known that the reaction can be applied to a variety of malononitriles, cyanoacetic esters and malonic esters[221,222], as well as to compounds having only one 'activating group', such as the cyano or carboxyl group[223].



(X, Y = CN or $CO_2C_2H_5$ or one is H; R^1, R^2, R^3, R^4 = alkyl)

The rates of rearrangement vary with structure, and the order of reactivity decreases as the cyano is replaced by the alkoxycarbonyl group, so that malononitriles are the most reactive and malonic esters least. In the generalized formula above, the radicals R^1, *etc.*, may all be alkyl groups, but in the case of cinnamyl compounds only decomposition occurs, and no rearrangement products can be isolated. The simplest example is vinyl allyl malonic ester, and this has been successfully rearranged[224]. The presence of an activating group is not essential, however: 3-phenyl-1,5-hexadiene is rearranged quantitatively to 1-phenyl-1,5-hexadiene and the 3-methyl analogue undergoes a similar reaction at higher temperatures although in slightly smaller yield (95%), the partial reversibility of the reaction in this case having been demonstrated[225]. The intramolecular nature of the reaction follows from the lack of mixed products when more than one vinyl allyl compound is heated in the same reaction mixture, and from the observation that the allyl group is inverted in cases where it is unsymmetrical. The energies of activation and entropy terms have been measured in certain instances of the reaction, and the appreciably negative values for the entropy of activation confirm the proposed cyclic transition state for the reaction, which is regarded as a concerted process although there is some evidence that bond making and bond breaking may not be completely simultaneous[226].

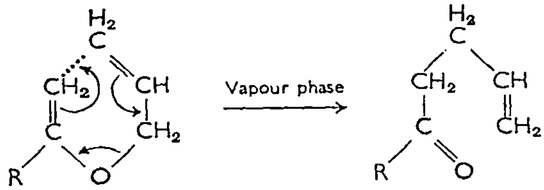
B. The Claisen Rearrangement of Alkene Ethers

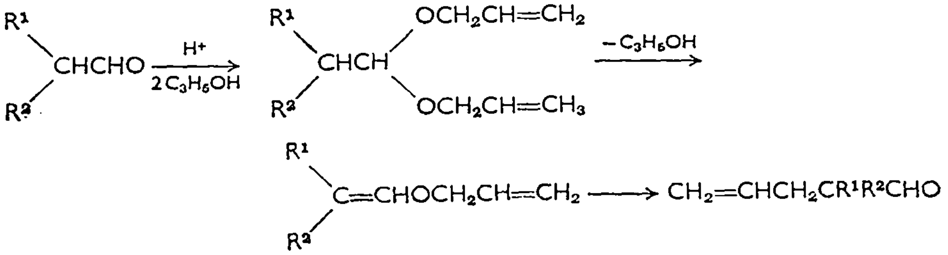
The thermal rearrangement of allyl phenyl ethers to give *o*-propenyl phenols—the *Claisen rearrangement*—is, of course, well known[227]. Almost simultaneously with the discovery of the Cope rearrangement, examples of the hitherto unknown allyl vinyl ethers **84a**, **84b** and **84c** became available for study[228]. Like the aryl analogues, these vinyl allyl ethers rearrange smoothly on heating giving aldehydes or ketones, the order of reactivity being **84a** ≫ **84b** > **84c**. Again a cyclic mechanism for the reaction is proposed and this receives

$$CH_2{=}CROCH_2CH{=}CH_2$$

(**84a**, R = CH_3; **84b**, R = Ph; **84c**, R = H)

support from kinetic studies[229], the reaction being first order in the vapour phase, and homogeneous. Further examples of this reaction are the synthesis of α,α-disubstituted 4-pentenals by heating the relevant aldehydes with allyl alcohol in the presence of an acidic

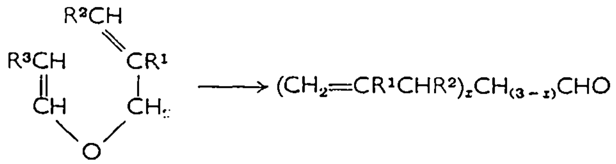




$$R^1R^2CHCHO \xrightarrow[2C_3H_6OH]{H^+} R^1R^2CHCH(OCH_2CH{=}CH_2)(OCH_2CH{=}CH_3) \xrightarrow{-C_3H_6OH} R^1R^2C{=}CHOCH_2CH{=}CH_2 \longrightarrow CH_2{=}CHCH_2CR^1R^2CHO$$

catalyst, the intermediate acetals decomposing, with subsequent rearrangement of the product[230].

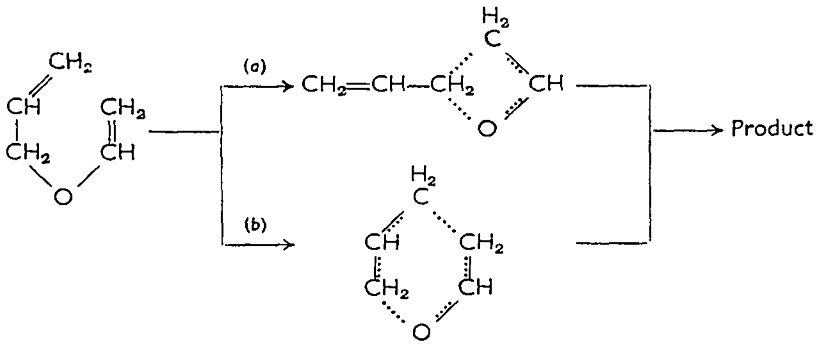
In order to secure a convenient rate of reaction, the rearrangement of allyl vinyl ethers has often to be carried out in the gas phase, under pressure to maintain a suitable temperature, but a smoother reaction and cleaner product can be achieved by the use of high boiling inert media, as, for example, in the case of the series of compounds **85** to **88**[231].



(R^3 = allyl when
$x = 2$; H when
$x = 1$)

(**85**, $R^1 = R^2 = H$, $x = 1$;
86, $R^1 = R^2 = H$, $x = 2$;
87, $R^2 = CH_3$, $R^2 = H$, $x = 1$;
88, $R^1 = H$, $R^2 = CH_3$, $x = 1$)

Detailed examination of the mechanism of the vapour phase Claisen rearrangement of allyl vinyl ether shows that the reaction is truly intramolecular, has an expected negative entropy of activation, and confirms that a six-membered cyclic transition state is involved[232]. Two possible transition states seem likely for the reaction represented as pathways (*a*) and (*b*) in equation (17).



(17)

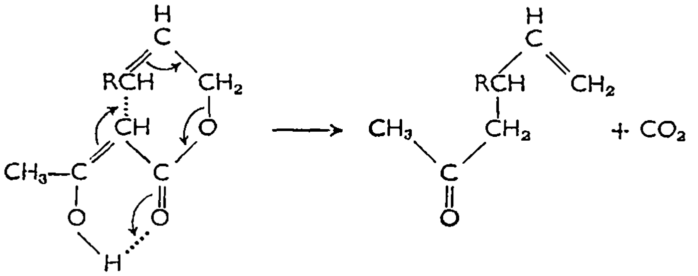
However, pent-4-enal produced from allyl vinyl ether labelled at the 1-position in the allyl group with ^{14}C (**89**) contains more than 97% of its labelled carbon in the form **90**, whilst when the label is on the terminal carbon of the allyl group, not more than 1% of the product labelled as in **90** is formed, both observations being consistent with the pathway (*b*). Deuterium labelling of the starting material as in **91** gives more than 97% of the compound **92**, and the combined labelling of the starting material as in **93** gives more than 96% of the compound **94**, again the expected products assuming pathway (*b*) is followed. Although these experiments clearly indicate the shape of the transition state, it is not possible to deduce the precise sequence of the bond-forming and bond-breaking reactions. It seems likely, however, that they are sufficiently synchronous to be regarded as concerted, since the rate of loss of optical activity in 1-methylallyl vinyl ether is practically identical with the rate of the thermal rearrangement.

$$\underset{(\mathbf{89})}{CH_2{=}CHO^{14}CH_2CH{=}CH_2} \xrightarrow{97\%} \underset{(\mathbf{90})}{{}^{14}CH_2{=}CHCH_2CH_2CHO}$$

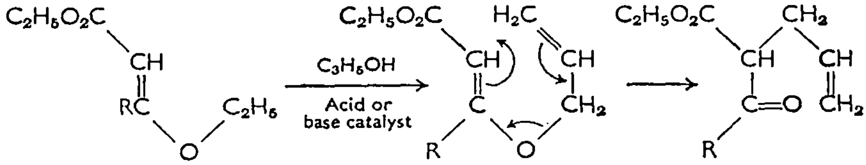
$$\underset{(\mathbf{91})}{CH_2{=}CHOCD_2CH{=}CH_2} \xrightarrow{>97\%} \underset{(\mathbf{92})}{CD_2{=}CHCH_2CH_2CHO}$$

$$\underset{(\mathbf{93})}{CH_2{=}CDO^{14}CH_2CH{=}CH_2} \xrightarrow{>96\%} \underset{(\mathbf{94})}{{}^{14}CH_2{=}CHCH_2CH_2CDO}$$

A closely similar reaction to the Claisen transformation occurs in the decarboxylative rearrangement of acetoacetates and benzoylacetates of β,γ-unsaturated alcohols to give γ,δ-unsaturated ketones, a reaction of considerable preparative value. Here inversion of the unsaturated allylic moiety occurs indicating that a cyclic mechanism is involved[233].



Mechanistic interpretation of the Carroll reaction, in which acetoacetates react with β,γ-unsaturated alcohols in the presence of basic catalysts to give γ,δ-unsaturated ketones[234], requires only that prior reesterification of the acetoacetate with the unsaturated alcohol occurs.

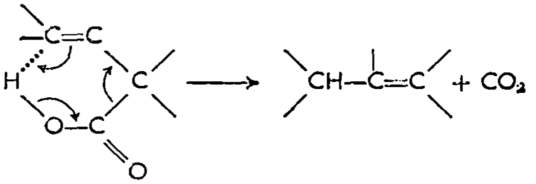


(R = H or alkyl)

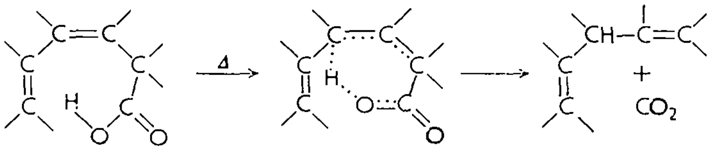
The catalysed rearrangement of β-ethoxyacrylates and crotonates[235,236] in the presence of allylic alcohols to give unsaturated ketones is similarly rationalized on the basis of a transetherification, followed by Claisen rearrangement of the allyl vinyl ethers formed.

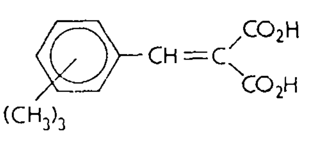
C. Rearrangement Involving Decarboxylation of Unsaturated Carboxylic Acids

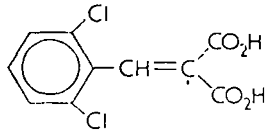
Decarboxylation of α,β-unsaturated carboxylic acids is frequently accompanied by rearrangement, the reaction once more involving a cyclic transition state[237].



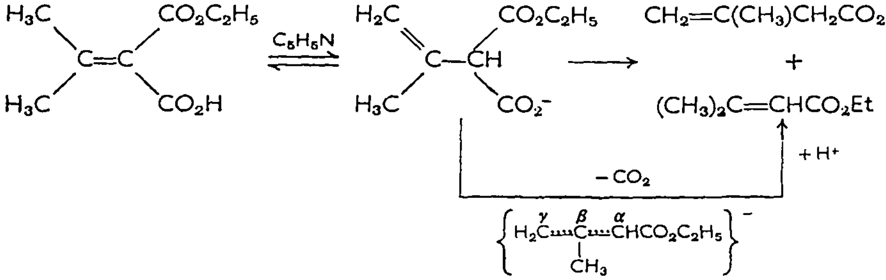
Strong evidence for the involvement of a cyclic transition state has been derived from a study of 3,5-dienoic acids, since, in a cyclic process, unconjugated acids must result from decarboxylation, and in fact this is observed[238]. The resistance of 4,4-disubstituted 2-enoic acids to decarboxylation is also explained if, in general, decarboxylation of α,β-unsaturated acids is preceded by isomerization to the β,γ-form. In the decarboxylation of α,β-unsaturated malonic half-esters in pyridine, for example, prototropic isomerization to the β,γ-forms first occurs. Decarboxylation of the conjugate base then ensues, the resulting mesomeric anion being capable of accepting a proton *irreversibly* at either the α- or the γ-positions, giving





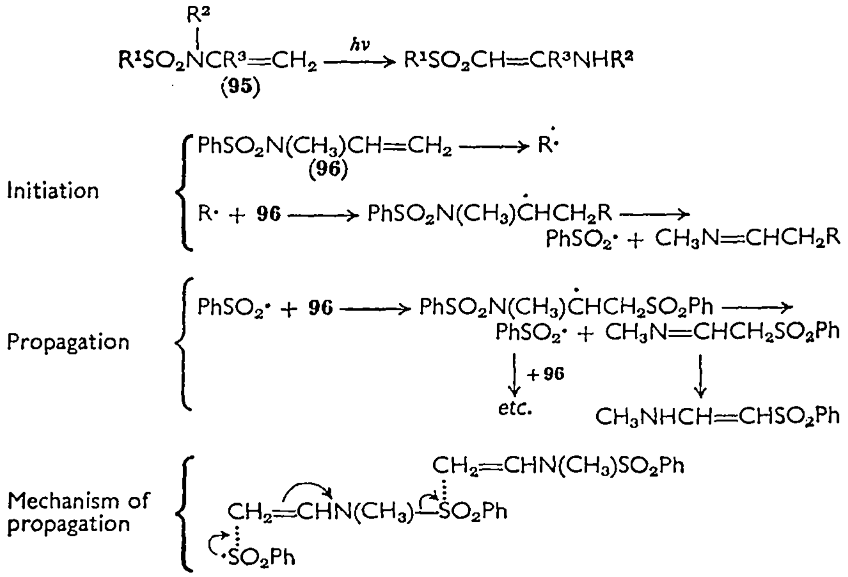


both α,β- and β,γ-unsaturated product. The product ratio remains constant under a variety of conditions which affect the rate, in accord with the view that a common intermediate is involved. Consistent with this scheme, neither of the substituted benzylidenemalonic acids shown above decarboxylates at a measurable rate in pyridine[239].



D. Rearrangement of N-Alkyl-N-Vinylsulfonamides

Most if not all of the transformations documented in this account of alkene rearrangements concern reactions in the gaseous or liquid phase. Propagation of isomerization is comparatively rare in the solid phase, and it is all the more interesting, therefore, when such processes are discovered. A recent example is the reaction of **95**.



Scheme 8.

Propagation of the reaction in the crystalline phase is rather sensitive, as might be expected, to the nature of the substituents on the nitrogen atom, and crystalline *N*-methyl-*N*-styryl-*p*-toluenesulfonamide is not affected by radiation doses which would cause isomerization in the liquid phase. In those cases where isomerization readily occurs in the solid, it seems probable that the geometry of the crystalline lattice allows radical propagation with little or no translational motion of the actual radicals concerned, as implied in Scheme 8[240].

V. ACKNOWLEDGEMENTS

The author is indebted to Professor P. B. D. de la Mare for his interest and encouragement, particularly in connexion with section III (Anionotropy), and to Professor Wilson Baker, F.R.S., for facilitating the completion of this work.

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 8

Nucleophilic attacks on carbon–carbon double bonds

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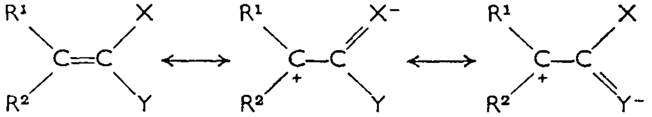
I. INTRODUCTION

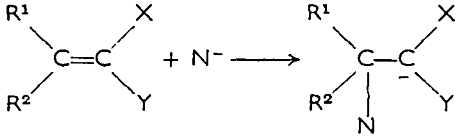
The very presence of π-electrons in a carbon–carbon double bond makes attack by electrophilic reagents rather facile, while special activating factors are required for nucleophilic attack. The most important among these is the presence of groups which diminish the electron density in the double bond. The effect of such groups may be either inductive ($-I$) or resonative ($-M$), distributing the negative charge over the molecule and polarizing the double bond with the result that, when C_α is the atom to which the activating groups X and Y are attached, a partial positive charge is developed on the β-carbon. In this case the main contributing resonance structures aiding the nucleophilic attack on the β-carbon are:



The relative magnitude of both inductive and resonative effects of various substituents at different positions in the molecule will be discussed in detail, as well as steric effects relating to the substrate and the attacking reagent. Some carbon–carbon double bonds in hydrocarbons of special structures, such as dibiphenyleneethylene[1,2], may also undergo nucleophilic attack.

Enhanced molecular symmetry in the substituted alkene lowers the polarization of the double bond and with it the reactivity of the β-carbon. On the other hand, multiple substitution, whether symmetrical, *e.g.* tetracyanoethylene, or not, enhances the overall reactivity of the system. In extended conjugated systems, 1,6-additions may compete with α,β-additions and may even become dominant[3a,4,5].

The multiplicity of substrates, nucleophilic agents (N or N^-) and reaction types notwithstanding, practically all mechanistic variations are based on the same initial nucleophilic attack by the reagent on the β-carbon of the double bond. The fate of the intermediate carbanion formed is determined in later stages of the reaction by the nature of the substrate, the reagent and the medium. Of course,


(1)

the geometrical structure of the intermediate is equally important. This, in different proposed mechanistic schemes, was described as tetrahedral or as planar, and each description is probably justified in separate cases.

A unified discussion of all reaction types based upon mechanistic similarities, while attractive, seems to be still premature on the basis of the information available. Therefore, we will deal separately with different reaction types, each posing its own problems, while endeavoring to point out the common features of these reactions and emphasize their interrelations.

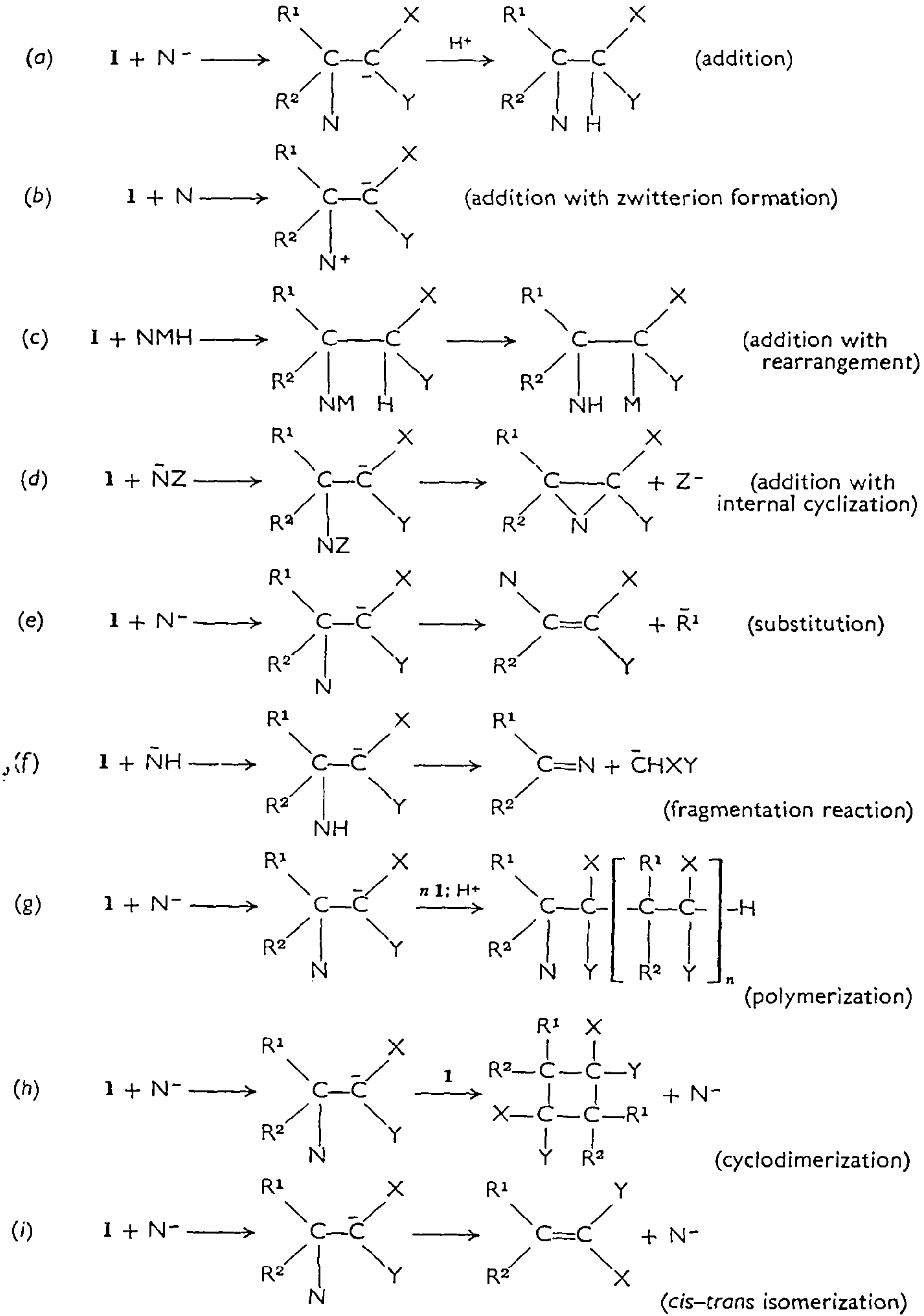
The main reaction routes are summarized in the Scheme 1[6]. In routes (*a*), (*b*), (*c*), (*d*), (*e*) and (*f*), the attacking nucleophile or a part of it is incorporated into the product, while in routes (*h*) and (*i*) the nucleophile has the role of a catalyst only. Nucleophilic polymerizations (*g*) do not fall within the scope of the present chapter. Neither will we discuss reactions which may formally be described as nucleophilic attacks, but which do not actually take place by a direct attack on the carbon–carbon double bond, such as isomerizations and base-catalyzed dimerizations[7,8], through removal of allylic protons, or alkali metal reductions in liquid ammonia[9]. S_N2' allylic reactions are discussed in a separate chapter.

The multiplicity of the reaction routes may be demonstrated on a single sufficiently active system, such as ethyl benzylidenecyanoacetates. Under various conditions, these may undergo addition of HCN or of $NaHSO_3$, cleavage by water or by hydroxide ions, exchange of the $=C(CN)CO_2Et$ group by a $=C(CN)_2$ group, zwitterion formation with phosphines, nucleophilic dimerization, and also nucleophilic isomerization. These variations obviously complicate kinetic and mechanistic investigations and, for that matter, even synthetic applications.

It is not our aim to give a complete coverage of the very large number of synthetic studies which deal with nucleophilic reactions on carbon–carbon double bonds. We will try only to summarize those studies which afford clarification of the mechanisms of these reactions and of their dependence on the various factors governing the interaction of the substrate with the attacking reagents, directing the reaction into one of the many available pathways.

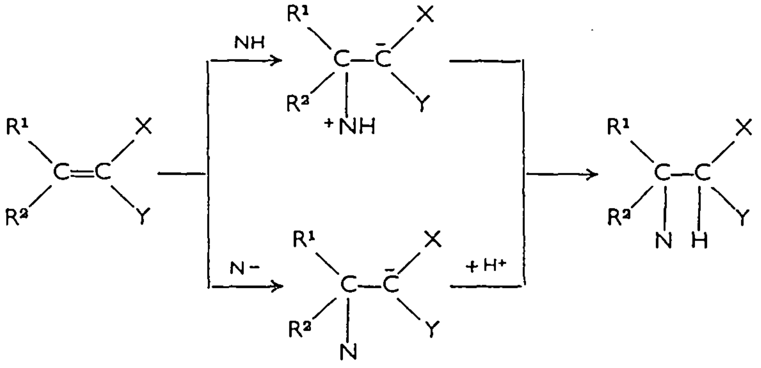
II. NUCLEOPHILIC ADDITIONS TO CARBON–CARBON DOUBLE BONDS

The most frequently met nucleophilic attack on double-bond systems, and the synthetically most useful one, is the addition in which a carbanion is formed initially, adding in later stages of the



SCHEME 1. Nucleophilic attacks on $R^1R^2C{=}CXY$ (**1**), intermediates and products.

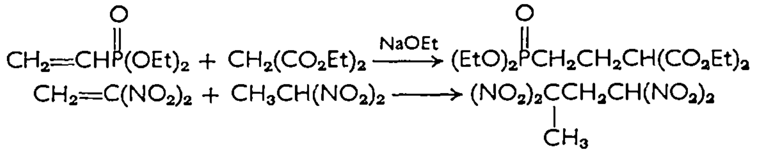
reaction generally a proton and, in rarer cases, other cations. We will describe first representative examples of the synthetic applications of nucleophilic additions, divided according to the various attacking agents. These are reactions with donors containing carbon, nitrogen, oxygen, sulfur or halogens as the nucleophilic center. Having summarized these, we will discuss the kinetics, mechanism and stereochemistry of the addition process, and finally special cases involving organometallic compounds and phosphines.



(NH = H_2O, ROH, R^1R^2NH, $HCR^1R^2R^3$)

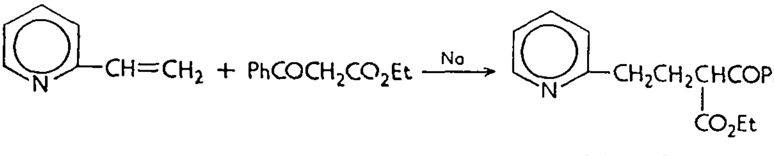
A. Scope of Addition of Nucleophiles

Best known of these reactions is the Michael condensation and one of its instances, the cyanoethylation reaction. Since comprehensive reviews of these are available[10,11,12], we will give only a few representative examples. Some of the analogs of the cyanoethylation reaction are the phosphonoethylation[13], dinitroethylation[14] and pyridylethylation[15] reactions.

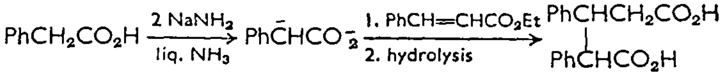


$$CH_2{=}CH\overset{O}{\overset{\|}{P}}(OEt)_2 + CH_2(CO_2Et)_2 \xrightarrow{NaOEt} (EtO)_2\overset{O}{\overset{\|}{P}}CH_2CH_2CH(CO_2Et)_2$$

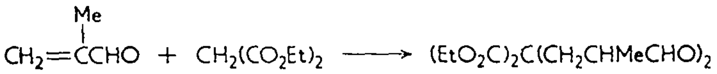
$$CH_2{=}C(NO_2)_2 + CH_3CH(NO_2)_2 \longrightarrow (NO_2)_2\underset{CH_3}{\underset{|}{C}}CH_2CH(NO_2)_2$$



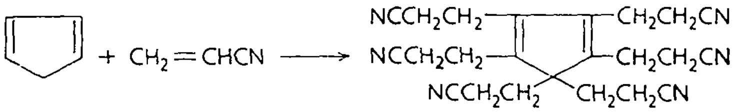
Compounds containing a potential carbanionoid carbon atom are widely used as donors in the presence of basic catalysts. These include malonic esters, alkylmalonic esters, cyano, nitro and carbamido compounds, as well as ketones, ketoesters and many others. In reactive systems, piperidine or pyridine may serve as the catalyst with relatively small intrusion of side reactions. Less active donors, such as esters, require the use of stronger catalysts, *e.g.* alkali metal amides in liquid ammonia[16]. Unsubstituted hydrocarbons may be employed as donors, if their conjugate base is strongly resonance stabilized, *e.g.* cyclopentadiene and fluorene[17]. If the donor molecule contains more than one acidic hydrogen atom, double or multiple Michael reactions may take place leading, for example, to double substitution of malonic ester[18], or, in the case of the cyanoethylation of cyclopentadiene, to the corresponding hexasubstituted product[19].



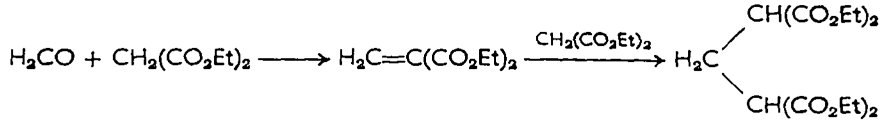
$$PhCH_2CO_2H \xrightarrow[\text{liq. }NH_3]{2\ NaNH_2} Ph\bar{C}HCO_2^- \xrightarrow[\text{2. hydrolysis}]{\text{1. }PhCH{=}CHCO_2Et} \begin{array}{l} PhCHCH_2CO_2H \\ \quad | \\ PhCHCO_2H \end{array}$$



$$CH_2{=}\overset{\overset{\displaystyle Me}{|}}{C}CHO + CH_2(CO_2Et)_2 \longrightarrow (EtO_2C)_2C(CH_2CHMeCHO)_2$$



Carbonyl–methylene condensations forming activated α,β-unsaturated systems are often accompanied by Michael condensations, especially in the presence of an excess of the methylene component, which then serves as a donor[20].



$$H_2CO + CH_2(CO_2Et)_2 \longrightarrow H_2C{=}C(CO_2Et)_2 \xrightarrow{CH_2(CO_2Et)_2} H_2C\begin{array}{l} \diagup CH(CO_2Et)_2 \\ \diagdown CH(CO_2Et)_2 \end{array}$$

Representative examples of the use of unsaturated aliphatic and aromatic aldehydes[21], ketones[22], nitriles[23], sulfones[24], esters[25] and amides[26a] as acceptors are given below. The inductive effect of fluorine substitution is strong enough to activate C=C bonds in fluoroolefins to add various reagents[26b].

$$CF_2{=}CF_2 + RSH \longrightarrow RSCF_2CHF_2$$

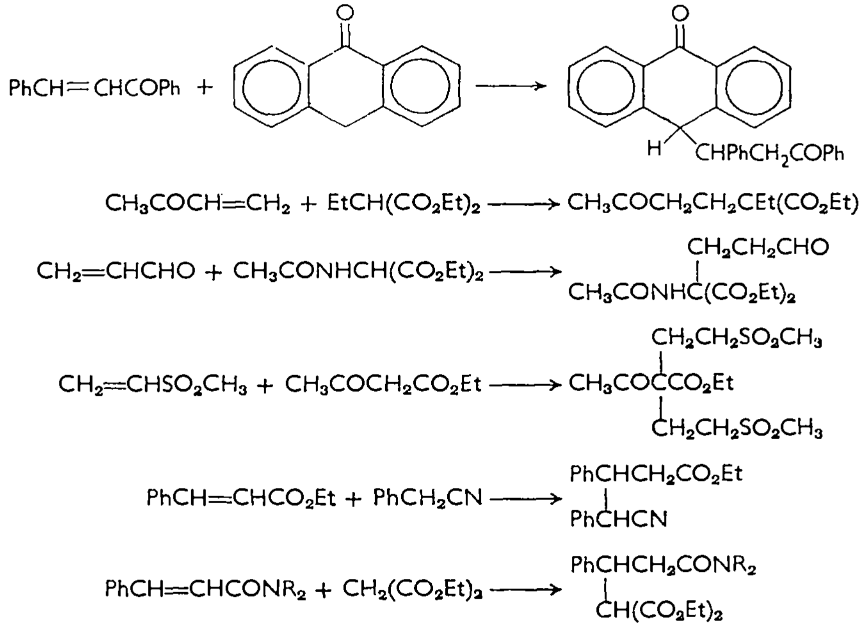
The important Robinson modification[27] of the Michael reaction is used for the generation of sensitive unsaturated carbonyl compounds *in situ* from quaternary salts of β-dialkylamino ketones,

$$[R^1COCH_2CH_2\overset{+}{N}R^2R^3R^4]X^- \longrightarrow R^1COCH{=}CH_2$$

in order to avoid side-reactions. β-Chloro ketones are also used for the *in situ* generation of vinyl ketones[28]. Although there was some

$$RCHClCH_2COR \longrightarrow RCH{=}CHCOR$$

doubt whether the unsaturated ketones are necessary intermediates in these reactions[29], a recent study shows this to be actually the case[30].



$$CH_3COCH{=}CH_2 + EtCH(CO_2Et)_2 \longrightarrow CH_3COCH_2CH_2CEt(CO_2Et)_2$$

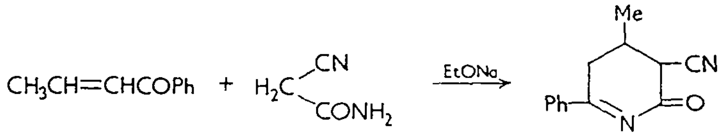
$$CH_2{=}CHCHO + CH_3CONHCH(CO_2Et)_2 \longrightarrow \begin{array}{l}CH_2CH_2CHO\\ |\\ CH_3CONHC(CO_2Et)_2\end{array}$$

$$CH_2{=}CHSO_2CH_3 + CH_3COCH_2CO_2Et \longrightarrow \begin{array}{l}CH_2CH_2SO_2CH_3\\ |\\ CH_3COCCO_2Et\\ |\\ CH_2CH_2SO_2CH_3\end{array}$$

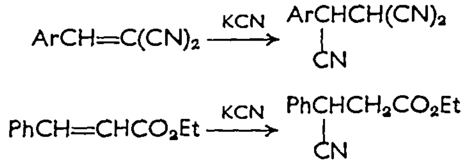
$$PhCH{=}CHCO_2Et + PhCH_2CN \longrightarrow \begin{array}{l}PhCHCH_2CO_2Et\\ |\\ PhCHCN\end{array}$$

$$PhCH{=}CHCONR_2 + CH_2(CO_2Et)_2 \longrightarrow \begin{array}{l}PhCHCH_2CONR_2\\ |\\ CH(CO_2Et)_2\end{array}$$

Some of the side-reactions, such as competitive addition of the catalyst anion when using alkoxides, may be avoided by working without solvent[31]. Dieckmann and similar cyclization reactions[32]



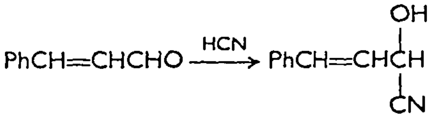
often occur in Michael condensations producing difunctional esters, nitriles or ketones. In nucleophilic attacks by cyanide ions, yields are high with active acceptors, such as chalcone[33] or benzylidene malononitriles[34], but fall considerably with the less reactive β-aryl unsaturated esters, such as ethyl cinnamate, or β,β-disubstituted esters, such as ethyl β,β-dimethylacrylate[35]. With unsaturated



$$\mathrm{ArCH{=}C(CN)_2 \xrightarrow{KCN} ArCH(CN)CH(CN)_2}$$

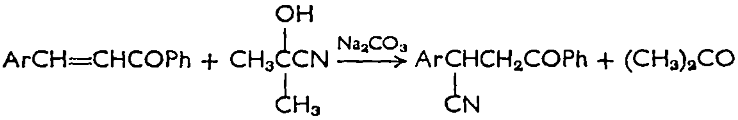
$$\mathrm{PhCH{=}CHCO_2Et \xrightarrow{KCN} PhCH(CN)CH_2CO_2Et}$$

aldehydes, only addition to the carbonyl group takes place[36].



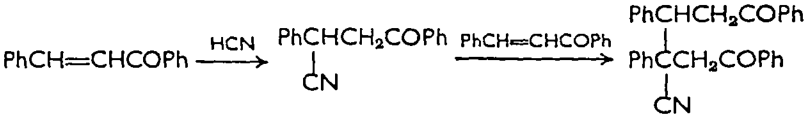
$$\mathrm{PhCH{=}CHCHO \xrightarrow{HCN} PhCH{=}CHC(OH)(CN)H}$$

On the other hand, α,β-addition products of acceptors activated by a keto group are so stable that they may be obtained in metathetical reactions using, for example, acetone cyanohydrin as the source of cyanide ions[37]. In cases when the addition of the cyano group



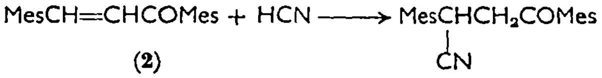
$$\mathrm{ArCH{=}CHCOPh + CH_3C(OH)(CH_3)CN \xrightarrow{Na_2CO_3} ArCH(CN)CH_2COPh + (CH_3)_2CO}$$

sufficiently enhances the acidity of a hydrogen atom in the adduct, the latter may become the donor in a second reaction[38] as shown below:

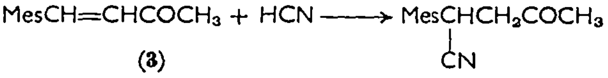


$$\mathrm{PhCH{=}CHCOPh \xrightarrow{HCN} PhCH(CN)CH_2COPh \xrightarrow{PhCH{=}CHCOPh} PhC(CN)(CH_2COPh)CH(Ph)CH_2COPh}$$

The presence of the large mesityl (Mes) group[39], either on the α- or the β-carbon, does not inhibit the reaction, and both **2** and **3** add HCN exclusively to the C=C bond.

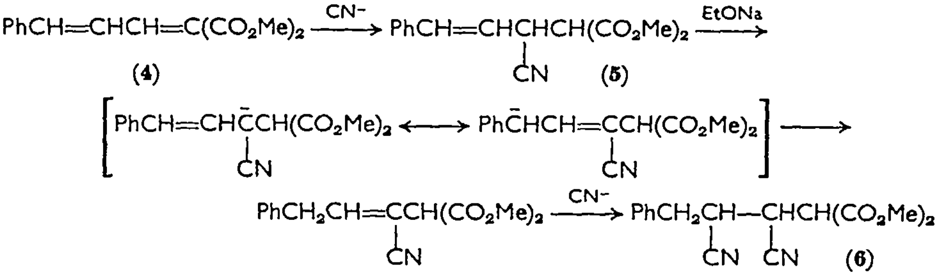


$$\mathrm{MesCH{=}CHCOMes + HCN \longrightarrow MesCH(CN)CH_2COMes}$$



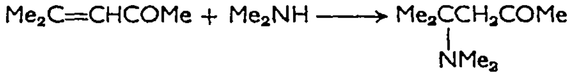
$$\mathrm{MesCH{=}CHCOCH_3 + HCN \longrightarrow MesCH(CN)CH_2COCH_3}$$

An interesting reaction is observed in the case of the conjugated system **4**, in which the primary addition to the β-position produces **5**, but which, in the presence of an excess of KCN, gives **6**. The following reaction sequence involving the formation of a new conjugated system has been proposed[36,40]:



$$\mathrm{PhCH{=}CHCH{=}C(CO_2Me)_2} \xrightarrow{\mathrm{CN^-}} \mathrm{PhCH{=}CH\underset{CN}{C}HCH(CO_2Me)_2} \xrightarrow{\mathrm{EtONa}}$$
$$\mathrm{(4)} \qquad\qquad \mathrm{(5)}$$
$$\left[\mathrm{PhCH{=}CH\underset{CN}{\overset{-}{C}}CH(CO_2Me)_2} \longleftrightarrow \mathrm{Ph\overset{-}{C}HCH{=}\underset{CN}{C}CH(CO_2Me)_2}\right] \longrightarrow$$
$$\mathrm{PhCH_2CH{=}\underset{CN}{C}CH(CO_2Me)_2} \xrightarrow{\mathrm{CN^-}} \mathrm{PhCH_2\underset{CN}{C}H{-}\underset{CN}{C}HCH(CO_2Me)_2} \quad \mathrm{(6)}$$

The addition of sufficiently basic nitrogenous nucleophiles, such as NH_3 or $MeNH_2$, to mesityl oxide[41] or of methoxylamine to chalcone[42] takes place as a rule in the absence of catalysts. Similar reactions, *e.g.* between acrylonitrile and ammonia, may proceed



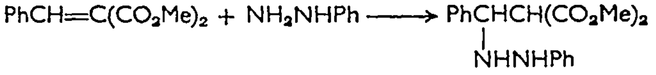
$$\mathrm{Me_2C{=}CHCOMe + Me_2NH \longrightarrow Me_2\underset{NMe_2}{C}CH_2COMe}$$

further than the monoaddition stage[43]. Facile addition takes place

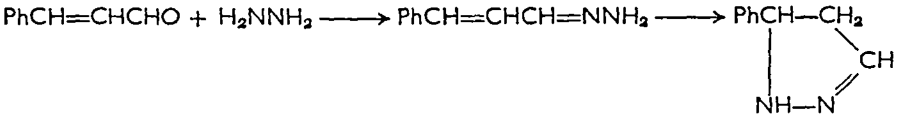
$$\mathrm{CH_2{=}CH(CN) + NH_3 \longrightarrow NH[CH_2CH_2(CN)]_2}$$

of both aliphatic and aromatic amines[44] to a wide variety of acceptors[45].

Phenylhydrazine or hydrazine may be used as donors[46]. Hydrazones of α,β-unsaturated aldehydes often yield pyrazolines through intramolecular nucleophilic cyclization[47].

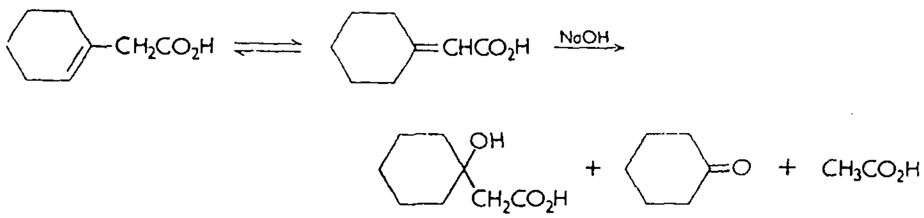


$$\mathrm{PhCH{=}C(CO_2Me)_2 + NH_2NHPh \longrightarrow Ph\underset{NHNHPh}{C}HCH(CO_2Me)_2}$$

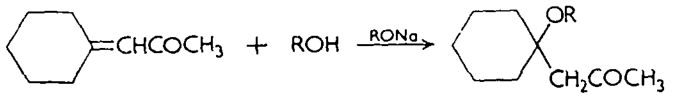


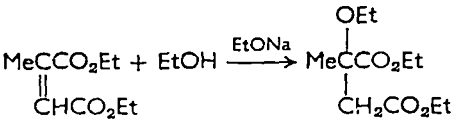
Turning to oxygen-containing nucleophiles, water can be added to relatively inert substrates, such as unsaturated acids, in the presence of basic catalysts, but the reaction is often accompanied by cleavage[48,49].

In adducts formed with alkoxide ions as the attacking agents, cleavage does not take place; stable products are obtained by cyanoethylation of alcohols or by addition of alcohols to cyclohexylidene



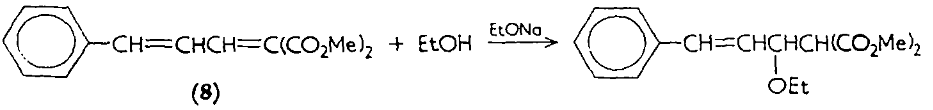
ketones[50] or to the ester 7[51]. Conjugate 1,4- (not 1,6-) addition to the ester 8[52] yields the α,β-product.





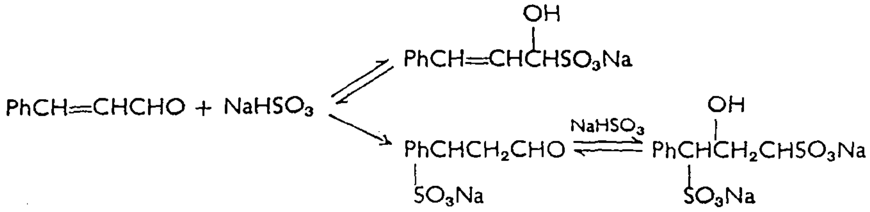
$$\underset{\displaystyle \text{CHCO}_2\text{Et}}{\text{MeCCO}_2\text{Et}} + \text{EtOH} \xrightarrow{\text{EtONa}} \text{Me}\overset{\displaystyle \text{OEt}}{\underset{\displaystyle \text{CH}_2\text{CO}_2\text{Et}}{\text{C}}}\text{CO}_2\text{Et}$$

(7)



(8)

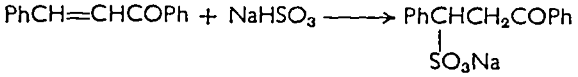
Multiple reaction paths are also observed in the reactions of sulfur-containing nucleophiles. Crotonaldehyde[53] or cinnamaldehyde[54] give with sodium bisulfite a fast carbonyl addition which is reversible, and a slower 1,4-addition leading to a more stable product. The introduction of the SO_3Na group in the β-position enhances the reactivity of the carbonyl group by destroying its conjugation with the double bond, so that the final product of the reaction is a bis adduct.



$$\text{PhCH}{=}\text{CHCHO} + \text{NaHSO}_3 \rightleftharpoons \text{PhCH}{=}\text{CH}\overset{\displaystyle \text{OH}}{\text{C}}\text{HSO}_3\text{Na}$$

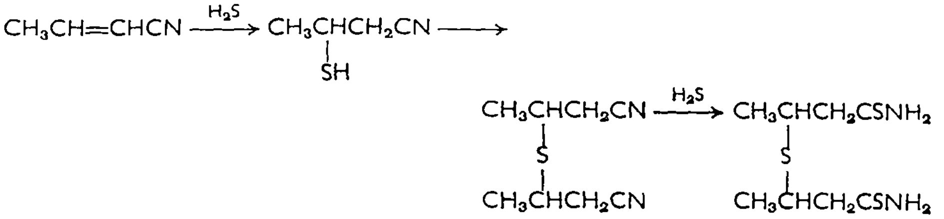
$$\text{PhCH}{=}\text{CHCHO} + \text{NaHSO}_3 \rightarrow \underset{\displaystyle \text{SO}_3\text{Na}}{\text{PhCH}}\text{CH}_2\text{CHO} \xrightleftharpoons{\text{NaHSO}_3} \underset{\displaystyle \text{SO}_3\text{Na}}{\text{PhCH}}\text{CH}_2\overset{\displaystyle \text{OH}}{\text{C}}\text{HSO}_3\text{Na}$$

With more hindered carbonyl groups, as in chalcone, only α,β-addition takes place[54].



$$PhCH{=}CHCOPh + NaHSO_3 \longrightarrow \underset{\substack{|\\ SO_3Na}}{PhCH}CH_2COPh$$

Sulfhydryl compounds, *i.e.* hydrogen sulfide[55] as well as its alkyl and aryl derivatives[56], give facile additions and bis-addition reactions.

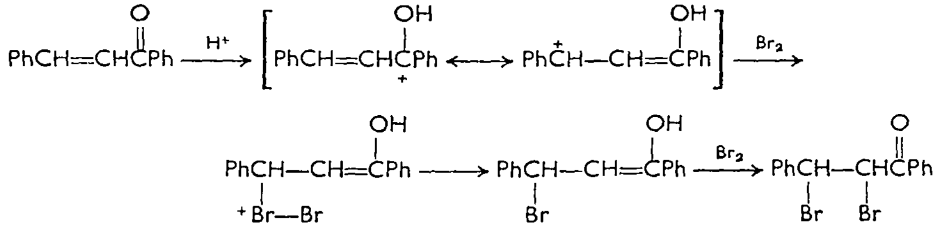


$$CH_3CH{=}CHCN \xrightarrow{H_2S} \underset{\substack{|\\ SH}}{CH_3CH}CH_2CN \longrightarrow$$

$$\begin{array}{c}CH_3CHCH_2CN\\ |\\ S\\ |\\ CH_3CHCH_2CN\end{array} \xrightarrow{H_2S} \begin{array}{c}CH_3CHCH_2CSNH_2\\ |\\ S\\ |\\ CH_3CHCH_2CSNH_2\end{array}$$

$$PhSH + CH_2{=}CHCO_2Me \xrightarrow{MeONa} PhSCH_2CH_2CO_2Me$$

Addition reactions of halogens to the β-carbon of the double bond are often acid catalyzed. These reactions take place through primary protonation of the activating groups in acids[57], aldehydes[58] or chalcones[59], enhancing the electrophilicity of the β-carbon to such a degree as to allow it to react even with very weak nucleophiles (towards C=C bonds), such as halogen molecules or halide ions. In a subsequent halogenation step, the α,β-dihalide of the substrate is formed.

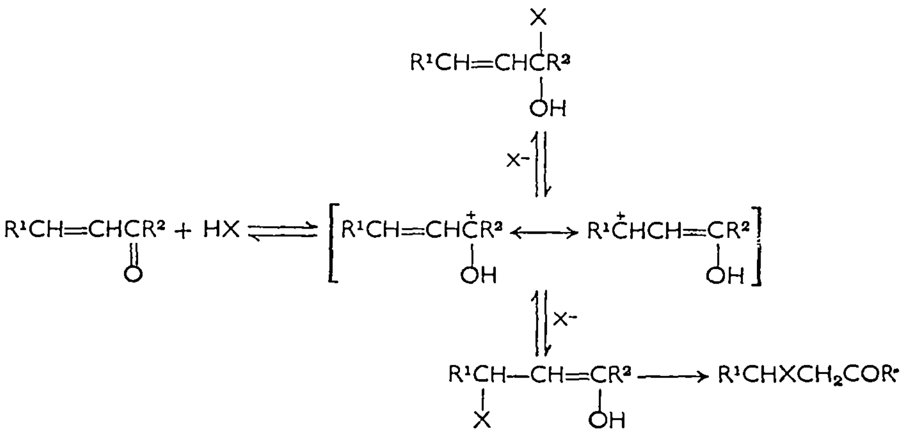


$$PhCH{=}CH\overset{\overset{O}{\|}}{C}Ph \xrightarrow{H^+} \left[PhCH{=}CH\underset{+}{\overset{\overset{OH}{|}}{C}}Ph \longleftrightarrow Ph\overset{+}{C}H{-}CH{=}\overset{\overset{OH}{|}}{C}Ph\right] \xrightarrow{Br_2}$$

$$\underset{\substack{|\\ {}^{+}Br{-}Br}}{PhCH}{-}CH{=}\overset{\overset{OH}{|}}{C}Ph \longrightarrow \underset{\substack{|\\ Br}}{PhCH}{-}CH{=}\overset{\overset{OH}{|}}{C}Ph \xrightarrow{Br_2} \underset{\substack{|\\ Br}}{PhCH}{-}\underset{\substack{|\\ Br}}{CH}\overset{\overset{O}{\|}}{C}Ph$$

Hydrogen halides may also add to the double bond by a nucleophilic mechanism, preceded by protonation of the activating carbonyl groups. The instability of the carbonyl addition product in which a hydroxyl group and a halogen atom are bound to the same carbon atom leads to preferred β-halogenation resulting, after ketonization, in the net addition of HX to the double bond. An example is the reaction of acrolein with hydrochloric acid[60].

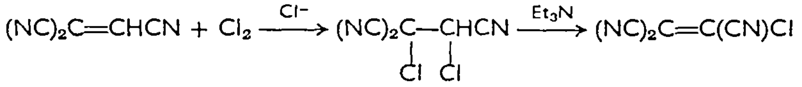
Azide ions add to the double bond[61], but other pseudo-halogens as well as halide ions are generally unreactive and no reaction is



observed between I^-, Br^- or SCN^- and either $PhCH{=}CHNO_2$ or p-$O_2NC_6H_4CH{=}C(CN)_2$[61]. With fluoroolefins, on the other hand, substitution and allylic rearrangement reactions are accompanied by addition of the fluoride ion[62].

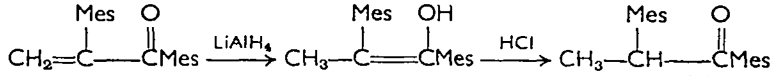
$$CF_3CF{=}CFCF_3 + F^- \longrightarrow CF_3CF_2\bar{C}FCF_3 \xrightarrow{H^+} CF_3CF_2CHFCF_3$$

A different reaction type has been demonstrated only in the addition of chlorine to tricyanoethylene[63]. This very slow uncatalyzed addition changes to a rapid one in the presence of tetramethylammonium chloride. The primary step in the catalyzed reaction is almost certainly the addition of the chloride ion to the double bond, made possible by the exceptional electrophilicity of the β-carbon in this substrate.



$$(NC)_2C{=}CHCN + Cl_2 \xrightarrow{Cl^-} (NC)_2C(Cl){-}CH(Cl)CN \xrightarrow{Et_3N} (NC)_2C{=}C(CN)Cl$$

Nucleophilic reduction of the double bond may take place by hydride ions, when the saturated compound is obtained by hydrolysis of the primary adduct with the reducing agent, *e.g.* $LiAlH_4$[64]. α,β-Unsaturated ketones may yield the enol form of the corresponding



$$CH_2{=}C(Mes){-}C(O)Mes \xrightarrow{LiAlH_4} CH_3{-}C(Mes){=}C(OH)Mes \xrightarrow{HCl} CH_3{-}CH(Mes){-}C(O)Mes$$

(Mes = mesityl)

reduced compound by 1,4-addition[65]. Hydride reductions are generally accompanied by reduction of the activating carbonyl or nitrile groups to the corresponding alcohols or amines.

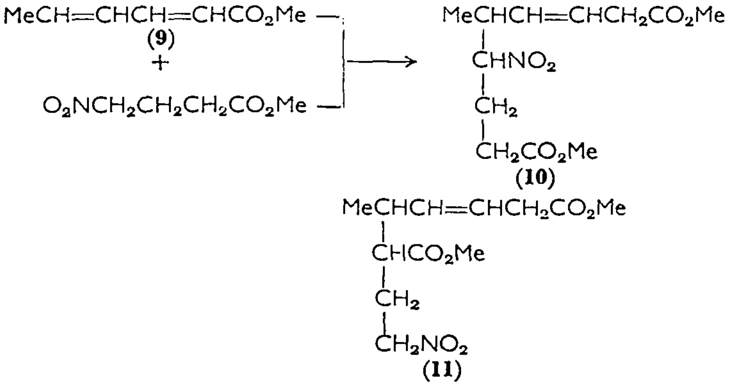
B. The Kinetics and Mechanism of Nucleophilic Additions

In view of the considerable synthetic importance of the nucleophilic addition reactions and the large number of investigations dealing with this subject, the scarcity of kinetic studies is rather surprising. A considerable part of the information available relating to the relative reactivity of substrates and of attacking agents is based on yields and on competition experiments, some of which reflect the position of final equilibria rather than actual reactivities. Kinetic investigations are complicated by the intrusion of side-reactions, such as cyclization, formation of bis adducts, polymerization, and addition of the catalyst, and often also by the lack of information on the dissociation of the reagents in the solvents used. Conclusions based on yields are notoriously unreliable. Nevertheless, the general trend is clear enough, showing the influence of steric hindrance and of electronic effects in directing the reaction into one of several possible reaction routes.

Yield determinations show that the presence of alkyl or aryl groups either at the α- or at the β-carbon atom of the double bond results in low yields, which may be attributed to both steric and electronic effects. Unsaturated esters containing one aryl group, such as ethyl cinnamate, or two β-methyl groups, such as ethyl β,β-dimethylacrylate, give with diethyl malonate yields of about 30%, while ethyl crotonate gives 60%. The introduction of a third alkyl group or a second aryl group inhibits the reaction completely[66].

Results based on positional competition experiments are more reliable than those based on yields only. The reactivity of different positions in the donor or in the acceptor can be determined by identifying the product obtained by using a donor with two (or more) potential nucleophilic centers, or by using an acceptor with two potential electrophilic centers. The preferred point of attachment shows the relative reactivity of these centers, *i.e.* the activating power of the substituent groups under study.

With donors which have two acidic hydrogens activated by two different groups, the carbon to which the more acid hydrogen atom was originally attached will add preferentially to the double bond. The activating effect of a nitro group is stronger than that of a carbethoxy group, as seen by the addition of methyl γ-nitrobutyrate to **9** to yield the product **10** rather than its isomer **11**[67]. The combined activating effect of two carbethoxy groups is stronger that that of a



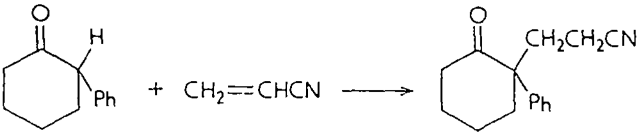
$$\left.\begin{array}{c}\mathrm{MeCH{=}CHCH{=}CHCO_2Me}\\ \textbf{(9)}\\ +\\ \mathrm{O_2NCH_2CH_2CH_2CO_2Me}\end{array}\right\} \longrightarrow \begin{array}{l}\mathrm{MeCHCH{=}CHCH_2CO_2Me}\\ \quad|\\ \mathrm{CHNO_2}\\ \quad|\\ \mathrm{CH_2}\\ \quad|\\ \mathrm{CH_2CO_2Me}\\ \quad\textbf{(10)}\end{array}$$

$$\begin{array}{l}\mathrm{MeCHCH{=}CHCH_2CO_2Me}\\ \quad|\\ \mathrm{CHCO_2Me}\\ \quad|\\ \mathrm{CH_2}\\ \quad|\\ \mathrm{CH_2NO_2}\\ \quad\textbf{(11)}\end{array}$$

formyl group[68], as shown by the formation of **13** from acrolein and **12.** Other studies[69] show that a carbonyl group is much more

$$\underset{\textbf{(12)}}{\mathrm{(EtO_2C)_2CHCH_2CH_2CHO}} + \mathrm{CH_2{=}CHCHO} \longrightarrow \underset{\textbf{(13)}}{\mathrm{(EtO_2C)_2C(CH_2CH_2CHO)_2}}$$

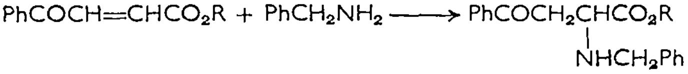
effective than a single carbethoxy group. The cyanoethylation of α-phenylcyclohexanone at the substituted α-position shows that the hydrogen in the —C(=O)CHPh— group is more reactive than that in the —C(=O)CH$_2$— group[70,71].



The application of a similar positional competition method to the study of various acceptors showed that activation of a double-bonded carbon atom β to a carbonyl group is much stronger than of the carbon β to a nitrile group. Exclusive addition of the nucleophile PhSH to the carbon atom adjacent to the nitrile group, *i.e.* β to the RCO— group, occurs in β-cyanovinyl ketones[72]. A ketonic carbonyl group

$$\mathrm{RCOCH{=}CHCN} + \mathrm{PhSH} \longrightarrow \mathrm{RCOCH_2CH(SPh)CN}$$

also governs the addition in the presence of a carbethoxy group, as in the exclusive addition of benzylamine to the position β to the former in β-benzoylacrylic acid and its esters[73].



$$\mathrm{PhCOCH{=}CHCO_2R} + \mathrm{PhCH_2NH_2} \longrightarrow \mathrm{PhCOCH_2}\underset{\mathrm{NHCH_2Ph}}{\underset{|}{\mathrm{C}}}\mathrm{HCO_2R}$$

Kinetic complications encountered in the normally required presence of strong basic catalysts may be overcome, at least in part, by using nearly neutral reaction media and by measuring the kinetically simpler retrograde reaction[74,75]. The ternary donor/acceptor/catalyst system may also be simplified by using the catalyst as the donor.

Two main points are emphasized by all kinetic studies: that the slowest step is the attack of the nucleophile on the double bond, as proposed by Ingold[3b], followed by fast protonation of the anionic product either by the solvent or by a second donor molecule; and that the reaction becomes faster with stronger electrophilicity of the β-carbon atom, *i.e.* when the substrates are activated by groups exerting stronger inductive or resonative effects.

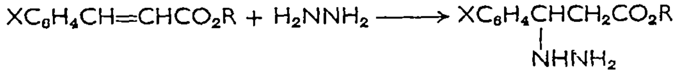
Steric and electronic effects on the rate of reactions with various acceptors are usually rather hard to distinguish. The data in Table 1 reflect the considerable loss of reactivity on α-methylation of the acceptor[76]. This is caused by both inductive and steric effects of the added methyl groups, resulting in higher activation energies (E_a) on the one hand and in lower frequency factors (A) on the other. In this series the carbethoxy group has a stronger activating effect than the nitrile group.

TABLE 1. Addition of sulfite ions to various acceptors at 25° in acetate buffer (pH 6)[76].

Acceptor	10^2k (l./mole sec)	E_a (kcal/mole)	A
Acrylonitrile	18	—[a]	—
Methyl acrylate	29	12	2×10^8
Methacrylonitrile	0·035	18	11×10^5
Methyl methacrylate	0·13	18	4×10^9

[a] Strongly temperature dependent.

Electronic effects can be isolated when an aryl group at the β-carbon atom is substituted by different p-substituents. In the addition of hydrazine to ring-substituted methyl cinnamates[77], the order of reactivity is p-NO_2 > m-NO_2 > m-Br > H > p-MeO, showing the importance of inductive effects exerted by the β-substituent. The reaction of barbituric acid with ring-substituted β-nitrostyrenes[78] again shows the requirement of a positive reaction center reflected



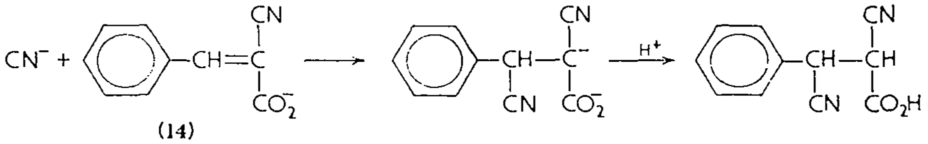
$$XC_6H_4CH{=}CHCO_2R + H_2NNH_2 \longrightarrow XC_6H_4\underset{\displaystyle NHNH_2}{CH}CH_2CO_2R$$

in the positive value (+0·739) of the Hammett reaction constant (Table 2).

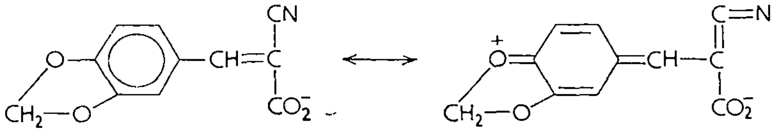
TABLE 2. Addition of barbiturate anions to $XC_6H_4CH{=}CHNO_2$ in 66⅔% dioxane at 30°C[78].

X	4-$(CH_3)_2N$	3-MeO	3,4-CH_2O_2	H	4-Cl	3-NO_2	4-NO_2
10*k* (l./mole sec)	2·32	7·0	7·4	12·9	17·7	31·4	46·5

The rate of the addition of HCN to potassium α-cyanocinnamate in aqueous solution[79] is proportional to the concentration of both cinnamate (**14**) and cyanide ions, but independent of the nature of the cations present in the reaction mixture. The reaction involves bond formation between two anions, followed by protonation of the resulting dianion. Using **15** in the place of **14**, the reaction becomes ten times slower, since the electrophilicity of the β-carbon is lowered by the resonance contribution of non-reactive forms, such as **16** (+*M* effect of the methylenedioxy group).



(14)



(15) (16)

Increasing symmetry in haloalkenes decreases their reactivity toward diethylamine[80a]. The reactivity order $F_2C{=}CFBr > F_2C{=}CFCl > F_2C{=}CF_2$ is correlated to the dipole moments of the substrates.

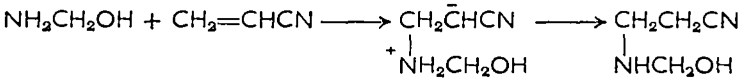
$$F_2C{=}CFX + Et_2NH \longrightarrow F_2C(NEt_2)CHFX$$

However, when the attacked system is strongly activated by two carbonyl groups as in the methoxide-catalyzed addition reaction of methanol to substituted *trans*-dibenzoylethylenes, the reactions are

$$Ar^1COCH{=}CHCOAr^2 + CH_3OH \xrightarrow{CH_3O^-} Ar^1COCH(OCH_3)CH_2COAr^2$$

quite rapid and even the uncatalyzed reaction can be observed[80b]. The interesting feature of this system is that a linear Hammett relation exists with the sum of the σ values of the *p*-substituents in both rings. Steric effects cause *cis*-dibenzoylethylene to react slower by a factor of 45 than the *trans* isomer.

Both electronic and steric effects also influence the effectiveness of the donor. Acrylonitrile is used most frequently as the substrate with a variety of nucleophiles, such as acetylacetone[81], ethanolamine[81], diethyl malonate[82], alkoxide ions[83] and various carbanions[84]. All these reactions are kinetically first order in each of the reactants. The measurements were carried out in different media, so that comparison of the results is difficult. However, the order of reactivity diethyl malonate > acetoacetic ester > ethanolamine > acetylacetone was observed[81, 82]. Because the nucleophilicity of the amino nitrogen atom is much higher than that of a hydroxylic oxygen atom, ethanolamine, at pH 7·5–9·4, attacks only through its nitrogen atom[81]. Still it can be expected that at higher pH, with increasing dissociation of the —OH group, the alkoxide oxygen should be able to compete effectively with the nitrogen as a nucleophile.



$$NH_2CH_2OH + CH_2{=}CHCN \longrightarrow CH_2\underset{\overset{+}{N}H_2CH_2OH}{\underset{|}{\bar{C}H}}CN \longrightarrow CH_2\underset{NHCH_2OH}{\underset{|}{CH}}_2CN$$

The reaction of acrylonitrile with various donors[84] (Table 3) shows that the influence of the two activating groups at the same carbon atom is by no means additive. At a constant catalyst concentration the rates were independent of the concentration of the active methylene compound, but in the rate equation $k_1 = k_2[\text{cat}]_{\text{eff.}}$, the 'effective' concentration of the catalyst $[\text{cat}]_{\text{eff.}}$ was lower than its stoichiometric concentration. Therefore, the measure of reliability of the rate data is not quite clear.

TABLE 3. Pseudo first-order rate coefficients for the reaction $BuCHXY + CH_2{=}CHCN \rightarrow CH_2(CBuXY)CH_2CN$ in *t*-butanol[84].

X	CN	CO_2Et	$COCH_3$	COSEt	CN	COSEt
Y	CN	CO_2Et	CO_2Et	CO_2Et	CO_2Et	COSEt
$10^3k_1(\text{sec}^{-1})$	3	2	1·65	0·66	0·21	0·13

The reactivity of various alkoxides (each dissolved in its parent alcohol) toward acrylonitrile is inversely proportional to the acidity of the parent alcohols[83]. This may be expected with anions of similar structure in which hydrogen basicities and nucleophilicities may be correlated[85]. Identical rates were obtained with lithium, sodium and potassium derivatives of the same alkoxide, showing complete dissociation under the conditions of the experiments (Table 4).

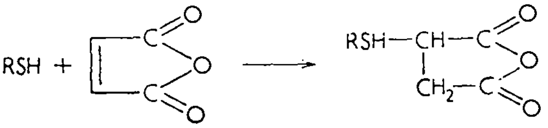
TABLE 4. Rate coefficients for the addition of alkoxides to acrylonitrile at 20°[83].

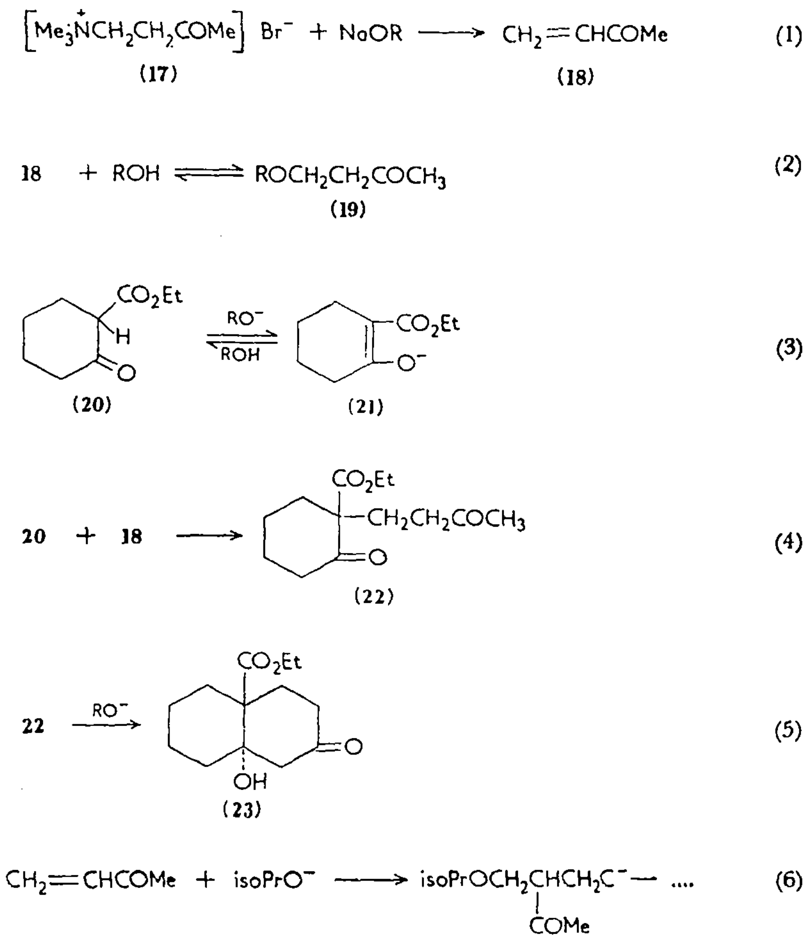
RO^-	MeO^-	EtO^-	$n\text{-}PrO^-$	$n\text{-}BuO^-$	$isoPrO^-$
10^2k_1 (l./mole sec)	0·58	5·25	9·58	9·58	28·75

Hence, the rate differences with different alkoxides are not due to differences in their dissociation or to the presence of different ion pairs. Kinetic analysis of the results shows that only the alkoxide ions (and not the alcohol molecules) serve as nucleophiles.

The same nucleophilic order $MeO^- < EtO^- < isoPrO^-$ was also observed[30] in step (2) of the alkylation of 2-butenone (**18**) with the enolate (**21**) of ethyl 2-cyclohexanone carboxylate (**20**). This alkylation was studied as an example of the Robinson modification of the Michael reaction. The butenone was prepared *in situ* from the metho salt of 4-dialkylaminobutan-2-one (**17**). Analysis of all stages of the reaction shown in Scheme 2 proved that **18** reacts rapidly with the solvent, so that the molecules undergoing alkylation do not originate directly from the decomposition of the metho salt, but from the keto ether **19**. Step (2) takes place through addition of alkoxide ions to **18**, and becomes especially important in the cases when its reversal is slow. This results in the fact that catalytic amounts of isopropoxide ions are much more effective in promoting the formation of **23** than methoxide or ethoxide ions. The competition for the RO^- ions, which are required in both steps (2) and (3), results in higher yields of **23** with $isoPrO^-$, which is easily regenerated from the ether **19**. This reaction is also complicated by the polymerization step (6), favored by the isopropoxide anion. The use of carefully selected catalysts, *e.g.* t-BuO^-, which themselves give no addition but still catalyze the alkylation, may be helpful[84,86].

In contrast to the alcohols, the reactivity order of mercaptans toward maleic anhydride[87] was found in the presence of traces of base to be





Scheme 2.

correlated to their relative acidities. In this case, the concentration of RS⁻ ions, determined by the acidity of RSH, governs the reaction

$$p\text{-}NO_2C_6H_4S^- > p\text{-}ClC_6H_4S^- > p\text{-}MeOC_6H_4S^-$$

rates. The reactivity of tertiary alkyl mercaptans is low, with both steric and electronic effects tending to inhibit their attack.

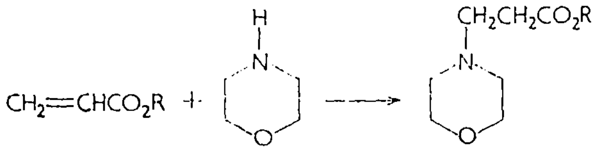
Working in the presence of large amounts of the catalyst, enabling practically complete ionization of the nucleophile, as in the reaction of substituted phenols with trifluorochloroethylene[88], the more acidic

2,4,6-trichlorophenol reacts very much slower than 1,3,4-xylenol, reflecting the stronger nucleophilicity of the less basic anion.

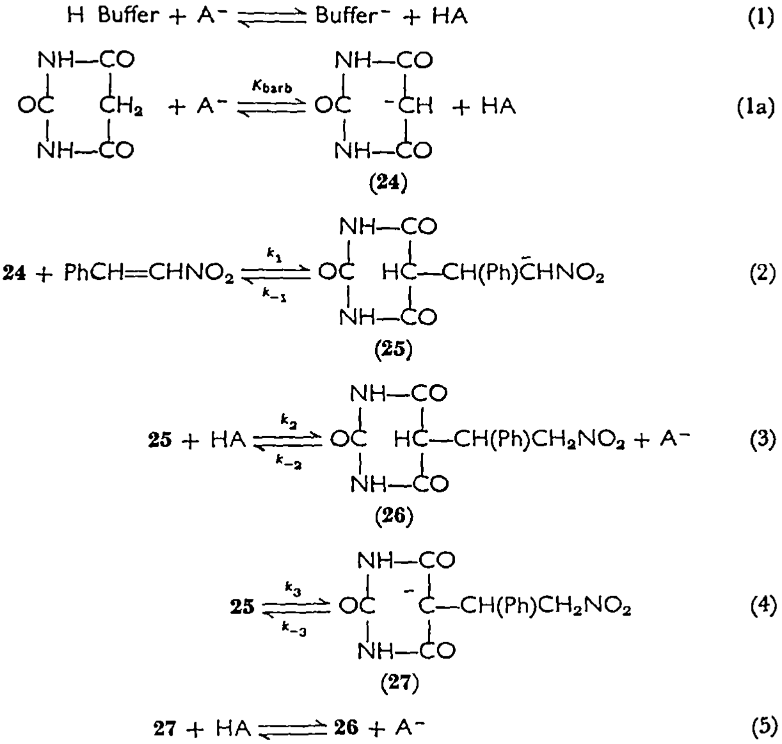
$$\mathrm{ArO^- + CF_2{=}CFCl \longrightarrow ArOCF_2\overset{-}{C}FCl \xrightarrow{ArOH} ArOCF_2CHFCl + ArO^-}$$

Amine addition rates are faster if the amine is more basic and if it is less hindered sterically. The reactivity order in the addition of amines to methyl methacrylate (based on yields) is as follows[89]: piperidine > Et_2NH > $PhNH_2$ > PhNHEt.

The attack on acrylic esters by piperidine or morpholine is of the second order, and, although not catalyzed by added bases, it is inhibited by acids proportionally to the lowering of the effective amine concentration. Hence, the rate-determining step is a direct attack by the amine on the β-carbon of the substrate. The rates were much faster with piperidine than with morpholine, as expected from the relative basicities of these two amines of similar bulk. Methyl substitution on the β-carbon of the acrylates lowered the rates both by steric inhibition and by electronic effects. The effect of the size of the esteric alkyl groups (Me, Et, Bu) is very small. The primary step is the formation of a zwitterion, favored by solvents of high dielectric constants; the reaction is immeasurably slow in pure benzene and becomes progressively faster on the addition of methanol to the solvent[90].



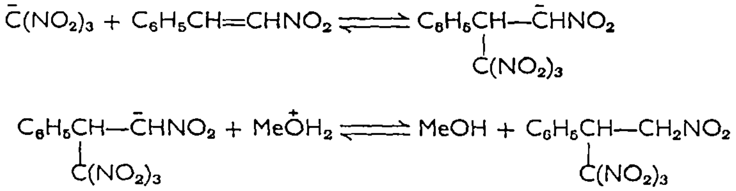
The fact that sufficiently strong carbon acids react also in the absence of catalysts and even in slightly acid media is a strong indication that the role of the basic catalysts in the addition is only the promotion of the ionization of the carbon acids. Kinetic results obtained under such conditions[74,78] often permit easier interpretation of the data. For example, in the reaction of aryl-substituted β-nitrostyrenes with barbituric acid in slightly acid buffered dioxane–water solvent (Scheme 3)[78], first-order dependency was found in both the styrene and in barbiturate ions. Step (2) was proposed to be rate determining, with the concentration of **24** being governed by the buffer/barbituric acid equilibrium. Protonation of the carbanion **25** may take place by the solvent (step 3) or intramolecularly (step 4). The kinetic form of the reaction would also fit a mechanism involving a rapid reversible nucleophilic attack followed by slow protonation by water molecules ($k_1 > k_2$) (but not by H_3O^+ or by H-buffer). However, analysis of the dependence of the equilibrium upon the pH of the medium points to the formation of a C—C bond in the rate-determining step, and protonation rates of carbanions are known to be generally fast[91]. In dioxane–water mixtures of higher dielectric constant,



Scheme 3.

the rate coefficients rise, contrary to the effect expected from the Hughes–Ingold theory of solvent effects[92a]. In this case, the entropy effect more than compensates for the rise in the activation energy caused by the more polar solvent on the ion–dipole reaction, although in a rather similar case, the addition of alkoxide ions to acrylonitrile[83], rate coefficients fall with increasing dielectric constant of dioxane–methanol mixtures, or by increasing the methanol content in dimethylformamide–methanol mixtures. Both the steep rise in the rate coefficients in the region approaching pure dioxane or pure dimethylformamide and the similar dielectric constant of dimethylformamide and of methanol show that the effect is a specific one, possibly a specific solvation of the methoxide ions by methanol resulting in much reduced reactivity of the solvated methoxide ions compared to the unsolvated ones[92b].

For the uncatalyzed reaction of the strong carbon acid trinitromethane with β-nitrostyrene[74], a similar mechanism was derived from the kinetic results, mainly relating to the reverse reaction, *i.e.* to the decomposition of **28**.

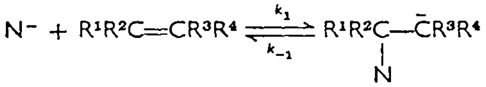


$$\bar{C}(NO_2)_3 + C_6H_5CH{=}CHNO_2 \rightleftharpoons C_6H_5\underset{\displaystyle C(NO_2)_3}{\underset{|}{C}}H{-}\bar{C}HNO_2$$

$$C_6H_5\underset{\displaystyle C(NO_2)_3}{\underset{|}{C}}H{-}\bar{C}HNO_2 + Me\overset{+}{O}H_2 \rightleftharpoons MeOH + C_6H_5\underset{\displaystyle C(NO_2)_3}{\underset{|}{C}}H{-}CH_2NO_2$$

(28)

Although protonation of the intermediate carbanions is usually very rapid, the question of the reversibility of the nucleophilic attack and the position of its equlibrium ($K = k_1/k_{-1}$) is important for the understanding of the reaction

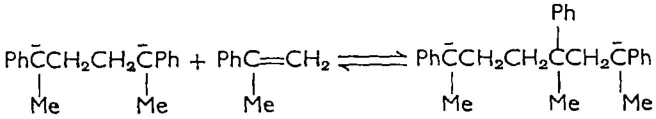


$$N^- + R^1R^2C{=}CR^3R^4 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^1R^2\underset{\displaystyle N}{\underset{|}{C}}{-}\bar{C}R^3R^4$$

Two limiting systems were studied recently[92c, 92d]. The exchange of $K^{14}CN$ with tetracyanoethylene in acetonitrile was complete within less than one hour showing the existence of the equilibrium

$$(NC)_2C{=}C(CN)_2 + CN^- \rightleftharpoons (NC)_3C{-}\bar{C}(CN)_2$$

while the equilibrium constant in the system[92d] 'living α-methylstyrene dimer' + monomer $\rightleftharpoons$ 'living trimer'



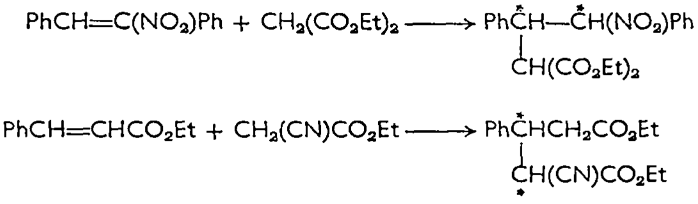
$$Ph\underset{\displaystyle Me}{\underset{|}{\bar{C}}}CH_2CH_2\underset{\displaystyle Me}{\underset{|}{\bar{C}}}Ph + Ph\underset{\displaystyle Me}{\underset{|}{C}}{=}CH_2 \rightleftharpoons Ph\underset{\displaystyle Me}{\underset{|}{\bar{C}}}CH_2CH_2\overset{\displaystyle Ph}{\overset{|}{\underset{\displaystyle Me}{\underset{|}{C}}}}CH_2\underset{\displaystyle Me}{\underset{|}{\bar{C}}}Ph$$

favors the trimer (K = 331 l./mole). The higher rate coefficient for the nucelophilic attack (k_2 = 17·1 l./mole sec) even with a very unreactive alkene is probably a result of the high reactivity of the hydrocarbon carbanion. It seems that the dispersion of the charge in the transition state, and thus the decrease in the repulsion between the two negative charges, is not the most important factor for the reactivity, as the reaction of the singly charged cumyl anion with α-methylstyrene gives an even higher value (k_2 = 155 l./mole sec).

C. Stereochemistry of the Addition Reaction

Open-chain substrates undergoing addition may yield products containing asymmetric carbon atoms, while with cyclic substrates the asymmetric carbons may also be the centers of *cis–trans* isomerization. Even so, relatively few studies deal with the stereochemistry of the reaction, and comparatively little is known about the factors governing it.

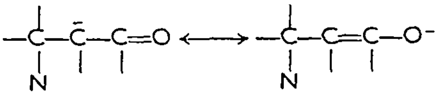
In many Michael reactions, two or three asymmetric carbon atoms appear in the adduct, one or two at the original α- and β-carbon atoms of the acceptor and one at the originally carbanionic carbon of the donor[93, 94] In some syntheses, two different racemic products



$$\mathrm{PhCH{=}C(NO_2)Ph + CH_2(CO_2Et)_2 \longrightarrow Ph\underset{\underset{\displaystyle CH(CO_2Et)_2}{|}}{\overset{*}{C}}H{-}\overset{*}{C}H(NO_2)Ph}$$

$$\mathrm{PhCH{=}CHCO_2Et + CH_2(CN)CO_2Et \longrightarrow Ph\underset{\underset{\displaystyle \underset{*}{C}H(CN)CO_2Et}{|}}{\overset{*}{C}}HCH_2CO_2Et}$$

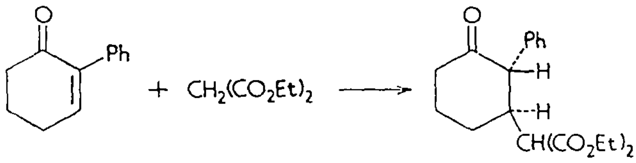
have been obtained[10a], but in most, when the addition could yield diastereoisomers, only one of these is isolated. The attack on the β-carbon takes place perpendicularly to the plane of the double bond[95] and generally is immediately followed by protonation of the substrate. The protonation of the enolate anion will be dominant compared to the protonation of the less important carbanionic contributing resonance structure. This 1,4-addition is followed by ketonization of the enolic adduct and leads to a final product, which

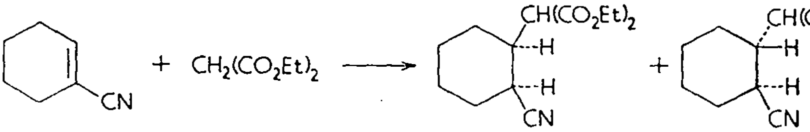


$$\underset{\text{(carbanion)}}{\mathrm{-\underset{\underset{\displaystyle N}{|}}{\overset{|}{C}}-\underset{|}{\overset{-}{C}}-\underset{|}{C}{=}O}} \longleftrightarrow \underset{\text{(enolate)}}{\mathrm{-\underset{\underset{\displaystyle N}{|}}{\overset{|}{C}}-\underset{|}{C}{=}\underset{|}{C}-O^-}}$$

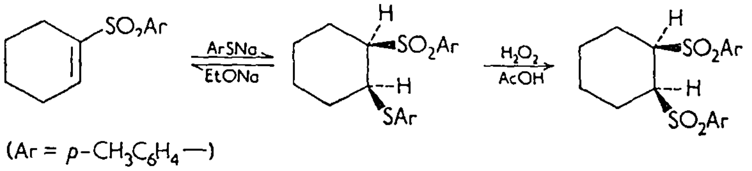
is an α,β-adduct. The important point is that the configuration of the final product does not depend upon the stereochemistry of a *cis* or *trans* addition process, as in the case of electrophilic additions to double bonds, but on the stereochemistry of the ketonization step. Apart from this, the addition process is reversible, and even in cases when the product formation is assumed to be kinetically controlled[96], the reaction mixture may undergo complete equilibration in the basic medium, so that the product actually obtained may be the thermodynamically more stable one. When two isomers are isolated, this again does not necessarily indicate the stereochemical path, but more often, the similar thermodynamical stability of the two isomers.

With cyclic acceptors, the identification of the two isomers is easier, since each of them can usually be degraded to reference compounds of known stereochemistry. The addition of diethyl malonate to 2-phenyl-2-cyclohexen-1-one gave exclusively the *trans* isomer (identified by degradation)[97,98]. However, the reaction was carried out under conditions permitting equilibration, so no conclusions can be drawn regarding the stereochemistry of the attack. *Trans* isomers were obtained in other cases[99,100], and the formation of *trans* products seems to be generally dominant. In cyclic systems, *cis* addition yields always the *trans* product, and *trans* addition always the *cis* product. Thermodynamic control in the equilibration may lead to the formation of the more stable *trans* isomer from the initially formed *cis* isomer, but not *vice versa*. Therefore, isolation of a *cis* product will be proof of a primary *trans* addition; since in the reaction of 1-cyanocyclohexene with malonic ester 72% of the product was the *cis* and only 28% the *trans* isomer[101] and probably no equilibration of the products takes place, it can be concluded that the primary process was a *trans* addition. Similarly, the addition of *p*-toluenethiol to *p*-tolylsulfonylcyclohexene[102] gave a *cis*-addition product, the identity of which was proved by oxidation to a compound which was obtained also independently (and necessarily in the *cis* form) by diene synthesis. The exclusive formation of the thermodynamically less stable product

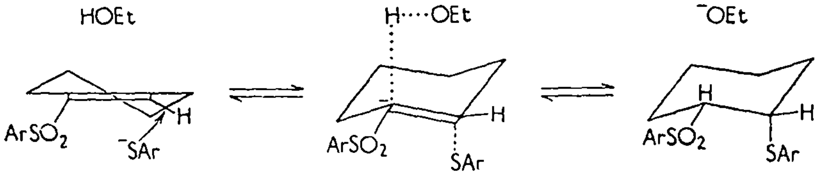




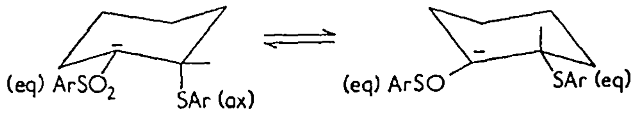
was explained as follows. The least hindered path of the attack by ArS⁻ corresponds to the axial direction. The carbanionoid carbon in the intermediate becomes tetrahedral, with the bulky arylsulfonyl group on the adjacent carbon in the equatorial position, so that protonation by the solvent can take place only by the axial route, with



formation of the *cis* product. However, the intermediate carbanion can have no more than at most a fleeting existence. Protonation must take place before it is able to isomerize, since otherwise the more stable product would be formed. In other words, the two stages of the addition occur in what is, for all practical purposes, a concerted

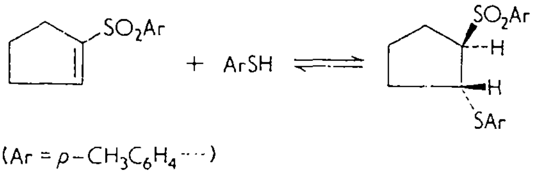


process. It could be predicted that in a solvent which is a poor supplier of protons, the lifetime of the carbanion will be enhanced and the concerted mechanism will change to a consecutive two-step process, permitting the isomerization of the carbanion and formation of the *trans* product. This prediction was verified, using dioxane



(*cis*) (*trans*)

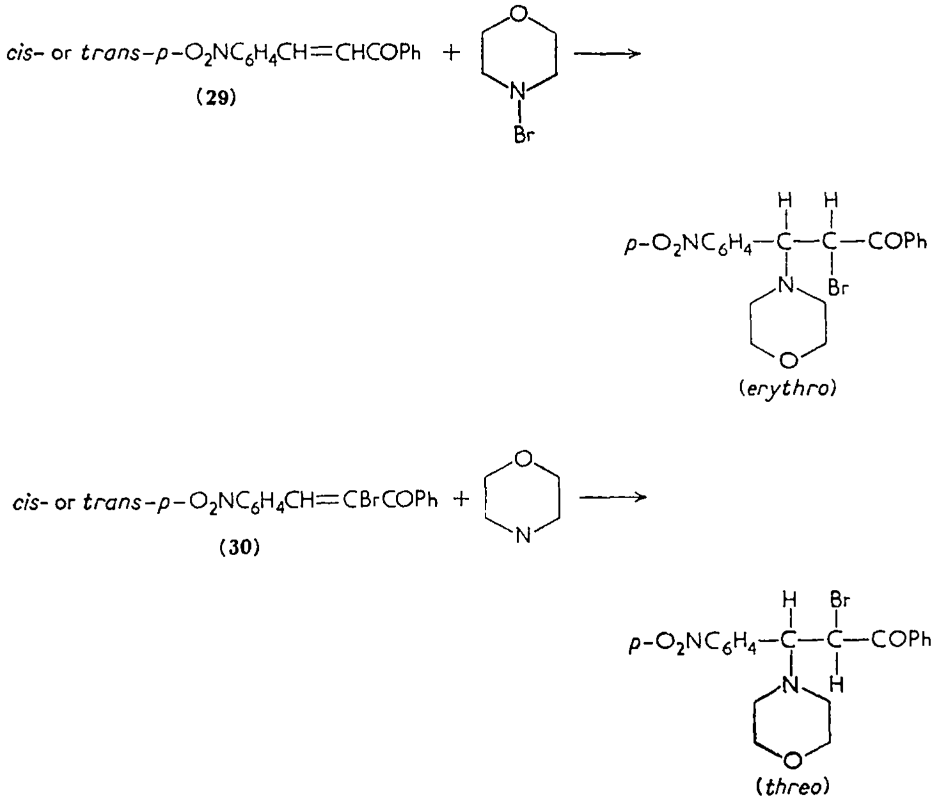
as the solvent in the presence of only a small amount of water and ethanol as proton sources. Under the conditions employed, the *cis* product is stable, so the *trans* isomer must originate from isomerization of the intermediate carbanion. The formation of *cis* products in other cyclic systems is probably governed by similar effects, determined by the geometry of substituent groups on the ring[103a]. However, the addition of *p*-toluenethiol to 1-*p*-tolylsulfonylcyclopentene yields both in ethanol and in dioxane the more stable *trans* isomer[103b].



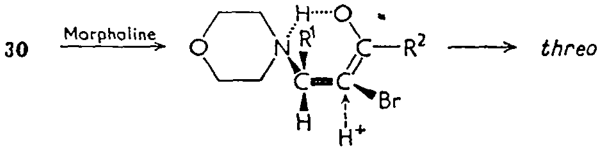
The different behavior was ascribed not to a change in mechanism, which is still basically a *trans* addition, but to a fast isomerization of the intermediate carbanion followed by a comparatively slow protonation. While in the cyclohexyl system strain results mainly from steric interaction between the —SAr group and the two axial hydrogens, in the nearly planar cyclopentyl system the interaction between the two large substituent groups becomes important, and enhances the isomerization in the direction of the less hindered product.

(*cis*) (*trans*)

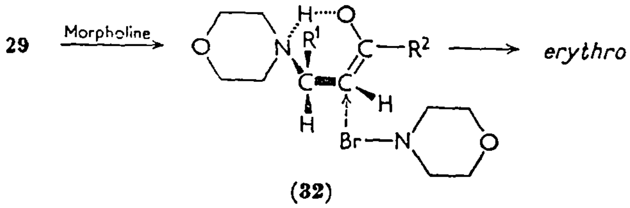
Stereochemical studies have been carried out in systems in which *N*-bromoamines with unsaturated ketones on the one hand or amines with bromo ketones on the other yield isomeric products: the addition of *N*-bromomorpholine to *trans*-chalcone yields the *erythro* isomer of α-bromo-β-morpholinobenzylideneacetophenone, while the *threo* isomer of the same product is obtained from the reaction of morpholine with α-bromochalcone[104,105]. The sterochemistry of the products is independent of the configuration of the starting materials, since only the *erythro* product is obtained in the reaction of either *cis*- or *trans*-4-nitrochalcone (**29**) with *N*-bromomorpholine, and only the *threo* product is obtained in the reaction of either *cis*- or *trans*-4-nitro-α-bromochalcone (**30**) with morpholine[105]. Even taking into account the possibility of isomerization in the strongly basic reaction medium, at least one of these reaction pairs must be kinetically controlled. According to equilibration experiments, this is the morpholine–**30** pair. The reaction is not stereospecific, but as the configuration of the product is also not due to equilibration, it must be governed by an addition step with a 'convergent configuration control'[105]. The convergence of the two routes starting with either *cis* or *trans* acceptors points to a common intermediate with only a single asymmetric center. Strict configuration control in the formation of the second asymmetric center during the last step of the reaction then accounts for the formation of a single product. The results of the



reaction of morpholine with **30** were explained by the formation of a chelated enol intermediate **31**[105], which is more stable than its open-chain configuration. Protonation of this intermediate by a morpholinium ion or by the solvent will take place from the least hindered direction, *i.e.* from the side of the hydrogen atom at the adjacent carbon, and will lead to the *threo* isomer, irrespectively of whether the starting material was *cis* or *trans*. In mixtures containing *N*-bromomorpholine, morpholine is always present at least in traces. Therefore, a similar chelated enol intermediate **32** may also be formed in the second reaction, and will be brominated from the least hindered direction to form the *erythro* isomer. This mechanism, incidentally, explains the relatively low rate with *N*-bromomorpholine, making it dependent upon the concentration of the morpholine initially present in the mixture, while the morpholine formed as a side-product in the reaction allows its continuation.

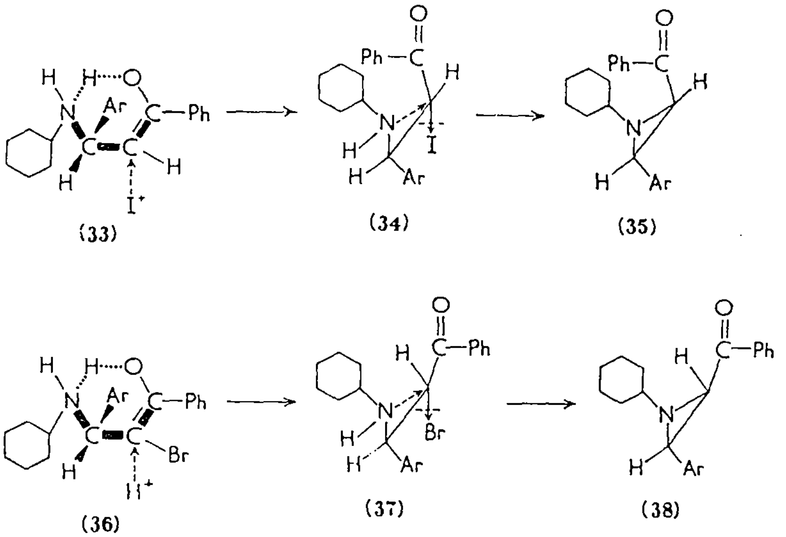


(31)



(32)

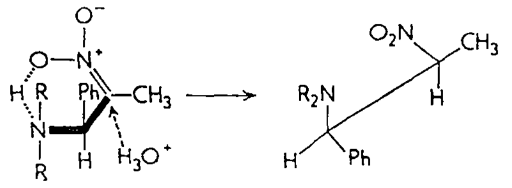
Formation of cyclic products often assists stereochemical elucidation. For example, α-halo-β-amino (or -β-alkylamino) ketones formed in additions undergo facile cyclization to the corresponding ethylenimine ketones. This involves only the inversion of the α-carbon atom without isomerization of the diastereoisomers formed by addition[106]. In Scheme 4, the *erythro* isomer **34** will produce only the *trans* compound **35**, and the *threo* isomer **37** only the *cis* compound **38**. Generally, the *trans* product is dominant in syntheses. In the *p*-nitrobenzylidene-acetophenone/cyclohexylamine/iodine system[107] (Ar = *p*-$O_2NC_6H_4$–) about equal amounts of the *cis* and *trans* products were obtained in benzene solution. Changing the medium from benzene to methanol enhanced the formation of the *trans* isomer. As this with a hydrogen-bonding solvent can hardly be ascribed to enhanced chelated enol (**33**) formation, it must be assumed that the mechanism is changed in the second (iodination) step of the addition. The stereochemistry of the products is then related to the relative populations of the chelated and open-chain conformations of the intermediate aminoenol, as well as to the relative size and reactivity of the iodinating species. The steric hindrance presented to the attacking reagent by the chelate is larger than that presented by the open-chain conformer. If the latter is the substrate, the similarity in size of the cyclohexyl and phenyl groups will lead to about equal formation of *cis* and *trans* isomers. Therefore, the formation of similar amounts of *cis* and *trans* products in benzene shows that, since the iodinating agent has also considerable steric requirements, the preferred attack is probably on the unchelated enol, even though its concentration is relatively small. On the other hand, the preferred formation of the *trans* product in methanol probably points to an attack by a reagent of small size on the prevalent chelate intermediate. This interpretation seems to be reasonable, since the attacking agent in benzene is probably the bulky iodine–amine complex or possibly



SCHEME 4.

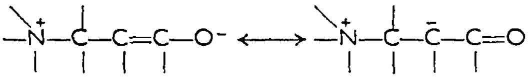
the equally bulky *N*-iodocyclohexylamine, while in methanol it is the relatively small I^+ cation or the CH_3OI molecule. Accordingly, by changing the solvent or by using different sized halogens, or by both together, the isomer ratio may be changed at will. This was verified experimentally in the reaction of cyclohexylamine with *trans*-α-bromochalcone or with *trans*-4-nitro-α-bromochalcone (**30**) in methanol, when the amount of the *cis* product is enhanced[107] in the reaction sequence **36** → **37** → **38**. Here the protonation of the enol **36** from the least hindered direction gives the *threo* ketone **37**, which in turn, by intramolecular reaction accompanied by inversion, gives the *cis*-ethylenimine ketone **38**. The protonation step is not hindered when the source of protons is methanol or its conjugate acid, but in benzene protonation takes place by the bulky cyclohexylammonium ions and, therefore, the attack probably will be again on the less hindered unchelated form.

The same hypothesis may be applied for the reaction of amines with (2-nitropropenyl)benzene, where formation of the *erythro* isomer **39** probably takes place through a chelate derived from the *aci*-nitro structure[108].

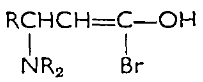


(39)

A different treatment emphasizes the importance of bulk interactions between the substituent groups on the α- and β-carbon atoms[109,110] and neglects the possible intramolecular functional group interactions. While pointing out[109] that the positively charged nitrogen attached to the β-position attracts the electrons in the π-bond of the enolate anion **40** so that the resonance contribution of the keto-zwitterionic form **41** is enhanced and may allow direct α,β-addition to take place, the emphasis in the stereochemical analysis is still placed on the ketonization step of the enol **42**. The factors affecting



(40) **(41)**



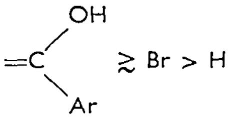
$$\underset{\mathrm{NR_2}}{\mathrm{RCH}}\mathrm{CH{=}}\underset{\mathrm{Br}}{\mathrm{C}}\mathrm{{-}OH}$$

(42)

the structure of the product will be similar to those found in other asymmetric inductions[111], mainly depending upon the 'effective' size of the substituents. This was given for the β-substituents as

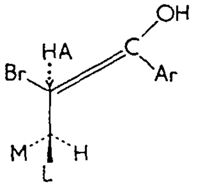
$$\text{Aryl} > \text{MeNH} > \text{NH}_2 > \text{H}; \quad \text{C}_6\text{H}_{11}\text{NH} \sim \text{C}_6\text{H}_5 > \text{CH}_3 > \text{H}$$

and for the substituents on the trigonal α-carbon as



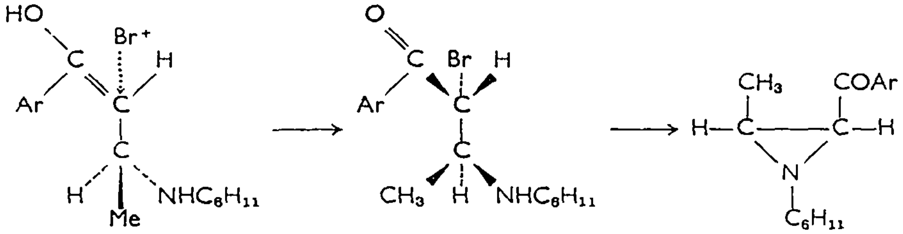
$\gtrsim$ Br > H

The most preferred structure of the enol with the least crowding of substituent groups in the transition state is the one in which the protonating agent approaches the enolic double bond from the least hindered direction, *i.e.* from the side of the two smallest groups attached to the adjacent asymmetric carbon atom:



(M = medium group;
L = large group.)

The configuration of the enol in which the aryl group and the subsubstituted β-carbon are *cis* to each other is preferred, since the strongly solvated hydroxyl group is probably more bulky than the less solvated phenyl group. Using this principle together with the above-mentioned series of relative 'effective sizes', the experimentally obtained *cis–trans* ratios in the formation of ethylenimine ketones can be rationalized. Similarly, in the phenylcrotonophenone/cyclohexylamine/bromine system, bromination of the enol intermediate **43** in its least crowded conformation, *i.e.* in which the enolic double bond is flanked by the two smallest groups (Me and H) attached to the β-carbon, gives through the bromoketone **44** exclusive formation



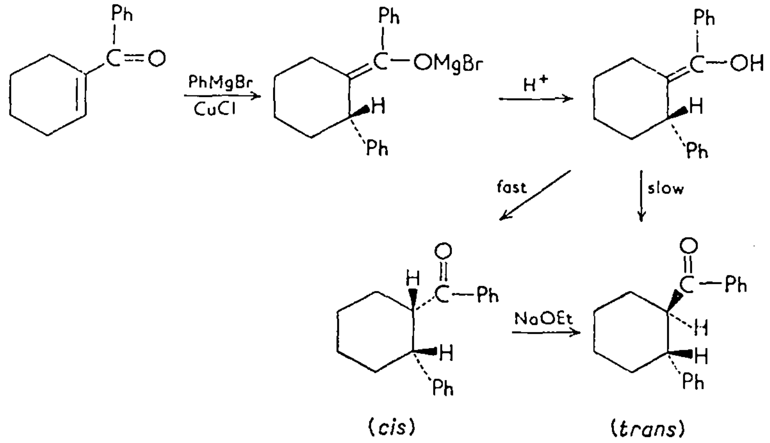
(43) **(44)** **(45)**

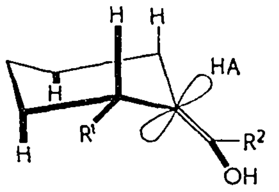
(Ar = p-$C_6H_5C_6H_4$—)

of *cis*-**45**. On the other hand, the *p*-phenylcrotonophenone/cyclohexylamine/iodine system yields mainly the *trans* product[112] showing the dependence of the stereochemical path upon the nature and size of the halogen.

This treatment was criticized[107] because it neglects the high degree of configurational control which may be obtained even with two C_β substituents of very similar size, as well as specific solvent effects and also the formation of different products from the ketone/*N*-bromomorpholine and the bromoketone/morpholine systems[105, 107].

The stereochemistry of the 1,4-addition of Grignard reagents (see section II.D) is also governed by the ketonization step, with preferred attack on the enol intermediate from its least hindered side. In the presence of CuCl, which promotes 1,4-addition, *cis*-1-phenyl-2-benzoylcyclohexene is the main product in the reaction of 1-benzoylcyclohexene with phenylmagnesium bromide[96], although the *trans* isomer is more stable. These results may be explained by kinetic





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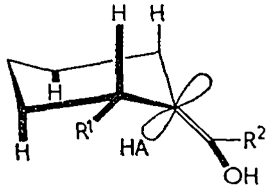
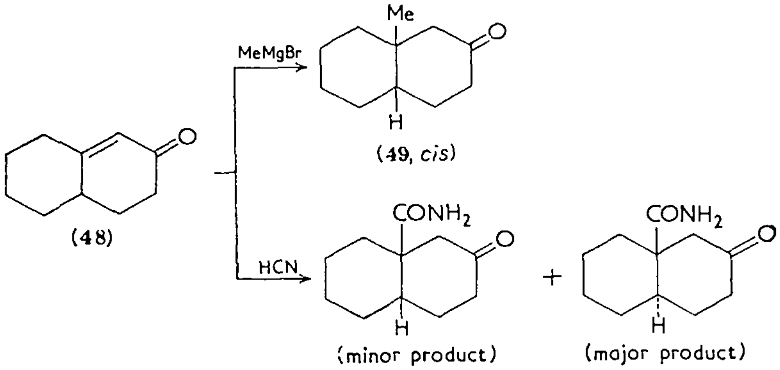


(47)

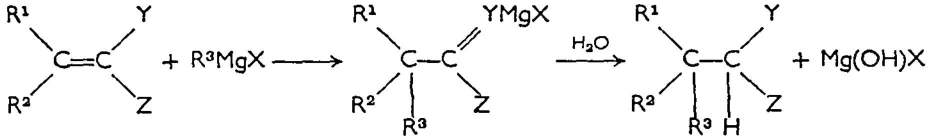


control in the two transition states shown above. The attack by the protonating agent HA on the enol as shown in **46** is much more facile than in **47**, when pronounced steric hindrance is caused by the axial hydrogen atoms.

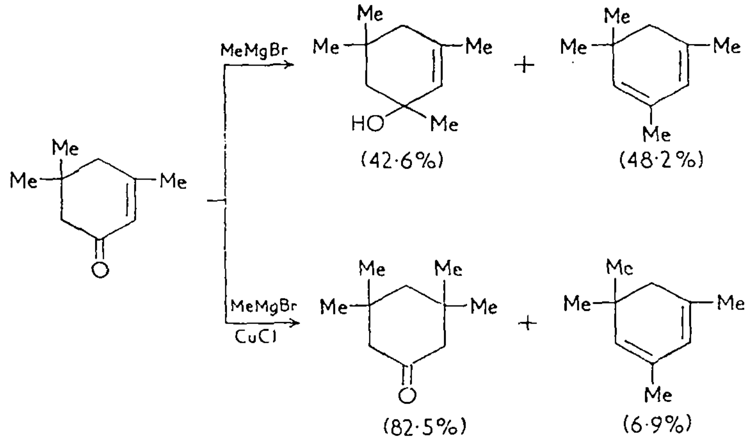
Finally, when the *β*-carbon is common to two rings, the primary nucleophilic attack itself may produce *cis* and *trans* isomers of the alicyclic carbanionic product. The reaction of **48** with MeMgBr gives the *cis* isomer **49** exclusively[113], while in the addition of HCN to the same substrate, a mixture of the *cis* and *trans* amides is produced in a 1:3·6 ratio[114].

D. Addition of Organometallic Compounds

1,4-Additions of organometallic compounds are fast and practically irreversible, yielding kinetically controlled products, while most other additions are generally thermodynamically controlled. Therefore, these reactions are especially valuable for studying the relations between carbonyl and α,β-additions and the factors governing them. The addition of Grignard reagents to unsaturated substrates is a well known and useful synthetic reaction[115]. Unsaturated aldehydes give mainly carbonyl addition products[116], but 1,4-additions are general with α,β-unsaturated ketones[115a], acids[117], nitriles[115e,118], esters[115c,119] and amides[115f,120].



Complicating the study of this reaction are its extreme rapidity, the instability of the reagent and various side-reactions. Some

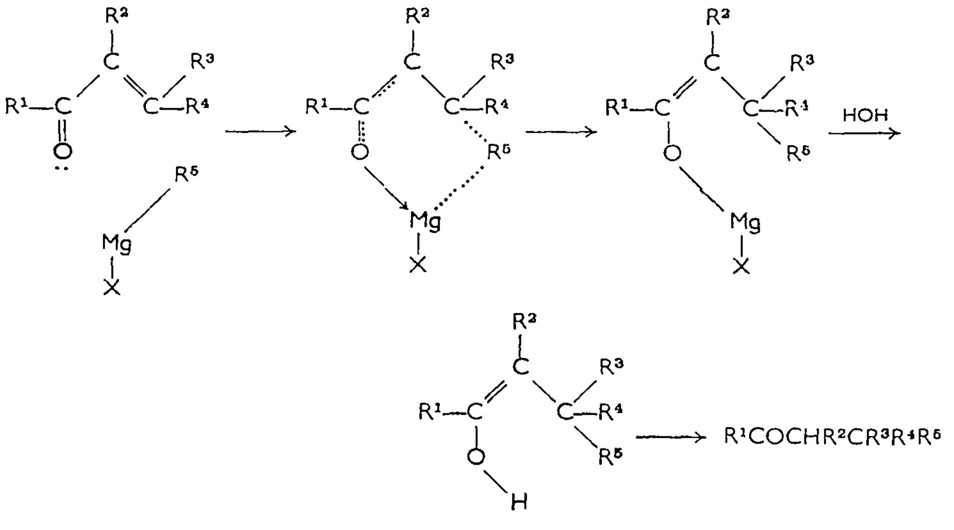


explanations for the ratio of carbonyl and α,β-additions were based on unreliable experiments, before the recognition of the strong effects of impurities. The latter is demonstrated in the reaction of isophorone with MeMgI in which the major product is normally that of carbonyl addition, while in the presence of 1% of CuCl, 1,4-addition is dominant[121].

It is not quite clear why the addition of a cuprous salt increases the yield of 1,4-addition products[113, 122, 123]. Possibly, a copper salt complex is formed with participation of the α-carbon atom, enhancing the electrophilicity of the β-carbon, or an alkylcopper may be formed[124] from the copper salt and the Grignard reagent (see below).

1,4-Addition is also preferred over carbonyl addition with alkyl- and arylcadmiums[125], -berylliums and -manganeses[126], while the use of more reactive potassium and calcium organometallics gives almost exclusively carbonyl addition[126]. Sodium and lithium derivatives give mainly carbonyl additions with the same systems which yield α,β-products with Grignard reagents[127, 128, 129].

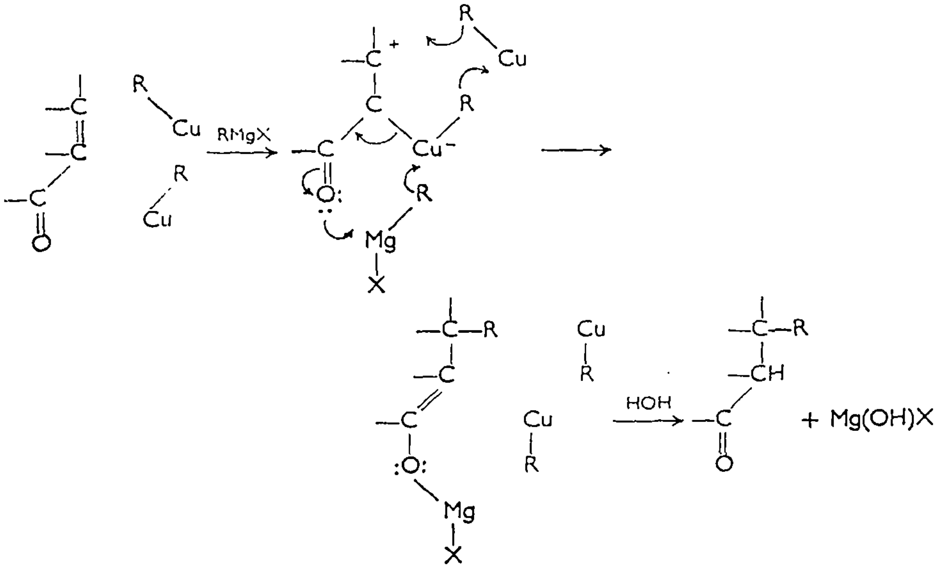
The accepted mechanism for the 1,4-addition of Grignard reagents[130] postulates the formation of a quasi-6-membered ring in the first stage of the reaction. The magnesium atom coordinates with the carbonyl oxygen atom and increases the electrophilicity of the β-carbon, while simultaneously the Mg—R^5 bond is weakened. When R^5 becomes attached to C$_\beta$, an enolate is formed which yields, after hydrolysis, the enol, and after ketonization, the final product.



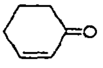
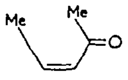
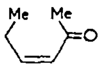
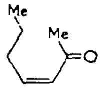
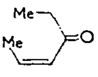
No similar cyclic mechanism will operate with lithium and sodium compounds, owing to their lower coordinative tendency. This explains their preference for carbonyl addition.

The Grignard reaction in the presence of copper salts has been formulated with the participation of alkylcoppers coordinating through

$$\mathrm{RMgBr + CuCl \longrightarrow MgBrCl + RCu}$$



their copper atom with the α-carbon atom[124]. The generality of this mechanism has been criticized[131] on the basis of the similarity of the carbonyl- and α,β-product ratios with a series of Grignard reagents, both with cyclohexenone and its open-chain analogs:

Substrate					
Yield of α,β-addition product with isoPrMgBr[131]	64%	65%	56%	63%	80%

The criticism was based mainly upon the assumption that the ring compound has much less flexibility than its open analogs, and that the formation of a cyclic intermediate with the former should demand considerable strain in valency angles and, therefore, different product ratios. This criticism did not take into account the enhanced flexibility of the bonds during the complex formation, allowing the cyclic mechanism to operate even with cyclohexenone[115b].

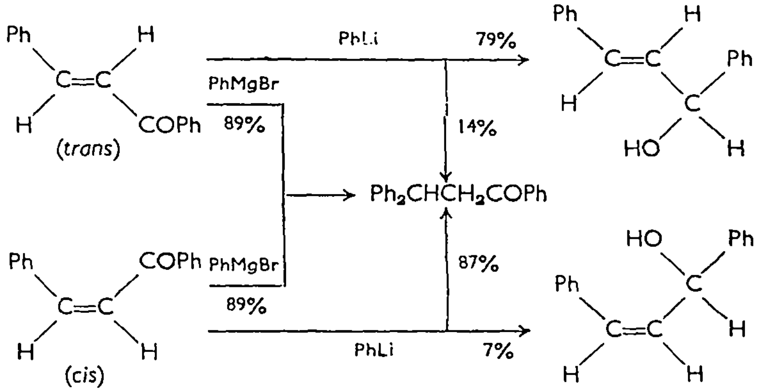
Regarding the influence of the structure of the reagent and substrate on the yields, it was observed that one relatively large substituent on the β-carbon hardly affects the reactivity of the system[132, 133, 134]. Facile reaction takes place in the presence of a β-mesityl group even with reagents of high steric demands, *e.g.* when the latter also contains a mesityl group[133]. On the other hand, a mesityl group on the carbonyl carbon atom generally inhibits the addition to the latter, in agreement with the widely observed steric sensitivity of carbonyl reactions. Accordingly, reactions may be directed to take the 1,4-addition route by using esters with a large alkyl group[135, 136], *e.g.* *s*-Bu. The percentage of α,β-adducts formed by 1,4-addition is similarly enhanced in sterically more hindered ketones (Table 5).

TABLE 5. Yields of α,β-adducts in Grignard reactions[137].

Carbonyl compound	PhMgBr	EtMgBr
$PhCH{=}CHCH{=}O$	0	0
$PhCH{=}CHCOCH_3$	12	60
$PhCH{=}CHCOC_2H_5$	40	71
$PhCH{=}CHCOCH(CH_3)_2$	88	100
$PhCH{=}CHCOC(CH_3)_3$	100	100
$PhCH{=}CHCOPh$	94	99
$Ph_2C{=}CHCOPh$	0	13
$PhCH{=}CPhCOPh$	100	100
$PhCMe{=}CHCOPh$	44	41

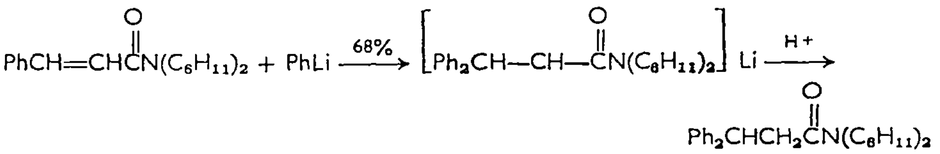
On the other hand, electronic effects in the substrate seem to be less important than steric ones in the determination of the carbonyl- and α,β-addition ratio, since the high reactivity of the reagent renders it rather undiscriminating. The factors affecting the carbonyl- and 1,4-addition ratio were discussed qualitatively[138, 139]. A single substituent either at C_α or at C_β enhances the ratio of α,β- *versus* carbonyl addition while disubstitution at C_β inhibits α,β-addition completely. Carbonyl addition takes place if both C_α and C_β are substituted. With aliphatic substrates, carbonyl addition, and with aryl-substituted substrates, α,β-addition is preferred as a rule, possibly owing to electronic effects.

The effect of the configuration of the double bond on the addition was studied in the chalcone system[128]. With either *cis*- or *trans*-chalcone, PhMgBr gives almost exclusively 1,4-addition (α,β-adduct), while in the addition of PhLi to the *trans*-chalcone, carbonyl addition, and to the *cis*-chalcone, again α,β-addition is dominant. Analogous results were obtained with α-phenylchalcones[127]. The main governing factor seems to be a steric one. Although both the carbonyl and the β-carbon are more reactive in the *trans* isomer, the benzoyl group is flanked by only one substituent, so that rapid carbonyl addition of PhLi will be easy. On the other hand, in the *cis* isomer the steric hindrance at the benzoyl group is pronounced, leading to 1,4-addition. In the α,β-diphenylchalcone, both reaction centers are strongly hindered, so that overall yields are low but carbonyl addition is pronounced[127].

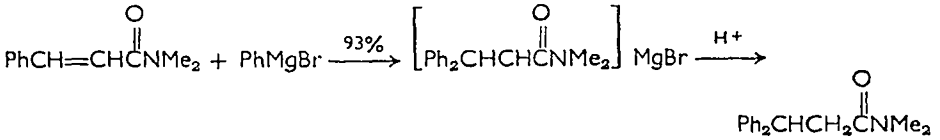


$$\mathrm{Ph_2C{=}CPhCOPh + PhLi \longrightarrow Ph_2C{=}CPhC(Ph)_2OH}$$

With α,β-unsaturated amides, 1,4-addition is preferred irrespective of the nature of the reagent used, with some exceptions involving carbonyl addition of MeMgI[140].



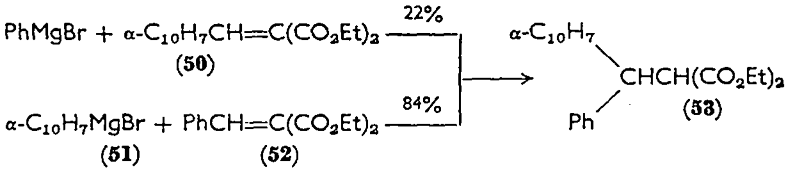
$$\mathrm{PhCH{=}CH\overset{O}{\overset{\|}{C}}N(C_6H_{11})_2 + PhLi \xrightarrow{68\%} \left[Ph_2CH{-}CH{-}\overset{O}{\overset{\|}{C}}N(C_6H_{11})_2\right] Li \xrightarrow{H+} Ph_2CHCH_2\overset{O}{\overset{\|}{C}}N(C_6H_{11})_2}$$



$$\mathrm{PhCH{=}CH\overset{O}{\overset{\|}{C}}NMe_2 + PhMgBr \xrightarrow{93\%} \left[Ph_2CHCH\overset{O}{\overset{\|}{C}}NMe_2\right] MgBr \xrightarrow{H+} Ph_2CHCH_2\overset{O}{\overset{\|}{C}}NMe_2}$$

The importance of steric effects in the reagent was studied with relatively unhindered substrates, such as crotonaldehyde or cinnamaldehyde. Here, the normal carbonyl addition of aldehydes is changed to 1,4-addition by the use of Grignard reagents of high steric demands (*t*-Bu, *t*-Am)[116,141]. The differences between the reactivities of alkylmagnesium chlorides, bromides and iodides may, at least in part, also be caused by steric effects[142]. The importance of steric hindrance is much larger in the double-bonded substrate than in the attacking agent[134]. Addition of PhMgBr to **50** gives only 22% yield, while the same product **53** is obtained in 84% yield from the reaction of **51** and **52**.

$$t\text{-BuMgCl} + \text{PhCH{=}CHCHO} \longrightarrow \text{PhCH}(t\text{-Bu})\text{CH}_2\text{CHO}$$

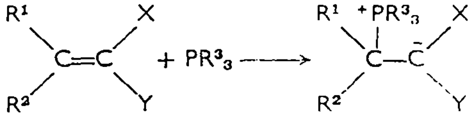


In the presence of a suitable leaving group, the addition is often accompanied by substitution. Thus, simultaneous reaction of phenyl- and naphthylmagnesium bromides with ethoxymethylene malonate (**54**) gives the product **55**[143].

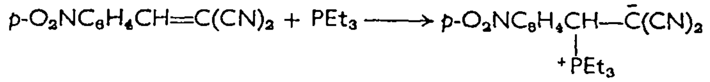
$$\underset{}{\text{PhMgBr}} + \alpha\text{-C}_{10}\text{H}_7\text{MgBr} + \underset{\textbf{(54)}}{\text{EtOCH{=}C(CO}_2\text{Et)}_2} \longrightarrow \underset{\textbf{(55)}}{\text{Ph}(\alpha\text{-C}_{10}\text{H}_7)\text{CHCH(CO}_2\text{Et)}_2} + \text{OEt}^-$$

E. Addition of Phosphines

The addition of tertiary phosphines to activated C=C bonds results in the formation of a zwitterionic product[144,145] which is analogous to the first intermediate in other nucleophilic attacks by neutral molecules, but is the end-product in this special case.



Electron-donating substituents at the *β*-position, especially in aromatic systems, inhibit the reaction and *vice versa*; no reaction takes place between *p*-dimethylaminobenzylidenemalononitrile and triethylphosphine, while the *p*-nitro derivative yields an especially stable product[144]. A *p*-hydroxy group inhibits the reaction completely, while the same group in the *m*-position yields adducts, although of



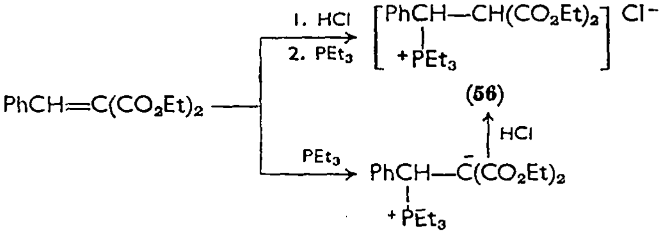
$$p\text{-}O_2NC_6H_4CH{=}C(CN)_2 + PEt_3 \longrightarrow p\text{-}O_2NC_6H_4\underset{\substack{|\\ {}^{+}PEt_3}}{CH}{-}\bar{C}(CN)_2$$

low stability, showing that the effect is largely a resonative one.

Triethylphosphine also adds to less activated systems, in which the α-position is disubstituted by two less efficient electron attracting groups, *e.g.* CO_2R[144]. With less extensively conjugated systems, such as acrolein, acrylonitrile or nitroolefins, in which the stabilization of the adducts is lower, nucleophilic polymerization takes place under the influence of phosphines[146].

$$PR_3 + CH_2{=}CHX \longrightarrow \overset{+}{P}R_3(CH_2CHX)_nCH_2\bar{C}HX \xrightarrow{HY} YPR_3(CH_2CHX)_nCH_2CH_2X$$
$$(X = CN,\ CO_2R,\ CHO,\ COMe)$$

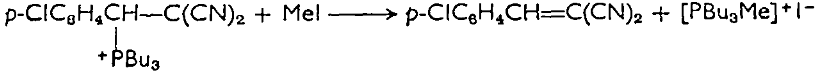
Phosphonium salts **56** may be obtained irrespectively of the order of the addition of the reagents, *i.e.* both by addition of HCl to the adduct **57** and by addition of HCl to the ester followed by addition of the phosphine[144,147]. Attempted alkylation of the zwitterions leads to



(56)

(57)

their decomposition giving the initial substrate and phosphonium halides[148]. The zwitterions derived from benzylidenemalononitriles



$$p\text{-}ClC_6H_4\underset{\substack{|\\ {}^{+}PBu_3}}{CH}{-}\bar{C}(CN)_2 + MeI \longrightarrow p\text{-}ClC_6H_4CH{=}C(CN)_2 + [PBu_3Me]^{+}I^{-}$$

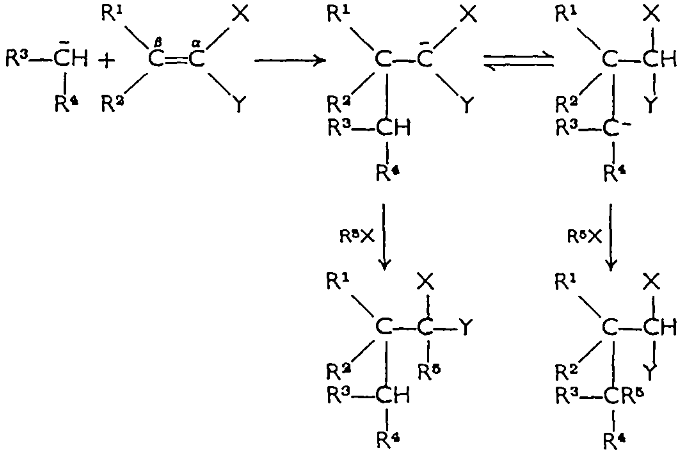
are insoluble in water[149], and their spectra in very dilute solutions in methanol, dioxane or benzene is similar to that of the starting materials[144,149]. Accordingly, an equilibrium may exist between the adduct and its components in the solution, and the adduct could be a π-complex and not a zwitterion. Adduct formation in methanol or dioxane is very fast even at room temperature. The equilibrium constants[149] calculated from the decrease of the alkene concentration show the larger stability of adducts formed from more reactive substrates (Table 6).

TABLE 6. Equilibrium constants $K = \frac{[\text{adduct}]}{[XC_6H_4CH{=}C(CN)_2][PBu_3]}$ in methanol at 44° [149].

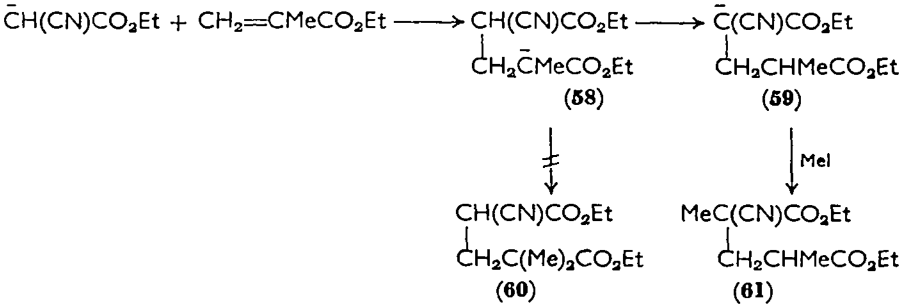
X	*p*-NO$_2$	*m*-NO$_2$	*o*-Cl	*p*-Cl	H	*p*-Me	*p*-MeO
K(l./mole)	6600	2940	2480	1600	1160	450	115

F. Rearrangement in the Intermediate Anion

The intermediate anion formed in the nucleophilic attack by carbanions may undergo rearrangement reactions, the driving force of which is the formation of a more stable anion. Prototropic rearrangement may take place in carbanions which contain an acid hydrogen atom on the carbon newly attached to C_β. Usually the rearrangement cannot be detected as the products obtained after protonation are identical, but, by further alkylation of the intermediates, two different products will be obtained. For instance, the ester **61** is obtained by methylation, instead of the normal product **60**, proving the rearrangement **58** → **59** in the example below[150].

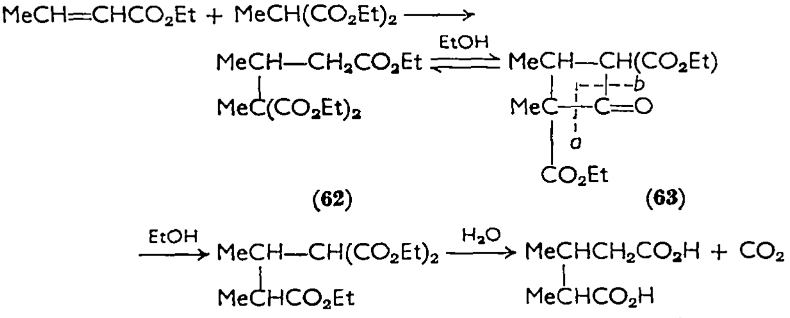


The 'abnormal' Michael reaction can take place in systems $R^1R^2C{=}CHX$, in which a hydrogen is attached to the α-carbon, but not with systems $R^1R^2C{=}CR^3X$[151]. Here, one of the substituent groups of the donor (other than hydrogen) appears attached to the α-carbon of the product as a result of rearrangement of the intermediate. The reaction of diethyl methylmalonate with ethyl crotonate gives the normal adduct **62** in the presence of $\frac{1}{6}$ mole of sodium ethoxide, but in the presence of one equivalent of the base, **64** is obtained[152], in which formally the methyl group is added to the first and the $CH(CO_2Et)_2$ group to a second carbon. It was believed[153] that this actually happens, but the generally accepted mechanism[154] supposes for all cases the formation of a normal primary addition product **62**, which may undergo intramolecular

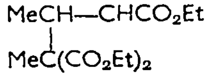


$$\begin{array}{lll}
\bar{C}H(CN)CO_2Et + CH_2{=}CMeCO_2Et \longrightarrow & \begin{array}{l} CH(CN)CO_2Et \\ | \\ CH_2\bar{C}MeCO_2Et \end{array} \longrightarrow & \begin{array}{l} \bar{C}(CN)CO_2Et \\ | \\ CH_2CHMeCO_2Et \end{array} \\
 & \quad (58) & \quad (59) \\
 & \quad \not\downarrow & \quad \downarrow \mathrm{MeI} \\
 & \begin{array}{l} CH(CN)CO_2Et \\ | \\ CH_2C(Me)_2CO_2Et \end{array} & \begin{array}{l} MeC(CN)CO_2Et \\ | \\ CH_2CHMeCO_2Et \end{array} \\
 & \quad (60) & \quad (61)
\end{array}$$

Dieckman reaction in the strongly basic medium, giving the cyclobutanone **63**. The latter is a β-keto ester, which undergoes facile alcoholysis in the strongly basic medium, either reverting to **62** by cleavage at *a*, or producing the 'abnormal' reaction product **64** by cleavage at *b*. The latter reaction is preferred, since the anion **67** is more stable that the anion **66**.

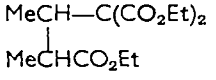


$$\begin{array}{lll}
MeCH{=}CHCO_2Et + MeCH(CO_2Et)_2 \longrightarrow & & \\
 & \begin{array}{l} MeCH{-}CH_2CO_2Et \\ | \\ MeC(CO_2Et)_2 \end{array} \overset{\mathrm{EtOH}}{\rightleftharpoons} & \begin{array}{l} MeCH{-}CH(CO_2Et) \\ |\qquad\quad | \;\; b \\ MeC{-}C{=}O \\ |\;\; a \\ CO_2Et \end{array} \\
 & \quad (62) & \quad (63) \\
\xrightarrow{\mathrm{EtOH}} & \begin{array}{l} MeCH{-}CH(CO_2Et)_2 \\ | \\ MeCHCO_2Et \end{array} \xrightarrow{H_2O} & \begin{array}{l} MeCHCH_2CO_2H + CO_2 \\ | \\ MeCHCO_2H \end{array} \\
 & \quad (64) & \quad (65)
\end{array}$$



$$\begin{array}{l} MeCH{-}\bar{C}HCO_2Et \\ | \\ MeC(CO_2Et)_2 \end{array}$$

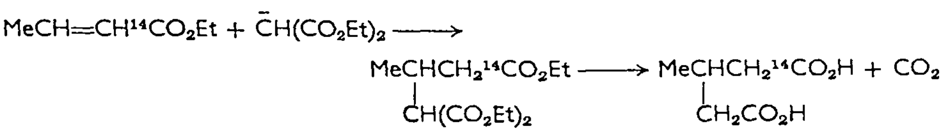
(66)



$$\begin{array}{l} MeCH{-}\bar{C}(CO_2Et)_2 \\ | \\ MeCHCO_2Et \end{array}$$

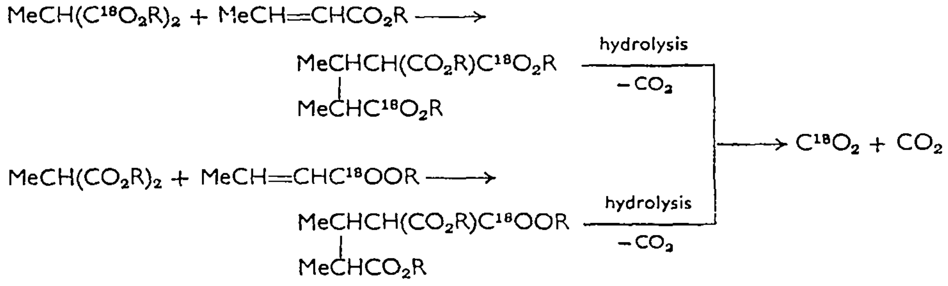
(67)

In the addition of malonic ester to ethyl crotonate, no such rearrangement takes place even under reaction conditions which promote the 'abnormal' route. In this case, the normal and 'abnormal' adducts are chemically identical, but, by isotopic labeling, it was shown that no migration of the carbethoxy group takes place[155], since no labeled carbon appears in the CO_2 liberated, and the only rearrangement this system does undergo is a prototropic one.



$$\mathrm{MeCH{=}CH^{14}CO_2Et + \bar{C}H(CO_2Et)_2 \longrightarrow \underset{CH(CO_2Et)_2}{MeCHCH_2{}^{14}CO_2Et} \longrightarrow \underset{CH_2CO_2H}{MeCHCH_2{}^{14}CO_2H} + CO_2}$$

The cyclobutanone mechanism was proved by isotopic labeling[156,157] to apply for 'abnormal' substitutions. Using carboxyl-carbon labeled crotonate in the reaction sequence **62** → **64** → **65** in conditions leading to the 'abnormal' product, 42% of the activity appeared in the carbon dioxide liberated from the reaction[156]. This definitely shows the migration of a carbethoxy group, since obviously one of the two carboxyl groups bound to the same carbon atom undergoes the decarboxylation. By labeling the oxygen in the crotonate in one set of experiments and in the malonate in another[158], and by hydrolysis and decarboxylation of the 'abnormal' ester, further proof was given for the migration of a carbethoxy group, and any mechanism involving methyl migration was eliminated.



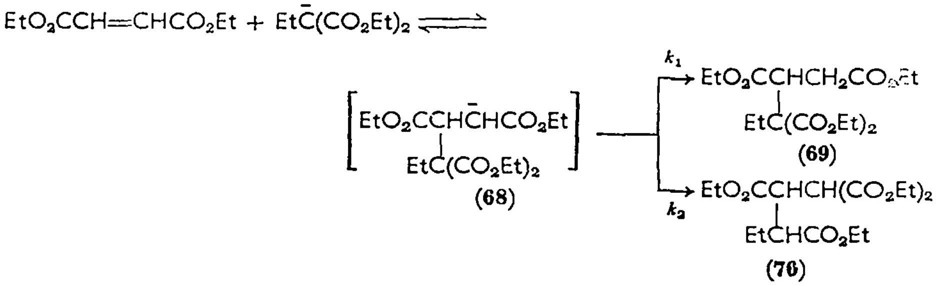
$$\mathrm{MeCH(C^{18}O_2R)_2 + MeCH{=}CHCO_2R \longrightarrow \underset{MeCHC^{18}O_2R}{MeCHCH(CO_2R)C^{18}O_2R} \xrightarrow[-CO_2]{hydrolysis} C^{18}O_2 + CO_2}$$

$$\mathrm{MeCH(CO_2R)_2 + MeCH{=}CHC^{18}OOR \longrightarrow \underset{MeCHCO_2R}{MeCHCH(CO_2R)C^{18}OOR} \xrightarrow[-CO_2]{hydrolysis} C^{18}O_2 + CO_2}$$

TABLE 7. Atom % excess ^{18}O in abnormal Michael condensation[158].

Reactants	^{18}O in labeled reactants	Found	Calc. for CO_2Et migration	Calc. for Me migration
$MeCH(C^{18}O_2Me)_2 + MeCH{=}CHCO_2Et$	1·68	0·52	0·42	1·68
$MeCH(CO_2Et)_2 + MeCH{=}CHC^{18}OOEt$	0·43	0·10	0·10	0·00
$MeCH(C^{18}O_2Me)_2 + PhCH{=}CHCO_2Et$	0·88	0·22	0·22	0·88

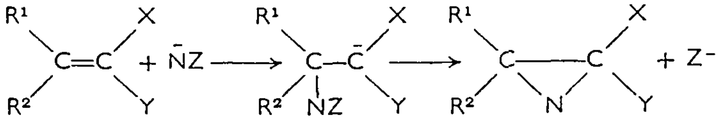
In the reaction of diethyl fumarate with diethyl ethylmalonate in benzene[159], again the first step is a fast formation of a carbanion **68**, which can be protonated to give the normal product **69** (k_1), or it can rearrange and give the 'abnormal' product **70** (k_2). The rate of formation of the normal product is proportional to the concentration of the anion **68** and also to the concentration of the free malonic ester, which is able to protonate the anion **68**. The relative amount of the normal product in the mixture is highest after short reaction times and becomes less with increasing reaction time, showing that it is an essential intermediate. A whole equivalent of base is required for the 'abnormal' reaction[160], since free malonic ester is able to block the abnormal route by protonation of **68**. Indeed, using two equivalents of the malonic ester with one of sodium ethoxide, only the normal product is obtained.



The cyclobutanone mechanism was criticized on the basis of the high strain in the intermediate[159], but it should be noted that even more highly strained compounds, such as cyclopropanes, are obtained as stable products from carbanionic intermediates in the Michael reaction. In another proposal, the formation of the anions of hemiacetals takes the place of the cyclobutanone intermediate[161]. It was noted that usually the normal product is transformed to the 'abnormal' one in lower yields than obtainable from the direct reaction of the starting materials[162]. The possibility of the presence of *para*-bridged intermediates was also discussed[10b, 163].

III. RING FORMATION BY NUCLEOPHILIC ATTACK

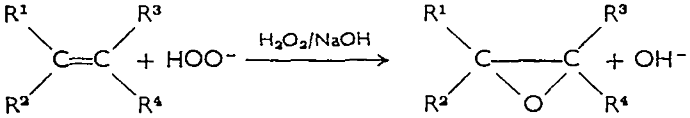
When the nucleophilic reagent contains a suitable leaving group, *i.e.* a stable anion or a neutral molecule attached to the attacking nucleophilic atom, the formation of the primary carbanion may be followed by an intramolecular nucleophilic substitution with the formation of a cyclic compound.



The most frequent example is the alkaline epoxidation with a hydroxide ion as the leaving group. Halogenated carbanionic nucleophiles may give cycloalkanes, halide ions leaving in the cyclization step. Nitrogen-containing nucleophiles, even when containing suitable leaving groups, do not as a rule produce cyclic compounds (aziridines) by direct reaction. However, the formation of such compounds in reactions of amines with bromoketones, or in amine/halogen/ketone systems, has already been discussed in section II.C.

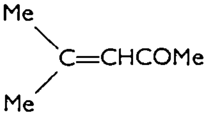
A. Alkaline Epoxidation

Epoxides (oxiranes) are formed with alkaline hydrogen peroxide when the attacking nucleophile is the hydroperoxide ion and the leaving group is a hydroxide ion:

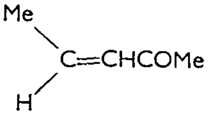


The reaction was first studied with α,β-unsaturated ketones[164] and extended later to other systems. Under carefully controlled conditions, epoxides may be obtained even in cases when the starting materials (acrolein, crotonaldehyde)[165,166] or the products are sensitive towards oxidation by the reagent.

The only kinetic study relating to the alkaline epoxidation reaction proved unequivocally that it involves a nucleophilic attack on the alkene double bond[167]. The reaction of H_2O_2 with mesityl oxide (**71**) or with ethylidene acetone (**72**) is first order both with respect to



(**71**)

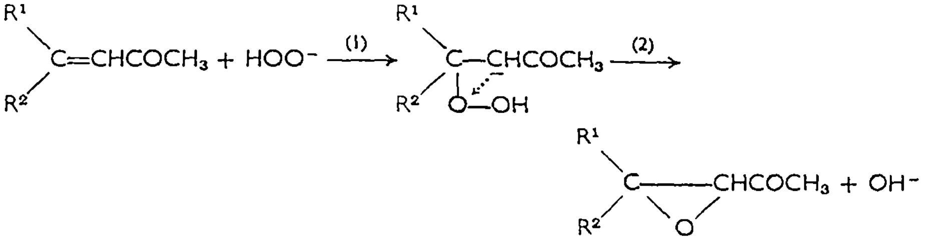


(**72**)

the unsaturated compound and the hydroperoxide ion, the concentration of which is calculated from the equilibrium:

$$OH^- + H_2O_2 \rightleftharpoons HOO^- + H_2O$$

The following reaction mechanism was proposed:

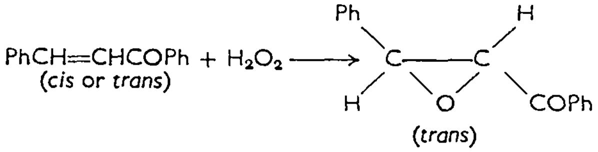


On the basis of the kinetic results alone, it cannot be decided whether steps (1) and (2) take place consecutively or with simultaneous formation of the C—O and breaking of the O—OH bond. The differences in the rates with **71** and **72** emphasize the nucleophilic character of the reaction. The second methyl group at the β-carbon atom lowers the rate by a factor of 5·6 owing mainly to its deactivating ($+I$) effect.

If the intermediate carbanion is sufficiently long-lived to permit rotation, no correlation can be expected between the stereochemistry of the epoxidation product and that of the starting material, and the thermodynamically more stable product should be obtained in a stereoselective reaction[168]. Moreover, both isomerization and epimerization may complicate or invalidate conclusions drawn from stereochemical studies in these systems in general[169].

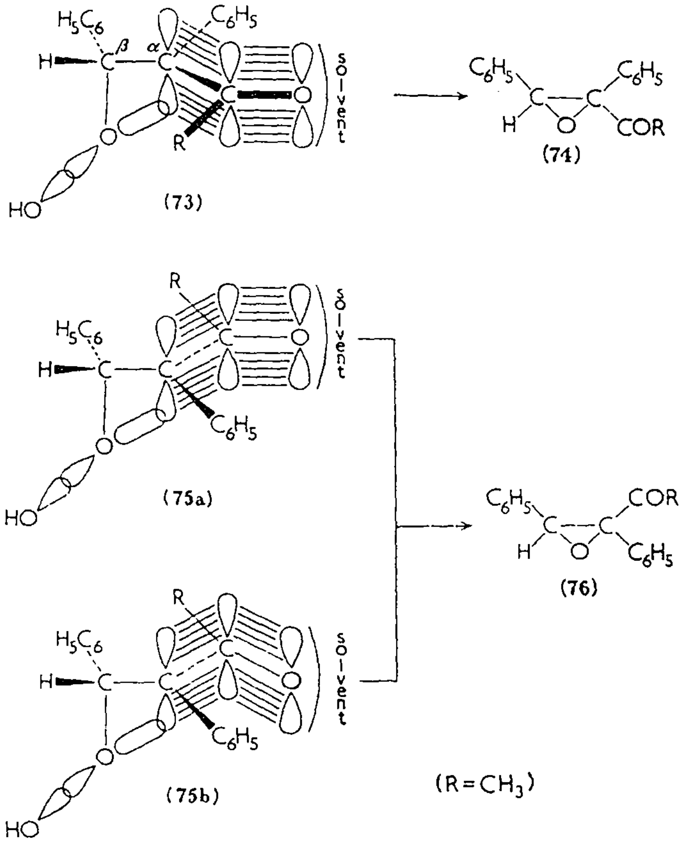
Base-catalyzed isomerization (by OH^- or OOH^-) of either the starting material or of the product may take place even if the formation of the latter is kinetically controlled and the epoxidation as such is stereospecific. The *cis–trans* isomerization and epoxidation of 3-methyl-3-penten-2-one (MeCH=CMeCOMe) were studied in comparable conditions[169]. In a reaction period, sufficient for the complete epoxidation, the initial *cis–trans* isomer ratio of 3·46 changed only to 2·65, and when starting with the pure *trans* isomer, no isomerization took place at all. These results do not give the complete picture, since they were obtained in the absence of hydroperoxide anions, which are much more nucleophilic towards unsaturated systems[170] than hydroxide ions. In the presence of the former, after 90% epoxidation the *cis–trans* ratio in the residual unreacted ketone was only 1·9 against 99 in the starting material. On the other hand, in conditions in which both *cis*- and *trans*-chalcone undergo epoxidation, no isomerization of the *cis* isomer takes place[128].

Base-catalyzed epimerization of the product may take place during epoxidations[171,172] and, therefore, later steoreochemical studies dealt with model systems not containing α-hydrogen atoms[168,169]. The epoxidation is nearly stereoselective[168] and, in most cases studied, both *cis* and *trans* isomers yield the same more stable *trans* epoxide, irrespectively of the configuration of the starting material[168,169,171–8]. For example, both *cis*- and *trans*-chalcone give the *trans* epoxide[173].

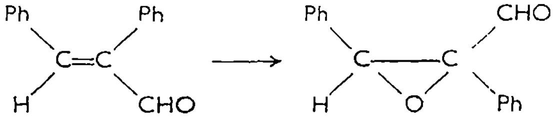


However, the epoxidation of α-phenyl-*trans*-chalcone gives the epoxide in which the two phenyl groups are in the *cis* position[171], although the spatial requirement of a phenyl group is somewhat higher than that of a benzoyl group. This was explained by Zimmerman[168], who assumed that it was not the van der Waals repulsion, but rather the overlap control in the transition state of the epoxidation which determines the configuration. The importance of this factor is shown by the very high difference (28 kcal/mole) between the free energy of the ionization of acetone (producing an anion in which overlap is possible) and that of methane. The van der Waals *cis* effect between two phenyl groups on adjacent carbons may be responsible only for a maximum value of 5·7 kcal/mole[179]. In the case of α-phenylbenzylideneacetone, the epoxide with the phenyl groups in the *cis* position (**74**) is formed through the transition state **73**. Maximum delocalization of the charge is possible in this transition state (**73**) with maximum overlap of orbitals in the conformation in which the acyl group is coplanar with C_β and the phenyl carbon bound to it. The steric interaction between the two phenyl groups in **73** can be minimized by assumption of the least hindered conformations about the C—Ph bonds.

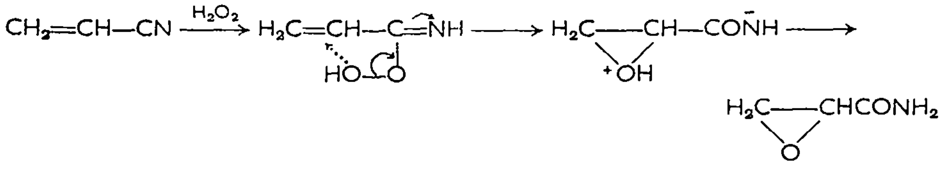
In the second possible transition state, two mutually incompatible situations may exist. The transition state depicted as **75a** allows maximum overlap, but van der Waals repulsions are very strong. On the other hand, if depicted as **75b**, the transition state is sterically unhindered, but at the same time overlap is minimized, since the acetyl group cannot assist in the charge distribution, and the energy will be raised considerably. Hence, **73** is much preferred, and it was concluded[168] that epoxidation is much more inhibited by *cis* interaction between a phenyl and an acetyl group than by interaction between two phenyl groups. Accordingly, the preferred product of the reaction will be the one with a less hindered acyl group, i.e. **74** and not **76**.



When the steric requirements of the activating group are smaller, with the formyl group, the factor governing the stereochemistry of the reaction will again be the steric interaction between the two much larger groups. Thus a 'normal' product with the two phenyl groups in the *trans* position is obtained in the epoxidation of α-phenyl-*trans*-cinnamaldehyde.



Similarly, alkaline epoxidation of α-phenyl-*cis*-cinnamonitrile, in which the linear nitrile group is always able to overlap, yields the epoxide with two phenyl groups in the *trans* position[168], isolated as the corresponding amide. However, α-phenyl-*trans*-cinnamonitrile (with two *cis* phenyl groups) gives as the major product the epoxide of α-phenyl-*trans*-cinnamamide[180], with retention of the *cis* position of the two phenyl groups; the second isomer is then the minor product. An intramolecular epoxidation mechanism[180,181] as shown below for acrylonitrile[181] accounts for the transformation of the cyano into an amido group, and, in the case of α-phenylcinnamonitriles,

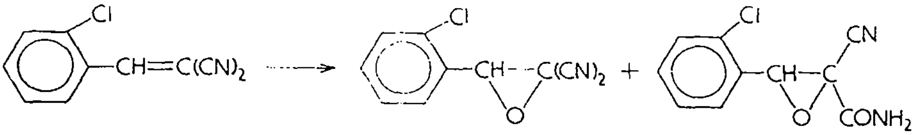


also for the retention of the configuration of the starting materials. The relative amount of the two isomeric products obtained from α-phenyl-*trans*-cinnamonitrile may be determined by the extent of base-catalyzed isomerization of the starting material *prior* to reaction with H_2O_2, each of the isomers retaining its configuration in the epoxidation process. This mechanism may be important only with nitriles, where the corresponding peroxycarboximidic acid intermediate may be formed, while carbonyl groups of α,β-unsaturated ketones are not attacked during epoxidation[167].

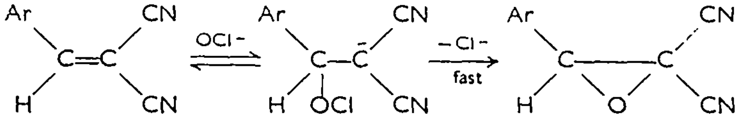
The consideration of overlap control also requires that the more nearly planar isomer allowing better conjugation should give the faster reaction, since it has the more electrophilic β-carbon. *trans*-Chalcones are usually several times more reactive than the *cis* isomers[128,173] and the latter become completely unreactive if their α-hydrogen is substituted by a phenyl[171] or an ethyl[176] group. In these cases, inductive $(+I)$ as well as steric effects operate, accounting for the low yield (25%) obtained, *e.g.* in the epoxidation of diethyl isopropylidenemalonate [$Me_2C{=}C(CO_2Et)_2$], as compared to the high yield (82%) obtained with diethyl ethylidenemalonate [$MeCH{=}C(CO_2Et)_2$][182].

t-Butylhydroperoxide (Me_3COOH) with the *t*-butoxy anion as the leaving group may be used advantageously for epoxidation in non-hydroxylic solvents[183]. Benzalacetophenone, methyl vinyl ketone or mesityl oxide in benzene give good yields of epoxides with this reagent. In some cases, the combined use of aprotic solvents and mild catalysts may lead to better yields and diminished side-reactions[180,184a].

Sodium hypochlorite (NaOCl), used only rarely before[184b], found more use recently for epoxidation of unsaturated aldehydes[184c], ketones[184d] and a nitrile[184e]. The reagent is less hazardous than peroxide, and quantitative yields can be obtained rapidly, *e.g.* with benzylideneacetophenone in pyridine[184d]. Epoxidation of *o*-chlorobenzylidene malononitrile with an excess of hypochlorite gave a mixture of the epoxydinitrile and of the epoxyamidonitrile:



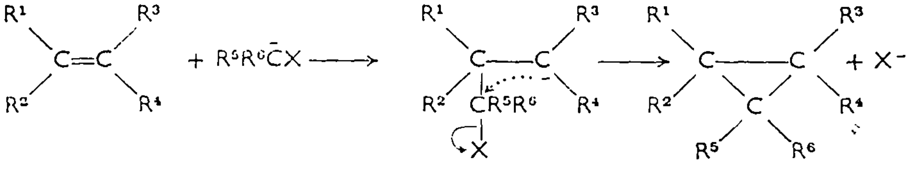
Using an equimolar amount of the reagent, no epoxyamidonitrile was obtained, eliminating the possibility of an intramolecular epoxidation mechanism *via* attack on the nitrile group[180,181]. As the rates are dependent upon both the HOCl and on the OH^- concentrations, a mechanism analogous to the one discussed above was postulated:



The hydroperoxide ion was shown to be about 20 times more reactive than the hypochlorite ion[184e]. However, as HOCl is much more acidic ($K_a = 4 \times 10^{-8}$) than H_2O_2 ($K_a = 2{\cdot}24 \times 10^{-12}$), it can be assumed that, at pH lower than 10, epoxidation by HOCl will be dominant. The rates of attack on the double bond are very high both with hydroperoxide ($k_2 = 4 \times 10^5$ l./mole sec) and with the hypochlorite anion ($k_2 = 2{\cdot}20 \times 10^4$ l./mole sec). In a similar reaction system with mesityl oxide as the substrate, the halohydrin was obtained at pH ~ 4·5–10, probably through intramolecular transfer of the chlorine to the carbanionic center in the intermediate[184f].

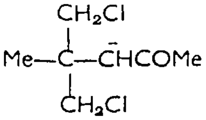
B. Cyclopropane Formation

Nucleophilic attack on a double bond by a carbanionic reagent containing a suitable leaving group usually leads to the formation of cyclopropanes. While no kinetic work has been carried out on this reaction, it can be assumed that primary attack by a carbanion (formed in the basic medium) on the β-carbon atom is followed by cyclization through an internal S_N2 reaction with the simultaneous elimination of the anionic leaving group.



A mechanism involving attack by a carbene intermediate would be equally reasonable, since the tendency of carbenes to react with double bonds to form cyclopropanes is well known. The following facts are relevant to this problem. Diethyl bromomalonate forms cyclopropanes with activated electrophilic double bonds, but not with styrene or with cyclohexene[185], although the latter reactions should be equally feasible by a carbenic mechanism. Moreover, *t*-butyl α-chloroacetate does not react in the presence of the n-butoxide anion[186] which is known to catalyze carbene reactions, but the same compound does react with double bonds in the presence of potassium *t*-butoxide to form cyclopropanes[187]. Lastly, the same carbanionic intermediate may also be formed by base-catalyzed elimination of a proton γ to a halogen atom. By this route, diethyl α-bromoglutarate gives, through the carbanion $EtO_2\bar{C}CHCH_2CHBrCO_2Et$, 1,2-dicarbethoxycyclopropane by internal cyclization[188].

It is questionable in the proposed carbanionic mechanism whether an internal S_N2 attack on a tertiary carbon atom is a practical route, taking into consideration the very low reaction rates obtained in S_N2 reactions with neopentyl halides[189]. Inspection of models of the anion **77** shows that, at least in this special case, the carbanionoid carbon atom is in a preferred position for the formation of a three-membered ring **78** by only relatively small distortion of the bonds[190].



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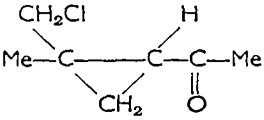
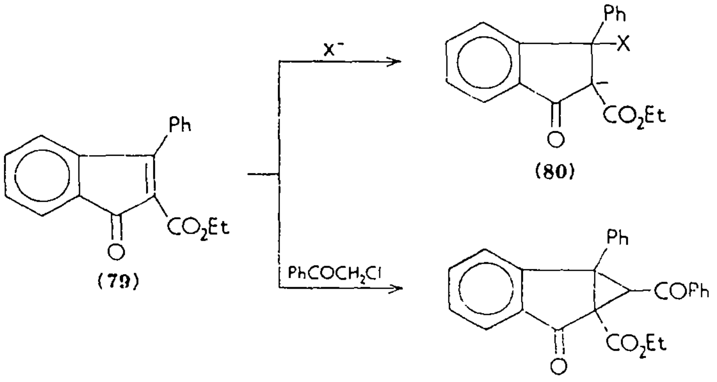


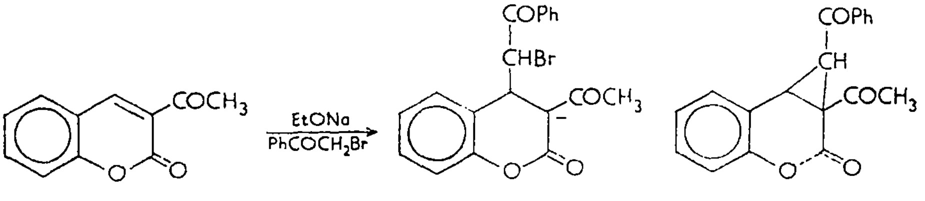
(78)

Preference for intramolecular alkylation is shown also by 2-carbethoxy-3-phenylindenone (**79**) which easily adds anions to form carbanions such as **80**[191] but the latter does not undergo alkylation by alkyl halides, since the charge-bearing atom is flanked by large groups. Similar sterically determined unreactivity is found with branched alkylated malonoesters in further alkylation attempts[192]. On the other hand, with phenacyl chloride in the presence of KOH in *t*-butanol **79** gives by intramolecular alkylation in the intermediate, the corresponding cyclopropane **81**[193]. Similarly, the reaction of

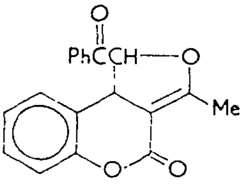


(79) (80) (81)

3-acetylcoumarine with phenacyl bromide[194] leads to the formation of **83** and even though the carbanion **82** may conceivably react also in its enolate form, actually no dihydrofuran derivative **84** is formed[195].

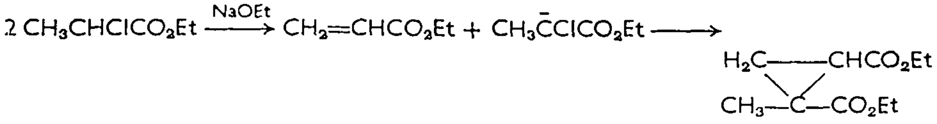


(82) **(83)**



(84)

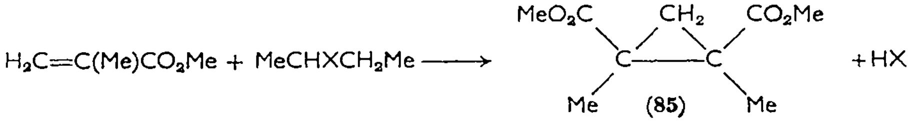
The general scope, synthetic applications and stereochemistry of the cyclopropane formation were studied only recently. The first compound prepared by this route and identified as a cyclopropane was obtained from ethyl α-chloropropionate[196]. In this case, one molecule of the ester yields ethyl acrylate by elimination of HCl and is attacked by a carbanion formed from a second molecule. As a



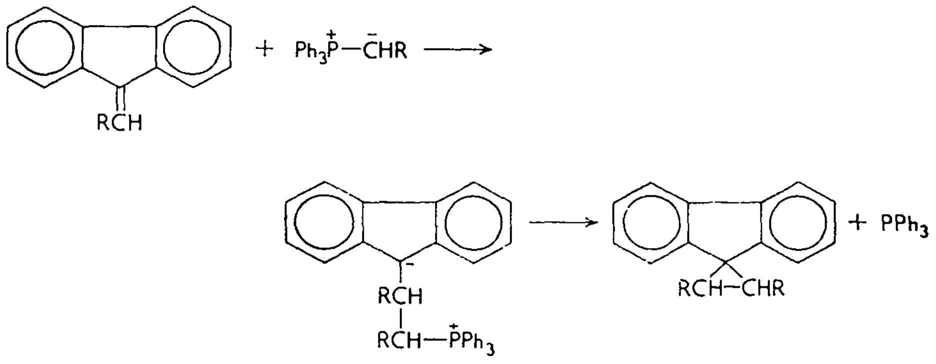
proof of this mechanism, much higher yields of the product were obtained from an equimolecular mixture of the acrylate and the chloropropionate under the same conditions[196]. Products obtained in the addition of diethyl halomalonates to acrolein, assumed originally to be linear adducts[197], were shown in later work to be cyclopropane derivatives[198]. The reaction was also extended to unsaturated aldehydes, ketones[198,199], esters[200,201,202] and nitriles[185,203].

Yields in the reaction are relatively unsensitive towards temperature differences[204] but are influenced strongly by the nature of the catalyst and the carbanion used. Strong carbon acids, such as diethyl bromomalonate, react well in the presence of catalysts, such as EtONa in ethanol. Very reactive acceptors, *e.g.* benzylidenemalononitriles, react with ethyl bromomalonate even in the presence of piperidine[205]. With weaker carbon acids, stronger catalysts such as Me_3COK or sodium amide are required, and the amount of side-products rises considerably[199]. With the same catalyst, the nature of the solvent may also be important; Me_3COK was found to give better yields in toluene than in *t*-butanol[206].

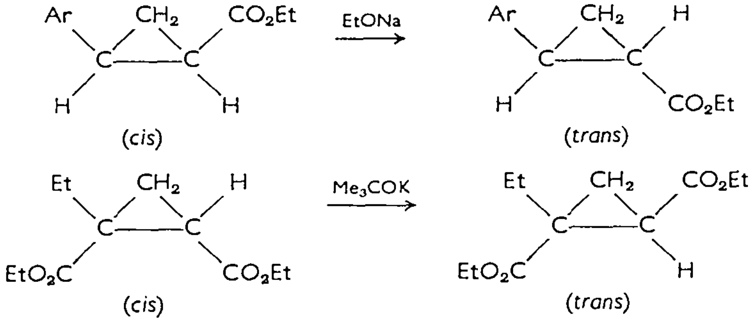
The nature of the anionic leaving group is also of consequence. With methyl methacrylate, the 2-chloro-, 2-bromo- and 2-iodomethyl propionates give 69, 32 and 14% yields, respectively, of the cyclopropane **85** and similarly with the same acceptor, chloropropionitrile gives 61% yield of the corresponding cyclopropane as against 33% with the bromo derivative[204]. Tosyl derivatives give low yields[206]. The lower yields obtained with nitriles compared to those obtained with esters are probably due to side-reactions shown by excessive tar formation. Competitive Claisen condensation of the starting material can be reduced by the use of sterically strongly hindered esters, *e.g.* *t*-Bu, which indeed give regularly higher yields of cyclopropanes than methyl or ethyl esters[207a]. The triphenylphosphine



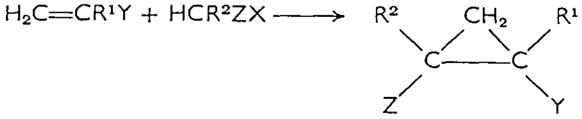
group may also serve as a leaving group, following attack of Wittig reagents $Ph_3\overset{+}{P}—\overset{-}{C}HR$ on polarized C=C bonds. Several cyclopropanes and also spirocyclopropane derivatives of fluorene have been obtained by this route in fair yields[207b].



The stereochemistry of the formation of fully substituted cyclopropanes has not yet been investigated. When α-hydrogen atoms are present in the product, these are generally sufficiently acidic to permit epimerization in the strongly alkaline reaction medium. The configuration of the product, therefore, is not necessarily determined in the cyclization step. For example, ethyl *cis*-2-arylcyclopropanecarboxylates isomerize to the more stable *trans* esters in the presence of sodium ethoxide in ethanol[208], and *cis* diesters are converted to the *trans* isomers by refluxing with Me_3COK[200,202].

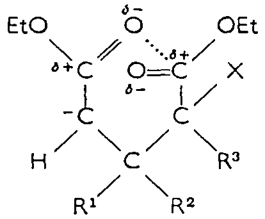


The activating groups Z of the donor and Y of the acceptor usually occupy the *cis* position in the primary product[200,202]. Whenever this is the major product, it is probably formed preferentially in the primary step, since subsequent epimerization can only lower its amount. The amount of *cis* product diminishes with growing size of the halogen in the donor[204] and becomes very small when the leaving group is the large tosylate ion[206].



The *cis–trans* ratio is also diminished when a nitrile is used as the acceptor instead of the corresponding ester[203], when the reaction temperature is raised[204], or when stronger bases are used as the catalysts. The last two effects are probably caused by epimerization of the product. Comparison of results is difficult because some reactions were carried out in heterogeneous systems, with considerable differences in the solubilities of the catalysts in the medium.

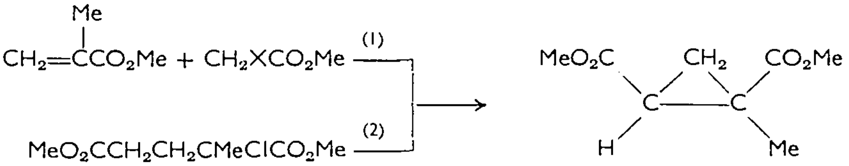
In a series of reactions, the α-positions of both donor and acceptor were substituted by alkyl groups and, therefore, no epimerization of the product was possible[204]. The *cis* product was found to be predominant throughout, although the *trans* product is more stable and, moreover, the carbanionic intermediate is probably long-lived enough to permit isomerization. This was explained by an 'attraction–interaction' due to the close proximity of the two activating groups in the carbanionic intermediate in a conformation which may permit the distribution of the negative charge on both. This conformer can yield the *cis* isomer of the product by small and almost unhindered rotation in the course of the displacement of the leaving group, while the rotation necessary for the formation of the *trans* isomer is considerably more hindered[209,210]. The nature of the interaction of the two electron-attracting groups in the carbanion



was elegantly identified as a mode of internal solvation[210], and can be schematically represented as a quasi six-membered ring. Such structures should be much less important with nitriles, owing to the linear structure of this group. Indeed, it was found that, under otherwise similar conditions, nitriles gave much larger relative amounts of the *trans* products than the corresponding esters[204, 210].

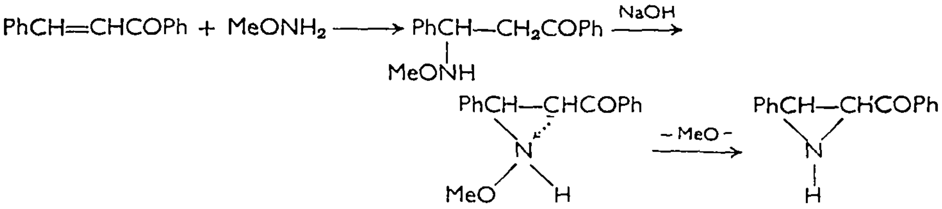
This effect is most important in solvents of low dielectric constants and becomes insignificant when solvation by the medium takes its place in more polar solvents. In the latter case, the transition states leading to the *cis* and *trans* isomers are similar and, therefore, the product ratio is determined by the thermodynamic stabilities of the two products. Accordingly, in the formation of various cyclopropanes, the *cis* product is predominant in pure benzene or toluene, and the *trans* in a 50/50% mixture of benzene with hexamethyl phosphoramide. The product ratio varies with the variation of the polarity of the solvent mixtures[210] giving, for example, 37, 50 and 64% of the *trans* isomer of dimethyl 1,2-dimethylcyclopropane-1,2-dicarboxylate in benzene–hexamethyl phosphoramide mixtures, containing 10, 20 and 40% of the latter respectively. This is an example of a stereoselective reaction which can be directed to either the *cis* or the *trans* route by choosing the appropriate solvent.

The stereoselectivity determined by the competition of normal and inner solvation is observed irrespectively of the path by which the carbanion is obtained. For example, dimethyl 1-methylcyclopropane-1,2-dicarboxylate may be prepared by route (1) or (2), and in both cases the *cis* product is preferred in benzene while the *trans* product is formed almost exclusively in mixtures of equal amounts of benzene and hexamethyl phosphoramide[210].

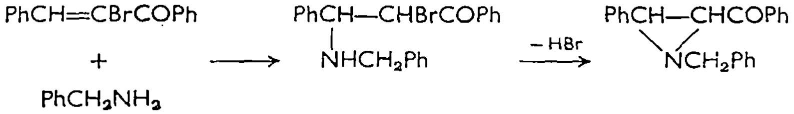


C. Formation of Nitrogen-containing Rings

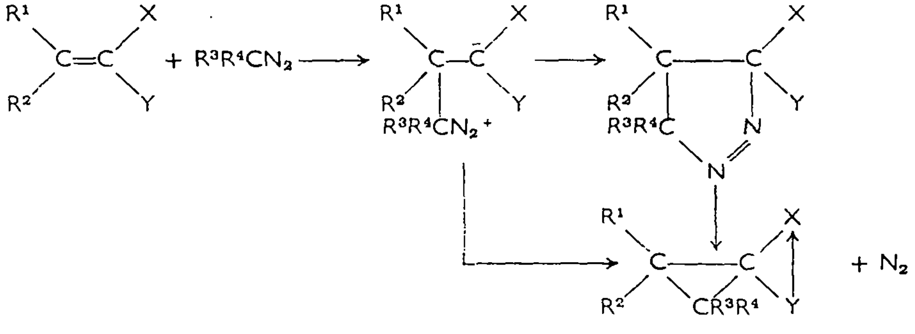
Aziridine formation should be possible with nucleophiles in which a suitable leaving group (OH, N_2, NO_2) is bound to a nitrogen atom. Actually, normal addition products are generally obtained in the reaction of hydroxylamine[211,212,213], hydrazoic acid[214] or nitramine[215] with various unsaturated compounds. The formation of aziridines, *e.g.* in the reaction of phenyl azide with styrene[216] or of carbamic acid azide with diethyl fumarate[217], is probably due either to secondary reactions of the primary product or to concerted cycloadditions. The base-catalyzed formation of an aziridine from the product of addition of methoxylamine to chalcone[42,45b] probably takes place analogously to epoxidation, with MeO as the leaving group[45c].



Aziridines may be obtained by the nucleophilic attack of primary or secondary amines on unsaturated compounds containing an α-halogen atom. Here the primary addition product contains a halogen atom and a labile nitrogen-bound hydrogen, the product being formed by γ-elimination of HX[218]. The formation of five-membered rings containing two nitrogen atoms is a more general reaction. Diazo compounds such as diazomethane or diazoacetic ester, on addition to activated double bonds, give pyrazolines[219]. The latter decompose easily on heating to yield cyclopropanes and, in many cases, cannot be isolated[220].

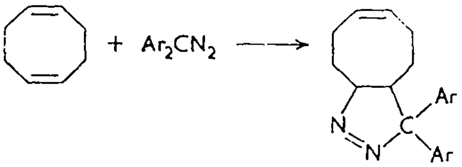


In the addition a zwitterionic intermediate is formed, with a positively charged nitrogen in the vicinity of a negative carbon atom, so that the formation of a five-membered ring will be facilitated. On the other hand, especially at high temperature, elimination of N_2 will be favored yielding a cyclopropane derivative:



The ambident nature[221] of the attacking diazo compound determined by its contributing resonance forms $R^3R^4\overset{-}{C}{-}\overset{+}{N}{\equiv}N$ and $R^3R^4C{=}\overset{+}{N}{=}\overset{-}{N}$

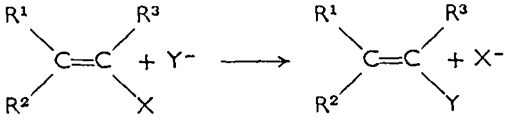
complicates the assignment of an exact reaction mechanism. In some cases, products were isolated which corresponded to a nucleophilic attack with carbon as the nucleophilic center[222] and in other cases to an attack with nitrogen as the nucleophilic center[223]. The high reactivity of α,β-activated compounds confirms the nucleophilic nature of the reaction, and the fact that both ethyl maleate and fumarate give the same product with diphenyldiazomethane[224] shows that this reaction at least occurs in two stages. On the other hand, pyrazolines are formed even from systems which are not normally subject to nucleophilic attacks as, for example, with acenaphthylene[225] or 1,5-cyclooctadiene[226]. In these and in similar cases, the reaction is probably a concerted 1,3-cycloaddition[227].



IV. VINYLIC SUBSTITUTION

The generally accepted thumb rule that vinylic substitutions are more difficult to carry out than substitutions in saturated systems is true only when comparing simple systems[228]. Actually, many substitutions in activated unsaturated systems are rather facile. Examples are the 'ketovinylation' with β-chlorovinyl ketones, which found wide synthetic application[229,230,231,232], and tricyanovinylation with tetracyanoethylene[233,234] or tricyanovinyl chloride[63]. Several alkoxymethylene derivatives of malononitrile, ethyl cyanoacetate and similar compounds are also used in syntheses[235].

Diverse routes may lead to the exchange of a group bound to a vinylic carbon atom by a second, usually anionoid, group. Among

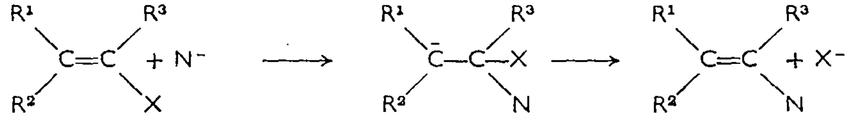


these, only the addition–elimination mechanism belongs directly to the nucelophilic attacks discussed in this chapter, but its interpretation is closely interwoven with other routes and these, consequently, will have to be discussed briefly.

The close similarity between nucleophilic vinylic and nucleophilic aromatic substitutions[236] gives added importance to the study of the former. The formation of *cis–trans* isomers in vinylic systems gives information on the transition state of the reaction, which is not available in aromatic systems.

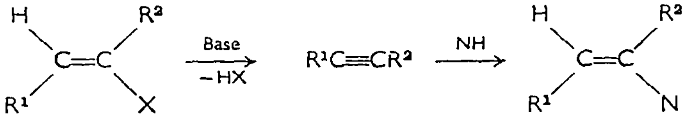
The five reaction mechanisms proposed for vinylic substitutions are (1) the addition–elimination mechanism, (2) the elimination–addition mechanism, (3) substitutions with primary rearrangements of the substrate, (4) substitution involving a vinyl carbanion, and (5) S_N1-type vinylic substitution. The most important routes are (1), (2) and (3), while (4) and (5) are observed only in special cases.

In the addition–elimination mechanism, the first step is a nucleophilic attack on an unsaturated carbon atom. The intermediate carbanion formed in this step eliminates an anion with regeneration of the double bond. As we will see, this overall addition–elimination process may take one of several closely related pathways.



Addition–elimination (1)

In the second (elimination–addition) mechanism, the primary step is an attack on a vinylic hydrogen atom. The elimination of the latter is accompanied by the elimination of an anionic leaving group (usually a halide ion) from the neighboring carbon atom with the formation of an acetylenic intermediate. This in turn adds the nucleophile and a proton to give the product of overall substitution.



Elimination–addition (2)

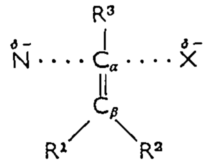
The prerequisite for reaction by route (1) is a reagent with a high carbon nucleophilicity. If this is at the same time also a reagent of high proton basicity, then, with hydrogen-containing substrates, mechanism (2) will intrude and compete with (1). On the other hand, the second mechanism is favored by nucleophiles of high proton basicity, with carbon basicity having only secondary importance in this case. The relative importance of routes (1) and (2) can be distinguished by isotope studies; deuterium exchange will take place if the primary step involves a proton elimination but not if the mechanism involves attack on carbon only (unless the exchange is possible through an independent equilibration route).

In the elimination–addition mechanism there will obviously be no relation between the configuration of the starting material and that of the product[12], since both *cis* and *trans* isomers give the same acetylenic intermediate, and the product configuration will be determined by the stereochemistry of the product-forming addition. On the other hand, in the addition–elimination mechanism, the product configuration will be mainly determined by the path of the attack and by the configuration and the lifetime of the carbanionic intermediate. With long-lived intermediates, as a rule, the product ratio will be determined by the relative stability of the two isomers. With very short-lived intermediate carbanions, the structure of the product is expected to be related to the structure of the starting material, as will be shown in detail.

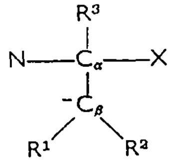
It has been pointed out[237] that the relative inertness of simple vinyl halides is caused by the resonance contribution of structures in which the carbon–halogen bond has a partial double bond character. The primary attack in vinylic substitution, therefore, takes place on a

$$\mathrm{CR^1R^2{=}CR^3{-}\ddot{X}} \longleftrightarrow \mathrm{\bar{C}R^1R^2{-}CR^3{=}\overset{+}{X}}$$

carbon atom which is much less electrophilic than the carbon attacked in alkyl halides. Two alternatives were proposed by Gold[238] for the structure of the addition–elimination intermediate. The first (**86**) is analogous to that in aliphatic S_N2 reactions with an *sp* hybridization for the collinear R^3—C_α—C_β σ-bonds where one of the *p* electrons is involved in the weak binding of the entering and the leaving groups, while the other participates in the formation of the π-bond between C_α and C_β. In the second structure (**87**), C_α is tetrahedral; the β-carbon has an sp^3 hybridization and the C_α—C_β bond has a single-bond character. At the time of the formulation of these proposals, no suitable example was known which could be used for deciding between



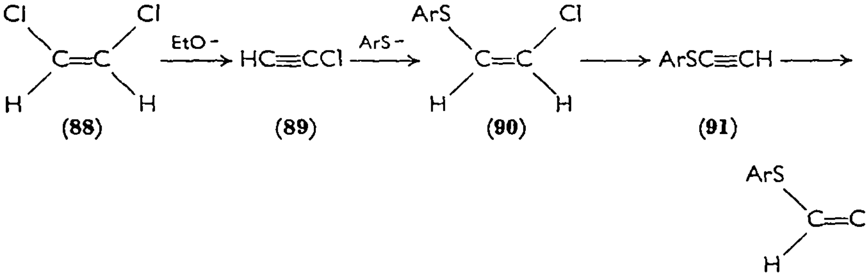
(**86**)



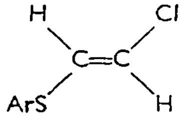
(**87**)

the alternatives and only later studies, discussed below in detail, excluded the S_N2-type mechanism.

The close relationships between the addition–elimination and the elimination–addition mechanisms, as well as their stereochemical differences, were investigated by Truce and his collaborators[239–245], who used simple polyhaloalkenes as the substrates and the *p*-toluenethiolate anion as the nucleophile. *trans*-Dichloroethylene does not react at all, while the *cis* isomer **88** yields *cis*-1,2-ditolylthioethylene (**92**) in which the configuration of the starting material is retained[239]. The inertness of the *trans* isomer is strongly indicative of an elimination–addition mechanism, since considerable differences between the reactivities of the two isomers can hardly be assumed in the addition–elimination mechanism. Moreover, the reaction gives the final product (**92**) almost quantitatively, while the compound **93**, which



(88) (89) (90) (91) (92)

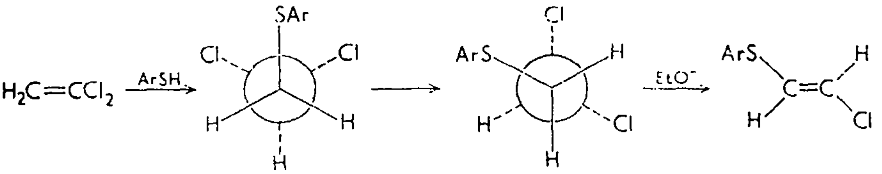


(93)

(Ar = p-$CH_3C_6H_4$—)

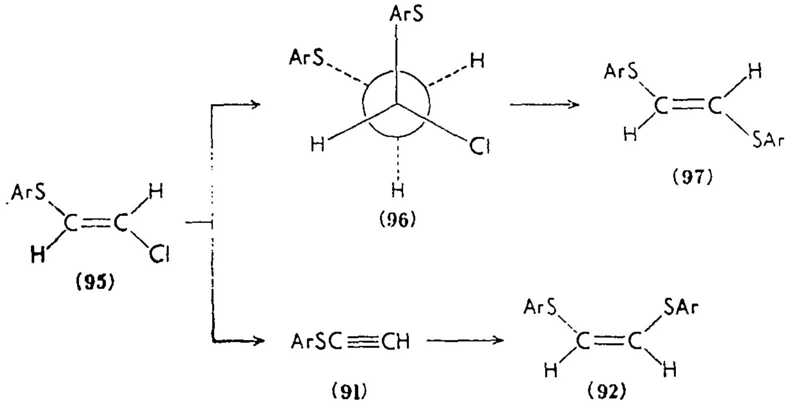
must be an intermediate in the addition–elimination route, gives only 10% conversion into **92** under the same conditions. The necessary presence of a strong base in the reaction mixture also points to the elimination–addition mechanism. In the *p*-toluenethiol/*cis*-1,2-dichloroethylene/EtO⁻ system, the reaction rate is proportional to the concentration of the two latter reagents but is independent of the concentration of thiolate ions[239]. Hence, the first, slow step of the reaction is a dehydrohalogenation, followed by fast addition of the thiolate. The energy of activation (34 kcal/mole) is also very similar to that of the dehydrohalogenation of **88** in methanol by methoxide ions (35 kcal/mole)[246]. Finally, in the presence of base, the independently prepared chloroacetylene **89** gave with *p*-toluenethiolate, according to the concentration of the latter, either the intermediate **90** or the final product **92**. Since **90** does not yield **92** in the absence of a strong base, this reaction must again take place by elimination–addition. The results above are explained by the favored *trans* elimination of hydrogen and halogen[246,247,248] from the *cis*-dihalo compound. The structure of the product is determined by the stereochemistry of the nucleophilic addition to the intermediate acetylene. As a rule, this is a *trans* addition[249–251] of the anion and the proton so that in the product (**90**) the arylthio and chloro groups are *cis* to each other. The same arguments hold for the formation of **92** with two thiol groups in *cis* positions. Thus, the overall retention of configuration is a result of two *trans* eliminations and two *trans* additions.

The influence of the polarization of the double bond can be seen in the reactions of vinylidene chloride[240]. Although *trans* elimination is possible, the elimination of a proton from a methylene group is more difficult than from a CHCl group, as in the previous case. On the other hand, the inductive effect of the two α-halogen atoms develops a partial positive charge on the β-carbon atom, favoring the addition–elimination mechanism over elimination–addition. Indeed, vinylidene chloride does not give with alkaline K_2HgI_4 the mercury derivative of chloroacetylene (which is obtained with 1,2-*cis*-dichloroethylene) and with *p*-toluenethiol in some cases the intermediate addition compound **94**, as well as its dehydrochlorination product **95**, can be isolated.



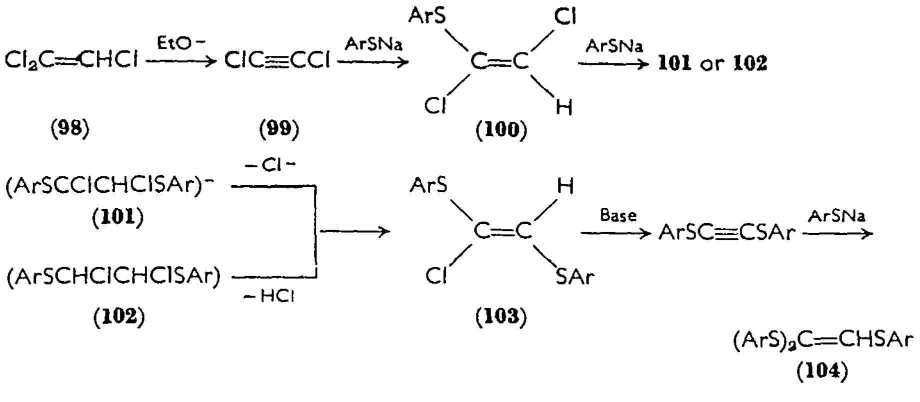
(94) **(94a)** **(95)**

The stereochemistry of the addition–elimination mechanism is mainly determined by the '*cis* effect'[252,253a]. The transition states leading to the *cis* or *trans* isomers resemble the products, and their formation is, as a rule, determined by the tendency to avoid steric interactions between large space-demanding groups. The preferred transition state of the elimination from **94** will be, therefore, **94a**, leading to the formation of **95**. The same principle applied to substitution in **95** demands that elimination from the intermediate **96** should give the *trans* product **97**. None of this isomer could be isolated from the reaction mixture and it has to be assumed that **95** is converted into **92** through the intermediate **91** in an elimination–addition reaction. This necessarily involves a very sluggish *cis* elimination of HCl from **95** and in ordinary reaction conditions only 10% of **92** is obtained. As a confirmation, it was shown that **95** cannot be converted by the thiol into **92** in the absence of a strong base.

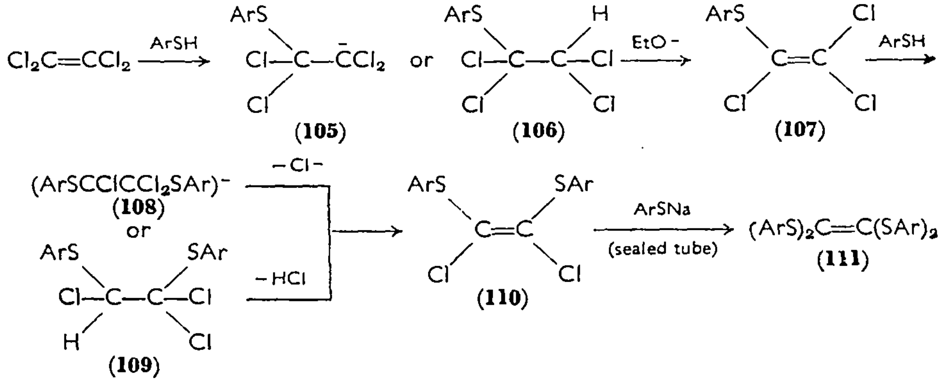


Trichloroethylene (**98**) combines the structures of both vinylidene chloride and 1,2-*cis*-dichloroethylene, making it difficult to predict the mechanism. In contrast to earlier studies[254], the final product with *p*-toluenethiol is the trisubstituted compound **104**[241]. In the first substitution, **100** is obtained in high yields in the presence of base but not at all in its absence, proving this to be an elimination–addition reaction. The addition–elimination route seems to be inhibited by the reduction of the polarity of the double bond (compared to vinylidene chloride), with the β-halogen counteracting the effect of the two α-halogen atoms, even though the double bond as a whole becomes more electrophilic.

Indeed, **98** is deuterated by $Ca(OD)_2$ and yields, with strong basic reagents, HCl and **99**; independently prepared **99** with sodium *p*-toluenethiolate yields **100**[255,256]. In **100**, the two chlorine atoms must be in the *trans* position as it is formed by *trans* addition of ArS and H to **99**. This is also confirmed by the difficulty of its dehydrochlorination. The step following is an addition–elimination and, with low concentrations of the thiolate, **103** containing two *trans* ArS groups was isolated. The last substitution is again an elimination–addition, to yield **104**[241].

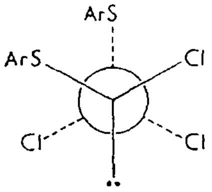


The last of the chlorinated series, tetrachloroethylene, can react only by addition–elimination[242], and, in view of the relative inertness of *trans*-1,2-dichloroethylene, it is somewhat surprising that it reacts at all. It seems that the combined inductive effect of four chlorine atoms sufficiently enhances the electrophilicity of the double bond, so that a direct attack on the carbon atoms becomes possible. This results in the formation of the carbanion **105** or possibly of the α,β-addition product **106**, either of which may yield **107** by elimination. The reaction **107** → **110** does not take place in the absence of base. Normally this is indicative of elimination–addition which, however, is

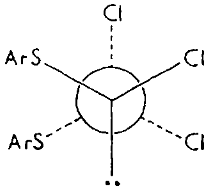


impossible in the present case. Therefore, this is an addition–elimination, but the actually feasible route is only through **108** and not through **109**, *i.e.* the base is necessary both for the formation of the attacking thiolate ions and for the inhibition of the protonation of **108**. This is one of the cases where the stereochemistry of the product (**110**) is determined by the higher thermodynamic stability of the *cis* isomer[257].

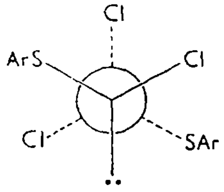
The primarily formed carbanion (**108a**) is present in the reaction mixture in equilibrium with the '*cis*' and '*trans*' carbanions '*cis*'-**108** and '*trans*'-**108** of which the former produces *cis*-**110** by *trans* elimination. The final substitution to yield **111** only takes place under forced conditions, as can be expected from the lowering of the reactivity of the substrate.



(**108a**)



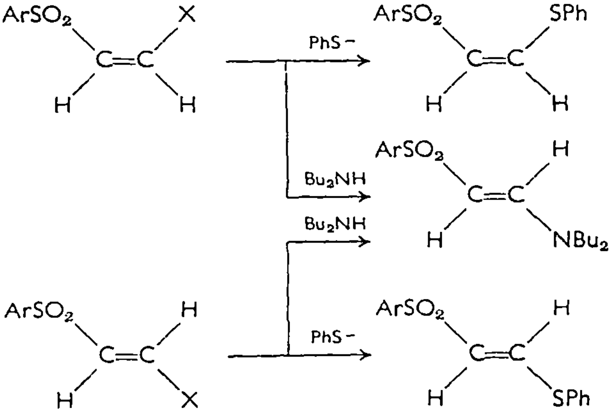
('*cis*'-**108**)



('*trans*'-**108**)

Other thiols react similarly with retention of configuration[258]. The use of sulfite ions[243] as nucelophiles lead to the same mechanistic conclusions with only minor differences, caused mainly by the activating effect of the entering sulfonate group on the intermediates and on the products of the reaction.

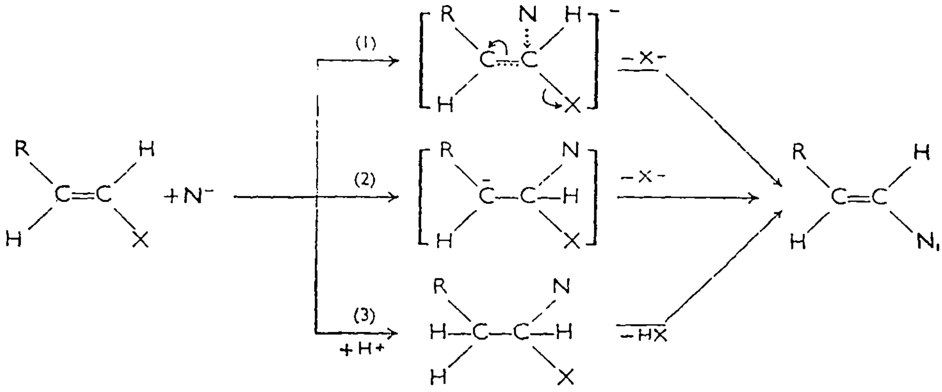
The addition–elimination mechanism was investigated in great detail by other workers[259–270]. In all cases the reaction was of first order with respect to the substrate and the nucelophile, pointing to the participation of both in the rate-determining step. Montanari and coworkers showed that, by using thiophenolate ions with a large variety of *cis* or *trans* substrates[271–274], the configuration of the starting material was retained in the product. Modena and coworkers found retention of configuration in the reaction of 1-halo-2-arylsulfonylethylenes with thiophenoxide, azide, methoxide and ethoxide



ions[259-261] using *cis*- and *trans*-chloro and -bromo compounds, and also substrates in which either the α- or the β-hydrogen was substituted by a methyl group[264,265]. On the other hand, when amines (cyclohexylamine, dibutylamine or piperidine) were used as the nucleophiles, the *trans* product was always obtained, both from *cis* and *trans* substrates[262].

A strong, although not complete, stereospecificity[267-269] is shown in the attack by EtS⁻ or PhS⁻ on sensitive[275] β-chlorocrotonate systems, but with EtO⁻ and PhO⁻ ions the same product is obtained from either the *cis* or the *trans* starting material in a non-stereospecific reaction.

The possibility that addition–elimination and elimination–addition reactions take place side by side was emphasized by Modena[260] who also pointed out the feasibility of three addition–elimination routes leading to the final product. The first (1) is a synchronous reaction in which bond breaking and bond forming take place simultaneously, and the direction of the attack is perpendicular to the plane of the double bond. The second route (2) is through the formation of a more or less stable carbanion which eliminates the leaving group directly, and the third route (3) is through the formation of a neutral α,β-addition product which subsequently undergoes elimination (Scheme 5). These three routes may be identified by the stereochemistry of the products, by the 'element effect'[276] and by isotope exchange studies. In path (1) the stereochemistry of the starting material and of the products will be related; in path (2) the same can be expected only in the special case when the lifetime of the intermediate is too short to permit its reorganization before the final



SCHEME 5.

product-forming step[260,261], otherwise both in path (2) and in path (3) the structure of the product will be determined by thermodynamic control.

The 'element effect' has been used as a mechanistic criterion in nucleophilic aromatic substitution[276,277]. For vinylic substitutions, this criterion is applied[263] by comparing the reaction rates of bromo and chloro derivatives of the same isomer and taking into consideration that, while the C—Br bond is broken more rapidly than the C—Cl bond, the polarization of the C=C bond caused by the two halogens is rather similar. Accordingly, if the reaction rates with the two halogens differ considerably, it can be assumed that the carbon–halogen bond cleavage is part of the rate-determining step and the activation energies will vary with different halogens. On the other hand, the absence of an element effect will indicate that the carbon–halogen bond is broken after the rate-determining nucleophilic attack on the double bond[263]. Hence, both the elimination–addition and the synchronous addition–elimination mechanism (path 1 in Scheme 5) will show the element effect.

Table 8 summarizes relevant data for several series of reactions. In similar reactions, the *cis*-bromo derivative reacts at a faster rate than the *cis*-chloro, with the largest differences observed when the nucelophile is an alkoxide, or in some cases cyclohexylamine or dibutylamine. The differences are much smaller or disappear completely with the corresponding *trans* compound, and the chloro compounds react somewhat faster than the bromo derivatives in attacks by the very reactive alkoxide ions.

The magnitude of the element effect varies considerably with the reagents, and it may be argued that the mechanism of the reaction depends on the nature of the attacking reagent. Indeed, nucleophiles having high carbon basicity, such as azide or thiophenoxide ions, show smaller rate differences when reacting with *cis* or *trans* and also with chloro or bromo derivatives of the same substrate. This may be rationalized by assuming a rate-determining attack on the β-carbon, followed by fast cleavage of the carbon–halogen bond for these cases in which only small differences will be caused by variations in the electrophilicity of the attacked carbon and by steric effects. The large element effects found with strong nucleophiles (alkoxides, amines) could be a result of fast initial attack followed by a comparatively slow carbon–halogen bond cleavage. More probably, the mechanism may be changed completely to elimination–addition with rate-determining C—X and C—H bond cleavages. In these cases the *cis* substrates (in which facile *trans* elimination is possible) are much more reactive than the *trans* compounds, as expected. Indeed, when the absence of α-hydrogens in a substrate makes the elimination–addition mechanism impossible, no element effect is observed[265] and the mechanism is again an addition–elimination even with alkoxides.

TABLE 8. Rate coefficients (k_2) of reactions $R^1C_6H_4SO_2CR^2{=}CR^3Y + N$ in methanol.

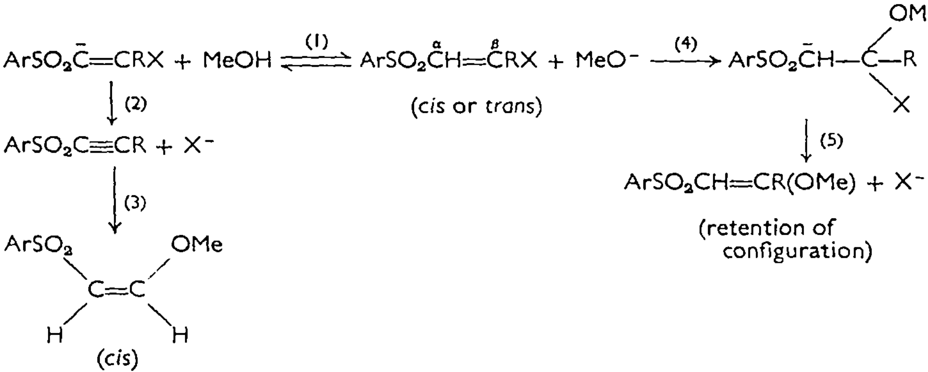
R^1	R^2	R^3	N	Temp. (°c)	10^3k_2(l./mole sec)				Ref.
					Y = Br		Y = Cl		
					cis	*trans*	*cis*	*trans*	
p-NO_2	H	H	MeO^-	0	—	—	280	168	260
p-NO_2	H	H	PhS^-	0	—	—	4800	2300	261
p-NO_2	H	H	$C_6H_{11}NH_2$	0	336	3·88	8·78	3·86	263
p-NO_2	H	H	Bu_2NH	0	271	55·3	64·8	65·8	263
p-NO_2	H	H	N_3^-	25	155	156	52	77	263
p-Me	H	H	MeO^-	0	1780	5·35	9·6	6·4	263
p-Me	H	H	PhS^-	0	248	86·4	109	40	263
p-Me	H	H	$C_6H_{11}NH_2$	0	8·41	0·22	0·46	0·23	263
p-Me	H	H	Bu_2NH	0	8·43	3·06	2·38	2·85	263
p-Me	H	H	N_3^-	25	2·31	3·0	0·90	1·45	263
H	H	H	MeO^-	0	2600	8·8	18	10·5	263
H	H	H	EtO^-	0	50000	30·3	—	41·0	263
H	H	H	PhS^-	0	482	154	200	69·0	263
H	H	H	$C_6H_{11}NH_2$	0	13·3	0·30	0·63	0·34	263
H	H	H	Bu_2NH	0	12·5	5·40	4·20	5·25	263
H	H	H	N_3^-	25	4·30	5·10	2·00	2·55	263
p-NO_2	Me	H	MeO^-	25	5·05	5·26	5·40	6·22	265
p-NO_2	Me	H	PhS^-	25	458	143	175	63	265
p-NO_2	Me	H	$C_6H_{11}NH_2$	25	0·20	0·067	0·14	0·059	265
p-NO_2	Me	H	Bu_2NH	25	0·54	0·20	0·39	0·27	265
p-NO_2	H	Me	MeO^-	0	7850	—	71·9	—	264
p-NO_2	H	Me	PhS^-	0	34·2	—	14·1	—	264
p-NO_2	H	Me	$C_6H_{11}NH_2$	0	105	—	0·45	—	264
p-NO_2	H	Me	Bu_2NH	0	210	—	0·77	—	264

Mechanistic differences are also reflected in the activation energies. Cases for which the addition–elimination mechanism can be assumed fall into the range of 12–15 kcal/mole; higher values (20–22 kcal/mole) are obtained for reactions probably taking the elimination–addition route[260,262,265].

Studies with the *cis* and *trans* isomers of the **112**, **113** and **114** systems in deuterated methanol[266] showed that none of the three substrates gave deuterium exchange with the solvent in the presence of thiophenoxide ions. Methoxide-catalyzed exchange of deuterium was found with **112** and **114** but not with **113** which has no α-hydrogen. Accordingly, substitution of the halogen by thiophenoxide must be an addition–elimination. The same is probably true for the reaction of **113** with other nucleophiles. The deuterium exchange in the other

$Ar\overset{\alpha}{C}H{=}\overset{\beta}{C}HX$ (**112**) $Ar\overset{\alpha}{C}Me{=}\overset{\beta}{C}HX$ (**113**) $Ar\overset{\alpha}{C}H{=}\overset{\beta}{C}MeX$ (**114**)   ($Ar = p\text{-}CH_3C_6H_4$—, $X = Cl, Br$)

cases is not a sufficient indication of the elimination–addition mechanism, since isotope exchange between C_α-deuterated **112** and the solvent, containing methoxide ions, was much faster than substitution by MeO^- and no kinetic isotope effect was observed for the substitution. Moreover, the *trans* product was obtained from the *trans* substrate, although the elimination–addition mechanism should produce the *cis* product. These results are explained by Scheme 6[266].



Scheme 6.

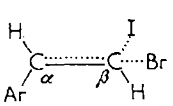
Fast equilibration with the solvent (step 1) in the first route is followed by elimination (step 2) and subsequent addition (step 3). In the second route, the equilibration is accompanied by a direct attack on the β-carbon (step 4), with elimination of the halogen in the product forming step (step 5). The route (1)–(4)–(5) is feasible both with the *cis* and *trans* isomers. The *cis* isomer by facile *trans* elimination of HX can react also through route (1)–(2)–(3), whereby it will show a strong 'element effect' and give the *cis* product. When using ArS^- instead of MeO^-, the results fit the (1)–(4)–(5) route with the added condition that step (4) must be much faster than step (1), owing to the low basicity of the thiophenoxide ions. In the absence of α-hydrogens, route (4)–(5) is the only possible one.

The modes of behavior of the intermediate carbanion were discussed by Miller and Yonan[270], who studied the reaction of *p*-nitro-β-bromostyrene with iodide ions. Complete retention of configuration was

$$p\text{-}O_2NC_6H_4CH{=}CHBr + I^- \longrightarrow p\text{-}O_2NC_6H_4CH{=}CHI + Br^-$$

found in the first step of the reaction, although isomerization occurred after prolonged reaction times. The primary attack of the nucleophile was described as occurring perpendicularly to the plane of the double bond with interaction of the π-orbitals, leading with the *cis* substrate to the transition state **115**.

The formation of a bond between the nucleophile and C_β gives a tetrahedral carbanion with an electron pair occupying one of the valences of C_α, which is in effect a *trans* addition of a halide ion and of an electron pair. It was assumed that only *trans* elimination of the electron pair and of one of the halogens in the appropriate conformation can complete the reaction. The carbanion **116** is one of three rotational *threo* isomers with a rotational barrier of about 3–5 kcal/mole[277]. The isomeric *erythro* carbanion **117**, which is also obtained by attack on the *trans* isomer, can be obtained by inversion of the configuration of **116** in a process probably demanding an energy of not more than 7 kcal/mole[270]. If the inversion of the carbanion is faster than its rotation, then, on the average, the carbon atom adjacent to the reaction site may be considered to be coplanar, and the structures **118** and **119** represent the intermediates responsible for the stereochemical pathway of the reaction. Elimination of the nucleophile from these carbanions will give a product with retention of the



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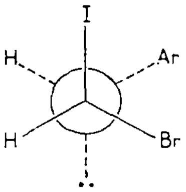

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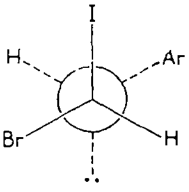

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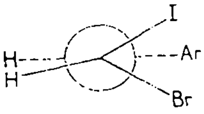

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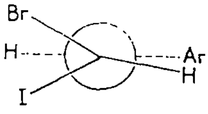


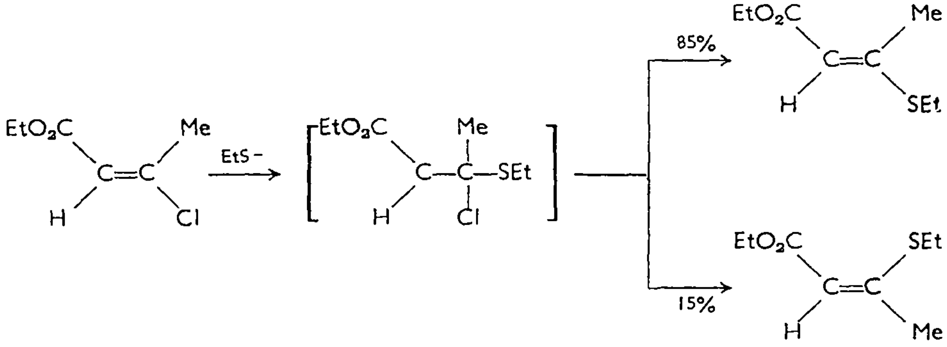
(119)

configuration of the starting material, while rotation will lead to interconversion and isomerization. Retention of configuration may, therefore, be consistent with a reaction in which the elimination of the nucleophile from the carbanion is faster than the rotation of the latter.

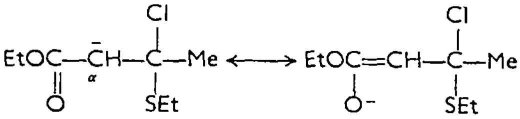
In cases when the inversion of the intermediate is slower than its rotation, the conversion of *cis* to *trans* will be governed by the former, but still isomerization will take place only if the inversion of the carbanion is also accompanied by rotation. While such a route is possible, the experimental results show that it cannot compete seriously with other pathways in which halide exchange occurs with retention of configuration.

Examination of a possible S_N2-type mechanism[238] with the aid of molecular models shows that the reaction site is highly shielded. Moreover, in the transition state **86** groups R^1 and N and also R^2 and X are at almost bonding distance, but since actual bond formation is impossible, the repulsion energy will be very high. Therefore, the S_N2-type mechanism is excluded.

In the study of the reaction of ethyl β-chloro-*cis*- and -*trans*-crotonate with thioethoxide, thiophenoxide, ethoxide and phenoxide ions, both isomers were produced with thioanions but with preferred retention, while only one isomer was obtained with oxyanions[267-269]. The extent of isotope exchange in deuterated ethanol containing thioethoxide ions was rather small, and different *cis–trans* ratios were obtained from the *cis* and the *trans* esters. Hence, the reaction cannot take place by elimination–addition. Neither can it involve prototropy, as this also requires a single intermediate leading to an identical *cis–trans* product ratio. In a manner similar to that proposed by Miller and Yonan[270], it was assumed that the primary attack takes place perpendicularly to the plane of the double bond and that the chloride ion leaves in the same way as also required by the principle of micro-

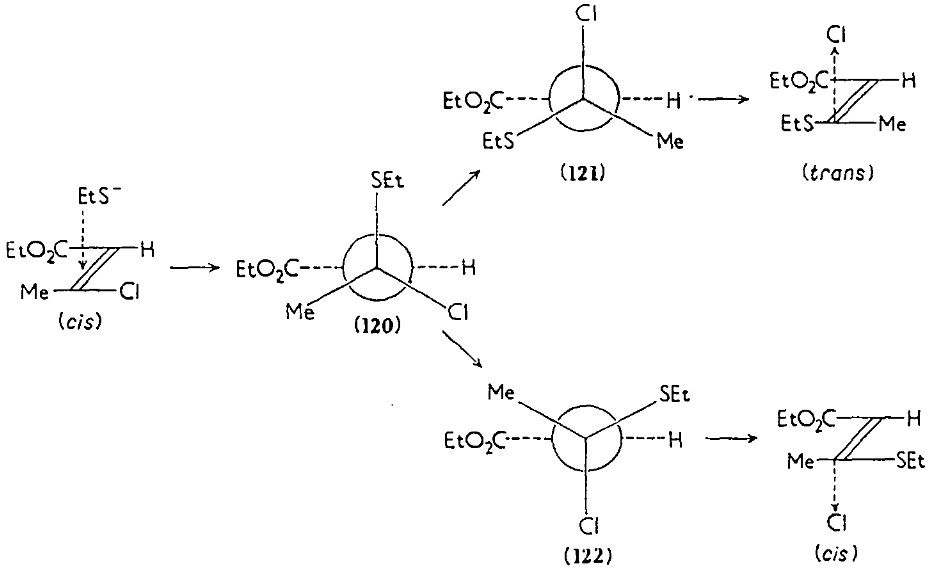


scopic reversibility. In the intermediate resonance hybrid, the negative charge is distributed between C_α and the carbonyl oxygen so that the two groups bound to C_α remain coplanar after the nucleophilic attack. Therefore, **120** and **123** could be obtained from the



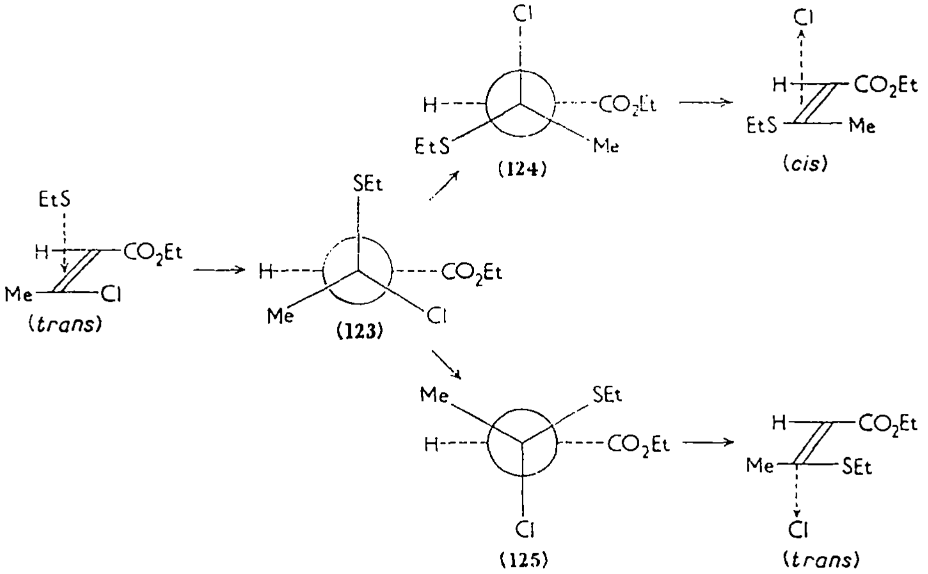
$$\mathrm{Et}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{OC}}-\overset{-}{\underset{\alpha}{\mathrm{C}}}\mathrm{H}-\overset{\mathrm{Cl}}{\underset{\mathrm{SEt}}{\mathrm{C}}}-\mathrm{Me} \longleftrightarrow \mathrm{Et}\underset{\underset{\mathrm{O^-}}{|}}{\mathrm{OC}}{=}\mathrm{CH}-\overset{\mathrm{Cl}}{\underset{\mathrm{SEt}}{\mathrm{C}}}-\mathrm{Me}$$

cis and *trans* isomers, respectively, and these, by rotation, will produce the rotamers **121**, **122**, **124** and **125**. In each of these rotations the intermediates have to pass through eclipsed conformations and steric compression will result in the eclipsing of the substituent pairs CO_2Et–EtS, CO_2Et–Cl and possibly CO_2Et–Me[269]. Therefore, the



Transformation	Steric course	Eclipsed pairs
120 → **121**	Inversion	EtS–CO_2Et; Cl–H
120 → **122**	Retention	CO_2Et–Me
123 → **124**	Inversion	EtS–H; CO_2Et–Cl
123 → **125**	Retention	Me–H

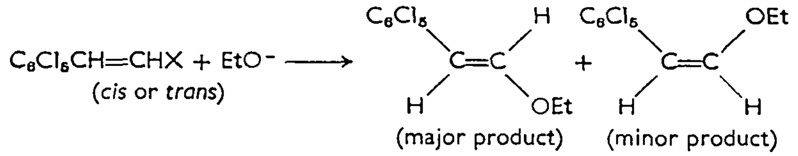
formation of **122** from **120** and of **125** from **123** will be preferred, both with retention of configuration, even though the differences between the energy barriers involved are rather small (about 1 kcal/mole was calculated for the *cis*-chloro ester on the basis of the 85% retention



observed). Accordingly, the steric course of the substitution may be predetermined by the proper choice of substituent groups. A substrate of the type YCH═CHCl (in which Y is the activating group) will tend to retain its configuration more than a compound of the type YCH═CRCl. Indeed, ethyl β-chlorocrotonates, which are of the latter type, give some inversion[269], while with *p*-nitro-β-bromostyrene, which is of the former type, retention of configuration is complete[270].

A further possibility, that of *cis* elimination of the nucleophile and of an electron pair, is discussed by Vernon and coworkers[269], who point out that overlap control between, for example, the chlorine atom and the electron pair in the *cis* position, could favor such a route.

Predictions based on the magnitude of steric compression in the intermediate are not confirmed in the reaction of *cis* and *trans* β-halopentachlorostyrenes with ethoxide ions, leading to mixtures rich in the

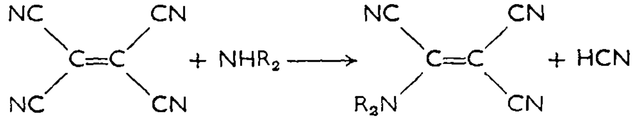


trans isomer[278]. Similarly, both *cis*- and *trans*-3,4-dinitro-3-hexene give with *p*-toluenethiolate ions only one product, probably the *trans* isomer[279], although retention of configuration would be predicted in both the *cis* and the *trans* isomers. It may well be possible that in these cases the intermediate carbanion has a sufficiently long lifetime to permit thermodynamic control to take the place of the kinetic control on which the above predictions are based.

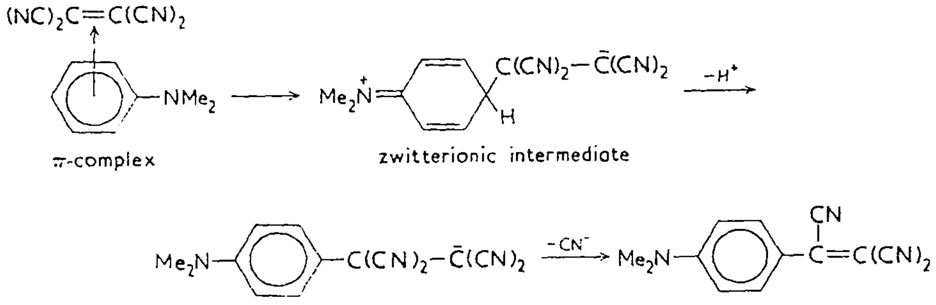
To summarize, the steric relations in the substitution are determined by the ratio of the rates of the elimination of the leaving group and of the rotation in the carbanion. If the elimination is the faster, the reaction will be kinetically controlled and the stereochemistry of the reaction will be determined by the rotational barriers in the intermediate. Conversely, if the rotation rate is the faster, the reaction will be thermodynamically controlled, yielding either the more stable product alone or a mixture rich in the latter.

Regarding the dependence of the reaction rates upon the structure of the attacked molecule, as in all mechanisms discussed in this chapter, groups withdrawing electrons from the reaction center will enhance the rate, while electron-donating ones will lower it. Systems activated by halogens only are very unreactive[270], and often give no reaction at all[280]. Substitution of hydrogen by a carbethoxy or similar group in the chloropropene system increases the reaction rates by a factor of 10^6 or 10^9 [269]. In the system (ArY)CH=CHCl the activating effect is in the order Y = SO_2 > SO > S, and the effect of a $PhSO_2$ group is similar to that of a carbethoxy group. When ArY is a thiol group the reactivity of the substrate is so low that the mechanism will be changed to elimination–addition[274].

Owing to the disinclination of carbon atoms to carry a negative charge, only systems in which this charge may be distributed on other groups will tend to react. With several such groups in the molecule, extensive charge distribution facilitates the nucleophilic attack. A good example of this is the high reactivity of tetracyanoethylene with various amines and even with the *para* position of mono- or dimethylaniline[234,281a].



In such active electrophilic double bonds π-complex formation can precede the formation of the carbanionic intermediate, as in the case of the substitution of tetracyanoethylene by dimethylaniline. In this system the stable carbanionic intermediate is formed irreversibly and accumulates, and its decomposition to the final substitution product, *N*,*N*-dimethyl-4-tricyanovinylaniline, is slow. As the cyano group is a sluggish leaving group in nucleophilic substitutions, the proton is eliminated first and the elimination is general base catalyzed[281a]:



In the substitution of the readily eliminated chlorine of tricyanovinyl chloride by dimethylaniline, the zwitterionic intermediate is not accumulated, and the chloride ion leaves before the proton removal and thus the reaction is not base catalyzed. The low activation energy (2·6 kcal/mole) showed that the measured process is not the nucleophilic attack but rather a composite process, in which the reversal of the formation of the zwitterionic intermediate has kinetic importance[281b].

Table 9 summarizes ρ values of the Hammett equation for the attack of various nucleophiles on *cis*- and *trans*-1-chloro-2-arylsulfonylethylenes. The relatively high values show the requirement of a rather strongly positive reaction center. Although the individual rate constants in the various series differ from each other by several orders of magnitude, the derived ρ values are nearly identical for each *cis–trans* pair and are rather similar also with different nucleophiles. Hence the primary importance of charge distribution in the attacked molecule is evident and the polarization caused by the reagents has only a secondary effect.

TABLE 9. ρ Values for the reaction of *cis*- and *trans*-$XC_6H_4SO_2CH{=}CHCl + N \rightarrow XC_6H_4SO_2CH{=}CHN + Cl^-$ in methanol.

N	Temp. (°c)	*cis*	*trans*	Reference
MeO^-	0	1·56	1·60	260
PhS^-	0	1·60	1·84	261
N_3^-	25	1·84	1·85	261
$C_6H_{11}NH_2$	25	1·22	1·21	262
Bu_2NH	0	1·50	1·48	262

The same picture is given by the study of the reaction of ethyl β-chloro-*cis*- and -*trans*-crotonate and ethyl β-chloro-α-methylcrotonate with EtO^-, EtS^- and PhS^- ions[269]. Probably owing to both steric and inductive effects, the introduction of the α-methyl group lowers the rates by a factor of 100 to 500. It is difficult to give a systematic explanation of the small rate differences with *cis* and *trans* isomers. These may be caused by the differences in the polarization of the attacked carbon, due to the different distances of the substituents in the two isomers, and also by lower electrophilicity of C_β, due to steric inhibition of resonance.

The results in some cases depend upon the nature of the nucleophile. For example, ethyl β-chloro-*cis*-crotonate reacts faster than the *trans* isomer with ethoxide ions, but the *trans* isomer reacts faster with thioethoxide ions (Table 10).

TABLE 10. Rates, relative rates and activation parameters for the reaction of chlorocrotonates with various nucleophiles[269].

Substrate	Temp. (°c)	Nucleophile	10^3k_2 (l./mole sec)	Relative k_2[a]	E (kcal/mole)	$\log_{10} B$
Ethyl β-chloro-*trans*-crotonate	20	EtO^-	10·2	1·00	19·2	12·4
	20	EtS^-	32·4	6·12	14·5	9·39
	20	PhS^-	1·78	0·24	16·0	9·19
Ethyl β-chloro-*cis*-crotonate	20	EtO^-	35·2	4·49	17·6	11·8
	20	EtS^-	15·1	2·66	14·1	8·71
	20	PhS^-	0·385	0·060	15·3	8·13
Ethyl β-chloro-α-methylcrotonate	35	EtO^-	0·71	0·011	20·5	11·4
	35	EtS^-	0·447	0·013	16·7	8·49

[a] The relative rates refer to 0°c.

The relative rates of the reaction of ethoxide ions with 1,1-diphenylvinyl chloride, bromide and fluoride, are 1, 4 and 270 respectively[282,283]. Since in these cases there is no possibility of elimination–addition and a rate-determining carbon–halogen bond cleavage must be slower with fluorine than with chlorine[276], the results probably reflect the relatively strong polarization caused by fluorine, combined with low steric hindrance presented to the nucleophile. Similar nucleophilic substitutions in other fluoroethylenes give facile formation of fluoroethers, fluorothioethers and other products under relatively mild conditions[284].

Only little is known about the relative reactivity of the nucleophiles used in vinylic substitution reactions, which also include, in addition to those already mentioned, arsenite ions[285], carbanions[143] (from

Grignard reagents) and selenophenols[286]. Some of the relevant data are given in Tables 10 and 11. Sulfur-containing nucleophiles give especially high rates and their reactivity seems to be proportional to their acidity. Chloride ions are very poor nucleophiles and the chlorine isotope exchange in the β-chlorocrotonate system is slower by a factor of 10^6 than the substitution by thioethoxide ions[269].

While the rate coefficients, in similar conditions, differ from each other by several orders of magnitude, the activation energies for reactions with identical mechanisms are rather similar. However, at least in the chlorocrotonates there is a clear trend in the activation energies, with different nucleophiles in the order

TABLE 11. Second-order rate coefficients (k_2) and activation energies of the reactions of various nucleophiles with *trans*-p-$MeC_6H_4SO_2CH{=}CHCl$

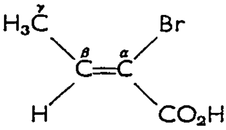
Nucleophile	10^3k_2 (l./mole sec)	E_a (kcal/mole)	Conditions	Reference
N_3^-	1·45	—	methanol, 25°	261
p-$MeC_6H_4CH_2S^-$	638	14·7	methanol, 25°	261
$C_6H_{11}NH_2$	0·23	13·2	methanol, 0°	262
Bu_2NH	2·85	12·7	methanol, 0°	262
Piperidine	60·0	—	methanol, 0°	261
PhS^-	40	14·7	methanol, 0°	261
p-$MeC_6H_4S^-$	67	—	methanol, 0°	261
$PhCH_2S^-$	1000	14·7	methanol, 0°	261
EtO^-	24·8	15·8	ethanol, 0°	260
MeO^-	6·4	16·9	methanol, 0°	260

$$EtO^- > PhS^- > EtS^-.$$

The three other mechanisms (3), (4) and (5) mentioned in the beginning of this section may operate in some special cases. In the carbanionic route (4), a halogen atom in systems such as 1,2-diphenyl-1-p-chlorophenyl-2-bromoethylene[287] or in α-bromostilbene[288] is exchanged for lithium. The resulting vinylic carbanion may undergo carbonation or methylation with the overall process being at least formally, a vinylic substitution.

Route (3) is more generally available, but only in systems allowing prototropic rearrangements. The reaction of both α-bromocrotonic (**126**) and of α-bromoisocrotonic acid (**127**) with concentrated methanolic potassium hydroxide gives α-methoxycrotonic acid (**128**)[289,290] and, by further addition, **129** is formed as a by-product. In the course of such reactions, the double bond migrates from the α,β- to the

β,γ-position[291–294], so that the initially vinylic halogen becomes capable of normal nucleophilic displacement. As a proof of this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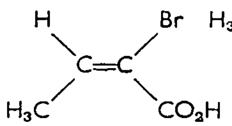
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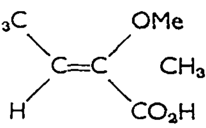

(128)

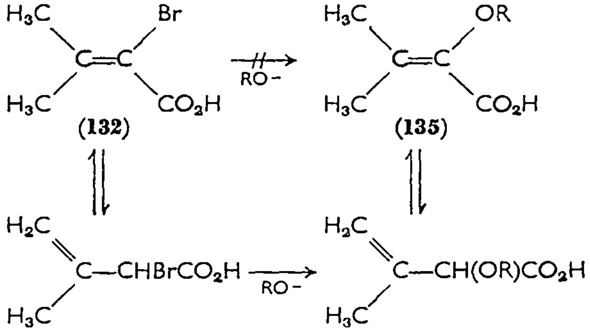
$CH_3CH(OMe)CH(OMe)CO_2H$

(129)

mechanism, it was shown that **130**, in which there can be no prototropic change, gives no α-alkoxyacrylic acid when treated with alkoxides[291] and similarly **131** gives no substitution but only dehydrobromination with alkali. A prototropic mechanism is summarized

$H_2C{=}CBrCO_2H$ **(130)** $PhCH{=}CBrCO_2H$ **(131)**

in the reaction sequence **132** → **133** → **134** → **135**. The β,γ-unsaturated acid **134** was actually isolated from the reaction mixture[292].


(132) **(135)** **(133)** **(134)**

In vinyl halides, heterolytic cleavage of the C—X bond with formation of vinyl cations is difficult[237] and therefore S_N1-type reactions are hardly expected to occur. Kinetic results[295] in the hydrolysis of **136** with R = H, Me or MeO at 65° show that the reaction is first order, allowing, for this case, a mechanistic interpretation with a cationic intermediate **137**. At 55° the reaction is

$$p\text{-}RC_6H_4COCBr{=}CHCO_2H \longrightarrow p\text{-}RC_6H_4CO\overset{+}{C}{=}CHCO_2H + Br^-$$

(136) **(137)**

still first order with R = H, but of intermediate order with R = Me or MeO, and the latter is the case also with R = H if the reaction is carried out at 45°. However, in most cases the experimental data fit second-order kinetics almost as well as first-order. The rates are slowest with R = MeO— and fastest with R = H, while the opposite would be expected in an S_N1-type reaction. To explain this, a hypothesis is presented according to which in this special system the *p*-Me and *p*-MeO groups by their conjugation with the carbonyl group, lower the S_N1 reactivity of the C—Br bond.

V. FRAGMENTATION REACTIONS

Nucleophilic attacks on the alkene bond may lead to the formation of two moieties, one of them containing the β-carbon of the original molecule together with the nucelophilic center (Z) of the attacking nucleophile, and the second containing the α-carbon with two hydrogen atoms obtained from the attacking reagent or from the medium.

$$R^1R^2\overset{\beta}{C}{=}\overset{\alpha}{C}XY + ZH_2 \longrightarrow R^1R^2C{=}Z + H_2CXY$$

Similar reactions may occur even if the nucelophile contains only one mobile hydrogen atom; a carbanionic fragment is formed first, and yields the product after abstraction of a proton from the medium. When the nucleophilic atom in the reagent is oxygen, the moiety containing C_β will be an aldehyde or a ketone:

$$R^1R^2C{=}CXY + H_2O \longrightarrow R^1R^2C{=}O + H_2CXY$$

With primary and secondary amines or with the amide anion a C=N

$$R^1R^2C{=}CXY + NH_3 \longrightarrow R^1R^2C{=}NH + CH_2XY$$

bond is formed and attack by carbanions derived from active methylene compounds will lead to the formation of a new carbon–carbon double bond. Formally, the last reaction is the transfer of the C_β moiety

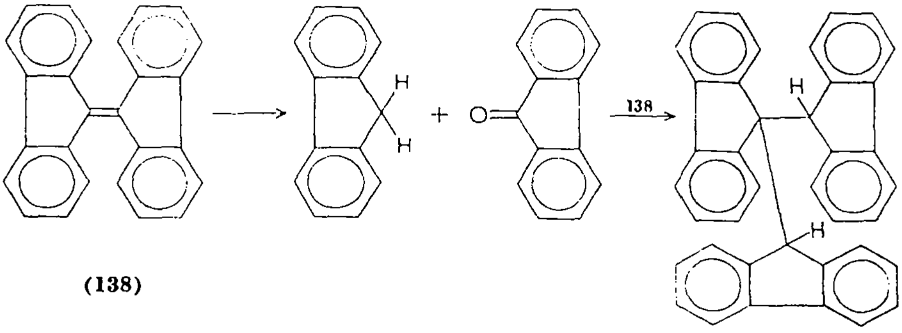
$$R^1R^2C{=}CX^1Y^1 + CH_2X^2Y^2 \longrightarrow R^1R^2C{=}CX^2Y^2 + CH_2X^1Y^1$$

from one active methylene residue to another (alkylidene or arylmethylene transfer). Since the second product containing C_α is an active methylene compound in all these cases, the fragmentation is often accompanied by secondary reactions. For example, 1,3-dinitro-2,2-diphenylpropane is formed from 1,1-diphenyl-2-nitroethylene in the presence of potassium *t*-butoxide[86] by the Michael addition of the nitromethane formed in the solvolysis, to the double bond of the starting material. Similarly the base-catalyzed frag-

$$Ph_2C{=}CHNO_2 \longrightarrow Ph_2C{=}O + CH_3NO_2$$

$$Ph_2C{=}CHNO_2 + CH_3NO_2 \longrightarrow Ph_2C(CH_2NO_2)_2$$

mentation of dibiphenyleneethylene (**138**) produces[296], among other products, tribiphenylenepropane (**139**).

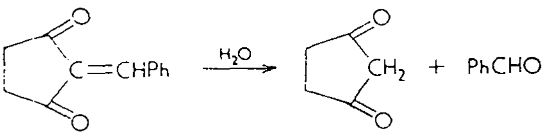


(138)

(139)

A. Cleavage by Oxygen- and Sulfur-containing Reagents

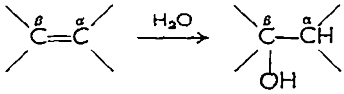
The cleavage of alkenes to carbonyl and active methylene compounds is the reversal of condensations such as the Perkin, Knoevenagel, Claisen and Claisen–Schmidt reactions. Examples are the base-catalyzed C=C bond cleavage of substituted benzylidenemalononitriles $ArCH{=}C(CN)_2$ to the corresponding aromatic aldehydes and to malononitrile[34], or of alkylidene esters $RCH{=}C(CO_2Et)_2$ to the corresponding aldehydes and malonic ester[297]. The cleavage of 2-benzylidene cyclopentane-1,3-dione takes place with catalytic concentrations of base in ethanol[298], vanillidenenitromethane is hydrolyzed in aqueous ammonium acetate buffer[299] and benzylidene malononitriles are cleaved even without a catalyst in aqueous ethanol[300,301]. The decrease in the ultraviolet absorption of tricyanovinylbenzene with time, which was originally attributed to complex formation with the solvent[302], was also found to be caused by the cleavage of the molecule to malononitrile and benzoyl cyanide[301].



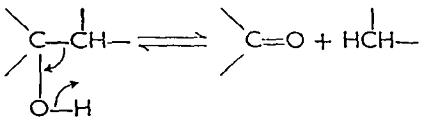
$$PhC(CN){=}C(CN)_2 + H_2O \longrightarrow PhCOCN + CH_2(CN)_2$$

No solvolysis by alcohol alone leading to the formation of an acetal and an active methylene compound has been described.

Shemyakin and coworkers have shown the special importance of such reactions, and especially of oxidative–hydrolytic reactions, in the field of quinones[303,304]. They investigated the ease of cleavage of various structures containing either double bonds or their hydration products, *i.e.* $\rangle\overset{\beta}{\mathrm{C}}(\mathrm{OH})—\overset{\alpha}{\mathrm{C}}\mathrm{H}\langle$ groups, which may be intermediates in the cleavage reaction. Electron-attracting substituents on the α-carbon and electron-donating ones on the β-carbon were shown to facilitate hydrolysis. In more symmetrical molecules, when the α- and β-substituents are comparable, the hydrolysis becomes more difficult or even impossible[305]. Thus symmetrical unsaturated dicarboxylic acids as well as acids in which two carboxyl groups are attached to the same carbon atom but remote from the double bond, *e.g.* systems such as $—C{=}CC(CO_2H)_2$, were found to be extremely resistant towards hydrolysis. When one carboxyl group is attached directly to an ethylenic carbon, *e.g.* α-phenylcinnamic acid, the acid is slowly cleaved by concentrated alkalies, and acids containing two carboxyl groups attached to the same ethylenic carbon atom undergo rapid cleavage even on heating with water alone[306]. Vinyl ketones are often cleaved on heating with water alone, although generally a basic catalyst is necessary. Unsaturated nitro compounds are as a rule hydrolyzed by boiling with water. According to Shemyakin the hydrolytic splitting of C=C bonds proceeds through a relatively facile primary hydration:



and is completed by a tautomeric change, which is in effect the reversal of an aldol condensation[307].

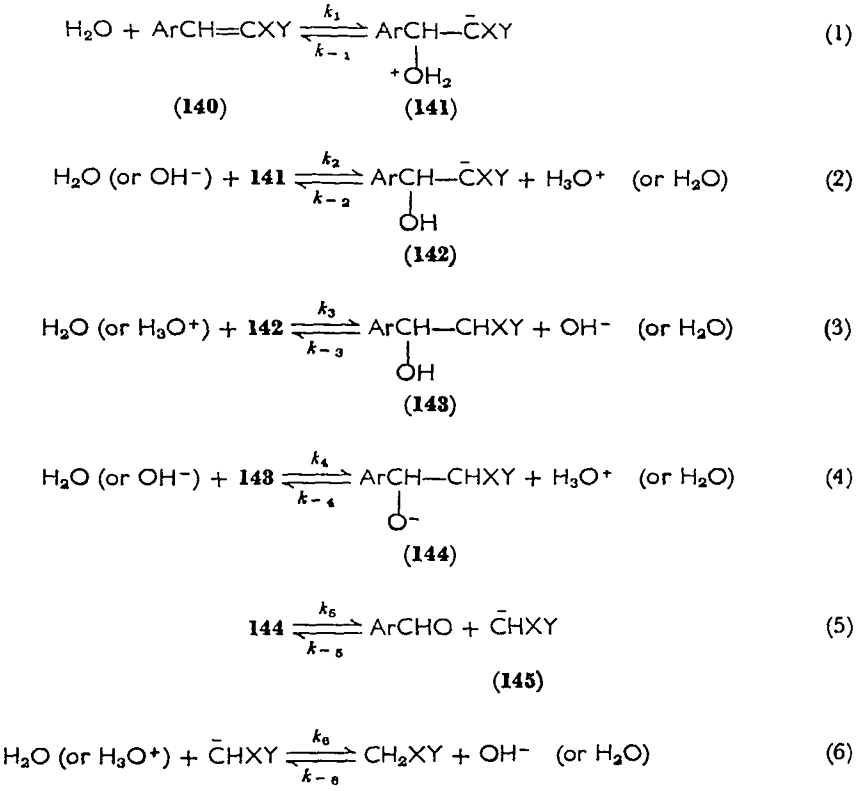


In qualitative experiments, the ease of hydrolysis of ring-substituted

$$\mathrm{ArCH{=}CHCOCH_3} \longrightarrow \mathrm{ArCHO} + \mathrm{CH_3COCH_3}$$

benzylidene acetones[308] was found to be 2,4-$(NO_2)_2$ < *o*-NO_2 < *m*-NO_2 < *p*-NO_2 < H, judged by the concentration of KOH necessary for complete cleavage on boiling for one hour. Such hydrolyses normally lead to equilibrium, which, in the presence of a large excess of alkali, may be displaced by side-reactions. Indeed, corresponding acids were isolated from the reaction mixtures and, therefore, the observed effect is not necessarily correlated to the reactivity of the substrates. In the very similar chalcone system, the effect of nitro substitution in the ring was found in kinetic investigations to be opposed to the above order (see below).

Investigations using kinetic and isotope exchange methods show that the cleavage follows an essentially identical route in all systems, with characteristic differences in the relative importance of different



$$H_2O + ArCH{=}CXY \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{{}^{+}OH_2}{ArCH}{-}\bar{C}XY \qquad (1)$$

(140) (141)

$$H_2O\ (\text{or } OH^-) + \mathbf{141} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \underset{OH}{ArCH}{-}\bar{C}XY + H_3O^+\ (\text{or } H_2O) \qquad (2)$$

(142)

$$H_2O\ (\text{or } H_3O^+) + \mathbf{142} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \underset{OH}{ArCH}{-}CHXY + OH^-\ (\text{or } H_2O) \qquad (3)$$

(143)

$$H_2O\ (\text{or } OH^-) + \mathbf{143} \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} \underset{O^-}{ArCH}{-}CHXY + H_3O^+\ (\text{or } H_2O) \qquad (4)$$

(144)

$$\mathbf{144} \underset{k_{-5}}{\overset{k_5}{\rightleftharpoons}} ArCHO + \bar{C}HXY \qquad (5)$$

(145)

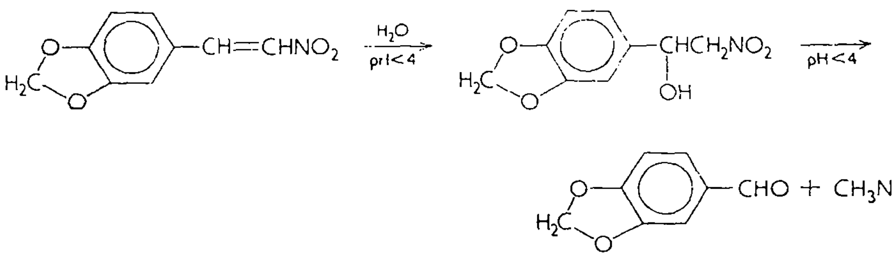
$$H_2O\ (\text{or } H_3O^+) + \bar{C}HXY \underset{k_{-6}}{\overset{k_6}{\rightleftharpoons}} CH_2XY + OH^-\ (\text{or } H_2O) \qquad (6)$$

SCHEME 7. General cleavage scheme.

steps for various systems. The generalized scheme for the uncatalyzed cleavage by water alone is shown in Scheme 7. When the attacking nucleophile is a hydroxide ion[301], step (1a) takes the place of steps (1) and (2):

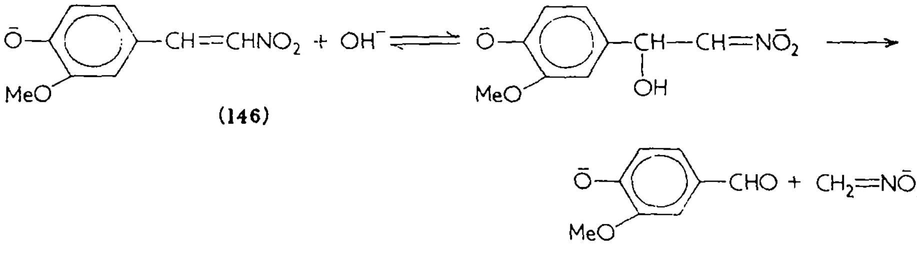
$$ArCH{=}CXY + OH^- \underset{k_{-7}}{\overset{k_7}{\rightleftharpoons}} \mathbf{142} \qquad (1a)$$

Varying the reaction conditions or the substituent groups attached to the C=C group changes both the absolute value and the relative magnitude of the rate coefficients of the various steps. For example, in the hydrolysis of piperonylidenenitromethane[309] (**140**, Ar = $(CH_2O_2)C_6H_3$—, X = NO_2, Y = H), the only reaction at pH < 4 is the reversible formation of an aldol **143** by attack of water molecules. At higher pH cleavage occurs with enhanced overall reaction rates and one of the stages of the process **140** → **143** becomes rate determining in product formation. At pH = 11 the nature of the primary step changes and it seems that hydroxyl ions become the attacking agents (step 1a) instead of water molecules (step 1).



The conversion of the aldol intermediate to the product requires deprotonation of the hydroxyl group, and is therefore inhibited by protonic acids and catalyzed by bases. This is also the case in the hydrolytic cleavage of hydroxyketones, *e.g.* in the dealdolization of diacetone alcohol[310], which takes place through steps (4) and (5) with the latter being rate determining[311]. Steps (4) and (5) of the general scheme may also take place in a single concerted process in which the deprotonation of the hydroxyl group and the cleavage of the C_α—C_β bond occur simultaneously. This was found in the dealdolization of complicated β-hydroxyketones[312] and in the cleavage of β-hydroxyacids and -esters[313].

In the alkaline cleavage of 4-hydroxy-3-methoxy-β-nitrostyrene[314], the yellow phenolate **146** loses its color on standing, owing to hydration. Kinetic analysis points to attack by hydroxide ions (step 1a). This is one of the systems in which there is an accumulation of an

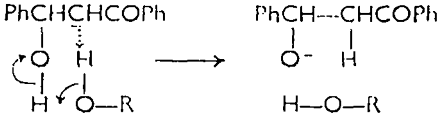

(146)

intermediate, and the decomposition of the latter is rate determining in product formation. Acidification of the mixture immediately after the disappearance of the color regenerates the latter, but does not do so in later stages of the reaction. This shows that step (1a) is reversible and **146** is reformed in the first case from the accumulated intermediate, but not from the end-products. Separate kinetic measurements for the disappearance of the color on the one hand and the appearance of the products on the other show that the concentration of the intermediate (**142** or **143** in Scheme 7), calculated at identical overall reaction percentages, becomes higher at higher pH, but at the same time its base-catalyzed decomposition is also accelerated.

The general cleavage scheme with variation (1a) applies also to the hydrolysis of chalcone and its six mononitro derivatives in 95% ethanol[315]. The ratio k_7/k_{-7} is very small and no ketolic intermediate

$$Ar^1CH{=}CHCOAr^2 + H_2O \xrightarrow{OH^-} Ar^1CHO + CH_3COAr^2$$

of type **143** is accumulated. This ketol has been prepared independently from benzaldehyde and acetophenone and the rate of its decomposition was shown to be very much faster than that of the chalcone[316]. In a possible modification of the general scheme, which may also be applied to other systems[315], the proton-transfer steps (2), (3) and (4) may be superseded by a direct transformation of **141** to **143** or of **142** to **144** with the participation of a solvent molecule in the transition state in a manner similar to that proposed for ester hydrolysis[317].



The cleavage of benzylidenemalononitriles in neutral 95% ethanol[301] is also in accordance with the general scheme, with no aldol accumulation. The attacking nucleophile was identified as a

$$ArCH{=}C(CN)_2 \xrightarrow{H_2O} ArCHO + CH_2(CN)_2$$

water molecule by analogy of the first step to that in the isomerization of ethyl *o*-methoxybenzylidenecyanoacetate (see section VII), and by the relatively small inhibition of the reaction by very dilute protonic acids. Since the extent of inhibition with identical acid concentrations is different with different substrates, it is not due to the lowering of the hydroxyl ion concentration in the medium, but again to inhibition in later proton-transfer steps. Competition between steps (1) and (1a) occurs in more basic solutions and depending upon the substrate used, the nucleophilicity of OH^- ions is found to be about 10^4 to 10^6 times higher than that of water molecules. A similar OH^-/H_2O reactivity ratio was observed in attacks on saturated carbon atoms[318]. Using buffers, the cleavage is accelerated by higher $Et_3N/Et_3N \cdot HCl$ buffer concentrations in the alcoholic medium, but phthalate buffer does not show the same effect. This was attributed to the non-ideal behavior of the first buffer in ethanol. However, general base catalysis by both buffers in the proton-abstraction steps (2) and (4) would also fit the results assuming that the catalytic coefficient of phthalate is much lower in these steps than that of triethylamine. The rates rose considerably on adding water to the medium, probably owing both to the stabilization of the zwitterionic intermediate **141** by the more polar solvent, and to the increase in the amount of the reagent.

Systems activated by only one carboxyl group are much less reactive. The negative charge of the carboxylate group lowers the electrophilic character of the β-carbon and also repulses approaching anions. Therefore, rather drastic conditions are necessary for the cleavage of the double bond, *i.e.* the use of alkali melts[319]. In unsaturated acids, in which the double bond is distant from the carboxyl group, the acid generally undergoes an initial base-catalyzed isomerization to the corresponding α,β-unsaturated acid. The products of the cleavage are acetic acid and a second acid containing two carbon atoms less than the starting material[319,320], obtained in the strongly alkaline medium by secondary reaction.

2-Phenylacrylic acid gives on alkaline cleavage formic and phenylacetic acids, according to the general scheme. By the use of ^{14}C either as shown below or by labeling C_α, the cleavage was shown[321] to take place according to (A) with only slight intrusion of (B).

$$\mathrm{CH_2{=}\!\!\!\!\mid\;C(Ph)^{14}COOH} \longrightarrow \mathrm{HCOOH + PhCH_2{}^{14}COOH} \qquad \text{(A)}$$

$$\mathrm{CH_2{=}C(Ph)\mid{}^{14}COOH} \longrightarrow \mathrm{H^{14}COOH + PhCH_2COOH} \qquad \text{(B)}$$

The influence of α- and β-substituents on the cleavage rates has been investigated quantitatively. Tables 12 and 14 summarize these results as well as activation parameters for solvent-catalyzed and for hydroxyl ion catalyzed reactions. With ring-substituted benzylidenemalononitriles, the Hammett reaction constants[322] were found to have high and positive values pointing to the requirements of a highly positive reaction site.

It is interesting to note that in this system any factor leading to enhanced overall reaction rates, *e.g.* addition of water or of basic buffers to the ethanolic solution or increase of temperature, causes a convergence of the rates with different substituents. This is reflected in the decrease in the ρ values of the Hammett equation in Table 13.

TABLE 12. Rate coefficients and activation parameters[301] for the solvent-catalyzed cleavage $XC_6H_4CH{=}C(CN)_2 + H_2O \rightarrow ArCHO + CH_2(CN)_2$ in 95% ethanol at 40°.

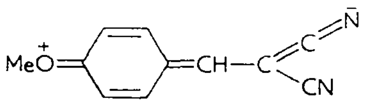
X	10^5k_1 (sec^{-1})	E_a (kcal/mole)	$-\Delta S^\ddagger$ (e.u.)
p-NO_2	131	7·3	53
o-Cl	28·9	16·2	27·4
m-Cl	21·9	16·5	27
p-Cl	11·3	13·8	37
H	3·46	20·3	18·5
p-MeO	0·239	15·5	39·3

TABLE 13. Hammett ρ values of the hydrolysis of benzylidenemalononitriles in different conditions[301].

Temperature (°c)	30		40						
ρ in 95% ethanol	2·36		2·04						
% of water in ethanol	1	2	4	6	8	10	20	32	50
ρ at 40°	2·12	2·14	2·10	2·00	2·02	1·92	1·80	1·58	1·56
10^3 [TEA[a],TEA·HCl] (mole/l.)	0	1	2	5					
ρ at 40°	2·04	1·80	1·72	1·55					

[a] TEA = triethylamine.

The strong effect of β-substituents can be seen from the tables. The reactivity order *ortho* > *meta* > *para* of the three chlorobenzylidenemalononitriles (Table 12) and the nitrochalcones (Table 14) shows that the effect of these groups is inductive, falling with increasing distance from the reaction site. An additional explanation is required for the effect of methoxy groups (which do not fall on the straight line determining the Hammett reaction constant), in the presence of which, resonance structures like **147** lower the contribution of reactive structures like **148**. In the *o*-methoxy derivatives, structures like **149** are less important than **150**, as the latter does not require coplanarity of the whole molecule and is therefore less hindered sterically so that the compound is more reactive than its *para* isomer[323]. Structure **149** will be even more hindered in the *cis* isomer (*cis* aryl/carbethoxy) and, accordingly, an additional rate enhancement is found in the hydrolysis



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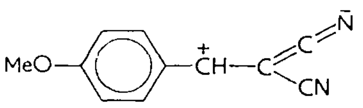

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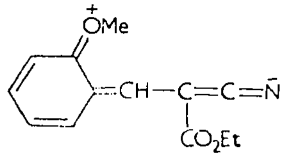

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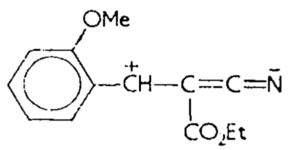


(150)

of the latter[324]. Substitution of the β-hydrogen atom by a cyano group enhances the cleavage rates[301], probably owing to its inductive effect. However, the resonance effect of the cyano group leads to an enhanced electrophilicity also on C_α and the overall reactivity of the double bond is increased. The same argument explains the exceptional sensitivity of the completely symmetrical tetracyanoethylene molecule towards nucleophilic attacks[233].

The effect of C_α substituents on cleavage reactions was studied in detail. The data in Table 14 also show clearly the relatively high activation exerted even by a single electron-attracting group at C_α compared to the inertness of unactivated systems. The effect of a second activating group added to an α-cyano group is CN > CO_2Et > $CONH_2$[323]. A linear correlation was found between log *k* for the hydrolysis of four compounds of the general formula p-$MeOC_6H_4CH{=}CXY$ and the maxima of the *K* bands in the corresponding ultraviolet spectra. This supports the proposed reaction mechanism since it may be assumed that forms like $Ar\overset{+}{C}H{-}CY{=}\overset{-}{X}$ are responsible both for the nucleophilic attack on the double bond and for the spectral transitions. No similar contributing structures in which a positive charge would appear on the β-carbon can be written formally for the nitro substituent in the aroyl group of chalcones. Nevertheless, it was proposed that the activation is due to a resonance effect here too, transmitted to the β-carbon through the crossconjugated carbonyl group, with inductive effects having only a minor role[315].

TABLE 14. Catalytic rate coefficients ($k_2 = k_1/[OH^-]$) and activation parameters for the base-catalyzed cleavage

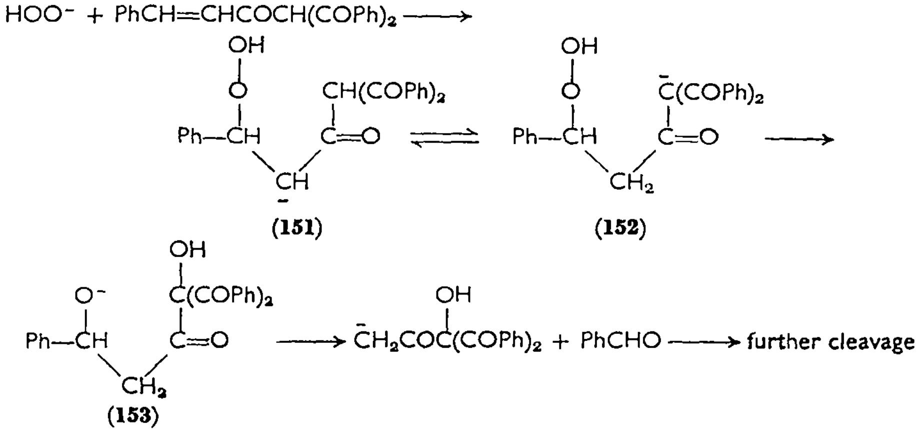
$$ArCH{=}CHXY + H_2O \xrightarrow{OH^-} ArCHO + CH_2XY \text{ in 95\% ethanol.}$$

Ar	X	Y	10^2k_2 (l./mole sec)	Temp. (°c)	E_a (kcal/mole)	$-\Delta S^\ddagger$ (e.u.)	Ref.
C_6H_5—	H	COC_6H_5	0·0075	35	20·0	14·9	315
o-$NO_2C_6H_4$—	H	COC_6H_5	0·200	35	12·6	32·8	315
m-$NO_2C_6H_4$—	H	COC_6H_5	0·0766	35	19·1	12·2	315
p-$NO_2C_6H_4$—	H	COC_6H_5	0·0583	35	20·3	9·4	315
C_6H_5—	H	$COC_6H_4NO_2$-o	0·030	35	18·1	18·1	315
C_6H_5—	H	$COC_6H_4NO_2$-m	0·100	35	20·0	9·6	315
C_6H_5—	H	$COC_6H_4NO_2$-p	0·135	35	18·4	14·0	315
p-HO(m-MeO)C_6H_3—[a]	H	NO_2	7·85	25	—	—	309
C_6H_5—	CN	CO_2Et	670	40	—	—	323
o-$MeOC_6H_4$—	CN	CO_2Et	198	40	—	—	323
p-$MeOC_6H_4$—	CN	CN	1410	40	11·7	18·3	323
p-$MeOC_6H_4$—	CN	CO_2Et	171	40	13·1	18·0	323
p-$MeOC_6H_4$—	CN	$CONH_2$	34·9	40	16·2	11·1	323
p-$MeOC_6H_4$—	$CONH_2$	$CONH_2$	0·026	40	—	—	323

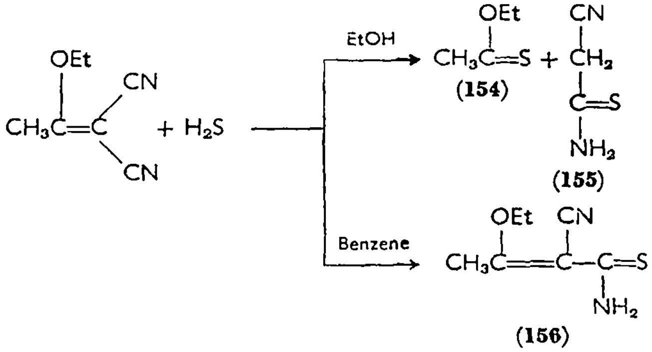
[a] In water.

In cases when step (1) of Scheme 7 is rate determining, this should produce a strongly negative entropy change, as a zwitterion with separated charges is formed from two neutral molecules. On the other hand, the attack of a small OH^- anion on a neutral molecule with the formation of a large carbanion (step 1a) will produce a relatively smaller change in the entropy. This is indeed reflected in Tables 12 and 14. In the hydrolysis of p-methoxybenzylidene-malononitrile, which was investigated both in the absence and presence of base, the change from step (1) to (1a) lowered the value of E_a by 3·8 kcal/mole, and the difference in the two $\Delta S^\ddagger$ values is 21 e.u.

The conditions used for alkaline epoxidation may also lead to fragmentations. With α,β-unsaturated ketones containing an enolizable hydrogen, two aldehydes are obtained, and not the epoxide. The main products obtained from $PhCH{=}CHCOCH(COPh)_2$ are benzaldehyde and acetaldehyde; here the mechanism probably involves a primary attack on the β-carbon by the hydroperoxide anion, followed by isomerization of **151** to the more stable anion **152**. Internal attack of the negative carbon on the hydroperoxide group and cleavage of the O—OH bond gives **153** (equal to **144** in Scheme 7 with Ar = Ph, X = $—COC(COPh)_2OH$, Y = H), which decomposes with the formation of benzaldehyde. Further cleavage analogous to the haloform reaction, gives acetaldehyde and more benzaldehyde[325].



Cleavage may be induced also by hydrogen sulfide. The reaction of ethoxyethylidenemalononitrile in ethanol or in dimethyl formamide leads to the formation of **154** and **155**, the latter being formed by addition of H_2S to one of the cyano groups of the malononitrile moiety[326]. In benzene only addition of H_2S to a cyano group occurs without cleavage of the C=C bond yielding **156**.



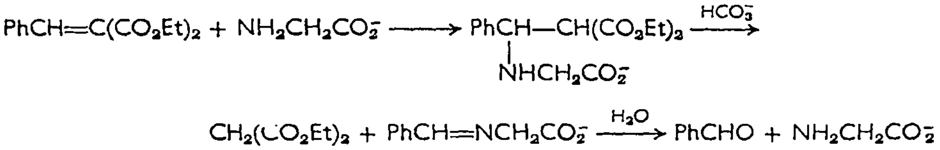
B. Cleavage by Nitrogen-containing Reagents

Fragmentation reactions with nitrogen-containing reagents leading to the formation of C=N bonds are less frequently met, although the

$$R^1R^2C{=}CR^3R^4 + H_2NX \rightleftharpoons R^1R^2C{=}NX + H_2CR^3R^4$$
$$(X = NH_2, NHAr, H, Et, NHCONH_2)$$

reverse condensation reaction of active methylene compounds with various compounds containing C=N groups takes place easily and usually in good yields[327]. The cleavage is complicated by the reactivity of the C=N bond, which especially in aqueous media gives the corresponding amine and carbonyl compounds. The Schiff bases which may be formed as primary reaction products in the amine-catalyzed hydrolysis are rapidly cleaved into the corresponding carbonyl compound with regeneration of the catalytic amines[298,328].

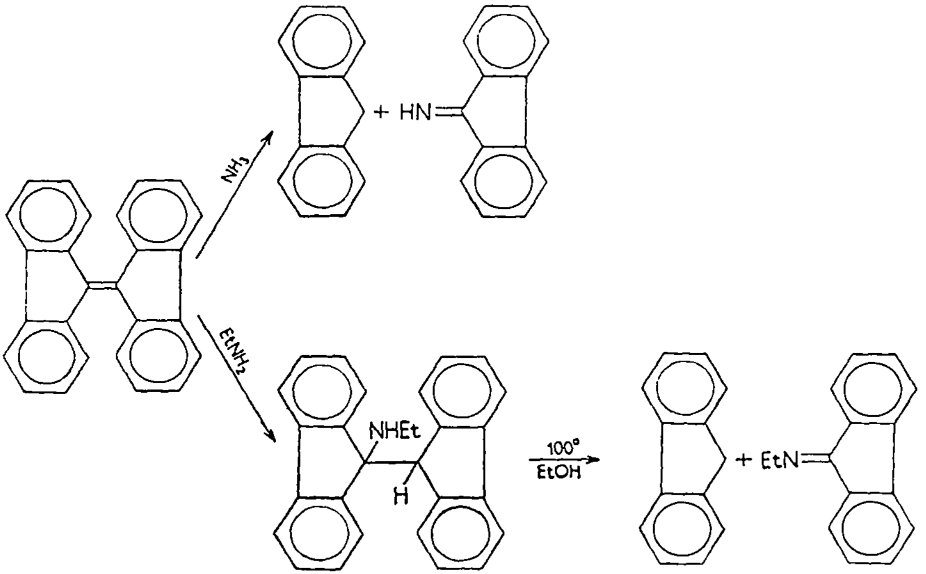
In the hydrolysis of diethylbenzylidene malonate catalyzed by amino acids the reaction rate at pH 8–10 is proportional to the concentration of the aminocarboxylate ions ($H_2NCH_2COO^-$), and leads to the formation of an addition product. In the presence of bicarbonate ions this adduct is rapidly cleaved to diethyl malonate and to the benzylideneglycinate anion, the latter decomposing further in the aqueous medium[329].



$$PhCH{=}C(CO_2Et)_2 + NH_2CH_2CO_2^- \longrightarrow \underset{\displaystyle NHCH_2CO_2^-}{PhCH}{-}CH(CO_2Et)_2 \xrightarrow{HCO_3^-}$$

$$CH_2(CO_2Et)_2 + PhCH{=}NCH_2CO_2^- \xrightarrow{H_2O} PhCHO + NH_2CH_2CO_2^-$$

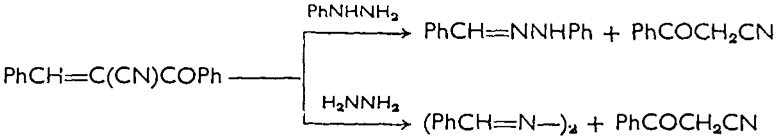
Dibiphenyleneethylene, although symmetrical and lacking the usual activating groups, reacts with ammonia or with ethylamine as shown[2]:



(157)

The second reaction goes through an amine–alkene addition product **157** which is analogous to aldols in the case of cleavage by water.

Hydrazine hydrochloride and hydroxylamine hydrochloride yield only the corresponding Michael adducts, but in the fragmentation of the double bond with other nitrogen-containing reagents, hydrazine yields hydrazones; phenylhydrazine, phenylhydrazones; semicarbazide, semicarbazones, and in each case also the appropriate active methylene compounds as shown in the examples below[330,331].



$$PhCH{=}C(CN)COPh \xrightarrow{PhNHNH_2} PhCH{=}NNHPh + PhCOCH_2CN$$

$$PhCH{=}C(CN)COPh \xrightarrow{H_2NNH_2} (PhCH{=}N{-})_2 + PhCOCH_2CN$$

$$PhCH{=}C(CN)COC_6H_4NO_2\text{-}p \xrightarrow{PhNHNH_2} PhCH{=}NNHPh + CH_2(CN)COC_6H_4NO_2\text{-}p$$

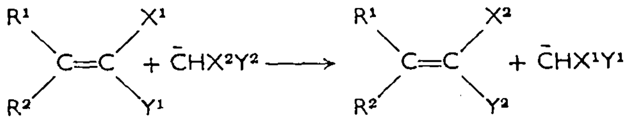
$$p\text{-}O_2NC_6H_4CH{=}C(CN)COPh \xrightarrow{H_2NNH_2} p\text{-}O_2NC_6H_4CH{=}NHNH_2 + CH_2(CN)COPh$$

$$XC_6H_4CH{=}CHCOPh \xrightarrow{H_2NNHCONH_2} XC_6H_4CH{=}NNHCONH_2 + PhCOCH_3$$

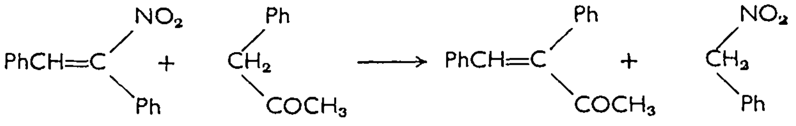
A mechanism involving a stable addition intermediate was proposed for each case, but its existence was not proved.

C. Arylmethylene and Alkylidene Transfer

The normal product of C=C bonds with carbanions is the Michael adduct, but in some cases cleavage occurs. A necessary condition for this seems to be that the attacking carbanion should contain a hydrogen atom bound to the carbon carrying the negative charge. The net reaction then is the exchange of a $=CX^1Y^1$ group for a different $=CX^2Y^2$ group. Reactions of this type were observed accompanying

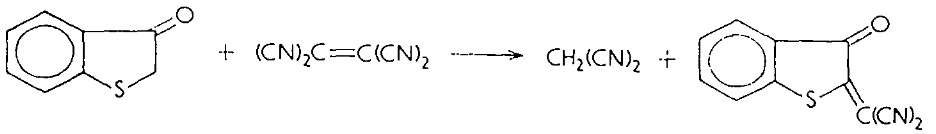


Michael condensations[332-336a], and a typical example is the formation of **160** among other products in the condensation of **158** with **159**[333].

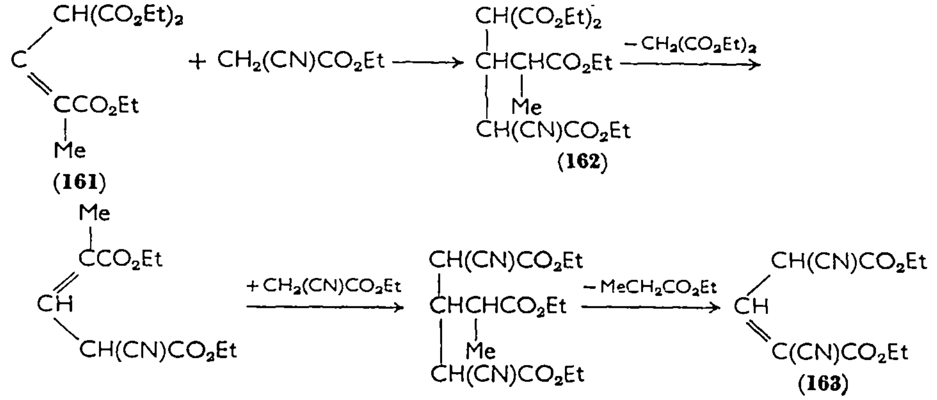


(158) **(159)** **(160)**

Recently it has been shown that even symmetrical alkenes can undergo cleavage by carbanionic attacks. Thus, tetracyanoethylene is cleaved, *e.g.* by 2*H*,3*H*-benzo[*b*]thiophen-3-one, to give malononitrile and the corresponding 2-dicyanomethylene compound[336b].



Two consecutive reactions of this type take place in the base-catalyzed reaction of the ester **161** with ethyl cyanoacetate, when the malonate residue is the leaving group in the first stage of the reaction, and the ethyl propionate group leaves after the second attack to give **163**[334].

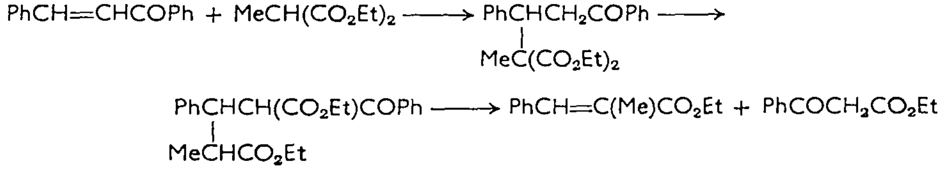


(161)

(162)

(163)

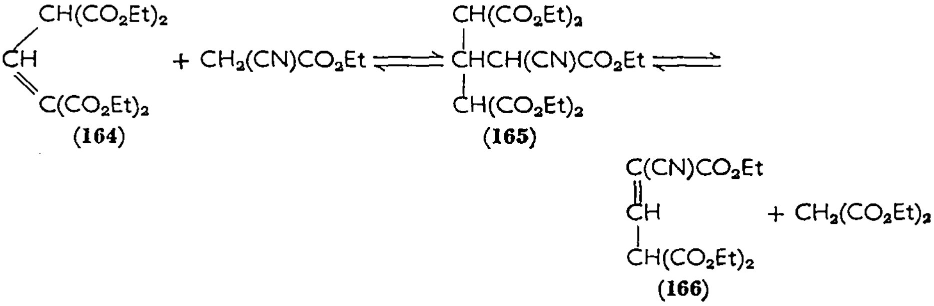
In another reaction sequence, both a rearrangement of the primary addition product (abnormal Michael reaction) and, at least formally, a cleavage of the starting material take place[336], although the attacking carbanionic site does not contain a hydrogen atom.



$$PhCH{=}CHCOPh + MeCH(CO_2Et)_2 \longrightarrow \underset{\textstyle MeC(CO_2Et)_2}{PhCHCH_2COPh} \longrightarrow$$

$$\underset{\textstyle MeCHCO_2Et}{PhCHCH(CO_2Et)COPh} \longrightarrow PhCH{=}C(Me)CO_2Et + PhCOCH_2CO_2Et$$

The extent of the cleavage and the position of the equilibria are influenced by the conditions of the reaction. Since the elimination of an active methylene compound, or rather of the corresponding carbanion, is a reaction with a high activation energy[75], addition products such as the tetraester **162** may be isolated when working at relatively low temperatures. The equilibrium in the presence of excess sodium ethoxide will favor the most stable carbanion, which is usually the donor of the Michael reaction. On the other hand, in the presence of only catalytic amounts of a strong base or in the presence of weak bases, the production of the adduct will be preferred. In the reaction of **164** with ethyl cyanoacetate, only cleavage products **166** and diethyl malonate can be isolated in the presence of an equimolecular amount of sodium ethoxide, whereas, by using piperidine as the catalyst, the adduct **165** is obtained[334].



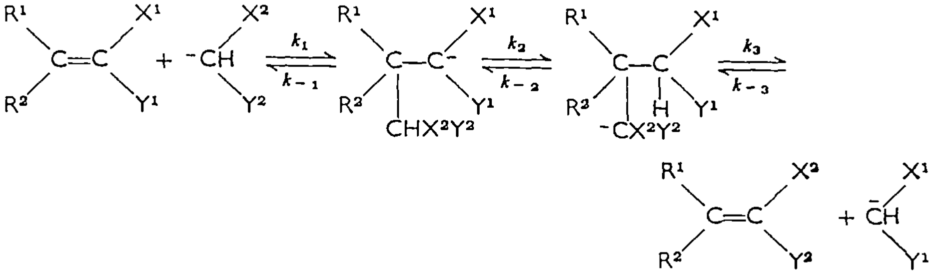
The catalytic effect of malononitrile on the hydrolysis of ethyl benzylidenecyanoacetates may also be due to a similar exchange reaction, since the cleavage of the dicyano derivative is much faster than that of the cyanocarbethoxy derivative[328].

Some information is available on preferentially formed products. Table 15 shows that the leaving group is as a rule a weaker carbon acid than the entering one.

TABLE 15. Leaving and entering groups in cleavage reactions of double bonds.

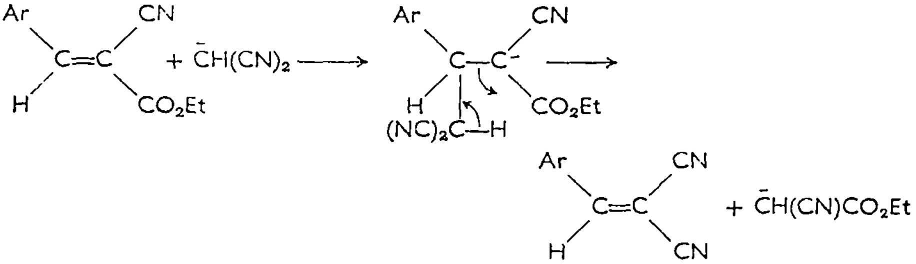
System	Leaving group	Entering group	Ref.
Ethyl dicarboxyglutaconate	$CH_2(CO_2Et)_2$	$CH_2(CN)CO_2Et$	334
Ethyl γ-methylcarboxyglutaconate	$MeCH(CO_2Et)_2$	$CH_2(CN)CO_2Et$	334
Ethyl benzylidenecyanoacetates	$CH_2(CN)CO_2Et$	$CH_2(CN)_2$	6
α-Nitrostilbene	$PhCH_2NO_2$	$PhCH_2COCH_3$	333
p-Methoxybenzylidene methyl isopropyl ketone	$CH_3COCH(CH_3)_2$	$CH_2(CO_2Et)_2$	335

The same factors which enhance the acidity of a carbon acid also give added resonance stabilization to the alkenic compound, and this may be the actual driving force for the exchange of groups. Using the detailed reaction scheme below it can be argued that when the anion $\bar{C}HX^2Y^2$ is more stable, the attacked system $R^1R^2C{=}CX^1Y^1$ is less reactive than the product $R^1R^2C{=}CX^2Y^2$ and, at the same time, the newly formed anion $\bar{C}HX^1Y^1$ is a stronger base and probably



also a stronger nucleophile. Accordingly, k_{-3} should be larger than k_1. In addition, the elimination of a more stable carbanion should be faster than that of a less stable one[75]. Therefore, the reaction seems to be governed not by kinetic, but by thermodynamic control, as mentioned above.

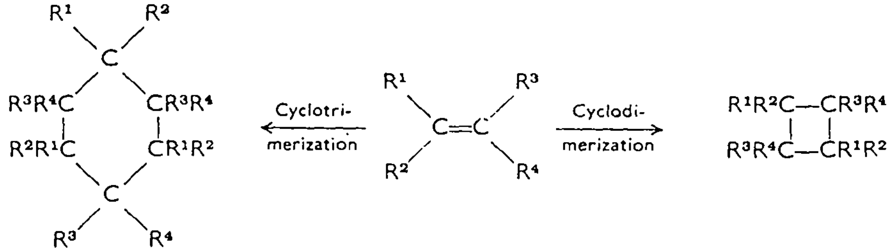
By using more reactive substrates or nucleophiles or both, milder experimental conditions suffice. Uncatalyzed arylmethylene transfer takes place with 95% yield between *o*-methoxybenzylidene cyanoacetate and malononitrile. In this strongly activated system, no addition product could be detected, and the mechanism proposed for this reaction[6] does not include any intermediate apart from the



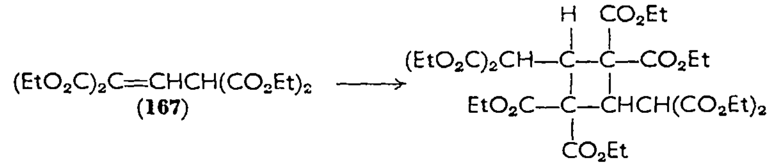
carbanion formed in the primary step. This is assumed to undergo cleavage by a four-center reaction, assisted by the presence of a negative charge in the vicinity of the acid hydrogen atom. This mechanism may possibly apply also for other facile cleavages of the C=C bond, both with carbanions and other nucleophiles.

VI. CYCLODIMERIZATION AND CYCLOTRIMERIZATION

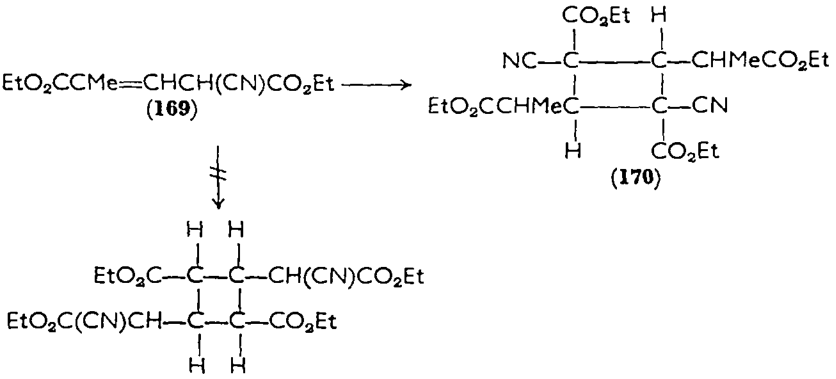
Nucleophilic attack on double bonds may lead to the formation of cyclic dimers (cyclobutane derivatives) and of cyclic trimers (cyclohexane derivatives). The role of the nucleophile in the cyclization reaction is purely catalytic, since it is eliminated from the intermediate during product formation.



In many cases the primary step in the dimerization is the abstraction of a proton from an allylic carbon atom, followed by Michael condensation of the anion with an additional molecule of the starting material. For instance, cyclic dimers **168** are obtained in the pyridine-catalyzed reaction of tetraethyl propene-1,1,3,3-tetracarboxylate **167**, but not all the original α- and β-carbon atoms are incorporated in the four-membered ring; in the reaction of diethyl 4-cyanobutene-2,4-dicarboxylate (**169**) the product obtained is **170** and not **171**[8].

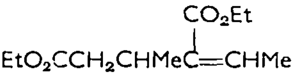


(167) **(168)**



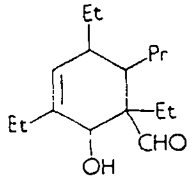
(169) **(170)** **(171)**

Similarly, by primary proton abstraction, linear dimerization of ethyl crotonate gives **172**[337,338] and the self-condensation of 2-ethyl-2-hexenal yields a cyclic dimer **173**[339].



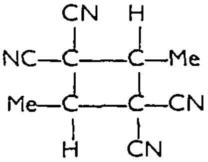
$EtO_2CCH_2CHMe\overset{CO_2Et}{C}{=}CHMe$

(172)



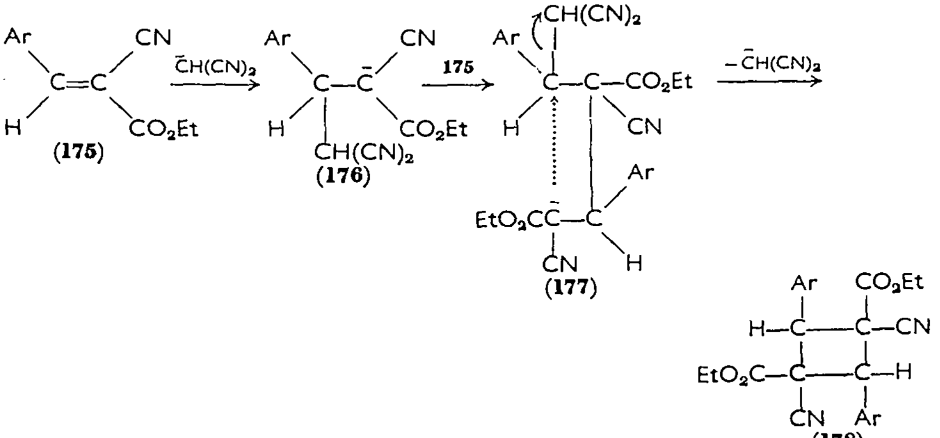
(173)

Dimers of unidentified structures were obtained as side products in the piperidine-catalyzed condensation of malononitrile with aromatic aldehydes[34] or from isopropylidenemalononitrile in piperidine[340a]. The product of the latter reaction was recently identified as an amino-substituted cyclohexene derivative[340b]. In the condensation of acetaldehyde with malononitrile, a cyclic dimer of the product (ethylidenemalononitrile) was obtained and identified as 2,2,4,4-tetracyano-1,3-dimethylcyclobutane (**174**)[341].



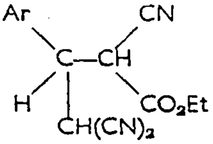
(174)

Ethyl 2-methoxybenzylidenecyanoacetate (**175**, Ar = *o*-$MeOC_6H_4$—) gives the corresponding cyclodimer **178** in a fast reaction, with rather irreproducible and low yields[6]. The following mechanism was proposed for this reaction, catalyzed by anions of carbon acids such as malononitrile or ethyl cyanoacetate:



(178)

Nucleophilic attack by the malononitrile anion produces the carbanion **176** which may react by two different intramolecular routes, leading either to the *trans* isomer of the starting material (if this was originally *cis*) by elimination of the attacking nucleophile, or to an arylmethylenemalononitrile by elimination of the ethyl cyanoacetate anion. Alternatively, **176** may react also by two different bimolecular routes: it may capture a proton from the solvent to give the Michael adduct **179** or react with a second molecule of the starting material to give the carbanion **177** which in turn yields the final cyclic product **178** after elimination of the nucleophile. As no second cyclobutane derivative **180** could be detected in the reaction mixture, it seems that the Michael adduct cannot be an intermediate in the formation of **178**,



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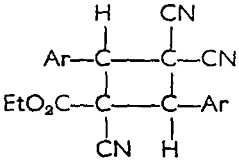


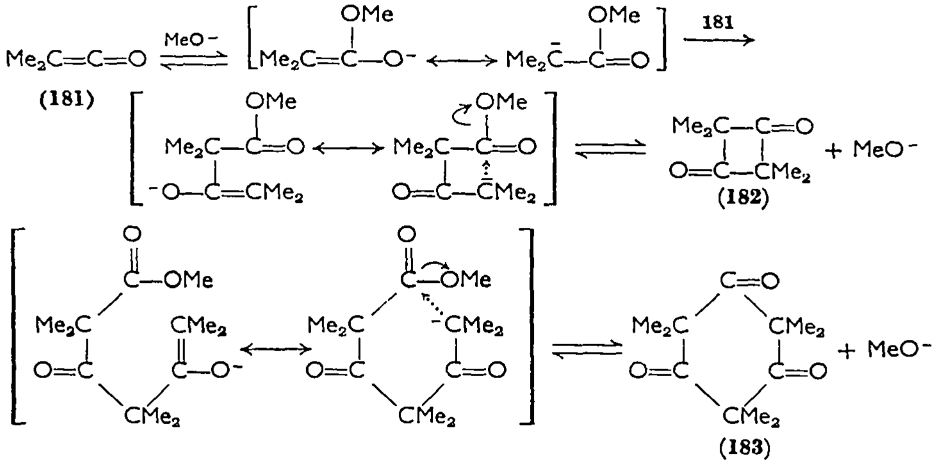
(180)

since **179**, by loss of a proton from its $CH(CN)_2$ group and reaction with **175**, should be able to produce **180** at least as easily as **178**.

The irreproducibility in the cyclobutane formation can be rationalized by taking into consideration the mechanistic similarity of the various possible routes leading to different products, so that very slight differences in the reaction conditions may suffice to give largely differing product ratios. The rapid unimolecular route leading to arylmethylene transfer will be preferred over the bimolecular dimerization in which only one discrete conformation of **177** can produce **178**[324]. The stereochemistry of the latter was not investigated, but it is identical to the product obtained by photodimerization[342], and it can be assumed that the aryl and carbethoxy groups retain their original *trans* configuration.

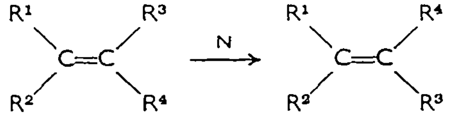
The mechanism of the cyclodimerization is a close analog of the benzoin condensation. Both reactions involve initial nucleophilic attack on a positively polarized carbon, followed by a nucleophilic attack of the carbanion (or its product of rearrangement in the benzoin case) on a second molecule, and are completed by formation of a stable dimer after elimination of the nucleophile.

Nucleophilic cyclotrimerizations in systems containing only C=C bonds are not known. However, the reversible reactions of dimethylketen (**181**) and its dimer tetramethyl-1,3-cyclobutanedione (**182**) to yield the trimer hexamethyl-1,3,5-cyclohexanetrione **183**[343], and the similar reaction of diphenylketen[344] have been formulated as occurring through a primary nucleophilic attack on the carbon atom common to the carboxyl and to the alkene groups with formation of a stable six membered ring[343].



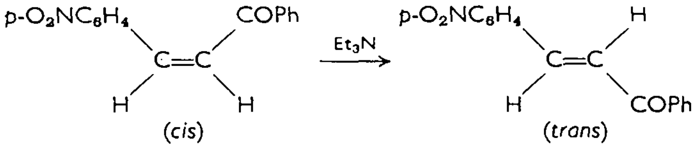
VII. NUCLEOPHILIC ISOMERIZATION

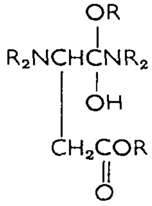
Nucleophilic *cis–trans* isomerizations of compounds containing an activated double bond seem formally to be simpler than other nucleophilic reactions, which cause larger changes in the substrate. The



isomerization reaction may serve as a useful tool for isolating the effects of the structure of the substrate and of the medium on the primary reversible nucleophilic attack on the one hand and on the stability of carbanionic intermediates on the other. In the absence of kinetic complications, and with reagents which give neither substitution nor addition products with the substrate, nucleophilic isomerizations using the same compound should allow the determination of reactivity series of diverse nucleophiles.

Cis–trans isomerizations have been the subject of many investigations[345], carried out in the gas phase[346], in acid solutions[347,348] or in the presence of free radicals[349]. Nucleophilic isomerizations were generally noted incidentally in the course of synthetic studies as in the isomerization of *cis*-2-methoxybenzylidenecyanoacetic acid in its preparation from 3-cyanocoumarine[342]. The amine-catalyzed isomerization of *cis*-4-nitrochalcone was studied in more detail[350]. In some cases the product of a nucleophilic addition to the double bond may be a stable intermediate in the isomerization. Thus, the addition product of ethanol with the lower melting isomer of 2-nitro-2-phenyl-1-(*p*-methoxyphenyl)ethylene can be isolated, but gives, on heating, the higher melting isomer of the starting material[351]. In the relatively unreactive maleate–fumarate system, ammonia[352] and pyridine[353] were shown to catalyze the conversion of maleic to fumaric acid, and a great variety of primary and secondary aliphatic, aromatic and heterocyclic amines convert dimethyl maleate to the fumarate[354]. Tertiary amines, even strongly basic ones, give no reaction, *e.g.* no conversion took place in the course of one year at room temperature in the presence of triethyl amine in ether. This lack of reactivity was ascribed to the absence of a hydrogen atom on the amino nitrogen, which was assumed to be necessary for the formation of coordinative bonds between the carbonyl oxygen atoms with two amine molecules, partially abolishing the double bond character of the central bond and permitting free rotation and isomerization. Since this mechanism is based on the proton-donating capacity of the amines, strong protonic acids should be much stronger catalysts, contrary to experimental results[355]. A modified mechanism in which one of the amine molecules in the intermediate **184** acts as an electron acceptor and the other as an electron donor was suggested[355,356]. This mechanism fits the observed kinetics (first order in the maleate and second order in the amine[355,356]), accounts for the correlation of the basic strength of





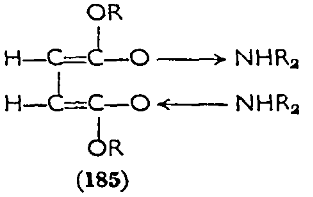
(184)

most primary and secondary amines used with the rate of the isomerization (Table 16), and also for the unreactivity of tertiary amines. It also explains why, in the isomerization of free maleic acid (in contrast to its esters), tertiary amines become effective catalysts; here the tertiary base acts as an electron donor only, while the ammonium ions formed from the organic acid and the base, can act as the proton donors.

TABLE 16. Catalytic effect of various amines on the isomerization of diethyl maleate[356] at 24·9°C.

Amine	k_3 (l.^{2}/mole^2 sec)	pK_a
Piperidine	$7{\cdot}66 \times 10^{-2}$	11·12
Me_2NH	$6{\cdot}49 \times 10^{-2}$	10·70
$MeNH_2$	$3{\cdot}84 \times 10^{-2}$	10·64
$EtNH_2$	$3{\cdot}13 \times 10^{-3}$	10·67
$PhCH_2NH_2$	$2{\cdot}36 \times 10^{-3}$	9·37
Et_2NH	$5{\cdot}1 \times 10^{-4}$	11·0
$PhNH_2$	$6{\cdot}34 \times 10^{-7}$	4·58
PhNHMe	$6{\cdot}34 \times 10^{-7}$	4·85
Et_3N	0·0	10·72
Me_3N	0·0	9·82
Pyridine	0·0	5·19
$PhNMe_2$	0·0	5·21

This mechanism was criticized[356] considering the difficulty of direct attack on the double bond and the lack of isotope exchange in acid-catalyzed reactions of maleic acid in the presence of DCl[357]. An association was suggested between two amine molecules and the diester through the two carbonyl oxygens, again with one of the amine molecules acting as an electron donor and the second as a proton donor (**185**).



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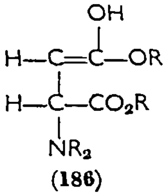
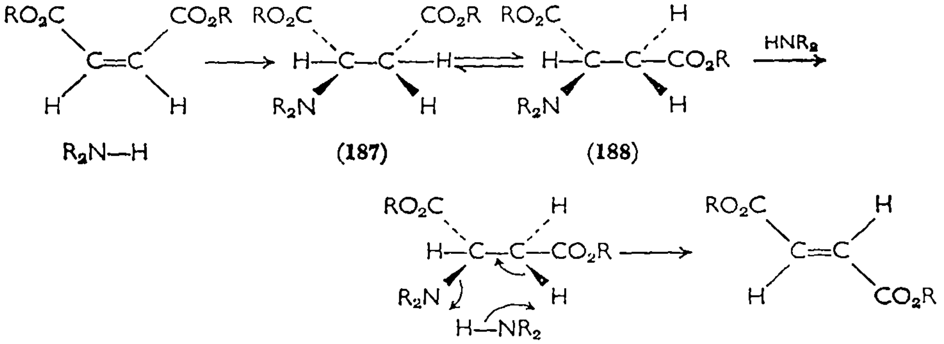


(186)

A mechanism involving a reversible 1,4-addition of the amine to the conjugated C═C—C═O system of the ester[253b] yielding **186** fits the lack of reactivity of tertiary amines, but does not account for the observed third-order kinetics. Moreover it implies the primary formation of a carbanion which, unless the reaction is a concerted one, should also be formed with tertiary amines, and should be able to isomerize.

The above-mentioned discrepancies may be explained by assuming an initial concerted (or very nearly concerted) addition of the amine to the C=C bond, in which the nucleophilic attack on the relatively weakly electrophilic C_β is assisted by a simultaneous electrophilic attack on C_α by the amino hydrogen:



(187) (188)

Without the intrusion of a second base molecule the addition product **187** and its rotamer **188** are stable and the reaction is essentially irreversible since the rate of uncatalyzed proton departure should be comparable to that found in the α-position of acetic acid (3×10^{-11} min^{-1})[91]. In the presence of an additional amine molecule, the rate determining step will be the elimination depicted as a concerted process, and the '*cis* effect'[252] leads to the formation of the fumarate.

This mechanism requires third-order kinetics, fits the fact that amine addition products were isolated in the course of the isomerization[355] and explains the correlation between the reactivity of the various amines and their proton basicity (pK_b). The electrophilic analog of this reaction is the third-order addition of bromine to double bonds where the second bromine molecule is required for the abstraction of bromide ions from the addition product in the form of Br_3^- ions[358].

According to this mechanism, enhanced electrophilicity of the β-carbon and enhanced stability of the carbanion formed will allow a change over the second-order kinetics with rate-determining attack on the β-carbon. In this case, electrophilic assistance will no longer be necessary, tertiary amines will also catalyze the reaction, and the isomerization rates should be correlated to the nucleophilicity of the amines towards unsaturated carbon. This was indeed observed in the nucleophilic isomerization of the reactive ethyl *o*-methoxybenzylidenecyanoacetate system[324], which isomerizes under the influence of such diverse nucleophiles as water, hydroxide ions, amines and various active methylene compounds. The isomerization rates at low catalyst concentrations are proportional to the concentration of the nucleophile (Table 17).

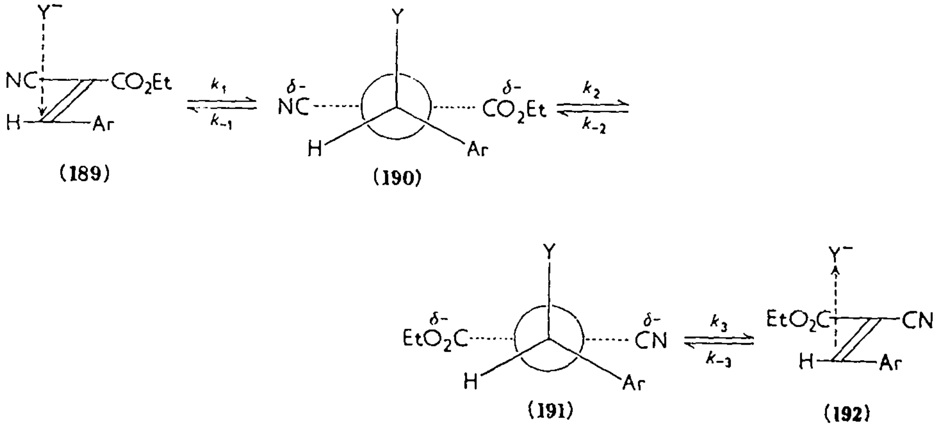
TABLE 17. Catalytic rate coefficients ($k_2 = k_{exp}$/stoichiometric catalyst concentration) for the *cis–trans* isomerization of ethyl 2-methoxybenzylidenecyanoacetate by various nucleophiles at 40° in ethanol[324].

Nucleophile	k_2 (l./mole sec)
OH^-	3·5
Et_3N	0·31
$CH_2(CN)_2$	0·11
$CH_2(CN)CO_2Et$	0·016
$KC(CN)_3$	0·3
H_2O	7×10^{-6}

As found already in fragmentation reactions, the reactivity of hydroxide ions is higher by almost six orders of magnitude than that of water molecules. The active methylene compounds most probably exert their catalytic influence through the corresponding carbanions, present in the reaction mixture only in very small concentrations. The nucleophilicity of these carbanions towards an unsaturated carbon atom should be very much higher than that of triethylamine, and indeed the catalytic effect of triethylamine–active methylene compound mixtures is much higher than the sum of the effect of the two catalysts separately. This exaltation can be accounted for by the equilibrium $R_3N + CH_2XY \rightleftharpoons R_3\overset{+}{N}H + \overset{-}{C}HXY$ which enhances the carbanion concentration. Under otherwise identical conditions, in a basic buffer solution in alcohol, the isomerization by malononitrile is 35 times faster than by ethyl cyanoacetate, in good agreement with the results obtained in the nucleophilic attack of the same compounds on carbonyl groups of aromatic aldehydes[359].

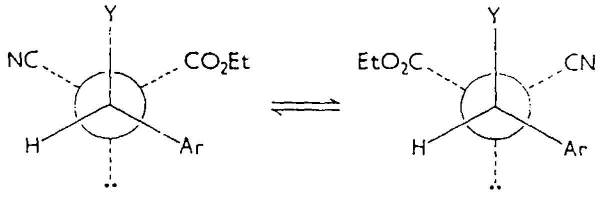
Isomerization studies help to identify the attacking reagent in other reactions of the same substrate. For example, in the fragmentation of benzylidenemalononitriles the nucleophile could be either a water molecule or a hydroxide ion. The fact that the isomerization rates do not change on adding up to 0·02 mole/l. perchloric acid to the mixture and are lowered only slightly in 0·2 molar acid is a clear indication that the nucleophilic species responsible for the isomerization is a neutral molecule and, hence by analogy, it can be assumed that the same species attacks in the first step of the fragmentation too.

The relative simplicity of isomerization reactions, in which the same product is always obtained from a substrate, irrespective of the nature of the attacking reagent, should in principle make it possible to determine the relative nucleophilicity of various nucleophiles towards unsaturated vinylic carbon atoms. Nevertheless, the study of the isomerization of ethyl *o*-methoxybenzylidenecyanoacetate[360] catalyzed by various amines, showed that complications arise. Although the reaction was first order in both the substrate and in the catalyst, the observed rate is not determined by the primary attack alone. The activation energies of these processes (Table 18) are so low that they certainly cannot be attributed to a step involving the formation of a carbon–nitrogen bond. The proposed reaction mechanism involves a perpendicular attack by the reagent Y^- and the formation of the carbanion **190** which by rotation can give its conformer **191**. Elimination from **190** or from **191** will give the isomers **189** or **192** respectively. The mechanism may also be formulated using tetrahedral carbanions, when the structures **193** and **194** take the place of **190** and **191**[324]. The step **193** $\rightleftharpoons$ **194** involves both rotation and inversion of the intermediates. It is doubtful whether the two pathways could be distinguished mechanistically, but the first formulation may be preferred for the present case, taking into account the high resonance stabilization of the planar carbanionic intermediates. Using the steady state



(189) (190) (191) (192)

approximation, the overall rate coefficient k_{exp} is determined by the ratio k_1k_2/k_{-1}, where k_1 and k_{-1} are the rate coefficients for the primary nucleophilic attack and its reversal, and k_2 is that for the rotation (and/or inversion) of the carbanion. Since only k_1 is a true measure of the carbon nucleophilicity of the amine, k_{exp} would measure this property only in two discrete cases, namely either when k_2/k_{-1} is constant for a series of amines, or when it is strictly proportional to k_1. Owing to the variety of steric and electronic factors involved, with the possible addition of electrostatic ones with zwitterionic intermediates, it is hardly probable that any one of the two above mentioned conditions should hold.



(193) **(194)**

The ratio $K = k_1/k_{-1}$ which is the equilibrium constant for the primary attack, was defined as the 'carbon basicity'[361] and a correlation may be expected between k_{exp} and K in the cases when k_2 is constant or nearly so for a series of amines. In a system with a zwitterionic intermediate, and in a solvent of low dielectric constant, it is well possible that the electrostatic factor dominates and nearly equalizes the values of k_2 with different amines. Alternatively, k_2 may be proportional to K as the same factors which increase the rotation rates also increase K by stabilizing the intermediate carbanion. The reactivity order of the secondary amines studied in the above system is identical with that found for their nucleophilic attack on 2,4-dinitrochlorobenzene[362].

No correlation can be expected between the isomerization rates governed by carbon basicity and between the proton basicity of the amines. In an attack on carbon, the steric requirements will be much more important than in the protonation of an amine. Indeed, the importance of steric effects is shown in the larger reactivity of the less hindered secondary amines as compared to the tertiary ones, although the electron availability on the nitrogen atom of the latter is greater. On the other hand, the low reactivity of heterocyclic as compared to other tertiary amines proves the importance of the electronic factor in the reaction (Table 18).

TABLE 18. Catalytic rate coefficients and activation parameters for the *cis–trans* isomerization of ethyl *o*-methoxybenzylidenecyanoacetate[360] in the presence of various amines in benzene at 40°.

Amine	k (l./mole sec)	E_a (kcal/mole)	$-\Delta S^{\ddagger}$ (e.u.)
n-Bu_2NH	7·5	5·06	42·5
n-Pr_2NH	7·5	4·0	45·8
iso-Bu_2NH	1·49	2·76	53·0
iso-Pr_2NH	0·58	4·6	53·7
n-Bu_3N	0·106	2·7	58·3
Et_3N	0·024	4·6	55·0
Pyridine	0·0106	3·1	66·0
2,6-Lutidine	0·00094	3·2	63·0

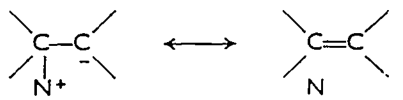
The low values for the activation energy and the high negative entropy changes can be rationalized by applying the equations

$$E_{\text{exp}} = E_1 + E_2 - E_{-1}$$

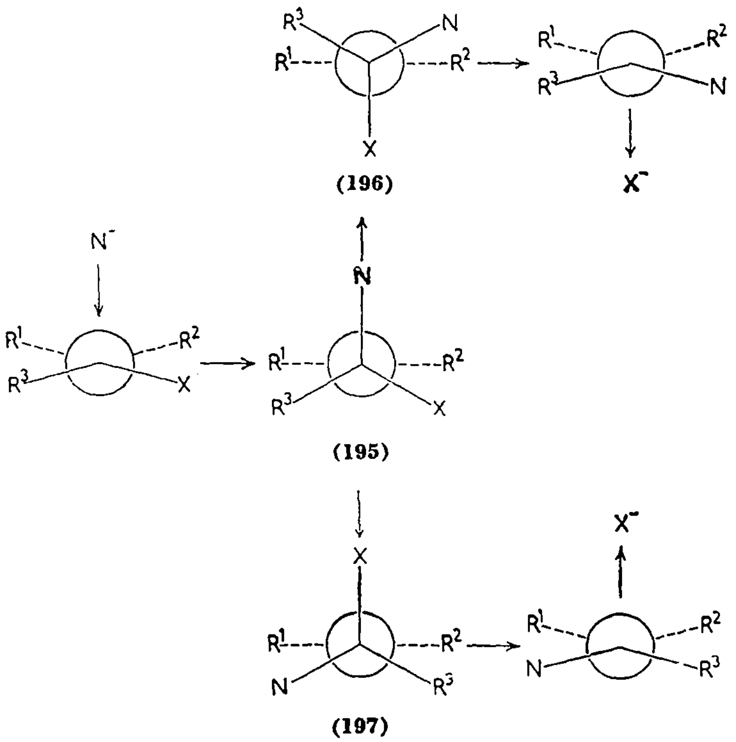
and

$$\Delta S^{\ddagger}_{\text{exp}} = \Delta S^{\ddagger}_1 + \Delta S^{\ddagger}_2 - \Delta S^{\ddagger}_{-1}$$

where the subscripts refer to the reaction steps in the sequence **189** → **192**. Using values found in the literature for similar reactions while assuming that the rotation in the intermediate is more than usually hindered owing to electrostatic causes and that the elimination step is more facile than in other *E*1cB reactions for the same reason (contribution of no-bond forms to the resonance hybrid), activation energy values can be calculated which are similar to the ones found experimentally. The values of the entropy of activation may be explained by the highly ordered state of the zwitterionic intermediate, when $\Delta S^{\ddagger}_{2(\text{rotation})}$ is low compared to the two other entropy values.



With the assumption $k_{-1} > k_2$ as argued above, the preferred retention of configuration in vinylic substitutions can be explained. If the nucleophile attacks perpendicularly to the plane of the double bond and the eliminated group leaves similarly, the elimination from the carbanionic intermediate can take place either from the conformer **196** formed by only 60° rotation in the primary intermediate **195**, or after 120° rotation, from conformer **197**. Since elimination is faster than rotation, it will occur preferentially from **196** with resulting overall retention of configuration. This analysis fits one of the reaction mechanisms proposed by Miller and Yonan[270].



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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 9

Reactions of alkenes with radicals and carbenes

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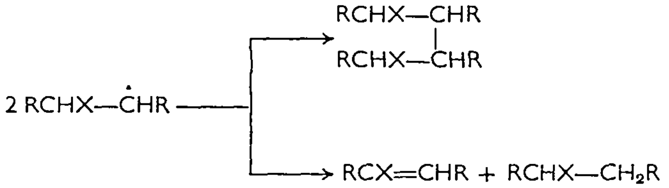
I. REACTIONS WITH RADICALS

A. Introduction

In general, the centre of highest reactivity in an alkene is at the double bond. In accord with this, free radicals usually react with olefins by addition to give new free radicals (equation 1), which subsequently react by dimerization, disproportionation, or radical transfer with another species present in the system (equations 2a, 2b and 3 respectively). In certain cases, dependent upon the structure of the alkene and upon the nature of the attacking radical, abstraction of an α-methylenic hydrogen atom may be a competing reaction. Such reactions derive activation in part from the high stability of the resulting substituted allyl radical (equation 4). Such allylic reactions

$$\mathrm{X\cdot + RCH{=}CHR \longrightarrow RCHX{-}\dot{C}HR} \tag{1}$$



$$2\,\mathrm{RCHX{-}\dot{C}HR} \longrightarrow \begin{matrix}\mathrm{RCHX{-}CHR}\\ |\\ \mathrm{RCHX{-}CHR}\end{matrix} \tag{2a}$$

$$2\,\mathrm{RCHX{-}\dot{C}HR} \longrightarrow \mathrm{RCX{=}CHR + RCHX{-}CH_2R} \tag{2b}$$

$$\mathrm{RCHX{-}\dot{C}HR + ZY \longrightarrow RCHX{-}CHZ{-}R + Y\cdot,\ etc.} \tag{3}$$

$$\mathrm{X\cdot + RCH_2{-}CH{=}CH_2 \longrightarrow XH + R\dot{C}H{-}CH{=}CH_2 \longleftrightarrow RCH{=}CH{-}\dot{C}H_2} \tag{4}$$

are particularly favoured if the abstracting radical X• is strongly electronegative, such as is the case with the succinimidyl radical derived from *N*-bromosuccinimide and with the *t*-butoxyl radical derived from di-*t*-butyl peroxide or *t*-butyl hypochlorite[1]. It is noteworthy, however, that the related benzoyloxy radical ($PhCO_2\cdot$) derived from dibenzoyl peroxide, prefers to add to the double bond rather than abstract an allylic hydrogen atom[2]. Since detailed discussion of allylic reactions of alkenes is presented in another chapter, this review is mainly directed at reactions involving addition of radicals to the double bond, although complications arising from competing allylic abstraction will be noted where relevant.

Before 1930, considerable research had been carried out with the addition of a variety of addenda to unsymmetrical olefins, with a view to the formulation of rules which would relate the observed orientation of the addition to contemporary theories of ionic reactions. In most cases the Markownikoff rule was found to be applicable[3], which requires that the cationic part of the addendum attach itself to the carbon atom which carries the greater number of hydrogen atoms, *i.e.* by way of the more stable intermediate carbonium ion. Conflicting and confusing results were reported in some cases involving the addition of hydrogen bromide, however, the classic case being that of allyl bromide.

In theory, the reaction between hydrogen bromide and allyl bromide may take one of two courses, either (5a) or (5b). Kharasch and Mayo[4] established that if the reactants were pure and freshly prepared, and if the reaction were allowed to proceed in the dark and in the absence of oxygen, a quantitative conversion into 1,2-dibromopropane was obtained after 10 days. The reaction thus proceeded according to the Markownikoff rule. Alternatively, the presence of small amounts of peroxides or oxygen introduced either deliberately or fortuitously by the use of old samples of allyl bromide caused the rapid formation (30 minutes) of 1,3-dibromopropane. Very many instances of reversal of addition under the influence of added peroxides were reported from Kharasch's laboratory during the following seven years, and this work has been reviewed by Mayo and Walling[5].

$$\mathrm{HBr} + \mathrm{CH_2{=}CHCH_2Br} \longrightarrow \begin{cases} \longrightarrow \mathrm{CH_3CHBrCH_2Br} & \text{(5a)} \\ \longrightarrow \mathrm{CH_2BrCH_2CH_2Br} & \text{(5b)} \end{cases}$$

A theoretical interpretation of these results was advanced in 1937 by Hey and Waters[6] and Kharasch, Engelmann and Mayo[7] who independently postulated that the fast abnormal addition was a radical chain process involving atomic bromine and a free radical intermediate. Thus, for initiation by a radical $R\cdot$, which need be present in only catalytic quantity, Scheme 1 was proposed. This

$$\mathrm{R\cdot + HBr \longrightarrow RH + Br\cdot}$$

$$\mathrm{Br\cdot + CH_2{=}CHCH_2Br \longrightarrow BrCH_2\dot{C}HCH_2Br}$$

$$\mathrm{BrCH_2\dot{C}HCH_2Br + HBr \longrightarrow BrCH_2CH_2CH_2Br + Br\cdot}$$

SCHEME 1.

mechanism has become the prototype for a large number of free-radical addition reactions involving a wide variety of addenda, many of which do not react with olefins at all in the absence of radical initiators such as peroxides or ultraviolet light. These reactions may be represented by the generalized Scheme 2.

$$\text{Initiation}\quad \mathrm{R\cdot + XY \longrightarrow RX + Y\cdot}\quad \mathrm{(or\ XY \xrightarrow{h\nu} X\cdot + Y\cdot)} \tag{6}$$

$$\text{Propagation}\quad \left\{\begin{aligned} &\mathrm{Y\cdot + RCH{=}CH_2 \longrightarrow R\dot{C}HCH_2Y} && (7)\\ &\mathrm{R\dot{C}HCH_2Y + XY \longrightarrow RCHXCH_2Y + Y\cdot} && (8)\end{aligned}\right.$$

SCHEME 2.

Thus the chain-propagation reaction consists of two steps: an addition step, reaction (7), and a radical displacement step, reaction (8). Addition polymerization may be regarded as a special case of this process which occurs when the radical $\mathrm{R\dot{C}HCH_2Y}$ generated in reaction (7) competes with the chain-carrying radical Y· for unreacted olefin (reaction 9).

$$\mathrm{R\dot{C}HCH_2Y + RCH{=}CH_2 \longrightarrow R\dot{C}HCH_2CHRCH_2Y} \tag{9a}$$

$$\mathrm{R\dot{C}HCH_2CHRCH_2Y + RCH{=}CH_2 \longrightarrow R\dot{C}HCH_2CHRCH_2CHRCH_2Y,\ etc.} \tag{9b}$$

$$\text{Chain transfer to XY}\quad \mathrm{R\dot{C}HCH_2CHRCH_2CHRCH_2Y + XY \longrightarrow RCHXCH_2CHRCH_2CHRCH_2Y + Y\cdot} \tag{10}$$

Reactions such as (10) with successive molecules of monomer rather than with the molecule XY give telomers, *i.e.* products containing more than one molecule of olefin per molecule of XY. The chain is assumed to be terminated by dimerization of radicals or by disproportionation, although in many cases experimental support for this does not exist.

In order that a significant kinetic chain length be maintained it is necessary that both attack by Y· on the double bond (reaction 7) and attack by the radical $\mathrm{R\dot{C}HCH_2Y}$ on XY (reaction 8) be fast in comparison with all chain-termination steps. It follows that if either of these propagation steps is significantly endothermic, addition by way of a chain mechanism is difficult or impossible, regardless of the efficiency of the initiators. If both propagation steps are exothermic, chain addition is possible but not certain, for even strongly exothermic reactions may have high energies of activation or highly negative entropies of activation. Gould[8] has recently derived approximate energies of the propagation steps in some radical additions to propylene and it is predictable from these that radical chain processes involving the addition of water or HCl are unlikely, because of the difficulty of breaking the H—OH and H—Cl bonds. The addition of iodine, or HI, is also unlikely but for a different reason, in this case as a result of the weakness of the C—I bond, *i.e.* in this case reaction (7) is reversible. These predictions have been suppported by experiment. In the experimentally realized chain additions of HBr, CH_3CHO and CCl_4 on the other hand, both the addition and displacement steps are exothermic.

B. Addition of Polyhalogenomethanes to Olefins

The possibility that carbon tetrachloride could be induced to undergo free-radical addition to olefins was foreshadowed by the observation[9] in 1937 that polystyrene prepared in carbon tetrachloride possessed a relatively low degree of polymerization. Mayo[10] rationalized this in terms of a chain-transfer process but it was not until 1945 that Jensen, Kharasch and Urry[11] reported that carbon tetrachloride and chloroform reacted with 1-octene by way of a radical chain to give 1,1,1,3-tetrachlorononane and 1,1,1-trichlorononane, respectively (*e.g.* equation 11). Later, it was shown that carbon tetrabromide[12]

$$\cdot CCl_3 + RCH{=}CH_2 \longrightarrow R\dot{C}HCH_2CCl_3 \tag{11a}$$

$$R\dot{C}HCH_2CCl_3 + CHCl_3 \longrightarrow RCH_2CH_2CCl_3 + \cdot CCl_3 \tag{11b}$$

and bromoform[13] also reacted additively with olefins containing a terminal double bond (1-octene, styrene, ethyl acrylate, diallyl, propylene) under the influence of added peroxides or light of suitable wavelength. The addition of bromoform follows a different course from the addition of chloroform owing to a difference at the initiation stage. Whereas chloroform yields a $\cdot CCl_3$ radical, bromoform gives a $\cdot CHBr_2$ radical (Scheme 3). The behaviour of chloroform is noteworthy since displacement occurs preferentially at the C—H bond, the greater resonance energy (12 kcal) of the $\cdot CCl_3$ radical formed[14] apparently having the effect of lowering the strength of the C—H bond to a value below that of C—Cl in this molecule. It has

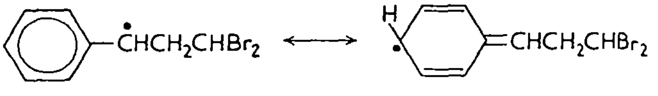
$$R\cdot + CHCl_3 \longrightarrow RH + \cdot CCl_3; \quad R\cdot + CHBr_3 \longrightarrow RBr + \cdot CHBr_2$$

$$\cdot CCl_3 \text{ (or } \cdot CHBr_2) + RCH{=}CH_2 \longrightarrow R\dot{C}HCH_2CCl_3 \text{ (or } R\dot{C}HCH_2CHBr_2)$$

SCHEME 3.

been reported[15], however, that in addition reactions involving $CDCl_3$, where the rate of C—D cleavage is reduced because of the isotope effect, a significant amount of C—Cl cleavage does in fact occur.

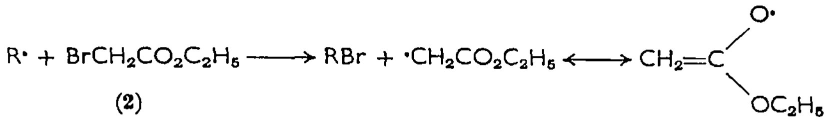
Telomerization sometimes becomes particularly pronounced in additions involving halogenomethanes, and in general becomes important when the halide employed is relatively unreactive or when its concentration is low, so that reaction (9a) rather than (8) is favoured. Thus telomer formation is appreciable in the reactions of carbon tetrachloride[13,16,17], chloroform[17] and dibromodifluoromethane[18] with ethylene, but not with the more reactive halides bromotrichloromethane[19] and carbon tetrabromide[13], which have the labile C—Br bond. A measure of the relative importance of reactions (8) and (9a) can be obtained by calculation of the chain-transfer constants[20], which express the ratio of the rates of reactions (8) and (9a); thus bromotrichloromethane has a high chain-transfer constant. The degree of telomerization is also dependent upon the stability of the intermediate free radical $R\dot{C}HCH_2Y$. Higher stability increases the selectivity of the radical so that it is more likely to exist long enough to react with another molecule of olefin, whereas a more reactive radical is more likely to react with the addendum XY, *e.g.* the halogenomethane. The addition of bromoform to styrene, but not to 1-octene, results largely in telomer formation, the addition proceeding by way of resonance-stabilized benzyl radical **1**.



(1)

Further, a reduction in the proportion of bromoform in the reaction mixture will lead to a telomer of much higher molecular weight and, in the limit, telomerization becomes indistinguishable from polymerization. In general, those factors which determine the occurrence and extent of radical chain polymerization of olefins also take the same role in telomerization, with the exception of course that the chain-ending and chain-transfer reactions in the latter case are dependent upon the nature of the chain-transfer reagent. In view of this, and also because an excellent account of radical polymerization has recently been published[21], it is not proposed to discuss this type of reaction here.

For the reaction $R\cdot + X{-}CCl_3 \rightarrow RX + \cdot CCl_3$, the reactivity increase in the series $CCl_4 < CBrCl_3 < ClCl_3$ follows the order of decreasing energies of the bonds broken, whilst the reactivity decrease in the series $X{-}CX_3 > X{-}CHX_2 > X{-}CH_2X > X{-}CH_3$, for a similar radical displacement, probably follows the corresponding decrease in resonance energies of the radicals produced. In general, halogenomethanes containing less than three halogen atoms do not readily undergo addition reactions. Exceptions are the halides whose radicals are stabilized by delocalization over neighbouring conjugated groups, as with bromoacetic ester (**2**)[22]. Recently, however, Cadogan, Hey and Hibbert have shown[23] that methylene dibromide can be induced to react with 1-octene to give mainly 1,3-dibromononane.



$$R\cdot + BrCH_2CO_2C_2H_5 \longrightarrow RBr + \cdot CH_2CO_2C_2H_5 \longleftrightarrow CH_2{=}C(O\cdot)OC_2H_5$$

(**2**)

The scope of radical-addition reactions involving olefins and polyhalogenomethanes is illustrated by selected examples given in Table 1.

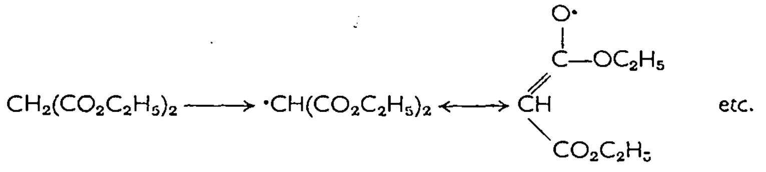
Table 1. Radical-addition reactions of polysubstituted methanes with olefins.

$RCH{=}CH_2$	XY	Initiating radical Y·	Product $RCHXCH_2Y$ (%)	Reference
$(CH_3)_2C{=}CH_2$	CCl_4	$\cdot CCl_3$	78	24
1-Octene	CCl_4	$\cdot CCl_3$	85	11, 13
$CH_2{=}CHOCOCH_3$	CCl_4	$\cdot CCl_3$	Low[a]	25
$CH_2{=}CHOCOCH_3$	$BrCCl_3$	$\cdot CCl_3$	90	19, 26
1-Octene	$BrCCl_3$	$\cdot CCl_3$	88	19, 26
Styrene	$BrCCl_3$	$\cdot CCl_3$	78	19, 26
$CH_2{=}CHCF_3$	CCl_3I	$\cdot CCl_3$	57	27
$CH_2{=}CHF$	CF_3I	$\cdot CF_3$	65	28
$CH_2{=}CHCN$	CF_3I	$\cdot CF_3$	72	29
1-Octene	$CHCl_3$	$\cdot CCl_3$	22	13
1-Octene	$CHBr_3$	$\cdot CHBr_2$	31	13
Styrene	$CHBr_3$	$\cdot CHBr_2$	Low[a]	13
1-Octene	$BrCH_2CN$	$\cdot CH_2CN$	66	30
1-Octene	$BrCH_2CO_2C_2H_5$	$\cdot CH_2CO_2C_2H_5$	48	22
1-Octene	CBr_4	$\cdot CBr_3$	96	13
Styrene	CBr_4	$\cdot CBr_3$	96	13

[a] Telomer present.

C. Addition of Carboxylic Acids and Derivatives to Alkenes

Until recently few radical-addition reactions of carboxylic acids and derivatives with olefins had been reported. Bromoacetic and related esters have been shown to undergo such reactions, the resonance stabilization of the $\cdot CH_2CO_2C_2H_5$ radical and the relative weakness of the C—Br bond contributing to the success of the reaction. On the other hand it has been stated[22] that in the case of methyl acetate, the radical $\cdot CH_2CO_2CH_3$ produced initially competes unsuccessfully with the initiating radical from the peroxide in their reactions with the olefin, *i.e.* chain propagation by abstraction of a α-hydrogen atom from methyl acetate is an unfavoured process. Recent work by Allen, Cadogan, Harris and Hey[31] has overcome this difficulty and provided important new synthetic routes to straight-chain esters. The esters chosen were diethyl malonate, ethyl cyanoacetate and ethyl acetoacetate. Such compounds would be expected to undergo the displacement reaction (8) and the initiation step (6) quite readily as a result of the energy gain in the formation of the corresponding resonance-stabilized radicals, *e.g.* **3**.



$$CH_2(CO_2C_2H_5)_2 \longrightarrow \cdot CH(CO_2C_2H_5)_2 \longleftrightarrow (\cdot O)(C_2H_5O)C{=}CH{-}CO_2C_2H_5 \quad \text{etc.}$$

(3)

Peroxide-induced chain-addition reactions between these esters and acyclic olefins have now been effected, diethyl malonate and 1-octene, for example, reacting to give diethyl n-octylmalonate. At a low ratio of ester to olefin (5:1) low conversions (20–25%) of the olefin to the octylmalonate were obtained and olefin was recovered. Using the same olefin to initiator ratio (20:1), but a much higher ratio of ester to olefin (20–50:1), however, the conversion to diethyl n-octylmalonate was much more satisfactory (67–85%). These reactions can be rationalized by the Scheme 4.

$$(t\text{-}C_4H_9O)_2 \longrightarrow 2\ t\text{-}C_4H_9O\cdot$$

$$t\text{-}C_4H_9O\cdot + RCH_2CH{=}CH_2 \longrightarrow RCH_2\dot{C}HCH_2OC_4H_9\text{-}t \qquad (12)$$

$$t\text{-}C_4H_9O\cdot + RCH_2CH{=}CH_2 \longrightarrow R\dot{C}HCH{=}CH_2 + t\text{-}C_4H_9OH \qquad (13)$$

$$t\text{-}C_4H_9O\cdot + CH_2(CO_2C_2H_5)_2 \longrightarrow \cdot CH(CO_2C_2H_5)_2 + t\text{-}C_4H_9OH \qquad (14)$$

$$\mathrm{RCH_2\dot{C}HCH_2OC_4H_9\text{-}\mathit{t} + CH_2(CO_2C_2H_5)_2 \longrightarrow RCH_2CH_2CH_2OC_4H_9\text{-}t + {\cdot}CH(CO_2C_2H_5)_2} \tag{15}$$

$$\mathrm{{\cdot}CH(CO_2C_2H_5)_2 + RCH_2CH{=}CH_2 \longrightarrow RCH_2\dot{C}HCH_2CH(CO_2C_2H_5)_2} \tag{16}$$

$$\mathrm{RCH_2\dot{C}HCH_2CH(CO_2C_2H_5)_2 + CH_2(CO_2C_2H_5)_2 \longrightarrow RCH_2CH_2CH_2CH(CO_2C_2H_5)_2 + {\cdot}CH(CO_2C_2H_5)_2} \tag{17}$$

$$\mathrm{RCH_2\dot{C}HCH_2CH(CO_2C_2H_5)_2 + RCH_2CH{=}CH_2 \longrightarrow telomers} \tag{18}$$

$$\mathrm{2\ RCH_2\dot{C}HCH_2OC_4H_9\text{-}\mathit{t} \longrightarrow products} \tag{19}$$

$$\mathrm{2\ R\dot{C}HCH{=}CH_2 \longrightarrow products} \tag{20}$$

Scheme 4.

Farmer and Moore[32] have shown that *t*-butoxy radicals react with 1-heptene in two ways: (*a*) by addition to give a radical (reaction 12; $R = C_4H_9$) which can subsequently react by dimerization, disproportionation, or combination with other radicals, and (*b*) by abstraction of an α-methylene hydrogen atom to give a resonance-stabilized allyl radical (reaction 13; $R = C_4H_9$) which can also be removed in electron pairing reactions. Hence, at low ratios of ester to olefin, reactions (19) and (20) which are chain-ending processes, are favoured compared with the chain-initiation and -propagation steps (14) and (15). At high ratios of esters to olefins, on the other hand, there is a reduced probability of occurrence of telomerization and, by working in dilute solution, of disproportionation or radical combination, *e.g.* reaction (21).

$$\mathrm{2\ RCH_2\dot{C}HCH_2OC_4H_9\text{-}\mathit{t} \longrightarrow RCH_2CH_2CH_2OC_4H_9\text{-}\mathit{t} + RCH_2CH{=}CHOC_4H_9\text{-}\mathit{t}} \tag{21}$$

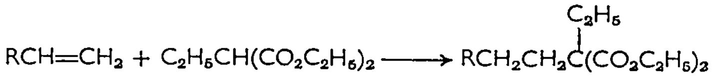
The use of a high addendum to olefin ratio (20–30:1) has also allowed the reactions (22)–(24) to proceed with ease in the presence of di-*t*-butyl peroxide or dibenzoyl peroxide. The products are those

$$\mathrm{RCH{=}CH_2 + CH_3COCH_2CO_2C_2H_5 \longrightarrow RCH_2CH_2CH(COCH_3)CO_2C_2H_5} \tag{22}$$

$$\mathrm{RCH{=}CH_2 + CH_2(CN)CO_2C_2H_5 \longrightarrow RCH_2CH_2CH(CN)CO_2C_2H_5} \tag{23}$$

$$\mathrm{RCH{=}CH_2 + CH_3COCH_2COCH_3 \longrightarrow RCH_2CH_2CH(COCH_3)_2} \tag{24}$$

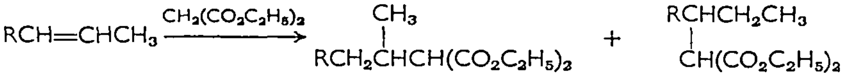
obtained by standard syntheses from malonic and acetoacetic esters, but in this case the starting material is the cheap terminal olefin and the use of base is obviated. Further, dialkylation, which often is a complication in the ionic reaction, does not occur to a significant extent in the radical process. A second alkyl group can be introduced, however, by the use of a monoalkylated ester, *e.g.* **4**.



$$RCH{=}CH_2 + C_2H_5CH(CO_2C_2H_5)_2 \longrightarrow RCH_2CH_2\overset{C_2H_5}{\overset{|}{C}}(CO_2C_2H_5)_2$$

(**4**)

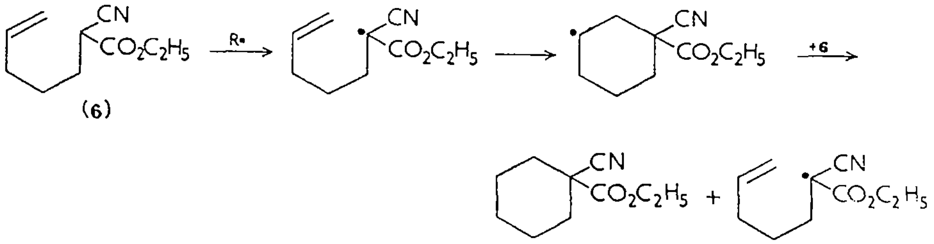
The reaction also occurs with non-terminal olefins such as 2-octene, but in this case both possible isomers (**5a** and **5b**) are produced in almost equal amounts.



$$RCH{=}CHCH_3 \xrightarrow{CH_2(CO_2C_2H_5)_2} RCH_2\underset{}{\overset{CH_3}{\overset{|}{C}}}HCH(CO_2C_2H_5)_2 + \begin{matrix} RCHCH_2CH_3 \\ | \\ CH(CO_2C_2H_5)_2 \end{matrix}$$

(**5a**) (**5b**)

An interesting variation of this reaction has been independently discovered by Julia[33], who noted that under suitable conditions intramolecular cyclization can be effected in pentenylcyanoacetic ester (**6**).



(6)

Similar reactions have been studied by Cadogan, Hey and Ong[34].

For many years the only recorded example of addition of acetic acid to an olefin was that of the peroxide-induced reaction with ethylene, which gave a mixture of homologous acids $CH_3(CH_2)_{2n}CO_2H$ of unstated composition[35]. More recently, it was reported[36] that homologues of acetic acid, but not acetic acid itself, undergo free-radical addition to olefins to give acids with substituents in the α-position (equation 25).

$$R^1CH{=}CH_2 + R^2\dot{C}HCO_2H \longrightarrow R^1\dot{C}HCH_2CHR^2CO_2H \qquad (25a)$$

$$R^1\dot{C}HCH_2CHR^2CO_2H + R^2CH_2CO_2H \longrightarrow RCH_2CH_2CHR^2CO_2H + R^2\dot{C}HCO_2H \qquad (25b)$$

Since it has been shown[22] that homolytic abstraction of an α-hydrogen atom from methyl acetate occurs to give carbomethoxymethyl radicals ($\cdot CH_2CO_2CH_3$), which subsequently dimerize, it appears reasonable to expect that under suitably modified conditions addition of acetic acid or its derivatives to olefins to give 1 : 1 adducts could be achieved, thus providing a valuable new homologation reaction for straight-chain acids and their derivatives. The experimental realization of this expectation was recently reported by Allen, Cadogan and Hey[37].

Reaction of 1-octene (1 mole), acetic acid (50 mole) and di-*t*-butyl peroxide (0·15 mole) at the boiling point for 48 hours gave decanoic acid in only 12% yield. Recovery of olefin indicated a low chain length under these conditions. Four- and six-fold increases in the proportion of acetic acid gave decanoic acid in 60% and 70% yields, respectively.

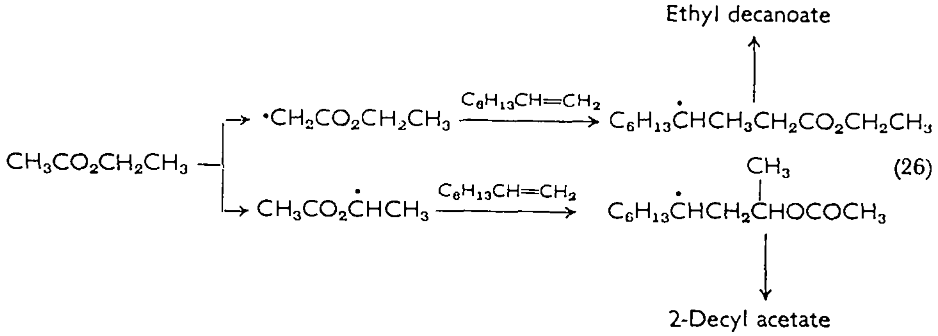
$$C_6H_{13}CH{=}CH_2 + \cdot CH_2CO_2H \longrightarrow C_6H_{13}\dot{C}HCH_2CH_2CO_2H$$

$$C_6H_{13}\dot{C}HCH_2CH_2CO_2H \xrightarrow{CH_3CO_2H} C_6H_{13}CH_2CH_2CH_2CO_2H + \cdot CH_2CO_2H$$

The reaction can also be carried out with derivatives of acetic acid. Thus reaction of acetic anhydride (100 mole) with 1-octene (1 mole) and di-*t*-butyl peroxide (0·15 mole) at the boiling point for 12 hours gave decanoic anhydride (63%), presumably arising by transformation of the first-produced 1 : 1 adduct, acetic decanoic anhydride, under the conditions of the experiment. A four-fold increase in the proportion of acetic anhydride led to the production of decanoic anhydride in 84% yield. Thus for high yields of the 1 : 1 adduct, high ratios of addendum to olefin are necessary. This condition can also be satisfied by gradual addition of a mixture of the olefin and peroxide to the addendum. The addition, for example, of a mixture of 1-octene (1 mole), di-*t*-butyl peroxide (0.15 mole) and acetic anhydride (2 mole) during 6 hours to boiling acetic anhydride (48 mole), followed by 1 hour at the reflux, gave decanoic anhydride in 72% yield. Acetonitrile can similarly be converted into decanoic nitrile and acetamide into decanoic amide[38].

On the other hand, *N*-methyl- or *N*,*N*-dimethylacetamide gives the alkylated acetamide $R^1CH_2CH_2CH_2NR^2COCH_3$, where $R^2 = H$ or CH_3 respectively[39], thus indicating that hydrogen-atom abstraction occurs more readily from a methyl group α to the amino group ($CH_3CONHCH_2$—H) compared with a methyl group α to the carbonyl group (H—$CH_2CONHCH_3$) and that abstraction from the amino group does not occur.

Ethyl acetate on reaction with 1-octene gives a mixture of ethyl decanoate, the expected 1 : 1 adduct, and the isomeric 2-decyl acetate (reaction 26), thus showing that α-hydrogen abstraction from the ethyl group in the ester also occurs in this instance[27].



(26)

Terminal alkenes may be converted by means of formamide into amides, and unsaturated esters and amides have been used instead of the olefin[40]. Similarly, *N*,*N*-dimethylformamide gives the amide $RCH_2CH_2CON(CH_3)_2$ together with the alkylated formamide $RCH_2CH_2CH_2NCH_3CHO$, thus resembling the reaction with ethyl acetate described above, whereas *t*-butylformamide gives only the amide $RCH_2CH_2CONHC_4H_9$-*t*[39], methyl formate gives only telomers with ethylene, but gives 1:1 adducts with higher olefins[41].

D. Addition of Aldehydes, Ketones and Alcohols to Olefins

The peroxide- and light-induced additions of aldehydes to terminal olefins result in the formation of ketones[42]. Equation (27) gives the

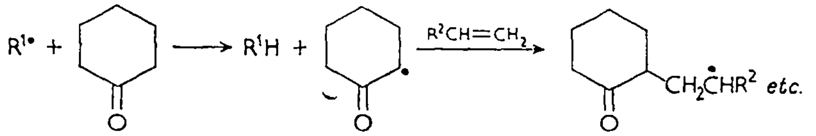
$$R^1CHO + R^2CH{=}CH_2 \longrightarrow R^2CH_2CH_2COR^1 \qquad (27)$$

overall reaction, but telomers, the alkane derived from the alkyl radical of the aldehyde, and carbon monoxide also appear. Thus reactions such as (28) also occur. This work has been extended by

$$R\dot{C}O \longrightarrow R\cdot + CO; \quad R\cdot + RCHO \longrightarrow RH + R\dot{C}O \qquad (28)$$

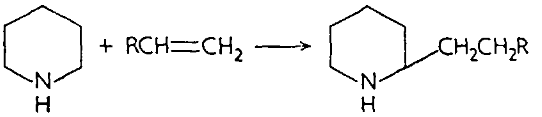
Patrick[43] to include additions to carbonyl-conjugated olefins, such as diethyl maleate and mesityl oxide. The high yields of 1:1 adducts obtained in these reactions and in similar reactions involving perfluoroolefins[44] suggest that polar effects are operative and the acyl radical, $R\dot{C}O$, may be considered to be electron donating or nucleophilic in character. This can be rationalized by assuming contributions of the type $R{-}\bar{C}{=}\dot{O}^{+} \leftrightarrow R{-}\dot{C}{=}O$, and also by remembering that the electron-donating properties of a radical are related to the stability of the corresponding cation formed by loss of one electron. In this case there is evidence that the $R-\overset{+}{C}=O$ is a fairly stable entity, and hence the analogous radical is electron donating in character.

Few examples of radical-addition reactions of ketones have been reported. It appears that cyclohexanone is the most reactive ketone in this sense[45], the course of the reaction with 1-octene being given in reaction (29).



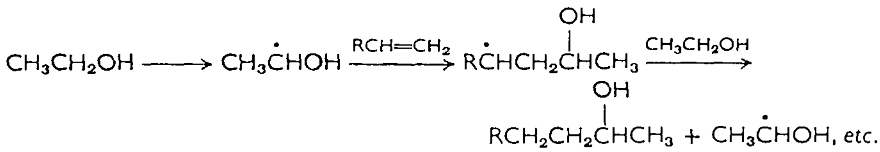
(29)

Application of the high-dilution technique has, however, recently resulted in the successful addition of acyclic ketones to olefins, *e.g.* 1-octene and methyl ethyl ketone gives rise to a mixture of ethyl nonyl ketone (1 part) and methyl 2-decyl ketone (9 parts)[37]. Initiation of such additions by abstraction of a hydrogen atom from cyclohexane-type compounds appears sometimes to be a favoured process, since piperidine has been made to add to 1-octene and to propene to give 2-octylpiperidine and (±)-coniine respectively[46].



Other amines are significantly less reactive, as reflected by the following chain-transfer constants with 1-octene: piperidine, 0·26; n-butylamine, 0·062; isopropylamine, 0·095. Russell[47], in an investigation of the ease of autoxidation of hydrocarbons, has also observed that hydrogen-atom abstraction from cyclohexane-type compounds occurs readily. On the other hand, the low transfer constant (0·0181) of cyclohexylamine does not appear to support this, but in this case the hydrogen atom undergoing abstraction would be axial and hence possibly subject to a steric barrier.

The radical-induced addition of primary and secondary alcohols to olefins results in the formation of secondary and tertiary alcohols (equation 30)[45]. The transfer constants for such reactions are



$$CH_3CH_2OH \longrightarrow CH_3\dot{C}HOH \xrightarrow{RCH=CH_2} R\dot{C}HCH_2\overset{OH}{\overset{|}{C}}HCH_3 \xrightarrow{CH_3CH_2OH} RCH_2CH_2\overset{OH}{\overset{|}{C}}HCH_3 + CH_3\dot{C}HOH, \text{etc.} \quad (30)$$

small, however[49] (*e.g.* for 1-octene: C_2H_5OH, 0·017; $(CH_3)_2CHOH$, 0·063; CH_3OH, 0·011), and extreme conditions of dilution are necessary in order to produce radical chains leading to low molecular weight products. Chain transfer takes place more readily with secondary alcohols, methanol having the lowest transfer constant, *e.g.* with a 20:1 molar ratio of 2-propanol and 1-octene a 40–50% conversion into 1:1 adduct is obtained, but with methanol the corresponding conversion is only 15% even when the alcohol to olefin ratio is 50:1. Alkyl peroxides or light of suitable wavelengths are effective initiators of these reactions, but diacyl peroxides and 2,2′-azobisisobutyronitrile are less useful, the former presumably because of their induced decompositions in the presence of alcohols[50].

E. Addition Reactions of Elements other than Carbon

1. Sulphur compounds

In the addition reactions cited above, the evidence for a free-radical chain mechanism is placed beyond doubt by the fact that either the products formed are different from those resulting from ionic addition, or the reactions do not proceed at all unless initiated by a free radical generated either thermally or photolytically. It is, however, possible that under certain conditions addition reactions may take place by both homolytic or heterolytic mechanisms and give the same product. An example of this has been provided by Kharasch and Fuchs[51] who showed that the addition of mercaptans to methyl acrylate proceeds in the presence of a strong base (heterolytic) or a peroxide (homolytic), and in both cases the same product $RSCH_2CH_2CO_2CH_3$ is formed. The formation of telomers in the reaction is in accord with its homolytic nature. The homolytic addition of a thiol R^2SH to an olefin, $R^1CH{=\!=}CH_2$, is inhibited by oxygen, and the product[52] is $R^1CH(OH)CH_2SOR^2$.

Many other radical chain reactions involving thiols have now been reported[53]. The addition step is sometimes reversible, for *cis–trans* isomerization of olefins may occur during thiol addition. Both the addition and displacement steps in the propagation reaction are exothermic and little energy appears to be required for the reaction. Appreciable quantities of telomers are formed from ethylene, for example, only at very high pressures (500 atmospheres)[51]. Thiol acids RCOSH also readily undergo addition reactions with olefins. Although here the chain-carrying radical is bidentate ($RCOS\cdot \leftrightarrow RCSO\cdot$) the product is formed entirely by thioyl radical addition, thus providing, by hydrolysis of the adduct, a very useful synthetic route to thiols (equation 31)[54,55]. The ease of reaction of thiols

$$R^1CH{=}CH_2 + R^2COSH \longrightarrow R^1CH_2CH_2SCOR^2 \xrightarrow{OH^-} R^1CH_2CH_2SH \qquad (31)$$

with olefins is reflected in the values of their chain transfer constants, *e.g.* for reaction with styrene at 60°: n-butyl mercaptan, 22[56]; ethyl thioglycollate, 58[57].

2. Phosphorus compounds

The addition of phosphorous trichloride to aliphatic olefins can take place under the influence of peroxides[58], as does that of phosphine[59]

$$PCl_3 \text{ (or } PH_3) + RCH{=}CH_2 \longrightarrow RCHClCH_2PCl_2 \text{ (or } RCH_2CH_2PH_2) \qquad (32)$$

(equation 32). The addition of phenylphosphorous dichloride proceeds more readily[60], presumably as a result of weakening of the P—Cl bond as a result of delocalization in the intermediate $Ph\dot{P}Cl$ radical. More recently, dialkyl phosphonates $(RO)_2P(O)H$ have been shown to react readily with olefins to give the useful dialkyl alkylphosphonates (equation 33)[61]. The chain-carrying radical

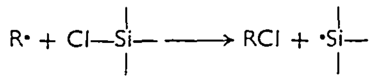
$$RCH{=}CH_2 + (RO)_2P(O)H \longrightarrow (RO)_2P(O)CH_2CH_2R \qquad (33)$$

$(RO)_2\dot{P}O$ is here analogous to that involved in the radical chain addition of aldehydes to olefins.

The addition of phosphines, R_2PH, has been shown to be reversible[62] thus indicating a close similarity between thiols and phosphines in this reaction.

3. Other elements

The energies of the displacement step in silicon hydride and halide additions resemble those of phosphorus. The displacement (34) is



$$R\cdot + Cl{-}\overset{|}{\underset{|}{Si}}{-} \longrightarrow RCl + \cdot\overset{|}{\underset{|}{Si}}{-} \qquad (34)$$

more endothermic, however, and additions of silicon compounds which would involve such displacements rarely occur[63]. Trichlorosilane readily suffers displacement at the Si—H bond and with 1-octene gives a very high yield (99%) of n-octyl trichlorosilane in the presence of acetyl peroxide[64]. The transfer constant for $SiHCl_3$ with styrene is 0·026 compared with $0{\cdot}5 \times 10^{-4}$ for chloroform, but even so, telomer formation occurs in the former case[65]. Many other addition reactions of silicon compounds with olefins have been reported and are summarized elsewhere[66].

Trichlorogermane behaves in these reactions analogously to chloroform and trichlorosilane (equation 35)[67]. The higher-row

$$C_4H_9CH{:}CH_2 + GeHCl_3 \xrightarrow[(22\%)]{} C_4H_9CH_2CH_2GeCl_3 \qquad (35)$$

elements which form stable bonds with carbon usually also form stable bonds with halogens so that successful addition reactions involving their halides are difficult to achieve.

Owing to the strong bonds which oxygen and nitogen form with hydrogen, addition reactions involving water and amines are unlikely, and hydrogen abstraction rather than addition by $RO\cdot$ and $R_2N\cdot$ radicals is favoured.

Addition reactions of other nitrogen compounds are also rare. Nitryl chloride[68] and dinitrogen tetroxide[69] will undergo radical chain additions with olefins, particularly the latter, since the N—N bond is weak. The initial attack is by $\cdot NO_2$ radicals in both cases but the nature of the subsequent displacement step on N_2O_4 is not clear (equation 36). The reaction is clearly homolytic because

$$RCH{=}CH_2 + \cdot NO_2 \longrightarrow R\dot{C}HCH_2NO_2 \xrightarrow[N_2O_4]{\cdot NO_2 \text{ or}}$$
$$RCH(NO_2)CH_2NO_2 \text{ or } RCH(ONO)CH_2NO_2 \qquad (36)$$

chain transfer with reactive solvents such as bromotrichloromethane readily occurs (equation 37)[67].

$$RCH{=}CH_2 + N_2O_4 \longrightarrow R\dot{C}HCH_2NO_2 + \cdot NO_2$$
$$R\dot{C}HCH_2NO_2 + BrCCl_3 \longrightarrow RCHBrCH_2NO_2 + \cdot CCl_3 \qquad (37)$$

F. Orientation of Free-radical Addition

In all examples of radical chain addition to olefins of the type $RCH{=}CH_2$ considered so far, the point of initial attack has been apparently exclusively at the terminal CH_2 group, although in many cases it is fair to state that the methods of analysis or of isolation of products have not been quantitative. This specificity, which at first sight is remarkable in view of the homolytic nature of the reaction, has generally been explained on the basis of the greater stability of the intermediate radical $R\dot{C}HCH_2Y$ formed by addition of the radical $Y\cdot$ to the olefin, compared with that of $RCHYCH_2\cdot$, while polar and steric factors have been considered to be less important[70].

Important contributions to our knowledge of the problem of the orientation in free-radical addition reactions have been made by Haszeldine and his school[71] who demonstrated the relative unimportance of the polarization of the double bond in $RCH{=}CH_2$ (where

$R = CF_3$, CN, CH_3, Cl, F or CO_2CH_3) in determining the point of attack (the CH_2 group) of a trifluoromethyl radical or bromine atom. Explanations of the direction of addition based solely on steric considerations were also shown to be unsuitable for general application, although large steric effects would obviously be expected to be important in influencing orientation. It has therefore been assumed that the main factor is the relative stability of the two possible radicals. There is indeed certain evidence derived from the study of radical rearrangements that tertiary radicals are more stable than secondary, which are in turn more stable than primary, $R_3C\cdot > R_2CH\cdot > RCH_2\cdot$ (see later).

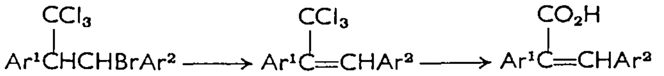
In view of the observed specificity of the additions to $RCH{=}CH_2$, clearly a more satisfactory system for a study of the factors which influence orientation of additions is the unsymmetrically substituted olefin, $R^1CH{=}CHR^2$, where the effect of variations in R^1 and R^2 on the direction of addition can be noted. Much less information is available about radical chain additions involving non-terminal olefins, however, although Huang[72] has obtained an order of stability of the intermediate radicals from such olefins. Unfortunately, few of the systems which he studied were capable of quantitative resolution, an essential requirement for the study of such reactions. Nevertheless, a very useful order of relative stabilizing effects was obtained. Thus, for addition of a trichloromethyl radical to olefins, the ability of substituents to stabilize the intermediate radical is in the order Ph > $CO_2C_2H_5$ or CN; COR > $CO_2C_2H_5$ > CO_2H > CH_3 > H.

The relative absence of quantitative data is characteristic of this field, and it was to meet this situation that a quantitative study of radical addition reactions of *trans*-stilbenes (**7**) was recently carried out[73].

The system had to fulfil the following requirements: (*i*) give a high yield of 1:1 adduct, preferably formed irreversibly, and a negligible yield of telomers, since telomer formation might take place by preferential reaction of one of the intermediate radicals, so that the observed ratio of isomeric 1:1 adducts would have little significance; (*ii*) the expected mixture of adducts **8** and **9** must be stable, non-interconvertible and capable of being analysed quantitatively. Undoubtedly, the reagent which best satisfies requirement (*i*) is bromotrichloromethane. Addition of this reagent to substituted stilbenes **7** would be expected to give either or both of the adducts **8** and **9**

$Ar^1CH{=}CHAr^2$ (**7**) $Ar^1CHXCHYAr^2$ (**8**) $Ar^1CHYCHXAr^2$ (**9**)

(X = CCl_3 or Br; Y = Br or CCl_3). Having obtained this mixture, it was proposed to convert it into a mixture of substituted α-phenylcinnamic acids, authentic samples of which are readily obtainable, which would then be analysed by ultraviolet spectroscopy.



$$Ar^1CH(CCl_3)CHBrAr^2 \longrightarrow Ar^1C(CCl_3){=}CHAr^2 \longrightarrow Ar^1C(CO_2H){=}CHAr^2 \qquad (38)$$

Preliminary experiments were carried out with *trans*-stilbene itself in order to establish the nature of the reaction and devise a quantitative method (equation 38). It was found that radical chain addition of bromotrichloromethane to *trans*-stilbene gave 1-bromo-3,3,3-trichloro-1,2-diphenylpropane (**10**) in good yield after initiation by ultraviolet light or peroxides. Reaction of the adduct **10** with lithium chloride in dimethylformamide gave an excellent yield (98%) of α-trichloromethylstilbene (**11**) which on hydrolysis gave α-phenyl-*trans*-cinnamic acid (98–100%). The results of similar reactions, expressed in terms of the isomeric composition of the mixture of substituted α-phenyl cinnamic acids produced from corresponding substituted *trans*-stilbenes, are given in Table 2.

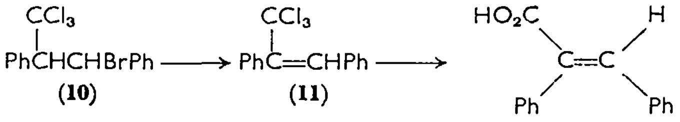
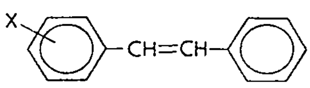
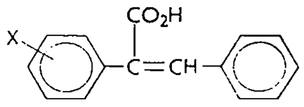
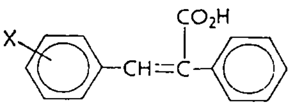
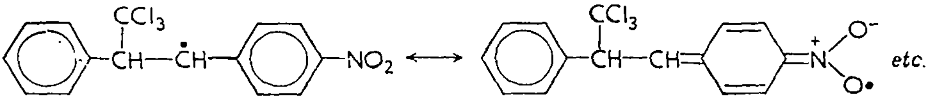


TABLE 2. Isomer ratios in the addition of $BrCCl_3$ to *trans*-stilbenes.

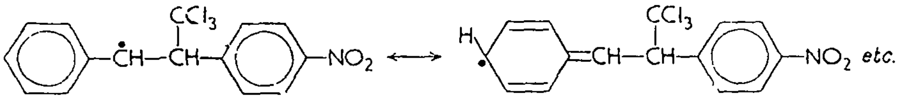
		
X		
4-NO_2	40	60
4-Br	47	53
3-NO_2	47	53
3-Br	45	55
3-CH_3	55	44
3-CH_3O	48	52

In the system used in this investigation, steric factors are considered to be unimportant, since they are likely to apply equally to both olefinic carbon atoms, so that discussion of the experimental results can be confined to the possible influences of polar and radical stability factors on the addition reaction. Little is known about the importance of polar effects in free-radical addition reactions, although there is evidence that the trichloromethyl radical can be considered to be electron accepting in character[15]. It is clear from the results given in Table 2, however, that a *selective* polar effect is not operative in the reactions with substituted stilbenes, since there is no significant variation in position of attack with change of polarity or position of the nuclear substituent.

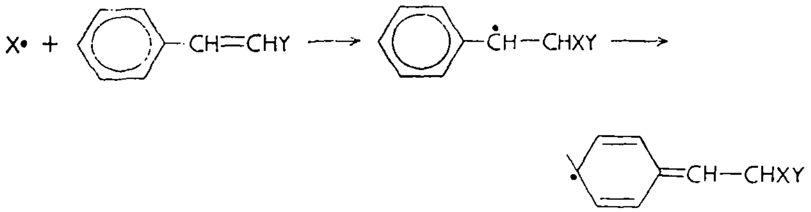
The absence of marked substituent effects in this reaction indicates, however, that addition to stilbene is governed largely by the stability of the resulting intermediate free radical. Thus, for 3-substituted stilbenes, there is no difference in stability between the two possible radicals in each case, since delocalization of the benzylic free electron with the non-conjugated 3-substituent cannot occur. In the case of 4-substituted stilbenes, particularly if the substituent is conjugated, such as nitro, greater stability of radical **12** compared with that of **13** might be expected as a result of the possible additional delocalization of the free electron in this case. In agreement with this, the largest real effect was obseved with 4-nitro-*trans*-stilbene and the orientation was as predicted. It is clear, however, that delocalization which arises from 4-substituents is low, *i.e.* the differences in stability between substituted benzyl radicals are small.



(12)

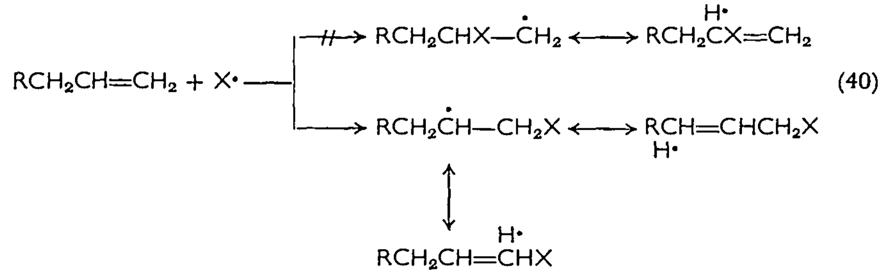


(13)



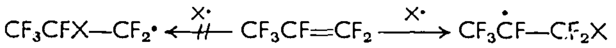
(39)

In the cases discussed so far, the direction of addition is governed by the relative stabilities of the possible intermediate free radicals. These, in turn, are dependent upon the structure of the alkene, *e.g.* addition to substituted styrenes always proceeds by way of the resonance stabilized benzyl radical (equation 39). Addition to the terminal CH_2 group of simple alkenes is influenced by the higher stability, due to a hyperconjugative effect, of the secondary radical involved (equation 40).



$$RCH_2CH{=}CH_2 + X\cdot \begin{cases} \xrightarrow{\;/\!/\;} RCH_2CHX{-}\dot{C}H_2 \longleftrightarrow RCH_2\overset{H\cdot}{C}X{=}CH_2 \\ \longrightarrow RCH_2\dot{C}H{-}CH_2X \longleftrightarrow R\underset{H\cdot}{C}H{=}CHCH_2X \\ \qquad\quad \updownarrow \\ \qquad\quad RCH_2\overset{H\cdot}{C}H{=}CHX \end{cases} \qquad (40)$$

However, in some cases reported recently, consideration of radical stability is not sufficient to account for the observed orientations. On the basis of the relative stabilities of the possible intermediate radicals, perfluoropropene (**14**) should react with a radical X• as shown[70,75]. Harris and Stacey[76] noted, however, that the isomer **15**,



$$\underset{(15)}{CF_3CFX{-}CF_2\cdot} \xleftarrow[\;/\!/\;]{X\cdot} \underset{(14)}{CF_3CF{=}CF_2} \xrightarrow{X\cdot} \underset{(16)}{CF_3\dot{C}F{-}CF_2X}$$

unfavoured on grounds of stability, is formed in increasing proportions during additions of thiols RSH (R = CH_3, CF_3CH_2, CF_3) (Table 3). Assuming that the polarization of perfluoropropene is the same for radical and ionic addition, $CF_3\overset{\delta-}{C}F{=}\overset{\delta+}{C}F_2$, these results can be rationalized by assuming that strong polar effects in the *radical* are operative, *i.e.* trifluoromethanethiyl ($CF_3S\cdot$) is strongly electrophilic as a result of the reduction of electron density at the sulphur atom by the strong inductive effect of the CF_3 group. The order of this polarization, $CF_3 > CF_3CH_2 > CH_3$, is paralleled by the relative amount of the isomer $CF_3CF(SR)CF_2H$ formed in each case. It is interesting that the polar effect is apparently not as pronounced in the reaction involving the CF_3 radical[79] compared with that of the $CF_3S\cdot$ radical. A similar rationalization can be invoked to explain the variation in isomer ratio arising from addition of various silanes to perfluoropropene (Table 3). In this case the inductive effect of the methyl group in the

TABLE 3. Addition of XY to $CF_3CF{=}CF_2$.

XY	Attacking radical X·	Products (%)		Reference
		CF_3CFYCF_2X	CF_3CFXCF_2Y	
CH_3SH	$CH_3S\cdot$	91	9	76
CF_3CH_2SH	$CF_3CH_2S\cdot$	70	30	76
CF_3SH	$CF_3S\cdot$	45	55	76
$(CH_3)_3SiH$	$(CH_3)_3Si\cdot$	96	4	77
$(CH_3)_2SiH_2$	$(CH_3)_2SiH\cdot$	95	5	77
CH_3SiH_3	$CH_3SiH_2\cdot$	76	24	77
SiH_4	$\cdot SiH_3$	60	40	77
PH_3	$\cdot PH_2$	66	34	78
CF_3I	$CF_3\cdot$	80	20	79
SF_5Cl	$Cl\cdot$	50	50	80

radicals induces electron-donating character in the radical, the order of relative electrophilicities of the radicals then becomes $\cdot SiH_3 > \cdot SiH_2CH_3 > \cdot SiH(CH_3)_2 > \cdot Si(CH_3)_3$ which is the order of the increased formation of the isomer CF_3CFXCF_2H.

Finally, it should be noted that Lovelace, Postelnek and Rausch[81] have formulated an empirical rule which enables the orientation of haloalkyl-radical addition to fluoroalkenes to be predicted with some success. Thus, if RX is added to the olefin $Ca^1a^2{=}Cb^1b^2$, and if $\sum (E.AR)_{a^1a^2} < \sum (E.AR)_{b^1b^2}$, where E is the Pauling electronegativity and AR is the atomic refraction of a^1, a^2, b^1, b^2, then the orientation will be $RCa^1a^2{-}Cb^1b^2X$. The radical R· attacks the olefinic carbon atom with the lowest $\sum (E.AR)$ of its substituents. The theoretical basis of this rule is, however, obscure.

G. The Relative Reactivity of Olefinic Double Bonds Towards Free Radicals

In an examination of the relationship between structure and reactivity, information can often be most readily obtained by the use of competitive reactions. In the general scheme for free-radical addition reactions given above (Scheme 2, section I.A) it is apparent that if the rate of addition of the radical Y· in reaction (7) is slow, then these radicals accumulate until their concentration becomes so high that the chain is terminated by dimerization or disproportionation. Alternatively, if reaction (8) is slow, the secondary free radical

$$Y\cdot + RCH{=}CH_2 \longrightarrow R\dot{C}H{-}CH_2Y \tag{7}$$

$$R\dot{C}HCH_2Y + XY \longrightarrow RCHX{-}CH_2Y + Y\cdot \tag{8}$$

formed in reaction (7) may dimerize or add to other molecules of olefin to yield telomers. Thus, in order to compare reactivities of olefins with respect to radical addition in reaction (7), reagents which react rapidly in reaction (8) must be selected. From the result of the investigations outlined above, it follows that bromotrichloromethane and thiols are such reagents. The former reagent has been used[26] in the determination of relative reactivities of several olefins with respect to addition of a $\cdot CCl_3$ radical. This was achieved by allowing a 1 : 1 mixture of two olefins to react with a large excess of halide until about 25% of the mixed olefins had been consumed, followed by analysis of the resulting mixture.

More recently, Walling and Helmreich[82] reported the results of a similar investigation involving thiyl ($RS\cdot$) radicals derived from dodecane thiol. Preliminary experiments indicated, however, that

$$R^1S\cdot + R^2CH{=}CH_2 \rightleftharpoons R^2\dot{C}H{-}CH_2SR^1 \tag{41}$$

$$R^2\dot{C}H{-}CH_2SR^1 + R^1SH \longrightarrow R^2CH_2CH_2SR^1 + R^1S\cdot \tag{42}$$

reaction (41) is reversible, since in the addition of methane thiol to *cis*-2-butene at 60°c in the presence of azobisisobutyronitrile as initiator, the *trans* isomer appeared in the unreacted olefin. It was found that the rate constant for the formation of *trans*-2-butene from the intermediate radical $CH_3\dot{C}HCH(SCH_3)CH_3$ in reaction (41) is 80 times that for product formation by transfer with thiol (reaction 42). It should be noted, however, that the corresponding ratio of rate constants is likely to be lower in the case of addition to β-methylstyrene and related compounds, since addition yields an intermediate radical highly stabilized by resonance. It is of interest to compare the former reaction with the addition of bromotrichloromethane to the isomeric 2-butenes[83]. Attack of the trichloromethyl radical is not reversible in this case, since there is no isomerization of the butene. Both *cis* and *trans* isomers give an identical mixture of addition products, showing that the intermediate radical is the same for each.

In the addition of thiol to olefins, the reversibility of the reaction had to be taken into account when measuring the relative reactivities of olefins towards attack by thiyl radicals. By means of an elegant gas–liquid chromatographic technique, Walling and Helmreich obtained values for such relative reactivities close to those obtained by Kharasch and Sage[26] for additions involving trichloromethyl radicals. The results of both series of experiments are given in Table 4.

TABLE 4. Relative reactivities of olefins towards $\cdot CCl_3$ and RS$\cdot$ radicals.

Olefin	Relative rate		Olefin	Relative rate	
	$\cdot CCl_3$	RS$\cdot$		$\cdot CCl_3$	RS$\cdot$
1-Octene	1·0	1·0	Ethyl cinnamate	0·8	—
β-Methylstyrene	1·4	1·5	Vinyl acetate	0·8	0·8
Butadiene	18	—	Allylbenzene	0·7	1·0
Methallyl chloride	1·6	—	Allyl chloride	0·5	0·7
2-Methyl-1-butene	0·9	1·2	Allyl cyanide	0·3	0·4
2-Ethyl-1-butene	1·4	—	Cyclohexene	0·24	0·25
Vinyl butyl ether	—	3·9	Cyclopentene	0·8	0·6
Styrene	100	17	4,4,4-Trichloro-1-butene	0·3	—
p-Chlorostyrene	100	—	—	—	—
α-Methylstyrene	420	—	—	—	—

Several generalizations seem to follow from these results.

(*i*) Compounds such as styrene and butadiene, that yield resonance-stabilized radicals, are very much more reactive than those which do not.

(*ii*) The large differences in reactivity between α- and β-methylstyrenes and between styrene and ethyl cinnamate are also noticeable. This has generally been attributed to steric hindrance, although the evidence on this point is limited.

(*iii*) Electron-donating groups in the olefin increase the reactivity of the double bond in these reactions; electron-accepting groups decrease the rate of reaction. These results suggest that both the trichloromethyl and thiyl radicals behave as electron-accepting or electrophilic radicals. In agreement with this it has been found[84] that incorporation of a *p*-methoxy group into α-methoxystyrene increases its reactivity towards $\cdot SCH_2CO_2H$ radicals by a factor of 100, whereas incorporation of a *p*-fluoro group decreases reactivity by a factor of 2. By an extension of this argument, the presence of electron-attracting groups in the thiol should increase the reactivity of the derived thiyl radical, and this too has been observed[54].

The relative reactivities of some olefins toward aryl radicals in the Meerwein reaction (section I.K) have also been measured[85] (Table 5).

Apart from the position of styrene, which is not yet understood, in the series of reactivities, the results parallel those obtained for the trichloromethyl and thiyl radicals, thus strongly suggesting that aryl radicals are electron accepting or electrophilic in character. Much information has been gathered by Hey and his school[86,87] which

TABLE 5. Relative reactivities of olefins towards aryl radicals.

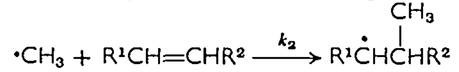
Olefin	Phenyl radical		*p*-Chlorophenyl radical
Acrylonitrile	1·00[a]	—	1·00[a]
Styrene	0·86	0·74	1·47
Methyl acrylate	0·79	0·69	0·97
Methyl methacrylate	1·07	0·93	1·52
Methacrylonitrile	—	1·00[a]	—

[a] Reference monomer.

shows that aryl radicals have varying degrees of *relative* electrophilicity according to the substituents present in the ring, but the work described above is the first which links aryl radicals as a class to other radicals in this context. The variation in the relative position of styrene in the series given in Table 5 may indeed be a function of the greater electrophilicity of the *p*-chlorophenyl compared with the phenyl radicals.

The reactivity data described above refer to *trans* isomers. Szwarc and coworkers[88] have made a kinetic study of the addition of methyl radicals to isomeric *cis*- and *trans*-olefins in a solvent. The reactivity of the methyl radical towards the olefin is expressed in the form of a ratio of velocity constants, k_2/k_1 (methyl affinity), as in equations

$$\cdot CH_3 + \text{solvent} \xrightarrow{k_1} CH_4 + \text{solvent radical} \qquad (43a)$$



$$\cdot CH_3 + R^1CH{=}CHR^2 \xrightarrow{k_2} R^1\dot{C}H\overset{CH_3}{\overset{|}{C}}HR^2 \qquad (43b)$$

(43a) and (43b). No products were isolated. The results are summarized in Table 6.

TABLE 6. Relative reactivities of *cis* and *trans* isomers (k_2/k_1)[a].

cis-2-Butene	3·4
trans-2-Butene	6·9
cis-Di-*t*-butylethylene	1·9
trans-Di-*t*-butylethylene	0·4
cis-Stilbene	29·0
trans-Stilbene	104·5
Diethyl maleate	333
Diethyl fumarate	1998

[a] In isooctane (2,2,4-trimethylpentane) at 65°c.

It is noteworthy that with the stilbenes, and also maleate and fumarate, the thermodynamically more stable isomer is the more reactive—an observation that has been confirmed by Cadogan and Inward[89].

The method of obtaining 'methyl affinities' is based on the assumption that $C_8H_{17}^\bullet$ radicals produced by hydrogen-atom abstraction from the 'solvent' (2,2,4-trimethylpentane) by methyl radicals do not react with the olefin $R^1CH{=}CHR^2$. Szwarc and coworkers have made a similar assumption when estimating the methyl affinities of a series of aromatic substrates. The validity of this assumption has been challenged in the latter case by Beckwith[90], who showed that reaction between $C_8H_{17}^\bullet$ radicals and the aromatic compound does occur in some cases. It remains to be seen whether the same objection applies to results obtained from the corresponding reactions of olefins.

More recently, the results of an investigation into the relative reactivities of the double bond in various substituted *trans*-stilbenes have been described[89]. Cadogan and Inward noted that to obtain a complete description of radical addition to an olefinic double bond, a knowledge of the overall rate of attack at an unsymmetrically substituted double bond relative to a standard is required, in addition to information concerning the position of attack. In the case of the stilbenes, some of the latter information was available (see above)[73]. For example, in the case of *trans*-4-nitrostilbene, it is conceivable that, although no selective polar effects are operative in its reaction with trichloromethyl radicals, the double bond might be deactivated relative to that in *trans*-stilbene. This could arise from a non-selective lowering of the electron density at the double bond, so that attack by the electron-accepting trichloromethyl radical would be less favoured than attack on stilbene. Under such circumstances, the direction of attack would be determined by radical stability factors while polar factors would influence its rate. Using the system devised earlier[73] whereby 1:1 adducts formed by radical chain addition of bromotrichloromethane to substituted stilbenes can be converted into the corresponding α-phenylcinnamic acids, Cadogan and Inward allowed pairs of such stilbenes and of related compounds to react in competition, with a limited amount of trichloromethyl radicals. The resulting mixture of substituted α-phenyl cinnamic acids was analysed by titration to give the relative rate k_A/k_B for the competition of two olefins A and B with trichloromethyl radicals. These results, in conjunction with those concerning directive effects reported earlier, represented the first quantitative analysis of relative reactivities of particular positions in unsymmetrical non-terminal olefins and are summarized in Table 7.

Examination of Table 7 reveals that *trans*-stilbene reacts with trichloromethyl radicals twice as quickly as *cis*-stilbene, whereas

TABLE 7. Relative reactivities (*trans*-stilbene = 1) of substituted stilbenes and related compounds towards trichloromethyl radicals.

Olefin	Relative reactivity	Olefin	Relative reactivity
trans-Stilbene	1·0	*cis*-4-Nitrostilbene	0·83
cis-Stilbene	0·55	*trans*-4-Nitrostilbene	0·86
trans-4,4′-Dibromostilbene	0·94	*trans*-β-Methylstyrene	2·0
trans-4,4′-Dibromostilbene[a]	1·09	*trans*-1-(β-Naphthyl)-2-phenylethylene	3·2

[a] Addition performed in the presence of nitromethane (2·5 mole) and bromotrichloromethane (1 mole).

4-nitro-*cis*- and -*trans*-stilbene are of comparable reactivity. This is partially explained by the observation that isomerization of 4-nitro-*cis*-stilbene to the thermodynamically more stable *trans* isomer occurred during the reaction. This presumably also took place with *cis*-stilbene although to a smaller extent. The isomerization is attributed to reversible addition of bromine atoms to the double bond, thus paralleling the isomerization of dimethyl maleate to fumarate[91] and that of 1,2-dibromoethylene[92]. It is further known[93] that light and peroxides accelerate the isomerization of *cis*-stilbene in the presence of hydrogen bromide, evidently by way of a mechanism involving bromine atoms. It should be noted, however, that Skell and Woodworth[83] did not observe isomerization of the *cis*- and *trans*-2-butenes during the photoinitiated addition of bromotrichloromethane at 0–10°c. It is clear, therefore, that generalization concerning reversibility in reactions of this type cannot be made, particularly since the reactivity of *cis*-stilbene relative to the *trans* isomer is significantly different from unity, the value to be expected if complete isomerization had occurred before addition. Since isomerization may occur in this reaction to a small but unknown extent, the relative rate ratio obtained for *cis*-stilbene must be considered to be a maximum figure.

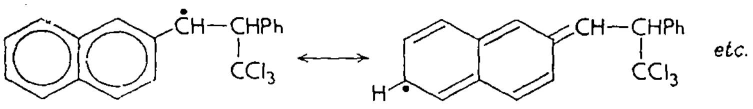
The value obtained, however, is in good agreement with that of the relative reactivity of *cis*- compared with *trans*-stilbene in other free radical reactions. Szwarc and coworkers[88] obtained a value of 0·28 for the addition of methyl radicals, and Lewis and Mayo[94] reported an approximate value of 0·5–0·67 obtained from rates of copolymerization of the two isomers with maleic anhydride. The reactivity of the *cis* isomer relative to *trans*-stilbene with respect to benzoyloxy radicals has also been found to be 0·5[95]. The higher reactivity of the *trans* isomer has been rationalized[88] in terms of the greater resonance stabilization of the transition state derived from the *trans* form.

With regard to the addition of trichloromethyl radicals to substituted stilbenes, it has been concluded earlier that the factor which mainly governs the orientation of addition is the relative stability of the possible intermediate radicals.

These conclusions are confirmed by the magnitude of the relative rate ratios of 4-nitro-*trans*-stilbene, 4,4′-dibromo-*trans*-stilbene, and *trans*-1-(β-naphthyl)-2-phenylethylene. It is clear that the polarity of the substituent group has no effect on the overall reactivity of the olefinic double bond in the stilbene series. It is also noteworthy that the presence of nitromethane, a solvent of high dielectric constant, in the reaction does not significantly affect the relative ratio obtained for 4,4′-dibromo-*trans*-stilbene.

These observations can be rationalized in terms of the stability of the intermediate radicals in each case. The reactivity of 4-nitro-*trans*-stilbene and 4,4′-dibromo-*trans*-stilbene are similar to that of *trans*-stilbene, reflecting once again the small effects of the nitro group and bromine atom in the 4-position on the stability of the intermediate free radical.

The effect is most marked with *trans*-1-(β-naphthyl)-2-phenylethylene, in which case the relative rate ratio is 3·2. In this case, additional resonance stabilization can occur in one of the possible intermediate radicals, thus explaining the higher reactivity of this olefin.



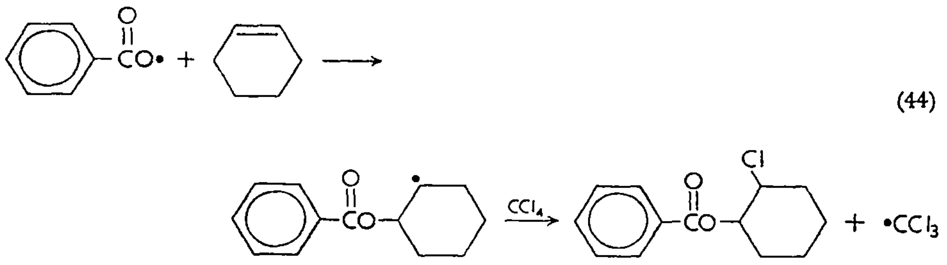
The overall picture for relative rates of addition to olefins, therefore, appears to be that where pronounced stabilization of the radical is possible, this will be the dominant factor. Only where radical stabilization is less important are we likely to observe effects attributable to polarization either in the radical or in the olefin.

H. Mechanisms of the Addition Reaction

In a discussion of the mechanism of the addition reaction, it is convenient to consider the three main stages separately. Although data about the initiation step are sparse, and no direct evidence that chain initiation takes place by the reaction $R\cdot + CX_4 \rightarrow \cdot CX_3 + RX$ has been presented in the work so far considered, the general reaction scheme for chain propagation has received ample support as a result of the isolation and identification of the various 1 : 1 adducts and telomers; this part of the reaction need not therefore be further discussed. As with the initiation step, only a few attempts have been made to isolate products which would give conclusive proof of the nature of the termination step.

I. Chain initiation

In most radical chain reactions, the average kinetic chain lengths are very large and consequently the proportions of groupings derived from the initiators are very small. Kooyman and Farenhorst noted[96], however, that only 20 to 40 moles of addition product are formed per mole of peroxide in the peroxide-catalysed addition of carbon tetrachloride to cyclohexene. They were accordingly able to isolate products derived from the decomposition of the peroxide initiator. Of the phenyl radicals from the peroxide, 55% appeared as 2-chlorocyclohexyl benzoate, thus indicating an addition–initiation process (equation 44). Chain initiation by abstraction ($R\cdot + CCl_4 \rightarrow RCl + \cdot CCl_3$) is less important in this case, since only 10% of the phenyl radicals appear as chlorobenzene and 12% as benzoic acid.



(44)

An abstraction process as a method of initiation is inferred from a recent study[73a] of the addition of bromotrichloromethane to *trans*-stilbene in the presence of a di-*t*-butyl peroxide. Most (64%) of the peroxide appeared as *t*-butyl hypobromite and 7% as *t*-butyl bromide, a small amount of deoxybenzoin was also formed. These results clearly show that the main initiation reaction involves the abstraction of a bromine atom from the solvent to give a trichloromethyl radical and *t*-butyl hypobromite. The genesis of *t*-butyl bromide is less obvious and suggests that a second mode of initiation is operative. It is well known[97] that the thermal decomposition of di-*t*-butyl peroxide in solvents does not lead to *t*-butyl radicals; hence the formation of *t*-butyl bromide in this case cannot be the result of a simple abstraction of a bromine atom from the solvent. Frey[98] has shown that some of the products of photolysis of pure di-*t*-butyl peroxide can be accounted for by invoking the formation (12%) of free *t*-butyl radicals, but these special conditions did not obtain in the case under discussion above.

The difference between modes of initiation in reactions involving bromotrichloromethane and carbon tetrachloride is probably a function of the great facility with which bromine atom abstraction occurs in the former case.

Initiation of chain-addition reactions by irradiation with light of suitable wavelength needs no further discussion. More recently, high-energy radiation has also been found to be useful in this respect[99]. Trace metals such as tin[100], cobalt or silver[101] have also been found to initiate free-radical addition reactions under much milder conditions than those employed with peroxidic catalysts. The mechanisms of these reactions are still obscure.

2. Chain termination

In general chain termination occurs by radical dimerization or disproportionation. In some cases, it has been found that large amounts of peroxide are needed to produce good yields of 1 : 1 adducts. In the reaction of carbon tetrachloride with cyclohexene (3:1) where chain termination by dimerization of trichloromethyl radicals does not take place, the chain-breaking step is considered to consist of the formation of radicals of low reactivity, such as the resonance-stabilized allylic radicals which are unable to continue the chain (equation 45)[96].

$$\cdot CCl_3 + RCH_2{-}CH{=}CH_2 \longrightarrow R\dot{C}H{-}CH{=}CH_2 + CHCl_3 \qquad (45)$$

This mechanism is supported by the isolation of chloroform and of bicyclohexen-2-yl formed by dimerization of the allyl-type radicals. The latter compound has also been detected in the products of the reaction of diethyl malonate with cyclohexene[31]. A similar abstraction of a hydrogen atom to give a resonance-stabilized radical probably explains the failure[43] of the addition of α,β-unsaturated aldehydes to olefins. This mechanism constitutes an example of 'degradative chain transfer'[102]. If allylic α-methylene hydrogen atoms are not available for abstraction, as in 3,3-dimethyl-1-butene, much less peroxide is necessary to produce a high yield of 1:1 adduct in the reaction of the olefin with carbon tetrachloride compared with 1-decene, say, since chain ending occurs by the much less efficient method of radical–radical interaction. This is supported by the isolation of hexachloroethane. On the other hand, allylbenzene, which gives an allyl-type radical of great stability, exhibits little (2%) addition owing to its faster rate of chain breaking. Further, in small amounts it inhibits the addition of carbon tetrachloride to 3,3-dimethyl-1-butene.

The overall picture of chain termination under these conditions is therefore consistent with a reaction of the type given in equation (46).

$$R^{1\cdot} + CH_2{=}CHCH_2R^2 \longrightarrow R^1H + CH_2{=}CH\dot{C}HR^2 \qquad (46)$$

Huyser[103] has recently measured the ratio of the rate of addition of a $\cdot CCl_3$ radical to the double bond to that of α-methylenic hydrogen abstraction for a series of olefins. He noted the amount of chloroform formed in a reaction of an olefin with bromotrichloromethane.

TABLE 8. Addition *versus* allylic abstraction by trichloromethyl radicals.

Alkene	Temp. (°c)	$\frac{k_{add.}}{k_{abs.}}$	Alkene	Temp. (°c)	$\frac{k_{add.}}{k_{abs.}}$
1-Octene	77·8	43	*cis*-2-Butene	99	34
1-Decene	77·8	44	*trans*-2-Butene	99	26
2-Pentene	77·8	6	Cyclohexene	77·8	1·2
3-Heptene	77·8	3·5	Cyclohexene	40·0	1·85
3-Heptene	40·0	5	Cyclopentene	77·8	5
4-Methyl-2-pentene	77·8	1·3	Cyclopentene	40·0	6·5
4-Methyl-2-pentene	40·0	1·7	Cycloheptene	77·8	5·5
			Cycloheptene	40·0	8

The results summarized in Table 8 indicate that the amount of hydrogen abstraction by the trichloromethyl radical with respect to addition to 1-octene and 1-decene is small. This is consistent with the absence of side products in addition of bromotrichloromethane to terminal alkenes. Hydrogen abstraction is more important in non-terminal olefins such as 2-pentene and 3-heptene. Here, the addition is sterically hindered and Huyser attributes the comparatively low ratio to a decrease in $k_{add.}$ rather than to an increase in $k_{abs.}$. In non-terminal olefins, however, $k_{abs.}$ appears to increase in the order primary allylic hydrogen < secondary < tertiary, which is the expected order, reflecting the stabilities of the radicals produced. Thus the 2-butenes display little abstraction compared with addition. 2-Pentene, with two allylic hydrogen atoms on a secondary carbon atom, undergoes considerable hydrogen abstraction. The increase in $k_{abs.}$ in 3-heptene is probably statistical, reflecting the greater number of secondary allylic hydrogen atoms in this case. 4-Methyl-2-pentene has a tertiary allylic hydrogen atom which results in a very low ratio of $k_{add.}/k_{abs.}$.

As already stated, the above order of reactivities can be explained in terms of the relative stabilities of the radicals formed, but Huyser points out that a further factor may involve the ease of formation of the transition state. If the $\cdot CCl_3$ radical is assumed to have some degree of carbanion character in the transition state, then for abstraction from 2-butene, 2-pentene and 4-methyl-2-pentene, the transition states

$$Cl_3\overset{\delta-}{C}\cdots H\cdots \overset{\delta+}{C}H_2CH{=}CHCH_3$$

(17)

$$Cl_3\overset{\delta-}{C}\cdots H\cdots \overset{\delta+}{C}H(CH_3)CH{=}CHCH_3$$

(18)

$$Cl_3\overset{\delta-}{C}\cdots H\cdots \overset{\delta+}{C}(CH_3)_2CH{=}CHCH_3$$

(19)

will be **17**, **18** and **19** respectively. The order of reactivities is then predicted to follow the order of stabilities of the incipient carbonium ions in the transition state, as observed.

The high rate of abstraction from cyclohexene is again noteworthy. The value of $k_{add.}$ may be low for steric reasons but this is probably not the entire explanation for the low ratio $k_{add.}/k_{abs.}$. Abstraction is probably favoured because two of the allylic hydrogen atoms present a favourable equatorial aspect to the approaching trichloromethyl radical. Further it is possible that loss of an allylic hydrogen atom leads to release of strain in the molecule. The ratios $k_{add.}/k_{abs.}$ obtained for reactions with cyclopentene and cycloheptene are less easily rationalized, but here again conformational factors probably govern the reaction.

Under different conditions, different mechanisms may be operative. Melville, Robb and Tutton[104], in a kinetic study of the addition of bromotrichlormethane to cyclohexene, have shown that at high concentration of halide (halide:olefin = 10:1), chain termination is due exclusively to dimerization of trichloromethyl radicals, while at low concentrations of halide (1:10), the rate-determining stage of the reaction becomes the debromination of bromotrichloromethane by the trichloromethylcyclohexyl radical, and dimerization of these radicals constitutes the chain-termination step. Corroboration of this by isolation of 2,2′-di(trichloromethyl)bicyclohexyl has not yet been attempted.

Chain termination in the reaction of $BrCCl_3$ with stilbene under the former conditions also involves dimerization of CCl_3 radicals[73a]. That the method of chain termination may vary with the type of compounds involved is clearly shown by the isolation of small quantities of acetaldehyde and cyclohexanone from the peroxide-induced additions of ethanol and cyclohexanol to olefins[49], as in equation (47),

$$R\cdot + CH_3\dot{C}HOH \longrightarrow RH + CH_3CHO \tag{47}$$

where R· is a free *t*-butoxy or an intermediate free radical. This type of reaction is evidently dominant in the attempted peroxide-induced addition of benzyl alcohol to ethylene, since benzaldehyde is obtained instead of the expected product. Termination of radical chains in addition reactions can also be brought about by interaction with metallic halides. Kochi[105] has shown, for example, that the polymerization of styrene can be inhibited by cupric and ferric chlorides with the formation of chlorides (equation 48). Such interaction of

$$R\cdot + PhCH{=}CH_2 \longrightarrow Ph\dot{C}H{-}CH_2R \tag{48a}$$

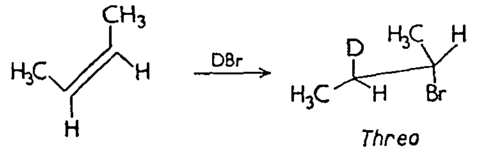
$$Ph\dot{C}H{-}CH_2R + PhCH{=}CH_2 \not\longrightarrow Ph\dot{C}H{-}CH_2CHPhCH_2R \tag{48b}$$

$$Ph\dot{C}H{-}CH_2R + FeCl_3 \longrightarrow PhCHClCH_2R + FeCl_2 \tag{48c}$$

radicals with metallic halides has great significance in relation to the mechanisms of the Sandmeyer and Meerwein reactions, and is discussed in greater detail in section I.K.

I. Stereochemistry of Radical-addition Reactions

The evidence relating to the stereochemistry of free-radical addition to olefins is sparse. The addition of bromotrichloromethane to *cis*- or to *trans*-2-butene produces in each case identical mixtures of the two diastereoisomeric 1:1 addition products. This indicates that the 3-trichloromethyl-2-butyl radical ($CH_3CH(CCl_3)\dot{C}HCH_3$), assumed to be pyramidal, formed by addition of a trichloromethyl radical to either *cis*- or *trans*-2-butene has a life sufficiently long for equilibrium among its conformers to be reached before reacting further[83]. The homolytic addition of HBr to acyclic olefins at room temperature and above is also non-stereospecific. At very low temperatures (−78°) on the other hand, DBr adds to both *cis*- and *trans*-2-butene in a stereospecifically *trans* manner, the *cis* isomer giving wholly *threo*-bromide (equation 49a), the *trans* isomer giving the *erythro* form (equation 49b)[106]. Similarly, Goering and Larsen[107], who assume a planar intermediate radical, showed that the additions of HBr and DBr to the isomeric 2-bromo-2-butenes are also completely stereospecifically *trans* at −78°, since addition to the *cis* and *trans* isomers produces different products, the *meso* and (±) forms respectively (equations 50a, 50b). As the temperature of the reaction is increased, however, the stereospecificity, as shown by the ratio of (*meso*/±) or (±/*meso*), diminishes to the point where both olefins give the same product at room temperature. Since HBr and DBr are particularly good transfer agents in radical-addition reactions, it would be expected that diastereoisomeric radicals produced in their presence would tend to abstract a hydrogen atom before attaining equilibrium among its conformations. The fact that such stereospecificity occurs only at low temperatures (when the concentration



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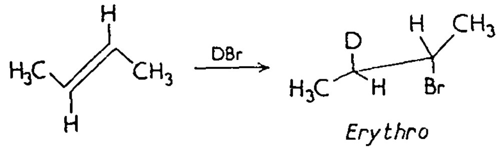

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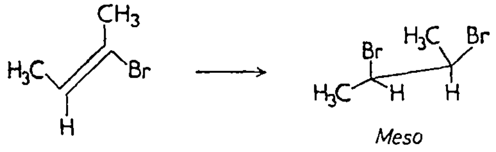
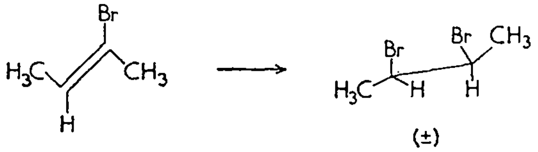


(50a)

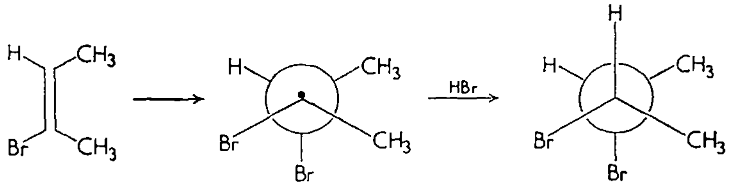


(50b)

of HBr is high, and rotation about the C—C bond in the intermediate radical is much less likely) suggests that stereospecific addition reactions in acyclic systems are unlikely to be observed with other addenda. In this connexion it is interesting to note that even additions of bromotrichloromethane are not usually stereospecific, nor is the addition of CH_3SD to *cis*- and *trans*-2-butenes[108] at −70°. The transfer agent next most likely to undergo stereospecific addition to open-chain olefins is RSH, although the addition of H_2S to the isomeric 2-chloro-2-butenes in liquid H_2S is not stereospecific[101]. More recently, however, conditions for the stereospecific (*trans*) addition of mercaptans to olefins have been established by Skell and Allen[108], who studied the reaction of methyl deuteromercaptan (CH_3SD) with the *cis*- and *trans*-2-butenes in the presence of DBr. In this case the 3-deutero-2-bromobutanes were formed in a stereospecifically *trans* process as were the 3-deutero-2-methylthiobutanes, the *cis* isomer producing the *threo* form of the latter, the *trans* isomer producing the *erythro*. Thus it can be concluded that DBr is the sole transfer agent with the radicals $CH_3CHX\dot{C}HCH_3$ and also that the equilibration (51) is more rapid

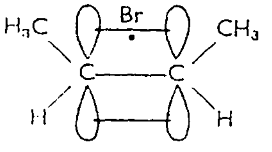
$$Br^{\bullet} + CH_3SD \longrightarrow DBr + CH_3S^{\bullet} \qquad (51)$$

than additions of $Br^{\bullet}$ and $CH_3S^{\bullet}$ to these olefins. Steric control of mercaptan additions is therefore achieved by the rapid reaction of the diastereoisomerically related 3-methylthio-2-butyl radicals with HBr, a reaction which is more rapid than the isomerization of the radicals. In the absence of HBr, these radicals achieve equilibration between their conformations before reacting with the transfer agent, CH_3SD (or CH_3SH).



(52)

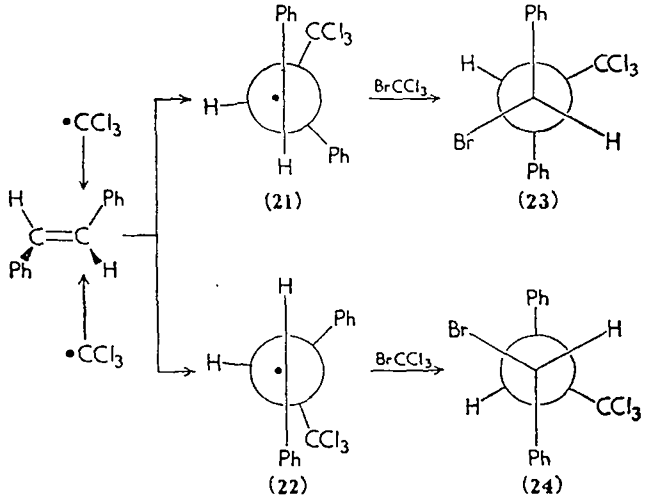
There are two possible explanations for the *trans*-addition reactions of open-chain olefins. For addition of HBr to *cis*-2-bromo-2-butene to give the *meso* dibromide, the intermediate radical may be considered to react with HBr before rotation, and in such a way that the newly acquired bromine atom is always as far removed as possible from the transfer agent (equation 52). It may also be that the bromine atom, instead of attacking a molecule of olefin, attacks a π-complex derived from olefin and HBr, a pathway also leading to stereospecific addition. Such a mechanism less satisfactorily explains the diminution of stereospecificity with rise in reaction temperature. Recently, Abell and Piette[109] have examined the electron paramagnetic resonance spectra of the intermediate free radicals produced during the ultraviolet-initiated addition of hydrogen bromide to various acyclic and alicyclic olefins at low temperatures. From such a study it was hoped that unequivocal conclusions concerning the structure of the intermediate radicals would be obtained, thus leading to a rationalization of the stereochemistry of the addition process. It was confirmed by the use of DBr instead of HBr that bromine atom addition is the initial step in this process since the spectra in each case were identical, but it was not possible to establish with certainty the structure of the intermediate, although these workers claim that the formation of a bridged structure **20** could be considered to be consistent with their observations. Clearly, much useful information



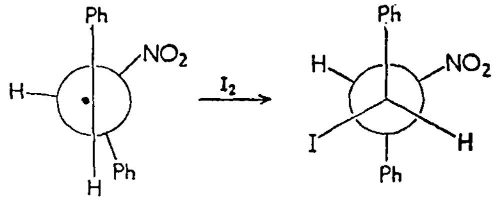
(20)

could be produced by extensive investigations of the electron spin resonance spectra of such radicals.

As already stated, additions of bromotrichloromethane to acyclic olefins are not usually stereospecific, but it has been shown[73a] that the results of the addition of bromotrichloromethane to *trans*-stilbene are explicable only if stereospecific control of the reaction is taken into account. Addition of trichloromethyl radicals to *trans*-stilbene will give equal amounts of the intermediate radicals **21** and **22**, which in theory would be expected to reach equilibrium between their conformers by inversion before abstraction of a bromine atom from the chain-transfer reagent, bromotrichloromethane, and thus give rise to four isomeric 1 : 1 adducts distributed between two different enantiomorphic pairs. This situation was found to obtain in the addition of bromotrichloromethane to *cis*- and to *trans*-2-butene[83]. In contrast, Cadogan and Duell[73a] detected only one racemic adduct to the stilbenes. This suggests that the *chain-transfer* reactions of the intermediate radicals in this case are stereospecific, proceeding through preferred conformations in which the bulky phenyl and trichloromethyl groups are as far apart as possible. It is thus reasonable that the bromotrichloromethane molecule should approach the radicals from the least hindered side in each case to give a single racemic mixture of isomeric 1 : 1 adducts **23** and **24**.



A similar explanation accounts for the observation that the reaction of dinitrogen tetroxide with *cis*- or *trans*-stilbene in the presence of iodine gives only one of the isomeric 1,2-diphenyl-2-nitroethyl iodides (equation 53)[110].

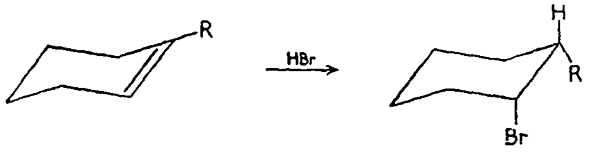


(53)

In contrast to reactions of acyclic radicals described above, equilibration between conformations by free rotation about C—C bonds is impossible in the radicals produced by addition to cyclic olefins. Use of such olefins is, therefore, helpful in deciding the extent of stereochemical control of radical addition reactions with reagents other than HBr.

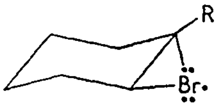
The homolytic additions of HBr to 1-methyl-[111], 1-chloro-[112] and 1-bromocyclohexenes have been shown to be stereospecifically *trans*.

Addition to 1-methylcyclohexene, for example, gives *cis*-1-bromo-2-methylcyclohexane in which the incoming hydrogen and bromine are *trans* to one another (equation 54). It is tempting to rationalize these observations in terms of a bridged intermediate **25**, but this is unlikely, since the bromine atom carries nine electrons.



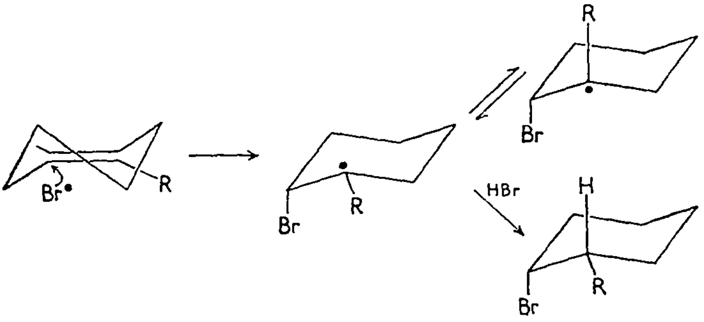
(54)

($R=CH_3$, Cl, Br)



(**25**)

It is more reasonable to assume that the bromine atom attacks the double bond by the least hindered route, which corresponds to an axial direction in the resulting intermediate cyclohexyl radical. It has been suggested by Brand and Stevens[69] that in the intermediate radical the bonds about the trivalent carbon atom are pyramidal rather than planar, so that two conformations are possible, the group R being either axial or equatorial. Sterically, the equatorial conformation is preferred, leaving an axial position open to attack by HBr. Thus the *cis* isomer is formed, provided chain transfer occurs before ring inversion, for such inversion would place the bromine atom in the thermodynamically more stable position.



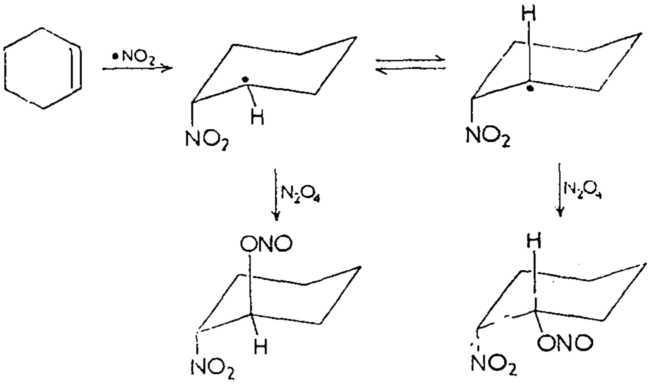
The addition of thiols to cyclohexene derivatives is non-stereospecific, although a preponderance of *trans* addition occurs[113,114]. Here, the same considerations which applied to the addition of HBr to cyclohexenes are operative, with the addition that thiols are considerably less active transfer agents that HBr, as discussed above;

hence the intermediate radical will have time to reach at least partial equilibration between its conformations, so that non-stereospecific addition occurs. Presumably, addition of mercaptans to such olefins in the presence of HBr would also lead stereospecifically to *trans* addition (*cf.* the addition of HBr/CH_3SH to the 2-butenes).

The addition of N_2O_4 to olefins has been shown to proceed by way of $\cdot NO_2$ radicals[69]:

$$RCH{=}CH_2 \xrightarrow{\cdot NO_2} R\dot{C}HCH_2NO_2 \xrightarrow{N_2O_4} RCH(NO)_2CH_2NO_2 \text{ (or } RCH(ONO)CH_2NO_2)$$

The addition to 1-methylcyclohexene is stereospecifically *trans*, whereas that to cyclohexene is non-stereospecific (58% *trans*). In the former case, the considerations discussed in connexion with the additions of HBr apply. In the case of cyclohexene, no stereochemical preference exists in the intermediate radical, and *cis* as well as *trans* addition can occur.



J. Rearrangements in Free-radical Reactions of Alkenes

In contrast to rearrangements of heterolytic intermediates, which have been frequently reported, fewer rearrangements which proceed by a homolytic mechanism have been described.

Since most of these have been 1,2-shifts, it is necessary to consider the possibility of their occurrence in radical addition reactions where the orientation data are derived largely from analysis based on the assumption of non-rearrangement of the intermediate radical. Such rearrangements also provide a direct measure of the relative stabilities of the radicals involved. Recently, examples of homolytic rearrangement during addition reactions have been reported. Nesmeyanov and coworkers[115], in a reinvestigation of the addition of HBr to

1,1,1-trichloropropene, noted that rearrangement of the intermediate radical occurred, *e.g.* equation (55). This school has also reported[115]

$$\mathrm{CCl_3CH{=}CH_2 + Br\cdot \longrightarrow CCl_3\dot{C}HCH_2Br \longrightarrow \cdot CCl_2CHClCH_2Br \xrightarrow{+HBr} CHCl_2CHClCH_2Br + Br\cdot} \tag{55}$$

a rearrangement of the intermediate radical produced in the addition of bromotrichloromethane to 1,1,1-trichloro-2-propene (Scheme 5)

$$\begin{gathered}
\mathrm{CCl_3CH{=}CH_2 + \cdot CCl_3 \longrightarrow CCl_3\dot{C}HCH_2CCl_3 \longrightarrow \cdot CCl_2CHClCH_2CCl_3} \\
\mathrm{\cdot CCl_2CHClCH_2CCl_3 + BrCCl_3 \longrightarrow CBrCl_2CHClCH_2CCl_3 + \cdot CCl_3} \\
\mathrm{\cdot CCl_2CHClCH_2CCl_3 \longrightarrow CCl_2{=}CHCH_2CCl_3 + Cl\cdot} \\
\mathrm{Cl\cdot + CCl_3CH{=}CH_2 \longrightarrow CCl_3\dot{C}HCH_2Cl \longrightarrow \cdot CCl_2CHClCH_2Cl} \\
\mathrm{CCl_3\dot{C}HCH_2Cl + BrCCl_3 \longrightarrow CCl_3CHBrCH_2Cl + \cdot CCl_3} \\
\mathrm{\cdot CCl_2CHClCH_2Cl + BrCCl_3 \longrightarrow CBrCl_2CHClCH_2Cl + \cdot CCl_3}
\end{gathered}$$

SCHEME 5.

and also the formation of 1,1,2,2-tetrachloro-3-bromopropane, 1,1,2,3-tetrachloro-1-propene, 1,1,2-trichloro-3-bromo-1-propene and 1,1,2,2,3-pentachloropropane from the peroxide-catalysed reaction of HBr with 1,1,1,2-tetrachloro-2-propene (Scheme 6)[116].

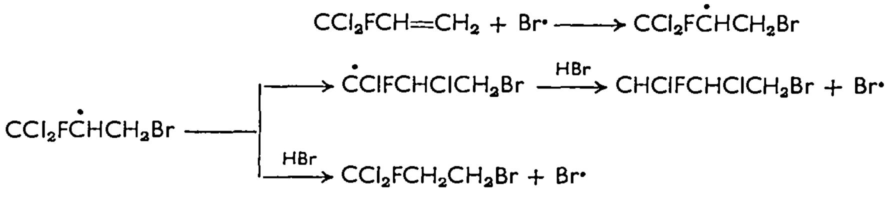
$$\begin{gathered}
\mathrm{CCl_3CCl{=}CH_2 \longrightarrow CCl_3\dot{C}{=}CH_2 + Cl\cdot} \\
\mathrm{Cl\cdot + CCl_3CCl{=}CH_2 \longrightarrow C\dot{C}l_3CClCH_2Cl \longrightarrow \cdot CCl_2CCl_2CH_2Cl} \\
\mathrm{\cdot CCl_2CCl_2CH_2Cl \longrightarrow CCl_2{=}CClCH_2Cl + Cl\cdot} \\
\mathrm{\cdot CCl_2CCl_2CH_2Cl + HBr \longrightarrow CHCl_2CCl_2CH_2Cl + Br\cdot} \\
\mathrm{Br\cdot + CCl_3CCl{=}CH_2 \longrightarrow CCl_3\dot{C}ClCH_2Br \longrightarrow \cdot CCl_2CCl_2CH_2Br} \\
\mathrm{\cdot CCl_2CCl_2CH_2Br \longrightarrow CCl_2{=}CClCH_2Br + Cl\cdot} \\
\mathrm{\cdot CCl_2CCl_2CH_2Br + HBr \longrightarrow CHCl_2CCl_2CH_2Br + Br\cdot}
\end{gathered}$$

SCHEME 6.

The formation of 1-bromo-2-methyl-2,3,3-trichloropropane from 2-methyl-3,3,3-trichloro-1-propene and HBr follows a similar route[117], as does the radical-catalysed addition of HBr to 3,3-dichloro-1-propene[118].

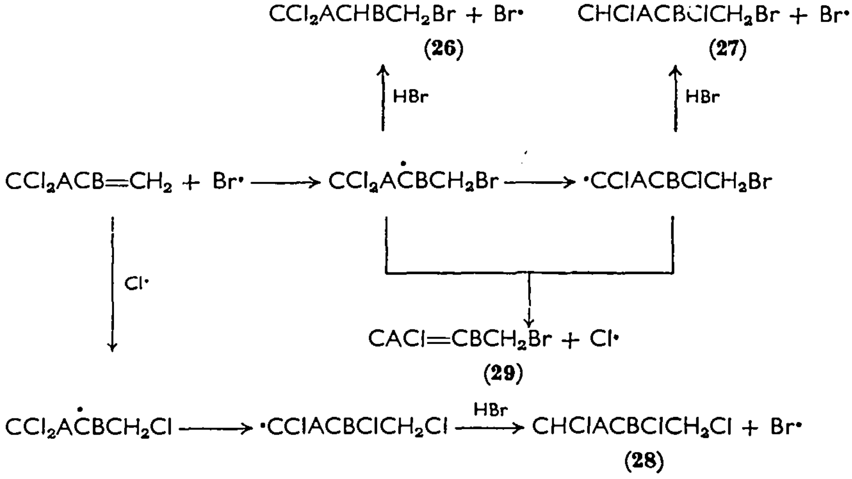
$$\mathrm{Br\cdot + Cl_2CHCH{=}CH_2 \longrightarrow Cl_2CH\dot{C}HCH_2Br \longrightarrow Cl\dot{C}HCHClCH_2Br \xrightarrow{HBr} ClCH_2CHClCH_2Br + Br\cdot}$$

In the cases so far discussed, where the intermediate radicals were of the type $CCl_3\dot{C}H$— or $CHCl_2\dot{C}H$—, exclusive rearrangement to the isomeric $\dot{C}Cl_2CHCl$— or $\dot{C}HClCHCl$— radicals occurs before chain transfer with the addendum, even when this is HBr, which is the most reactive chain-transfer agent. Recently, however, partial rearrangement of the intermediate radical has been observed during the addition of HBr to 3,3-dichloro-3-fluoro-1-propene, when both 1-bromo-3,3-dichloro-3-fluoropropane and 1-bromo-2,3-dichloro-3-fluoropropane were formed[119], showing that the introduction of fluorine into a radical markedly affects its stability.



Scheme 7.

The above examples which, together with others, are summarized in Table 9, allow an estimate to be made of the relative stabilities of various haloalkyl free radicals and, further, allow a common mechanism (Scheme 8) to be put forward, *e.g.* for reaction with HBr.



Scheme 8.

It is therefore clear that the presence of a free electron in a molecule can, under certain circumstances, facilitate homolysis of an adjacent C—Cl or C—Br bond, thus leading to 1,2-halogen shifts. In accord

TABLE 9. Rearrangements occurring in radical additions of polyhaloalkenes.

Alkene	Addendum	'Normal' product (26)	Rearranged products			Rearrangement (%)	Reference
			(27)	(28)	(29)		
$CCl_3CH{=}CH_2$	HBr		$CHCl_2CHClCH_2Br$ (77)[a]			100	115
$CCl_3C(CH_3){=}CH_2$	HBr		$CHCl_2C(CH_3)ClCH_2Br$ (59)	$CHCl_2C(CH_3)ClCH_2Cl$ (11)[a]	$CCl_2{=}C(CH_3)CH_2Br$ (15)[a]	100	120
$CCl_3CCl{=}CH_2$	HBr		$CHCl_2CCl_2CH_2Br$ (34)	$CHCl_2CCl_2CH_2Cl$ (14)	$CCl_2{=}CClCH_2Br$ (15)	100	116
$CHCl_2CH{=}CH_2$	HBr	$CHCl_2CH_2CH_2Br$ (5)[a]	$CH_2ClCHClCH_2Br$ (46)			90	118, 121
$CH_3CCl_2CH{=}CH_2$	HBr		$CH_3CHClCHClCH_2Br$ (73)			100	121
$CFCl_2CH{=}CH_2$	HBr	$CFCl_2CH_2CH_2Br$ (39)	$HCFClCHClCH_2Br$ (18)			30	119
$CHCl_2CCl{=}CH_2$	HBr	$CHCl_2CHClCH_2Br$ (30)				0	116
$CHCl_2C(CH_3){=}CH_2$	HBr	$CHCl_2CH(CH_3)CH_2Br$ (34)	$CH_2ClC(CH_3)ClCH_2Br$ (30)		$CHCl{=}C(CH_3)CH_2Br$ (12)	47	121
$CCl_3CH{=}CH_2$	$BrCCl_3$		$BrCCl_2CHClCH_2CCl_3$ (18)	$BrCCl_2CHClCH_2Cl$ (14)	$CCl_2{=}CHCH_2CCl_3$ (26)	100	115
$CCl_3CH{=}CH_2$	PhSH		$CHCl_2CHClCH_2SPh$ (30)		$CCl_2{=}CHCH_2SPh$ (11)	100	122

[a] Figures in parentheses represent percentage yields.

with this Nesmeyanov, Freidlina and coworkers have been able to induce homolytic isomerization of certain polyhaloalkenes, *e.g.* that of 1,1,1-trichloro-2-bromo-2-propene into 1,1,2-trichloro-3-bromo-1-propene (Scheme 9)[123].

$$\begin{aligned}
CCl_3CBr{=}CH_2 &\xrightarrow{h\nu} CCl_3\dot{C}{=}CH_2 + Br\cdot \\
CCl_3CBr{=}CH_2 + Br\cdot &\longrightarrow CCl_3\dot{C}BrCH_2Br \\
CCl_3\dot{C}BrCH_2Br &\longrightarrow \cdot CCl_2CBrClCH_2Br \\
\cdot CCl_2CBrClCH_2Br &\longrightarrow CCl_2{=}CClCH_2Br + Br\cdot
\end{aligned}$$

SCHEME 9.

It appears from these results that a radical with the structure $\cdot CCl_2C\!<$ is more stable than are the secondary and tertiary radicals $>\!C\dot{C}HC\!<$, $>\!C\dot{C}ClC\!<$, and $(>\!C)_3C\cdot$. Nesmeyanov and coworkers[124] have extended this classification of relative radical stability as follows:

$$RCH_2\cdot < R_2CH\cdot < R_3C\cdot \ll RCHCl\cdot < R_2CCl\cdot < RCCl_2\cdot \text{ (most stable)}$$

This series is derived for systems where R is a polyhaloalkyl group, although it is noteworthy that the order of the first three members of the sequence is in accord with the corresponding sequence when R is alkyl.

Among the most significant observations on radical rearrangements are those of Skell, Allen and Gilmour[125] and of Wiley and coworkers[126]. The former showed that radical chain chlorination of isopropyl bromide gives, among other products, 1-bromo-2-chloropropane and that of *t*-butyl bromide gives 1-bromo-2-chloro-2-methylpropane. These experiments indicate that 100% rearrangement results from the removal of hydrogen atoms from the methyl groups of isopropyl and *t*-butyl bromides (equations 56 and 57).

$$CH_3CHBrCH_3 \longrightarrow \underset{\textbf{(30)}}{CH_3CHBrCH_2\cdot} \longrightarrow \underset{\textbf{(31)}}{CH_3\dot{C}HCH_2Br} \xrightarrow{Cl_2} CH_3CHClCH_2Br \qquad (56)$$

$$(CH_3)_2CBrCH_3 \longrightarrow (CH_3)_2CBrCH_2\cdot \longrightarrow (CH_3)_2\dot{C}CH_2Br \xrightarrow{Cl_2} (CH_3)_2CClCH_2Br \qquad (57)$$

Since the intermediate radicals **30** and **31** might also be expected from the homolytic addition of HBr to 1-propene, it is possible that the observed terminal addition of bromine atoms in this case arises by way of rearrangement of the non-terminal intermediate radical. On the other hand, hydrogen bromide is the most reactive transfer agent known, and it is probable that chain transfer of the intermediate radical **30** with HBr would occur before rearrangement, so that the observed absence of non-terminal addition product ($RCHBrCH_3$) is due to reasons (outlined above) other than radical rearrangement.

The possibility of rearrangements in less reactive systems, however, must be borne in mind when discussing the orientation of free-radical addition reactions, although no experimental support for this possibility has been advanced.

Wiley and coworkers[126a], in a study of the γ-radiolysis of n-propyl chloride, have invoked 1,2-radical shifts to explain the formation of small amounts of isopropyl chloride (equation 58). In this case a

$$CH_3CH_2CH_2Cl \longrightarrow CH_3CH_2CH_2\cdot \longrightarrow CH_3\dot{C}HCH_3 \xrightarrow{+CH_3CH_2CH_2Cl} CH_3CHClCH_3 + CH_2CH_2CH_2\cdot \qquad (58)$$

similar rearrangement to that reported by Skell occurs. It should be noted, however, that radicals formed by high-energy radiation are likely to have properties different from those produced in peroxide-induced reactions.

Benson and Willard[126b] later showed that the radiolysis of propyl chloride is catalysed by hydrogen chloride and retarded by propylene, that hydrogen in the hydrogen chloride exchanges but chlorine does not, and that high *G* values* for the formation of 2-chloropropane are obtained. They thus established that the mechanism of the rearrangement was as in equation (59). The last step in this reaction, which

$$CH_3CH_3CH_2Cl \xrightarrow{Cl\cdot} CH_3\dot{C}HCH_2Cl \longrightarrow CH_3CHClCH_2\cdot \xrightarrow{+HCl} CH_3CHClCH_3 + Cl\cdot \qquad (59)$$

must be reversible, is noteworthy, as pointed out by Mayo[126c], since it corresponds to radical displacement on hydrogen chloride which is usually energetically unfavourable and also involves rearrangement of a secondary to a primary radical. Mayo therefore concludes that in reactions of radicals of the type under discussion, which require little activation energy, the products correspond to the more stable radical ($CH_3\dot{C}HCH_2Cl$), at least when the halogen is bromide. In reactions which are more difficult, as with hydrogen chloride, then the more stable product, Me_2CHCl, is formed from minor proportions of the less stable but more reactive radical ($CH_3CHClCH_2\cdot$). These

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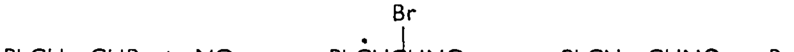
* G = molecules formed per 100 ev absorbed.

considerations will not necessarily apply, of course, when the intermediate radicals contain several halogen atoms, since the stabilities and hence reactivities of the radicals will also be altered.

In addition to complications arising from rearrangements of intermediate radicals in these systems, it is important to note the possibility of reversibility of the addition step. This has been discussed above for the addition of thiols and phosphines to olefins, and it has been shown that isomerization of the olefin can occur in these reactions. Radical elimination is an extension of reversibility, as shown by the results of the addition of $\cdot NO_2$ radicals derived from N_2O_4 to β-bromostyrene[127]. Here the isolation of β-nitrostyrene shows that elimination had occurred as in equation (60).



$$PhCH{=}CHBr + \cdot NO_2 \longrightarrow Ph\dot{C}H\overset{Br}{\overset{|}{C}}HNO_2 \longrightarrow PhCH{=}CHNO_2 + Br\cdot \qquad (60)$$

Kharasch and Sage also observed unexpected products resulting from elimination of a halogen atom from the intermediate radical produced during the addition of bromotrichloromethane to allyl bromide[128]. The products isolated vary with the proportions of reactants. Irradiation of a mixture of bromotrichloromethane and allyl bromide (4:1) gave 1,2,3-tribromopropane and 1,1,1,5,5,5-hexachloro-3-bromopentane, which could have arisen as in Scheme 10.

$$\cdot CCl_3 + CH_2{=}CHCH_2Br \longrightarrow CCl_3CH_2\dot{C}HCH_2Br \longrightarrow CCl_3CH_2CH{=}CH_2 + Br\cdot$$

$$\cdot CCl_3 + CCl_3CH_2CH{=}CH_2 \longrightarrow CCl_3CH_2\dot{C}HCH_2CCl_3$$

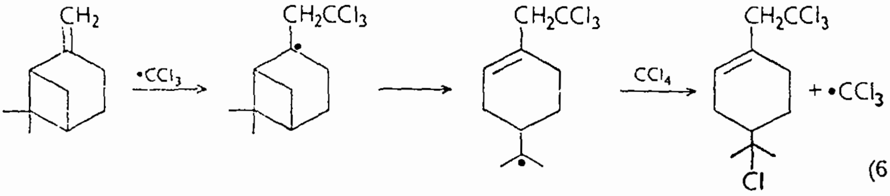
$$CCl_3CH_2\dot{C}HCH_2CCl_3 + BrCCl_3 \longrightarrow CCl_3CH_2CHBrCH_2CCl_3 + \cdot CCl_3$$

$$Br\cdot + CH_2{=}CHCH_2Br \longrightarrow CH_2Br\dot{C}HCH_2Br \xrightarrow{BrCCl_3} CH_2BrCHBrCH_2Br + \cdot CCl_3$$

SCHEME 10.

The intermediate product, 4,4,4-trichloro-1-butene, can be isolated if an excess of allyl bromide is used.

It is of interest that the addition of carbon tetrachloride to β-pinene, catalysed by benzoyl peroxide[129], results in the two fragments adding to *non-adjacent* carbon atoms (equation 61). Similar rearrangements occur during the additions of chloroform and bromoacetic ester[130]. It is probable that the relief of strain produced by rupture of the cyclobutane ring contributes to the ease with which rearrangement occurs.



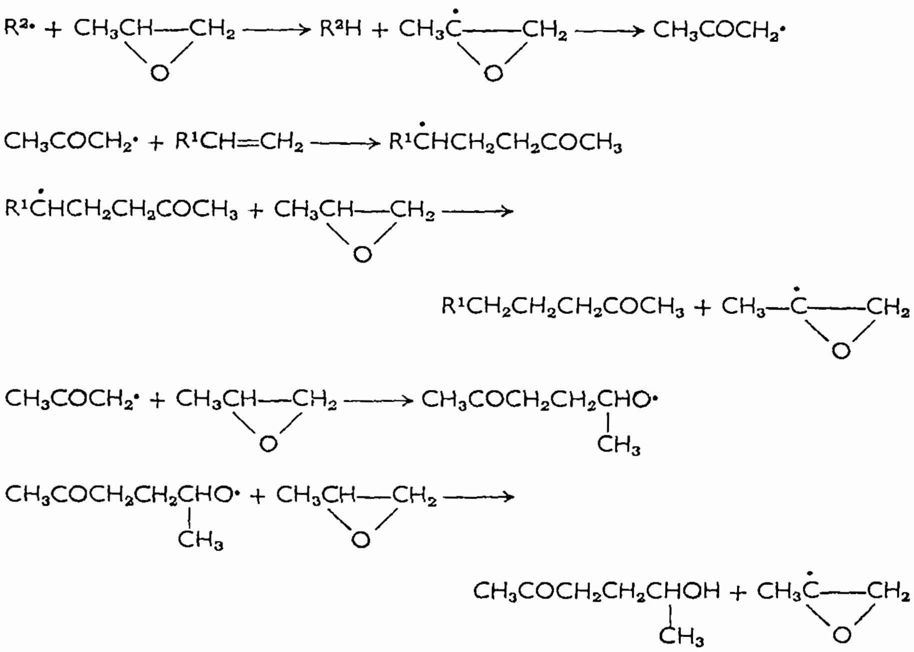
(61)

The addition of sulphuryl chloride to $\mathrm{RCH{=}CH_2}$ in the presence of sulphur dioxide[131], which suppresses the dissociation of the intermediate $\mathrm{{}^{\bullet}SO_2Cl}$ radical to give a dichlorinated sulphone, also proceeds by isomerization of the intermediate free radical, as in equation (62).

$$\mathrm{RCH{=}CH_2 + {}^{\bullet}SO_2Cl \longrightarrow R\dot{C}HCH_2SO_2Cl \longrightarrow RCHClCH_2SO_2{}^{\bullet} \xrightarrow{RCH{=}CH_2}}$$

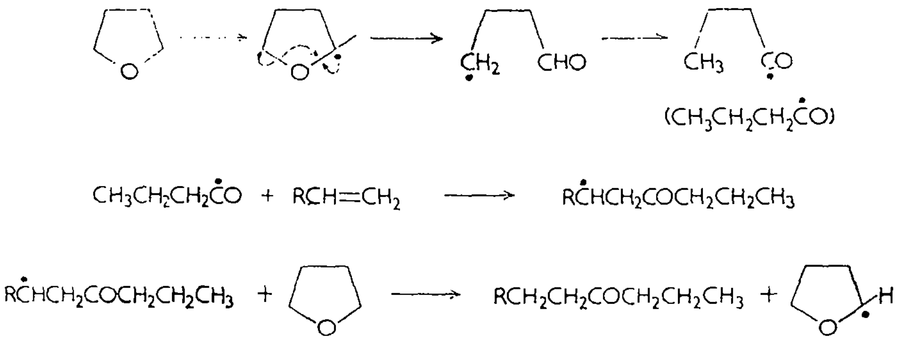
$$\mathrm{RH\dot{C}CH_2SO_2CH_2CHClR \xrightarrow{SO_2Cl_2} (RCHClCH_2)_2SO_2 + {}^{\bullet}SO_2Cl} \tag{62}$$

A different type of 1,2-shift occurs[132] during the addition of propylene oxide to 1-decene. The formation of small amounts of 2-undecanone and 5-hydroxy-2-hexanone suggests that the sequence of reactions occurs as defined in Scheme 11.



Scheme 11.

In a related reaction with 1-octene, tetrahydrofuran undergoes ring scission followed by intramolecular hydrogen transfer (Scheme 12)[133]



SCHEME 12*.

K. The Influence of Copper Salts on Radical Reactions of Alkenes: Meerwein Arylation and Related Reactions

As a result of the favourably small oxidation–reduction potentials of the system $Cu^0 \rightleftharpoons Cu^I \rightleftharpoons Cu^{II}$, copper salts readily enter into one electron-transfer process and are thus capable of initiating and terminating free-radical chain reactions, and also in some cases can alter the course of a chain reaction by their participation.

The reaction between aromatic diazonium salts and α,β-unsaturated carbonyl compounds in the presence of cupric chloride and aqueous acetone was discovered by Meerwein and his collaborators[134] and is exemplified by the reactions (63) and (64). This reaction has

$$ArN_2^+Cl^- + PhCH{=}CHCHO \longrightarrow PhCH{=}CArCHO + N_2 + HCl \qquad (63)$$

$$ArN_2^+Cl^- + PhCH{=}CHCO_2CH_3 \longrightarrow PhCHClCHArCO_2CH_3 + N_2 \qquad (64)$$

received wide study and it is now clear that it is not restricted to α,β-unsaturated carbonyl compounds, but is capable of extension. The preparative aspects of the Meerwein reaction have been recently summarized[135] and it is here considered sufficient to consider only the mechanistic implications.

Although originally believed to be a heterolytic reaction, radical mechanisms were soon proposed by Waters[136], Koelsch[137] and Muller[138]. Conclusive evidence that diazonium salts generated free aryl radicals under Meerwein conditions was provided by Dickerman

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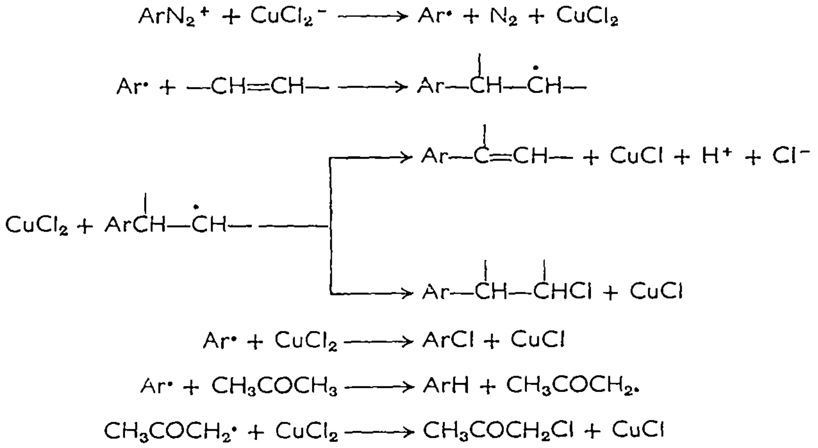
* Curved arrows represent movement of *single* electrons.

and Weiss[139] who used chlorobenzene instead of an olefin and obtained a mixture of isomeric chlorobiphenyls of composition corresponding to that produced by radical phenylation. Dickerman, Weiss and Ingberman, after a study of the kinetics of the reaction[140], were able to advance a satisfactory reaction scheme, in which it is assumed that an aryl radical is generated by a redox reaction with a complex formed between chloride ion and cuprous chloride, which is assumed to be present in small quantities. The aryl radical then reacts by addition to the double bond to give an intermediate which can react either by elimination or abstraction, both reactions involving cupric chloride as an oxidizing agent. The concomitant formation of chloroacetone in Meerwein reactions is also accommodated by Dickerman's reaction scheme, as is the need for both cupric and cuprous salts (Scheme 13).



SCHEME 13.

In theory, the intermediate radicals formed in these processes should be able to initiate polymerization of the olefin. That they do not in practice is attributed to their reaction with cupric chloride.

That the presence of copper salts can profoundly alter the course of a radical reaction of alkenes also follows from recent observations by Asscher and Vofsi[141]. They showed that whereas styrene, butadiene, acrylonitrile or ethyl acrylate gave polymers on radical-induced reaction in the presence of carbon tetrachloride, similar reactions carried out in the presence of cuprous, cupric, ferrous or ferric chlorides gave high yields of the one to one adduct $RCHClCH_2CCl_3$. Thus even highly stabilized radicals will rapidly undergo chain transfer with chloride ion in the presence of copper (and iron) ions (Scheme 14).

$$\mathrm{CCl_4 + Cu^+ \longrightarrow \cdot CCl_3 + Cu^{2+} + Cl^-}$$

$$\mathrm{PhCH{=}CH_2 + \cdot CCl_3 \longrightarrow Ph\dot{C}HCH_2CCl_3}$$

$$\mathrm{Ph\dot{C}HCH_2CCl_3 + Cl^- + Cu^{2+} \longrightarrow PhCHClCH_2CCl_3 + Cu^+}$$

SCHEME 14.

Such redox transfer, therefore, provides for specific chlorine activation, a further interesting example of which is provided in reactions involving chloroform. As described above, chloroform reacts with alkenes in the absence of copper salts by addition of a trichloromethyl radical to give the adduct $\mathrm{RCH_2CH_2CCl_3}$. In the presence of cuprous chloride, however, the isomeric 1,1,3-trichloride is formed (Scheme 15). Similarly, a ferrous chloride catalysed reaction of chloroform with 2-butene gave a diastereoisomeric mixture of adducts $\mathrm{CH_3CHClCH(CHCl_2)CH_3}$, whereas the di-*t*-butyl peroxide induced reaction gave one adduct only ($\mathrm{CH_3CHCCl_3\text{-}CH_2CH_3}$). In these reactions, the role of the copper is twofold: acting in a reducing capacity in the initiation step, and as an oxidizing agent in the termination reaction.

$$\mathrm{CHCl_3 + Cu^+ \longrightarrow \cdot CHCl_2 + Cu^{2+} + Cl^-}$$

$$\mathrm{RCH{=}CH_2 + \cdot CHCl_2 \longrightarrow R\dot{C}HCH_2CHCl_2}$$

$$\mathrm{R\dot{C}HCH_2CHCl_2 + Cu^{2+} + Cl^- \longrightarrow RCHClCH_2CHCl_2 + Cu^+}$$

SCHEME 15.

Cadogan and Siddiqui[142] have shown that metallic copper itself can act as a redox initiator of radical reactions, although in this case it is not known whether bromotrichloromethane (equation 65b) or cuprous bromide (equation 65c) is involved in the chain transfer process.

$$\mathrm{BrCCl_3 + Cu \longrightarrow CuBr + \cdot CCl_3} \qquad (65a)$$

$$\mathrm{R\dot{C}HCH_2CCl_3 \xrightarrow{BrCCl_3} RCHBrCH_2CCl_3 + \cdot CCl_3\ etc.} \qquad (65b)$$

$$\mathrm{R\dot{C}HCH_2CCl_3 \xrightarrow{CuBr} RCHBrCH_2CCl_3 + Cu\ etc.} \qquad (65c)$$

II. REACTIONS WITH CARBENES AND METHYLENES

A. Introduction

The possibility that divalent carbon compounds might be intermediates in certain chemical reactions was suggested a hundred years ago to account for the products of the alkaline hydrolysis of chloroform[143]. Divalent carbon intermediates were also invoked from time to time during the first half of the present century, particularly as intermediates in the decompositions of diazoalkanes and of ketenes, but it was not until the last decade that the 'carbenes' and their reactions were subjected to close scrutiny*.

The generic name 'carbene' was 'collaboratively conceived by Doering, Winstein and Woodward, in a nocturnal Chicago Taxi'[148], to be descriptive of derivatives of methylene (CH_2), by analogy with the derivation of 'carbinols' from methanol.

One of the major problems of carbene chemistry has been the determination of the configuration of the non-bonding electrons on the divalent carbon atom. It has now been established that in most, but not all, divalent carbon intermediates which have been identified, these electrons are paired, *i.e.* their spin quantum numbers have opposite signs. It has been suggested that the term 'carbene' should be reserved for these species, while those with unpaired electrons, and which exhibit the reactions characteristic of free radicals, should be termed 'methylenes'[149]. This distinction is adhered to in the present article, with the exception that the parent molecule, CH_2, is always called 'methylene'.

The current interest in divalent carbon species seems to date from 1950, when Hine published his first paper on a reinvestigation of the alkaline hydrolysis of chloroform, and concluded that dichlorocarbene ($:CCl_2$) was probably an intermediate in this reaction[150]. In subsequent studies, Hine and collaborators have extended their work to a series of haloforms, and the mass of data obtained from kinetic and product analysis leaves no doubt that intermediates of the type $:CX_2$ (X = halogen) are common to all the hydrolyses investigated, and that they are formed by α-elimination of hydrogen halide from the haloform.

It was not until 1954 that Doering and Hoffmann showed that dihalocarbenes from the haloforms could be trapped by addition to olefins to give cyclopropane derivatives[151]. Thus cyclohexene,

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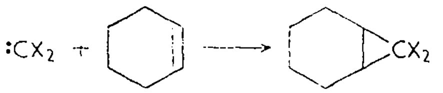
* For recent reviews, see refs. 144–147a.

chloroform (or bromoform) and potassium *t*-butoxide react to give 7,7-dihalonorcarane (equation 66).

While α-elimination reactions have furnished a route to the dihalocarbenes, and, more recently, to a variety of other substituted carbenes, a second route to divalent carbon intermediates involves the thermal or photochemical decomposition of diazoalkanes and ketenes. Earlier work on this subject was reviewed in 1938 by Pearson, Purcell and Saigh[152], who themselves showed that both diazomethane and ketene gave, on photolysis, reactive species which would remove a tellurium mirror to give telluroformaldehyde. More work has demonstrated that in the case of ketene, they were probably observing the radical $\cdot CH_2COCH_2\cdot$[153], but that with diazomethane the reactive species was indeed methylene ($:CH_2$). The decomposition of diazomethane, and more particularly of ethyl diazoacetate, catalysed by copper or copper salts in the presence of an olefin, has long been known as a route to cyclopropane derivatives, and it seems that until recently this reaction has generally been assumed to involve divalent carbon intermediates. Such a view was expressed, for example, in 1949 by D'yakanov[154], who had made an extensive study of this reaction. It now seems more likely that the intermediate is not a free methylene or carbene, but a complex of the divalent carbon bound to copper.



(66)

The photochemical decompositions of diazomethane and ketene, and related compounds, and the reactions of the divalent species produced, have mainly fallen within the province of the physical chemists, in particular Kistiakowsky and coworkers in America, and Frey in England. However, it was again Doering who, with Knox, first observed the addition of methylene, produced by photolysis of diazomethane, to an olefinic double bond*. Irradiation of a solution of diazomethane in cyclohexene gave a low yield of norcarane, identical with a specimen obtained by reduction of the dihalonorcarane from the haloform route.

The interest in divalent carbon may, perhaps, be divided into three main categories. Two of these are of a physicochemical nature: namely, the study of the energetics of methylene production and of its reactions, and the configuration of the non-bonding electrons. Much

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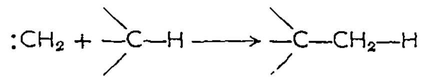
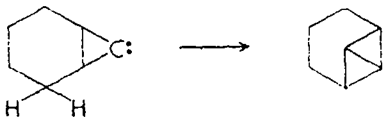
* Footnote in ref. 151.

light has been shed on the latter problem by the techniques of the organic chemist, in particular by the researches of Skell and his collaborators. The arguments used by Skell will be considered in some detail later. The third major aspect of carbene chemistry concerns the synthetic utility of divalent carbon intermediates. In favourable cases, yields of cyclopropanes of the order of 90%, based on carbene source, may be obtained from olefins. A further synthetic application makes use of the 'insertion reaction', in which methylene itself, and the more reactive carbenes, can directly insert into a carbon–hydrogen bond (equation 67). The synthesis of an otherwise inaccessible carbocyclic compound, by an intramolecular reaction of this type, is shown in equation (68)[155]. A full survey of this type of reaction is, however, beyond the scope of this review.



$$:CH_2 + \text{—}\overset{\diagdown}{\underset{\diagup}{C}}\text{—}H \longrightarrow \text{—}\overset{\diagdown}{\underset{\diagup}{C}}\text{—}CH_2\text{—}H \qquad (67)$$



(68)

Before considering in detail any aspects of the reactions of divalent carbon compounds with olefins, mention should be made of the possibility of obtaining other reactive intermediates analogous to the carbenes. Thus photolysis of hydrazoic acid, and of nitrous oxide, give initially 'nitrene' (imine) ($:\ddot{N}H$), and an oxygen atom ($:\ddot{O}:$), respectively. Each of these is isoelectronic with methylene. Little work has as yet been carried out on the reactions of these species with olefins, but that which has been reported will be discussed where relevant.

B. Reactions of Carbenes Formed by Base-catalysed α-Eliminations

The earliest compelling evidence for carbene addition to olefins to give cyclopropanes was obtained by Doering and Hoffmann[151]. They used Hine's method of generating dihalocarbenes (but in the presence of cyclohexene or other olefins), and were able to isolate a number of cyclopropane derivatives. Although Hine at that time already regarded the hydrolysis of chloroform by strong base to proceed according to Scheme 16, his evidence was not completely conclusive[150]. However, the reduction of the rate of hydrolysis in

$$\mathrm{CHCl_3 + {}^-OC(CH_3)_3 \xrightleftharpoons{\text{fast}} {}^-CCl_3 + HOC(CH_3)_3}$$
$$\mathrm{{}^-CCl_3 \xrightarrow{\text{slow}} :CCl_2 + Cl^-}$$
$$\mathrm{:CCl_2 \longrightarrow \text{products}}$$

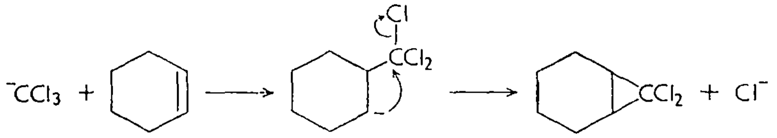
SCHEME 16.

the presence of halide ions, and the isolation of dichloroiodomethane when the reaction is carried out in the presence of iodide ions, leave little doubt that the species $:\mathrm{CCl_2}$ is an intermediate[156].

$$\mathrm{:CCl_2 + Cl^- \longrightarrow {}^-CCl_3}$$
$$\mathrm{:CCl_2 + I^- \longrightarrow {}^-CCl_2I}$$
$$\mathrm{{}^-CCl_2I + HOC(CH_3)_3 \longrightarrow HCCl_2I + {}^-OC(CH_3)_3}$$

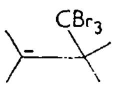
SCHEME 17.

This, however, still did not provide conclusive evidence that the olefin addition reaction involved a carbene. Doering and Hoffmann considered, and rejected, an alternative reaction scheme involving attack on the double bond by the trihalomethyl anion, followed by a rapid elimination of halide ion, *i.e.* equation (69). Rejection of this



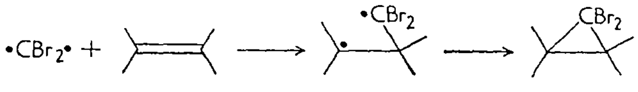
(69)

mechanism was based largely on the lack of precedent for the attack of a carbanion on an unpolarized double bond. Such a reaction was soon to be reported[157]. However, in 1956 Skell and Garner[158] were able to show that the reaction between bromoform, potassium *t*-butoxide and *cis*- or *trans*-2-butene gives in each case a single di-



(32)

bromocyclopropane derivative, *i.e.* the addition is stereospecific. This was regarded as powerful evidence against the carbanion mechanism, because the intermediate anion **32** would be expected to undergo internal rotation to give a mixture of stereoisomeric cyclopropane derivatives, unless the elimination of a bromide ion were extremely rapid. Similar arguments have been raised against the addition of dibromocarbene as a diradical, *i.e.* reaction in a state in which the non-bonding electrons are unpaired. Again, internal rotation in the intermediate diradical (**33**) would be likely to occur faster than cyclization, and consequently the reaction would be non-stereospecific*.



(**33**)

In a later paper, Skell and Garner[159] showed that a parallel may be drawn between the reactivities of different olefins towards addition of dibromocarbene and addition of bromine. On the other hand, there is no correlation with the reactivities of free-radical species such as $\cdot CCl_3$. These results are illustrated in Table 10. This again argued against dibromomethylene having unpaired electrons,

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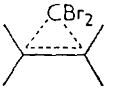
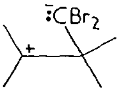
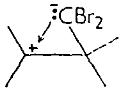
* A certain amount of confusion concerning the stereochemistry of carbene addition has crept into the literature. One of Skell's preliminary communications has the wrong numbers appended to two structural formulae[192]. In a full paper, also by Skell[159], the authors set out to distinguish between a diradical intermediate such as **33**, which might cyclize very rapidly, and a cyclic transition state **34**. In their final discussions they decide in favour of 'a partially formed cyclopropane' which they write as **35**. This is apparently differentiated from **34** only in order to emphasize its partial carbonium-ion character; however, in a review of Skell's work, Zollinger[254] states that the transition state **35** (which is in fact rewritten as **35a**) is a correct formulation, and that **33** and **34** are excluded. In addition, Hine[146] considers that the zwitterionic intermediate **36** is also ruled out by the stereospecific addition. This zwitterion is presumably considered to have normal tetrahedral bond angles at the tetracovalent carbon, and to be capable of internal rotation. However, such an intermediate would necessarily suffer a large electrostatic distortion, and occurrence of internal rotation before cyclization seems doubtful. The distinction, therefore, between **36** and **37** (p. 638) seems to be a fine one and in our view **37** satisfactorily represents the transition state of the addition as it is currently understood.



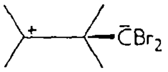
(**34**)



(**35**)



(**35a**)



(**36**)

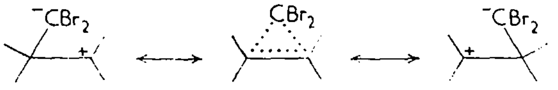
TABLE 10. Reactivities of olefins towards $:CCl_2$, $:CBr_2$, $\cdot CCl_3$ and Br_2, relative to that of isobutylene[159,161]

Olefin	Relative reactivity			
	$:CCl_2$	$:CBr_2$	Br_2	$\cdot CCl_3$
$(CH_3)_2C{=}C(CH_3)_2$	6·6	3·5	2·5	—
$(CH_3)_2C{=}CHCH_3$	2·9	3·2	1·9	0·17
$(CH_3)_2C{=}CH_2$	1·00	1·00	1·00	1·00
1,3-Butadiene	—	0·5	—	40
Cyclohexene	0·12	0·4	—	0·045
n-1-Hexene	0·023	0·07	0·36	0·19[a]

[a] n-1-Octene

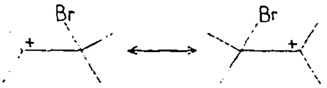
and further, the similarity in reactivity between $:CBr_2$ and Br^+, an electrophilic species, finally excluded the possibility that the reactive intermediate could be a trihalomethyl carbanion.

The electrophilic nature of dibromocarbene is consistent with a structure in which the non-bonding electrons on the carbon atom are spin-paired leaving an unoccupied (probably *p*) orbital. Reaction with an olefin can then be regarded as proceeding through a transition state such as **37**. The vacant orbital on the carbene is electron-seeking,



(37)

and reacts with the π electrons of the olefin in a concerted process such that in the cyclic transition state internal rotation is impossible. Hence stereospecific addition is observed. Examination of the dipolar contributions to the transition state reveals why it is that electron-donating alkyl substituents on the double bond promote the reaction, just as they promote the addition of bromine (equation 70).



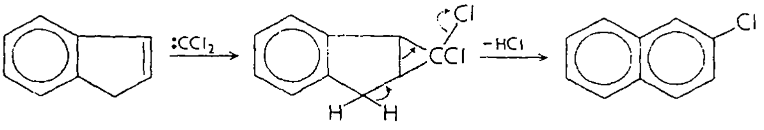
(70)

At about the same time, Doering and LaFlamme[160] confirmed that the stereospecificity of cyclopropane formation is *cis*, in accord with the proposed transition state **37**.

Doering and Henderson[161] later reported some further competitive experiments to determine the reactivities of different olefins towards dihalocarbenes (Table 10). They concluded that both $:CCl_2$ and

:CBr_2 were electrophilic, though there is possibly an appreciable steric effect with the more bulky dibromocarbene. They, like Skell, considered that the results were best explained by a spin-paired structure for the carbene. It was noticed that ethylene itself did not appear to form a cyclopropane under the reaction conditions, and this was attributed to a faster reaction of the dihalocarbene with unreacted butoxide anion. It had previously been observed that with more reactive olefins, better yields of adduct are formed with *t*-butoxide than with other alkoxides, possibly because the side reaction between carbene and *t*-butoxide ion is sterically inhibited.

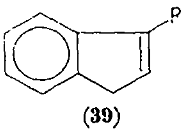
A significant contribution to the early work on the addition of halocarbenes to olefins was made by Parham and coworkers. By analogy with the well-known ring expansions of pyrrole and indole to 3-chloropyridine and 3-chloroquinoline, using chloroform and strong base, Parham studied the reactions of indene under similar conditions. He was able to show that ring expansion occurred here also, to give β-chloronaphthalene[162], and under carefully controlled conditions, the isolation of the intermediate carbene adduct **38** was possible[163].



(38)

This was readily converted to the chloronaphthalene by treatment with a protic solvent, the overall yield being about 60%. Similar results were obtained when chloroform was replaced by bromoform, β-bromonaphthalene being isolated.

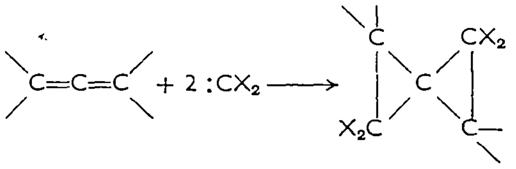
When a 1-alkylindene was employed, then a 1-alkyl-2-halonaphthalene was the only product, in accord with the expectation that the indene would react entirely as the more stable isomer **39**. 2,3-Disubstituted naphthalenes were obtained when 2-substituted



(39)

indenes were used[164], and the yields in these reactions varied with the nature of the substituent. Thus, in accord with the electrophilic nature of the dihalocarbenes, side-reactions compete more favourably with addition when the indene carries an electron-withdrawing substituent such as $CO_2C_2H_5$, than when it is unsubstituted, or has an alkyl substituent. In other work :CClBr and :CClF, from $HClBr_2$ and $HCCl_2F$ respectively, were successfully added to indene[165].

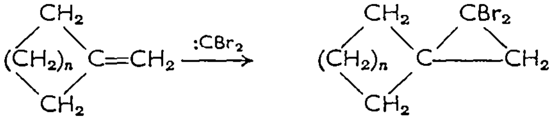
More recent applications of addition reactions of carbenes from haloforms have been concerned with the synthesis of unusual ring systems. For example, carbene addition to allenes may be visualized as providing a route to spiropentanes (equation 71). A number of



(71)

syntheses of this type will be considered under later headings, but a few may. conveniently be discussed now.

Dihalocarbenes have, for example, been added to methylenecycloalkanes to give good yields of spiranes (equation 72)[166]. In the particular case where $n = 3$, the dibromocarbene adduct was readily reduced by lithium aluminium hydride to spiro[2.5]octane.



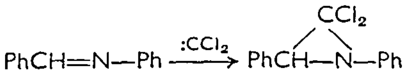
(72)

(n = 1–3, yield = 60–75%)

Dichlorocarbene and phenylchlorocarbene (:CClPh) (obtained by the action of potassium *t*-butoxide on benzylidene chloride) have been added to ketene acetals to give cyclopropanone acetals in yields of up to 75%, and the properties of the products have been studied[167]. In a similar reaction with dibromocarbene, only rearranged products were isolated[168].

Dichlorocarbene has recently been added, though in low yield, to tetrachloroethylene, giving perchlorocyclopropane[169]. The success of this reaction may be regarded as somewhat surprising in view of the electron-withdrawing nature of the chlorine substituents on the olefin, particularly in view of Doering's failure to add dihalocarbenes to unsubstituted ethylene[161], and a similar failure with perchlorobutadiene[170].

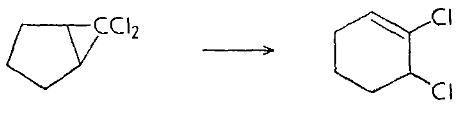
Dichlorocarbene has successfully been added to the carbon–nitrogen double bond[171].



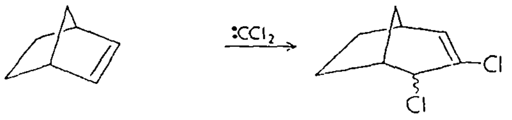
$$PhCH{=}N{-}Ph \xrightarrow{:CCl_2} PhCH{-}N{-}Ph \quad (\text{bridged by } CCl_2)$$

(73)

Instances have already been cited of reactions in which the dihalocyclopropane adducts are unstable (addition to indenes), or even unobserved (addition to indole). Further examples of this type of phenomenon are found when the expected cyclopropane adduct suffers considerable conformational strain. Thus, cyclopentadiene with base and chloroform gives chlorobenzene[172], and the adduct from cyclopentene and dichlorcarbene rearranges under mild conditions to 2,3-dichlorocyclohexene (equation 74)[173a]. The primary adduct with norbornene cannot be isolated (equation 75)[173a]*. A general method of increasing the length of a carbon chain by a carbene

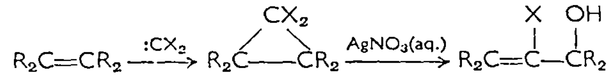


(74)



(75)

route was discovered by Skell and Sandler[174]. It involves treatment of a *gem*-dihalocyclopropane with aqueous silver nitrate (equation 76). The reaction is particularly rapid with the cyclopentene adduct, also reflecting the strain in this molecule.



$$R_2C{=}CR_2 \xrightarrow{:CX_2} R_2\overset{CX_2}{C{-}C}R_2 \xrightarrow{AgNO_3(aq.)} R_2C{=}\overset{X}{C}{-}\overset{OH}{C}R_2 \qquad (76)$$

Except in the case of particularly reactive olefins, such as tetramethylethylene, the haloform route to carbenes does not give yields of cyclopropanes greatly in excess of 50% (based on haloform or alkoxide ion). This has been ascribed to side-reactions of the carbenes with the alkoxide ion or the alcohol produced from it, and it has already been mentioned that the occurrence of these side-reactions can be reduced by using *t*-butoxide as the base. Similar limitations would appear to apply to a number of other base-catalysed reactions which have been used as sources of dihalocarbenes. However, Parham and Schweitzer[175] have added dichlorocarbene to several olefins by the reaction of potassium *t*-butoxide with ethyl trichloro-

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* The primary adduct from norbornene and dichlorocarbene has now been isolated, and the stereochemistry of its rearrangement product has been determined[173b].

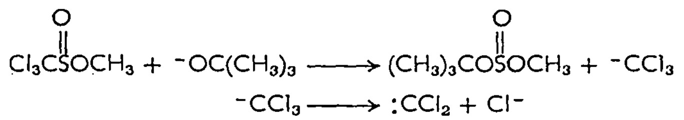
acetate, giving yields of 70–90% of cyclopropane (based on trichloroacetate). This reaction does not give any alcohol (equation 77), and it was considered that its absence could be associated with the improved yields of cyclopropanes.

$$\begin{gathered} {}^{-}OC(CH_3)_3 + CCl_3CO_2C_2H_5 \longrightarrow {}^{-}CCl_3 + (CH_3)_3COCO_2C_2H_5 \\ {}^{-}CCl_3 \longrightarrow :CCl_2 + Cl^{-} \end{gathered} \tag{77}$$

The reaction of hexachloroacetone with sodium methoxide and cyclohexene[176] gives dichloronorcarane in 60% yield (based on the formation of two molecules of :CCl$_2$/molecule of hexachloroacetone).

$$2\ {}^{-}OCH_3 + CCl_3COCCl_3 \longrightarrow (CH_3O)_2CO + 2\ :CCl_2 + 2\ Cl^{-} \tag{78}$$

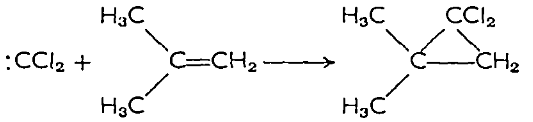
The reaction of methyl trichloromethylsulfinate with potassium *t*-butoxide has recently been found to provide a further route to dichlorocarbene adducts of olefins[177].



$$\begin{gathered} Cl_3C\overset{O}{\overset{\|}{S}}OCH_3 + {}^{-}OC(CH_3)_3 \longrightarrow (CH_3)_3CO\overset{O}{\overset{\|}{S}}OCH_3 + {}^{-}CCl_3 \\ {}^{-}CCl_3 \longrightarrow :CCl_2 + Cl^{-} \end{gathered} \tag{79}$$

The reaction of ethyl trichloroacetate with base (equation 77) is, at first sight, similar to the reaction of *t*-butyl dichloroacetate with base. However, when the latter reaction is carried out in the presence of an olefin it is again the dichlorocarbene adduct which is produced, though in low yield (equations 80 and 81)[178].

$$\begin{gathered} HCl_2CCO_2C(CH_3)_3 \xrightarrow{{}^{-}OC(CH_3)_3} {}^{-}Cl_2CCO_2C(CH_3)_3 \longrightarrow \\ :CCl_2 + CO + {}^{-}OC(CH_3)_3 \end{gathered} \tag{80}$$



(81)

Apart from the side-reactions already considered, the presence of base in halocarbene syntheses can often promote undesirable complications. The first addition of dichlorocarbene to an olefin under essentially neutral conditions was reported in 1959 by Wagner[179]. The carbene was generated by pyrolysis of sodium trichloroacetate in boiling dimethoxyethane. In the presence of excess cyclohexene, a 65% yield of dichloronorcarane was obtained. This reaction has been extended to additions to a number of other olefins, including base-sensitive ones, such as allyl chloride, with fair to good yields of adducts[180]. The presence of a polar, but aprotic, solvent is essential, and the yields are sensitive to the proportions of reactants and solvent, owing to a side-reaction between the carbene and the trichloroacetate anion.

Difluorocarbene, from sodium chlorodifluoroacetate has also been added to cyclohexene, though in poor yield[181].

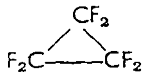
A number of other pyrolytic reactions which give dihalocarbene adducts with olefins has been reported recently. These reactions also occur under neutral conditions, but may again involve transient formation of trihalomethyl carbanions. While these reactions are generally regarded as occurring under neutral conditions, it should be noted that the trihalomethyl ion itself is a strong base. Thus Rees and Smithen have observed the formation of chloroform in the reaction of 2,3-dimethylindole with sodium trichloroacetate, as well as products of the reactions of the dimethylindolyl anion[181a].

Pyrolysis of trichloromethyltrichlorosilane (**40**) at 250° in the presence of cyclohexene gives dichloronorcarane, but the high temperature involved must greatly reduce the usefulness of this

$$\underset{\textbf{(40)}}{Cl_3CSiCl_3} \xrightarrow{250^\circ} :CCl_2 + SiCl_4$$

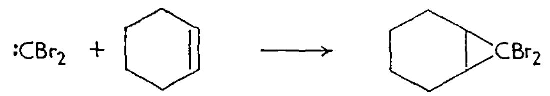
reaction[182]. In the report of this work, it was suggested that the pyrolysis of trimethyltrifluoromethyltin (**41**), which in the presence of tetrafluoroethylene gives perfluorocyclopropane (equation 82)[183], may involve difluorocarbene.

$$\underset{\textbf{(41)}}{F_3CSn(CH_3)_3} \xrightarrow{150^\circ} :CF_2 + (CH_3)_3SnF$$

$$:CF_2 + C_2F_4 \longrightarrow$$  (82)

Of great potential value is the observation that, under neutral conditions in boiling benzene, phenyltribromomethylmercury (**42**) smoothly splits out dibromocarbene which will add to cyclohexene; a yield of adduct of nearly 90% being obtained after two hours (equation 83). The corresponding trichloro compound gives similar yields only after two days[184]. The phenylmercuric halide is precipitated quantitatively.

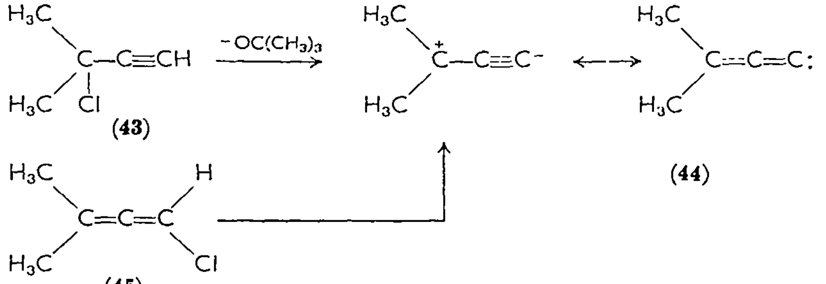
$$\underset{\textbf{(42)}}{PhHgCBr_3} \longrightarrow PhHgBr + :CBr_2$$



(83)

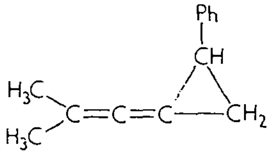
Several other carbenes, which, with olefins, give substituted cyclopropanes, have been reported as products of α-elimination reactions. Most of these will be discussed in a later section, as their existence as *free* carbenes cannot be considered to have been established with certainty.

Attempts to prepare diphenylcarbene by α-elimination from benzhydryl chloride appear to have failed[167]. Dimethylvinylidenecarbene (**44**)[185] has been obtained by dehydrochlorination of the

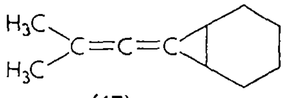


(**43**) (**44**) (**45**)

acetylene **43**, and has been trapped by addition to styrene and to cyclohexene, giving **46** and **47** respectively. Addition to *cis*- or *trans*-2-butene is stereospecific, which result, by application of arguments similar to those used for the dihalocarbenes, suggests that the non-bonding electrons are spin-paired[186]. This reaction does not involve



(**46**)



(**47**)

an α-elimination, but it seems likely that the same carbene might be obtained from the chloroallene (**45**).

Attempts to trap ethylidenes ($R_2C{=}C\colon$) with olefins have been unsuccessful. From projected α-eliminations in which such species might be formed, acetylenes are usually isolated. There is no evidence that ethylidenes are even formed as intermediates, as elimination and rearrangement to form acetylenes may occur in concert[146,p.497].

C. Formation and Reactions of Unsubstituted Carbene (Methylene)

By 1938 the formation of methylene (CH_2) during pyrolysis or photolysis of diazomethane and photolysis of ketene was considered to be established[152], but evidence for reactions in which methylene adds to olefins was not forthcoming until 1954[151], and spectroscopic observation of methylene was not reported until 1959, by Herzberg and Shoosmith[187].

It is convenient to consider the spectroscopic evidence first, as it is unambiguous, and a knowledge of it assists in the understanding of some of the earlier work. Quantum-mechanical calculations had differed in their predictions concerning the ground state of the CH_2 species. The experimental resolution of these differences was lucidly described by Herzberg in a recent lecture to the Royal Society[188].

Rapidly decaying spectral bands, which could only be associated with the methylene molecule, were observed after the flash-photolysis of diazomethane in a large excess of inert gas. However, the bands fell into two classes, one of which faded less rapidly than the other. The shorter-lived spectrum was associated with singlet methylene (*i.e.* having the two non-bonding electrons spin-paired); the longer-lived with triplet methylene (having unpaired electrons in different orbitals). The singlet methylene, shown to have an H—C—H bond angle of about 103° in its lowest energy level, was considered to be formed first in a highly excited state, and to decay to the triplet or diradical form. The lowest energy of the triplet molecule is linear, and is the true ground state of methylene. Ironically, the earlier extensive searches for the spectrum of methylene formed by the flash-photolysis of ketene (considered to be safer to handle than diazomethane), were necessarily in vain, as the main bands would have been obscured by the absorption of the ketene.

The reactions of methylene have now been examined in some detail, particularly in the gas phase. The methylene is usually generated by photolysis of ketene or of diazomethane, though that obtained by pyrolysis of diazomethane reacts in an essentially similar manner to that formed photolytically[189].

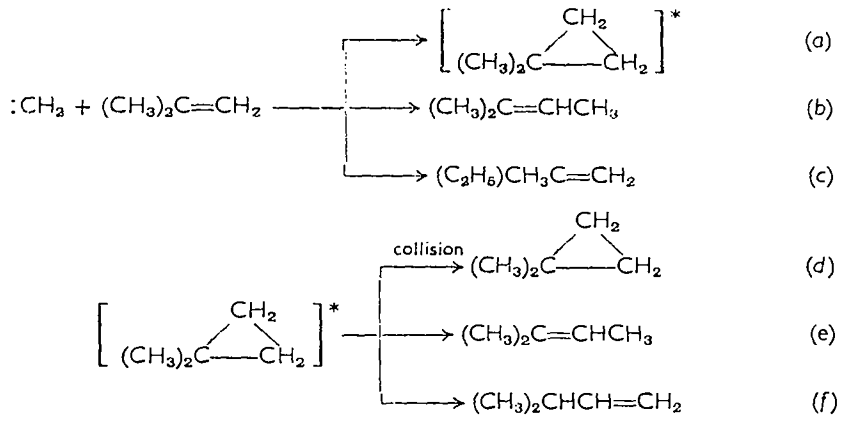
It was mentioned in the introduction that methylene is capable of reacting by insertion into a carbon–hydrogen bond. The halocarbenes, whose reactions have already been discussed, do not participate in this insertion reaction. This is probably because interaction between the vacant orbital on the carbon atom and the electrons on the halogen atoms, makes the halocarbenes unreactive by comparison with methylene. Methylene itself, by contrast, has been referred to as 'the most indiscriminate reagent known to organic chemistry'[148]. It inserts in aliphatic primary, secondary and tertiary C—H bonds almost statistically[190].

Initial attack on an olefin may be at the carbon–carbon double bond, or by C—H insertion, and is the same both in the gas phase and in solution. Insertion into carbon–carbon single bonds is negligible. In the gas phase, the observed products are pressure dependent, as the cyclopropane formed by addition contains an excess of vibrational energy which is sufficient to rupture the ring unless the molecule is rapidly deactivated by collision.

Photolysis of diazomethane in cyclohexene was first reported in detail by Doering and colleagues in 1956[190]. It was found that the insertion in different C—H bonds is roughly statistical, and the ratio of the reactivity of any one C—H bond to that of the carbon–carbon double bond is approximately 1 : 6. This result has been substantiated by more recent work of Hammond and his collaborators[191]. Skell and Woodworth found that dimethylcyclopropanes were formed stereospecifically when diazomethane was photolysed in *cis*- or *trans*-2-butene[192,193]. By use of similar arguments to those outlined above, they concluded that the methylene was reacting in a singlet (spin-paired) state. Further, in view of the high reactivity of the methylene (suggesting a very short lifetime), they considered that the methylene was probably formed in a singlet state. This seems inherently likely, as there is no reason to suspect spin-inversion during photolysis, though, as Frey and Kistiakowsky had pointed out[194], and as is now known to be the case[188], the singlet state is not necessarily the ground state. Evidence for singlet methylene is also provided by the failure of oxygen to modify the reactions seriously, though some of the minor products are not formed when oxygen is present, indicating that they may have been formed by free-radical processes.

It was noticed that the insertion reactions of methylene from the photolysis of ketene in the gas phase were slightly less random than those from diazomethane, tertiary hydrogens being attacked most readily[194]. This suggested that a somewhat less reactive species was being observed in the ketene reactions. The possibility that the difference was due to the fact that the comparison was with photolysis of diazomethane *in solution* was eliminated by repeating the latter reaction in the gas phase, when almost statistical randomness was observed[195]. Calculations by Frey and Kistiakowsky indicated that the methylene molecules from ketene and from diazomethane under the commonly used conditions of photolysis, had roughly 15 and 30 kcal/mole respectively of energy in excess of the ground-state value[194]. Implications of this fact have been discussed at some length, and reactions have been carried out in an excess of an unreactive gas, such as nitrogen, to remove most of the excess energy by collision.

Frey has made a detailed study of the reactions of methylene from diazomethane with the three isomeric butenes[196,197]. In the particular case of isobutene[196], and in the absence of an inert gas, the processes in Scheme 18 are though to account for the major products.



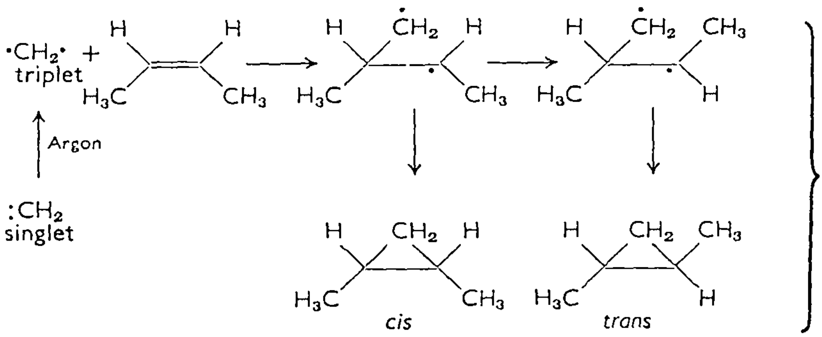
Scheme 18.

The initial addition process (*a*) gives an excited dimethylcyclopropane carrying the thermal equilibrium energy of the reactants, the heat of the reaction, and any excess kinetic or vibrational energy carried by the methylene. At very low pressures the excited dimethylcyclopropane rearranges (paths *e* and *f*), at higher pressures it may be deactivated by collision (path *d*), and the limiting high-pressure yield is approximately 55%. It is interesting that a much lower pressure is necessary to approach the limiting yield than is required in the addition to ethylene[194,198] where the excited cyclopropane cannot distribute its excess energy among so many vibrational modes.

When the reaction with isobutene is carried out in the presence of a molar excess of an inert gas, there is greater discrimination between the initial processes of addition and insertion (*a*–*c*). Yields of cyclopropane of up to 70% are possible, and the difference is attributed to removal of excess translational kinetic energy from the methylene by collision, before it reacts with the olefin.

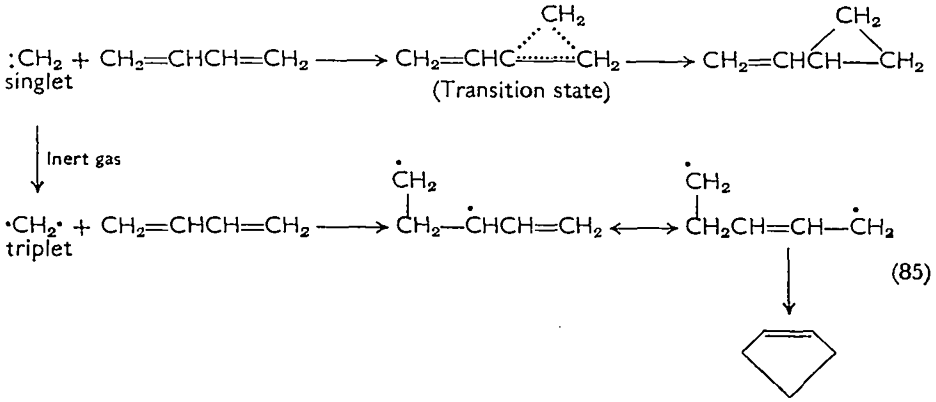
Three other points deserve mention. The methylene, when formed, has excess vibrational energy as well as excess translational energy, and the former is carried into the excited cyclopropane. It is found that the pressure-dependence of cyclopropane yield varies with the wavelength of the light used to decompose the diazomethane, and this is associated with the fact that methylene carries different amounts of vibrational energy into the excited cyclopropane molecule. Secondly, comparison with the reactions of methylene from ketene indicate that the latter species has a much lower excess of energy. Frey has also found evidence that in the case of addition to *cis*- or *trans*-butene[197], the excited cyclopropane may undergo geometrical isomerization before being deactivated.

When much higher proportions of inert gas are employed, rather different results are obtained. Studies of this kind have been made by Anet and coworkers[199] and by Frey[200] in the presence of alkenes, and it has been found that in such reactions the addition of methylene to double bonds is no longer stereospecific. This has been attributed to deactivation of the methylene and partial spin-inversion from the singlet to a lower energy triplet state. The triplet methylene adds to the olefin to give a diradical intermediate which may undergo internal rotation prior to cyclization (equation 84). It was found, for example, by Frey[200], using *cis*-2-butene in a thousand-fold excess of argon, that roughly equal proportions of *cis*- and *trans*-dimethylcyclopropane were obtained. When a small quantity of oxygen was added, the yield of the *trans* isomer was greatly reduced, in accord with its postulated formation solely by way of diradical intermediates (84).



(84)

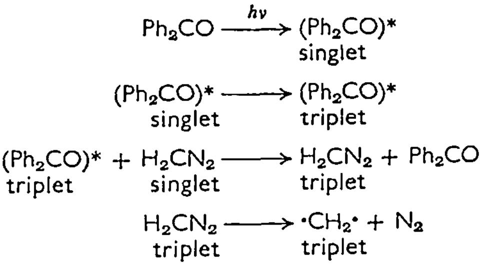
Further evidence, based on product analyses, that the methylene from photolysis of diazomethane may suffer spin-inversion to a more stable triplet state by collision with an inert gas, has been obtained from studies of its reaction with 1,3-butadiene. Under the conditions normally employed for the study of methylene, the addition reaction with butadiene leads almost exclusively to vinylcyclopropane[201]. In the presence of excess inert gas, however, significant quantities of cyclopentene are produced by 1,4-addition; this is a typical radical-addition reaction, anticipated for triplet methylene[202].



(85)

The addition of singlet methylene to butadiene has been reported to differ from the addition to the butenes considered above in that the limiting low-pressure yield of vinylcyclopropane is non-zero[201]. It is thought that this may be due to internal conversion of energy in the excited vinylcyclopropane formed initially, to give an electronically excited molecule which is either relatively stable, or can lose its excess energy by some process other than collision. On the other hand, the limiting yield of vinylcyclopropane at low-pressure has been found to be zero in more recent work[201a].

Triplet methylene has recently been obtained by two ingenious new routes, and its diradical nature demonstrated by the non-stereospecificity of its reactions with olefins. Both methods are photochemical. The first, due to Kopecky, Hammond and Leermakers[191],



$$\mathrm{Ph_2CO} \xrightarrow{h\nu} \underset{\text{singlet}}{(\mathrm{Ph_2CO})^*}$$

$$\underset{\text{singlet}}{(\mathrm{Ph_2CO})^*} \longrightarrow \underset{\text{triplet}}{(\mathrm{Ph_2CO})^*}$$

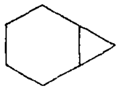
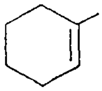
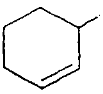
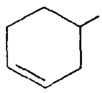
$$\underset{\text{triplet}}{(\mathrm{Ph_2CO})^*} + \underset{\text{singlet}}{\mathrm{H_2CN_2}} \longrightarrow \underset{\text{triplet}}{\mathrm{H_2CN_2}} + \mathrm{Ph_2CO}$$

$$\underset{\text{triplet}}{\mathrm{H_2CN_2}} \longrightarrow \underset{\text{triplet}}{\cdot\mathrm{CH_2}\cdot} + \mathrm{N_2}$$

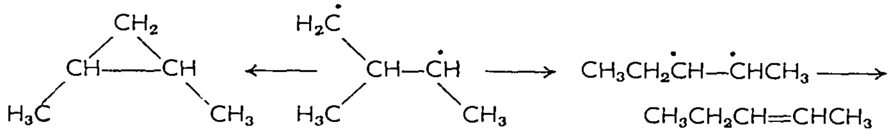
SCHEME 19.

makes use of the photosensitized decomposition of diazomethane using benzophenone. The diazomethane shows only weak absorption at 3130 Å, and when a solution of it and benzophenone in an olefin is irradiated with this wavelength, the sequence of reactions in Scheme 19 is believed to occur. In either *cis*- or *trans*-2-butene, both *cis*- and *trans*-dimethylcyclopropane are produced, but the relative yields of these two products are quite different, suggesting that in the intermediate diradical, rotation is not significantly more rapid than cyclization. In Table 11, the relative yields of C_7 products from cyclohexene are compared for the direct photolysis of diazomethane and the photosensitized reaction. It will be seen that the yields of insertion products are much lower in the photosensitized reaction. Furthermore, the methylcyclohexenes that are obtained are probably formed by insertion reactions of a small amount of singlet methylene. Triplet methylene would be expected to prefer allylic attack, whereas the 3- and 4-methylcyclohexenes, indistinguishable by vapour-phase chromatography, were shown by infrared spectroscopy to be present in the products of the photosensitized reaction in roughly equivalent amounts.

TABLE 11. Relative yields of products from the reaction of methylene with cyclohexene in solution.

Source of methylene			 + 
$h\nu + CH_2N_2$	1	0·24	1·3
$h\nu(3130\,\text{Å}) + CH_2N_2 + Ph_2CO$	1	trace	0·42

The procedure for obtaining triplet methylene described recently by Duncan and Cvetanovic[202a], involves the triplet mercury photosensitized decomposition of ketene. The reaction was conducted in the gas phase, and the products were pressure dependent. However, the work was carried out at sufficiently high pressure for the yields of products to approach their limiting values. In the reactions with each of the 2-butenes, non-stereospecific addition was observed. The insertion products *cis*- and *trans*-2-pentene were also formed, but as no similar products were obtained from isobutene these were thought to arise from rearrangement of the intermediate diradical, by an intramolecular 1,2-shift not possible with isobutene.



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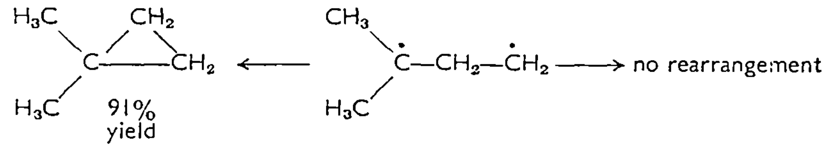
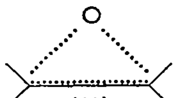


(87)

As yet there appears to be no report of the addition of photolytically produced nitrene $(:\ddot{\mathrm{N}}\text{—H})$ to an olefinic double bond, but both atomic oxygen[203] and sulphur[203a] have been added to olefins. Cvetanovic and Sato[203] have examined the photolysis of nitrous oxide and of nitrogen dioxide in the presence of olefins, and have observed a number of phenomena similar to those found in the reactions of methylene. Photolysis of nitrogen dioxide, for example, gives oxygen atoms which in part add to olefins to give epoxides. With light of wavelength 2450 Å, the epoxide formation is non-stereospecific, indicating that the oxygen is reacting in a triplet state. On the other hand, use of a wavelength of 2288 Å gives an almost stereospecific addition, suggesting that it is singlet oxygen that is reacting; a transition state such as 48 being envisaged.



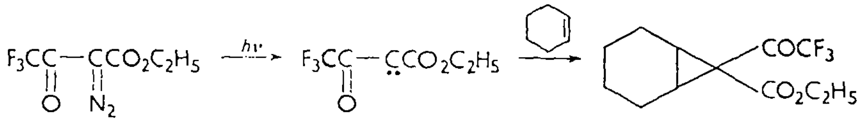
(48)

D. *Formation and Reactions of Carbenes (other than Methylene) from Ketenes and Diazo Compounds*

Just as diazomethane or ketene gives methylene on photolysis, so methylketene and diazoethane give ethylidene (methylcarbene, $CH_3CH:$). This, however, rearranges very rapidly to ethylene. The same is true of other alkylcarbenes obtained in this way, rearrangement to the corresponding alkene being rapid. Very recently[204] methylcarbene was trapped by addition to propene, but only in low yield and at high pressure. The addition could not be repeated with *cis*- or *trans*-butene, and therefore whether or not the reaction is stereospecific is not known.

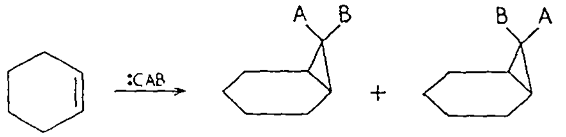
Perhaps the most familiar synthesis of cyclopropanes involves the thermal, or copper or copper salt catalysed, decomposition of diazoacetic ester in the presence of an olefin. Less work has been carried out on the photochemical induction of this reaction, but photolysis of diazoacetic ester gives carbethoxycarbene, and of diazomalonic ester gives dicarbethoxycarbene. The insertion reactions of these carbenes have been studied, and it has been found that there is greater selectivity than in the case of free methylene[148,205].

It is likely that the thermal decomposition of diazoacetic ester provides an alternative route to carbethoxycarbene, but better product yields may be expected with the lower temperatures associated with the photolytic process. The catalysed decompositions probably do not involve free carbenes (*vide infra*).

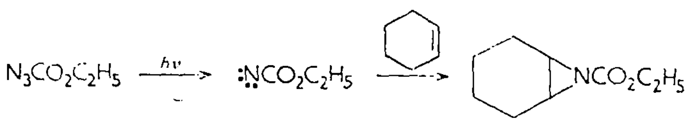


(49) (+ products of allylic insertion)

The related trifluoromethylcarbonylcarbethoxycarbene (**49**), obtained photochemically from the corresponding diazo compound, has also been added to olefins[206]. It should be noted that when a carbene bears two different substituents, most olefins give two stereoisomeric adducts, in proportions governed chiefly by steric factors, *e.g.* equation (88).



(88)



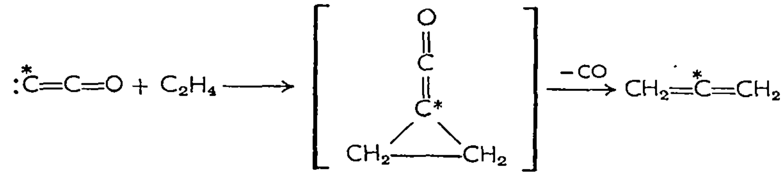
(**50**) (**51**)

Similar to diazoacetic ester is ethyl azidoformate (**50**), which on photolysis in cyclohexene, gives the nitrene adduct (**51**)[207].

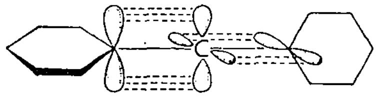
The photolysis of carbon suboxide in the presence of ethylene has recently been reported[208]. By labelling the central carbon atom of the reagent, and examining the isotopic composition of the major product (allene), it was possible to conclude that a reaction involving carbonylcarbene (**52**) probably occurred.

$$O{=}C{=}\overset{*}{C}{=}C{=}O \xrightarrow{h\nu} CO + :\overset{*}{C}{=}C{=}O$$

(52)



With the exception of unsubstituted methylene, there has been no evidence to indicate that the carbenes considered so far do not react in the singlet state. However, the lowest singlet and triplet states of methylene probably do not differ greatly in energy. Therefore, while substituents generally appear to stabilize the singlet rather than the triplet state, it seems reasonable that certain substituents might have the reverse effect, giving rise to triplet intermediates. Indeed, two diazo compounds photolysed in the presence of olefins by Skell and colleagues, were found to give cyclopropanes non-stereospecifically, and it was inferred that the divalent carbon intermediates must be reacting in the triplet state. The two intermediates in question were diphenylmethylene from diphenyldiazomethane[149], and propargylene $(HC{\equiv}C{-}\ddot{C}H)$ from $HC{\equiv}C{-}\ddot{C}HN_2$[209]. The diphenylmethylene was known to react with oxygen, and in addition, it was found that the rates of its reactions with different olefins were characteristic of radical rather than of electrophilic attack. For example, the reaction with butadiene was a hundred times faster than that with cyclohexene[149]. The conclusion that diphenylmethylene is formed in, or once formed, rapidly changes to, the triplet state, has now been substantiated by the observation of an electron spin resonance signal from the products of photolysis of diphenyldiazomethane in a glass at 77°K[210]. While the results of this work suggest that the ground state is indeed a triplet, it is likely that the diphenylmethylene does not have the simple linear structure **53** visualized by Skell[149].



(53)

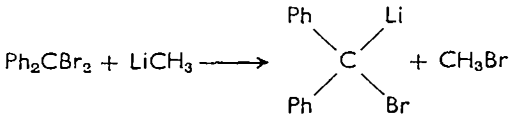
Electron spin resonance signals have also been observed from phenylnitrene obtained by the photolysis of phenyl azide[211].

The addition reactions of diphenylmethylene (or of propargylene) to *cis*- or *trans*-2-butene do not give the same proportions of isomers, indicating that in each case cyclization of the intermediate diradical occurs at a rate comparable with that of internal rotation.

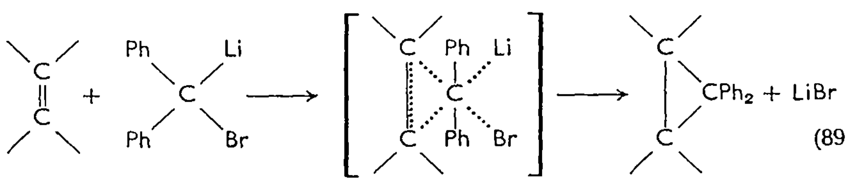
E. The Reactions of Carbenoid Species with Olefins

In the foregoing sections, a few reactions have been mentioned but not discussed on the grounds that they do not involve free carbene intermediates. It is the purpose of the present section to examine these and related reactions for which evidence preponderates in favour of 'carbenoid' intermediates which can readily transfer to an olefin a divalent carbon moiety in a bimolecular process. Reactions which probably fall into this category include certain α-eliminations catalysed by very strong base such as butyllithium or phenylsodium, as well as the copper-catalysed decompositions of the diazo compounds.

In the former reactions, the mechanism implied is α-metalation, followed by elimination of the metal salt concomitantly with attack on an olefin. A mechanism of this type was invoked by Closs and Closs[212] to explain the observation that diphenylcyclopropane formation in the reaction of diphenyldibromomethane, methyllithium and an olefin, is stereospecific (equation 89). Here, the difference from the reaction of diphenylmethylene from diphenyldiazomethane requires a difference in mechanism, but the alternative possibility that singlet diphenylcarbene is reacting cannot be excluded. A similar mechanism has been proposed for the analogous reaction of benzylidene bromide[213].

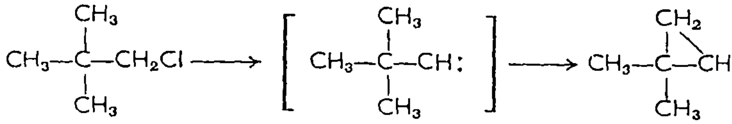


(89a)

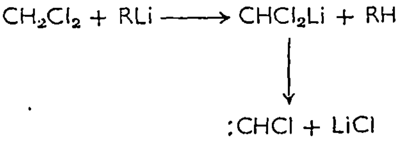


(89b)

Friedman and Berger[214] have obtained a 3% yield of norcarane from the reaction of methyl chloride, phenylsodium, and cyclohexene. The reaction with *cis*-2-butene gives *cis*-dimethylcyclopropane (1%) stereospecifically, which seems to exclude the participation of triplet methylene. The failure to observe insertion products argues against singlet methylene, and so a concerted mechanism is again preferred. However, some α-eliminations catalysed by strong bases, for example from the neopentyl halides, do give products of *intra*molecular insertion (equation 90)[215].


(90)

A variety of other base-catalysed α-elimination reactions have been reported to give substituted cyclopropanes when carried out in the presence of olefins and some of them are outlined in Table 12. Many of these reactions probably involve *C*-metalation followed by elimination of a metal halide, but whether or not this elimination leads to free carbenes, or gives cyclopropanes by simultaneous attack on the olefin cannot be stated with certainty. In particular Closs has studied the addition of [CHCl] to a variety of unsaturated compounds[216-218], and has discussed the results in terms of free chlorocarbene (equation 91). Attempts to trap the intermediate lithium compound with carbon dioxide have so far proved unsuccessful. α-Elimination from

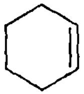
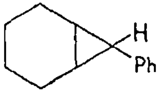
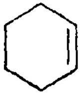
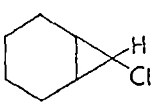
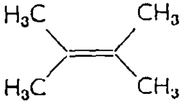
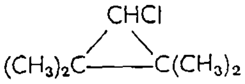
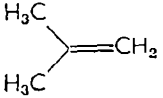
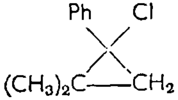
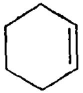
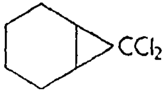
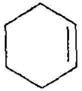
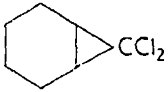
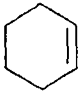
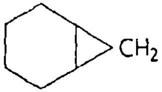
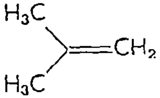
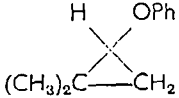
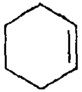
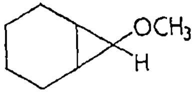
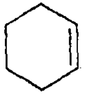
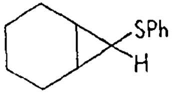


$$\begin{tikzcd} CH_2Cl_2 + RLi \arrow[r] & CHCl_2Li + RH \arrow[d] \\ & :CHCl + LiCl \end{tikzcd} \qquad (91)$$

methylene chloride can, however, be brought about by *t*-butoxide[226], in which case metalation prior to elimination presumably does not occur, and formation of a free carbene seems likely. This may also be true when an alkyllithium is used as the base. In any case, competitive additions to a series of olefins have been carried out by the alkyllithium procedure, and the order of reactivities is characteristic of electrophilic attack[218]. The reagent, which adds stereospecifically *cis*[217], is less discriminating than is dichlorocarbene.

While evidence for free chlorocarbene does not appear to be conclusive, Closs has recently reported compelling evidence for the formation of free alkylcarbenes in the reaction of methylene chloride with excess alkyllithium[227]. The products of the reaction are

TABLE 12. The synthesis of some cyclopropanes by means of α-elimination reactions.

Reagent	Base	Olefin	Adduct	Yield	Reference
$PhCH_2Cl$	n-C_4H_9Li		 *cis* + *trans*	14%	219
CH_2Cl_2	n-C_4H_9Li		 *cis* + *trans*	48%	216, 217
CH_2Cl_2	n-C_4H_9Li			67%	216, 217
$PhCHCl_2$	CH_3Li			54%	220
CCl_4	n-C_4H_9Li			50%	221
$CBrCl_3$	n-C_4H_9Li			91%	221
CH_2Br_2	CH_3Li			14%	221
$PhOCH_2Cl$	*t*-C_4H_9Li			50%	222, 223
CH_3OCH_2Cl	*t*-C_4H_9Li		 *cis* + *trans*	—	223, 224
$PhSCH_2Cl$	*t*-C_4H_9Li		 *cis* + *trans*	~90%	224, 225

similar to those generated by base-catalysed decomposition of tosylhydrazones (a reaction believed to involve alkylcarbenes), and include cyclopropanes formed by intramolecular insertion. Closs regards the formation of alkylcarbenes as occurring *via* the sequence (92).

$$:\mathrm{CHCl} + \mathrm{RLi} \longrightarrow \mathrm{RCHLiCl} \qquad (92a)$$

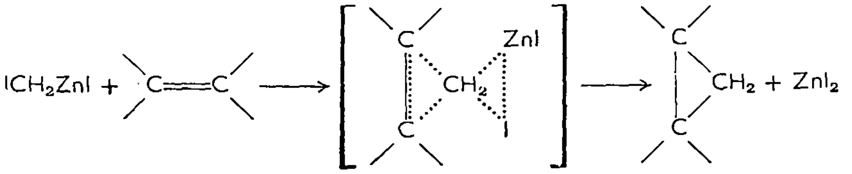
$$\mathrm{RCHLiCl} \longrightarrow \mathrm{R\ddot{C}H} + \mathrm{LiCl} \qquad (92b)$$

More recently still, Closs has prepared and photolysed chlorodiazomethane in the presence of olefins. The discovery that this procedure gives rather different products from those of the methylene chloride–alkyllithium–olefin reactions, argues against the formation of free chlorocarbene in the latter system[227a]. However, by an ingenious flow technique, Franzen has shown that free difluorocarbene is formed in the particular case of the reaction between bromotrifluoromethane and alkyllithium, and it was even possible to obtain an estimate of the lifetime of this intermediate in ether solution[227b].

A direct comparison between the use of potassium *t*-butoxide and methyllithium as the base in carbene-addition reactions has been made in the case of phenylchlorocarbene[220]. Whereas α-elimination from benzylidene chloride catalysed by *t*-butoxide requires temperatures of the order of 70°, when methyllithium is used as the base the reaction may be conducted at much lower temperatures (~0°) and gives improved yields. Whether this reflects the stronger basicity of the methyllithium or a change in mechanism cannot yet be decided.

Simmons and Smith[228] found that methylene iodide reacts with a zinc–copper couple in ether to give a solution which, after filtration from unreacted couple, contains essentially no copper, but which reacts with olefins to give cyclopropanes. Typically cyclohexene gives norcarane in 48% yield (based on methylene iodide). The yields with other olefins varied from 10–70%. They were markedly dependent on the nature of the zinc–copper couple. It seems likely that this convenient cyclopropane synthesis, which is again stereospecifically *cis*[228], involves a bimolecular reaction between the olefin and iodomethylzinc iodide (equation 93).

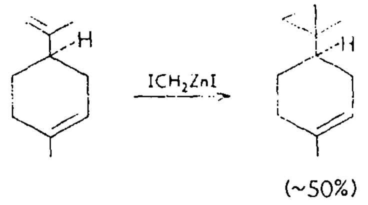
$$\mathrm{Zn/Cu} + \mathrm{CH_2I_2} \xrightarrow{(\mathrm{C_2H_5})_2\mathrm{O}} \mathrm{ICH_2ZnI} + \mathrm{Cu}$$



(93)

Although Simmons and Smith had discounted an alternative mechanism in which the organozinc intermediate adds to an alkene ($R_2C{=}CR_2$) in a classical sense to form $R_2C(ZnI)CR_2CH_2I$ which subsequently suffers 1,3-elimination of zinc iodide, evidence in support of such a mechanism has recently been presented by Hoberg[228a].

The organozinc intermediate is relatively unreactive towards esters and ketones, and the reaction permits the preparation of, for example, cyclopropyl acetate from vinyl acetate. That the carbene donor is a bulky molecule is demonstrated by the reaction of D-limonene (equation 94). Only the less-hindered double bond is attacked.



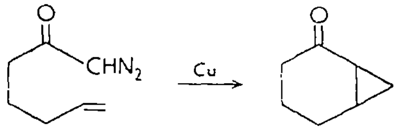
(94)

Bisiodomethylzinc also forms cyclopropanes with olefins[228b].

The synthesis of cyclopropanes from olefins by means of the copper or copper salt catalysed decompositions of diazo compounds, particularly of diazoacetic ester, is well known[e.g. 229,230], and has been regarded as proceeding *via* divalent carbon intermediates[154]. Yates suggested in 1952 that the intermediate (RCOCH:) formed in the copper-catalysed reactions of diazoketones may be bound to the copper surface[231]. Recently, it has been shown that norcarane is the only C_7 product obtained (in low yield) from the copper-catalysed decomposition of diazomethane in cyclohexene[191]. The absence of insertion products suggests that free methylene, either in the singlet or triplet state, is probably not an intermediate. The intermediate is probably also complexed in the copper salt catalysed decompositions. However, Skell and Etter have carried out competitive experiments with a series of olefins, using the copper sulphate catalysed decomposition of diazoacetic ester, and have found that the carbethoxycarbene moiety adds stereospecifically, and that the order of reactivities parallels that of the electrophilic dihalocarbenes[232a]. Attack on the olefins is less discriminating than that by the dihalocarbenes[232a], though considerably more so than that by carbethoxycarbene produced photochemically[232b].

Sorm and coworkers[233] have studied some copper and copper salt catalysed decompositions of diazoketones in the presence of olefins and have isolated some cyclopropyl ketones. This reaction has been extended to include intramolecular addition to a double bond[234].

Other diazocompounds which have been employed in copper or copper salt additions to olefins are diazoacetonitrile[235] and diazoethane[209].

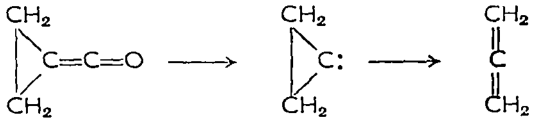


(95)

Closs has compared certain carbenoid reactions with S_N2 processes[212]. This comparison suggests kinetic experiments which might be devised to distinguish between carbenoid and free carbene mechanisms in favourable cases, though it seems that in many instances neither bimolecular transfer of a divalent carbon fragment, nor unimolecular formation of a free carbene, would be the rate-controlling step. Furthermore, Hine has shown that certain free carbenes can be formed by concerted (bimolecular) α-eliminations from haloforms[236], rather than by the two-step elimination process described in section II.B.

F. *Cyclopropylidenes: The Carbene Route to Allenes*

Photolysis of carbon suboxide in ethylene has been shown to give allene (section II.D). It is possible that an intermediate in the reaction is cyclopropylidene (**54**). A number of potentially useful allene syntheses have recently been described, in which derivatives of

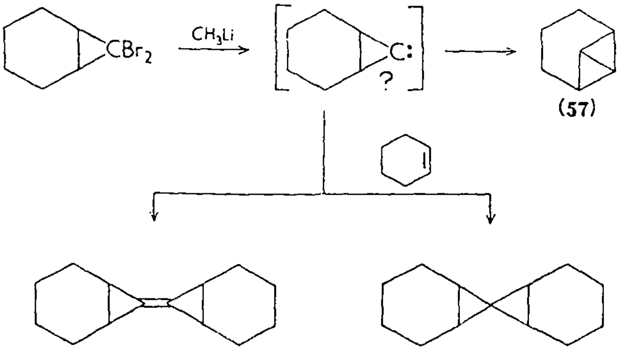


(**54**)

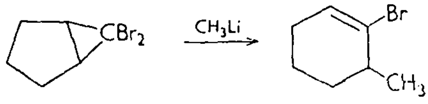
cyclopropylidene may be intermediates. In some of the reactions, the cyclopropylidene has, in part, been trapped by addition to an olefin to form a spiropentane, though in most of these cases the question of whether free cyclopropylidenes are formed has not been answered.

The first instance of a reaction of this type was reported by Doering and LaFlamme[237], who found that 1,1-dibromocyclopropanes react with magnesium in ether, or with sodium on alumina either alone or in dry decalin, at room temperature, to give allene in fair yields.

They suggested that the reaction might involve the intermediate formation of a cyclopropylidene which collapsed to the observed allenic product. Moore and Ward[238] found that a similar bromine elimination could be effected using Miller and Kim's procedure[221] with alkyllithium in ether at −80°. Dibromonorcarane was exceptional, presumably because of the enormous strain in cycloheptane-1,2-diene; one product isolated was the polycyclic compound **55**, and when the reaction was carried out in the presence of cyclohexene, the spiropentane **56** could be isolated. Later work[155] has shown that intramolecular insertion to give **57** may also occur, suggesting that the free carbene may be involved. 6,6-Dibromobicyclo-[3.1.0]hexane (**58**) also reacts differently with methyllithium, giving 2-bromo-3-methylcyclohexene[239].



(55) (56)



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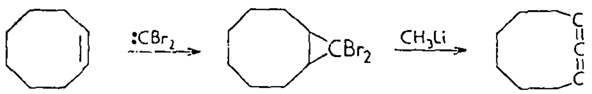
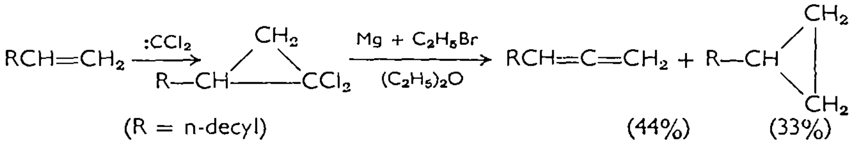


(59)

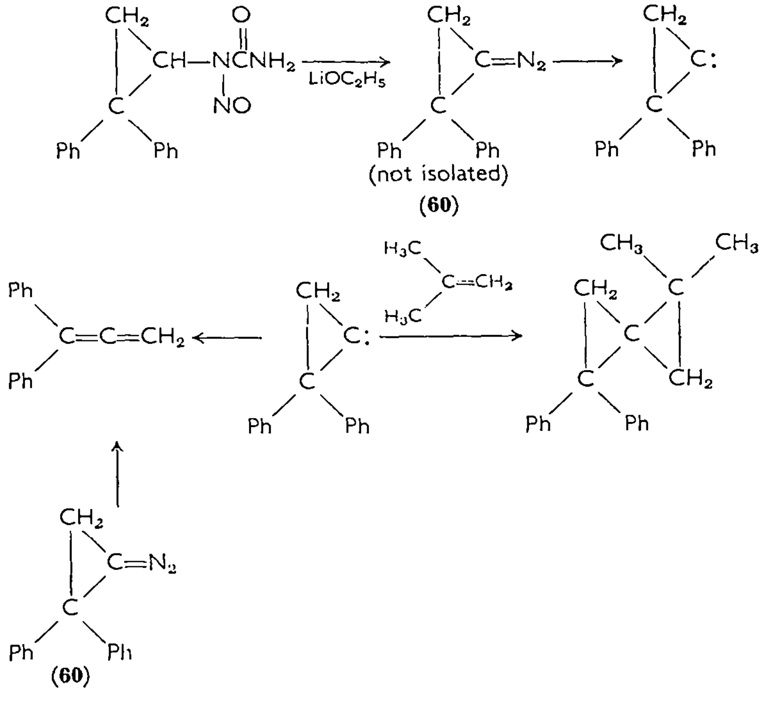
When larger rings are fused to the dibromocyclopropane, cyclic allenes may be synthesized successfully[239], *e.g.* cyclonona-1,2-diene (**59**).

Logan[240] has extended Doering and LaFlamme's procedure to *gem*-dichlorocyclopropanes by using magnesium and ethyl bromide in ether (equation 96). No carbene intermediates could be trapped by an olefin.



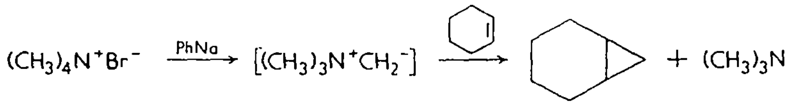
(96)

Jones[241] has observed reactions of 2,2-diphenylcyclopropylidene obtained from the corresponding diazo compound **60.** Its reaction with olefins gives spiropentanes in a stereospecifically *cis* process, suggesting a singlet electron configuration of the carbene. 1,1-Diphenylallene is always obtained as a by-product. Evidence is presented[242] which indicates that the allene is a product of two simultaneous reactions, and it is suggested that these might be the collapse of the cyclopropylidene and a direct decomposition of the diazo compound.



G. Miscellaneous Syntheses Involving Carbenes

A few other syntheses of cyclopropanes which involve carbene or carbenoid intermediates have been reported. Some of these involve the reactions of ylides with olefins. For example, Franzen and Wittig[243] have obtained norcarane from tetramethylammonium bromide, phenylsodium and cyclohexene (equation 97); and Hruby and Johnson[244] have obtained a cyclopropane *via* a sulphur ylide (equation 98).



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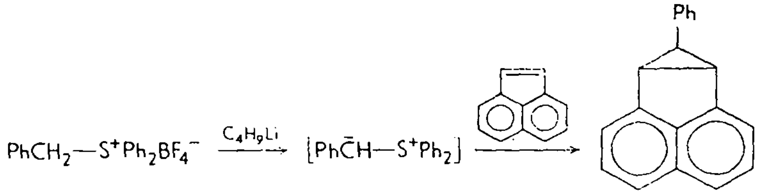
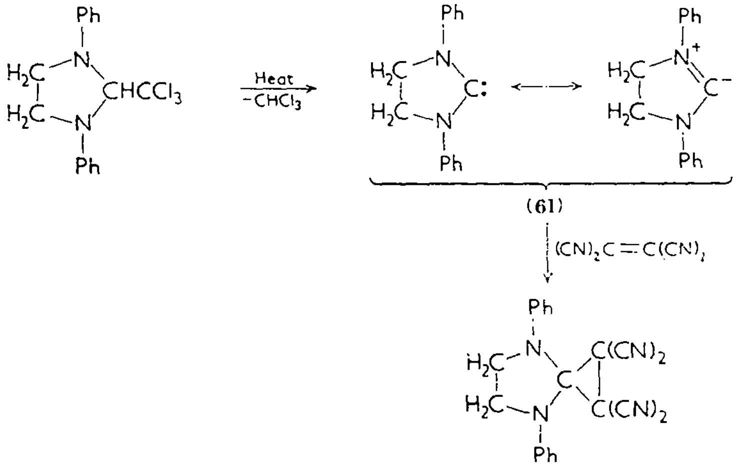


(98)

Wanzlick has made an intensive study[245] of the ‘nucleophilic carbene’ **61** in which two strongly electron-donating substituents are joined to the divalent carbon. One of its reactions is with the

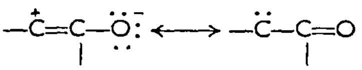


(62)

‘electrophilic olefin’ tetracyanoethylene, to give the spiro compound **62** in good yield.

H. 1,3-Dipolar Additions of Substituted Carbenes

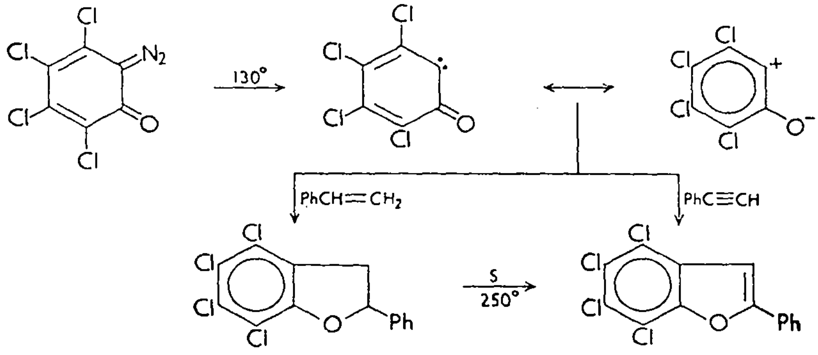
Huisgen and his school have recently elaborated the reactions of 1,3-dipoles with double and triple bonds to give a large variety of different five-membered ring heterocycles*. Many of the new ring systems are obtained by reactions of 1,3-dipoles, which may be written in uncharged canonical forms which possess electron deficient carbon or nitrogen. Typical of these are the ketocarbenes **63**. 1,3-



$$-\underset{|}{\overset{+}{C}}=C-\underset{\cdot\cdot}{\ddot{O}}{:}^{-} \longleftrightarrow -\ddot{C}-\underset{|}{C}=O$$

(**63a**) (**63b**)

Dipolar additions of ketocarbenes[278] and of 1,3-dipoles generally[279] have been the subjects of recent reviews. The addition is exemplified by the reactions in equation (99). The dipolarophile must normally contain a relatively polar or highly strained double or triple bond.



(99)

I. *Reactions of Carbenes with Polyenes and Acetylenes*

Reactions of carbenes with compounds having greater unsaturation than a single olefinic bond have so far only been referred to where such reference can help to throw light on some fundamental point. Typically, the reactions of singlet and triplet methylene with butadiene have already been considered. Some other reactions of carbenes with highly unsaturated compounds are collected below.

1. Conjugated dienes

The dihalocarbenes have been found to undergo 1,2-addition with conjugated double-bond systems[170], and, consistent with their electrophilic nature, they normally attack the most heavily alkylated double bond in the molecule. For example, dichlorocarbene reacts with isoprene to give 2,2-dichloro-1-methyl-1-vinylcyclopropane (**64**)[246]. The same double bond of isoprene is attacked in the copper catalysed reaction with diazoacetic ester[247]. Whereas it has been

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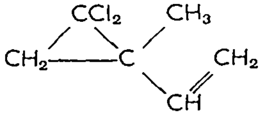
* See Chapter 11.

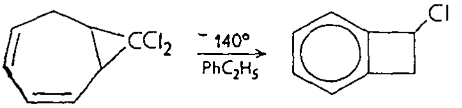
noted that cyclopentadiene gives chlorobenzene with dichlorocarbene, cycloheptatriene[172,248] and cyclooctatetraene[249] give normal adducts,



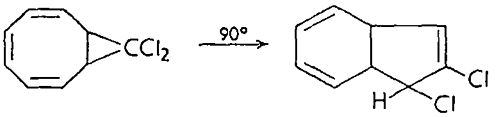
(64)

but these are unstable to heat, and rearrange as shown in equations (100) and (101) respectively.

An interesting reaction reported recently[250] is the formation of pyrroline (in low yield) when hydroxylamine-*O*-sulphonic acid is

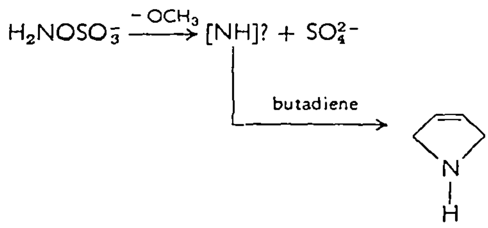


(100)



(101)

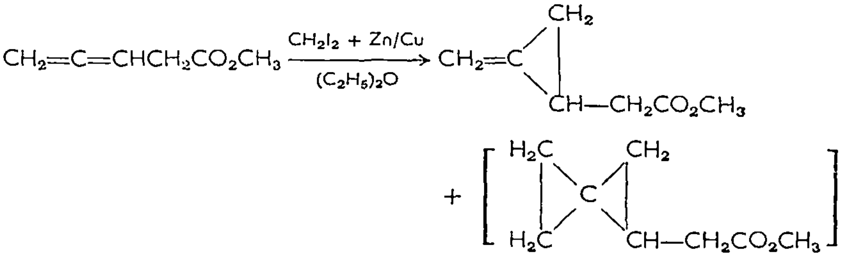
treated with sodium methoxide in methanol containing butadiene (equation 102). The suggested nitrene intermediate could not be trapped with a non-conjugated olefin[250a].



(102)

2. Allenes

Very little work has been carried out on the addition of carbenes to allenes. Frey[251] has found that a major product of the gas-phase photolysis of diazomethane or ketene in the presence of allene is methylenecyclopropane, providing the reaction is conducted at fairly high pressure. The insertion product, methylallene, is also formed. Substituted methylenecyclopropanes have been obtained in fairly good yields by the addition of dibromocarbene to allenes[252], and application of the Simmons–Smith procedure[253] has also produced methylenecyclopropanes, together with spiropentanes, as by-products. In both of these reactions, initial attack is at the more alkylated double bond, *e.g.* equation (103).

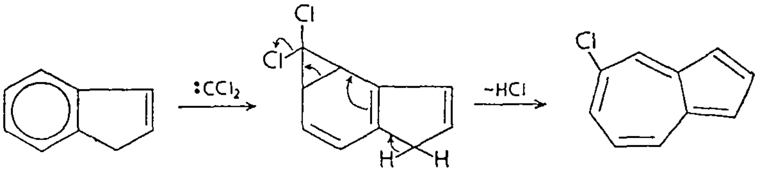


(103)

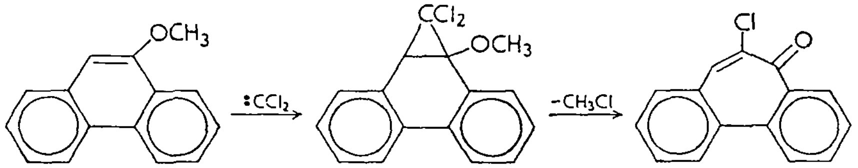
3. Aromatic compounds

Detailed discussion of the reactions of methylene and of carbethoxycarbene with aromatic compounds is beyond the scope of this article. A number of recent reviews are available which consider this subject[147,230,254].

Most benzenoid systems seem to be too unreactive to add dihalocarbenes, though in their work with indene, Parham and Reiff[162] obtained evidence of a by-product containing the azulene chromophore



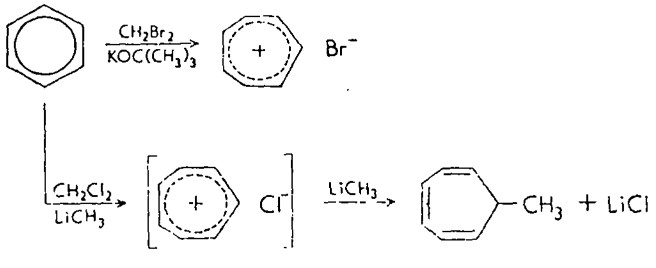
(104)



(105)

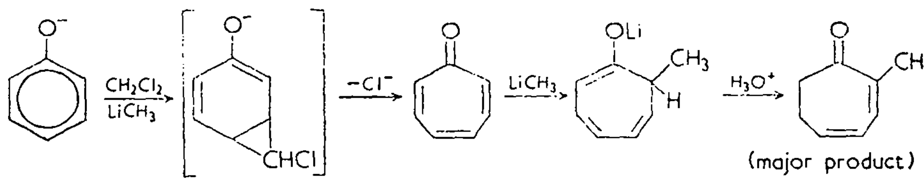
(equation 104), and recently Parham, Bolon and Schweitzer[255] have reported the formation of tropones from some methoxyl substituted aromatics (equation 105). Volpin and coworkers[226] have obtained low yields of tropylium ion from the reaction between benzene and monohalocarbenes, formed from methylene dihalides and potassium *t*-butoxide (equation 106). Closs and Closs have also expanded benzene rings by the methylene chloride–alkyllithium reaction (equations 107 and 108), and the same reagents have been employed to expand pyrrole to unsubstituted pyridine (equation 109)[257].

Dewar and Pettit's synthesis of tropylium bromide[258], outlined in equation (110), has received a number of interesting extensions. Acenaphthylene has been converted to the perinaphthylenium cation[259], and thiophene to thiapyrilium salts[260]. Other reactions of the intermediate cyclopropane adduct of carbethoxycarbene with thiophene, as well as that with furan, have been reported[261].



(106)

(107)



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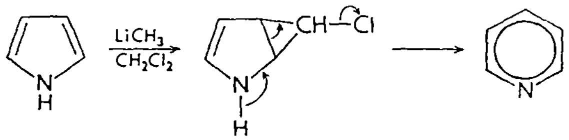
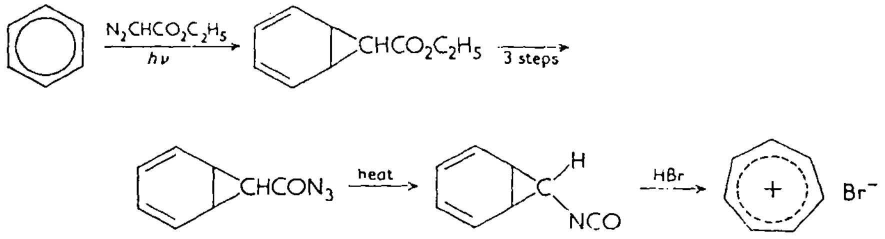


(109)

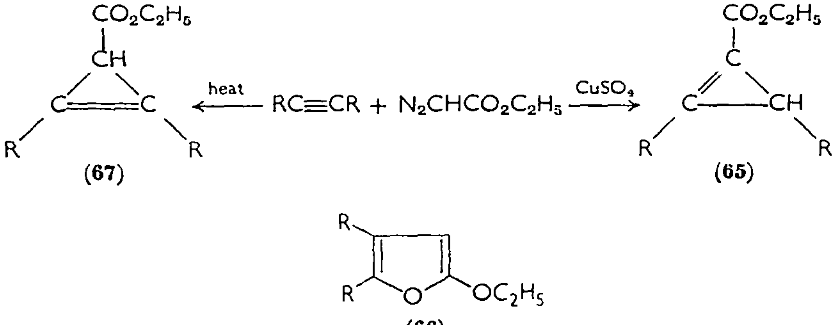


(110)

4. Acetylenes

Most of the major carbene and carbenoid reactions for converting olefins into cyclopropanes have now been repeated with acetylenes. Many of the resulting cyclopropene adducts have been found to have remarkable stability, in view of the necessarily large Bayer strain in such rings.

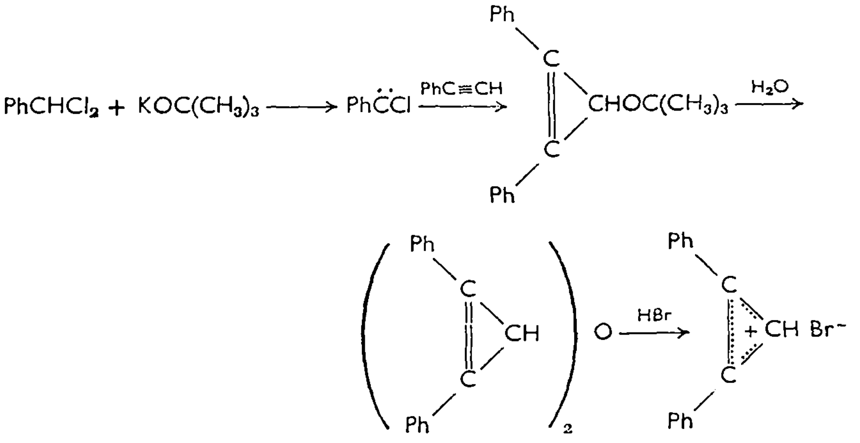
D'yakanov and Komendatov were the first to prepare a cyclopropene by one of these routes[262]. They used the decomposition of diazoacetic ester. In more recent work by D'yakanov's school, it was reported that the position of the double bond in the cyclopropene ring depends upon whether or not the decomposition of the diazo compound is catalysed[263]. Breslow and Chipman, however, have shown[264] that the unexpected cyclopropenes **65** are in reality the isomeric furan derivatives **66**, and D'yakanov has agreed with this formulation[265]. The furan appears to be the major product if the decomposition is catalysed by copper sulphate, while the expected cyclopropene **67** is formed in the copper catalysed or uncatalysed reaction. The furan is the product expected from a 1,3-dipolar addition of the carbethoxycarbene (section II.H).



(67) (65)

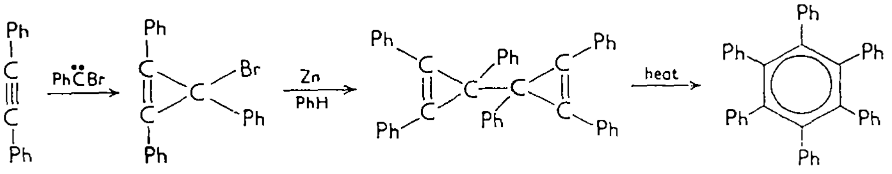
(66)

Perhaps the biggest contribution to cyclopropene chemistry has come from Breslow and colleagues. Often using carbene reactions (*e.g.* equation 111), this school has synthesized a variety of substituted

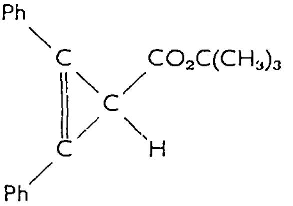


(111)

cyclopropenium salts[266]. Molecular-orbital theory has predicted that the cyclopropenium cation should exhibit aromatic stability, but this is not so for either the cyclopropenyl free radical, or for the corresponding anion. Breslow has obtained experimental evidence in support of the latter two predictions, in addition to isolating salts of the cations. The compound **68** shows no evidence of dissociation into radicals[267]; unexpectedly, on heating, it rearranges to hexaphenylbenzene. The *t*-butyl ester **69** does undergo very slow deuterium exchange when heated with potassium *t*-butoxide in deutero-*t*-butanol, but the rate of the reaction gives no indication that the carbanion is stabilized[268].



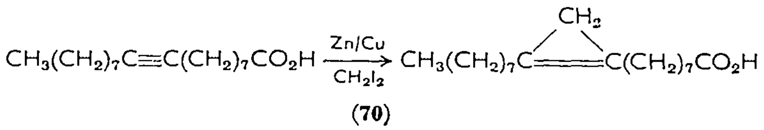
(68)



(69)

Both Breslow and Hover[266], and Doering[269] have made cyclopropenes without any aromatic substituents, and Breslow has also prepared 1,2-di-n-propylcyclopropenium perchlorate[266].

Castallucci and Griffin[270] have achieved a one-step synthesis of the naturally occurring sterculic acid (**70**) from stearolic acid, using the Simmons–Smith procedure, and Frey has obtained evidence that

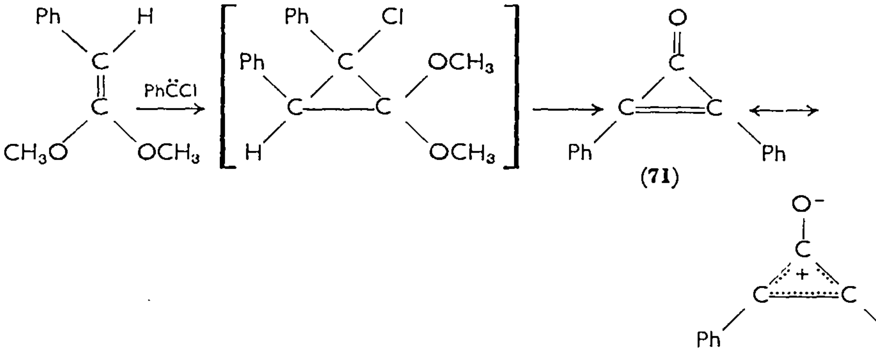


$$CH_3(CH_2)_7C{\equiv}C(CH_2)_7CO_2H \xrightarrow[CH_2I_2]{Zn/Cu} CH_3(CH_2)_7\overset{CH_2}{C{=}C}(CH_2)_7CO_2H$$

(70)

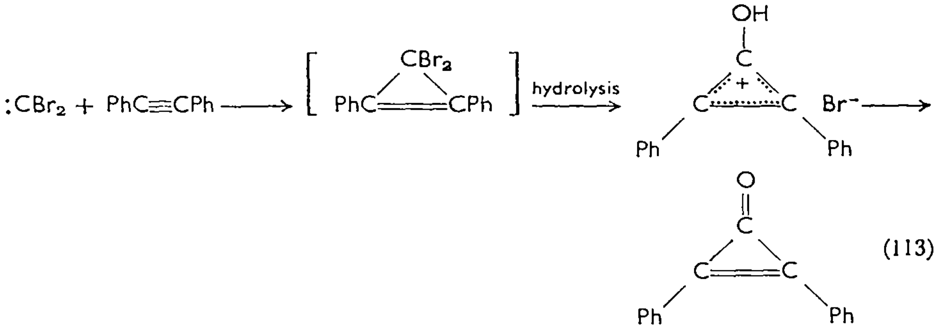
unsubstituted cyclopropene has a transient existence during the photolysis of diazomethane in the presence of acetylene[271].

Although cyclopropanone acetals cannot be hydrolysed to the parent cyclopropanone, diphenylcyclopropenone (**71**) has been prepared (equation 112)[272]. It is presumably stabilized in the same way as is tropone.



(112)

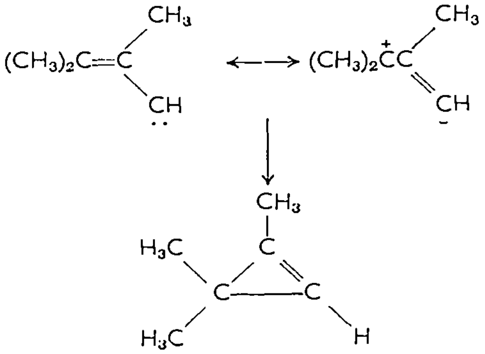
Dichloro- or dibromocarbene reacts with diphenylacetylene to give a cyclopropenone on treatment of the reaction mixture with sodium bicarbonate (equation 113)[273].



(113)

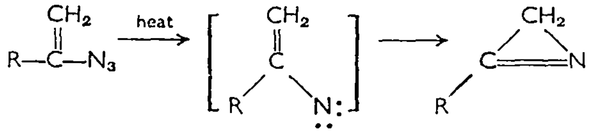
When dichlorocarbene reacts with an enyne, the preferred attack is at the double bond[274].

Closs and Closs have found that cyclopropenes are also formed by cyclization of alkenylcarbenes[275], *e.g.* equation (113). Smolinsky[276]

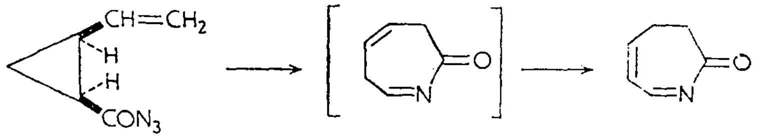


(114)

has obtained azirine derivatives from the pyrolysis of alkenyl azides (equation 115), possibly by a similar mechanism, and pyrolysis of the azide **72** may also involve a nitrene intermediate[277].



(115)



(72)

J. Recent Developments *

Interest in carbene reactions is at a high pitch, and many papers pertinent to this review have appeared since the end of 1962. Some of the more significant of these are mentioned briefly below.

Carbenes and nitrenes successfully added to alkenes for the first time include nitrene (:NH) (at 4°K)[280], phenylselenocarbene[281], and the dicarbene $:C{=}C{=}C:$[282]. A convenient source of chlorofluorocarbene has been reported[283], and allylcarbene (from allyldiazomethane) has been shown to undergo internal cycloaddition to form bicylobutane[284]. A bicyclobutane derivative has also been obtained by double carbene addition to an acetylene[285].

Seyferth's organomercurial synthesis of dihalocyclopropanes has successfully been extended to a variety of unreactive alkenes[286]. By this method perchlorocyclopropane was obtained in 70% yield.

Reactions of carbenes with steroids have been used to synthesize cyclopropane derivatives[287] as well as ring-expanded products[288, 289]. The cuprous chloride (or bromide) catalysed decomposition of diazomethane in benzene provides a convenient route to cycloheptatriene which is free from toluene[290], and photolysis of ethyl azidoformate in benzene has been shown to give carbethoxyazepine[291]. This is the first example of a monocyclic azepine. Several other reactions between aromatic compounds and carbenes or carbenoid intermediates have been reported. Among the more interesting of these is the application of Dewar and Pettit's procedure[258] to benzothiophene[292]. Surprisingly, it is the carbocyclic ring which is expanded, the product being the thienotropylium ion.

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* This section was added at the proof stage.

Several interesting observations on the stereochemistry of carbene additions have been made. Thus it has been shown that the major product from the alkyllithium–methylene chloride–alkene reaction is the sterically least favoured isomer[293]. This unexpected result suggests that tentative configurational assignments of other alkene–carbene adducts should be reexamined. A possible explanation involves charge separation and electrostatic effects in the transition state. Doubt has also been cast on the stereochemical evidence for the triplet nature of diphenylmethylene generated by photolysis of the corresponding diazo compound. In a similar reaction with diazofluorene, it has been found that the cyclopropanes produced from *cis-* or *trans*-2-butene undergo photochemical stereoisomerization[294]. Finally, it has been observed that an allylic or homoallylic hydroxyl group exhibits a strong *cis*-orienting influence in the Simmons–Smith synthesis[295].

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 10

Allylic reactions

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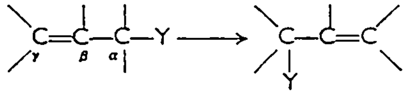
I. INTRODUCTION

A carbon–carbon double bond may profoundly influence the reactivity of a substituent or functional group in the molecule containing it. The effects of alkene linkages on the chemical properties of adjacent groups are of practical importance to synthetic chemists, and the nature and cause of these effects are of considerable interest to theoretical chemists.

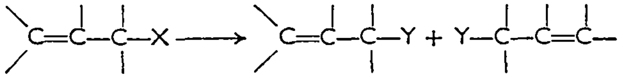
The effect of alkene unsaturation on the reactivity of a replaceable functional group or substituent depends upon the position of the alkene bond relative to the substituent, and is greatest in vinyl and allyl derivatives. The inertness of vinyl compounds, in which the replaceable group is bonded to one of the unsaturated carbon atoms, is well known. Allylic compounds, in which a replaceable atom or group other than hydrogen, is bonded to a saturated carbon atom attached to an alkene carbon atom, exhibit greatly enhanced reactivity relative to analogous saturated compounds.

Allylic compounds are characterized not only by enhanced reactivity in substitution reactions, but also by the ease with which they undergo allylic isomerization (equation 1a), and by their tendency to undergo



(1a)

partial or complete rearrangement in substitution reactions (equation 1b). The purpose of this chapter is to survey the kinds of substitution,



(1b)

isomerization and rearrangement reactions which allylic compounds undergo, with particular emphasis on the mechanisms of these reactions.

Allylic isomerization reactions are reactions in which the group Y migrates from the α- to the γ-carbon atom of the allylic system (equation 1a), with or without rearrangement of the atoms comprising Y. The term allylic rearrangement is arbitrarily limited to substitution reactions in which the entering group becomes bonded to the γ-carbon atom of the allylic system (see equation 1b).

In order to establish the occurrence of either allylic isomerization or allylic rearrangement (without using isotopic labels), it is necessary that the allylic compound be unsymmetrically substituted. For this reason, most of the examples of allylic reactions discussed below involve unsymmetrically substituted allylic compounds. Symmetrically substituted allylic compounds which are optically active by virtue of asymmetric α-carbon atoms also yield valuable information on the mechanisms of allylic reactions, and such compounds are frequently referred to.

Since much of the following discussion is concerned with the effects of substituents on the three-carbon allylic system on reactivity and reaction mechanism, acyclic allylic compounds are named as α-, β- and γ-substituted derivatives of the parent allyl compound, rather than systematically. While this violates the rules of systematic nomenclature, it serves the purpose of focusing attention on the allylic system, and also makes it much easier to visualize structures in the absence of written formulas.

II. NUCLEOPHILIC SUBSTITUTION REACTIONS

Nucleophilic substitution reactions of allylic compounds are similar in many respects to the analogous reactions of saturated aliphatic compounds. The allylic substitutions differ from their aliphatic analogues in the nature of the reactive intermediates and transition states involved, and in the fact that the entering group sometimes becomes bonded to the γ-carbon atom of the allylic system, rather than to the same carbon atom as the group which it replaced. In addition to the S_N2, S_N1 and S_Ni mechanisms available to saturated compounds[1], allylic compounds undergo nucleophilic substitution by two other mechanisms, S_N2' and S_N1', both of which involve allylic rearrangements.

Allylic nucleophilic substitution reactions were reviewed by DeWolfe and Young in 1956[2]. The following discussion summarizes the survey given in the review article, and brings it up to date.

A. Normal Bimolecular Nucleophilic Substitution

The normal bimolecular mechanism of nucleophilic substitution of allylic compounds most closely resembles the corresponding mechanism of saturated compounds, and bears the same mechanistic designation, S_N2. S_N2 reactions of allylic compounds involve a concerted attack by the nucleophile at the backside of the α-carbon atom of the allylic system, and give *only* unrearranged substitution products of inverted configuration (equation 2).

$$\mathrm{RCH{=}CHCH_2{-}X + Y\!: \longrightarrow RCH{=}CHCH_2{-}Y + X\!:} \qquad (2)$$

Practically all of the theoretical considerations which apply to S_N2 reactions of saturated compounds[1] apply equally to S_N2 reactions of allylic compounds. The present discussion is limited to a survey of the structural and environmental factors which affect the rates of allylic S_N2 reactions.

As shown in Table 1, allylic halides are considerably more reactive in S_N2 reactions than are the corresponding saturated halides. This appears to be true regardless of the structure of the carbon skeleton, the nucleophile used, the nature of the displaced group, or the reaction conditions. The rate difference between S_N2 reactions of allylic compounds and those of their saturated analogs is due mainly

TABLE 1. Relative reactivities in bimolecular displacement reactions of allylic and saturated halides.

Compounds	Nucleophile	Reaction conditions	$k_{\text{allylic}}/k_{\text{saturated}}$
$CH_2{=}CHCH_2Cl$ $CH_3CH_2CH_2Cl$	$C_2H_5O^-$	ethanol, 44·6°	27[a]
$CH_3CH{=}CHCH_2Cl$ $CH_3CH_2CH_2CH_2Cl$	$C_2H_5O^-$	ethanol, 44·6°	88[a]
$CH_2{=}C(CH_3)CH_2Cl$ $(CH_3)_2CHCH_2Cl$	$C_2H_5O^-$	ethanol, 44·6°	340[a]
$CH_3CHClCH{=}CH_2$ $CH_3CHClCH_2CH_3$	$C_2H_5O^-$	ethanol, 44·6°	26[a]
$CH_2{=}CHCH_2Cl$ $CH_3CH_2CH_2Cl$	I^-	acetone, 50°	73[b]
$CH_2{=}CHCH_2Br$ $CH_3CH_2CH_2Br$	C_5H_5N	nitromethane, 60°	78[c]
$CH_2{=}CH_2CH_2Br$ $CH_3CH_2CH_2Br$	C_5H_5N	ethanol, 55·6°	70[d]
$CH_2{=}CHCH_2Br$ $CH_3CH_2CH_2Br$	NH_3	ethanol, 40°	55[e]
$CH_2{=}CHCH_2Cl$ $CH_3CH_2CH_2Cl$	$(NH_2)_2CS$	methanol, 50°	167[f]
$CH_2{=}CHCH_2Br$ $CH_3CH_2CH_2Br$	$(NH_2)_2CS$	methanol, 50°	81[f]
$CH_2{=}CHCH_2I$ $CH_3CH_2CH_2I$	$(NH_2)_2CS$	methanol, 50°	57[f]

[a] C. A. Vernon, *J. Chem. Soc.*, 4462 (1954).

[b] J. B. Conant, N. R. Kirner and R. E. Hussey, *J. Am. Chem. Soc.*, **47**, 488 (1925).

[c] K. Clarke and K. Rothwell, *J. Chem. Soc.*, 1885 (1960).

[d] H. T. Clarke, *J. Chem. Soc.*, 416 (1910).

[e] S. Henchoz, *Compt. Rend.*, **244**, 1203 (1957).

[f] F. G. Bordwell, P. E. Sokol and J. D. Spainhour, *J. Am. Chem. Soc.*, **82**, 2883 (1960).

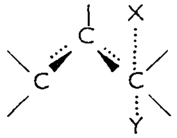
to the lower energy of activation of the allylic reactions[3-5], which may be attributed to resonance stabilization of the transition state of an allylic S_N2 reaction by overlap of the π-orbital on the α-carbon atom with the π-orbitals of the double bond[6].

The effect of substituents on rates of S_N2 reactions depends upon the size, electronic structure, electronegativity, polarizability and point of attachment of the substituent; on the nature of the leaving group and the nucleophile; on the structure of the rest of the molecule; and on the solvent, temperature and other environmental factors. Two reactions have been applied to a large enough number of allylic compounds to permit generalizations to be made regarding substituent effects on allylic S_N2 reactions: the reaction of allylic chlorides with potassium iodide in acetone, and with sodium ethoxide in ethanol. Data for both of these reactions are summarized in Table 2.

The interpretation of substituent effects in S_N2 reactions of alkyl halides is complicated by the difficulty encountered in separating electronic from steric effects[7]. In the more rigid allylic system, steric effects predominate in the case of α-substituents, but are relatively unimportant for β- and γ-substituents.

Steric retardation of S_N2 reactions by allylic α-substituents is illustrated by the fact that both α-methylallyl chloride and α-chloroallyl chloride are much less reactive than allyl chloride in S_N2 reactions. When there are two substituents on the α-carbon atom, displacement by the S_N2 mechanism is usually so hindered that it is not observed. In such cases, substitution occurs either by the unimolecular mechanism or the abnormal bimolecular mechanism.

The conformation of lowest energy for the transition state of an allylic S_N2 reaction is that in which the leaving group, the α-carbon and the entering group are in a line perpendicular to the plane formed by the α-, β- and γ-carbon atoms (**1**)[4,6,8]. This is the only configuration which permits resonance interaction of the double bond with the developing π-orbital of the α-carbon. Bonds to β- and γ-substituents will lie in the plane described by the allylic carbon atoms, both in the ground state and in the transition state.



(1)

Table 2. Relative reactivities of allylic chlorides[a].

Compound	KI in acetone (20°c)	$NaOC_2H_5$ in ethanol (50°c)
$CH_2{=}CHCH_2Cl$	1·00	1·00
$CH_2{=}CHCHCl_2$	0·01	0·012
$CH_2{=}CHCHClCH_3$	0·023	0·06
$CH_2{=}CClCH_2Cl$	0·72	0·47
$CH_2{=}CBrCH_2Cl$	0·87	0·82
$CH_2{=}C(CH_3)CH_2Cl$	1·58	1·03
$CH_2{=}C(C_6H_5)CH_2Cl$	2·27	1·12
cis-$ClCH{=}CHCH_2Cl$	8·58	2·8
trans-$ClCH{=}CHCH_2Cl$	2·90	3·47
cis-$BrCH{=}CHCH_2Cl$	20	5·8
trans-$BrCH{=}CHCH_2Cl$	1·2	2·9
cis-$CH_3CH{=}CHCH_2Cl$	8·35	5·14
trans-$CH_3CH{=}CHCH_2Cl$	1·56	4·43
trans-$C_6H_5CH{=}CHCH_2Cl$	11·0	6·83
$(CH_3)_2C{=}CHCH_2Cl$	28·1	15
cis-$CH_3CH{=}C(CH_3)CH_2Cl$	5·57	3·94
trans-$CH_3CH{=}C(CH_3)CH_2Cl$	41·8	4·36
$(CH_3)_2C{=}C(CH_3)CH_2Cl$[b]	150	—
$C_2H_5C(CH_3){=}CHCH_2Cl$	—	20
α-$CH_3CCl{=}CHCH_2Cl$	23·3	4·8
β-$CH_3CCl{=}CHCH_2Cl$	27·8	6·16
$CH_3CH{=}CHCHCl_2$	2·37	3·7
$CH_3CHClCH{=}CHCH_2Cl$	—	0·23
$Cl_2C{=}C(CH_3)CH_2Cl$	> 33	7·42
$CH_2{=}C(CH_3)CCl_2CH_3$	0·07	0·11
α-$CHCl{=}C(CH_3)CH_2Cl$	32·8	—
β-$CHCl{=}C(CH_3)CH_2Cl$	8·45	—
cis-$CH_3CCl{=}CClCH_2Cl$	69	5·95
trans-$CH_3CCl{=}CClCH_2Cl$	23	6·66
$CCl_2{=}CHCH_2Cl$[c]	98	12·1
$CBr_2{=}CHCH_2Cl$[c]	very fast	19·1
cis-n-$C_4H_9CH{=}CHCH_2Cl$[d]	10·7	3·13
trans-n-$C_4H_9CH{=}CHCH_2Cl$[d]	2·37	2·77
cis-$(CH_3)_3CCH{=}CHCH_2Cl$[d]	5·92	1·55
trans-$(CH_3)_3CCH{=}CHCH_2Cl$[d]	1·38	2·33
trans-$CF_3CH{=}CHCH_2Cl$[e]	17·00	—
p-$CH_3C_6H_4SO_2CH{=}CHCH_2Cl$[f]	13·8	—
$C_6H_5SO_2CH{=}CHCH_2Cl$[f]	15·9	—
$NCCH{=}CHCH_2Cl$[f]	17·5	—

[a] Data from R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 765–66 (1956), except as otherwise noted.

[b] L. F. Hatch and P. R. Noyes, *J. Am. Chem. Soc.*, **79**, 345 (1957).

[c] L. F. Hatch and S. D. Zimmerman, *J. Am. Chem. Soc.*, **79**, 3091 (1957).

[d] L. F. Hatch, H. D. Weiss and T. P. Li, *J. Org. Chem.*, **26**, 61 (1961).

[e] J. A. Pegolotti and W. G. Young, *J. Am. Chem. Soc.*, **83**, 3258 (1961).

[f] F. G. Bordwell and G. D. Cooper, *J. Am. Chem. Soc.*, **73**, 5184 (1951).

Because of the geometry of the ground and transition states, allylic S_N2 reactions should be nearly free from the steric hindrance which β-substituents produce in the corresponding saturated compounds[9], and γ-substituents should have negligible steric effect on reactivity. It follows that the effects of β- and γ-substituents on allylic S_N2 reactivity must be largely electronic.

The data in Table 2 show that both electron-attracting and electron-repelling γ-substituents facilitate reaction of allylic chlorides with potassium iodide in acetone, and with sodium ethoxide in ethanol. A similar situation exists in several bimolecular displacement reactions of substituted benzyl halides[10,11]. Halogen, alkyl, aryl, cyano and sulfonyl γ-substituents all accelerate allylic S_N2 reactions, and the effect of two γ-substituents is invariably greater than that of one. Since all of these groups can interact with the allylic double bond by resonance or hyperconjugation, and hence should stabilize the transition state of the reaction, no definite decision regarding inductive effects of these groups on reactivity can be made. To add to the confusion, both the γ-*t*-butyl group and the γ-trifluoromethyl group—neither of which can interact mesomerically with the reaction center—increase S_N2 reactivity. It is conceivable that a strongly electron-attracting γ-substituent could cause a reversal in the relative importance of bond making and bond breaking in formation of the transition state[12]. The powerfully electronegative trifluoromethyl group may exert its activating influence by so polarizing the allylic double bond that the allylic halide is electronically similar to an α-halocarbonyl compound, and, therefore, owes its enhanced reactivity to its ability to form a more stable, cyclic transition state[13].

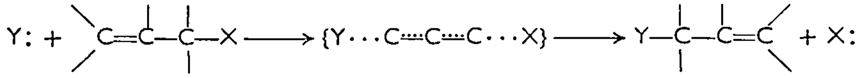
Allylic chlorides having a single γ-substituent *cis* to the CH_2Cl group appear invariably to be more reactive with iodide ion in acetone than are their geometric isomers. This effect may be due in part to release of steric strain on formation of the transition state, but is probably due mainly to Bunnett's polarizability effect[4,14]. This effect is thought to be due to van der Waal's forces acting between the substituent and the nucleophile, which should increase with increasing polarizability of both the substituent and the nucleophile, and with increasing proximity of the substituent to the reaction center. This hypothesis accounts for the fact that the *cis* isomer is consistently the more reactive with the highly polarizable reagent, iodide ion, but is sometimes the less reactive isomer with ethoxide ion. It also explains why the *cis–trans* reactivity ratio is considerably larger for γ-bromo (16·7) than for γ-chloro (2·95) or γ-methyl (5·57).

Substituents on the allylic β-carbon atom cannot bring into play the conjugative mechanism of electron release, and their influence on S_N2 reactivity must be due to a combination of inductive, steric and polarizability effects which nearly cancel. In reactions with both iodide ion and ethoxide ion, reactivity increases slightly in the order $CH_2{=}CClCH_2Cl < CH_2{=}CBrCH_2Cl < CH_2{=}CHCH_2Cl < CH_2{=}C(CH_3)CH_2Cl < CH_2{=}C(C_6H_5)CH_2Cl$ (Table 2).

The complexity of the factors which determine S_N2 reactivity of allylic compounds is demonstrated by data on the few reaction series for which energies and entropies of activation are available. Rate differences in the reactions of allyl, β-methylallyl and γ-methylallyl chlorides with ethoxide ion in ethanol are due mainly to different entropies of activation[3], while the differences in reactivity of γ-methyl, γ-phenyl and γ-*p*-tolylallyl chlorides with potassium iodide in acetone are due to differences in both E_a and $\Delta S^{\ddagger}$[15]. In the reaction of four allylic chlorides with sodium thiosulfate in aqueous ethanol, there is a steady increase in E_a as the electron-attracting power of the γ-substituent increases, accompanied by a diminution in the negative value of $\Delta S^{\ddagger}$ which more than compensates for it[16]. Just the reverse is true in the reaction of thiourea with allyl and γ-*p*-toluenesulfonylallyl chlorides in methanol[4].

B. The Abnormal Bimolecular Mechanism of Nucleophilic Substitution

A second mechanism of bimolecular substitution should be available to allylic compounds[17,18], in which the nucleophilic reagent attacks the unsaturated γ-carbon atom of the allylic system, displacing the α-substituent in a concerted process (equation 3). This process is



$$Y\colon + \;\rangle C{=}\overset{|}{C}{-}\underset{|}{\overset{|}{C}}{-}X \longrightarrow \{Y\cdots C{\cdots}C{\cdots}C\cdots X\} \longrightarrow Y{-}\underset{|}{\overset{|}{C}}{-}\overset{|}{C}{=}C\langle \; + X\colon \qquad (3)$$

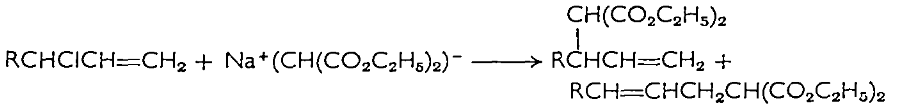
called abnormal bimolecular substitution and is represented by the symbol S_N2'.

At least three conditions must be met before a reaction can be definitely classified as an example of abnormal bimolecular substitution:

1. The rate of the reaction must be proportional to the concentration of both the nucleophilic reagent and the allylic reactant.

2. The reaction must give isolable amounts of rearranged substitution products.
3. Neither the starting material nor the normal substitution product must undergo allylic isomerization at an appreciable rate under the conditions of the reaction.

Early attempts to establish the existence of the S_N2' mechanism were fruitless[19-22], and led to the conclusion that the S_N2' mechanism is not ordinarily involved in bimolecular replacement reactions of primary and secondary allylic compounds[23,24]. The first example of an allylic S_N2' reaction was reported in a Ph.D. thesis by Webb[25]. However, the first case which met all three of the conditions listed above was reported by Kepner, Winstein and Young in 1949[26]. They found that α-methylallyl and α-ethylallyl chlorides react with the sodium salt of malonic ester in ethanol to give 10 and 23%, respectively, of the rearranged products to be expected from S_N2' displacements (equation 4). Kinetic studies of the reaction with α-ethylallyl chloride showed that it was second order, and it was shown that neither the reactant nor the normal product isomerizes under the reaction conditions used. Dewar[27] questioned the validity of the conclusions reached from these results on the grounds that the abnormal product might have been formed by *O*-alkylation of the malonate ion, followed by Claisen rearrangement of the resulting vinyl ether. It is unlikely that the postulated ether would rearrange under the mild conditions used, even if it were formed, and Stork and White demonstrated that *O*-alkylation followed by isomerization definitely does not occur in S_N2' reactions of alkylcyclohexenyl 2,6-dichlorobenzoates with malonate ion[28].



$$RCHClCH{=}CH_2 + Na^+(CH(CO_2C_2H_5)_2)^- \longrightarrow R\overset{CH(CO_2C_2H_5)_2}{\overset{|}{C}}HCH{=}CH_2 + RCH{=}CHCH_2CH(CO_2C_2H_5)_2 \qquad (4)$$

Once the existence of the S_N2' mechanism had been demonstrated, further examples were soon discovered. Young, Webb and Goering[29] found that α-methylallyl chloride undergoes a bimolecular reaction with diethylamine, and demonstrated that the S_N2' mechanism is involved. A short time later, England and Hughes[30] published the results of a study of bromide-exchange reactions of α- and γ-methylallyl bromides, presumably by mechanisms S_N2 and S_N2'. De la Mare and Vernon[31-35] published a series of papers on S_N2' reactions of allylic chlorides having sterically hindered α-carbon atoms, and

Stork and White[36] described S_N2' reactions of substituted cyclohexenyl 2,6-dichlorobenzoates. These and other reactions are discussed in more detail in the following paragraphs.

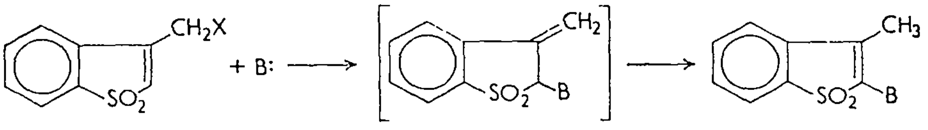
The number of allylic replacement reactions which probably involve the S_N2' mechanism is quite large. Only in a few cases, however, have the kinetics, product compositions, and product stabilities been sufficiently well established to prove definitely that this mechanism is responsible for the formation of rearranged products.

The S_N2' mechanism is a potential competitor to the normal S_N2 mechanism whenever an allylic compound undergoes a bimolecular displacement reaction. The competitive advantage of the abnormal mechanism is increased by structural and environmental factors which suppress the normal S_N2 reaction, or which increase the rate of the abnormal reaction relative to the rate of normal substitution.

The most obvious means of suppressing normal bimolecular substitution is to introduce bulky substituents at the α-carbon atom. S_N2' substitution by anionic reagents is usually not detectable unless there is at least one α-substituent, and two α-substituents or a single very bulky α-substituent (a *t*-butyl group, for example) are necessary before the abnormal mechanism predominates. Thus, the reaction of α-methylallyl chloride with ethoxide ion in ethanol yields less than 5% of the abnormal product[19,20,22,35], while α-*t*-butylallyl chloride forms the abnormal product exclusively[37]. Similarly, in reactions with sodium thiophenoxide in ethanol, α-methylallyl chloride formed a small amount of rearranged product, while the abnormal product formed exclusively from α,α-dimethylallyl chloride[35]. α,α-Dimethylallyl chloride also reacts with thiourea in acetone solution by the S_N2' mechanism[38]. A single α-halogen substituent renders abnormal bimolecular substitution observable (α-chloroallyl chloride forms substantial amounts of abnormal products in reactions with ethoxide, phenoxide and thiophenoxide[33]), and two α-halogens suffice to cause substitution to proceed predominantly or exclusively by this mechanism[34].

An α-chloro substituent is more effective than an α-methyl group in increasing the ratio of S_N2' to S_N2 substitution. This is probably due in part to the fact that α-chloro is more effective than α-methyl in retarding normal substitution (see Table 2). An α-halogeno substituent should also facilitate the S_N2' reaction relative to the normal reaction by shifting the π-electron cloud away from the γ-carbon atom, thus aiding γ-attack by the nucleophile[23,32,34]. If this idea is correct, a secondary allylic compound having a sufficiently powerful electron-attracting α-substituent should react exclusively by the S_N2' mechanism in bimolecular substitution reactions, as appears to be the case in reactions of α-trifluoromethyl *p*-bromobenzenesulfonate with iodide and azide ions[13].

The steric and electronic effects of β- and γ-substituents on S_N2' reactivity are largely unknown. γ-Substituents in general facilitate S_N2 reactions of allylic compounds (Table 2), and in the great majority of cases γ-substituted primary allylic compounds appear to undergo substitution exclusively by the normal mechanism. An interesting exception to this rule is the reaction of 3-halomethylbenzothiophene-1,1-dioxides with piperidine, morpholine, thiourea, and thiophenoxide ion[39]. All of these reagents yield the rearranged product exclusively and kinetic and other evidence indicates that this is the result of substitution by the S_N2' mechanism (equation 5).

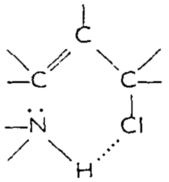


(5)

This result is attributed to π-electron delocalization by the sulfonyl group in the transition state of the S_N2' reaction, plus the fact that the only conformation available for displacement is particularly favorable to the S_N2' reaction.

The effect of α-substituents on rates of S_N2' reactions is qualitatively similar to the effect of γ-substituents on S_N2 reactivity[32,34,35]. α-Substituents which can release electrons to the α-carbon atom by either the inductive or the mesomeric process should stabilize the S_N2' transition state, and hence lower the free energy of activation.

The nature of the nucleophilic reagent affects both the rates of S_N2' reactions and the ratio of normal to abnormal bimolecular substitution. The limited evidence available indicates that uncharged nucleophilic reagents—amines, for example—are less discriminating between the α- and γ-carbon atoms of the allylic system than are anionic reagents. α-Methylallyl chloride yields a substantial amount of abnormal substitution product in bimolecular reactions with trimethylamine, and appears to give only the product of abnormal substitution in reactions with secondary amines such as diethylamine and dimethylamine[29,40-42]. The exclusive formation of abnormal products in reactions of α-methylallyl chloride with secondary amines is probably due to initial hydrogen bonding between the amine and the allylic chlorine atom[25], which would orient the nucleophile properly for attack on the γ-carbon atom of the allylic system **2**.



(2)

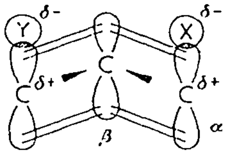
That α-substituents are not required for the occurrence of abnormal reactions of allylic chlorides with amines is demonstrated by the fact that 7% of rearranged product was formed in the reaction of trimethylamine with allyl chloride-1-^{14}C[43].

In contrast, reactions of α-methylallyl chloride with alcoholic sodium ethoxide or sodium thiophenoxide give mainly or entirely the normal products[20,22,35]. Sodium ethylmalonate in ethanol, an anionic nucleophile whose negative charge is dispersed over three centers, gives appreciable amounts of rearranged products in bimolecular reactions with α-methyl- and α-ethylallyl chlorides[25], but only normal product in the reaction with allyl chloride-1-^{14}C[44].

The conclusion reached is that uncharged reagents and anionic reagents in which the charge is dispersed over more than one center yield higher proportions of abnormal products in bimolecular reactions with allylic halides than do anionic reagents whose charge is concentrated on one atom. Any acceptable explanation of S_N2–S_N2' rate ratios will also have to allow for steric effects due to the bulk of the reagent, an aspect of these reactions which has not been investigated. The observed variation of product ratios with the charge-type of the nucleophile is probably due to electrostatic repulsion between anionic reagents and the π-electron cloud of the allylic double bond, and to electrostatic assistance to the departure of the chloride ion by anionic reagents being greater for α-attack than for γ-attack.

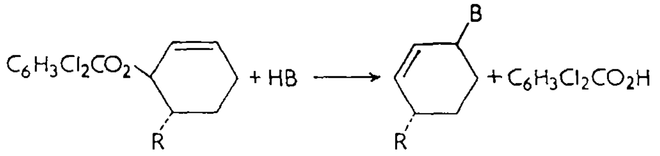
Data on solvent effects on S_N2' reactions are meager. The rates of S_N2' reactions of α-chloroallyl chloride and α,α-dichloro-β-methylallyl chloride with sodium thiophenoxide are greater in 75% ethanol–water mixture than in absolute ethanol[45], contrary to expectation for reactions between charged nucleophiles and uncharged substrates. On the other hand, the S_N2' reaction of α-methylallyl chloride with dimethylamine is about ten times faster in benzene than in the less polar solvent, cyclohexane, as expected for bimolecular substitutions of this charge type.

The electronic and stereochemical details of the S_N2' reaction have been fairly well established. It has long been tacitly assumed that S_N2' displacements are concerted processes, rather than addition–elimination reactions; this view has been substantiated by Bordwell, Sokol and Spainhour[4], who showed that the reactivities of 3-halomethylbenzothiophene-1,1-dioxides in S_N2' displacements by thiourea in methanol vary with the nature of the displaced halogen in very nearly the same way as do the reactivities of allyl halides in S_N2 displacements by the same reagent. The observed reactivity ratios in the S_N2' reaction, Cl:Br:I::1·0:79:230, are very much larger than would be expected if the reaction involves slow formation of an intermediate adduct, followed by rapid loss of halide ion.



(3)

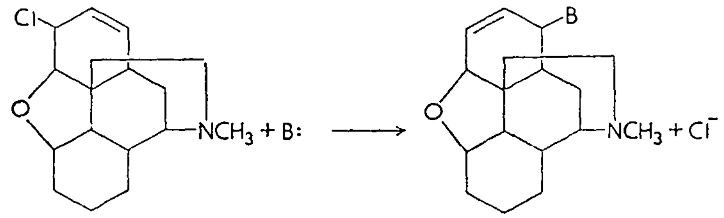
The concerted S_N2' displacement involves simultaneous bond breaking at the α-carbon and bond making at the γ-carbon atom. In the transition state, all three carbon atoms of the allylic system are trigonally hybridized, and lie in a plane perpendicular to the plane of the partial bonds to the entering and leaving groups. Winstein suggested that the electronic requirements for transforming the α-carbon atom from a tetrahedral to a trigonal configuration are best satisfied if the entering and leaving groups are on the same side of the plane formed by the allylic carbons, *i.e.* in a *cis* configuration[29]. This leads to **3** as a picture of the S_N2' transition state.



(6)

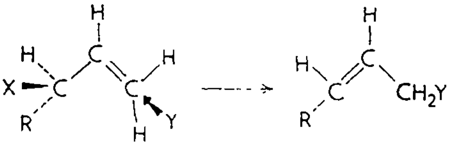
This model for the transition state is compatible with the effects of substituents on reactivity, and accounts very satisfactorily for the stereochemistry of S_N2' reactions of cyclic allylic compounds. Stork and White[28,36] found that *trans*-6-alkyl-2-cyclohexenyl 2,6-dichlorobenzoates undergo abnormal bimolecular displacement reactions with morpholine in xylene solution and with sodiodibutylmalonate in butanol solution to form rearranged products in which the new group is attached to the side of the ring from which the dichlorobenzoate ion departed (equation 6).

Stork also suggested a *cis*-S_N2' mechanism to account for the product formed in the reaction of α-chlorocodide with methoxide ion[46], and obtained kinetic evidence for the S_N2' mechanism in the reaction of α-chlorocodide with piperidine in benzene, in which the nucleophile also enters *cis* to the leaving group (equation 7)[47].

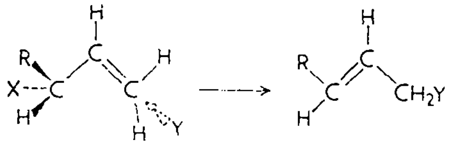


(7)

The stereochemistry of S_N2' displacements in acyclic allylic systems has not been worked out, and it is not known to what extent steric hindrance to *trans*-S_N2' displacement is responsible for the observed stereochemical course of abnormal substitution reactions of cyclic compounds. It should be pointed out that the formation of a mixture of *cis* and *trans* γ-substituted reaction products in an S_N2' reaction of an α-substituted allylic compound does not necessarily mean that transition states having both *cis* and *trans* configurations are involved. This result could be due to exclusive *cis* displacement on two different conformations of the allylic reactant (equations 8a and 8b).



(8a)



(8b)

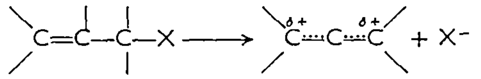
C. The Unimolecular Mechanism of Substitution and Rearrangement

The unimolecular mechanism of substitution in allylic compounds is similar to the S_N1 mechanism of nucleophilic aliphatic substitution[48], in that its rate-determining step involves formation of an ionic intermediate. There is one important difference, however: the cationic intermediate formed by an allylic compound is mesomeric and can react with the solvent or other nucleophilic reagent to yield, in the case of an unsymmetrically substituted allylic cation, a mixture of isomeric products (equation 9). If X and Y are different, substitution with partial allylic rearrangement is the result. When they are the same, the result is isomerization. In either case the essential features of the reaction are identical, and the substitution and the isomerizations are both examples of mechanism S_N1. Formation of the intermediate may be aided by interaction of the leaving group with solvent molecules, metal ions or acids. The leaving group X may or may not become completely free of the carbonium ion—all that is necessary is that heterolytic bond fission occur at least to the point where an ion pair is formed.

$$\mathrm{R^1CH{=}CH{-}CHXR^2} \xrightarrow{-X^-} \{\mathrm{R^1CH{=}CH{-}\overset{+}{C}HR^2} \longleftrightarrow \mathrm{R^1\overset{+}{C}H{-}CH{=}CHR^2}\} \xrightarrow{+Y:} \mathrm{R^1CH{=}CHCHYR^2} + \mathrm{R^1CHY{-}CH{=}CHR^2} \quad (9)$$

Factors influencing reactivity in allylic S_N1 reactions

S_N1 reactions in general are facilitated by structural features in the reactant which stabilize the cationic intermediate. Tautomeric electron release by the allylic double bond should increase reactivity by stabilizing the allylic carbonium ion (equation 10)[19]. The observed acceleration is smaller than expected, possibly because of the inductive effect of the vinyl group, which should strengthen the C—X bond. Allyl chloride is solvolyzed only 25 times faster than n-propyl chloride in slightly aqueous formic acid[49].



(10)

Electron-releasing alkyl or aryl substituents on the α- and γ-carbon atoms of the allylic system stabilize the ionic intermediate in S_N1 reactions, and in so doing decrease the energy of activation and increase reactivity. γ-Substituents are almost as effective as α-substituents in this respect and γ-alkyl substituted primary allylic halides resemble secondary and tertiary alkyl halides in their reactivity.

Most of the data pertinent to allylic S_N1 reactivity are from studies of solvolysis reactions of allylic halides, which are discussed below. Since the kinetic criterion of reaction molecularity is not ordinarily applicable to solvolysis reactions, there is usually at least a possibility that some of the experimental rate data refer to S_N2 reactions of the halides with the solvent. This is least likely to be a complicating factor when the solvent has low nucleophilicity coupled with high ionizing power, as is the case with slightly aqueous formic acid. Relative rates of solvolysis of a number of allylic chlorides in 99·5% formic acid are recorded in Table 3.

TABLE 3. Relative rates of solvolysis of allylic chlorides[a].

Compound	Solvent	
	C_2H_5OH (25°c)	99·5% HCO_2H 44·6°c)
$CH_2{=}CHCH_2Cl$	1·00	1·00
$CH_2{=}C(CH_3)CH_2Cl$	1·3	0·5
cis-$CHCl{=}CHCH_2Cl$	0·6	2·1
trans-$CHCl{=}CHCH_2Cl$	0·6	3·09
$CH_2{=}CHCHCl_2$	—	65·4
$(CH_3)_3CCH{=}CHCH_2Cl$	—	2260
$(CH_3)_3CCHClCH{=}CH_2$	—	2520
$CH_3CH{=}CHCH_2Cl$	17	3550
$CH_3CHClCH{=}CH_2$	3·0	5670
$C_6H_5CH{=}CHCH_2Cl$	150	—
$(CH_3)_2C{=}CHCH_2Cl$	2200	—
$(CH_3)_2CClCH{=}CH_2$	6000	—
$C_2H_5C(CH_3){=}CHCH_2Cl$	1800	—
$C_2H_5C(CH_3)ClCH{=}CH_2$	3300	—
$CH_3CH{=}CHCHClCH_3$	22000	—
$C_6H_5CH{=}CHCHCl_2$	33000	—

[a] Data from R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 786 (1956).

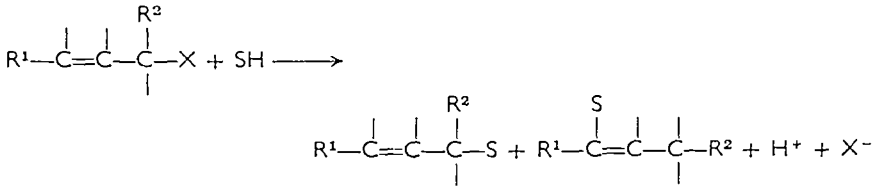
A chlorine substituent on either the α- or γ-carbon atom of allyl chloride causes an increase in the rate of formolysis, indicating that mesomeric electron release is more important than inductive electron withdrawal in determining the effect of halogen substituents on rates of allylic S_N1 reactions. An alkyl group on either the α- or the γ-carbon atom produces a 2000–5000-fold increase in reactivity, an α-alkyl group being slightly more effective than the same group in the γ-position. The data for solvolysis in aqueous ethanol, which occurs by the S_N1 mechanism in the case of the more reactive allylic compounds, show that the activating effect of a γ-phenyl substituent is about 100 times that of a single α- or γ-methyl substituent, while two α- or γ-methyl substituents are two to ten thousand times as effective as only one. The data for formolysis of α- and γ-*t*-butylallyl chlorides indicate that steric hindrance is of negligible importance in S_N1 reactions, as expected.

Few data are available concerning the influence of the nature of the displaced group on S_N1 reactions of allylic compounds. Qualitatively, leaving-group effects are similar to those observed in unimolecular reactions of aliphatic compounds, with reactivity decreasing in the order RI > RBr > RCl > RF. The S_N1 reactivity of allylic esters correlates with the acid strength of the conjugate acid of the leaving group. Thus, $ROSO_2C_6H_4CH_3 > ROCOC_6H_4NO_2 > ROCOC_6H_5$.

As expected for reactions whose rates are determined by ionization, the rates of unimolecular reactions of allylic compounds are highly dependent on the ionizing power of the solvent, and only slightly on solvent nucleophilicity. Most of the pertinent data refer to solvolysis reactions, which are discussed below. Ions such as Ag^+, Cu_2^{2+} and H^+ and Lewis acids such as BF_3 accelerate many allylic substitution and isomerization reactions. This acceleration is due to electrophilic interaction between the catalyst and the leaving group, and is similar in nature to that produced by increasing the ionizing power of the solvent.

D. *Allylic Solvolysis Reactions*

Much of our knowledge of the structures and properties of the cationic intermediates involved in a number of reactions of allylic compounds—including unimolecular substitutions—has come from studies of solvolysis reactions such as equation (11).



$$R^1{-}\overset{|}{C}{=}\overset{|}{C}{-}\overset{\overset{R^2}{|}}{\underset{|}{C}}{-}X + SH \longrightarrow R^1{-}\overset{|}{C}{=}\overset{|}{C}{-}\overset{\overset{R^2}{|}}{\underset{|}{C}}{-}S + R^1{-}\overset{\overset{S}{|}}{\underset{|}{C}}{-}\overset{|}{C}{=}\overset{|}{C}{-}R^2 + H^+ + X^- \qquad (11)$$

It is ordinarily impossible to establish the kinetic order of a solvolysis reaction with respect to the solvent, since the solvent is usually present in large excess. Nucleophilic substitution by solvent molecules could involve concerted displacement of the allylic substituent (S_N2 and S_N2'), or reaction of the solvent with an allylic carbonium ion (S_N1). The decision as to which, if either, of these mechanisms is involved in a particular allylic solvolysis reaction must be based on indirect evidence.

It now seems probable that the classical S_N1 and S_N2 mechanisms of Hughes and Ingold are only the extremes in a continuous spectrum of mechanisms. Winstein and Swain and their collaborators[12,50–52] postulated that mechanisms intermediate between S_N1 and S_N2 should exist, in which electrophilic solvation of the leaving group and nucleophilic interaction of the solvent with the substituted carbon atom both contribute to the driving-force of the reaction. The evidence bearing on intermediate mechanisms of nucleophilic substitution has been critically reviewed by Streitwieser[53]. One compelling argument for the existence of intermediate mechanisms is based on the effect of solvent ionizing power on reaction rate for borderline reactions. If competing S_N1 and S_N2 reactions are involved in a solvolysis reaction, a plot of log (solvolysis rate) *versus* solvent ionizing power should show a distinct curvature or even a break at the region of transition from one mechanism to the other[50,51]. Actually, very good straight lines of slopes intermediate between those for limiting S_N1 and S_N2 reactions are obtained[54], evidence that the reaction occurs by a single mechanism intermediate between S_N1 and S_N2.

The concept of a graded range of mechanisms is particularly useful in accounting for the kinetics and product compositions of allylic solvolysis reactions.

The response of a solvolysis reaction to changes in solvent composition provides valuable information on its mechanism. Two properties of the solvent, ionizing power and nucleophilicity, are particularly important in determining the rate of a solvolysis reaction. Ionizing power is a measure of the ability of the solvent to dissociate covalent molecules into pairs of oppositely charged ions, and depends upon both the dielectric constant of the solvent and its ability to solvate ions. A convenient experimental measure of solvent ionizing power is Winstein's Y parameter[50,51] defined by equation (12), where k and

$$Y = \log \frac{k}{k_0} \tag{12}$$

k_0 are rate coefficients for solvolysis of a substrate in the experimental solvent and in a standard solvent such as 80% ethanol, the substrate being a compound such as t-butyl chloride whose solvolyses are at the extreme S_N1 end of the mechanistic spectrum. Solvent nucleophilicity is more difficult to define precisely, but is a measure of the tendency of the solvent to undergo covalent interaction with substituted carbon atoms. In cases where the nucleophilic atom is constant, nucleophilicity toward carbon roughly parallels basicity (nucleophilicity toward hydrogen)[55].

The fact that solvent ionizing power and nucleophilicity can be varied independently is the basis of a useful criterion of mechanism for solvolysis reactions. Briefly, the rates of solvolysis reactions at the S_N1 end of the mechanistic spectrum should be very sensitive to solvent ionizing power and relatively insensitive to solvent nucleophilicity, while the reverse should be true of reactions at the S_N2 end of the spectrum. Reactions having mechanisms intermediate between 'pure' S_N1 and 'pure' S_N2 respond to changes in both ionizing power and nucleophilicity.

The variation in solvolysis rate with solvent ionizing power is measured quantitatively by the parameter m of the Winstein–Grunwald equation (13)[51], where k and k_0 refer to rate coefficients for

$$\log \frac{k}{k_0} = mY \tag{13}$$

solvolysis of the compound in the experimental solvent and in 80% ethanol, respectively, and Y is the ionizing power of the experimental solvent, determined as described above. Reactions at the S_N2 end of the spectrum have m values in the neighborhood of 0·4, while those at the S_N1 end have m values of about 1·0. Reactions having intermediate or 'borderline' mechanisms have m-values between these extremes. Values of m for solvolysis of several allylic chlorides in aqueous ethanol are recorded in Table 4.

Insofar as m values are a reliable criterion of mechanism, these results are in substantial agreement with conclusions arrived at from

TABLE 4. Solvent effects on rates of solvolysis reactions of allylic chlorides[a].

Compound	m Value for aqueous ethanol	$\frac{k_{50\%C_2H_5OH}}{k_{HCO_2H}}$	$\frac{k_{50\%C_2H_5OH}}{k_{C_2H_5OH}}$
$CH_2{=}CHCH_2Cl$	0·455	47	27
$CHCl{=}CHCH_2Cl$	—	11	42
$CH_2{=}CHCHCl_2$	—	0·9	—
$CH_3CH{=}CHCH_2Cl$	0·655	1·2	154
$CH_3CHClCH{=}CH_2$	0·875	0·7	650
$(CH_3)_2C{=}CHCH_2Cl$	0·974	—	3400
$(CH_3)_2CClCH{=}CH_2$	0·99	—	4800
$C_6H_5CH{=}CHCH_2Cl$	—	—	1500

[a] Data from R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 790–791 (1956).

other evidence. Solvolyses of allyl and β-methylallyl chlorides in aqueous ethanol are by mechanism S_N2; α- and γ-methylallyl chlorides solvolyze by intermediate mechanisms, and allylic chlorides having two α,γ-alkyl substituents or a single γ-aryl substituent solvolyze by the S_Ni mechanism.

Comparison of solvolysis rates in solvents of similar ionizing power, but widely different nucleophilicities leads to a similar conclusion. 50% aqueous ethanol and moist formic acid is such a pair of solvents. As expected, reactions at the S_N1 extreme have nearly the same rates in both of these solvents, while reactions toward the S_N2 extreme are faster in the more nucleophilic solvent, aqueous ethanol (Table 4).

A comparison of solvolysis rates in 50% ethanol and absolute ethanol shows the effect of varying solvent ionizing power while keeping nucleophilicity almost constant (see Table 4). Allyl chloride, β-methylallyl chloride and γ-chloroallyl chloride, whose solvolyses in aqueous ethanol are probably bimolecular, are fairly insensitive to solvent polarity, while α,α- and γ,γ-dimethylallyl chloride, whose solvolyses are plainly unimolecular, are several thousand times more reactive in aqueous ethanol than in absolute ethanol.

The data on solvent effects indicate that, in a given solvent, the solvolysis of allyl chloride is closest to the bimolecular end of the mechanistic range, and that the mechanism shifts toward limiting S_N1 in the sequence $CH_2{=}CHCH_2Cl$, $CH_2{=}C(CH_3)CH_2Cl$, $CH_3CH{=}CHCH_2Cl$, $CH_3CHClCH{=}CH_2$, $C_6H_5CH{=}CHCH_2Cl$, $(CH_3)_2C{=}CHCH_2Cl$, $(CH_3)_2CClCH{=}CH_2$, with the last two compounds listed reacting by the classical S_N1 mechanism.

The addition of a much more powerful nucleophile than the solvent to a solvolysis reaction mixture should have a much smaller effect on the rate of a solvolysis occurring by the limiting S_N1 mechanism than on the rate of one occurring by the S_N2 mechanism. This is true because any added nucleophile which can compete with the solvent in a bimolecular process will accelerate the reaction, whereas the fate of the carbonium-ion intermediate formed in a unimolecular reaction does not ordinarily enter into the rate equation. The effects of added lyate ions on the rates of allylic solvolysis reactions are in agreement with mechanistic conclusions arrived at from studies of solvent effects. For example, Young and Andrews found that the rate of hydrolysis of γ-methylallyl chloride in aqueous ethanol is increased much more by addition of hydroxide ion than is that of α-methylallyl chloride, in agreement with the conclusion reached above that the mechanism of solvolysis of the secondary chloride is closer to the S_N1 limit[56]. This criterion of mechanism has also been applied by de la Mare and Vernon[45,49], who found that the rates of reaction of allyl chloride, β-methylallyl chloride and 1,3-dichloropropene with ethanol and aqueous ethanol are quite sensitive to added alkali, while the solvolyses of α,α- and γ,γ-dimethylallyl chlorides are unaffected by added alkali. Solvolyses of cinnamyl and α-methylallyl chlorides were only slightly affected by the addition of alkali, while the solvolysis of crotyl chloride falls between those of allyl and α-methylallyl chlorides in sensitivity to added base. The mechanistic conclusions reached from these observations are in complete agreement with those based on solvent effects.

Much can be learned about the mechanisms of solvolysis reactions of unsymmetrically substituted allylic compounds from the products they form. If only unrearranged substitution product is formed, a bimolecular mechanism is clearly implied but not necessarily required. Solvolysis of most allylic compounds yields mixtures of normal and rearranged substitution products, and this is usually assumed to be evidence for unimolecular substitution. In cases where isomeric allylic compounds form identical mixtures of products, it is probable not only that limiting unimolecular substitution is involved, but also that both isomers react *via* a common intermediate—either a classical mesomeric carbonium ion or an ion pair. In reaching mechanistic conclusions from product composition data, however, the possibility of isomerization of the normal reaction product should be kept in mind.

Typically, the two members of an isomeric pair of allylic compounds yield somewhat different mixtures of solvolysis products under identical reaction conditions. That is, a 'product spread' is observed. Product spread is defined as the difference in the percentages of one of the isomeric reaction products between the two mixtures of products obtained from the isomeric starting materials. The existence of a product spread means that both allylic isomers do not react by formation of the *same* intermediate, be it a solvated carbonium ion or an ion pair.

As kinetic and relative reactivity data would lead one to expect, product spreads are greater in solvents of low ionizing power than in those of higher ionizing power but similar nucleophilicity. This is true because solvolysis of both allylic isomers will approach the limiting S_N1 mechanism as solvent nucleophilicity is decreased and solvent ionizing power is increased. When both isomers react by the limiting mechanism, they will, of course, give identical product mixtures, and the product spread will be zero. The primary member of an isomeric pair is more susceptible to nucleophilic interaction with solvent than the secondary or tertiary member, and invariably gives the larger percentage of primary reaction product (see Table 5).

Electrophilic catalysts such as silver ion facilitate the formation of carbonium ions, and product spreads are smaller in their presence than in pure solvent (see Table 5).

TABLE 5. Product spreads in solvolyses of allylic chlorides under standard conditions[a].

Compound	C_2H_5OH		C_2H_5OH-Ag_2O		H_2O		H_2O Ag_2O		CH_3CO_2H-CH_3CO_2Ag	
	%P[b]	S[b]	%P	S	%P	S	%P	S	%P	S
$CH_3CH{=}CHCH_2Cl$	91	38	70	24	55	19	45	11	60	4
$CH_3CHClCH{=}CH_2$	53		46		36		34		56	
$C_2H_5CH{=}CHCH_2Cl$					45	14			58	5
$C_2H_5CHClCH{=}CH_2$					31				53	
$(CH_3)_2C{=}CHCH_2Cl$	48	18	35	15	15	0	17	1	55	0
$(CH_3)_2CClCH{=}CH_2$	30		20		15		16		55	
$C_2H_5C(CH_3){=}CHCH_2Cl$	49	23[c]	39	13	12	0	14	2	55	1
$C_2H_5C(CH_3)ClCH{=}CH_2$	—		26		12		12		54	

[a] Data from R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 794 (1956).

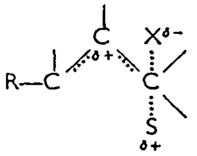
[b] %P = percent primary solvolysis product in product mixture; S = product spread.

[c] Calculated by assuming that the tertiary chloride would give the same product mixture in both presence and absence of silver oxide.

In any given solvent, product spreads are greater for primary–secondary isomer pairs than for primary–tertiary isomer pairs. This is not surprising since kinetic data indicate that reactions of dialkylallylic halides are more nearly limiting S_N1 than are those of monoalkylallylic halides. The butenyl chlorides, for example, give product spreads in all solvents studied, while the dimethylallyl and methylethylallyl chlorides give product spreads only in ethanol, the least ionizing and most nucleophilic solvent used.

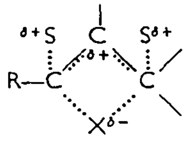
The problem of product spreads in allylic solvolysis reactions could be dismissed by assuming that one or both of the allylic isomers undergoes substitution by competing S_N1 and S_N2 reactions. The reasons for rejecting this possibility and assuming instead that one or both isomers react by a mechanism intermediate between the limiting S_N1 and S_N2 mechanisms have already been discussed. Solvolysis of an unsymmetrical allylic compound by an intermediate mechanism gives a mixture of isomeric products richer in the unrearranged product than the mixture formed by the limiting S_N1 mechanism. If the intermediate mechanism involves a reactive intermediate rather than a transition state, this intermediate must differ in some way from the 'free' mesomeric carbonium ion of the limiting S_N1 mechanism. The difficulty in visualizing an intermediate other than the S_N1 carbonium ion has been a major stumbling block to the application of the borderline-mechanism hypothesis to allylic substitution reactions.

This difficulty may be resolved by applying Streitwieser's structural hypothesis[57]. The transition state for an allylic solvolysis occurring by mechanism S_N2 is represented by **4**. If the nucleophilic interaction



(4)

of the solvent molecule is somewhat weaker, and electrophilic solvation of the leaving group somewhat stronger, this structure can represent a highly reactive ion-pair intermediate as well as a transition state. The fate of the ion-pair intermediate represented by **4** will depend upon its stability. It could form a covalent bond to the nucleophile before solvent molecules become oriented properly to solvate the positive charge developed on the α-carbon atom, thus yielding normal substitution product. If the lifetime of **4** is long enough, however, it will rearrange to the more stable solvated intimate ion pair **5**. It is



(5)

important to note that intermediate **4** is different for each member of a pair of allylic isomers, but that both members yield the same intermediate **5**.

Intermediate **4** is clearly implicated in reactions of primary γ-alkylallylic compounds, but solvolysis reactions of secondary and tertiary allylic compounds are so little dependent on solvent nucleophilicity that **5** may be formed directly.

The large rate accelerating effect of γ-alkyl substituents on reactions presumably proceeding through intermediate **4** indicates that there is a considerable resonance delocalization of positive charge in this intermediate. A somewhat different type of intermediate appears to be involved in deamination reactions of allylic primary amines. The product compositions and stereochemistry of deaminations of butenyl and pentenyl amines in acetic acid at room temperature are best accounted for by assuming that a substantial part of the product is formed from a 'hot' carbonium ion, which differs from **4** only in that the γ-carbon atom is not oriented so as to permit π-orbital overlap with the double bond[58]. Once π-orbital overlap occurs, the 'hot' ion is indistinguishable from **4**, and the remainder of the product arises from **4** and/or **5**.

Intermediate **5** can either undergo internal return to the starting material and its allylic isomer[59], or it can react with solvent to form a mixture of isomeric solvolysis products; in general, it will do both. The conversion of **5** to substitution products may involve two additional intermediates—a solvent separated ion pair, or a fully dissociated carbonium ion[60].

The problem of determining experimentally which of these three possible carbonium-ion intermediates gives rise to solvolysis products is a complex one[59-61]. In solvolyses of α,α-dimethylallyl chloride and optically active *cis-* and *trans*-5-methyl-2-cyclohexenyl chlorides[62], intimate ion pairs are probably the source of solvolysis products as well as isomeric chlorides. For each of these compounds, the ratio of solvolysis to isomerization is much greater in ethanol than in acetic acid, and the rate of acetolysis relative to ethanolysis is abnormally small.

These observations are rationalized by a mechanism involving competition between solvent and internal return for a common intermediate, presumably the intimate ion pair. The nucleophilic solvent ethanol is so much more effective in this competition than acetic acid that it not only yields a larger proportion of solvolysis product, but does so more rapidly than would be expected from its ionizing power due to its ability to swamp out internal return to starting material. The assertion that the common intermediate is an intimate ion pair is supported by the fact that racemization of the cyclohexenyl chlorides (equivalent to allylic isomerization) occurs without *cis–trans* isomerization.

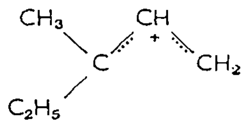
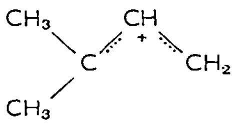
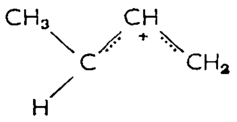
A different situation exists in the solvolysis of α-aryl-γ-methylallyl *p*-nitrobenzoates in methanol and aqueous dioxane[63]. Addition of azide ion to the reaction mixture resulted in the formation of allylic azide, but had little effect on total reaction rate or rate of isomerization.

Overlap of the π orbital of the double bond with the developing π orbital at the α-carbon atom should preserve the geometry of the allylic system when an allylic carbonium ion is formed[64,65]. That this overlap constitutes a substantial barrier to rotation about the allylic C—C bonds was recently demonstrated by Young, Sharman and Winstein[66], who found that the initially formed primary substitution products of solvolysis of *cis*- and *trans*-γ-methylallyl chlorides in aqueous silver nitrate have the same geometric configuration as the starting materials.

Allylic solvolysis reactions occurring by the limiting S_N1 mechanism involve mesomeric ionic intermediates which can react with the solvent at either of the two allylic positions to give mixtures of normal and rearranged products. It is interesting that the thermodynamically less stable product is almost always formed in greater than equilibrium proportion, and is frequently the major product. At equilibrium, the primary member of a pair of allylic isomers predominates by a factor of about 5 to 1 for a primary–secondary pair, and by a factor of about 10 to 1 for a primary–tertiary pair—probably because of hyperconjugative stabilization of the primary isomers by the γ-alkyl groups[67].

Table 6 gives product compositions for reactions of allylic carbonium ions with water, ethanol and acetic acid. Figures quoted for the primary–tertiary systems are, wherever possible, for reactions under conditions which gave zero product spreads. Product com-

TABLE 6. Products from allylic carbonium ions[a].

Solvent			
H_2O	12[b]	15	36
C_2H_5OH	26	20	46
CH_3CO_2H	54	55	56

[a] Data from Table 5.

[b] % Primary substitution product in product mixture.

positions in ethanol are those given by the tertiary halides in the presence of silver oxide. The values given for the butenyl carbonium ion are product compositions for silver-ion catalyzed reactions of the secondary halide. For all three carbonium ions, the less stable product predominates in ethanol and water, while the two products are formed in approximately equal amounts in acetic acid. The proportion of primary product given by the butenyl carbonium ion is greater than that given by the primary–tertiary systems in all three solvents.

The activation energy for formation of either product from an allylic carbonium ion should be small, and the transition states should not differ greatly in structure from the solvated ion or ion pair. This being so, one would expect the nucleophile to react preferentially with the allylic carbon atom bearing the largest positive charge, since this should be more strongly solvated in the ground state[68]. This hypothesis provides a logical explanation for the data of Table 6. High solvent polarity favors the concentration of ionic charge, and it should be concentrated preferentially on the most alkylated carbon atom. It is not surprising, then, that the amount of product formed by reaction of solvent with the most alkylated allylic carbon is greatest in water, less in ethanol, and least in acetic acid for all three of the allylic ions listed. Furthermore, since two alkyl groups attached to the allylic system should stabilize the positive charge at a tertiary allylic carbon more than a single alkyl group would stabilize it at a secondary carbon, less primary product should be formed from a dialkylallylic cation than from a monoalkylallylic cation in any particular solvent. If charge distribution in the allylic carbonium ion is indeed the chief factor determining product composition, it follows that *the lower the dielectric constant of the solvent, the less it will discriminate between the two charged centers of an unsymmetrical allylic cation in forming solvolysis products*. This generalization is supported by the data of Table 6, and also by data of Sneen and Rosenberg[69], who found that solvolysis of α-phenyl-γ-methylallyl *p*-nitrobenzoate in 60% aqueous dioxane gives only 16% of α-aryl product, while solvolysis in the less polar solvent, methanol, gives 34% α-aryl product.

The interpretation of solvent and structural effects on allylic solvolysis product compositions is hampered by the paucity of reliable data, and complicated by the possibility that different kinds of intermediates—*e.g.* solvated carbonium ions and intimate ion pairs—may be involved in different reactions.

E. The S_Ni' Mechanism of Substitution

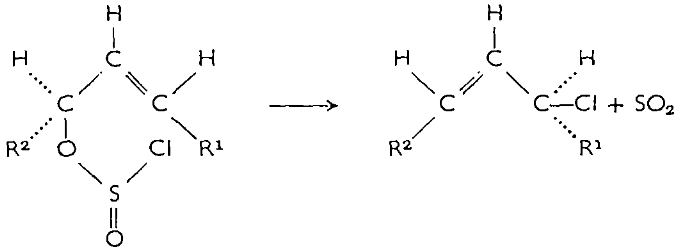
In reactions involving the S_N1, S_N2 and S_N2' mechanisms, the nucleophilic reagent is a separate species from the compound undergoing substitution. One additional mechanism of substitution remains to be considered: that in which the nucleophilic atom is part of the compound being substituted. This mechanism was labeled intramolecular nucleophilic substitution by Hughes and Ingold[70], and given the symbol S_Ni. In the case of allylic compounds, if this mechanism involves rearrangement or isomerization, it is designated by the symbol S_Ni'. Most S_Ni' reactions of allylic compounds are isomerizations, which are discussed elsewhere.

The S_Ni' mechanism was first postulated by Roberts, Young and Winstein[20] to explain the predominant formation of rearranged chlorides in reactions of isomeric allylic alcohols with thionyl chloride[71]. Allylic chlorosulfinate decomposition is the most thoroughly studied class of intramolecular allylic substitutions. It is assumed that allylic chlorosulfinates are intermediates in the conversion of allylic alcohols to chlorides by reaction with thionyl chloride (equation 14). Allyl chlorosulfinate[72] and α- and γ-trifluoromethyl-

$$\begin{aligned} &\mathrm{R^1CH{=}CHCH(OH)R^2 + SOCl_2 \xrightarrow{-HCl} R^1CH{=}CHCH(OSOCl)R^2} \longrightarrow \\ &\qquad \mathrm{R^1CH{=}CHCHClR^2 + R^2CHClCH{=}CHR^2 + SO_2} \end{aligned} \tag{14}$$

allyl chlorosulfinates[73] have actually been isolated, but the instability of alkyl- and aryl-substituted chlorosulfinates has precluded their isolation.

The conversion of allylic chlorosulfinates to allylic chlorides could involve mechanisms S_N2, S_N1, S_Ni and S_Ni', separately or in combination. In the S_Ni' mechanism, chlorine attacks the γ-carbon atom of the allylic system, with simultaneous shift of the double bond and elimination of sulfur dioxide. It is reasonable to expect that optically active chlorides of rearranged structure would be formed from optically active α,γ-disubstituted chlorosulfinates reacting by this mechanism, since one particular conformation of the transition state may be favored above all others (equation 15).



(15)

Young and coworkers established the existence of this mechanism by carrying out thionyl chloride reactions in non-polar solvents containing no chloride ion, conditions which eliminated competition by mechanism S_N1 and S_N2. The exclusion of chloride ion presented a problem, since hydrogen chloride is generated during formation of the chlorosulfinates. This difficulty was overcome by carrying out the reactions in relatively dilute solution (0·5 to 1 M) in anhydrous ethyl ether[74], which forms a hydrogen-bonded complex with dry hydrogen chloride[75,76,77]. Using the ether technique, it is possible to convert many primary and secondary allylic alcohols almost quantitatively into chlorides of rearranged allylic structure[74,78,79]. These results not only established the existence of the S_Ni' mechanism, but also demonstrated that the S_Ni mechanism does not compete with it in dilute ether solutions. If the thionyl chloride concentration is too high, reactions in ether solution lead to mixtures of isomeric chlorides[71,80,81]. This may be due to increased polarity of the solvent or to saturation of the ether with HCl, both of which could result in reaction by other mechanisms.

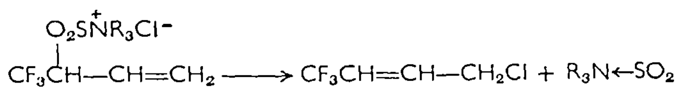
Decomposition of α- and γ-methylallyl chlorosulfinates in solvents other than ether was found to occur by more than one mechanism. In pentane solution, the chlorosulfinate from optically active α-methylallyl alcohol yielded a mixture of γ-methylallyl chloride and α-methylallyl chloride of partially inverted configuration. This result may be attributed to partial decomposition by the S_N2 mechanism. In dioxane and sulfur dioxide solutions, and in the absence of a solvent the secondary chloride in the product mixture had partially retained the configuration of the ester, indicating that partial decomposition by the S_Ni mechanism occurs under these conditions.

Examples of the stereospecific nature of the S_Ni' reaction include the conversion of (−)-*trans*-α,γ-dimethylallyl alcohol into (−)-*trans*-α,γ-dimethylallyl chloride[78], formation of (+)-*cis*-5-methyl-2-cyclohexenyl chloride from (+)-*cis*-5-methyl-2-cyclohexenol[82], conversion of 4β-hydroxycholest-5-ene and 6β-hydroxycholest-4-ene into the 6β- and 4β-chlorides, respectively[83], and preparation of 6β-chloro-3β-benzoyloxy-4-cholestene from 4β-hydroxycholesteryl benzoate[84].

Although the ether technique has successfully achieved reaction by the S_Ni' mechanism in many cases, allylic alcohols having multiple or especially strong activating groups may form chlorosulfinates which decompose by other mechanisms. In the case of cinnamyl alcohol, S_Ni' reaction was achieved by keeping the thionyl chloride concentration below 0·1 M. This has the disadvantage of slow formation of the chlorosulfinate from the alcohol and requires handling large volumes of solvent. It is also possible for the structure of the allylic system to be such that S_Ni' reaction is ruled out by geometrical considerations. This appears to be the case with a number of steroid allylic alcohols[4,85,86].

The S_Ni' mechanism could involve either a one-stage, concerted process, or ionization to a rigidly oriented intimate carbonium chlorosulfinate ion pair followed by internal return of the chlorine component of the chlorosulfinate anion to give rearranged chloride[78,87]. The stereochemical consequences of either process would be identical. A decision between these alternatives is possible on the basis of solvent and structural effects on rates of chlorosulfinate decomposition. If an ion-pair intermediate is involved in the S_Ni' reaction, its rate should be very sensitive to solvent polarity and should be greatly increased by electron-releasing α- and γ-substituents. Most S_Ni' allylic chlorosulfinate decompositions probably involve ion-pair intermediates. The decomposition of allyl chlorosulfinate-1-^{14}C in decane, n-butyl ether, thionyl chloride and liquid sulfur dioxide gives mostly rearranged chloride[72], and the decomposition is more than a thousand times faster in sulfur dioxide, a highly polar solvent, than in n-decane. The reaction is also greatly accelerated by electron-releasing α- and γ-substituents. The decompositions of α- and γ-methylallyl chlorosulfinates are at least four powers of ten faster than the decomposition of allyl chlorosulfinate.

Strongly electron-attracting substituents increase the stability of allylic chlorosulfinates, and shift the mechanism of their decomposition toward a concerted process. α-Trifluoromethylallyl chlorosulfinate decomposes much more slowly than allyl chlorosulfinate, and its rate of decomposition is only slightly affected by changes in solvent polarity[73]. The S_Ni' decomposition of α-trifluoromethylallyl chlorosulfinate in ether solution is catalyzed by tertiary amines, possibly due to the formation of a quaternary salt by reaction of the amine with the ester as in equation (16). Similar complexes may be

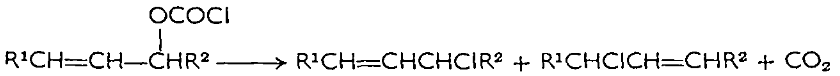


$$CF_3\overset{O_2S\overset{+}{N}R_3Cl^-}{\overset{|}{C}}H{-}CH{=}CH_2 \longrightarrow CF_3CH{=}CH{-}CH_2Cl + R_3N{\leftarrow}SO_2 \tag{16}$$

intermediates in the S_N2 decompositions of other allylic chlorosulfinates in the presence of amines[74].

The reaction of primary and secondary allylic alcohols with thionyl chloride is an interesting example of the extent to which mechanism can be controlled in allylic substitutions. As discussed above, the intermediate chlorosulfinates decompose entirely by the S_Ni' mechanism in dilute ether solutions, yielding rearranged allylic chlorides. Addition of a source of chloride ion to the ether solution results in reaction by the S_N2 mechanism. In the presence of amine hydrochlorides, primary chlorosulfinates yield only the primary chloride, while secondary chlorosulfinates yield secondary chloride of inverted configuration plus some primary chloride. If the secondary alcohol is converted to the diallylic sulfonate and this is treated with an amine hydrochloride, secondary chloride of inverted configuration is the only product. Finally, if a secondary allylic chlorosulfinate is decomposed in a solvent such as dioxane or sulfur dioxide, which can solvate the backside of the ion-pair intermediate, a mixture of chlorides is obtained in which the secondary chloride has partially retained the configuration of the starting material.

The decomposition of allylic chloroformates (equation 17) should

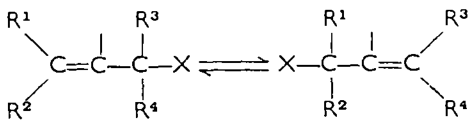
 (17)

$$R^1CH{=}CH{-}\overset{\displaystyle OCOCl}{\overset{|}{C}}HR^2 \longrightarrow R^1CH{=}CHCHClR^2 + R^1CHClCH{=}CHR^2 + CO_2 \quad (17)$$

resemble that of allylic chlorosulfinates. Olivier and Young[88] studied the decomposition of α- and γ-methylallyl chloroformates in a variety of solvents, and found that mixtures of isomeric chlorides and butadiene are formed in all solvents used, even in ether. The rate of the reaction is very sensitive to solvent polarity, being about four powers of ten faster in nitrobenzene than in decane. These results are evidence for the formation of very unstable carbonium chloroformate ion-pair intermediates, which collapse to products before the proper structural orientation for selective S_Ni' substitution is attained.

III. ALLYLIC ISOMERIZATION REACTIONS

Typical allylic isomerization reactions (equation 18) involve migration of a functional group from one end of an allylic system to the other.

 (18)

The migrating group may separate from the α-carbon of the allylic system as an anion, a radical or a neutral molecule, or may not separate from it at all. Isomerization reactions may precede, accompany, or follow substitution reactions of allylic compounds. For this reason, the synthetic chemist should be aware of the nature of these reactions, and of the structural and environmental factors which influence their rates and equilibrium positions.

Most allylic isomerizations involve no change in the structure of the migrating group. A few, such as the Claisen rearrangement and the allylic thiocyanate–isothiocyanate interconversions, involve rearrangement of the migrating group as well as rearrangement of the allylic system. These two classes of reactions are discussed separately.

A. Isomerization of Allylic Alcohols

The most thoroughly studied allylic isomerizations, as well as the most useful in organic synthesis, are those of the allylic alcohols. Alcohol isomerizations are useful when the most convenient synthetic approach yields the allylic isomer of the desired alcohol, and these reactions have been widely used in the synthesis of terpene derivatives and related compounds[89]. Braude, who conducted an extensive study of allylic alcohol isomerizations, reviewed them in 1950[90,91].

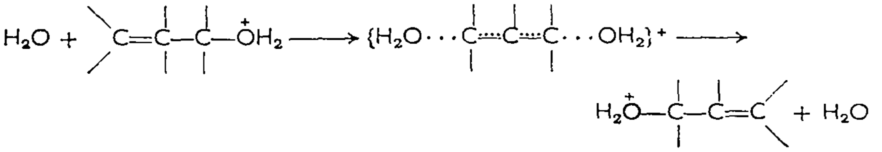
Allylic alcohol isomerizations are catalyzed by proton and Lewis acids[92], and rarely occur at measurable rates in the absence of acids. The dependence of rate of isomerization upon acid concentration was studied by Braude[93,94] and by Bunton[95], who found that these reactions are first order in acid concentration in dilute solutions of mineral acids, but that in more concentrated solutions rate of isomerization is proportional to Hammett's acidity function[96].

The rate of acid-catalyzed alcohol isomerization is greatly increased by α- and γ-alkyl substituents. Allylic alcohols having a single alkyl substituent in the α- or γ-position isomerize at appreciable rates only if treated with mineral acids at elevated temperatures—conditions which usually cause simultaneous formation of ethers, dienes and carbonyl compounds[97-99]. The α,α- and γ,γ-dialkylallyl alcohols are isomerized to equilibrium mixtures by treatment with 1% aqueous sulfuric acid for 60 hours at room temperature[100]. Braude and coworkers found that α-, β- and γ-methyl substituents on the allylic system increase the rate of isomerization of allylic alcohols by factors of the order of 10^2, 10^1 and 10^3, respectively, and that alkyl substituents increase the reaction rate mainly by lowering the energy of activation[101-105]. The effects of multiple substituents on activation energies are approximately additive, in the absence of steric hindrance.

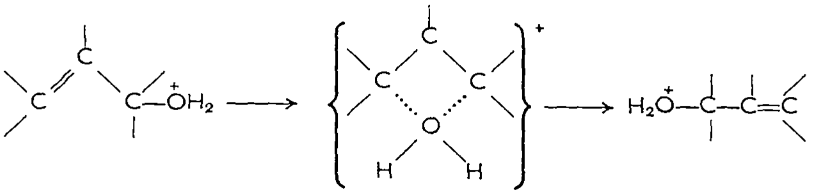
Unsaturated substituents on the α-carbon atom greatly facilitate the isomerization of allylic alcohols. For example, α-phenylallyl alcohol is readily isomerized to cinnamyl alcohol by treatment with dilute sulfuric acid, while α-cyclohexylallyl alcohol is not affected by these conditions[106]. An α-aryl group has a rate-accelerating effect similar to that of two α-alkyl groups, and an α-vinyl group is only slightly less activating than an α-aryl group. Probably because of their electronegativity, α-ethynyl and α-acetyl groups are much less activating than α-aryl and α-vinyl groups[1,93,107]. The relative rates of isomerization of $RCH(OH)CH{=}CH_2$ in 60% aqueous ethanol–hydrochloric acid solutions at 30° are: $R = HC{\equiv}C{—}$, 1·0; $R = CH_2{=}CH{—}$, $1{\cdot}2 \times 10^4$; and $R = C_6H_5{—}$, $2{\cdot}9 \times 10^4$[4,108]. The activating effect of unsaturated α-substituents is probably due to π-orbital overlap with the allylic system in the transition state of the rate-determining step of the reaction. This hypothesis is supported by the fact that α- and β-methyl substituents which sterically hinder attainment of coplanarity of the allylic system and the unsaturated substituent produce much smaller than normal rate accelerations, and may actually retard isomerization[103].

As would be expected from the substituent effects described above, aryl substituents which can release electrons to the allylic system either inductively or mesomerically increase the ease of isomerization of α-aryl-γ-methylallyl alcohols[109–111]. A plot of log (specific rate coefficient) *versus* Brown's σ^+ substituent constants[112] is nearly linear, with a slope of $-3{\cdot}4$. A similar graph, using the usual Hammett σ constants of the aromatic substituents[113], exhibits much greater scattering of points.

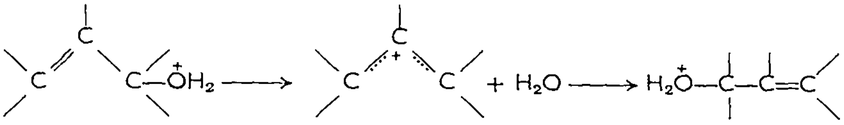
The fact that allylic alcohol isomerizations are acid catalyzed implies that the conjugate acid of the alcohol, ROH_2^+, is a reactive intermediate. Protonation of the hydroxyl group weakens the carbon–oxygen bond and renders unnecessary the separation of opposite charges in the transition state of the rate-limiting step of the reaction. Therefore, it is not surprising that the oxonium ion isomerizes much more readily than the unprotonated alcohol. Isomerization of the conjugate acid could conceivably occur by the S_N2' mechanism (equation 19), by the S_Ni' mechanism (equation 20),



$$H_2O + {>}C{=}C{-}C{-}\overset{+}{O}H_2 \longrightarrow \{H_2O\cdots C{\cdots}C{\cdots}C\cdots OH_2\}^+ \longrightarrow H_2\overset{+}{O}{-}C{-}C{=}C{<} + H_2O \qquad (19)$$

 (20)

or by the S_N1 mechanism (equation 21). In principle, there is no

 (21)

sharp dividing line between the bimolecular and the unimolecular mechanisms, since varying amounts of nucleophilic interaction of water with the incipient carbonium ion can be visualized. Similarly, the S_Ni' mechanism may merge imperceptibly with the S_N1 mechanism: as the degree of bond breaking becomes greater, and the degree of bond making becomes less, the S_Ni' transition state becomes a solvated S_N1 carbonium-ion intermediate.

The fact that rate of isomerization is proportional to Hammett's acidity function rather than to hydrogen ion concentration might be taken as evidence favoring the S_N1 mechanism, since this type of acidity dependence is usually held to indicate that the transition state of the rate-limiting step of the reaction is composed of the reactant plus a proton, but does not involve a water molecule[114]. However, Bunnett recently pointed out that reactions having only one or two water molecules tied up in the transition state will give nearly linear plots of log (rate coefficients) *versus* H_0[115]. This fact, plus the fact that allylic alcohol isomerizations were studied in mixed solvents, in which the exact significance of the acidity function is open to question, makes it impossible to rule out the S_N2' mechanism on the basis of kinetic acidity dependence alone.

However, two other kinds of evidence make the S_N2' mechanism extremely unlikely. The first is the very large rate-accelerating effect of electron-releasing substituents in these reactions. Substituent effects on rates of isomerizations of allylic alcohols are similar in magnitude to those observed in unimolecular substitution reactions of allylic halides and esters. It is also highly significant that, in the case of isomerization of α-aryl-γ-methylallyl alcohols, a much better linear free energy plot is obtained using Brown's σ^+ aryl substituent constants rather than Hammett's σ substituent constants. The σ^+ constants consistently give better fits than do σ constants in reactions which involve conjugation of the aromatic ring with a positively-charged α-atom in the reacting side chain during the rate-determining step of the reaction. It is also significant that the slope ($\rho = 3{\cdot}4$) of the *k versus* σ^+ plot for allylic alcohol isomerizations is nearly identical with that for acid-catalyzed ionization of triarylmethanols ($\rho = 3{\cdot}44$)[112].

A second kind of evidence ruling against the S_N2' mechanism is the effect of solvent composition on rate of isomerization in mixed solvents such as aqueous ethanol. Braude, Jones and Stern[93,109] studied the isomerization of α-phenyl-γ-methylallyl alcohol in aqueous ethanol–0·1 N hydrochloric acid solutions, and found that the rate goes through a maximum at about 80% ethanol. Gutbezahl and Grunwald[116] have shown that, if allowance is made for the effect of solvent composition on the concentration of the reactive conjugate acid of the alcohol, the rate of isomerization of the conjugate acid is independent of solvent composition. This result would be most unlikely if the reaction involved nucleophilic attack by solvent molecules on the conjugate acid.

In summary, kinetic acidity dependence is ambiguous in allylic alcohol isomerizations, but substituent effects and solvent effects make it possible to rule out bimolecular isomerization with a high degree of confidence. Substituent effects on rates suggest a transition state or reaction intermediate with considerable carbonium-ion character. This could either be a free, solvated allylic cation, or an S_Ni' transition state in which the migrating water molecule is very loosely bound to the allylic system.

Some recent experiments on racemization, *cis–trans* isomerization, allylic isomerization, and oxygen exchange of optically active allylic alcohols indicate that these reactions involve carbonium-ion intermediates, which may, however, have different lifetimes and be solvated in different ways. Bunton and Pocker[95] found that α-phenylallyl alcohol undergoes simultaneous oxygen exchange and isomerization in acidic 60% aqueous dioxane solutions, and that the isomerization reaction has a small positive entropy of activation. Goering and Dilgren studied the simultaneous isomerization, racemization, and oxygen exchange of optically active α-phenylallyl alcohol in 40% dioxane–aqueous perchloric acid solutions[117,118]; they found that racemization is about twice as fast as isomerization, and that about 4% of the cinnamyl alcohol and about 20% of the initially formed racemic α-phenylallyl alcohol are produced without oxygen exchange. The data are consistent with a carbonium-ion mechanism in which the water molecule formed in the dissociation step has a greater than average probability of being involved in the recombination step. The fact that part of the isomerization occurred without exchange means that isomerization cannot involve the S_N2' mechanism exclusively, while the fact that 96% of the isomerized product had undergone exchange means that the S_Ni' mechanism is unimportant in this reaction.

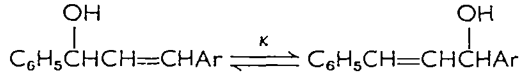
Harris and Weale[119] found that acid-catalyzed isomerization of α-phenylallyl alcohol in 45·7% aqueous acetone has a small negative volume of activation (-5 cm^3/mole). Whalley interpreted this fact as evidence against the S_N1 mechanism for this reaction[120]. The small value of the pressure effect, plus the fact that it is due at least in part to the increase in catalyst concentration as the solution is compressed, make the volume of activation a dubious mechanistic criterion for this reaction.

The acid-catalyzed racemization, isomerization and oxygen exchange of *cis*- and *trans*-5-methyl-2-cyclohexenols were studied by Goering and Josephson[121,122]. In 35% aqueous acetone–perchloric acid solutions these alcohols undergo simultaneous racemization (allylic isomerization) and *cis–trans* isomerization. With each isomer, the rate of racemization is several times the rate of *cis–trans* isomerization. By using ^{18}O-labeled alcohols it was shown that with the *cis* alcohol most of the racemization is intramolecular (*i.e.* occurs without oxygen exchange), while with the *trans* alcohol, interconversion of enantiomers results in nearly complete oxygen exchange.

These reactions almost certainly involve carbonium-ion intermediates, as do nearly all other interconversions in the 5-methyl-2-cyclohexenyl system[123]. The kinetic and stereochemical results, however, lead to the surprising conclusion that the *cis* and *trans* isomers do not form the same carbonium ion. Goering has rationalized the experimental data convincingly by assuming that the isomeric alcohols react mainly *via* the quasi-axial conformations, which give rise to carbonium ions which differ conformationally and in the way in which they are solvated. These carbonium ions collapse to products more rapidly than they are interconverted.

It is difficult to measure equilibrium constants for isomerizations of simple mono- and dialkylallyl alcohols, due to concurrent side reactions such as ether formation, dehydration and isomerization to carbonyl compounds. The limited data available indicate that similar amounts of the isomeric alcohols are present at equilibrium[97,100]. Most acid-catalyzed alcohol isomerizations which have been studied in detail involve alcohols with unsaturated α-substituents such as vinyl, aryl, ethynyl and carbonyl groups. In these cases, the equilibrium greatly favors the resonance-stabilized isomer having the unsaturated substituent on the γ-carbon atom. For example, isomerization of α-phenylallyl alcohol leads to an equilibrium mixture consisting almost entirely of cinnamyl alcohol.

In α,γ-diarylallyl alcohols the equilibrium constant is rather insensitive to the nature of the aryl groups. For example, in the equilibrium (22), the equilibrium constant is close to unity when



$$C_6H_5\overset{\overset{OH}{|}}{C}HCH{=}CHAr \overset{K}{\rightleftharpoons} C_6H_5CH{=}CH\overset{\overset{OH}{|}}{C}HAr \qquad (22)$$

Ar = p-$NO_2C_6H_4$, α-$C_{10}H_7$ and β-$C_{10}H_7$[124,125], although the rate of the forward reaction is about two hundred times faster for the γ-naphthyl alcohols than for the γ-p-nitrophenyl alcohol. This implies that the *sum* of the aryl substituent effects on isomerization rate is about the same, regardless of which member of a pair of substituents is attached to the α-carbon and which to the γ-carbon.

In some cases the equilibrium is displaced due to a rapid reaction of the initially formed isomerization product. Acid-catalyzed isomerizations of γ-halo- or γ-alkoxyallylic alcohols yield reactive halohydrins and hemiacetals, which readily hydrolyze to unsaturated carbonyl compounds[126,127].

B. Isomerization of Allylic Esters

Ester isomerizations were among the first allylic reactions to be studied systematically. From their investigations of the effects of structural and environmental factors on ease of isomerization, Burton and Ingold[128-133] concluded that allylic ester isomerizations involve dissociation of the esters into allylic cations and carboxylate anions, followed by recombination of the ions to give the starting material and its allylic isomer. The term *anionotropy* was used to describe these anionic migrations. This descriptive term was later broadened to include allylic isomerization and rearrangement reactions occurring by other mechanisms, and is still widely used today.

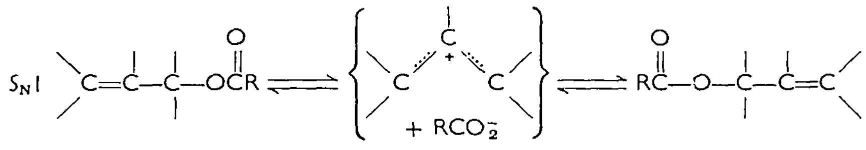
Many early discussions of allylic ester mobility are unreliable due to the failure of early workers to appreciate the extreme susceptibility of these reactions to acid catalysis. In some cases traces of acidic impurities may have caused acid-catalyzed isomerization to become the predominant reaction. α-Arylallyl *p*-nitrobenzoate isomerizations exhibit autocatalysis due to the formation of traces of *p*-nitrobenzoic acid by side reactions[134-136]. Similar catalysis may have been involved in other ester isomerizations which were assumed to have been uncatalyzed. In the presence of strong acids, acid-catalyzed isomerization may be the only observable reaction[135,137]. Acid catalysis is not a requirement for allylic ester isomerization[134,135,138,139] even in aprotic solvents such as those used by Burton[128-133]; however, data gathered without cognizance of the possibility of concurrent acid-catalyzed and uncatalyzed reactions must be viewed with suspicion.

If uncatalyzed ester isomerizations occur by the S_N1 mechanism suggested by Burton and Ingold, they should be facilitated by structural features which weaken the carbon–oxygen bond between the allylic group and the carboxylate group. This is indeed the case. The effect of allylic substituents on ease of ester isomerization closely parallels their effect on rates of allylic solvolyses occurring by the unimolecular mechanism. Esters having a single α- or γ-alkyl substituent isomerize at ordinary temperatures only in the presence of mineral acids[140], and undergo uncatalyzed isomerization only on being heated to high temperatures[141]. α,γ-Dialkylallyl and α-arylallyl esters isomerize at measurable rates at temperatures below 100°[142], and α-aryl-γ-alkylallyl esters isomerize readily at room temperature[143].

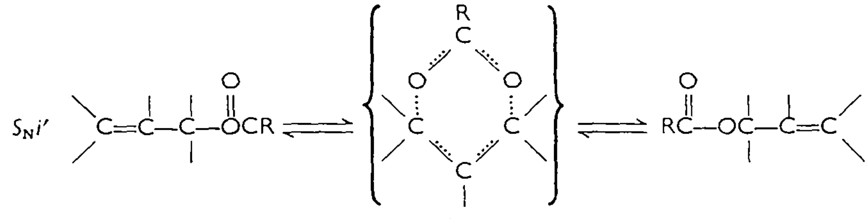
Substituents which increase the stability of the potential carboxylate ion (*i.e.* which render it less basic) enhance mobility, although carboxyl substituent effects are small compared to allylic substituent effects. Allylic benzoates isomerize more readily than acetates, and *p*-nitrobenzoate esters isomerize faster than benzoates. The relative rates of uncatalyzed isomerizations of α-phenylallyl esters in chlorobenzene at 130° are: acetate, 0·038; benzoate, 0·14; *p*-nitrobenzoate, 1·0[135], and similar relative rates are observed for the benzoate and *p*-nitrobenzoate in chlorobenzene at 155°[138,144].

The effect of solvent polarity on rates of uncatalyzed ester isomerizations also supports the S_N1 mechanism. The more polar the solvent, the more rapidly isomerization occurs. Solvent effects on isomerization reactions which accompany the neutral solvolyses of allylic esters are particularly significant. The rates of unimolecular solvolysis and isomerization of α,γ-dialkylallyl and α-aryl-γ-alkylallyl esters are both increased by increasing the ionizing power of the solvent[143,145,146], and the increase in isomerization closely parallels the increase in solvolysis rate.

Substituent and solvent effects on rates of uncatalyzed ester isomerizations require that the transition states for these reactions involve considerable separation of charge. The reactivity data alone could be rationalized equally well by the classical S_N1 mechanism (equation 23a), or by a cyclic, concerted S_Ni' process (equation 23b) in which the transition state resembles a rigidly oriented carbonium–carboxylate ion pair. There is no sharp dividing line between an S_N1 mechanism involving internal return from an intimate ion pair and a true S_Ni' mechanism.



(23a)



(23b)

(6)

If **6** is an intermediate, the mechanism is S_N1; if it is a transition state, the mechanism is S_Ni'. Since the kinetic and stereochemical consequences are the same in either case, the question cannot be resolved experimentally.

A dissociated carbonium-ion intermediate is quite unlikely for these reactions. The absence of common-ion rate acceleration or exchange in isomerizations accompanying hydrolysis of α-phenyl-γ-methylallyl *p*-nitrobenzoate[143], *trans*-5-methyl-2-cyclohexenyl-*p*-nitrobenzoate[147], and α,γ-dimethylallyl *p*-nitrobenzoate[142] rules out free carbonium ions as intermediates in these reactions, as does the observation that solvolyses of optically active *cis*- and *trans*-5-methyl-2-cyclohexenyl esters are accompanied by racemization (allylic isomerization) but not by *cis-trans* isomerization[146–148].

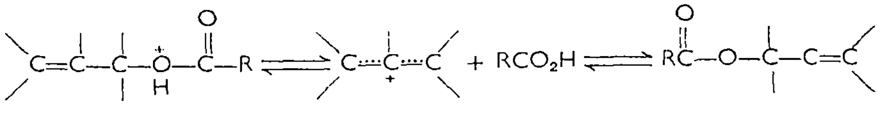
The situation in aprotic solvents is not so clear-cut. Added lithium *p*-nitrobenzoate caused only a small increase in the rate of isomerization of α-phenylallyl *p*-nitrobenzoate in acetic anhydride and acetonitrile solutions, the increase being of the order of magnitude of a primary salt effect[21]. This finding rules out a dissociated carbonium-ion intermediate, as well as isomerization by S_N2', displacement. When ^{18}O-labeled α-phenylallyl benzoate was heated with benzoate ion in chlorobenzene, the rates of isomerization and isotopic exchange showed that only a fraction of the benzoate groups in the cinnamyl benzoate product came from the added benzoate salt[144]. Allylic isomerization of *cis*- and *trans*-5-methyl-2-cyclohexenyl hydrogen phthalates in acetonitrile solutions is accompanied by a small amount of *cis–trans* isomerization, evidence for partial isomerization *via* a carbonium-ion intermediate[139]. Since these esters possess an acidic proton, part of the reaction may have been acid-catalyzed; acid-catalyzed isomerizations are much more likely to involve free carbonium ions than are the uncatalyzed reactions.

In summary, a considerable body of evidence supports the hypothesis that in most uncatalyzed allylic ester isomerizations, a carboxyl group migrates without at any time becoming dissociated from the allylic group. This rules out the classical S_N1 mechanism, but permits no choice between S_Ni, and internal return from an ion-pair intermediate.

The finding that in certain cases the carbonyl oxygen atom of the original ester becomes the alkyl oxygen of its isomer at first glance seems evidence for the S_Ni' mechanism. This was observed for isomerization of α-phenylallyl-*p*-nitrobenzoate[149-150] and α-phenyl-γ-methylallyl-*p*-nitrobenzoate[123]. However, as pointed out by Winstein and Robinson[61], these results can be explained in terms of an intimate ion-pair intermediate, in which the ions can be rotated relative to each other only by overcoming fairly strong electrostatic forces.

An ion-pair mechanism for the isomerization of labile allylic esters is supported by the observation of Goering and Pombo[142] that, during isomerization of ^{18}O-labeled *trans*-α,γ-dimethylallyl *p*-nitrobenzoate in aqueous acetone, the carboxyl groups undergo concurrent oxygen scrambling and allylic migration about one-fifth of the time. In other words, this reaction appears to involve an ion-pair intermediate in which rotation of the carboxylate ion prior to internal return occurs about 20% of the time.

Acid-catalyzed ester isomerization (equation 24) involves heterolysis of protonated ester molecules, and hence is mechanistically quite similar to acid-catalyzed alcohol isomerization. Most of the con-



(24)

siderations regarding substituent and acidity effects on alcohol isomerizations apply equally well to acid-catalyzed ester isomerizations. The rates of isomerization of α-ethynyl-γ-methylallyl acetate and α-phenylallyl acetate parallel H_0 rather than lyonium-ion concentration[94,151]. α- and γ-Alkyl, aryl and vinyl substituents speed up the acid-catalyzed isomerization of allylic esters to about the same degree that they do acid-catalyzed isomerization of the corresponding alcohols.

Under neutral conditions, allylic esters isomerize much more readily than allylic alcohols. This difference in reactivity largely disappears in the acid-catalyzed isomerizations. Under acidic conditions, esters isomerize at about the same rates as do the corresponding alcohols[94,137]. Inductive polarization of the alkyl carbon–oxygen bond and resonance stabilization of the transition state of the dissociation step are jointly responsible for greater anionotropic mobility of allylic esters than allylic alcohols in the absence of catalysts. In the acid-catalyzed isomerization of allylic esters, the transition state has about the same or perhaps less resonance stabilization than the protonated ester. This is probably the principal cause of the relatively small difference in reactivity of allylic alcohols and esters toward acid-catalyzed isomerization.

Another consequence of protonation of the ester is that dissociation yields a solvated allylic carbonium ion, rather than an ion pair. The strong electrostatic attraction which holds the ion pair together is lacking between the carbonium ion and the carboxylic acid molecule, and it is not surprising that internal return is not ordinarily observed in acid-catalyzed ester isomerization[148]. Pocker found that, in the perchloric acid-catalyzed racemization and isotopic exchange of $(-)$-α-phenylallyl acetate-carboxyl-^{14}C in acetic acid solution, racemization and isotope exchange occur at the same rate[151].

C. *Isomerization of Allylic Halides*

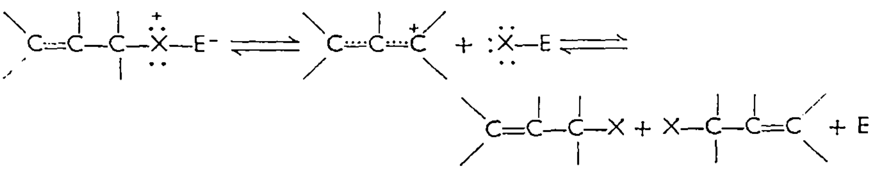
Isomerization reactions of allylic halides are frequently described in the literature, and are of considerable practical importance. Yet, with the exception of the isomerizations which accompany solvolyses of allylic chlorides (see section II.D), the detailed mechanisms of these reactions have received little attention.

Allylic chlorides are relatively stable in the absence of polar solvents and electrophilic catalysts. Chlorides having only one α- or γ-alkyl substituent are quite stable at ordinary temperatures. However, tertiary allylic chlorides and α-arylallylic chlorides isomerize rapidly at elevated temperatures[152-156], and at appreciable rates even at room temperature[157-160]. Even though no catalysts were added to the labile chlorides, traces of catalytic impurities were probably present in some cases. The uncatalyzed isomerizations of allylic chlorides probably involve formation and recombination of ion-pair intermediates. This hypothesis is supported by the large increase in lability produced by α- or γ-alkyl and aryl substituents. The fact that the rate of isomerization of α-phenylallyl chloride in both aprotic and hydroxylic solvents parallels solvent ionizing power is compelling evidence for an ionic mechanism for this reaction[159].

The less labile allylic chlorides isomerize at appreciable rates at moderate temperatures only in the presence of acidic catalysts such as proton acids and various metal salts. Among the salts which have been used are cuprous chloride[161-170] and cyanide[171], ferric chloride[164,170,172], aluminum chloride[170,173-177], zinc chloride[178-180], stannic chloride[177] and antimony pentachloride[173]. Strong acids such as hydrogen chloride catalyze the isomerization of allylic chlorides[159,162,181-184], and the isomerization of α-phenylallyl chloride is accelerated even by carboxylic acids[159].

Isomerization may also occur on the surface of solid salts. Silver oxide and colloidal silver chloride have been reported to catalyze allylic chloride isomerizations[185-186], as has a suspension of sodium chloride and phenylallylsodium in pentane[187]. The sodium salts are much less effective catalytically in liquid ammonia than in pentane, probably due to solvation of the sodium ions by ammonia.

The catalytic activity of Lewis and proton acids is probably a consequence of formation of complexes of the type R—X$^+$—E$^-$ or R—X···HA between the catalyst and allylic halide. Such complexes should dissociate much more readily than the allylic halide itself, and subsequent recombination would lead to a mixture of allylic isomers (equation 25, E = Lewis acid). The fact that the com-



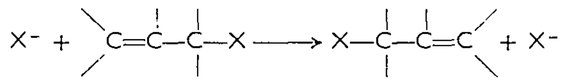
(25)

position of the butenyl chloride mixtures obtained by equilibration of α- and γ-methylallyl chlorides in the presence of high concentrations of anhydrous hydrogen chloride differs from that observed when catalytic quantities of the acid are used is evidence for the formation of complexes between hydrogen chloride and allylic chlorides[188].

Allylic chloride isomerizations are not nearly as susceptible to catalysis by free radicals as are isomerizations of the corresponding bromides. Exposure to peroxides and air, which causes rapid equilibration of allylic bromides, has no effect on α- and γ-methylallyl chlorides[188]. However, the same chlorides undergo simultaneous coupling and isomerization when treated with nickel carbonyl in methanol and ether solutions, and a radical mechanism is probably involved in both reactions[189].

Allylic bromides isomerize so readily that it is difficult to obtain pure samples of unsymmetrically substituted bromides. There are many reports in the literature of presumably pure bromides undergoing isomerization when heated or allowed to stand at room temperature[190-193]. Hydrobromic acid[194] and cuprous salts[195-197] catalyze the isomerization reaction, and hydrogen bromide in the presence of peroxides causes particularly rapid isomerization to occur[198-199], probably by a free radical chain mechanism[200]. Traces of hydrogen bromide and peroxides, formed by hydrolysis and oxidation reactions, are very difficult to exclude from allylic bromide preparations. This fact probably accounts for the difficulty of obtaining reproducible kinetic data for 'thermal' isomerizations of allylic bromides[201]. The stability of allylic bromides in the complete absence of Lewis acids and radical sources has not been established.

It is possible that some allylic halide isomerizations are the result of abnormal bimolecular displacement (S_N2') reactions (equation 26).



$$X^- + \rangle C{=}\overset{|}{C}{-}\overset{|}{\underset{|}{C}}{-}X \longrightarrow X{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{C}{=}C\langle + X^- \qquad (26)$$

This was claimed to be the case for the isomerization which accompanied exchange reactions of α- and γ-methylallyl bromide with radioactive lithium bromide in acetone solutions[30,202]. However, a lithium-ion catalyzed carbonium-ion mechanism is not excluded by the experimental data, and the S_N2' mechanism of halide isomerization has not been established with certainty.

The primary member of a primary–secondary or primary–tertiary pair of isomeric allylic halides predominates at equilibrium. The γ-alkyl isomer comprises 55–75% of the equilibrium mixtures of monoalkylallyl chlorides[188,203], and 80–90% of equilibrium mixtures of monoalkylallyl bromides[190,201,204]. In the case of allylic bromides, the equilibrium constant is rather insensitive to temperature changes:

butenyl bromide equilibrium mixtures contain 87% of the primary isomer at 20°, and 85·5% at 100°[190]. As expected, a second alkyl group shifts the equilibrium further in favor of the primary isomer. Thus, β,γ,γ-trimethylallyl chloride comprises 87% and α,α,γ-trimethylallyl chloride 13% of the equilibrium mixture[153].

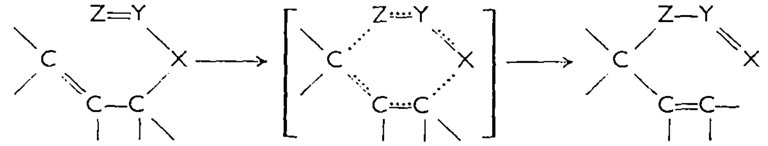
The greater thermodynamic stability of the γ-alkyl member of a primary–secondary or primary–tertiary pair of isomeric allylic halides is presumably due to hyperconjugative interaction of the alkyl group with the allylic double bond. Direct resonance interaction of an aryl or chloro substituent with the double bond results in still greater stabilization of the γ-substituted isomer; cinnamyl chloride is the only identifiable constituent of the α-phenylallyl chloride–cinnamyl chloride equilibrium mixture[159], and the γ-chloro isomer greatly predominates in equilibrium mixtures of dichloro- and trichloropropenes[182,205,206].

Many allylic replacement reactions which give rise to rearranged products probably do so at least in part because of isomerization of initially formed normal products. This was shown to be the case in the conversion of α- and γ-methylallyl alcohols to mixtures of bromides under a variety of conditions[194]. It is also likely that isomerization of initially formed α-chloroallyl chlorides is responsible for the conversions of α,β-unsaturated carbonyl compounds into γ-chloroallyl chlorides on treatment with phosphorus pentachloride[206-209].

It is often possible to obtain both members of a pair of labile isomeric allylic halides in pure form. Low-temperature fractional distillation of the equilibrium mixture is usually the most convenient method of obtaining the predominant primary isomer. If the secondary or tertiary isomer is desired, a mixture containing a non-volatile catalyst may be distilled slowly, and the more volatile secondary or tertiary halide removed at the still-head as it is formed. Even very labile, thermodynamically unstable halides such as α-phenylallyl chloride keep satisfactorily if stored at sufficiently low temperatures.

D. Concerted Intramolecular Isomerization Reactions

The thermal isomerizations of allyl aryl ethers, allyl vinyl ethers, allylic thiocyanates and allylic azides have several features in common. They all occur at rates which are relatively insensitive to changes in solvent polarity and the structure of the allylic system, they have negative entropies of activation, and (with the exception of the azide isomerizations) rearrangement of the allylic substituent accompanies allylic migration. These reactions occur by the S_Ni' mechanism, and usually involve cyclic six-membered transition states in which there is little separation of charge (equation 27).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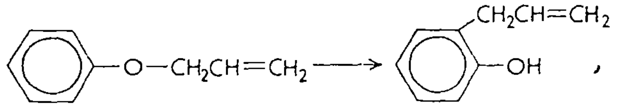
The Claisen rearrangements of allyl aryl and allyl vinyl ethers (equations 28, 29) differ from the other thermal isomerizations in

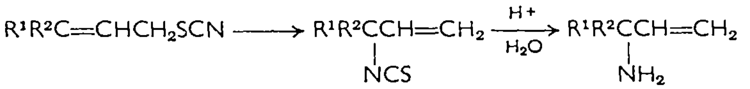

(28)

$$CH_2{=}CH{-}O{-}CH_2CH{=}CH_2 \longrightarrow CH_2{=}CHCH_2CH_2CHO \qquad (29)$$

that they form non-allylic products. For this reason, and because they are reviewed elsewhere[210-213], Claisen rearrangements are not discussed here.

It has been known since 1875[214] that allyl thiocyanate rearranges to allyl isothiocyanate, slowly at room temperature, and rapidly at its boiling point (equation 30). It was later reported that crotyl thiocyanate undergoes a similar rearrangement to crotyl isothiocyanate[215,216]. Actually, the product of this reaction is α-methylallyl isothiocyanate[29,41,217-220]. This isomerization, like isomerizations of most other unsymmetrically substituted allylic thiocyanates[178], involves rearrangement of the allylic system as well as of the functional group. These rearrangements are of practical interest because they afford an unambiguous synthetic route to α-substituted allylic primary amines (equation 31), substances otherwise difficult to prepare.

$$CH_2{=}CHCH_2SCN \longrightarrow CH_2{=}CHCH_2NCS \qquad (30)$$


$$R^1R^2C{=}CHCH_2SCN \longrightarrow R^1R^2\underset{\displaystyle NCS}{\underset{|}{C}}CH{=}CH_2 \xrightarrow[H_2O]{H^+} R^1R^2\underset{\displaystyle NH_2}{\underset{|}{C}}CH{=}CH_2 \qquad (31)$$

Allyl thiocyanate isomerizes at almost the same rate in toluene, nitrobenzene and dimethylformamide at 68°[221]. The reaction is slowest in the most polar solvent, dimethylformamide, and its rate is not appreciably affected by dissolved potassium thiocyanate. Allyl and β-methylallyl thiocyanates isomerize at almost the same rate.

γ-Alkyl substituents appear to increase the ionic character of the reaction somewhat, but even two γ-methyl substituents do not markedly alter the mechanism. γ-Methylallyl thiocyanate isomerizes about fifteen times more rapidly than allyl thiocyanate, while γ,γ-dimethylallyl thiocyanate isomerizes about 150 times more rapidly[222,223]. The rate increase produced by γ-alkyl substituents is small compared to that observed for S_N1 reactions of allylic halides, however. Allyl and γ-methylallyl thiocyanates isomerize more slowly in acetonitrile than in cyclohexane, while γ,γ-dimethylallyl thiocyanate isomerizes about three times faster in acetonitrile than in cyclohexane.

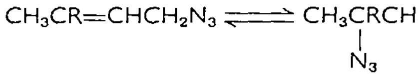
The relative insensitivity of isomerization rate to solvent and structural changes suggests that the isomerizations of allyl and γ-alkylallyl thiocyanates are intramolecular and involve transition states in which there is little or no charge separation. This view is supported by the fact that the isomerizations of allyl and β-methylallyl thiocyanates have substantial negative entropies of activation, as would be expected for reactions having a cyclic intramolecular mechanism.

It was long assumed that the isomerization of allyl and γ-alkylallyl thiocyanates is essentially irreversible. This conclusion was recently found to be erroneous. While the isomerization of allyl thiocyanate proceeds nearly to completion in the absence of solvents or in non-polar solvents, the reaction is measurably reversible in acetonitrile. γ-Alkyl substitution increases the amount of allylic thiocyanate in the equilibrium mixture, probably due to hyperconjugative stabilization of the thiocyanate by the γ-alkyl groups. γ-Methyl- and γ,γ-dimethylallyl thiocyanates isomerize to equilibrium mixtures containing appreciable amounts of thiocyanate under all conditions studied[222,224]. The amount of thiocyanate in the equilibrium mixture is greater in polar than in non-polar solvents. γ,γ-Dimethylallyl thiocyanate gives an equilibrium mixture containing 40% of thiocyanate in the absence of a solvent, 18% in cyclohexane solution, and 50% in acetonitrile solution. This observation can be explained by assuming that the functional group of alkyl thiocyanates involves more separation of charge than that of alkyl isothiocyanates[225]. This assumption also accounts for the fact that allyl and γ-methylallyl thiocyanates isomerize more slowly in acetonitrile solutions than in cyclohexane solutions. Presumably, the ground state is stabilized relative to the transition state by the more polar solvent in these reactions.

γ-Aryl and γ-halogeno substituents greatly retard the rate of isomerization of allylic thiocyanates, and may even alter the mechanism of the reactions. For example, γ-phenylallyl thiocyanate isomerizes very much more slowly than allyl thiocyanate[221], and yields γ-phenylallyl isothiocyanate rather than α-phenylallyl isothiocyanate[226]. The reaction is about ten times faster in nitrobenzene than in decalin, which indicates a mechanism with more ionic character than that of ordinary allylic thiocyanate isomerizations. In contrast, α-phenylallyl isothiocyanate, prepared from α-phenylallyl amine, isomerizes smoothly and completely to γ-phenylallyl thiocyanate[224]. Apparently, the loss of resonance energy on formation of the expected α-phenylallyl isothiocyanate from γ-phenylallyl thiocyanate precludes the concerted mechanism followed by most other allylic thiocyanate isomerizations.

A γ-chloro substituent also hinders allylic thiocyanate isomerization, and probably for the same reason. Thus, γ-chloroallyl thiocyanate and γ-chloro-γ-methylallyl thiocyanate undergo extensive decomposition on heating, but do not yield isolable amounts of isomerization products[227,228].

The isomerizations of butenyl and pentenyl azides also appear to involve non-ionic transition states[229]. α- and γ-Methylallyl azides isomerize slowly at room temperature in a variety of solvents, as do α,α- and γ,γ-dimethylallyl azides (equation 32).



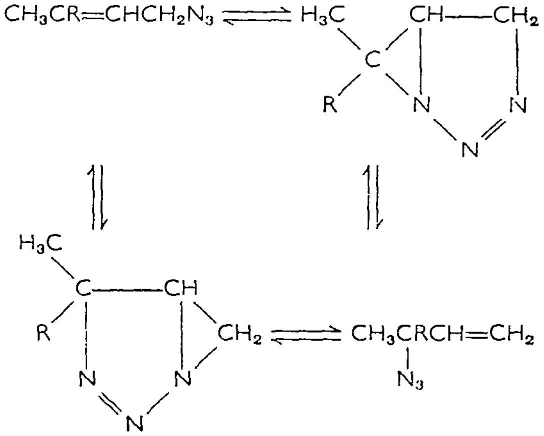
$$CH_3CR{=}CHCH_2N_3 \rightleftharpoons CH_3\underset{\overset{|}{N_3}}{C}RCH{=}CH_2 \qquad (32)$$

$(R = H, CH_3)$

The rate of allylic azide isomerization is remarkably insensitive to methyl substitution and to solvent ionizing power. The pentenyl azides ($R = CH_3$) isomerize only 2–4 times more rapidly than the butenyl azides ($R = H$) in a given solvent, and the rates of isomerization of both the butenyl and pentenyl azides are changed by a factor of only about one power of ten on changing the solvent from pentane to 70% aqueous acetone. In contrast, isomerization of the analogous pentenyl chlorides, which almost certainly involves ion-pair intermediates, is many powers of ten faster in 70% acetone than in n-pentane[230]. The very great effect of methyl substitution on rates of allylic chloride isomerizations has already been commented on (section III.C).

The azide isomerizations resemble allylic thiocyanate isomerizations in their low sensitivity to solvent ionizing power and in their negative entropies of activation. $\Delta S^{\ddagger}$ values average -10 to -11 e.u. for pentenyl azide isomerizations in pentane, ether and acetone, compared to $\Delta S^{\ddagger} = -9$ e.u. for isomerization of allyl thiocyanate in toluene[221]. The azide isomerizations are even less sensitive to methyl substitution than are the thiocyanate isomerizations.

The known ability[231,232] of alkyl and aryl azides to add to olefins suggests that allylic azide isomerizations may involve an intramolecular addition–elimination mechanism. However, the hypothetical intermediate has not been identified yet (equation 33).



(33)

IV. ALLYLIC GRIGNARD REAGENTS

The organometallic compounds formed by reactions of allylic halides with magnesium comprise a group of reagents of considerable theoretical interest and practical importance. Since the preparation and synthetic applications of allylic Grignard reagents are reviewed elsewhere[233,234], only recent research on the structure and constitution of these organomagnesium compounds is discussed here.

For more than two decades, the structure and constitution of allylic Grignard reagents has been the subject of many investigations and much debate. Both members of a pair of isomeric allylic halides form Grignard reagents which are chemically indistinguishable, and it is quite likely that isomeric halides yield the same Grignard reagent.

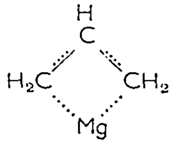
Since allylic rearrangement can occur both during preparation of the Grignard reagents and during their subsequent reactions, the chemical properties of these substances shed no light on their structures. A study of their physical properties has proved to be more fruitful, in spite of the experimental difficulties involved in preparing and handling pure samples of organomagnesium halides. Ultraviolet, infrared and nuclear magnetic resonance spectrometry have been particularly useful tools.

There are two facets to the problem of allylic Grignard reagent structure and constitution. First, there is the complex problem, common to all Grignard reagents, of the nature and composition of the chemical species present in ethereal solutions of 'organomagnesium halides'. It appears, on the basis of several kinds of evidence, that allylic and other Grignard reagents in ether solution consist of mixtures of diorganomagnesiums and magnesium halides, associated and solvated in complex ways[235-238].

More interesting, from the standpoint of allylic chemistry, is the question of the structure of the allylic groups in allylic Grignard reagents. A growing body of evidence indicates that the Grignard reagent prepared from either member of a primary–secondary or primary–tertiary pair of allylic halides has most or all of the allylic groups covalently bonded to magnesium at the primary carbon atom.

The ultraviolet absorption spectrum of the Grignard reagent prepared from cinnamyl bromide is qualitatively that of a compound having a styrene chromophore ($C_6H_5CH{=}CH$—), as is that of dicynnamylmagnesium[239]. Similarly, the infrared spectra of Grignard reagents prepared from α- and γ-methylallyl bromides support the primary structure for the butenyl groups of these organomagnesium derivatives[240,241].

The nuclear magnetic resonance spectra of allylic Grignard reagents are particularly pertinent to the question of their structure. The n.m.r. spectrum of allylmagnesium bromide precludes a non-classical bridged structure **7** for the allyl group:



(7)

and indicates that rapid equilibration of the two classical structures occurs as in equation (34)[242]. The two classical allylic structures

$$CH_2{=}CHCH_2{-}Mg{-} \rightleftharpoons {-}Mg{-}CH_2CH{=}CH_2 \qquad (34)$$

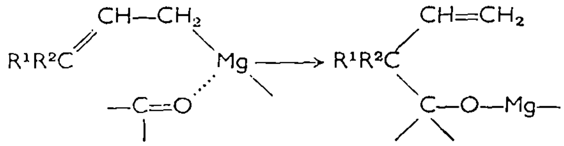
appear to be interconverted faster than 1000 times per second at ordinary temperatures.

The n.m.r. spectra of the Grignard reagent formed by α- and γ-methylallyl bromide are even more revealing. The organomagnesium derivatives of both halides have identical spectra which indicate that the butenyl groups are present predominantly or exclusively as classical crotyl groups, $CH_3CH{=}CHCH_2$—Mg—[237]. The spectrum of dibutenylmagnesium shows the same chemical shifts as the Grignard reagent, which argues against the RMgBr formula for the Grignard reagent.

While it is not possible on the basis of available evidence to decide definitely whether a small fraction of the butenyl groups in the butenyl Grignard reagent are present in the secondary form, it is necessary to postulate that a small fraction of the pentenyl groups in the Grignard reagent from γ,γ-dimethylallyl bromide are present in the classical tertiary form, and that the tertiary and primary groups are rapidly interconverted at ordinary temperatures[243]. The n.m.r. spectrum of this reagent shows a sharp singlet in the methyl region at ordinary temperatures, which splits to a doublet at low temperatures. These results exclude a symmetrical, bridged structure for the Grignard reagent. The methyl singlet at higher temperatures indicates that the *cis*- and *trans*-methyl groups undergo averaging of their chemical shifts through rotation about the C—C bond in the α,α-dimethylallyl form of the reagent, present only in very low concentration[243].

In coupling reactions with organic halides and reduction reactions with active hydrogen compounds, allylic Grignard reagents give mixtures of isomeric hydrocarbons[233,234]. In contrast, their reactions with carbonyl compounds are highly specific. The Grignard reagents prepared from either member of a primary–secondary or primary–tertiary pair of allylic halides react with aldehydes, ketones, esters, carbon dioxide and phenyl isocyanate to give mainly or exclusively the product of addition at the secondary (or tertiary) carbon atom of the allylic system[233]. Only with a very highly hindered ketone, di-*t*-butyl ketone, did extensive addition take place at the primary carbon atom of the butenyl Grignard reagent[244].

The formation of products of addition at the secondary or tertiary carbon atoms of allylic Grignard reagents, in which it is highly probable that primary allylic groups greatly predominate over secondary or tertiary groups, was first rationalized by Young and Roberts[245], who proposed a special cyclic addition mechanism (35).

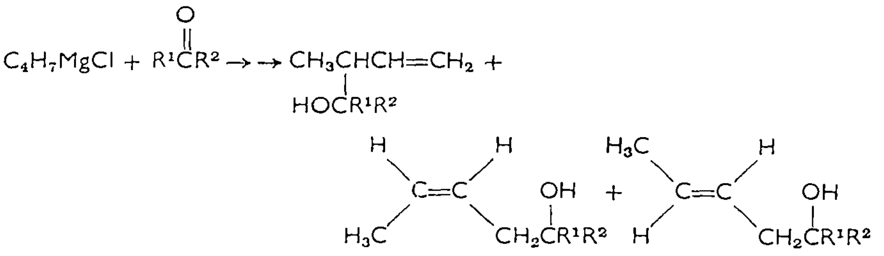


(35)

The existence of such a special mechanism would not only account for the products formed, but would explain why highly hindered and easily enolizable ketones give excellent yields of addition products with allylic Grignard reagents, but poor yields with other Grignard reagents. It might also account for the small amount of 1,4-addition products formed in reactions of allylic Grignard reagents with substances such as phenyl vinyl ketone and *t*-butyl cinnamate, to which other Grignard reagents add almost exclusively in the 1,4 manner.

The predominant formation of products of addition at the secondary or tertiary carbons of allylic Grignard reagents can also be explained by assuming that normal addition of the secondary (or tertiary) allylic groups takes place so much more rapidly than normal addition of the primary allylic groups that secondary or tertiary addition products predominate even though most of the allylic groups of the Grignard reagent are primary groups. This explanation has been invoked to account for the fact that butenylmagnesium bromide forms equal amounts of *erythro*- and *threo*-3-methyl-4-penten-2-ol in reactions with acetaldehyde at temperatures from $-70°$ to $+35°$[246,247], on the grounds that a cyclic transition state having a cyclohexanelike chair conformation with both methyl groups equatorial should give the *threo* alcohol from the *trans*-γ-methylallyl Grignard reagent. It should be pointed out that there is no experimental evidence bearing on the geometry or stereochemistry of the hypothetical cyclic six-membered transition state, and no compelling reason for accepting cyclohexane as a conformational model for it. Further, the postulate that the secondary form of the Grignard reagent is so much more reactive than the greatly predominant primary form that it gives rise to most or all of the addition product seems unreasonable. This hypothesis also fails to account for the unique behavior of allylic Grignard reagents in reactions with sterically hindered and α,β-unsaturated ketones.

Reactions of the Grignard reagent prepared from *trans*-crotyl chloride with highly hindered ketones such as diisopropyl ketone, isopropyl *t*-butyl ketone and di-*t*-butyl ketone give mixtures of addition products containing varying amounts of the products of addition at the primary carbon atom of the allylic system (equation 36)[248]. It is interesting that the primary addition product contains both the *cis* and *trans* isomers. This result furnishes independent chemical evidence for the existence of a mobile equilibrium between the primary and secondary forms of the Grignard reagent. If the primary addition products are formed by a cyclic six-membered mechanism from two different conformations of the Grignard reagent, as seems likely, it is necessary to assume that some secondary C_4H_7MgX is present, and that its reaction by a cyclic process is much faster with highly hindered ketones than is the analogous reaction of the primary isomer. If, on the other hand, it is assumed that primary addition product is formed



(36)

from the primary Grignard reagent, *cis–trans* isomerization must have occurred by rotation about the $CH_3CH—CH$ bonds of the small amount of secondary Grignard reagent present in the equilibrium mixture.

In summary, physical evidence indicates that the allylic groups in allylic Grignard reagents are present as classical structures covalently bonded to magnesium at the α-carbon atom, rather than as bridged structures in which magnesium is bonded to both ends of the allylic system. Equilibration of the two possible isomeric allylic structures occurs extremely rapidly at room temperature, and the primary isomer of a primary–secondary or primary–tertiary pair greatly predominates at equilibrium. The only data which bear on the detailed mechanisms of reactions of allylic Grignard reagents with halides, active hydrogen compounds and carbonyl compounds are product composition data. For this reason, allylic Grignard reactions require much more study before any but tentative conclusions can be reached regarding their mechanisms.

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 11

Cycloaddition reactions of alkenes

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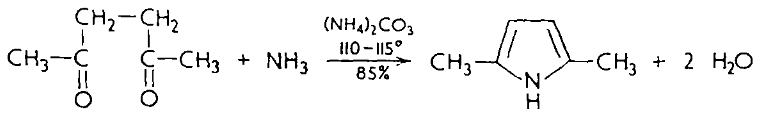
I. DEFINITION AND CLASSIFICATION

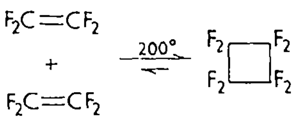
A. The Concept of Cycloaddition

What are cycloadditions? Unfortunately, natural phenomena do not present themselves in neatly ordered categories. It is left to us to define and classify them, and the results may often seem arbitrary. Recognizing that ambiguity may be found in borderline cases, let us set out some criteria distinguishing cycloaddition reactions.

In the reaction of acetonylacetone with ammonia[1,2] a ring is closed with incorporation of a nitrogen atom. This involves a multi-step reaction sequence in which two molecules of water are eliminated.

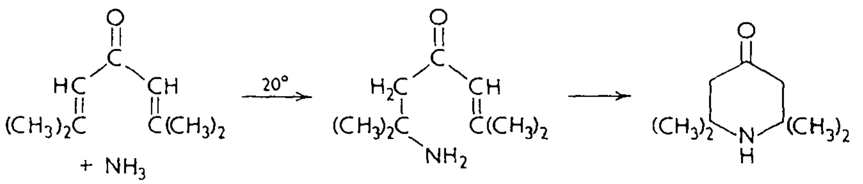


Against this process may be contrasted a true cycloaddition, the thermal dimerization of tetrafluoroethylene[3].



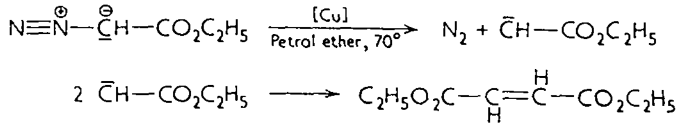
Rule 1. The product of a cycloaddition corresponds to the sum of the components. Cycloadditions are not accompanied by the elimination of small molecules.

The reaction of phorone with ammonia which yields 2,2,6,6-tetramethyl-4-piperidone[4,5] fits this requirement, but it is not purposeful to consider this multi-step nucleophilic addition to the α,β-unsaturated ketone as a cycloaddition. Here σ bonds of one component are broken, in contrast to the dimerization of tetrafluoroethylene.



Rule 2. Cycloadditions do not involve the breaking of σ bonds.

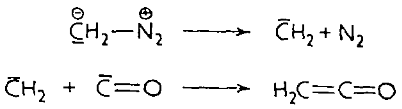
In the copper powder catalyzed decomposition of ethyl diazoacetate a 70% yield of diethyl fumarate can be obtained[6]. As is now known, copper is able to induce elimination of nitrogen from the diazo compound (*cf.* p. 759). The resulting carbethoxycarbene collects on the surface of the catalyst in relatively high concentration and dimerization takes place with the formation of a double bond.



$$N\equiv\overset{\oplus}{N}-\overset{\ominus}{\underline{C}}H-CO_2C_2H_5 \xrightarrow[\text{Petrol ether, 70°}]{[Cu]} N_2 + \bar{C}H-CO_2C_2H_5$$

$$2\ \bar{C}H-CO_2C_2H_5 \longrightarrow C_2H_5O_2C-\underset{H}{C}=\overset{H}{C}-CO_2C_2H_5$$

If diazomethane is heated in an atmosphere of carbon monoxide, the latter adds to the methylene produced as an intermediate to form ketene[7].



$$\overset{\ominus}{\underline{C}}H_2-\overset{\oplus}{N}_2 \longrightarrow \bar{C}H_2 + N_2$$

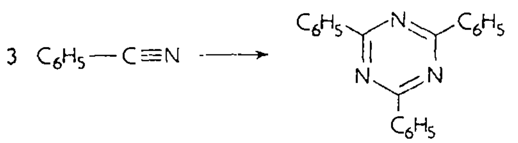
$$\bar{C}H_2 + \bar{C}=O \longrightarrow H_2C=C=O$$

Are these reactions cycloadditions? Van't Hoff considered the double bond to be a two-membered ring. However, this is not the commonly accepted concept today. Instead we think of a double bond as consisting of one σ and one π bond. This division into two bonds of different kinds has proved fruitful, even if there has been some recent dissension[8]. The formation of a two-membered ring should not be considered a cycloaddition.

Rule 3. The number of σ bonds is increased in cycloadditions.

Thus we need not include the formation of alkene–silver complexes or of ferrocene and dibenzenechromium as cycloadditions since the new metal–carbon bonds formed are not normal σ bonds.

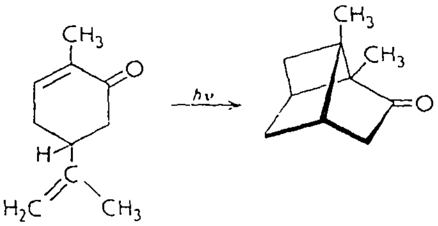
Is it possible that more than two components are involved in a cycloaddition? If benzonitrile is treated with metallic sodium or with cold chlorosulfonic acid, three molecules combine to form 2,4,6-triphenyl-1,3,5-triazine[9,10]. The trimerization of acetaldehyde, thioacetone, phenylisocyanate, *etc.*, corresponds formally to this reaction type.



It is doubtful that termolecular reactions exist in which all six centers are properly oriented with respect to one another in the rate-determining process. In fact, there is no evidence that tri- or tetramerizations proceed in a single step; a path of successive steps is more probable. If the product from two units reacts with a third, then the latter step could well be a cycloaddition. In any case a closer investigation of the catalytic process itself is always needed. Possibly more complex mechanisms, unrelated to cycloaddition, will prove to be involved.

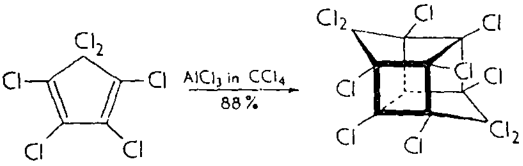
Rule 4. Cycloadditions of more than two reactants are multi-step processes; only the last step, leading to the ring structure, is strictly speaking a cycloaddition.

It does not contradict the concept of cycloaddition if the two participating functional groups are attached to one another in the same molecule. In the photoisomerization of carvone to carvonecamphor[11,12] there is an intramolecular cycloaddition of two olefinic double bonds.

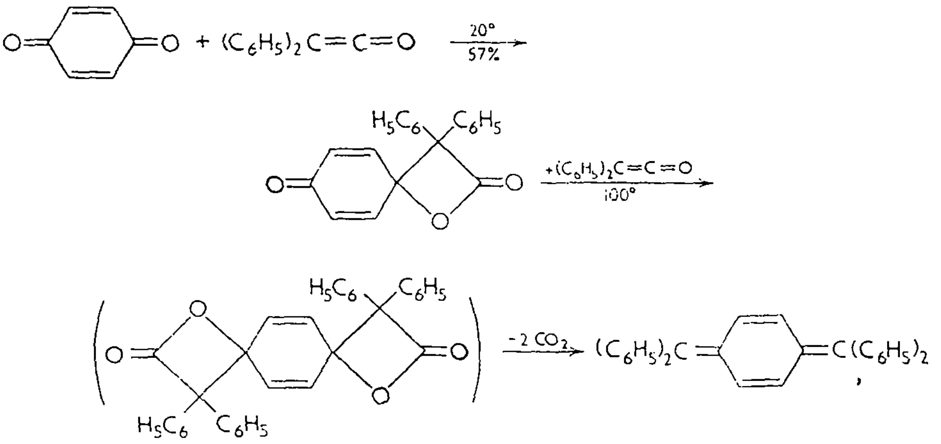


Rule 5. Intramolecular cycloadditions are possible if the necessary functional groups are linked in the same molecule.

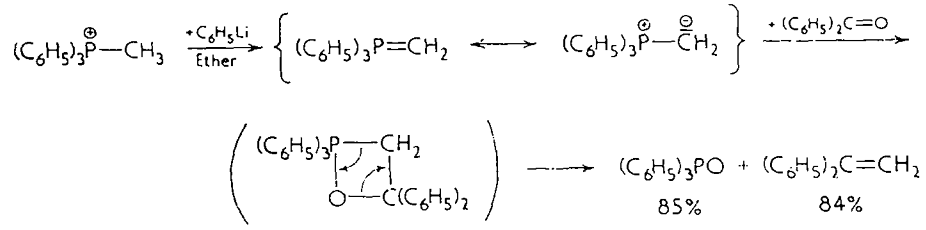
Two molecules may also undergo more than *one* cycloaddition with each other. An example is the dimerization of hexachlorocyclopentadiene in the presence of aluminum chloride, which produces in high yield a cage-like chlorocarbon[13]. In the scope of the rule it is not at all required that the two cycloadditions be completed simultaneously; usually they will take place successively.



Must the cyclic products necessarily be stable? Thermal stability is a relative thing; we recognize that organic chemistry is bounded by narrow temperature limits. On reacting benzoquinone with one equivalent of diphenylketene a crystalline monoadduct is obtained as the result of a cycloaddition. If this is heated with additional diphenylketene at 100°, a good yield of tetraphenyl-*p*-quinodimethane is isolated. Even though the bis-β-lactone cannot be isolated, there can be little doubt that the second cycloaddition does occur, followed by carbon dioxide elimination[14].

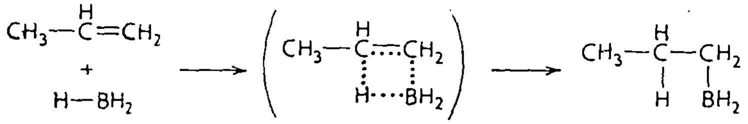


Consequently, cycloadditions may also be postulated in those cases where the subsequent opening of the ring apparently occurs faster than its formation. This may be true, for example, in the Wittig olefin synthesis, in which phosphine ylides react with carbonyl compounds[15]. The formulation of an intermediate having a four-membered ring appears to be required in this reaction. Probably this

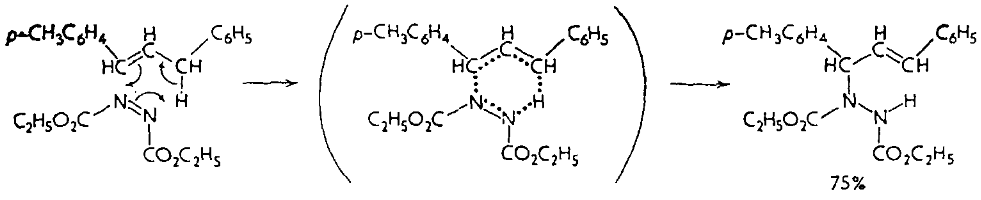


is the second intermediate, preceded by another one in which the nucleophilic ylide-carbon has become attached to the carbonyl group.

However, if a ring merely occurs as a transition state and thus has no significant lifetime, the reaction should not be considered a cycloaddition. Hydroboration, the formation of organoboron compounds from diborane and olefins, takes place, according to Brown[16], as a *cis* addition and is satisfactorily represented as proceeding through a transition state in which a four-membered ring occurs.



The allylic substitution of olefins can be explained similarly in those cases where a shift of the double bond is required. In the reaction of diethyl azodicarboxylate with 3-phenyl-1-(*p*-tolyl)propene, a mechanism involving a cyclic six-membered transition state is supported by the small solvent dependence, the lack of catalysis by acids or bases, and the kinetic isotope effect[17].



The decision as to whether an intermediate, *i.e.* a dip in the energy curve, occurs or not requires a fundamental study of the reaction mechanism. As a rule of thumb, however, it may be considered that a state which cannot be written with principal valences only, does not normally have the character of a true intermediate.

Rule 6. The term cycloaddition should only be used if the cyclic product has a finite lifetime. The ring structure must be an intermediate, not only a transition state.

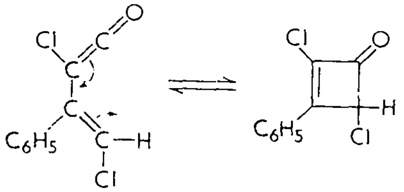
B. The Principles of the Classification

A classification of cycloaddition reactions can be based upon (1) the number of new σ bonds, and (2) the size of the ring which is formed, or the number of ring atoms which each reactant contributes. Together these two criteria present a scheme in which all cycloadditions can be neatly pigeon-holed.

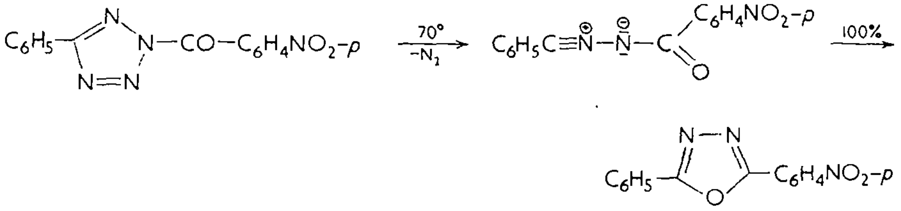
Cycloadditions in which *two* new σ bonds are formed are of particular interest because of their number and significance. The succeeding sections will deal exclusively with such reactions. A few examples of other cycloaddition classes will be considered first.

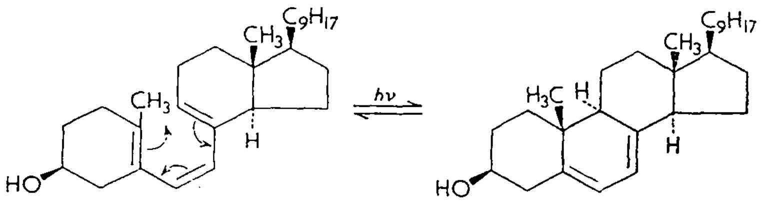
I. Some cycloadditions with formation of more or less than two new σ bonds

Cycloadditions which lead to *one* new σ bond are necessarily *intramolecular* reactions. The formation of 2,4-dichloro-3-phenylcyclobutenone from (1-phenyl-2-chlorovinyl)chloroketene in the equilibrium reaction shown below offers a convincing explanation for the racemization of the optically active cyclobutenone derivative[18].



The *N*-acylated nitrilimines formed initially by elimination of nitrogen from 2-acyltetrazoles spontaneously cyclize to give 1,3,4-oxadiazoles[19]. Similarly, 1,2,4-triazoles and 1,3,4-thiadiazoles are obtained from *N*-imidoyl- or *N*-thioacyltetrazoles[20]. The key step of these processes is the conversion of a π bond of the open-chain intermediate into a σ bond in the cyclic product.



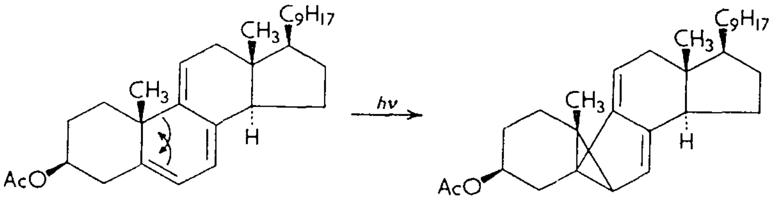


Precalciferol Ergosterol

The photochemically induced equilibration of ergosterol with precalciferol[21] embodies in the reverse reaction a ring closure in which a σ bond is formed at the expense of a π bond. An excellent example from the field of the simple olefins is found in the photoisomerization of 2,3-dimethylbutadiene to give 1,2-dimethylcyclobutene in 70%

yield[22]. The formation of an unsaturated pyrone ring occurs in the photoisomerization of β-ionone[23].

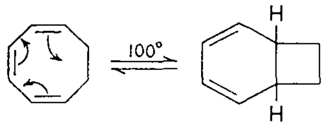
A more complicated type of cycloaddition is found in the photochemical rearrangement of dehydroergosterol acetate[24,25]. Here



Dehydroergosterol acetate Lumi isomer

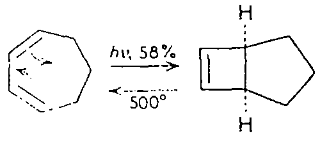
one σ and one π bond are transformed into two new σ bonds. Rule 2 (p. 742) is no longer obeyed in this case. The rearrangement of santonine to lumisantonine[26] and some related photoisomerizations[27] also illustrate this type of transformation.

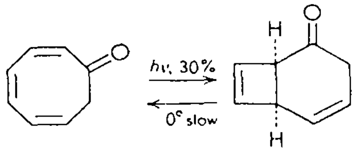
The development of a transannular σ bond at the expense of a π bond is not an uncommon variation. Establishment of a thermal equilibrium between cycloocta-1,3,5-triene and bicyclo[4.2.0]octadiene[28] includes such a step and its reversal.

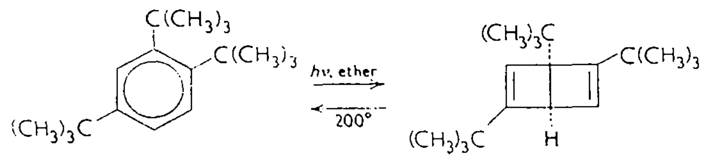


85% 15%

Numerous photoisomerizations which have been discovered in recent years belong in this category; examples are the reactions of cyclohepta-1,3-diene[29] and cycloocta-1,3,5-trien-7-one[30]. The transformation of 1,2,4-tri-*t*-butylbenzene into a Dewar benzene structure



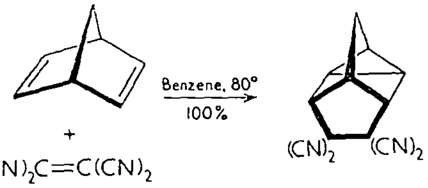




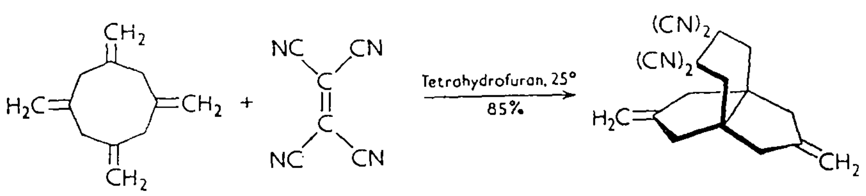
by irradiation may also be cited[31]. The configuration of the bicyclo[2.2.0]hexane derivative is of course quite different from 'Dewar benzene'. The large steric interaction of the *ortho* *t*-butyl groups in the starting material favors isomerization to the interesting bicyclic form in this case.

Perhaps these valence tautomerizations ought not to be considered as cycloadditions. Certainly such cases should not be included where there is no gain in the number of σ bonds. In the ring expansion of *cis*-divinylcyclobutane to 1,5-cyclooctadiene (p. 784) as well as in numerous other Cope rearrangements, the number of σ and π bonds remains unchanged[32].

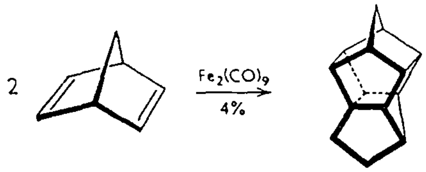
In the homo-Diels–Alder reactions of bicyclo[2.2.1]heptadiene, *three* π bonds are converted to *three* σ bonds with the closure of two new rings. Tetracyanoethylene[33], *N*-phenylazodicarboximide[34], and less readily acrylonitrile[35] take part in cycloadditions of this interesting type.



If the cyclization of reactive double bond systems with bicyclo[2.2.1]heptadiene is considered to be a 1,5-addition, then the reaction of 1,3,5,7-tetramethylenecyclooctane with tetracyanoethylene[36] corresponds to a 1,7-addition. In this case too, three σ bonds are derived from three π bonds.



Still more rare are cases in which *four* new σ bonds arise in a cycloaddition. When bicyclo[2.2.1]heptadiene is irradiated in the presence of iron pentacarbonyl several products are formed. Present to the extent of about 4% is a saturated dimer whose nuclear magnetic resonance spectrum indicates a structure in which two molecules of bicycloheptadiene are coupled together with the ensuing loss of all four double bonds[37,38]. The role of the iron carbonyl in this reaction has not been clarified.



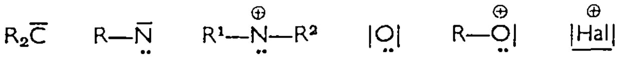
An example in the inorganic field is the dimerization of P_2. At temperatures above 800° the tetrahedral P_4 molecule is in equilibrium with 2 P_2; at 1200° about 50% of the P_4 is dissociated It is conceivable that the formation of the four new σ bonds in the reverse reaction takes place simultaneously.

2. Classification of cycloadditions in which two new σ bonds are formed

The size of the new ring offers an advantageous as well as a simple principle for the classification of these cycloadditions. The number of ring atoms contributed by each reactant then can be used for subclassification. Each class will be illustrated with one or two examples.

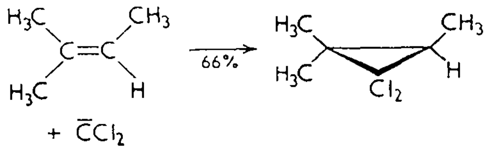
2 + 1 → 3

The component which provides one ring atom must combine nucleophilic and electrophilic character, as is the case with the following structures:



$$R_2\overline{C} \quad R-\underset{\cdot\cdot}{\overline{N}} \quad R^1-\underset{\cdot\cdot}{\overset{\oplus}{N}}-R^2 \quad |\underset{\cdot\cdot}{O}| \quad R-\underset{\cdot\cdot}{\overset{\oplus}{O}}| \quad \overset{\oplus}{\underline{|Hal|}}$$

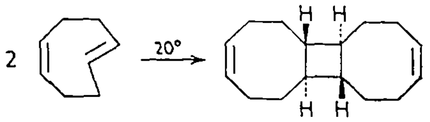
Compounds containing double or triple bonds may be the reaction partners. A wealth of information has been recorded concerning the



reactions of 'divalent carbon', even though carbene chemistry *per se* has blossomed forth only in recent years. The preparation of dichlorocarbene from chloroform and potassium *t*-butoxide[39] initiated this fruitful development.

2 + 2 → 4

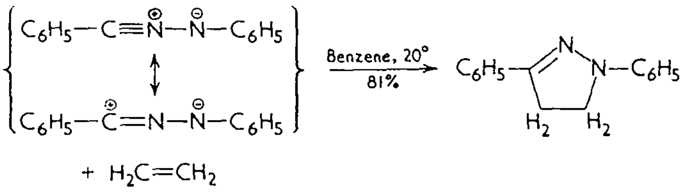
In this class belong the numerous thermal or photochemically induced formations of cyclobutanes, cyclobutenes, and four-membered heterocyclic compounds. The classic case of the spontaneous dimerization of *cis-trans*-1,5-cyclooctadiene[40] is an illustration.



Cycloadditions of the 3 + 1 → 4 type have not been described thus far.

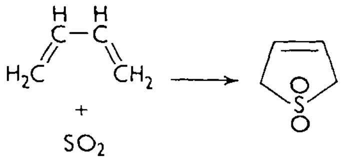
3 + 2 → 5

Although a large number of examples of 1,3-dipolar cycloadditions, especially reactions of diazoalkanes and azides, have long been known, it has only been in the last few years that the usefulness and broad scope of this synthetic principle has been recognized[41]. As an example may be cited the room-temperature addition of ethylene to diphenylnitrilimine generated *in situ* by reaction of *N*-phenylbenzhydrazide chloride with triethylamine[42].



4 + 1 → 5

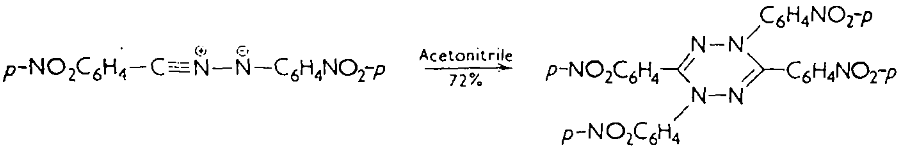
The industrially important 1,4-addition of sulfur dioxide to 1,3-butadiene[43] is probably the best example of this type of addition; pyrogallol is used to inhibit polymerization of the diene. Isoprene[44] and 2,3-dimethylbutadiene[45] react in the same way.

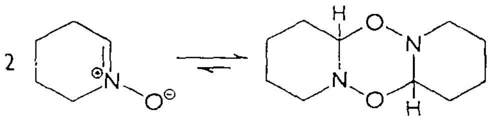


Methylene generated by the photolysis of diazomethane also adds, to a small degree, to the 1,4-positions of butadiene to give cyclopentene (6–10%)[46].

$3 + 3 \rightarrow 6$

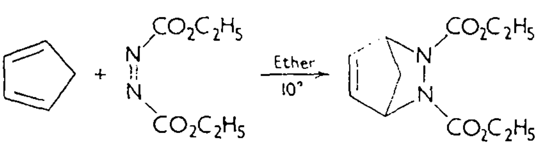
Several 1,3-dipoles tend to dimerize according to this scheme. Di-*p*-nitrophenylnitrilimine, prepared *in situ*, dimerizes spontaneously and irreversibly to give the 1,4-dihydro-1,2,4,5-tetrazine derivative[47]. Piperideine *N*-oxide exists in equilibrium with its head-to-tail dimer[48].





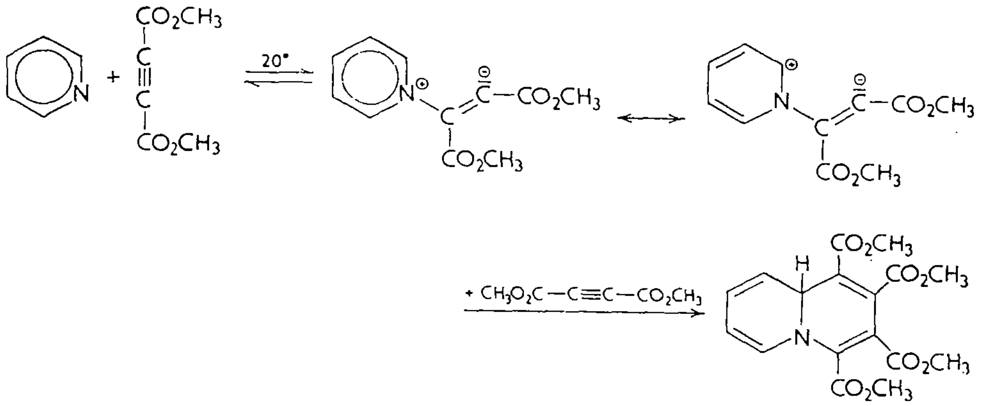
$4 + 2 \rightarrow 6$

No other cycloaddition has received so much attention as the broadly useful synthesis of six-membered rings discovered by Diels and Alder. The yearly flow of publications dealing with the preparative use or the theoretical aspects of the 'Diene synthesis' shows no sign of abatement. When the structure of the adduct from cyclopentadiene and diethyl azodicarboxylate had been clarified[49], the idea emerged that this synthetic principle is of general applicability.

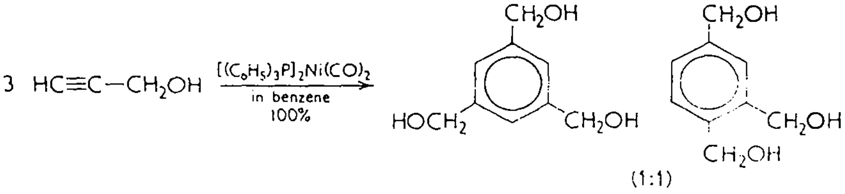


1,4-Dipolar addition belongs in the same category. Diels and Alder[50] reacted pyridine with dimethyl acetylenedicarboxylate and obtained a red 1:2 adduct whose structure was fully established only much later.

With the strongly electrophilic acetylenedicarboxylate, pyridine forms a 1,4-dipole which unites with a second molecule of the acetylene derivative in a cycloaddition. Recent successful replacement of the second molecule of acetylenedicarboxylate by other dipolarophiles supports the indicated mechanism[51].

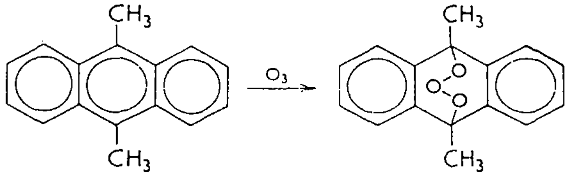


Rule 4 (p. 744) permits inclusion of many trimerizations in the 4 + 2 → 6 category. However, very little is known about the detailed mechanisms of these reactions. In no case has the nature of the final ring closure been established. As an example may be cited the elegant synthesis of benzene derivatives from acetylenes which proceeds under the catalytic influence of bis(triphenylphosphine)-dicarbonylnickel[52], triphenylchromium tetrahydrofuranate[53] or di-cobalt octacarbonyl[54] under very mild conditions.



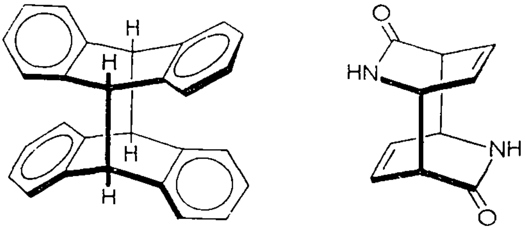
4 + 3 → 7

Verified examples of this class are rare. The product from 9,10-dimethylanthracene and ozone[55] very probably contains a seven-membered ring.



4 + 4 → 8

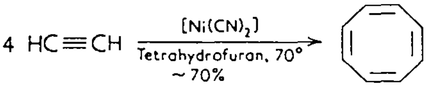
One of the earliest known photodimerizations, that of anthracene[56], belongs to this class. The coupling of two molecules through the 9,10-positions takes place with the sacrifice of the aromaticity of the central rings. The dimerization of α-pyridone[57] and its derivatives upon irradiation appears to be similar.



The supposition that the thermal dimerization of 1,3-butadiene to *cis-cis*-1,5-cyclooctadiene[58] also falls in this category can no longer be accepted in view of the elucidation of the mechanism (see p. 784). Possibly certain dimerizations of *o*-quinodimethanes to derivatives of 1,2,5,6-dibenzocyclooctadienes[59] are of this type, but further clarification is needed.

6 + 2 → 8

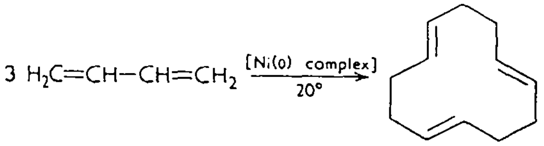
Reppe's synthesis of cyclooctatetraene from acetylene[60] fits formally into the classification at this point. However, if the synthetic route discussed on page 793 is correct, the eight-membered ring is not formed by cyclization of the last acetylene unit with a preformed six-membered intermediate. It is more likely that a sequence of two cycloadditions of the 2 + 2 → 4 type takes place with participation of the nickel ion followed by a valence tautomerization to form the eight-membered ring. Such a reclassification will probably become more



prevalent in the cycloaddition field as additional reaction mechanisms are elucidated.

8 + 4 → 12

The trimerization of butadiene which occurs at ordinary temperature under the influence of chromium or nickel(0) catalysts to give all-*trans*- or *trans*-*trans*-*cis*-cyclododeca-1,5,9-triene[61] may be an example of this class. Here also investigation of the reaction path has not been completed. A cycloaddition rapidly becomes less probable with increasing ring size, but in the orienting field of a metal complex the expense in activation entropy may be less.



In the development of this classification of cycloaddition reactions we have sometimes left the field of alkene chemistry. However, our further detailed discussion of the main types will be limited to components with a carbon–carbon double bond. Selected examples should make the essential features of cycloaddition processes familiar to the reader; a complete survey is not intended.

II. THREE-MEMBERED RINGS

A. Cyclopropane Derivatives from Carbenes and Alkenes

The chemistry of methylenes or carbenes[62] has been characterized by explosive development in the last decade. Nevertheless, its roots reach back into the last century. In 1885 Buchner[63] originated the study of the reaction of benzene and related compounds with diazoacetic ester. The attack on naphthalene was suggested by Buchner and Hediger[64] to involve primary loss of nitrogen from the ethyl diazoacetate followed by addition of the reactive fragment, $:CHCO_2C_2H_5$, to a 'double bond' of the aromatic hydrocarbon.

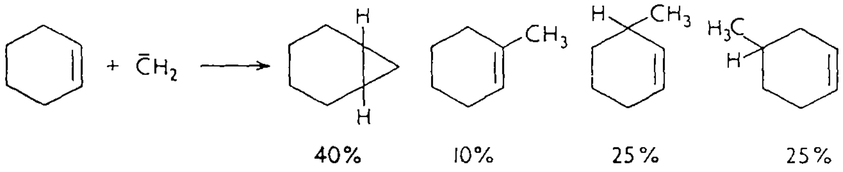
Carbenes are not isolable substances; unlike carbon monoxide and the isocyanides, their divalent carbon structures are not stabilized by resonance with an all-octet canonical form (octet stabilization). Carbenes therefore must be generated for reaction *in situ*. That they occur as discrete intermediates is supported by a great body of experimental data. In recent years the view has been advocated that there are two structural types of carbenes which differ characteristically in their reactivity. The relation will be explained first with reference to the parent compound, methylene.

1. The reactions of methylene

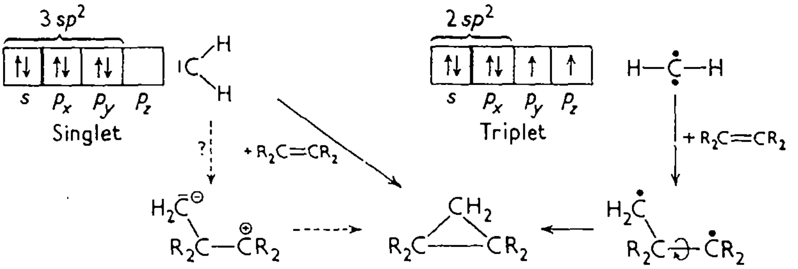
Thermolysis or photolysis of diazomethane or ketene are useful processes for the generation of methylene, the simplest carbene. The volatilization of arsenic, selenium or tellurium mirrors by gaseous reaction products is evidence for the presence of free methylene[65]. The more recent preparative and analytical investigations stem from the observation of Meerwein[66] who photolyzed diazomethane in diethyl ether and recovered n-propyl as well as isopropyl ethyl ether. Under the same conditions, benzene was smoothly transformed into cycloheptatriene[67,68].

Methylene generated by the photolysis of diazomethane is not only able to add to the double bond of an alkene to form a cyclopropane derivative, but also reacts with carbon–hydrogen bonds in saturated and unsaturated hydrocarbons to insert the methylene group. The equally rapid transformation of primary, secondary and tertiary carbon–hydrogen bonds to *C*-methyl structures led Doering to the conclusion that 'methylene must be classed as the most indiscriminate reagent known in organic chemistry'[69]. The reaction with cyclohexene is an example.

$$H_2\overset{\ominus}{\bar{C}}-\overset{\oplus}{N}\equiv N \xrightarrow{h\nu} H_2\bar{C} + N\equiv N$$

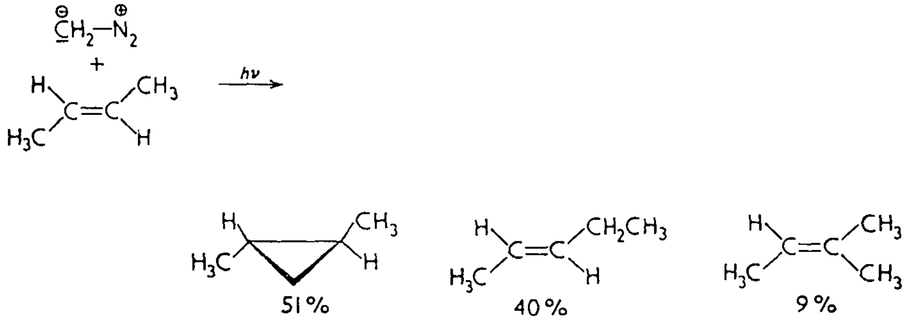


What geometry and electronic structure can be assigned to this active species? *A priori* two somewhat simplified possibilities may be discussed. With sp^2 hybridization the orbitals of the carbon atom would form an obtuse angle. The third electron pair, which is not employed in the bonding, would occupy the third sp^2 orbital. With an electron deficiency as well as an unshared electron pair, such a singlet methylene molecule should show both electrophilic and nucleophilic character. An electrophilic attack on an olefinic carbon atom should lead to a relatively energy-rich zwitterionic intermediate, which could then close a ring with neutralization of the charges. However, an energetically more favorable and more probable process would be a concerted three-center addition to give the cyclopropane ring. In this case the methylene would display its electrophilic and nucleophilic properties simultaneously.



The alternative is a linear methylene structure with carbon–hydrogen bonds of the *sp* type, for which Hund's rule requires only one electron in each of the two remaining equivalent *p* orbitals. Such a biradical methylene (triplet state) can react only in a two-stage addition with the carbon–carbon double bond. Furthermore, since the primary adduct is still a biradical, the final ring closure must be accompanied by a change in multiplicity. The forbidden transition from triplet to singlet state presumably does not take place immeasurably fast.

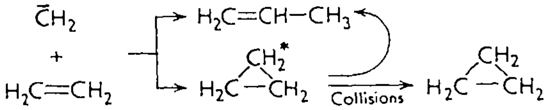
Irradiation of diazomethane in liquid *trans*-2-butene at −70° or in the gas phase at 25° at pressures of at least 1200 Torr gives only



trans-1,2-dimethylcyclopropane together with products of insertion of methylene into carbon–hydrogen bonds; reaction with *cis*-2-butene is no less stereospecific[70–72]. The thermolysis of diazomethane in 2-butene at 300° yields the same products[73].

The stereospecific *cis* addition offers a strong argument for the bent singlet state of methylene. In the primary adduct from triplet methylene the original double bond of the alkene has become a single bond which is capable of rotation. It may be supposed that the lifetime of the intermediate is sufficient to cause some, if not complete, loss of stereospecificity.

In the gas reactions of methylene with butene, particularly at low pressure, removal of the heat of reaction is difficult; the 'hot' 1,2-dimethylcyclopropane to some extent suffers ring opening to give 2-pentene. This phenomenon is still more apparent in the reaction of ethylene with methylene[74]. At low gas pressure energy-dissipating collisions are relatively rare, and the energy-rich cyclopropane molecules decompose to propylene. With increasing inert gas pressure the yield of cyclopropane improves.

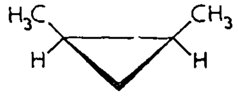
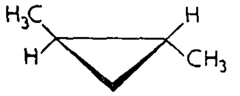


The experience of recent years has revealed that the pressure of an added inert gas also alters the picture of methylene reactivity itself in a characteristic way. In the photolysis of diazomethane in a mixture of argon and *cis*-2-butene at pressures of 2100–3200 Toor, Frey observed that as the ratio of argon to butene was increased the yield of addition product improved at the expense of the insertion reaction and that stereoselectivity decreased[75,76]. At an argon/*cis*-butene ratio of 1600 the recovered C_5 fraction contained 27% each of *cis*- and *trans*-1,2-dimethylcyclopropane, 16% each of *cis*- and *trans*-2-pentene, 10% 3-methyl-1-butene, and 4% 2-methyl-2-butene[76]. It was concluded that the longer lifetime and greater number of collisions with inert molecules promoted conversion of singlet methylene to the triplet state. This finds additional support in the fact that oxygen, a known radical trap, is able to prevent such addition of triplet methylene to the alkene.

Spectroscopic studies of the gas-phase photolysis of diazomethane support this concept. It is indicated that the initially formed singlet methylene undergoes a transition to the triplet state at high inert gas pressure[77].

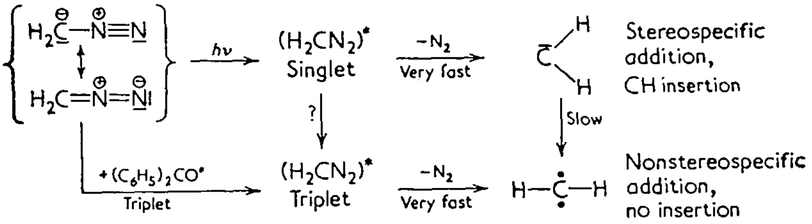
Apparently biradical methylene is energetically favored over the spin-coupled singlet species. The lack of stereospecificity is the result of the two-step mechanism of the addition to double bonds and not due to the 'hot' character of the reagent. The insertion reaction appears to be possible only through a one-step three-center reaction and thus cannot be attributed to triplet methylene.

The singlet methylene arises from an activated singlet state of diazomethane or ketene. It is possible, however, to bring about a photosensitized decomposition of these methylene generators which leads directly to triplet methylene; in solution, benzophenone serves as the sensitizer[78], in the gas phase, triplet mercury (Hg 6 $^3P_1$) may be used[79]. Under such circumstances, the insertion reaction with cyclohexene is greatly depressed in favor of norcarane formation. The photosensitized reaction with isobutene gives 91% 1,1-dimethylcyclopropane, while with singlet methylene a large amount of insertion is observed[80]. In the sensitized gas reactions of the isomeric 2-butenes at a ketene/olefin ratio of 1 : 10, the product mixtures obtained (in percent of C_5 fraction) are quite similar, although not identical[79].

			2-Pentenes	Methylbutenes
trans-2-Butene	14	52	24	9
cis-2-Butene	25	31	32	12

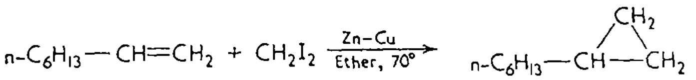
The agreement of the results for *cis*-2-butene with those obtained in the diazomethane photolysis in argon/*cis*-2-butene mixtures (p. 758) is noteworthy. Cvetanovic proposed that the pentenes and methylbutenes obtained in this work do not reflect the insertion reaction characteristic of singlet methylene but instead arise from isomerization of the primary biradical adduct of triplet methylene and the alkene[79].

The following scheme summarizes the phenomena which occur in the production of methylene from diazomethane; a similar one could be constructed for ketene as the methylene source.

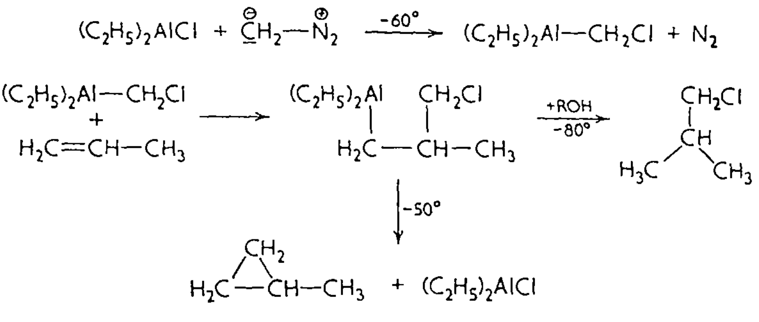


Metallic copper not only catalyzes the evolution of nitrogen from diazoalkanes but also modifies the reactivity of the carbene. Hammond found that methylene liberated in this way added stereospecifically to carbon–carbon double bonds but showed no tendency to give insertion reactions[78]. Such behavior corresponds to neither singlet nor triplet methylene. A bonding interaction between the metal and the carbene carbon atom is for the time being a satisfactory explanation. Similar results were also obtained in the presence of iron(III) complexes[78].

One must avoid indiscriminately attributing all *in situ* methylenations to free methylene. For example, according to Simmons, stereospecific methylene addition is obtained by reaction of alkenes with methylene iodide and the zinc–copper couple[81].



The fact that filtered ethereal solutions can be used contraindicates the existence of a short-livid intermediate. It seems very likely that the active reagent is iodomethylzinc iodide, ICH_2ZnI. The same reagent was obtained from diazomethane and zinc iodide[82]. A recent study using $(C_2H_5)_2AlCH_2X$ (X = halogen) as a model brought to light a reaction path which is supported in each step by sound analogies[83]. If, in fact, both the addition of the organometallic reagent and the closure of the cyclopropane ring proceed stereoselectively, the interpretation of the *cis* methylenation causes no difficulty.



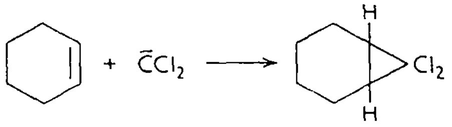
If tetramethylammonium bromide is reacted in cyclohexene with $C_6H_5Li\cdot C_6H_5Na$, the formation of 5–18% norcarane is observed[84]. Whether or not this reaction as well as the decomposition of sulfonium ylides[85,86] involves the formation of free carbene intermediates clearly requires further investigation.

2. Halocarbenes

Hine was the first to prove the transitory existence of CCl_2 in the reaction of chloroform with alkali[87]. Dichlorocarbene and its analog, dibromocarbene, generated from bromoform, were shown by Doering and Hoffmann to add to olefinic double bonds with the formation of 1,1-dihalocyclopropane derivatives[88]. A suspension of potassium *t*-butoxide in cyclohexene, for example, is treated at room temperature with the haloform. Chloroform gives a 59% yield of dichloronorcarane, while bromoform yields 75% of the dibromo compound.

$$HCCl_3 + \overset{\ominus}{O}-C(CH_3)_3 \rightleftharpoons \overset{\ominus}{C}Cl_3 + HO-C(CH_3)_3$$

$$\overset{\ominus}{C}Cl_3 \longrightarrow \bar{C}Cl_2 + Cl^{\ominus}$$



59%

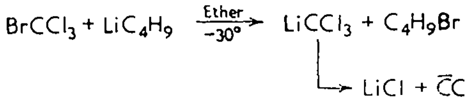
A great number of alkenes have been subjected to this reaction, as a few examples will illustrate: *β*-pinene, 50% CCl_2 adduct[88]; 1,3-butadiene, 51% CCl_2 and 64% CBr_2 adduct[89]; styrene, 76% CCl_2 and 72% CBr_2 adduct[90]. The reactions proceed more cleanly than those with CH_2, inasmuch as the addition to the double bond is not accompanied by insertion reactions. CH bonds in aromatic side chains[91], methylmalonic ester[92] and 2,5-dihydrofuran[93] appear to be susceptible to some $CHal_2$ insertion.

Ethyl trichloroacetate[94], hexachloroacetone[95,96] and methyl trichloromethanesulfinate[97] also give dichlorocarbene when treated with sodium ethoxide or potassium *t*-butoxide. The decomposition of sodium trichloroacetate in boiling 1,2-dimethoxyethane offers a neutral source for dichlorocarbene[98].

$$Cl_3C-CO_2C_2H_5 + NaOCH_3 \longrightarrow \bar{C}Cl_2 + CH_3O-CO_2C_2H_5 + NaCl$$

$$Cl_3C-CO_2Na \xrightarrow{80-120^\circ} \bar{C}Cl_2 + CO_2 + NaCl$$

As a final example, the action of n-butyllithium on bromotrichloromethane at −30° leads to bromine–metal interconversion; it has been suggested that the organolithium compound decomposes spontaneously into CCl_2 and lithium bromide. Cyclohexene gives a 91% yield of dichloronorcarane with this system[99]. As an alternate path one must consider an initial addition of trichloromethyllithium to the olefinic double bond followed by subsequent closure of the three-membered ring (see p. 760).

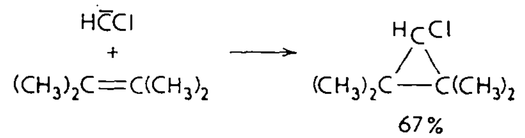


$$BrCCl_3 + LiC_4H_9 \xrightarrow[-30^\circ]{Ether} LiCCl_3 + C_4H_9Br$$
$$LiCCl_3 \longrightarrow LiCl + \bar{C}Cl_2$$

Methylene chloride is metallated by butyllithium. Cycloadditions which have been carried out on olefins with this system are not unequivocal in mechanism. The following formulation has been proposed by Closs[100].

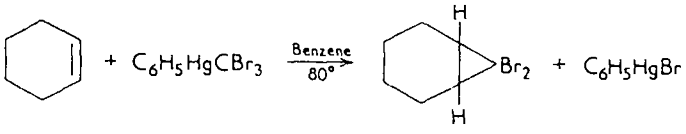
$$H_2CCl_2 + LiC_4H_9 \xrightarrow[-25^\circ]{Ether} LiCHCl_2 + C_4H_{10}$$

$$LiCHCl_2 \longrightarrow \bar{C}HCl + LiCl$$



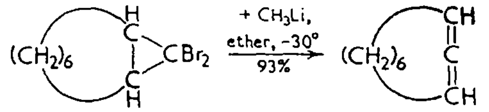
67%

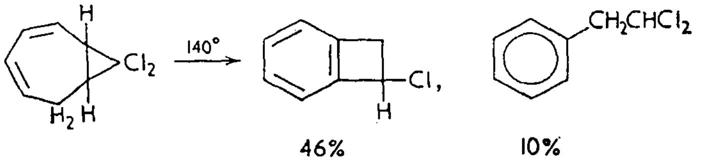
The suspicion that free carbene may not be involved here finds support in experiments recently published by the same author. Chlorocarbene (HCCl), generated from chlorodiazomethane, shows some CH insertion besides *cis* addition to double bonds[101]. Trihalomethylphenylmercury has also been recommended as a dihalocarbene generator[102]; mechanistic studies are still lacking.



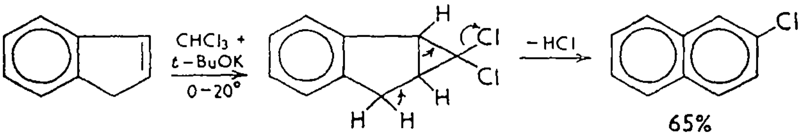
88%

The dihalocyclopropane derivatives which have become easily available are able to undergo useful transformations. Reductive dehalogenation offers an elegant synthesis of allenes[103]. Thus, the action of magnesium or methyllithium on the CBr_2 adduct from cyclooctene results in the strained allene having a nine-membered ring[104]. Thermolysis of the CCl_2 adduct from cycloheptatriene opens a route into the benzocyclobutene series[105].

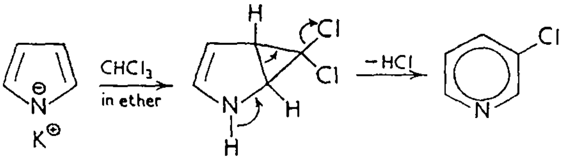




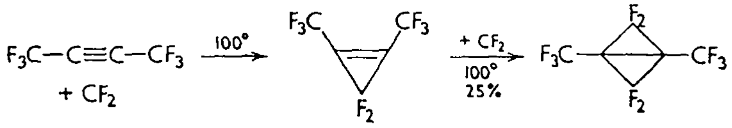
The addition of CCl_2 to the olefinic double bond of indene is followed by a ring expansion which leads with evolution of hydrogen chloride to *β*-chloronaphthalene. The primary adduct is isolable[106].



A classic precedent for this transformation is the reaction discovered by Ciamician[107] of pyrrole with chloroform and alkali to form *β*-chloropyridine. α-Formylpyrrole, the product of a Reimer–Tiemann synthesis, of which the essential step is the nucleophilic addition of a pyrrole anion to CCl_2, has been found only in minor amounts. The formation of *β*-phenylpyridine on heating pyrrole with benzal chloride and sodium ethoxide probably involves phenylchlorocarbene as an intermediate[108,109]. Indole reacts analogously with chloroform and alkali to give *β*-chloroquinoline[110].

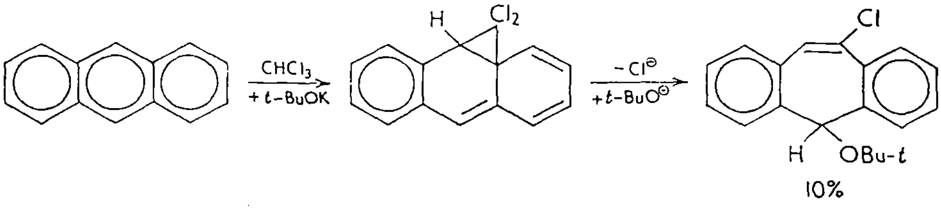


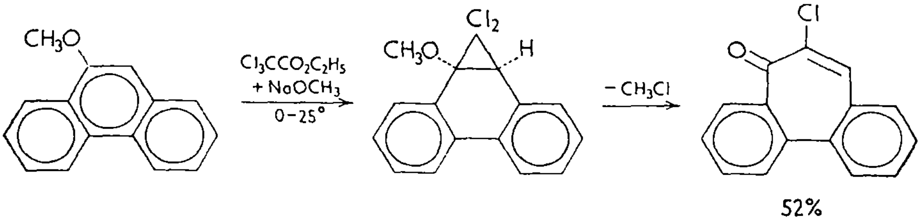
A cyclopropene derivative which stems from the addition of difluorocarbene to hexafluoro-2-butyne is able to accept another molecule of difluorocarbene. The bicyclobutane structure of the



double adduct has been confirmed by ^{19}F nuclear magnetic resonance[111].

Only the electron-rich aromatic carbon–carbon bonds add dichlorocarbene. Benzene and naphthalene do not react, while anthracene[112] as well as 1- and 2-methoxynaphthalene[113] give poor yields of ring-enlargement products. However, 9-methoxyphenanthrene reacts smoothly[113].





With mono- and dihalocarbenes stereospecific *cis* addition to olefins is observed exclusively; with CBr_2 careful investigations have been carried out[71,114].

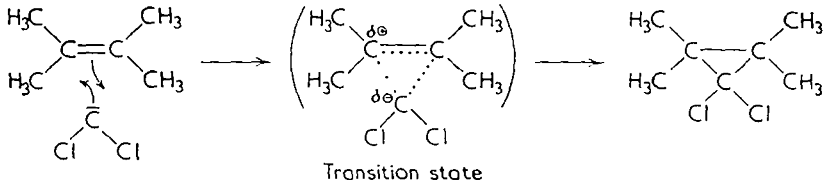
A comparison of the reactivity of alkenes toward dihalocarbenes is not possible by means of a direct kinetic measurement, since the addition of the carbene takes place much faster than the reaction in

TABLE 1. Relative rate coefficients for the reaction of alkenes with CBr_2 (bromoform + potassium *t*-butoxide) based on isobutene as standard[114,115].

Alkene	k_2 (rel.)
Tetramethylethylene	3·5
Trimethylethylene	3·2
Isobutene	≡ 1·0
1,1-Diphenylethylene	0·8
Butadiene	0·5
Cyclohexene	0·4
Styrene	0·4
1-Hexene	0·07
Allylbenzene	0·02

which it is generated. However, pairs of olefinic components can be allowed to compete, say for CBr_2, and from the product analysis their relative activities can be calculated. The data in Table 1 show that increased methylation of the ethylene accelerates the reaction.

How does this effect arise? The concept of concerted addition does not require that the two new bonds be formed at identical rates, even though bond formation begins simultaneously. Let us tentatively assume that the alkene double bond is able to mobilize its π electrons for the formation of the σ bond more easily than the electron-deficient carbene can provide its electron pair. This would lead to a certain charge separation in the transition state, that is, at the peak of the energy profile. If the carbene carbon atom gains more electrons than it loses, it will carry a partial negative charge while the olefin will have to accommodate an equal positive charge. The electron-donating methyl groups—the sp^3 hybridized carbon atoms have lower electronegativity than the olefinic sp^2 centers—are now able to accept part of the positive charge and thus to lower the activation barrier.

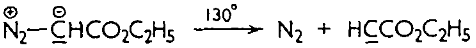


That the positive partial charge in the transition state cannot be particularly large is disclosed by the relatively low activity of butadiene and styrene toward CBr_2. The vinyl group and the aromatic nucleus are inductively electron-attracting. The extent of the opposing electromeric effect depends upon the magnitude of the positive charge to be stabilized. In the cases of butadiene and styrene the reaction-impeding inductive effect is scarcely compensated by the promoting electromeric effect. In allylbenzene only the inhibiting effect is apparent. An electrophilic two-step addition of the carbene leading to a carbonium ylide should take place several orders of magnitude faster with styrene and butadiene than with the methylated ethylenes. The relative rate coefficients thus support the assumption that in the case of the dihalocarbenes we are dealing with 'electrophilic–nucleophilic' reagents.

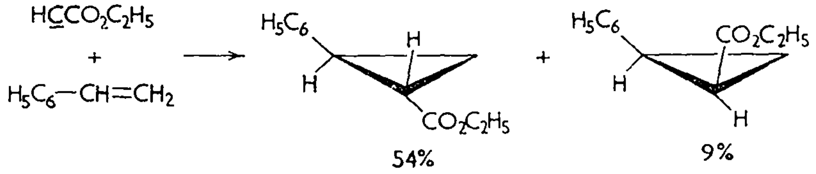
The singlet carbenes may be considered as amphoteric reagents in that they possess both an electron-deficient center and an unshared electron pair. In the discussion to follow the most predominant tendency will be noted first.

3. Other carbenes

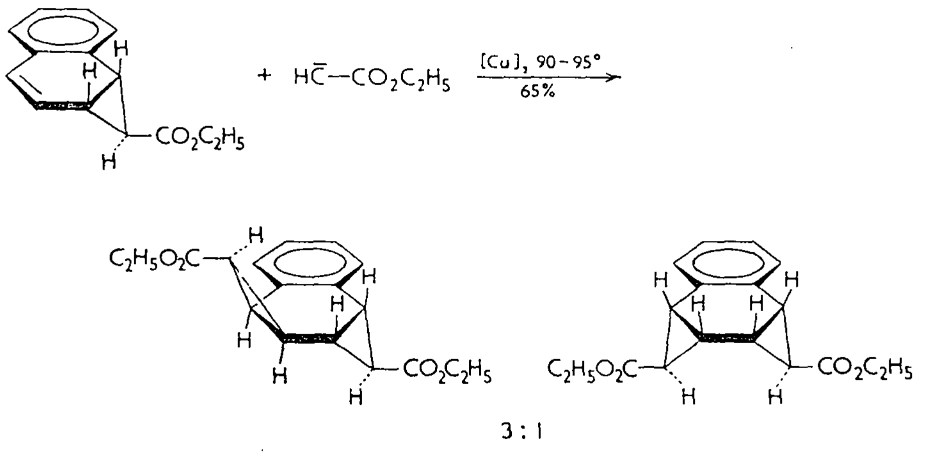
The thermolysis, photolysis or metal-catalyzed decomposition of ethyl diazoacetate lead to carbethoxycarbene. Its addition to monosubstituted ethylenes yields cyclopropane derivatives having two asymmetric centers. The reaction with styrene reveals that the paths to both stereoisomeric adducts are used, but that the sterically better course is favored[116-118].



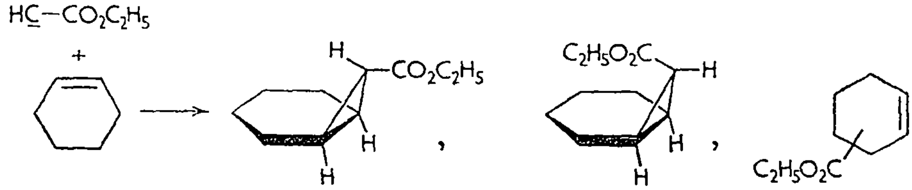
$$\overset{\oplus}{N_2}-\overset{\ominus}{\underline{C}}HCO_2C_2H_5 \xrightarrow{130°} N_2 + H\underline{C}CO_2C_2H_5$$



This also appears to hold in the additions of carbethoxycarbene to aromatic compounds. As a 'double-bond reagent' it attacks predominantly the aromatic bond of highest bond order[119]. The product from benzene and carbethoxycarbene, because of its tautomeric relationship to 7-carbethoxycycloheptatriene, gives no indication of the steric course of the addition. However, the product of 1,2-addition to naphthalene, *i.e.* 2,3-benzo-7-carbethoxynorcaradiene, has the ester group in a *trans* configuration[120]. This ester in turn accepts a second carbethoxycarbene molecule exclusively at the olefinic bond to give isomeric products whose ratio reflects the influence of steric factors[120].



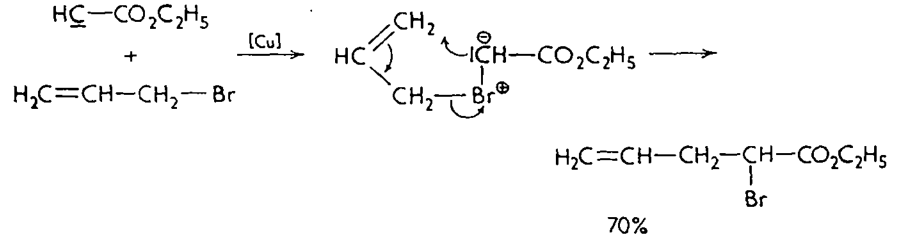
The thermal additions of carbethoxycarbene to olefinic or aromatic bonds have frequently reduced its preparative value because of the intrusion of CH-insertion reactions. For example, the photolysis of ethyl diazoacetate in cyclohexene produces substantial amounts of ethyl cyclohexenylacetates in addition to the *cis*- and *trans*-norcaranecarboxylic esters[121].



Photolysis	16%	10%	21%
Cu catalysis	69%	4%	0%

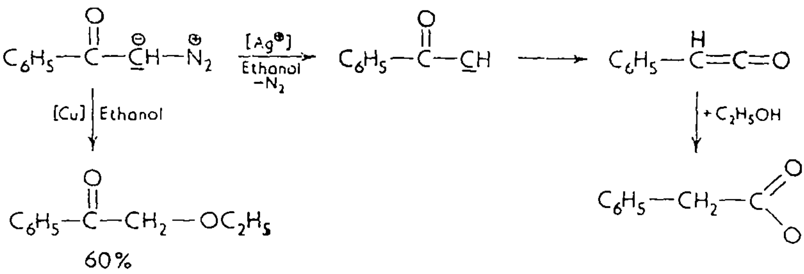
Although the thermolysis of ethyl diazoacetate requires temperatures of 130–140°, the nitrogen elimination can be brought about by copper catalysis at 70–90°. Like methylene, its carbethoxy derivative also exhibits substantially different reactivity under such conditions. Experiments of Skell and Etter with cyclohexene show that the carbene, presumably now bound to copper, is no longer capable of insertion and also behaves more stereoselectively in additions. In the union with the double bond of vinyl ethyl ether, the presence of copper has also been observed to cause an increase in the *trans/cis* ratio of the diastereomeric cyclopropanes obtained[121].

Occasionally, the electrophilic reactivity of carbethoxycarbene competes with the bridging function needed for the three-center addition path. The copper-catalyzed decomposition of diazoacetic ester in allyl alcohol gives a 52% yield of ethyl allyloxyacetate together with 7% of *trans*-2-hydroxymethylcyclopropanecarboxylic ester[122].

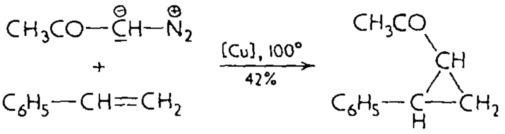


The formation of 70% ethyl 2-bromo-4-pentenoate from allyl bromide[123] indicates a primary attack of the carbethoxycarbene at the bromine atom with subsequent allylic rearrangement of the ylide. That the rearrangement takes place through a quasi five-membered ring is shown by the behavior of methallyl chloride[124]. In the case of allyl chloride itself reaction occurs about equally well at both the double bond and the chlorine atom[123].

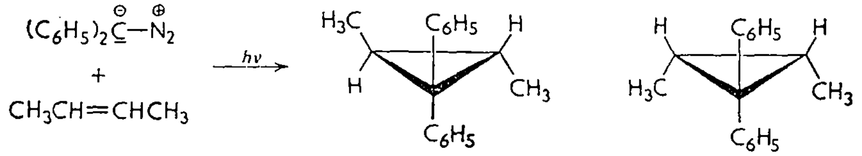
The Wolff rearrangement of diazoketones to ketenes demonstrates that the intermediary ketocarbenes rapidly undergo an intramolecular rearrangement[125–127]. The chain-lengthening procedure of Arndt and Eistert is based on this rearrangement[128]. Under the influence of silver ions, which accelerate the decomposition of the diazoketone, the reaction in ethanol leads directly to the ethyl ester of the carboxylic acid. If copper is used as the catalyst only the α-ethoxyketone is obtained[129].



The bond to copper—anhydrous copper sulfate displays the same activity—suppresses the Wolff rearrangement of the ketocarbene and makes possible its addition to styrene, cycloalkenes, vinyl acetate, dihydropyran and other alkenes[130]. Intramolecular additions of this type are also known[131]. In the absence of a suitable reaction partner even dimerization to diacylethylenes may take place[132].

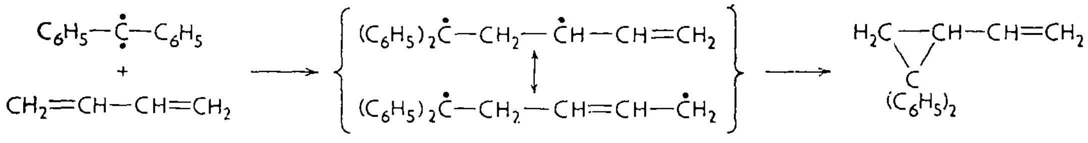


In the cases of the alkylated or dialkylated carbenes which can be prepared *via* the diazoalkanes or by reaction of alkali metals with alkyl chlorides, the interaction with olefinic double bonds is generally less likely than isomerization to alkenes or cyclopropanes[133,134]. Diphenylcarbene which is easily obtained by photolysis or thermolysis of diphenyldiazomethane surprisingly fails to demonstrate the expected stereospecificity in additions to geometrically isomeric alkenes[135]. Identical product mixtures are not actually obtained from *cis*- and *trans*-2-butene, but the 'false' isomers occur in substantial amounts. The system diphenyldibromomethane + methyllithium is capable of stereospecific methylenation of *cis-* and *trans*-2-butenes[136]; the occurrence of a free carbene, however, seems doubtful here.



trans-2-Butene	15	:	1
cis-2-Butene	2·3	:	1

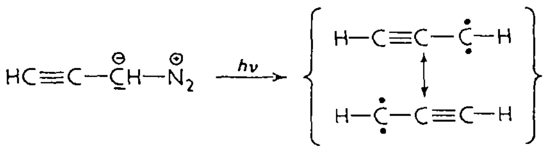
The suggestion that diphenylmethylene exists as a diradical and enters two-step additions to olefinic double bonds[135] (see p. 757) has been supported by its sensitivity to oxygen. The formation of benzophenone[137] proceeds through the carbonyl oxide[138]. The reaction with oxygen also made possible detection of a thermal dissociation of tetra-α-naphthylethylene into the carbene at 150°[139]. Recently it was shown by electron paramagnetic resonance measurements that diphenylcarbene, generated in a 'rigid solvent' by photolysis of diphenyldiazomethane, exists in a long-lived triplet state[140]. Apparently the singlet → triplet transition is faster in the case of the diphenyl derivative than in methylene itself or the conversion has already occurred at the stage of the photoexcited diphenyldiazomethane molecule. A linear bond system with the benzene nuclei in planes at right angles to one another would permit the orbitals of the unpaired electrons to overlap with the aromatic π clouds. Problematically enough, the angular structure of biphenylene carbene likewise undergoes non-stereospecific additions[140a].



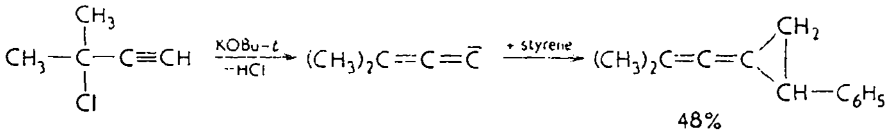
In agreement with the two-step mechanism for the addition, the reaction of diphenylmethylene with butadiene is about 100 times faster than with isobutene[135]; the intermediate profits from the resonance stabilization of the allyl radical. Here we find a striking difference between the one- (see p. 757) and two-step addition paths.

Propargylene, which is obtained by irradiation of diazopropyne, was shown by Skell and Klebe[141] to be another carbene which does not react stereospecifically. The striking cylindrical symmetry of the bond system in this molecule arises from a linear skeleton, where the orbitals at the carbene carbon atom are singly occupied; thus the

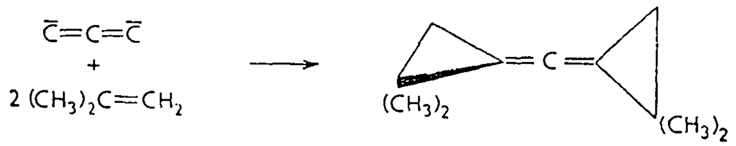
π orbitals extend over all three carbon atoms. Besides the normal *cis*-addition product, this reagent gives with *trans*-butene 5%, and with *cis*-butene 13%, of the adduct with the 'wrong' configuration.



An unusual carbene of the allene series which is capable of addition to alkenes has been obtained by 1,3-elimination of hydrogen chloride from 3-chloro-3-methylbutyne[142].



Still more exotic is the dicarbene of the formula C_3. Skell and Wescott[143] recognized that C_3, first detected spectroscopically in the atmosphere of comets and later found to be a main constituent in vaporized carbon, shows the properties of a dicarbene. The product obtained with isobutene at −180° seems to be the bisadduct and occurs in three stereoisomers.



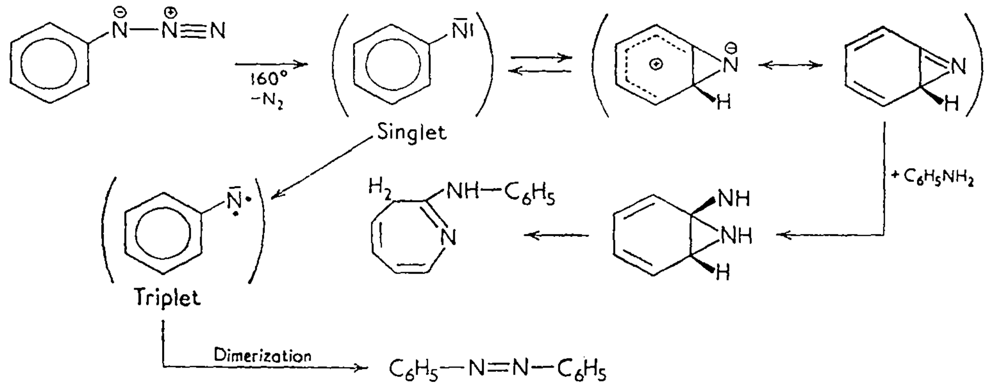
B. Aziridines from Azenes

The name 'azene'[144] for the singly bonded neutral nitrogen function is analogous to 'carbene'. In the azenes the same alternatives of formulation as singlet or triplet states are offered as with the carbon analogs. Compared with the wealth of carbene chemistry the azenes must still be regarded as 'underdeveloped'[144a].

The parent compound, NH, has been postulated as an intermediate in the familiar hydrazine synthesis of Raschig, but the pros[145–147] and cons[148, 148a] of this proposal will not be discussed here.

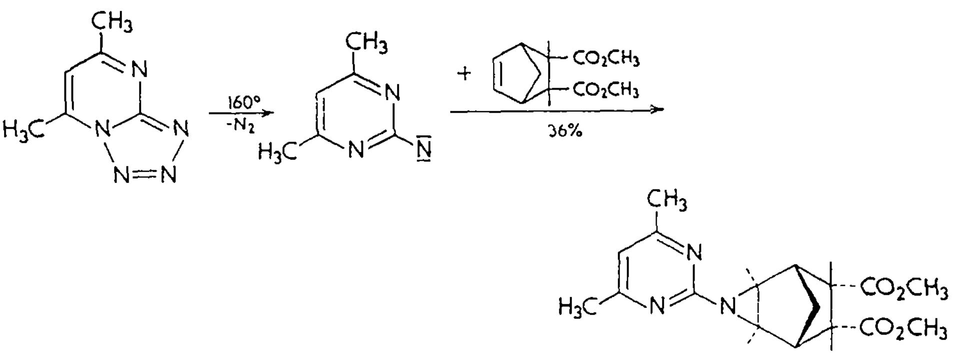
In his classic work on azides, Curtius long ago assumed the existence of the molecular fragment $\mathrm{R{-}\overset{\bullet}{\underset{\bullet}{N}}|}$ which remained after the loss of a nitrogen molecule from the organic azide. Based on the tendency of this fragment to undergo rearrangements, Curtius even set up a classification of azides into 'rigid' and 'non-rigid' types[149]. The ketoazenes are hypothetical intermediates in the Curtius rearrangement to form isocyanates[150]; their behavior suggests that the carboxylic acid azides should be considered prototypes of the 'non-rigid' azides.

The thermolysis rates of aromatic azides show only a small solvent dependence and a modest influence of *m*- and *p*-substituents[151,152]. This suggests an initial formation of an arylazene. The 9% yield of azobenzene obtained in the thermolysis of phenyl azide in benzene at 160°[153] possibly arises from dimerization of C_6H_5—N; gas-phase pyrolysis at 360° gives 72% azobenzene[154]. The ring-expansion reaction which takes place in aniline at 160° to give a 3*H*-azepine derivative is consistent with an intramolecular electrophilic substitution of the phenylazene[155,156]. Nitrogen elimination from phenyl azide is not induced by aniline as shown by the small solvent dependence on the decomposition rate[151]. Can the same species, phenylazene, give rise to dimerization and ring enlargement? Possibly a singlet and a triplet intermediate are involved as suggested in the following hypothetical scheme.

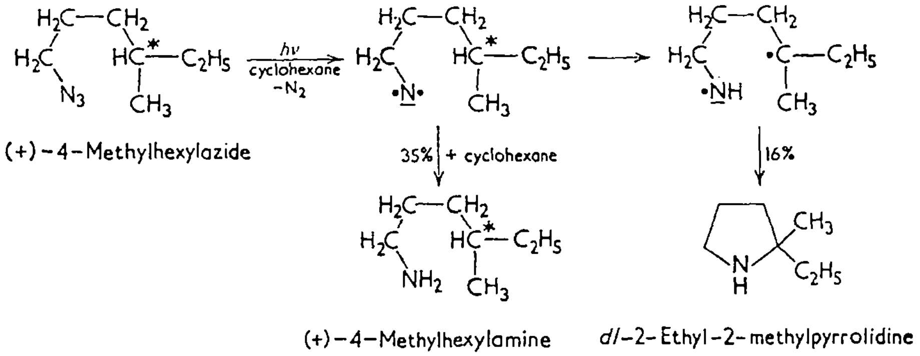


A similar reaction is the formation of 2-phenylazirine from α-azidostyrene at 360° which was recently reported by Smolinsky[157]. The nearly quantitative formation of carbazole from *o*-azidobiphenyl indicates the occurrence of an electrophilic substitution in the neighboring benzene nucleus[158].

The tendency toward intramolecular stabilizing reactions appears to be smaller with 2-pyridyl- and pyrimidylazenes. 2-Pyridylazene can be detected as a thermolysis product of tetrazolopyridine by its trapping reaction with triphenylphosphine[159]. Addition of such azenes to strained double bonds yields aziridine derivatives[160]. However, proof is not yet available that in these cases primary addition to give a Δ^2-triazoline is not involved.

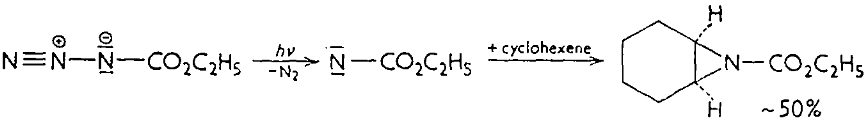


New investigations on the thermolysis[161] and photolysis[162] of organic azides have brought to light a surprising tendency of the azenes to react by intramolecular CH insertion. According to Barton and Morgan this is associated with loss of optical activity[162], which points to a multi-step mechanism and a triplet structure for the reaction azene. The reduction to a primary amine which occurs in both saturated and unsaturated solvents also may be explained on this basis.



Ketoazenes have been designated above as hypothetical intermediates in the Curtius rearrangement of acyl azides. However, a systematic study of the correlation between structure and rate strongly suggests that elimination of nitrogen and migration of the alkyl or aryl group are concerted[163]. The free ketoazene appears to be involved not in the thermolysis, but in the photolysis of acyl azides. Some intramolecular CH insertions forming γ- or δ-lactams have recently been observed upon irradiation of suitable cycloalkanecarboxylic acid azides[164,165].

An azene incapable of Curtius rearrangement is the ethoxycarbonyl derivative. Lwowski and Mattingly[166] have described the photolysis of ethyl azidoformate in cyclohexene which leads to an aziridine-*N*-carboxylic ester. Since a triazoline intermediate is rather improbable, possibly this case represents a true azene addition to the olefinic double bond. Thermolysis in cyclohexane gave about 50% of ethyl *N*-cyclohexylcarbamate. Hafner and König succeeded in adding ethoxycarbonylazene to benzene; they obtained 70% of the ring-enlarged *N*-ethoxycarbonylazepine[167]. Huisgen and Blaschke[167a] have observed a 1,3-addition of ethoxycarbonylazene to diphenylacetylene to give 33% 2-ethoxy-4,5-diphenyloxazole.



The simplest azene, NH, supposedly generated in the reaction of hydroxylamine-*O*-sulfonic acid with sodium methoxide in methanol, has been reported to give some pyrroline in its reaction with butadiene, but no 2-vinylethylenimine was found[168]. On the other hand, photolysis of hydrazoic acid in an argon matrix containing ethylene at 4°K has been shown to produce ethylenimine[169].

As a working hypothesis it may be proposed that the azenes are first liberated as singlet structures and then, perhaps even faster than carbenes, undergo a transition to the triplet state. The singlet azene may well be responsible for the formation of an azepine derivative from phenyl azide and of an azirine from α-styryl azide, while the CH insertion reaction and hydrogen abstraction from the solvent presumably are reflections of the biradical structure. The CH insertions by carbenes and by azenes apparently follow different mechanistic paths. It is a safe expectation that the reactions of azenes with alkenes will receive greater attention in the coming years.

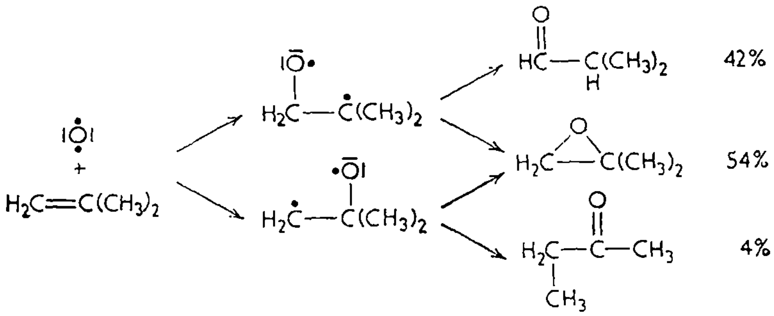
It should also be added that the ultraviolet irradiation of phenyl, *o*-trifluoromethylphenyl, and benzenesulfonyl azides dissolved in a polychlorotrifluoroethylene glass at 77°K produces the azene in a stable triplet state, as demonstrated by electron paramagnetic resonance[170]. However, photolysis of cyclohexyl and styryl azides or azidoformic ester produced no resonance signal.

C. Oxiranes from Oxygen Atoms and Alkenes

The reaction of ethylene with atmospheric oxygen on a silver catalyst at 230–240° and 50–100 atm pressure is used industrially for the production of ethylene oxide[171]. It might be supposed that either addition of an oxygen atom to the double bond or a redox reaction with silver oxide is involved; however, there is no experimental evidence to throw light on the reaction mechanism.

On the other hand, it is quite clear that the mercury-sensitized decomposition of nitrous oxide in an oxygen-free atmosphere produces oxygen atoms in the triplet ground state. Cvetanovic[172] allowed such oxygen atoms to react with olefins in the gas phase and isolated the products of oxygen addition as well as cleavage fragments. In the case of propylene, the adduct fraction consisted of about equal amounts of propylene oxide, propionaldehyde and acetone. As the gas pressure was increased the yield of the adduct fraction rose, reaching 60% at 700 Torr. It appears, therefore, that an energy-rich intermediate is formed which decomposes if it is not able to distribute its energy rapidly.

The case of isobutene is no less instructive; the yields given in the accompanying chart refer to the unfragmented products.



Evidently the addition of the biradical oxygen atom takes place predominantly at the less-substituted ethylenic carbon atom. The intermediate adduct (triplet state) stabilizes itself either by ring closure to the epoxide or by radical rearrangement in which a hydrogen atom or a methyl group migrates to the neighboring carbon atom.

Analysis of the products having fewer carbon atoms indicated fragmentation by a radical process. Just as with triplet carbenes, the addition of the oxygen atom is not stereospecific; *cis*-2-butene gives a mixture of *cis*- and *trans*-2-butene oxide.

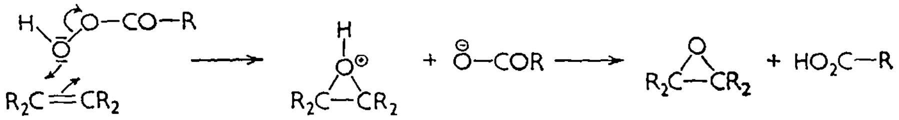
From ethylene itself no ethylene oxide could be obtained under these conditions; apparently removal of the heat of reaction is too difficult. Larger molecules are able to accommodate substantial amounts of energy, at least temporarily, in their vibrational and rotational degrees of freedom.

Competitive experiments of several olefins for the oxygen atom lead to conclusions concerning their relative reactivities[173]. The increased activity which results from the introduction of a methyl group at the olefinic bond shows that the radical-like oxygen atom is electrophilic. The limited data do not permit further conclusions.

TABLE 2. Reaction rate coefficients for the reactions of alkenes with the oxygen atom[173] and with peracetic acid (in acetic acid at 25·8°)[174].

Alkene	O atom k_2 (rel.)	CH_3CO_3H 10^3k_2
Ethylene	0·038	0·19
Propylene	0·23	4·2
trans-2-Butene	1·13	93
cis-2-Butene	0·84	
Isobutene	≡ 1·00	92
Trimethylethylene		1240
Tetramethylethylene	4·18	immeasurably fast
Cyclopentene	1·20	195
Styrene		46
1,1-Diphenylethylene		48

In Table 2 the relative activities toward the triplet oxygen atom are contrasted with the rate coefficients for the epoxidation of olefins by peracetic acid[174]. Peracids are hydroxyl cation donors. However, the HO^+ cation is no more free in solution reactions than the proton; it merely exchanges its bonding partner in a multi-center process. The stereoselective *cis* addition as well as the relatively low rate coefficient for styrene leave no doubt that the epoxidation of the alkenes with peracids does not begin with primary electrophilic attack, but rather is a multi-center addition. One can feel sure that the HO^+ cation with its electron sextet does not undergo a change in spin coupling in transferring to the alkene. However, in this case we are not dealing with a true cycloaddition, since in the course of the reaction the carboxylate ion is eliminated, or in other words, a σ bond is broken. It is also possible to represent the final proton transfer as part of the multi-center process[175].



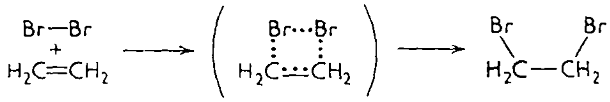
The comparison above shows that methyl substitution at the double bond increases the reactivity of the alkene to both the triplet oxygen atom and the donor of the singlet hydroxyl cation. The spread of the reactivities is smaller in the first case because the oxygen atom is the 'hotter' or less selective reagent. The parallel effects in the two series indicate that caution is necessary when correlating rate data with reaction mechanism or even with the electronic state of the reagent. It is to be expected that the two series will diverge in the cases of butadiene and styrene.

Kinetic measurements of the epoxidation of substituted *trans*-stilbenes with perbenzoic acid in benzene at 30° furnish a ρ value of $-1{\cdot}2$, a measure of the promoting effect of electron release to the alkene double bond[175]. As expected, the rate coefficients for substituted perbenzoic acids reacting with *trans*-stilbene increase with the strength of the related benzoic acid, in accordance with a ρ value of $+1{\cdot}4$.

D. The Addition of Halogens to Alkenes

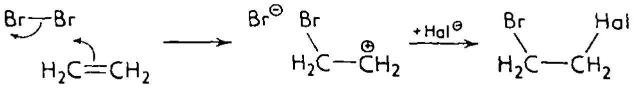
One of the longest recognized properties of alkenes is their ability to add halogens at the double bond. Here only a few mechanistic aspects will be considered briefly.

Over a hundred years ago in his textbook, Kekulé formulated the addition of bromine to a molecule of ethylene as involving a quasi four-membered ring:

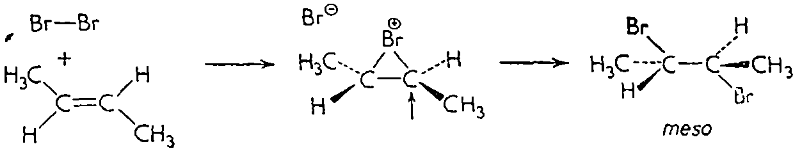


The succession of revisions on the mechanism of this formally simple addition reflects the historical development of our knowledge concerning elementary reaction mechanisms.

The addition of bromine to ethylene in sodium chloride solution yields besides ethylene dibromide some 1-bromo-2-chloroethane[176]. Similarly, the bromination of stilbene in methanol produces chiefly the methoxybromo derivative. Careful kinetic studies by Bartlett and Tarbell[177] showed that in these cases neither BrCl nor $BrOCH_3$ react with the olefin in a simple addition process. The attacking species must therefore, at least formally, be a bromine cation, which possibly is transferred from a polarized bromine molecule to the alkene carbon atom.



The occurrence of an open-chain carbonium ion in this mechanism would mean that rotation about the central C—C bond could take place. However, the addition of chlorine or bromine to *cis*- and *trans*-2-butene is highly stereoselective according to the *trans* principle. It would, in fact, be unlikely that an electron-deficient carbon atom could exist in the presence of the available electron pairs on the neighboring, covalently bonded halogen atom. The more probable cyclic bromonium ion structure was first postulated as an intermediate by Roberts and Kimball[178]. The nucleophilic attack of the bromide ion in the second step takes place from the opposite side of the molecule and thus involves a Walden inversion at the β-carbon.



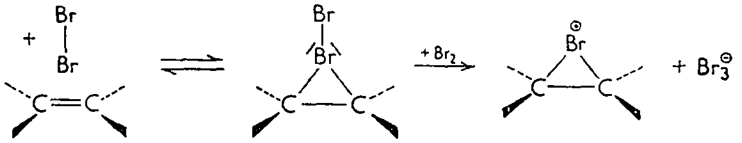
The formulation of the halogenonium ion as the first intermediate of the halogen addition offers a clue to the kinetic effects of substituents. Stabilization of the intermediate ion by hyperconjugative delocalization of the positive charge can result from alkyl substitution at either olefinic carbon. This accounts for the observed accelerating effect of methyl substituents; carboxyl groups adversely affect the stability of the ion and are retarding. Table 3 shows that a phenyl residue has a greater effect than *one* methyl but less than *two* methyl groups. Recollecting the discussion on p. 765, one learns here that the phenyl-carrying carbon atom bears a modest positive charge in the transition state but is still far from being properly represented as an open carbonium ion.

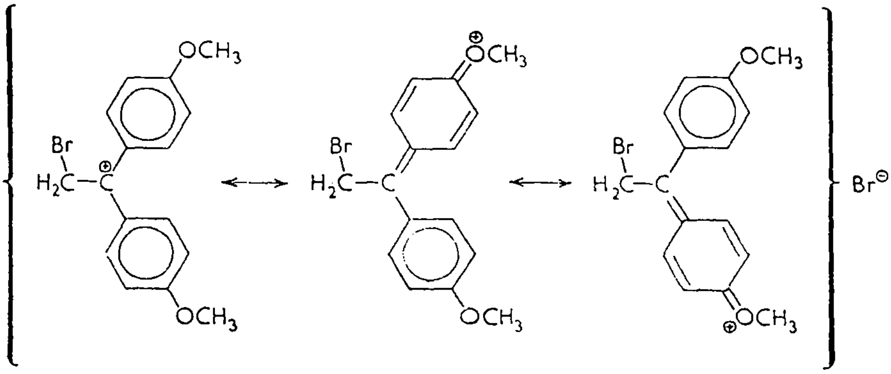
In contrast to chlorination, the addition rates of Br_2, I_2, ICl, BrCl, and IBr in acetic acid are second order with respect to the

TABLE 3. Reaction rate coefficients for the addition of chlorine to α,β-unsaturated carboxylic acids in acetic acid at 24°[179].

Carboxylic acid	k_2 (l./mole min)
$CH_2{=}CHCO_2H$	0·018
$CH_3CH{=}CHCO_2H$ (*trans*)	0·62
$(CH_3)_2C{=}CHCO_2H$	51
$C_6H_5CH{=}CHCO_2H$ (*trans*)	4·9

halogen[180]. There are several possible ways to visualize the role of the second molecule of halogen in the rate-determining step[179-181]. One unproved explanation deserving serious consideration is that the bromine addition in the primary step is a true cycloaddition of the bromine molecule. Following this addition equilibrium, the second bromine molecule acts as an acceptor of the bromide ion by forming the tribromide anion. The ring opening of the bromonium ion then takes place as described above. The reagents which show halogen addition of higher kinetic order possess a greater tendency than chlorine to expand their valence electron shell. According to the preceding scheme, an equilibrium constant and the rate coefficient of the step leading to the bromonium ion both enter the specific reaction rate. The expected substituent effects are again those discussed above. However, the role of the primary adduct could also be played by a π complex of the alkene and the halogen.





In limiting cases, incidentally, the three-center addition of the halogen can give way to a two-center process. In the bromination of 1,1-di-(*p*-anisyl)ethylene or 1,1-bis-(*p*-dimethylaminophenyl)ethylene a violet or deep blue cation, respectively, occurs which subsequently loses a proton[182]. Thus the result here is substitution rather than addition. The readiness of the methoxy or dimethylamino groups to accept the positive charge is responsible for this deviation from the usual primary mode of attack.

III. FOUR-MEMBERED RINGS

A. Thermal Additions of Alkenes to Form Cyclobutanes and Cyclobutenes

Ethylene and other simple alkenes are unable to undergo dimerization to form four-membered rings. Such a closure is a special property of certain classes of unsaturated compounds[183].

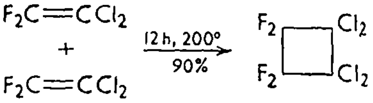
1. Polyfluorinated alkenes

Tetrafluoroethylene is metastable at room temperature. At as low as 200° smooth dimerization to octafluorocyclobutane takes place[184] (p. 742); the reverse reaction occurs above 500°. The activation energies for the forward and backward reactions (25·4 and 74·1 kcal) disclose that this dimerization is exothermic by about 50 kcal[185], while the hypothetical cyclodimerization of ethylene to cyclobutane should only result in the liberation of about 16 kcal. The polyfluorinated olefin evidently has a higher energy level than ethylene itself.

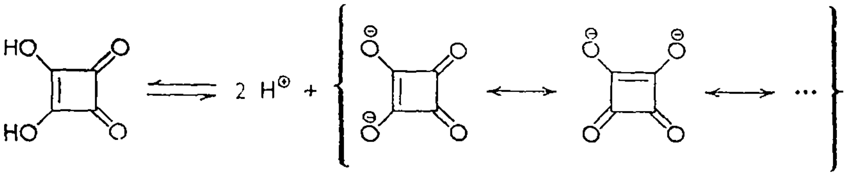
It is tempting to explain this behavior of polyfluorinated olefins as due to the repulsion forces between the fluorine atoms which are bound to the same carbon atom. A spreading of the F—C—F bond angle to greater than 109° should cause compression of the angles of the two remaining valences of the carbon atom; the Baeyer strain in the cyclobutane ring would then be diminished. However, structural analysis of such polyfluorinated compounds by electron diffraction does not support this hypothesis. Octafluoropropane has F—C—F bonds with the normal tetrahedral angle of 109·5°[186], while for tetrafluoroethylene the angle is 114°, even less than the 120° angle expected for sp^2 hybridized carbon[187].

The dimerization of trifluorochloroethylene takes place about five times slower than that of tetrafluoroethylene and gives exclusively

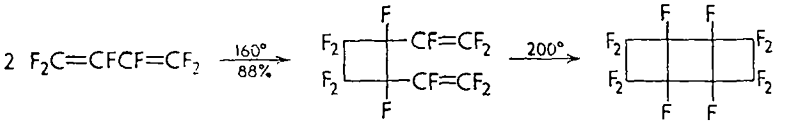
1,2-dichlorohexafluorocyclobutane; the *cis*- and *trans*-dichloro configurations occur in the ratio of 5 : 1 [188]. This head-to-head dimerization is frequently observed, for example, in the case of 1,1-dichloro-2,2-difluoroethylene[189], but it is not without exception. In the dimerization of perfluoropropene both possible dimer-types are obtained[190].



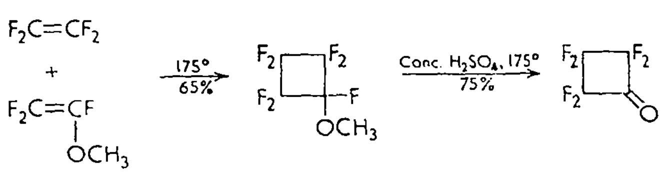
The easy access to the fluorinated cyclobutanes has greatly contributed in recent years to the development of the chemistry of four-membered ring compounds. For example, Park was able to convert the dichlorohexafluorocyclobutane above to 1,2-dihydroxycyclobutene-3,4-dione, whose p*K* value approaches that of sulfuric acid[191].



The especially reactive hexafluorobutadiene dimerizes in a head-to-head fashion to give a diene which at 200° isomerizes to a saturated compound[192]. Presumably the latter contains a condensed system of

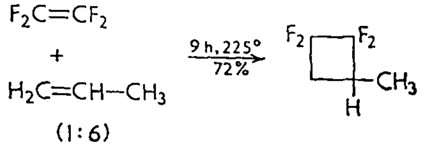


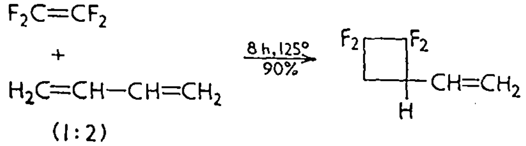
three cyclobutane rings. The second step represents the intramolecular variant of dimerization which is favored by a lower entropy but is expensive in terms of the strain in the tricyclo[2.0.0.2]octane system.



The codimerization of different fluoroalkenes can also be accomplished. The product from tetrafluoroethylene and trifluorovinyl methyl ether can be converted into perfluorocyclobutanone, whose carbonyl group exhibits an unusual capacity for addition reactions[193].

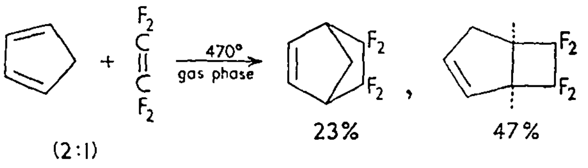
Still more noteworthy is the work of the research group at DuPont de Nemours on the mixed dimerization of polyfluorinated alkenes with olefinic hydrocarbons which do not themselves undergo dimerization[194]. With an excess of propylene, for example, it is easily possible to prepare the hydrogen- and fluorine-containing cyclobutane derivative the principal product. While the dimerization of tetrafluoroethylene has a useful rate only at 200°, the 1,2-addition of this compound to butadiene to give a cyclobutane derivative takes place readily at 120°.



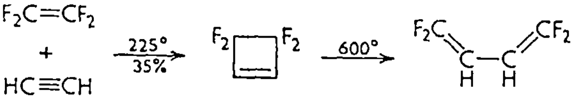


This phenomenon is all the more significant since the reaction enthalpy in the case of butadiene must be smaller than with ethylene; in the course of the cycloaddition the conjugation energy of the diene is lost. The question of why additions to conjugated systems pass over a lower activation-energy barrier will be considered further on page 782.

In this connection, particular notice should be given to the fact that only the cycloaddition to the four-membered ring occurs and not the Diels–Alder reaction leading to a cyclohexene derivative. The case of cyclopentadiene is less clearcut since here both possible modes of reaction are observed. The major product, incidentally, has been used as the basis for an effective synthesis of tropolone[195].

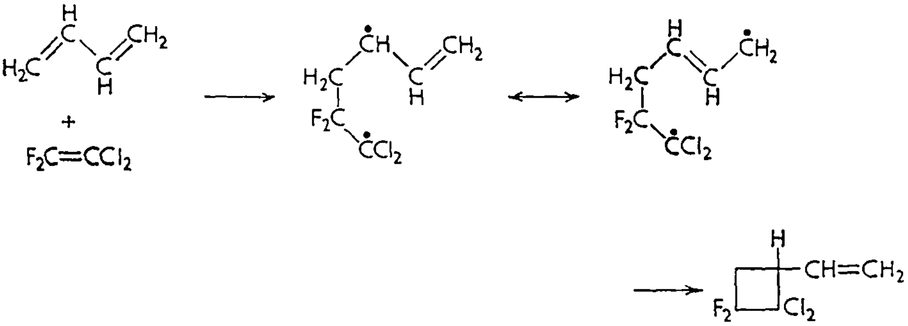


It is not surprising that styrene and vinylacetylene also give adducts with tetrafluoroethylene; in the latter case, the double and triple bonds display about the same reactivity. Cycloaddition to acetylene itself can also be accomplished; at higher temperatures ring opening of the 3,3,4,4-tetrafluorocyclobutene is observed[196].

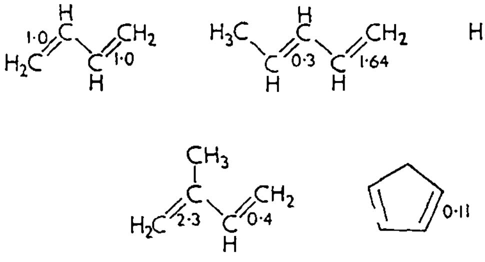


The union of 1,1-dichloro-2,2-difluoroethylene and phenylacetylene takes place at 130° giving exclusively 1-phenyl-3,3-difluoro-4,4-dichlorocyclobutene in 71% yield[197].

The suggestion was made several years ago that the dimerization of tetrafluoroethylene occurs in two stages, the first of which produces a diradical[198]. Recent work and theoretical considerations support this view. The high rate of addition of tetrafluoroethylene to butadiene (p. 781) could be related to the resonance stabilization of the substituted allyl radical obtained. The head-to-head dimerization of 1,1-dichloro-2,2-difluoroethylene and the orientation observed in the 'mixed' cyclobutane formations require that a lower energy level be ascribed to the polychloroalkyl than to the polyfluoroalkyl radical. The comparatively higher selectivity of chlorinated alkyl radicals has been recognized and thus is in line with this interpretation.



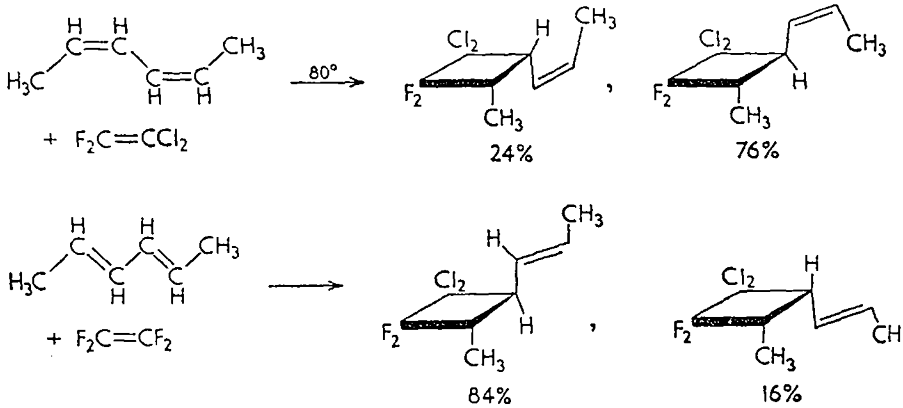
Partial rate factors :



Convincing arguments for this mechanism have been presented recently by Bartlett and Montgomery[199]. 1,1-Dichloro-2,2-difluoroethylene adds exclusively in one direction to butadiene. By a combination of kinetic measurements and product analyses, it was possible to obtain partial rate factors for the addition of this perhaloethylene to the three methylbutadienes. The result is that in both *cis*- and *trans*-1-methylbutadienes the unmethylated double bond is more reactive while in 2-methylbutadiene the opposite is true. This provides an excellent explanation for the stabilization of the allyl radicals by methyl substitution in the α- or γ-position.

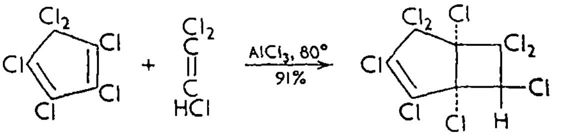
The two odd electrons need not lose their spin coupling in the short-lived intermediate diradical; the transition to the triplet state is forbidden and hence slow. The closure of the diradical to a four-membered rather than a six-membered ring might be explained in terms of the activation entropy.

The original olefinic double bonds have become single bonds in the intermediate and rotation is impeded by only low energy barriers. In agreement with expectation, Bartlett and Montgomery[199] observed the additions to be non-stereoselective. The union of dichlorodifluoroethylene with *cis-cis*- and *trans-trans*-hexa-2,4-diene gave diastereoisomeric pairs in which only the double bonds not involved in cycloaddition retained their configuration. From *cis-trans*-hexa-2,4-diene all four possible diastereoisomers were actually produced. The yields given in the chart below are percentage distributions of the total adduct obtained.



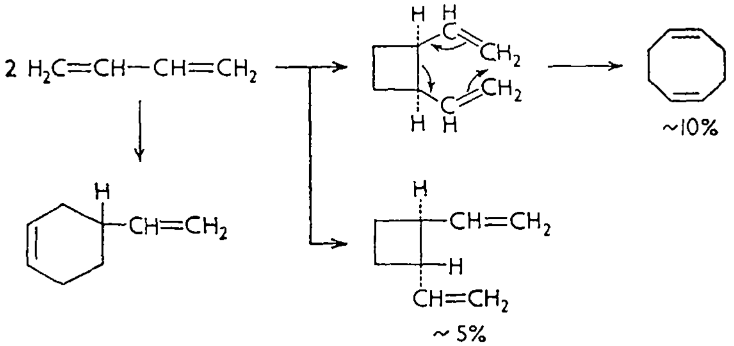
Polychloroalkenes show no tendency to undergo thermal cycloaddition, probably because of the greater double bond strength of the ground state compared to the polyfluoroalkenes. Hexachlorocyclopentadiene can be dimerized as mentioned earlier (p. 744) and also enters a number of addition reactions with chlorinated olefins[200,201].

However, here thermal reactions are not involved; the role of the aluminum chloride catalyst has not been clarified.



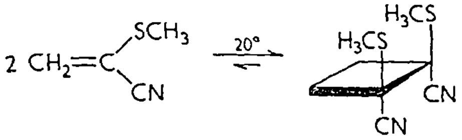
2. Conjugated alkenes

If butadiene is heated to 150–250° in the presence of polymerization inhibitors, the Diels–Alder reaction leading to 4-vinylcyclohexene predominates. As by-products, about 10% of *cis-cis*-cycloocta-1,5-diene[202] and 5% of *trans*-1,2-divinylcyclobutane[203] are obtained. Presumably, three different types of cycloaddition reactions are not actually involved here. Vogel pointed out that *cis*-1,2-divinylcyclobutane as it is formed immediately undergoes a so-called Cope rearrangement to the doubly unsaturated eight-membered ring[204]. Probably the primary dimerizations of butadiene are limited to the formation of four- and six-membered rings.

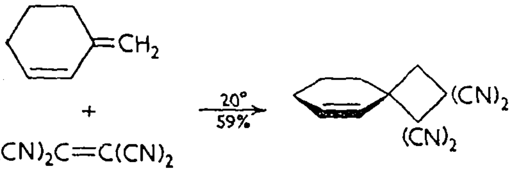


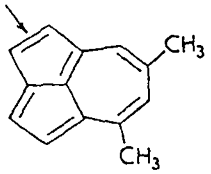
Here also one can imagine a diradical intermediate being formed by 1,1-coupling of two butadiene molecules. While ethylene does not dimerize, butadiene enters a head-to-head dimerization even though the resonance energy of two diene molecules has to be sacrificed. This loss of about 6 kcal is slight, however, compared to the gain in the intermediate of about 50 kcal, twice the resonance energy of an allyl radical[205].

Acrylonitrile dimerizes at 200–300° to give a mixture of *cis*- and *trans*- 1,2-dicyanocyclobutane to the extent of 5%[206]. Again the orientation may be controlled by the stabilization of the intermediate diradical, this time by the two nitrile groups. A thioether group in the α-position so effectively promotes the dimerization of the substituted acrylonitrile that even at room temperature in alcohol an equilibrium is established, which lies well on the side of the four-membered ring. On vacuum distillation at 140° the monomer is recovered[207].

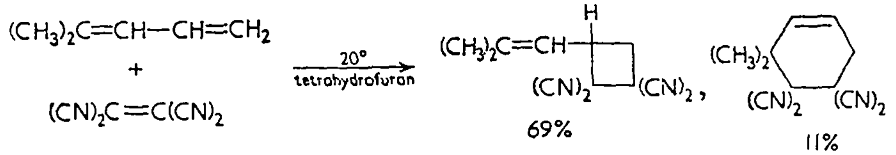


Tetracyanoethylene combines with dienes exceptionally easily to form Diels–Alder adducts (p. 921). If this reaction is hindered by a *transoid* structure in the 1,3-diene, then the closure of a four-membered ring can be achieved; the case of methylenecyclohexene[208] is illustrated below. With 3,4-dimethylene-1,2-diphenylcyclobutene the system avoids the Diels–Alder reaction which would form a cyclobutadiene structure by closing instead a new cyclobutane ring[208]. The cycloaddition of tetracyanoethylene with a tricyclic pentalene derivative leads to a derivative of azulene[209].

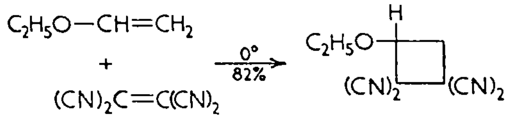




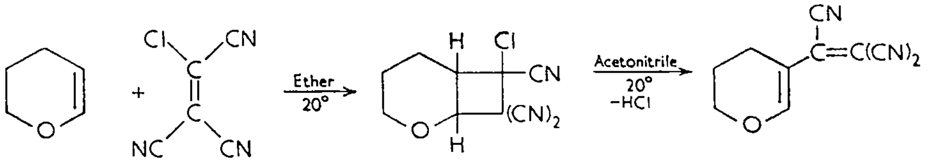
With 1,1-dimethylbutadiene the Diels–Alder reaction is sterically impeded. Although the reaction with tetracyanoethylene in tetrahydrofuran still produces a low yield of the Diels–Alder adduct, in nitromethane solution the cyclobutane derivative is formed exclusively[210]. Apparently only the 2 + 2 → 4 type of cycloaddition profits from the strong accelerating influence of the more polar solvent.



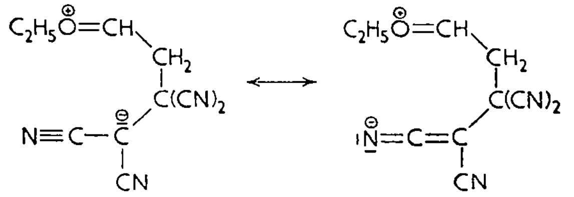
Besides the 1,3-dienes, the electron-rich double bonds of vinyl ethers, vinyl thioethers and enamines combine exceptionally easily with tetracyanoethylene to form cyclobutane derivatives, as Williams, Wiley and McKusick have recently reported[211]. Even at 0–30°, the deep colors of the π complexes with ethyl vinyl ether, dihydropyran or *p*-methoxystyrene fade rapidly; the adducts are obtained in yields of 81%, 94% and 93%, respectively. *N*-Vinylpyrrolidone (90% adduct) and *N*-vinyl-*N*-methylbenzenesulfonamide (94%) serve to illustrate the *N*-conjugated alkenes investigated.



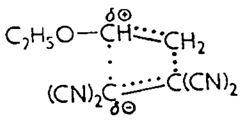
The analogous reactions with tricyanoethylene and tricyanovinyl chloride are somewhat slower. Actually the latter does not give cyclobutene derivatives with vinyl ethers or enamines but rather products in which a hydrogen at the double bond is replaced by the tricyanovinyl residue. The isolation of a cyclic intermediate in the case of dihydropyran suggests that in these reactions a cycloaddition always occurs as the initial step.



Although in all cases of cyclobutane formation from tetracyanoethylene and 1,3-dienes a diradical intermediate may still be involved, another mechanistic picture for the addition to the electron-rich alkenes is advocated. The surprisingly large dependence upon the solvent polarity is significant. Provisional kinetic measurements[211]



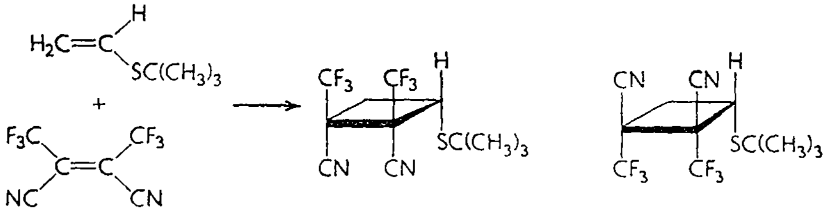
(1)



(2)

indicate that the relative rate coefficients for the reaction of *p*-methoxystyrene with tricyanovinyl chloride in acetonitrile, ether and cyclohexane are in the ratios 200:80:1. In view of such a solvent effect one is inclined to think of the formation of an exceptionally resonance-stabilized zwitterionic intermediate in the rate-determining step; for example, the structure **1** for the reaction with ethyl vinyl ether.

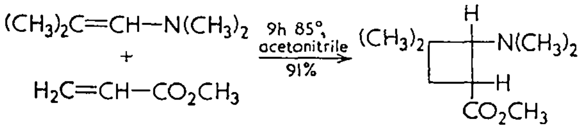
One would expect that the open-chain zwitterion **1** should be able to rotate about both of the original double bonds. However, this concept must be abandoned in consideration of recent evidence that such cycloadditions are stereoselectively *cis*[212]. The geometric isomers of 1,2-bistrifluoromethyl-1,2-dicyanoethylene are converted with vinyl *t*-butyl sulfide into the expected pairs of diastereoisomeric cyclobutanes without contamination from isomerization products. Furthermore, the addition of tetracyanoethylene to *cis*- and *trans*-propenyl propyl ether is distinctly *cis*. This stereospecificity is not even disturbed in such a polar solvent as methanol.



Electrostatic attraction in an intermediate such as **1** could fix the configuration so strongly that rotation about the bonds in question is blocked. Since such an electrostatic bonding force must be assumed to be significant at the start of the activation process, in order to guarantee the stereoselectivity of the addition, this would amount to a multi-center addition reaction. The transition state **2**—the different lengths of the two new bonds indicate their different bond energy—corresponds in essence to that drawn on page 765 for the addition of dichlorocarbene; here a greater charge separation is anticipated. From an entropy point of view, **2** is less favorable than the open-chain, freely mobile zwitterion, **1**; **2** would, however, have substantially greater bond energy. If one expresses **2** in the symbolism of the valence-bond method, besides the canonical forms of the starting materials and products the configurationally fixed dipolar structures related to **1** contribute to a substantial degree as hyperconjugated forms.

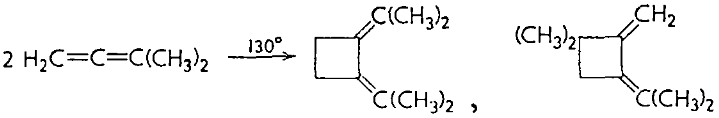
The question as to whether the multi-center addition *via* **2** goes through an intermediate or has a single-peak energy profile must remain open for the time being. One might imagine an intermediate in which the charge centers are bound as in an 'intimate ion pair'[213]. It must be remembered, however, that such ion pairs are capable of configurational changes, which often demonstrate their existence as discrete intermediates. Therefore, as long as exclusive *cis* addition is observed in polar solvents, no basis exists for assuming a dip in the energy profile of the cycloadditions under discussion.

It should also be mentioned that extremely electron-depleted double bonds such as those found in tri- and tetracyanoethylenes are not necessary prerequisites for cycloadditions to enamines. Even methyl acrylate, diethyl maleate, methyl vinyl sulfone or β-nitrostyrene are suitable[214].



3. Cumulated double bonds

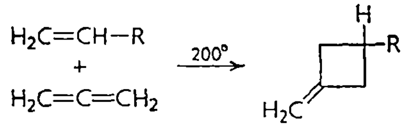
The tendency of *allenes* to dimerize was recognized over 50 years ago by Lebedew. Allene itself is converted into 1,2-dimethylenecyclobutane to a small extent when heated to 150°; in a flow process at 500°, a 50% yield can be obtained[215]. Following a recent report, this dimer is composed of 1,2- and 1,3-dimethylenecyclobutane in a 3 : 1 ratio[215a]. 1,1- and 1,3-Dimethylallene as well as tri- and tetramethylallene also undergo head-to-head dimerization at 130–150°[216]. As a final example, tetrachloroallene can be isolated only with special precautions; at room temperature it dimerizes to perchloro-1,2-dimethylenecyclobutane[217,218].



Under the catalytic influence of bis(triphenylphosphite)nickel dicarbonyl at 100°, allene undergoes an interesting tri- and tetramerization which yields 28% 1,2,4- and 7% 1,3,5-trimethylenecyclohexane as well as 6% 1,3,5,7-tetramethylenecyclooctane (p. 749)[219].

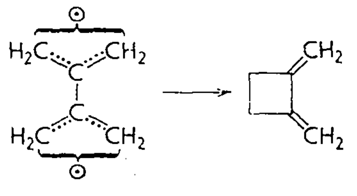
The heats of hydrogenation of allene (71 kcal) and of propylene (30 kcal)[220] leave no doubt that the cumulated bond system of allene has a higher energy than a system with two isolated double bonds. Consequently, cycloadditions with allene are thermodynamically favored.

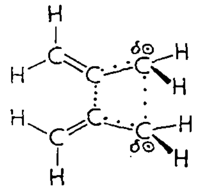
Allene not only dimerizes but also reacts at 200° with a wide variety of α,β-unsaturated carboxylic acids, esters, aldehydes, and nitriles, as well as with phenyl-conjugated alkenes to form 3-substituted 1-methylenecyclobutanes[221]. In analogous cycloadditions, 1,1-difluoroallene furnishes 3-substituted 2,2-difluoro-1-methylenecyclobutanes[221a].



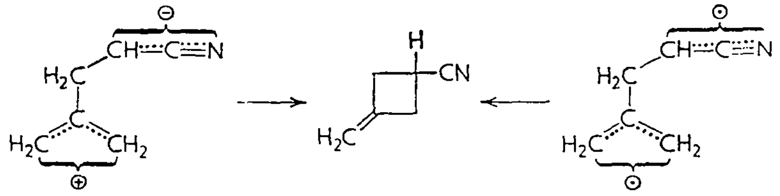
R =	yield
CO_2CH_3	25% yield
CN	60%
C_6H_5	22%

We have discussed above two alternative mechanisms for the closure of four-membered rings by cycloaddition. Where is the dividing line between them? The orientation observed in the dimerization of allene indicates the formation of the 2,2'-coupled diradical intermediate **3** stabilized by twofold allyl resonance. A multi-center process is less probable because allyl resonance, whether as radical, cation or anion, would be sterically impossible in structures contributing to a transition state like **4**.

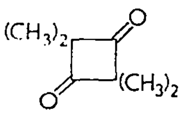

(**3**)


(**4**)

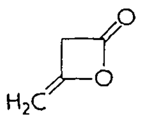
The same orienting forces direct the reaction with styrene or acrylonitrile to the respective 3-substituted methylenecyclobutanes. Here also a primary two-center addition giving a diradical or zwitterionic intermediate would be preferred, since this would be stabilized by allyl resonance.



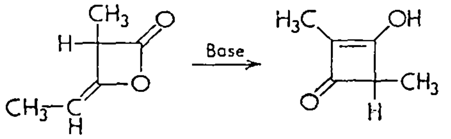
The discoverer of the ketenes, Staudinger, observed not only the notorious tendency of these compounds to dimerize but also their ability to combine with alkenes to form cyclobutane derivatives. The dimerization can follow either of two paths, one leading to cyclobutane-1,3-diones (*e.g.* **5**), the other to γ-methylene-β-lactones (*e.g.* **6**). In the case of ketoketenes the formation of the carbocyclic ring takes precedence. However, the parent compound, ketene, gives γ-methylene-β-propiolactone (**6**), and the aldoketenes generally furnish both types of dimers[222]. The ketene dimers can be dissociated to the monomers at an incandescent wire.



(**5**)

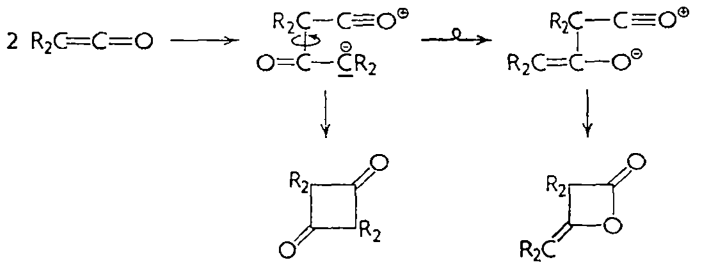


(**6**)



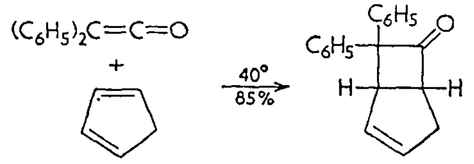
(**7**) (**8**)

With methylketene one obtains both the β-lactone **7** and the cyclobutane-1,3-dione **8**. The latter is in fact an enol and a relatively strong acid. As indicated in the chart above, it is possible to rearrange the β-lactone to the enolate anion of the carbocyclic isomer **8** by base[223]. Conversely, tetramethylcyclobutane-1,3-dione is isomerized by aluminum chloride at 150° to the β-lactone in 87% yield[224]. Since each of these inverse processes requires the breaking of *one* carbon–carbon bond only, it is possible that the spontaneous dimerization of ketenes goes through an analogous intermediate stage in which the two units are connected by one bond.

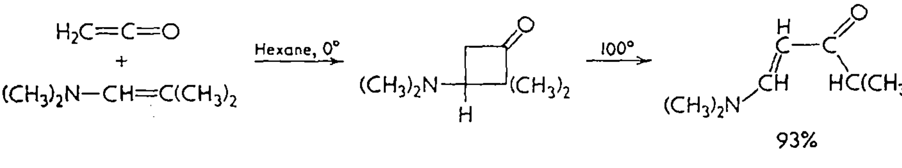


The exceptional stabilization of such an intermediate with the formal charges localized on the oxygen atoms makes this reaction path attractive, but not necessary. The zwitterionic intermediate was no less plausible in the case of the addition of tetracyanoethylene to vinyl ethers, yet there the stereospecific course (p. 787) substantiated the four-center mechanism. Unfortunately, in the ketene dimerization the stereochemical criterion is not applicable; neither is there information available on the solvent dependence of the reaction.

In the dimerization reaction, the addition of the carbon–carbon double bond of one ketene molecule to that of another gives a cyclobutanedione; addition to the carbon–oxygen double bond yields the β-lactone. Both types of reaction can also be realized with alkenes and aldehydes as second components. The addition of diphenylketene to styrene (60% yield), ethyl vinyl ether (80%), cyclohexene (60%), cyclopentadiene (85%), and other olefins takes place at 40–60° to give products of a single orientation[225,226]. The contribution of zwitterionic structures to the transition state appears to control the direction of addition in all cases. Nevertheless, the cycloadditions of dimethylketene and diphenylketene to *cis*- and *trans*-propenyl propyl ether proceed stereospecifically[227].

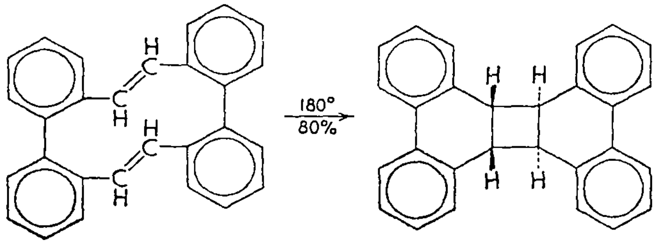


The limited number of investigations on the addition of simple ketenes to alkenes do not yet permit a clear decision as to whether or not ketene dimerization occurs as a serious side-reaction. However, the adducts of ketene and its *t*-butyl derivative with cyclopentadiene were obtained in only 34% and 22% yields, respectively[228,229]. On the other hand, the interaction of ketene or dimethylketene with enamines takes place smoothly and completely as has recently been demonstrated by three independent groups[230–232].

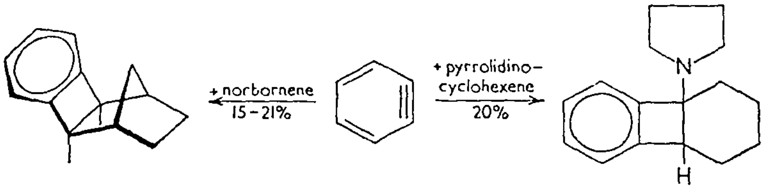


4. Strained multiple bonds and cyclobutadienes

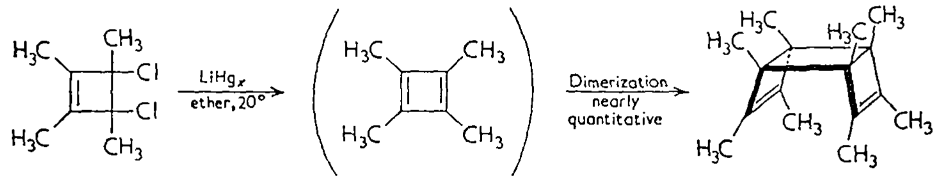
The incorporation of a *trans* double bond in an eight-membered ring leads to considerable angle strain, amounting in *trans*-cyclooctene to 9 kcal. The 1,5-cyclooctadiene, obtained by degradation of the alkaloid pseudopelletierine, has recently been shown to have the strained *cis-trans* configuration[233]; on storage at room temperature, it is converted into a crystalline dimer[40] (p. 751). In *trans-trans*-tetrabenzocyclodecahexaene the closure of a cyclobutane ring is probably promoted by the juxtaposition of the olefinic double bonds[234]; above 240° the polycyclic system breaks into two molecules of phenanthrene.



Benzyne can be regarded as an acetylenic system which suffers from severe angle strain[235] and thus displays an uncommon capacity for addition reactions. Besides dimerization to form biphenylene, which is attained in 24% yield in the treatment of *o*-fluorobromobenzene with lithium amalgam[236], addition reactions with norbornene, norbornadiene[237] and pyrrolidinocyclohexene[238] have also been described.

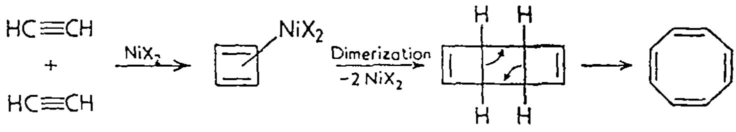


The possible aromatic character of cyclobutadiene is an old theoretical problem. Criegee and Louis succeeded in dehalogenating 3,4-dichloro-1,2,3,4-tetramethylcyclobutene[239]; instead of the cyclobutadiene derivative they obtained its dimer, the permethylated tricyclo[2.0.0.2]octadiene, in which the two outside four-membered rings are in a *syn* configuration. The violet π complex of the monomer



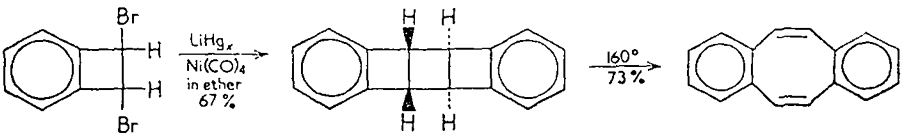
with $NiCl_2$ is stable[240]. Whether or not the tendency of the cyclobutadiene derivative to dimerize stems from a triplet ground state, which molecular-orbital theory has predicted, or merely from high strain in the double bond is a question that cannot yet be answered.

The nickel complex mentioned is transformed in boiling water to the *anti*-fused stereoisomer of octamethyltricyclo[2.0.0.2]octadiene in 65% yield[241]. Thermal decomposition of the nickel complex at 185° gives octamethylcyclooctatetraene among other products. The theoretical predictions that cyclobutadiene would be stabilizable by complex formation with transition metals and that it occurs as an intermediate in the cyclooctatetraene synthesis of Reppe[242] as depicted below, have thus found experimental confirmation. This mode of formation of cyclooctatetraene includes two cycloadditions of the $2 + 2 \rightarrow 4$ type. However, an alternative reaction path for the Reppe process has recently been proposed[242a].

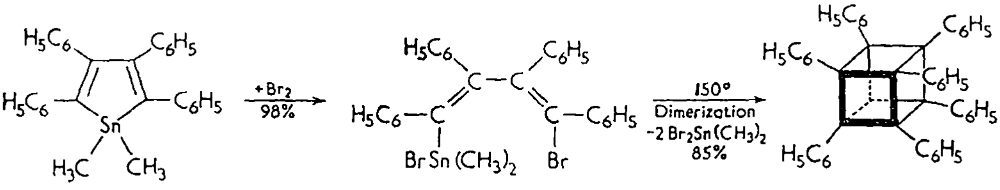


Also the formation of *syn*-tricyclo[2.0.0.2]octadiene from 1,2,3,4-tetrabromocyclobutane by lithium amalgam[243] is pertinent in this connection. The tricyclic diene yields a silver complex which is not derived from cyclobutadiene as originally alleged, but instead is silver cyclooctatetraene[243a].

Dimerization to tricyclo[2.0.0.2]octadienes appears also to be the fate of 1,3-diphenylcyclobutadiene[244] and 1,2,3-triphenyl-4-fluorocyclobutadiene[245]. In the latter case, the dimer was shown to have the *anti* configuration[246]. Nenitzescu and colleagues generated benzocyclobutadiene from its dibromide in the presence of nickel carbonyl[247] and obtained the *anti*-oriented[248] tricyclooctadiene derivative, which isomerized on heating to 1,2,5,6-dibenzocyclooctatetraene. 1,2-Diphenylnaphtho[*b*]cyclobutadiene has been isolated recently as red needles[248a].

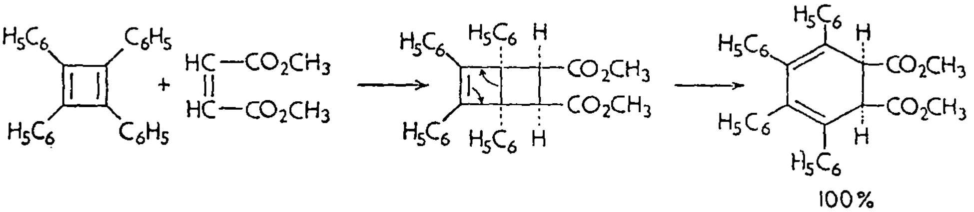


Stable complexes of tetraphenylcyclobutadiene with iron carbonyl [249], palladium chloride[250,251] and nickel bromide[252] are also known. Free tetraphenylcyclobutadiene prepared in various ways dimerizes at once. By way of an unsaturated intermediate, a product melting at 430° is formed to which Freedman and Petersen[253] assign the interesting octaphenylcubane structure (**9**). Here we face a noteworthy double cycloaddition.



(**9**)

The generation of tetraphenylcyclobutadiene at 150° in dimethyl acetylenedicarboxylate or maleate leads to the 3,4,5,6-tetraphenylphthalate or its 1,2-*cis*-dihydro derivative, respectively[252]. Here, too, primary cycloadditions of the type 2 + 2 → 4 are plausible. The reaction is stereospecific, as is shown by the formation of diastereomeric products from the maleic and fumaric esters. Tetramethylcyclobutadiene can react similarly with double or triple bonds to give six-membered rings[254,255].



In view of the extraordinary level of current interest, one can probably expect rapid development and consolidation of the chemistry of cyclobutadiene. However, all the evidence for the occurrence of mononuclear derivatives of cyclobutadiene is of an indirect nature, and can only be considered satisfactory if other available interpretations have been excluded. In a recent critical discussion of the possible formation of free tetramethylcyclobutadiene as an intermediate, Criegee arrived at a cautious rejection of the hypothesis[255].

B. Photochemical Formation of Cyclobutanes and Cyclobutenes

Good reviews which have appeared during the last decade[256,257] permit us to limit this discussion to a few characteristic examples. Emphasis will be given to the work of recent years.

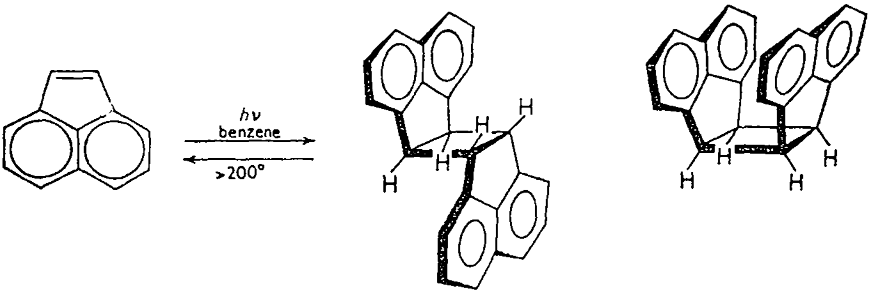
In the early period of preparative photochemistry, sunlight was used exclusively. It is not surprising, therefore, that the beginnings of this branch of chemistry date back to the sunny lands of Italy and Egypt.

Today immersion lamps and irradiation apparatus are on the market which will deliver light in various regions of the spectrum to suit special purposes. This equipment makes the chemist independent of the sun and weather and has given the development of photochemistry a strong impetus.

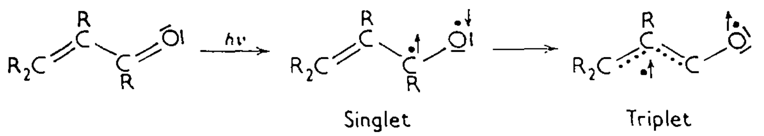
1. Photodimerization of alkenes

The formation of four-membered rings through irradiation of olefins, particularly α,β-unsaturated carbonyl compounds, is one of the oldest photoreactions of organic chemistry. The practical use of such dimerizations depends not only upon the lifetime of the photoexcited state but also on the availability of a sufficiently large amount of light energy in the specific absorption band of the unsaturated compound. Photoadditions of this type are not chain reactions.

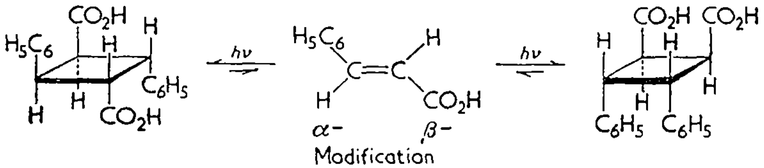
Probably, the predominance of the conjugated alkenes in this field is chiefly a reflection of their high ultraviolet extinction at long wavelengths. Although stilbene itself undergoes only slight transformation to tetraphenylcyclobutane in the course of irradiation for two years[258], the dimerization of acenaphthylene is more facile[259]. In the two stereoisomers obtained, the five-membered rings are arranged in *syn* or *anti* configuration at the newly formed cyclobutane ring. It is presumed that the photoexcitation must take place in an associated complex of two molecules in order to be effective[260].



α,β-Unsaturated carbonyl compounds offer much more favorable circumstances for the photoreaction. By absorption of a light quantum, the bond system of the carbonyl group attains an excited singlet state which then degenerates with loss of energy to the lowest triplet state. One may suppose that this triplet state, in which one unpaired electron participates in allylic resonance, then attacks a nearby olefinic double bond and brings about cyclobutane formation.

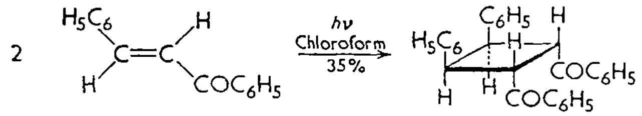


The establishment of the photochemical equilibrium between the *crystalline* cinnamic acids and their stereoisomeric cyclodimers is a classic illustration of this reaction type, whose exploration is due to Liebermann, Stoermer and Stobbe[256]. In *solutions* of cinnamic acid, ultraviolet light merely causes an equilibration between the *cis* and *trans* isomers. The orientation of the cycloaddition reaction depends mainly upon the arrangement of the building blocks in the crystal lattice. The crystallographically different α- and β-forms of *trans*-cinnamic acid give α-truxillic acid (**10**) and β-truxinic acid (**11**) respectively, by head-to-tail and head-to-head dimerization[261].



(10) **(11)**

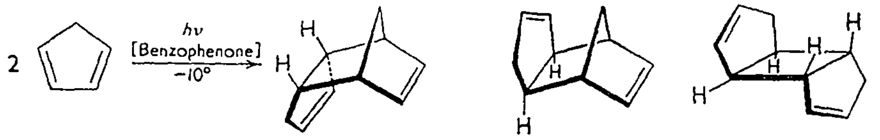
Numerous ultraviolet-induced dimerizations of α,β-unsaturated acids, esters, nitriles and ketones, as well as quinones, fit into the same pattern. In the case of fumaronitrile it has been proved that the direction of addition reflects the orientation of the molecules in the crystal[262]. Mechanistic conclusions, however, may only be drawn from the orientation data on photochemical dimerizations *in solution*. Benzalacetophenone[263], dibenzalacetone[264] and benzalpyruvic acid[265] undergo a head-to-head dimerization under such conditions. If one ascribes an active role to the triplet state, then β,β'-coupling permits optimum resonance in the allyl radicals involved; head-to-head dimerization must then result.



To be sure, this rule is occasionally broken. Irradiation of cyclopenten-3-one with ultraviolet light gives comparable amounts of the head-to-head and head-to-tail dimers, both with *anti* configuration of the cyclopentanone rings[266]. Possibly another mechanism comes into play in this case. Cinnamalbenzyl cyanide yields exclusively a dimer of the truxillic acid type[267].

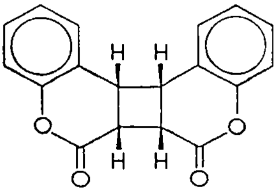
The carbonyl group absorbs the light energy and transfers it to the carbon–carbon double bond; one can consider the carbonyl a built-in photosensitizer. The sensitizer need not, however, be part of the alkene molecule. Thus, the dye Bengal Rose is able to act as a sensitizer for the dimerization of acenaphthylene (p. 795) at a wavelength (590 $m\mu$), which does not cause direct photodimerization[268]. Apparently the triplet state sensitizer is able to transfer its energy to the alkene through collision and thereby excite the π-electron system of the latter to the lowest triplet state. The diastereomeric bis-acenaphthylenes are obtained in the same ratio as in the normal photoreaction.

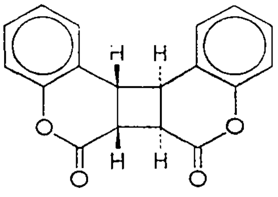
Sensitization in this manner greatly extends the usefulness of the alkene photodimerization. Hammond, Turro and Liu observed that when benzophenone or other ketones were used as sensitizers a dimerization of cyclopentadiene resulted which differed from the thermal Diels–Alder reaction[269]. In addition to *endo*-dicyclopentadiene equal amounts of the *exo* isomer and of *trans*-tricyclo[3.0.0.3] deca-2,8-diene were also obtained. Thermal and photosensitized dimerizations also follow different paths in the cases of butadiene and isoprene[270,271].

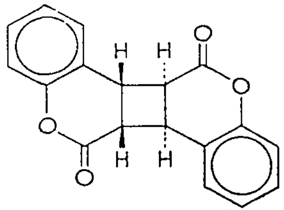


An indication that photodimerization and photosensitized dimerization need not inevitably occur by the same mechanism is found in the behavior of coumarin. On irradiation in water or alcohol the *cis* head-to-head dimer is obtained[257,272]. However, from the β-carotene or benzophenone photosensitized reaction, Schenck, Wilucki and Krauch isolated the *trans* head-to-head dimer in addition to some of the *trans* head-to-tail isomer[273]; a complex of the photo-activated sensitizer with the coumarin is presumed to be an intermediate.

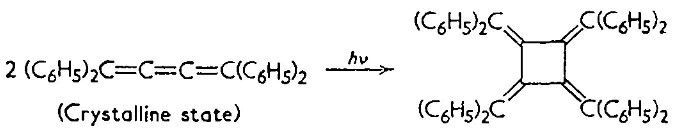
The mercury-photosensitized formation of small amounts of cyclobutane from ethylene has recently been described by Chesick[273a].


cis head-to-head


trans head-to-head


trans head-to-tail

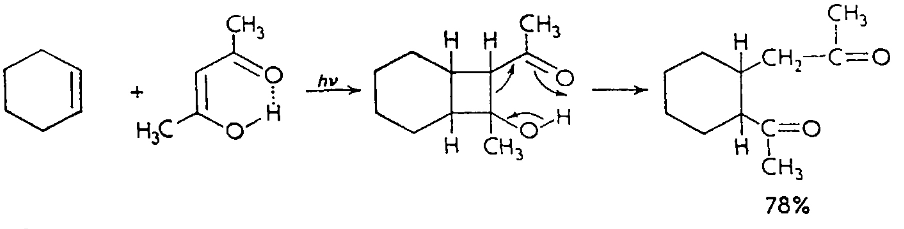
Another noteworthy photodimerization may be cited in conclusion: that of 1,1,4,4-tetraphenylbutatriene in sunlight. It was recently shown that here coupling of two molecules of the cumulene occurs at the central double bond, leading to the formation of perphenylated tetramethylenecyclobutane[274].



2. Reactions of photoactivated alkenes with other alkenes or aromatic nuclei

In the dimerizations discussed it is very probable that only *one* molecule of the monomer need be photoexcited; the second is brought into the reaction 'cold'. There is no obvious reason why both roles should be played by molecules of the same compound. Only very recently 'mixed' photodimerizations have become known.

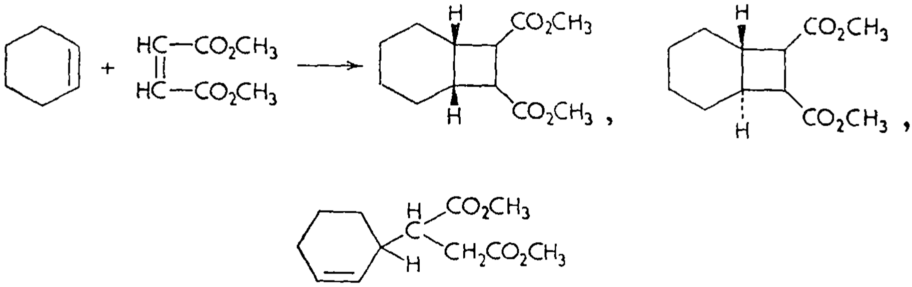
By ultraviolet irradiation of a solution of cyclopenten-3-one in cyclopentene, Eaton[266] obtained 67% of the 'mixed cyclobutane' with the five-membered rings in a *trans* configuration. The formation of 1,5-diketones in the irradiation of acetylacetone with cyclopentene, cyclohexene or 1-octene involves a subsequent opening of the initially formed carbocyclic four-membered rings and provides a valuable practical application[275].



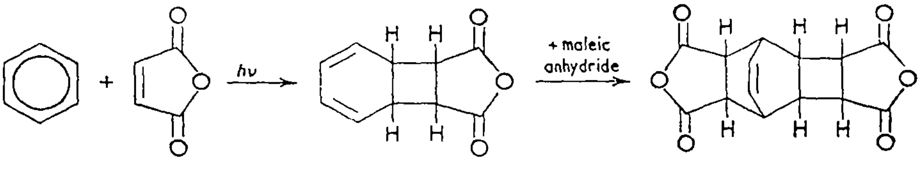
Furan adds dimethylmaleic anhydride at the 2,3-position under benzophenone-sensitized irradiation with closure of a four-membered ring according to Schenck[276], while under the conditions of the thermal Diels–Alder reaction dienophiles add to the 2,5-positions to form 1,4-endoxo compounds. The quantum yield is 0·18; the non-sensitized reaction gives the same product but with lower efficiency.

Cyclohexene, tetramethylethylene and trichloroethylene, but not tetrachloroethylene, also have the faculty of accepting photosensitized dimethylmaleic anhydride. The single cyclobutanes formed in good yields are regarded as *cis* adducts; *cis*- and *trans*-1,2-dichloroethylene give rise to diastereomeric adducts[277].

Interestingly enough, the irradiation of dimethyl maleate in cyclohexene produces four stereoisomeric cyclobutane derivatives besides dimethyl cyclohex-3-enylsuccinate[278]. Structures with *cis* fusion of the carbocyclic rings have been assigned to two of the cycloadducts while the remaining two are suggested to be *trans* fused. The product of the *trans* fusion is angle-strained to an unusual extent. Moreover, the *trans* addition to form an energetically unfavorable product poses a difficult mechanistic question. Analogous *cis*- and *trans*-fused structures have been proposed[279] for the photoproducts from cyclohexene and maleic anhydride.

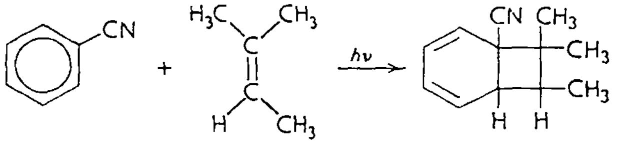


By ultraviolet irradiation of a benzene solution of maleic anhydride, Angus and Bryce-Smith, were able to obtain a small yield of a 1:2 adduct[280]. In this case photocycloaddition involves a loss of aromatic resonance. The Diels–Alder addition of a second molecule of maleic anhydride follows in a subsequent step.



In the presence of benzophenone as photosensitizer, the yield of the same adduct increases to 12% if ultraviolet light is used[281]; surprisingly, sunlight is more efficient and produces 93% of the bisadduct[282]. Toluene, *o*-xylene and chlorobenzene give analogous 1:2 adducts[281], while phenanthrene, as might be anticipated, furnishes a mono-adduct[283]. Oxygen causes no disturbance of the non-sensitized reaction; this leads to the conclusion that an excited singlet state might be responsible for the ring closure within the charge-transfer complex from the hydrocarbon and maleic anhydride[284]. On the other hand, oxygen inhibits the benzophenone-sensitized addition of maleic anhydride to benzene.

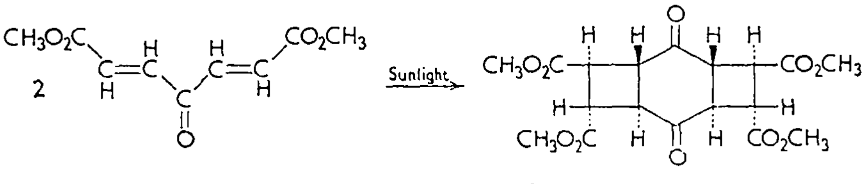
Finally, the studies of Ayer and Büchi deserve mention[285]. Aromatic nitriles undergo photoadditions to ethylene, simple alkenes or vinyl acetate. The products which are obtained in low yield have the nitrile group on a quaternary carbon atom.



It is apparent that one cannot speak of a *single* mechanism for the photochemical cycloaddition of alkenes. To unveil the domains of the competing mechanisms and to develop preparatively the multitude of possibilities which are offered is an important and potentially rewarding task for future investigations.

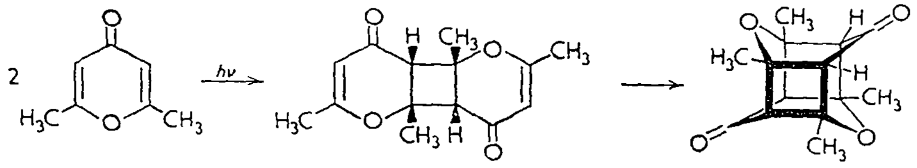
3. Intramolecular photoaddition reactions

The spatial proximity of the reacting groups and the smaller decrease in entropy in the cycloaddition reactions favor intramolecular processes. The photoisomerization of carvone to carvonecamphor (p. 744) is an early example[286]. The structure conceived intuitively by Ciamician has recently been proved unequivocally by degradation reactions[287]. By irradiation of dimethyl 3-oxopenta-1,4-diene-1,5-dicarboxylate in the crystalline state, two molecules are coupled



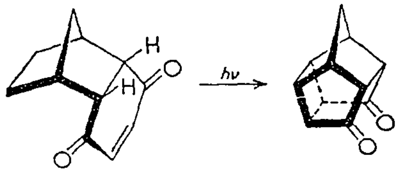
through four carbon–carbon single bonds[288]; the second cycloaddition is intramolecular; the structure of the product is supported by nuclear magnetic resonance spectroscopy[289].

A photodimer of 2,6-dimethyl-γ-pyrone isolated earlier by Paterno[290] was recently recognized by Yates and Jorgenson as having a cage structure[291]. There is no reason, however, to consider that the two cycloadditions involved occur simultaneously; again the dimerization takes place in the crystal.

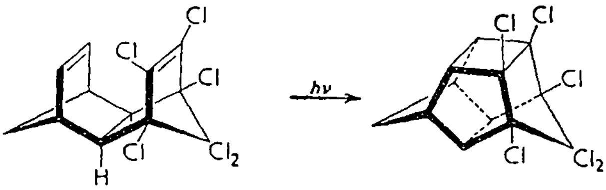


The dimerizations of the three dimethyl-*p*-benzoquinones take the same course when these compounds are irradiated in the solid phase. One obtains the *cis* or *trans* dimers with only *one* cyclobutane ring closed and also the rigid cage structures which arise from the *cis* dimers by further cycloaddition and have no residual unsaturation[292]. The monomeric quinones can be regenerated by pyrolysis. In the case of 1,4-naphthoquinone only a single ring closure occurs, leaving the benzene resonance untouched.

Interesting intramolecular photoadditions leading to cage molecules have been studied in recent years by Cookson. For example, the *endo* adduct from cyclopentadiene and *p*-benzoquinone forms a four-membered ring on irradiation[293].

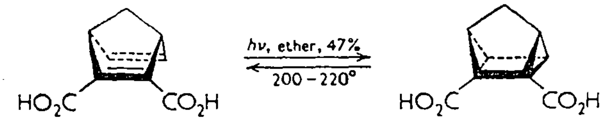


In isodrin, the stereoisomer of the insecticide aldrin, the double bonds interact to form a hexachloro derivative of the 'bird cage hydrocarbon'[294]. The intramolecular photoaddition here no longer

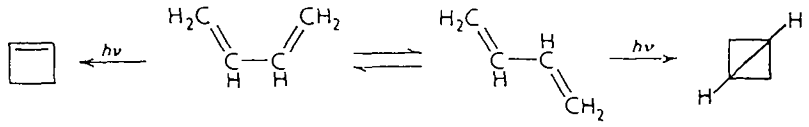


requires carbonyl conjugation. The same transformation can, in fact, be brought about by bromine in carbon tetrachloride[294]. However, in the latter case a many-act drama of additions and eliminations is undoubtedly at play, which no longer corresponds to our definition of cycloaddition.

In the bicyclo[2.2.1]heptene system, the tub form of the cyclohexene ring is fixed. By irradiation of bicyclo[2.2.1]heptadiene-2,3-dicarboxylic acid, Cristol and Snell obtained a quadricyclenedicarboxylic acid[295]. With the formation of a new cyclobutane ring, the 'tub' has been given a 'bottom'. The structure of this densely packed ring system has been proved[296]. Here, too, the carboxyl groups are not essential; as was recently shown, the light of a mercury lamp converts bicyclo[2.2.1]heptadiene in 67% yield into quadricyclene, which at 200° dissociates into the original doubly unsaturated hydrocarbon[270, 297].



An interesting case of intramolecular addition has been offered by Srinivasan[297a] in the photoisomerization of butadiene to bicyclo[1.1.0]butane in cyclohexane solution. Cyclobutene and the highly strained bicyclic hydrocarbon have been obtained in a 10:1 ratio. 1,5-Hexadiene undergoes a similar transformation to a saturated bicyclic system[297b].

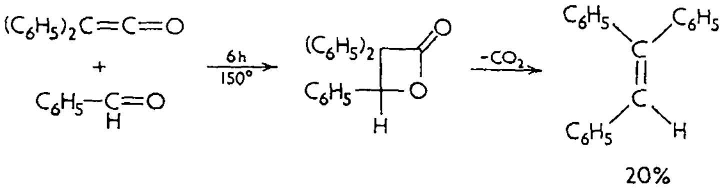


C. Four-membered Heterocyclic Compounds

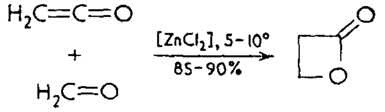
1. β-Lactones and oxetanes

The dimerization of ketenes to γ-methylene-β-lactones (p. 790) illustrates the ability of the cumulated carbon–carbon bond to add carbonyl compounds. The carbonyl groups of quinones combine even at or near room temperature with diphenylketene to form β-lactones (p. 790)[298]. Benzaldehyde or fluorenone add to the carbon–carbon double bond of diphenylketene only at 150°. At this temperature β-lactones are unstable and decompose at once to alkenes and carbon dioxide; triphenylethylene and 2,2-diphenylbiphenylene-ethylene, respectively, are obtained in 20% and 50% yields in these cases[299].

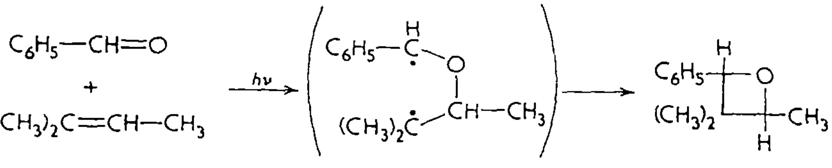
The rapid dimerization of the parent substance, ketene itself, prevents other reactions except at low temperature. Addition to carbonyl compounds has only been successful since the importance of acid catalysis has been recognized. β-Propiolactone, prepared from



ketene and formaldehyde[300], is a highly reactive and valuable starting material for industrial processes. Numerous aldehydes and ketones react analogously[301]. The electrophilic catalysis makes a multi-step mechanism probable.

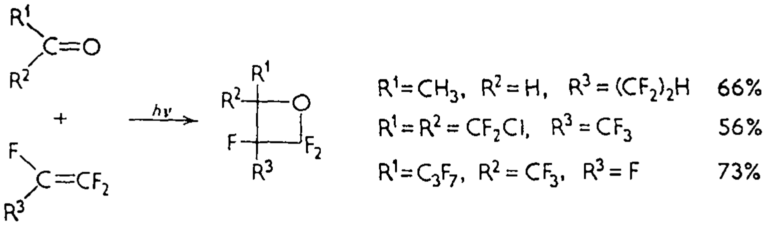


The photoaddition of carbonyl compounds to alkenes was discovered and correctly formulated[302] as long ago as 1909; however, the structure of the adducts has only been established recently[303]. The yields of oxetanes from trimethylethylene and benzaldehyde, acetophenone or butyraldehyde only amount to 4–10%. If it is assumed that the carbonyl group reacts in the triplet state, then the orientation is that which would be expected from a primary attack of the carbonyl oxygen at the olefinic double bond. An intramolecular addition of the same type occurs in the irradiation of 1-hexen-5-one[304].

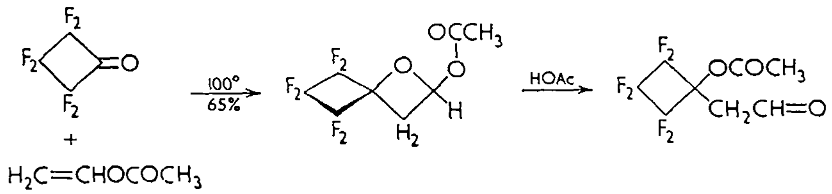


The low efficiency of the photoaddition reactions above stems from the multiplicity of competing side-reactions, such as photoinitiated polymerization[305]. In contrast, the thoroughly investigated photoreactions of fluorinated aldehydes, ketones and carboxylic acid fluorides with the terminal double bonds of fluoroalkenes, to form oxetanes, take place smoothly as shown by Harris and Coffman[306].

The eludication of the structure of the adducts rests principally on the fluorine nuclear magnetic resonance spectra.

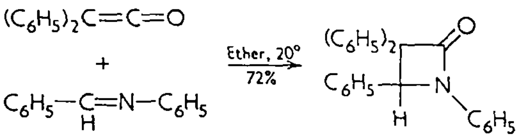


With perfluorocyclobutanone such additions do not require the assistance of light. Spiro-ring systems have been obtained by England with propylene, cyclohexene or vinylacetate at 25–100°[307]. Frequently subsequent ring-opening reactions take place under mild conditions.

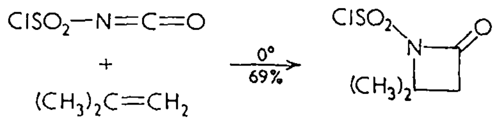


2. β-Lactams

Azomethines or Schiff bases react somewhat more easily than aldehydes in cycloaddition reactions with ketenes. The addition of diphenylketene to benzalaniline which was early reported by Staudinger[298], described a new class of compounds, the β-lactams. With the discovery of this structural element in penicillin, the reaction, which is predominantly one of ketoketenes, received much attention[308]; unfortunately its applicability is limited.



In a manner similar to that of the β-lactones, the β-lactams decompose on heating into an alkene and an isocyanate[309]. With highly reactive isocyanates, the reaction can be carried out in the reverse direction as a cycloaddition. Chlorosulfonyl isocyanate, which can be prepared from cyanogen chloride and sulfur trioxide, adds to isobutene, tetramethylethylene, styrene and other olefins at 0–50°, as the studies of Graf[310] have disclosed.

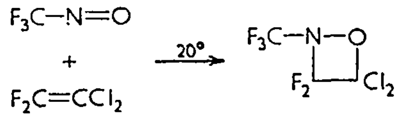


The electron-rich double bond of enamines undergoes cycloaddition even with phenylisocyanate to form β-dialkylamino-β-lactams[311]. The cycloaddition of tosylisocyanate to enol ethers has also been reported[312].

3. 1,2-Oxazetidines

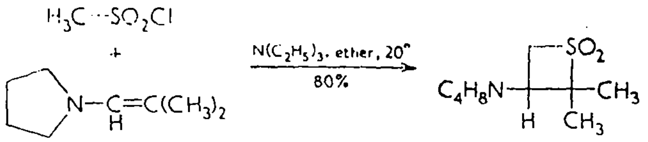
Ingold and Weaver[313] reported the addition of nitrosobenzene to ethyl methylenemalonate and 1,1-diphenylethylene. They described the 1 : 1 adducts as derivatives of 1,2-oxazetidine. However, Burkhardt and Lapworth[313a] have shown that these were *N*-(2,2-bis-ethoxycarbonylvinyl)-*N*-phenylhydroxylamine and triphenylnitrone, respectively. Nitrosobenzene and styrene were found to form 2:1 adducts containing five-membered rings[313b].

The interaction of nitrosotrifluoromethane with 1,1-dichloro-2,2-difluoroethylene or other polyfluoroalkenes gives rise to a four-membered oxygen- and nitrogen-containing ring system besides a 1 : 1 copolymer[314,315]. Only one of the two possible orientations is chosen.

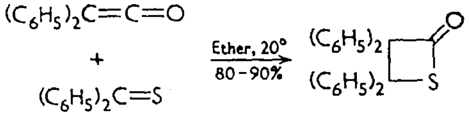


4. Thietanes and oxathietanes

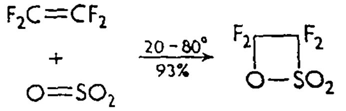
From several quarters it has recently been reported that hydrogen chloride can be abstracted from aliphatic sulfonyl chlorides by reaction with triethylamine. The hypothetical 'sulfenes', $R_2C{=}SO_2$, obtained correspond to the ketenes which are prepared analogously from acyl chlorides. The lability of this new class of compounds is too great to permit their isolation. However, the sulfenes combine *in situ* with the electron-rich double bond of enamines or ketene acetals to give thietane derivatives[316–319].



Thiobenzophenone is able to add to diphenylketene to give a colorless adduct which becomes blue at the melting point, indicating regeneration of the thioketone[320]. With *p,p'*-bisdimethylaminothiobenzophenone, the addition to diphenylketene at room temperature is followed by the elimination of carbon oxysulfide and the formation of 1,1-bis-(*p*-dimethylaminophenyl)-2,2-diphenylethylene.



Tetrafluoroethylene has the remarkable property of adding sulfur trioxide to its double bond. The product of this exothermic reaction is formulated as the sultone of 2-hydroxytetrafluoroethanesulfonic acid[321].

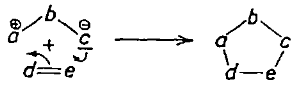


IV. 1,3-DIPOLAR CYCLOADDITIONS

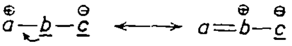
If additions of the type 3 + 2 → 5 are to be used for the formation of uncharged five-membered rings, it is necessary that the components bear formal charges. In the most important subgroup of this type, the formal charges are associated with the building block which contributes three members to the ring. Reactions of this class have, in fact, long been known, although the generality and utility of the concept was only recognized in recent years by the authors' Munich research group[41].

A. The Concept and Classification Scheme

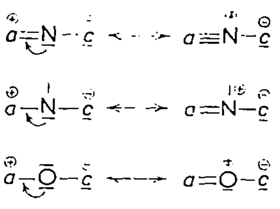
A 1,3-dipole may be defined as a system *a—b—c*, in which *a* has an electron sextet and carries a formal positive charge, and *c* is an anionic center having a free electron pair. In the union of such a 1,3-dipole with a multiple bond system *d*=*e*, the so-called dipolarophile, a cyclic shift of electrons accompanies and consummates closure of a five-membered ring. The following discussion will be concerned only with those 1,3-dipoles in which carbon, oxygen or nitrogen are found in the roles of *a*, *b* and *c*.



Compounds in which the positive center *a* is an electron-deficient carbon, nitrogen or oxygen atom are not capable of long-lived existence. When the 1,3-dipole is an isolable substance, then the symbol employed above can only refer to a resonance structure of minor weight. Stabilization of the reactive system is possible if a lone pair at *b* fills the electron gap at *a* by forming an additional bond. An all-octet structure is thus attained in which *b* has become the seat of the formal positive charge. We will refer to betaines of this kind as octet-stabilized 1,3-dipoles.



Sextet structures of 1,3-dipoles can be formulated in which *a* and *b* are connected by a single bond or by a double bond. Octet-stabilized *1,3-dipoles with double bond* must necessarily have nitrogen as the central atom *b*, since only this element can supply an unshared electron pair while in the trivalent neutral state. Systems *without double bond* may also contain oxygen as the central atom in the 1,3-dipole.



Systematic variation of the elements, carbon, oxygen and nitrogen, in accordance with these considerations leads to six '1,3-dipoles with double bond', which fall into two groups, nitrilium and diazonium betaines (Table 4).

A greater number of '1,3-dipoles without double bond' is possible. In addition to the six systems with nitrogen as the central atom, six others can be added with oxygen in this position (Table 5).

TABLE 4. Octet-stabilized 1,3-dipoles with double bond.

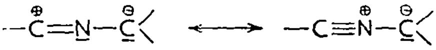
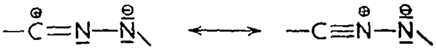
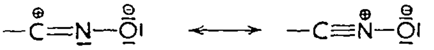
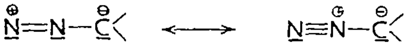
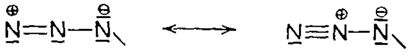
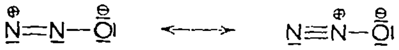
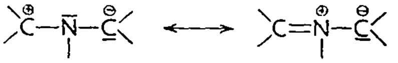
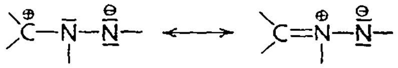
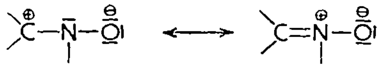
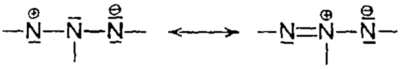
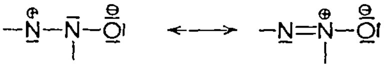
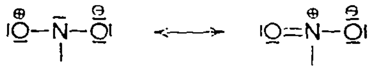
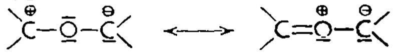
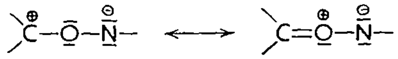
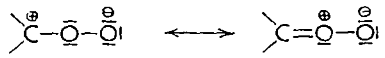
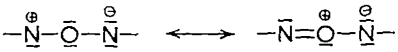
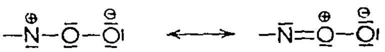
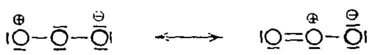
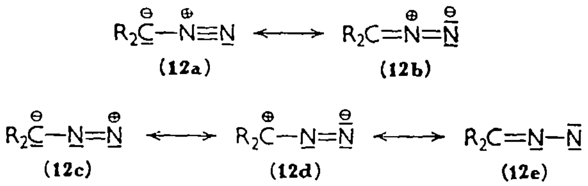
Nitrilium betaines	
	Nitrile ylides
	Nitrilimines
	Nitrile oxides
Diazonium betaines	
	Diazoalkanes
	Azides
	Nitrous oxide

TABLE 5. Octet-stabilized 1,3-dipoles without double bond.

Nitrogen as the center atom	
	Azomethine ylides
	Azomethine imines
	Nitrones
	Azimines
	Azoxy compounds
	Nitro compounds
Oxygen as the center atom	
	Carbonyl ylides
	Carbonyl imines
	Carbonyl oxides
	Nitroso imines
	Nitroso oxides
	Ozone

Although all of the members of the class of 1,3-dipoles with double bond are known and have been shown to undergo dipolar additions with multiple bonds, some of the systems without double bond, such as the azimines, carbonyl imines, nitroso imines, and nitroso oxides, have not yet been prepared. All other representatives of this class exhibit pronounced 1,3-dipolar reactivity.

In the schematic compilation of the 1,3-dipoles in Tables 4 and 5, the all-octet structures upon which the names are based are listed with one sextet structure in each case. However, additional resonance structures contribute to the stability of the compounds, as may be exemplified for diazoalkanes. Undoubtedly, the ground state of the molecule is well represented by the two all-octet structures **12a** and **12b**, while **12c**–**12e** are less significant. However, it is just these sextet structures which signal the electrophilic-nucleophilic character of these compounds.



$$R_2\overset{\ominus}{C}-\overset{\oplus}{N}\equiv N \longleftrightarrow R_2C=\overset{\oplus}{N}=\overset{\ominus}{N}$$

(12a) (12b)

$$R_2\overset{\ominus}{C}-N=\overset{\oplus}{N} \longleftrightarrow R_2\overset{\oplus}{C}-N=\overset{\ominus}{N} \longleftrightarrow R_2C=N-N$$

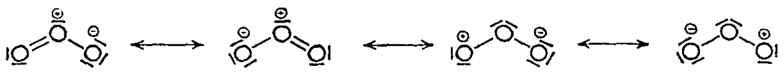
(12c) (12d) (12e)

Inspection of the sextet structures also discloses that the formal charges are inherently interchangeable. Therefore it is, in general, not meaningful to ascribe to a certain center electrophilic activity and to the second one nucleophilic activity. For the same reason, the number of 1,3-dipolar systems would not be doubled by interchange of the atoms *a* and *c*; in the illustration, **12c** and **12d** are merely alternative representations of the same compound.

The term '1,3-dipole' should not mislead one into expecting that such compounds necessarily have high dipole moments. Actually, it might be anticipated that the charge distributions in the two octet structures largely balance one another. The result is an electric moment of only 1·42 D for diphenyldiazomethane.

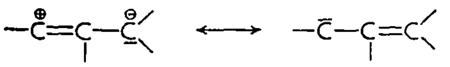
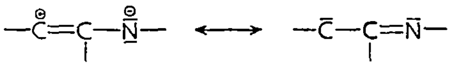
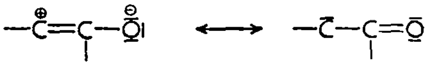
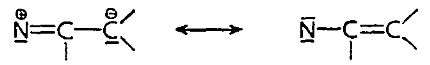
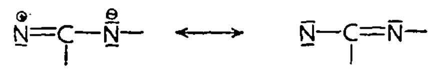
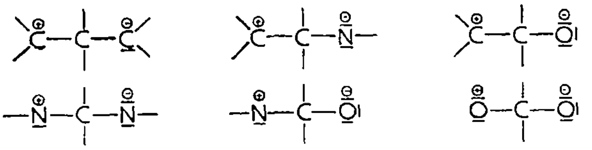
The same considerations apply to the 1,3-dipoles without double bond (Table 5). In these systems, however, a charge-free sextet structure, such as the azene **12e** above, can no longer be formulated. The possible contributing resonance structures for ozone are indicated below.

Not all of the 1,3-dipoles listed are sufficiently stable to permit isolation in pure form. It is often necessary to liberate the reactive system *in situ* from a suitable precursor which has good storage stability, and to trap the dipole at once by its reaction with a multiple bond. If we do not require that the 1,3-dipole be isolable, the scope of the concept is further broadened by inclusion of all those types for which no octet-stabilized structures can be formulated. Carbon can then also function as the central atom *b* (Table 6). All representatives of this group are highly reactive systems which at best can only occur as short-lived intermediates in the course of a reaction. Still other resonance structures could be written for the carbenes (formulated below for ketocarbenes) and azenes, but all lack octet-stabilization. Several systems of this kind have been proved capable of cycloaddition to form five-membered rings.

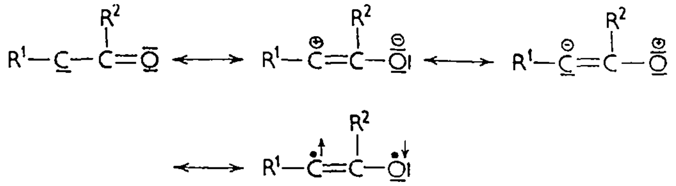


In the unsaturated carbenes and azenes the charges can still be interchanged; however, in those 1,3-dipoles where the formal charges are

TABLE 6. 1,3-Dipoles without octet-stabilization.

Systems with double bond	
	Vinylcarbenes
	Iminocarbenes
	Ketocarbenes
	Vinylazenes
	Iminoazenes
	Ketoazenes
Systems without double bond	
	

separated by a saturated center *b*, no resonance stabilization whatever is possible.



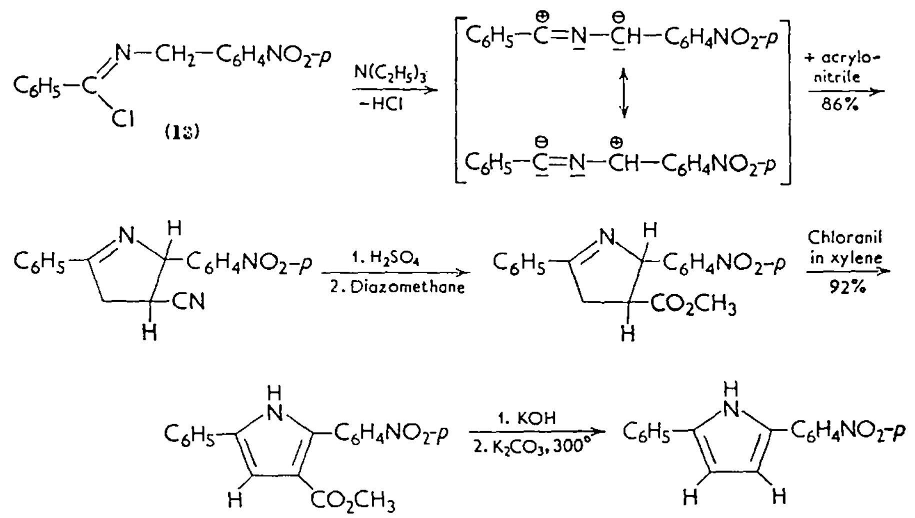
The systematic outline developed above is limited to 1,3-dipoles based on carbon, nitrogen and oxygen. This is an arbitrary restriction, and it is perfectly possible to formulate 1,3-dipolar systems with elements of the second row of the periodic table, such as sulfur and phosphorus. Experiments with thioketocarbenes[322] indicate that such a substantial expansion of the field of cycloaddition is within grasp. Finally, one can also imagine, using elements of the third and seventh groups of the periodic table in formulating 1,3-dipoles; cycloaddition with such systems would, of course, be of a different charge type.

1,3-Dipolar additions have been shown to be an astonishingly fruitful synthetic method for the preparation of five-ring heterocycles[41,323]. For the following discussion, only illustrations of the reactions with olefinic dipolarophiles have been selected from the wealth of available material. It is merely pointed out that numerous other multiple bond systems also combine smoothly with 1,3-dipoles. Sometimes the olefins are exceeded in dipolarophilic reactivity by the acetylenes. Numerous possibilities for variation are available through the use of dipolarophiles with heteromultiple bonds. Compounds with carbon–nitrogen double and triple bonds, as well as many carbonyl functions, combine with suitable 1,3-dipoles. The sulfur–nitrogen double bond of *N*-sulfinylaniline and, in several cases, the nitrogen–nitrogen double bond are also able to participate. Thiocarbonyl compounds possess an especially high reactivity; here a characteristic difference between dipolarophiles and the dienophiles of the Diels–Alder reaction can be seen. A recent review of the subject also includes a discussion of 1,3-dipolar cycloadditions to non-olefinic dipolarophiles[323].

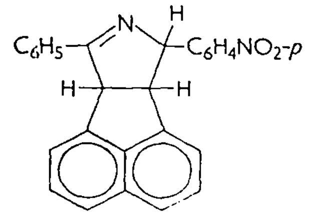
B. Cycloadditions of '1,3-Dipoles with Double Bond'

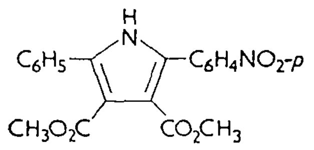
1. Nitrile ylides

Reaction of triethylamine with a benzene solution of *N*-(*p*-nitrobenzyl)benzimidoyl chloride (**13**) produces triethylamine hydrochloride and a violet solution, which presumably contains the unstable 1-phenyl-3-(*p*-nitrophenyl)nitrilylide[324]. This 1,3-dipole displays its activity when acrylonitrile is present in the reaction mixture; an 86% yield of two diastereomeric Δ^1-pyrrolines is obtained. The degradation to 2-(*p*-nitrophenyl)-5-phenylpyrrole formulated below proves the structure of the cycloadduct.



The reaction of **13** with acenaphthylene is similar. However, with dimethyl fumarate the cyclization reaction is followed by dehydrogenation, yielding dimethyl 2-(*p*-nitrophenyl)-5-phenylpyrrole-3,4-dicarboxylate. It is particularly interesting that the same ethyl acrylate adduct is obtained with the isomeric nitrile ylides derived from *N*-(*p*-nitrobenzyl)benzimidoyl chloride, and *N*-benzyl-*p*-nitrobenzimidoyl chloride[325]. A 3*H*-azirine intermediate has been ruled out.

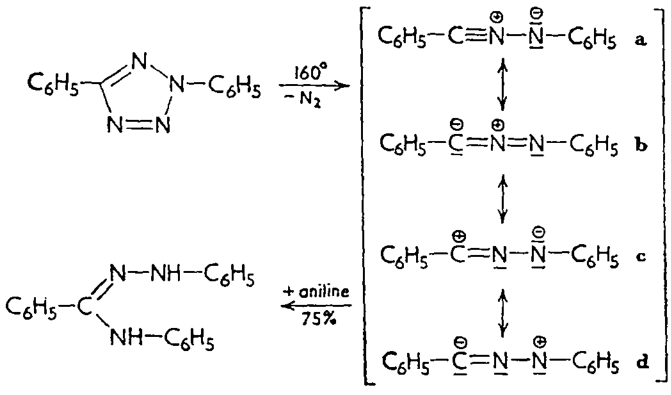




2. Nitrilimines

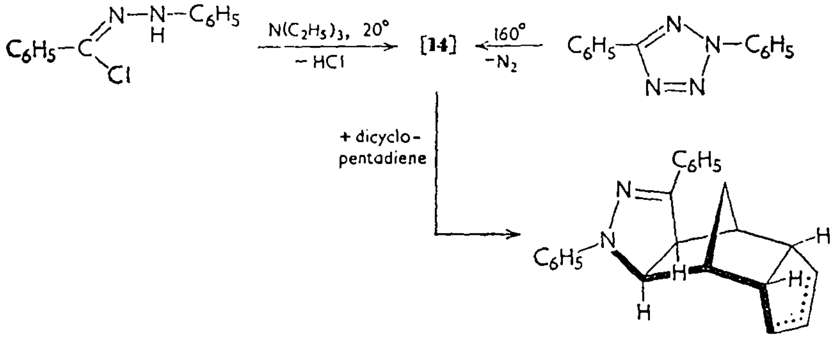
a. Preparation. Until recently the only nitrilimine described was the parent compound of the class, isodiazomethane, prepared by Müller[326]. Cycloadditions of this compound with olefins are not known, however.

A simple procedure for the preparation of reactive nitrilimines *in situ* is afforded by the thermal elimination of nitrogen from 2,5-disubstituted tetrazoles. The decomposition of 2,5-diphenyltetrazole takes place at 160–180° to form diphenylnitrilimine (**14**) which is capable of participating in a great variety of 1,3-additions. Union with aniline gives *N*-phenylbenzamide phenylhydrazone[327] in 75% yield. Liberation of **14** in the presence of olefins leads to the formation of Δ^2-pyrazolines in high yield.



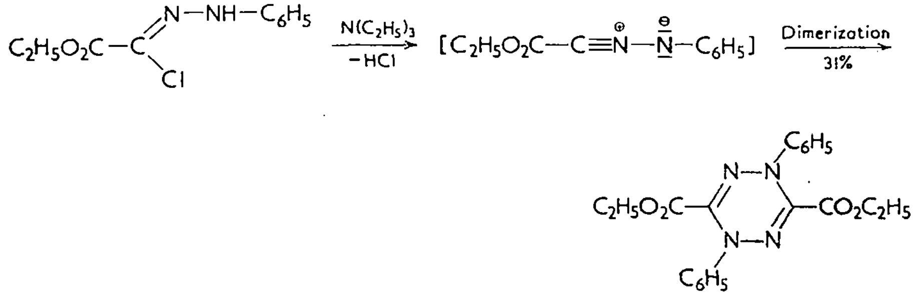
(**14**)

Thermolysis of 2-alkyl-5-aryltetrazoles is less smooth, requiring temperatures near 220°, yet cycloadditions are also possible under these conditions[328]. The disadvantage of this high-temperature procedure was circumvented when it was found that nitrilimines could be generated even at room temperature by the action of tertiary bases on hydrazidoyl halides[329]. Here again the 1,3-dipole cannot be isolated, and the dipolarophile must be present in the reaction mixture

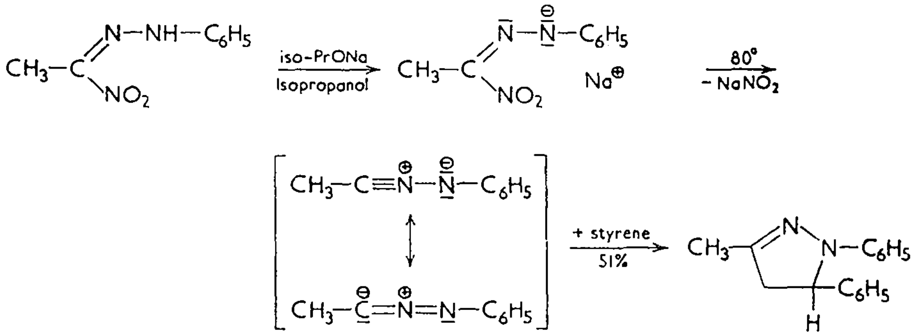


from the outset. It is thus possible to obtain an 83% yield of the Δ^2-pyrazoline from **14** and dicyclopentadiene. The same addition to the strained double bond can also be realized in 68% yield by thermolysis of 2,5-diphenyltetrazole in dicyclopentadiene[329].

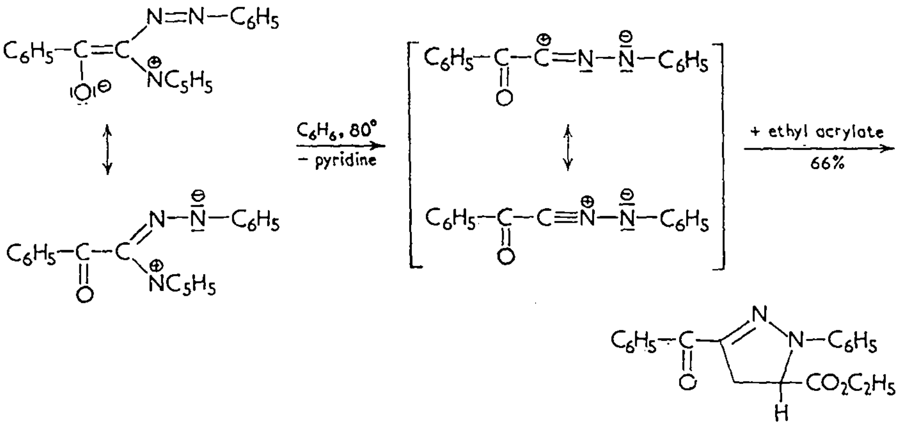
In the absence of a sufficiently reactive dipolarophile, dimerization of the 1,3-dipole to form a derivative of 1,4-dihydro-1,2,4,5-tetrazine is frequently observed, as illustrated below for the nitrilimine derived from 1-carbethoxyformyl(phenylhydrazidoyl) chloride[330].



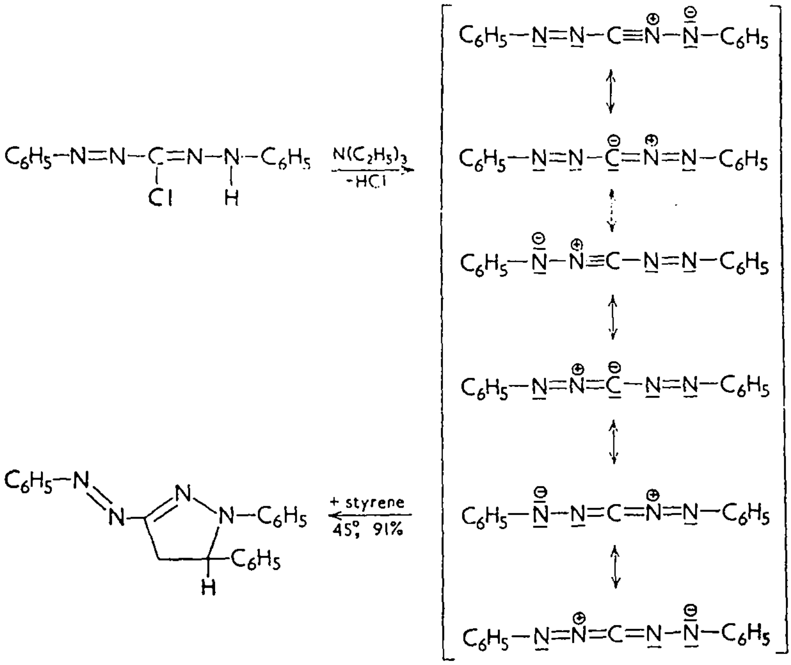
The α-nitroaldehyde phenylhydrazones, which are prepared by azo coupling as described by Bamberger[331], are useful for the preparation of C-alkylnitrilimines. By heating the sodium salts of these compounds with dipolarophilic olefins, Δ^2-pyrazolines are obtained[47,332]. The assumption that a nitrilimine intermediate is responsible for the reaction seems reasonable.



Access to the *C*-acylnitrilimines is available through use of the pyridinium enol betaines discovered by Krollpfeiffer and Braun[333]. These substances decompose on warming to give pyridine and the 1,3-dipole which can easily be trapped through cycloaddition reactions[334]. In the absence of dipolarophiles, dimerization to diacyldihydrotetrazines occurs.

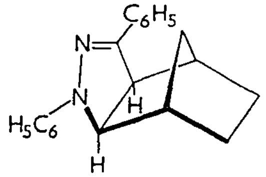


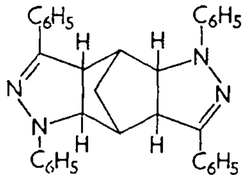
As a final class of nitrilimine generators the diarylhaloformazanes may be mentioned. Treatment of *N*,*N*-diphenylchloroformazan[335] with triethylamine leads to a nitrilimine which is of particular interest because of its symmetry and resonance stabilization. The 1,3-dipole cannot actually be isolated but is readily intercepted with styrene[330]. The structure of the adduct, 1,5-diphenyl-3-phenyiazo-Δ^2-pyrazoline, has been established. Only the octet-stabilized resonance structures of the dipole are indicated in the formulation below.



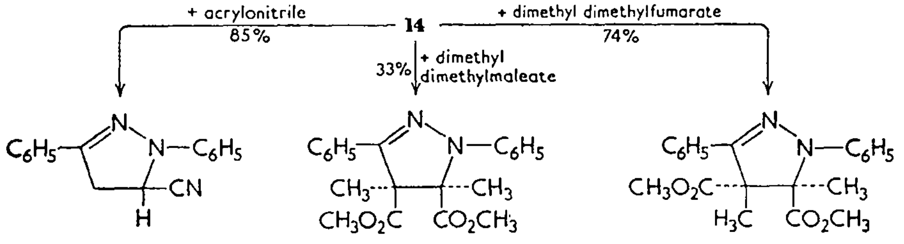
b. Cycloadditions to olefins. Reactions of nitrilimines with olefins generally furnish excellent yields of Δ^2-pyrazolines, as already indicated by the examples above. The reactions of diphenylnitrilimine (**14**) have been studied in detail.

The high angular strain which is present in derivatives of bicyclo-[2.2.1]heptene causes olefins of this type to be especially reactive dipolarophiles. Even at 20°, norbornene combines with diphenylnitrilimine, generated from benzphenylhydrazidoyl chloride and triethylamine, to give an 80% yield of a tricyclic Δ^2-pyrazoline[329]. The *exo* structure of the adduct was established unequivocally[336]. Bicyclo[2.2.1]hepta-2,5-diene gives a 79% yield of the 1:1 adduct together with 6% of a bisadduct.

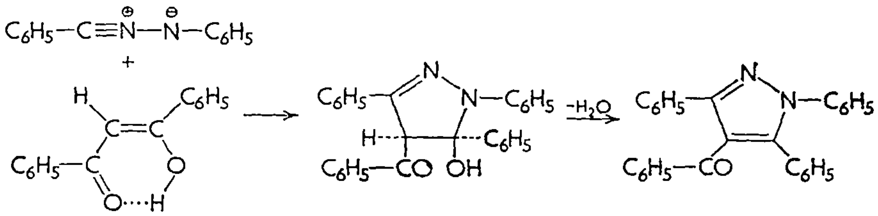




α,β-Unsaturated carbonyl compounds and nitriles also exhibit a high capacity for such cycloaddition reactions. Thus from benzphenylhydrazidoyl chloride and acrylonitrile at room temperature in the presence of triethylamine, 1,3-diphenyl-5-cyano-Δ^2-pyrazoline is obtained in 85% yield[329]. Reactions with ethyl acrylate and ethyl crotonate occur just as smoothly. It is of theoretical significance that diastereomeric adducts are isolated from dimethyl dimethylmaleate and dimethyl dimethylfumarate without contamination by the epimer in either case. This result is strong evidence for a true *cis* addition, in which the two new σ bonds are formed simultaneously[329]. Dimethyl maleate itself gives chiefly the dimethyl fumarate adduct because of subsequent base-catalyzed epimerization.

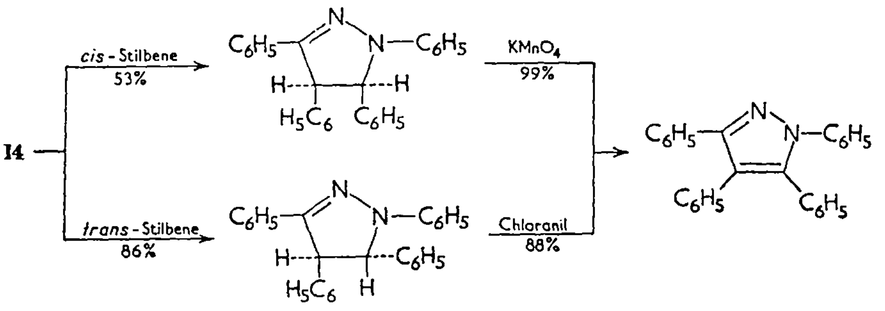


The reaction of carboxylic acid hydrazidoyl chlorides with sodium salts of acidic CH compounds to form pyrazoles has long been known from the work of Fusco and coworkers[337,338] who investigated numerous examples. These authors attempted to explain the mechanism of the reaction by assuming a primary nucleophilic attack by the enolate anion. On the basis of data now available, it is reasonable to suggest that here also nitrilimines occur as intermediates and add to the double bond of the enol.



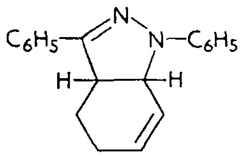
In general, any conjugation enhances the dipolarophilic reactivity of an alkene. Thus, phenyl-conjugated olefins readily accept diphenylnitrilimine. With styrene, for example, an 88% yield of 1,3,5-triphenyl-Δ^2-pyrazoline is the result; addition to acenaphthylene takes place in 90% yield[329].

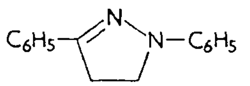
Addition of **14** to *cis*- and *trans*-stilbene is stereospecific. Dehydrogenation of the two disastereomeric pyrazolines leads to the same 1,3,4,5-tetraphenylpyrazole[329].

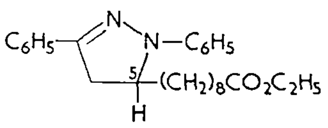


Nitrilimines also react smoothly with dienes. If triethylamine is added at 80° to a mixture of benzphenylhydrazidoyl chloride and cyclohexa-1,3-diene one obtains a 73% yield of a tetrahydroindazole derivative, which has been aromatized to 1,3-diphenylindazole[329]. Butadiene combines with **14** almost quantitatively at 20° to give 1,3-diphenyl-5-vinyl-Δ^2-pyrazoline; oxidative degradation to 1,3-diphenylpyrazole-5-carboxylic acid serves to prove the structure.

Cycloaddition of diphenylnitrilimine to unconjugated olefins requires longer reaction times, but, nevertheless, often gives high yields. For example, **14** prepared from benzphenylhydrazidoyl chloride and triethylamine in benzene solution absorbs ethylene to form 1,3-diphenyl-Δ^2-pyrazoline in 81% yield[42]. Ethyl undecylenate is converted to a 5-substituted dihydropyrazole[329]. Cyclopentene







exceeds cyclohexene in reactivity. Only when the latter itself is used as a solvent one does obtain an appreciable amount of the adduct with **14.**

c. Dipolarophilic reactivity, mechanism and orientation phenomena. The dependence of the reaction rate upon the nature of the dipolarophile permits interesting conclusions regarding the mechanism of 1,3-dipolar cycloadditions. The necessity for carrying out reactions with diphenylnitrilimine *in situ* makes direct kinetic measurements of the reaction rate impossible. Consequently one must use competition experiments to determine the relative rate coefficients: a large excess of two olefins in a known molar ratio is permitted to compete for the 1,3-dipole. Quantitative analysis of the product mixture makes possible calculation of the relative rate coefficients[336] (Table 7, p. 819).

The observed differences in reactivity permit a numerical comparison of the promoting or retarding influence of many functional groups. The favorable effect of conjugation in the dipolarophile, already established qualitatively (p. 817), is here illustrated by the very active α,β-unsaturated carbonyl compounds and nitriles. Thus, ethyl acrylate reacts 250 times faster than unconjugated methyl 4-pentenoate. A second carboxylic ester group shows a further effect, as comparison of the data for the fumaric and acrylic esters demonstrates. The rate enhancement by phenyl-conjugation is smaller; this is clear from a comparison of styrene with 1-heptene, where the rate coefficients differ by a factor of 11.

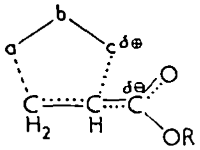
Steric effects frequently are found to be of particular significance in multi-center reactions. Here we find that introduction of a methyl group at the α-position in an acrylic ester reduces the reactivity by a factor of 3, while a β-methyl group causes a 48-fold reduction. Comparison of styrene with 1,1- and 1,2-diphenylethylene teaches that the inhibiting steric effect of a second phenyl group exceeds the additional activation resulting from extended conjugation. It is further illuminating in this connection that tetraethyl ethylenetetracarboxylate still adds diphenylnitrilimine smoothly, while no reaction occurs with tri- and tetraalkylated or -arylated olefins.

TABLE 7. Relative rates of addition of diphenylnitrilimine in boiling benzene (ethyl crotonate ≡ 1·0).

Compound	k_2 (rel.)
Dimethyl fumarate	283
Fumaronitrile	112
Ethyl acrylate	48·2
Methyl methacrylate	16·6
Dimethyl maleate	7·94
Norbornene	3·12
Styrene	1·60
Ethyl crotonate	≡ 1·00
Acenaphthylene	0·99
Tetraethyl ethylenetetracarboxylate	0·91
trans-Stilbene	0·274
Methyl 4-pentenoate	0·197
Indene	0·197
1,2-Dihydronaphthalene	0·157
1-Heptene	0·146
Cyclopentene (20°)	0·128
1,1-Diphenylethylene	0·112
cis-Stilbene	0·011
Cyclohexene	0·011

The enhancing influence of conjugation on the dipolarophilic capacity of an alkene requires some discussion. If one compares the cycloaddition of a 1,3-dipole to an isolated double bond with that to a conjugated system, it is apparent that the reaction enthalpy should be smaller in the second case, since the conjugation energy is necessarily sacrificed in the course of the reaction. Nevertheless, the activation barrier must be lowered as is shown by the increased reactivity of conjugated systems.

One underlying reason for this effect can be found in the stabilization of partial charges in the transition state. Concerted closure of the two new σ bonds does not necessarily mean that the development of the bonds has proceeded to an equal degree in the activated complex. Any difference between the bond-forming rates during the activation process would lead to a partial charge at the dipolarophile. Neighboring unsaturated substituents would stabilize such a charge to a greater or lesser degree and thus lower the energy level of the transition state.

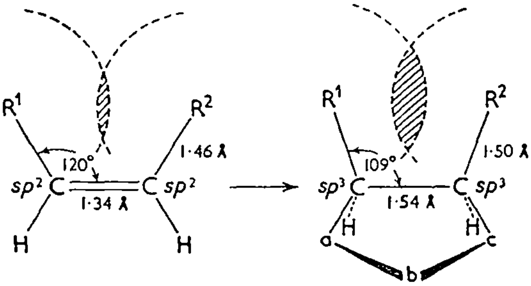


An additional factor which may be partly responsible for the high dipolarophilic reactivity of conjugated multiple bonds is the accentuated polarizability of such systems[339]. Apparently, the greater mobility of the bonding electrons facilitates the cyclic shift of electrons which is the essence of a multi-center addition.

As Table 7 shows, norbornene leads the non-conjugated olefins in reactivity. The heat of hydrogenation of the angle-strained double bond of bicyclo[2.2.1]heptene is about 6 kcal larger than that of cyclohexene[340]. 1,3-Dipolar cycloaddition, like addition of hydrogen, is enhanced by relaxation of the angular strain.

The higher reactivity of *trans*-alkenes compared to the related *cis* isomers is also an interesting phenomenon. The relative rate coefficients for dimethyl fumarate and maleate differ by a factor of 36, while *trans*-stilbene reacts 26 times faster than the *cis* compound. These data are surprising at first sight inasmuch as the more energy-rich maleate adds bromine or sulfite ion more rapidly than the fumarate.

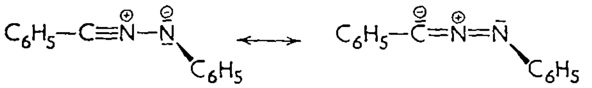
The explanation is not hard to find: the 120° bond angles at the two sp^2-hybridized centers may cause significant van der Waals compression between *cis* substituents in the ground state. Steric inhibition of resonance arising from this crowding reduces the activating influence of *cis*-carbonyl or -phenyl substituents on the cycloaddition reaction. Furthermore, in the course of the multi-center process the sp^2 centers



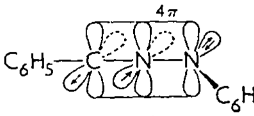
must be transformed to sp^3 hybridization. The accompanying shrinkage of the bond angles causes increased steric interaction of the eclipsed *cis* substituents, despite the slightly lengthened carbon–carbon bond joining the two tetrahedral atoms. Scale models show clearly this enhanced overlapping of *cis* substituents, which must result in an increase in activation energy. The *trans*-alkene is free from this rate-retarding factor^{341}.

Olefins lacking a center of symmetry can add nitrilimines in either of two directions. Regardless of the nature of the substituents, however, monosubstituted alkenes invariably unite with **14** to form 5-substituted pyrazolines^{329}. Since the orientation is the same with styrene as with ethyl acrylate, it seems improbable that electronic substituent effects influence the direction of addition.

A wealth of experimental material supports the view that steric effects dominate the orientation. In the two octet structures of the nitrilimines, the nitrile carbon and the external nitrogen atom bear the anionic charge. Resonance between the two forms **14a** and **14b** is only possible when the molecular geometry is as indicated in the figure below. With four electrons in three p orbitals, the delocalized π system in **14c** corresponds to that of the allyl anion^{339}. It is easy to perceive that the terminal nitrogen is more readily accessible than the carbon atom of the 1,3-dipole. If steric factors are controlling, then bulky substituents may always be expected to appear at the 5-position of the Δ^2-pyrazoline, adjacent to the imine nitrogen.



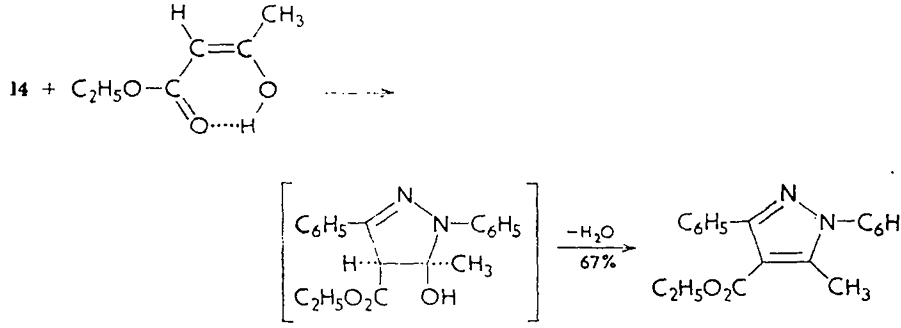
(**14a**) (**14b**)



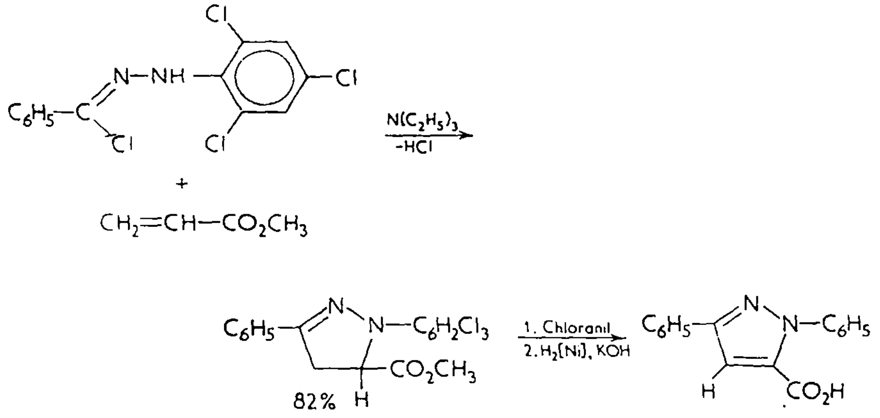
(**14c**)

It is in fact observed that styrene, ethyl acrylate, acrylonitrile, butadiene and even 1-heptene yield 5-substituted pyrazolines exclusively. Ethyl crotonate and cinnamate give mixtures of the pyrazoline-4- and -5-carboxylates in ratios of 35:65 and 27:73, respectively^{342}. On the other hand, addition to acetoacetic ester, which in the enol form may be viewed as a trisubstituted ethylene, leads to a single product. Spontaneous elimination of water from this pyrazoline produces ethyl 1,3-diphenyl-5-methylpyrazole-4-carboxylate^{329}, suggesting that again the addition reaction is sterically controlled (formulation on p. 822).

The rigor with which this orientation rule is obeyed is surprising. Although with acrylonitrile, for example, the steric interference at the α-carbon is certainly small, no trace of a second isomer of the diphenylnitrilimine adduct could be found. *C*-Phenyl-*N*-(trihalophenyl)-nitrilimines also add to mono- and 1,1-disubstituted ethylenes to give



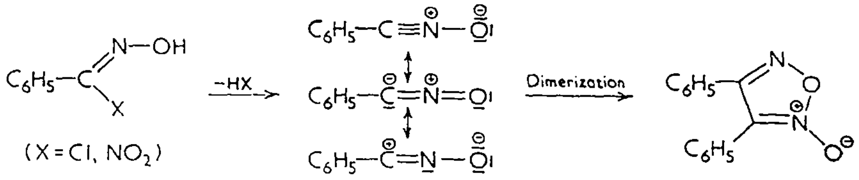
5-substituted Δ^2-pyrazolines[42]. One might have expected a reversal of the orientation because of the bulky substituent at the imine nitrogen. A satisfactory interpretation of this result is still lacking.



3. Nitrile oxides

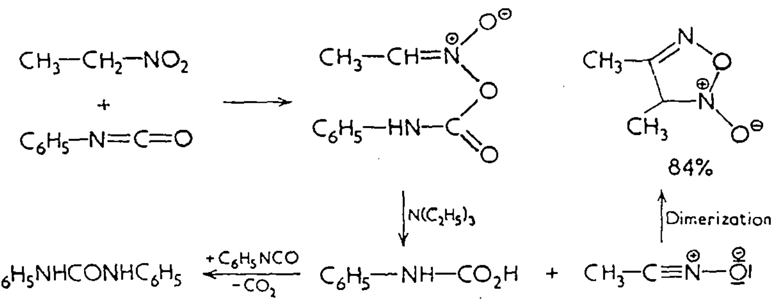
In contrast to the other nitrilium betaines discussed so far, the nitrile oxides are a long known and thoroughly investigated class of compounds. Numerous cycloadditions, particularly those involving benzonitrile oxide, had already been described when the general concept of the 1,3-dipolar addition was formulated by Huisgen.

Probably Werner and Buss[343] were the first to prepare benzonitrile oxide, but they isolated only diphenylfuroxan, the product of its spontaneous dimerization. The experimental skill of Wieland was responsible for the later isolation of the free nitrile oxide[344]. Hydroxamic acid chlorides or nitrolic acids are commonly used as precursors.

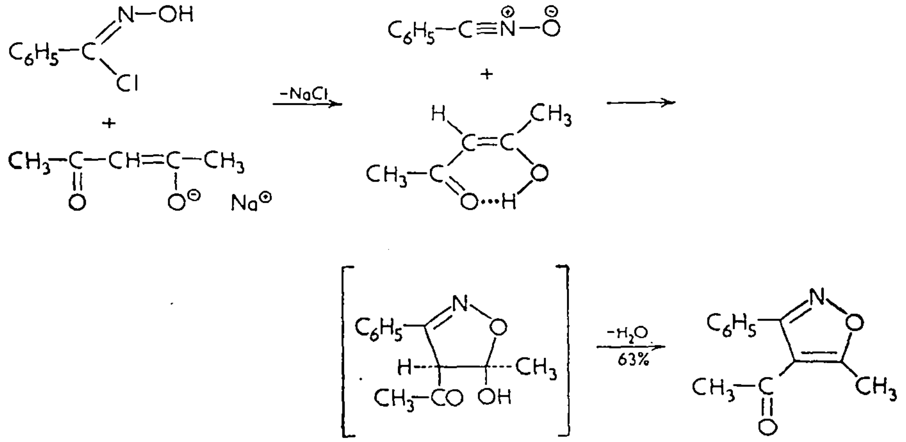


The free nitrile oxides can, of course, be used in cycloaddition reactions, but it is advantageous and more convenient to generate the nitrile oxide *in situ* in the presence of the dipolarophile by gradual addition of a tertiary base to a solution of the hydroxamic acid chloride[345]. The nitrile oxide which is then present only at low concentration is quickly intercepted by the dipolarophile. It is thus possible to minimize wasteful dimerization to the furoxan[346].

Among the aliphatic nitrile oxides, those related to ethyl cyanoformate and trimethylacetonitrile are accessible by the methods mentioned. A route to nitrile oxides with simple alkyl groups was recently described by Mukaiyama and Hoshino[347]. These authors isolated good yields of the alkylfuroxans and substituted ureas from the reactions of isocyanates and nitroalkanes with tertiary bases. The mechanism of this reaction, in which the critical step involves a base-induced elimination, is outlined below.



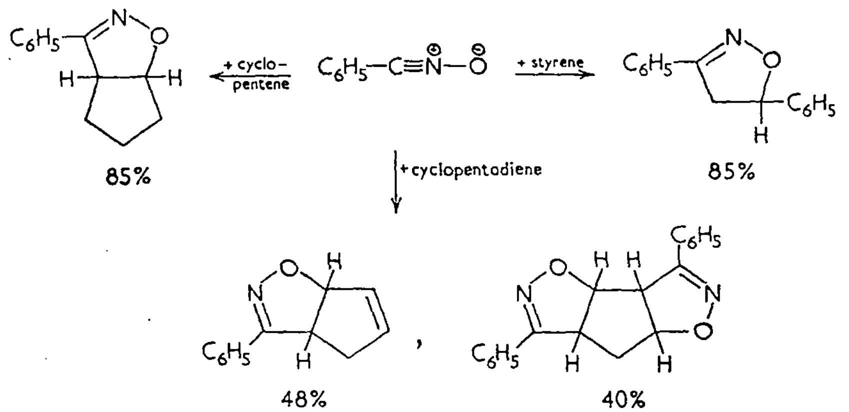
Quilico and Fusco[348] obtained ethyl 3,5-diphenylisoxazole-4-carboxylate in 63% yield from the reaction of benzhydroxamic acid chloride with ethyl sodiobenzoylacetate. The sodium salts of numerous other β-dicarbonyl compounds have been reacted in the same manner. The mechanism was first explained by assuming a nucleophilic displacement of the halogen by the carbanion. However, a few years later Quilico and Speroni[349] provided evidence for the occurrence of a nitrile oxide intermediate. The reaction of benzhydroxamic acid chloride with sodioacetylacetone may thus be written as follows:



The Italian authors studied the reactions of aromatic nitrile oxides, principally, with nearly all types of olefins to form Δ^2-isoxazolines. Ethylene and its alkyl derivatives reacted relatively sluggishly, so that considerable dimerization of the 1,3-dipole was observed when the free nitrile was employed[350]. As in the case of nitrilimines, the reactivity of cyclopentene (85% yield of benzonitrile oxide adduct) exceeded that of cyclohexene which did not give an isolable adduct with free benzonitrile oxide[351]. However, under more favorable conditions where the 1,3-dipole is generated *in situ*, a 55% yield of the fused isoxazoline system can be obtained from cyclohexene[352]. Quantitative yields were isolated in the *in situ* additions of benzonitrile oxide to the angle-strained double bonds of bicyclo[2.2.1]heptene and its derivatives[351,352].

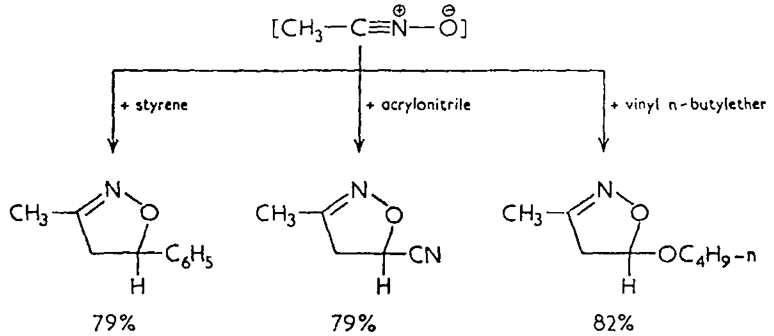
Phenyl-conjugated olefins[353] and 1,3-dienes[354] often react faster than those with isolated double bonds. 1,3-Dienes are able to add one or two molecules of the nitrile oxide; addition of benzonitrile oxide to cyclopentadiene, formulated on page 825, serves as an example[353]. A bisadduct was also obtained from allene[355].

α,β-Unsaturated ketones[356], carboxylic acids, esters and anhydrides[357,358] are highly reactive towards nitrile oxides. Use of a low stationary concentration of the 1,3-dipole often permits nearly quantitative yields[352]. The stereospecificity of the addition has been established by the isolation of diastereoisomeric Δ^2-isoxazolines from benzonitrile oxide and the *cis/trans* pair, dimethyl maleate and fumarate[358].



Ketene gives a lower yield of cycloaddition product than do the related acetals. Acid hydrolysis of the product from benzonitrile oxide and ketene diethyl acetal gives 3-phenyl-Δ^2-isoxazolin-5-one[359].

Aliphatic nitrile oxides (p. 823) also can be added *in situ* to carbon–carbon double bonds[347].



The examples given illustrate the highly specific orientation observed in cycloadditions to mono- or 1,1-disubstituted olefins. The substituents invariably appear in the 5-position of the Δ^2-isoxazoline; it is readily appreciated that the sterically favored reaction path is followed. The analogy between nitrilimines (p. 821) and nitrile oxides is obvious.

The close mechanistic parallel between the nitrilimine and nitrile oxide additions is also revealed by the relative reaction rates of olefinic dipolarophiles, which have been determined by competition experiments[352] (Table 8). Slight differences are apparent here: norbornene is somewhat more reactive than the unsaturated esters, and the reactivity of styrene is also enhanced over that observed with nitrilimines.

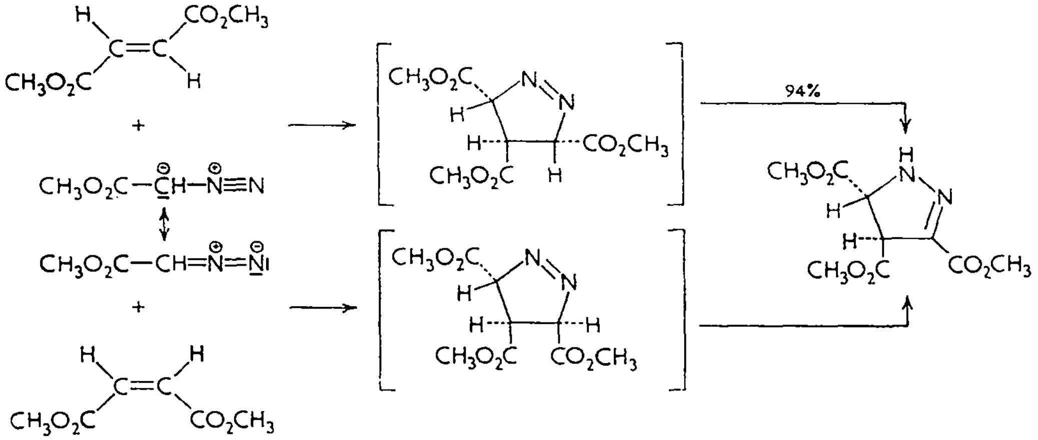
Table 8. Relative rates of addition of benzonitrile oxide to olefins in ether at 20°.

Dipolarophile	k_2 (rel.)
Norbornene	97
Dimethyl fumarate	94
Ethyl acrylate	66
Methyl methacrylate	23
Vinyl n-butyl ether	15
Styrene	9·3
1,1-Diphenylethylene	3·3
Cyclopentadiene	3·7
1-Hexene	2·6
Dimethyl maleate	1·61
Cyclopentene	1·04
Ethyl crotonate	≡ 1·00
trans-Stilbene	0·24
Cyclohexene	0·055

4. Diazoalkanes[360]

The resonance structures of the diazoalkanes formulated on page 809 facilitate recognition of the rather complete charge compensation. The dipole moments of diphenyldiazomethane, 1·42 D, and of ethyl diazoacetate, 2·03 D (in benzene at 25°)[361], confirm this deduction.

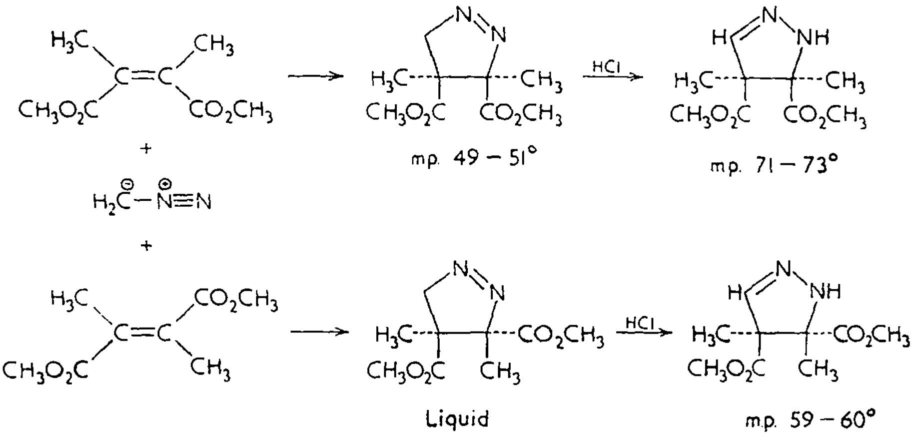
Formation of five-membered rings through the addition of diazoalkanes to α,β-unsaturated esters was first observed in 1888 by Buchner[362]. The adduct from methyl diazoacetate and dimethyl



fumarate is not the expected Δ^1-pyrazoline, but instead the more stable trimethyl Δ^2-pyrazoline-3,4,5-tricarboxylate; the silver salt of the triacid yields pyrazole on heating[362].

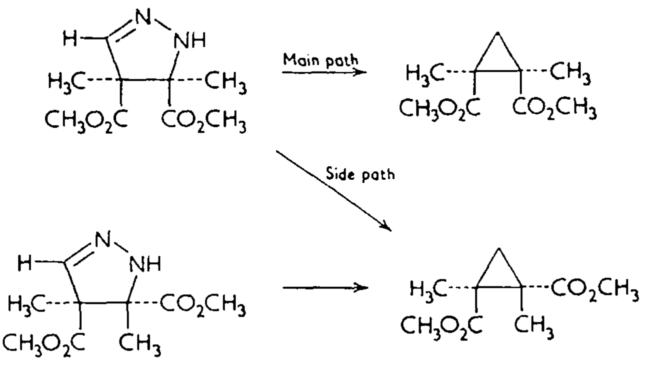
It is noteworthy that the addition of methyl diazoacetate to dimethyl fumarate or to dimethyl maleate gives the same product. This violation of the principle of *cis* addition is more apparent than real; tautomerization of the initial Δ^1-pyrazolines involves loss of the asymmetric center in question.

Diastereomeric primary adducts possessing Δ^1-pyrazoline structures can be isolated from the additions of diazomethane to dimethyl dimethylfumarate and dimethyl dimethylmaleate[363]. The lower acidity of the carbon–hydrogen bond adjacent to the nitrogen in this case makes isomerization to the more stable Δ^2-pyrazolines possible only

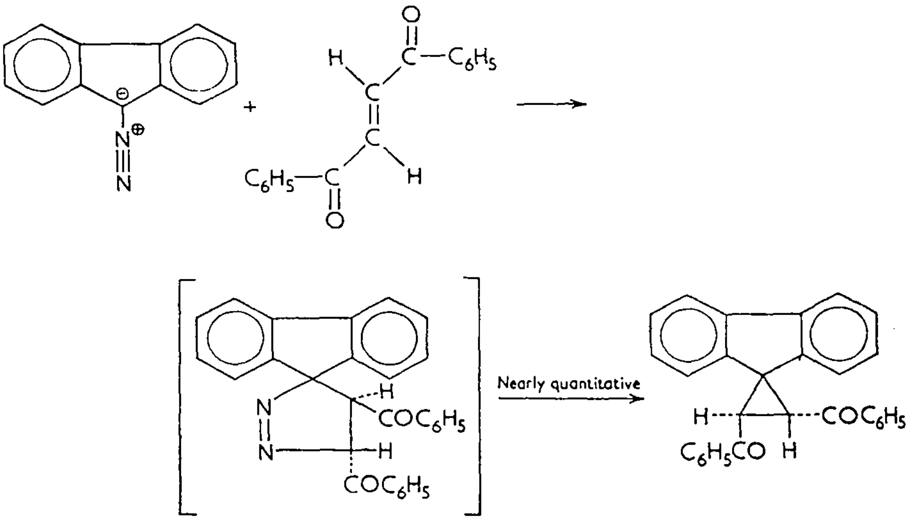


in the presence of a catalyst. The stereospecificity of the reaction emerges clearly, since the asymmetric centers arising from the carbon atoms of the olefinic double bond are not disturbed.

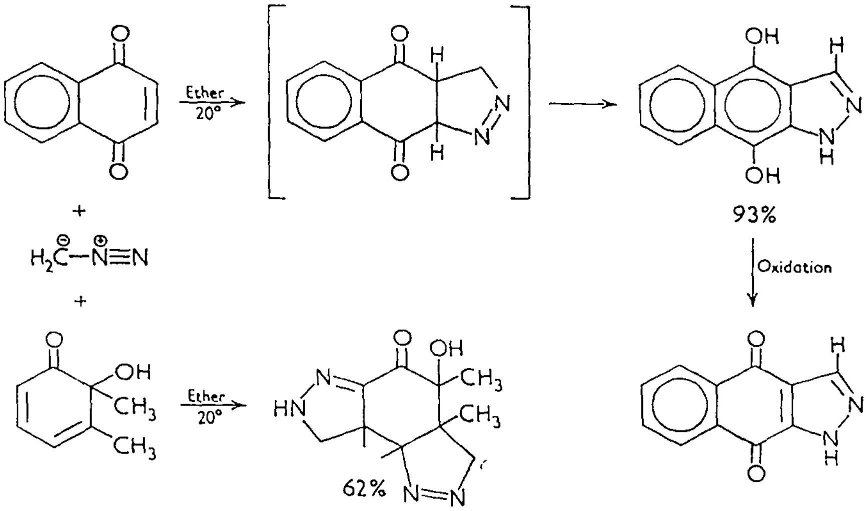
Thermolysis at 180° affirms the configurations of the two Δ^2-pyrazolines formulated above. Expulsion of nitrogen leads to *cis*- and *trans*-1,2-dimethylcyclopropane-1,2-dicarboxylates, respectively. Presumably the loss of nitrogen involves initial isomerization to the Δ^1-pyrazoline; more recent studies make it likely that this transformation is often the rate-determining step[364,365]. Decomposition of the Δ^1-pyrazoline is not rigorously stereospecific[366], as shown below; the photochemical conversion of Δ^1-pyrazolines to cyclopropanes is more stereoselective[366]. In addition to the cyclopropanecarboxylates, α,β-unsaturated esters are obtained and frequently may be the major products.



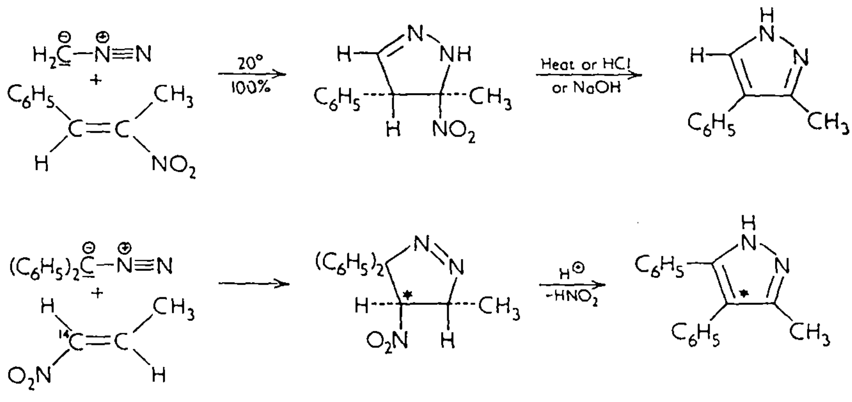
Reactions of diazoalkanes with α,β-unsaturated carbonyl compounds provide a convenient method for the preparation of a great variety of pyrazolines[367]. Those derived from diazodiphenylmethane are unstable in many cases; the maleic anhydride adduct, to which van Alphen ascribed a Δ^1-pyrazoline structure, decomposes in solution at room temperature[368]. Reaction of the same diazo compound with *N*-substituted maleimides takes place at room temperature, forming the Δ^1-pyrazoline; in boiling benzene thermolysis leads to the cyclopropane derivative[369]. When 9-diazofluorene is used, very often the cyclopropane is obtained directly, as indicated for the reaction with dibenzoylethylene[370].



Several research groups have investigated the action of diazoalkanes on quinones[371,372]. Depending upon the structure of the reactants and the conditions, 1:1 or 1:2 adducts may be isolated. Similar behavior has been observed in the cycloadditions to *o*-quinols studied by Wessely[373].



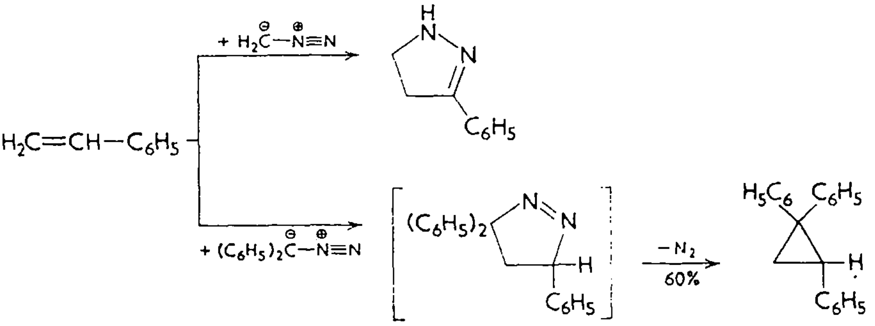
Additions of diazomethane to α,β-unsaturated nitroalkanes frequently produce isolable nitropyrazolines as the primary products. These, however, undergo aromatization at higher temperatures with loss of nitrous acid[374]. In these reactions as with α,β-unsaturated carbonyl compounds, the products have the structures expected on the basis of electronic effects; that is, the nucleophilic diazomethane carbon becomes attached to the electrophilic β-carbon of the dipolarophile. In contrast, additions of diazodiphenylmethane to nitroolefins



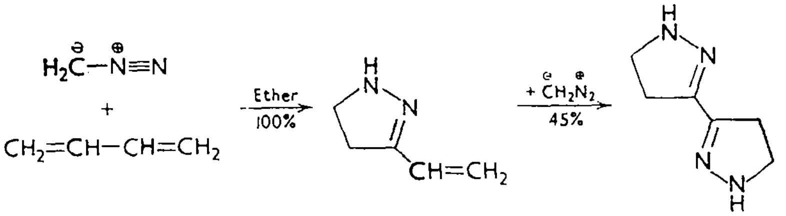
take place in the inverse sense. Aromatization of the primary adduct in this case necessitates phenyl migration[375]. Obviously, the electronically anomalous orientation is the one favored by steric factors.

Competition of the alternative modes of addition has been observed by Parham in the reactions of diazoalkanes with styryl alkyl sulfones[376].

Compared with the intensive study which the reactions of diazoalkanes with α,β-unsaturated carbonyl and nitro compounds have received, relatively little has been done with phenyl-substituted ethylenes and unconjugated olefins. Oliveri-Mandala reported the formation of 3-phenyl-Δ^2-pyrazoline from diazomethane and styrene[377]. Although in this case the heterocycle could be isolated, the corresponding addition involving diazodiphenylmethane is followed by spontaneous nitrogen elimination[378]. Since the rate of nitrogen loss exceeds the self-decomposition rate of the diazo compounds, a Δ^1-pyrazoline is postulated as an intermediate with the exclusion of a carbene mechanism.

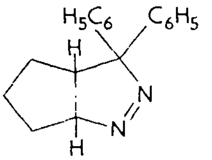


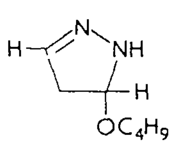
1,3-Butadiene also adds diazomethane relatively easily. The initial product, 3-vinyl-Δ^2-pyrazoline, is converted by an excess of diazomethane into bis-3-pyrazolinyl[379].



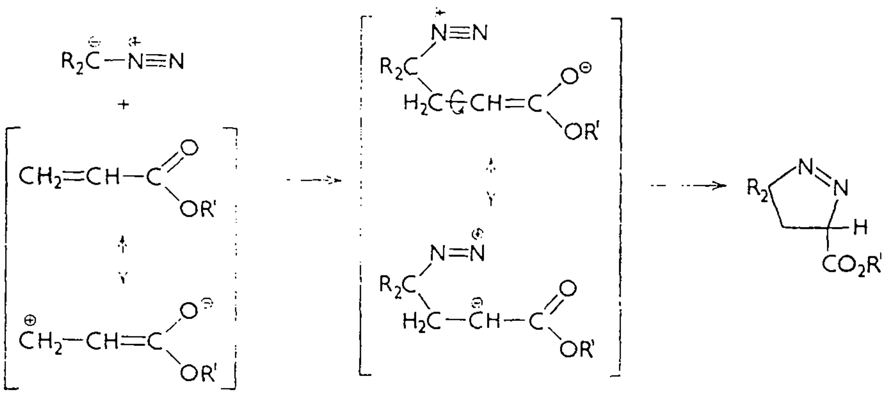
The yields are lower when simple olefins are used. Diazomethane gives only 9% adduct with ethylene[380] and an even smaller amount with cyclohexene[381]. The superior reactivity of cyclopentene here emerges again; with diazodiphenylmethane at 40° an adduct is obtained in 30% yield, which has been shown by nuclear magnetic resonance to be the Δ^1-pyrazoline[382]. Ethyl diazoacetate and cyclopentene at 80° form 89% adduct; with 1-heptene the yield is 39%[382].

The union of vinyl n-butyl ether with diazomethane results in a 55% yield of 4-butoxy-Δ^2-pyrazoline[383].





For many years the outstanding capacity of α,β-unsaturated carbonyl compounds and nitriles to react with diazoalkanes has been explained on the basis of a two-step mechanism[384,385]. It has been supposed that the rate-determining step is an electrophilic attack of the carbon–carbon double bond upon the diazo compound to form a zwitterion **15**. The possibility of delocalization of the negative charge would enhance the stability of the betaine. Ring closure to the Δ^1-pyrazoline would presumably take place in a rapid second step.



(15)

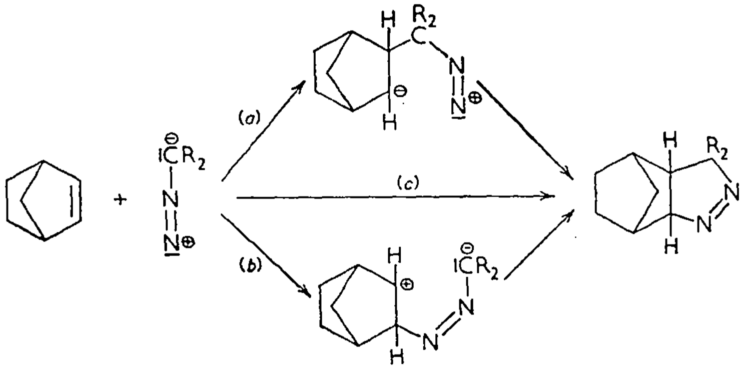
A weakness of this mechanistic interpretation is apparent in the nature of the diazonium intermediate **15**. Alkyldiazonium ions tend to lose nitrogen very rapidly; in fact this seems to be the only known exothermic ionization leading to a carbonium ion[386]. The expectation that reactions of diazoalkanes with electrophilic alkenes would be accompanied by nitrogen elimination is not fulfilled; many such additions go to completion without perceptible gas evolution.

If indeed nitrogen evolution is occasionally observed in the course of the reaction, decomposition of the often labile Δ^1-pyrazolines provides a plausible explanation. The two-step mechanism outlined above would lead one to expect a competition between the diazonium ion decomposition and the ring closure of the betaine to form the stable pyrazoline, but in no case have a stable pyrazoline and the product of nitrogen elimination been found together.

An additional argument against the intermediate **15** lies in the stereospecificity of the addition. As has been pointed out, reactions of suitable *cis-trans* olefin pairs with diazoalkanes produce diastereoisomeric products without mutual contamination (p. 827). The two-step process can only be sustained by the assumption that rotation about the indicated carbon–carbon bond in **15** is much slower than the ring closure. Finally, the addition of diazoalkanes to nucleophilic olefins (p. 830) also speaks against a two-step process.

A strong argument in support of a single-step multi-center addition has been found in the study of pyrazoline formation from diazoalkanes and angle-strained bicylo[2.2.1]heptene derivatives[387]. Huisgen and Fleischmann investigated the dependence of the rate of addition upon the constitution of the diazoalkane and related this to the reaction mechanism[388].

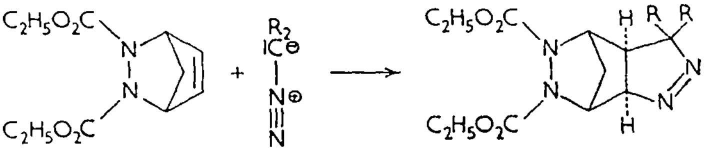
Of the three conceivable reaction paths, (*a*) which represents a nucleophilic addition of the diazoalkane to the double bond has no analogy in the chemistry of alkenes. Path (*b*) is initiated by an electrophilic attack of the terminal diazo nitrogen atom and completed by rapid cyclization to the pyrazoline. The third possibility is the concerted addition (*c*).



(16)

Additions of nucleophiles, for example, sulfite or cyanide ion[360], at the terminal nitrogen atom of the diazo group occur more rapidly since the anionic charge is better stabilized in the intermediate, an analog of **16**. This would also lead one to expect increasing reaction rates in the series, diazomethane, ethyl diazoacetate, diazoacetophenone, diazobenzoylacetone towards a strained double bond. However, in agreement with preparative experience[388], the kinetic data in Table 9 established quite the reverse order of reactivity. On the other hand, these rate data are in accord with the multi-center addition (*c*). The decrease in rate coefficients merely reflects the increase in resonance stabilization of the ground state of the diazoalkane.

TABLE 9. Rates of cycloaddition of diazoalkanes to diethyl-2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate in *N,N*-dimethylformamide at 60°[382].



1,3-Dipole	10^6k_2 (l./mole sec)
Diazomethane	97,000
Diazodiphenylmethane	1,020
Diazofluorene	293
Ethyl diazoacetate	93
Diazoacetophenone	18
Diazo-*p*-nitroacetophenone	8·5
Diazobenzoylacetone	< 1

Additional strong support for the concerted mechanism may be drawn from the observed minor dependence of the addition rate upon solvent polarity. In the two-step reaction paths (*a*) and (*b*), the primary step involves development of a zwitterion having distant charges separated by a tetrahedral carbon atom. Since, in contrast to the diazoalkane itself, exchange of the charges is here no longer possible, the activated complex in the rate-determining step should possess a considerably higher electric moment. A drastic enhancement in rate with increasing solvent polarity should result. On the other hand, little or no solvent effect would be predicted for the multicenter process.

Rate coefficients have been measured for several cycloadditions of diazoalkanes to dimethyl fumarate and to an angle-strained double bond in a variety of solvents[389]. Within the polarity range between benzene and N,N-dimethylformamide, the k_2 data do not show a regular trend; their variation does not exceed a factor of 3·2. These results are in agreement with the multi-center process.

Multi-center reactions require strict orientation of the components in the activation step. As a consequence large negative entropies of activation are the rule, associated with only small values for the activation enthalpy. The thermodynamic parameters for the reaction of diazodiphenylmethane with suitable olefins (Table 10) do, in fact, exhibit these characteristics[389]. Large negative entropy values have been observed in all 1,3-dipolar additions investigated kinetically.

TABLE 10. Activation parameters for some additions of diazodiphenylmethane in N,N-dimethylformamide[389].

Dipolarophile	$\Delta H^\ddagger$ (kcal/mole)	$\Delta S^\ddagger$ (e.u.)
Ethyl acrylate	8·0	−43
Dimethyl fumarate	8·4	−39
Diethyl 2,3-diazabicyclo[2,2,1]hept-5-ene-2,3-dicarboxylate	12·7	−34

The rules discussed in connection with nitrilimines and nitrile oxides also hold for predicting the relative reactivities of substituted

TABLE 11. Rate coefficients for the addition of diazodiphenylmethane to alkenes in N,N-dimethylformamide at 40°[389].

Dipolarophile	$10^5 k_2$ (l./mole sec)
Maleic anhydride	5,830
Phenyl acrylate	2,500
Dimethyl fumarate	2,450
trans-Dibenzoylethylene	979
Ethyl acrylate	707
Acrylonitrile	434
Dimethyl maleate	68·5
Ethyl methacrylate	50·5
Dicyclopentadiene	3·45
Norbornene	2·86
Ethyl crotonate	2·46
Styrene	1·40
Ethyl cinnamate	1·25
Acenaphthylene	0·32
1,1-Diphenylethylene	0·27

olefins toward diazoalkanes. The activating influence of conjugated carbonyl and nitrile functions is clearly apparent in the data of Table 11. Phenyl acrylate exceeds the ethyl ester by a factor of 3·5; phenyl esters are generally intermediate in reactivity between the alkyl esters and acid anhydrides. The rate coefficients for ethyl acrylate, methacrylate and crotonate reflect the retarding effect of methyl substitution in the dipolarophile with the ratio of 280:20:1.

The enhanced dipolarophilic reactivity of *trans* olefins over the *cis* isomers has already been explained on page 820. As would be expected, the rate ratio k_{trans}/k_{cis} increases with the steric requirements of the eclipsed substituents in the *cis* configuration[341] (Table 12). While *trans*-dibenzoylethylene reacts 110 times faster than its *cis* isomer, the factor is only 2·6 for ethyl crotonate where the small methyl–ethoxycarbonyl interaction is involved.

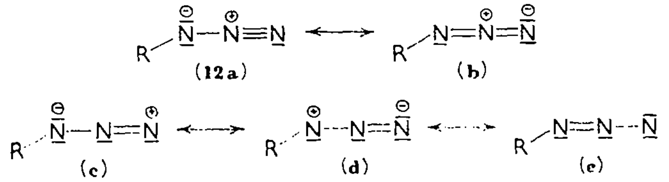
TABLE 12. Rate coefficients for the addition of diazodiphenylmethane to *cis–trans* isomeric alkenes at 40°[341].

Dipolarophile	Solvent	$10^5 k_2$ (l./mole sec)	$\frac{k_{2\ trans}}{k_{2\ cis}}$
trans-Dibenzoylethylene	Dioxane	562	110
cis-Dibenzoylethylene	Dioxane	5·14	
Dimethyl fumarate	*N*,*N*-Dimethylformamide	2450	36
Dimethyl maleate	*N*,*N*-Dimethylformamide	68·5	
Dimethyl mesaconate	*N*,*N*-Dimethylformamide	13·9	8·5
Dimethyl citraconate	*N*,*N*-Dimethylformamide	1·65	
Ethyl *trans*-crotonate	*N*,*N*-Dimethylformamide	2·46	2·6
Ethyl *cis*-crotonate	*N*,*N*-Dimethylformamide	0·95	

5. Azides

Hydrazoic acid and organic azides can be regarded as imides of molecular nitrogen (Table 4). The stability of this array of three nitrogen atoms rests on its substantial resonance energy. The mutual charge compensation of the two all-octet structures **a** and **b** is evident from the fact that the dipole moment of phenyl azide is only 1·55 D[361]. Moreover, x-ray structural analysis[390] has established that the nitrogen–nitrogen bond orders are intermediate between a single and double, and a double and triple bond, respectively.

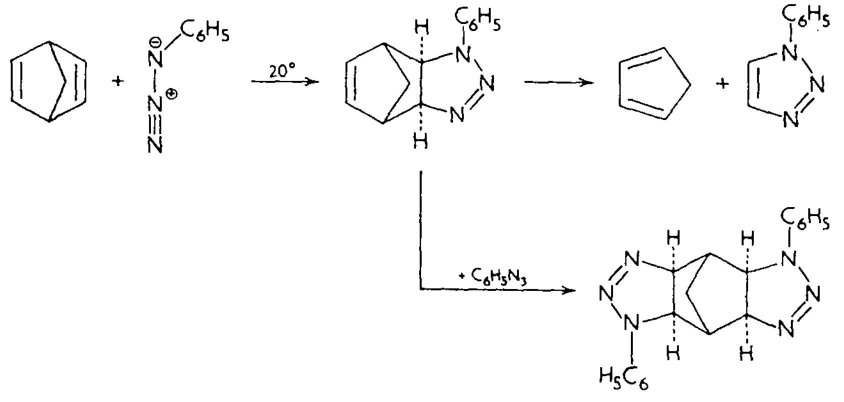
sp Hybridization of the σ bonds of the central nitrogen atom leads to a linear chain of three nitrogen atoms in the ground state. In order that the first and third nitrogen atoms may make contact with the π bond of an olefinic dipolarophile in the course of a cycloaddition, bending of the linear azide system is required. An LCAO calculation by Roberts[391] has shown that such bending is possible without too great an expenditure of energy. It appears that the energy lost in breaking one π bond is partially compensated by a regain through



rehybridization. We suppose that these relationships may be assumed to hold for the other five 1,3-dipoles 'with double bond' (Table 4, p. 808).

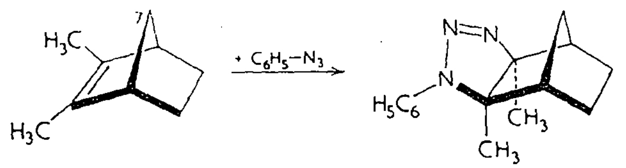
While the addition of azides to acetylenes leads to the stable aromatic 1,2,3-triazole ring system, reaction with olefins produces derivatives of 4,5-dihydro-1,2,3-triazole, whose thermal lability frequently causes preparative difficulties. Many of the Δ^2-triazolines lose nitrogen below 100°.

a. Angle-strained double bonds and cycloalkenes. The most thoroughly studied additions of azides are those to the angle-strained double bonds of bicyclo[2.2.1]heptene derivatives. In the hands of Alder and Stein[387], facile phenyl azide addition served well as a diagnostic tool for the bicyclo[2.2.1]heptene double bond. Norbornene and dicyclopentadiene afford good illustrations, each reacting exothermically and quantitatively with phenyl azide[387,392]. Norbornadiene is

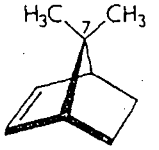


able to add two moles of phenyl or *p*-nitrophenyl azide[393]. The monoadducts obtained when excess of norbornadiene is used decompose easily in a retro-Diels–Alder reaction, giving cyclopentadiene and 1-aryltriazoles[393]. Aliphatic azides also combine with norbornadiene and dicyclopentadiene, but the yields obtained are often low[394].

Alder and Stein pointed out that azide addition to the bicyclo[2.2.1]-heptene system takes place with exclusive *exo* orientation[395]. Cycloaddition fails if *exo* attack is sterically hindered by substituents at the methylene bridge (position 7). Even though the tetrasubstituted ethylenic bond of santene (**17**) adds phenyl azide smoothly, apobornylene (**18**) is incapable of reaction. Conclusive proof of this selectivity was provided by the nuclear magnetic resonance spectrum of the adduct of phenylazide and norbornene which clearly showed that only the *exo* attack occurred[393].

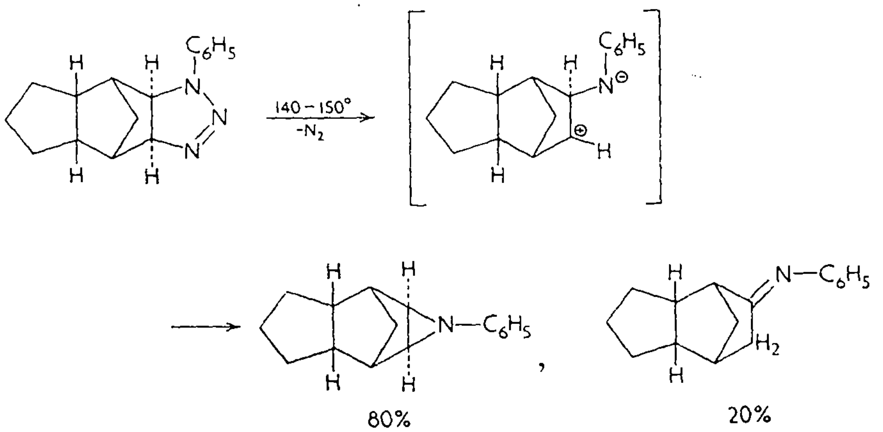


(**17**)



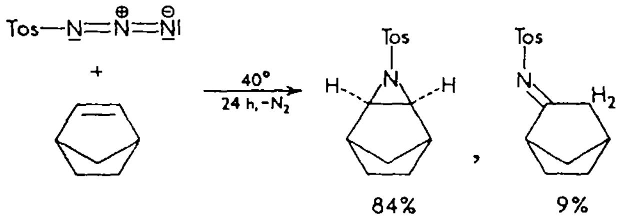
(**18**)

The adducts formed by organic azides and bicycloheptene derivatives are relatively stable to heat. Elimination of nitrogen takes place only at about 150°, with formation of a mixture of an aziridine and a Schiff base, as illustrated below for dihydrodicyclopentadiene[395].



The presumed zwitterionic intermediate may stabilize itself through closure of a three-membered ring or by hydride shift. The intermediate, which would be a 1,3-dipole without octet stabilization, has not however been experimentally substantiated. Incidentally, photolysis of the dihydrotriazoles leads to aziridines exclusively[395a].

The cleavage of triazolines in the presence of acid catalysts usually occurs at room temperature. Addition of a proton at $N_{(1)}$ blocks the stabilizing resonance of the triazoline system. In view of this, it is not surprising that *N*-acyl groups also promote elimination of nitrogen from a triazoline. For this reason, the adduct of benzazide and norbornene cannot be isolated; at 40° the induction period for nitrogen evolution shows that the rates of cycloaddition and of triazoline decomposition are comparable. The products are a *N*-benzoylaziridine in 65% yield, together with 22% of a substituted oxazoline[396]. The same is true for the addition of *p*-toluenesulfonyl azide which is followed by a rapid nitrogen elimination[396,397].

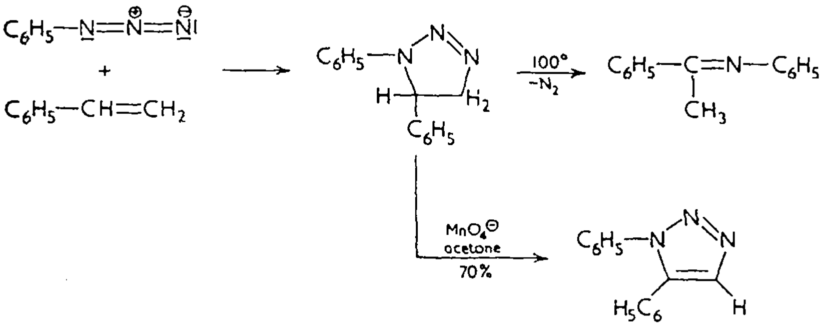


It is recognized that *trans*-cyclooctene, the smallest known cyclic olefin with a *trans* configuration, possesses an angle-strained double bond; the heat of hydrogenation exceeds that of *cis*-cyclooctene by approximately 9 kcal[340]. Even at room temperature the *trans* isomer adds phenyl azide exothermically[397], while formation of the diastereoisomeric triazoline from the *cis* isomer requires several months[395]. This observation is the only evidence for stereoselectivity in the cycloaddition of azides. The enhanced reactivity of the *trans* configuration is also apparent in higher cyclic olefins[398,399].

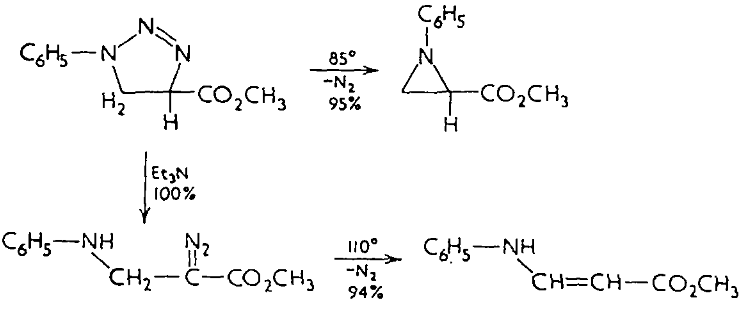
b. Simple and conjugated alkenes. Similar to *cis*-cyclooctene, cyclopentene and unstrained cycloalkenes require a higher temperature for the azide addition or a very long reaction time at lower temperatures to reduce degradation of the resulting labile triazolines[395,400]. The triazoline from cyclopentene and phenyl azide loses nitrogen below 100° with quantitative formation of cyclopentanone anil[395]. In the analogous reaction of cyclopentene with tosyl azide nitrogen is evolved even at 40°[393].

Little is known about the reactions of simple acyclic olefins with azides. *p*-Nitrophenyl azide reacts with *trans*-2-butene during forty days at 25° to give a 31% yield of 1-(*p*-nitrophenyl)-4,5-dimethyl-Δ^2-triazoline[400]. The reaction of phenyl azide with trimethylethylene described by Wolff[401] probably needs checking.

Conjugated olefins have been investigated somewhat more thoroughly. Phenyl azide adds to styrene to form 1,5-diphenyl-Δ^2-triazoline[400,401], which at 100° decomposes to give a mixture of 1,2-diphenylaziridine and acetophenone anil with evolution of nitrogen. Oxidation of the triazoline with potassium permanganate leads to the known 1,5-diphenyl-1,2,3-triazole[393]. Nuclear substituted styrenes and indene react similarly[400,402].



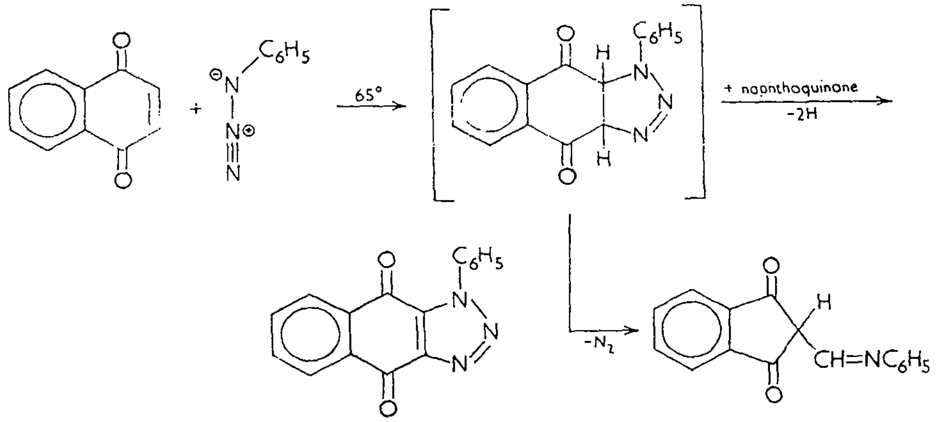
The superiority of α,β-unsaturated carbonyl compounds over unconjugated olefins in their dipolarophilic activity is much less pronounced toward azides than toward the diazoalkanes (p. 818). Phenylazide adds to methyl acrylate to give methyl 1-phenyl-Δ^2-triazoline-4-carboxylate, the structure of which was proven by dehydrogenation to the known triazole derivative[393]. Thus styrene and methyl acrylate differ in their orientation of addition.



With base catalysis the methyl 1-phenyltriazoline-4-carboxylate undergoes an unexpected ring opening to form methyl 2-diazo-3-anilinopropionate. It is interesting to note that the thermolysis of the triazoline gives exclusively the aziridine, while the isomeric diazo compound decomposes with the sole formation of methyl 3-anilinoacrylate[393].

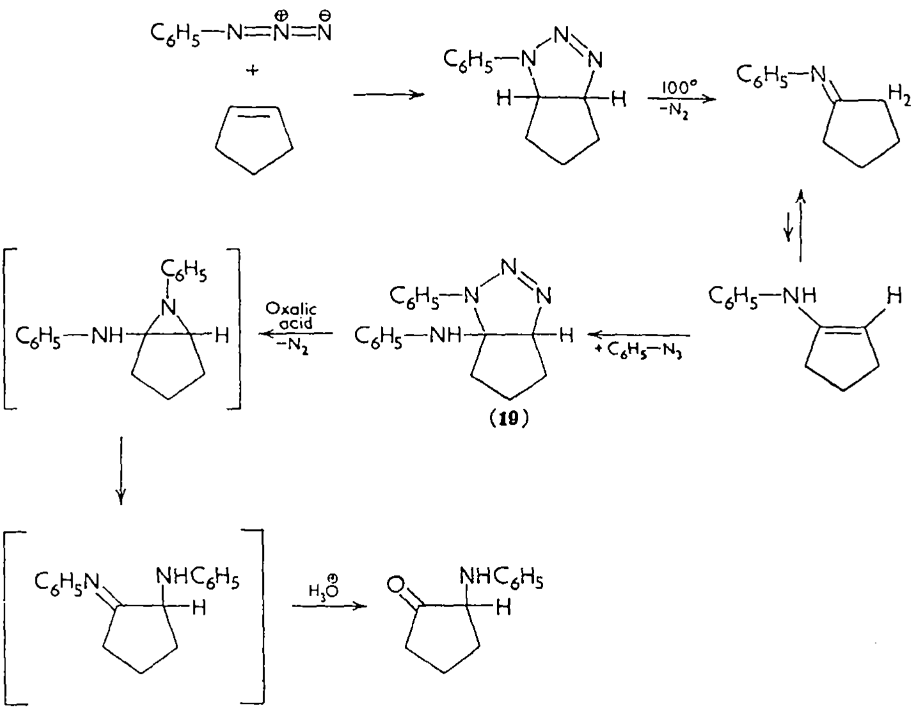
In contrast to earlier reports[401], dimethyl 2-diazo-3-anilinosuccinate, formed *via* the triazoline, has now been shown to be the product from phenylazide and dimethyl fumarate[393]. Upon pyrolysis at 130°, dimethyl 2-anilinofumarate is obtained.

Cycloadditions of aromatic azides to maleimides and to unsaturated sulfonamides have also been reported[369,403,404]. The action of azides on quinones of the benzene series leads to mono- or bisadducts depending on the reaction conditions[401,405,406]. The triazolines formed first are easily dehydrogenated by excess quinone to *vic*-triazoloquinones, probably through a hydroquinone intermediate. It is presumed that aziridines are present among the products of thermal degradation. According to Wolff[407], 1-phenyl-4,9-dioxo-3a,4,9,9a-tetrahydronaphtho[2,3-*d*]triazole suffers a ring contraction under thermolytic conditions; nitrogen evolution is accompanied by an interesting acyl migration.

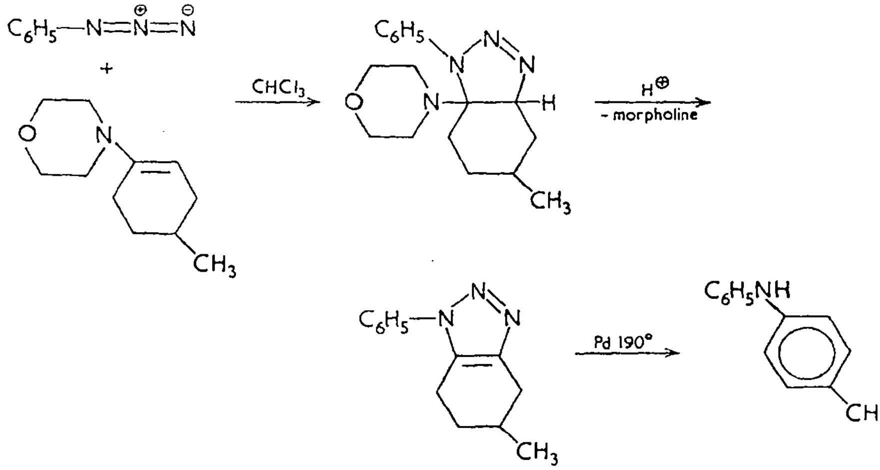


c. Enamines and enol ethers. The electron-rich double bonds of enamines are particularly receptive to organic azides. Alder and Stein[395,408] observed that heating cyclopentene with excess phenyl azide leads to an 'N$_4$ compound', which probably is formed by addition of a second molecule of the azide to an enamine or anil derived from the primary adduct. The structure proposed by the authors probably needs revision to **19** in the light of recent work; the reaction scheme on page 841 offers a new interpretation of the acid degradation to 2-anilinocyclopentanone.

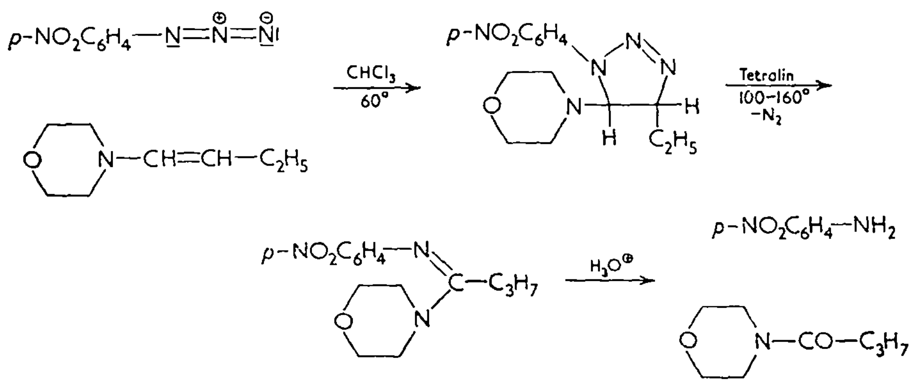
Fusco and coworkers studied the reactions of aromatic azides with enamines. Their structure proof for the adduct from 1-morpholino-



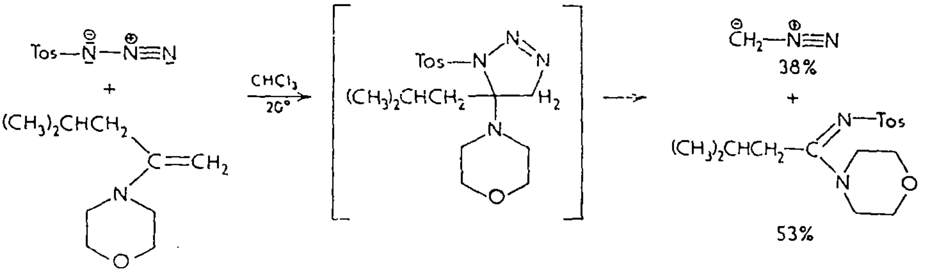
4-methylcyclohex-1-ene and phenyl azide is indicated below[409]. The orientation is that favored by electronic rather than steric considerations. The readiness with which enamine adducts aromatize to *vic*-triazoles by acid-catalyzed elimination of the secondary amine, has also been noted by our research group in Munich[400].



The enamine adducts from *p*-nitrophenyl azide rearrange on pyrolysis with elimination of nitrogen and formation of an amidine[409]. Here also the degradation products provide evidence for the orientation in the 1 : 1 adduct.



A series of enamine adducts from tosyl azide have been shown to undergo an interesting 1,3-dipolar elimination. For example, **20**, prepared from 2-morpholino-4-methylpent-1-ene, decomposes at room temperature to diazomethane and an amidine having one less carbon atom[410].



(20)

Enol ethers are inferior to enamines in their rates of azide addition. The dominant orienting factor, stabilization of a positive charge by the neighboring oxygen atom, is equivalent to that in the enamine case. 2,3-Dihydrofuran and 2,3-dihydropyran give single adducts with aromatic azides[400] or with tosyl azide[393] (formulation on p. 843).

d. Kinetic studies. The low solvent dependence observed for the addition of phenyl azide or *p*-nitrophenyl azide to the strained double bond of diethyl 2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate is again good evidence for the small charge separation in the transition state[378]. The rate coefficients for the reactions of phenyl azide with olefinic dipolarophiles (Table 13) exhibit typical phenomena, such as steric hindrance due to an α- or β-methyl substituent in ethyl acrylate, which have previously been discussed. The carboxylate function is moderately activating, while the second group of this kind (fumarate and maleate) causes deactivation despite the additional favorable electronic effect. Probably, steric factors come into play.

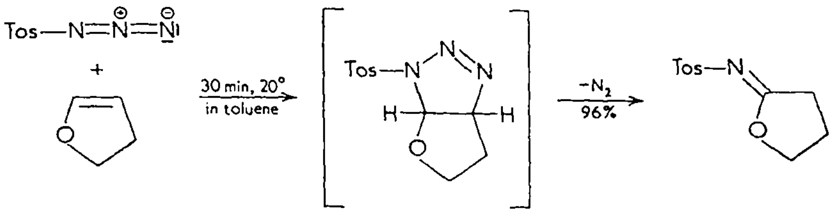


Table 13. Rate coefficients for the addition of phenyl azide to carbon–carbon double bonds in carbon tetrachloride at 25°[393,400].

Dipolarophile	$10^7 k_2$ (l./mole sec)
1-Pyrrolidinocyclopentene[a]	115,000
1-Pyrrolidinocyclohexene[a]	9,930
1-Morpholinocyclopentene[a]	2,580
Norbornadiene	194
Norbornene	188
Ethyl acrylate	9·85
Diethyl fumarate	8·36
Cyclopentene	1·86
Methyl methacrylate	0·72
Vinyl n-butyl ether	0·40
Styrene	0·40
Dimethyl maleate	0·34
Ethyl crotonate	0·27
1-Heptene	0·24

[a] In benzene

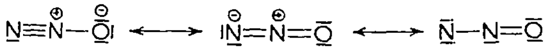
Electron-attracting as well as electron-donating substituents conjugated with the double bond have an activating influence on the dipolarophile. Enamines attain a 10^6-fold increase in reaction rate over conjugated alkenes, which illustrates the importance of the electron density at the double bond. 1-Pyrrolidinocyclopentene reacts 45 times faster than 1-morpholinocyclopentene.

An abnormally large effect is also found for the influence of nuclear substituents on the rate of addition of phenyl azide. Electron-rich azides add particularly easily to electron-poor olefins and the converse is also true. The rate ratio of *p*-nitrophenyl azide to *p*-methoxyphenyl azide in their cycloadditions is with *N*-phenylmaleimide but 440 with 1-pyrrolidinocyclohexene. The substituted phenyl azides follow the Hammett equation; the ρ values (in benzene at 25°) are $+0{\cdot}8$ for cyclopentene, $+0{\cdot}9$ for norbornene, $-1{\cdot}2$ for maleic anhydride, and $+2{\cdot}6$ for 1-pyrrolidinocyclohexene[393].

This Hammett correlation in itself makes it improbable that two mechanistic schemes are competing. The rate coefficient for the addition of phenyl azide to 1-pyrrolidinocyclopentene at 25° increases only by a factor of 10 as the solvent is changed from cyclohexane to *N*,*N*-dimethylformamide[393]. This small solvent dependence is incompatible with a two-step mechanism. Thus there is reason to believe that the addition of azides to enamines follows the usual concerted path despite a relatively high substituent influence. Following our definitions on page 765, organic azides display electrophilicnucleophilic reactivity.

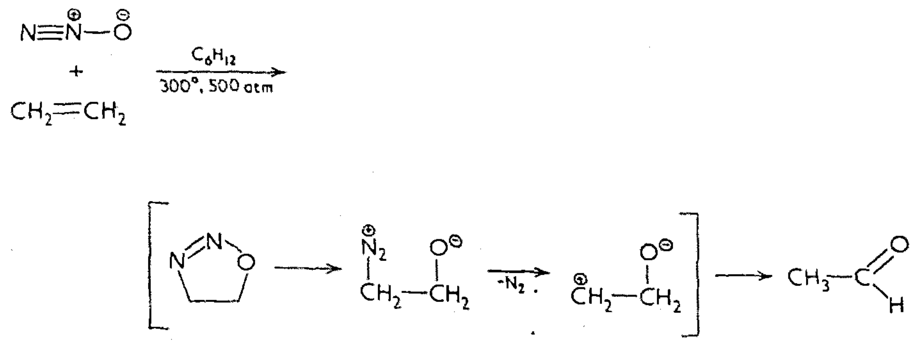
6. Nitrous oxide

The dipole moment of the linear[411] nitrous oxide molecule is only 0·17 D[412], which is good evidence for the nearly equal contribution of the two octet resonance structures to the ground state. The nitrogen–nitrogen distance is 1·13 Å, intermediate between values for the double and triple bonds; the nitrogen–oxygen distance of 1·19 Å is between those of double and single bonds[413].



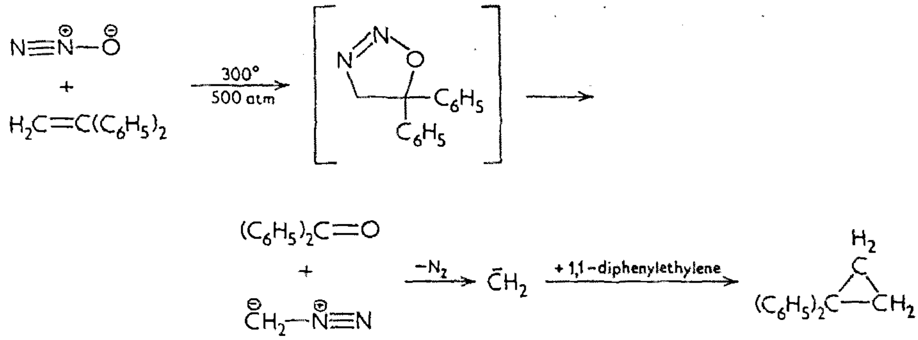
$$\underline{N}\equiv\overset{\oplus}{N}-\overset{\ominus}{\overline{\underline{O}}}| \longleftrightarrow |\overset{\ominus}{\underline{N}}=\overset{\oplus}{N}=\overline{\underline{O}} \longleftrightarrow \overline{\underline{N}}-\underline{N}=\overline{\underline{O}}$$

The reactions of nitrous oxide with alkenes and alkynes, studied by Buckley and colleagues[414], may be considered 1,3-dipolar additions. Although cyclic adducts could not actually be isolated, the nature of the subsequent products leaves little doubt of the occurrence of oxadiazoline and oxadiazole intermediates, respectively. Thus the reaction with ethylene at 300° which leads to acetaldehyde and nitrogen can be interpreted as involving the primary formation of 1,2,3-oxadiazoline. The 'diazo oxide' resulting from ring opening is converted to acetaldehyde by elimination of nitrogen and a hydride transfer. The intermediate **21** is the same as that postulated for the primary product from formaldehyde and diazomethane.



(21)

The reaction with 1,1-diphenylethylene takes a different course. Here the intermediate appears to dissociate to benzophenone and diazomethane; the latter decomposes further to methylene which combines with excess olefin forming diphenylcyclopropane.

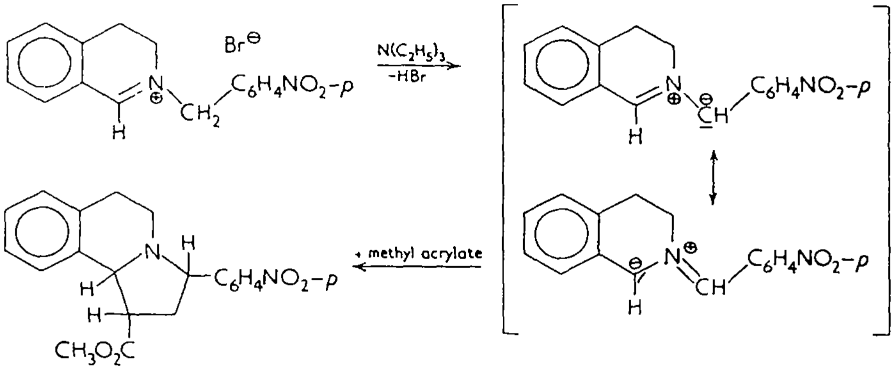


C. *Cycloadditions of '1,3-Dipoles without Double Bond'*

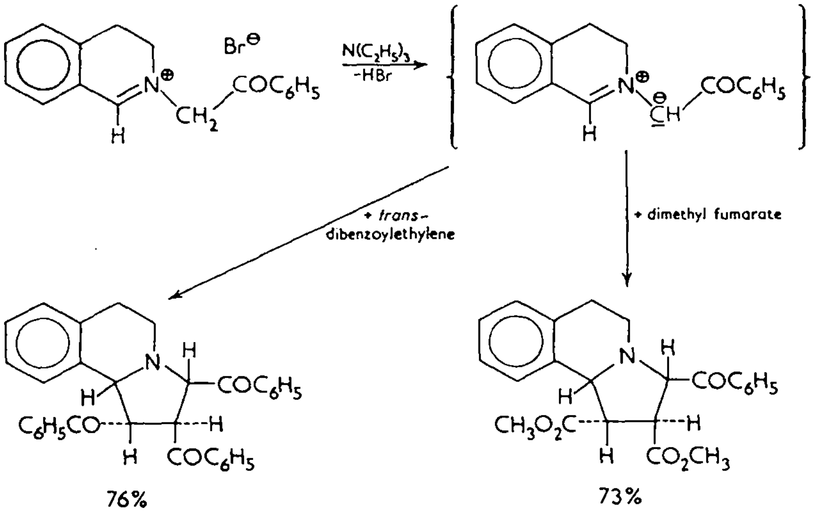
1. Azomethine ylides (Nitrenes)

The azomethine ylide system was made accessible for the first time by the research group in Munich. Staudinger and Miescher assigned the structure of a 'nitrene', *i.e.* an azomethine ylide by our definition, to products obtained from *N*-arylnitrones and diphenylketene. Later experiments revealed a different structure for these products.

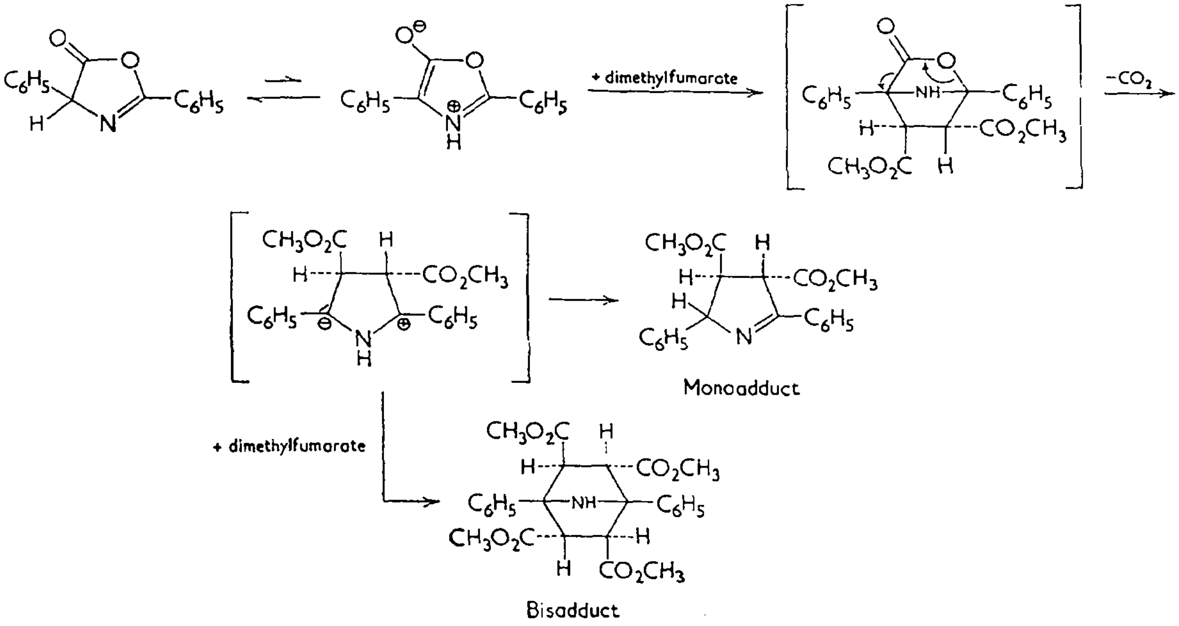
1,3-Dipoles of this class may be prepared *in situ* by the action of a tertiary base on certain immonium salts. Thus triethylamine liberates from *N*(*p*-nitrobenzyl)3,4-dihydroisoquinolinium bromide an orange-yellow azomethine ylide which combines with methyl acrylate to form a 1:1 adduct[415]. Degradation of this compound to 3-phenylbenzo[*g*]pyrrocoline establishes its constitution. Similar adducts are obtained from dimethyl fumarate or acrylonitrile.



The short-lived ylide from *N*-phenacyl-3,4-dihydroisoquinolinium bromide, which likewise must be prepared *in situ*, similarly combines smoothly with α,β-unsaturated carbonyl compounds.

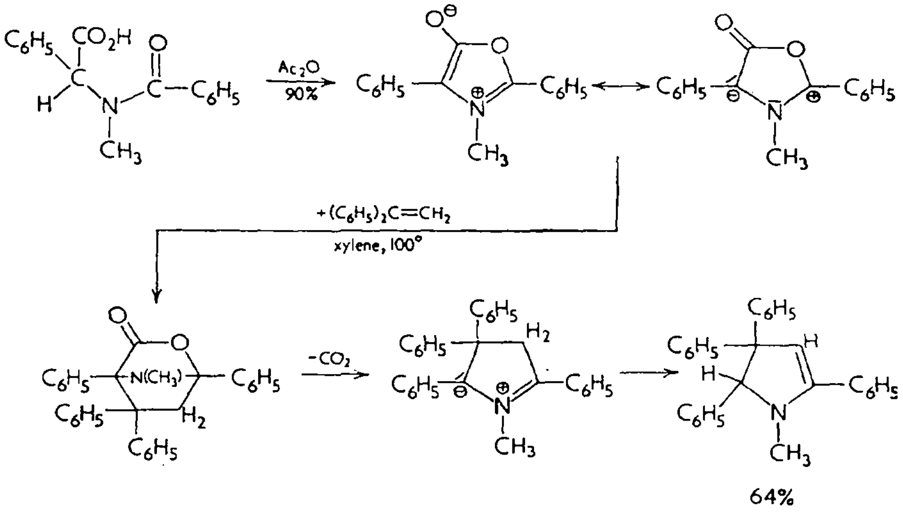


Surprisingly, azlactones behave in their reactivity towards alkenes as azomethine ylides. 2,4-Diphenyloxazolone reacts with 1·1 equivalent of dimethyl fumarate at 120° to give 67% dimethyl 2,5-diphenyl-Δ^1-pyrroline-3,4-dicarboxylate in addition to carbon dioxide[415a]. If one introduces the above oxazolone into an excess of molten dimethyl fumarate, 76% of a bisadduct is obtained which is a derivative of the



7-azabicyclo[2.2.1]heptane system[415a]. The above reaction scheme requires no comment. Decarboxylation yields a new azomethine ylide which can then tautomerize or can enter into a second 1,3-dipolar cycloaddition.

Azlactones appear to be in equilibrium with mesoionic oxazoles

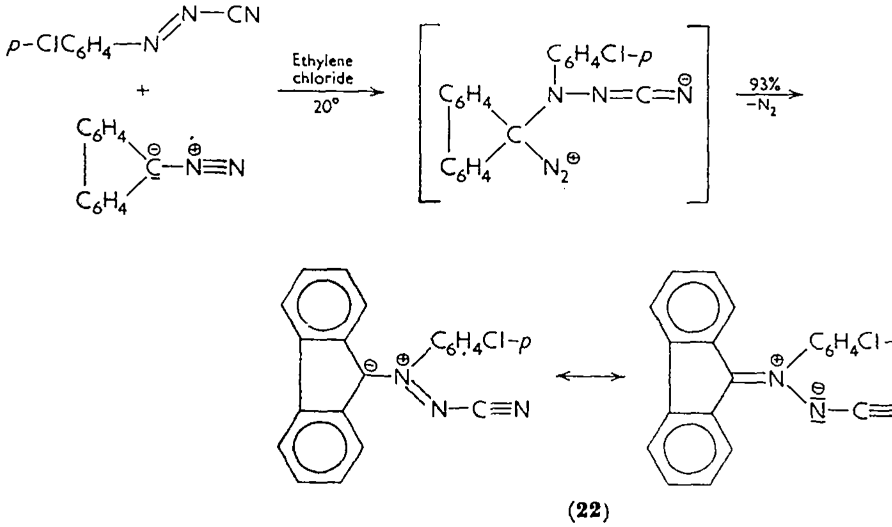


which may be regarded as azomethine ylides. By warming *N*-benzoyl-*N*-methylphenylglycine with acetic anhydride, the mesoionic *N*-methyl derivative of the tautomeric diphenyloxazolone mentioned above can be isolated as yellow crystals. Despite its aromaticity, this anhydro-5-hydroxy-3-methyl-2,4-diphenyloxazolium hydroxide displays a rather unique azomethine ylide activity. For example, α,β-unsaturated carboxylic esters or nitriles undergo exothermic additions at room temperature followed by carbon dioxide expulsion. Even poor dipolarophiles, *e.g.* 1,1-diphenylethylene, react smoothly[415b].

2. Azomethine imines

A few years ago, the synthetic routes to these zwitterionic derivatives of azomethines were disclosed, and the new 1,3-dipoles were shown to enter into cycloadditions. A number of compounds described earlier were recognized as aromatic variations of the azomethine imine system and were likewise drawn into the investigation.

a. N_β-Cyano(azomethine imines). A class of stable, isolable azomethine imines was found by Huisgen, Fleischmann and Eckell to result from the reaction of diazocyanides with aliphatic diazo compounds[416]. Thus, from *p*-chlorophenyl-*anti*-diazocyanide and diazofluorene elimination of one equivalent of nitrogen is observed even at room temperature. The bright orange azomethine imine **22** results in 93% yield; the two all-octet structures of **22** are given above. Analogous azomethine imines were prepared from diphenyldiazomethane and its

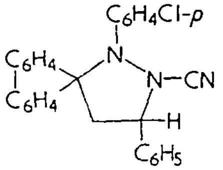


(22)

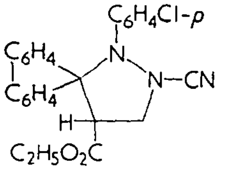
nuclear substituted derivatives, as well as from other diazocyanides and from ethyl *p*-nitrobenzeneazocarboxylate.

Degradation results as well as ultraviolet and infrared spectra are in agreement with the structure **22**. Thus, the infrared nitrile band at 2118 cm^{-1} is in a region typical for cyanamide anions. The strong immonium band occurs at 1548 cm^{-1}. The cyclic adducts prepared from **22** do not exhibit this band, while the nitrile frequency is found in the usual region near 2240 cm^{-1}.

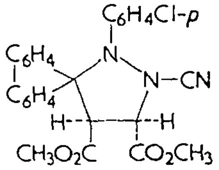
Azomethine imines of the type **22** combine with olefins to produce pyrazolidines[417]. For instance, the reactions with norbornene and norbornadiene form adducts in near quantitative yields. Even the sluggish unconjugated alkenes give good yields of adducts after 50–100 hours at 80°: ethyl undecylenate, 74%; 1-heptene, 84%; cyclopentene, 84%. Several additions to conjugated alkenes are indicated below with reaction conditions, yields and orientation noted.



13 h, 70°
92 %



6 h, 80°
85 %



7 h, 80°
93 %

Kinetic measurements disclose that ethyl acrylate in chlorobenzene at 80° reacts 20 times as fast as styrene and 55 times faster than 1-hexene. The activation parameters for the addition of **22** to ethyl acrylate (in chlorobenzene) are again of an order characteristic of a multi-center addition[418]:

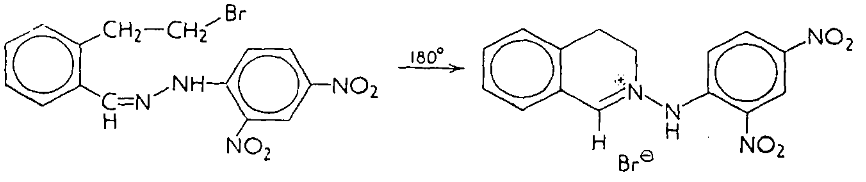
$$\Delta H^{\ddagger} = 12{\cdot}5\ \text{kcal/mole};\ \Delta S^{\ddagger} = -34\ \text{e.u.}$$

The stereospecificity of the reaction has been established through isolation of diastereoisomeric adducts from dimethyl maleate and fumarate. The excellent yields obtained even from simple olefins, as well as the exclusive formation of a single crystalline product in each case, suggest the use of such azomethine imines for the characterization of liquid olefins.

b. Azomethine imines of the 3,4-dihydroisoquinoline series. Owing to their great reactivity, the azomethine imines of the 3,4-dihydroisoquinoline series have been the subject of intensive study in the last few years.

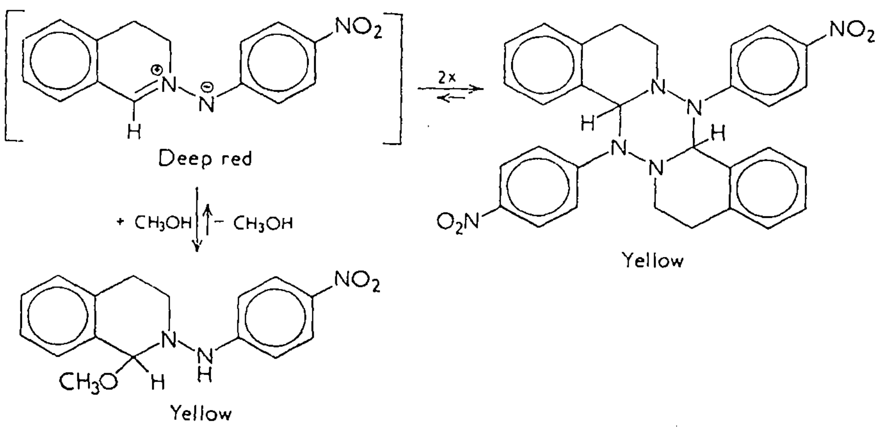
These 1,3-dipoles are not actually isolable, but their easy preparation *in situ* from storable precursors makes them easy to use.

As Schmitz has reported[419], *o*-(β-bromoethyl)benzaldehyde 2,4-dinitrophenylhydrazone undergoes an intramolecular alkylation on heating to form *N*-(2,4-dinitrophenylamino)-3,4-dihydroisoquinolinium bromide (**23**). Analogous hydrazonium salts may be prepared from aryl- or alkylhydrazones of *o*-(β-bromoethyl)benzaldehyde[420–422].



(**23**)

Abstraction of the hydrazone proton by a base, for instance triethylamine, generates the typical azomethine imine system which is depicted below in one of the two all-octet structures. The red azomethine imine dimerizes in a head-to-tail fashion to form a derivative of hexahydro-1,2,4,5-tetrazine[420–422]; such dimers are yellow or colorless depending upon the substituents in the benzene ring. Redevelopment of a red color on gentle warming in an inert solvent reveals the existence of a mobile equilibrium between the dimer and the monomeric azomethine imine. This dissociation equilibrium makes the dimer, which has an excellent shelf-life, a convenient source of the monomeric 1,3-dipole for use in neutral media. Additional masked 1,3-dipoles are the crystalline alcohol

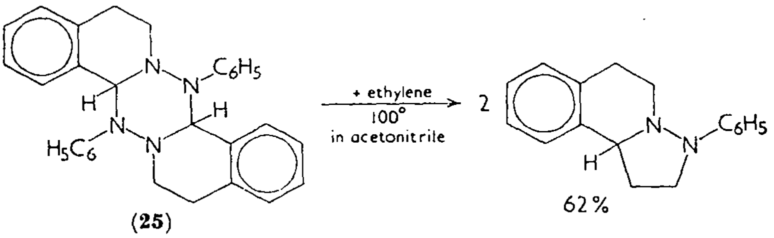


(**24**)

adducts (**24**), which likewise exhibit thermochromism and dissociate reversibly to the starting materials[419,420,423]. These relationships are illustrated for 3,4-dihydroisoquinoline *N*(*p*-nitrophenyl)imine.

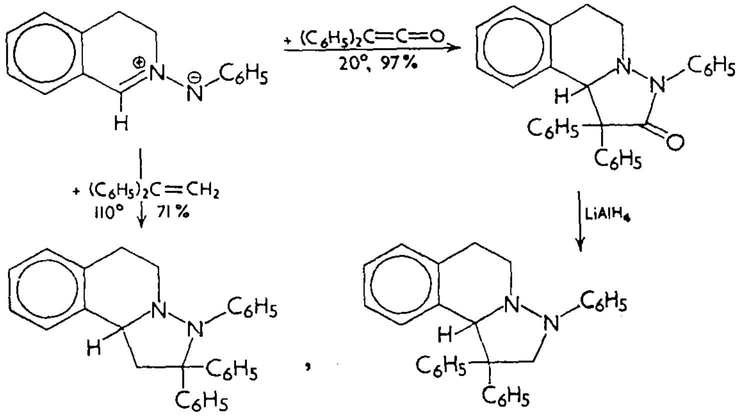
These azomethine imines enter cycloadditions with practically all types of multiple bonds; they are apparently among the most active of the known 1,3-dipoles.

If the hexahydrotetrazine derivative **25** is heated with ethylene (15 atm) in an autoclave at 100°, the dipole generated *in situ* combines with the olefin to give the adduct in 62% yield[421].



(25)

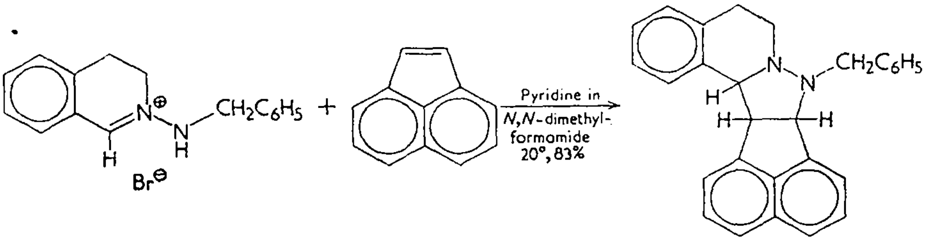
Monosubstituted ethylenes frequently give structural isomers or stereoisomeric adducts. Cycloolefins combine readily with **24** to form well-crystallized pyrazolidines: cyclopentene, 87%; norbornene, 99%; dicyclopentadiene, 100%; norbornadiene, 97%[420,422,424]. The action of *cis-* and *trans*-cyclooctene on **23** in the presence of tertiary bases produces the diastereomeric adducts without mutual contamination[422].



Examples of the reaction of 3,4-dihydroisoquinoline *N*-arylimines with phenyl-conjugated olefins are abundant. Styrene and the *N*-phenylazomethine imine from **25** give an 86% yield of two structural isomers. Reductive ring cleavage reveals that both possible modes of addition are realized[421].

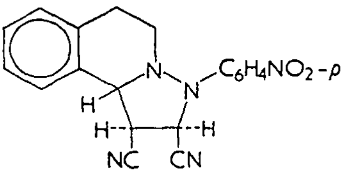
Reaction of **25** with 1,1-diphenylethylene similarly leads to two structurally isomeric pyrazolidines. One of the products can also be obtained by reduction of the diphenylketene adduct. The latter is a lactam which in turn establishes the orientation in the two diphenylethylene adducts[421,422] (formulation on p. 851).

As would be anticipated, *cis*- and *trans*-stilbene combine with **25** to form diastereoisomeric adducts[421,422] without mutual admixture. An example which illustrates the reactivity of *N*-alkylated azomethine imines is the reaction of *N*-benzyldihydroisoquinolinium bromide with acenaphthylene[422].

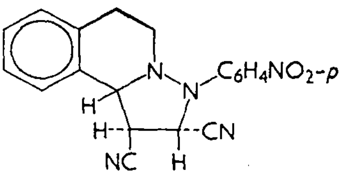


The rapid additions of α,β-unsaturated carbonyl compounds and nitriles frequently lead to diastereoisomers; thus acrylonitrile and **25** give two crystalline adducts in 99% total yield. Maleic anhydride, the 'classic' dienophile, is also an exceptionally good dipolarophile. With both it and the related compound, *N*-phenylmaleimide, addition of the 1,3-dipole generated from **24** takes place in 94% yield in boiling acetonitrile or benzene[422]. Quinones also react smoothly with azomethine imines[425].

As with dimethyl maleate and fumarate, the corresponding nitriles combine with dihydroisoquinoline *N*-(*p*-nitrophenyl)imine in a highly stereoselective manner to give excellent yields of dicyanopyrazolidines[420,422]. Additions to the isomeric dibenzoylethylenes proceed similarly.

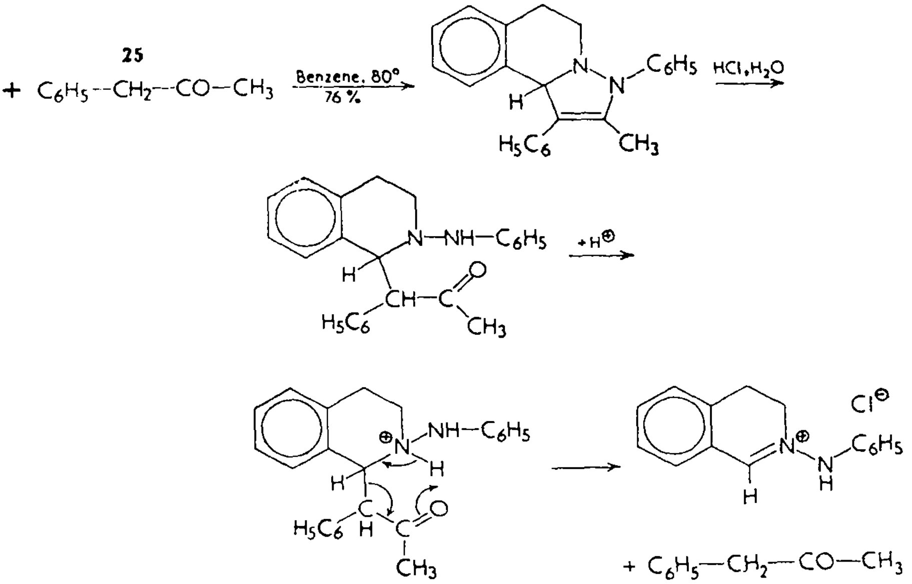


96 %

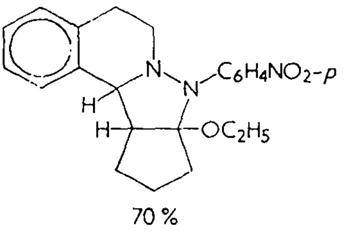


94 %

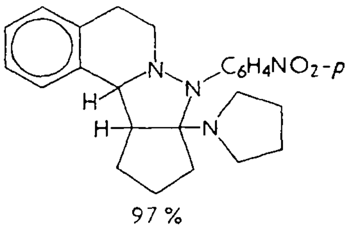
Reactions of enolizable β-dicarbonyl compounds with azomethine imines of the 3,4-dihydroisoquinoline series usually lead, after elimination of water, to Δ^3-pyrazolines, which may also be prepared by addition of the 1,3-dipoles to the respective acetylenes[422]. For instance, **25** combines with acetylacetone to form the dehydrated adduct in 94% yield. Conclusive evidence for the direction of addition is provided by acid hydrolysis, as illustrated for the case of the adduct from **25** and phenylacetone.



Finally, the reaction of azomethine imines with enol ethers and enamines deserves mention. The 1,3-dipole from **24** adds smoothly in boiling benzene to cyclopentenyl ethyl ether, morpholinocyclopentene, and pyrrolidinocyclopentene. Acid hydrolysis of the adducts to cyclopentanone supports the structures indicated below[422].



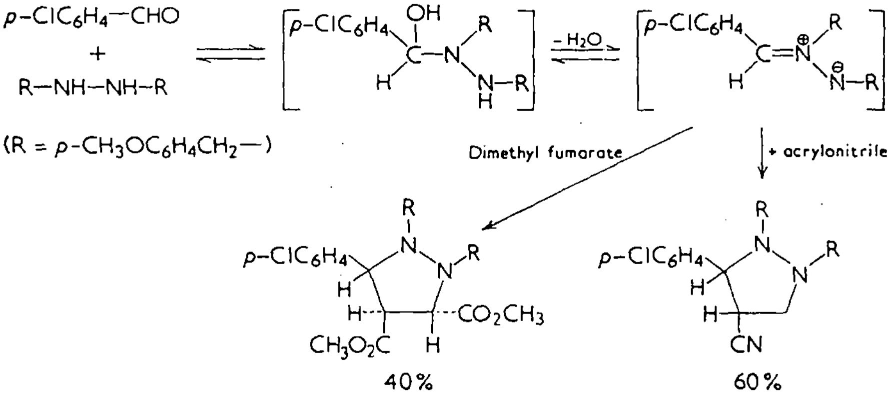
70 %



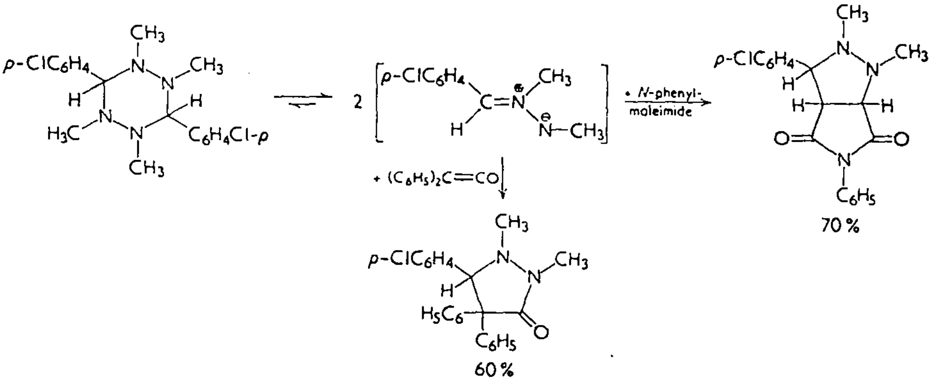
97 %

c. Azomethine imines from 1,2-disubstituted hydrazines and aldehydes. The synthetic methods discussed thus far make available a number of specially substituted azomethine imines. Greater opportunity for structural variation is offered by a new procedure, the reaction of

1,2-disubstituted hydrazines with carbonyl compounds. The 1,3-dipoles which are presumed to be in equilibrium with the α-hydrazinocarbinols should be capable of interception through cycloaddition. As examples may be chosen the reactions of 1,2-bis-(*p*-methoxybenzyl)-hydrazine with *p*-chlorobenzaldehyde and dimethyl fumarate or acrylonitrile[426].



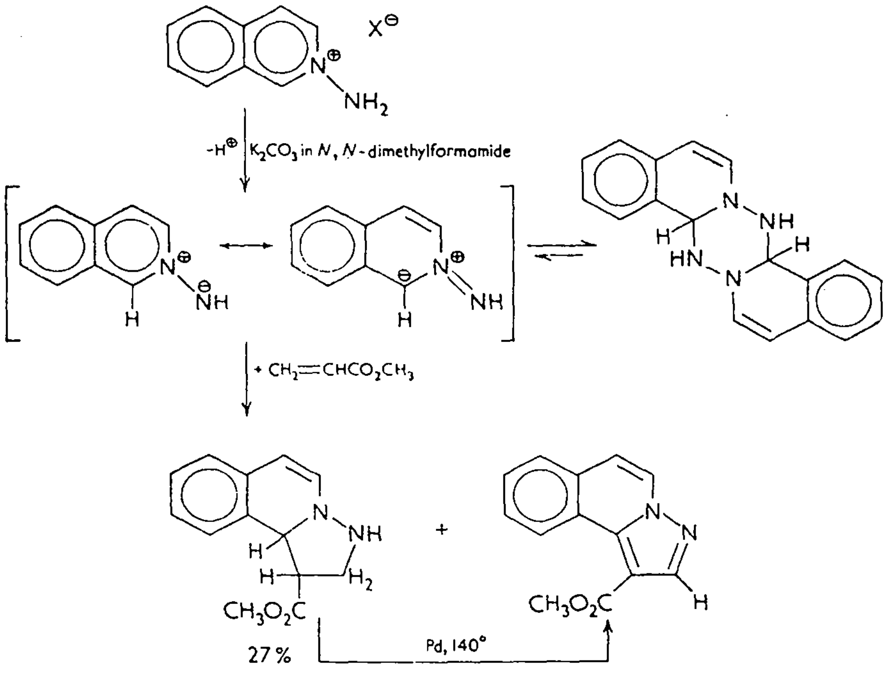
These reactions do not proceed as smoothly as those employing the hexahydrotetrazines discussed earlier. The formation of derivatives of this ring system through reactions of aliphatic aldehydes with hydrazobenzene has long been known[427]. It is possible, although not verified, that this involves dimerization of an azomethine imine. Reactive hexahydrotetrazines are obtained by the condensation of aliphatic hydrazo compounds with aromatic aldehydes.



As an example, the product from two molecules of hydrazomethane and *p*-chlorobenzaldehyde adds to *N*-phenylmaleimide or diphenylketene to form crystalline 1:1 adducts[428].

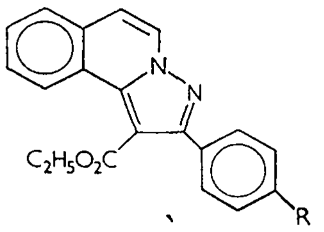
The mechanism of these reactions still requires elucidation; either a one-step cycloaddition of the monomeric azomethine imine or a primary electrophilic attack of the dipolarophile on the hexahydrotetrazine may account for the products. Evidence for support of a multi-center process is found in the isolation of diastereoisomeric pyrazolidines in the combination of the hexahydrotetrazine above with dimethyl maleate and fumarate. Furthermore, the formation of an adduct with acenaphthylene is not easily compatible with the concept of an electrophilic attack.

d. Isoquinoline N-imines. In the isoquinoline *N*-imines the carbon-nitrogen double bond portion of the 1,3-dipole is part of an aromatic system. Such *N*-imines of aromatic nitrogen bases have actually long been known[429,430], although 1,3-dipolar additions involving them have only been described recently[431].

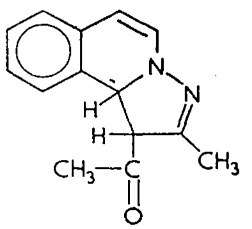


If one treats the *N*-aminoisoquinolinium salt[432] prepared from isoquinoline and hydroxylamine-*O*-sulfonic acid with potassium carbonate, the isoquinoline imine dimerizes immediately to a hexahydrotetrazine derivative[431]. Cycloadditions with this system may proceed *via* a small equilibrium concentration of the monomeric zwitterion. Since the pyridine ring resonance is sacrificed in the course of the cycloaddition, it is not surprizing that considerably less reactivity is found here than with the azomethine imines of the 3,4-dihydroisoquinoline series. It may be mentioned that carboxylic esters of the acetylene series and carbon–sulfur double bonds react more readily than the olefins discussed below.

If the dimer is warmed with methyl acrylate to 70°, in addition to the expected pyrazolidine adduct one obtains a minor amount of the dehydrogenated compound, methyl pyrazolo[1,5-*a*]isoquinoline-3-carboxylate. The reactions of isoquinoline *N*-imine with ethyl cinnamate or *p*-nitrocinnamate lead only to the dehydrogenated pyrazoles (**26**). Surprisingly, the reaction of the hexahydrotetrazine with boiling mesityl oxide proceeds with elimination of the elements of methane; the product isolated in 37% yield may have the structure **27**[431].

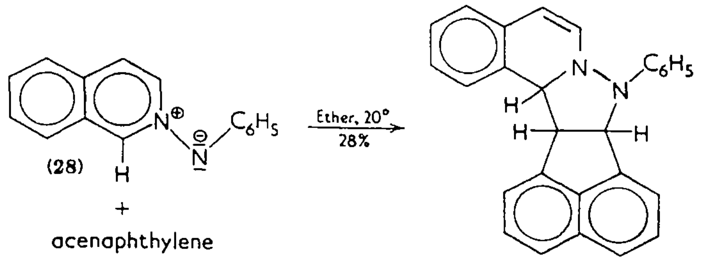


(**26**, R = H, NO_2)



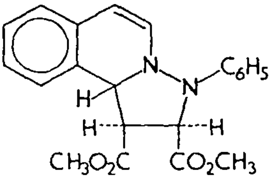
(**27**)

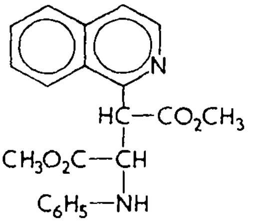
N-Arylamino-3,4-dihydroisoquinolinium salts can be aromatized in the nitrogen-containing ring by oxidation with nitrosobenzene[422]. The same *N*-arylaminoisoquinolinium salts are also obtained from *N*-(2,4-dinitrophenyl)isoquinolinium chloride by way of the ring-opened derivatives with arylhydrazines[433]. Treatment of the salts with aqueous sodium carbonate liberates the highly colored isoquinoline *N*-arylimines, which can be taken up in ether and reacted with olefins[434]. The *N*-(*p*-nitrophenyl)imine can be isolated in analytically pure form.

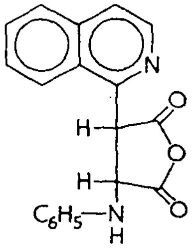


The isoquinoline *N*-arylimines exhibit notable 1,3-dipolar reactivity. An ether solution of the *N*-phenylimine **28** reacts with acenaphthylene at 20° to give a hexacyclic pyrazolidine which can be converted by hydrogenation to the corresponding adduct of the 3,4-dihydroisoquinoline series.

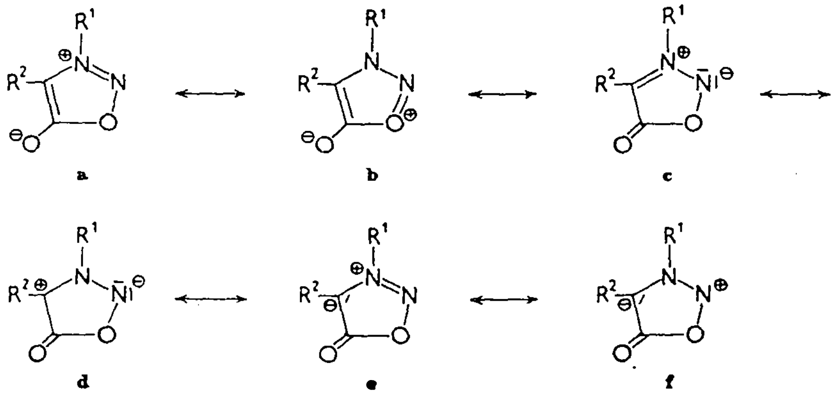
Yields of 61% and 60% are obtained in cycloadditions of **28** to 1,4-naphthoquinone and dimethyl maleate, respectively. The reactions with dimethyl fumarate and maleic anhydride apparently proceed with cleavage of the pyrazolidine ring and regeneration of the aromatic isoquinoline structure, as is indicated by the occurrence of an NH bond in the infrared spectrum and changes in the ultraviolet spectrum[434].


60 %


69%


63 %

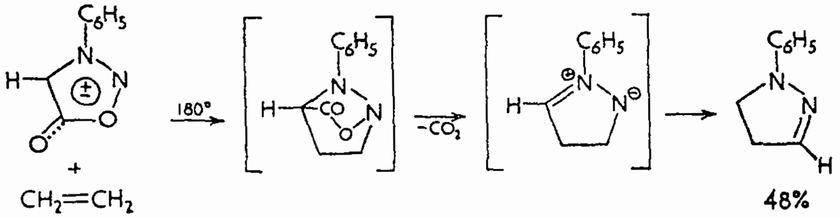
e. Sydnones. Cyclization of *N*-nitroso-α-arylamino or -alkylamino acids with acetic anhydride produces the 'sydnones', discovered by Earl and Mackney in 1935[435]. Later work has shown that these compounds contain a 'mesoionic' aromatic system which can only be depicted with di- and tetrapolar resonance structures[436,437].



A choice of possible octet structures is offered by the formulae **a**–**c**; the resonance contributors **d**–**f** in every case have an electron sextet. The structures **c** and **d** suggest a potential azomethine imine system. The correctness of this hypothesis is established by the reactions of sydnones with carbon–carbon triple bonds which lead with carbon dioxide elimination to good yields of pyrazoles[438].

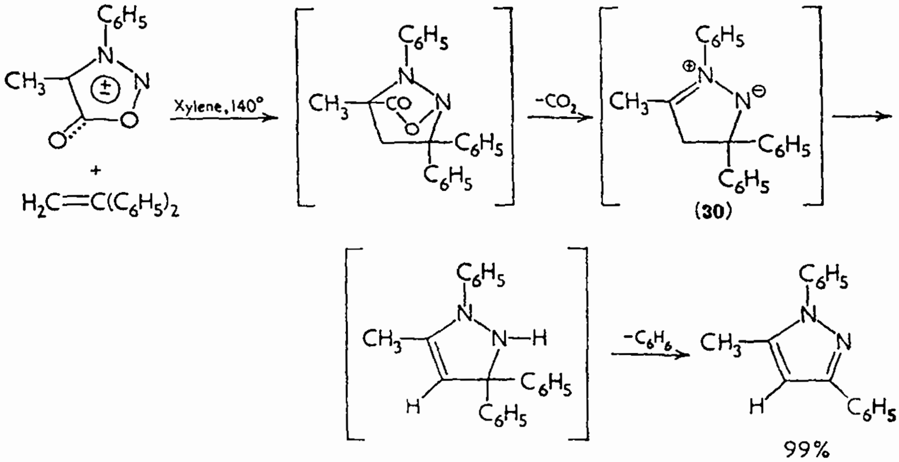
Additions of sydnones to olefins at 120–180° are followed by a variety of secondary reactions[439,440]. Kinetic experiments, however, leave no doubt that the 1,3-dipole adds to the olefinic double bond in the rate-determining step; the elimination of carbon dioxide is a subsequent fast reaction.

On heating *N*-phenylsydnone with ethylene in a sealed tube at 180°, a 48% yield of 1-phenyl-Δ^2-pyrazoline is obtained. The primary cycloadduct **29** loses carbon dioxide to give a new cyclic azomethine imine which is stabilized by migration of a proton and formation of the Δ^2-pyrazoline.



(29)

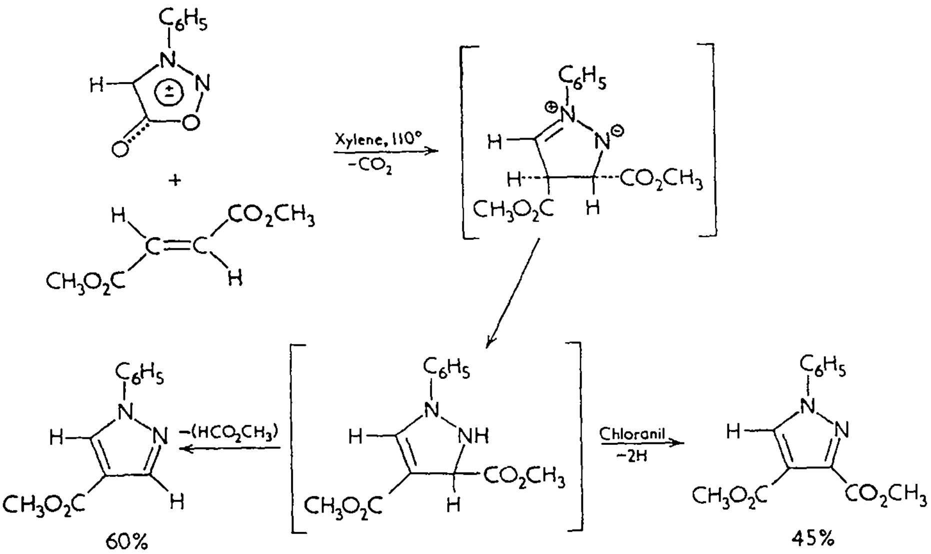
The same path is followed in reactions with propylene, ethyl undecylenate, safrole, and other monosubstituted ethylenes. When styrene is used the phenyl residue appears exclusively in the 3-position: *N*-(p-tolyl)sydnone at 140° is converted quantitatively to 1-(*p*-tolyl)-3-phenyl-Δ^2-pyrazoline[440].



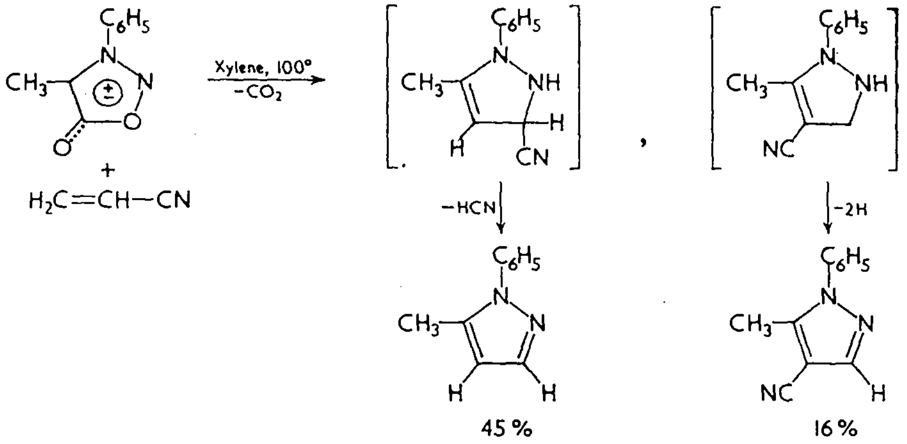
(30)

If a 1,1-disubstituted ethylene is used as the dipolarophile, the zwitterion resulting from carbon dioxide elimination does not have hydrogen available for the tautomeric shift to a Δ^2-pyrazoline. The betaine **30** arising from *N*-phenyl-*C*-methylsydnone and 1,1-diphenylethylene in boiling xylene decomposes to the aromatic pyrazole system with the expulsion of benzene; 1,3-diphenyl-5-methylpyrazole is isolated in almost quantitative yield. Assumption of a Δ^4-pyrazoline intermediate seems plausible[439]. The same reaction course is followed in the addition of *N*-phenylsydnone to α-methylstyrene to give 1,3-diphenylpyrazole with loss of methane and carbon dioxide.

In the reaction of dimethyl fumarate with *N*-phenylsydnone in xylene, stabilization of the adduct by rearrangement to the Δ^2-pyrazoline could be expected. In fact, however, elimination of the elements of methyl formate takes place, and a 60% yield of methyl 1-phenylpyrazole-4-carboxylate is obtained[439]. If the reaction is carried out in the presence of chloranil, an intermediate—presumably the Δ^4-pyrazoline—is dehydrogenated *in situ* to dimethyl 1-phenylpyrazole-3,4-dicarboxylate. When diphenyl fumarate is used, phenol and carbon monoxide rather than phenyl formate can be identified as elimination products[440].

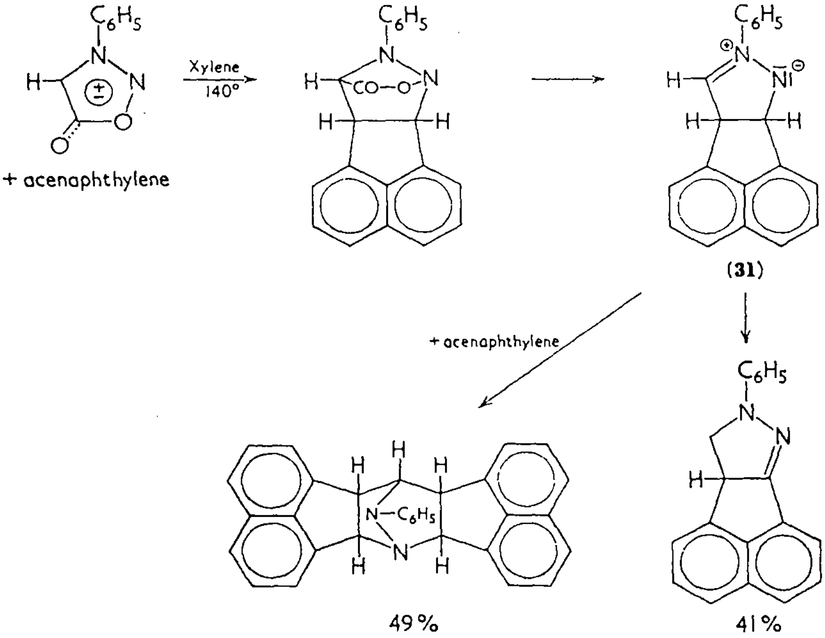


On the other hand, the reaction of sydnones with ethyl acrylate leads to Δ^2-pyrazolines; slight amounts of the pyrazolecarboxylate and an uncertain 1:2 adduct are found as by-products[441]. Addition



of *N*-phenyl-*C*-methylsydnone to acrylonitrile gives both 1-phenyl-5-methylpyrazole and its 4-nitrile. There is reason to think that the addition in this case is not selectively oriented[440].

Dehydrogenation during the course of reaction is observed in the addition of *N*-phenyl-*C*-methylsydnone to *cis*- and *trans*-stilbene; in both cases the tolane adduct, 1,3,4-triphenyl-5-methylpyrazole, was isolated. The same type of reaction was observed with ethyl cinnamate and benzalacetone[440]. Pyrazoles also arise in the reactions of


(31)

sydnones with quinones; excess quinone acts as a dehydrogenating agent in these cases. Depending upon the reaction conditions, formation of a bis-adduct can also occur[442].

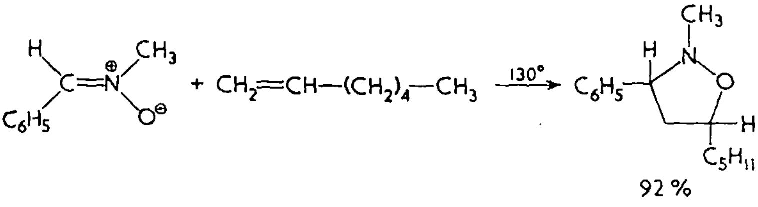
Finally, the remarkable course of the reaction of *N*-phenylsydnone with acenaphthylene may be noted[439]. As mentioned above, the intermediate resulting from the initial adduct by elimination of carbon dioxide possesses an azomethine imine character. This new azomethine imine **31** is partly stabilized in the recognized manner as the Δ^2-pyrazoline. As the major product, however, a 49% yield of a 1:2 adduct is obtained, stemming from further addition of acenaphthylene to **31**. The Baeyer strain in the five-membered ring of acenaphthylene causes a tendency in **31** to keep the formerly olefinic carbon atoms in the now sp^3-hybridized state. This slows down isomerization to the Δ^2-pyrazoline and favors addition of a second molecule of the dipolarophile (formulation on p. 860).

3. Nitrones (Azomethine oxides)

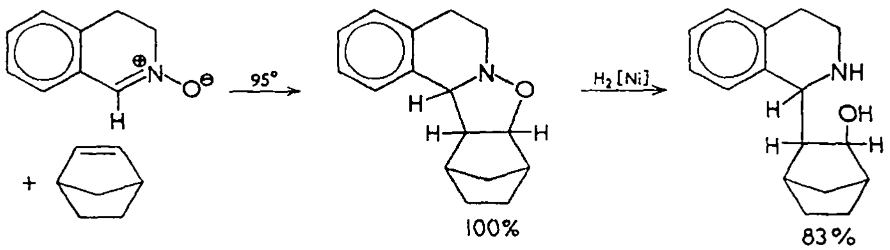
Azomethine oxides or nitrones have been known since 1887, and several syntheses are available for their preparation. Probably the most useful are the reactions of *N*-monosubstituted hydroxylamines with carbonyl compounds, the dehydrogenation of *N,N*-disubstituted hydroxylamines and the alkylation of oximes. The older literature has been reviewed by Smith[443].

Until recently cycloadditions of nitrones were essentially unknown. Only the reaction with phenyl isocyanate, which was studied by Beckmann[444], had been reported earlier. Recently, however, several research groups have independently directed their attention to the synthesis of isoxazolidines utilizing the 1,3-dipolar addition of nitrones to olefins[445-448].

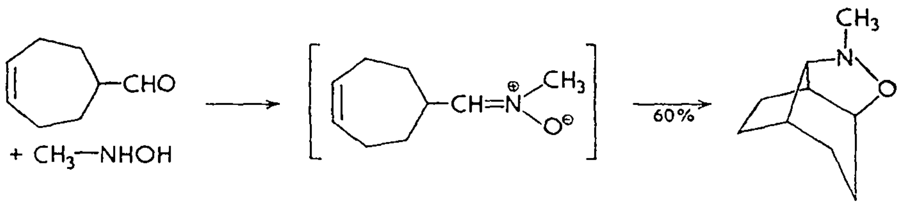
a. Synthesis of isoxazolidines. Because of the absence of side-reactions, stable nitrones combine even with sluggish olefins to give excellent yields of adducts. Thus, *C*-phenyl-*N*-methylnitrone adds to 1-heptene at 130° to give 92% of 2-methyl-3-phenyl-5-(*n*-amyl)isoxazolidine[449].



Cyclohexene, which is usually quite unreactive, also accepts nitrones to give satisfactory yields[447,448]. 3,4-Dihydroisoquinoline *N*-oxide combines quantitatively with norbornene to form a pentacyclic isoxazolidine[448]. Hydrogenolysis of the *exo* adduct with Raney nickel catalysis produces an amino alcohol, showing that the oxygen atom in the adduct is no longer present as an *N*-oxide function.

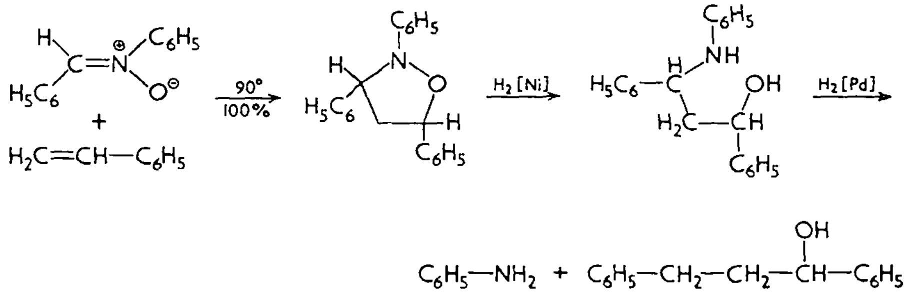


Nitrones are also involved as intermediates in certain intramolecular addition reactions investigated recently by LeBel[446]. For example,



N-methylhydroxylamine reacts with 4-formylcycloheptene to give a tricyclic isoxazolidine in 60% yield.

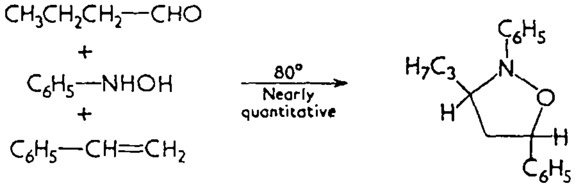
If piperideine oxide is allowed to react with butadiene one obtains four different mono- and bisadducts whose structures remain uncertain[447]. Styrene and diphenylnitrone combine quantitatively to produce a mixture of two stereoisomeric 2,3,5-triphenylisoxazolidines.



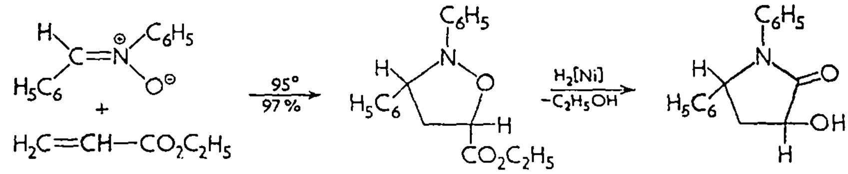
In each case, catalytic reduction on palladium breaks the nitrogen–oxygen bond and hydrogenolysis of the *N*-benzyl group leads to

1,3-diphenylpropan-1-ol[334,448]. Reactions of the same nitrone with α-methylstyrene or acenaphthylene similarly furnish diastereoisomeric adducts[334,422].

The isoxazolidine syntheses outlined do not require the use of pure, isolated nitrones. In place of the nitrones derived from aliphatic aldehydes, which are difficult to purify, one can use the *N*-substituted hydroxylamine and the appropriate aldehyde in an excess of the olefinic dipolarophile which then serves as a solvent. The nitrone formed *in situ* is immediately captured through cycloaddition. Butyraldehyde and *N*-phenylhydroxylamine serve as components in the following example[448].



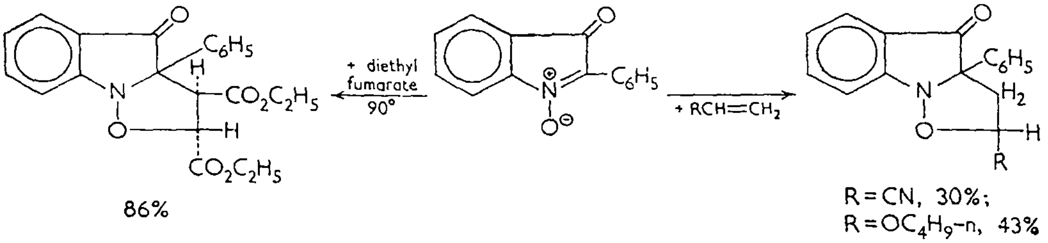
The rapid and efficient addition of nitrones to α,β-unsaturated carboxylic esters is highly stereospecific, as is demonstrated by the isolation of diastereoisomeric adducts of dihydroisoquinoline *N*-oxide with dimethyl maleate and fumarate in yields of 95% and 100%, respectively[422]. The amino alcohol produced by hydrogenation of the adduct from diphenylnitrone and ethyl acrylate in the presence of Raney nickel cyclizes immediately to the five-membered ring lactam; this ring closure reveals the orientation in the adduct[334]. It should be



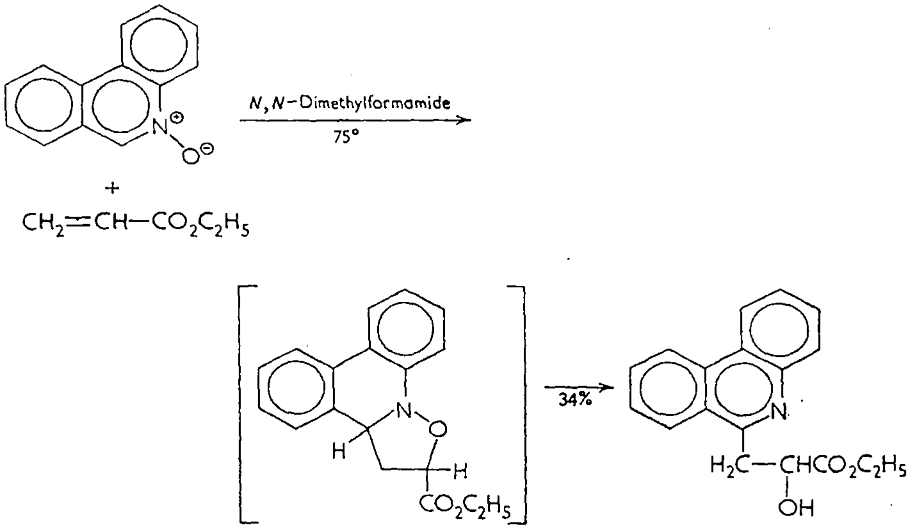
noted that the adduct from diphenylnitrone and ethyl acrylate undergoes partial dissociation into its components during distillation in high vacuum[334]. As with the Diels–Alder reaction, the 1,3-dipolar cycloaddition is reversible in principle. From the reaction of 5,5-dimethylpyrroline-1-oxide and ethyl acrylate both the kinetically and the thermodynamically controlled products have been obtained[450].

Regardless of electronic influences which might be present, mono- and 1,1-disubstituted ethylenes invariably react with nitrones to form 5-substituted isoxazolidines. The dominating steric factor in these reactions is clearly demonstrated by the following orientations: methacrylic ester adds in the same sense as acrylic ester, while crotonic and β,β-dimethylacrylic esters add in the opposite direction with respect to the methoxycarbonyl group[334].

C-Acylnitrones are substantially more reactive than the *C*-alkyl and *C*-aryl compounds[449]. Isatogens, which may be considered cyclic acylnitrones, also enter cycloadditions with remarkable ease. Although 2-phenylisatogen produces only a 30% yield of adduct with acrylonitrile[451], with diethyl fumarate 86% of the 1:1 adduct is obtained[334]. The electron-rich double bonds of enol ethers also combine readily with isatogens[334].



As with the azomethine imines the carbon–nitrogen bond of the nitrone 1,3-dipole may be part of an aromatic system. Isoquinoline and phenanthridine *N*-oxides do, in fact, enter cycloadditions, although only with the more active dipolarophiles. The adduct from



ethyl acrylate yields a more stable compound by fission of the isoxazolidine ring and regeneration of the aromatic system[452].

b. Kinetic studies. The rates of cycloadditions of nitrones to a wide variety of olefins have been measured by a dilatometric method[449]. Table 14 presents data for various reactions using *C*-phenyl-*N*-methylnitrone in toluene at two different temperatures.

The rules of relative reactivity toward '1,3-dipoles with double bond' which have already been discussed apparently hold for the

TABLE 14. Rate coefficients for cycloadditions of *C*-phenyl-*N*-methylnitrone in toluene[449].

Dipolarophile	10^5k_2 (l./mole sec)	
	85°	120°
α,β-Unsaturated carbonyl compounds		
Maleic anhydride	1,000	
trans-Dibenzoylethylene	327	
Diethyl fumarate	72·5	
Methyl acrylate	44·0	
Dimethyl mesaconate	25·8	
Diethyl maleate	24·7	
Methyl methacrylate	13·9	129
Ethyl crotonate	3·96	36·4
Dimethyl citraconate	3·17	13·4
Ethyl *β,β*-dimethylacrylate		2·70
Ethyl trimethylacrylate		0·10
Aryl-conjugated alkenes		
p-Nitrostyrene	5·45	51
p-Chlorostyrene		19·7
Styrene		11·7
p-Methylstyrene		9·3
p-Methoxystyrene		8·72
Acenaphthylene		5·70
Indene		1·90
α-Methylstyrene		1·07
1,1-Diphenylethylene		0·97
Non-conjugated alkenes		
Allyl acetate		7·25
Norbornene		4·90
Methyl allylacetate		3·75
Ethyl undecylenate		3·00
n-Hept-1-ene		2·64
Cyclopentene		0·82

nitrones as well. The favorable effect of aryl conjugation is less significant than that of a neighboring carbonyl function. Comparison of the isomeric maleate–fumarate and citraconate–mesaconate pairs discloses the higher dipolarophilic quality of the *trans*-olefin, in line with the discussion on page 820.

The influence of steric factors is illustrated by the impeding effect of the methyl substituents in the series: acrylate, methacrylate, crotonate, β,β-dimethylacrylate and trimethylacrylate. Here the rate coefficients are in the ratios, 4970:1500:364:27:1.

The greater reactivity of electron-deficient carbon–carbon double bonds can be recognized in the influence of *p*-substituents in the styrene nucleus. The series of substituted styrenes obey the Hammett relation; the ρ value of $+0{\cdot}9$ is quite small, however.

The angle-strained double bond of norbornene has been shown to be highly reactive toward nitrilimines, nitrile oxides, diazoalkanes and azides. For reasons which are not yet clear, its reactivity is much less pronounced toward nitrones. Kinetic data from azomethine imine reactions bring to light a similar relationship[418]. The advantage of norbornene over ordinary olefins is slight in these cases.

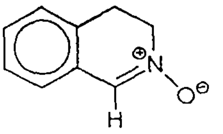
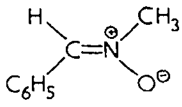
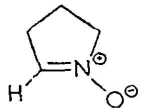
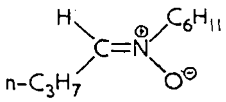
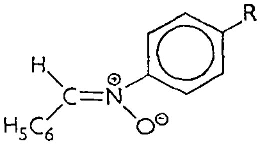
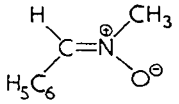
The thermodynamic parameters have been determined for several nitrone additions[449]. The entropies of activation are in the range of -23 to -32 e.u., in agreement with the high order required for a multi-center reaction.

In conclusion, a brief discussion of the influence of structural variations in the nitrone is required. The dipole moments[453] and ultraviolet spectra[454] of the open-chain aldonitrones certify that a *trans* configuration of the two groups at the carbon–nitrogen bond is preferred. However, cyclic nitrones such as 3,4-dihydroisoquinoline *N*-oxide or Δ^1-pyrroline *N*-oxide must necessarily have a *cis* configuration. Comparison of the reactivity of these compounds with some *trans* representatives, such as *C*-phenyl-*N*-methylnitrone and *C*-propyl-*N*-cyclohexylnitrone, makes it apparent that the *cis* reagents possess a greater dipolar activity. Presumably entropy factors are responsible for this advantage in the case of the rigid cyclic systems (Table 15).

In the ground state there can be little aniline-type resonance in *N*-arylnitrones, inasmuch as the nitrogen atom has substantial ammonium character. In the course of the cycloaddition the nitrogen becomes trivalent, however, and aniline resonance is possible; greater dipolar reactivity is consequently observed in *N*-arylnitrones. The influence of *p*-substituents in the *N*-phenyl group is that expected

TABLE 15. Rate coefficients (10^4k_2 l./mole sec) for the addition of various nitrones to ethyl crotonate in toluene at 100°[449].

Influence of configuration

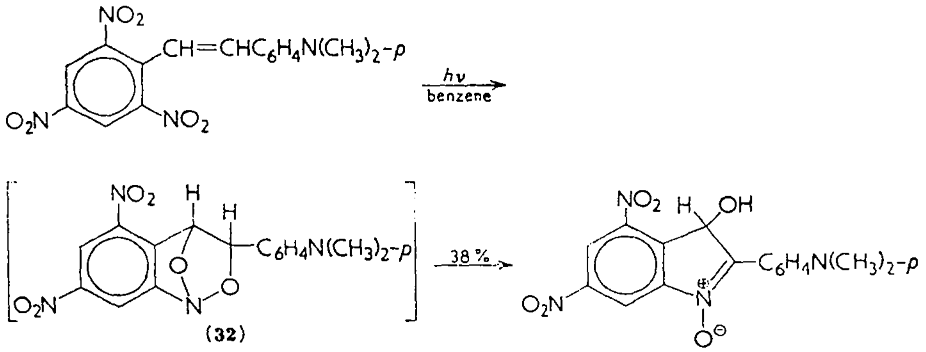
cis	*trans*
 240	 1·1
 160	 0·97
Influence of N-substituents	
 R = OCH_3 H Cl 3·9 5·5 8·8	 1·1

on this basis. Variation of the *C*-substituent points out that an aryl group is also favorable in this position.

4. Nitro compounds

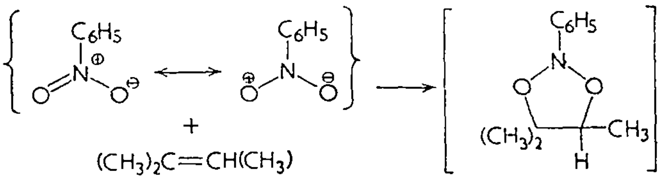
Little is known about cycloaddition of the nitro group to carbon–carbon double bonds. Occasionally the occurrence of a transitory 1,3,2-dioxazolidine ring has been inferred from isolated reaction products. In most of the cases studied a multi-step mechanism is also possible and probably preferable. The high resonance stabilization of the nitro group would, *a priori*, lead one to expect little tendency toward cycloaddition.

Examples of intramolecular interactions of aromatic nitro groups with neighboring multiple bonds are quite numerous. In many instances light-induced redox reactions are involved which could reasonably be initiated by a primary 1,3-dipolar cycloaddition, although in no case is the evidence convincing. Splitter and Calvin[455] have, for example, suggested the structure **32** for a spectroscopically detected intermediate in the photochemical formation of isatogens from *o*-nitrostilbene derivatives.



(32)

Büchi and Ayer[456] studied the light-catalyzed reaction of nitrobenzene with trimethylethylene. The final products isolated were acetone, acetaldehyde, acetanilide, azobenzene and a compound of unknown constitution which decomposed to acetone and *p*-chloroaniline under the influence of hydrochloric acid. The intermediate **33** was postulated as the primary product.

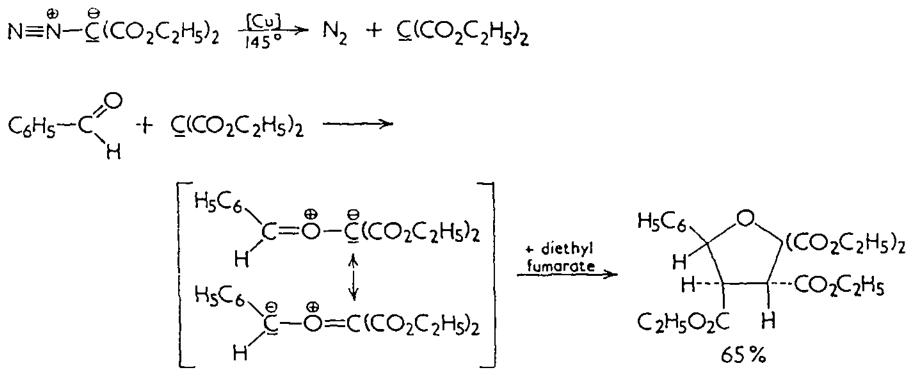


(33)

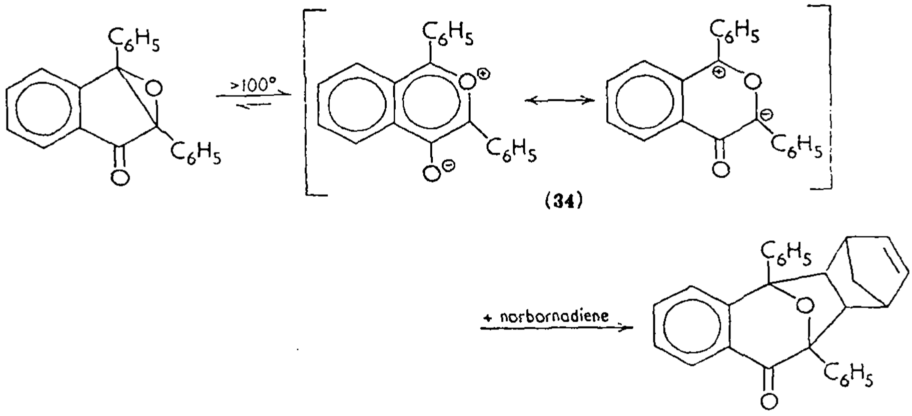
5. Carbonyl ylides

If one excludes the reactions of isobenzofuran derivatives, our knowledge of cycloadditions of carbonyl ylides to olefins is still meager. The simplest route to 1,3-dipoles of this type would be the reaction of carbenes with carbonyl compounds. In an investigation by Kharasch which appears to deal with this simplest scheme, the carbonyl ylide from ethoxycarbonylcarbene and acetone was intercepted by cycloaddition with excess acetone and a 9% yield of ethyl 2,2,4,4-tetramethyl-1,3-dioxolane-5-carboxylate obtained[457].

Dioxolane derivatives are also formed in the copper-catalyzed decomposition of ethyl diazomalonate in benzaldehyde, in this case in good yield. If this decomposition of the aliphatic diazo compound is carried out in a mixture of benzaldehyde and diethyl fumarate, one obtains a 1 : 1 : 1 adduct of the bisethoxycarbonylcarbene, aldehyde and unsaturated ester in 65% yield[458]. The synthetic route outlined below and the constitution of the tetraethyl 2-phenyltetrahydrofuran-3,4,5,5-tetracarboxylate require further confirmation. The formation of 2,2,4,4-tetramethyl-1,3-dioxolane by irradiation of diazomethane in acetone has been reported recently[459].



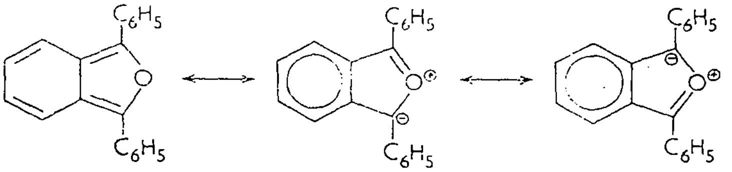
Ullmann and Milks attributed the reversible thermochromism of 2,3-diphenylindenone oxide at temperatures above 100° to a valence-tautomeric equilibrium with the pyrylium oxide **34**. The latter is readily recognized as an aromatic carbonyl ylide. Supporting evidence was found in the addition of the compound to norbornadiene and to dimethyl acetylenedicarboxylate[460].



(34)

According to a recent report, tetracyanoethylene oxide equilibrates at 130° with the corresponding open-chain carbonyl ylide; this undergoes cycloadditions with ethylene, acetylene and even with benzene[461].

Reactions of 1,3-diphenylisobenzofuran (**35**) with olefins have long been known[462]. Although the neutral resonance structure **35a** portrays the compound as a diene, one can perceive in the equivalent zwitterionic structures, **35b** and **35c**, a carbonyl ylide system. The Janus-headed reagent here does not permit distinguishing between diene and 1,3-dipolar reactivity.



(35a) **(35b)** **(35c)**

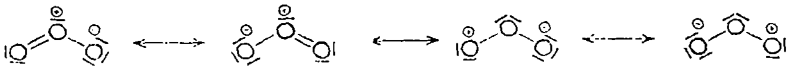
In accord with its place in the historical development, the cycloadditions of **35** will be treated in connection with the Diels–Alder reaction (p. 895). A review of the older literature is given by Elderfield[463]; more recent work is summarized in ref. 458.

6. Carbonyl oxides

The 1,3-dipolar carbonyl oxide system arises as the key intermediate in the ozonolysis of carbon–carbon double bonds. Inasmuch as no additions to olefins are known, no detailed discussion is needed here. We will return to the essential reactions of the carbonyl oxides in connection with the chemistry of ozone (see also ref. 323).

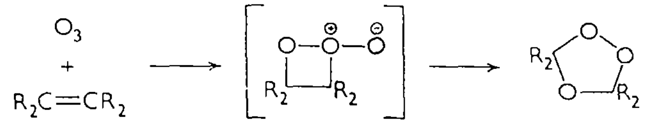
7. Ozone

In the ozone molecule the three oxygen atoms occupy the corners of an isosceles triangle. The bond lengths as obtained from spectral data are 1·28 Å; the bond angle is 116° 45′[477]. These values together with the small dipole moment of 0·53 D substantiate the fully symmetrical 1,3-dipolar system in ozone.



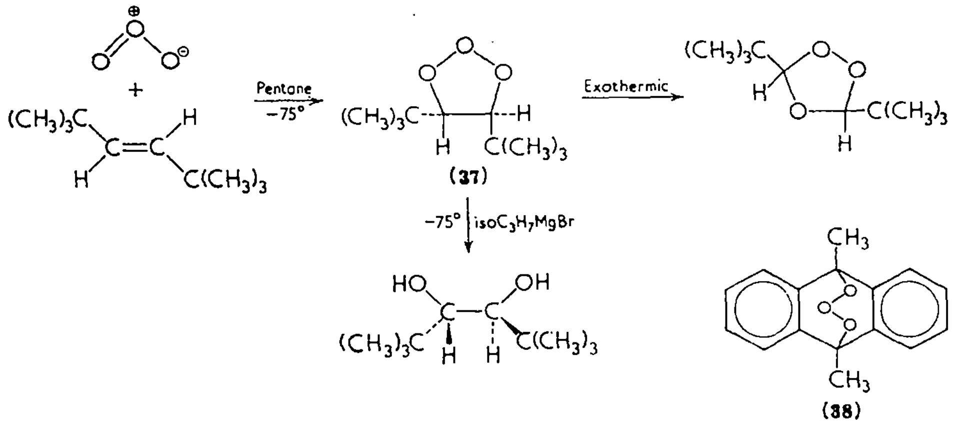
a. Primary ozonide formation as a cycloaddition. Ozone reacts with carbon–carbon double bonds even at low temperature; aromatic systems are also susceptible to attack, though at a slower rate. The much-debated course of the reaction has been clarified in recent years by the brilliant studies of Criegee. Without going into the details of earlier misconceptions, the current view of the course of ozonolysis and the nature of the products will be described briefly.

Subsequent to the pioneering work of Harries[464], Staudinger was probably the first to recognize that the rapid reaction masked a multi-step sequence[465]. He postulated the molozonide **36** as the first product of ozone attack, and suggested that this quickly isomerized to the isolable ozonide; the latter was correctly formulated as a cyclic peroxidic acetal.



(36)

The primary molozonide served for many years as a hypothetical intermediate. Only recently Criegee and Schröder succeeded in isolating such a compound[466]. Following ozonization of *trans*-di-*t*-butylethylene at −75°, they were able to recover a crystalline 1:1 adduct in which the original σ bond of the olefin was still intact.



(37)

(38)

Exothermic isomerization of this primary ozonide begins at −60° leading to the normal ozonide, a derivative of 1,2,4-trioxolan. At −95°, ozone attack on many olefins seems to stop with the formation of the primary ozonide[467].

Good evidence permitting a choice between a five-membered ring structure such as **37** for the primary ozonide and a four-membered ring corresponding to **36** was obtained by a nuclear magnetic resonance study of the relatively stable primary ozonide **38** from 9,10-dimethylanthracene[468]. The formation of the primary alkene ozonide can analogously be formulated as a 1,3-dipolar cycloaddition.

b. Kinetic data and reaction with aromatic compounds. Very little kinetic data on the ozonization of unsaturated compounds have been published. The faster reaction of the *trans* isomer of the dimethyl maleate–fumarate and citraconic–mesaconic acid isomer pairs[469] is in agreement with the rules deduced previously for multi-center additions. Quantitative competition experiments with alkene mixtures and ozone in the gas phase have recently been described by Cvetanovic and colleagues[470]. The data for simple alkenes permit recognition of enhanced dipolarophilic reactivity due to alkyl substitutions at the double bond (Table 16). Apparently with ozone, an ambivalent reagent, the electrophilic character is accentuated over the nucleophilic. *trans*-1,2-Dialkylethylenes are only slightly more reactive than the *cis* isomers, which is not surprising in view of the relatively low steric interaction of alkyl substituents (see p. 820). Only substituents with high steric requirements reduce the dipolarophilic activity[471].

TABLE 16. Relative rate coefficients of alkenes toward ozone. Competition experiments in the gas phase in the presence of nitrogen[470].

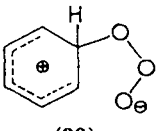
	k_2 (rel.)		k_2 (rel.)
Ethylene	$\equiv 1{\cdot}0$	2-Methyl-1-butene	6·0
Propylene	4·5	*cis*-2-Butene	9·5
1-Butene	4·0	*trans*-2-Butene	11
1-Pentene	4·0	Trimethylethylene	15
Isobutene	4·8	Tetramethylethylene	26

Data on the solvent dependence of the ozonolysis rate are available for ozonization of benzene (Table 17). In consideration of the differing reaction temperatures, the effect is quite small.

TABLE 17. Rate coefficients for the ozonization of benzene in various solvents[472,473].

	k_2 (l./mole sec)
Chloroform (−28°)	$0{\cdot}72 \times 10^{-4}$
Nitromethane (−28°)	$2{\cdot}1 \times 10^{-4}$
Carbon tetrachloride (25·2°)	$2{\cdot}8 \times 10^{-2}$
Acetic acid (25·2°)	$9{\cdot}1 \times 10^{-2}$

We would expect that in an electrophilic primary attack by ozone the large increase in charge separation in the zwitterionic intermediate **39** would be reflected in a considerably greater solvent effect. A solvent dependence of the observed magnitude is, however, in accord with a multi-center addition mechanism since there is very likely a moderate increase in polar character in going from ozone with its small dipole moment to the transition state **40** of the cycloaddition.



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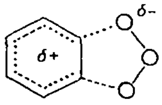


(40)

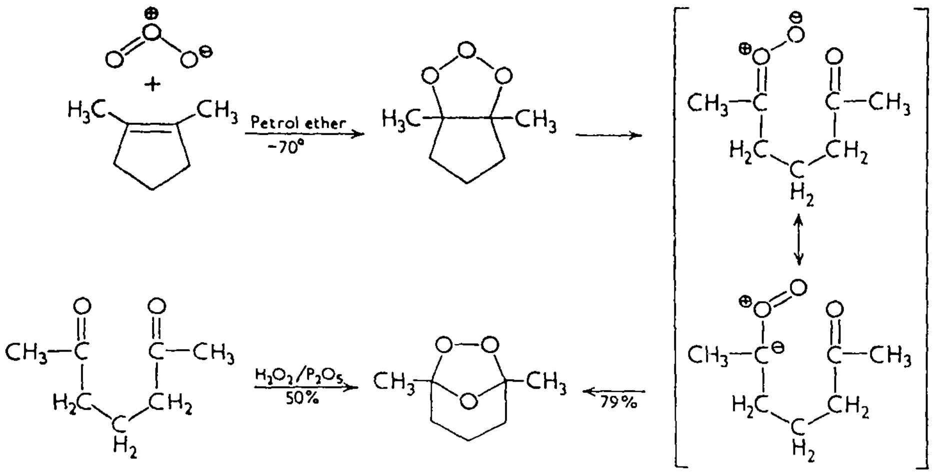
The high negative activation entropies observed for the ozonization of aromatic compounds can also be taken as evidence for a multi-center process[472].

Wibaut and coworkers interpreted the accelerating influence of aluminum chloride, boron trifluoride and ferric chloride on the ozonization of benzene in nitromethane as evidence for an electrophilic attack by the ozone molecule[473]. However, the greatest acceleration observed corresponded only to a factor of 3·5; rate enhancements are normally larger in reactions involving an initial electrophilic attack. Possibly the addition of the Lewis acid merely increases the solvent polarity.

The point of initial attachment of the ozone molecule to *aromatic* compounds is also mechanistically significant. According to Badger, 'double-bond reagents' such as ozone attack polycyclic aromatic nuclei at the carbon–carbon bond of 'maximum double-bond character' rather than at the center of highest electron density (to which electrophilic agents are directed)[474]. In other words, the addition takes place at the points of lowest localization energy[475]. The case of pyrene is particularly informative; electrophilic substitution takes place at position 1, but ozone attacks the 3,4-bond[476].

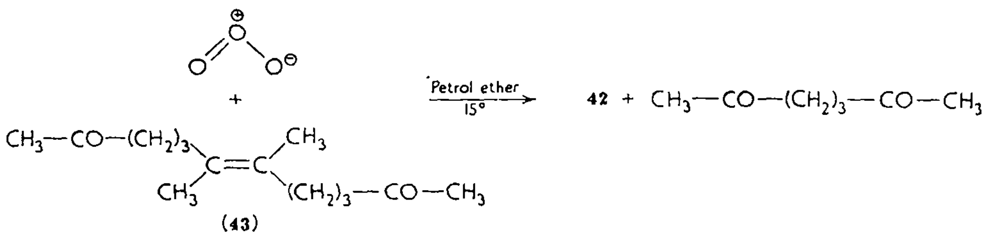
c. The mechanism of ozonide formation. How does the rearrangement of the primary ozonide to the isolable 1,2,4-trioxolane derivative occur? The driving force must come from the attendant increase in the σ bond energy, which amounts to approximately 52 kcal; one carbon–carbon bond and one oxygen–oxygen bond are lost and two carbon–oxygen bonds are formed. Quite generally in 1,3-dipolar cycloadditions to hetero multiple bonds, one observes the orientation which results in the greatest gain in σ-bond energy[339].

As Criegee[478] has proven, the primary ozonide decomposes into two independent fragments, a carbonyl oxide and a carbonyl compound. By a new cycloaddition of these two species, two carbon–oxygen bonds are closed and the ozonide is obtained. Ozonide formation proceeds in a particularly good yield with cyclopentene derivatives since in these cases (**41**) the carbonyl oxide and carbonyl function remain united by a polymethylene chain and are thus better able to locate each other for cycloaddition.



(**42**) (**41**)

The bicyclic ozonide **42** which is formed in 79% yield can also be obtained in an independent synthesis from heptane-2,6-dione by treatment of the hydrogen peroxide adduct with phosphorus pentoxide in ether[479]. Additional elegant support for the proposed reaction path is provided by the formation of the same ozonide **42** from the diketone **43** and ozone[480].



(**43**)

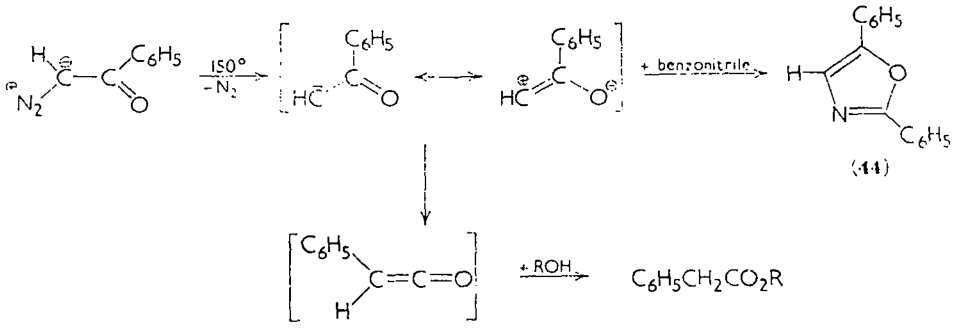
D. Reactions of 1,3-Dipoles without Octet Stabilization

Little material is yet available on the reactions of 1,3-dipoles without octet stabilization (see p. 810). Since representatives of this class in all cases occur only as short-lived reactive intermediates, isolation is excluded in principle. Interception of the 1,3-dipolar system generated *in situ*, however, offers important preparative possibilities.

For a number of examples of this class of dipoles only cycloadditions to hetero multiple bonds have yet been demonstrated. Additions to alkenes have been carried out only with ketocarbenes (Table 6, p. 810).

Ketocarbenes have long been postulated as hypothetical intermediates in the Wolff rearrangement of diazoketones[481,482]. Normally ketenes or their further reaction products are isolated. The fragment remaining after elimination of a nitrogen molecule can be formulated as a 1,3-dipole and should be capable of cycloaddition.

When thermolysis of diazoacetophenone is carried out in benzonitrile, the phenylketocarbene does in fact add to the carbon-nitrogen triple bond of the solvent, although only in 0·4% yield[483]; the remainder of the material consists of subsequent reaction products derived from phenylketene formed by the Wolff rearrangement. If the decomposition is carried out in the presence of copper, the ketocarbene is probably stabilized as a metal complex, and the yield of the cycloadduct **44** rises to 17%[483].



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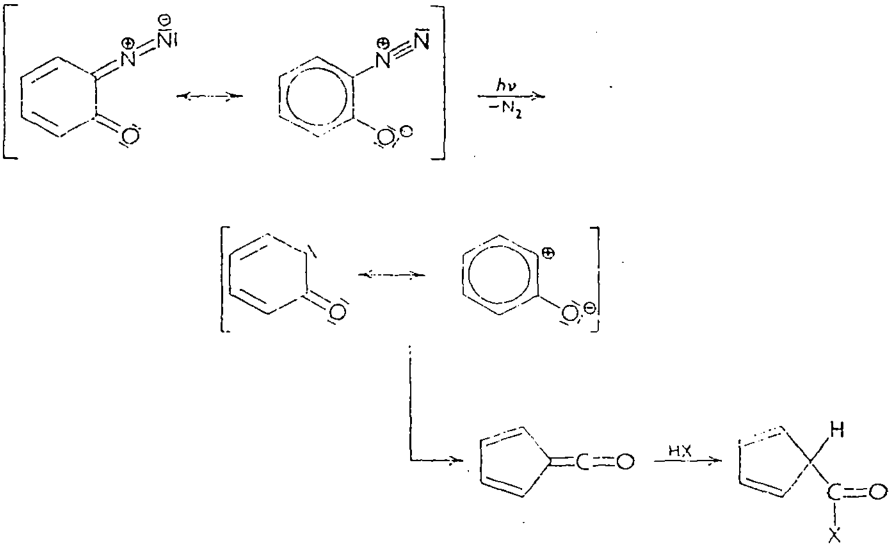
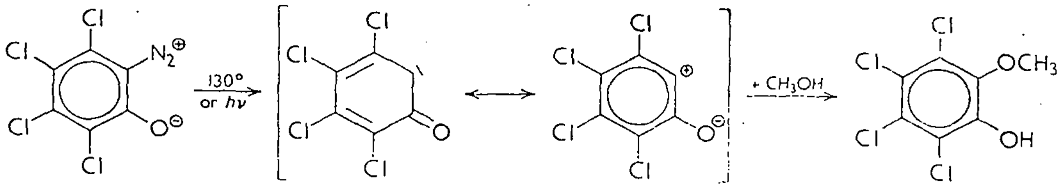
Since *intermolecular* addition reactions have a natural disadvantage compared with the *intramolecular* Wolff rearrangement, the only chance of trapping the short-lived intermediate efficiently lies in selection of proper model systems in which the Wolff rearrangement is impeded.

The benzene-*o*-diazooxides occupy a middle position in reactivity between the aliphatic diazoketones and the aromatic diazonium salts. The aromatic ketocarbenes produced by photolysis are, according to

Süs[484], still capable of undergoing the Wolff rearrangement. However, one can anticipate a longer lifetime for the carbenoid intermediate in this case since ring contraction in the course of rearrangement must be accompanied by sacrifice of the aromatic resonance energy.

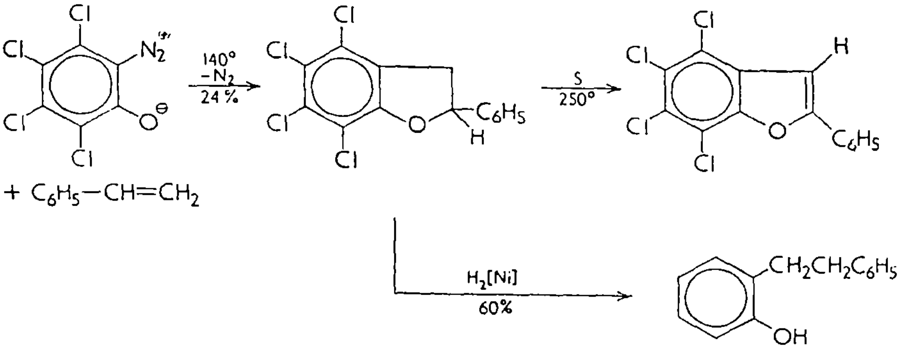


Tetrachlorobenzene-*o*-diazooxide is particularly suitable for study. The ketocarbene **45** produced by thermal decomposition at 130° or by photolysis no longer tends to undergo rearrangement and, as expected, can be added to numerous multiple bond systems as shown by Huisgen, König, Binsch and Sturm[483].

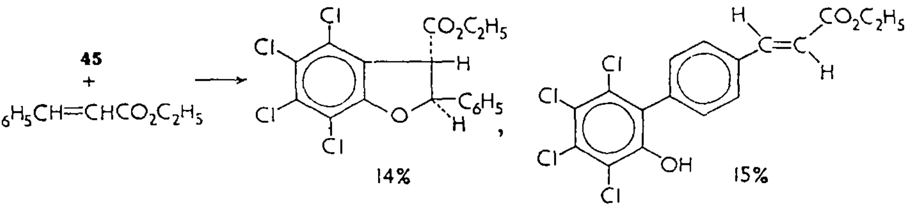


(45)

If **45** is allowed to react with boiling styrene, the 2,3-dihydrobenzofuran derivative is formed in 24% yield. The structure of the adduct follows from its dehydrogenation to the related aromatic system and from its degradation to *o*-hydroxydibenzyl by dehalogenation and ether hydrogenolysis. Both derivatives could be synthesized by independent routes.

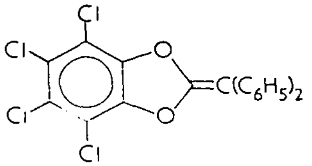


Addition of **45** to ethyl cinnamate produces the expected cycloadduct accompanied by a diphenyl derivative which results from attack of the carbene at the *para* position of the cinnamate nucleus[482]. A similar aromatic substitution by **45** has been observed in the case of *trans*-stilbene.



Surprisingly, decomposition of the *o*-diazooxide in dimethyl maleate and fumarate leads to the same product[483], for which a *trans* configuration with respect to the ester groups has been established by nuclear magnetic resonance spectroscopy[482]. Whether this lack of stereospecificity arises from a two-step mechanism or from thermal isomerization of an initial *cis* adduct must be clarified by further experiments.

The occurrence of the ketocarbene **45** as an intermediate in all these reactions is supported by measurements of the decomposition rate of the *o*-diazooxide which proves to be virtually independent of the dipolarophile present[482]. The sole exception to this is diphenylketene, which causes an induced decomposition of the *o*-diazooxide even at room temperature. The dioxole **46** is formed in 50% yield. Here we are not dealing with the addition of a ketocarbene, but rather with an initial electrophilic attack of the ketene on the diazooxide. Derivatives of this ring system had been obtained earlier in reactions of ketenes with quinone diazides[485].



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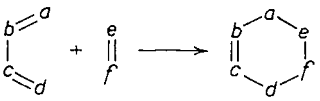
Cycloadditions of ketocarbenes are not limited to carbon–carbon double bonds. Many reactions with alkynes, nitriles, carbonyl and thiocarbonyl compounds have been investigated. The preparation and addition of substituted ketocarbenes from other diazoketones as well as from ethyl diazoacetate[483,486] and ethyl diazotrifluoroacetoacetate[487] will only be noted in passing since reactions with carbon–carbon double bonds have not yet been described.

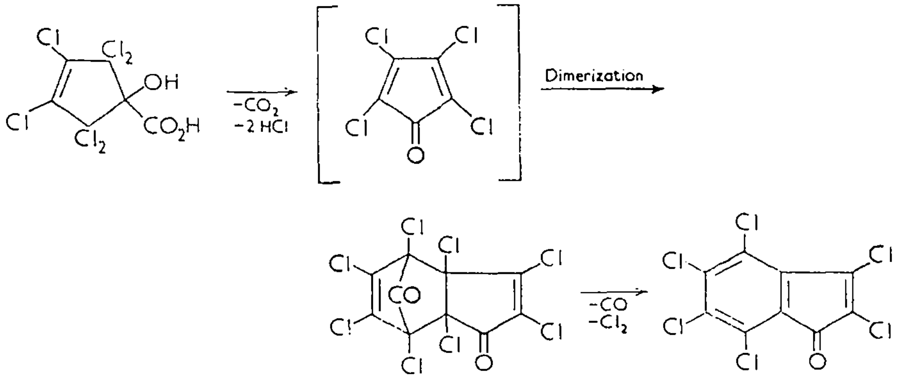
V. THE DIELS-ALDER REACTION

A. Classification and Historical Introduction

The publications of Diels and Alder beginning in 1928 disclosed the generality of the reaction:



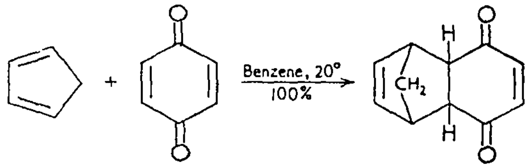
In a cycloaddition of the type 4 + 2 → 6, the olefinic component adds to the conjugated diene to form a six-membered ring. The almost unlimited possibilities for variation of both the *diene* and the *dienophile* make the Diels–Alder reaction a synthetic method of outstanding utility.



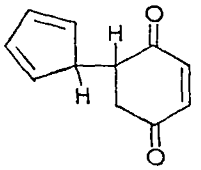
As early as the turn of the century, reactions were known which can be formulated according to the Diels–Alder concept; incorrect structures were occasionally proposed, thus preventing earlier recognition of the generality of the reaction.

Zincke and colleagues[488] isolated perchloroindenone from the pyrolysis of perchlorinated 4-hydroxycyclopentene-4-carboxylic acid. In this reaction, tetrachlorocyclopentadienone formed initially is presumably converted to the dimer which loses carbon monoxide and chlorine to give the aromatic product (formulation on p. 878).

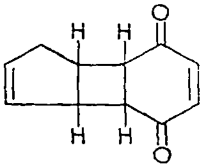
The 1:1 adduct from cyclopentadiene and *p*-benzoquinone[489] was later proved to have the bicyclic structure expected from the Diels–Alder formulation of the reaction.



Diels and Alder (1928)

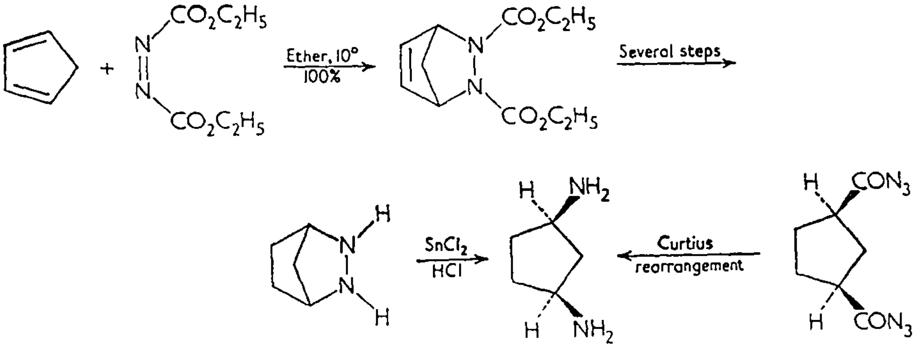


Albrecht (1906)



Staudinger (1912)

Degradation of the 1:1 adduct from diethyl azodicarboxylate and cyclopentadiene to *cis*-1,3-diaminocyclopentane[490] laid the basis for the classical work of Diels and Alder[491]. In the following decade these authors established the preparative scope of the reaction and



contributed important stereochemical criteria for the formulation of the mechanism.

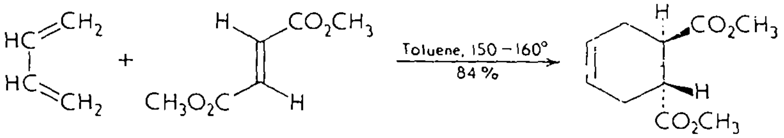
Excellent summaries of the literature through 1955 are available[492–499]. The following discussion, in which full coverage is not attempted, reflects the newer literature as much as possible. Since a separate systematic treatment of the diene and dienophile components would strain the seams of this review, particular open-chain dienophiles will be considered with the discussion of the dienes.

B. The Diene Component

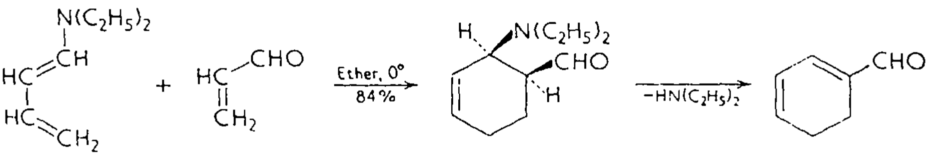
I. Open-chain dienes

Butadiene and its derivatives are capable of taking part in the Diels–Alder reaction almost without exception. Monosubstitution or polysubstitution progressively alter the reactivity of the diene but do not prevent the addition except in special cases (see p. 913).

Butadiene itself reacts with dimethyl fumarate at elevated temperatures to give the cyclohexene-*trans*-4,5-dicarboxylic ester[500].

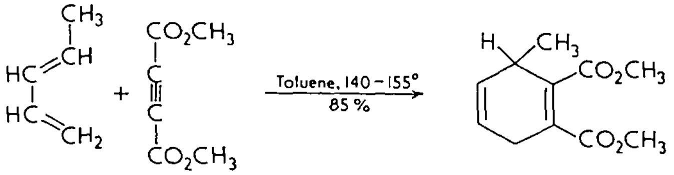


An acid-labile adduct between 1-(diethylamino)butadiene and acrolein is formed even at low temperatures thus making 2,3-dihydrobenzaldehyde readily available[501]. Elimination of two molecules of amine from the corresponding adducts of the substituted 1,4-diaminobutadiene leads analogously to a benzene derivative[502].

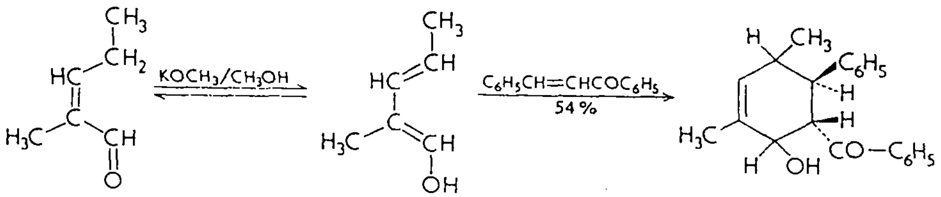


A 3,6-dihydrophthalate derivative is formed by the addition of the triple-bonded dienophile, dimethyl acetylenedicarboxylate, to 1-methylbutadiene (piperylene)[503] as formulated on p. 881.

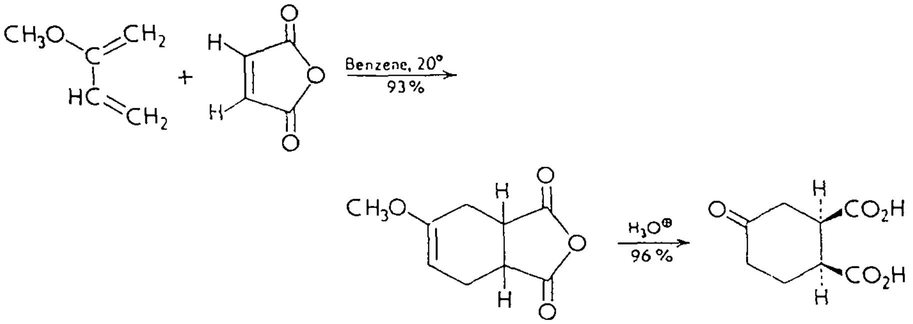
It is not certain that the addition of 1-hydroxybutadiene to dienophiles is mechanistically a Diels–Alder reaction. The initial adduct



which is obtained from benzalacetophenone and 1-methyl-2-ethylacrolein is formally a cycloadduct of 1-hydroxy-2,4-dimethylbutadiene, but it is formed only in the presence of a basic catalyst[504], as Meerwein has found.

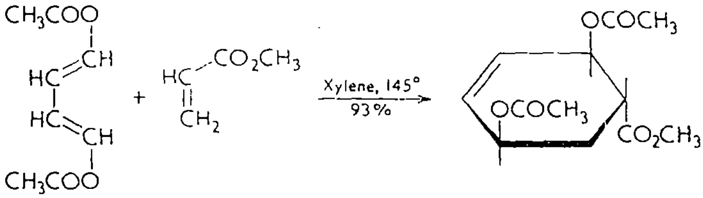


Cyclohexanone derivatives can be obtained by acid hydrolysis of the adducts from 2-alkoxybutadienes[505].

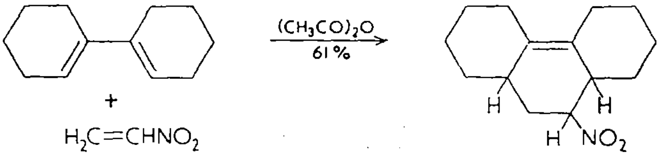


In the reaction product from 2-vinylbutadiene and maleic anhydride the components are found in a 1:2 ratio; the primary adduct contains a new diene system which accepts a second molecule of the dienophile[506].

The ability to take part in addition reactions is not destroyed by substitution of the diene in the 1,4-positions. A synthesis of the biochemically important shikimic acid recently described involves the addition of methyl acrylate to *trans-trans*-1,4-diacetoxybutadiene as the initial step[507]. Diels–Alder reactions with 2,3-diphenylbutadiene make derivatives of *o*-terphenyl easily accessible[508].

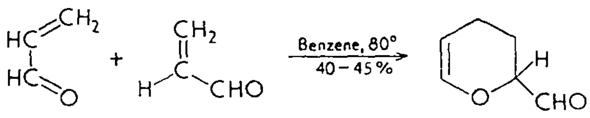


Even 1,2,3,4-tetrasubstitution of butadiene does not always prevent the cycloaddition. 1,1′-Bicyclohexenyl adds nitroethylene exothermically to give the hydrogenated phenanthrene derivative[509].



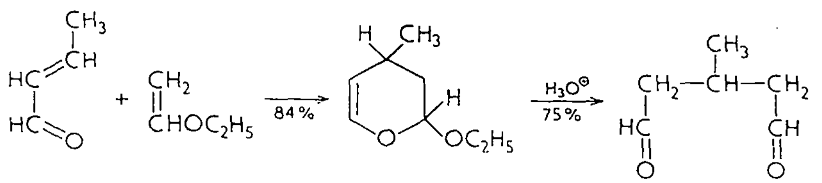
2. Open-chain dienes containing heteroatoms

By formal substitution of an oxygen atom for the terminal methylene group in butadiene, *i.e.* transition to acrolein, the reactivity of the diene system is substantially modified. The dimerization of acrolein to dihydropyranecarboxaldehyde[510] now competes with addition to the less active dienophiles.



Although the reaction of acrolein with maleic anhydride fails, dienophiles having electron-rich double bonds add very well[511]. The addition of enol ethers requires heating to 180–200°[512]. The substituted glutardialdehydes, which can be obtained by acid hydrolysis of adducts derived from substituted acroleins, are useful starting materials for alkaloid syntheses[513].

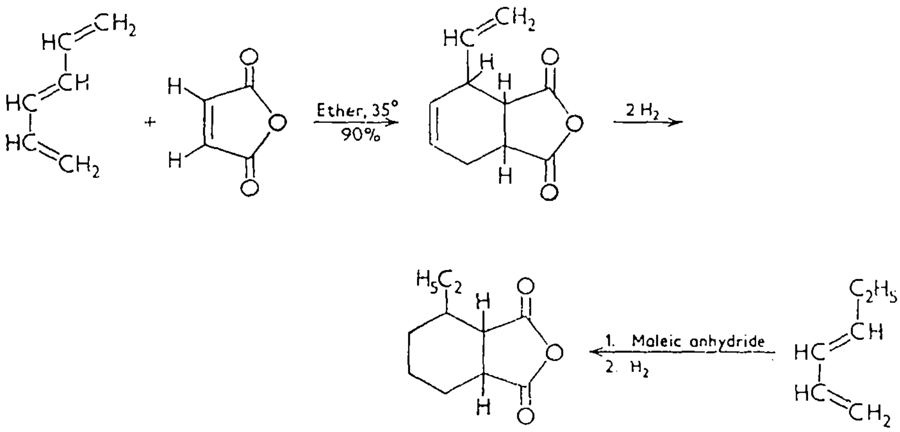
The smooth addition of acrolein and its derivatives to enamines[514] provides another valuable route to glutardialdehydes. The union of esters of *N*-vinylcarbamic acid and of *N*-vinylureas with α,β-unsaturated carbonyl compounds occurs at 20–120°[515].



Incorporation of a nitrogen atom in the diene system is only possible in special cases. The 1:1-addition compounds from 1-styryl-3,4-dihydroisoquinoline derivatives and maleic anhydride and that from the bisanil of glyoxal and *p*-dimethylaminoaniline with *p*-benzoquinone have been ascribed the structures of Diels–Alder adducts[511].

3. Polyenes

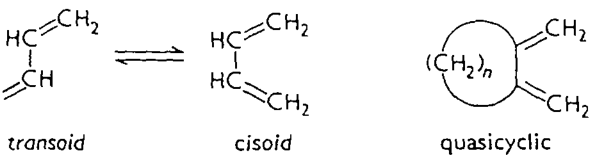
Polyenes take part as substituted butadienes in the Diels–Alder reaction. Thus, *trans*-1,3,5-hexatriene combines with maleic anhydride to form 3-vinylcyclohexene-4,5-dicarboxylic anhydride. Hydrogenation of this product gives the 3-ethyl compound which is also obtainable from *trans*-1-ethylbutadiene[516]. The less reactive *cis* isomer of 1,3,5-hexatriene (see also p. 913) can be freed of the *trans* isomer through reaction of the latter with maleic anhydride[517]. In work with ω,ω′-tetraphenylpolyenes, Alder and Schumacher observed interesting relationships between the chain length and the position of the diene addition[518].



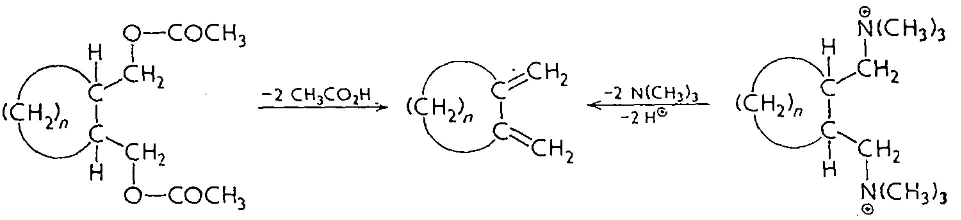
4. Bismethylenecycloalkanes

Butadiene and its simple alkyl derivatives exist predominantly in the *transoid* conformation[519]. However, only the *cisoid* conformers which are in equilibrium can participate in the Diels–Alder addition.

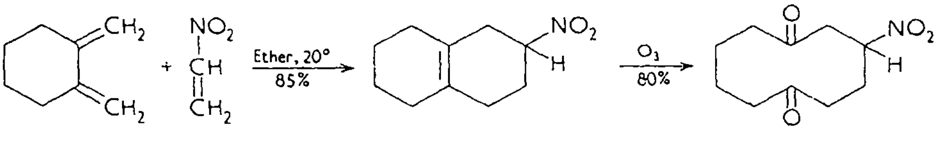
An increase in the equilibrium concentration of the *cisoid* form through suitable substitution in the diene is reflected by an enhancement of the addition rate (see p. 913). In the 1,2-bismethylenecyclo-



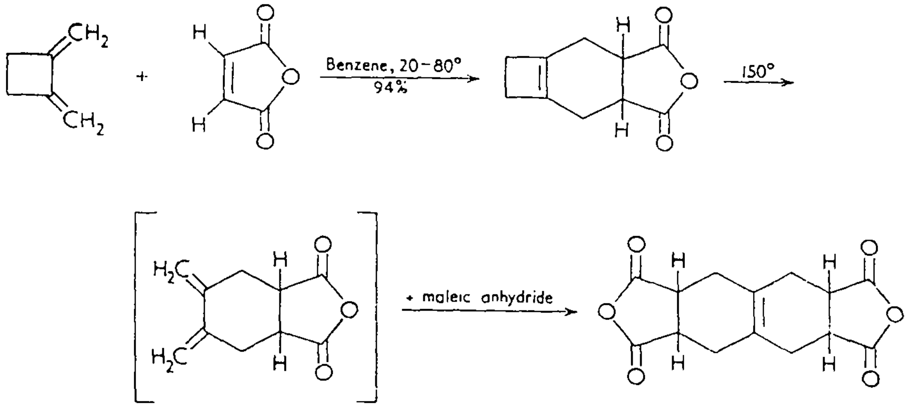
alkanes, inclusion of the 2- and 3-positions of the diene in a ring freezes the *cisoid* conformation. These quasicyclic dienes which may be prepared by ester pyrolysis or by Hofmann elimination of the bifunctional ammonium salts[520], are among the most reactive dienes.



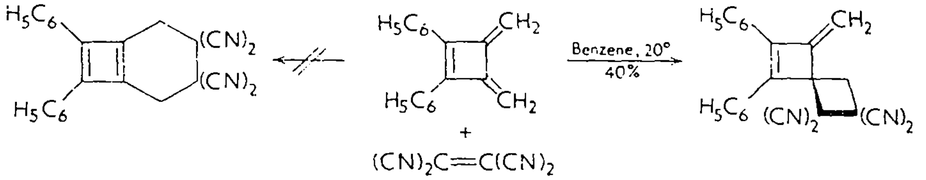
Even at 0°, 1,2-bismethylenecyclohexane reacts with nitroethylene to give a Diels–Alder adduct, the ozonization of which provides a route to 3-nitrocyclodecane-1,6-dione[521]. Reactions of 1,2,4,5-tetrakismethylenecyclohexane with tetracyanoethylene, maleic anhydride or *p*-benzoquinone produce the bisadducts[522]. Interestingly, 4,5-bismethylenedioxolanes[523] react only with tetracyanoethylene[524], a particularly active dienophile.



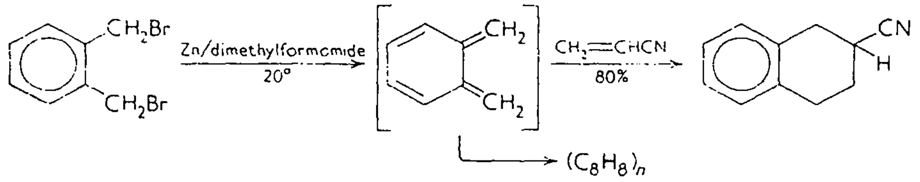
1,2-Dimethylenecyclobutane yields a 1:1 adduct at 20°; at 150° ring opening occurs, followed by addition of a second molecule of dienophile to the new quasicyclic diene system[525].



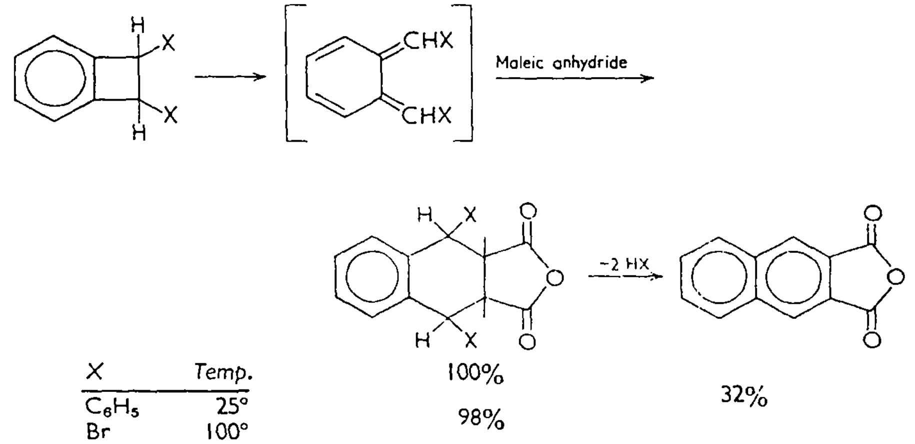
The formation of an energy-rich cyclobutadiene system is avoided in the reaction of 1,2-bismethylene-3,4-diphenylcyclobut-3-ene with tetracyanoethylene. In this case four-ring cycloaddition to give a spiro compound takes precedence over the Diels–Alder reaction[33,526].



Some cyclic 1,2-bismethylene compounds are too reactive to be isolated, nevertheless, their existence has been demonstrated by trapping reactions. ω,ω′-Dibromo-*o*-xylene is debrominated by powdered zinc to form a polymer of *o*-quinodimethane. However, the monomer can be captured as a stable adduct with maleic anhydride, acrylonitrile or other dienophiles[527]. 2,3-Dihydronaphthalene[528] and dimethylisoindene[527] appear in the analogous dehalogenations of the corresponding dibromo compounds.



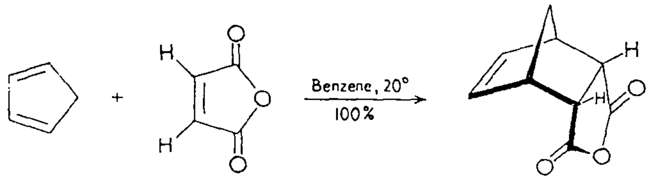
Benzocyclobutenes react with dienophiles at 25–200°, depending upon the substituents in the four-membered ring, to form naphthalene or hydronaphthalene derivatives[529,530]. A valence tautomerism with *o*-quinodimethanes seems to offer the simplest explanation. The parent compound itself can be converted reversibly to a cyclic sulfone by reaction with sulfur dioxide.



X	Temp.
C_6H_5	25°
Br	100°
H	200°

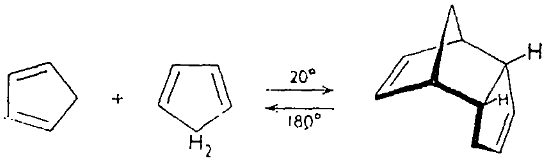
5. Alicyclic dienes

Just as the simple butadiene derivatives are eminently suitable for the preparation of six-membered carbocyclic rings, so the addition reactions of cyclic dienes open the way to various bicyclic compounds.



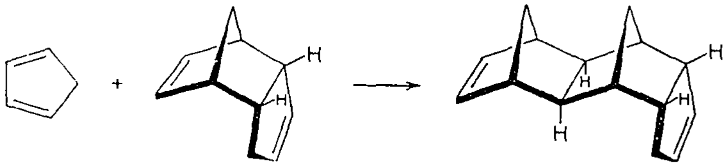
The Diels–Alder pattern is plainly discernible in the reactions of cyclopentadiene. An adduct with maleic anhydride, for example, is formed quantitatively at room temperature in an exothermic and stereospecific reaction[491].

Cyclopentadiene is readily obtained by pyrolysis of its dimer; the reverse reaction takes place slowly at room temperature, faster on warming. Cyclopentadiene thus functions as both a diene and a

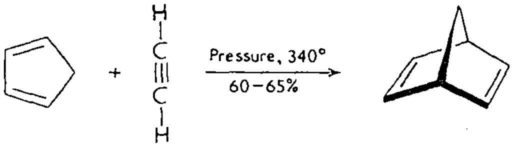


dienophile, a behavior which we shall meet again with cyclopentadienones and *o*-quinones (see pp. 890, 891). Butadiene also shows the same dualistic reactivity in its dimerization to 4-vinylcyclohexene.

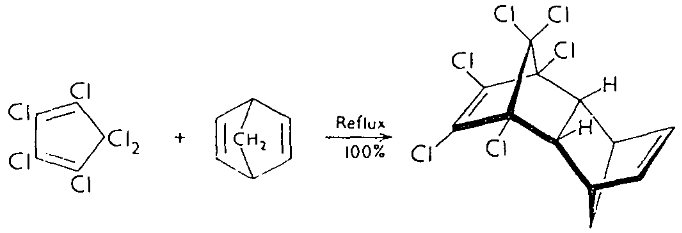
The capacity of cyclopentadiene to polymerize is not lost at the dimer stage. Brilliant investigations by Alder and his students[531] have clarified the structures and stereochemistry of the higher oligomers.



The reactivity of cyclopentadiene makes an abundance of valuable bicyclo[2.2.1]heptenes easily available, as the Alder school has shown. The use of substituted cyclopentadienes leads with relatively few steps to naturally occurring camphor derivatives[494]. Under more stringent conditions the sluggish dienophile, acetylene, yields the interesting bicyclo[2.2.1]heptadiene[532].

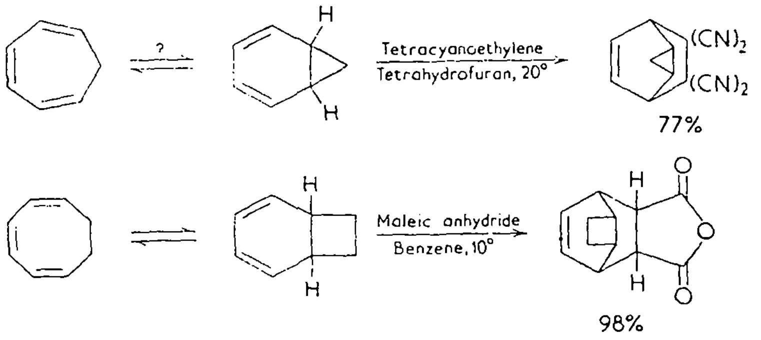


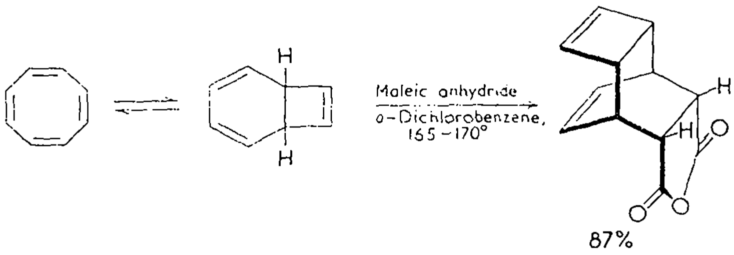
Hexachlorocyclopentadiene[533] shows no tendency to dimerize thermally. However, it reacts with the strained double bond of bicycloheptadiene to give an adduct which is used as an insecticide ('Aldrin').



As the ring size is increased in the series, cyclopentadiene, cyclohexa-1,3-diene and cyclohepta-1,3-diene, the reactivity falls and vanishes when one reaches the eight-membered cyclic diene. Only after climbing to the fourteen- and eighteen-membered rings do we again see a small reactivity[495].

Cycloheptatriene[534,535] and cyclooctatriene[60,536] add tetracyanoethylene or maleic anhydride to give tricyclic compounds. In these cases the hydrocarbons react in their valence–tautomeric, bicyclic diene form. Both valence tautomers of cycloocta-1,3,5-triene can be isolated; at 100° the bicyclic form amounts to 15% of the equilibrium mixture, as Cope has demonstrated[536]. Cyclooctatetraene combines through an 0·01% equilibrium concentration of the tautomeric bicyclooctatriene with the dienophile as a recent kinetic investigation has shown[537]. The configuration of the cyclooctatetraene–maleic anhydride adduct[538] is the one expected from the less hindered approach.



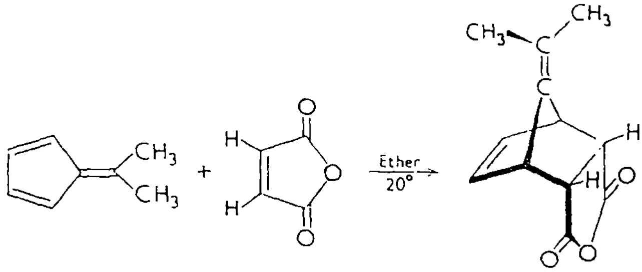


It has been suggested that cycloheptatriene can also combine *directly* with dienophiles; using nitrosobenzene as the dienophile, the adduct formed seems to be derived from the seven-membered ring[539]. The anomalous reaction with azodicarboxylic ester may also be mentioned here as it opens a useful route to tropylium salts[540].

6. Fulvenes

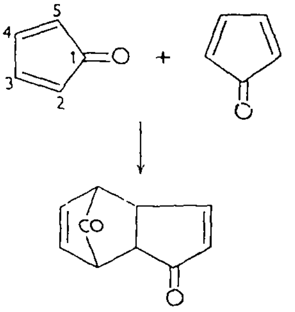
The fulvenes[541], which can be easily prepared by condensation of cyclopentadiene with ketones or aldehydes, will add dienophiles at the endocyclic double bond system as expected[542].

The reversibility of the Diels–Alder reactions of the fulvene system for a long time impeded establishment of the adduct configurations. A critical study by Woodward and Baer[543] clarified the course of the reaction in the pentamethylenefulvene–maleic anhydride system.



7. Cyclopentadienone and derivatives

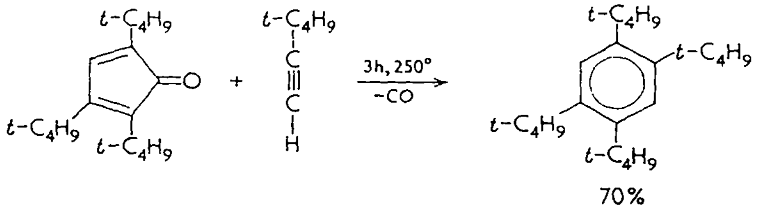
The tendency of cyclopentadienones to dimerize, formally a Diels–Alder reaction, is strongly dependent upon the nature and number of substituents[544]. The dimers, which can dissociate in solution, as well as the monomers themselves, sometimes show considerable reactivity in cycloadditions.



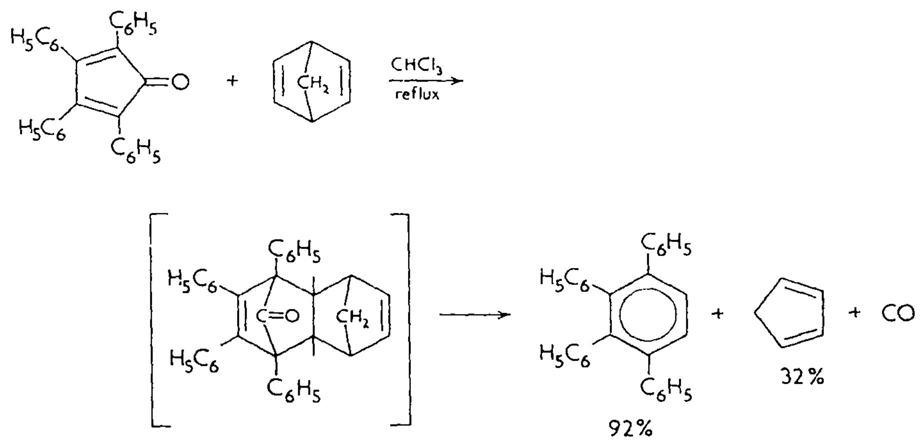
Substituent in position			
2	3	4	5
Non-dissociating dimers			
H	H	H	H
Cl	Cl	Cl	Cl
H	C_6H_5	C_6H_5	H
H	C_6H_5	C_6H_5	C_6H_5
Dissociating dimers			
CH_3	C_6H_5	C_6H_5	CH_3
C_6H_5	C_6H_5	H	C_6H_5
Monomers			
C_2H_5	C_6H_5	C_6H_5	C_2H_5
CH_3	C_6H_5	C_6H_5	C_6H_5
C_6H_5	C_6H_5	C_6H_5	C_6H_5

With olefinic dienophiles, it is usually possible to isolate the initial bicyclic adducts, which generally lose carbon monoxide at elevated temperatures[544]. With acetylenic dienophiles, the tendency toward aromatization causes elimination of carbon monoxide to be a rapid second step following the Diels–Alder reactions[544,545]. 1,2,4,5-Tetra-*t*-butylbenzene, with its extremely high van der Waals compression, is obtained from easily accessible starting materials[546].

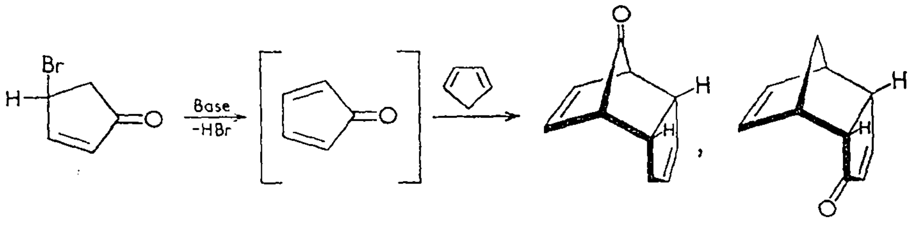
The preparation of polyphenylated polyphenyls can be carried out smoothly from tetracyclone and bifunctional acetylene derivatives[547].



The primary adduct from tetracyclone and bicycloheptadiene loses cyclopentadiene as well as carbon monoxide to form a benzene derivative[548]. Frequently the use of bicyclo[2.2.1]heptadiene leads through a retro-Diels–Alder reaction to the same product as obtained from acetylene (*cf.* p. 906).



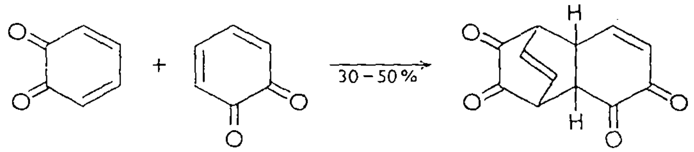
Efforts to obtain the parent compound, monomeric cyclopentadienone have failed; only the *N*,*N*-dimethylhydrazone of cyclopentadienone has been isolated as a monomer[459]. In agreement with



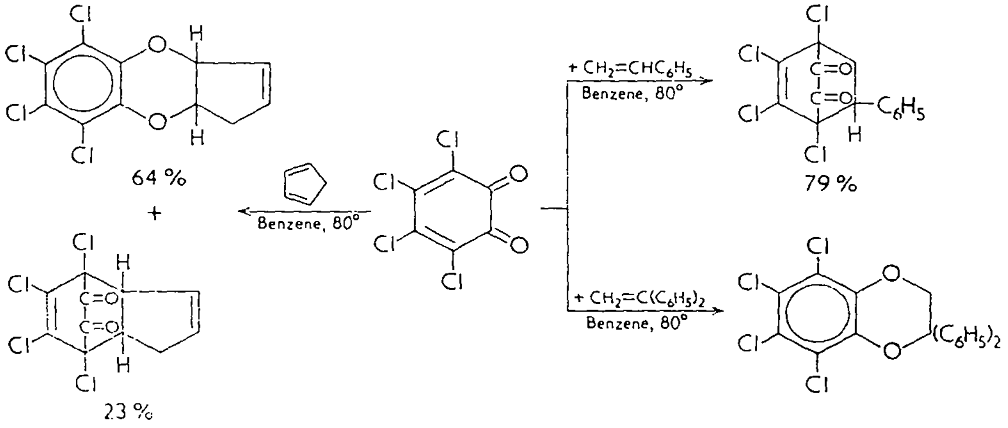
calculations of the electron distribution and free valence[550] for this molecule, attempts to prepare cyclopentadienone by the retro-Diels–Alder reaction (see p. 906) lead only to the dimer or further reaction products[551]. However, two reports have disclosed the interception of the intermediary cyclopentadienone with cyclopentadiene. In its dimerization cyclopentadienone behaves as both a diene and a dienophile[552,553].

8. o-Quinones and o-quinonoid systems

The literature notes only a few examples of dienophilic behavior by *o*-quinones[554]. The structure originally proposed[555] for the adduct from cyclopentadiene and tetramethyl-*o*-benzoquinone has been revised[556]; the *o*-quinone derivative functions as the diene, cyclopentadiene as the dienophile. The great tendency of many *o*-benzoquinones to dimerize is evidence for the underlying readiness of these compounds to accept also the role of the dienophile in Diels–Alder reactions[557,558].



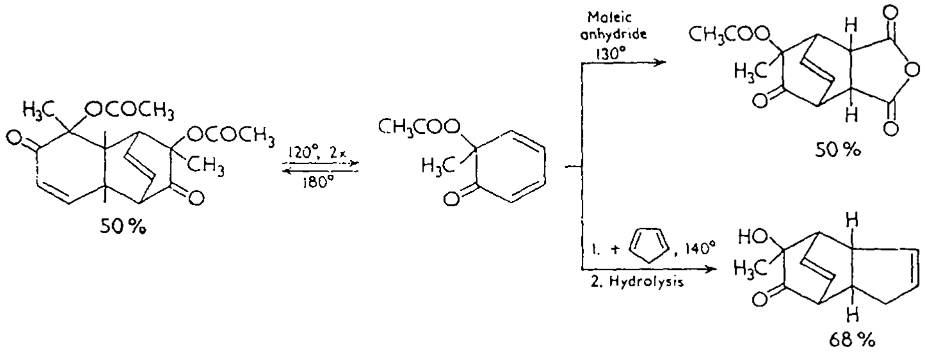
A surprising phenomenon was observed by Horner and Merz[559] in the reactions of monomeric tetrachloro-*o*-benzoquinone with alkenes. Depending upon the dienophile used, addition involved either the six-membered ring or the 1,2-diketo group. The photochemical reaction



yields 1:1 adducts of a different structure[257]. Use of cyclopentadiene in the thermal reaction leads to the formation of comparable amounts of the two possible 1:1 adducts[559]. It is worth mentioning

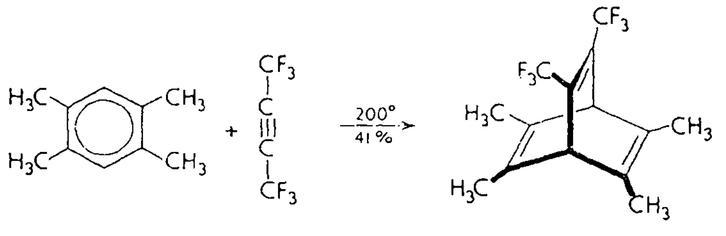
that tetrachloro-*o*-benzoquinone is inert toward typical dienophiles such as acrylonitrile and maleic anhydride[559].

The tendency toward dimerization and diene addition reactions is also found in 6,6-disubstituted cyclohexadienones[560,561] and methyl-*o*-quinol acetates[562]. Besides maleic anhydride, simple olefins and dienes can be added under mild conditions, as illustrated by the reactions of 2-methyl-*o*-quinol acetate.



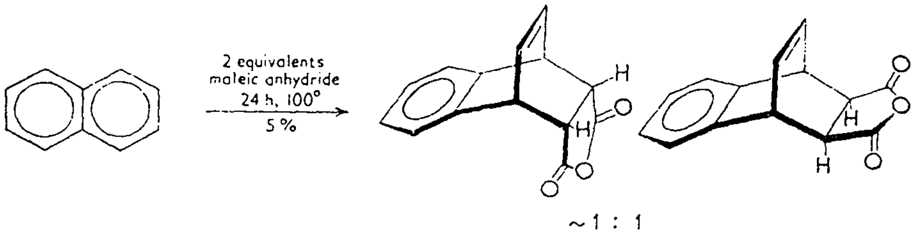
9. Aromatic nuclei

As might be expected, aromatic compounds are found to be sluggish diene components. In addition reactions the aromatic resonance of benzene or naphthalene is wholly or partly sacrificed. A portion of the resonance energy must be expended in the rate-determining step as activation energy. The readiness of the aromatic systems to function as dienes therefore increases in the series, benzene, naphthalene, anthracene. The position of dienophilic attack on polycyclic aromatic systems can be deduced from theoretical considerations[563] (see p. 873 regarding localization energies for ozonization).

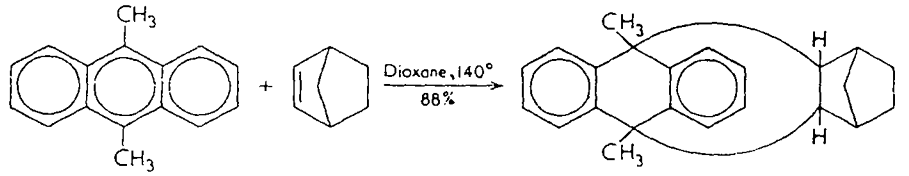


The only known diene additions of a simple benzene derivative are those of durene with hexafluoro-2-butyne[564] or dicyanoacetylene[565] which lead to unsaturated bicyclo[2.2.2]octanes. The formation of 1,2-bistrifluoromethylbenzene, the product from benzene itself and hexafluoro-2-butyne, can similarly be formulated as involving a primary 1 : 1 adduct.

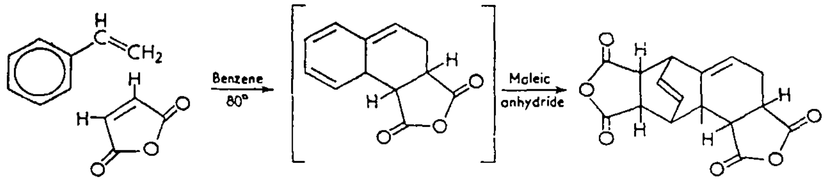
The conversion of naphthalene to diene adducts also requires drastic conditions[566,567]. However, the 1,2,3,4-tetramethyl derivative reacts readily at 100°. Interestingly, an excess of maleic anhydride appears to impede the reaction of naphthalene[567].

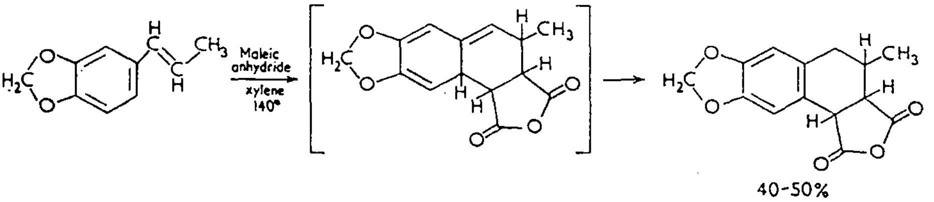


The 9,10-addition of hydrogen to anthracene finds a parallel in the addition of dienophiles across the same positions. Preparative experience leaves no doubt that the rate of addition with anthracene exceeds that with naphthalene. The highly reactive vinylidene cyanide[568] produces the 1 : 1 adduct at room temperature; the angle-strained dienophile bicycloheptene requires heating, even with the active component 9,10-dimethylanthracene[569]. The addition of C_6O_6, the double anhydride of ethylene tetracarboxylic acid, to the 9,10-position of 9,10-dimethoxyanthracene is reversible at 30° in dioxane. At higher temperatures the reactive C_6O_6 adds to the 1,4-position of the anthracene nucleus[569].

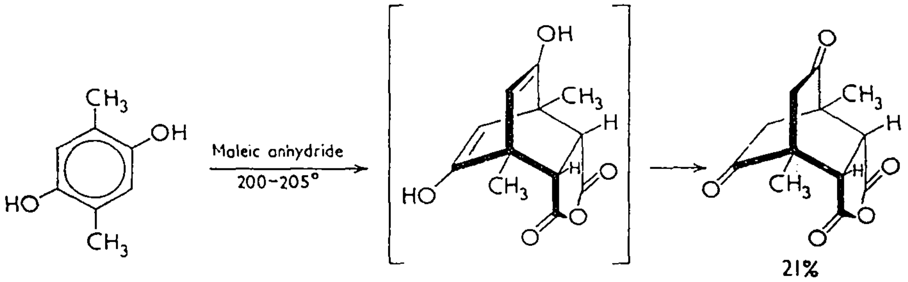


In compounds such as styrene, only one double bond of the diene is part of the aromatic system. The tendency of styrene to polymerize or copolymerize often makes the Diels–Alder reaction unprofitable. The primary addition of maleic anhydride converts styrene to a cyclohexadiene derivative which combines with a second molecule of the dienophile[570]. Rearomatization through migration of a double bond is also possible, as illustrated for isosafrole[571]. In the case of 1-vinylnaphthalene a 95% yield of the primary adduct with tetracyanoethylene is obtained at room temperature[572].





Phenols react with maleic anhydride only upon fusion; the adducts are structurally derived from the tautomeric keto-form, as has been shown with 2,5-dimethylhydroquinone[573], hydroquinone[574], and β-naphthol[575].

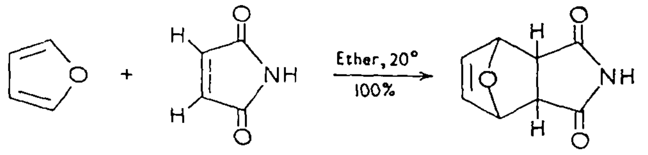


Of the pseudoaromatic azulenes and tropolones, only a few derivatives of the latter are amenable to Diels-Alder reactions[576].

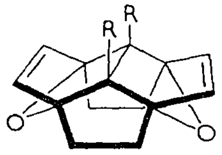
10. Heterocyclic compounds

Ever since the original studies of the Diels-Alder reactions, heterocyclic compounds of the furan, pyrrole and thiophene classes have been the subject of systematic investigations. The diene reactivity is known to fall in the above series.

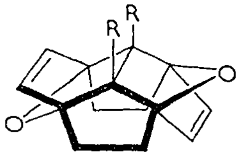
Furan reacts with maleic acid derivatives in the cold to give thermolabile adducts[577-579]. This reactivity persists in the alkyl derivatives as well as in the recently prepared polycyanofurans[580]. In the furan analogs of the paracyclophanes, both furan nuclei participate in the diene addition with dimethyl acetylenedicarboxylate[581]. The



two possible isomers, **47** and **48**, are formulated below; the configuration of the isolated product remains uncertain. In an analogous manner two molecules of furan combine with one of acetylenedicarboxylate to **49**[482]. Photooxidation of the heterocyclophane includes an interesting intramolecular Diels–Alder reaction[583].

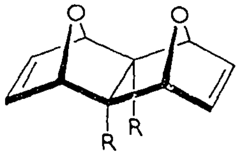


(47)



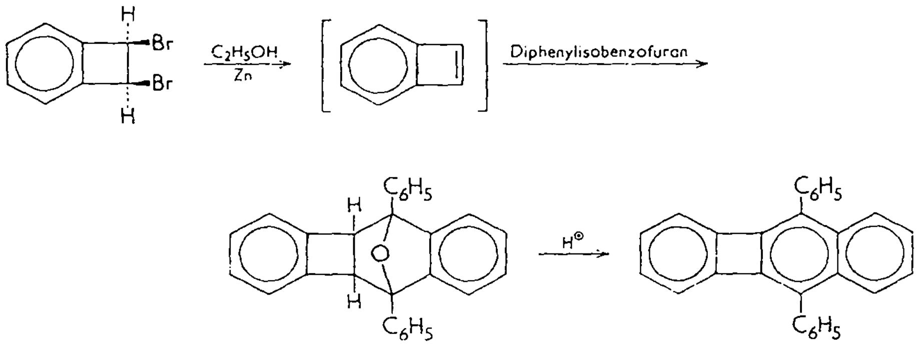
($R = CO_2CH_3$)

(48)

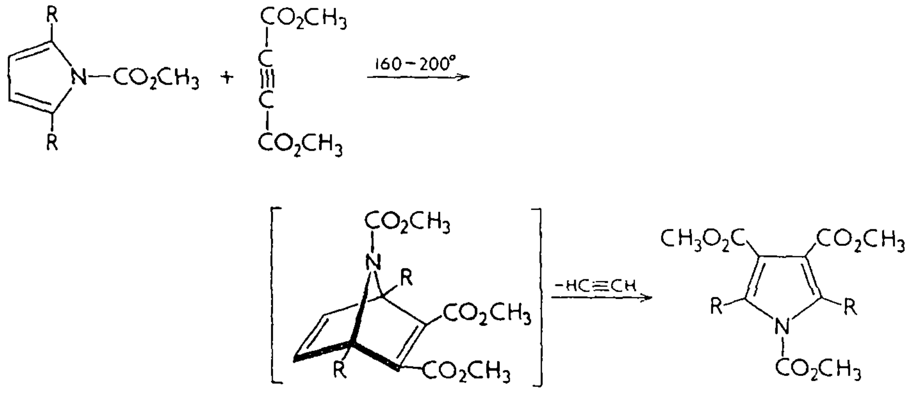


(49)

Diphenylisobenzofuran (p. 870), which itself can be obtained *via* a Diels–Alder reaction[584], was recently used to trap the short-lived benzocyclobutadiene[585]; hydrolytic ring opening leads to diphenylbenzobiphenylene.



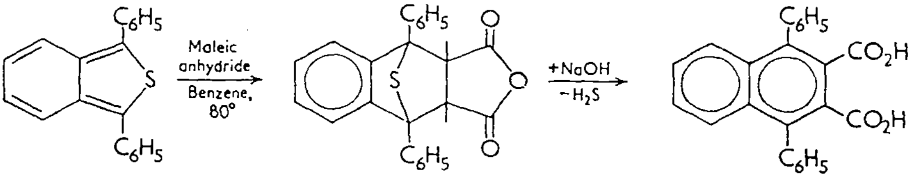
The sensitivity of pyrroles towards electrophilic attack at the α-position causes side-reactions with diverse dienophiles; maleic anhydride, for example, combines with pyrrole to give, after hydrolysis, α-pyrrylsuccinic acid. With *N*-benzyl-[586,587] and *N*-carbomethoxypyrrole[588] and acetylenic dienophiles, normal Diels–Alder additions at the 2,5-position have been observed. The reaction of methyl pyrrole-*N*-carboxylate with dimethyl acetylenedicarboxylate forms not the 1:1 adduct, but instead, due to the high reaction temperature, a product resulting from acetylene elimination (retro-Diels–Alder reaction; see p. 906).



R = CH$_3$, 51%
R = H, 43%

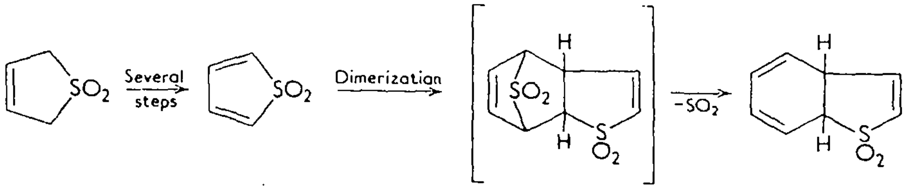
The formation of substituted phthalic esters from arylphospholes[589] and dimethyl acetylenedicarboxylate can be attributed to a diene synthesis; the fate of the phosphorus containing fragment is uncertain. Pentaphenylphosphole gives in 88% yield dimethyl tetraphenylphthalate[590].

Thiophene itself and simple derivatives show no inclination to add dienophiles. Toward hexachlorocyclopentadiene the parent compound acts as a dienophile to form a bisadduct[591]. With 2- and 3-vinylthiophene the reaction proceeds as with styrene[592]. A few isobenzothiophene derivatives have been shown to add maleic anhydride to the diene system of the heterocycle[593]; the reaction of the diphenyl derivative may serve as an example[594].

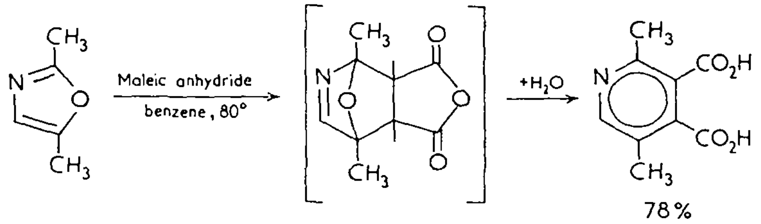


Thiophene 1,1-dioxide offers an interesting analogy to cyclopentadienone. Its preparation from the 1:1 adduct of butadiene with sulfur dioxide by a multi-step procedure has been described by

Bailey[595]. Attempts to isolate or trap the monomer have yielded only a derivative of the dimer.



Of the five-membered aromatic compounds containing several heteroatoms, so far only oxazole derivatives[596] and benzoxazole[597] have been induced to react with maleic anhydride. 2,5-Dimethyloxazole gives 2,5-dimethylcinchomeronic acid as secondary product. An elegant synthesis of pyridoxine has been achieved employing the adduct obtained from 5-ethoxy-4-methyloxazole and diethyl maleate[598].

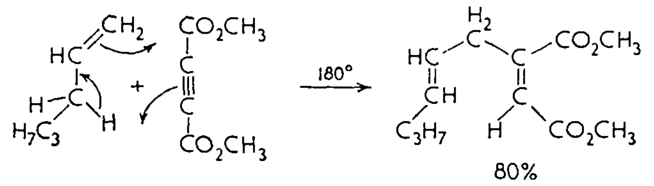


From the six-membered heterocycles, α-pyrone may be mentioned. With olefinic dienophiles, 1:1 adducts can often be obtained; those from acetylenic dienophiles lose carbon dioxide to form aromatic products[599].

Acridizinium bromide, a nitrogen analog of anthracene, adds maleic anhydride at the center ring in 87% yield[600]. The so-called diene adducts of 2,3-dimethylquinoxaline have recently been disproved[601]. The interesting reactions of 1,2,4,5-tetrazines as dienes will be discussed on page 923.

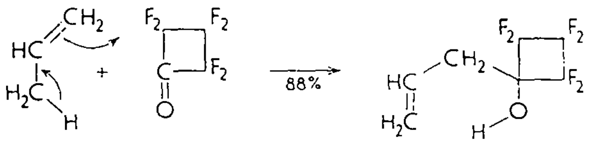
II. Simple olefins and non-conjugated dienes

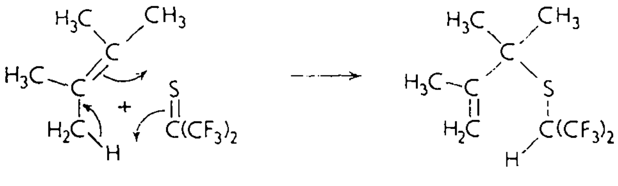
Simple alkenes often react with dienophiles in a fashion which seems to bear some mechanistic analogy with the diene synthesis. The net result is an allylic substitution which is brought about by a cyclic electron shift and migration of the olefinic double bond. Alder has termed this reaction type an 'indirect substitution–addition' or 'ene synthesis'[494]. The strongly oriented *cis* addition observed when acetylenic dienophiles are employed points to a concerted mechanism[602, 603], which is also in agreement with recent investigations concerning the asymmetric induction in the 'ene synthesis'[604].



The addition reactions of diethyl azodicarboxylate with 1,3-diarylpropenes and with 1,2- and 1,4-dihydronaphthalene follow the pattern of the 'ene synthesis' and proceed with obligatory double-bond migration[17]. A mechanistic study has established the synchronous mechanism in these cases and excluded radical or ionic paths[17] (p. 746).

Aldehydes, ketones and thioketones with electron-deficient C=O or C=S functions, such as chloral[605], carbonyl cyanide[606], pyruvic ester[607], perfluorocyclobutanone[307] or hexafluorothioacetone[608], are all heterodienophiles which are capable of participating in the 'ene synthesis'. Interestingly, the direction of addition observed with carbonyl compounds is reversed with the thioketones, as the example with hexafluorothioacetone illustrates.





The reversibility of the reaction of pyruvic ester with olefins makes a common transition state probable for the 'ene synthesis' with carbonyl compounds and the pyrolysis of β-hydroxyolefins[607].

As already noted, the homo-Diels–Alder reactions, *i.e.* transannular reactions of non-conjugated dienes illustrated on page 749, do not obey the classification rule of the diene addition reaction, $2\ \pi \rightarrow 2\ \sigma$ bonds. To the examples provided earlier we may now include the 1:1 adducts of azodicarboxylates[609,610], of dicyanoacetylene[565] and of the double anhydride from ethylenetetracarboxylic acid, C_6O_6[569], with norbornadiene.

C. The Dienophile Component

Systematic discussion of the dienes has already given an indication as to the great variety of operative open-chain dienophiles. A brief summarizing classification will now be added. In accordance with a rule already given by Alder, the rate of the addition reaction increases as the electron density at the double bond is diminished by conjugation with electron-attracting groups X. Kinetic measurements (see p. 919) with cyclopentadiene and 9,10-dimethylanthracene provide quantitative support for this statement.

1. Open-chain olefinic dienophiles

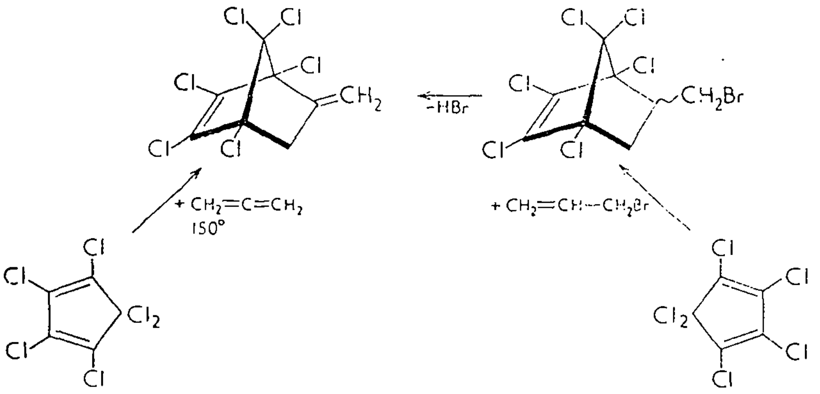
Ethylene itself and allyl compounds in general exhibit only slight dienophilic activity. Acrolein and acrylic acid derivatives are the most reactive of the monosubstituted ethylenes. The asymmetrically disubstituted ethylenes, such as vinylidene cyanide and methylenemalonic ester, are in some cases prone to polymerize and difficult to use. 1,2-Disubstituted ethylenes can exist in geometrically isomeric forms, which permit the formation of diastereoisomeric adducts. The possibility here, as well as with tri- and tetrasubstituted ethylenes, of combining various kinds of ligands broadens the range of utility considerably. Tri-[611] and tetracyanoethylene[524], as representatives of the last two types, have claimed much preparative interest.

2. Open-chain acetylenic dienophiles

Acetylene itself is only able to participate in addition reactions under stringent conditions[532]. The difficulties in handling laboratory quantities may be circumvented by addition of vinyl bromide to the diene followed by subsequent dehydrobromination which thus leads to the same product which would be obtained from free acetylene. Methyl propiolate, acetylenedicarboxylic esters and ethyl phenylpropiolate are especially useful examples of mono- and di-substituted acetylenes.

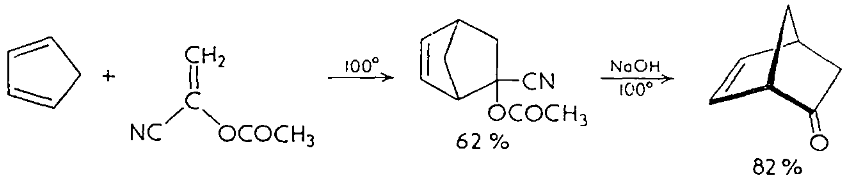
3. Allenes

Because of its poor reactivity, the parent compound has found use only rarely. With polychlorinated dienes, such as hexachlorocyclopentadiene, the reaction proceeds in satisfactory yield[612]; the structure of the product was established in a straightforward way[613].



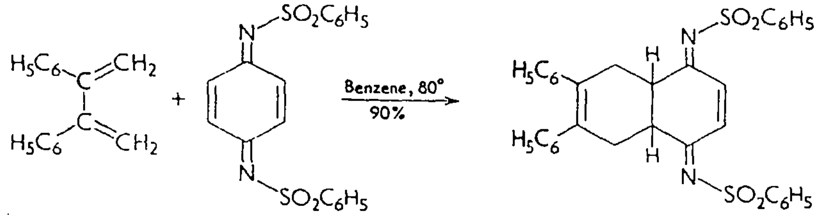
Allenecarboxylic acid reacts with cyclopentadiene as an acrylic acid derivative to give 86% yield of the adduct having the carboxyl group in the *endo* configuration[614]. Stereospecific addition of allenedicarboxylic acid[615] to the same diene has recently permitted conclusions about the absolute configuration of the allene.

The inability of ketenes to undergo diene addition has long been recognized; with dienes, cyclobutane derivatives are formed (p. 789). However, use of α-acetoxyacrylonitrile provides an indirect route to the diene adducts of ketene[616].

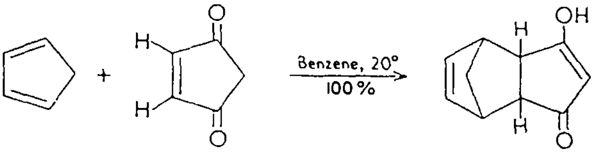


4. Cyclic dienophiles

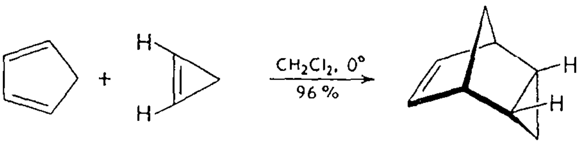
Crossed conjugation of two carbon–carbon double bonds with carbonyl groups as in the *p*-quinones makes these compounds favorite dienophiles; their reactivity remains unaltered even in the *N,N*-disulfonylquinonediimine derivatives[617].



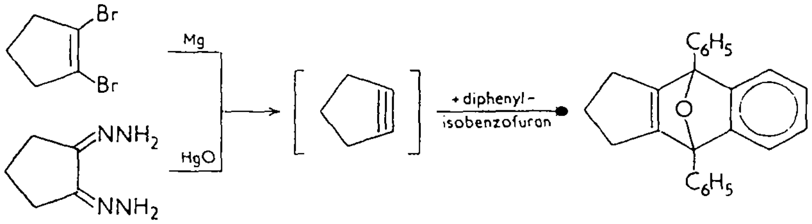
Cyclopent-2-ene-1,3-dione offers a convenient route to cyclopentane-1,3-dione derivatives *via* its diene adducts[618]. The dienophile exists completely in the diketone form.



Addition reactions at the double bond of cyclopropene are outstanding for their great ease; the $sp^2 \rightarrow sp^3$ transition during the diene addition is associated with a significant reduction of the strain in the three-membered ring. While ethylene only reacts with cyclopentadiene under drastic conditions, cyclopropene gives the *endo* adduct even at 0°, as Wiberg has shown[619]. The stereoisomeric *exo* adduct is obtainable from bicyclo[2.2.1]heptadiene by reaction with methylene iodide in the presence of the zinc/copper couple[81].



The linear arrangement of the *sp*-hybridized carbon–carbon triple bond can only be incorporated in a strain-free condition in rings of nine or more members. The lower homolog, cyclooctyne, shows accentuated dienophilic reactivity. Cycloheptyne, -hexyne and



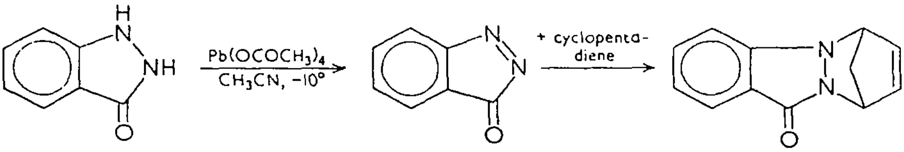
-pentyne are not isolable compounds, but by trapping with diphenylisobenzofuran (p. 895) their existence can be demonstrated[620,621].

Arynes formally contain a carbon–carbon triple bond in the aromatic nucleus; however, the bond system undoubtedly is not that of an acetylene. Wittig brilliantly brought to light the dienophilic character of the arynes[622]; for instance, cyclopentadiene[622] and cyclohexadiene[623] have been used as olefinic dienes. Stiles[624] observed, that even benzene and naphthalene react as diene components with benzyne.

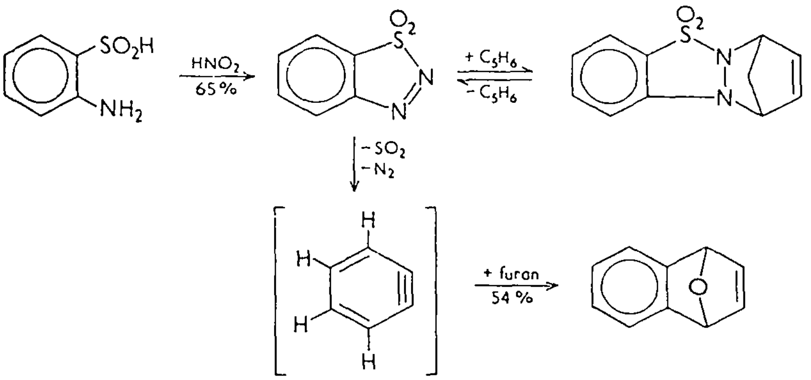
Formal exchange of one CH group in benzyne by nitrogen leads to dehydroaromatic compounds of the pyridine series which likewise are able to react as dienophiles[625].

5. Cyclic azo compounds

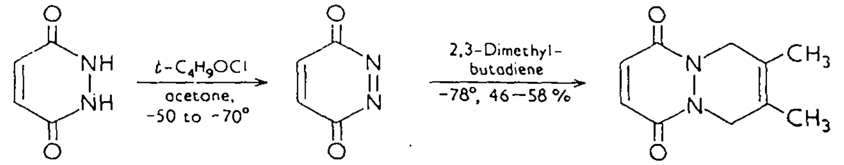
High dienophilic activity is common to several cyclic azo compounds which have only recently come into view. From the unstable deep red solutions obtained by oxidation of indazolin-3-one, diene adducts of indazol-3-one can be recovered[626].



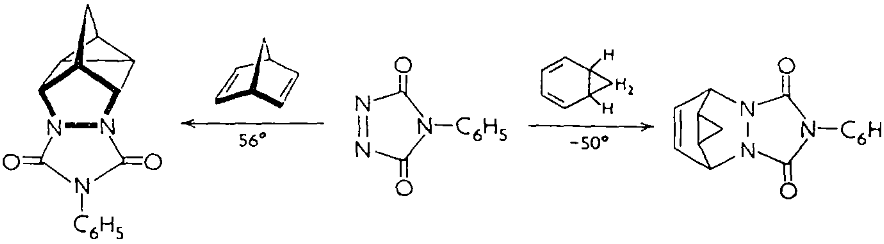
The diazonium betaine produced by diazotization of *o*-aminobenzenesulfinic acid cyclizes to form a covalent ring[627]. Its decomposition at room temperature gives benzyne; addition of cyclopentadiene to the nitrogen–nitrogen double bond is reversible at higher temperatures.



Among other interesting modes of reaction, the diaza analogs of *p*-benzoquinone or 1,4-naphthoquinone show a tendency to undergo the diene addition even at low temperature[628,629].

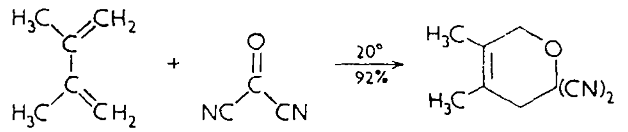


In 4-phenyl-1,2,4-triazoline-3,5-dione an extremely active dienophile is present[630]. The homo-Diels–Alder reaction with norbornadiene also takes place smoothly.

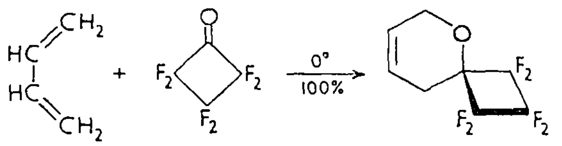


6. Other dienophiles with heteroatoms

In contrast to their activity as dipolarophiles in 1,3-dipolar additions, the bond systems C=X (X = O, S, N) and C≡N show only slight inclination to act as dienophiles[511]. Aldehydes and ketones with

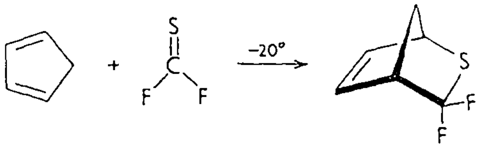


electron-deficient carbonyl groups (*e.g.* formaldehyde[631], chloral[632], carbonyl cyanide and mesoxalic ester[633]) are able to add dienes to form dihydropyrans.



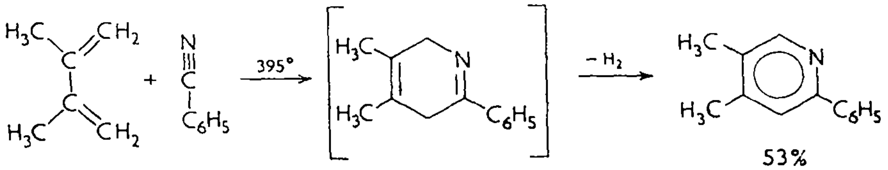
A heterodienophile comparable in reactivity to tetracyanoethylene is perfluorocyclobutanone, which has recently been studied by England; its reactions make spirodihydropyrans readily accessible[307].

Only under the influence of electron-withdrawing substituents is the C=S bond able to function as a dienophile. The reactions of hexafluorothioacetone, trifluorothioacetyl fluoride and thiocarbonyl fluoride[608] with open-chain and cyclic dienes yield interesting dihydrothiopyran derivatives.

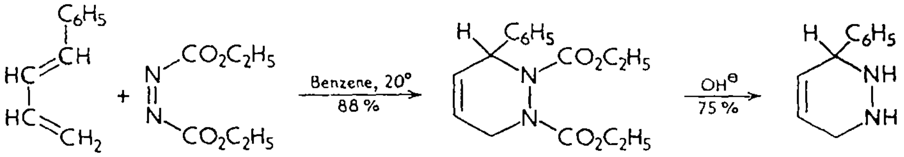


Similar to the C=S double bond, the C=N double bond found in Schiff bases when substituted with electron-withdrawing groups add to dienes. Kresze and Albrecht were able to react $Hal_3C—CH=N—Tos$ with several dienes to form isolable adducts in more than 90% yield[634]. α-Halogenated amines combine with dienes to give Δ^3-piperidinium salts; here it is probably the immonium ion that functions as the dienophile[635].

The nitrile function exhibits dienophilic reactivity only under drastic conditions. α-Ketonitriles react with tetracyclone at 250–270° followed by immediate carbon monoxide elimination to give acylpyridine derivatives[636]. The simple nitriles, acetonitrile and benzonitrile, as well as cyanogen, can be combined with dienes in a flow process in which an alumina catalyst is used at temperatures above 400°[637]. Under these conditions the Diels–Alder adduct is dehydrogenated to the aromatic pyridine derivative.

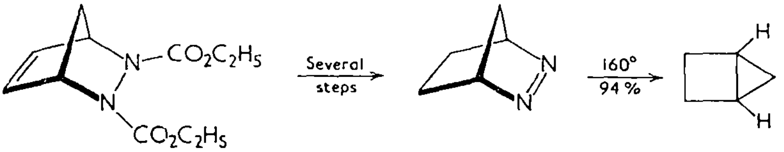


Of the dienophiles with two heteroatoms, the —N=N—, —N=O and —N=S=O systems as found in azo, nitroso, and *N*-sulfinyl compounds may be given special consideration.

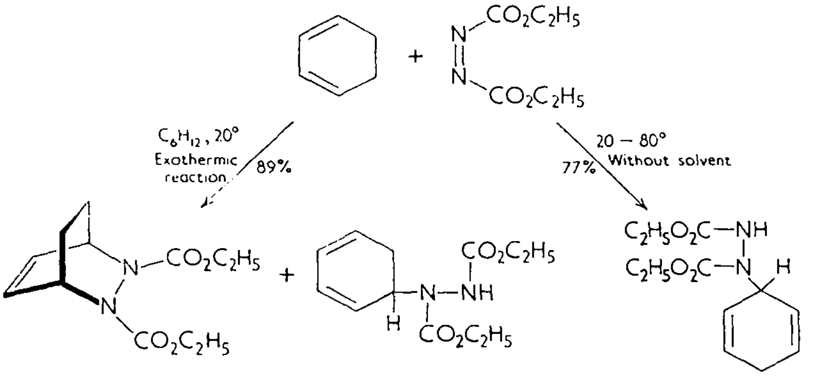


The high reactivity and ready availability of azodicarboxylic ester make it a useful starting point for the synthesis of cyclic and bicyclic hydrazo and azo compounds as well as pyridazine derivatives[638,639].

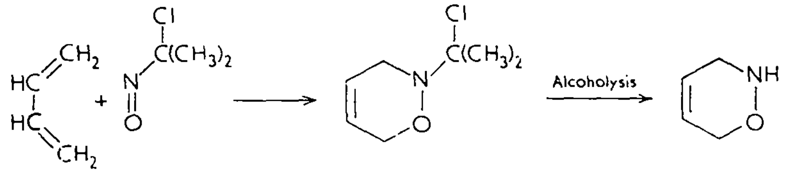
The bicyclic azo compound derived from the adduct of cyclopentadiene and azodicarboxylic ester is converted thermally to the highly strained bicyclopentane[640,641].



The tendency of the azodicarboxylate to cause radical allylic substitution[642] and to undergo multi-center addition with migration of the double bond[17] warns us not to ascribe Diels–Alder structures uncritically to all 1 : 1 adducts. Small changes in the reaction conditions result in fundamental changes in the course of the reaction with cyclohexadiene[643].

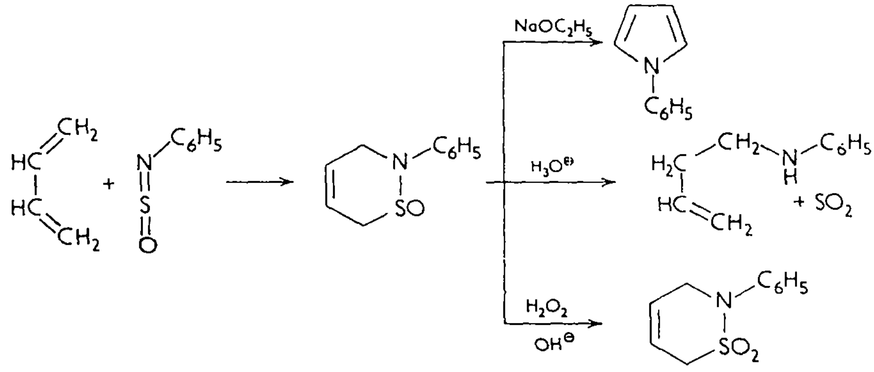


The nitroso group is only able to participate in diene additions when adjacent to an electron-attracting ligand or when attached to an aromatic nucleus[511]. Hydrogenolysis of the N—O bond in the adducts from nitrosobenzene makes *cis*-1,4-amino alcohols available.



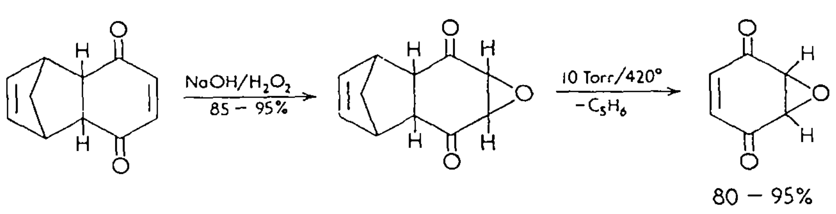
The addition of oxygen to dienes under the influence of light leads formally to a Diels–Alder adduct[257,494,644]. There is yet no foundation for believing that the reaction, which perhaps involves a triplet intermediate, has a common mechanism with the thermal diene additions.

The 1 : 1 adducts obtained from *N*-sulfinyl compounds, RN=S=O, and dienes provide new synthetic routes; the additions take place at the N=S double bond, as is also the case with the even more reactive *N*-sulfinylsulfonamides[645].



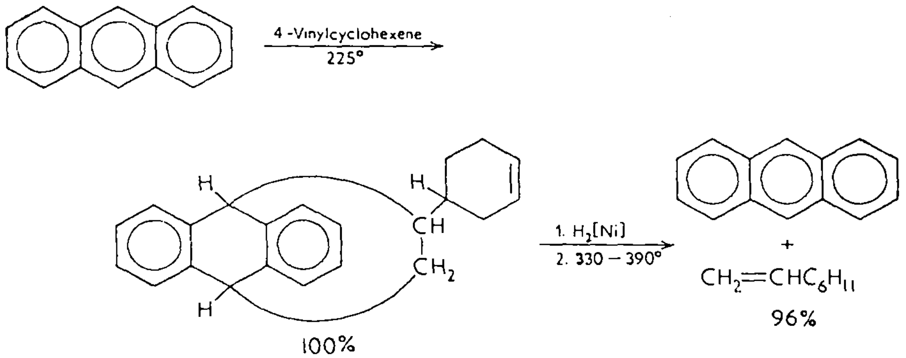
D. Retro-Diels–Alder Reactions

The spontaneous occurrence of the diene addition at moderate temperatures is one of the characteristics of the reaction. At higher temperatures redissociation to the components is often observed. This long-recognized phenomenon often is of preparative use. However, this is only of practical significance when one is able to modify the adduct chemically and obtain a 'new' diene or dienophile through the retro-Diels–Alder reaction. For the following discussion a number of illustrations are arbitrarily selected from the abundant experimental examples.

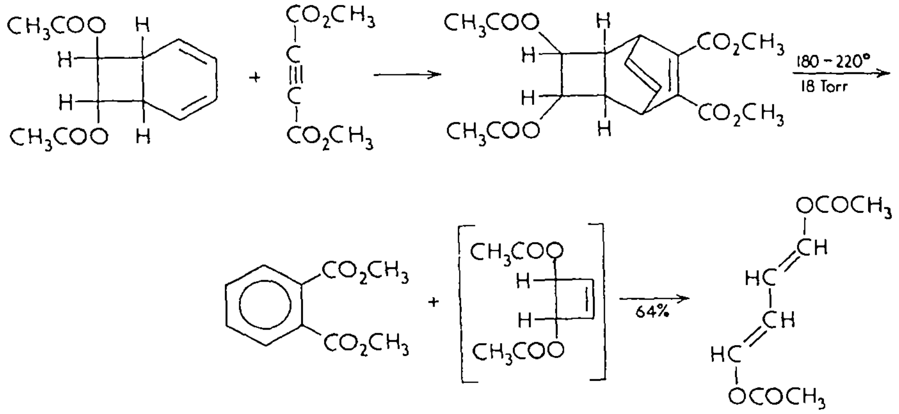


The notorious alkali-sensitivity of *p*-benzoquinone prevents its conversion into the epoxide; in the cyclopentadiene adduct alkaline epoxidation is possible. Subsequent thermolysis makes the desired epoxide and its simple substituted derivatives accessible in surprisingly good yield[646].

4-Vinylcyclohexene, which is obtained by dimerization of butadiene, can be transformed in three steps to vinylcyclohexane[647].



From the large number of additional examples may be mentioned the preparation of 1,3-dioxole derivatives[648], of 6,6-disubstituted cyclohexadienones from dimeric fulvene epoxides[561], of *o*-quinodimethane[529,530], and of acetylenedicarboxylic acid dichloride[649]. The importance of the retro-Diels–Alder reaction in locating the substituents on the cycloheptatriene ring may also be recalled[650,651].

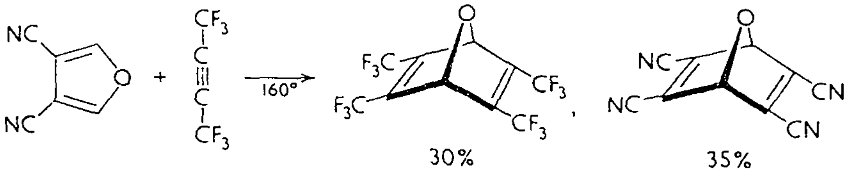


It is not essential in the retro-Diels–Alder reaction that the same bonds be broken as were formed in making the adduct. For example, the adduct from 7,8-diacetoxybicyclo[4.2.0]octa-2,4-diene and dimethyl acetylenedicarboxylate[60] dissociates to dimethyl phthalate and *trans-trans*-1,4-diacetoxybutadiene[652].

A series of adduct cleavages take place even under mild temperature conditions. The reversibility of the diene additions of furans and fulvenes (see pp. 894, 888) for a long time impeded analyses of the steric course of these reactions. The product of alkaline hydrolysis of the anthracene/diethyl azodicarboxylate adduct decomposes even in boiling ethanol into anthracene and diimide, which was recognized by its ability to cause stereospecific *cis* hydrogenation[653, 654].

Unusually facile cleavage has also been demonstrated recently with various tetracyanoethylene adducts. In the fulvene[655] and substituted anthracene series[569] the decomposition sometimes occurs immeasurably fast. In one case, the phenomenon has been used for the preparation of the double anhydride of ethylenetetracarboxylic acid[569].

The following amusing reaction quite possibly depends upon a repetition of diene additions and retro-Diels–Alder reactions; presumably the reaction conditions here guarantee establishment of the thermodynamic equilibrium[656].

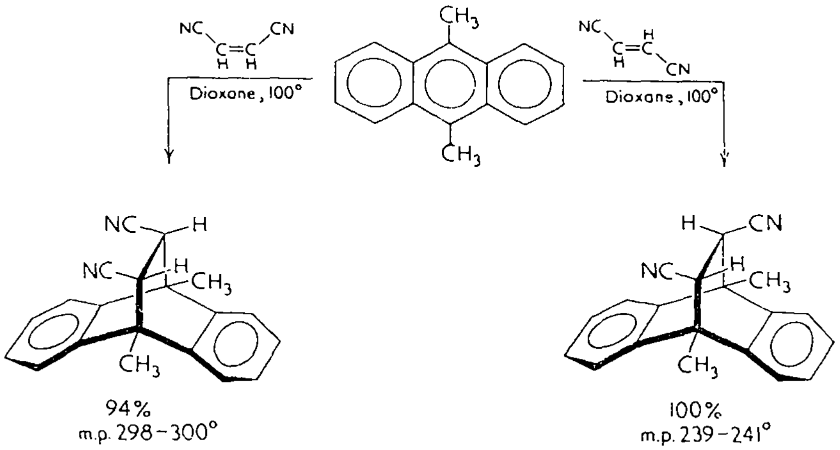


E. The Stereochemistry of the Diels–Alder Reaction

The long-recognized stereoselective course of the diene-addition reaction poses problems of theoretical as well as practical interest. Outstanding contributions to the subject have been made by Alder and his students, in particular. Appearance of a review article recently[657] permits restriction of the present discussion to a few special features. The value of the stereochemical results in the diagnosis of the course of diene additions may sometimes be seriously reduced. Epimerization of either the starting materials or the product has in some cases falsely indicated a non-stereoselective process. The reversibility of the Diels–Alder reaction necessitates special caution; with furans and fulvenes only reactions at low temperature lead to the kinetically controlled adduct.

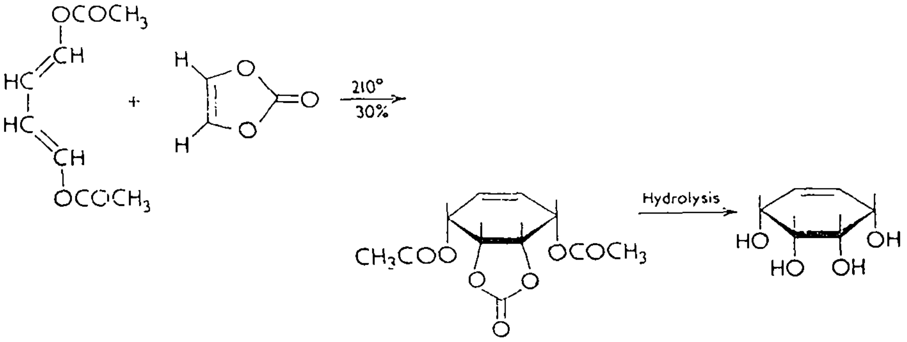
1. The '*cis* principle'

The large amount of experimental data already available in 1937 made possible formulation of the so-called '*cis* principle'[658], which states that the configurational relationship of the dienophile and diene is retained in the adduct. Thus, *cis–trans* isomeric dienophiles react with dienes to give high yields of pure diastereoisomeric 1 : 1 adducts as is illustrated by the following example[569]:



With respect to the mechanistic consequences, it is intriguing that a vast number of additional examples are opposed by only a *single* violation of the *cis* principle: *cis*- and *trans*-β-sulfoacrylic acid give with cyclopentadiene the same product, having a *trans* ligand structure[660]. Although an isomerization of the dienophile before or of the product after the addition could be excluded, the low yields suggest that this finding should not be overemphasized and that further work should be done.

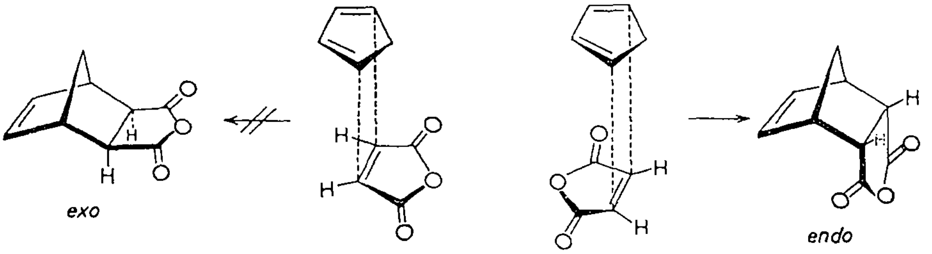
The configuration of the diene component also is retained in the adduct[657]. Thus, the maleic anhydride addition product from *trans-trans*-1,4-diphenylbutadiene contains the phenyl groups in



a *cis* arrangement[661]. Analogously, from *trans-trans*-1,4-diacetoxybutadiene and vinylene carbonate one obtains after hydrolysis the cyclohexenetetrol with an all-*cis* structure[652].

2. The '*endo* addition rule'

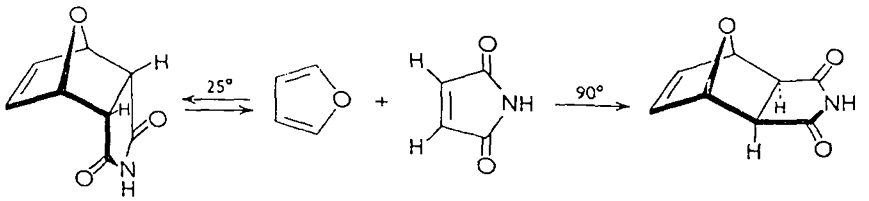
Basically, there are two stereochemical alternatives for the addition of maleic anhydride to cyclopentadiene. Of these, only the mode leading to the product with an *endo* anhydride configuration is used. This result led Alder and Stein[658] to formulate the '*endo* addition rule', which requires that the reaction partners arrange themselves in parallel planes; addition proceeds from that orientation of the components which has the 'maximum accumulation' of double bonds. Not only the double bonds which take part directly in the addition step must be counted, but also the π bonds of the so-called activating groups in the diene or dienophile. In the cyclopentadiene–maleic anhydride system this rule requires that only the '*endo*' product be formed. Its configuration has been firmly established[658].



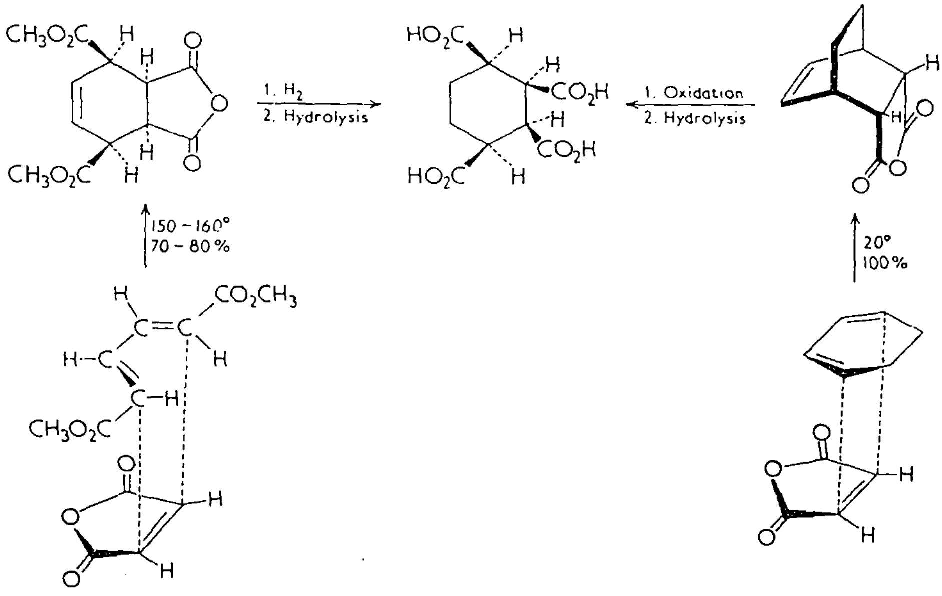
A simple method for the detection of the *endo* carboxyl function in the bicyclo[2.2.1]heptene system is that of bromo- or iodolactonization[657]. The latter, unlike bromolactonization, is not limited in usefulness by Wagner–Meerwein rearrangements and has found acceptance as a rapid titrimetric method for the analysis of *endo*/*exo* isomer mixtures[662]. With the help of this sensitive test, the presence of a small amount (< 1·5%) of the *exo* adduct from cyclopentadiene and maleic anhydride in the crude product has recently been demonstrated[662].

The *endo* addition rule proposed by Alder is quite closely obeyed in the addition of cyclic dienes to cyclic dienophiles. In the cases of the adducts from cyclooctatetraene or cyclopentadiene with benzoquinone and of hexachlorobicyclo[2.2.1]heptadiene with cyclopentadiene, the elegant photoisomerization reaction of Cookson[663] provides proof for the *endo* structure (p. 801).

With furans[664-666] and fulvenes[543, 667], one obtains the *endo* adduct by kinetically controlled reactions at low temperatures. The easy reversibility of the reaction on warming allows isomerization to the thermodynamically more stable *exo* isomer.



The stereochemistry of the compounds obtained from open-chain dienes and cyclic dienophiles also is often determined by the rule of maximum accumulation of double bonds. The adduct from diethyl *trans-trans*-muconate and maleic anhydride is transformed by hydrogenation and saponification into all-*cis*-cyclohexane-1,2,3,4-tetracarboxylic acid, which can also be prepared from the configurationally certain cyclohexadiene–maleic anhydride adduct[668, 669].



In the addition of open-chain dienophiles to cyclic dienes, the *endo* addition rule is not always obeyed. From cyclopentadiene and ethyl acrylate the *endo* and *exo* adducts are obtained in a ratio of 76:24[670, 671]. When acrylonitrile is used as the dienophile, the product ratio of 60:40 approaches the statistical value[672]. Substitution of a methyl or phenyl group or a chlorine atom in the α- or β-position of the acrylic ester, for example, has a marked influence on the stereochemical course[673,674].

Open-chain dienes and dienophiles fulfil the 'rule of maximum accumulation of double bonds' only at low temperatures; one obtains cyclohexene derivatives with substituents in the *cis* arrangement[657]. At higher temperatures the stereoselectivity is often lost.

The problem of the origin of the stereoselectivity is an intriguing one which has not been completely clarified[674]. The predominant *endo* addition of *p*-benzoquinone to cyclopentadiene has been attributed to dipole inductive forces between polar groups in the dienophile and the easily polarized diene[675]. Today this phenomenon could better be termed as a charge-transfer interaction. Astonishingly, the addition of the dienophiles, cyclopropene[619], cyclopentene[676], and even propene[659], all which lack polar groups, yield almost exclusively the products of *endo* addition.

Berson[674] found an appreciable effect of the solvent upon the stereochemical course of the addition[677]. As the polarity increased, the *endo* isomer content of the adduct mixture from cyclopentadiene and methyl acrylate became greater; the transition state leading to *endo* addition, which has the higher dipole moment, profits more from solvation. The surprising fact that the energetically unfavored transition state having the higher dipole moment is preferred at all points to a second stronger directive effect, presumably the dipole induction forces. On the other hand, Horner and Dürckheimer[678] proposed on the basis of their results with *o*-quinone dimerizations that reactants possessing a high dipole moment tend to orient themselves with respect to one another to form the transition state of the lowest total dipole moment.

It must not be forgotten that the forces which determine the steric course are relatively small. Even predominance of one isomer by a 99:1 ratio in the product mixture corresponds to a difference of less than 3 kcal in the activation energies of the two possible modes of addition. The interplay of the factors discussed above makes it impossible as yet to predict precisely the steric course of addition for many open-chain dienophiles.

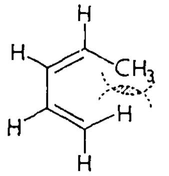
3. *Cisoid* and *transoid* dienes

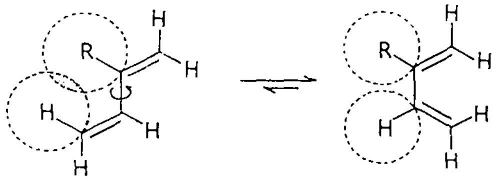
The planar *cisoid* conformation of the diene system is an absolute prerequisite for the Diels–Alder addition; steroids, in which for structural reasons the *transoid* form is frozen, fail to give the reaction[494]. All factors which can have an influence on the conformational equilibrium between the *cisoid* and *transoid* forms or on the coplanarity of the diene system should also affect the rate of the addition reaction.

cis-1-Methylbutadiene is much less reactive than the *trans* isomer in the addition with maleic anhydride[679]. The steric interaction of the 1-methyl group with the hydrogen atom at $C_{(4)}$ causes deformation of the molecule through a small rotation around the single bond between positions 2 and 3. Presumably the deviation from coplanarity in the case of *cis*-1-methylbutadiene is still small. As the spatial requirement of the *cis* ligand at $C_{(1)}$ increases in the series, methyl, ethyl and isopropyl, the ability to take part in the addition reaction decreases further and is completely lost when one reaches 1-*t*-butyl- and 1-phenylbutadiene[494].

The different addition rates of the isomers with maleic anhydride makes possible the separation and purification of the sluggish *cis* isomers of 1-phenylbutadiene[680], hexatriene[681], and the 1-halobutadienes[682]. In contrast, hexaethylidenecyclohexane, which contains three *cis*-1-substituted dienes, has been reported to yield bisadducts with reactive dienophiles[683]; however, no mono- or triadducts were found.

1,1-Disubstituted butadienes have been thought to react only after preliminary isomerization to the 1,3-disubstituted dienes[684]. Recently, however, it has been shown that very reactive dienophiles can add directly to 1,1-disubstituted butadienes[685]. The decreasing addition rates of the three isomeric 1,4-diacetoxybutadienes to juglone[686] support their configurational assignments as *trans-trans*, *cis-trans* and *cis-cis* forms on the basis of infrared and ultraviolet data.





With the 2-substituted butadienes, on the other hand, an astonishing rise in reactivity is found with increasing size of the substituent[687]. In going from butadiene to the 2-neopentyl derivative, the bimolecular rate coefficient for the addition to maleic anhydride (benzene, 25°) increases by a factor of approximately 50. In these cases, the van der Waals compression of the group R at $C_{(2)}$ and the hydrogen at $C_{(3)}$

favors the *cisoid* conformation required for reaction, to a degree dependant on the spatial demand of R.

It comes as no surprise that bulky groups in 2,3-disubstituted butadienes prevent the reaction by freezing the conformational equilibrium on the side of the *transoid* form; 2,3-di-*t*-butylbutadiene and analogous compounds, for example, are inert toward maleic anhydride[688].

F. Orientation Rules for the Addition of Unsymmetrical Compounds

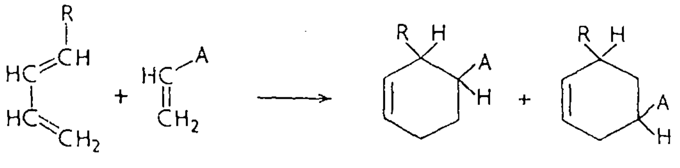
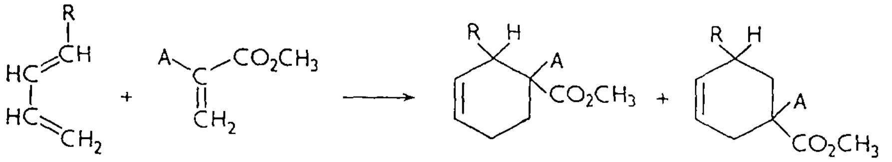
Reactions of symmetrical dienes or dienophiles cause no problems in regard to the structures of the products. From the combinations of unsymmetrical components, mixtures of isomers should be obtained. Usually, however, formation of a single isomer is strongly favored. Application of improved analytical techniques has weakened somewhat the authority of the older work, which often reported the formation of only *one* isomer[494]; many times this conclusion was based merely upon the isolation of the crystalline part of the reaction product. A review article[689] on the correlation of reactant structure with orientation in diene synthesis allows a limitation of the discussion to some characteristic phenomena.

1. 1-Substituted dienes

Table 18 contains a selection of isomer mixtures which have been recovered in reactions of 1-substituted butadienes with unsymmetrical dienophiles. Surprisingly, the electronic character of the substituents has practically no influence on the direction of addition; in every case the principal product is the cyclohexene derivative having neighboring ligands. With increasing temperature and greater spatial demand of the ligands, the fraction of the cyclohexene product possessing substituents in 1,3-relation increases; in the extreme case the isomer distribution approaches the statistical value.

The very strong orientation observed in the addition of *trans*-butadiene-1-carboxylic acid to acrylic acid is lost when the anions are used; presumably, here the Coulomb repulsion of the two charged groups causes the 1,3-isomer to increase to about 50%. The isomer ratio of the mixtures listed in the second and third sections were not obtained from the composition of the isomeric primary adduct but from the mixture of phthalic and isophthalic acids recovered by

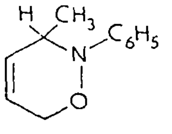
Table 18. Reactions of 1-substituted butadienes with unsymmetrical dienophiles[689].

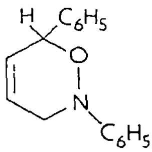
Diene R	Dienophile A	Reaction temperature	Ratio **50**:**51** of isomeric adducts	% Yield **50** + **51**
 **(50)** **(51)**				
	Electronic influence of substituents			
$N(C_2H_5)_2$	$CO_2C_2H_5$	20	only *cis*-**50**	94
CH_3	CO_2CH_3	20	18:1	64
C_6H_5	CO_2CH_3	150	39:1	61
CO_2H	CO_2H	150	8·8:1	86
CO_2H	CO_2H	70–75	only *cis*-**50**	67
CO_2Na	CO_2Na	220	1:1	50–60
	Steric influence of substituents in the diene			
CH_3	CO_2CH_3	200	6·8:1	85
$CH(CH_3)_2$	CO_2CH_3	200	5:1	60
$C(CH_3)_3$	CO_2CH_3	200	4·1:1	76
	Steric influence of α-substituents in methyl acrylate as dienophile			
				
$C(CH_3)_3$	H	200	4·1:1	76
$C(CH_3)_3$	CH_3	200	2·6:1	75
$C(CH_3)_3$	$CH(CH_3)_2$	200	0·9:1	19

degradation; the high yields obtained in the separate reaction steps make a serious error in the isomer ratios unlikely.

Preferential formation of *one* structural isomer was also observed when acetylenic dienophiles were employed. The reaction of 1-methylbutadiene with ethyl propiolate as well as the addition of 1-phenylbutadiene to propiolic acid furnish adducts in 85% and 30% yield, respectively, containing neighboring ligands without contamination by a second isomer[690].

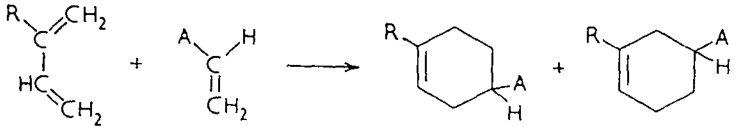
Anthracene derivatives with substituents in position 9 might also be considered as 1-substituted dienes. Here an interesting influence of the nature of the 9-substituent on the addition orientation of unsymmetrical dienophiles is observed[691,692].





The question of orientation in the addition of nitrosobenzene to 1-substituted butadienes will briefly be mentioned at this point. With 1-methylbutadiene the predominant product is 3-methyl-2-phenyl-1,2-2*H*-oxazine, while 1-phenylbutadiene and its nuclear substituted derivatives (*p*-CH_3O, *p*-Cl, *p*-NO_2) choose the second possible orientation in their addition to nitrosobenzene[511,693].

TABLE 19. Reactions of 2-substituted butadienes with unsymmetrical dienophiles[689].



(52) (53)

Diene R	Dienophile A	Reaction temperature	Ratio **52**:**53** of isomeric adducts	% Yield **52** + **53**
		Electronic influence of substituents		
OC_2H_5	CO_2CH_3	160	only **52**	50
CH_3	CO_2CH_3	20	5·4:1	54
C_6H_5	CO_2CH_3	150	4·5:1	73
Cl	CO_2CH_3	160	only **52**	60
CN	$COCH_3$	95	only **52**	86
		Steric influence of substituents		
n-C_3H_7	CO_2CH_3	200	2·4:1	81
$CH(CH_3)_2$	CO_2CH_3	200	3·0:1	65
$C(CH_3)_3$	CO_2CH_3	200	3·5:1	47
		Influence of temperature		
CH_3	CO_2CH_3	20	5·4:1	54
CH_3	CO_2CH_3	120	4·0:1	74
CH_3	CO_2CH_3	200	2·0:1	84
CH_3	CO_2CH_3	400	1·4:1	18

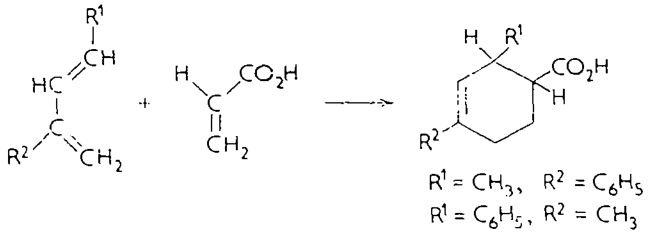
2. 2-Substituted dienes

As the examples of Table 19 show, in the adducts derived from 2-substituted butadienes and unsymmetrical dienophiles a single isomer once again predominates, in this case that which bears the substituents in the 1,4-positions. Often, however, the selectivity is not as pronounced as in the case of the 1-substituted dienes. Electronic factors apparently do not influence the sense of addition; the data thus completely parallel the results given in Table 18. Increasing steric requirements of substituents in the diene and dienophile favor the formation of the 1,4-disubstituted cyclohexene.

Acetylenic dienophiles again join the olefins in their behavior; isoprene reacts with propiolic acid to give 2,5-dihydro-4-methylbenzoic acid in 77% yield[694].

3. Disubstituted dienes

In 1,3-disubstituted butadienes the directive influences of the substituents are additive. 1-Methyl-3-phenylbutadiene and its 3,1-isomer both react with acrylic acid at 115–145° to form 2,4-disubstituted cyclohexene-3-carboxylic acids[695].



From 1,3-dimethylbutadiene and methyl acrylate at 200°, one obtains a small amount of the second possible structural isomer as a by-product[696].

Through the use of 1,4-disubstituted butadienes it is possible to compare the directive power of various substituents. Experiments by Alder and his coworkers[697] with 1-methyl-4-phenylbutadiene and 4-methyl- or 4-phenylbutadiene-1-carboxylic acid established the following descending order of directivities:

$$C_6H_5 \gg CH_3 \geqslant CO_2H.$$

Additions of 2,3-disubstituted butadienes with acrylic acid give approximately equal amounts of the two possible position isomers[698].

G. The Kinetics of the Diels–Alder Reaction

1. Activation parameters; the influence of solvent and substituents

The often quantitative nature of the reaction has long made kinetic studies attractive. The investigations of Wassermann[699] and Kistiakowsky[700] in the thirties led to important early discoveries. The values of the activation parameters exhibited characteristic peculiarities. Low activation energies (E_A = 9–17 kcal) are normal and are associated with similarly low frequency factors A; thus collisions producing reaction are relatively rare, and the steric configuration in the rate-determining step must be highly ordered. High negative values of the activation entropy are obtained by application of the Eyring equation[701].

The solvent effect on the bimolecular rate coefficient is quite small. As a rule, in going from non-polar to polar solvents, the rate constant increases only by a factor of 3–8[702]. Evidently the transition state is not much more polar than the ground state. The dimerization of cyclopentadiene serves to illustrate this point (Table 20). Addition reactions of more polar components also show similar variations in the rate coefficients[702,704].

TABLE 20. Solvent dependence of the dimerization of cyclopentadiene[703].

Solvent	10^7k_2 at 20° (l./mole sec)	E_A (kcal/mole)	log A
Ethanol	19	16·4	6·4
Nitrobenzene	13	15·1	5·5
Acetic acid	10	14·7	5·0
Paraffin oil	9·8	17·4	7·1
Dioxane[705]	9·4	17·3	6·8
Carbon disulfide	9·3	16·9	6·2
Carbon tetrachloride	7·9	17·1	6·7
Benzene	6·6	16·4	6·1
Cyclopentadiene	5·6	16·2	5·8

The Hammett ρ value[706] measures the electron demand at the reaction center. The influence of substituents is small as is shown by the reactions of *p*-substituted 1-phenylbutadienes with maleic anhydride[707] and of *p*-substituted ethyl phenylpropiolates with tetraphenylcyclopentadienone[708]. The replacement of *p*-CH_3O by *p*-NO_2 causes less than a ten-fold change in the rate coefficient. Consequently the rate-determining transition state bears only small partial charges. In comparison, it may be mentioned that the solvolysis of *p*-$CH_3OC_6H_4C(CH_3)_2Cl$ is about 13,000,000 times as fast as that of the corresponding *p*-nitro compound[709].

2. The reactivity of various dienophiles toward cyclopentadiene and 9,10-dimethylanthracene

A comparison of dienophile reactivity is of both preparative and theoretical importance. Kinetic measurements for reactions of a large number of dienophiles with cyclopentadiene or 9,10-dimethylanthracene in dioxane can be carried out advantageously by a spectroscopic technique[705]. The rule proposed by Alder[495], that electron-attracting substituents at the carbon–carbon double bond of the dienophile increase the rate of reaction, is confirmed quantitatively by the bimolecular rate constants collected in Table 21 as measured by Sauer and his colleagues[705]. A number of essential points merit special attention:

a. The dominating role of the activating groups in the dienophile is evident, for example, in an increase of k_2 by a factor of more than 10^7 in going from acrylonitrile to the record-holding dienophile, tetracyanoethylene (Table 21). The activating power of various ligands at the dienophilic double bond decreases in the following series for the reaction with cyclopentadiene:

$$\text{—COCl} \gg \text{—SO}_2\text{C}_6\text{H}_5 > \text{—COC}_6\text{H}_5 > \text{—COCH}_3 > \text{—CN, —CO}_2\text{CH}_3$$

In the reaction with 9,10-dimethylanthracene the series is:

$$\text{—COCl} > \text{—CN} > \text{—CO}_2\text{CH}_3 > \text{—C}_6\text{H}_5$$

The inversion of the relative activities of the —CN and —CO_2CH_3 groups warns against uncritical application of these dienophile scales to other dienes.

b. In pairs of *cis–trans* isomeric dienophiles, the *trans* isomer proves to be the more reactive despite the higher energy content of the *cis* form[710]. Interestingly however, the difference is lost in the case of the isomeric 1,2-dicyanoethylenes, fumaro- and maleonitrile. The origin of the reactivity difference may be the same as in 1,3-dipolar additions (see p. 820). The significance of this guiding principle in diagnosing the mechanism of cycloadditions has already been indicated[341].

TABLE 21. Reaction of various dienophiles with cyclopentadiene and 9,10-dimethylanthracene in dioxane at 20°[705].

Dienophile	Cyclopentadiene $10^6 k_2$ at 20° (l./mole sec)	9,10-Dimethylanthracene $10^6 k_2$ at 20° (l./mole sec)
	Cyanoethylenes	
Tetracyanoethylene	~43,000,000	~13,000,000,000
Tricyanoethylene	483,000	5,880,000
1,1-Dicyanoethylene	45,500	127,000
Fumaronitrile	81	139
Maleonitrile	91	131
Acrylonitrile	1·04	0·89
	cis-/trans-*Isomeric dienophiles*	$10^6 k_2$ at 130°
trans-Bisbenzenesulfonylethylene	11,500	—
cis-Bisbenzenesulfonylethylene	194	—
trans-Dibenzoylethylene	1,360	—
cis-Dibenzoylethylene	6·7	—
Dimethyl fumarate	74·2	2,150
Dimethyl maleate	0·63	20·5
Fumaronitrile	80·6	45,300
Maleonitrile	91	43,500
	Triple-bond and double-bond dienophiles	
Dimethyl fumarate	74	2,150
Dimethyl acetylenedicarboxylate	31	1,390
Methyl acrylate	—	718
Methyl propiolate	—	113
	α- and β-Substituted dienophiles	
Acrylonitrile	—	1,450
Methacrylonitrile	—	205
trans-Crotononitrile	—	11
Methyl acrylate	—	718
Methyl methacrylate	—	148
Methyl crotonate	—	5·0

c. In all cases studied the olefinic dienophile is slightly superior to the related acetylene.

d. The variable influence of a methyl group in the α- or β-position of acrylic ester or acrylonitrile is a phenomenon already recognized in 1,3-dipolar additions (p. 818). An interplay of steric and electronic substituent effects presumably is responsible.

e. The abnormally low values of $\log A$, in agreement with other data in the literature[699,700], exhibit a remarkable constancy (5·5 ± 1·5) in spite of a wide variation in the absolute rates. The conclusion seems sound that all of the reactions investigated follow the same mechanistic pattern.

3. Comparison of the reactivity of dienes toward maleic anhydride

The difference in reactivity of the various dienes shown in Table 22 toward maleic anhydride amounts to approximately seven powers of ten. With tetracyanoethylene as the dienophile, the rate coefficients for 9,10-dimethylanthracene and 2-chlorobutadiene differ by a factor of 10^{10}. The substituent influence observed for the dienophiles is reversed in the case of the dienes: here electron-donating ligands are accelerating, while electron-attracting groups impede the reaction. The higher reactivity of 2-phenylbutadiene compared with the 1-isomer in the reaction with maleic anhydride is presumably due to

TABLE 22. Reaction of dienes with maleic anhydride and tetracyanoethylene in dioxane[711,712].

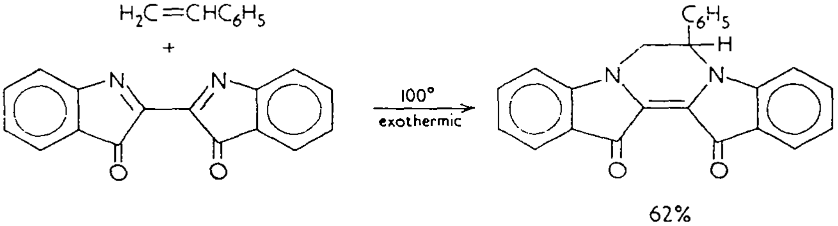
Diene	Maleic anhydride 10^8k_2 at 30° (l./mole sec)	Tetracyanoethylene 10^5k_2 at 20° (l./mole sec)
Cyclic dienes		
Cyclopentadiene	9,210,000	~43,000,000
9,10-Dimethylanthracene	1,600,000	~ 1,300,000,000
Cyclohexadiene	13,200	7,290
Hexachlorocyclopentadiene	1.14	—
Phenyl substituted butadienes		
2-Phenylbutadiene	~60,000	3,370
trans-1-Phenylbutadiene	11,200	6,680
Butadiene	6,830	519
trans-trans-1,4-Diphenylbutadiene	296	840
Other substituted butadienes		
1,2-Bismethylenecyclohexane	755,000	1,230,000
1,1′-Bicyclopentenyl	118,000	1,900,000
1-Methoxybutadiene	84,100	598,000
2,3-Dimethylbutadiene	33,600	24,300
trans-1-Methylbutadiene	22,700	2,060
2-Methylbutadiene	15,400	1,130
Butadiene	6,830	519
2-Chlorobutadiene	690	1·02

conformational effects (p. 913). One must be cautious, however, when applying these diene series to other dienophiles; with tetracyanoethylene, for instance, substantial differences are observed, particularly with the phenylbutadienes[712]. The low reactivity of hexachlorocyclopentadiene against maleic anhydride is astonishing in view of its very widespread use as a diene[533]. With tetracyanoethylene, hexachlorocyclopentadiene does not react even at 130°. A kinetic study has revealed an interesting reversal in its dienophilic reactivity[713].

4. Diels–Alder reactions with inverse electron demand

The figures in Tables 21 and 22 affirm the Alder rule: electron-attracting substituents in the dienophile and electron-releasing substituents in the diene favor the addition; thus the dienophile reacts as the electron-poor and the diene as the electron-rich component.

A series of examples in the literature are not in agreement with this principle. The abnormally high reactivity of enamines[514,515], enol ethers[512,513], and of simple olefins toward α,β-unsaturated aldehydes and ketones as well as toward certain *o*-quinones, has already been mentioned (p. 882). To this group may be added the reactions of dehydroindigo[714], substituted tetracyclones[715], and hexachlorocyclopentadiene[713]. Dehydroindigo combines with olefins such as styrene to give indigo dyes of the *cis* series having the structure of Diels–Alder adducts. The formal analogy with the Diels–Alder reaction is again weakened, however, since no reaction occurs with maleic anhydride.



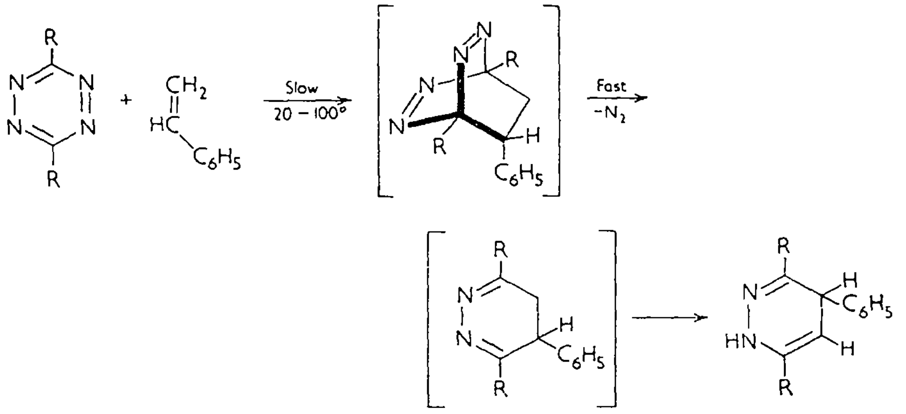
The addition of ethyl phenylpropiolate to tetracyclone, contrary to the Alder rule, is promoted by electron-attracting *p*-substituents in the 3- and 4-phenyl nuclei and retarded by electron donors[715].

A kinetic investigation concerning the behavior of hexachlorocyclopentadiene has revealed a reversal of the Alder dienophile scale. Here, electron-donating substituents in the dienophile facilitate addition, as is shown particularly well by the cyclopentene–maleic anhydride reactivity ratio, as well as by the bimolecular rate coefficients for *p*-substituted styrenes when these are contrasted with the data for 9,10-dimethylanthracene (Table 23).

TABLE 23. Rate constants for the additions of various dienophiles to hexachlorocyclopentadiene and 9,10-dimethylanthracene in dioxane at 130°[713].

Dienophile	$10^6 k_2$ (l./mole sec)	
	Hexachlorocyclopentadiene	9,10-Dimethylanthracene
Cyclopentadiene	15,200	—
p-Methoxystyrene	1,580	50
Styrene	793	70
p-Nitrostyrene	538	602
2,3-Dihydrofuran	333	—
Norbornene	72	36
Cyclopentene	59	7·8
Maleic anhydride	29	1,410,000

Contrary to the Alder rule, it is evident that hexachlorocyclopentadiene reacts as the electron-poor component; no addition has yet been achieved with the most electrophilic dienophile, tetracyanoethylene.



(R = $-CHFCF_3$, $-CHF_2$, $-C_6H_5$, $-CO_2CH_3$)

It is tempting to classify the reactions of symmetric tetrazines with olefins, discovered by Carboni[716,717], as additional examples of the same type. Additions at the electron-poor 3- and 6-positions occur most readily with dienophiles having electron-rich double bonds. The relative reactivity of different olefins, the activation parameters and solvent effects parallel completely the results with hexachlorocyclopentadiene[713]. Interestingly, with the extremely reactive 'diene', bismethoxycarbonyltetrazine, out of fourteen different olefins studied kinetically ethylene, cyclopentene, and ethylvinylether were found to be much more reactive than electron-poor olefins, *i.e.* acrylonitrile[712]. The structure of the 1,4-dihydropyridazines produced in these 'diene additions' has been substantiated by nuclear magnetic resonance spectroscopy[712,717].

5. Acceleration of the Diels–Alder reactions by catalysts and pressure

Although many diene additions take place readily under mild conditions, acceleration of more sluggish systems by catalysis is of interest. Until recently the reaction rate of Diels–Alder additions could not be influenced appreciably[718,719]. Thus the cyclopentadiene/*p*-benzoquinone system showed only slight response to the presence of toluenesulfonic acid, iodoacetic acid, pyridine, iodine or oxygen. A series of halogenated acetic acids exhibited low catalytic activity on the dimerization of cyclopentadiene and on its addition to *p*-benzoquinone[718].

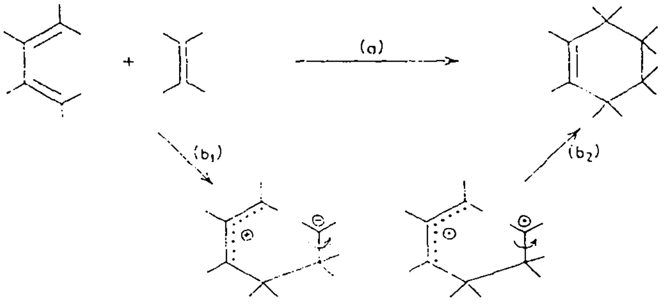
Substantially stronger catalytic properties are displayed by Lewis acids, such as $AlCl_3$[720], BF_3 or $SnCl_4$[721], as has been shown by Yates. Presumably, this catalysis depends upon formation of a primary complex of the Lewis acid with the polar groups of the dienophile, which causes further reduction in the electron density at the double bond and increased dienophilic character. Interestingly, the addition rate of ethylene to tetracyclone is also increased by aluminum chloride[722]; in this case the dienophile has no polar group. It is not yet proved that the mechanism of the Lewis acid-catalyzed reactions and the uncatalyzed ones are the same, although this is suggested by the highly stereospecific *cis* addition[710,720] which is observed with geometrically isomeric dienophiles.

Diene additions are accompanied by a decrease in volume; increased pressure should, therefore, favor the reaction. That the addition of the less reactive dienophiles (ethylene, propylene, acetylene, *etc.*) can be promoted in this way is well known. Addition of maleic anhydride to naphthalene gives a 78% yield at 10,000 atm but less than 1% at normal pressure[723]. Because of experimental difficulties, this technique has not yet been widely used. Some preparative value in special cases might be expected.

H. The Mechanism of the Diels-Alder Reaction

The question as to whether the two bonds between the diene and dienophile are formed simultaneously or in sequence is still under active discussion.

Formation of the two bonds in a multi-center process needs not take place at precisely the same rate. A difference in the degree of bond formation in the transition state generates partial charges (see p. 765). The possibility of an intermediate step in the multi-center mechanism, as discussed in connection with the additions to form four-membered rings (p. 787), is equally plausible for the Diels-Alder reactions.



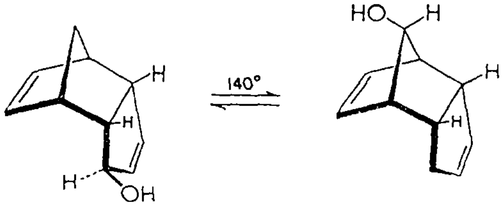
(54) (55)

For the two-step cyclization (path b), the possibilities for ionic or radical attack on the diene may be discussed. The Diels-Alder reaction with inverse electron demand also makes an intermediate with reversed charges reasonable. In the case of a radical reaction, one must in principle consider both a singlet and a triplet intermediate. Ring closure of the intermediate **54** or **55** requires additional activation energy. With a sufficiently long lifetime for **54** or **55**, rotation around the carbon-carbon single bond should be possible, which would have significant stereochemical consequences.

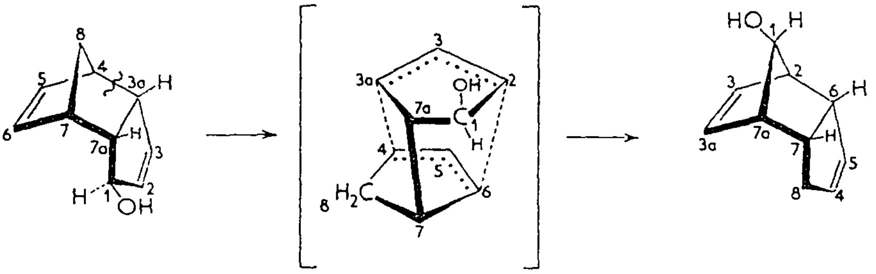
I. Rearrangements of Diels-Alder adducts

The thermal rearrangement of 1-hydroxydicyclopentadiene, discovered by Woodward and Katz[724], recently enlivened the discussion of the Diels-Alder mechanism and inspired some brilliant experiments.

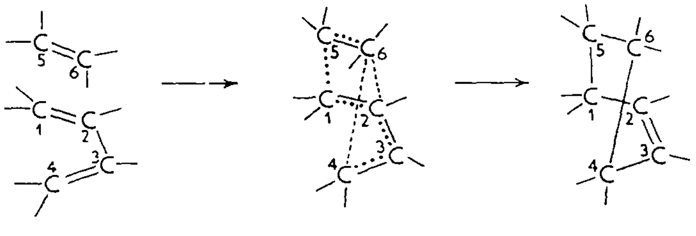
At 140°, α-(1-hydroxy)dicyclopentadiene is in equilibrium with about 50% of the 8-*syn*-hydroxy isomer. Similarly the epimeric β-form is transformed to the 8-*anti* alcohol. Experiments with optically active compounds have established the intramolecular course of this rearrangement and have ruled out intermediary dissociation to cyclopentadiene and its hydroxy derivative; recombination of these fragments would be expected to lead to their respective dimers.



A satisfactory interpretation of the rearrangement can be based on the assumption that only the bond $C_{(3a)}$—$C_{(4)}$ between the components is broken while simultaneously a new one, $C_{(2)}$—$C_{(6)}$, between the diene units is formed. Only at higher temperatures the second bond, $C_{(7)}$—$C_{(7a)}$, between the diene units is broken.



On the basis of the principle of microscopic reversibility, the American authors[724] proposed a 'two-stage' mechanism for the Diels–Alder reaction. The diene and dienophile approach one another in parallel planes, and in the rate-determining step only the bond between $C_{(1)}$ and $C_{(5)}$ is established. The stereospecificity



of the addition is guaranteed by 'secondary attractive forces' (the dashed lines between $C_{(6)}$ and $C_{(2)}$ or $C_{(4)}$) which come into play.

This mechanistic concept has not gone uncontested[725,726]. The isomerization described above can be construed as a special case of the Cope rearrangement[727]. Since there is no basis for postulating an intermediate stage for this process, which is characterized by synchronous bond reorganizations, the isomerization does not necessarily have a bearing on the Diels–Alder mechanism.

This type of rearrangement, moreover, appears to be restricted to those adducts in which both components have diene character[728]. The isomerization of methacrolein dimer[729] is included in this group; at 180° the retro-Diels–Alder decomposition competes successfully with the stereospecific rearrangement. In the case of the *endo–exo* isomerization of the cyclopentadiene–maleic anhydride adduct[730], the different activation parameters for the two reaction paths indicate that rearrangement by way of the retro-Diels–Alder reaction is not related mechanistically to the intramolecular isomerization which is also possible[731]. A number of other isomerizations of Diels–Alder adducts[726,732] may also be interpreted as due to the retro-Diels–Alder reaction.

With regard to the two-stage mechanism, one should expect a common intermediate, **54** or **55**, for cycloadditions leading to four- and six-membered rings. It has already been mentioned on page 785 that 1,1-dimethylbutadiene reacts with tetracyanoethylene in cyclohexane to form the cyclobutane and cyclohexene derivatives in approximately 7:3 ratio; the considerably greater tendency in more polar solvents to form the four-membered ring, however, suggests that a common intermediate for the two reactions is improbable.

2. The alternatives: one-step or two-step reaction

Virtually all Diels–Alder reactions may at this time be satisfactorily interpreted by the multi-center mechanism outlined on page 925. Stereoselective *cis* addition is an immediate consequence of the one-step mechanism, and therefore an intermediate like **54** or **55** is rather improbable but not entirely ruled out by this stereochemical finding.

The question of whether or not the components pass through a 'charge-transfer' complex on the way to the adduct was discussed by Woodward as early as 1942[733]. The parallelism repeatedly observed between increasing dienophilic reactivity and acceptor strength in the formation of 'charge-transfer' complexes as well as the frequent observance of fugitive colors during diene additions are in agreement with the primary formation of such a complex. The exclusive *endo* addition, which is frequently encountered and has already been mentioned on page 910, can also be explained by assuming a 'charge-transfer' complex. In principle one cannot rule out kinetically the mechanistic alternative that the formation of the charge-transfer complex is a competing reaction and does not contribute to the Diels–Alder addition[734].

The low log *A* values as well as the small dependence of the reaction rate upon solvent polarity or *p*-substituents in phenyl-substituted dienes and dienophiles are evidence for a highly ordered transition state with relatively little charge separation, such as is predicted by the synchronous mechanism. The similarity of these kinetic aspects in a great number of cases, independent of the absolute reaction rate as well as of the nature of the diene or dienophile, makes a common mechanism highly probable. The kinetic and steric results correspond substantially with those for 1,3-dipolar additions.

Attention has already been directed on page 914 to the fact that the electronic nature of the substituents in positions 1 or 2 of the diene has surprisingly little influence on the direction of addition of unsymmetrical dienophiles. Even though a satisfactory interpretation of the orientation phenomena is still lacking[735], they appear to be inconsistent with an ionic two-step mechanism.

A biradical intermediate (**55**) would also satisfy the orientation rules (p. 914); both electron-attracting and electron-donating substituents would be able to stabilize the odd electrons. Postulation of an intermediate, of course, requires the auxiliary hypothesis that free rotation is impeded or that the second step b_2 (p. 925) is very fast. However, kinetic studies[199] make a biradical intermediate rather improbable.

The pressure dependence of the rate of dimerization of isoprene permits calculation of the activation volume $\Delta V^{\ddagger}$. From the fact that $\Delta V^{\ddagger}$ is approximately equal to one-half of the total volume contraction in the reaction, Walling and Peisach[736] postulated that a two-step process with a biradical intermediate (**55**) was involved. The same relationship was found for the addition of butyl acrylate to 2,3-dimethylbutadiene, but for the dimerization of cyclopentadiene such a simple conclusion may not be justified[737]. The rearrangement of 1-hydroxydicyclopentadiene (p. 925) and the retro-Diels–Alder reaction are thought to possess a common energy profile since they deviate in the same way from several Cope rearrangements[738] with respect to $\Delta V^{\ddagger}$[737]. However, due to the experimental and theoretical difficulties of these high-pressure experiments, the above conclusions should be viewed with scepticism[739].

There is still no evidence for a biradical intermediate of triplet nature. Compounds which catalyze the singlet–triplet transition have no influence on the rate of the Diels–Alder reaction[726]. The log *A* values for the retro-Diels–Alder reaction are 'normal', so that a change in multiplicity, as would be demanded by a triplet transition state, is also excluded for the diene addition (see ref. 726). The fact that different products are obtained in the dimerization of cyclopentadiene in thermal and photoinduced reactions (p. 797) is a further argument against a triplet transition state.

R. D. Brown[740], assuming a synchronous reaction mechanism, carried out molecular-orbital calculations. In favorable cases, satisfactory predictions of the reactive positions and relative reactivity series for dienes were obtained. The calculations were based on the assumption that reactivity differences were primarily a reflection of changes in the activation energy, E_A, with steric factors playing only a minor role. This simplification is certainly only permissible within narrow limits; the experimental values for $\log A$ or $\Delta S^\ddagger$ vary perceptibly around an average figure.

Although primary isotope effects have often made important mechanistic conclusions possible, theoretical interpretation of the secondary isotope effect is considerably less clear. The addition of deuterated maleic anhydride to cyclopentadiene shows only an inverse secondary isotope effect, $k_D/k_H = 1{\cdot}06$[741]. The influence of deuterium in various positions of the α-methylfuran–maleic anhydride adduct upon the rate of its dissociation has also been investigated and according to Seltzer the results point to a one-step mechanism[742].

VI. ACKNOWLEDGMENTS

The authors gratefully acknowledge the translation of the German manuscript by Dr. F. C. Schaefer of the Central Research Division of the American Cyanamid Company during his stay in Munich. Also, thanks are due to Dr. J. R. Norell of Purdue University who has assisted in proofreading and in attaining a smooth 'American English'.

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 12

Conjugated dienes

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I. INTRODUCTION

Alkenes which have alternate double and single bonds are usually referred to as *conjugated* dienes, trienes or polyenes. Their structural features and chemical properties are so strikingly different from those of the non-conjugated alkenes that they deserve special discussion in a separate chapter.

The simplest conjugated diene is 1,3-butadiene (henceforward referred to as butadiene), and is commonly formulated as **1**, although

$$\overset{1}{C}H_2{=}\overset{2}{C}H{-}\overset{3}{C}H{=}\overset{4}{C}H_2$$

(**1**)

this formulation fails to disclose the true nature of the molecule. A much more satisfactory representation of butadiene is obtained by applying the molecular-orbital concept to the formulation of its structure. Because the theoretical aspects of the bonding in alkenes have been discussed in Chapter 1, only a very brief outline is given here for butadiene.

It is convenient to discuss the orbitals of butadiene in the same terms of σ and π symmetry classification as used for ethylene. Since each carbon atom in butadiene is attached to only three other atoms, sp^2 hybrid orbitals of carbon are involved. These then form the σ-bond skeleton which establishes the geometry of the molecule. The remaining four electrons, one from each carbon atom, are left in four $p\pi$ orbitals (Figure 1) which combine to form four molecular orbitals delocalized over all four carbon atoms. These π-molecular orbitals ψ_1, ψ_2, ψ_3 and ψ_4 are shown schematically in Figure 2 and the energy-level diagram for butadiene is shown in Figure 3.

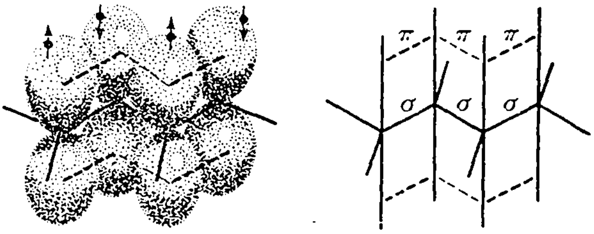


FIGURE 1. The interaction of $p\pi$ orbitals in butadiene. [Reproduced, by permission, from J. D. Roberts, *Molecular Orbital Calculations*, W. A. Benjamin Inc., New York, 1961.]

It can be seen that ψ_1 and ψ_2 are bonding orbitals and are doubly occupied in the ground state. Both the ψ_1 and the ψ_2 orbitals contribute to the $C_{(1)}$—$C_{(2)}$ and $C_{(3)}$—$C_{(4)}$ bonds which are consequently shorter and stronger than a single bond. These bonds are represented as double bonds in the formulation **1** and are called *essential double bonds.* The combined effects of ψ_1 (bonding) and ψ_2 (antibonding) on the $C_{(2)}$—$C_{(3)}$ bond result in the latter being only very slightly shorter and stronger than a single sp^2—sp^2 bond. This bond is represented as a single bond in formula **1** and it is called an *essential single bond.* The molecular orbitals ψ_3 and ψ_4 are antibonding and not occupied in the ground state.

The effects of these structural features on the physical and chemical

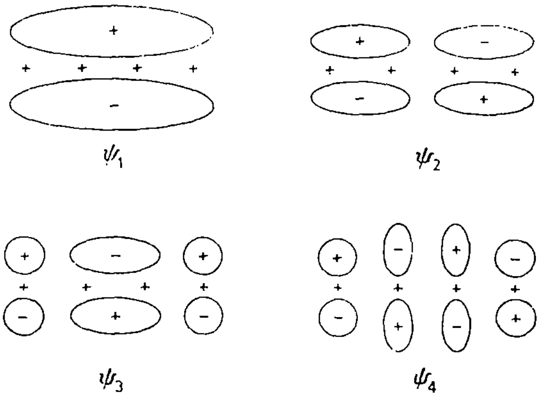


FIGURE 2. The four molecular orbitals of butadiene. [Reproduced from H. H. Jaffé and M. Orchin, *Theory and Applications of Ultraviolet Spectroscopy*, John Wiley and Sons, New York, 1962.]

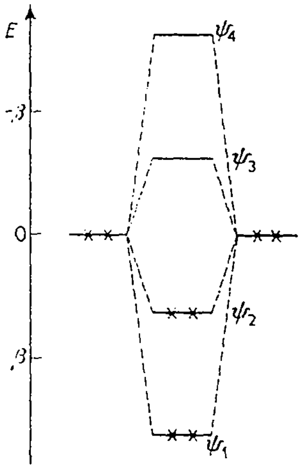


FIGURE 3. The energy-level diagram for butadiene. [Reproduced from H. H. Jaffé and M. Orchin, *Theory and Applications of Ultraviolet Spectroscopy*, John Wiley and Sons, New York, 1962.]

properties of conjugated diene systems will be illustrated in the rest of this chapter.

II. SYNTHESIS OF CONJUGATED DIENES

As early as 1913 it was stated[1] that butadiene is obtainable from any organic compound by thermal treatment alone; Ostromyslenskii supported this statement by listing twenty-one methods for preparing alkadienes, principally butadiene[2]. In a review[2] published in 1944, Egloff and Hulla indicated that over eighty-five distinct organic reactions yield butadiene*.

It may be convenient here to summarize the general methods of preparing[3] conjugated dienes, which are as follows:

(*i*) The direct conversion of hydrocarbons, mainly catalytic dehydrogenation of olefins;
(*ii*) Dehydration of the appropriate saturated diols;
(*iii*) Pyrolysis of the esters of the diols in (*ii*);
(*iv*) Dehydration of α,β- or β,γ-unsaturated alcohols;
(*v*) Dehydrohalogenation of the corresponding saturated dihalides;
(*vi*) Partial hydrogenation of the corresponding vinylacetylenic hydrocarbons;
(*vii*) Hofmann degradation of the appropriate 1,4-diamines; and
(*viii*) Miscellaneous reactions.

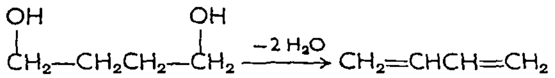
Catalytic dehydrogenation of olefins yields the corresponding conjugated dienes.

$$\underset{(2)}{CH_2{=}CHCH_2{-}CH_3} \longrightarrow CH_2{=}CHCH{=}CH_2 + H_2$$

The dehydrogenation of butenes is an important technical process for the production of butadiene in yields of up to 80%. This reaction as well as the general conversion of hydrocarbons into butadiene has been comprehensively reviewed[2].

Another reaction which has found wide use in the laboratory as well as important technical applications is the dehydration of alcohols or the pyrolysis of their esters.

The dehydrations are normally carried out in the presence of a dehydrating catalyst such as acid phosphates, silicic acid, phosphotungstic acid, phosphomolybdic acid or boric acid[4].



$$\underset{(3)}{\overset{OH}{CH_2}{-}CH_2CH_2{-}\overset{OH}{CH_2}} \xrightarrow{-2\,H_2O} CH_2{=}CHCH{=}CH_2$$

In the Lebedev process[4], the use of a catalyst mixture having a dehydrogenating component (A) and a dehydrating component (B) affords the direct conversion of ethanol into butadiene.

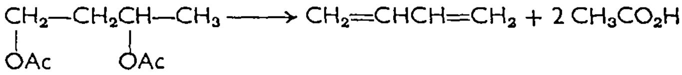
$$2\,CH_3CH_2OH \longrightarrow CH_2{=}CHCH{=}CH_2 + H_2 + 2\,H_2O$$

* If one remembers that butadiene is one of the key hydrocarbons in the synthetic rubber industry, it is not surprising that methods for the production of alkadienes have been so widely investigated.

For a review on this reaction and the general conversion of hydrocarbon oxygen derivatives into butadiene, the reader is referred to an article by Egloff and Hulla[4], which covers the literature up to 1944.

In the following pages examples from the more recent literature will be presented to illustrate various methods for the formation of alkene systems with conjugated double bonds.

It has been known for several decades[3,4] that the pyrolytic formation of butadiene is often facilitated by using the esters, particularly the acetates, of the appropriate diols. Thus 1,3-butanediol diacetate (**4**) forms 1,3-butadiene on catalytic pyrolysis.

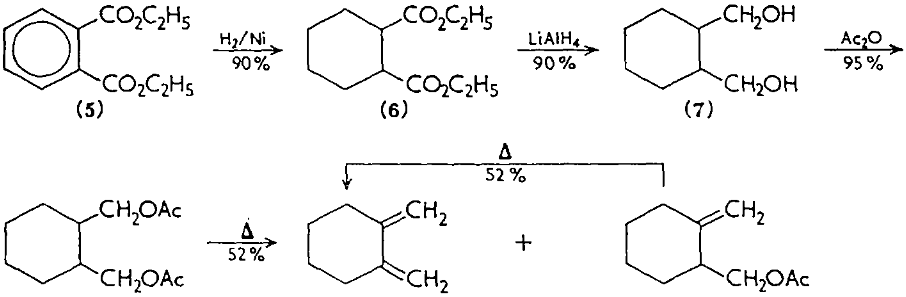


$$\underset{OAc}{CH_2}-CH_2\underset{OAc}{CH}-CH_3 \longrightarrow CH_2{=}CHCH{=}CH_2 + 2\,CH_3CO_2H$$

(4)

In more recent years, Bailey and coworkers[5-26] have used ester pyrolysis for the synthesis of dienes which are not easily obtained by other methods.

1,2-Dimethylenecyclohexane (**9**) has been prepared[5] in a four-step synthesis from diethylphthalate in an overall yield of 77%. The crucial step, the pyrolysis of the diester **8**, takes place with an 89% yield. For optimum pyrolytic conditions, the temperature and contact time should be such that only 65% of the theoretical acetic acid is cracked out. The diene **9** has been polymerized to a high molecular weight all-1,4-, all-*cis* diene polymer[6].



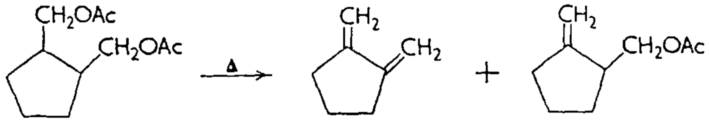
(5) (6) (7)

(8) (9) (10)

[λ_{max} = 220 mμ (ε = 10,500)]

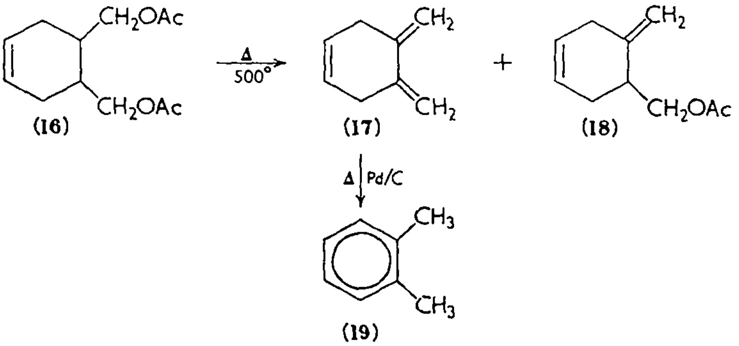
By a similar pyrolytic procedure 4-methyl- and 4,5-dimethyl-1,2-dimethylenecyclohexane (**11** and **12** respectively) have been synthesized[7] in overall yields of 75% and pyrolysis of 1,2-di(acetoxymethyl)-cyclopentane (**13**) has produced 1,2-dimethylenecyclopentane (**14**) in a 44% yield[8].

A good demonstration that the pyrolysis of esters is a satisfactory synthetic procedure is given by the synthesis of 1,2-dimethylene-4-cyclohexene (**17**) in 92% yield without the formation of any of the isomeric *o*-xylene (**19**)[9].



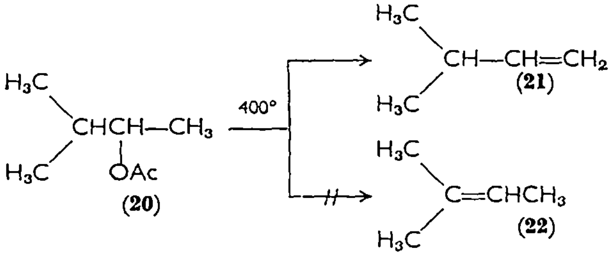
(**13**) (**14**) (**15**)

Significantly, it appears that simple secondary aliphatic acetates[10a] as well as tertiary esters[10b] undergo pyrolytic dehydroacetoxylation according to the Hofmann rule to form with very high selectivity

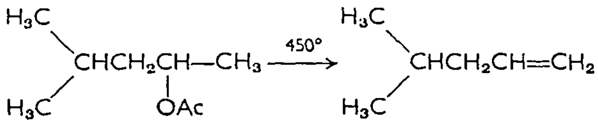


(**16**) (**17**) (**18**) (**19**)

the least highly alkylated olefin. For example[10], methylisopropylcarbinyl acetate (**20**) yielded on pyrolysis at 400° only 3-methyl-1-butene (**21**), no 2-methyl-2-butene (**22**) being detected. Similarly,

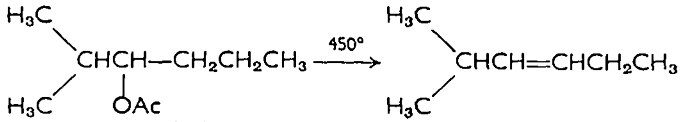


(**20**) (**21**) (**22**)



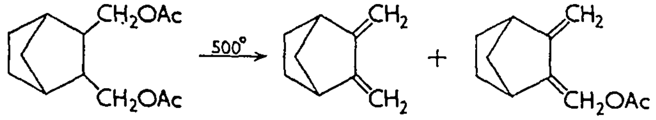
(**23**) (**24**)

4-methyl-1-pentene (**24**) and 2-methyl-3-hexene (**26**) were the only products isolated from the pyrolysis of the respective esters **23** and **25**. Substituted derivatives of **17** have also been made by this method[11].

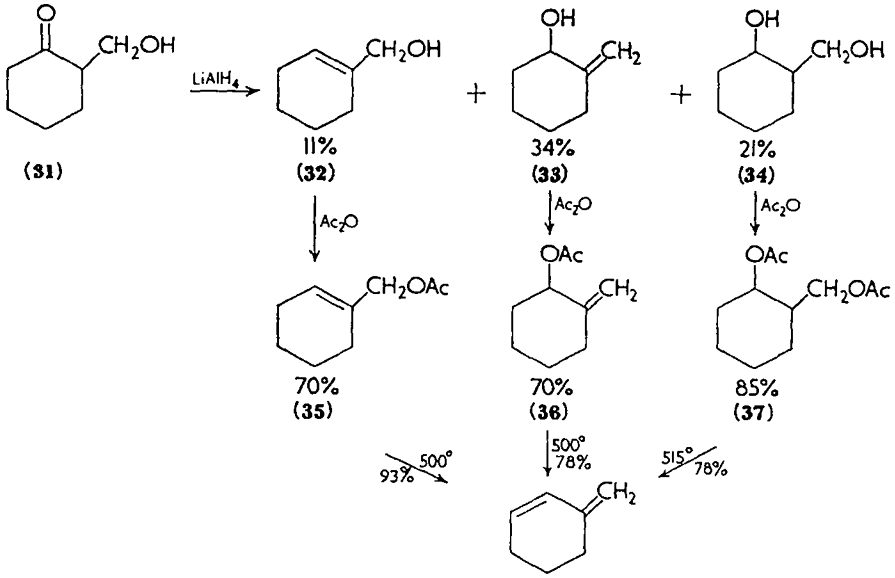


(**25**) (**26**)

The diene 1,2-dimethylenecyclohexane (**9**) has been used[12] as starting material for the synthesis of 2,3-dimethylenedecalin (**27**), and this procedure has been developed into a general method for the synthesis of linear condensed polynuclear hydrocarbons[13a]. The isomer 1,2-dimethylenedecalin has also been synthesized[13b] to serve as starting material for the synthesis of angular polycyclic aromatic compounds.



(**28**) (**29**) (**30**)



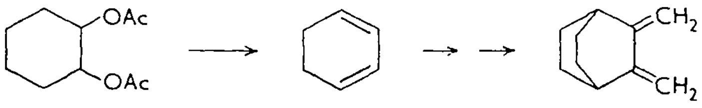
(**31**) (**32**) (**33**) (**34**) (**35**) (**36**) (**37**) (**38**)

[λ_{max} = 231 mμ (ε = 21,000)]

The bicyclic diene **29** has been obtained[14] in a 79% yield from the pyrolysis of the corresponding acetate **28**.

As potential starting material for the production of an all-*trans* polymer, 3-methylenecyclohexene (**38**) has been prepared[15] in three steps from 2-hydroxymethylcyclohexanone (**31**) in an overall yield of 42%.

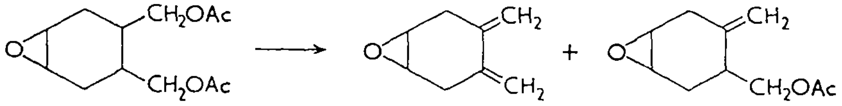
A convenient synthesis of 1,3-cyclohexadiene (**40**) has been developed[16] by the pyrolysis of a mixture of *cis*- and *trans*-1,2-diacetoxycyclohexane (**39**). The cyclohexadiene was then used as starting material for the synthesis of 2,3-dimethylenebicyclo[2.2.2]octane (**41**).



(39) **(40)** **(41)**

Commercially available alkenylsuccinic anhydride has been used[17] as starting material for the synthesis of a 2-alkyl-1,3-butadiene.

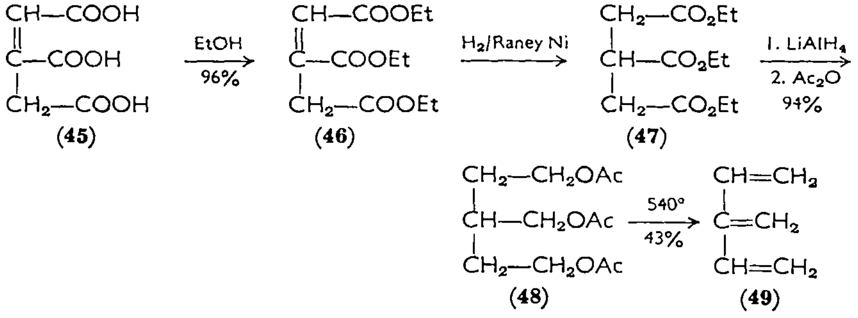
The pyrolysis of the epoxydiacetate **42** has afforded[18] the epoxydiene 3,4-dimethylene-7-oxabicyclo[4.1.0]heptane (**43**).



(42) **(43)** **(44)**

[λ_{max} = 225 mμ (ε = 4500)]

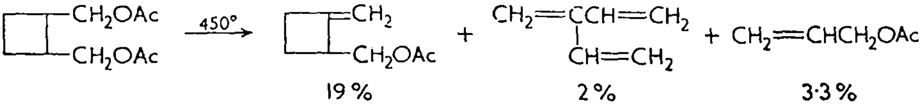
The pyrolysis of a triacetate has been used[19] to produce 2-vinyl-1,3-butadiene (**49**) in an overall yield of 40% from aconitic ester (**46**).



[λ_{max} = 231 mμ (ε = 205,000)]

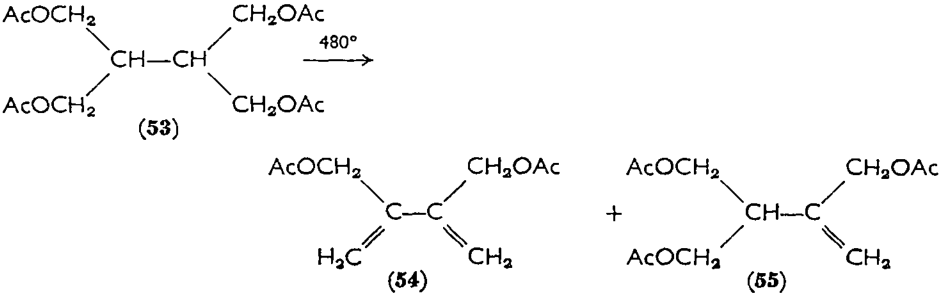
The reductive acetylation, whereby the saturated ester **47** is first reduced with lithium aluminum hydride and the complex is decomposed with acetic acid and acetic anhydride, gives the triacetate **48** in one step.

It is of interest to note that when 1,2-di(acetoxymethyl)cyclobutane (**50**) was pyrolyzed[20], no dimethylenecyclobutane was isolated but instead, cleavage of the cyclobutane ring took place in two different ways to produce allyl acetate (**52**) and 2-vinylbutadiene (**49**).



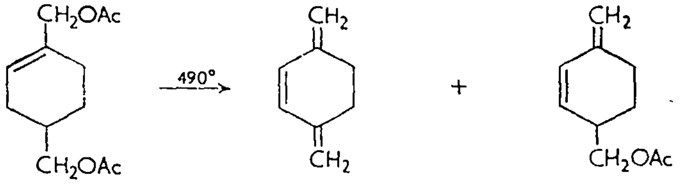
(**50**) (**51**) (**49**) (**52**)

The tetraacetate **53** on pyrolysis[21] gave 84% of 2,3-di(acetoxymethyl)-1,3-butadiene (**54**).



[$\varepsilon_{220\ m\mu}$ = 19,500]

The conjugated triene 1,4-dimethylene-2-cyclohexene (**57**), isomeric with *p*-xylene, has been prepared[22] by a six-step synthesis starting from dimethyl terephthalate. In the last step, the unsaturated diacetate 1,4-di(acetoxymethyl)-2-cyclohexene (**56**) is pyrolyzed at 490° to give a 61% yield of the triene **57**. Little or no *p*-xylene seems to be formed during the pyrolysis.

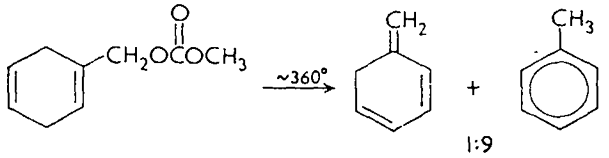


(**56**) (**57**) (**58**)

[λ_{inf} = 256 mμ (ε = 25,200)
λ_{max} = 264 mμ (ε = 30,000)
= 274·5 mμ (ε = 21,200)]

[λ_{max} = 232 mμ
(ε = 11,700)]

The successful synthesis of the dienes **17**, **38** and **40** as well as that of the triene **57** has been extended to the synthesis of the alicyclic isomer of toluene, 5-methylene-1,3-cyclohexadiene (**60**). This has been accomplished[23] by the pyrolysis of 1,4-cyclohexadiene-1-methanol methyl carbonate (**59**) followed by isolation through gas chromatography. The triene **60** appears[16] to be quite stable at the



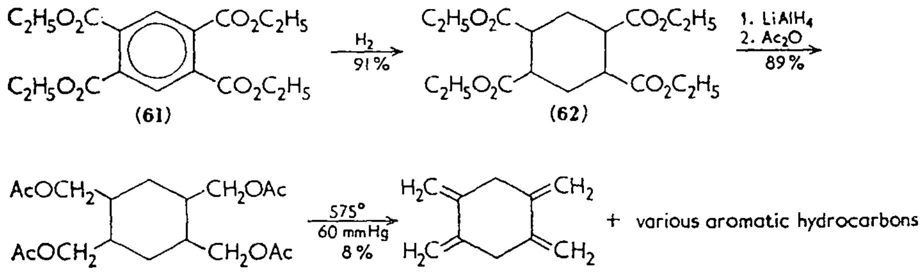
(**59**) (**60**)

[λ_{max} = 303 mμ (ε = 4400)]

dry-ice temperature and in dilute solutions, as shown by its stability at 110° in the gas-phase chromatographic column. However, in the pure liquid it isomerizes to toluene at a moderately rapid rate at room temperature.

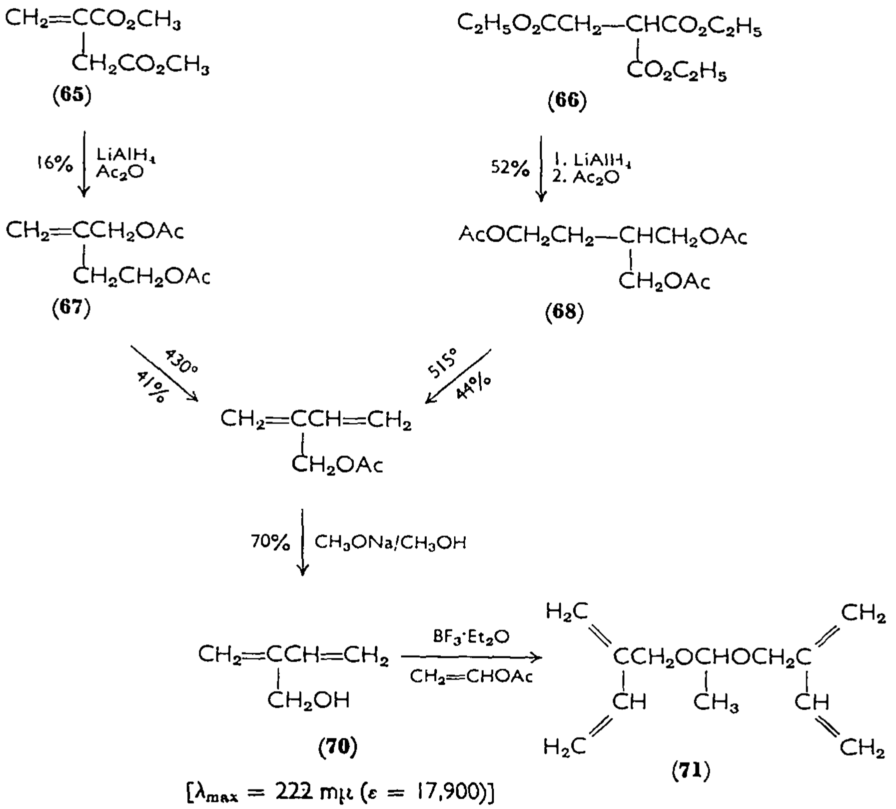
These data are presented as evidence for the efficacy of the pyrolysis of esters to synthesize highly unstable isomers of aromatic compounds.

The tetraene 1,2,4,5-tetramethylenecyclohexane (**64**) has been synthesized[24] in three steps from tetraethyl pyromellitate (**61**). The pure tetraene was separated from the reaction mixture, which consisted of a large variety of aromatic hydrocarbons, by preparative gas chromatography.



[λ_{max} = 224 mμ (ε = 10,500)]

In order to produce a convenient starting material for a series of bifunctional dienes, of which 2-vinyl-1,3-butadiene (**49**) is the simplest member, the synthesis of 2-hydroxymethyl-1,3-butadiene (**70**) has been carried out by two different routes involving the pyrolysis of an ester as the key step[25].

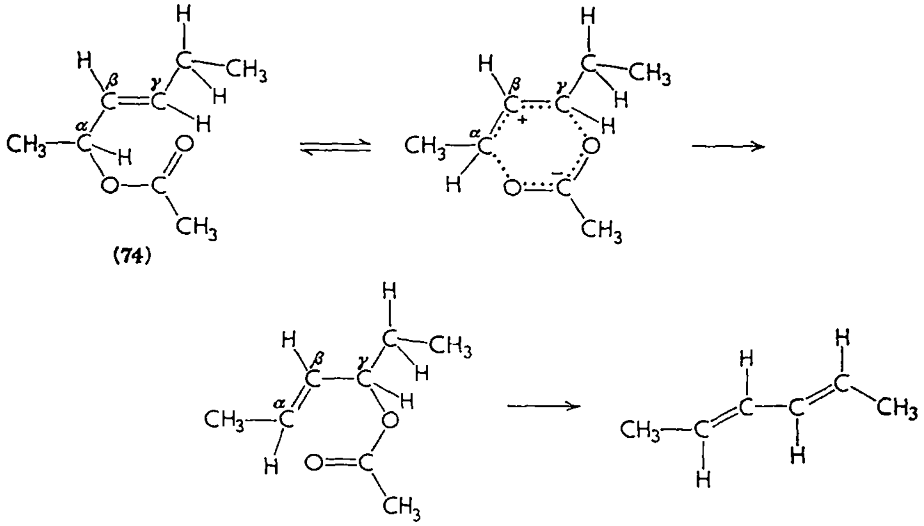


The same substituted diene **70** has been obtained[26] by a route involving the pyrolysis of an amine oxide as well as the pyrolysis of an ester.

The reaction of **70** with vinylacetate in the presence of a mercuric oxide–boron trifluoride etherate mixture afforded a 38% yield of the bis-(2-butadienylmethyl)acetal (**71**).

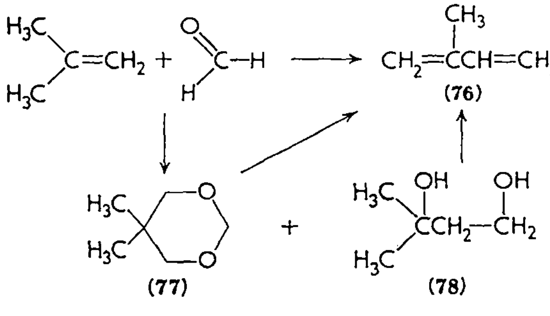
The isomerization which takes place during the pyrolysis of allylic acetates has been investigated by Greenwood[27,28]. Both 2-acetoxy-*trans*-3-heptene (**72**) and 4-acetoxy-*trans*-2-heptene (**73**) gave[27], on pyrolysis, a mixture of 1,3- and 2,4-heptadienes in which the *trans* configuration of the carbon–carbon double bond was essentially retained. Similar results were obtained[28] from the pyrolysis of 2-acetoxy-*trans*-3-hexene (**74**) and 4-acetoxy-*trans*-2-hexene (**75**).

It is suggested[28] that in this, as in other known cases of isomerization of allylic esters[29], the isomerization is intramolecular and that some kind of a cyclic transition state is involved. In this transition state the carbonyl oxygen atom must come into bond-forming distance of the γ-carbon atom of the allylic system. Since the *trans*-alkene configuration is essentially retained after pyrolysis, the hydrogen atoms on the α- and β-carbon atoms (the carbon atoms between which the double bond will appear in the isomerized ester) of the allylic system must be in a *trans* conformation in the cyclic transition state.



(74)

As an example of the synthesis of conjugated dienes from aldehydes and olefins, isoprene (**76**) may be prepared in a yield of over 75% by the reaction of formaldehyde with isobutylene in a flow system over a mixed catalyst of calcium phosphates[30]. The reaction is best run with



(76)

(77)

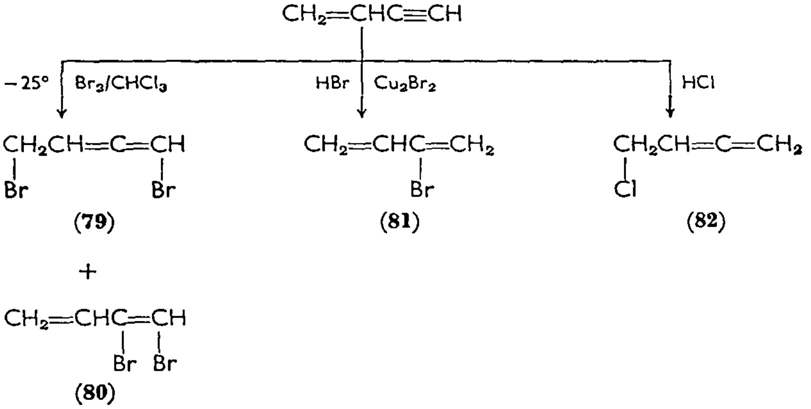
(78)

4,4-dimethyl-1,3-dioxane (**77**) (formed by acid condensation of formaldehyde with isobutylene) at 325°. The by-products in the preparation of dioxane are also usable. Thus, the alcohol **78** yields isoprene in over 75% yields. The alcohol **78** is considered to be an intermediate in the direct formation of isoprene from the dioxane **77**.

The same reaction, starting with formaldehyde and propylene, has been used, with similar results, for the production of butadiene[30].

Addition reactions to the triple bond of vinylacetylenes can be used to synthesize unsubstituted or substituted conjugated dienes. Alkenylacetylenes of the type RCH=CHC≡CH hydrogenate more selectively than do compounds such as CH_2=CHC≡CR and the former readily yield the corresponding dienes on hydrogenation over paladium in methanol[31]. The difference in behavior is explained by greater difference in the adsorbability of the starting materials and the hydrogenation products on the catalyst surface.

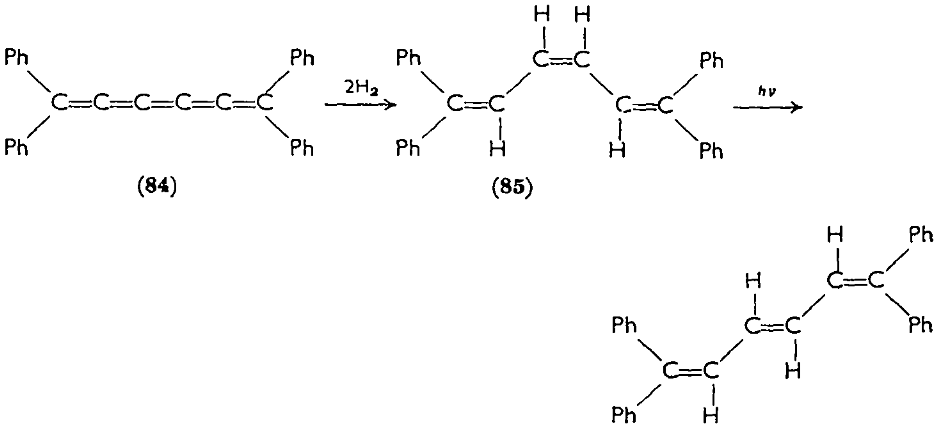
Addition of a chloroform solution of bromine to vinylacetylene at −25° gave[32], on fractionation of the products, mostly 1,4-dibromo-1,2-butadiene (**79**) and a lesser amount of 1,2-dibromo-1,3-butadiene (**80**). On the other hand, addition of hydrogen bromide to vinylacetylene in the presence of cuprous bromide gave 2-bromo-1,3-butadiene (**81**), and addition of hydrogen chloride to vinylacetylene gave 4-chloro-1,2-butadiene (**82**). Propenylacetylene and hydrogen chloride react[33] to form 2-chloro-1,3-pentadiene (**83**).



The catalytic hydrogenation of cumulenes over Lindlar catalyst has afforded[34] the corresponding *cis*-polyenes which upon irradiation were rearranged to known *trans*-polyenes.

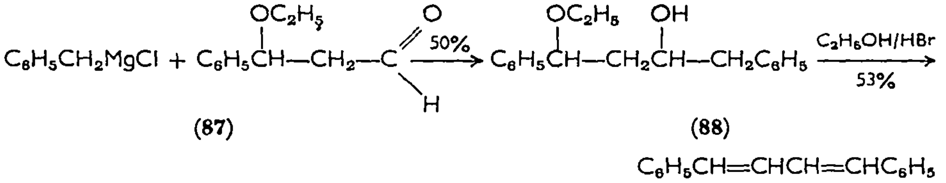
The Grignard and related reactions have been widely used for the synthesis of α,β- or β,γ-unsaturated alcohols, which upon dehydration formed the corresponding conjugated dienes or polyenes.

α,ω-Diphenylpolyenes have been prepared[35a] by reacting benzylmagnesium with aldehydes, substituted on the terminal carbon atom with C_6H_5— and C_2H_5O— groups, and refluxing the resulting hydroxy ether with a 45% solution of hydrobromic acid in ethanol.



(84) (85) (86)

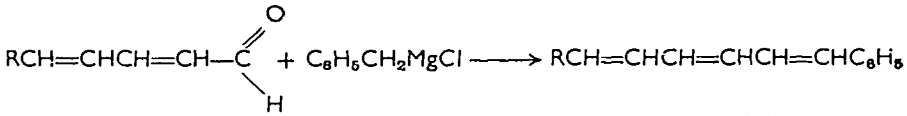
Using the same method as for 1,4-diphenylbutadiene, Mikhailov and Povarov[35a] have also prepared 1,6-diphenyl-1,3,5-hexatriene (**90**) in 11·3% yield; 1,8-diphenyl-1,3,5,7-octatetraene (**91**) in 38·3% yield; and 1,10-diphenyl-1,3,5,7,9-decapentaene (**92**) in 37·4% yield.



$$C_6H_5CH_2MgCl + C_6H_5CH(OC_2H_5){-}CH_2{-}CHO \xrightarrow{50\%} C_6H_5CH(OC_2H_5){-}CH_2CH(OH){-}CH_2C_6H_5 \xrightarrow[53\%]{C_2H_5OH/HBr} C_6H_5CH{=}CHCH{=}CHC_6H_5$$

(87) (88) (89)

By a similar method, unsymmetric 1,6-diaryl-substituted 1,3,5-hexatrienes have been prepared[35b].



$$RCH{=}CHCH{=}CH{-}CHO + C_6H_5CH_2MgCl \longrightarrow RCH{=}CHCH{=}CHCH{=}CHC_6H_5$$

(93) (94)

(R = α-naphthyl, 9-phenanthryl, *p*-xenyl, 2-pyridyl, 2-quinolyl)

The transformation

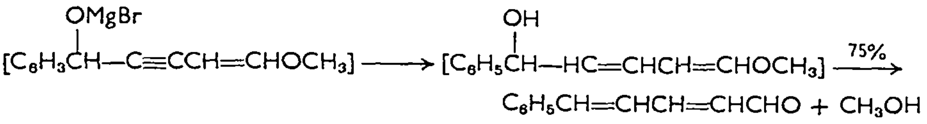
$$RCHO \longrightarrow RCH{=}CHCH{=}CHCHO$$

in a single stage has been reported[36]. This reaction, a modification of a previously described[37] two-stage process, consists of the condensation of the bromomagnesium derivative of methoxybutenyne

(**95**) with the aldehyde. Addition of lithium aluminum hydride followed by addition of mineral acid affords the dienal in good yields.

$$C_6H_5CHO + BrMg{-}C{\equiv}CCH{=}CHOCH_3 \longrightarrow$$

(95)

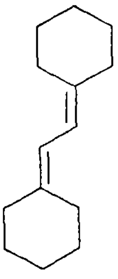


$$[C_6H_3\overset{OMgBr}{\overset{|}{C}}H{-}C{\equiv}CCH{=}CHOCH_3] \longrightarrow [C_6H_5\overset{OH}{\overset{|}{C}}H{-}HC{=}CHCH{=}CHOCH_3] \xrightarrow{75\%} C_6H_5CH{=}CHCH{=}CHCHO + CH_3OH$$

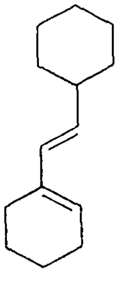
(96)

Interaction of the Grignard reagent of 2-bromophenanthrene with crotonaldehyde, followed by dehydration (*p*-toluenesulfonic acid in benzene) of the isolated *trans*-1-(2-phenanthryl)-2-buten-1-ol (**97**), afforded[38] *trans*-1-(2-phenanthryl)-1,3-butadiene (**98**). The latter polymerized during two months at −30° in the absence of bright light. Irradiation with ultraviolet light rapidly reduced the intensity of the absorption maxima at 323 and 209 mμ. The same dehydration method was used to prepare *trans*-1-(2-naphthyl)-1,3-butadiene (**99**).

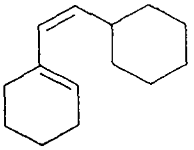
For comparison with the non-stereoisomeric dicyclohexylidene-ethane[39a] (**100**), Viscontini and Burgherr[39b] have prepared 1-(1-cyclohexen-1-yl)-2-cyclohexylethylene (**101**) which can exist as the *trans* and *cis* stereoisomers (**101a** and **101b** respectively). Compound



(100)



(101a)



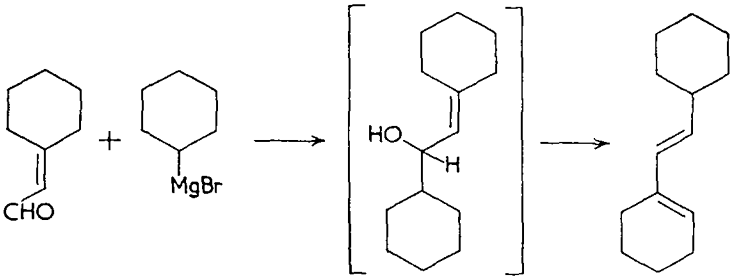
(101b)

101a was prepared by reacting cyclohexylideneacetaldehyde (**102**) with cyclohexylmagnesium bromide to obtain directly the allylic rearrangement product **101a**.

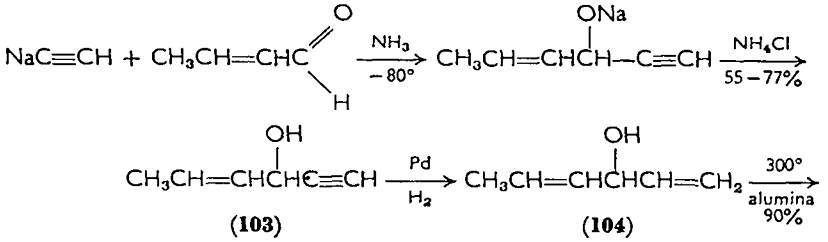
The infrared spectrum of **101a** showed a characteristic *trans* double linkage band at 960 cm^{-1} and a shift of 15 mμ in the ultraviolet on comparison with **100**.

A new and convenient synthesis of 1,3,5-hexatriene (**105**) has recently been described[40]. The method involves the synthesis of 4-hexen-1-yn-3-ol (**103**) from sodium acetylide and crotonaldehyde.

Reduction of **103** to the corresponding 1,4-hexadien-3-ol (**104**) and vapor-phase dehydration over alumina gave **105** in an overall yield of about 60%. In the reduction of the alcohol **103** to **104** the use of 5% palladium on calcium carbonate, poisoned with 40% by weight of lead acetate, is reported[40] to be more than 99% selective.



(102) **(101a)**



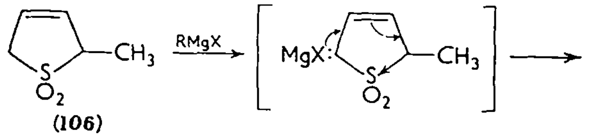
$$NaC\equiv CH + CH_3CH{=}CHC\overset{O}{\underset{H}{}} \xrightarrow[-80^\circ]{NH_3} CH_3CH{=}CH\overset{ONa}{C}H{-}C\equiv CH \xrightarrow[55-77\%]{NH_4Cl}$$

$$\underset{\mathbf{(103)}}{CH_3CH{=}CH\overset{OH}{C}HC\equiv CH} \xrightarrow[H_2]{Pd} \underset{\mathbf{(104)}}{CH_3CH{=}CH\overset{OH}{C}HCH{=}CH_2} \xrightarrow[\text{alumina } 90\%]{300^\circ}$$

$$CH_2{=}CHCH{=}CHCH{=}CH_2$$

(105)

[λ_{max} = 247 mμ (ε = 34,000);
= 256 mμ (ε = 48,000);
= 267 mμ (ε = 40,600).]



(106)

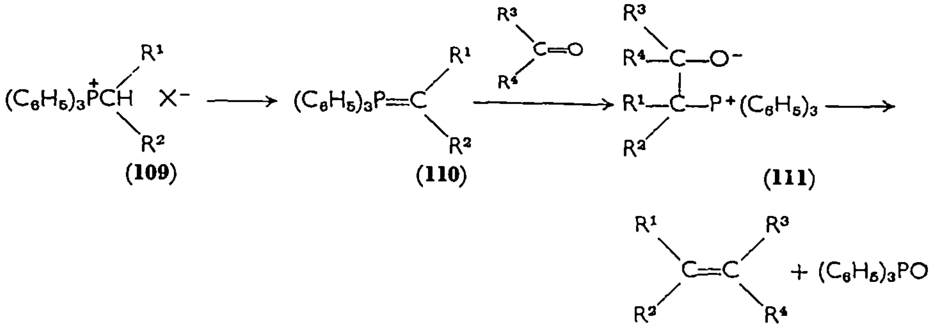
$$CH_3CH{=}CHCH{=}CHSO_2MgX \xrightarrow{C_6H_5CH_2Cl} CH_3CH{=}CHCH{=}CHSO_2CH_2C_6H_5$$

(107) (108)

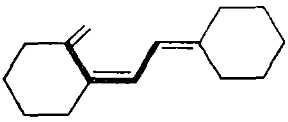
[λ_{max} = 248 mμ]

The use of Grignard reagents has been recently reported[41] in a novel synthesis of benzylsulfonyldienes. Addition of an ether solution of ethylmagnesium bromide to a solution of 2-methyl-2,5-dihydrothiophene-1,1-dioxide (**106**) followed by alkylation of the butadienylsulfinic salt (**107**) with benzylchloride affords 1-benzylsulfonyl-1,3-pentadiene (**108**) in a 26% yield.

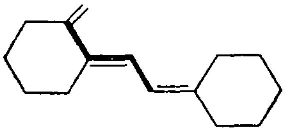
In 1954, Wittig and Schöllkopf[42] showed that triphenylphosphoranes (**110**), prepared from triphenylphosphonium halides **109** react readily with aldehydes and ketones to form the intermediates **111** which eliminate triphenylphosphine oxide to form a carbon–carbon double bond in the compound **112**. The mild reaction conditions required for the various steps and the non-ambiguity with regard to the position where the double bond is introduced make the Wittig reaction an excellent tool for the synthesis of mono-, di- and polyolefins[43]. Several pertinent examples are given in the following paragraphs.



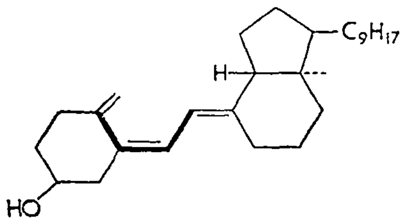
(**109**) (**110**) (**111**) (**112**)



(**113**)
[λ_{max} = 261 mμ (ε = 17,000)]

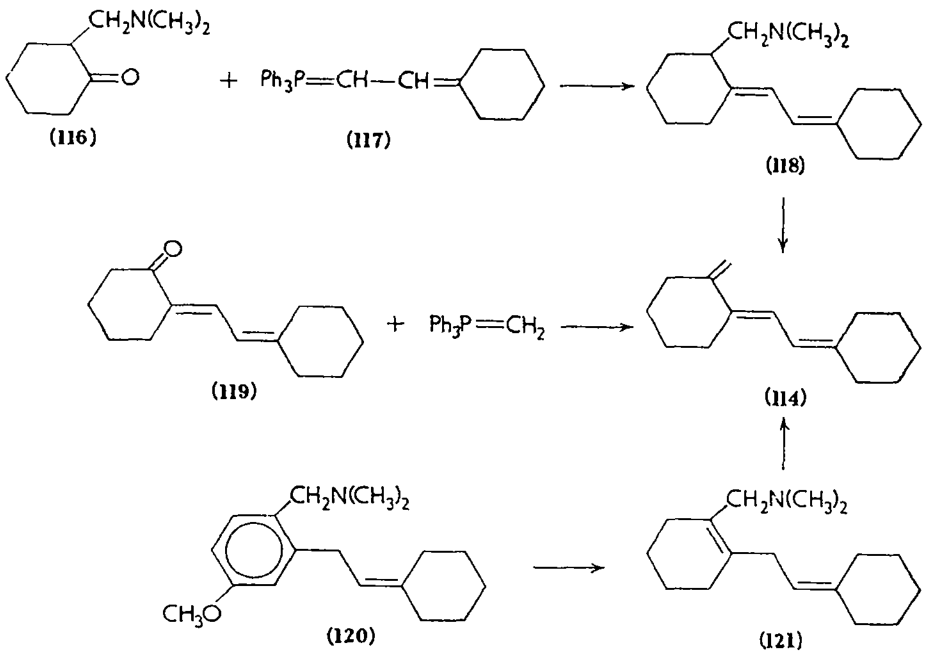


(**114**)
[λ_{max} = 269·5 mμ (ε = 22,700)]



(**115**)
[λ_{max} = 265 mμ (ε = 18,300)]

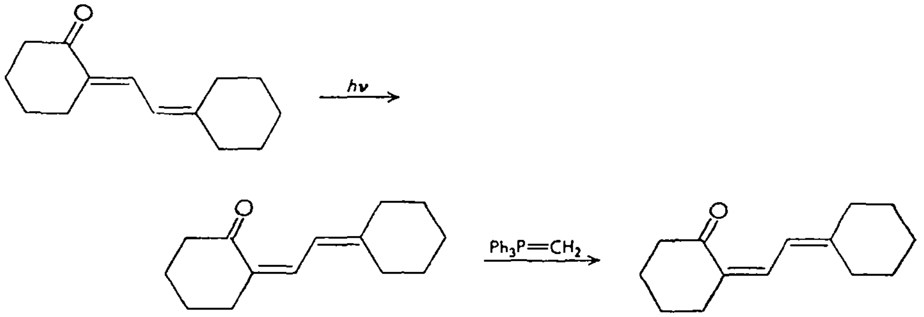
In the course of synthesis work on calciferol and related compounds,



Lythgoe and coworkers have reported[39a] the preparation of the simple model trienes **113** and **114** containing the system of calciferol (**115**).

Reaction of the phosphorane **117** with 2-dimethylaminomethylcyclohexanone (**116**) gave[39a] the *trans* diene **118** which upon thermal decomposition yielded the *trans* triene **114**. The same triene was obtained from the reaction of 1,2′-cyclohexylideneethylidenecyclohexanone (**119**).

A much lower overall yield of the triene **114** was obtained[44] by the reduction of the amine **120** with sodium and alcohol in liquid ammonia

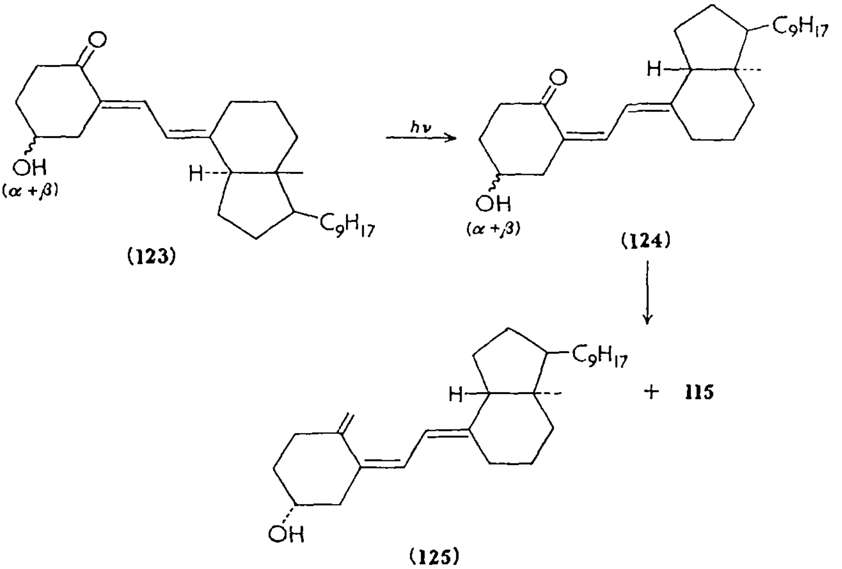


(**119**) [λ_{max} = 309–310 mμ (ε = 22,500)]

(**122**) [λ_{max} = 304–305 mμ (ε = 15,200)] followed by thermal decomposition of the isolated 2-dimethylaminomethyl-1,2′-cyclohexylideneethylcyclohexene (**121**).

The *cis* isomer of **113** has been prepared in the following way[45]: Irradiation of a methanolic solution of the *trans* dienone **119** afforded, after chromatography, the *cis* dienone **122** (in over 50% yield); upon reaction with methylenetriphenylphosphorane, **122** yielded the *cis* triene **113**. The latter is a rather unstable oil which decomposes in the presence of air at room temperature and also in its absence above 70°.

By applying the same series of reactions to the dienone **123**, Harrison and Lythgoe[45] claimed to have carried out the first partial synthesis of calciferol[46].



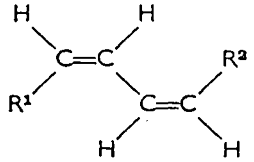
(123)

(124)

(125)

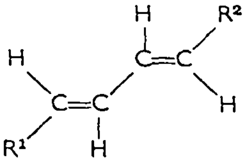
Harrison and Lythgoe[47] have also reported a non-photochemical synthesis of the model *cis* triene **113**. Reduction of the bicyclic γ-lactone **126** to the diol **127** was followed by conversion of the latter into the crystalline phosphonium bromide **128**. The Wittig reaction of **128** with cyclohexanone afforded the dienol **129** which, on oxidation with manganese dioxide, yielded the *cis* dienone **122**. The conversion of **122** into the *cis* triene **113** has already been mentioned.

The sex-attractant principle bombykol, isolated from the silkworm *Bombyx mori* L, has been shown by Butenandt and coworkers[48] to be 10,12-hexadecadien-1-ol. In order to arrive at an unambiguous



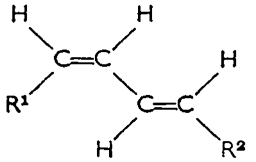
(10-*cis*-12-*cis*-)

(130)



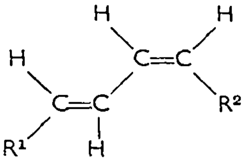
(10-*trans*-12-*trans*-)

(131)



(10-*trans*-12-*cis*-)

(132)

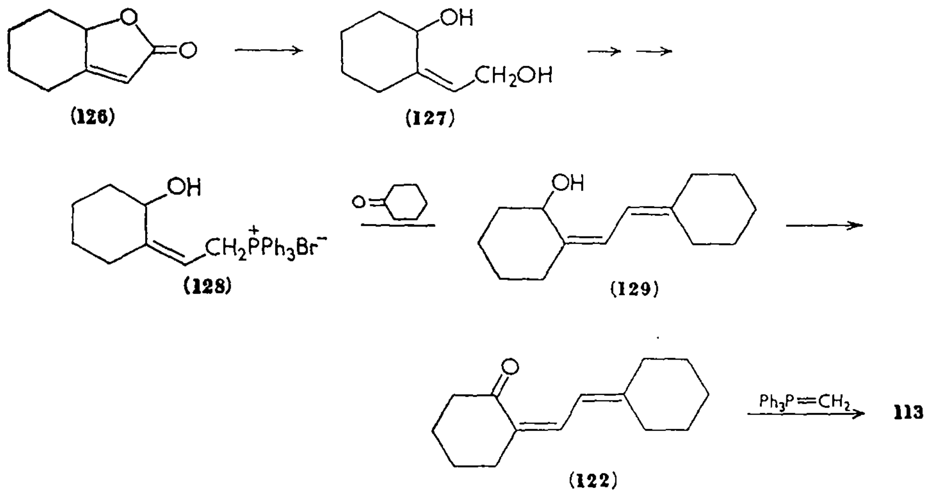


(10-*cis*-12-*trans*-)

(133)

[$R^1 = CH_3(CH_2)_2$—, R^2 = —$(CH_2)_8CH_2OH$]

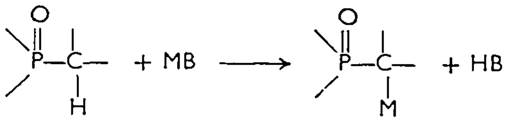
structure of this diene the four isomeric dienes **130–133** have been synthesized[48,49] by way of the Wittig reaction.



(126) **(127)** **(128)** **(129)** **(122)**

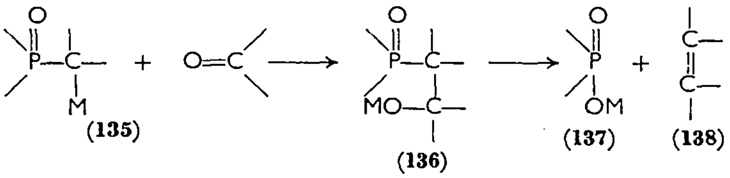
It has been shown by both groups of workers[48,49] that the synthesized 10-*trans*-12-*cis*-hexadecadien-1-ol (**132**) is identical, in all physical, chemical and biological properties, with the natural compound bombykol. The various schemes used in the synthesis of these isomers provide an excellent example of the versatility of the Wittig reaction for the introduction of conjugated double bonds in organic compounds.

Another reaction which appears to provide a general method for the synthesis of mono- and polyolefins has been recently described by Horner, Hoffmann and coworkers[50]. This reaction is based on the metalation of a carbon atom in the α-position to a $\rangle P{=}O$ group, followed by the reaction of the metalated compound **135**, with carbonyl derivatives such as aldehydes or ketones. The resulting product (**136**) readily breaks up into the corresponding phosphorus-containing acid anion **137** and the olefin **138**.



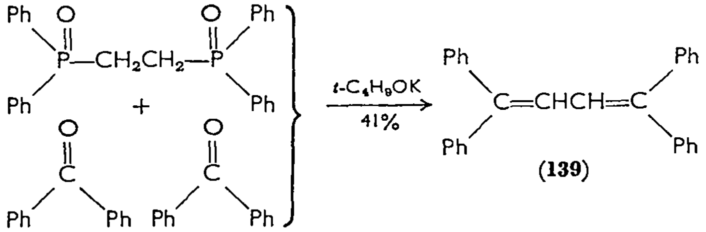
(134) **(135)**

(M = Li, K, Na; B = base)



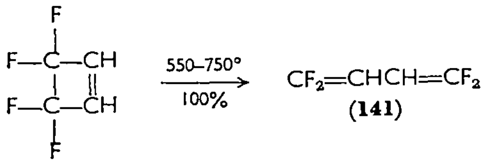
(135) **(136)** **(137)** **(138)**

Esters of mono- and bisphosphonic as well as -phosphinic acids have been used in about fifty examples of this reaction[50]. The synthesis of 1,1,4,4-tetraphenyl-1,3-butadiene (**139**) follows.



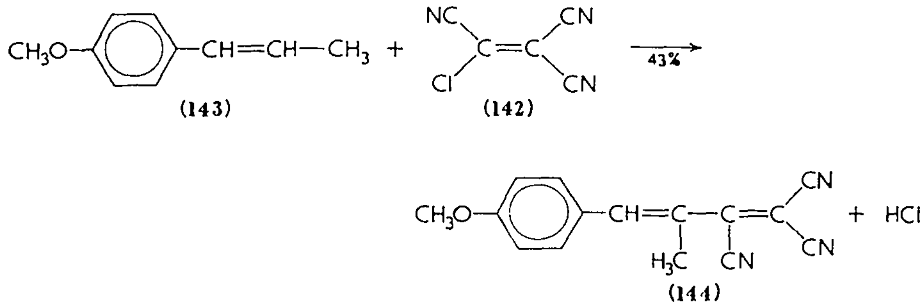
(139)

Several fluorinated butadienes have been recently prepared[51–54] by pyrolysis of cyclobutenes and cyclobutyl acetates.



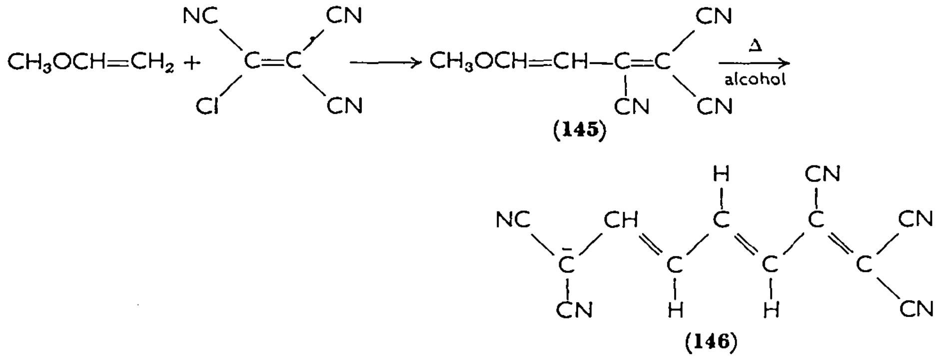
(140) **(141)**

A number of 1,1,2-tricyano-1,3-butadienes have been made[55] by reacting tricyanovinyl chloride (**142**) with electron-rich olefins such as methyl vinyl ether, anethole (**143**), and *N*-vinylpyrrolidone.



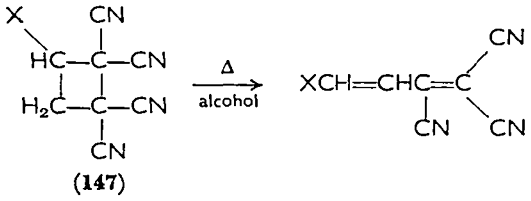
(143) (142) (144)

1,1,2-Tricyano-4-methoxy-1,3-butadiene (**145**) reacts readily in alcohol to give the intensely blue anion of the cyanocarbon acid 1,1,2,6,7,7-hexacyano-1,3,5-heptatriene (**146**), isolated as the ammonium or sodium salt.



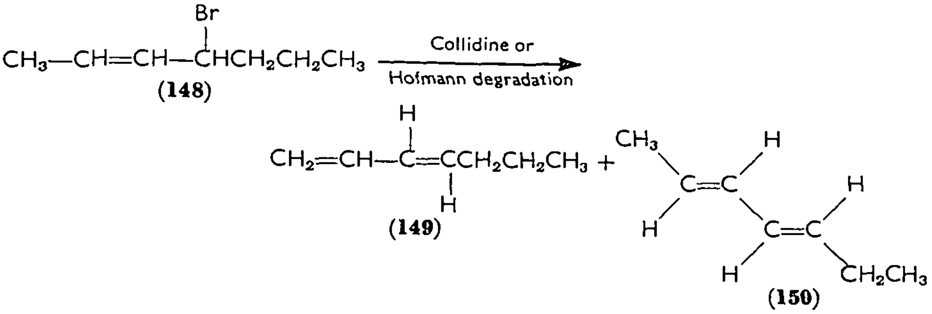
(145) (146)

Some of the cyano-substituted butadienes can also be made[55] by the cleavage, in hot alcohol, of 3-substituted 1,1,2,2-tetracyanocyclobutanes (**147**).



(147)

In their original publication[56] on allylic bromination, Ziegler and collaborators advocated the reaction of an alkene with *N*-bromosuccinimide followed by dehydrobromination as a method for the preparation of conjugated dienes. This procedure has been widely used[57] for the introduction of a conjugated diene system into cyclic compounds, but the method has seen little application in open-chain compounds[58]. When 4-bromo-2-heptene (**148**) was subjected[58] to various dehydrobromination procedures (such as refluxing with collidine or using the Hofmann degradation method), a mixture of 1,3- and 2,4-heptadiene, **149** and **150** respectively, was always obtained. The mixtures obtained by the two procedures differed both in the ratio of structural isomers and in the distribution of geometrical isomers.



(148) **(149)** **(150)**

III. PHYSICAL PROPERTIES OF CONJUGATED DIENES

It is outside the scope of the present discussion to attempt a review of all the physical data for conjugated dienes, even though these are frequently used and undoubtedly may be of great value. Such physical properties as heat capacity and other thermal data, viscosity, refractive index, will find little or no mention here. This section will be concerned mainly with a discussion of spectral properties of conjugated dienes since, in the opinion of this author, these data are of most immediate practical interest to the organic chemist.

A. *Boiling Points*

In a recent study[59] on the influence of chemical structure on the boiling points of acetylenic and olefinic hydrocarbons, it has been found that in the series of diolefins each double bond increases the boiling point by about 5°. If the two double bonds are positioned at adjoining carbons, the boiling point increases by 14°; if the double bonds are separated by one carbon atom the rise in boiling points is only 10°, and when the double bonds are separated by two or more carbon atoms the increase in boiling points becomes progressively less significant.

Consequently, it is concluded[59] that among normal olefins, the highest boiling points are found for compounds having several double bonds placed as much as possible near one another, and in particular for compounds having the double bonds at the first and second carbon atoms.

With a substituting methyl group, the highest boiling points are found for compounds having the two double bonds at the first and second carbon atoms and the methyl group on the third carbon atom.

B. *Magnetic Properties*

In a study on the magnetic properties of conjugated molecules, Hoaran[60] has shown that π electrons in conjugated systems, contrary to previous views, considerably decrease the implane components of the magnetic susceptibility (χ) of the skeleton of nuclei, kernel and σ electrons. By extending London's theory[61] and introducing new correction terms, a greatly improved agreement is obtained between theory and experiment for a number of conjugated dienes and polyenes. Table 1 shows the data for several butadiene derivatives.

TABLE 1. Magnetic susceptibilities of butadiene derivatives.

Compound	χ_M[a]	χ_{calc}[b]	Λ_{exp}[c]	r_{exp}[d]	r_{theory}[e]	ρ_{London}[f]
1,3-Butadiene	—	—	—	—	0·06	0
2-Methylbutadiene	46·0	42·8	3·2	0·21	—	0
2,3-Dimethylbutadiene	57·0	55·1	1·9	0·13	—	0
1-Phenylbutadiene	82·6	66·5	16·1	1·07	1·05	0·903
1,4-Diphenyl-butadiene	131·0	102·4	28·6	1·89	2·00	1·760
1,1,4,4-Tetraphenyl-butadiene	228	174·2	53·8	3·56	—	—

[a] Average molecular susceptibility measured experimentally.

[b] Calculated molecular susceptibility.

[c] $\chi_M - \chi_{calc}$.

[d] The ratio $\Lambda_{exp\ compound}/\Lambda_{exp\ benzene}(= -15{\cdot}1 \times 10^{-6})$.

[e] The ratio $\Lambda_{theory\ compound}/\Lambda_{theory\ benzene}$.

[f] The ratio anisotropy $\Delta K_{London,\ compound}/\Delta K_{London,\ benzene}$.

In a study of molecular polarizabilities, Bramley and LeFèvre[62] report the molar Kerr constants mK_2 for the α,ω-diphenylpolyenes $C_6H_5[CH{=}CH]_nC_6H_5$ with n = 1–4. The molar Kerr constants increase more rapidly with the number of vinyl groups (n) than would be expected from additivity (Table 2).

TABLE 2. Polarizations and molar Kerr constants[62] for $C_6H_5[CH{=}CH]_nC_6H_5$ in benzene at 25°.

n	$_\infty P_2$ (cm^3)	$10^{12}mK_{obs}$	$10^{12}mK_{calc}$	
1	65·3	124	111[a]	119[b]
2	82·7	357	358[a]	311[b]
3	101·0	692	764[a]	775[b]
4	148·4	1740	1759[a]	1777[b]

[a] Calculated from spectral data and the appropriate bisector axis length.

[b] Calculation includes both the σ and isolated π polarizabilities.

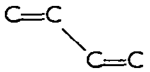
C. Electronic Absorption Spectra

The reader will have noticed that throughout section II, data have been given, whenever available, for the electronic absorption maxima, λ_{max}, of the compounds reported. This has been done because the application of ultraviolet spectroscopy to the problem in hand has become routine procedure in most organic laboratories and it may be useful to have available a compilation of absorption maxima for conjugated olefins.

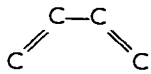
The remainder of this section will be concerned mainly with qualitative differences between closely related compounds and the enumeration of several empirical rules which help in the interpretation of electronic absorption spectra of conjugated dienes[63].

The energy-level diagram for butadiene has already been given in Figure 3. In Figure 4 are shown the energies of the molecular orbitals of this compound so as to indicate the combination of atomic orbitals of carbon to form ethylene and the combination of the two ethylene units to form butadiene. The electronic transitions which are of interest to this discussion are the V $\leftarrow$ N (*i.e.* Valence from Normal) or π–π^* transitions which are generally the most intense in an absorption spectrum.

A further point which requires consideration is the geometry of butadiene around the $C_{(2)}$—$C_{(3)}$ bond. It is possible to represent the two vinyl groups as being *trans* or *cis* as shown in **151** and **152** respectively. Configuration **151** is called *s-trans*-butadiene and **152** is



(151)



(152)

called *s-cis*-butadiene[64a]. The symbol *s-* signifies that the nomenclature refers to the *transoid* and *cisoid* configuration around an essential single bond.

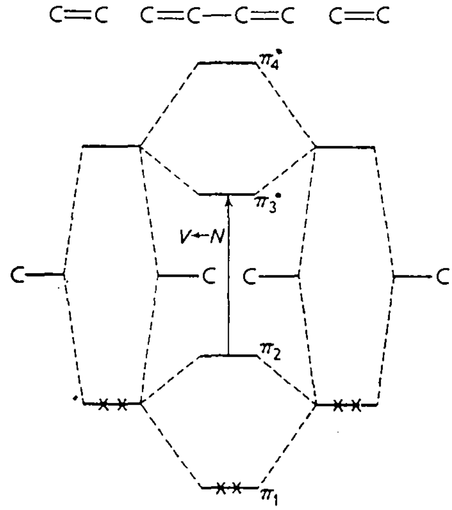


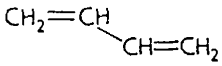
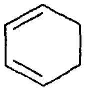
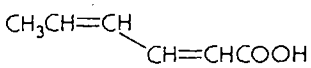
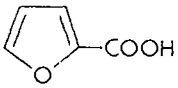
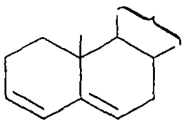
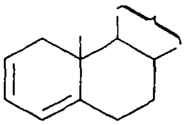
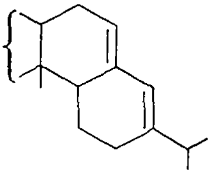
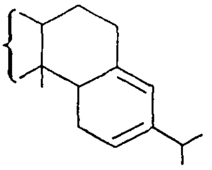
FIGURE 4. Energy levels of ethylene and butadiene. [Reproduced from H. H. Jaffé and M. Orchin, *Theory and Applications of Ultraviolet Spectroscopy*, John Wiley and Sons, New York, 1962.]

It is obvious that in an *s-cis* system the ends of the chromophore are much closer together than in an *s-trans* system and since it has been shown that the more elongated the molecule the greater the intensity of absorption[64,65], we should expect that the intensity of the absorption band of **152** should be less than that of **151**.

These differences in intensity of absorption have been used as criteria of configuration in pairs of geometrical isomerides differing only in the spatial arrangement of their unsaturated system[65–68], as shown in Table 3.

For butadiene, the longest wavelength band occurs at 217 mμ and, since the lowest unoccupied orbitals is the antibonding π_3^* orbital, this band must be due to a V ← N transition (see Figure 4). The intensity of absorption (Table 4) shows that the *s-trans* form predominates in butadiene. It is of interest to note that the energy barrier for conversion of the *s-trans* to the *s-cis* form is about 4·9 kcal/mole[69].

TABLE 3. Intensities of absorption, expressed as extinction coefficients of *s-cis-* and *s-trans-*1,3-dienes[a].

Compound	Conformation	ε_{max}
 $CH_2{=}CH{-}CH{=}CH_2$	*s-trans*	21,000
	*s-cis*	8,000
 $CH_3CH{=}CH{-}CH{=}CHCOOH$	*s-trans*	25,000
	*s-cis*	11,000
	*s-trans*	23,000
	*s-cis*	6,500
	*s-trans*	23,000
	*s-cis*	7,100

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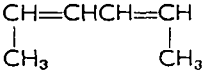
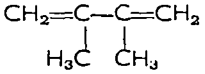
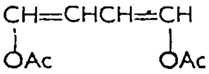
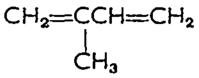
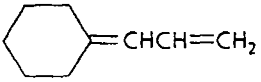
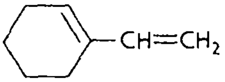
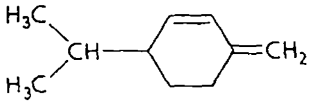
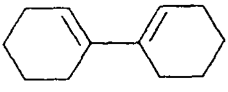
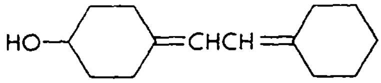
[a] For sources of data see refs. 65–68.

The bathochromic shifts produced in the absorption spectrum of butadiene by alkyl substituents have been summarized in an empirical rule by Woodward[70]. By taking the observed absorption maximum for butadiene $\lambda_{max} = 217$ mμ as base value, the expected absorption maximum for a substituted conjugated diene can be calculated by

TABLE 4. Spectra of conjugated dienes[70].

Compound	λ_{max}(mμ)	
	Calculated	Observed
$CH_2{=}CHCH{=}CH_2$	—	217
 $\underset{CH_3}{CH}{=}CHCH{=}\underset{CH_3}{CH}$	227	227
 $CH_2{=}\underset{H_3C}{C}{-}\underset{CH_3}{C}{=}CH_2$	227	226
 $\underset{OAc}{CH}{=}CHCH{=}\underset{OAc}{CH}$	227	228
 $CH_2{=}\underset{CH_3}{C}CH{=}CH_2$	222	220
	232	236·5
	227	230
	232	232
	237	236
	247	248

adding (to the base value) 5 mμ for each alkyl substituent on the diene and by adding a further 5 mμ for each exocyclic double bond present in the diene system. The data presented in Table 4 show the usefulness of this rule.

In an extension of the Woodward rule concerning alkyl substituents in conjugated aliphatic systems, Forbes and Shilton[71] have shown that in the case of α,β-unsaturated aldehydes and ketones a second β-methyl substituent gives rise to a considerably larger displacement than the first and that an analogous effect is observed for conjugated dienes, as shown in Table 5.

TABLE 5. Effect of terminal methyl groups on λ_{max} in $R^1R^2C{=}CHCH{=}CR^3R^4$ in ethanol[71].

Substituents				λ_{max} (mμ)	$\Delta\lambda_{max}$ (on replacement of H by CH_3)
R^1	R^2	R^3	R^4		
H	H	H	H	217·5	—
CH_3	H	H	H	223	5·5
CH_3	CH_3	H	H	232·5	9·5
CH_3	H	H	CH_3	226	8·5
CH_3	CH_3	CH_3	CH_3	241	15

Fieser and Fieser[72] have evolved a set of empirical rules for steroidal dienes and polyenes which are summarized in Table 6. Examples of the application of these rules are shown in Table 7[72,73].

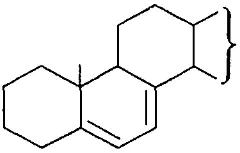
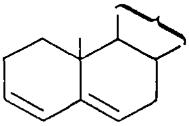
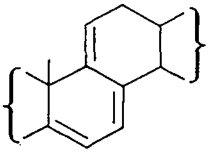
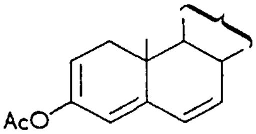
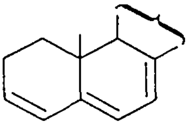
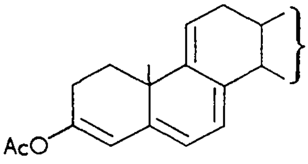
In a study on the dependence of spectral absorption upon structure, Hirayama has proposed[74] that the equation

$$(\lambda_{max})^2 = a + B(1 - C^N)$$

TABLE 6. Steroid dienes and polyenes[72].

	$\Delta\lambda_{max}$ (mμ)
Parent heteroannular diene	214
Parent homoannular diene	253
Double bond extending conjugation	30
Alkyl substituent or ring residue	5
Exocyclic location of double bond	5
Groups —OAc or —OR on diene system	0
Solvent correction	0
	total = λ_{max}

TABLE 7. Spectra of steroid dienes and trienes[72,73].

Compound	λ_{max}(mμ)		ε_{max}
	Calculated	Observed	
	253 + (4 × 5) + (2 × 5) = 283	282	11,900
	214 + (3 × 5) + 5 = 234	234	20,000
	253 + 30 + (5 × 5) + (3 × 5) = 323[a]	324	11,800
	253 + 30 + (3 × 5) + 5 = 303[a]	306	14,500
	253 + 30 + (4 × 5) + (2 × 5) = 313[a]	315	19,800
	253 + (2 × 30) + (5 × 5) + (3 × 5) = 353[a]	355	19,700

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[a] When both homoannular- and heteroannular-diene systems are present, the calculation is based upon the homoannular chromophore which absorbs at the longer wavelength.

establishes a relationship between the first absorption maximum of polyenes and the number of conjugated homochromophores present in the molecule (*a* and *C* are constants for the conjugated chromophoric system, *B* is a factor dependent upon the solvent, and *N* is an index defined by the number of conjugated homochromophores and corrected for the number and type of substituents, and of spectroscopically effective structures).

The above relationship has been tested on a large number of dienes and polyenes and it has been shown that there is a linear relation between *B* and the refractive index n_D^{20} of the solvent[74].

Panouse[75] has shown that for substituted polyenes this relationship can be improved by modification of the empirical constants and by the introduction of new correction terms, in particular for the substituents on the carbon atoms in the α-position to the double bonds.

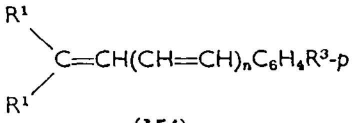
The spectra of a number of chlorophenylpolyenes have been found to resemble those of the corresponding α,ω-diphenylpolyenes and unless the conjugation in the chlorophenylpolyenes is affected by steric hindrance the absorption maxima determined experimentally agree very well with those calculated from Hirayama's empirical equation for alkyl substituted butadiene derivatives[76].

Hausser and coworkers[77] have shown that, in the system **153**,

$$C_6H_5CH{=}CH(CH{=}CH)_nC_6H_5$$

(153)

the bathochromic shift decreases in value from 28 mμ ($n = 0 \rightarrow n = 1$) with each integral increase in the value of n (*e.g.* $n = 5 \rightarrow n = 6$ there is an increase of only 15 mμ). Wizinger and coworkers[78,79] have investigated the bathochromic effect of the introduction of the first vinylene group and the convergence of the series for the system **154**



$$(R^1)_2C{=}CH(CH{=}CH)_nC_6H_4R^3\text{-}p$$

(154)

where R^1 is a chromophore group and R^2 is either a chromophore group, hydrogen or a group capable of ring formation with R^1 and R^3 is either hydrogen or a methoxy group.

From tabulated values[78,79] it is seen that the combined bathochromic effect for five vinylene groups varies from 76 mμ to 194 mμ and that the introduction of the first vinylene group gives shifts ranging from 24 to 48 mμ. It is surprising that the shift following the introduction of the first vinylene group is smaller in the anisyl (R^3 = OCH_3) than in the phenyl (R^3 = H) series. It is also shown that the effect of the —OCH_3 group is weaker after the introduction of one vinylene group.

The data[80] for several dimethylpolyenes are shown in Table 8.

TABLE 8. The principal maxima in the ultraviolet spectra of the dimethylpolyenes[80] $CH_3(CH{=}CH)_nCH_3$.

n	λ_{max} (mμ)	$\Delta\lambda$ ($\lambda_n - \lambda_{n=2}$) (mμ)
2	227	0
3	263	36
4	299	72
5	326	99
6	352	125
8	395·5	168·5
9	412·5	185·5
10	432[a]	205

[a] For $C_6H_{13}(CH{=}CH)_{10}C_6H_{13}$.

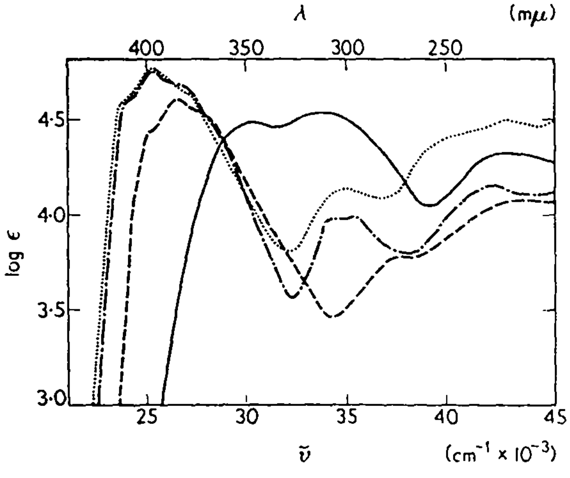
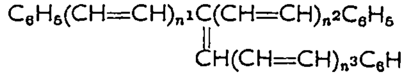


FIGURE 5. The ultraviolet spectra of **155b** (———), **155c** (– – – – –), **155d** (–·–·–·–) and **155f** (........) in methanol. [Reproduced, by permission, from F. Bohlman, *Chem. Ber.*, **89**, 2191 (1956).]

The Wittig reaction (*vide supra*) has been used[81] to prepare a number of hydrocarbons with cross-conjugated chromophoric systems as in

155, in order to investigate the effect of cross-conjugation on the ultraviolet absorption spectra. The ultraviolet spectra results show,



$$C_6H_5(CH{=}CH)_{n^1}\underset{\underset{\displaystyle CH(CH{=}CH)_{n^3}C_6H_5}{\|}}{C}(CH{=}CH)_{n^2}C_6H_5$$

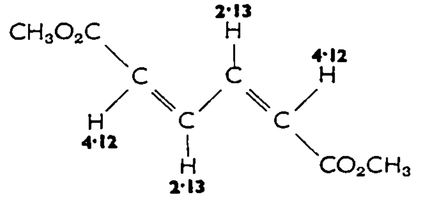
	n^1	n^2	n^3
155 a	1	0	0
b	1	1	0
c	1	1	1
d	2	1	1
e	2	2	0
f	2	2	1
g	2	0	1
h	1	0	1

Figure 5, that whenever a coplanar configuration is possible in systems such as **155**, cross-conjugation can have a considerable effect on the absorption spectra.

D. *Nuclear Magnetic Resonance Spectra*

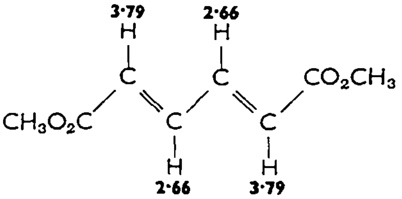
Nuclear magnetic resonance spectroscopy has been successfully used to distinguish between *cis* and *trans* forms of substituted mono-olefins[82] and the method has been extended to conjugated dienes.

The n.m.r. spectra for the three isomeric dimethyl muconates **156**, **157** and **158** provide unequivocal examples of a change in the sign of H – H coupling constants along a conjugated diene[83]. The chemical shifts (τ) for the olefinic protons of the muconic esters[83] are shown in the formulae **156–158** and the coupling constants (J) are given in Table 9.



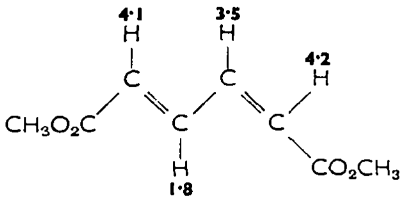
cis-cis

(**156**)



trans-trans

(**157**)



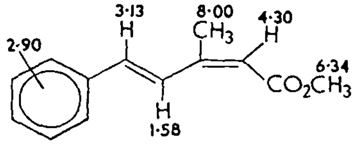
cis-trans

(**158**)

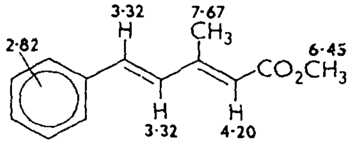
TABLE 9. Coupling constant (J) for
$CH_3OOC\overset{\delta}{C}H{=}\overset{\gamma}{C}H\overset{\beta}{C}H{=}\overset{\alpha}{C}HCOOCH_3$[83].

Muconic ester		$J_{\alpha\beta}$	$J_{\alpha\gamma}$	$J_{\alpha\delta}$	$J_{\beta\gamma}$	$J_{\gamma\delta}$
Configuration	Formulae					
cis-cis	**156**	11·8	−1·3	±1·3	11·3	$J_{\alpha\beta}$
trans-trans	**157**	11·2	−0·7	±0·6	16·5	$J_{\alpha\beta}$
cis(αβ)-*trans*(γδ)	**158**	10·7	0	0	10·7	14·8

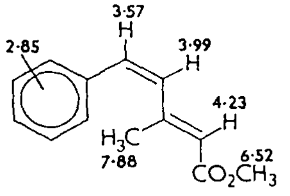
The four geometrical isomers of 3-methyl-5-phenyl-2,4-pentadienoic acid (**159**–**162**) have been characterized by means of n.m.r. spectroscopy. The n.m.r. characteristics of the 2-*cis*-4-*cis* (**162**) and 2-*trans*-4-*cis* (**161**) isomers have been obtained from 30% and 95% pure samples of these compounds prepared by partial hydrogenation of the acetylenic esters[84]. Nuclear magnetic resonance spectroscopy has shown that the 2-*cis*-4-*cis* isomer (**162**) is isomerized rather readily under conditions where the 2-*trans*-4-*cis* isomer (**161**) remains unchanged.



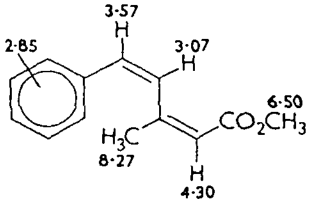
2-*cis*-4-*trans*
(J_{4-5} coupling 16 c.p.s.)
(**159**)



2-*trans*-4-*trans*
(J_{4-5} coupling 16 c.p.s.)
(**160**)



2-*trans*-4-*cis*
(J_{4-5} coupling 12 c.p.s.)
(**161**)



2-*cis*-4-*cis*
(J_{4-5} coupling 12 c.p.s.)
(**162**)

As can be seen from the n.m.r. data of **159**–**162**, the 3-methyl groups in these four structures occur in different environments. This has been accounted for[84] as follows. The methyl protons in the 2-*cis*-4-*trans* isomer (**159**) can be assumed to occur in a normal position, free from the magnetic anisotropic effect of neighbouring groups, at $\tau = 8{\cdot}00$. In the 2-*trans*-4-*trans* isomer (**160**) the carbonyl group is *cis* to the methyl protons and it exerts a deshielding effect on the latter with consequent absorption at $\tau = 7{\cdot}67$. The deshielding $\Delta\tau = -0{\cdot}33$ has been observed with other pairs of isomers[85]. However, in the 2-*trans*-4-*trans* isomer (**161**) the deshielding effect is only $\Delta\tau = -0{\cdot}12$, *i.e.* relative to **160** the methyl protons are subjected to a shielding influence $\Delta\tau = +0{\cdot}21$. The structural unit capable of exerting such a shielding effect is the phenyl group which can do so when the molecule is in the 3-*s*-*trans* conformation shown in **161**. Although models show this conformation to be somewhat more crowded than the alternative 3-*s*-*cis* conformation, such a structure would bring the $C_{(2)}$ proton in the shielding zone of the benzene ring. The occurrence of the $C_{(2)}$ proton absorption at $\tau = 4{\cdot}23$, almost exactly as in the *trans-trans* isomer ($\tau = 4{\cdot}20$) precludes the 3-*s*-*cis* conformation. By a similar argument the shielding of the methyl protons by the phenyl group, $\Delta\tau = 0{\cdot}27$, in the *cis-cis* isomer (**162**) can take place in the 3-*s*-*trans* conformation. This explanation thus establishes that the 4-*cis* isomer **161** and **162** exist in a preferred 3-*s*-*trans* conformation. The deshielding influence on the $C_{(2)}$ protons of both 2-*trans* isomers **160** and **161** ($\tau = 4{\cdot}20$ and $4{\cdot}23$ respectively) as compared to their position for the pair of 2-*cis* isomers **159** and **162** ($\tau = 4{\cdot}30$ and $4{\cdot}30$ respectively) is attributed to the $C_{(4)}$—$C_{(5)}$ olefinic bond.

The methyl protons of the *trans-trans* isomer **160** which for the methyl ester in carbon tetrachloride solution absorb at $\tau = 7{\cdot}67$, are shifted to $\tau = 7{\cdot}42$ for the acid in pyridine. This shift is very valuable in establishing the correct assignment of the n.m.r. absorption bands attributable to 3-*cis* methyl groups in geometrical isomers of unsaturated acids. Thus, a study of the iodine-catalyzed, ultraviolet irradiation-induced isomerization of the 2-*cis*-4-*trans* or 2-*trans*-4-*trans* isomers of 3-methyl-5-phenyl-2,4-pentadienoic acid (**163**) or of 3-methyl-5-(*p*-chlorophenyl)-2,4-pentadienoic acid (**164**) gives mixtures of all four geometric isomers with up to 37% of the 4-*cis* structure as indicated by n.m.r. spectroscopy[86]. The n.m.r. absorption maxima for the methyl protons of the acids **163** and **164** are shown in Table 10.

The geometrical isomers of several substituted 2,4,6-heptatrienoic acids have been characterized with the help of n.m.r. spectroscopy[87,88].

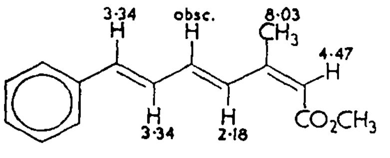
Of the eight possible geometrical isomers of 3-methyl-7-phenyl-2,4,6-heptatrienoic acid, three compounds having this composition with

TABLE 10. Nuclear magnetic resonance data for methyl protons in p-$XC_6H_4CH{=}CHC(CH_3){=}CHCOOH$[86].

Acid	τ^a X = H	τ^a X = Cl	τ^b methyl ester of acid X = H
2-*trans*-4-*trans*	7·42	7·47	7·67
2-*trans*-4-*cis*	7·61	7·69	7·88
2-*cis*-4-*trans*	7·95	7·98	8·00
2-*cis*-4-*cis*	8·18	8·24	8·27

[a] In pyridine.
[b] In carbon tetrachloride.

melting points of 203°, 169° and 192° have been reported[89-91]. Wiley and coworkers[87] have reinvestigated these acids and their methyl esters. The methyl esters of the acids melting at 194° and 203° have been shown to have the 2-*cis*-4-*trans*-6-*trans* (**165**) and the all-*trans* (**166**) configurations respectively. The product, m.p. 169°, formerly thought to be a third isomer, appears to be a mixture of the other two acids. The n.m.r. absorption data of the methyl esters **165** and **166** are shown in the formulae.

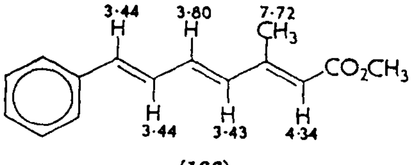


(J = 15 c.p.s.)

(**165**)

[Ultraviolet (CH$_3$OH): $\lambda\lambda_{max}$ = 246 mμ (ε = 10,900)
= 337 mμ (ε = 48,000)]

2-*cis*-4-*trans*-6-*trans*

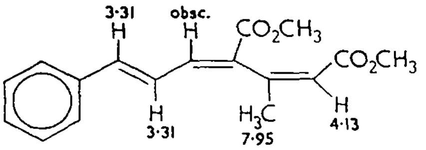


(**166**)

[Ultraviolet (CH$_3$OH): $\lambda\lambda_{max}$ = 243 mμ (ε = 9,250)
= 336·5 mμ (ε = 62,300)]

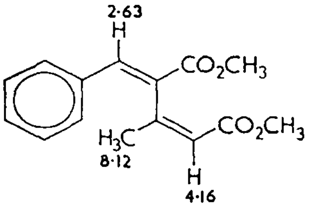
2-*trans*-4-*trans*-6-*trans*

The 3-methyl group in the ester **166** derived from the 203° acid is deshielded by the *cis*-carbonyl group a characteristic amount ($\Delta\tau = -0{\cdot}31$) with respect to that in the isomeric (194° acid) ester **165.** The deshielded $C_{(4)}$ proton of the 194° acid ester **165** appears as a low field ($\tau = 2{\cdot}18$) doublet with a coupling constant of 15 c.p.s. characteristic of a *trans* relationship between the $C_{(4)}$ and $C_{(5)}$ protons. The strong peaks at $\tau = 3{\cdot}34$ (**165**) and $\tau = 3{\cdot}44$ (**166**) are characteristic of a *trans* structure as observed in previous cases, *e.g.* **160.** The correctness of the above conformational assignments on the two isomers **165** and **166** is supported by the n.m.r. data for the two known dicarboxylic acid esters, **167** and **168**[87].



(167)

[Ultraviolet (CH_3OH): $\lambda_{max} = 319{\cdot}4$ mμ ($\varepsilon = 48{,}500$)]
2-*cis*-4-*cis*



(168)

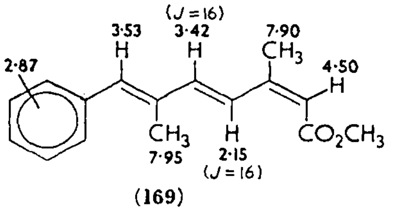
[Ultraviolet (CH_3OH): $\lambda_{max} = 279{\cdot}5$ mμ ($\varepsilon = 18{,}600$)]
2-*cis*-4-*cis*

The methyl protons absorption ($\tau = 8{\cdot}12$) for **168** is characteristic for a *trans* (to carbonyl) structure. The previously recorded values[85] for such a methyl group are $\tau = 7{\cdot}96$–$8{\cdot}27$ (*trans*) against $7{\cdot}71$–$8{\cdot}03$ (*cis*). The absorption band at $\tau = 2{\cdot}63$ is assigned to the $C_{(5)}$ proton deshielded by the $C_{(4)}$ carbomethoxy group. The two assignments $H_{(2)} = 4{\cdot}16$ and $H_{(5)} = 2{\cdot}63$ cannot be reversed since this would mean assigning an absorption to an olefinic proton alpha to a benzene ring well above the highest ($\tau = 3{\cdot}68$) value previously observed.

The methyl protons absorption ($\tau = 7{\cdot}95$) for the heptatrienoate **167** is ambiguously in the middle of the range for *cis* (to carboxyl) methyl and at the lower limit of the *trans* (to carboxyl) range. However, the 2-*cis* structure is supported by the $C_{(2)}$ olefinic proton absorption at $\tau = 4{\cdot}13$. The alternative 2-*trans* structure would place this proton within the deshielding ($\tau \sim 0{\cdot}80$) range of the 4-carboxyl to give an estimated[85] $\tau = 3{\cdot}3$, a region in which there is no observed absorption. Similarly, absence of absorption in this region shows that $H_{(5)}$ is *cis* to the 4-carbomethoxy. Such a structure would shift the $H_{(5)}$ absorption to a lower field ($\tau \sim 2{\cdot}9$) where it is obscured by the aromatic proton absorption.

By analogy to **160**, the singlet $\tau = 3{\cdot}31$ is assigned to the *trans* $H_{(6)}$—$H_{(7)}$ structure. If *cis*, these protons would probably be observed as an unsymmetrical doublet with $J = 9$–12 c.p.s. All these data, which confirm the 2-*cis*-4-*cis*-6-*trans* structure would be inconsistent with any of the seven alternative structures.

Similar arguments have been used[88] to establish the structures of the geometrical isomers of 3,6-dimethyl-7-phenyl-2,4,6-heptatrienoic acid esters (**169** and **170**) and the related compounds **171** and **172**. The n.m.r. absorption maxima are shown in the respective formulae **169–172**.



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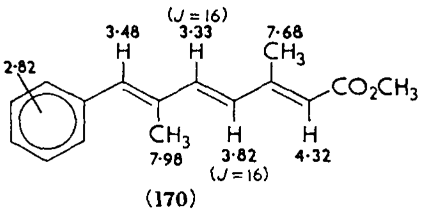

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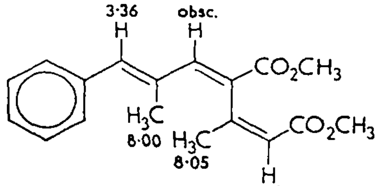

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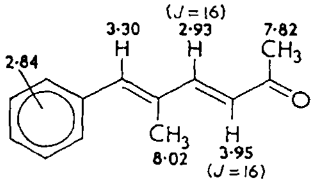

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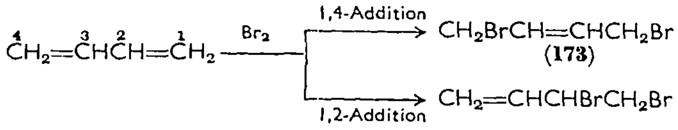
IV. CHEMICAL PROPERTIES OF CONJUGATED DIENES

The conjugated dienes show greatly enhanced chemical reactivity compared with monoolefins and non-conjugated dienes. The most significant difference is that the two centers of unsaturation appear to function as a single unit rather than as two independent double bonds.

Thus, the bromination of butadiene results in the formation of two products, 1,4-dibromo-2-butene (**173**) and 3,4-dibromo-1-butene (**174**). Compound **173** is the result of 1,4-addition to the conjugated



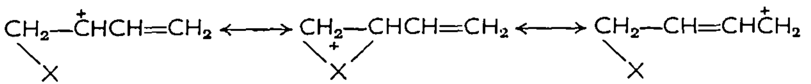
(**174**)

system and it involves the disappearance of the original double bonds with the formation of a new double bond at the 2,3-position. The rest of this chapter will be concerned mainly with a discussion of 1,4- *versus* 1,2-addition reactions between conjugated dienes and a variety of reagents. Since in most cases the products of the reactions of conjugated dienes constitute a mixture of 1,4- and 1,2-adducts, it will be more convenient to classify the various reactions according to the reagent adding to the diene, rather than according to the more obvious classification of 1,4- and 1,2-addition reactions.

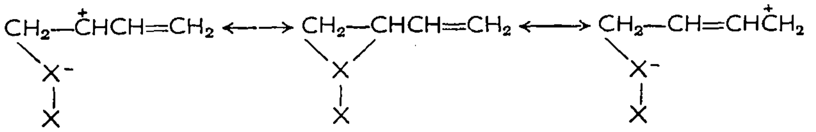
The most general reaction of conjugated dienes, the so-called 'diene reaction' or Diels–Alder reaction, has been thoroughly discussed in Chapter 11 on cycloadditions and it will not be treated here any further.

A. Addition of Halogens

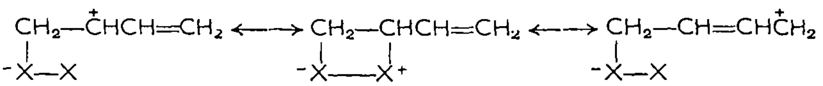
Addition of halogens to conjugated systems is generally regarded as a two-stage process: electrophilic attack by halogen or halonium ion followed by nucleophilic attack by halide ion[92]. A transition stage is envisaged in which the attacking reagent coordinates with one of the terminal double bonds, as shown in the contributing structures **175, 176** and **177.**



(**175a**) (**175b**) (**175c**)



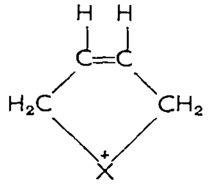
(**176**)



$$\underset{^-X—X}{CH_2}—\overset{+}{C}HCH{=}CH_2 \longleftrightarrow \underset{^-X}{CH_2}—\underset{X^+}{C}HCH{=}CH_2 \longleftrightarrow \underset{^-X—X}{CH_2}—CH{=}CH\overset{+}{C}H_2$$

(177)

If the electrophilic attack were to occur with the attacking reagent disposed centrally and symmetrically with respect to, and coplanar with, the diene, one could write the contributing structures **178**, **179** and **180** for the transition states.



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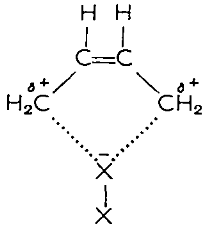

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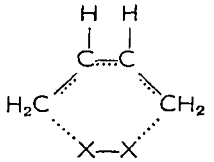


(180)

Mislow and Hellman[92] upon investigation of the chlorination of butadiene under conditions not inducive to *cis–trans* isomerization, have found that *trans*-1,4-dichloro-2-butene is the only 1,4-adduct formed in the reaction. The absence of any *cis*-1,4-adduct from the reaction products rules out the intermediates **178** to **180**, all of which have a *cis*-2-butenoid structure. In other words, the electrophilic reagent (chlorine) can coordinate with only one double bond of butadiene at a time, and not with both simultaneously. The resulting intermediate, which may be either a chloronium ion (**175b**) or a carbonium ion (**175a** ↔ **175c**), may combine with a chloride ion at either of two carbon atoms.

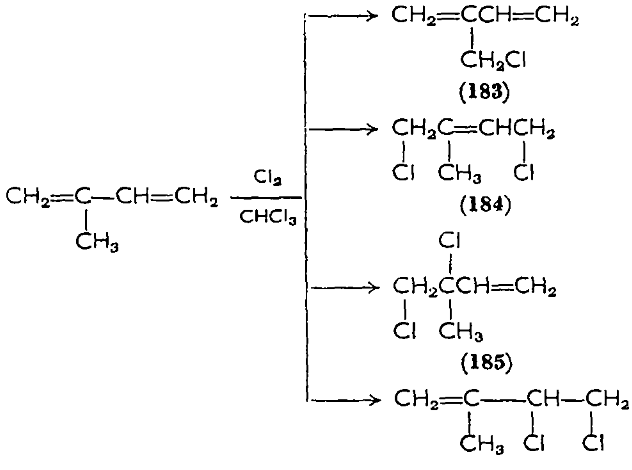
The product isolated must not necessarily be the one formed more rapidly from the reactive intermediate since the allyl halides formed may ionize to the reactive intermediate cation[93]. The *thermodynamically controlled*, *i.e.* the more stable product, will be formed preferentially if the two possible products are interconvertible under the reaction conditions. If the possible products are *not* interconvertible under the reaction conditions, the *kinetically controlled*, *i.e.* the more rapidly formed product, will be obtained in larger yield.

When the chlorination of butadiene was carried out[94] under reaction conditions where the two possible products were *not* interconvertible, 1,2-dichloro-3-butene (**181**) and 1,4-dichloro-2-butene (**182**) were obtained in a ratio of 2:1. This would indicate that **181** is the kinetically controlled product. On the other hand, it has been observed[95] that both **181** and **182** isomerize in the presence of zinc chloride and at equilibrium the mixture contains about 70% of the 1,4-adduct and 30% of the 1,2-isomer, an indication that the former, **182**, is the thermodynamically controlled product.

$CH_2{=}CHCHClCH_2Cl$ **(181)** $CH_2ClCH{=}CHCH_2Cl$ **(182)**

The chlorination of isoprene has recently been reinvestigated[96]. Passage of gaseous chlorine into a solution of isoprene in chloroform at ~20° yields mainly 2-chloromethylbutadiene (**183**) and 1,4-dichloro-2-methyl-2-butene (**184**), together with some 3,4-dichloro-3-methyl-1-butene (**185**) and 3,4-dichloro-2-methyl-1-butene (**186**).

The formation of **183** from isoprene must be the result of allylic chlorination, because **184**, **185** and **186** were recovered unchanged from control experiments under normal chlorination conditions. The dichloropentenes are probably the result of the three possible modes (1,4; 1,2; 3,4) of chlorine addition with a preference for 1,4-addition. However, experiments have shown that part of **185** may have been formed by the addition of hydrogen chloride to 2-chloromethylbutadiene (**183**).



$CH_2{=}C(CH_3){-}CH{=}CH_2 \xrightarrow[CHCl_3]{Cl_2}$

$CH_2{=}C(CH_2Cl)CH{=}CH_2$ **(183)**

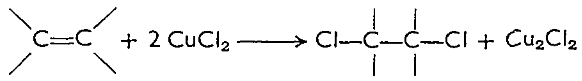
$ClCH_2C(CH_3){=}CHCH_2Cl$ **(184)**

$ClCH_2CCl(CH_3)CH{=}CH_2$ **(185)**

$CH_2{=}C(CH_3){-}CHCl{-}CH_2Cl$ **(186)**

It is interesting to note that when 1,4-dichloro-2-methyl-2-butene (**184**) was heated at 140° with a catalytic amount of cuprous chloride and copper powder, the reaction mixture contained about 45% of the 1,2-adduct **185** and about 5% of **186**.

The reaction of olefins with pumice-supported cupric chloride, which has the stoichiometry



has been applied to butadiene[97]. The products of the reaction at 220° had the following composition: 3,4-dichloro-1-butene, 42%; *cis*-1,4-dichloro-2-butene, 15%; *trans*-1,4-dichloro-2-butene, 41%; and 1-chlorobutadiene, 2%. The authors[97] envisage a chloronium ion intermediate in the reaction of simple olefins with cupric chloride since there appears to be predominantly a *trans* addition. It should be pointed out, however, that the formation of both *cis* and *trans* 1,4-adducts in the reaction with butadiene need not necessarily be construed as involving a butenoid chloronium ion intermediate, such as **178**, because the reaction conditions are definitely inducive[98] to *trans–cis* isomerization (*vide supra*).

The rapid, quantitative absorption of conjugated dienes and vinylbenzenes on solid cuprous chloride at low temperatures (−25 to +7°) has been used to separate these compounds from other olefins and paraffin hydrocarbons[99]. The reaction appears to be catalyzed by methanol, ethanol and n-propanol but not by isopropanol, benzyl alcohol and phenol. The conjugated diene recovered from the absorbent by heating to 70–130° was assayed to be 85–96% pure. The initial mixtures used in the experiments contained 20–70% of the conjugated diene.

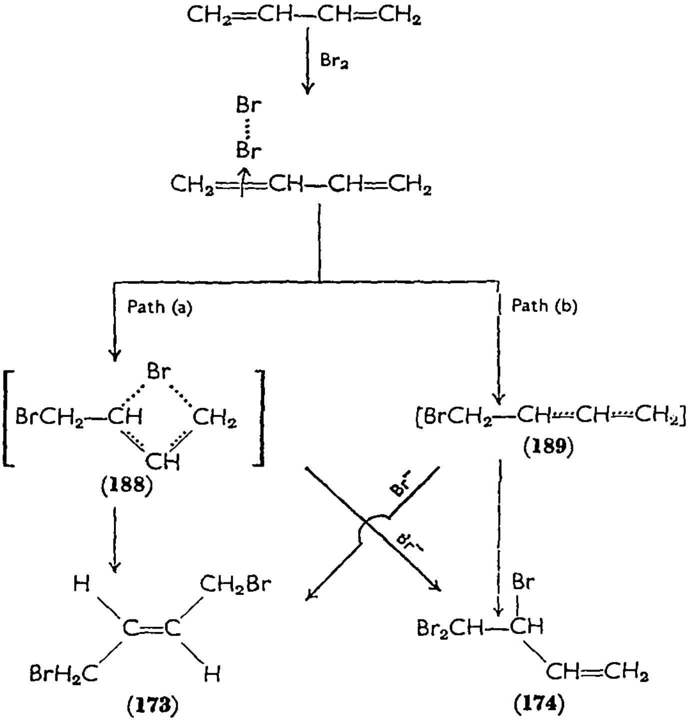
It has already been mentioned that the products of the addition of bromine to 1,3-butadiene are 1,4-dibromo-2-butene (**173**) and 3,4-dibromo-1-butene (**174**). As reported in an earlier paper[100], the ratio of the two dibromides appeared to be dependent upon the type of solvent used for the reaction. Thus the proportion of the 1,4-adduct **173** varied from 38·4% in hexane to 70·0% in acetic acid. This result would seem to indicate that the formation of **173** and **174** is kinetically controlled, with the former being favored by more polar solvents. The fact that both **173** and **174** undergo rearrangement to an equilibrium mixture of the two and the importance of solvent effect to the question of reaction mechanism have prompted a recent reinvestigation[101] of the bromine addition to butadiene. Quantitative data confirm that **173** and **174** are the products of the reaction. Moreover, of the two possible 1,4-adducts, only the *trans*-1,4-dibromo-2-butene has been obtained, the *cis* isomer not having been formed under the reaction conditions. As can be seen from Table 11, contrary to the conclusions of Farmer and colleagues[100], the ratio of **173** to **174** is not dependent upon solvent polarity.

TABLE 11. Equimolar bromination of 1,3-butadiene in various solvents at −15°[101].

Solvent	% of **173** (1,4-adduct)
Carbon disulfide	48
Trichloroethylene	49
Chloroform	45
Carbon tetrachloride	50
Hexane	46

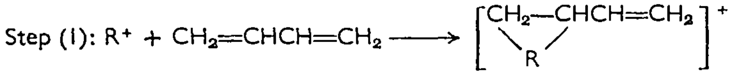
Hatch, Gardner and Gilbert have considered two mechanisms for the bromine addition to butadiene[101].

It is argued that since the transition state **189** shown in path (b) should require more extensive solvation than that involved in path (a), the latter would seem the more likely. It is further argued that



path (a) mechanism is in agreement with the observed complete stereospecificity of the reaction (only the *trans* 1,4-isomer is formed). Similarly, the observed unimolecular kinetics of the rearrangement of the 1,2-adduct **174** to the *trans* 1,4-adduct **173** and the large negative entropy of activation are said to be consistent with the mechanism involving a cyclic intermediate such as shown in path (a).

The compatibility of both 1,2- and 1,4-addition with molecular-orbital theory has been discussed by Wheland[102] who concludes that one cannot predict which of the two possible products will predominate. More recently, Pilar[103] has treated the 1,2- *versus* 1,4-addition to 1,3-butadiene by a simple LCAO–MO method. The treatment assumes that the ionic mechanism for the addition of a reagent R—A (*e.g.* Br—Br or H—Cl) occurs in two steps:



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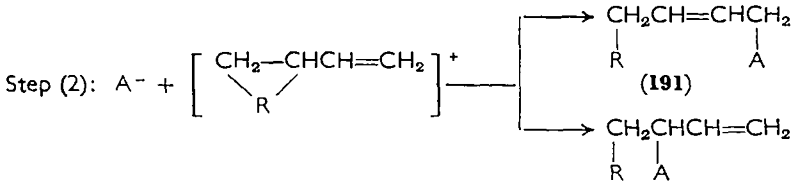
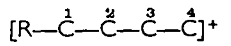


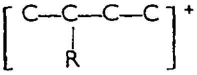
(192)

It is further assumed that at some point prior to attack by the nucleophilic species A⁻, the configuration of the transition state may be represented by **193** or **194** where the remaining two π electrons



$[\mathrm{R{-}\overset{1}{C}{-}\overset{2}{C}{-}\overset{3}{C}{-}\overset{4}{C}}]^+$

(193)



$$\left[\begin{matrix}\mathrm{C{-}\underset{\displaystyle\underset{R}{|}}{C}{-}C{-}C}\end{matrix}\right]^+$$

(194)

are confined to three $2p\pi$ orbitals of carbon. Among several other assumptions that are made[103b], in addition to the usual assumptions and approximations of the simple LCAO–MO method, are the following:

(*i*) The reactivity of the allylic-type transition state is independent of the attacking nucleophilic species A⁻.

(*ii*) The inductive effects of R are more important than conjugative effects.

Within the framework of the assumptions made, atom-stabilization energies, frontier-electron densities and total electron densities have been calculated. The results have been used to predict the direction of addition reactions to 1,3-butadiene, isoprene and chloroprene and it is claimed[103] that these predictions are in agreement with experiment (with the exception of chlorination of 1,3-butadiene).

B. *Addition of Hydrogen*

In a study of the kinetics of the catalytic hydrogenation of conjugated double bond systems, Kazanskii and collaborators[104] have found that the structure of the initial dienes affects strongly the direction of hydrogen addition. During hydrogenation over platinum, there takes place a simultaneous addition of one and two moles of hydrogen to produce a mixture of monoolefins, saturated hydrocarbons and unreacted dienes.

For all dienes studied, the rate of 1,2-addition is greater than that of 1,4-addition but the direction of the addition is governed by the structure of the initial diene. Thus, the amount of 1,4-addition of hydrogen is greater for dienes having alkyl substituents on the $C_{(2)}$ and $C_{(3)}$ atoms of the conjugated system and the rate of 1,4-addition of hydrogen decreases with an increase in the number of alkyl substituents on the $C_{(1)}$ and $C_{(4)}$ atoms of the butadiene system.

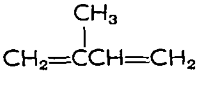
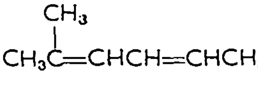
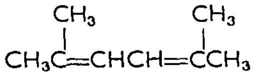
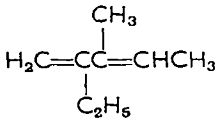
However, with platinum catalysts the structure of the initial diene has less effect on the direction of hydrogen addition than with palladium or nickel catalysts. It is claimed that the variation in the composition of the hydrogenation products of the dienes in passing from one catalyst to another is not accidental, but is governed by very definite rules. The change from platinum to palladium and nickel catalysts results in an increase in the amount of more thermodynamically stable monoolefins.

The composition of the mixture of monoolefins from the hydrogenation reaction depends also upon the secondary polymerization reaction of the olefins resulting from the displacement of the double bonds. It has been found that with platinum black, for all studied monoolefins, addition of hydrogen occurs only at the double bond and consequently no side polymerization reactions take place with this catalyst. On the other hand with palladium black and—to a lesser extent—with nickel, displacement of the double bond takes place, thus affecting the composition of the final products.

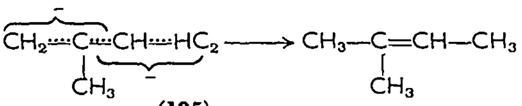
Table 12 shows the percentage composition of the hydrogenation products of various dienes.

Although isolated double bonds are not generally reduced by alkali

TABLE 12. Composition of hydrogenation products of dienes[104].

Diene	Catalyst	% Composition		
		Starting material	Monoolefin	Paraffin
 $CH_2{=}C(CH_3)CH{=}CH_2$	Pt	26	48	26
	Pd	2	96	2
	Ni	2	96	2
$CH_3CH{=}CHCH{=}CHCH_3$	Pt	32	41	27
	Pd	0	90–95	5–10
	Ni	0	95	5
 $CH_3C(CH_3){=}CHCH{=}CHCH_3$	Pt	17	55	28
	Pd	0	96	4
	Ni	0	95	5
 $CH_3C(CH_3){=}CHCH{=}C(CH_3)CH_3$	Pt	11	76	13
	Pd	0	93	7
	Ni	0	99	1
 $H_2C{=}C(C_2H_5)C(CH_3){=}CHCH_3$	Pd	0	100	0

metals in liquid ammonia or amines, conjugated dienes are reduced to monoenes by these reagents[105–107]. Thus isoprene and sodium in liquid ammonia give a 60% yield of 2-methyl-2-butene together with high molecular weight hydrocarbons[106]. It is believed[105] that this reaction occurs through the dianion **195**.

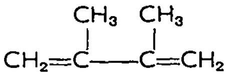
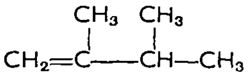
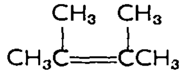
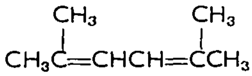
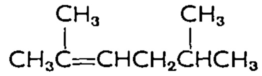
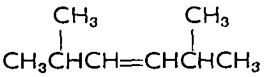


(195)

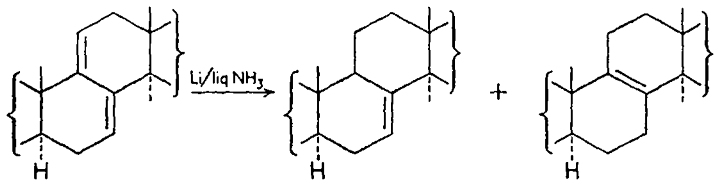
Reduction of 2-methyl-2,4-hexadiene with sodium in liquid ammonia gives a 53·5% yield of a mixture of products containing 12% of 1,2-reduction, 43% of 1,4-reduction and 45% of 3,4-reduction product[108].

The data in Table 13 show that the results of chemical reduction of conjugated diene systems are affected by the position of alkyl substitution on the diene system[109]. Alkyl substitution on the $C_{(2)}$ and $C_{(3)}$ atoms of the diene system appears to favor 1,4-addition, whereas alkyl substitution on the $C_{(1)}$ and $C_{(4)}$ atoms of the conjugated diene system results mainly in 1,2-addition. However, in the latter case the reaction also appears to be more dependent on the nature of the reagent.

TABLE 13. Effect of alkyl substitution on chemical reduction of diene systems[109].

Diene	Product	Reduction reagent		
		$Ca(NH_3)_6$	Na/EtOH	Na/liq NH_3
 $CH_2{=}\overset{CH_3}{C}{-}\overset{CH_3}{C}{=}CH_2$	 $CH_2{=}\overset{CH_3}{C}{-}\overset{CH_3}{C}H{-}CH_3$	9%	>4%	—
	 $CH_3\overset{CH_3}{C}{=}\overset{CH_3}{C}CH_3$	91%	<96%	—
 $CH_3\overset{CH_3}{C}{=}CHCH{=}\overset{CH_3}{C}CH_3$	 $CH_3\overset{CH_3}{C}{=}CHCH_2\overset{CH_3}{C}HCH_3$	—	71%	84%
	 $CH_3\overset{CH_3}{C}HCH{=}CH\overset{CH_3}{C}HCH_3$	—	29%	16%

A recent study[110] of the reduction of the 7,9(11)-diene group in tetracyclic triterpenes (**196**) with lithium in liquid ammonia has shown that both 1,2- and 1,4-addition of hydrogen takes place leading to Δ^7- and Δ^8-double bonds.



(**196**) (**197**) (**198**)

In a recent communication[111] it has been reported that aliphatic dienes, conjugated aromatic olefins, α,β-unsaturated acids (as salt or ester) and aldehydes, 1,2-diketones, epoxides and azoxy compounds can be hydrogenated by means of potassium cyanocobaltate(II), $K_3[Co(CN)_5]$, in aqueous solution at room temperature and a hydrogen pressure of one atmosphere. Thus, hydrogenation of isoprene gave a mixture of 85% 1,4-addition and 15% 1,2-addition products. It is claimed[111] that no other homogeneous hydrogenation system is known to reduce catalytically such a wide variety of substrates under such mild conditions.

The reduction of various α,ω-diphenyl polyenes, *e.g.* 1,4-diphenylbutadiene, in dimethylformamide has been investigated[112] by d.c. and a.c. polarography. The reduction appears to proceed in two steps:

$$M + e \rightleftharpoons M^-$$

and at a more negative potential:

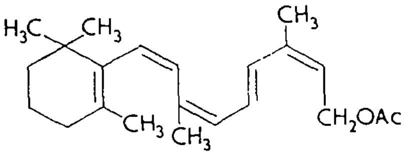
$$M^- + e \rightleftharpoons M^{2-}$$

The first electron addition is very fast, $k \approx 1$ cm/sec. The addition of the second electron is more or less irreversible owing to proton addition to the dinegative ions as well as to a relatively low rate of electron transfer.

C. Proton Addition to Conjugated Double Bonds

The mode of proton addition to conjugated double bonds in polyenes has been recently studied by Wassermann[113].

The light absorption and electrical conductance of vitamin A acetate (**199**) have been measured in benzene, with and without the

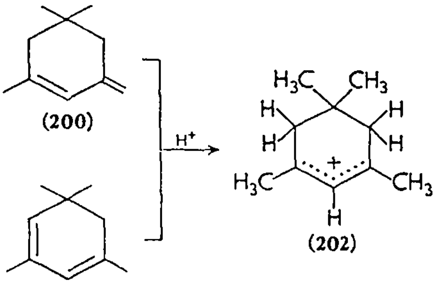


(**199**)

addition of trichloroacetic acid, CCl_3COOH. It has been found that the light absorption of **199** is markedly altered on addition of trichloroacetic acid owing to proton transfer, and the equilibrium constant K, relating to the proton uptake, has been found to be $K = 0{\cdot}10 \pm 0{\cdot}02$ l./mole in benzene at 20°. Measurements with different polyene concentrations indicate that only one acid molecule reacts with the carbon–carbon double bond of the polyene and the proton transfer leads to electrically conducting species. Experiments with dioxane, which acts as a competitive proton acceptor, have shown (within an accuracy of ± 20%) that the proton transfer from trichloroacetic acid to the polyene is reversible. From the experimentally determined light-absorption curve it appears that the proton uptake by vitamin A acetate leads to the mesomeric ion having the maximum number of formal double bonds.

Proton addition to a mixture of the conjugated dienes **200** and **201** results[114] in the formation of the allylic cation **202**.

The n.m.r. spectrum of a dichloromethane solution of **202** has four bands at 1·98, 6·67, 6·93 and 8·79 τ with relative areas of 1:4:6:6. The sharp band at lowest field is assigned to the hydrogen attached to a carbon that is both multiply bonded and part of a positively charged conjugated system. The four methylene hydrogens and six of the twelve methyl hydrogens which are alpha to the allylic system exhibit τ values (6·67 and 6·93 respectively) which reflect the proximity of a positive charge. The six hydrogens of the *gem*-dimethyl grouping absorb at a value (8·79 τ) only slightly lower than that of methyl hydrogens in saturated hydrocarbons[115]. The infrared spectrum of **202** in the range 2850–1450 cm^{-1} shows only one intense band at 1533 cm^{-1} and the ultraviolet spectrum of **202** (in sulfuric acid) has λ_{max} = 314 mμ (ε = 9130). The properties of cation **202** may serve as prototypes in structure elucidation of other aliphatic alkenyl cations.

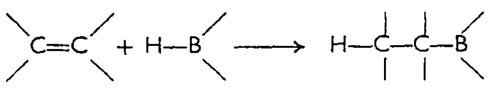

(200)

(201)

(202)

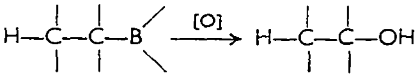
D. Hydroboration of Dienes

The addition of the boron–hydrogen linkage to multiple bonds between carbon and carbon (as well as to carbon–oxygen double bonds and carbon–nitrogen double and triple bonds) has been exploited by Brown and coworkers for the development of a powerful synthetic tool in organic chemistry[116].



The hydroboration of olefins proceeds readily to form the organoborane **203** in which the boron atom is placed predominantly at the less substituted of the two carbon atoms of the double bond.

The organoborane **203** is readily converted into the corresponding alcohol by oxidation with alkaline hydrogen peroxide.

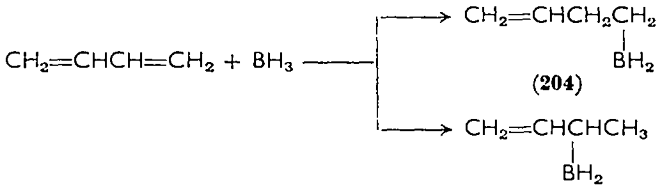


$$\mathrm{H{-}C{-}C{-}B}\langle \xrightarrow{[O]} \mathrm{H{-}C{-}C{-}OH}$$

(203)

The reaction has been extended to dienes in an attempt to find a possible synthetic route to diols and unsaturated alcohols[116-118].

Diborane reacts with 1,3-butadiene to form a polymeric organoborane which, when oxidized by alkaline hydrogen peroxide, yields over 75% of a mixture of butanediols. This mixture contains between 65–76% of 1,4- and 24–35% of 1,3-butanediol, depending upon the mode of addition of the reagents in the hydroboration reaction[117]. It is suggested that the change in the relative amounts of 1,3- and 1,4-diols formed are probably due to the fact that the hydroboration of butadiene does not proceed through a single, simple reaction path[116]. The initial stage probably involves addition of the boron–hydrogen bond to give the two intermediates **204** and **205**.

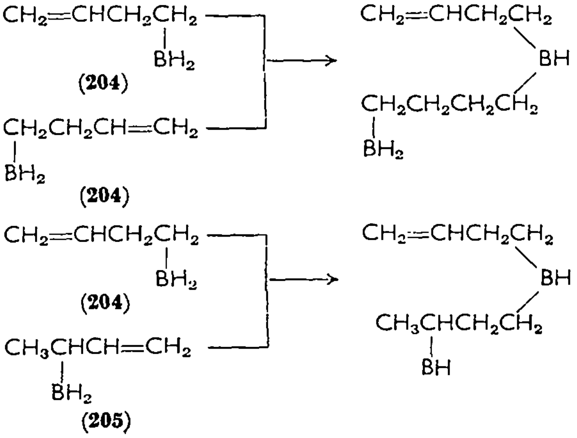


$$CH_2{=}CHCH{=}CH_2 + BH_3 \longrightarrow CH_2{=}CHCH_2CH_2BH_2\ \mathbf{(204)} \quad \text{and} \quad CH_2{=}CHCH(BH_2)CH_3\ \mathbf{(205)}$$

(204)

(205)

The second stage may involve a second addition due to the fact that the isolated double bond in either **204** or **205** is more reactive than the conjugated diene.



$$CH_2{=}CHCH_2CH_2BH_2\ \mathbf{(204)} + BH_2CH_2CH_2CH{=}CH_2\ \mathbf{(204)} \longrightarrow (CH_2{=}CHCH_2CH_2)BH(CH_2CH_2CH_2CH_2BH_2)$$

$$CH_2{=}CHCH_2CH_2BH_2\ \mathbf{(204)} + CH_3CH(BH_2)CH{=}CH_2\ \mathbf{(205)} \longrightarrow (CH_2{=}CHCH_2CH_2)BH(CH_2CH_2CH(BH)CH_3)$$

(204)

(204)

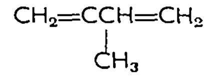
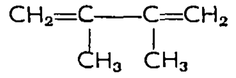
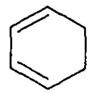
(204)

(205)

Since BH_3 possesses three hydrogen atoms capable of adding to the bifunctional butadiene molecule, a series of competing addition reactions may take place with the formation of a complex polymer. Oxidation of this polymer then yields the mixture of 1,3- and 1,4-butanediols[116].

Hydroboration of methyl-substituted 1,3-dienes results in an increased preference of the boron atom for the terminal position[117]. This can be seen from the data in Table 14.

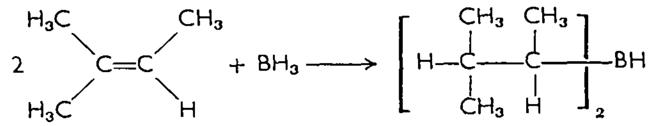
TABLE 14. Dihydroboration of conjugated dienes with diborane[117].

Diene	Total yield of mixture of diols[a] (%)	Composition of mixture of diols[b] (%)
$CH_2{=}CHCH{=}CH_2$	75	24 1,3- 76 1,4-
 $CH_2{=}\underset{CH_3}{C}CH{=}CH_2$	68	13 1,3- 87 1,4-
 $CH_2{=}\underset{CH_3}{C}{-}\underset{CH_3}{C}{=}CH_2$	66	100 1,4-
	61	two peaks

[a] Isolated.

[b] Gas chromatography analysis of crude reaction product.

A more selective reagent for the dihydroboration of butadiene is disiamylborane* (**206**) prepared by reacting 2-methyl-2-butene with diborane in tetrahydrofuran solution[116,118].



(**206**)

The fact that disiamylborane (**206**) is a monofunctional reagent as well as the large steric requirements of the siamyl groups probably account for the greater ability of **206** to place the boron atom at the

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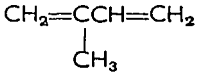
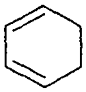
* The name 'siamyl', a contraction from *s*-isoamyl, has been suggested as a convenient term for the group $(CH_3)_2CHCH(CH_3)$—.

terminal carbon of the double bond. Thus the dihydroboration of butadiene with disiamylborane yields a 10:90 distribution of the 1,3- and 1,4-butanediol as compared with the 30:70 distribution from the reaction with diborane[117].

The selectivity of disiamylborane as a hydroborating agent is seen also in the monohydroboration of dienes to yield the respective unsaturated alcohols. The data presented in Table 15 compare the two reagents disiamylborane and diborane in the monohydroboration of dienes.

TABLE 15. Monohydroboration of conjugated dienes with disiamylborane and diborane[117,118].

Diene	Monohydroboration (%)	
	Disiamylborane	Diborane
$CH_2{=}CHCH{=}CH_2$	8	4
 $CH_2{=}C(CH_3)CH{=}CH_2$	24	4
$CH_2{=}CHCH{=}CHCH_3$	74[a]	12
	88[b]	51[c]

[a] Mixture of *cis*- and *trans*-3-penten-1-ol.
[b] 90% of 2-cyclohexen-1-ol.
[c] 35% of 3- and 65% of 2-cyclohexen-1-ol.

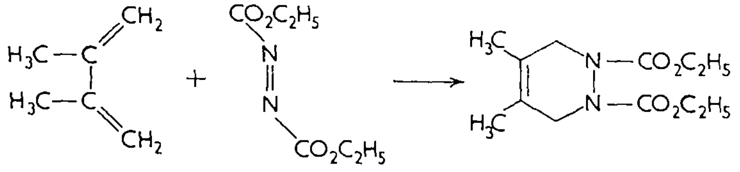
It has been suggested[116] that an intensive study of the hydroboration of dienes and polyenes may bring forth many new synthetic possibilities in organic chemistry.

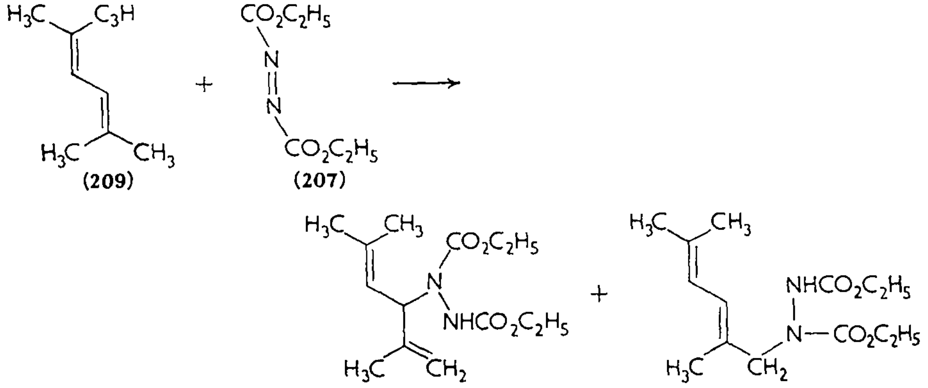
E. Addition of Dialkyl Azodicarboxylates to Dienes

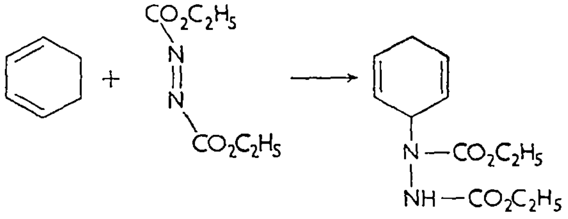
The addition of ethyl azodicarboxylate (**207**) to conjugated dienes is known to provide a good synthetic route for the preparation of various pyridazines and other hydrazine derivatives[119]. Thus, 2,3-dimethylbutadiene reacts readily with **207** to give the normal 1,4-addition compound **208**.

The recent claim by Levina and coworkers[120] that addition of **207** to conjugated diene systems takes place in the allyl position has been reinvestigated by Gillis and Beck[119]. The latter authors have shown that when the 1,4-position of the diene is highly substituted, Diels–Alder addition is prevented and addition takes place by other routes.

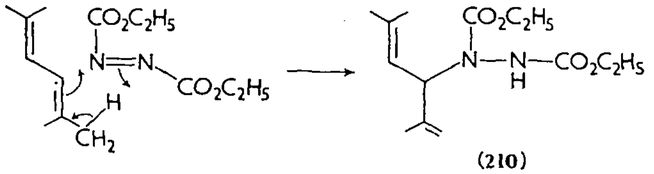
The reaction of 2,5-dimethyl-2,4-hexadiene (**209**) with ethyl azodicarboxylate forms[119] an adduct in 65% yield. Gas chromatography shows this adduct to consist of a mixture of three products in a ratio of 2%, 83% and 15% respectively. The 83% component is assigned structure 1,2-dicarbethoxy-1-[3-(2,5-dimethyl-1,4-hexadienyl)]hydrazine (**210**) and the 15% component is assigned structure 1,2-dicarbethoxy-1-[1-(2,5-dimethyl-2,4-hexadienyl)]hydrazine (**211**). Similarly[119], the addition of **207** to 1,3-cyclohexadiene yields 77% of 1,2-dicarbethoxy-1-[1-(2,5-cyclohexadienyl)]hydrazine (**212**).


(207) **(208)**

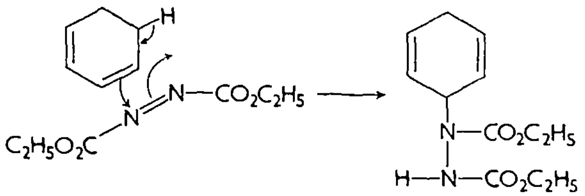

(209) **(207)** **(210)** **(211)**


(212)

The mechanism envisaged for these reactions consists of addition in the allyl position (similar to that reported[121] for simple olefins) and a cyclic mechanism, similar to that reported[122] for 1,3-diarylpropenes, resulting in a shift of the double bond out of conjugation.

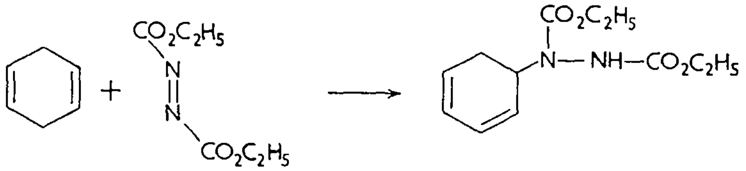


(210)

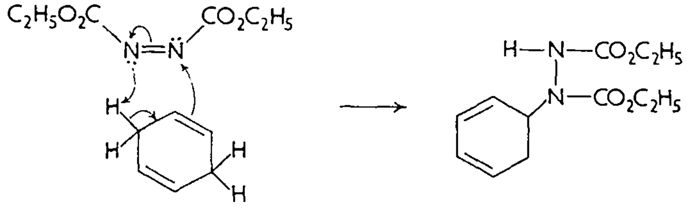


(212)

Franzus and Surridge[123] have also found that the reaction of 1,3-cyclohexadiene with ethyl azodicarboxylate does not proceed *via* a Diels–Alder addition and instead they suggest an addition–abstraction mechanism resulting in the formation of **212**. Moreover, these authors[123] have shown that 1,4-cyclohexadiene reacts with ethyl azodicarboxylate to form the conjugated diene derivative **213**, isomeric with **212**.



(213)



(212)

The formation of **213** can only take place by a concerted addition–abstraction mechanism, because a mechanism *via* hydrogen abstraction at the allyl position in a chain process should have resulted in the formation of **212**.

F. Addition of Radicals to Dienes

Rajbenbach and Szwarc[124] have determined the relative reactivities of various classes of olefins towards methyl radical additions. The respective relative rate constants of the addition, frequently referred to as *methyl affinities*, are determined as ratios k_2/k_1 where the subscripts refer to the two reactions

$$CH_3^{\bullet} + \text{isooctane} \longrightarrow CH_4 + \text{isooctyl radical} \qquad (1)$$

$$CH_3^{\bullet} + M \longrightarrow CH_3{-}M^{\bullet}\ \text{radical} \qquad (2)$$

$$(M = \text{olefin})$$

The results for conjugated dienes are given in Table 16.

TABLE 16. Methyl affinities for conjugated dienes[124-126].

Compound	Temp. (°c)	k_2/k_1
1,3-Budadiene	54·8	2350 ± 35
	64·9	2015 ± 30
	75·0	1790 ± 40
	85·1	1630 ± 10
Isoprene	54·8	2460 ± 70
	64·9	2090 ± 50
	75·0	1800 ± 30
	85·1	1470 ± 30
2,3-Dimethyl-1,3-butadiene	64·9	2230 ± 70
1,4-Diphenyl-1,3-butadiene	64·9	378 ± 6
2,5-Dimethyl-2,4-hexadiene	64·9	21·3
1,1,4,4-Tetraphenyl-1,3-butadiene	64·9	~60
1,5-Hexadiene	64·9	68
Allene	64·9	17·6 ± 0·2
1,2-Dimethylenecyclobutane (**214**)	65	4750 ± 35
1,2-Dimethylene-3-methylcyclopentane (**215**)	65	6575 ± 110
1,2-Dimethylenecyclohexane (**216**)	65	1015 ± 55

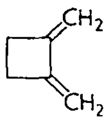
The isolated dienes show reactivities which are approximately twice as high as those of the corresponding monoolefins whilst the cumulated dienes show surprisingly low reactivities, lower even than those of simple monoolefins.

On the other hand, the reactivities of conjugated dienes are very high, probably due to substantial lowering of the activation energy of the addition process. The presence of methyl groups on atoms $C_{(2)}$ or $C_{(3)}$ of the conjugated diene system, slightly increases the reactivity probably because of hyperconjugation effects. Substituents on atoms $C_{(1)}$ and $C_{(4)}$ of the diene system exhibit a blocking effect, strikingly shown by 2,5-dimethyl-2,4-hexadiene.

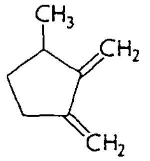
Pullman[127] has correlated the conjugated dienes methyl affinities data of Rajbenbach and Szwarc[124] with the radical-localization energies calculated for these compounds.

The reaction center is predicted to be the terminal carbon atom. Methyl substitution on the terminal carbon atom of the diene system decreases reactivity but methyl substitution elsewhere increases it. It appears that steric hindrance has a minor effect on reactivity.

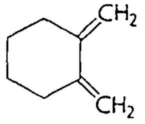
In an attempt to determine the relation between the reactivities of conjugated dienes and their conformations, Szwarc and coworkers[126] have investigated the methyl affinities of 1,2-dimethylenecyclobutane (**214**), 1,2-dimethylene-3-methylcyclopentane (**215**) and 1,2-dimethylenecyclohexane (**216**). The data are included in Table 16 and it can be seen that the reactivities of **214** and **215** are larger by factors of about 2·3 and 3·3 respectively than those of the linear conjugated dienes, whilst the reactivity of the six-membered ring compound **216** is about one-half of that of butadiene. The relatively low reactivity of **216** is explained by the lack of coplanarity of its vinyl groups. The unusually high reactivity of **214** and **215** is tentatively ascribed to the possibility that the considerable steric strain due to the coplanar *cis* conformation of the vinyl groups is released in the transition state as a result of the change from the sp^2 to sp^3 configurations. This may result in a lowering of the activation energy of the process and thereby increasing the respective methyl affinity. This may also account for the higher reactivity of the five-membered ring compound **215**, as compared to the four-membered ring derivative **214**, since the reactive —CH_2 centers in the former compound are more closely placed than in the latter (see Table 17).



(214)



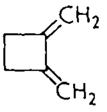
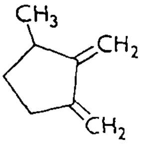
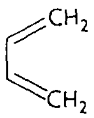
(215)



(216)

These arguments are said to disprove the suggestion[128] that the

TABLE 17. Bond angles and distances in exocyclic conjugated dienes[126].

Compound	Angle between vinyl groups	Distance between CH_2's of vinyl groups (Å)	Distance between H's of vinyl CH_2's (Å)
	90°	3·3	2·75
	72°	3·0	2·05
	60°	2·75	1·70

preferred conformation of isoprene is *cis* as compared to the favored *trans* conformation for butadiene.

The reaction of a 1,3-diene, a monofunctional compound and hydroxyl radicals, generated from hydrogen peroxide with ferrous sulfate, provides a one-step synthesis for long-chain unsaturated dicarboxylic acids, diketones, glycols and other difunctional compounds[129]. The hydroxyl radicals, generated in step (i), remove a

$$H_2O_2 + Fe^{2+} \longrightarrow \cdot OH + OH^- + Fe^{3+} \qquad \text{(i)}$$

$$R{-}H + \cdot OH \longrightarrow R\cdot + H_2O \qquad \text{(ii)}$$

$$R\cdot + M \longrightarrow R{-}M\cdot \qquad \text{(iii)}$$

$$2\,R{-}M\cdot \longrightarrow R{-}M{-}M{-}R \qquad \text{(iv)}$$

hydrogen atom from the monofunctional compound to form the radical R• (step ii) which adds to the 1,3-diene (M) to produce a new free radical, R—M• (step iii), which dimerizes (step iv).

This sequence, in which the unsaturated compound (M) is converted to a dimer containing residues (R) of the saturated compound as terminating groups is called *additive dimerization.* The additive dimers can be straight-chain or branched-chain compounds formed by 1,4- or 1,2-addition to the diene.

Under the conditions reported [129] the additive dimers were obtained in yields of upwards of 60% (based on hydrogen peroxide) and comprised a mixture of 1,4- and 1,2-adducts, with predomination of the former.

Through additive dimerization, reduction of *t*-cycloalkyl hydroperoxides with ferrous salts in the presence of 1,3-dienes provides a route for the formation of unsaturated long-chain diketones[130], and reductive cleavage of keto ester peroxides in the presence of butadiene affords the synthesis of long-chain unsaturated dicarboxylic esters[131].

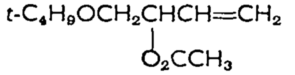
In a study on the behavior of *t*-butoxy radicals towards butadiene it has been found that the predominant reaction is addition at the terminal position to produce allylic radicals[132,133].

$$t\text{-}C_4H_9O\cdot + CH_2{=}CHCH{=}CH_2 \longrightarrow \underset{\textbf{(217)}}{t\text{-}C_4H_9OCH_2CH\overset{\cdots}{-}CH\overset{\cdots}{-}CH_2\cdot}$$

In order to explore the behavior of allylic radicals such as **217**, a recent study has been carried out[134] on the reaction between peroxy esters and conjugated olefins, such as butadiene, isoprene and styrene, in the presence of copper salts. The stoichiometry of the addition of peroxy esters to butadiene, catalyzed by copper salts, is given by

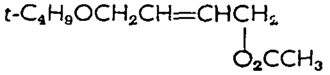
$$t\text{-}C_4H_9OO_2CR + C_4H_6 \xrightarrow{Cu^{I}} t\text{-}C_4H_9OC_4H_6O_2CR$$

The above reaction with *t*-butyl peracetate has been found to yield a mixture of acetic acid (~10%), *t*-butyl alcohol (~5%) and ester (~92%) as well as a minor amount of polymeric butadiene. The ester has been found to consist of about 50% 1:1 adduct and about 30% of 2:1 adduct of butadiene and *t*-butyl peracetate. The 1:1 adduct has been shown to consist of two isomers, 4-*t*-butoxy-3-acetoxy-1-butene (**218**, ~80%) and 4-*t*-butoxy-1-acetoxy-2-butene (**219**). In the presence of excess cupric ion the formation of 2:1 and higher adducts is drastically reduced.



$$t\text{-}C_4H_9OCH_2\underset{\displaystyle O_2CCH_3}{\underset{|}{C}}HCH{=}CH_2$$

(218)



$$t\text{-}C_4H_9OCH_2CH{=}CH\underset{\displaystyle O_2CCH_3}{\underset{|}{C}}H_2$$

(219)

The copper salt-catalyzed reaction of *t*-butyl peroxy esters with conjugated dienes has been formulated to occur *via* the following steps[134]:

(*i*) The formation of *t*-butoxy radicals by reaction of cuprous salt with *t*-butyl perester.

$$t\text{-}C_4H_9OO_2CR + Cu^{I} \longrightarrow t\text{-}C_4H_9O\cdot + Cu^{II}O_2CR$$

(*ii*) The chain transfer reaction to produce allylic radicals by addition to the diene.

$$t\text{-}C_4H_9O^{\bullet} + C_4H_6 \longrightarrow t\text{-}C_4H_9OCH_2CH\overset{\cdots}{-}CH\overset{\cdots}{-}CH_2^{\bullet}$$

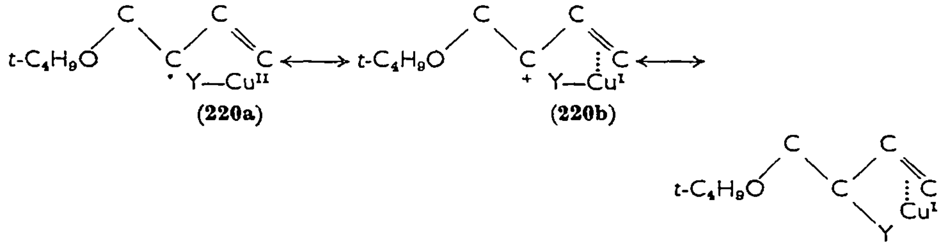
(217)

(*iii*) The oxidation–reduction reaction of the allylic radical with cupric salt to yield substituted monoolefins

$$t\text{-}C_4H_9OC_4H_6^{\bullet} + Cu^{II}O_2CR \longrightarrow t\text{-}C_4H_9OC_4H_6O_2CR + Cu^{I}$$

In the various reactions investigated[134] the 1,2-addition product, *e.g.* **218**, is always the major product irrespective of the solvent employed. The predominance of the more highly substituted allylic secondary isomer is unique in non-stereospecific reactions which involve the equilibrated allylic moieties[135]. If either free-radical or carbonium-ion processes were involved in the substitution step, it would be expected that the primary allylic isomer, *e.g.* **219**, would constitute *at least* 50% of the isomeric fractions[135].

The observed specificity and non-dependence on solvent have led to the postulate that the oxidation of allylic radicals by cupric salts is subject to ligand transfer and to electron transfer control[135]. The degree to which each contributes is a function of the free radical, metal ion and ligand. If a transition state such as **220** is considered for oxyanions such as acetate, benzoate and methoxide, then **220** is largely characterized by the oxidation of the free radical to the carbonium ion **220b**.

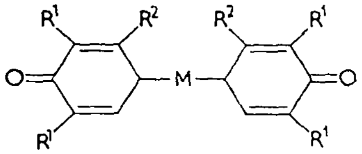


(220a) **(220b)** **(220c)**

In this mechanism for the oxidation–reduction reaction, the copper transfers one electron as well as the ligand, whilst at the same time it coordinates with the carbon–carbon π bond of the allylic radical. The differences in the transition states of the ligand transfer and electron transfer processes can be found in the relative contributions of the carbonium ion and the free radical forms[134,135]. The carbonium ion contribution is minimal in the ligand transfer process but it becomes important as part of the driving force of the oxidation. The converse is applicable to the role played by the free radical forms. The conversion of Cu^{II} to Cu^{I} may be responsible for attainment of carbonium ion character in the transition state and the importance of the coordination of copper with the π bond of the allylic radical during the oxidation step is consistent with the electron transfer process. On the other hand, since the driving force for ligand transfer is associated with the free radical character of the transition state, *e.g.* **220a**, the reaction would be expected to proceed like other radical chain reactions so that the coordination of the π bond with copper in the transition state would be minimal[134].

Stable aryloxy radicals derived from 2,4,6-tri-*t*-butylphenol and 2,6-di-*t*-butyl-4-phenylphenol react[136] with butadiene or chloroprene to give good yields (60–80%) of yellow crystalline solids in which two aryloxy radicals are combined with one unsaturated molecule.

The 2:1 adducts have been assigned structure **221** where M represents the unsaturated molecule



(**221**, $R^1 = C(CH_3)_3$;
$R^2 = C(CH_3)_3$ or C_6H_5;
$M = -CH_2CH{=}CHCH_2-$ or
$-CH_2CH{=}CClCH_2-$.)

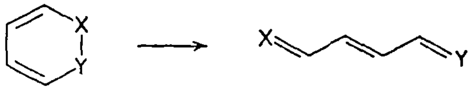
In a discussion on the localization of π electrons and the mechanism of free-radical reactions, it has been shown[137], by the use of simple molecular-orbital theory, that part of the mechanism of free-radical attack upon the conjugated molecules consists of a collision process between the conjugated molecule and an attacking reagent in which the C—H bond at the position of attack is displaced out of the plane of the molecule. This would tend to produce a free electron derived from the π-electron system at the position of attack.

G. Photochemical Transformations

In recent years there has been great activity in the study of photochemical transformations[138].

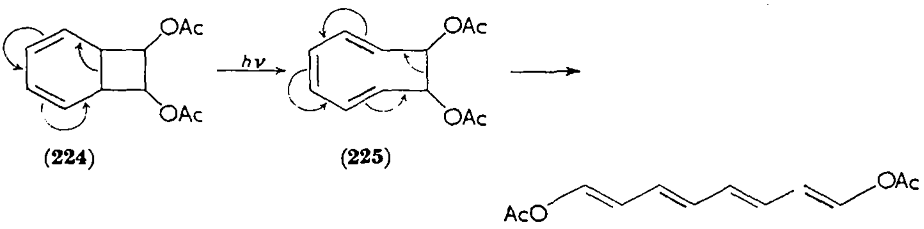
The application of photochemical reactions for the *cis–trans* isomerization about a double bond has been widely used but little other information has been recorded as to results of the irradiation of open-chain dienes[138]. On the other hand, the ultraviolet irradiation of various cyclic dienes has received considerable attention in recent years[139,140].

In preliminary experiments it has been shown that 1,3-cyclohexadiene affords on irradiation 1,3,5-hexatriene and this is believed to be a general reaction[139].



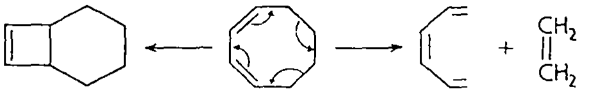
(222) **(223)**

This generalization has been extended as follows: irradiation with ultraviolet light of the appropriate wavelength of a ring system containing ($n-1$) conjugated double bonds can yield either an open-chain compound possessing n conjugated double bonds or a bicyclic valence tautomer[139,141]. Thus, irradiation of **224** in ether produces[139] the tetraene **226**. In the ring-opening step, the excited state is deactivated *via* rearrangement of the bonding electrons with concomitant breaking of a saturated carbon–carbon bond.



(224) **(225)** **(226)**

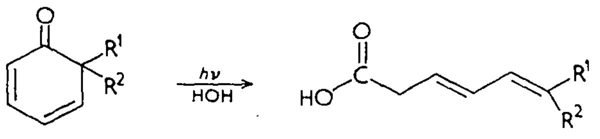
In the case of 1,3-cyclooctadiene (**227**) the excited state could be deactivated to yield 1,3,5-hexatriene and ethylene or it could collapse to the valence tautomer Δ^7-bicyclo[4.2.0]octene (**228**).



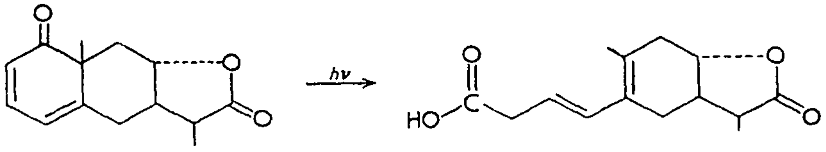
(228) **(227)**

It has been found[141] that upon irradiation in ether solution, **227** yields a single product which has been identified as **228**. The n.m.r. spectrum of **228** shows a sharp singlet at 4·04 τ, corresponding to two identical vinyl protons on a cyclobutene ring[141].

The photochemical transformation of cyclohexadienones of structure **229** has been shown by Barton and Quinkert[142] to yield $\beta,\gamma,\delta,\varepsilon$-dienoic acid derivatives (**230**). Dauben and coworkers[143] have recently extended this reaction to the fused ring system **231**.

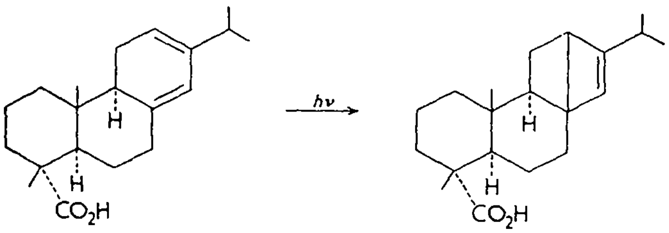


(229) **(230)**



(231) **(232)**

Other examples of photochemical transformations and leading references may also be found in the recently reported[144] results of the ultraviolet irradiation of levopimaric acid (**233**), a derivative of 1,3-cyclohexadiene.



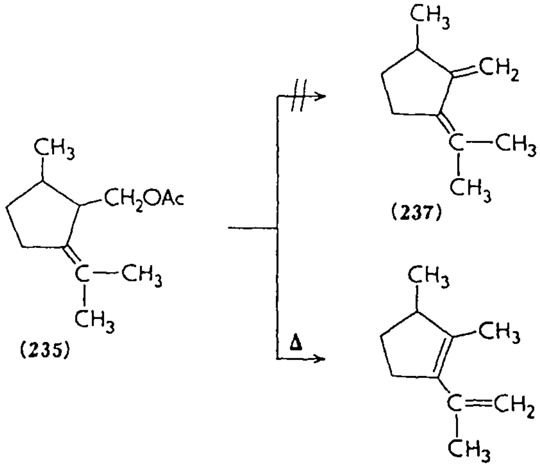
(233) **(234)**

The photosensitized oxygenation of olefins and homoannular dienes has been recently reviewed[145,146].

H. Thermal Rearrangement of 1,3-Dienes

The observation that pyrolysis of 2-acetoxymethyl-3-isopropylidene-1-methylcyclopentane (**235**) produces 2-isopropenyl-1,5-dimethyl-1-cyclopentene (**236**) rather than the expected 3-isopropylidene-2-methylene-1-methylcyclopentane (**237**) has recently prompted an investigation of thermal rearrangements of the type described in (**238**).

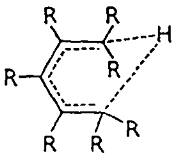
Although thermal rearrangements such as **238** have been reported by several authors[147], the generality of such isomerizations has not been previously explored.



(235) (237) (236)

(**238**)

Wolinsky and coworkers[147] have demonstrated that 1,3-dienes in which a vinyl and an alkyl group are *cis* undergo a reversible thermal isomerization involving the overall 1,5-transfer of a hydrogen with concomitant migration of both carbon–carbon double bonds. The systems investigated and the results of thermal isomerizations at different temperatures are shown in Table 18.

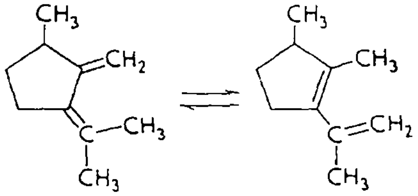
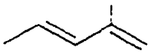
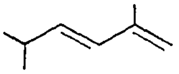


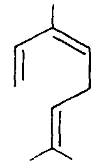
(**249**)

Since dienes in which a vinyl group and an alkyl group are *trans* appear to be thermally stable, it is suggested[147] that this difference in thermal behavior may serve as a method for distinguishing between *cis*- and *trans*-1,3-dienes. By this means, α- and β-ocimene have been assigned the geometric configurations **247** and **248** respectively.

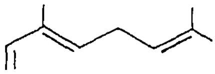
The selective isomerization of *cis*-1,3-dienes is thought[147] to occur *via* the six-membered transition state **249** in which the five carbon

TABLE 18. Thermal rearrangements of 1,3-dienes[147].

System investigated	Starting diene	Temp. of injector (°c)	Products (%)		
 **(237)** **(236)**	**237**	260	85·5 (**237**)	14·5 (**236**)	
		310	40	60	
		360	5	95	
 **(239)** **(240)**	**239**	260	97 (**239**)	2·3 (**240**)	
		360	66·8	33·2	
		450	20·7	79·3	
	240	360	0	100·0	
		400	3·8	96·2	
		450	6·3	93·7	
 **(241)** **(242)**	**241**	360	99·0 (**241**)	1·0 (**242**)	
		450	93·8	6·2	
	242	260	35·7	64·3	
		360	94·3	5·7	
		400	95·5	4·5	
 **(243)** **(244)**	**243**	320	95 (**243**)	2·4 (**244**)	2·4 (**245**)
		400	80	14	5·8
		450	78	16·4	5·5
	244	450	74	21	4·4
 **(245)**	**245**	450	99 (**245**)		
 **(246)**	**246**	450	99 (**246**)		



(247)



(248)

atoms are coplanar, or nearly so, the migrating hydrogen remaining out of this plane.

Thus it is pointed out[147] that the planar dienes **237** and **236** require a temperature of 350° to approach equilibrium whereas an equilibrium mixture was never completely reached at 450° with the non-planar dienes **239** and **240**.

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The Chemistry of Alkenes
Edited by Saul Patai

CHAPTER 13

Cumulenes

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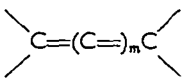
I. INTRODUCTION

A. Synthetic Cumulenes

Cumulenes can be defined[1] as compounds which contain a unit of n carbon atoms with $(n - 1)$ double bonds between them $(n \geqslant 3)$. They are therefore the members of the series* propadiene (allene), butatriene, pentatetraene, hexapentaene, *etc.*, and obey the general formula **1.**



(**1**, $m = 1, 2, 3, \ldots$)

The first appearance of cumulenes in the literature was as early as 1864, when Reboul[2] reported on valerylen (C_5H_8), believing it to be 1,1-dimethylpropadiene. Though this was later shown to be only a

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* Note that no numbers are required to specify the position of the double bonds.

mixture of C_5 hydrocarbons, he was apparently the first one to contrive the formula of an allene. In 1875, Henry[3] proposed the trivial name 'allene' for propadienes in connexion with his alleged synthesis of tetramethylpropadiene which again seems to have been only a mixture[4]. Curiously enough, Burton and Pechmann synthesized glutinic acid in 1887[5], and assigned to it the structure **2**, discarding the allenic formula **3** on the grounds that the new compound reacted in an analogous way to acetylenedicarboxylic acid. They even went so far as to claim that this demonstrated the impossibility of a single carbon atom forming two double bonds. Yet these investigators were the first to have a pure cumulene in their hands! This was revealed 67 years later when Jones and coworkers[6] showed that 'glutinic acid' had the allenic structure **3**. Burton and Pechmann's pessimistic view was proved to be unfounded only one year later when, in 1888, both Russian and American investigators succeeded in synthesizing allene itself and several alkyl-substituted propadienes, whose structures were proved conclusively[7,8,9].

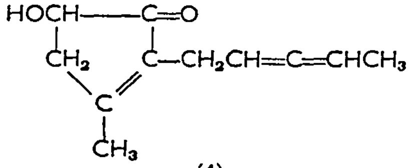
$$\mathrm{HOOCC{\equiv}C{-}CH_2COOH} \quad \textbf{(2)}$$

$$\mathrm{HOOCCH{=}C{=}CHCOOH} \quad \textbf{(3)}$$

There seems to have been the general belief that compounds with more than two consecutive cumulated double bonds would be unstable, and it was only in 1921 that Brand[10] obtained the next higher homolog of allene, namely a butatriene. Even this appears to have been more of an accidental discovery than the result of a systematic search in this field. It took another 17 years to extend the series of cumulenes still further. This was done by Kuhn and coworkers[1] who synthesized tetraphenylhexapentaene, which turned out to be almost as stable as its forerunner. However, an accumulation of more than five double bonds proved to be difficult. Such compounds can so far only be obtained in solution.

B. Naturally Occurring Cumulenes

Although the history of cumulenes begins as early as 1864, the right of priority has to be given to nature. In 1906, Semmler[11] had already suggested that carlina oxide, which he had obtained from the essential oil of *Carlina acaulis*, should have an allenic formula. However, this was later shown to be the isomeric acetylene[12]. In 1924, Staudinger and Ruzicka[13] proposed formula **4** for pyrethrolone, a component of pyrethrins contained in the blossoms of composite *Chrysanthemum cinerariifolium.*

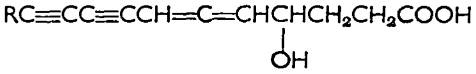


(4)

After a considerable amount of work, La Forge and Acree in 1942[14] confirmed that pyrethrolone really has an allenic side-chain. This was admitted only tentatively because the occurrence of cumulenes in nature was unheard of at that time. Ten years later, Celmer and Solomons[15] produced conclusive evidence that the highly unstable antibiotic mycomycin (**5**) contains an allenic grouping to which it owes its optical activity. On treating **5** with alkali, it undergoes a retro-propargylic rearrangement to the optically inactive isomycomycin (**6**).

$$\underset{(\mathbf{5})}{HC{\equiv}CC{\equiv}CCH{=}C{=}CHCH{=}CHCH{=}CHCH_2COOH} \xrightarrow{OH^-} \underset{(\mathbf{6})}{CH_3C{\equiv}CC{\equiv}CC{\equiv}CCH{=}CHCH{=}CHCH_2COOH}$$

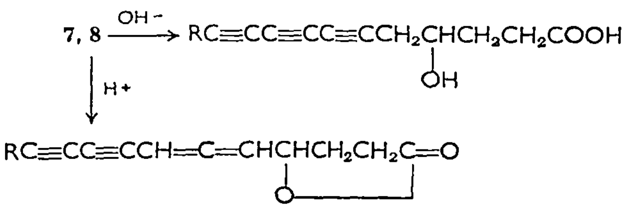
From *Basidiomycetes*, Jones and colleagues isolated similar compounds (**7** to **10**), whose high optical activity was again partly due to asymmetrically substituted allenes. These acids are accompanied



$$RC{\equiv}CC{\equiv}CCH{=}C{=}CH\underset{OH}{\underset{|}{C}}HCH_2CH_2COOH$$

[**7**, R = H (nemotinic acid); **8**, R = CH_3 (odyssic acid).]

by their lactones [nemotin (**9**, R = H) and odyssin (**10**, R = CH_3)]. Alkali treatment also caused the allenes to rearrange to acetylenes with partial loss of optical activity[16,17].



(**9**, R = H; **10**, R = CH_3)

Even a terminal allene grouping was encountered in drosophilin (**11**) whose natural precursor must be the acetylenic isomer drosophilin-C (**12**), because the rearrangement **12** → **11** could also be accomplished *in vitro*[18]. Another antibiotic which has allenic structure is marasin (**13**) occurring in *Marasmius ramealis*[19].

$$HC\equiv CCH_2C\equiv CC\equiv CCH{=}CHCH_2COOH \longrightarrow$$

(12)

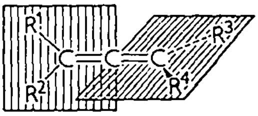
$$H_2C{=}C{=}CHC\equiv CC\equiv CCH{=}CHCH_2COOH$$

(11)

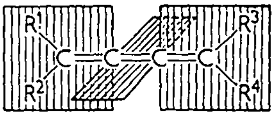
$$HC\equiv CC\equiv CCH{=}C{=}CHCH_2CH_2OH$$

(13)

Although these highly unsaturated compounds are exceedingly unstable and difficult to handle, their constitution can be established in a rather straightforward manner. Catalytic hydrogenation affords the corresponding saturated aliphatic chain which is identified by comparison methods. The number of moles of hydrogen consumed indicates the total number of multiple bonds and the study of the ultraviolet and infrared spectra permits the assignment of the correct distribution of multiple bonds. Closely related substances obtained synthetically are used to support the interpretation of the spectra.



(14)



(15)

The main stimulation in the cumulene field proved to be van't Hoff's theory of the tetrahedral carbon valences[20]. According to this, in cumulenes with an even number of double bonds the four substituents must be arranged in two perpendicular planes (**14**), whereas in the case of an odd number of double bonds the substituents must be in the same plane (**15**). This implies that members of the former type (allenes, pentatetraenes, *etc.*) must occur in optically active forms if $R^1 \neq R^2$ and $R^3 \neq R^4$ and provided that free rotation about the double bonds is sufficiently blocked. On the other hand, in the series with an odd number of double bonds (butatrienes, hexapentaenes, *etc.*), *cis–trans* isomerism should be found under the same conditions. These predictions have both been verified. Optically active allenes were obtained in 1935[21,22] and *cis–trans* butatrienes in 1954[23]. Details will be given later.

With respect to stereoisomerism, cumulenes can therefore be subdivided into two distinct series: those which exhibit optical activity and those which show *cis–trans* isomerism. This division is also justified from the point of view of the possibilities for syntheses. For cumulenes with an odd number of double bonds, there exist standard methods which make possible the synthesis of molecules with as many as nine cumulated double bonds, whereas in the other series it is difficult to think of a general synthetic scheme, each member seeming to have its own particular features.

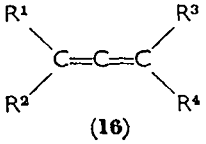
The excellent review article by Cadiot and colleagues[24] has been found most valuable for the preparation of the present chapter.

II. CUMULENES WITH AN EVEN NUMBER OF DOUBLE BONDS

Only allenes and pentatetraenes have so far been prepared, and the latter only very recently. The pentatetraenes are still quite stable so that there is hope for the future syntheses of heptahexaenes.

A. Allenes

In this section, methods of preparation will first be discussed and the most important representatives collected in tables. This will be followed by a discussion of the general properties of allenes, but theoretical considerations are deferred to section IV which gives a survey of the molecular spectra of all the cumulenes and their interpretation. In the present section, molecules of the general type **16** will be considered.

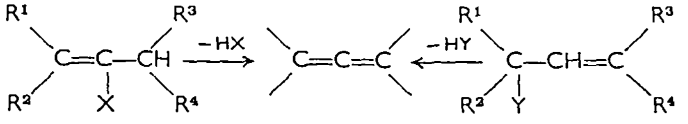


(**16**)

1. Methods of preparation

These may be roughly divided into seven different types on the basis of the starting materials which are suitable for allene synthesis.

a. Elimination from halo- and hydroxypropenes. As may be seen from equation (1), two types of halo- or hydroxypropenes have to be considered (**17** and **18**). The elimination of HX from the 2-halopropenes (**17**) is usually brought about by the action of alcoholic



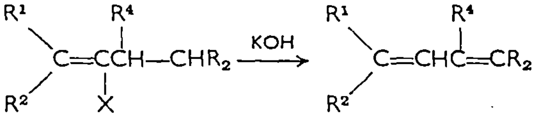
(**17**, X = halogen) (**18**, Y = halogen, hydroxy, alkoxy) (1)

potassium hydroxide, but the reaction is not always satisfactory for the following reasons:

i. If $R^1 = H$ in **17**, then the expected allenes are contaminated with the isomeric acetylenes[e.g. 25, 26, 27, 35].

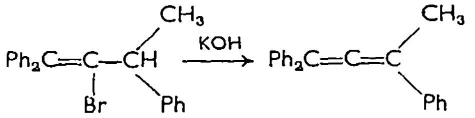
ii. If R^1 to R^4 in **17** are certain aromatic substituents then, on treatment with bases, stable carbanions may occur as intermediates which show no tendency to lose the halogen as X^- [28].

iii. If R^3 in **17** is of the form R_2CH ($R \neq H$), conjugated dienes (**19**) are obtained rather than allenes, due to prototropic rearrangement of the latter[29]. However, Ziegler's[30] triphenylmethylallene



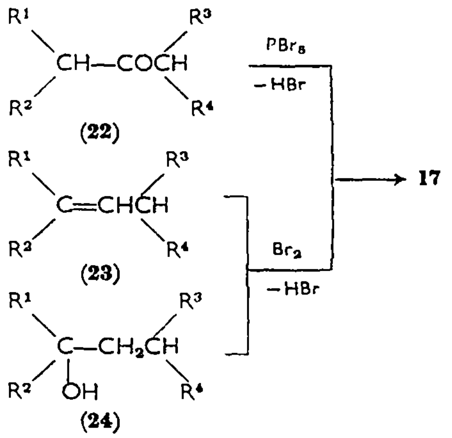
(**19**)

(**20**), which he prepared from the corresponding bromopropene **21**, is stable. Evidence for the allenic structure was indicated by ozonization which gave benzophenone and acetophenone.



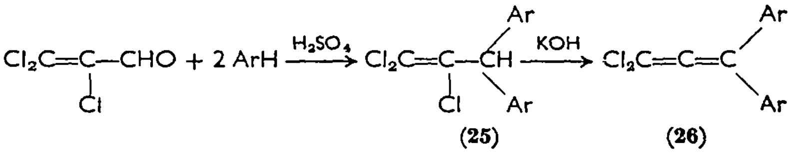
(**21**) (**20**)

Apart from these limitations, the method is very useful because the required halopropenes **17** are almost always readily available. There exist two general routes and a number of special procedures for their synthesis: (*i*) action of phosphorus pentahalide on substituted acetones **22**[5]; or (*ii*) bromination of propenes **23** or propanols **24** by the method of Ipatiew[31].

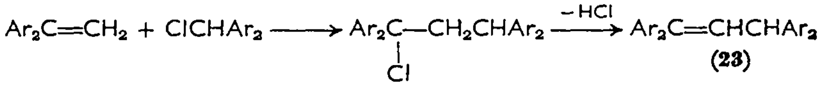


(2)

Roedig and colleagues[185] condensed trichloroacraldehyde with substituted benzenes and obtained diaryltrichloropropenes (**25**). On treatment with alkali, diaryldichloroallenes (**26**) are formed which tend to dimerize (see Table 5).

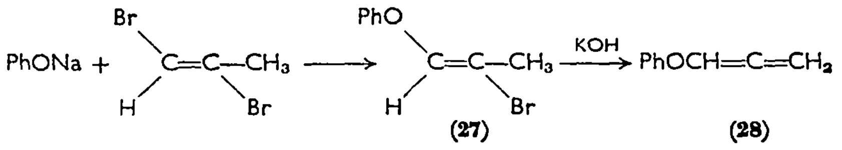


Asymmetric diarylethylenes have been found to add diarylhalomethanes to form tetraarylpropenes **23** (R^1 to R^4 = Ar) which can be converted to tetraarylallenes according to equations (2) and (1)[300].



$$Ar_2C{=}CH_2 + ClCHAr_2 \longrightarrow \underset{\displaystyle Cl}{Ar_2C}{-}CH_2CHAr_2 \xrightarrow{-HCl} \underset{\textbf{(23)}}{Ar_2C{=}CHCHAr_2}$$

1,2-Dibromopropene reacted with sodium phenolate to give phenoxybromopropene (**27**) which could be converted into phenoxyallene (**28**). Since *trans* elimination of HX from ethylenes is usually favored, the chances for formation of the isomeric acetylene could be expected to be lower[25] when hydrogen and bromine in **27** were in the *cis* position.



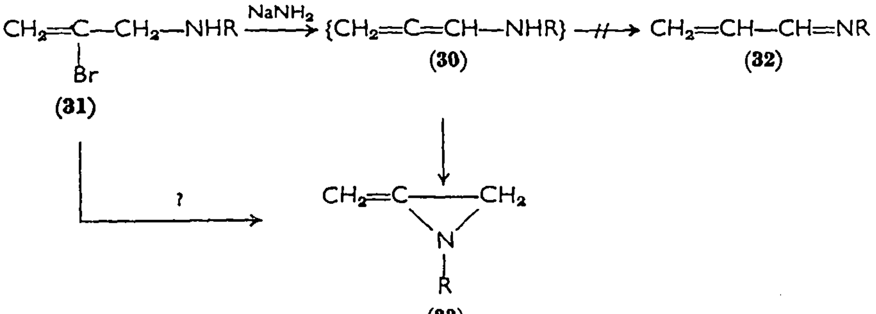
Arens[26] found spectroscopic evidence that alkoxyallenes may probably be synthesized along similar lines. Aliphatic allenes of the general type **29** can be built up using the route *via* the alcohols **24**[31].

$$R_2C{=}C{=}CH(CH_2)_nCHR_2$$

(**29**, R = alkyl; n = 1, 2, ...)

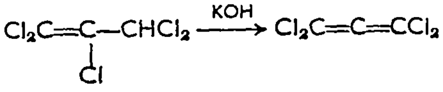
Allenedicarboxylic acid (**3**) is obtained in almost quantitative yield and free from the acetylenic acid **2** starting with acetonedicarboxylic acid according to equation (2)[5].

Aminoallenes **30** were assumed as intermediates in the elimination of HBr from the bromoallylamines **31**, which were reported to yield the allylidenimines **32**[33]. However, the latter have been shown, by means of infrared and nuclear magnetic resonance spectroscopy, as well as by degradation reactions, to possess a three-membered ring structure **33**, and received the name allenimines. It is conceivable that they are directly formed from **31** without involving the aminoallenes as precursors[34].



(**31**) (**30**) (**32**) (**33**)

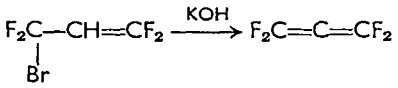
Tetrachloroallene can be prepared from pentachloropropene **34** in the gas phase by the action of KOH, but it dimerizes quickly on standing even in dilute solution. The existence of the monomeric tetrachloroallene has been proved by its very characteristic infrared spectrum[32].



$$Cl_2C{=}\underset{\displaystyle Cl}{\underset{|}{C}}{-}CHCl_2 \xrightarrow{KOH} Cl_2C{=}C{=}CCl_2$$

(**34**)

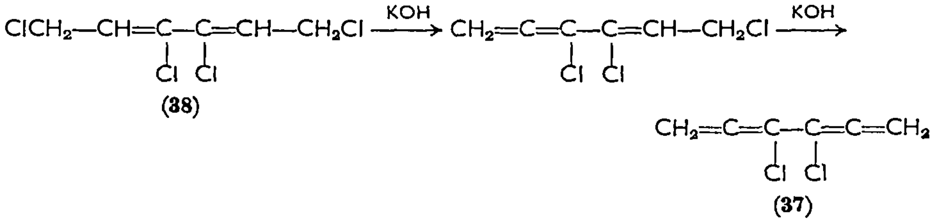
Returning to equation (1), the allyl-type propenes **18** will now be considered. If Y represents a halogen or (less frequently) an alkoxy group, then the elimination of HY has to be produced by means of a base. This means that the first attack is the abstraction of a proton from the double-bonded carbon atom, where it is usually very firmly attached. The method, therefore, has obvious limitations. Nevertheless, there are some cases where it proves useful. Tetrafluoroallene (**35**) is obtained from the bromopropene **36**, and does exist in monomeric form[35]. The synthesis of the conjugated diallene **37** has been



$$F_2\underset{\mathrm{Br}}{\underset{|}{C}}-CH=CF_2 \xrightarrow{KOH} F_2C=C=CF_2$$

(**36**) (**35**)

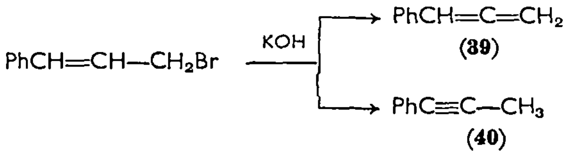
reported. It involves a twofold elimination of HCl from the tetrachlorohexadiene **38**, where the chlorine atoms in question occupy allylic positions[36]. Compound **38** is prepared by addition of chlorine to divinylacetylene, a process whereby allenes also may be formed, as will be seen later (section II.A.1.e).



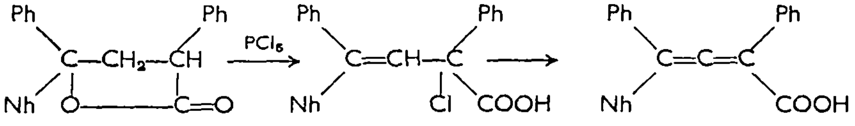
$$ClCH_2-CH=\underset{Cl}{C}-\underset{Cl}{C}=CH-CH_2Cl \xrightarrow{KOH} CH_2=C=\underset{Cl}{C}-\underset{Cl}{C}=CH-CH_2Cl \xrightarrow{KOH} CH_2=C=\underset{Cl}{C}-\underset{Cl}{C}=C=CH_2$$

(**38**) (**37**)

Phenylallene (**39**) has been found among the products when phenylallyl bromide is treated with KOH. The main contaminant is the isomeric acetylene **40**[37]. Pure **39** can be obtained by other methods to be mentioned later in this section.

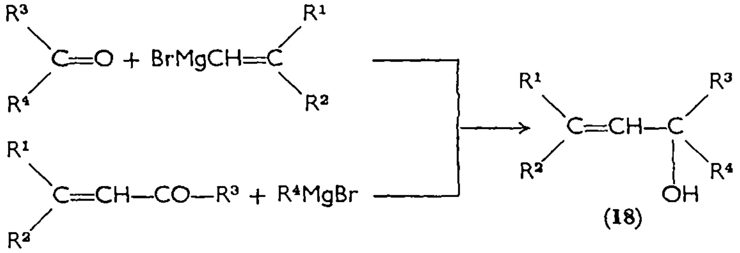


The synthesis of the triarylallenecarboxylic acid (**41**) must also occur *via* an elimination of halogen from the allyl position; it is reasonable to assume that the hydrogen atom adjacent to the carbonyl group is replaced by chlorine, leading to **42** as intermediate. The preparation



(Nh = α-naphthyl) (**42**) (not isolated) (**41**) of this acid was attempted in 1910[38] with the purpose of resolving it into optically active components, a problem which was solved 25 years later[22] (see section II.A.2.b).

Of more general applicability is the elimination of water from allyl alcohols (**18**, Y = OH) which is usually carried out by acids, or thermally. The hydroxy group is very mobile, especially in the case of tertiary allyl alcohols. The method is particularly useful when all four substituents are aromatic. It was first applied to the synthesis of tetraphenylallene by Vorländer and Siebert in 1906[39], and since then a great many tetraarylallenes have been obtained by this procedure[40,41,42]. The allyl alcohols **18** can be built up by straightforward Grignard syntheses of the type shown in equations (3)[40] or (4)[39,41].

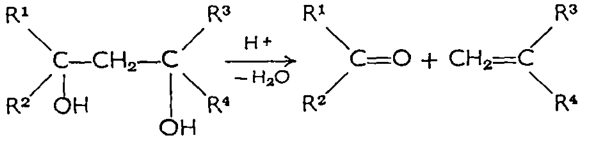


(18)

(3)

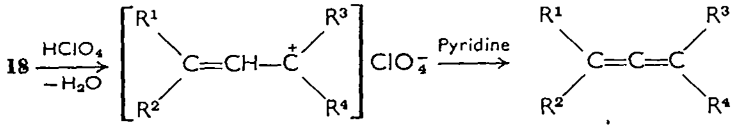
(4)

It is interesting to note that the propanediols **43** have been found to fragment on attempted elimination of water, without involving the allyl alcohols **18** as intermediates[42]. Extensive work by Ziegler and



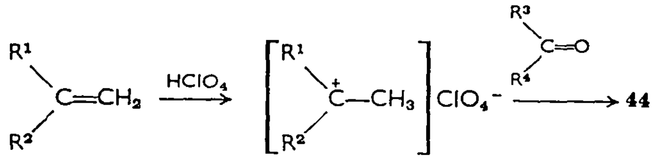
(43)

his group[40,43] and Wizinger[44] revealed that, if the allyl alcohols **18** are properly substituted (*e.g.* with *p*-methoxyphenyl or *p*-aminophenyl), then stable carbonium salts **44** can be isolated as precursors of the allenes **16**. By Wizinger's method it is possible to synthesize



(44) **(45) = (16)**

directly the carbonium salts **44** (equation 5). On treatment with pyridine they lose one molecule of acid and give rise to the desired allenes **16**. These exist only if none of the substituents is a hydrogen atom, otherwise only dimeric allenes of as yet unknown constitution arise. Wizinger and colleagues[45] also prepared carbonium salts **46**

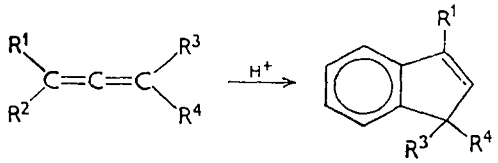


which are the vinylogs of **44**; on treatment with pyridine, the expected allenes **47** polymerized, except in the case when R = $CH_3OC_6H_4$—[297].

$$[R_2\overset{+}{C}\text{—}CH{=}CHCH{=}CR_2]X^- \xrightarrow{\text{Pyridine}} R_2C{=}C{=}CHCH{=}CR_2$$

(46) **(47)**

The tetraarylallenes (**16**, R^1 to R^4 = Ar) are transformed by acids into triarylindene derivatives **48**. Because of this, care must be taken that the allyl alcohols **18** are not exposed to acids for too long periods during the preparation of allenes[39,299].

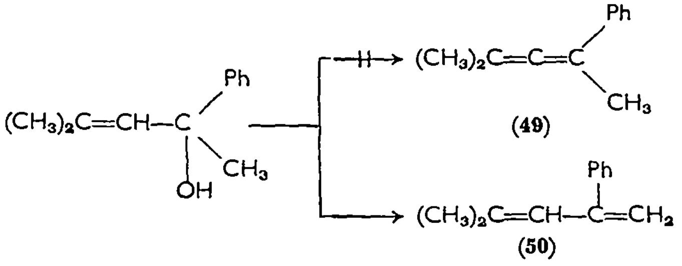


(45) **(48)**

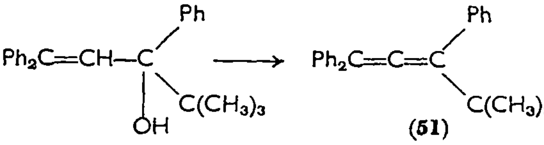
Aliphatic instead of aromatic substituents render the allyl alcohols **18** (R^1 to R^4 = alkyl) unsuitable as allene precursors because conjugated dienes are formed rather than cumulated ones. Only *t*-butyl groups permit the extension of the method into the series of aliphatically substituted allenes. Thus Klages thought[46] he had prepared trimethylphenylallene (**49**) but this was later shown to be the butadiene **50**[47]. On the other hand, triphenyl-*t*-butylallene (**51**) could easily be obtained by this procedure[48].

In conclusion, it can be said that the elimination method for allene syntheses is convenient because the starting materials **17** and **18** are readily available; but its applicability is limited by a number of requirements that have to be fulfilled by the substituents R^1 to R^4.

The reverse situation prevails in the dehalogenation method where there are practically no restrictions as to the substituents, but the starting materials are more difficult to prepare.

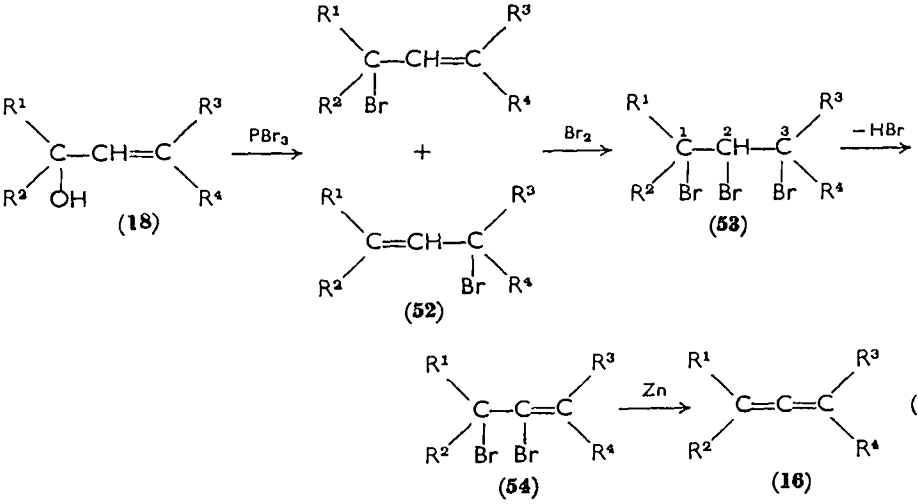


(49)
(50)



(51)

b. Dehalogenation of dihalopropenes. In 1927 Bouis[49] devised a general method (whose foundations go in fact back to Gustavson[50] in 1888) which could, in principle, be applied to the synthesis of any desired allene. The vital step consists in a reductive elimination of two vicinal halogen atoms which leaves the position of the double bond unaltered. Allyl alcohols **18** are transformed into the allyl halides **52**; subsequent addition of halogen furnishes a trihalopropane **53** and this, on elimination of HX, yields a dihalopropene **54** which is dehalogenated by zinc to the desired allene.



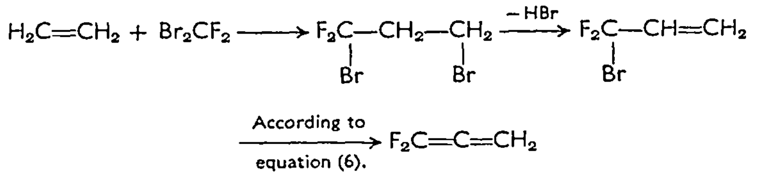
(18)
(52)
(53)
(54)
(16)
(6)

It is worth pointing out that irrespective of the nature of the substituents R^1 to R^4, the elimination of HBr from **53** will nearly always produce the desired dihalopropene **54** rather than an unwanted double bond in one of the substituents. This is due to the fact that the hydrogen at $C_{(2)}$ in **53** is the most mobile one.

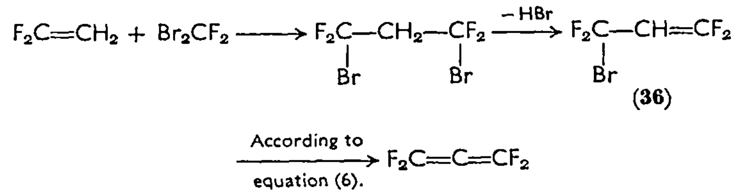
This method has been widely applied for the synthesis of various 1-alkyl- and 1,3-dialkylallenes[49,50,51]. Allene itself (C_3H_4) is most conveniently prepared from 2,3-dibromo- or 2,3-dichloropropene. Very recently, Slobodin and Khitrov[52] reported a 98% yield of pure allene by carrying out the dehalogenation of dibromopropene (**54**, R^1 to R^4 = H) in butyl acetate or isoamyl acetate rather than in an alcoholic solvent. Earlier procedures[53,54] using alcoholic solvents always suffered from the fact that the allene contained varying amounts of 2-bromopropene which is difficult to remove completely and which affects the polymerization of the allene.

The five different deuterated allenes have all been synthesized by this method. They are important for assigning the various spectral transitions to the normal modes of vibration of the allene molecule. Starting materials are appropriately substituted polychloropropanes which are converted into the corresponding deuterated 2,3-dichloropropenes by reaction with zinc in heavy water; on dehalogenation, the required deuteroallenes are produced[54,55].

Difluoro- and tetrafluoroallene were obtained by this method, although in the latter case the dehydrohalogenation mentioned previously is superior[35,56].



$$H_2C{=}CH_2 + Br_2CF_2 \longrightarrow \underset{Br}{F_2C}\text{—}CH_2\text{—}\underset{Br}{CH_2} \xrightarrow{-HBr} \underset{Br}{F_2C}\text{—}CH{=}CH_2 \xrightarrow[\text{equation (6).}]{\text{According to}} F_2C{=}C{=}CH_2$$



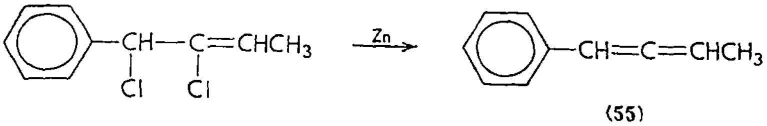
$$F_2C{=}CH_2 + Br_2CF_2 \longrightarrow \underset{Br}{F_2C}\text{—}CH_2\text{—}\underset{Br}{CF_2} \xrightarrow{-HBr} \underset{Br}{F_2C}\text{—}CH{=}CF_2 \xrightarrow[\text{equation (6).}]{\text{According to}} F_2C{=}C{=}CF_2$$

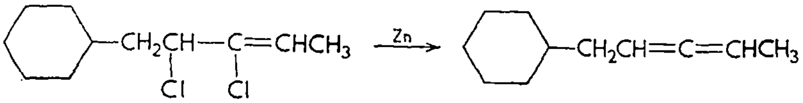
(36)

(35)

La Forge and Acree prepared various model substances for pyrethrolone **4** (*e.g.* **55** and **56**). Here, it was important that no shift of the double bonds occurred since this would have produced conjugated dienes[57].

Phenylallene was prepared[58] from phenyldichloropropene in better yield than by the earlier mentioned process, but an even better process is the anionotropic rearrangement of phenylpropargylic halides (Table 2, **75b**).

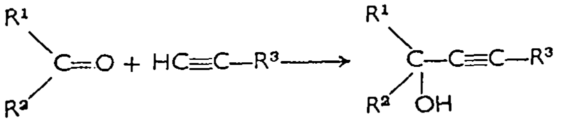

(55)


(56)

The great advantages of the method just discussed are its general applicability and the high purity of the products; however, it suffers from the disadvantage that many steps are necessary to reach the required 2,3-dihalopropenes. It was therefore gratifying that in the 1940's a more convenient (even if less general) procedure was developed.

c. Reduction of halopropynes and -allenes. Propargylic halides **58** are readily available from the reaction of various terminal acetylenes with carbonyl compounds followed by substitution[59]. In 1940 Ginzburg[60] found that these compounds easily exchange halogen with hydrogen on treatment with a zinc–copper couple in alcohol[64], and in the majority of the cases a simultaneous propargylic rearrangement produces the corresponding allenes **60**. This rearrangement may in some cases already occur on esterification of the propargylic alcohols **57**, resulting in allenic halides **59**. However, the latter behave exactly like their acetylenic isomers on subsequent reduction[60].

The ratio of allene **60** to acetylene **61** produced in this reaction depends upon the substituents. Primary halides (**58**, $R^1 = R^2 = H$) usually give acetylenes, whereas secondary and tertiary halides very often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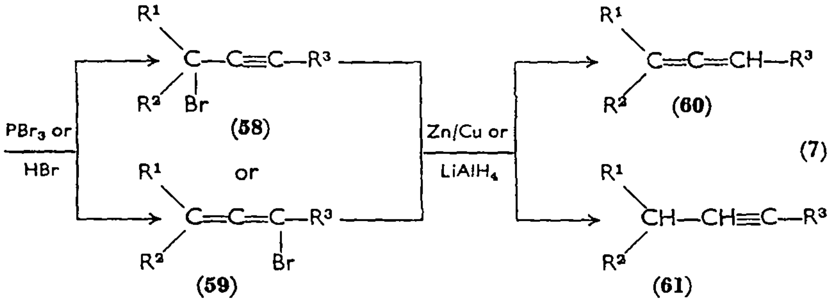
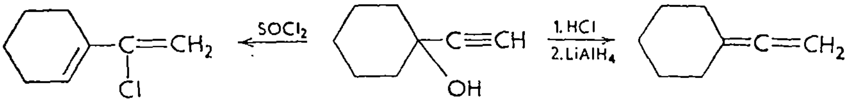


(58) (59) (60) (61) (7)

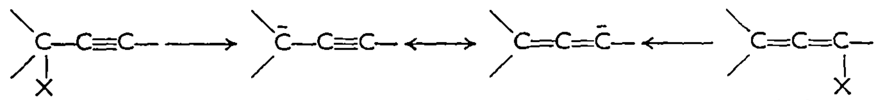
give allenes only[62,63]. Unfortunately, the use of tertiary halides (**58**, $R^1, R^2 \neq H$) is hampered by their instability. In some cases this inconvenience can be overcome if no attempt is made to isolate these halides in a pure state prior to their reduction. Thus 1-chloro-1-ethinylcyclohexane cannot be isolated from the reaction of the corresponding alcohol **62** with thionyl chloride, since this produces 1-(chlorovinyl)-1-cyclohexene. However, treatment of **62** with HCl followed immediately by reduction afforded pentamethyleneallene **63**[64].



(62) (63)

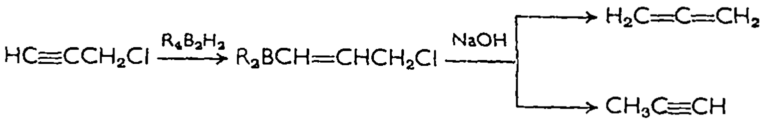
As has been shown by Wotiz, and Bailey and Pfeifer[64], the zinc–copper couple can be replaced by lithium aluminum hydride without seriously affecting the yields of allenes.

The mechanism of this reaction does not seem to be fully understood yet[62]. It is clear, however, that the halides **58** and **59** do not rearrange into one another prior to reduction[63]. Rather, it must be assumed that both halides react *via* a common intermediate when being converted into allenes. The assumption that this might be the anion **64** seems logical but has no experimental foundation[62]. On the other hand,



(58) (64a) (64b) (59)

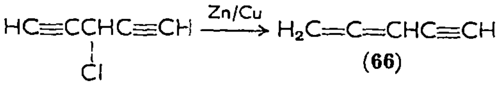
when tetraalkyldiborane was used as a reducing agent for propargyl chloride it was found that the borane added to the triple bond first. Alkali converted this adduct to a mixture of allene and propyne (ratio 20 : 1)[303]. However, it is not likely that the reduction with the zinc–copper couple follows a similar mechanism.



$$HC{\equiv}CCH_2Cl \xrightarrow{R_4B_2H_2} R_2BCH{=}CHCH_2Cl \xrightarrow{NaOH} H_2C{=}C{=}CH_2 + CH_3C{\equiv}CH$$

The high selectivity of this method was demonstrated when Jones and coworkers[65] were able to obtain pentatriene (**65**) and pentadienyne (**66**).

$$HC{\equiv}CCH{=}CHCH_2Cl \xrightarrow{Zn/Cu} \underset{(65)}{H_2C{=}C{=}CHCH{=}CH_2}$$



$$\underset{\displaystyle Cl}{HC{\equiv}CCHC{\equiv}CH} \xrightarrow{Zn/Cu} \underset{(66)}{H_2C{=}C{=}CHC{\equiv}CH}$$

It seems established that neither an allenic nor an acetylenic system is attacked by these reducing agents once it has been formed from its halogen-containing precursors **58** or **59**, provided that no hydroxy groups are in the α-position[66]. It would have been valuable had the propargylic alcohols **57** been capable of giving allenes because of the previously mentioned difficulties in esterifying them. However, Bailey and Pfeifer[66] showed that this is not the case. Thus, while 1-chloro-4-hydroxybutyne loses its halogen on reduction and furnishes the allenic alcohol **67**, the same treatment of dihydroxybutyne leaves the hydroxy groups untouched but readily brings about hydrogenation of the triple bond. An obvious explanation for these findings is to

$$ClCH_2C{\equiv}CCH_2OH \xrightarrow{LiAlH_4} \underset{(67)}{CH_2{=}C{=}CHCH_2OH}$$

$$HOCH_2C{\equiv}CCH_2OH \xrightarrow{LiAlH_4} HOCH_2CH{=}CHCH_2OH$$

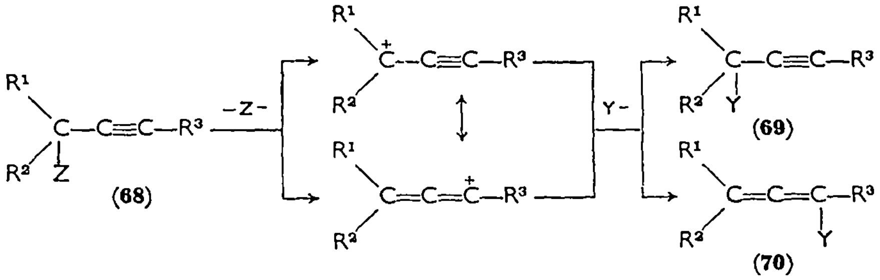
assume that the hydroxy groups are metalated before reduction takes place, so that they can no longer function as electronegative substituents.

The limitations of the allene synthesis just discussed lie, of course, in the fact that mixtures of allenes and acetylenes may be produced which are often difficult to separate, and, as is obvious, no tetrasubstituted allenes are obtainable.

d. Propargylic rearrangement. This term is understood here to mean a conversion of a propyne into a propadiene *via* an ionic mechanism. In many cases this involves a propargyl ion as a transition state, whose electron distribution will often be closer to that of a propadiene ion. Conditions which enable a propargylic species to dissociate should therefore bring about the isomerization.

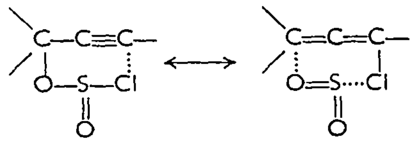
These syntheses may be subdivided into those rearrangements with a propargyl cation as a likely transition state and into those where the transition state is probably a propargyl anion, although there is not always general agreement on the mechanism of the rearrangement in the literature.

Cationic transition state—The basic reaction is pictured in equation (8) and Table 1 collects special examples.



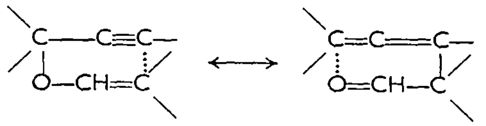
(8)

Meyer and Schuster[67] were the first to observe an anionotropic rearrangement of a propargyl alcohol, catalyzed by acids. However, their allenol (**70a**, Table 1) ketonized immediately. This Meyer–Schuster rearrangement is very useful for the syntheses of α,β-unsaturated ketones[68] and aldydehes[69]. The transition state is most likely to be the propargyl cation. However, in most of the other examples quoted in Table 1, this is not certain. For instance, esterification of propargylic alcohols by means of thionyl chloride (or phosphorous tribromide) is assumed to go *via* the chlorosulfite (or dibromophosphite) ester **71**[70]. Here the transition state is best pictured by **71** rather than by a free propargyl cation. Strong support for this view comes from the observation that optically active propargyl alcohol leads to an active chloroallene[71].



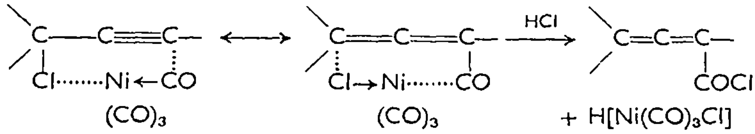
(71)

The same arguments apply to the transition state of the Claisen-type rearrangements of **68p** to **68r**, which should be like **72**[72].



(72)

Favorskaya's observations that certain propargyl halides rearrange to haloallenes only in the presence of copper halides can again be explained on the basis of a six-membered cyclic transition state which involves the metal. The same will be true for Jones' allenecarboxylic acid syntheses (**70n** and **70o**) with nickel carbonyl; and the reaction of propargyl halides with Grignard reagents (**70u** to **70ff**), discovered by Sacharowa. One example of these metal-containing transition states is pictured in **73**. It is striking that the quantity of the isomeric



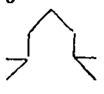
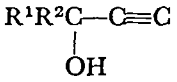
(73)

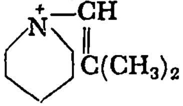
acetylene **69** produced according to equation (8) is always far less than the quantity of allene. This also supports the importance of the cyclic transition state which is, of course, not capable of giving rise to acetylenes.

The assets of the rearrangement based on equation (8) are that haloallenes become readily accessible, and also that almost any alkyl or aryl group may be introduced as a last step of the allene synthesis, using the elegant variation with the Grignard reagents. An unfavorable aspect is that the allenes are often obtained in an impure state only, owing to side-reactions of the relatively unstable propargyl halides.

Anionic transition state—Propargylmetal compounds will be more or less polarized in the direction of a propargyl anion. Prevost and coworkers investigated a number of propargyl Grignard reagents by infrared spectroscopy and concluded that there is only one propargylmagnesium bromide, and that this is obtained irrespective of whether it is prepared from bromopropyne or from bromoallene. The infrared band of this Grignard reagent lies close to the region where allenes

TABLE 1. Propargylic rearrangements according to equation (8).

Example	Substituents			Migrating groups		Yield of allene **70** (%)	Remarks	Reference
68	R¹	R²	R³	Z	Y			
a[a]	Ph	Ph	Ph	OH	OH	—	Ketonizes; with H_2SO_4	67
b, c, d	CH_3, C_2H_5, C_3H_7	H	H	OH	Cl	30	With $SOCl_2$	73
e	CH_3	CH_3	H	OH	Cl	15	With $SOCl_2$	
f	CH_3	$C(CH_3)_3$	H	OH	Cl	47	With $SOCl_2$	70, 71
g			H	OH	Cl	83	With $SOCl_2$	70, 71
h			 $R^1R^2C(OH)—C\equiv C$	OH	Br	71	With PBr_3	74
i	*o,o*-$C_6H_4C_6H_4$[b]		H	OH	Cl	55	With $SOCl_2$	69
j	H	H	H	Br	Br	65	Cu_2Br_2	75
k	CH_3	CH_3	H	Cl	Cl	33	HCl, Cu_2Cl_2	76, 77
l	CH_3	$C(CH_3)_3$	H	OH	Cl	88	HCl, Cu_2Cl_2	78
m	H	H	C_4H_9	Cl	COOH	38	With $Ni(CO)_4$ + HCl	79
n	CH_3	CH_3	H	Cl	COOH	34	With $Ni(CO)_4$ + HCl	79
o	Ph	H	H	Cl	COOH	12	With $Ni(CO)_4$ + HCl	79

p, q	H, CH_3	H	H	$OCH{=}C(CH_3)_2$	$C(CH_3)_2CHO$	—	Claisen rearrangement	72
r	H	H	H		$C(CH_3)_2CHO$	—	Enamine salt; Claisen rearrangement	80
s	CH_3	CH_3	H	$OC(=O)CH_2COCH_3$	CH_2COCH_3	—	Ketone splitting of acetoacetic ester	81
t	CH_3	CH_3	H	Cl	$OP(OC_2H_5)_2$	30	With $P(OC_2H_5)_3$	82
u^c	H	H	H	Br	$H_2C{=}CH$	25	10% acetylene	83
v^c	H	H	H	Br	C_4H_9	—	No acetylene	84, 85
w^c	H	H	H	Br	C_5H_{11}	—	No acetylene	84, 85
x^c	H	H	H	Br	$C_{12}H_{25}$	—	No acetylene	84, 85
y^c	H	H	H	Br	Ph	32	Best synthesis; 48% acetylene	84, 86
z^c	H	H	C_4H_9	Br	C_2H_5	25		87
aa^c	CH_3	CH_3	CH_3	Cl	CH_3	50		88
bb^c	CH_3	CH_3	CH_3	Cl	Ph	40		88
cc^c	CH_3	C_4H_9	CH_3	Cl	CH_3	35	35% acetylene	88
dd^c	CH_3	C_4H_9	CH_3	Cl	Ph	36	No acetylene	88
ee^c	CH_3	C_4H_9	H	Br	CH_3	95	No acetylene	304
ff^c	CH_3	C_2H_5	H	Br	C_2H_5	95	No acetylene	304

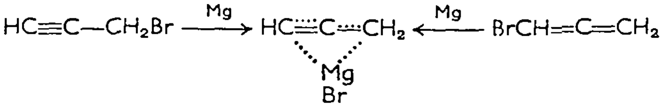
---

[a] These should be read as example **68a**, **68b**, *etc.*, and similarly in the tables following.

[b] *o,o*-$C_6H_4C_6H_4$ indicates the biphenylene radical.

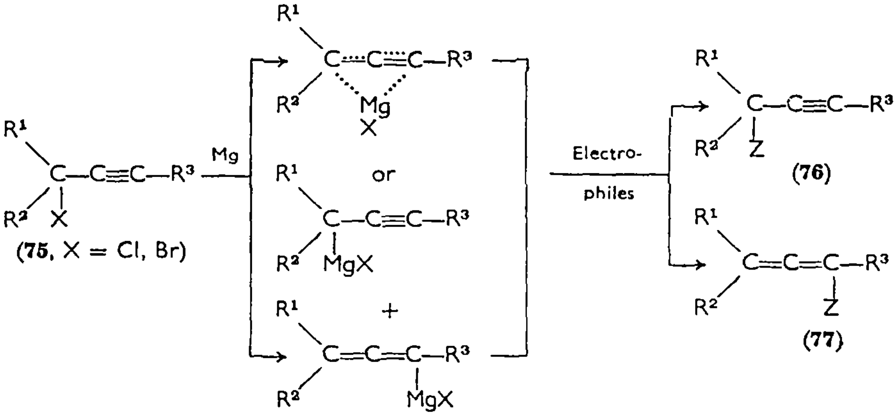
[c] Examples **u** to **ff** are reactions of YMgBr with **68**.

normally absorb[89]. Perhaps a formula like **74** is an adequate description of the electronic ground state. However, most of the Grignard



(**74**)

reagents from substituted propargyl halides are actually mixtures of two different compounds (as was revealed by the infrared spectrum); one is largely allenic and the other more propynic, and they are formed simultaneously from the same parent halide. The allene synthesis from propargyl Grignard reagents can be generalized as in equation (9); Table 2 records some examples.



(9)

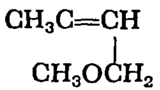
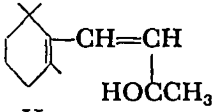
Although propargylmagnesium bromide has been found to have an electron distribution which is close to an allene, it reacts with carbonyl compounds to give acetylenic alcohols only (**76a**, Table 2). It has been shown that whenever allenes are produced, this is due to a subsequent prototropic rearrangement of **76a**. On the other hand propargyl Grignard reagents, which exist as acetylenes according to their infrared spectrum, furnish allenes on condensation with carbonyl compounds. This odd behavior has been explained on the basis of a cyclic electron-transfer mechanism (p. 1050). Whether the metal compound of a propargyl halide **75** is allenic or propynic depends entirely upon the bulk and the electronegativity of the substituents R^1 to R^3 in **75**[89,305]. If this theory is correct, then the allenes **77r** and **77s** must be due to a prototropic rearrangement of the acetylenes **76r** and **76s**, and they should be recorded in Table 3.

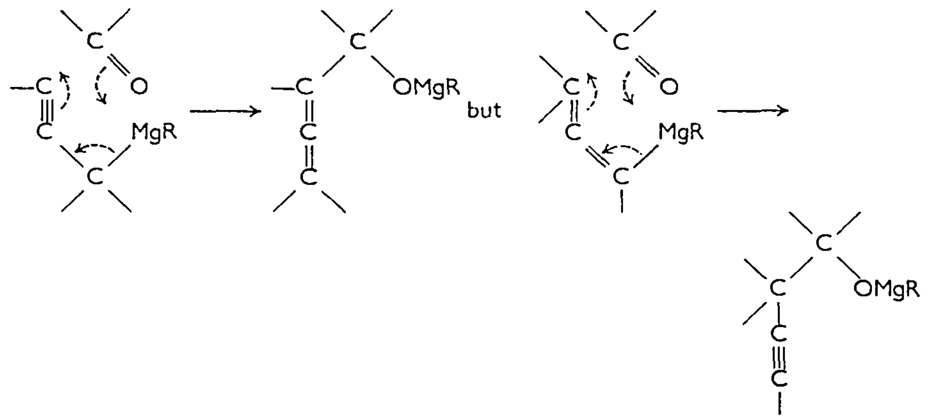
Table 2. Allene syntheses according to equation (9).

Example	Substituents			Electrophile	Substituent Z	Yield %		Remarks	Reference
75	R^1	R^2	R^3			Allene **77**	Acetylene **76**		
a	H	H	H	R^4R^5CO	R^4R^5COH	0	50–90	Any carbonyl compounds	89, 90, 100, 101, 102
b	Ph	H	H	H_2O	H	25	5	Acetylene easy to remove	86
c	H	H	Ph	H_2O	H	8	10	Acetylene difficult to remove	91
d	H	H	Ph	CO_2	COOH	—	—	Not isolated	91
e	H	H	CH_3	$PhCON(CH_3)_2$	PhCO	32	30		92, 93
f	CH_3	H	CH_3	$PhCON(CH_3)_2$	PhCO	55	—		92, 93
g	H	H	C_4H_9	$PhCON(CH_3)_2$	PhCO	20		**76** unstable	92, 93
h	CH_3	H	C_4H_9	CO_2	COOH	20	25	Resolved	94
i	CH_3	CH_3	C_4H_9	CO_2	COOH	9	0		94
j	H	H	C_3H_7	CO_2	COOH	38	16		95
k	H	H	C_4H_9	CO_2	COOH	41	9		95
l	H	H	C_6H_{11}	CO_2	COOH	23	13		95
m	C_4H_9	Ph	$C(CH_3)_3$	H_2O	H	82	0		96
n	C_4H_9	Ph	$C(CH_3)_3$	CO_2	COOH	72	0		96
o	C_4H_9	Ph	$C(CH_3)_3$	$ClCOOCH_3$	$COOCH_3$	64	0		96
p	Ph	Ph	$C(CH_3)_3$	H_2O	H	34	0		97
q	Ph	Ph	$C(CH_3)_3$	CO_2	COOH	34	0		97
r	H	H	H	$H_2C{=}CHCH_2Br$	$H_2C{=}CHCH_2$	49	21	Only in tetrahydrofuran or with Cu_2Br_2	98
s	H	H	H	$HC{\equiv}CCH_2Br$	$HC{\equiv}CCH_2$	35	5		99

TABLE 3. Allene syntheses according to equation (10).

Example (78)	Substituents R¹	R²	R³	Reaction conditions	Yield of allene **79** (%)	Unchanged acetylene (%)	Remarks	Reference
a	CH_3	CH_3	H	Alcoholic alkali 150°				105
b	H	H	H	325°, floridin	39	61	See also section II.4	106
c	H	H	H	Active carbon at 250°	19	—		133
d	C_2H_5	H	H	4 N alcoholic alkali; 180°	3	1	Equilibrium of 2 acetylenes and allene	107
e	H	H	C_2H_5	4 N alcoholic alkali; 180°	3	96		
f	C_5H_{11}	H	H	4 N alcoholic alkali; 180°	3	1	Equilibrium of 2 acetylenes and allene	108
g	H	H	C_5H_{11}		3	96		108
h	R^4R^5COH	H	H	Grignard reagents; see also **76a**	50	50	R^4,R^5 aliphatic substituents	89
i	Ar	H	Ar	Al_2O_3 column	20–75	—	Ar = Ph, BrC_6H_4, naphthyl or ferrocenyl	109 110
j	$CH_2{=}CH$	H	H	NaOH, 65°, 4h	64	4		111
k	$CH_3CH{=}CH$	H	H	NaOH, 65°, 4h	58	7		111
l	$C_2H_5CH{=}CH$	H	H	NaOH, 65°, 4h	58	4		111

m	$CH_2{=}CH$	H	$(CH_3)_2COH$	NaOH, 65°, 4h	88	—		111
n	$CH_2{=}CH$	H	C_2H_5CHOH	NaOH, 65°, 4h	85	—		111
o	$CH_3CH{=}CH$	H	C_2H_5CHOH	NaOH, 65°, 4h	83	—		111
p	 $CH_3\underset{CH_3OCH_2}{\underset{\vert}{C}}{=}CH$	H		NaOH, 65°, 4h	75	—	Carotene-type molecule	112
q	$C_4H_9C{\equiv}C$	H	H	NaOH, 20°, 3h	71	16		113
r	CN	H	H	Cu^I or NaOPh	80	—	Allenes are reactive dienophiles	114
s	CN	H	$H_2C{=}CHCH_2$	Cu^I or NaOPh	80	—		114
t	CN	H	$CH_3CH{=}CHCH_2$	Cu^I or NaOPh	80	—		114
u	CN	CH_3	CH_3	$NaOCH_3$	28	—		115
v	C_2H_5CO	H	H	Spontaneously				116
w	C_4H_9CO	H	H	Spontaneously				116
x	PhCO	H	H	Spontaneously			Not isolated in pure state	116
y	PhCO	H	PhCO	Spontaneously				93
z	$CH_3(CH_2)_5CO$	H	$(CH_2)_7COOH$	$NaHCO_3$; 3 h	100	—		100
aa	COOH	H	H	K_2CO_3	90	—		117
bb	COOH	H	H	$KHCO_3$	80	8		117
cc	COOH	H	Ph	K_2CO_3	52	40		118
dd	Ph	OH	$COOCH_3$	$(C_2H_5)_3N$	—	—	Allene ketonizes	119
ee	$PhCH_2$	Ph	H	Alcoholic alkali, 6 h	20	60		120

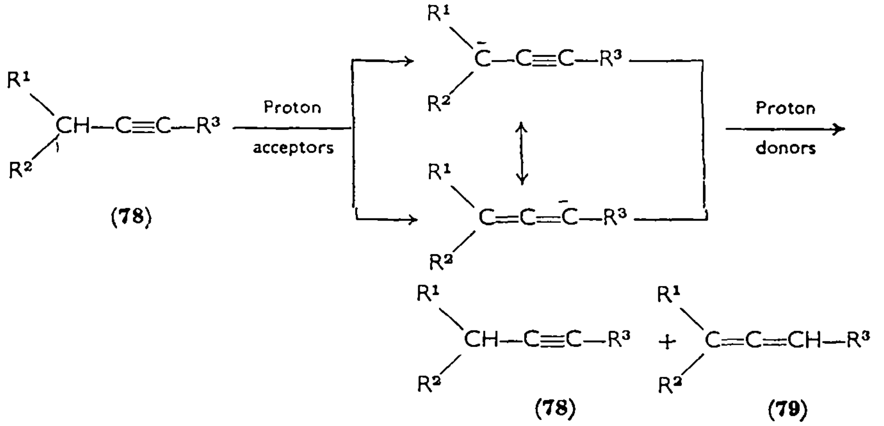


It is worth mentioning that propargylmagnesium bromide does not react with propargyl bromide or allyl bromide in ethereal solution. However, if tetrahydrofuran is added, condensation takes place immediately[98]. Propargylmagnesium bromide cannot therefore be prepared in tetrahydrofuran.

It is of interest that certain propargyl halides only react with magnesium if they are irradiated with sunlight[306].

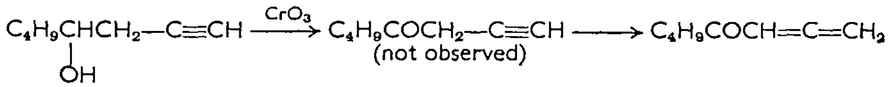
A final type of propargylic rearrangement (*via* an anionic transition state) is the prototropic isomerization of propynes in the presence of a base. Here it is justified to represent the transition state as the propargyl anion. It can be kept unchanged if the base is stronger than the propargyl anion, provided that no other reactions occur.

The basic reaction is given in equation (10) and Table 3 collects the more important examples of prototropic rearrangements of propynes to allenes.



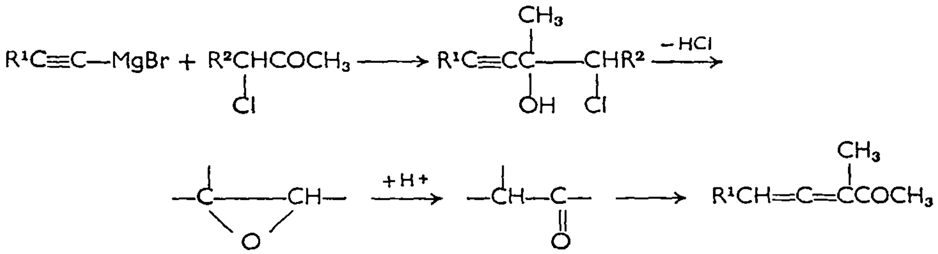
(10)

The ease of this rearrangement depends strongly upon the substituents R^1 and R^2 in **78**. The activating influence on the rearrangement increases according to the following series of substituents in the 1-position of the 2-propyne **78**: alkyl, carbinol, dialkyl, aryl, vinyl, ethinyl, cyano, carbonyl, carboxyl. Thus, secondary butynols **76a** (Table 2) are, in general, difficult to isomerize to allenes. However, if the alcoholic group is oxidized to the ketone function, then the rearrangement of the expected acetylenic ketones (**78v** to **y**) takes place spontaneously, even in an acidic medium.



$$\underset{\displaystyle OH}{C_4H_9CHCH_2{-}C{\equiv}CH} \xrightarrow{CrO_3} \underset{\text{(not observed)}}{C_4H_9COCH_2{-}C{\equiv}CH} \longrightarrow C_4H_9COCH{=}C{=}CH_2$$

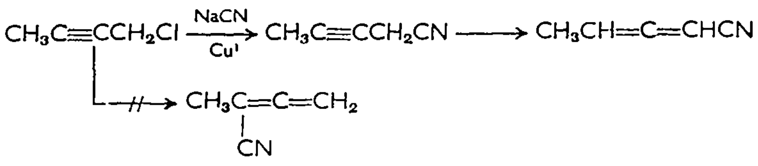
A similar observation was made by Perveev[103] and by Favorsky[104]: the epoxides **80** were opened and should have furnished the acetylenic ketones **81**. The latter, however, isomerized spontaneously to allenic ketones.



(80) **(81)**

$(R^1 = (CH_3)_2CH, (CH_3)_3C;\ R^2 = H, CH_3)$

The synthesis of the cyanides **79r** to **79u** represents an exception to reaction (8). For instance, 1-chloro-2-butyne is treated with alkali cyanide in the presence of copper salts. From the argument given on page 1043, formation of 1-cyano-1-methylallene *via* a cyclic transition state would be expected, but actually 3-cyano-1-methylallene is obtained, and this can only arise from 1-cyano-2-butyne by prototropy.



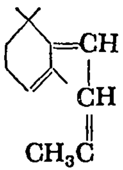
$$CH_3C{\equiv}CCH_2Cl \xrightarrow[Cu^I]{NaCN} CH_3C{\equiv}CCH_2CN \longrightarrow CH_3CH{=}C{=}CHCN$$

$$CH_3C{\equiv}CCH_2Cl \not\longrightarrow \underset{\displaystyle CN}{CH_3C}{=}C{=}CH_2$$

(not observed)

TABLE 4. Allene syntheses according to equation (11).

Example	Substituents				Y—X added	Yield of allene **84** (%)	Remarks	Reference
83	R^1	R^2	R^3	R^4				
a	H	H	H	H	HCl	30		122
b	H	H	H	H	HOR	—	**84b** only intermediate at −25°C	123
c	H	H	H	H	Br_2	70		124
d	H	H	H	H	$HN(CH_3)_2$	60	Presence of H_2O	125
e	H	H	H	H	ClPh	40	Radical addition?	126
f	H	H	H	H	ICl	25		127
g	CH_3	H	H	H	Br_2	84		128
h	CH_3	H	H	H	LiC_2H_5	72	−40°	129
i	CH_3	H	H	H	LiC_4H_9	16	40°	129
j	CH_3	H	H	H	LiC_4H_9	58	−40°	129
k	CH_3	H	H	H	LiC_4H_9-*t*	51	−40°	129
l	C_2H_5	H	H	H	LiC_2H_5	36	10°	129
m	C_2H_5	H	H	H	LiC_3H_7	74	−10°	129
n	C_2H_5	H	H	H	LiC_3H_7	81	−40°	129
o	C_2H_5	H	H	H	LiC_4H_9	16	30°	129
p	C_2H_5	H	H	H	LiC_4H_9-*t*	52	−40°	129

q	C_2H_5	H	H	H	$LiN(C_2H_5)_2$			129
r	t-C_4H_9	H	H	H	$LiN(C_2H_5)_2$			129
s	H	CH_3	H	H	HBr	10		130
t	H	CH_3	H	H	Ph_3CCPh_3	47	Radical addition	131
u	H	H	CH_3	H	ICl	10		127
v	H	H	Ph	H	Br_2			132
w	$H_2C{=}CH$	H	H	H	Cl_2	25		36
x	H	H	$H_2C{=}CH$	H	Cl_2	40	1,6-addition!	134
y	R^5R^6COH	H	H	H	$HN(CH_3)_2$	35	H_2O, pressure; R^5, R^6 = alkyl	135
z	H	H	CH_3CHOH	H	H_2	65	With $LiAlH_4$; the hydroxyl is vital	
aa	H	H	H_2COH	H	H_2	85		136
bb		H	CH_3CHOH	CH_3	H_2			137
cc	H	H	H	H	H_2		Fe catalyst; R^1 to R^4 also alkyl	138

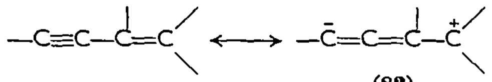
The synthesis of 1,3-diarylallenes has long been a problem[121]. The application of methods given in sections II.A.1.a and 1.b leads only to dimeric or polymeric material[109]. 1,3-Diarylpropynes (**78i**) are easily accessible, but they are resistant to rearrangement with alcoholic

$$Ar^1C{\equiv}CMgBr + C_7H_7SO_3CH_2Ar^2 \longrightarrow Ar^1C{\equiv}CCH_2Ar^2$$

alkali[121]. It was therefore gratifying that Jacobs[109,110] succeeded in enforcing the rearrangement on an alumina column.

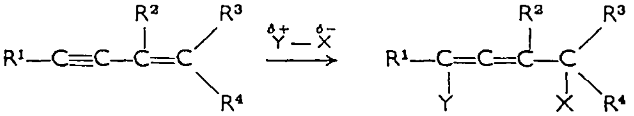
The prototropic propargylic rearrangement is thus only useful if the substituents in the 1-position of the 2-propyne are activating enough (at least an aryl group), otherwise only allene ⇌ propyne equilibrium mixtures will result, with very little allene.

e. 1,4-Addition to vinylacetylenes. Vinylacetylenes are usually slightly polarized in the sense of the mesomeric structure **82**. Most of the



(82)

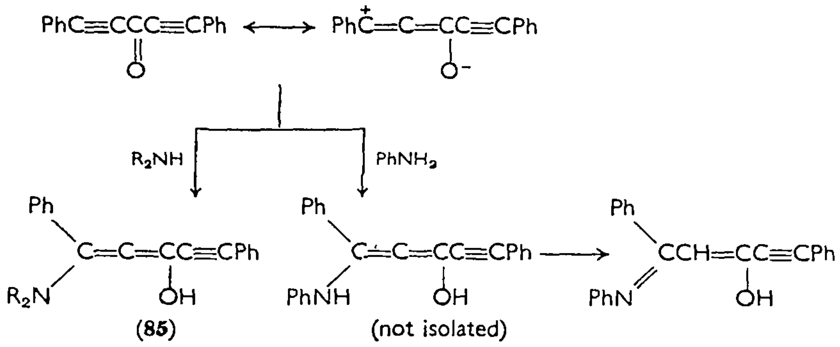
polar additions to vinylacetylenes go *via* structure **82** and furnish allenes. The reaction is pictured in equation (11) and examples of this elegant allene synthesis are collected in Table 4.



(83) **(84)** (11)

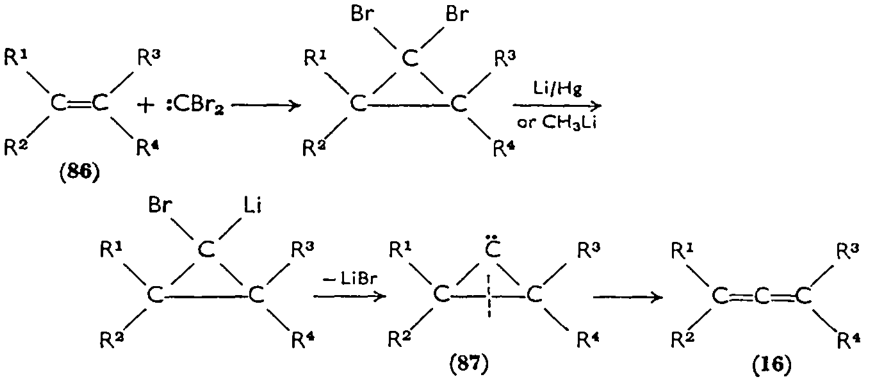
Carothers[122] in 1932 seems to have been the first to observe a 1,4-addition to vinylacetylenes when he synthesized **84a** (Table 4). In a patent published later, he and Berchet[139] reported a vast number of other 1-substituted buta-2,3-dienes all prepared from butadienyl chloride. Amongst them are buta-2,3-dien-1-yl alcohol, alkylethers, phenylether, esters of carboxylic acids, ester of chloroformic acid (and urethans thereof), amines, cyanide, thiocyanide, acetic acid, and all sorts of esters. Some of these products have medicinal properties; others may be used in the manufacture of dyes and pharmaceutical chemicals.

α-Acetylenic carbonyl compounds can also be regarded in a wider sense as vinylacetylenes. However, owing to the electronegative properties of oxygen, this system will be polarized in the opposite direction to the polarization of true vinylacetylenes as represented by **82**. In these carbonyl compounds, the addition will therefore be reversed, as shown by their reaction with primary and secondary amines[140]. The most striking property of the allenols **85** is that they do not ketonize, even on heating.



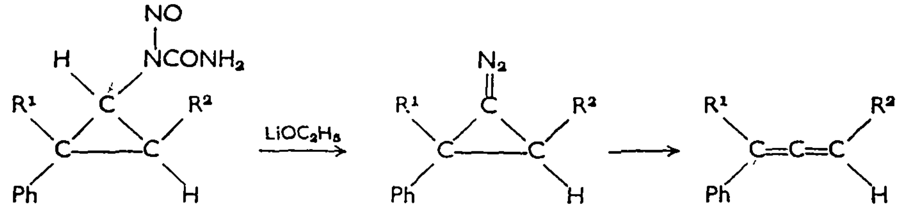
Certain hexapentaenes and butatrienes also furnish allenes on addition, as will be seen in Section III.

f. Doering's method; cyclic allenes. In 1958 Doering[141] found that dibromocarbene adds to olefins to form *gem*-dibromocyclopropanes. If the latter are dehalogenated by alkali amalgam, or better by methyllithium[142,143], then allene formation is observed. The question as to



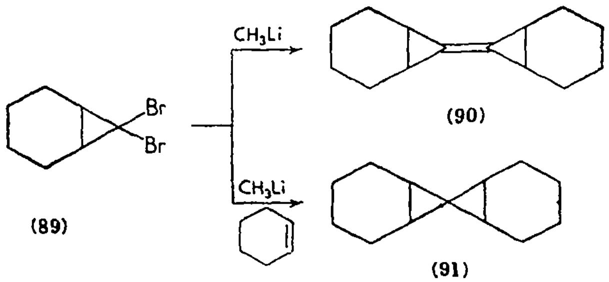
(12)

whether the cyclopropanecarbene **87** is an intermediate in this reaction has received some attention but remains, as yet, unanswered. At any rate, the diazocyclopropanes 88 also gave allenes after elimination of nitrogen. This reaction is highly stereospecific, since optically active **88b** gave 1,3-diphenylallene with an enormously high specific rotation ($[\alpha]_D = 797°$)[370]. Kinetic and mechanistic studies point to a cyclopropanecarbene precursor of the allenes[149,301].



(**88a**, R¹ = Ph, R² = H; **88b**, R¹ = H, R² = Ph)

Doering's method permits the synthesis of cyclic allenes[142,143,144] and even cyclic diallenes[143], if the ring contains at least 9 carbon atoms. The dehalogenation of dibromobicycloheptane (**89**) (obtained according to equation (12) with **86** = cyclohexene) does not yield cyclohepta-1,2-diene but the dimerization product **90**. If the dehalogenation of **89** is carried out in the presence of cyclohexene, then the interesting spiropentane **91** is formed. Both these observations are best explained on the basis of a carbene intermediate like **87**[142].

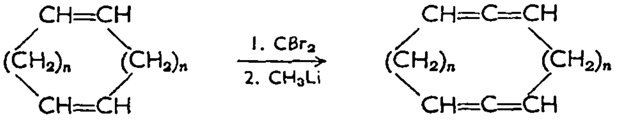


(89)

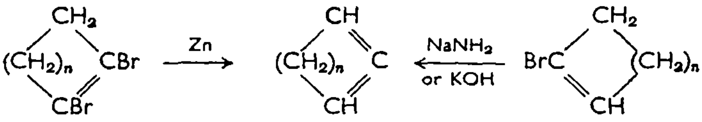
(90)

(91)

Starting with cyclooctadiene and cyclotetradecadiene Skatteböl[143] was able to build up the cyclic diallenes **92** whose structures were ascertained by spectroscopic and degradation experiments. Cyclic allenes have also been obtained by ordinary dehalogenation methods, but again only if the ring contained at least 9 carbon atoms[145,146].



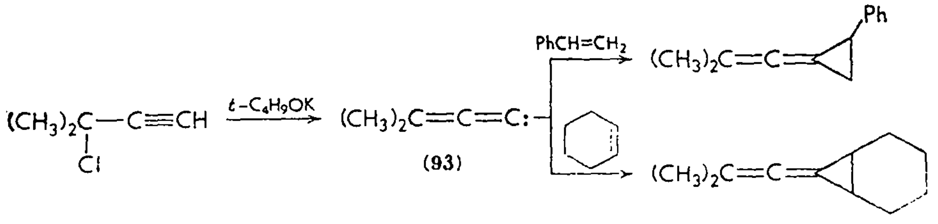
(**92**, n = 2, 5)



($n \geq 6$)

Earlier reports by Russian authors, that cyclohepta-1,2-dienes and cycloocta-1,2-dienes had also been observed, could not be substantiated[146].

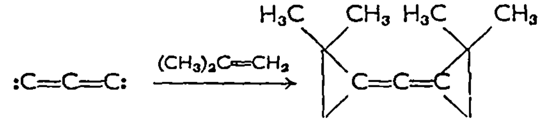
Hartzler[147] prepared an allenecarbene (**93**) which could be stabilized, like the dibromocarbenes, by cyclohexene or styrene to form interesting ethanoallenes **94**. Their structures were proved by oxidation and halogenation.



(93)

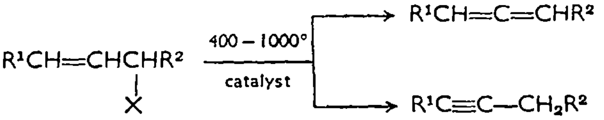
(94)

An interesting substance is C_3, a dicarbene whose presence in the atmosphere of comets has long been known. Skell and Wescott[369] prepared it in the laboratory and found that it behaves like a dicarbene, *e.g.* on reaction with isobutene it gave rise to a bisethanoallene:



The scope and limitation of Doering's method have not yet been fully tested. Sterically hindered olefins usually do not react with dihalocarbenes, and the dihalocyclopropanes are sometimes very resistant towards dehalogenation. Thus dichlorocyclopropanes can only be converted into allenes if they are treated with Grignard reagents[148].

g. Photolytic and pyrolytic allene formation; miscellaneous methods. Simple aliphatic allenes can be obtained by the elimination of HX at temperatures from 400 to 1000° in the presence of catalysts such as platinum, alumina or silica gel[150]. Normally the allenes polymerize at such high temperatures, but this can largely be avoided

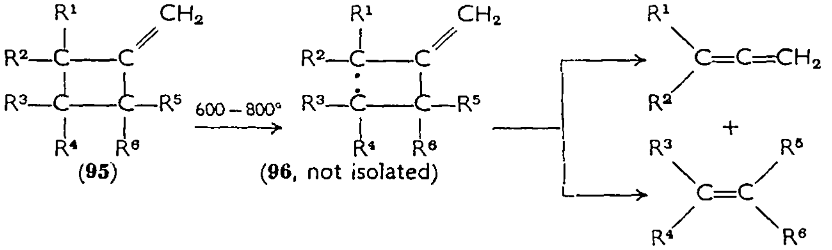


$$R^1CH{=}CH\underset{\displaystyle X}{\underset{|}{C}}HR^2 \xrightarrow[\text{catalyst}]{400-1000°} \begin{cases} R^1CH{=}C{=}CHR^2 \\ R^1C{\equiv}C{-}CH_2R^2 \end{cases}$$

$(X = Cl, Br, OCH_3, \overset{+}{N}(CH_3)_3;\ R^1, R^2 = H, CH_3)$

by rapidly cooling the gases after they have left the reaction vessel. Mixtures of propyne and propadiene are obtained when isobutane[151], isobutene[152], or *t*-butanol[151] are cracked at temperatures from 700 to 1000°. The combined yield of allene and methylacetylene reaches 60–70%, especially in the presence of water.

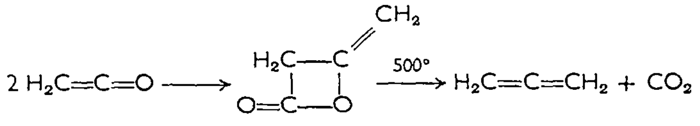
Methylenecyclobutanes (**95**) generally decompose into allenes and ethylenes at temperatures around 700°. This is a reversion of their formation reaction which takes place at about 200°. Certain by-products suggest that the reaction proceeds *via* the transient diradical **96**.



(**95**) (**96**, not isolated)

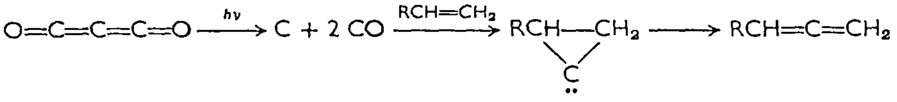
(**a**[153], R^1 to R^4 = F, R^5 = R^6 = H;
b[154], R^1 = R^2 = R^5 = R^6 = H, R^3 = CH_3, R^4 = CN;
c[154], R^1 = R^2 = R^5 = R^6 = H, R^3 = CH_3, R^4 = CO_2CH_3;
d[154], R^1 = R^2 = H, R^4 = CN, R^3 = R^5 = R^6 = CH_3;
e[154], R^1 = R^3 = R^5 = R^6 = H, R^2 = R^4 = CO_2CH_3.)

From the observation that diketene gives equal amounts of allene and carbon dioxide on heating, the lactone formula **97** was proposed for diketene[155]. Under certain conditions, between 500 and 600° ketene itself also gives equal amounts of allene and carbon dioxide[156]. This suggests that diketene might here be an intermediate.

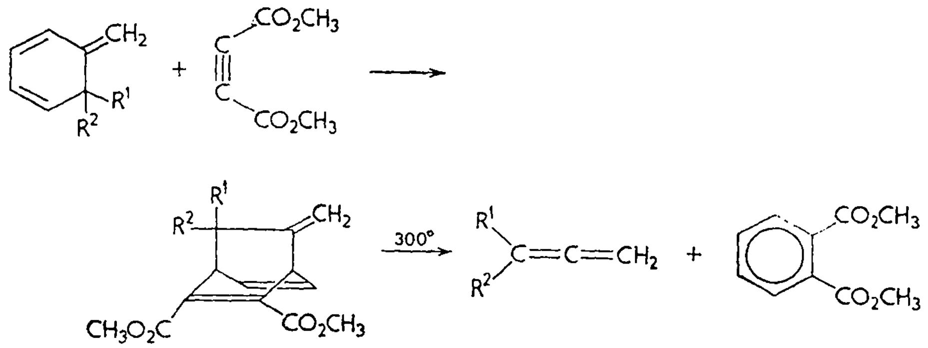


(**97**)

Irradiation of carbon suboxide in the presence of ethylenes gives rise to allenes and to twice as much carbon monoxide. It is assumed that the central carbon atom of the suboxide is inserted into the ethylenic double bond, involving carbene-type reactions[157].

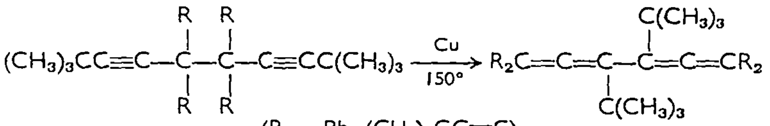


Methylenebicyclo[2.2.2]octadiene derivatives (**98**), arising from a Diels–Alder condensation, behave like the methylenecyclobutanes and furnish allenes on heating, besides benzene derivatives[158].



(**98a**, $R^1 = R^2 = CH_3$; **98b**, $R^1 + R^2 = (CH_2)_5$;
98c, $R^1 = CH_3$, $R^2 = Ph$.)

Marvel was interested in whether hexaethinylethanes would behave like hexaphenylethane and dissociate into radicals. He found this to be the case, but the radicals, after redistribution of the electrons, reassociated immediately to produce diallenes[159].



$$(CH_3)_3CC{\equiv}C-\underset{R}{\overset{R}{C}}-\underset{R}{\overset{R}{C}}-C{\equiv}CC(CH_3)_3 \xrightarrow[150^\circ]{Cu} R_2C{=}C{=}C-\underset{C(CH_3)_3}{\overset{C(CH_3)_3}{C}}{=}C{=}CR_2$$

($R = Ph$, $(CH_3)_3CC{\equiv}C$)

The first tetraarylallene synthesis was carried out by distilling the barium salt of diphenyl acetic acid[39]. Attempts to extend this method to other diaryl acetic acids failed, however[160].

$$(Ph_2CHCOO)_2Ba \xrightarrow{\text{Distillation}} Ph_2C{=}C{=}CPh_2 + BaCO_3 + H_2O$$

Wittig's olefin synthesis with triphenylphosphine ylides has also been applied in the cumulene field. Two different synthetic schemes can be envisaged for allenes: (i) condensation of a ketone with a vinylidenetriphenylphosphine, or (ii) condensation of a ketene with an alkylidenetriphenylphosphine. The yields are in both cases up to 70%.

$$R_2C{=}C{=}PPh_3 + O{=}CR_2 \longrightarrow R_2C{=}C{=}CR_2 + Ph_3P{=}O$$

($R = Ph$[161])

$$R^1{}_2C{=}PPh_3 + O{=}C{=}CR^2{}_2 \longrightarrow R^1{}_2C{=}C{=}CR^2{}_2 + Ph_3P{=}O$$

($R^1 = CH_3$; $R^2 = Ph$, mesityl[367]
$R^1 = R^2 = Ph$[162])

A slightly different course follows the condensation of Schiff bases with ethylidenetriphenylphosphines which involves a dehydration[368].

$$RCH_2CH{=}PPh_3 + PhCH{=}NPh \longrightarrow RCH{=}C{=}CHPh + Ph_3P + PhNH_2$$
$$(R = H, C_3H_7)$$

2. Chemical properties and reactions of allenes

a. General properties. Alkyl-substituted allenes are in general stable at temperatures up to 100°—even conjugated diallenes and cyclic allenes with more than 9 carbon atoms. Vinyl- and ethinylallenes are stable to at least room temperature. On the other hand, aryl- and diarylallenes can only be obtained if special precautions are taken, and triarylallenes have never been observed at all. However, tetraarylallenes are in most cases stable up to 200°.

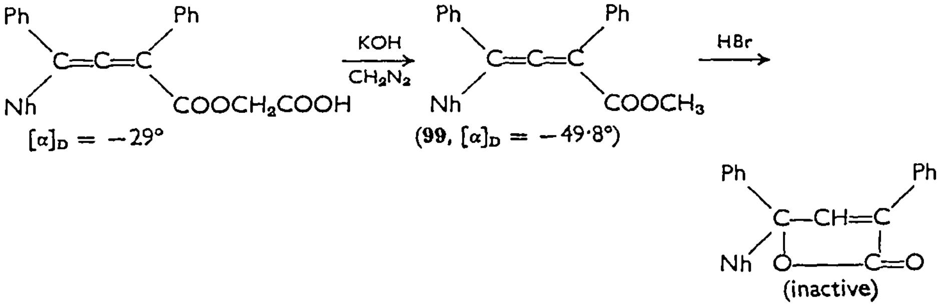
Allenes are sensitive towards acids, which give additions, while bases often cause double bond shifts.

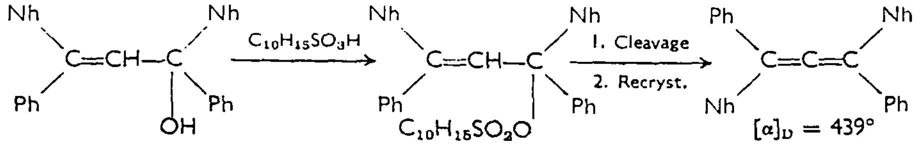
Unlike higher cumulative double-bond systems the allenic system has no pronounced influence on the solubility of the whole molecule. There is no characteristic ultraviolet absorption of the 1,2-diene, in contrast to the very characteristic infrared band near 1950 cm^{-1} which almost all allenes exhibit (for its assignment to a particular normal mode of vibration, see Section IV). This property has been widely used to establish the constitution of unknown allenes. Oxidation to the corresponding carbonyl compounds and hydrogenation to propanes are further possibilities of proving the constitution. Tetranitromethane gives yellow colors with allenes[163]. A special publication deals with reactions of cobalt carbonyls with allenes and acetylenes[164].

The determination and separation of allenic material in mixtures is of importance in industry. A crude method has been suggested by Lebedew[165]: a sample is heated and then oxidized. If allenes are present, they polymerize to cyclobutanes which yield succinic acid on oxidation. A short method for the determination of 1,2-butadiene in 1,3-butadiene is based on infrared spectroscopy[166]. In the quantitative analysis of mixtures of C_4 hydrocarbons by chemical methods, the former interferes and its percentage must be known in advance[167]. Modern methods of analyzing hydrocarbon mixtures that contain allenes make use of gas chromatography which is far superior to previous techniques. Thus traces of allene in propene can be accurately determined[168]. Mixtures of propene, propadiene and propyne are easily separated by gas chromatography[169]. Magnesium silicates used as a packing in the column have been found to give good results for analyzing C_1 to C_4 hydrocarbon mixtures[170]. Of interest is the observation that allene forms an azeotrope with ammonia and can thus be distilled from mixtures. The distillate forms two layers so that the allene can conveniently be separated from the ammonia[171].

Several simple alkylallenes have been purified thoroughly, and accurate melting point and boiling point determinations have been made. The knock characteristics of such highly pure allenes have also been investigated[172].

b. Optical activity. Many unsuccessful attempts to resolve suitably substituted allenes into optically active components have appeared in the literature up until 1930[30,38,173]. In that year, Faltis[174] failed to resolve the dimethyl ester of allenetetracarboxylic acid. He suggested that, contrary to van't Hoff's theory, the four valences in the allene molecule should all lie in the same plane which would make resolution impossible. However, Ingold[175] showed that Faltis did not actually have an allene so that his arguments had lost their basis. Moreover, five years later, two research groups independently succeeded in solving the long-pending problem. Kohler and co-workers[22,176] esterified the triarylallenecarboxylic acid (**41**) with glycolic acid and were able to separate the brucine salts. Careful saponification in the presence of diazomethane permitted the isolation of the optically active carboxylic ester **99**. The free acid, however, lactonizes and looses its activity. Maitland and Mills[41] performed an optically active synthesis by elimination of water from the tetra-arylallyl alcohol **100**, using *d*-camphorsulfonic acid. They assumed that the racemic alcohol was esterified by the optically active acid which gave rise to two diastereomeric esters with different chemical behavior. Elimination of the acid would then no longer produce racemic allene, but a mixture enriched in one isomer. Recrystallizations gave pure *d*-allene with the high specific rotation of $[\alpha]_D = 439°$.





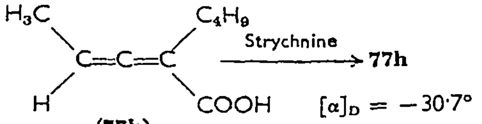
(100) (not isolated)

$[\alpha]_D = 439°$

(Nh = α-naphthyl)

Attempts to extend Maitland and Mills' elegant method to other tetraarylallenes (replacing one naphthyl group by pentadeuterophenyl or tolyl) have failed[177].

In 1951 Wotiz[94] resolved another allenecarboxylic acid (**77h**) synthesized by the method of equation (9) using strychnine. From



(77h)

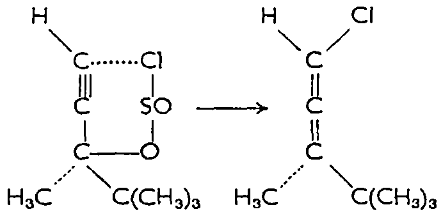
$[\alpha]_D = -30{\cdot}7°$

1952 onwards several optically active allenes were discovered in nature, as mentioned in the introduction of this chapter.

In 1957 Jacobs[110] observed that 1,3-diarylpropynes were converted into partially active 1,3-diarylallenes (**79i**) when treated with alumina impregnated with brucine. The synthesis of optically pure 1,3-diphenylallene has been mentioned on page 1055.

After this beautiful confirmation of one of the essential parts of van't Hoff's theory there remained one problem: how to establish the absolute configuration of a given optically active allene. Since allene isomerism is one of molecular asymmetry rather than atomic asymmetry, the conventional degradation methods are unsuitable for this purpose.

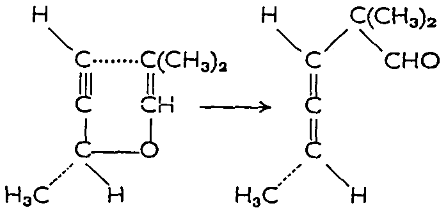
In 1959 Landor[71] observed that the optically active propargyl alcohol **68f** furnished the active haloallene **70f**. The assumption of the cyclic transition state **71** led Landor to anticipate that this reaction might be useful for finding the absolute configuration of an allene. For this, the absolute configuration of the propargyl alcohol **68f** had to be known. This was carried out by Eliel[178] who used



S-(+)-**71** S-(+)-**70f**

Brewster's method[179] of determining the sequence of the polarizabilities of the substituents around an asymmetric carbon atom and deducing from this its absolute configuration.

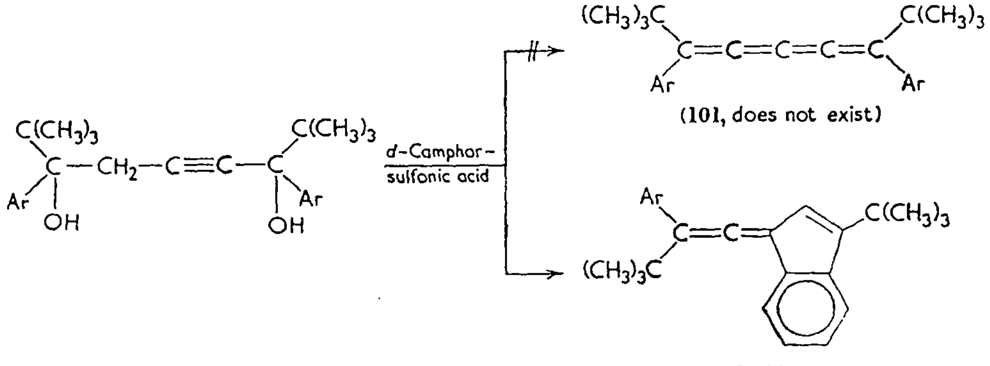
Jones and colleagues[72] resolved 2-butynol and hydrogenated to 2-butanol whose absolute configuration was known. The enol ether with dimethylethenol (**68q**) undergoes Claisen rearrangement. Again the shape of the cyclic transition state affords knowledge about the absolute configuration of the resulting allene aldehyde **70q**.



R-(+)-**68q** R-(+)-**70q**

Allenedicarboxylic acid has been resolved and its absolute configuration has been established *via* its Diels–Alder adduct with cyclopentadiene. The adduct can be related to norcamphor whose absolute configuration is known[302].

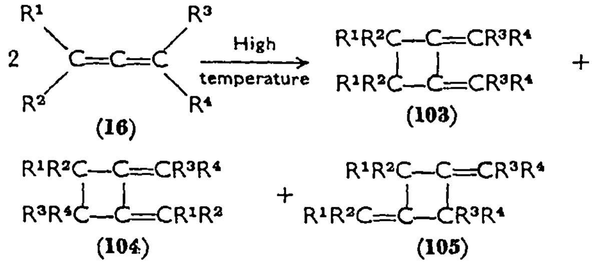
Very recently, Japanese workers[180] reported the resolution of the pentatetraene **101**. However, this was shown soon afterwards[181] to be most likely the indenoallene **102**, which would then constitute another example of an optically active allene. Its half-life of racemization at 150° is 800 min. It can generally be said that optically active allenes are more resistant towards thermal racemization than to racemization by acids or bases.



(**101**, does not exist)

(**102**)

c. Polymerization. All allenes will polymerize if kept at high temperatures for long enough. However, if the conditions are properly chosen (depending upon each particular case) then dimeric allenes can often be isolated which have the methylenecyclobutane structures **103**, **104** and **105**. Table 5 gives an idea of the scope and limitations of this allene dimerization.



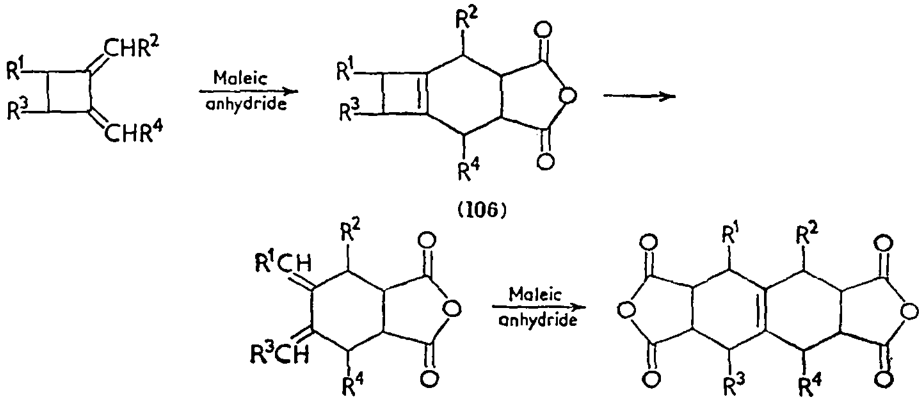
(16) (103) (104) (105) (13)

TABLE 5. Dimerization of allenes according to equation (13).

Example 16	Substituents				Reaction conditions	Yield of cyclobutanes (%)			Ref.
	R^1	R^2	R^3	R^4		**103**	**104**	**105**	
a	H	H	H	H	500°; seconds	50	—	0	54
b	H	H	H	H	400°	85	—	15	182
c	H	H	CH_3	CH_3	150°; days				183
d	CH_3	H	CH_3	H	150°; days	80	—	0	183
e	CH_3	H	CH_3	CH_3	150°; days	70	traces		183
f	Cl	Cl	Cl	Cl	0°	90	—	—	32, 184
g	F	F	F	F	40°	83	—	0	35
h	Cl	Cl	Ar	Ar	60°	60	—	?	185
i	F	F	H	H	300°	—	35	—	198

The 1,2-dimethylenecyclobutanes are powerful dienophiles. Thus if the dimerization of certain allenes is carried out in the presence of maleic anhydride, two moles of the anhydride are added. (The intermediate cyclobutene **106** undergoes a ring cleavage and furnishes a dimethylenecyclohexane which can add a second mole of maleic anhydride to form a naphthalene-type ring system.)

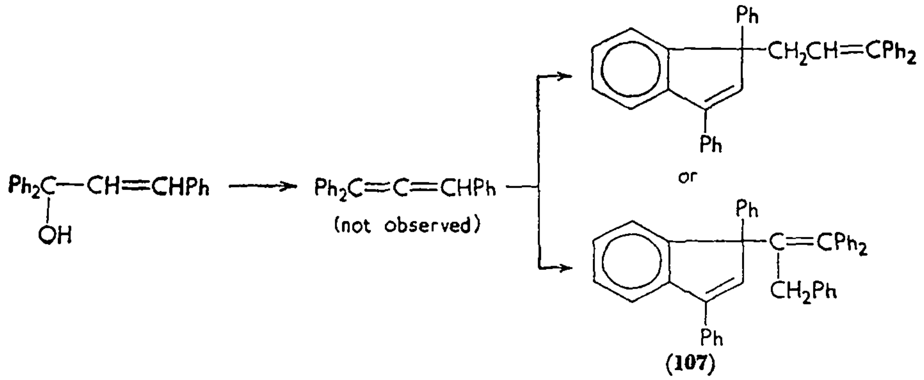
Certain arylallenes dimerize so that one of the aromatic substituents participates in forming a new ring. The structure of the dimeric triphenylallene has been the object of some controversy in the 1920's[43,187]. The indene structures **107** put forward by Straus[188]



(106)

(a^{186}, $R^1 = R^2 = R^3 = R^4 = H$;
b^{146}, $R^1 + R^2 = R^3 + R^4 = (CH_2)_4$;
c^{146}, $R^1 + R^2 = R^3 + R^4 = (CH_2)_5$.)

seem to be well substantiated by degradation experiments. Conclusive evidence for the existence of the monomeric triphenylallene has not yet been published*.



(107)

Triphenylchloroallene (**108**) undergoes the so-called rubrenic reaction and dimerizes to tetraphenyltetracene (rubrene). Regarding the mechanism of this reaction, it was proposed that the allene first dimerizes in a Diels–Alder-type condensation to a dichlorotetrahydrotetracene derivative which is then aromatized to rubrene[190].

Marvel[191] investigated various trisubstituted haloallenes and found that they dimerized more or less spontaneously without loss of halogen. The structures of the dimeric products have not yet been established.

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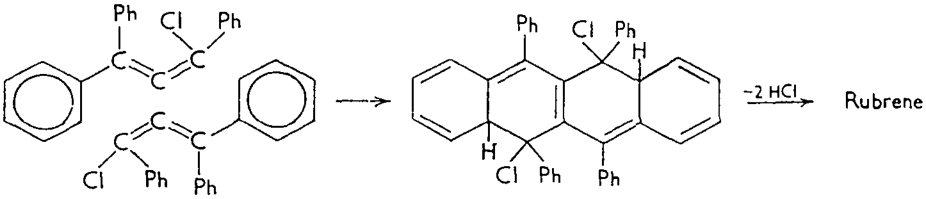
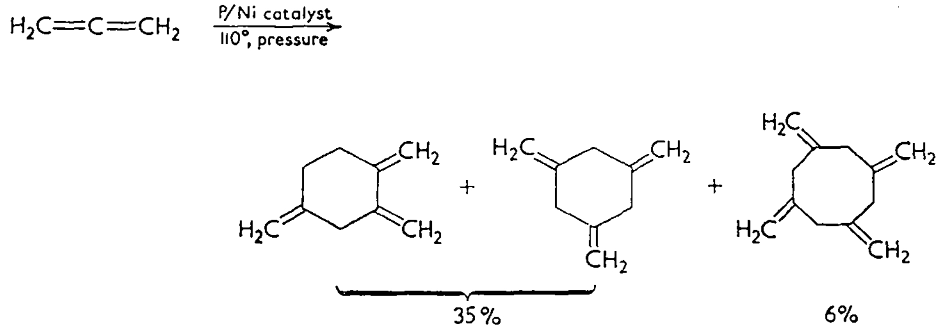
* See, however, ref. 189.



(108)

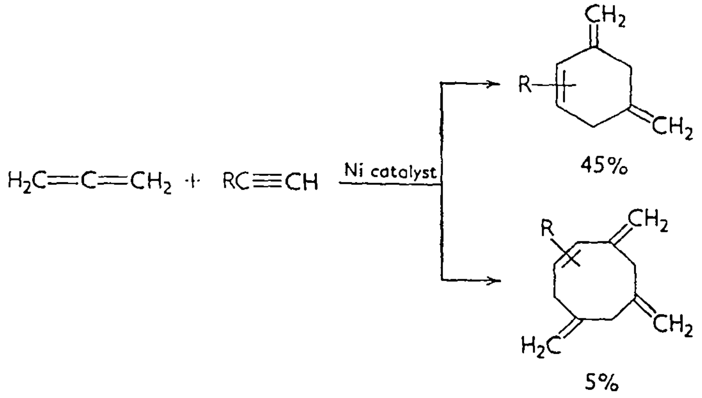
Allenecarboxylic acid is actually anhydroacetoacetic acid and it is therefore not surprising that it dimerizes to dehydracetic acid, as does acetoacetic acid[117].

The course of polymerization of allenes is changed if metal catalysts are present. This had already been observed by Lebedew in 1913, who found trimers, tetramers, pentamers and hexamers in addition to the dimers when he kept simple alkylallenes for several days at 140°[183]. Meinert and Hurd[199] achieved the same result in 80 seconds by increasing the reaction temperature to 500°. Of particular interest was the observation that the ratio of these oligomers changed considerably when the polymerization was carried out in iron vessels rather than in glass vessels[183]. Using a phosphorus-nickel catalyst Benson and Lindsey[192] were able to convert allene to a mixture of trimethylenecyclohexanes and tetramethylenecyclooctane with no detectable quantity of dimers being formed. If certain acetylenes



are added, then a copolymerization of allene and acetylene occurs, whereby dimethylenecyclohexenes and trimethylenecyclooctenes are produced[193].

1,2-Butadiene can be extracted from hydrocarbon mixtures (together with vinylacetylene and 1,3-butadiene) by aqueous solutions of copper salts in ammonium acetate. On heating these extracts, a liquid dimer of 1,2-butadiene is obtained, whose structure has not been determined[194].

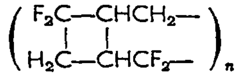


(R = H, CH_3, $CH_2{=}CH$, Ph)

Cobaltcarbonyl forms complexes with certain allenes which catalyze their own polymerization to products which are at least tetrameric[195].

Certain metal catalysts obtained from Grignard reagents have been found particularly suitable for the synthesis of linear polymers from allene[196]. Poly(difluoroallene), which is obtained by heating the allene at 20° under autogenous pressure, seems to be a linear chain with difluoromethylene groups[35] $-[CH_2C({=}CF_2){-}]_n$. This is supported by x-ray studies.

1,1-Difluoroallene polymerizes *via* the dimethylenecyclobutane **104i**:



$$\left(\begin{array}{l} F_2C{-}CHCH_2{-} \\ \;\;|\quad\;\;| \\ H_2C{-}CHCF_2{-} \end{array}\right)_n$$

It forms clear flexible films, resistent to boiling nitric acid[198].

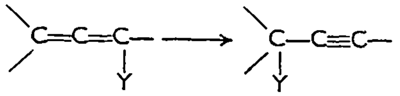
Poly(1,2-dienes) are of less importance than poly(1,3-dienes). Polymerization products of 1,2-butadiene may be used for covering roofs or as drying oils[200]; polymerized 1-chloro-2,3-butadiene is used for coatings[201]. The effect of allenic impurities on the polymerization of 1,3-butadiene, isoprene and styrene has been studied[202]. Catalytic amounts of methylallene improve the quality of the rubber[203], whereas larger amounts of allene allow only short chain polymers to be formed[204].

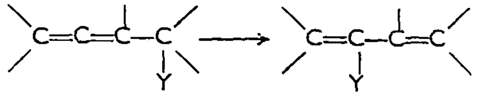
d. Isomerization. Allenes can undergo two types of double-bond isomerizations, producing either acetylenes or conjugated dienes, or

Table 6. Prototropic rearrangement of allenes.

Allene	Reaction conditions	Diene or acetylene	Yield (%)	Reference
$CH_3CH{=}C{=}CH_2$	Activated fuller earth	$CH_2{=}CHCH{=}CH_2$		209
$CH_3CH{=}C{=}CH_2$	Floridin; 200–330°	$CH_2{=}CHCH{=}CH_2$	20	205
		$C_2H_5C{\equiv}CH$	4	
$C_3H_7CH{=}C{=}CH_2$	Floridin; 230°	$CH_3CH{=}CHCH{=}CHCH_3$		206
$(CH_3)_2C{=}C{=}CH_2$	Floridin; 300°	$CH_2{=}C(CH_3)CH{=}CH_2$	20	
		$(CH_3)_2CHC{\equiv}CH$	60	207
$(CH_3)_2C{=}C{=}CHCl$	Cu_2Cl, NH_4Cl	$CH_2{=}C(CH_3)CH{=}CHCl$	40	208
$HOOCCH_2CH{=}C{=}CH_2$	K_2CO_3; 60°	$HOOCCH{=}CHCH{=}CH_2$	80	29
$Ph_2CHCH{=}C{=}CPh_2$	KOH	$Ph_2C{=}CHCH{=}CPh_2$	70	210
$Ph_2C{=}C{=}CHCH{=}C{=}CPh_2$	KOH	$Ph_2C{=}C{=}C{=}CHCH{=}CPh_2$	80	210
$CH_3CH{=}C{=}CHCH_3$	KOH	$C_2H_5C{\equiv}CCH_3$	—	51
$H_2C{=}C{=}CHCH_2N(CH_3)_2$	KOH	$CH_3C{\equiv}CCH_2N(CH_3)_2$	75	125
$C_4H_9C{\equiv}CCH{=}C{=}CH_2$	KOH	$C_4H_9C{\equiv}CC{\equiv}CCH_3$	~80	113

both simultaneously. The first type of isomerization can be considered as a *retro*-propargylic rearrangement (equation 14). The second type can only occur if the migrating group Y is conjugated to the allenic system (equation 15). If Y = H in these equations, then

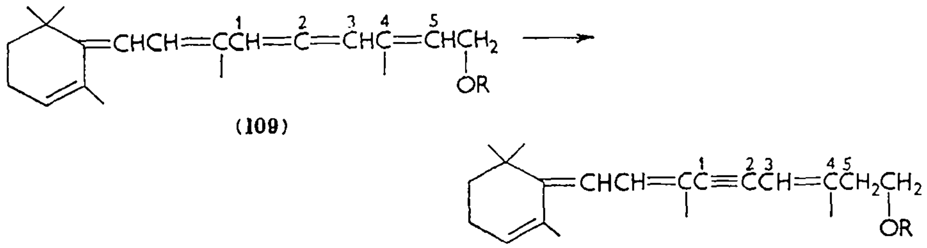

(14)


(15)

(Y = H, halogen)

the rearrangement is of prototropic type and will need basic conditions. Table 6 collects examples of prototropic rearrangements of allenes to acetylenes or possibly 1,3-dienes.

In the carotene-type vinylallene **109** the retro-propargylic rearrangement is coupled with an allylic rearrangement, so that ultimately the proton has been shifted from the 1- to the 5-position of the vinylallene system[112].


(109)

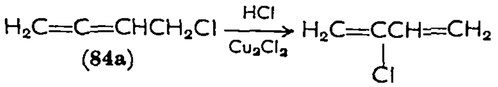
The very unstable decatetraenediyne **110** (obtained by oxidative dimerization of pentadienyne (**66**)) undergoes a double isomerization and furnishes dimethyltetraacetylene which is more stable than the parent diallene[65]. Other examples of prototropic isomerizations

$$H_2C{=}C{=}CHC{\equiv}CC{\equiv}CCH{=}C{=}CH_2 \longrightarrow CH_3(C{\equiv}C)_4CH_3$$

(110)

include the naturally occurring allenes mentioned in the introduction.

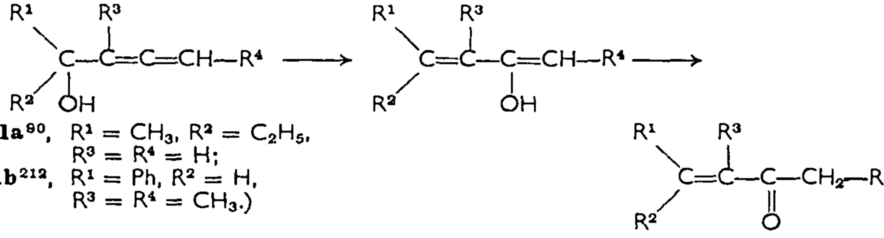
Equations (14) and (15) represent anionotropic rearrangements of allenes if Y is an electronegative substituent (*e.g.* halogen or hydroxyl). One of the most important examples from a practical point of view is Carother's isoprene synthesis. He treated vinylacetylene with hydrogen chloride in the presence of cuprous chloride and obtained chloroprene. This is not due to a 1,2-addition to the triple bond, however. Instead, the 1,4-addition product, 1-chloro-2,3-butadiene (**84a**) which is first formed rearranges under the influence of the copper salt in 90% yield[122]. The corresponding bromo and iodo



$$\underset{(\mathbf{84a})}{\mathrm{H_2C{=}C{=}CHCH_2Cl}} \xrightarrow[\mathrm{Cu_2Cl_2}]{\mathrm{HCl}} \mathrm{H_2C{=}\underset{\underset{\displaystyle Cl}{|}}{C}CH{=}CH_2}$$

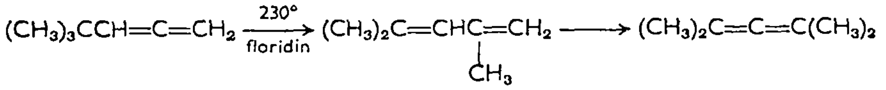
compounds rearrange even more easily to the haloprenes[211].

If allenylcarbinols **111** undergo the rearrangement of equation (15) (Y = OH) then α,β-unsaturated ketones are obtained due to a subsequent ketonization of primarily formed vinyl alcohols.



(**111a**[90], $R^1 = CH_3$, $R^2 = C_2H_5$,
$R^3 = R^4 = H$;
111b[212], $R^1 = Ph$, $R^2 = H$,
$R^3 = R^4 = CH_3$.)

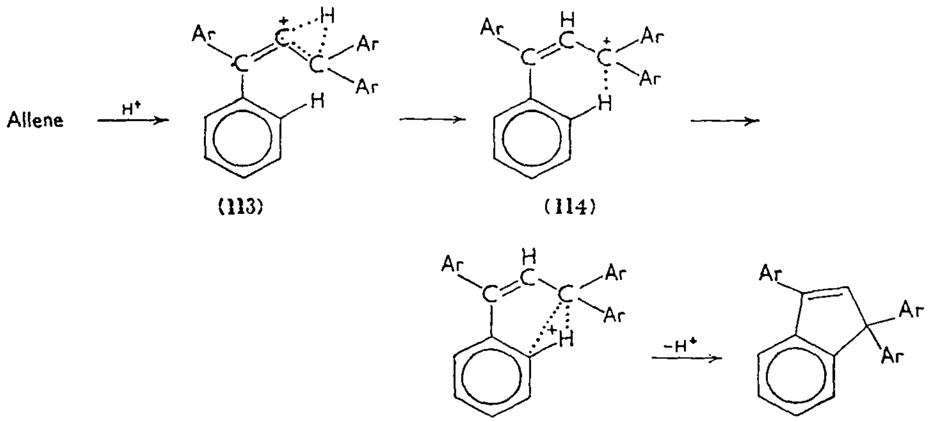
Slobodin passed *t*-butylallene over floridin at 230° and observed migration of a methyl group. It is interesting that under these conditions the 1,3-diene **112** rearranges to an allene again, which is one of the rare examples of conjugated double bonds isomerizing to cumulated ones[213].



$$\mathrm{(CH_3)_3CCH{=}C{=}CH_2} \xrightarrow[\text{floridin}]{230°} \mathrm{(CH_3)_2C{=}CH\underset{\underset{\displaystyle CH_3}{|}}{C}{=}CH_2} \longrightarrow \mathrm{(CH_3)_2C{=}C{=}C(CH_3)_2}$$

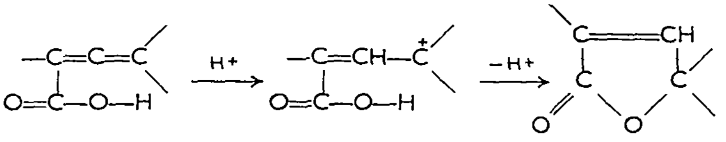
(**112**)

Tetraarylallenes (and certain allene carboxylic acids) undergo isomerization in the presence of acids to yield triarylindene derivatives[30,39,41,43,44,177]. It is not difficult to envisage a plausible mechanism: The proton of the acid approaches one of the double bonds of the allene to form first the π complex **113**. However, the carbonium ion **114** will have a lower energy than any other possible arrangement of the proton and electrons, due to a gain in resonance energy. The positive charge is now close to the *ortho* position of one of the aromatic rings and in the sphere of the σ electrons bonding the hydrogen atom. Since the proton is less electrophilic than the carbonium ion, the proton will soon be eliminated and a normal σ bond will be formed. This mechanism may be pictured as follows:



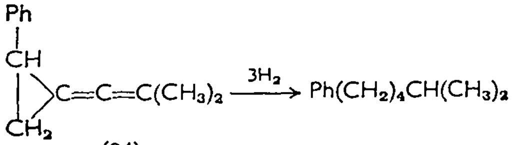
(113) (114)

The lactonization of certain allene carboxylic acids can be treated similarly[38,79,176]:



It should be noted that in the case of a tetraarylallene with different aryl groups, the structure of the isomeric triphenylindene is ambiguous and has not always been fully elucidated.

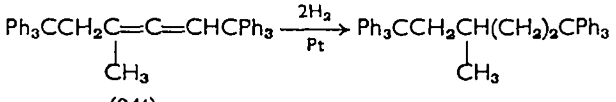
e. Hydrogenation. On catalytic hydrogenation, using nickel, palladium or platinum catalysts, allenes normally take up two moles of hydrogen. The resulting propanes can be identified by an independent synthesis, so that this procedure may help to prove the constitution of an unknown allene. Care must be exercised in case of three-membered rings which will also be hydrogenated, as, for example, with **94**. In the presence of a palladium catalyst it takes up three moles of hydrogen to give 5-methyl-1-phenylhexane.



$$\begin{matrix}\text{Ph}\\ |\\ \text{CH}\\ |\\ \text{CH}_2\end{matrix}\!\!>\!C{=}C{=}C(CH_3)_2 \xrightarrow{3H_2} Ph(CH_2)_4CH(CH_3)_2$$

(94)

Some allenes show surprising resistance towards catalytic hydrogenation. This may either be due to steric hindrance or to poisoning of the catalyst. Thus Mills and Maitland's diphenyldinaphthylallene cannot be hydrogenated catalytically, and even with hydrogen iodide and phosphorus only one double bond is attacked[41]. Kohler[22] made a similar observation with his diphenylnaphthylallenecarboxylic acid. Here, apparently, the bulky naphthyl group prevents a smooth reaction. Surprisingly enough, the equally overcrowded allene **84t** with its trityl group did consume two moles of hydrogen in the presence of a platinum catalyst. Perhaps the incomplete shielding of the allene from one side is responsible for this positive result.



$$Ph_3CCH_2\underset{\displaystyle CH_3}{C}=C=CHCPh_3 \xrightarrow[Pt]{2H_2} Ph_3CCH_2\underset{\displaystyle CH_3}{CH}(CH_2)_2CPh_3$$

(84t)

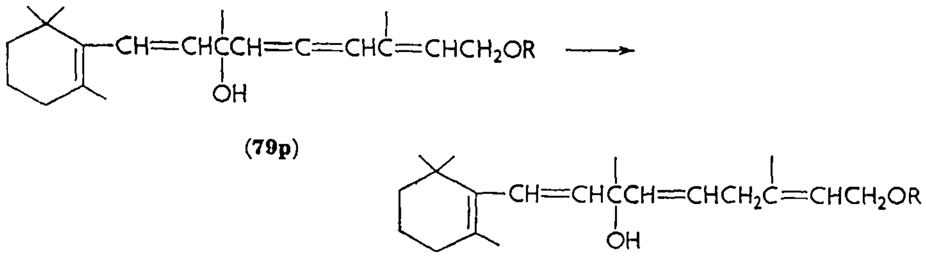
Roedig's diaryldichloroallenes (**26**) are completely unreactive towards catalytic hydrogenation; after removal of the chlorine atoms, however, hydrogenation becomes possible.

$$Ar_2C=C=CCl_2 \xrightarrow[Zn]{Pyridine} Ar_2C=C=CH_2 \xrightarrow{Raney\ Ni} Ar_2CHC_2H_5$$

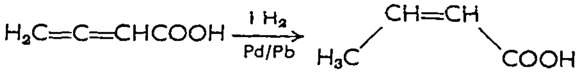
Cyano-1,3-dimethylallene (**79u**) can only be hydrogenated with Raney nickel under a considerable pressure of hydrogen[115]. It is possible that the pseudo-halogen also poisons the catalyst and prevents a smooth reaction.

Catalysts, reduced in efficiency by certain admixtures, permit partial hydrogenation of the allenic system. This problem is also of importance for large-scale industrial processes, where the conversion of compounds containing triple or cumulative bonds into simple olefins is required; considerable progress has been made in this field in recent years[314,215].

On a laboratory scale, poisoned Raney nickel afforded a specific partial hydrogenation of the polyene alcohol **79p** of vitamin A type[112], and a special palladium catalyst was used by Jones[117] in converting allenecarboxylic acid into crotonic acid. In this case, the catalyst was not only selective but also stereospecific, the hydrogenated product being pure *cis*-crotonic acid. Also, the β-allenic ketone **70s** gave an olefinic ketone when subjected to hydrogenation with a poisoned Pd catalyst[81].



(79p)



An interesting example of a partial hydrogenation was found by Kuhn and coworkers[210] in the conjugated diallene **115**. Half a double bond is reduced in each allene unit and the whole system becomes fully conjugated.

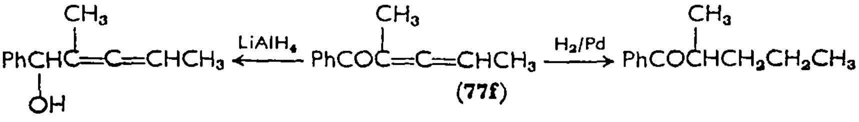
$$\mathrm{Ph_2C{=}C{=}CHCH{=}C{=}CPh_2} \xrightarrow[\mathrm{Pd/Pb}]{1\ \mathrm{H_2}} \mathrm{Ph_2C{=}CHCH{=}CHCH{=}CPh_2}$$

(115)

Higher cumulenes can also provide a test for the selectivity of a deactivated catalyst (section III). On the whole, little has been published on the selective hydrogenation of cumulative double bonds, in contrast to the extensive research on the partial hydrogenation of triple bonds.

Nascent hydrogen (from sodium in alcohol) or hydrogen iodide and phosphorus usually brings about complete saturation[39] with the possible exception of sterically hindered allenes[41,216]. However, somewhat milder conditions (zinc in pyridine or aluminum amalgam in the presence of water) may well leave certain allenes untouched; for example, the conjugated diallene **115** is produced from the treatment of the hexapentaene with aluminum amalgam in aqueous tetrahydrofuran and is not hydrogenated further. Haloallenes may be dehalogenated by a zinc–copper couple without loss of a double bond (method (c) for preparation of allenes).

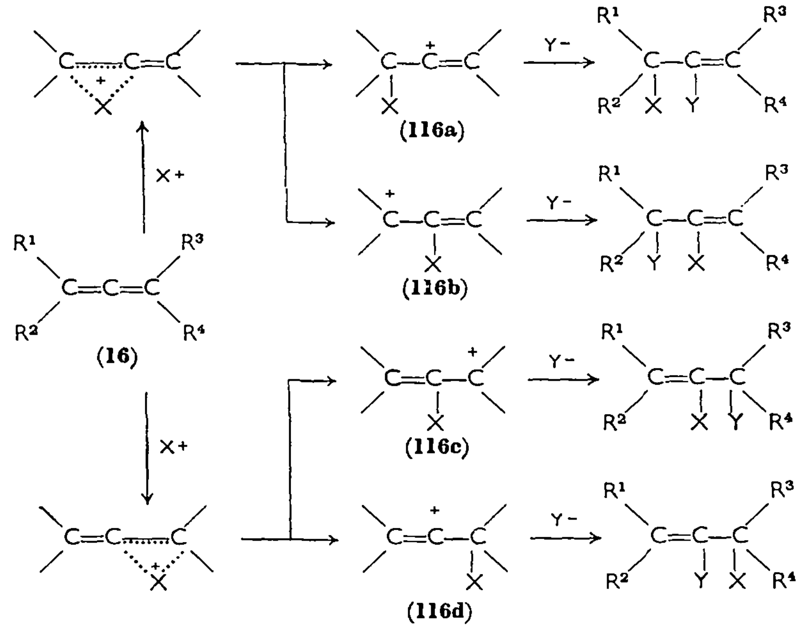
Lithium aluminum hydride does not normally attack the allenic bond. This reagent may therefore be used to reduce selectively other unsaturations in an allene molecule, such as carbonyl groups. The reduction of the α-allenic ketone **77f** is an example of how hydrogenation with the hydride can complement the catalytic hydrogenation. Thus the hydride gives an α-allenic alcohol while the catalytic procedure leads to a saturated ketone[93].



$$\mathrm{PhCH(OH)C(CH_3){=}C{=}CHCH_3} \xleftarrow{\mathrm{LiAlH_4}} \mathrm{PhCOC(CH_3){=}C{=}CHCH_3} \xrightarrow{\mathrm{H_2/Pd}} \mathrm{PhCOCH(CH_3)CH_2CH_2CH_3}$$

(77f)

f. Halogenation. The halogenation of allenes to tetrahalopropanes is a two-step process, the first step being the formation of a 1,2-dihalo-2-propene which may or may not then take up one more mole of halogen. The difference in the rates of these two steps is so large that in most cases only forced treatment can provide the tetrahalopropanes[217]. Obviously, chlorine will be more favorable for that purpose than bromine[35,49,51,86,185]; iodine does not react with allenes at all. Since these halogenations take place at low temperatures and in the dark, it can be assumed that they follow an ionic mechanism. The reactive agent will then be the bromonium or chloronium ion, and this will form a π complex with the double bond of the allene. The π complex, however, will soon be transformed into a halopropene carbonium ion **116** which has a lower energy. There are four possibilities (**a**, **b**, **c**, **d**) for the structure of this ion: **116b** and **c**, being allyl cations, usually have lower energy than **116a** and **d**, although it must be remembered that in the π complex the remaining 2,3-double bond can have no influence on the appearance of a positive



(16)

(116a)

(116b)

(116c)

(116d)

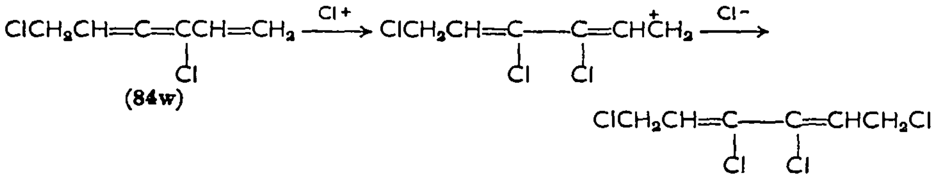
Table 7. Halogenation of allenes.

Example	Substituents				Halogen	Product	Reference
16	R^1	R^2	R^3	R^4			
a	H	H	H	H	Br_2	$H_2C{=}CBrCH_2Br$	217
b	H	H	H	H	Cl_2	$H_2C{=}CClCH_2Cl$	217
c	H	H	H	H	BrCl	$H_2C{=}CBrCH_2Cl$	217
d	C_3H_7	H	H	H	Br_2	$C_3H_7CHBrCBr{=}CH_2$	217
e	CH_3	CH_3	H	H	Br_2	$(CH_3)_2CBrCBr{=}CH_2$	218
f	F	F	H	H	Br_2	$F_2CBrCBr{=}CH_2$	56
g	CH_3	H	CH_3	H	Br_2	$CH_3CHBrCBr{=}CHCH_3$	219
h	CH_3	H	Ph	H	Br_2	$CH_3CHBrCBr{=}CHPh$	219
i	CH_3	H	$PhCH_2$	H	Br_2	$CH_3CHBrCBr{=}CHCH_2Ph$	219
j	Ph	Ph	Cl	Cl	Br_2	$Ph_2C{=}CBrCBrCl_2$	185
k	Cl	H	$ClCH_2CH{=}CH$	H	Cl_2	$ClCH{=}CClCHClCH{=}CHCH_2Cl$	134
l	H	H	CH_2Cl	H	Cl_2	$CH_2{=}CClCHClCH_2Cl$ $CH_2ClCCl{=}CHCH_2Cl$	220
m	H	H	CH_2Cl	H	$(SCN)_2$	$CH_2{=}C(SCN)CH(SCN)CH_2Cl$	221

charge in the 1-position due to the perpendicular arrangement of the two double bonds in the allene molecule.

Halogenation with bromine or chlorine does not provide any distinction between a haloallyl cation (**116b** or **c**) or a halopropenyl cation (**116a** or **d**), since both give the same dihalopropenes. In halogenations with bromine chloride, the bromonium ion (rather than the chloronium ion) will form the π complex. If bromopropenyl cations are the intermediates, then 1-bromo-2-chloropropenes must be formed. Experimentally, 1-chloro-2-bromopropenes are obtained, which proves that the bromoallyl cation must be the transition state. Equation (16) is the basic equation for the halogenation of allenes and Table 7 records some special examples.

The vinylallene **84w** has been reported to undergo 1,4-addition on chlorination[36], which is easily understood from the argument given above. Here the intermediate allyl cation is actually a pentadienyl cation.



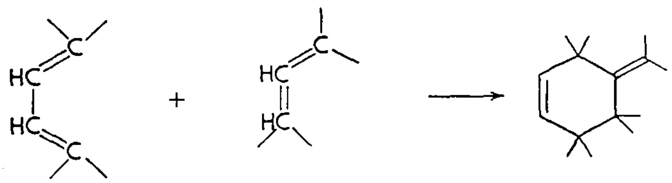
(**84w**)

$$\mathrm{ClCH_2CH{=}C{=}\underset{\displaystyle |\atop Cl}{C}CH{=}CH_2} \xrightarrow{\mathrm{Cl^+}} \mathrm{ClCH_2CH{=}\underset{\displaystyle |\atop Cl}{C}{-\!\!-}\underset{\displaystyle |\atop Cl}{C}{=}CH\overset{+}{C}H_2} \xrightarrow{\mathrm{Cl^-}}$$

$$\mathrm{ClCH_2CH{=}\underset{\displaystyle |\atop Cl}{C}{-\!\!-}\underset{\displaystyle |\atop Cl}{C}{=}CHCH_2Cl}$$

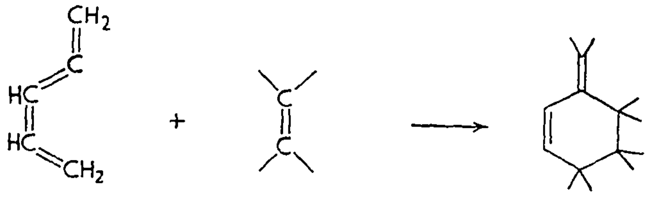
Tetraphenylallene forms a bromoindene on bromination[39]. This is explained in the same way as the indene formation with acids, discussed on page 1071 (replace H^+ by Br^+).

g. Addition (*other than halogenation and hydrogenation*). Simple allenes are reactive dienophiles in Diels–Alder syntheses. They give *exo*-methylenecyclohexenes according to the scheme:

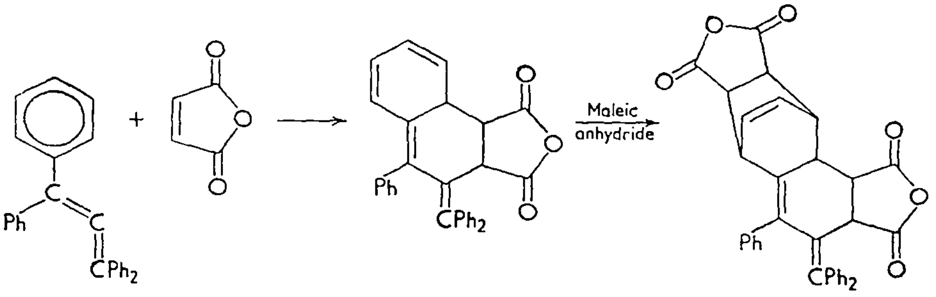


Dienes which have been used are butadiene, cyclopentadiene, hexachlorocyclopentadiene, and 2,5-dimethylfuran. Allenes suitable for Diels–Alder reactions include allene, difluoroallene, cyanoallene, allenecarboxylic acid and allene-1,3-dicarboxylic acid[6,114,198,230].

Vinylallene, on the other hand, can react as the diene component in a Diels–Alder synthesis and also gives *exo*-methylenecyclohexenes, this time, however, conjugated ones:

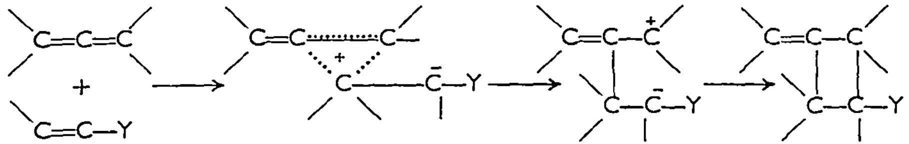


Dienophiles which have been used are benzoquinone, naphthoquinone, maleic anhydride and tetracyanoethylene[65]. Tetraphenylallene behaves like vinylallene towards maleic anhydride. The initially formed (benzo)methylenecyclohexene (**117**) cannot be isolated since it adds one more mole of maleic anhydride[241].



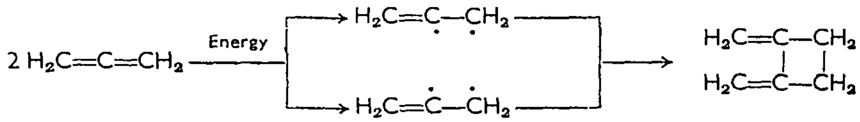
(**117**, not isolated)

At temperatures around 200°, even unconjugated allenes add to certain activated double bonds. When Y is an electron-attracting group, this addition will produce 1-Y-3-methylenecyclobutanes, in accordance with the arguments put forward for the mechanism of the halogenation of allenes. The allene as a nucleophile forms a π complex with the positively polarized end of the ethylene and the cyclobutane ring is then closed *via* the allyl cation **118**.

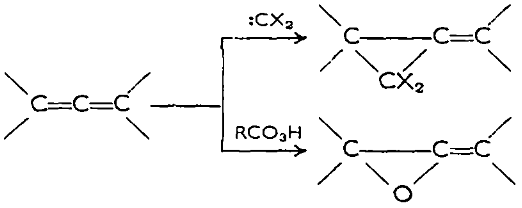


(**118**)

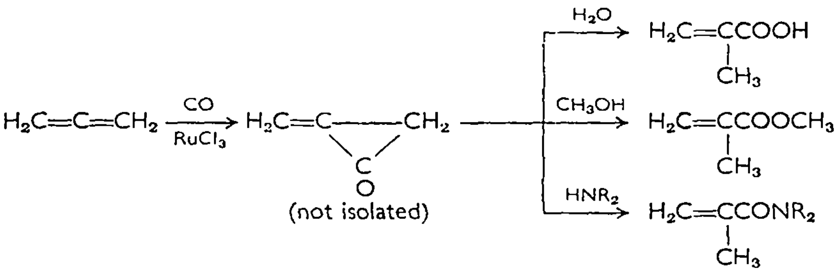
Allenes which have been used are allene, ethylallene and 1,1-difluoroallene; ethylenes which are suitable for this purpose include acraldehyde, acrylic acid (esters), acrylonitrile, styrene, maleic anhydride, azodicarboxylic ester (yielding a diazacyclobutane) and difluoroethylene[198,231,232,234]. Since these reactions are carried out at high temperatures, radical mechanisms will also be important. For instance, the fact that the thermal dimerization of allene gives largely 1,2-dimethylenecyclobutane cannot be reconciled with an ionic mechanism. Rather, it must be assumed that the allene is raised to a triplet state by thermal energy and then dimerizes through a four-center reaction.



Carbenes are even more electrophilic than the activated ethylenes mentioned above. Very recently it was found that they react smoothly with the more nucleophilic double bond of certain allenes to form methylenecyclopropanes[227,314,315]. The oxygen atom of peroxy acids has been assigned electrophilic properties in order to explain its addition to the more nucleophilic double bond of the allene in the formation of epoxides[31,228].



The carbonylation of allene in the presence of ruthenium catalysts leads to methacrylic acid derivatives. This is probably also a reaction of the allene as a nucleophile, with methylenecyclopropanone as a possible intermediate. Lactones composed of three allene units and

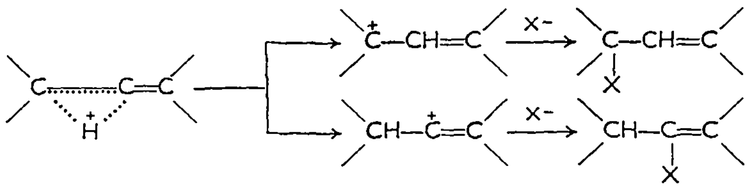


(not isolated)

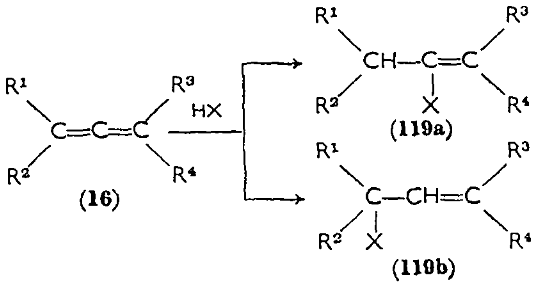
one molecule of carbon monoxide are also obtained, in addition to the methacrylic acid derivatives. They probably arise from a Diels–Alder condensation of 1,2-dimethylenecyclobutane (dimeric allene) with methacrylic acid[229].

Additions to allenes of substances which are more polar than ethylenes (*e.g.* acids, water, Grignard reagents and amines) will now be considered, although these reactions are not yet fully understood. It has not been proved that they always follow an ionic mechanism.

Allenes behave as nucleophiles in reactions with hydrochloric and perchloric acid and first add a proton to the more nucleophilic double bond. Depending upon the substituents, either an allyl cation or a vinyl cation is formed. The former is clearly favored in the case of tetraarylallenes, whereas allene itself and monosubstituted allenes may also undergo the addition *via* a vinyl cation, leading to 2-halopropenes.

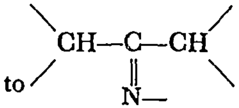


Allenes will behave as electrophiles in reactions with amines, water in the presence of mercuric salts, Grignard reagents, and hydrohalo acids in the presence of metal catalysts. These additions are best represented by an attack of the nucleophilic reactant on the most electrophilic carbon atom of the allene. In allene itself, and allenes with electron-attracting substituents, it is assumed that the central carbon atom is positively polarized $(>\overset{\delta^-}{C}=\overset{\delta^+}{C}=C<)^{27}$, this also being supported by quantum-chemical calculations; a nucleophilic reactant, therefore, would be expected to prefer the 2-position of an allene. This is confirmed by experiment, since an attack by nucleo-



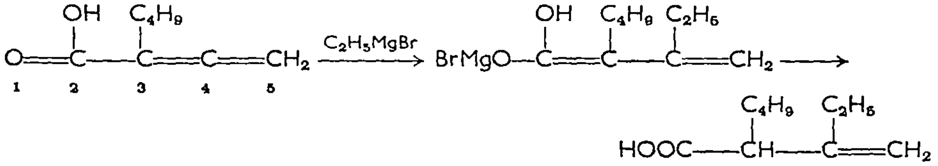
(17)

TABLE 8. Addition of HX to allenes according to equation (17).

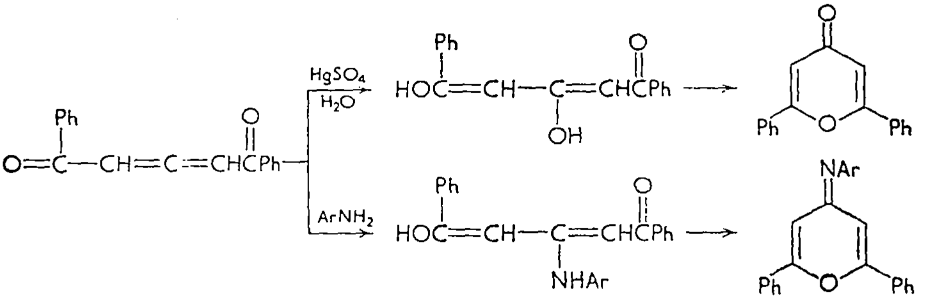
Example	Substituents				HX added	Reaction product	Remarks	Reference
16	R^1	R^2	R^3	R^4		119		
a	H	H	H	H	HCl	a	At −78°; $BiCl_3$	222
b	H	H	H	H	HF	a	At −78°; only $(CH_3)_2CF_2$ isolated	223
c	H	H	H	H	HOH	a	Ketonizes to acetone	40
d	H	H	H	H	HCN	a	ZnO, 425°	224
e	CH_3	H	H	H	HCl	a	At −78°	222
f	CH_3	CH_3	H	H	HCl	b	and $(CH_3)_2C{=}CHCH_2Cl$	222
g	H	H	C_3H_7	H	HCl	a	$BiCl_3$	61
h	H	H	CH_3	CH_3	HBr	b		225
i	CH_3	CH_3	Cl	H	HCl	b		76
j	CH_3	C_4H_9	Cl	Cl	HCl	b		226
k	$CH_2{=}CH$	Cl	H	CH_2Cl	HCl	b		36
l	H	H	C_3H_7	H	HBr	a		225
m	H	H	C_3H_7	H	HOH	a	$HgSO_4$; ketonizes	61
n	Various aromatic substituents				$HClO_4$	b	Carbonium salts are formed	43, 44
o	Various aromatic substituents				HOH	b	*Via* the hydrolysis of carbonium salts	43, 44
p	CN	H	H	H	HCl	a		114
q	CN	H	H	H	HOR	a	R = CH_3, C_2H_5, C_4H_9 or Ph	114
r	CN	H	H	H	HNR_2	a		
s	CN	H	H	H	H_2NNHR	a	Rearrange to 	114
t	H	H	$COOC_2H_5$	H	H_2NPh	a		117
u	PhCO	CH_3	CH_3	H	HOH	a	$HgSO_4$; ketonizes	93
v	H	H	$COOC_2H_5$	H	$HOCH_3$	a		154

philes on the terminal carbon atom of an allene has never been observed. The addition of nucleophiles to allenes is thus more uniform than the addition of electrophiles. This may also be seen from Table 8, where some polar additions to allenes according to equation (17) have been collected.

α-Allenic carbonyl compounds are analogs of vinylallenes and as such can undergo 1,4-addition reactions. Wotiz[235] showed that the reaction of butylallenecarboxylic acid with ethylmagnesium bromide involves a 1,4-addition of the Grignard reagent, and that the addition of water, amines, or Grignard reagents to α-allenic ketones prepared by Gaudemar-Bardone[93] is likely to follow the same pattern. The addition products of 1,3-dibenzoylallene undergo an interesting ring closure to γ-pyrone derivatives (**120**)[236].



$$O{=}C(OH){-}C(C_4H_9){=}C{=}CH_2 \xrightarrow{C_2H_5MgBr} BrMgO{-}C(OH){=}C(C_4H_9){-}C(C_2H_5){=}CH_2 \longrightarrow HOOC{-}CH(C_4H_9){-}C(C_2H_5){=}CH_2$$

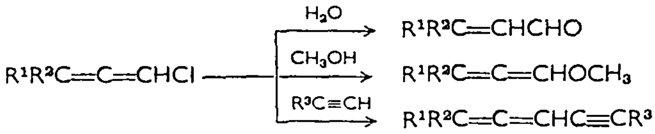


(**120**)

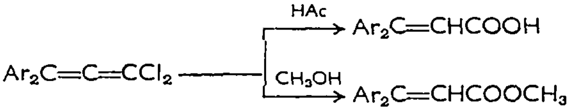
Radical additions to allenes are more sluggish than to isolated and conjugated dienes. Moreover, the rate coefficients of the addition of methyl radicals to allenes were independent of the size of the substituents on the allene. From this it was concluded that the addition took place on the central carbon atom[237]. On the other hand, Haszeldine[27] found that trifluoromethyl radicals (produced by irradiation of trifluoroiodomethane) add to the terminal carbon atom of allene. This discrepancy was resolved by ascribing nucleophilic properties to the methyl group, but electrophilic properties to the trifluoromethyl group[237]. Sulfur radicals (from thiols at high temperatures) give equal amounts of the 1- and the 2-addition products with allene[238].

Recent studies with thiyl radicals point to a preferential attack at the terminal positions of the allene system[373]. Acetoxyl radicals (from lead tetraacetate) give rise to 1,2-diacetoxypropenes with allenes[239]. Schlenk[240] found that two atoms of sodium add to tetraphenylallene and he claimed to have a 1,3-disodio-addition product. This would be surprising, since all known radical reactions of allenes involve 1,2-diradicals.

Certain allenes with functional groups undergo reactions which do not change the allene system (see also the hydrogenation with lithium aluminum hydride, page 1073). Haloallenes can exchange halogen with alkoxyl, hydroxyl or alkinyl[372] groups. Kinetic studies indicate that the tendency to form an allene carbonium ion as an intermediate is not great[185,242].

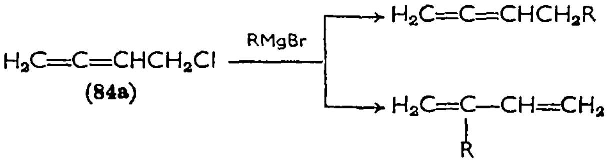


(R^1, R^2, R^3 = alkyl)

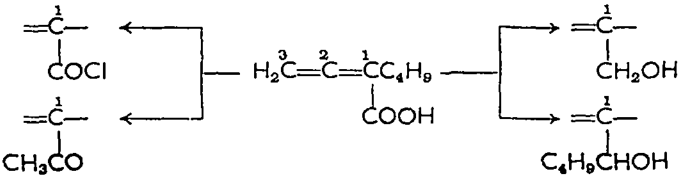


The chlorobutadiene **84a** reacts with most Grignard reagents, retaining the allene structure; with a few, however, a rearrangement to conjugated dienes occurs, analogous to the rearrangement of **84a** to isoprene[243].

Wotiz[189] prepared a series of new allenes from 1-butylallene-1-

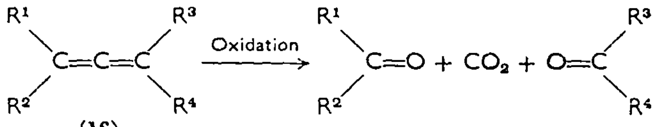


(R = CH_3, C_4H_9, C_7H_{15}, C_6H_5, $C_6H_5CH_2$)



carboxylic acid in which the allene system survived surprisingly drastic conditions.

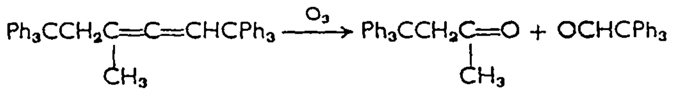
h. Oxidation. Forced oxidation splits allenes into the corresponding carbonyl compounds.



(16)

This is often sufficient proof of the structure of the parent allene[22,41,48,57,61]. The reagents employed include potassium permanganate in acetone or pyridine, chromic acid in acetic acid, and ozone. Slight difficulty is experienced in oxidizing sterically hindered allenes. Thus tetraphenylallene is resistant to permanganate but is cleaved by chromic acid[39]. The ozonization of an allene is always the cleanest oxidation method and has been widely used to establish the constitution of unknown allenes[103,120,131,147,181,243]. It has the advantage over other oxidizing agents in that aldehydes are not oxidized further to carboxylic acids. This may be of importance when allenes are investigated which are not tetrasubstituted.

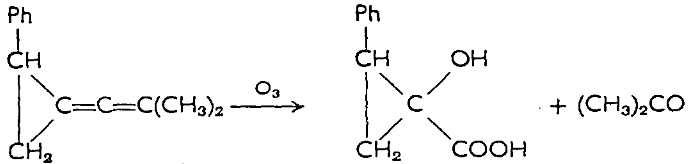
One special example may be sufficient to illustrate the ozonization method: If the substance obtained from isopropenylacetylene and triphenylmethyl is the allene **84t**, then it should give triphenylbutanone and triphenylacetaldehyde on ozonization. This was indeed observed[131].



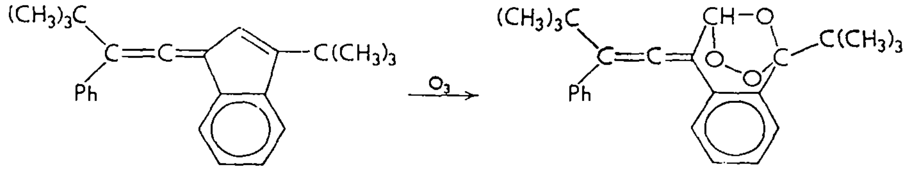
$$\underset{\displaystyle CH_3}{Ph_3CCH_2\underset{|}{C}{=}C{=}CHCPh_3} \xrightarrow{O_3} \underset{\displaystyle CH_3}{Ph_3CCH_2\underset{|}{C}{=}O} + OCHCPh_3$$

(84t)

The ozonization does not always break up the allenes completely. In the vinylidenecyclopropane **94** only one double bond was broken[147], and in the indenoallene **102** the whole allene group survived mild ozonization[244].



(94)

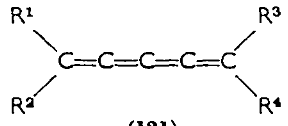


(102)

B. Pentatetraenes

1. Introduction

Pentatetraenes are cumulenes of type **121**. They proved to be inaccessible until very recently when Kuhn and Fischer[375] succeeded in preparing two tetraarylpentatetraenes which are still quite stable. The stability is in agreement with quantum-chemical calculations which did not predict a marked instability for such compounds[350].

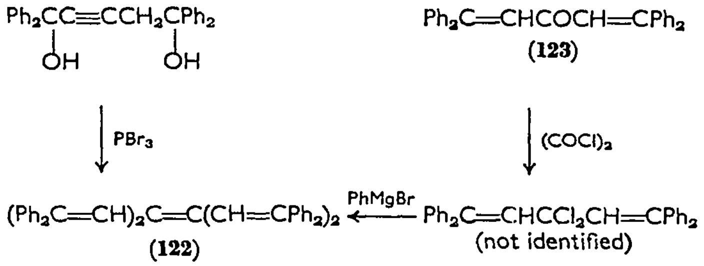


(121)

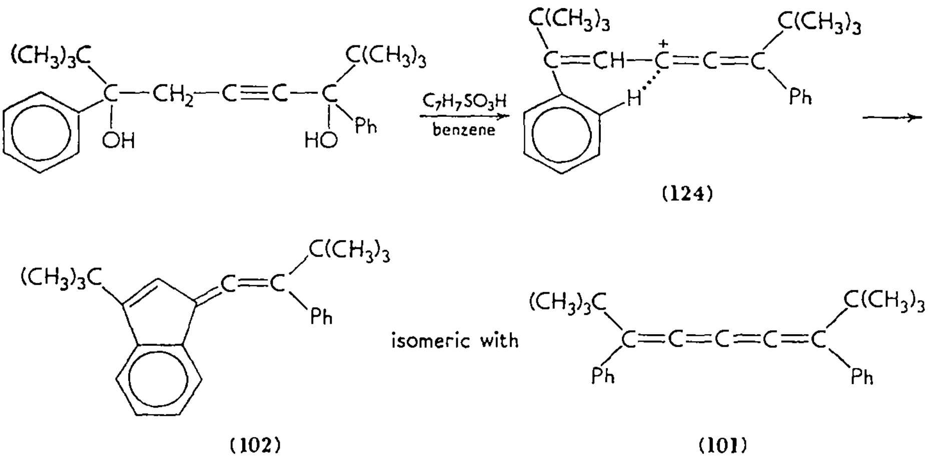
2. Earlier attempts to prepare pentatetraenes

a. 1,1,5,5-Tetraphenylpentyne-1,5-diol has been dehydrated by means of phosphorous tribromide[245]. A yellow, strongly fluorescent hydrocarbon (λ_{max} = 405 mμ) was obtained to which the structure of tetraphenylpentatetraene was assigned, mainly on the basis of its ultraviolet spectrum. Ozonization gave 1·3 moles of benzophenone as expected for the pentatetraene. However, molecular-weight determinations showed this hydrocarbon to be a dimeric pentatetraene and the nuclear magnetic resonance spectrum exhibited vinyl protons, a fact that cannot be reconciled with the pentatetraene formula.

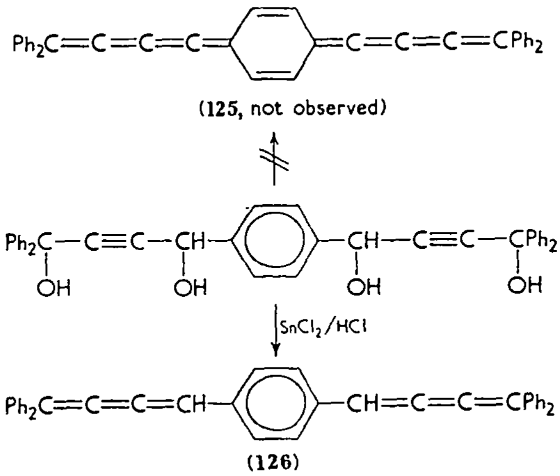
Subsequently Kuhn and Schulz[244] showed by an independent synthesis that the dimeric pentatetraene is the tetrakis-(1,1-diphenylvinyl)ethylene **122**. Marin [246] obtained **122** from the pentadienone **123** and also thought to have prepared tetraphenylpentatetraene. The formation of **122** from the ketone is more easy to interpret (dimerization on the central carbon atom by elimination of MgBrCl) than its formation from the pentynediol.



b. Japanese workers dehydrated 1,5-di-*t*-butyl-1,5-diphenylpentynediol and obtained a hydrocarbon which possessed the correct analytical data for the expected pentatetraene **101**. Moreover, when the dehydration was carried out with *d*-camphorsulfonic acid, an optically active hydrocarbon appeared, to which the structure of a pentatetraene was assigned. However, it was puzzling that this 'pentatetraene' consumed exactly three moles of hydrogen rather than four moles on catalytic hydrogenation[180]. Kuhn and Schulz[181] found on ozonization *o*-trimethylacetylbenzoic acid in addition to *t*-butyl phenyl ketone. This is not in agreement with a pentatetraene formula but fits perfectly for the indenoallene **102**. Its formation can be explained in close analogy to the indene formation from arylallenes, as going *via* the carbonium ion **124**. If this is correct then the expected pentatetraene did not even occur as an (unstable) intermediate.



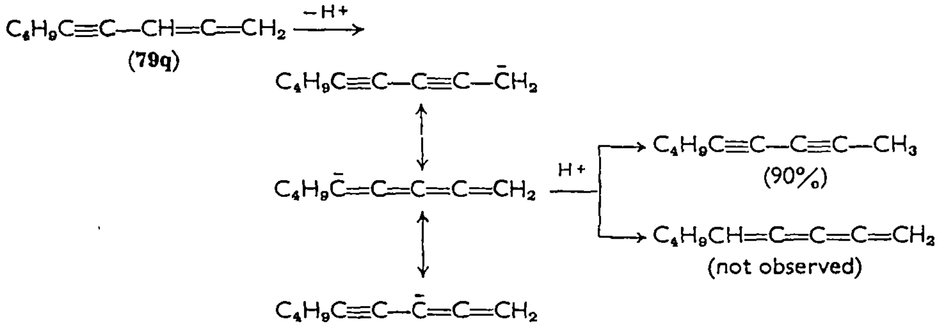
c. Kuhn and Fischer[247] reported the synthesis of the bispentatetraene **125**, thought to arise from the treatment of a tetraol with stannous chloride in ethereal hydrogenchloride. However, in a subsequent paper[248] they corrected the bispentatetraene formula in favor of the bisbutatriene formula **126**.



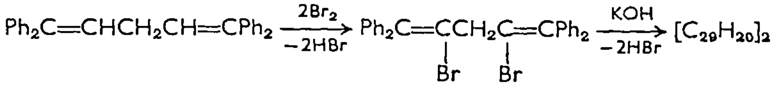
d. Coffman[249] claimed to have obtained pentatetraene by a Hofmann degradation. The hydrocarbon was described as a colorless liquid, boiling at 80–90°. No experiments to prove the exact location of the double bonds were, however, reported.

$$CH_2{=}CH{-}C{\equiv}C{-}CH_2\overset{+}{N}(CH_3)_3 \xrightarrow{AgOH} CH_2{=}C{=}C{=}C{=}CH_2$$

e. Butylpentadienyne **79q** is isomeric with butylpentatetraene. The prototropic rearrangement of **79q** goes *via* a mesomeric anion where the pentadiyne-like structure has apparently more weight than the pentatetraene-like structure, because this rearrangement gives a 90% yield of butylpentadiyne[113].



f. 1,1,5,5-Tetraphenyl-1,4-pentadiene reacts smoothly with bromine to give the dibromopentadiene **127**. Alkali in alcoholic solvents converts **127** into a hydrocarbon (λ_{max} = 297 mμ) which has the formula $C_{58}H_{40}$ and is thus a dimeric pentatetraene. Attempts to gain insight into its constitution have remained unsuccessful[28].

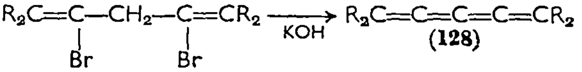


$$\mathrm{Ph_2C{=}CHCH_2CH{=}CPh_2 \xrightarrow[-2HBr]{2Br_2} Ph_2C{=}\underset{Br}{\underset{|}{C}}CH_2\underset{Br}{\underset{|}{C}}{=}CPh_2 \xrightarrow[-2HBr]{KOH} [C_{29}H_{20}]_2}$$

(127)

3. Preparation and reactions of pentatetraenes*

When the dibromopentadiene **127** was dehydrohalogenated in dimethylformamide with alcoholic alkali, tetraphenylpentatetraene (**128**) could be obtained as pale yellow prisms (m.p. 120° dec.). Tetraanisyldibromopentadiene gave the corresponding pentatetraene in yellow needles (yield 90%). Hydrogenation of **128** (R = anisyl) with



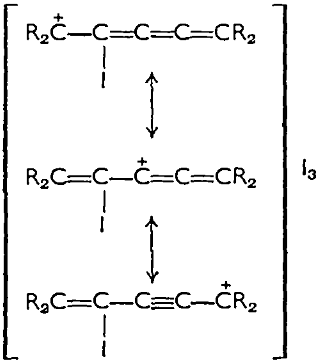
$$\mathrm{R_2C{=}\underset{Br}{\underset{|}{C}}{-}CH_2{-}\underset{Br}{\underset{|}{C}}{=}CR_2 \xrightarrow[KOH]{} \underset{(128)}{R_2C{=}C{=}C{=}C{=}CR_2}}$$

(R = Ph, p-$CH_3OC_6H_4$)

Raney nickel (4·0 moles of H_2) afforded tetraanisylpentane, identified by an independent synthesis. The nuclear magnetic resonance is in accord with the formula **128** (no vinyl protons). The main band in the ultraviolet spectrum lies in the region predicted by molecular-orbital calculations (section IV)[375].

Tetraanisylpentatetraene has pronounced nucleophilic properties. It can be protonated by acetic acid and with iodine a crystalline periodide is obtained (λ_{max} = 685 mμ; strong infrared absorption at 4·80 μ, characteristic for butatriene)[376]:

128 $\xrightarrow{I_2}$



Further investigations in this field are at present in progress in our laboratory.

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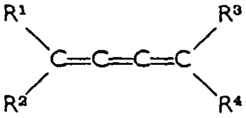
* The results reported in the following paragraph were obtained in our laboratory after the manuscript had been submitted to the editor.

III. CUMULENES WITH AN ODD NUMBER OF DOUBLE BONDS

This section covers compounds containing from three to as many as nine consecutive carbon–carbon double bonds. However, decanonaenes and octaheptaenes are not very stable, and only a limited number of them appear in the literature. There seems to be a large gap in stability between hexapentaenes and octaheptaenes; the latter exist only in solution while some of the hexapentaenes melt as high as 300° without decomposition. Butatrienes are even more stable.

A. Butatrienes

Butatrienes are compounds with three cumulated double bonds of type **129**. It is striking that, with two exceptions, no alkyl-substituted butatrienes are known. Approximately 80% of all known butatrienes are tetraarylbutatrienes. It is hoped that all known butatrienes are either recorded in Tables 9 to 12 or mentioned in the text.



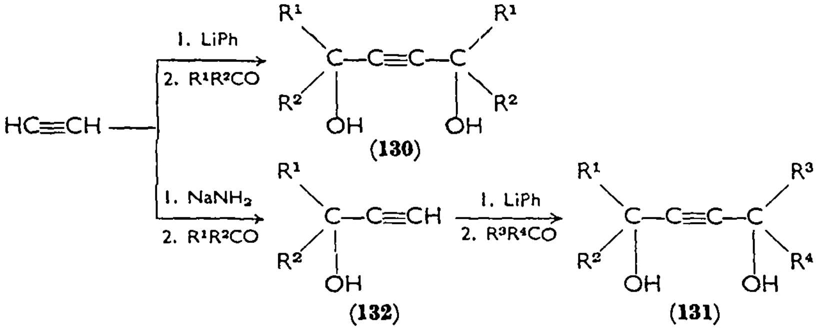
(129)

1. Methods of preparation

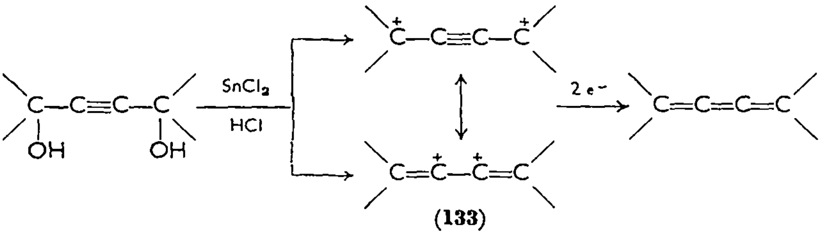
Methods for synthesizing butatrienes are much less numerous than those for allenes; only three different methods have to be considered here, the first (reduction of butynediols) being far superior to all other techniques.

a. Reduction of butyne-1,4-*diols.* This is the best route to butatrienes. The required butynediols are readily available from the condensation of carbonyl compounds with acetylene. Symmetrically substituted butynediols **130** are best prepared from dimetalated acetylene (from acetylene and phenyllithium in ether) and an appropriate carbonyl compound. Unsymmetrically substituted butynediols **131** are obtained in two steps: monometalated acetylene (from acetylene and sodamide in liquid ammonia, or ethylmagnesium bromide in tetrahydrofuran) is condensed with a carbonyl compound to give the propynols **132**; these are metalated again (by phenyllithium in ether) and condensed with a second carbonyl compound to give **131** (equation

18)*. Reduction of the butynediols is carried out with stannous chloride in ethereal hydrogen chloride or with phosphorous tribromide in pyridine. It is most likely that the halide ions facilitate the formation of a dicarbonium ion **133** which takes up two electrons (coming from the reaction $Sn^{II} \rightarrow Sn^{IV} + 2e$ or $P^{III} \rightarrow P^{V} + 2e$) rather than two halide ions. (Later, examples will be encountered where the halide ions compete successfully with the electrons, and where then no reduction of the butynediols will take place.)

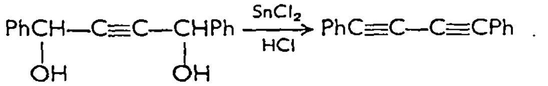


(18)



(19)

Di-*s*-butynediols (**131**, $R^1 = R^2 = H$) are unsuitable for reduction. Here, the dicarbonium ion forms a diacetylene by loss of two protons[256], *e.g.*



$$\underset{\displaystyle OH}{PhCH}{-}C{\equiv}C{-}\underset{\displaystyle OH}{CHPh} \xrightarrow[HCl]{SnCl_2} PhC{\equiv}C{-}C{\equiv}CPh\ .$$

Butynediols **131** with $R^1 \neq R^2$ and $R^3 \neq R^4$ should exist in meso and racemic forms. Simamura[257] succeeded in separating certain tetraarylbutynediols into meso and racemic forms. On reduction he observed the same butatrienes in each case, with no preferential formation of *cis* or *trans* butatrienes. This finding is in accord with the idea that the reduction proceeds *via* planar carbonium ions.

Table 9 records butatrienes which have been obtained by the reduction of butynediols.

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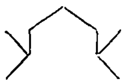
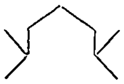
* Experimental details can be found in refs. 74 and 250–254.

TABLE 9. Butatriene syntheses according to equations (18) and (19).

Example 129	Substituents of butatriene				Yield (%)	M.p.	λ_{max} ($m\mu$)		Reference
	R^1	R^2	R^3	R^4					
a	PhCH=CH	H	PhCH=CH	H	—	309—311	400	430	254
b					16	150	230	272	74
c	Ph	α-C_4H_3S	Ph	α-C_4H_3S	27	205		466	255
d	Ph	$(CH_3)_3C$	Ph	$(CH_3)_3C$	30	105	245	323	258, 259
e	2-$BrC_6H_3C_6H_4$		2-$BrC_6H_3C_6H_4$		64	345	450	481	23
f	2-$NO_2C_6H_3C_6H_4$		2-$NO_2C_6H_3C_6H_4$		24	—	360	491	23
g	o,o-$C_6H_4C_6H_4$		o,o-$C_6H_4C_6H_4$		90	330	451	483	260, 261, 262
h	o,o-$C_6H_4C_6H_4$		Ph	p-BrC_6H_4	46	242		456	250
i	Ph	Ph	2-$NO_2C_6H_3C_6H_4$		20–30	188		470	248
j	Ph	Ph	o,o-$C_6H_4C_6H_4$		51	215		455	248, 250, 253
k	Ph	m-BrC_6H_4	Ph	m-BrC_6H_4	44	200	275	427	253
l	Ph	p-BrC_6H_4	Ph	p-BrC_6H_4	49–60	268		428	250, 253
m	Ph	o-ClC_6H_4	Ph	o-BrC_6H_4	20	173	322	398	253
n	Ph	o-ClC_6H_4	Ph	m-BrC_6H_4	20	182	325	405	253
o	Ph	o-ClC_6H_4	Ph	p-BrC_6H_4	20	180	270	408	253
p	Ph	p-ClC_6H_4	Ph	o-BrC_6H_4	20–35	208	276	426	253
q	Ph	p-ClC_6H_4	Ph	p-BrC_6H_4	25	251	282	430	253
r	Ph	p-ClC_6H_4	Ph	p-ClC_6H_4	25	250	282	430	253, 255 257, 262

s	Ph	p-$NO_2C_6H_4$	Ph	o-ClC_6H_4	20	173	258	425	253
t	Ph	m-$NO_2C_6H_4$	Ph	m-$NO_2C_6H_4$	35	209		426	263
u	Ph	p-$NO_2C_6H_4$	Ph	p-$NO_2C_6H_4$	10	293	273	466	253, 263
v	Ph	o-BrC_6H_4	Ph	Ph	30	141	273	415	253
w	Ph	Ph	Ph	p-BrC_6H_4	56	223		424	250
x	Ph	o-ClC_6H_4	Ph	Ph	18	163	270	414	253
y	Ph	Ph	Ph	m-$NO_2C_6H_4$	—	203		420	248
z	Ph	Ph	Ph	p-$NO_2C_6H_4$	20	195	274	453	248, 253
aa	Ph	Ph	Ph	Ph	30	237	318	420	252, 253, 254, 262
bb	Ph	p-$CH_3OC_6H_4$	Ph	p-ClC_6H_4	25	210	281	435	253
cc	Ph	p-$CH_3OC_6H_4$	Ph	m-$NO_2C_6H_4$	20–30	173		432	248
dd	Ph	p-$CH_3OC_6H_4$	Ph	p-$NO_2C_6H_4$	20–30	251		470	248
ee	Ph	Ph	Ph	β-$C_{10}H_7$	35	196		433	250
ff	Ph	p-$CH_3C_6H_4$	Ph	p-$CH_3C_6H_4$	23	236			257
gg	Ph	Ph	p-$CH_3OC_6H_4$	p-$CH_3OC_6H_4$	44	236	286	440	248, 253
hh	Ph	α-$C_{10}H_7$	Ph	α-$C_{10}H_7$	32	236		408	255
ii	Ph	β-$C_{10}H_7$	Ph	β-$C_{10}H_7$	31	248		445	250, 262
jj	p-$CH_3C_6H_4$	p-$CH_3C_6H_4$	p-$CH_3C_6H_4$	p-$CH_3C_6H_4$	—	240		449	261
kk	p-$CH_3OC_6H_4$	β-$C_{10}H_7$	Ph	p-BrC_6H_4	32	224		445	250
ll	β-$C_{10}H_7$	p-$CH_3OC_6H_4$	p-$CH_3C_6H_4$	β-$C_{10}H_7$	30	262		459	250
mm	Ph	p-PhC_6H_4	Ph	p-PhC_6H_4	64	276		448	255
nn	Ph	Ph	H	9-Br-10-anthracenyl	30	168			210

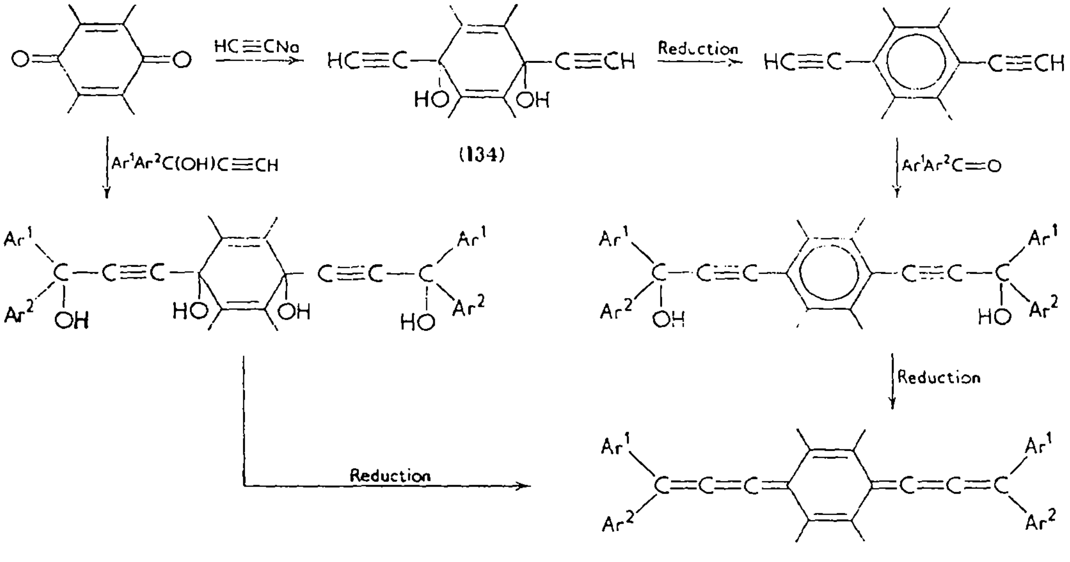
Table 10. Bisbutatrienes **135** from quinones, according to equation (20).

Example **135**	Substituents		Quinone underlying **135**	Yield (%)	M.p.	λ_{max} (mμ)	Reference
	Ar^1	Ar^2					
a[a]	Ph	Ph	Benzoquinone			360 539	281
b	Ph	Ph	Anthraquinone	65	365	258 294 540 583	281
c	Ph	p-BrC_6H_4	Anthraquinone	51	560	253 307 345 360 440 560 597 603	282
d	Ph	p-$CH_3C_6H_4$	Anthraquinone	75	540	253 302 343 360 439 557 590 599 606	282
e[a]	o,o-$C_6H_4C_6H_4$		Anthraquinone				281 282
f	Ph	Ph	Pentacenequinone	61	370	280 346 362 528 565	281

[a] Unstable, not isolated in pure state.

Bisbutatrienes can be prepared if bifunctional carbonyl compounds are introduced into equation (18) instead of R^3R^4CO. Dicarbonyl compounds used for this purpose include benzoquinone, anthraquinone, pentacenequinone, phenanthrenequinone, terephthalophenone, terephthalaldehyde and 9,10-diformylanthracene.

Equation (20) represents a slight variation of the equation (18), insofar as the intermediate dipropynols **134** may be reduced to diethinylaromatics before further reaction with carbonyl compounds. Table 10 collects the bisbutatrienes **135** prepared from quinones according to equation (20).

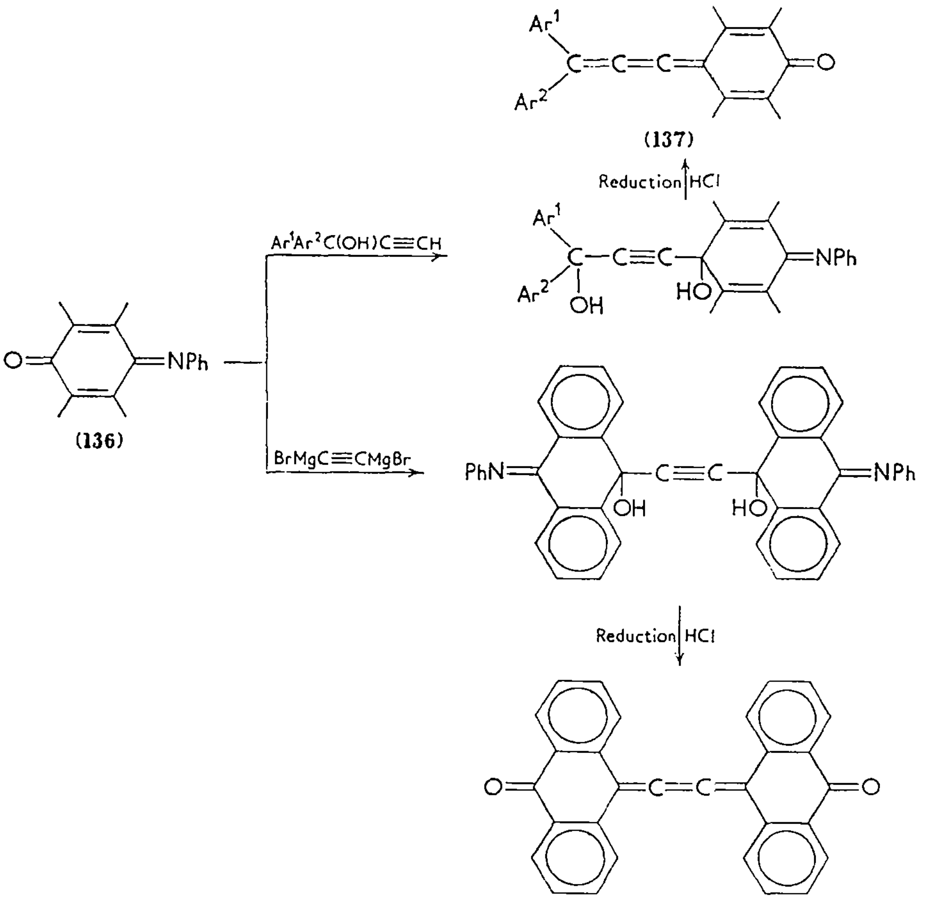


(135)

(20)

The bisbutatrienes **135** are stable, well crystalline, black-violet compounds. They can be regarded as quinodimethane derivatives. Quinomethane derivatives can also be prepared on a cumulene base if one of the carbonyl groups in the quinones is blocked by forming the anils **136**. The reaction with diarylpropynols according to equation (18) and reduction according to equation (19) leads then to the propadienylidenequinones **137**. If anthraquinone monoanil is condensed with dimetalated acetylene, followed by reduction, an interesting higher homolog **138** of anthradiquinone is produced[283]. These reactions are shown in equation (21) and Table 11 collects the propadienylidenequinones that have been prepared.

It is found that the reactivity of the carbonyl group in the propadienylideneanthrones is considerably diminished as compared with the two lower members of this series (**139**, $n = 0$ and $n = 1$). Thus in



(21)

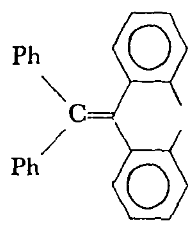
the butatriene **139**, $n = 2$, the carbonyl group does not undergo alkinylation, while in the allene **139**, $n = 1$, and in the ethylene **139**, $n = 0$, the carbonyl group behaves normally.

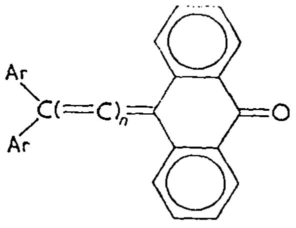
Another type of bisbutatrienes is obtained if diacyl aromatics are used instead of quinones. Here the conjugation between the two cumulene units is provided by an aromatic ring rather than by a quinoid system. Their syntheses are straightforward according to equations (18) and (19) (with a diacyl aromatic compound instead

TABLE 11. Propadienylidenequinones (**137**) prepared according to equation (21).

Example **137**	Substituents Ar¹	Substituents Ar²	Quinone underlying **137**	Yield (%)	M.p.	λ_{max} (mμ)	Reference
a	Ph	Ph	Anthraquinone	93	242	258 269 288 334 496	282
b	Ph	*p*-ClC_6H_4	Anthraquinone	45	220	257 288 332 378 497	284
c	Ph	*o*-ClC_6H_4	Anthraquinone	23	164	256 277 331 381 481	284
d	Ph	*p*-BrC_6H_4	Anthraquinone	40	228	257 292 499	284
e	*o,o*-$C_6H_4C_6H_4$		Anthraquinone	76	278	248 277 339 488 515	281, 283
f	Ph	Ph	Phenanthrenequinone			342 520	281
g	Ph	Ph	Pentacenequinone	50	234	283 325 376 494 530	281
h	*o,o*-$C_6H_4C_6H_4$		Pentacenequinone	37	296	244 284 325 515 553	281

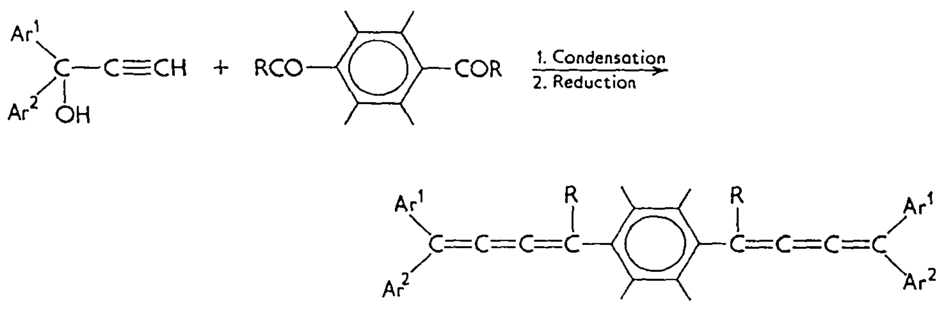
Table 12. Bisbutatrienylarenes (**140**).

Example **140**	Substituents Ar¹	Ar²	R	Diacyl aromatic underlying **140**	Yield (%)	M.p.	λ_{max} (mμ)	Reference
a	Ph	Ph	H	Terephthalaldehyde	75	235	285 370 475 507	248
b	Ph	Ph	H	Nitroterephthalaldehyde	67	360		248
c	Ph	Ph	Ph	Isophthalophenone	82	180	325 423	294
d	Ph	Ph	Ph	Terephthalophenone	70	264	280 405 485	294, 248
e	p-BrC$_6$H$_4$	p-BrC$_6$H$_4$	Ph	Isophthalophenone	61	168	324 435	294
f	p-BrC$_6$H$_4$	p-BrC$_6$H$_4$	Ph	Terephthalophenone	50	530	410 495	294
g	o,o-C$_6$H$_4$C$_6$H$_4$		Ph	Terephthalophenone	55	388	432 524	294
h	o,o-C$_6$H$_4$C$_6$H$_4$		Ph	Isophthalophenone	53	244	330 471	294
i			Ph	Terephthalophenone	15	387	449 544	294
j			Ph	Isophthalophenone	20	199	335 487	294
k	Ph	Ph	H	9,10-Diformylanthracene	60	360	285 395 600	248



(**139**, $n = 0, 1, 2$)

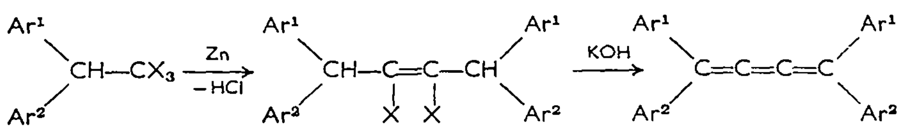
of R^3R^4CO). Table 12 records the known examples of these bis-butatrienylarenes **140**.



(**140**)

b. Elimination from suitably substituted butenes. This was the method which led to the discovery of cumulenes higher than allenes. Out of the 14 possible butenes disubstituted by X (X = halogen, hydroxy), only the two symmetrical ones provide a basis for the synthesis of butatrienes.

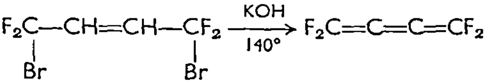
Brand treated 1,1,4,4-tetraaryl-2,3-dihalo-2-butenes (**141**) with alcoholic alkali and obtained excellent yields of the corresponding butatrienes **142**. The dihalobutenes are prepared by condensing two molecules of a 1,1-diaryl-2,2,2-trihaloethane:



(**141**) (**142**)

This method has been applied so far only to the syntheses of tetraarylbutatrienes of the symmetric type **142**[10,264–272].

Martin and Sharkey treated 1,1,4,4-tetrafluoro-1,4-dibromo-2-butene with KOH in the absence of oxygen and obtained tetrafluorobutatriene, a highly explosive colorless gas (b.p. −5°). Its



$$\underset{\text{Br}}{\overset{|}{\text{F}_2\text{C}}}\text{—CH=CH—}\underset{\text{Br}}{\overset{|}{\text{CF}_2}} \xrightarrow[140^\circ]{\text{KOH}} \text{F}_2\text{C=C=C=CF}_2$$

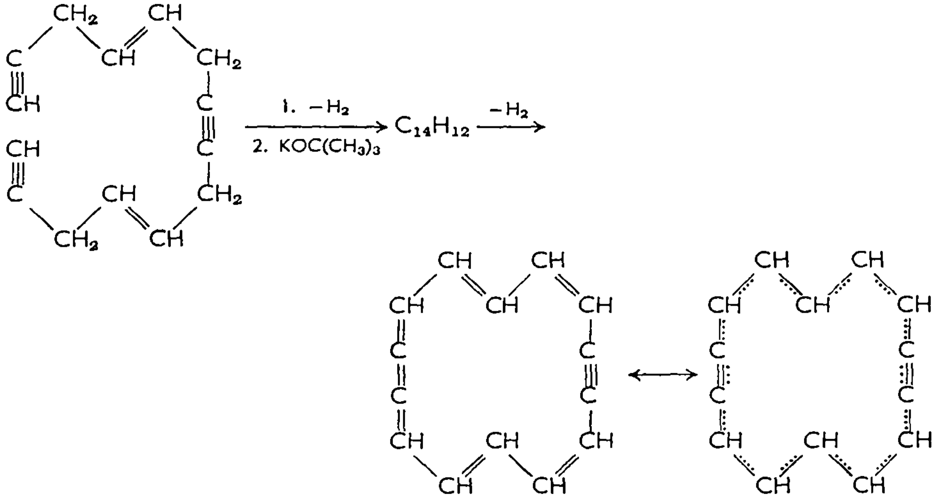
constitution has been established by mass spectrographic and by infrared spectrographic analysis, by the nuclear magnetic resonance spectrum which indicated that all the fluorine atoms are equivalent, and by reaction with bromine and chlorine which converted it to well defined polyhalobutanes[273,274].

Brand's tetraarylbutatrienes can, of course, also be obtained by the reduction of the corresponding butynediols; but it would not be possible to prepare tetrafluorobutatriene by the reduction of the corresponding butynediol, since the latter does not exist.

c. Double-bond rearrangements; miscellaneous methods. The 3,4-dihydrohexapentaene **115** (a diallene) underwent a prototropic rearrangement, yielding the 2,3-dihydrohexapentaene **143** (a vinylbutatriene) (see also Table 6). The constitution of **143** has been

$$\underset{\textbf{(115)}}{\text{Ph}_2\text{C=C=CH—CH=C=CPh}_2} \xrightarrow{\text{KOH}} \underset{\textbf{(143)}}{\text{Ph}_2\text{C=C=C=CH—CH=CPh}_2}$$

proved by analysis of the infrared and nuclear magnetic resonance spectra and by partial and complete hydrogenation[210]. Sondheimer prepared many macrocyclic polyenes (annulenes) by oxidative



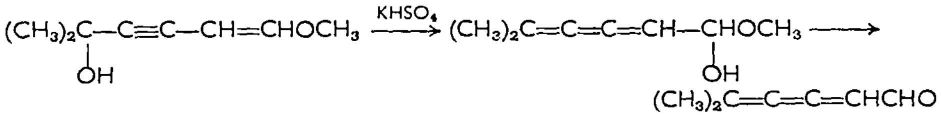
(144) **(145)**

coupling of α,ω-polyenynes and subsequent prototropic rearrangement. Tetradeca-4,10-diene-1,7,13-triyne gave dehydro[14]annulene and 1,8-bisdehydro[14]annulene **144**. The latter behaves as an aromatic system, and a Kékulé structure of this hydrocarbon can only be formulated if the ring contains a butatriene unit in addition to a triple bond[316]. However, according to a nuclear magnetic resonance analysis, the butatriene unit cannot be located in one side, and a formula like **145** is considered to be more adequate than **144**.

As mentioned in Section II, vinylacetylenes undergo 1,4-additions to give allenes. Divinylacetylene undergoes a 1,6-addition of hydrogen (from sodium amalgam in alcohol) and furnishes 1,3-dimethylbutatriene. Its structure seems to be confirmed by oxidative degradation, although it is surprising that a disubstituted butatriene should be so stable. Equally surprising is the existence of the 1,1-dimethyl-4-

$$H_2C{=}CH{-}C{\equiv}C{-}CH{=}CH_2 \xrightarrow[Na/Hg]{H_2} CH_3CH{=}C{=}C{=}CHCH_3$$

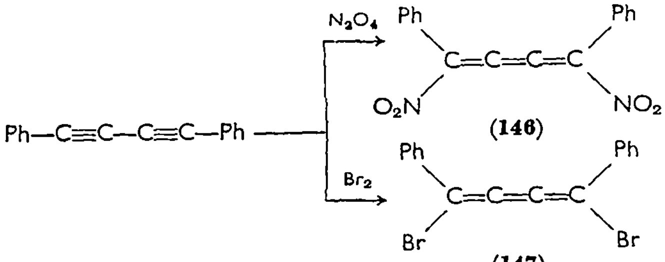
formylbutatriene, arising from a propargylic rearrangement coupled with an allylic shift of a double bond. The structure of this aldehyde



$$(CH_3)_2\underset{OH}{\underset{|}{C}}{-}C{\equiv}C{-}CH{=}CHOCH_3 \xrightarrow{KHSO_4} (CH_3)_2C{=}C{=}C{=}CH{-}\underset{OH}{\underset{|}{C}}HOCH_3 \longrightarrow (CH_3)_2C{=}C{=}C{=}CHCHO$$

was ascertained unequivocally by infrared spectroscopy (strong band at 2066 cm^{-1}) and by its nuclear magnetic resonance spectrum. Hydrogenation yielded small quantities of the expected saturated alcohol[298]. A very similar rearrangement was recently reported by Wartanjan and Badanjan[371].

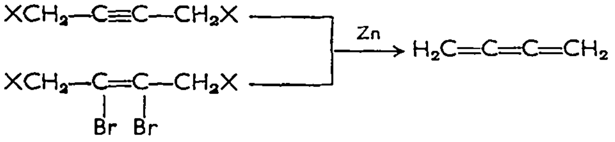
The 1,4-addition of nitrogen tetroxide and of bromine to diphenyldiacetylene has been claimed. The structures of the resulting butatrienes (**146** and **147**) are, however, mainly based on ultraviolet spectroscopic considerations[278,279].



(146)

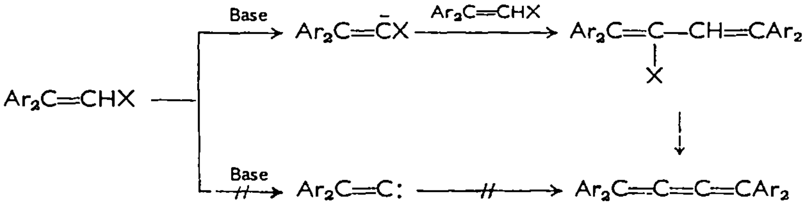
(147)

Butatriene itself can be prepared by the action of zinc on various halobutynes or halobutenes. It seems to be somewhat more stable than tetrafluorobutatriene. Its constitution has been established



by essentially the same methods as described for tetrafluorobutatriene[276,277].

The elimination of HX from certain 2-substituted 1,1-diarylethylenes leads to butatrienes through a dimerization. This reaction does probably not proceed *via* a carbene intermediate (no trapping was possible) but must be considered as a normal *C*-substitution[311,312,313]. This is also suggested by Köbrich's[374] synthesis of tetrabenzylbutatriene.



(X = Cl, Br, NO_2; Ar_2 = Ph_2, *o,o*-$C_6H_4C_6H_4$, $(C_3H_7)_2C(o\text{-}C_6H_4)_2$)

$$(PhCH_2)_2C{=}CHCl \xrightarrow[AgCl]{C_4H_9Li} (PhCH_2)_2C{=}C{=}C{=}C(CH_2Ph)_2$$

2. Chemical properties and reactions of butatrienes*

a. General properties. As may be seen from Tables 9 to 12, most of the butatrienes are stable compounds with remarkably high melting points. The stability is decreased if one or more of the four substituents are hydrogen atoms. Thus 1,4-distyrylbutatriene (**129a**) can

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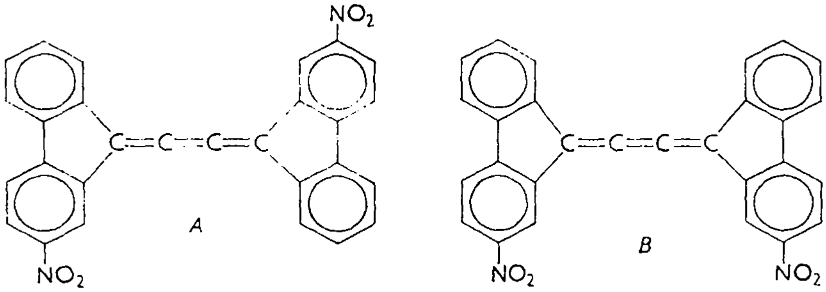
* A discussion of the ultraviolet and infrared spectra of butatrienes has been postponed to section IV because they are of particular interest when compared with the spectra of the hexapentaenes and the higher members of this cumulene series.

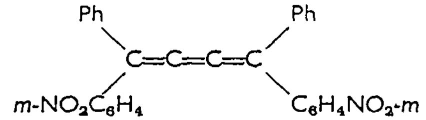
only be obtained by a very careful process of isolation[254], and butatriene itself is extremely labile. The instability of substituted butatrienes can be mainly attributed to a facile prototropic rearrangement, which will be dealt with later. Tetraarylbutatrienes are insoluble in ether, alcohol and petroleum ether. They show an increased solubility in the series of solvents: benzene, chloroform and dimethylformamide. Alkyl-substituted butatrienes are much more soluble. Tetrasubstituted butatrienes are less sensitive towards acids and bases than the corresponding allenes. Contrary to allenes, butatrienes have a characteristic ultraviolet spectrum and in general an uncharacteristic infrared spectrum.

b. cis–trans *Isomerism.* As has been pointed out in the introduction to this chapter, if the valences of the carbon atom are directed to the vertices of a tetrahedron, then it follows that in butatrienes the four substituents are all in the same plane; and if there is no rotation along the cumulene system *cis–trans* isomeric butatrienes should exist. There had been many unsuccessful attempts to verify this isomerism, before Kuhn and Scholler[23] succeeded in separating bis-(2-nitrobiphenylene)butatriene (**129f**) into the two isomers *A* and *B*. They subjected the mixture of butatrienes **129f**, as obtained by the usual synthesis, to chromatography on alumina and isolated two pure compounds, which had identical ultraviolet spectra but differed in their infrared absorption. On heating one of the isomers, it was transformed into the other. The small difference in the dipole moments of these two isomers permitted the assignment of the *trans* formula to isomer A.

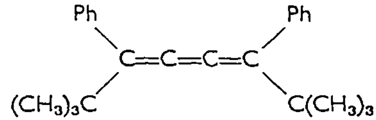


(129f)

Only two further butatrienes have been separated into *cis–trans* forms: 1,3-diphenyl-1,3-di-*m*-nitrophenylbutatriene (**129t**) and 1,3-diphenyl-1,3-di-*t*-butylbutatriene (**129d**). Similar arguments to those



(129t)

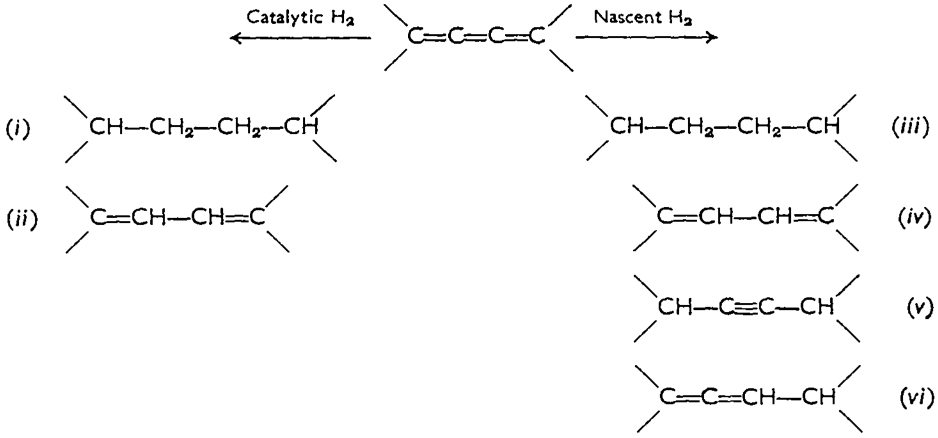


(129d)

quoted above were used to prove the *cis–trans* isomerism[259,263].

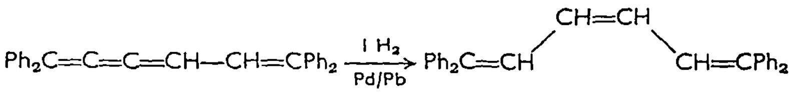
There are certain theories concerning the electronic structure of cumulenes according to which the central double bond exhibits some triple bond character. In this case, a separation into *cis–trans* forms would be expected to become more difficult, because the energy of activation for transforming the isomers into one another will be decreased (see also section IV).

c. Hydrogenation. The following scheme shows the products that can be obtained from butatrienes by catalytic hydrogenation on the one hand and by reaction with nascent hydrogen on the other:

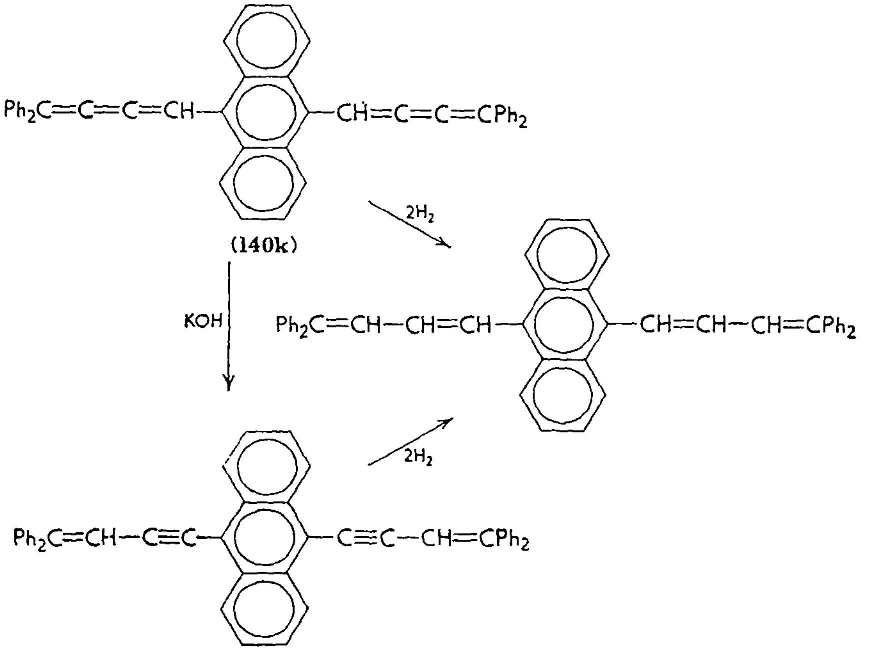


(*i*) In the presence of Raney nickel or palladium, butatrienes take up three moles of hydrogen leading to the corresponding butanes. The latter may be identified by independent synthesis, and thus the complete hydrogenation can make an important contribution to the proof of the structure of any butatriene[10].

(*ii*) A palladium catalyst poisoned by lead[215] affords a specific partial hydrogenation of butatrienes to give conjugated butadienes[210]. In the case of properly substituted butatrienes, the hydrogenation is stereospecific. Thus the vinylbutatriene **143** gave pure *cis*-hexatriene; the bisbutatriene **140k** gave a bisbutadiene which is identical with a compound obtained by partial hydrogenation of the bisbutenyne **148**. Since it is well known that acetylenes afford *cis*-ethylenes on partial hydrogenation, it follows that the hydrogenation of the cumulene must have been stereospecific too. Karrer and colleagues[285] found that the bisbutatriene **149** (which is related to the carotenes) takes up two moles of hydrogen, yielding a mixture of polyenes, at least two of which have *cis* configurations.



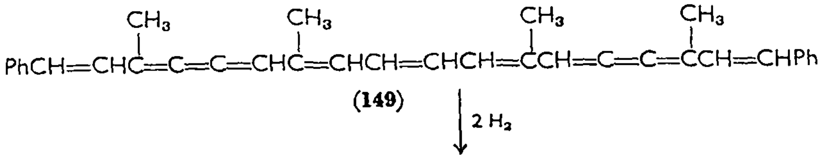
(143)



(140k)

(148)

(22)



$$\mathrm{PhCH{=}CH\overset{CH_3}{C}{=}C{=}C{=}CH\overset{CH_3}{C}{=}CHCH{=}CHCH{=}\overset{CH_3}{C}CH{=}C{=}C{=}\overset{CH_3}{C}CH{=}CHPh}\xrightarrow{2\,H_2}$$

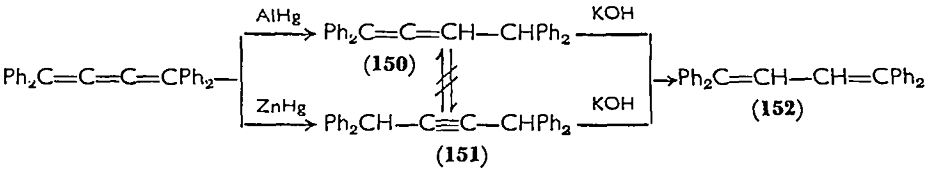
(149)

cis-Octadecanonaenes

A possible explanation for these observations is to assume that the hydrogenation goes *via* the butenyne structures $>C{=}CH{-}C{\equiv}C{-}$ in which the triple bond would account for the occurrence of *cis* double bonds after their hydrogenation. A support for this theory is the fact that all the butatrienes in question can be rearranged to the butenynes, as will be shown later. Similar problems will arise when the partial hydrogenation of hexapentaenes is considered.

(*iii*) Prolonged heating of butatrienes in high-boiling alcohols with alkali metals leads to a complete saturation[10]. However, this rather drastic treatment is not always of preparative importance.

(*iv*), (*v*) and (*vi*) Zinc amalgam or zinc dust in boiling pentanol in the presence of acetic acid converts tetraarylbutatrienes into 1,3-butadienes or 2-butynes. There is evidence that the butynes are the primary products, but are then rearranged to the symmetrical butadienes[10,266,267,270]. Aluminum amalgam in aqueous tetrahydrofuran (a very mild hydrogenation method) converted tetraphenylbutatriene into the 1,2-butadiene **150**, which is in this case the primary product, since the butyne **151** and the 1,2-butadiene **150** do not rearrange into one another under any conditions. However, both **150** and **151** can be isomerized to the conjugated butadiene **152**[210].

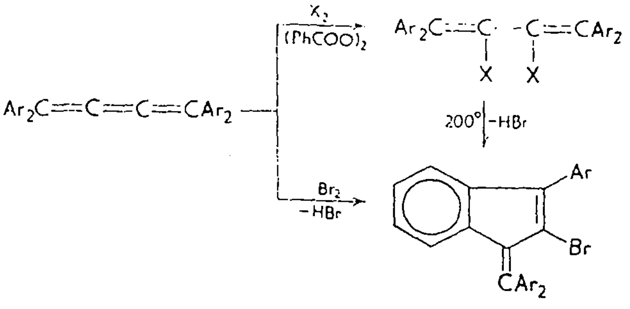


Thus, nascent hydrogen attacks butatrienes in such a way that the conjugation between the substituents on the opposite ends is interrupted. This rule applies also to hexapentaenes (see below), and to α,ω-diphenylpolyenes. In the case of the latter, Kuhn and coworkers[286] found that the corresponding dibenzylpolyenes were produced when they treated the diphenylpolyenes with alkali amalgam.

The hydrogenation of cumulenes with nascent hydrogen thus complements the partial catalytic hydrogenation which converts butatrienes to the conjugated butadienes.

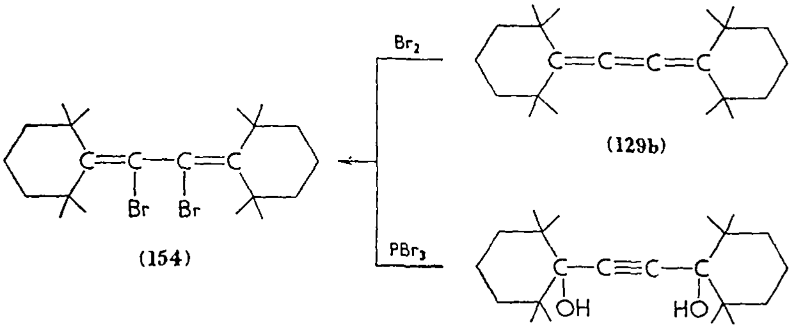
d. Halogenation. Butatrienes generally take up halogen in the 2- and 3-position and furnish 2,3-dihalo-1,3-butadienes. In the case of tetraarylbutatrienes, the yields reach 90% if dibenzoylperoxide is used as a catalyst. Without this catalyst, however, the formation of the methylenebromoindenes **153** becomes a competitive reaction[281,287].

The sterically hindered butatriene **129b** needs forced treatment with excess bromine to convert it into the 2,3-dibromobutadiene **154**.



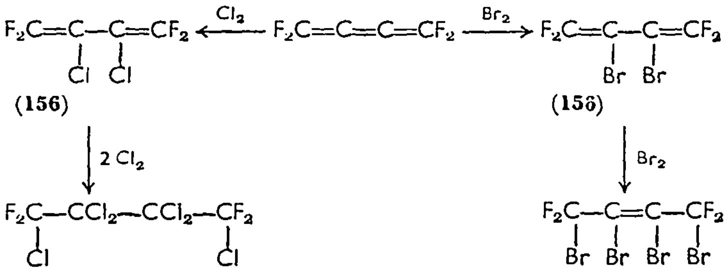
(153)

The latter can also be obtained from the butynediol **155** by reaction with phosphorous tribromide[74].



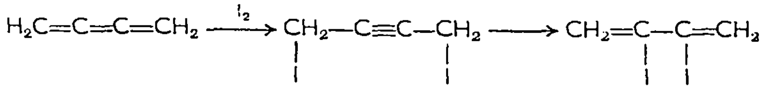
(154) (129b) (155)

Tetrafluorobutatriene and butatriene itself undergo also 2,3-halogenation, but the reaction does not stop at the 2,3-dihalobutadiene **156**; one more mole of bromine is taken up by a 1,4-addition and gives the tetrabromo-2-butene. Chlorination proceeds still further; all the double bonds of the butatriene are saturated with chlorine, yielding hexachlorotetrafluorobutane. Butatriene reacts even with iodine;



(156) (156)

here the isolable 1,4-addition product 1,4-diiodo-2-butyne **157** rearranges to 2,3-diiodo-1,3-butadiene[288].

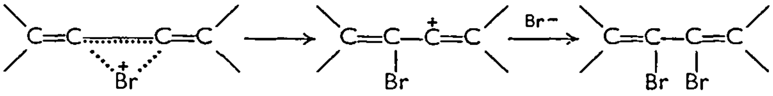


$$H_2C{=}C{=}C{=}CH_2 \xrightarrow{I_2} \underset{\mathrm{I}}{CH_2}{-}C{\equiv}C{-}\underset{\mathrm{I}}{CH_2} \longrightarrow CH_2{=}\underset{\mathrm{I}}{C}{-}\underset{\mathrm{I}}{C}{=}CH_2$$

(157)

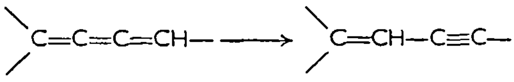
The results of the halogenation of butatrienes may be interpreted as follows: the halogenation (especially the iodination) under the influence of light or in the presence of peroxides is a radical reaction and goes *via* the (mesomeric) butyne diradical form of the butatriene. The 1,4-dihalobutynes which are formed initially will, in most cases, rearrange spontaneously to 2,3-dihalo-1,3-butadienes (compare the work by Krestinsky, Salkind and coworkers[289] on 1,4-dihalo-2-butynes).

If the halogenation of butatrienes follows an ionic mechanism, the bromonium ion would be expected to form a π complex with the central double bond, this again giving rise to 2,3-dibromobutadienes:



The bromocarbonium cation can alternatively form bromoindenes by ring closure if aryl substituents are present. The reasoning presented here is analogous to that advanced for the bromination of tetraaryl-allenes (p. 1076).

e. Isomerization. Tetrasubstituted butatrienes are resistant towards basic reagents, but if at least one hydrogen atom is attached to the butatriene chain then bases may cause a sort of retro-propargylic rearrangement which will produce butenynes (vinylacetylenes).



This rearrangement seems to be irreversible because in no instance has it yet been possible to rearrange vinylacetylenes to butatrienes. Besides the bisbutatriene **140k**, there are two further butatrienes (**143** and **129nn**) which can be isomerized to butenynes[210,290].

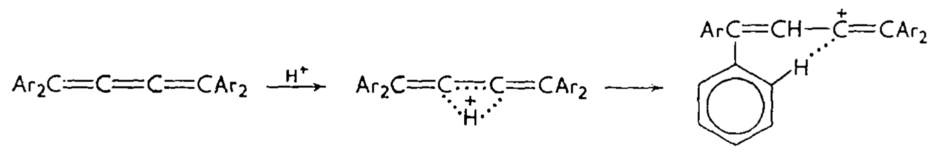
$$\underset{\textbf{(143)}}{Ph_2C{=}C{=}C{=}CH{-}CH{=}CPh_2} \xrightarrow{KOH} Ph_2C{=}CH{-}C{\equiv}C{-}CH{=}CPh_2 \qquad (23a)$$

$$\underset{\textbf{(129nn)}}{Ph_2C{=}C{=}C{=}CH{-}An\text{-}Br} \xrightarrow{KOH} Ph_2C{=}CH{-}C{\equiv}C{-}An\text{-}Br \qquad (23b)$$

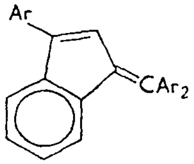
(An-Br = 9-bromo-10-anthracenyl)

They are shown in equation (23). Karrer's bisbutatriene **149** is probably also liable to butenyne formation because the latter is found together with the cumulene in the course of its preparation[285].

Acids isomerize tetraarylbutatrienes to methyleneindenes **159**[270]. This behavior is exactly analogous to the indene formation from tetraarylallenes (p. 1071). Here the tendency to form the carbonium ion **160** should be less pronounced than the formation of the allyl cation **114**, because **160** does not bring about an increase in resonance energy.

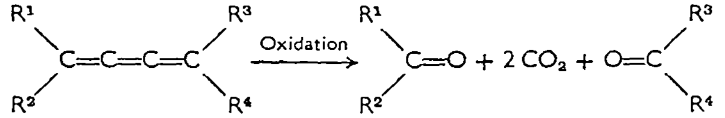


(160)



(159)

f. Oxidation; miscellaneous reactions. Forced oxidation splits butatrienes into the corresponding carbonyl compounds, a reaction which serves to prove the constitution of these cumulenes[10]. The same oxidizing

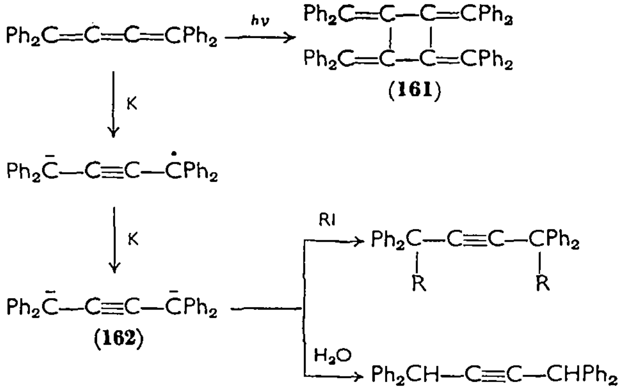


(129)

agents (chromic acid, permanganate, ozone) can be used here as in the allenic field. Ozonization is again the cleanest method. Unlike in the case of allenes, it has not been possible to interrupt the oxidation of a butatriene at an intermediate stage with a (partly) unbroken C_4 chain.

In 1921 Brand[10] had already observed that tetraphenylbutatriene dimerized on exposure to sunlight. Quite recently it has been found that the dimer is a tetramethylenecyclobutane derivative (**161**). Oxidative degradation and spectroscopic arguments were used to confirm this structure[291].

Potassium metal has been found to transfer one electron to tetraphenylbutatriene. The electronic structure of the resulting radical-ion has been studied by electron-spin resonance. Further action of potassium produces a dinegative ion (**162**) whose electronic structure must be close to the one indicated, since electrophilic reagents enter in the 1- and 4-positions[308].

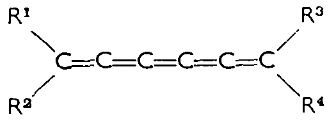


(161)

(162)

B. Hexapentaenes

These are compounds of type **163**, with five double bonds between six carbon atoms. No hexapentaene that contains one or more hydrogen atoms as substituents is known with certainty. As in the case of the butatrienes, aromatic substituents predominate.



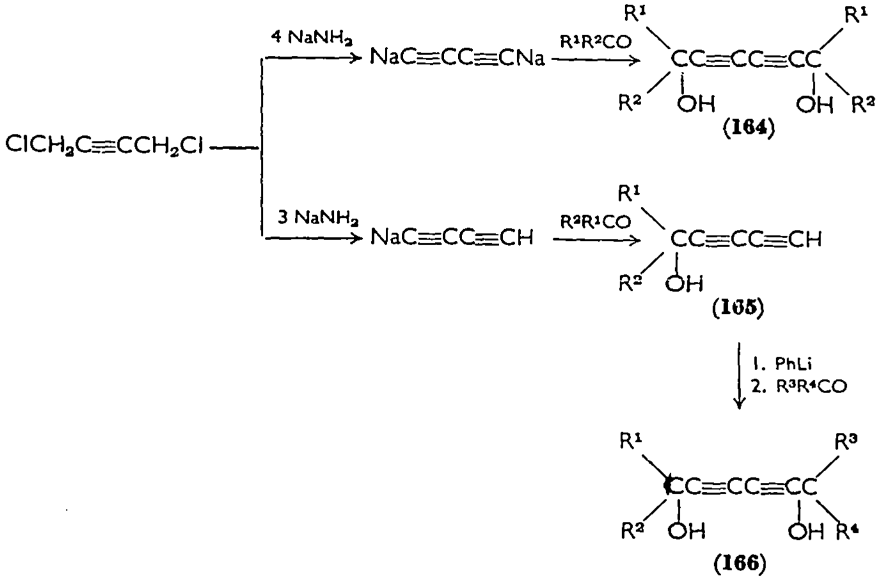
(163)

1. Methods of preparation

There are two pathways to hexapentaenes: reduction of hexadiynediols, and self-condensation of diarylpropynols according to Cadiot. Every known hexapentaene has been synthesized by one of these two methods.

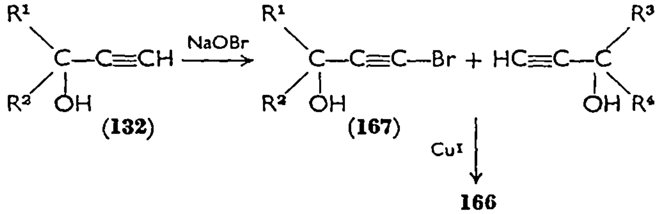
a. Reduction of hexa-2,4-diyne-1,6-diols. This method is the general one. The hexadiynediols are synthesized from diacetylene and carbonyl compounds as shown in equation (24).

Symmetrically substituted hexadiynediols **164** are easily obtained from dimetalated diacetylene and carbonyl compounds. Dimetalated diacetylene is prepared from 1,4-dichloro-2-butyne with four moles of sodamide in liquid ammonia (two moles of the amide are consumed for eliminating hydrogen chloride from dichlorobutyne)[263,275]. Difficulty is experienced in preparing unsymmetrically substituted hexadiynediols according to equation (24), because monometalated



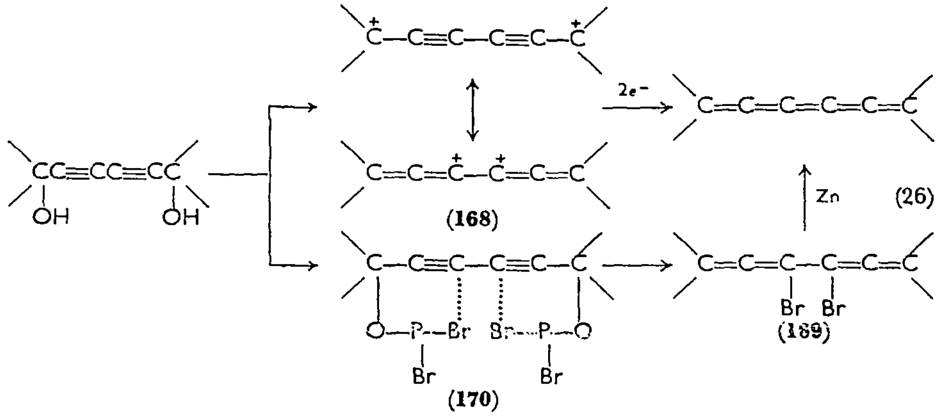
(24)

diacetylene is not easy to obtain (the hydrogen atom of sodiodiacetylide has about the same acidity as the two hydrogen atoms of diacetylene). Moreover, the pentadiynols **165** show a pronounced tendency to revert to diacetylene and carbonyl compound[292]. Chodkiewicz developed a procedure which made the asymmetric hexadiynediols **166** readily available: two different propynols **132** (say A and B) are joined together with the aid of copper(I) salts. Normally this would give rise to a mixture of three different hexadiynediols: A—A, B—B and A—B. However, if one of the propynols is transformed into a bromopropynol (**167**) and is then condensed with the second propynol, then only the desired asymmetric hexadiynediol **166** will be produced, as shown in equation (25)[293].



(25)

The reduction of the hexadiynediols to hexapentaenes is analogous to the conversion of butynediols to butatrienes and can be done by chromium(II) chloride or, more conveniently, by phosphorous tribromide in pyridine or stannous chloride in ethereal hydrogen chloride[275,263,254]. It is reasonable to assume the dicarbonium ion **168** as a transition state of this reaction, as pictured in equation (26). Alkyl-substituted hexadiynediols have been found to give 3,4-dibromohexatetraenes (conjugated diallenes) **169** on attempted reduction with phosphorous tribromide. This behavior can be understood from the



argument given in connexion with the propargylic rearrangement (p. 1042): alkyl-substituted hexadiynediols show less tendency to form a dicarbonium ion **168**; they will rather form a dibromophosphite ester **170**, and yield dibromohexatetraenes *via* the cyclic transition state **170**. Dibromohexatetraenes may be subsequently dehalogenated by zinc to the hexapentaenes[74,258]. Table 13 shows the hexapentaenes that have been prepared according to equations (24), (25) and (26).

Bishexapentaenes **171** have been obtained from terephthalophenone or isophthalophenone *via* the corresponding bishexadiynediols. This is shown in equation (27) and Table 14 collects the known examples. The bishexapentaenes derived from terephthalophenone are remarkably stable, whereas those derived from isophthalophenone, for which classically no conjugation can be formulated between the two hexapentaene units, are comparatively labile[294].

b. Self-condensation of diarylpropynols. Cadiot[292] found that diarylpropynols when treated with potassium hydroxide followed by acetic anhydride lead directly to hexapentaenes. As an intermediate product he could isolate *O*-acetylpropynols (**172**). The mechanism suggested by Cadiot has been questioned by Hartzler[147] who interpreted this reaction as proceeding *via* the diarylvinylidene carbenes **174**: the acetylpropynols **172** are deprotonated by the base to give the anions **173** which loose the acetyl group to form the carbenes **174**. The electrophilic carbene then condenses with the anion **173** and

TABLE 13. Hexapentaenes prepared by reduction of hexadiynediols.

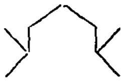
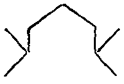
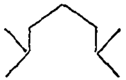
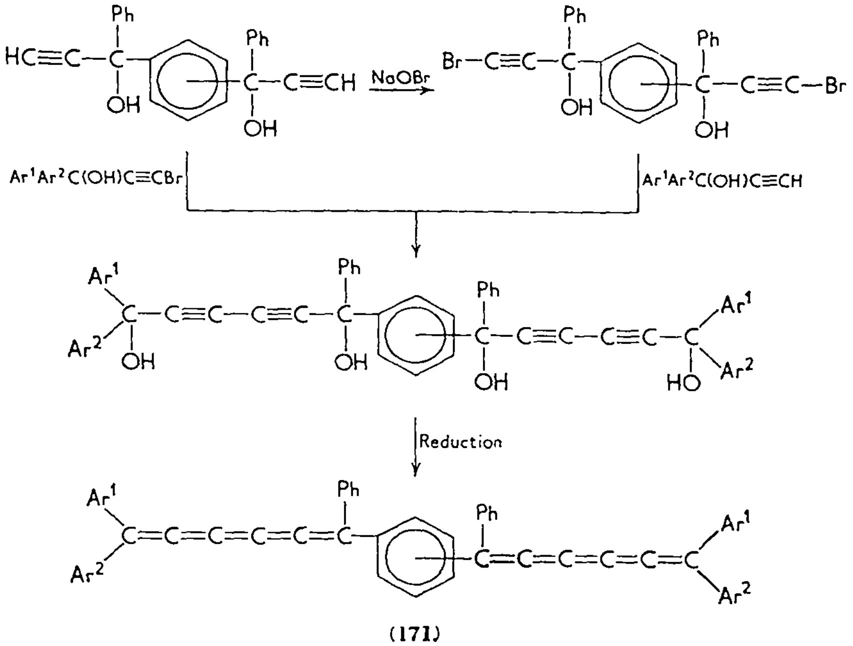
Example 163	Substituents R¹	R²	R³	R⁴	Yield (%)	M.p.	λ_{max} (mμ)				Reference
a	Ph	CH_3	Ph	CH_3			246	351	437		254, 258
b					92	204	225	238	317	339	74
c	Ph	Ph	Ph	CH_3			247	280	359	460	258
d	Ph	$C(CH_3)_3$			40	140	227	245	335	373	258
e	Ph	$C(CH_3)_3$	Ph	$C(CH_3)_3$	60	128	224	253	336	385	258
f	Ph	Ph			1	132	219	259	344	409	258
g	*o,o*-$C_6H_4C_6H_4$		*o,o*-$C_6H_4C_6H_4$		95	442	370	460	542		254, 310
h	Ph	Ph	Ph	Ph	94	301	370	440	488		310, 254
i	2-$NO_2C_6H_3C_6H_4$		2-$NO_2C_6H_3C_6H_4$				466	520	554		263
j	Ph	*m*-$NO_2C_6H_4$	Ph	*m*-$NO_2C_6H_4$			365	435	495		263
k	Ph	*p*-$NO_2C_6H_4$	Ph	*p*-$NO_2C_6H_4$			344	440	532		263
l	Ph	*m*-BrC_6H_4	Ph	Ph			369	436	492		309
m	Ph	*p*-BrC_6H_4	Ph	Ph	30	163	365	439	495		309
n	Ph	*o*-ClC_6H_4	Ph	Ph	30	139	364	438	475		309
o	*p*-ClC_6H_4	*p*-ClC_6H_4	*p*-ClC_6H_4	*p*-ClC_6H_4	87	218	503				261
p	Ph	*m*-$CH_3OC_6H_4$	Ph	Ph			366	430	487		309
q	Ph	*p*-$CH_3OC_6H_4$	Ph	Ph	24	174	373	432	502		309
r	*p*-$CH_3C_6H_4$	*p*-$CH_3C_6H_4$	*p*-$CH_3C_6H_4$	*p*-$CH_3C_6H_4$	70	326	506				261

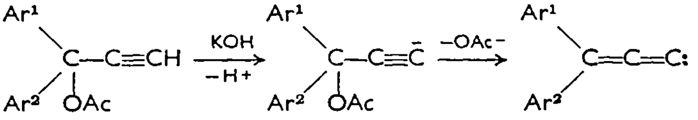
TABLE 14. Bishexapentaenes (**171**).

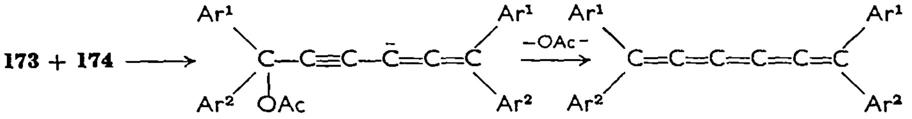
Example **171**	Substituents Ar^1	Ar^2	Diacyl compound underlying **171**	Yield (%)	M.p.	λ_{max} (mμ)				Reference
a	Ph	Ph	Isophthalophenone	55	364	369	435	500		309
b	Ph	Ph	Terephthalophenone	90	485	372	437	476	585	294
c	Ph	*o*-BrC_6H_4	Isophthalophenone	55		367	434	494		294
d	Ph	*o*-BrC_6H_4	Terephthalophenone	78	435	371	442	467	580	294
e	Ph	*m*-BrC_6H_4	Isophthalophenone			369	437	507		294
f	Ph	*m*-BrC_6H_4	Terephthalophenone	80	445	372	433	476	597	294
g	Ph	*p*-BrC_6H_4	Terephthalophenone	85	475	375	432	492	600	294
h	Ph	*p*-ClC_6H_4	Isophthalophenone			372	432	504		294
i	Ph	*p*-ClC_6H_4	Terephthalophenone	87	480	373	440	478	595	294
j	Ph	*p*-$NO_2C_6H_4$	Isophthalophenone			370	438	513		294
k	Ph	*p*-$NO_2C_6H_4$	Terephthalophenone	90	430	353	440	500	605	294
l	Ph	*m*-$CH_3OC_6H_4$	Terephthalophenone	80	440	372	442	479	596	294
m	Ph	*p*-$CH_3OC_6H_4$	Isophthalophenone			374	428	519		294
n	Ph	*p*-$CH_3OC_6H_4$	Terephthalophenone	80	450	377	431	486	599	294


(171)

(27)

gives the C_6 chain which looses the second acetate group to form the hexapentaene. The evidence for the carbene intermediate **174** was


(172) **(173)** **(174)**



that in the presence of styrene a 14% yield of the diarylvinylidenecyclopropane **175** was obtained, in addition to the tetraarylhexapentaene[147]. The formation of the allene **175** is analogous to the synthesis of the corresponding alkyl-substituted allenes **94** (p. 1057).

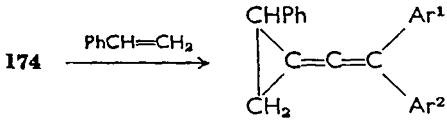
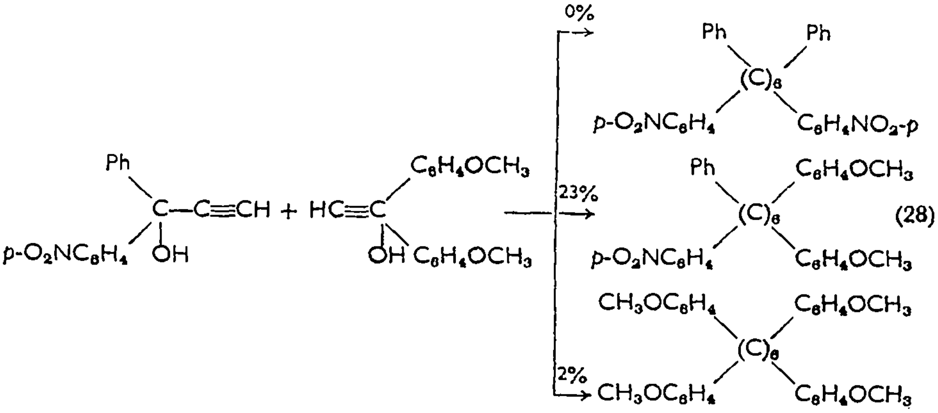

(**175**, $Ar^1 = Ar^2 = Ph$)

TABLE 15. Hexapentaenes synthesized by self-condensation of diarylpropynols.

Example 163	Substituents				Yield (%)	M.p.	λ_{max} (mμ)			Reference
	R^1	R^2	R^3	R^4						
h	Ph	Ph	Ph	Ph	60	204	370	440	488	292
g	*o,o*-$C_6H_4C_6H_4$		*o,o*-$C_6H_4C_6H_4$		13	350	370	460	542	292
s	*p*-BrC_6H_4	*p*-BrC_6H_4	*p*-BrC_6H_4	*p*-BrC_6H_4	47	217	370	425	507	292
t	Ph	*o*-BrC_6H_4	Ph	*o*-BrC_6H_4			367	435	465	309
u	Ph	*m*-BrC_6H_4	Ph	*m*-BrC_6H_4	39	165	368	438	491	309
v	Ph	*p*-BrC_6H_4	Ph	*p*-BrC_6H_4	69	203	365	435	495	292
w	Ph	*o*-ClC_6H_4	Ph	*o*-ClC_6H_4			366	438	466	309
x	Ph	*p*-ClC_6H_4	Ph	*p*-ClC_6H_4	41	220	368	439	467	309
y	Ph	*p*-$NO_2C_6H_4$	Ph	Ph	17	200	355	445	512	292
z	*p*-$NO_2C_6H_4$	*p*-$CH_3OC_6H_4$	*p*-$NO_2C_6H_4$	*p*-$CH_3OC_6H_4$	11		363	435	555	292
aa	Ph	*p*-BrC_6H_4	*p*-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	13		372	425	510	292
bb	Ph	*p*-$NO_2C_6H_4$	*p*-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	2		372	440	537	292
cc	Ph	*p*-$CH_3OC_6H_4$	Ph	*p*-$CH_3OC_6H_4$	12	165	375	425	503	292
dd	Ph	Ph	Ph	*β*-$C_{10}H_7$	9	170	370	435	500	292
ee	*p*-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	10	270	380	422	517	292
ff	Ph	*p*-BrC_6H_4	*p*-$CH_3OC_6H_4$	*β*-$C_{10}H_7$	15	195	372	435	512	292
gg	Ph	*p*-$NO_2C_6H_4$	*p*-$CH_3OC_6H_4$	*β*-$C_{10}H_7$	10			425	529	292
hh	*p*-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	*β*-$C_{10}H_7$			373	424	522	292
ii	Ph	*β*-$C_{10}H_7$	Ph	*β*-$C_{10}H_7$	34	135	370	435	510	292
jj	*p*-$CH_3OC_6H_4$	*β*-$C_{10}H_7$	*p*-$CH_3OC_6H_4$	*β*-$C_{10}H_7$	20	235	377	430	525	292

Cadiot observed that the condensation of a mixture of two different propynols led to the asymmetric hexapentaene only (equation 28).



(28)

This is easily explained on the basis of the above mechanism: the step **172** → **173** is not appreciably affected by the aryl groups; the step **173** → **174**, however, is enhanced by electron-donating (methoxyphenyl) groups and suppressed by electron-attracting (nitrophenyl) aryl groups. In the reaction mixture of equation (28) therefore, much of the anion **173** (Ar^1 = phenyl, Ar^2 = nitrophenyl) will be present, and also much of the carbene **174** ($Ar^1 = Ar^2$ = methoxyphenyl), which explains the preferential formation of the asymmetric hexapentaene. Table 15 records the hexapentaenes that have been obtained by this method.

2. Chemical properties and reactions of hexapentaenes

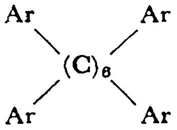
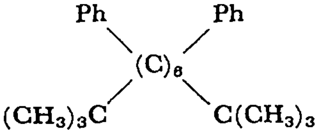
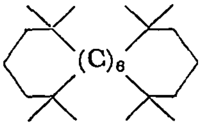
Spectroscopic properties will be considered in a comparative study of the cumulene spectra in section IV.

a. General properties. All the hexapentaenes described in the literature are tetrasubstituted; attempted syntheses with hydrogen atoms in the cumulene chain have been unsuccessful. Recalling the rearrangement of butatriene to butenyne, this tendency should be expected to be even more pronounced in the case of substituted hexapentaenes.

In Table 16 the different types of hexapentaenes (with respect to substitution) have been collected, together with some basic properties.

b. cis–trans *Isomerism.* All attempts to separate properly substituted hexapentaenes in *cis* and *trans* forms have failed. If the electron distribution in a cumulene chain is calculated, it is found

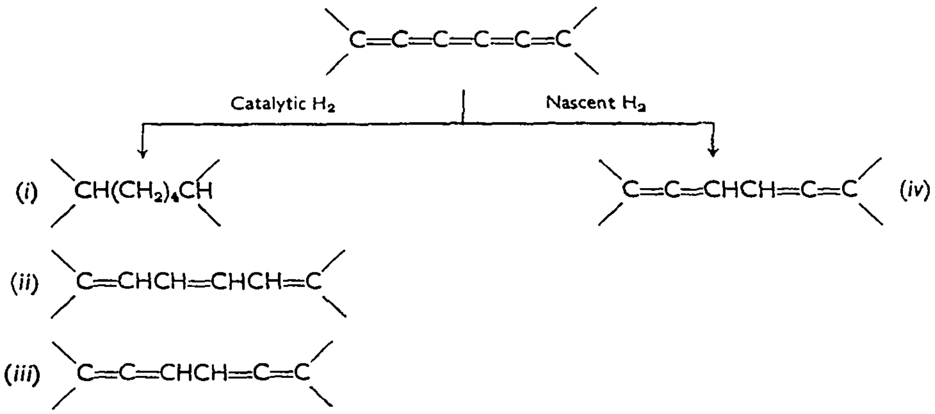
TABLE 16. Properties of hexapentaenes.

Type of hexapentaene	Color	Stability	Soluble in*
	Red to violet	Generally stable	C_6H_6, $CHCl_3$ Thf, Dmf
	Yellow	Stable	ether, C_6H_6, Thf, Dmf, $CHCl_3$
	Colorless	Stable	petroleum ether, alcohol, ether, C_6H_6, $CHCl_3$, Thf, Dmf
Bishexapentaenes **171**			
meta series	Red	Less stable	C_6H_6, $CHCl_3$, Thf, Dmf
para series	Violet	Stable	Thf, Dmf

* Thf = Tetrahydrofuran
Dmf = Dimethylformamide

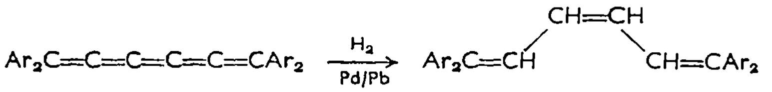
that, with increasing chain length of the cumulene, an alternation of the bond lengths becomes more apparent, *i.e.* certain double bonds tend to become single bonds. This means a decrease of the energy of activation for the *cis–trans* isomerization of the cumulene (see also section IV).

c. Hydrogenation. The following scheme shows the hydrogenation products that were obtained from hexapentaenes:



(*i*) Palladium or Raney nickel cause an uptake of five moles of hydrogen to give the corresponding hexanes. The latter may be identified by an independent synthesis, which provides a proof of the constitution of an unknown hexapentaene[1,74].

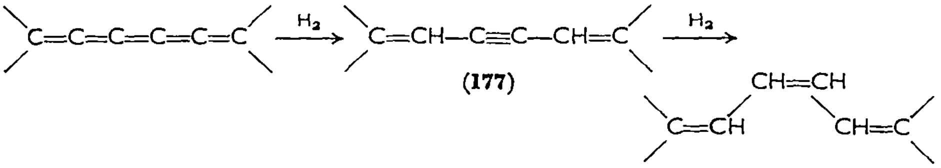
(*ii*) In the presence of a lead-poisoned palladium catalyst[215], tetraarylhexapentaenes take up only two moles of hydrogen, and furnish hexatrienes in which the central double bond is in a *cis* configuration (**176**). The trienes **176** can be readily rearranged to the



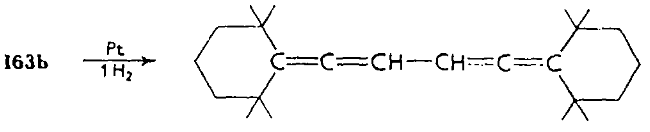
(**176**)

trans compounds by the action of light in the presence of traces of iodine. This reaction, together with the spectroscopic properties, proves that they are really *cis*-hexatrienes[295]. The partial hydrogenation of hexapentaenes is thus stereospecific, and is, as yet, the only route to *cis*-tetraarylhexatrienes.

To explain this stereospecificity, the participation of triple bonds could be assumed, as in the case of the partial hydrogenation of butatrienes. For instance, if the first mole of hydrogen adds to the 2- and 5-positions of the hexapentaene, a divinylacetylene (**177**) would be formed, which would give a *cis*-hexatriene on further hydrogenation. The 2,5-addition of the first mole of hydrogen is not unusual, since the conjugated diallene **115** also undergoes a 2,5-addition of hydrogen[210] (p. 1073).



(*iii*) In the overcrowded hexapentaene **163b**, the outer double bonds are shielded so that the hydrogenation with platinum could be stopped after one mole of hydrogen had been taken up on the central double bond. The result was the bisallene **178**[74].



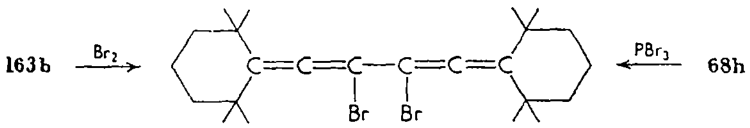
(178)

(*iv*) Aluminum amalgam in aqueous tetrahydrofuran converts tetraphenylhexapentaene into the diallene **115** which is absolutely resistant towards further reaction with nascent hydrogen under these conditions[210]. Since in this case no steric hindrance is involved,

$$\underset{\textbf{(163h)}}{Ph_2C{=}C{=}C{=}C{=}C{=}CPh_2} \xrightarrow[H_2]{Al/Hg} \underset{\textbf{(115)}}{Ph_2C{=}C{=}CHCH{=}C{=}CPh_2}$$

this hydrogenation result is a further confirmation of the rule mentioned on page 1104 that nascent hydrogen attacks cumulenes just by interrupting the conjugation between the substituents on opposite ends.

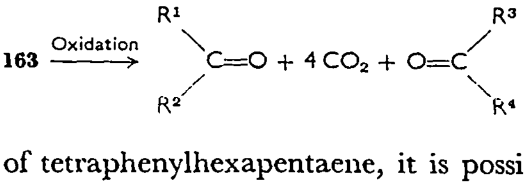
d. Halogenation. Hexapentaenes react with bromine and even with iodine but only in one instance has it been possible to isolate a well defined halogenation product: the sterically hindered hexapentaene **163b** takes up two atoms of bromine on the central double bond and yields the diallene dibromide **70h**, which is also obtained from the hexadiynediol **68h** with phosphorous tribromide. Its ultraviolet spectrum is almost identical with that of the diallene **178**[74].



(70h)

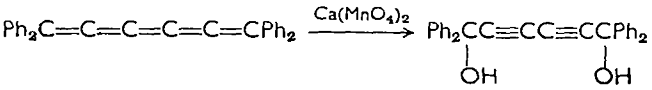
It is not sensible to reach conclusions as to a mechanism of the halogenation of hexapentaenes from this example, since steric factors seem to play a decisive role.

e. Oxidation; miscellaneous reactions. Forced oxidation splits hexapentaenes into the corresponding carbonyl compounds, a reaction which serves to prove the structure of these cumulenes[292].



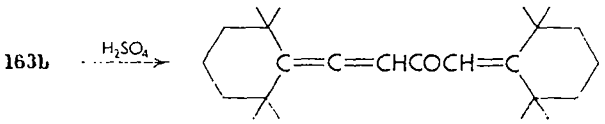
$$\textbf{163} \xrightarrow{\text{Oxidation}} R^1R^2C{=}O + 4\,CO_2 + O{=}CR^3R^4$$

In the case of tetraphenylhexapentaene, it is possible, under mild conditions, to stop the oxidation at an intermediate stage, and to isolate the hexadiynediol[292].



$$\mathrm{Ph_2C{=}C{=}C{=}C{=}C{=}CPh_2} \xrightarrow{\mathrm{Ca(MnO_4)_2}} \mathrm{Ph_2\underset{OH}{C}C{\equiv}CC{\equiv}C\underset{OH}{C}Ph_2}$$

Acid isomerization products (indenes) of hexapentaenes do not exist, and no halochromy is observed with strong acids. However, the sterically hindered hexapentaene **163b** could be hydrated to give the α-allenic ketone **179**. Again this is not a typical reaction of the hexapentaene system but depends upon the bulky substituents[74].

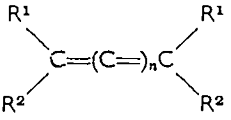


(179)

In conclusion it can be said that, apart from hydrogenation, no typical reactions of the hexapentaene system have yet been found.

C. Octaheptaenes and Decanonaenes

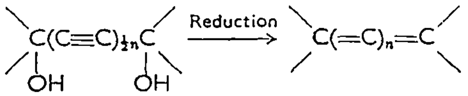
These are cumulenes of type **180**. Three octaheptaenes and two decanonaenes have been mentioned in the literature. None of them could be isolated in a pure state owing to their instability.



(**180**, n = 6 and 8.)

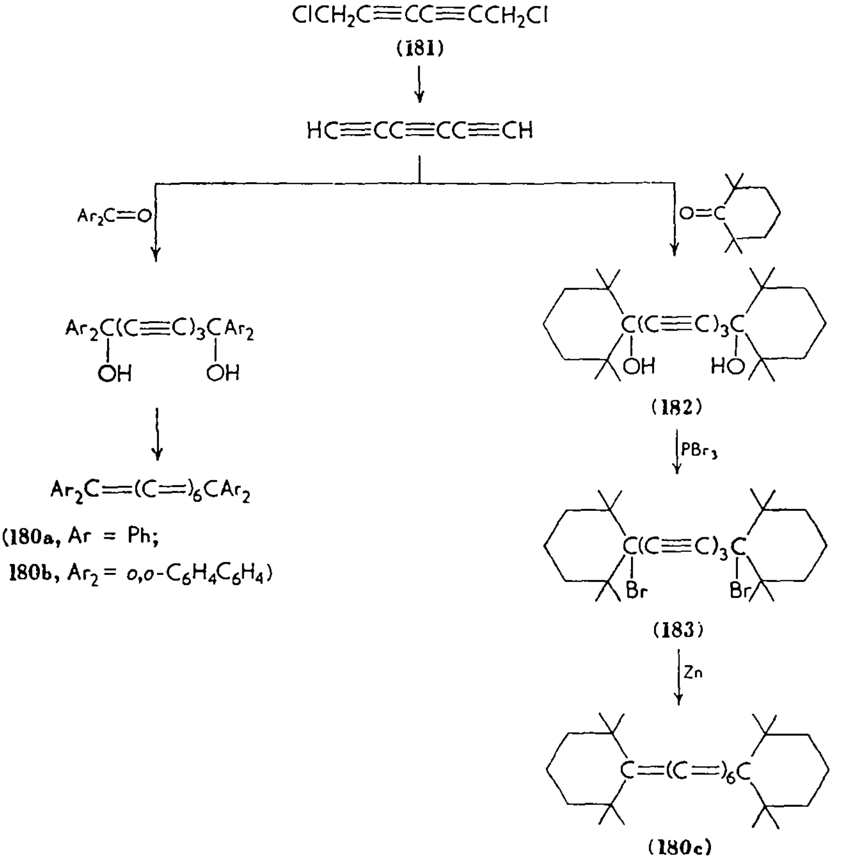
1. Method of preparation

The only method is the reduction of the poliyne-α,ω-diols. The octatriyne-1,8-diols were obtained from the reaction of carbonyl compounds with triacetylene which in turn is prepared by a twofold elimination of hydrogen chloride from 1,6-dichloro-2,4-hexadiyne (**181**). Equation (29) illustrates the basic reactions.



$$\mathrm{\underset{OH}{C}(C{\equiv}C)_{\frac{1}{2}n}\underset{OH}{C}} \xrightarrow{\text{Reduction}} \mathrm{C({=}C)_n{=}C}$$

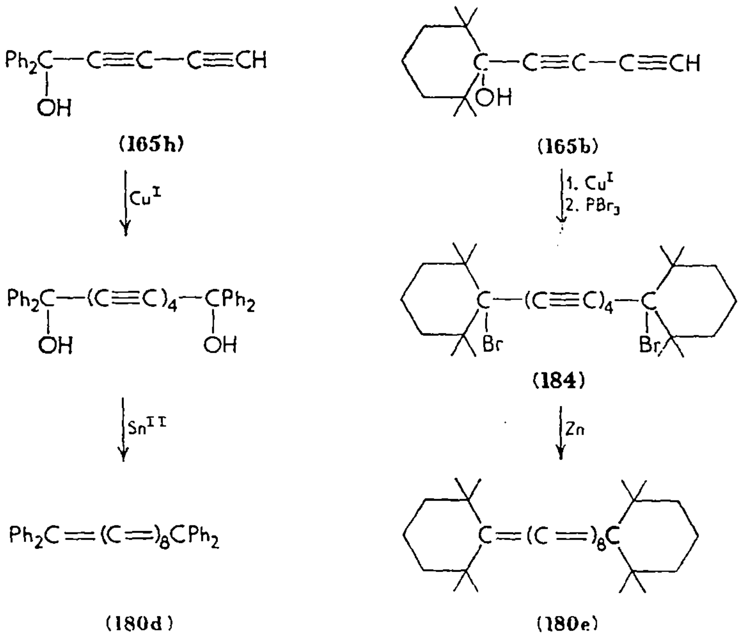
Neither **180a** nor **180b** could be obtained in the crystalline state. Evaporation of the violet or blue solutions respectively furnished only brown polymerization products. The benzene solutions, however, are relatively stable[296]. This may be due to a stabilization by solvation; and in fact it was even possible to separate these highly unsaturated compounds in solid form by embedding them in the crystal lattice of benzophenone or diphenylmethane. It is assumed that in benzene solution or in these mixed crystals, van der Waals forces provide a shield of solvent molecules for the cumulene and thus prevent cumulene molecules from reacting with one another[296].



(29)

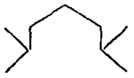
The aliphatic octaheptaene **180c** can only be prepared by reduction of the dibromide **183** with zinc, because the octatriynediol **182**, like the corresponding hexadiynediol, cannot be reduced directly. The octaheptaene **180c** could be isolated in the form of yellow crystals which decomposed within a few seconds[74]. Proof that the octaheptaenes do exist in solution is obtained by comparison of the ultraviolet spectra of these solutions with those of the other members of the cumulene series (see section IV).

To prepare decanonaenes, decatetrayne-1,10-diols are required. They are obtained by oxidative dimerization of pentadiynols **165**.



Again the alkyl-substituted decatetraynediol cannot be reduced directly; instead, the corresponding dibromide **184** must be dehalogenated with zinc.

TABLE 17. Octaheptaenes and decanonaenes.

Example 180	Substituents and chain length of cumulene			M.p.	λ_{max} ($m\mu$)	Reference
	R^1	R^2	n			
a	Ph	Ph	8	—	530 557	254, 296
b	o,o-$C_6H_4C_6H_4$		8	—	540 597	254, 296
c			8	—	267 284 401	74
d	Ph	Ph	10	—	314 338 365 454 526 573 606 663	245
e			10	—	280 305 325 390 465	74

Both decanonaenes are very unstable[74,245]. It was only possible to measure the ultraviolet spectrum of the colored solutions. They showed exactly the behavior that was to be expected from comparison with the lower members of the cumulene series (see Table 17).

IV. THEORY OF THE CUMULENE BOND

A. Thermodynamics

While there is only sparse literature on the thermodynamic properties of higher cumulenes,[324] allene itself and methylallene have been thoroughly investigated with respect to their thermodynamic behavior. Among the quantities that have been measured are: vapor pressure[317], triple point[317], heat capacity[318], specific heat[319], heat of vaporization[320], heat of formation[321] and heat of cumbustion[321]. Kistiakovsky[322] compared the heat of hydrogenation of allene with that of 1,3-butadiene, 1,4-pentadiene and benzene. He found that 1,4-pentadiene gives approximately twice the value for ethylene, showing that there is no interaction between the two isolated double bonds. The cumulative bond of allene, however, exhibits a destabilizing effect as compared with two isolated double bonds. From the experimental measurements, empirical formulae for the thermodynamic functions (entropy, enthalpy, virial coefficients) have been calculated[323]. The question has been raised whether allenes could replace acetylenes in welding. To this end flame temperature, heat of cumbustion and burning velocity of several simple allenes were measured and compared with the corresponding quantities for acetylene[324].

Kinetic studies of the allene polymerization and of the thermal decomposition of isobutylene to allene have been reported[325].

Of considerable technical importance is the interconversion of alkynes into 1,2- and 1,3-alkadienes in the gas phase in the presence of catalysts[326]. In particular, the equilibrium propyne $\rightleftharpoons$ propadiene has been repeatedly investigated and the equilibrium constants in the presence of various catalysts were determined as functions of temperature[327].

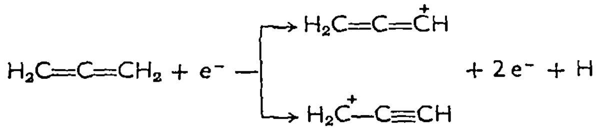
B. Electric and Magnetic Properties

In 1930 Faltis[174] had suggested that, contrary to van't Hoff's theory, the valences in allenes should all lie in the same plane. This was later refuted by separating allenes into optical isomers. But the first convincing argument against Faltis' hypothesis came from dipole moment measurements on 1,3-diphenyl-1,3-di-*p*-bromophenylallene. Here the dipole moment of the whole molecule is nearly exclusively determined by the polarity of the C—Br bond. From the known dipole moment of bromobenzene, vector addition indicates that the allene formula should give rise to a dipole moment of 1·85 D, while Faltis' formula should either give no dipole moment (*trans* configuration) or 2·62 D (*cis* configuration). Experimentally, 1·92 D is found. It was also possible to determine the valence angle of the end substituents. The dipole moment of 1,1-di-*p*-chlorophenyl-3,3-diphenylallene was measured and, from the known moment of chlorobenzene, an angle of 119° had to be assumed between the two chlorophenyl groups in order to obtain the measured dipole moment for the allene[328].

Another problem in cumulene chemistry that could be solved by dipole-moment measurements was the *cis–trans* assignment of the isomeric 1,4-diphenyl-1,4-di-*m*-nitrophenylbutatrienes (**129t**). When calculating the dipole moments by vector addition, using the known moment of the nitrophenyl group, the fact that the aryl groups can rotate has to be taken into account. On this basis, values of 4·9 D for the *trans* isomer and 6·0 D for the *cis* isomer are calculated. Experimental values are 5·2 D for isomer *A* and 5·9 D for isomer *B*. Therefore *A* must be the *trans*-butatriene[329].

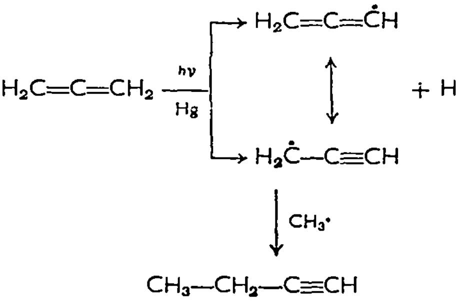
The diamagnetic susceptibility of simple allenes has been measured and found to be in agreement with calculations from bond increments[330]. The diamagnetic anisotropy of tetraphenylbutatriene has been investigated[331].

The mass difference between allene and argon has been determined in the mass spectrometer by electron impact[332]. The allenyl ion is also found, arising from the following reaction:



$$H_2C{=}C{=}CH_2 + e^- \longrightarrow \left\{ \begin{array}{l} H_2C{=}C{=}\overset{+}{C}H \\ H_2\overset{+}{C}{-}C{\equiv}CH \end{array} \right. + 2e^- + H$$

The appearance potential of this ion is measured and from that can be deduced the ionization potential of allene, the heat of formation of the ion, and the bond-dissociation energies. From the observation that 1-butyne also gave the allenyl ion on electron bombardment, it was concluded (invoking thermodynamic arguments) that the ion must have the propargyl structure rather than the propadiene structure[333]. This is also supported by the photosensitized decomposition of allene whereby the allenyl radical was produced. Addition of methyl radicals yielded 1-butyne rather than 1,2-butadiene, showing that the radical must also have a propargyl structure (equation 30).



(30)

The mass spectra of some 1,3-dialkylallenes and also of tetrafluoroallene have been taken, and the ionization potentials deduced[35, 335]. In each case the formation of an allenyl ion is indicated by a high peak at the corresponding mass number. This shows that the system of two cumulated bonds is largely conserved when one more electron is injected into the system[35,336].

Cumulenes containing hydrogen atoms in the α- and ω-position of the cumulene system provide an interesting test for the theory of the proton spin–spin coupling constants in nuclear magnetic resonance experiments. The proton spins on different carbon atoms can interact with one another *via* the (spins of the) σ electrons between the two protons in question. π Electrons in between provide only a small contribution to this interaction, *i.e.* to the spin–spin coupling constant (about 0·5 c/sec), since they do not have the appropriate symmetry. If the two protons are separated by more than three bonds then even the σ electrons do not bring about a larger contribution than 0·5 c/sec to the coupling constant. Now in allene the coupling constant is 7 c/sec for the spin–spin interaction between the protons in 1- and 3-position, which are separated by four bonds[337,366]. Karplus[338] showed that this unusually high coupling constant for 1,3-protons in allenes is due to a σ–π-exchange term in the Hamiltonian which would be small for such delocalized electrons as occur in aromatics. The same theory applied to butatriene predicts a coupling constant of 7.8 c/sec for the protons in 1- and 4-position which are separated by five bonds. The experimental value is as yet unknown.

The question of the signs of these coupling constants in allenes has been investigated in two recent papers[339].

C. Vibration–Rotation Phenomena

The cumulenes $H_2(C)_nH_2$ in the ground state cannot give rise to infrared absorption for pure rotational transitions, since they have no permanent dipole moment. However, if they are raised to a degenerate vibrational level then the Jahn–Teller effect will operate in the sense that the degeneracy is removed by distortion of the molecule. The distorted species should have a dipole moment and should show infrared absorption due to rotational transitions[340]. In the Raman effect the rotational transitions are allowed. From the spacings of the lines and the theoretically derived selection rules, the rotational constant B is determined which is inversely proportional to the moment of inertia and this in turn involves the internuclear distances. The connexion between rotational spectrum and internuclear distances is as follows:

$$\nu = 2B(J + 1)$$

$$B = \frac{h}{8\pi^2 c I_A}$$

where ν is the observed frequency in wave numbers, J is the rotational quantum number and I_A is the moment of inertia with respect to the A—A axis (see Figure 1).

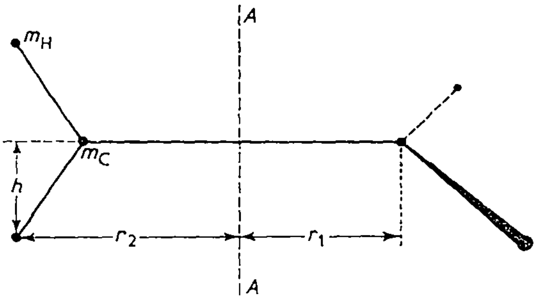
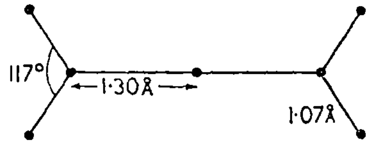


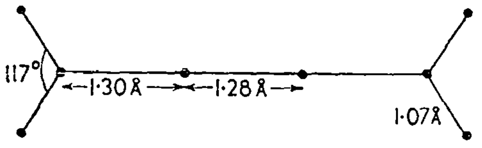
FIGURE 1.

$$I_A = \sum_i m_i r_i^2 = 2m_C r_1^2 + 2m_H r_2^2 + 2m_H(r_2^2 + h^2) \qquad (31)$$

In equation (31) I_A is taken from the spectrum and m_C and m_H are the known masses of the carbon and hydrogen atoms, whereas the distances r_1, r_2 and h are unknown. Since there is only one equation for three unknown quantities, either the C—H bond length has to be assumed, or two further equations in r_1, r_2 and h must be obtained by measuring the rotational spectrum of dideutero- and tetradeuteroallene. A similar analysis was done with butatriene[342] and the results obtained were confirmed by electron-diffraction experiments with butatriene[343]. The following geometry is then found for allene and butatriene:



$H_2C{=}C{=}CH_2$



$H_2C{=}C{=}C{=}CH_2$

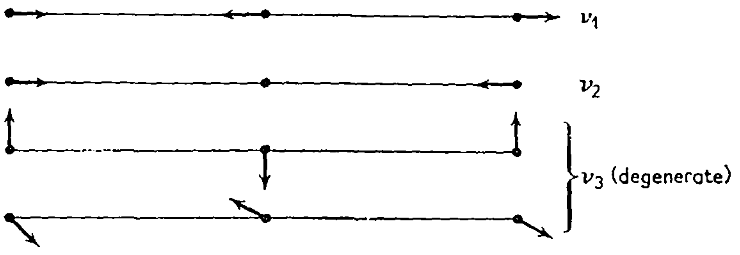
It is striking that the double bonds in allene are considerably shorter than the double bond in ethylene (1·34 Å). This double-bond contraction has also been observed in ketenes.

The fine structure of certain vibrational bands of allene due to vibration–rotation interaction has been investigated experimentally and theoretically[344].

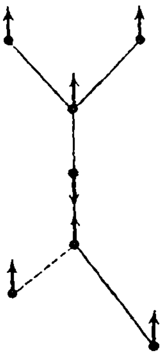
Cumulenes are of particular interest in vibrational spectroscopy, since they contain a system which can be identified with a linear n-atomic molecule. Allene (C_3H_4) with its seven atoms has 15 vibrational degrees of freedom. If normal coordinates are introduced 11 distinct normal modes of vibration are found, four of which are doubly degenerate. These normal modes as calculated for instance by Wilson's F–G-matrix method[345] have all been assigned to the observed frequencies[346]. The assignment is complicated by the appearance of overtones and combination frequencies. In part this complication can be overcome by investigating the frequency shifts that occur when some of the hydrogen atoms of allene are replaced by deuterium[347]. An easy process of correlating the observed frequencies with interatomic-force constants, as devised by Linnett and colleagues[348], is to assume a potential function for the vibrations which is quadratic in the displacements of the nuclei (this being tantamount to making an harmonic-oscillator approximation for the nuclear vibrations). This potential function contains a set of force constants as adjustable parameters. By a suitable choice of the latter the observed frequencies can be reproduced; moreover these same force constants can then be used in similar molecules (for instance those from ethylene can be used for allene).

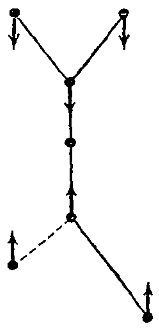
Only a few very simply substituted allenes have been subjected to a rigorous normal coordinate analysis[354]. Practical organic chemistry, however, is particularly interested in those normal modes of the allenes which are typical vibrations of the three carbon atoms since it is expected that they are not altered profoundly on varying the substituents. This would amount to treating allenes as linear triatomic molecules, perhaps with certain corrections for the substituents[349].

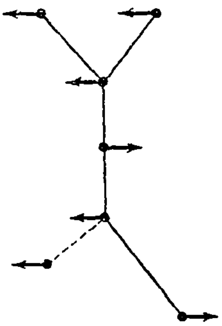
A linear triatomic molecule has four vibrational degrees of freedom. Carrying out a normal coordinate treatment, the following normal modes are found:



Now we have to look at those modes and frequencies of the complete C_3H_4 molecule which correspond most closely to the vibrations of the triatomic molecule. The following ones have to be chosen:


$\nu_1 \approx 1950\ cm^{-1}$


$\nu_2 \approx 1070\ cm^{-1}$


$\nu_3 \approx 350\ cm^{-1}$

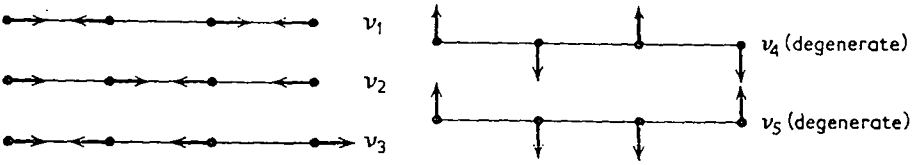
Experimentally it is found that most allenes exhibit an infrared absorption at 1920 to 2000 cm^{-1}. This frequency is thus largely independent of the substituents of the allene. This means that it is possible to calculate the 1950 cm^{-1} band of allenes from the antisymmetric stretching vibration of a linear triatomic molecule. However, for substituted allenes, the bands at 1070 cm^{-1} and 350 cm^{-1}

cannot be assigned easily due to other bands which normally lie in this region. Therefore, confining our attention to the antisymmetrical stretching frequency ν_1, we have to enquire whether it will appear in the spectrum, and with what intensity. It is principally allowed in absorption, irrespective of substitution; its intensity depends upon the rate of change of the dipole moment during the vibration. Two possibilities can be envisaged: (*a*) a symmetrically substituted allene with no permanent dipole moment, but with polarized double bonds; (*b*) an unsymmetrically substituted allene with a permanent dipole moment. The change of dipole moment during a vibration can be pictured as follows:

Type of allene	(*a*)	(*b*)
Equilibrium position of the nuclei	δ^- $\delta\delta^+$ δ^- •———•———•	δ^- δ^+ •———•———•
Dipole moment at equilibrium position	none	←———
Maximum displacement of the nuclei in one direction	δ^- $\delta\delta^+$ δ^- •——•————•	δ^- δ^+ •———•———•
Dipole moment	———→	←———
Maximum displacement of the nuclei in opposite direction	δ^- $\delta\delta^+$ δ^- •————•——•	δ^- δ^+ •————•——•
Dipole moment	←———	←———
Change of dipole moment	large	none

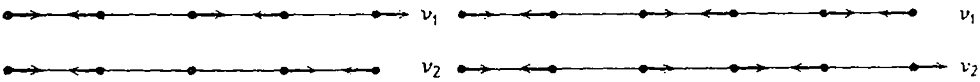
Thus allenes of type (*a*) should have an intense absorption band near 1950 cm^{-1} whereas allenes of type (*b*) should show no absorption in this region, but in practice a permanent dipole moment along the allene chain will often cause a polarization of the double bonds as well, *i.e.* case (*a*) will be admixed. This qualitative picture is verified by experiment: bisbiphenyleneallene has strongly polarized double bonds due to the electron-withdrawing properties of the five-membered ring, also confirmed by the facile addition of nucleophiles to the central carbon atom. In the infrared spectrum a very intense absorption band is found at 1925 cm^{-1}[377]. On the other hand, 1,1-diphenyl-3-biphenyleneallene has a permanent dipole moment, but only a weak absorption band at 1940 cm^{-1}[377]. Thus the intensity of the antisymmetric stretching frequency of allenes (the 'allene band') is largely determined by the polarization of the double bonds.

A model for the most characteristic vibrations of butatrienes is a linear 4-atomic molecule. It has 7 normal vibrations which can be represented as follows:



Calculations by Otting and Fischer[351] suggest that ν_1 should be about 2000 cm^{-1}. All the other frequencies would lie in a region which is either obscured by bands due to other vibrations of the cumulene molecule or in a range which is not covered by the usual spectrometers. However, ν_1 for a symmetrical linear 4-atomic molecule is infrared inactive since this transition is forbidden by symmetry. Therefore only butatrienes which have no symmetry can show infrared absorption in the 2000 cm^{-1} region, and the intensity of the band depends again on the rate of change of the dipole moment during that vibration. A further example is the 1,1-dimethyl-4-formyl-butatriene mentioned on page 1099.

The linear 5-atomic model for pentatetraenes has four stretching vibrations and the linear 6-atomic model for hexapentaenes has five stretching vibrations. The two vibrations which have the highest frequencies in each case may be pictured as follows:



According to unpublished calculations[351] it is expected that for pentatetraenes $\nu_1 \approx 2100$ cm^{-1} and $\nu_2 \approx 1600$ cm^{-1}. For hexapentaenes, the corresponding result is $\nu_1 \approx 2100$ cm^{-1} and $\nu_2 \approx 1900$ cm^{-1}. Pentatetraenes with polarized outer double bonds should thus have an infrared band in the 2100 cm^{-1} region. The same should be true for unsymmetrically substituted hexapentaenes with a permanent dipole moment. The hexapentaenes should in addition show infrared absorption in the 1900 cm^{-1} region (which is also usually free from other bands). These predictions have not yet been borne out by experiment. There are not many butatrienes which have such a dipole moment. Otting[352] investigated symmetrically substituted butatrienes and found no appreciable absorption near 2000 cm^{-1}. On the other hand, Kuhn and coworkers[248], Cadiot and coworkers[253] and Ried and coworkers[281] synthesized a number of unsymmetrically substituted tetraarylbutatrienes which showed infared absorption at 2032 cm^{-1}. The intensity of this band was roughly proportional to the permanent dipole moment component parallel to the chain, and in the 1,1-diphenyl-4-(2-nitrobiphenylene)butatriene (**129i**) it reached the intensity that is usually found for carbonyl bonds[248]. The band at 2032 cm^{-1} may therefore be used for identifying unknown butatrienes, provided they have a dipole moment parallel to the cumulene chain. Thus the bisbutatriene **140a** was originally formulated as a bispentatetraene **125**[247]. Introduction of a nitro group into the central benzene ring created a dipole moment, and compound **140b** showed an absorption band at 2032 cm^{-1}, indicating a butatriene structure[248].

A similar analysis as was done for the triatomic model (page 1028) reveals that a polarization of the outer double bonds of the butatriene does not bring about a change of the dipole moment during the vibration. In contrast to the allene case, the intensity of the high frequency transition ν_1 depends upon a permanent dipole moment along the butatriene chain.

Wotiz and coworkers[189] have published a survey on the infrared spectra of 58 allenes. In addition to the typical allene band in the 1950 cm^{-1} region, they also found absorption near 850 cm^{-1} which is characteristic of terminal allenes. In the spectrum of allene itself this band is also located at 850 cm^{-1} and is assigned to the torsional vibration of the CH_2 group. In terminal allenes which are substituted by electron-withdrawing groups (COOR, COR, CN, CF_3, COCl) the band at 1950 cm^{-1} appears as a doublet. Since the antisymmetric stretching vibration of the triatomic molecule is non-degenerate, it seems that the above splitting cannot be explained on the basis of the triatomic model (removal of a degeneracy would have explained the splitting). Another experimental observation concerns the shift of the allene band on fluoro substitution[56,353].

$H_2C{=}C{=}CH_2$	$F_2C{=}C{=}CH_2$	$F_2C{=}C{=}CF_2$
$\nu_1 = 1957\ \mathrm{cm}^{-1}$	$\nu_1 = 2020\ \mathrm{cm}^{-1}$	$\nu_1 = 2053\ \mathrm{cm}^{-1}$

Butatriene shows absorption at 2990, 1708, 1610 and 860 cm^{-1}[277], but an assignment to the normal modes has not yet been published.

D. Electronic Theory

Cumulenes can be defined (along with acetylenes) as carbon compounds that have two π-electron systems whose nodal planes are perpendicular and intersect at a line which joins the carbon atoms. In addition there is experimental as well as theoretical evidence that the two perpendicular π-electron systems interact only very little. Already van't Hoff's theory of the tetrahedral carbon valences implies that two consecutive double bonds should be perpendicular (if we represent a double bond by two tetrahedrons which have one edge in common).

Quantum-mechanically one can describe the π electrons of the cumulenes in terms of LCAO–MO theory[355]. The inner carbon atoms of cumulenes each contribute two $2p$ atomic orbitals to the molecular orbitals, and it is now important to know which resonance integrals will be different from zero. It will be recalled that the resonance integrals β_{ik} are defined as follows: let $\hat{\mathbf{H}}$ be the π-electron Hamiltonian operator of the cumulene under consideration and let $\psi_1(x, y, z), \ldots \psi_m(x, y, z)$ be all the carbon $2p$ atomic orbitals that contribute to the π-electron system, then the β_{ik} are (an asterisk (*) denotes the complex conjugate):

$$\beta_{ik} = \beta^{*}_{ki} = \mathbf{H}_{ik} = \iiint \psi^{*}_{i}(x,y,z)\hat{\mathbf{H}}\psi_k(x,y,z)\mathrm{d}x\mathrm{d}y\mathrm{d}z \qquad (32)$$
$$(i \neq k; i, k = 1,2 \ldots m)$$

Physically they represent the interaction of the 2 atomic orbitals ψ_i and ψ_k. This interaction will be roughly proportional to the extent of overlap of the orbitals ψ_i and ψ_k.

The following assumptions about the β_{ik} are made in Hückel's molecular-orbital (HMO) theory:

1. $\beta_{ik} = 0$ if ψ_i and ψ_k come from two carbon atoms that are not directly bonded.
2. $\beta_{ik} = 0$ if ψ_i and ψ_k are the orthogonal atomic orbitals $2p_y$ and $2p_z$ of one single carbon atom. If in such a case, ψ_j is a p orbital of a neighboring carbon atom which overlaps with ψ_i then it follows from the principle of maximum overlap that ψ_j will not overlap with ψ_k, *i.e.* if $\beta_{ji} \neq 0$, then $\beta_{jk} = 0$.

3. $\beta_{ik} = \beta(r) \neq 0$ if ψ_i and ψ_k have the same symmetry and come from two carbon atoms that are directly bonded. The resonance integral is assumed to be a real function of the distance r between the two carbon atoms, and will be the greater the smaller r is. Since β_{ik} is real in HMO theory, it follows from equation (32) that $\beta_{ik} = \beta_{ki}$.

The following set of resonance integrals will be adopted here for the various bonds; the resonance integrals are given in terms of an empirical parameter β, which is negative and for most π systems approximately -2 ev:

1 β for double bonds (bond length 1·28 to 1·34 Å) and for the bonds in benzene rings;
0·7 β for single bonds (bond length about 1·45 Å); and
1·3 β for triple bonds (bond length about 1·20 Å).

According to HMO theory, the orbital energies are obtained as the eigenvalues of the matrix (β_{ik}) with $\beta_{ii} = 0$. The sum of the energies of the occupied orbitals gives the total π-electron energy which is a negative quantity. If a given π-electron system has two possibilities of π-electron arrangement, and a transition from one arrangement into the other is possible, then the one with the lower (*i.e.* the more negative) π-electron energy will be the more stable arrangement. The difference between the lowest unoccupied and the highest occupied orbital will be called 'excitation energy'. It is a measure for the longest wavelength absorption of the molecule.

The following experimental observations will now be explained on the basis of HMO theory:

1. The substituents of allenes are fixed in two perpendicular planes; those of butatrienes are fixed in the same plane [as evidenced by the preparation of stereoisomers (pp. 1061 and 1101)].
2. The first absorption bands of tetraphenylallene and of 1,1-diphenylethylene coincide (Figure 2)*.

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* Compare refs. 15, 110, 112 and 377 for other examples where similar observations were made.

3. The longest wavelength absorption bands in the ultraviolet spectra of tetraphenylcumulenes C_nPh_4, $n = 3, 4, 5, 6, 7, 8$ (Figure 3).

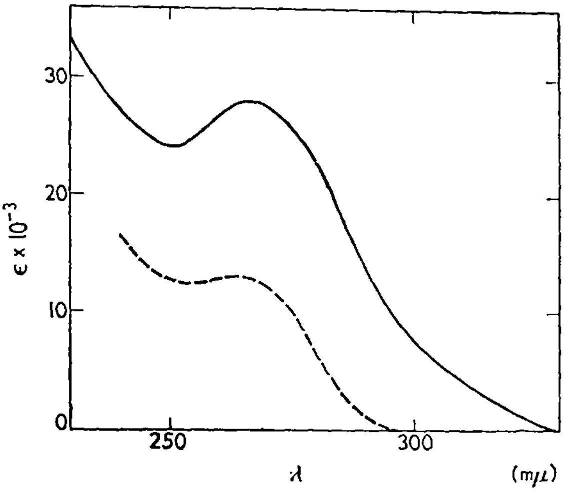


FIGURE 2. Absorption spectra of tetraphenylallene (———) and 1,1-diphenylethylene (– – – – –) in benzene.

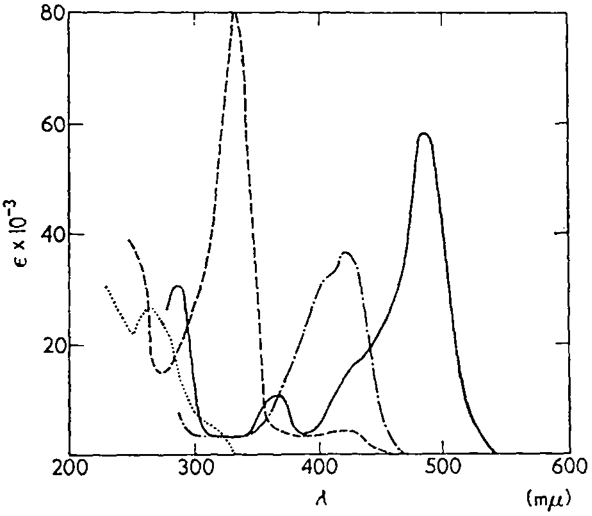


FIGURE 3. Absorption spectra of tetraphenylcumulenes in benzene: allene (·····), butatriene (—·—·—), pentatetraene (– – – –) and hexapentaene (———).

4. Partially unsubstituted butatrienes rearrange irreversibly to butenynes. The butenynes absorb at substantially shorter wavelengths than the butatrienes (p. 1106 and Figures 4 and 5).

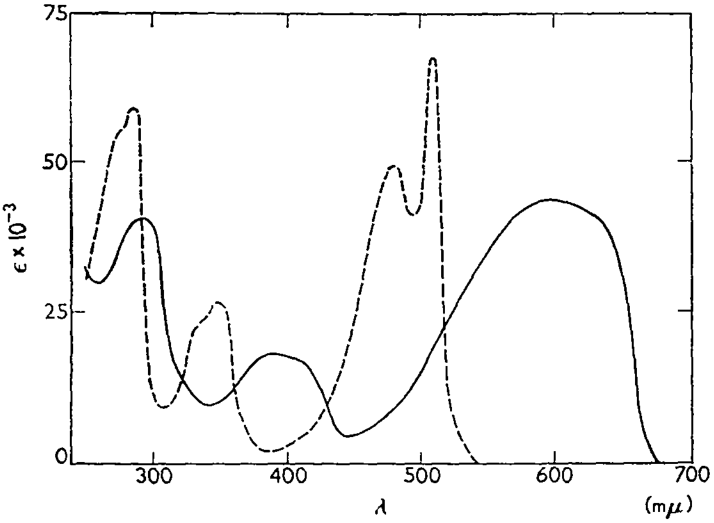


FIGURE 4. Absorption spectra of bis(diphenylbutatrienyl)anthracene (**140k**) (————) and bis(diphenylbutenynyl)anthracene (**148**) (– – – – –) in chloroform.

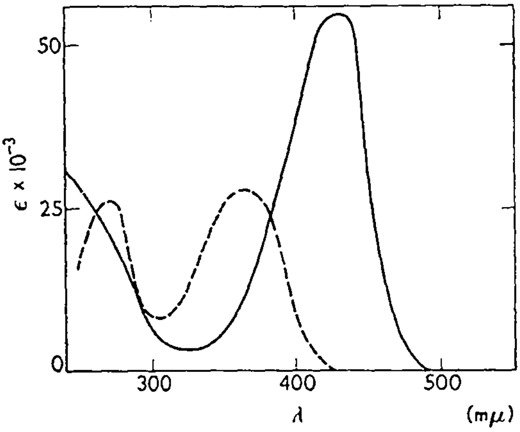


FIGURE 5. Absorption spectra of 1,1,6,6-tetraphenyl-1,2,3,5-hexatetraene (————) and 1,1,6,6-tetraphenyl-1,5-hexadien-3-yne (– – – – –) in benzene.

5. Tetraphenyl-1,2,4,5-hexatetraene rearranges irreversibly to tetraphenyl-1,2,3,5-hexatetraene and this in turn rearranges irreversibly to tetraphenyl-1,5-hexadien-3-yne (Table 6 and equation 23a).

6. The longest wavelength absorption bands of tetraphenylcumulenes lie at substantially longer wavelengths than those of the tetraphenylpolyenes (compare Figures 6 and 7).

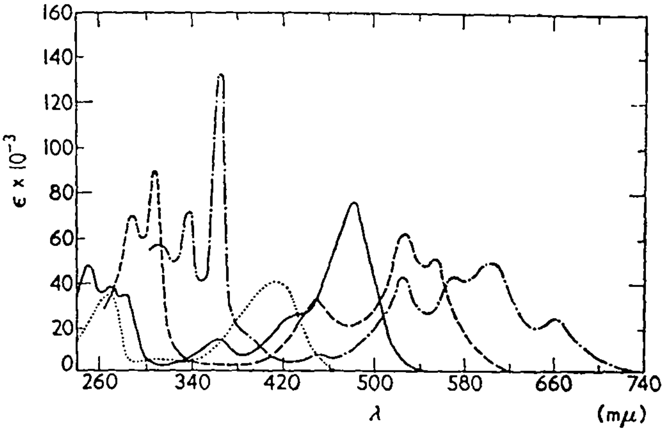


FIGURE 6. Absorption spectra of tetraphenylcumulenes in benzene: butatriene (· · · · · ·), hexapentaene (———), octaheptaene (– – – – –) and decanonaene (—·—·—).

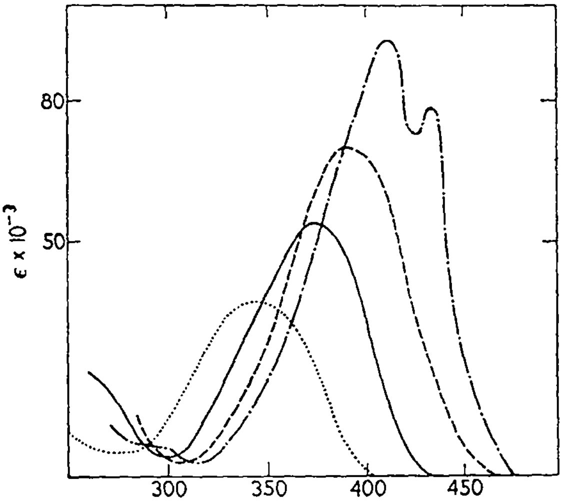


FIGURE 7. Absorption spectra of tetraphenylpolyenes in cyclohexane: butadiene (· · · · · ·), hexatriene (———), octatetraene (– – – – –) and decapentaene (—·—·—).

7. 1-Butyl-1,4-pentadiyne rearranges irreversibly to 1-butyl-3,4-pentadien-1-yne (**79q**) and this in turn rearranges irreversibly to 1-butyl-1,3-pentadiyne. Butylpentatetraene which could conceivably have been formed by these rearrangements, is not observed (Table 6 and p. 1086).
8. Tetraanisylpentatetraene can be readily protonated by acetic acid. Tetraanisylbutatriene is not protonated even by sulfuric acid.
9. 1,5-Disubstituted hexapentaenes have not yet been observed with certainty.

The explanations for the above observations, point by point, are as follows:

1. For allene there are four atomic orbitals: ψ_1 centered at $C_{(1)}$, ψ_2 and ψ_3 centered at $C_{(2)}$ and ψ_4 centered at $C_{(3)}$. On account of $\beta_{ik} = \beta_{ki}$ there are six resonance integrals to be considered: β_{12}, β_{13}, β_{14}, β_{23}, β_{24}, β_{34}. It follows from the first assumption of HMO theory that $\beta_{14} = 0$, and from the second that $\beta_{23} = 0$. Since a double bond is observed experimentally from $C_{(1)}$ to $C_{(2)}$ in allene, then at least one of β_{12} and β_{13} must be equal to β. Assuming that $\beta_{12} = \beta$, then β_{13} must be zero because of the second assumption of HMO theory; similarly, one of β_{24} and β_{34} must be equal to β and the other one equal to zero. There are thus two possible sets of resonance integrals in allene, and an investigation will now be made to find which one gives the lower π-electron energy:

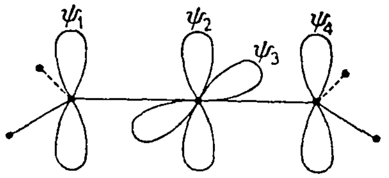
	β_{12}	β_{13}	β_{14}	β_{23}	β_{24}	β_{34}
Set I	β	0	0	0	β	0
Set II	β	0	0	0	0	β

Set I gives the matrix (β_{ik})

$$\begin{pmatrix} 0 & \beta & 0 & 0 \\ \beta & 0 & 0 & \beta \\ 0 & 0 & 0 & 0 \\ 0 & \beta & 0 & 0 \end{pmatrix}$$

for which the eigenvalues are $1{\cdot}4\beta$, 0, 0, $-1{\cdot}4\beta$. The π-electron energy for Set I is $2{\cdot}8\beta$.

Resonance between orbitals ψ_1 and ψ_2 and between ψ_2 and ψ_4 implies that they must have the same symmetry. Set I leads thus to a planar allene:

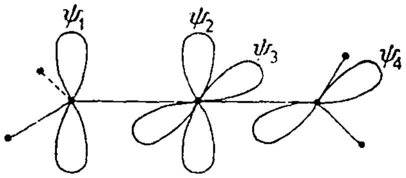


For Set II the matrix (β_{ik}) is

$$\begin{pmatrix} 0 & \beta & 0 & 0 \\ \beta & 0 & 0 & 0 \\ 0 & 0 & 0 & \beta \\ 0 & 0 & \beta & 0 \end{pmatrix} \tag{33}$$

for which the eigenvalues are: β, β, $-\beta$, $-\beta$; the π-electron energy is 4β.

Set II of resonance integrals which gives the lower π-electron energy leads to a perpendicular allene:



For Set I the highest filled molecular orbital is doubly degenerate and it is occupied by two electrons. In such a case Hund's rule applies which states that the two electrons must be filled in the two degenerate orbitals with parallel spin, *i.e.* the substance is then a diradical and would be expected to be unstable and to polymerize. A similar analysis for higher cumulenes yields the results recorded in Table 18[356].

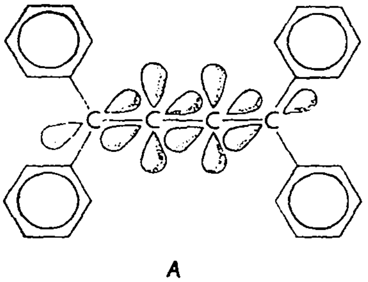
It is seen that the energy difference between the classical van't Hoff arrangement and the diradical arrangement of cumulenes decreases gradually. This explains the instability of higher cumulenes, since the thermal energy will gradually become sufficient to excite them to the unstable diradical form; HMO theory does not predict a marked tendency for the pentatetraene to form a diradical. Excitation

TABLE 18. π-Electron energy of planar and perpendicular arrangement of cumulenes C_nH_4 in HMO theory.

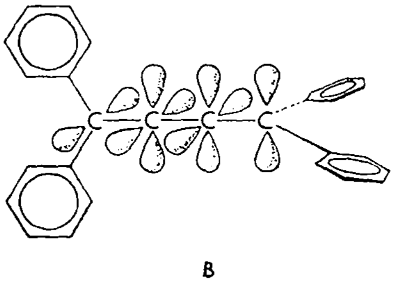
Cumulene	π-Electron energy of planar arrangement (in β)	π-Electron energy of perpendicular arrangement (in β)	Difference
Allene	2·82	4·00	1·18
Butatriene	6·48	5·66	0·82
Pentatetraene	8·26	8·94	0·68
Hexapentaene	11·46	10·86	0·60
. . . . . .			
Tridecadodecaene	28·76	29·00	0·24
Tetradecatridecaene	31·50	31·28	0·22

to the diradical form requires about the same energy as is necessary to excite the hexapentaene. Tetra-substituted hexapentaenes, however, are very stable and do not polymerize.

On the other hand, Zweig and coworkers[308] found that for tetraphenylbutatriene the planar configuration *A* had the same π-electron energy as the perpendicular butyne diradical configuration *B*. They did not take a smaller resonance integral between the phenyl groups and the cumulene chain, although this resonance is undoubtedly diminished, since two *gem*-phenyl groups cannot be planar simultaneously. If this resonance integral is taken to be 0·7β, then the van't Hoff configuration of tetraphenylbutatriene is found to be more stable than the perpendicular butyne diradical configuration. However, the main conclusion of Zweig is independent of this. The addition of two more electrons to tetraphenylbutatriene makes a perpendicular configuration of the substituents more likely. This is due to the fact that in the planar configuration the two additional electrons would go to an antibonding orbital (thus increasing the π-electron energy of the whole species), while for the perpendicular configuration the two additional electrons would go to a non-bonding



A



B

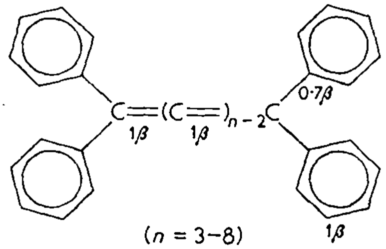
orbital (leaving the π-electron energy unaltered). The spectra of the mono- and dinegative ion of this cumulene support this view[363].

2. The matrix (33), which is relevant for the π electrons of allene, has the property that its characteristic polynomial in determinantal form (whose roots are the eigenvalues of (β_{ik})) factorizes into two identical 2 by 2 determinants:

$$\begin{vmatrix} -x & \beta & 0 & 0 \\ \beta & -x & 0 & 0 \\ 0 & 0 & -x & \beta \\ 0 & 0 & \beta & -x \end{vmatrix} = \begin{vmatrix} -x & \beta \\ \beta & -x \end{vmatrix} \cdot \begin{vmatrix} -x & \beta \\ \beta & -x \end{vmatrix} = 0$$

These 2 by 2 determinants are identical with the one that would be obtained for the π electrons of ethylene. Thus HMO theory treats allenes as two independent ethylenes which is in agreement with the experimental observation mentioned.

3. For tetraphenylcumulenes the following resonance integrals will be adopted:



The eigenvalues of the matrix (β_{ik}) are determined for each cumulene from which the energy for the first excitation can be deduced. In Figure 8 these theoretical excitation energies are correlated with the observed long wavelength absorption bands of these cumulenes. The latter are shown in Figure 3. It can be seen that the agreement is quite good so that one can be hopeful as regards the prediction of the absorption band for the still unknown tetraphenylheptahexaene*.

---

* When the manuscript for this chapter was originally submitted to the editor (March 1963) pentatetraenes were still unknown. An absorption band around 360 mμ for tetraphenylpentatetraene was then predicted (found 335 mμ). This prediction was based upon a comparison with the calculated excitation energy for tetraphenylbutatriene only. However, if a correlation line is drawn for the whole series of tetraphenylcumulenes, a better prediction can be made (345 mμ).

For a purely alkyl-substituted pentatetraene the same first absorption band is predicted as for the corresponding butatriene. Pullman and colleagues[357] applied HMO theory to the series C_nH_4 but allowed for hyperconjugation effects of the CH_2 groups (such effects would be much smaller for tetraalkylcumulenes). In this case they get a slight red shift of the first absorption band when going from butatriene to pentatetraene.

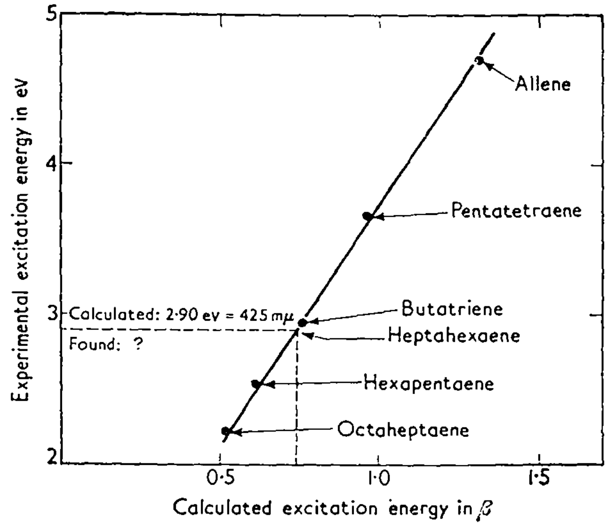
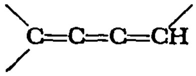
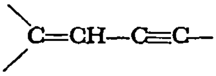


FIGURE 8. Correlation diagram for tetraphenylcumulenes.

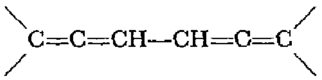
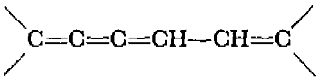
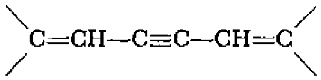
4. It can be shown that butenyne has a lower π-electron energy but a higher excitation energy than butatriene (Table 19).

TABLE 19. HMO calculations of butenyne and butatriene.

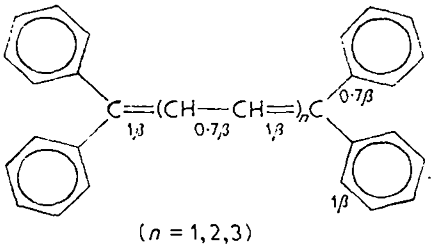
Compound	 $>C{=}C{=}C{=}CH<$	 $>C{=}CH{-}C{\equiv}C{-}$
Resonance integrals in terms of β	1 1 1	1, 0·7, 1·3
Orbital energies in terms of β (bonding orbitals)	0·62, 1·00, 1·62	0·82, 1·30, 1·58
Excitation energy in terms of β	−1·24	−1·64
π-Electron energy in terms of β	6·48	7·40

5. It can be shown that the π-electron energy decreases in the series hexa-1,2,4,5-tetraene → hexa-1,2,3,5-tetraene → hexa-1,5-dien-3-yne (Table 20).

TABLE 20. HMO calculations of hexatetraenes and hexadienyne.

Compound	 $>C{=}C{=}CH{-}CH{=}C{=}C<$	 $>C{=}C{=}C{=}CH{-}CH{=}C<$	 $>C{=}CH{-}C{\equiv}C{-}CH{=}C<$
Resonance integrals in terms of β	1 1 0·7 1 1	1 1 1 0·7 1	1 0·7 0·7 1 1·3
Orbital energies in terms of β (bonding orbitals)	0·55, 1·00, 1·00, 1·30	0·51, 1·00, 1·16, 1·60	0·70, 1·11, 1·30, 1·70
Excitation energy in terms of β	−1·10	−1·02	−1·40
π-Electron energy in terms of β	7·70	8·54	9·62

6. The calculated excitation energies for the tetraphenylcumulenes have been given previously (Figure 8). For tetraphenylpolyenes the following resonance integrals will be adopted:



The eigenvalues of the matrices (β_{ik}) are determined and from these the excitation energies for these polyenes are obtained in terms of β. Figure 9 correlates the calculated and experimental first excitation energies of three tetraphenylcumulenes and three tetraphenylpolyenes. The deviations from the straight line are seen to be quite small.

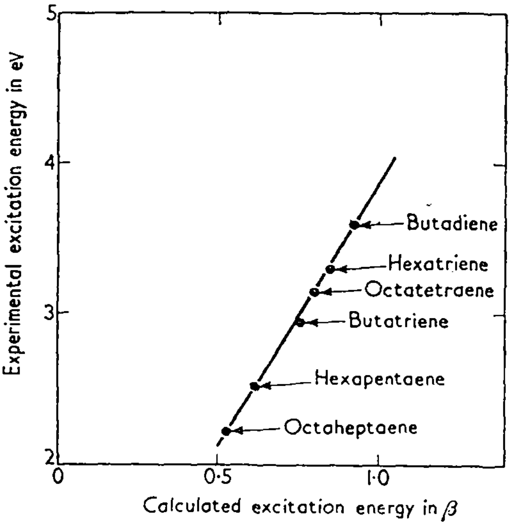


FIGURE 9. Correlation diagram for tetraphenylcumulenes and tetraphenylpolyenes.

7. The π-electron energies in the series penta-1,3-diyne → penta-1,2-diene-4-yne → pentatetraene increase (Table 21). From these results it would seem useless to try to synthesize pentatetraenes which have hydrogen atoms at the ends. Such pentatetraenes would probably rearrange spontaneously to pentadienynes and further to penta-1,3-diynes.

Table 21. HMO calculations of pentadiyne, pentadienyne and pentatetraene.

Compound	$-C\equiv C-C\equiv C-CH_2-$	$-CH=C=CH-C\equiv C-$	$-CH=C=C=C=CH-$
Resonance integrals in terms of β	1·3 1·3 0·7	1 1 0·7 1·3	1 1 1 1
Orbital energies in terms of β (bonding orbitals)	1·00, 1·00, 1·70, 1·70	0·82, 1·00, 1·30, 1·58	0·62, 0·62, 1·62, 1·62
Excitation energy in terms of β	−2·00	−1·64	−1·24
π-Electron energy in terms of β	10·80	9·40	8·96

8. A comparison between the increase in π-electron energy due to protonation of tetraphenylbutatriene on the one hand and tetraphenylpentatetraene on the other is given in Table 22. It is evident that the pentatetraene should be more easy to protonate than the butatriene. Analogous results would be obtained for tetraanisylcumulenes which explains the experimental observations.

TABLE 22. HMO calculations for tetraphenylbutatriene and tetraphenylpentatetraene and their protonation products.

Compound	Total π-electron energy	Difference
$Ph_2C{=}C{=}C{=}CPh_2$	$30\alpha + 39{\cdot}38\beta$	
$Ph_2\overset{+}{C}{-}CH{=}C{=}CPh_2$	$28\alpha + 37{\cdot}82\beta$	$2\alpha + 1{\cdot}56\beta$
$Ph_2C{=}C{=}C{=}C{=}CPh_2$	$32\alpha + 41{\cdot}88\beta$	
$Ph_2\overset{+}{C}{-}CH{=}C{=}C{=}CPh_2$	$30\alpha + 40{\cdot}80\beta$	$2\alpha + 1{\cdot}08\beta$

9. Hexenediynes or hexatetraenyne have a lower π-electron energy than the hexapentaene. Partially unsubstituted hexapentaenes would therefore probably rearrange spontaneously and irreversibly to compounds containing triple bonds (Table 23).

From the HMO theory information can also be gained about charge distribution and bond order in a π-electron system. Such calculations have been carried out by Pullman and coworkers[357] and by Longuet-Higgins and coworkers[358]. Bond lengths and force constants have been deduced. Experimental bond lengths now availabe for butatriene are, however, only in moderate agreement with the calculated ones.

A few more sophisticated quantum-mechanical calculations on cumulenes have been performed[364]. Serre[359] used the Pariser–Parr approach for allene and butatriene and assigned the various energy levels to the irreducible representations of the symmetry group of the cumulenes. Such calculations make possible the singling out of allowed and forbidden transitions. Streitwieser[360] showed that introduction of the so-called ω-technique into HMO theory greatly improves the results for the ionization potentials of allene and butatriene whereas simple HMO theory is, in general, only useful for getting information about π-electron energy and perhaps the position of the first absorption band.

TABLE 23. HMO calculations of hexenediyne, hexatetraenyne and hexapentaene.

Compound	—CH=C=C=C=C=CH—	—CH=C=C=CH—C≡C—	—C≡C—CH=CH—C≡C—
Resonance integrals	1 1 1 1 1	1 1 1 0·7 1·3	1·3 1 1·3 0·7 0·7
Orbital energies in terms of β (bonding orbitals)	0·44, 0·62, 1·25, 1·62, 1·80	0·55, 1·00, 1·30, 1·35, 1·74	0·71, 1·30, 1·30, 1·41, 1·70
Excitation energy in terms of β	−0·88	−1·10	−1·42
π-Electron energy in terms of β	11·46	11·88	12·84

Regarding the intensities of the bands in the cumulene spectra, it is found (see *e.g.* Figure 10) that the intensity of certain bands shows an approximately linear increase with increasing chain length, while other bands remain nearly constant in intensity. Closer analysis reveals that there is an optical transition in a cumulene chain with n carbon atoms whose transition dipole moment vector can be obtained by vector addition of $(n-1)$ ethylene transition dipole moments. Since the cumulene chain is not bent the vector addition of the ethylene moments can be replaced by algebraic summation and such a transition moment for the cumulene should be roughly proportional to the chain length. There is another transition in the cumulenes which (theoretically) shows no connexion with the ethylene transition. Its intensity will therefore not depend upon the chain length.

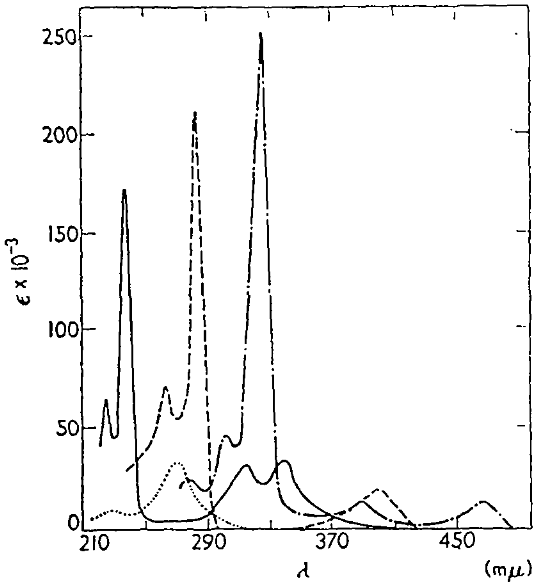
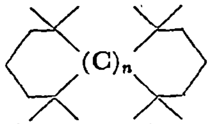


Figure 10. Absorption spectra of the cumulenes  in ether: butatriene (·····), hexapentaene (———), octaheptaene (– – – –) and decanonaene (—·—·—).

On the whole, not much theoretical work has been done in the field of analyzing cumulene spectra[361]. The spectrum of allene from 1200 to 2000 Å has been interpreted in terms of numerous Rydberg series which all converge to the same limit and give an ionization potential of 10·19 ev[362]. (Experimental values from electron impact data range from 10·2 to 10·4 ev.)

V. ACKNOWLEDGMENT

I am indebted to Professor R. Kuhn for valuable criticism and advice in preparing this chapter.

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The Chemistry of Alkenes
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CHAPTER 14

Ketenes

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[*] It is with regret that I must record Dr. Lacey's death on July 31, 1964. My thanks are due to his former colleagues for reading the proofs of this chapter —Editor

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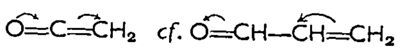
I. INTRODUCTION

The cumulative system of olefin and carbonyl double bond (C=C=O) in the ketene grouping presents some problems in classification in works of organic chemistry. Since many of the derivatives of ketenes are derivatives of carboxylic acids, which also provide starting materials for many ketenes, it is common to find an account of ketene chemistry associated with a section devoted to carboxylic acids. To consider the chemistry of ketenes alongside that of aldehydes and ketones is quite inappropriate since ketenes are quite without the properties commonly associated with the carbonyl group.

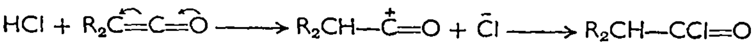
In many of their most typical reactions, however, ketenes exhibit strong resemblances to simple olefins: they are formed by typical olefin-forming reactions such as pyrolysis, dehalogenation, and dehydrohalogenation; they exhibit oxidation and polymerization reactions and a wide variety of addition reactions in which, almost without exception, the reagent adds to the olefin linkage rather than to the carbonyl group. In addition, however, to reactions with halogens, hydrogen halides, *etc.*, exhibited by normal olefins, ketenes react rapidly with alcohols, carboxylic acids, thiols, and phenols, which normally add to simple olefins only with difficulty, and with ammonia and amines, which do not react with simple olefins and add only to double bonds activated by conjugation with electron-attractive groupings such as carbonyl.

It is clear from the orientation observed in the products of addition reactions to ketenes that the carbonyl group is exerting an electron-repulsive ($+M$) effect increasing the covalency in the olefin double bond. The data for dipole moments of ketene and homologs show this electron displacement to be considerable and in ketene itself, for example, there is a *decrease* of 1·4 D as compared with the dipole moment for acetone, whereas in acraldehyde where the olefin and carbonyl groups are in conjugation there is an *increase* of 0·35 D relative to acetaldehyde, *e.g.*



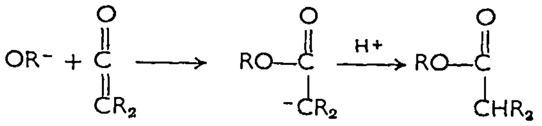
$$O{=}C{=}CH_2 \quad \textit{cf.}\ O{=}CH{-}CH{=}CH_2$$

The mechanism of the reaction of ketenes with electrophilic reagents such as halogens, hydrogen halides, *etc.*, is illustrated below.



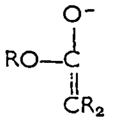
$$HCl + R_2C{=}C{=}O \longrightarrow R_2CH{-}\overset{+}{C}{=}O + \overset{-}{Cl} \longrightarrow R_2CH{-}CCl{=}O$$

With nucleophilic reagents, *e.g.*, RNH_2, OR^-, *etc.*, the mechanism is similar to the reaction of these reagents with acid anhydrides, halides, *etc.*, as, for example, in :



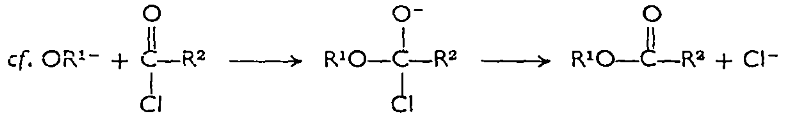
$$OR^- + \underset{\overset{\|}{CR_2}}{\overset{\overset{O}{\|}}{C}} \longrightarrow RO{-}\underset{\overset{|}{^-CR_2}}{\overset{\overset{O}{\|}}{C}} \xrightarrow{H^+} RO{-}\underset{\overset{|}{CHR_2}}{\overset{\overset{O}{\|}}{C}}$$

(1)



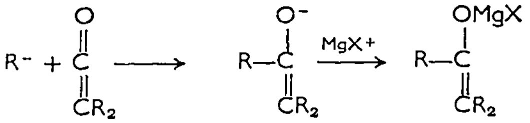
$$RO{-}\underset{\overset{\|}{CR_2}}{\overset{\overset{O^-}{|}}{C}}$$

(2)



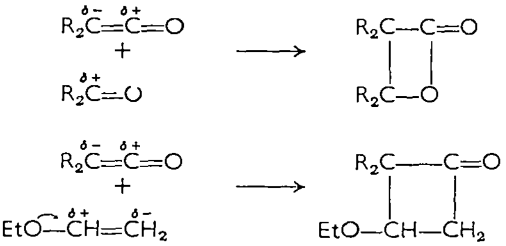
$$\textit{cf.}\ OR^{1-} + \underset{\overset{|}{Cl}}{\overset{\overset{O}{\|}}{C}}{-}R^2 \longrightarrow R^1O{-}\underset{\overset{|}{Cl}}{\overset{\overset{O^-}{|}}{C}}{-}R^2 \longrightarrow R^1O{-}\overset{\overset{O}{\|}}{C}{-}R^2 + Cl^-$$

In this case it is not possible to distinguish between the intermediate formation of **1** or **2** since both would add H^+ and rearrange to the carbonyl-containing final product rather than $ROC(OH){=}CR_2$. The contention that such reagents add to the olefin group is therefore a formal statement; indeed, one demonstrable exception exists since it is proved that Grignard reagents add to the carbonyl group, as in:

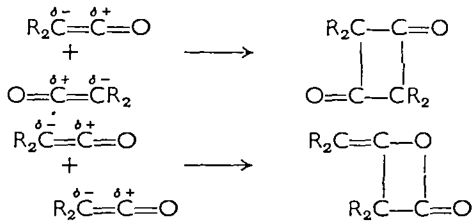


$$R^- + \underset{\overset{\|}{CR_2}}{\overset{\overset{O}{\|}}{C}} \longrightarrow R{-}\underset{\overset{\|}{CR_2}}{\overset{\overset{O^-}{|}}{C}} \xrightarrow{MgX^+} R{-}\underset{\overset{\|}{CR_2}}{\overset{\overset{OMgX}{|}}{C}}$$

A large class of ketene reactions involves cyclic transition states, particularly those with four members. Additions of ketenes with C=C, C=O, C=S, C=N, N=N are widely known. Their facility must be associated with the electron density at the olefin linkage polarized as $\overset{\delta-}{C}=\overset{\delta+}{C}\overset{\curvearrowright}{=}O$, the products being those to be predicted from the polarization of the unsaturated system employed, *e.g.*



Similar four-membered cyclic additions can take place in ketene dimerization reactions and a tendency to dimerize is a general characteristic. Two modes of addition are possible, as will be described later.



Implicit in a four-center transition state is the possibility of decomposition of the four-membered ring to the starting materials; the reactions are, in general, reversible although the reverse reactions are often complicated by alternative decomposition mechanisms.

Staudinger in his early papers drew a distinction between 'aldoketenes', $RHC=C=O$, and 'ketoketenes', $R^1R^2C=C=O$ (where R^1,R^2 are alkyl, aryl, but not alkoxycarbonyl) as indicated in Table 1. Amongst the ketoketenes, Staudinger found that the more strongly colored ketenes, *e.g.* diphenyleneketenes (red), diphenylketene (orange), were markedly more readily susceptible to reactions with

TABLE 1.

Property	Aldoketenes	Ketoketenes
Color	Colorless	Colored
Polymerization	Strong tendency	Less strong tendency
Addition reactions	Less strong tendency	Strong tendency
Autoxidation	Not susceptible	Slightly susceptible

nucleophilic reagents (*e.g.* alcohols, amines) and in four-center cyclic reactions (*e.g.* with $Ph_2C{=}NPh$) than the less strongly colored ketenes such as dimethylketene (yellow). The aldoketenes are not reported to be sensitive to oxygen and although reactions with alcohols and amines are well known, additions with C=C, C=O, N=N, *etc.*, have been observed only comparatively recently; in all cases with aldoketenes, polymerization can obscure all but moderately rapid reactions.

It seems probable that the more extensive electron-delocalization associated with color in the ketoketenes can account for greater reactivity in nucleophilic and four-center reactions. The lower tendency to polymerize is, however, inconsistent with this reasoning, but here it seems likely that steric effects, which must be strong with the bulky substitution in, say, $Ph_2C{=}C{=}O$ are controlling.

It is appropriate to point out that the present article is being written (1962) just half a century after the publication of Hermann Staudinger's *Die Ketene*[182]. No apology need be made for repeated reference to this work throughout the present review. It is seldom indeed that the chemistry of a class of compounds typified by a unique functional group can have been so extensively studied by one man. Staudinger has, however, been proved wrong in the prediction made in his preface that ketenes would only most rarely be used in technical processes. Ketene is today an important large-scale intermediate with many important applications and the study of its chemistry and that of its homologs continues to attract attention.

II. PREPARATION

A. From α-Haloacyl Halides

The dehalogenation of α-haloacyl halides may be regarded as a direct modification of a general method for the preparation of olefins; it was the method used by Staudinger in his first classical synthesis of ketenes[183].

$$R^1R^2CXCOY + M \longrightarrow R^1R^2C{=}C{=}O + MXY$$

The reaction is a general one for the synthesis of simple ketenes; it fails only for the dehalogenation of α,β-unsaturated α-haloacyl halides. The solvents generally used are dry ether or ethyl acetate and, apart from a few reported uses of magnesium[216], the dehalogenation agent generally employed is zinc. More recently, mercury[29, *cf.* 195] has been used for the preparation of several diarylketenes. The method is successful for ketoketenes, particularly for diphenylketene

(95%)[183,195], diphenyleneketene (90%)[184], carbonsuboxide (80%)[199], and methylphenylketene (80–90%)[222], but aldoketenes are formed in only poor yields[cf.190,216,212]. In many cases, the presence of aldoketenes in reaction products has been indicated only by the formation of derivatives[183,212]. The effects of variation of the nature of the halogen substituents, solvent, and dehalogenating agent have been most extensively investigated for the preparation of ketene itself[216], an unfortunate choice, perhaps, since the yields were in all cases poor. Indeed Hurd and coworkers[97] attempted the dehalogenation of α-bromoacetyl bromide, Staudinger's classical route to ketene, with negative results under a wide range of experimental conditions.

B. *Pyrolysis of Ketones, Acids, and Derivatives*

This route has its main practical importance for the preparation of the first member of the ketene group. Since the manufacture of ketene is of considerable industrial importance, the study of its formation has been the subject of considerable development work. Ketene was first prepared by Wilsmore[241] by the pyrolysis of acetone, ethyl acetate, and acetic anhydride. Today this important intermediate is made on a large scale either by the cracking of acetic acid at about 700°, generally under reduced pressure and in the presence of a phosphoric acid derivative which acts as a catalyst[37], or by the pyrolysis of acetone at 700–800° without catalyst [e.g.91].

$$CH_3CO_2H \longrightarrow CH_2{=}C{=}O + H_2O$$
$$CH_3COCH_3 \longrightarrow CH_2{=}C{=}O + CH_4$$

The thermal decomposition of acetone is the method most generally used in the laboratory; the equipment, consisting of an electrically heated filament of nickel–chromium wire suspended in acetone vapour, has been fully described[73]. The pyrolysis has been described as a free-radical chain reaction[160] in which initiation was attributed to the generation of carbon monoxide and methyl radicals. Concurrent thermal decomposition of ketene to carbon monoxide and methylene radicals, which combine to ethylene, contribute with the methane arising from the main reaction to dilute the ketene with inert materials. Pure ketene may, however, be obtained by low-temperature condensation followed by fractional distillation.

$$\begin{array}{ll} \text{Initiation:} & CH_3COCH_3 \longrightarrow 2\,CH_3\cdot + CO \\ \text{Chain reaction:} & CH_3COCH_3 + CH_3\cdot \longrightarrow CH_3COCH_2\cdot + CH_4 \\ & CH_3COCH_2\cdot \longrightarrow CH_3\cdot + CH_2{=}C{=}O \end{array}$$

The pyrolysis of acetic acid has been studied by Hurd and Martin[106] and by Bamford and Dewar[10]. Numerous patent applications indicate the weight of industrial development effort in this field. Hurd and his collaborators have studied the pyrolysis of various esters of acetic acid and methyl ketones such as methyl ethyl ketone, acetylacetone, biacetyl, *etc.*[93]. The pyrolysis of acetic anhydride is a convenient laboratory route to ketene[58].

Small yields of the corresponding ketenes have been obtained from the pyrolysis of phenyl- and diphenylacetic acids in a stream of toluene vapour at 515–636°[9]. Small yields of diphenylketene have been reported by the pyrolysis of diphenylacetylphthalimide[100], benzilic acid[191] and diphenylacetyl chloride[192]. The pyrolysis of isobutyrylphthalimide, however, gave a 30% yield of dimethylketene[100].

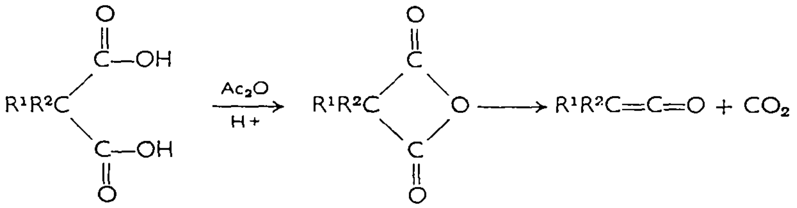
It had been generally believed that the thermal cracking of aliphatic acids was suitable for the preparation of only ketene itself. Recently, however, Enk and Spes[50] have published an account indicating that the continuous cracking of higher aliphatic acids to methyl-, ethyl-, and isopropylketenes may successfully be carried out under much the same conditions (30–60° lower temperature) as for ketene preparation. A much higher catalyst concentration (1–3%, *cf.* 0·2% for ketene manufacture) and shorter contact times were used to offset the rapid polymerization of higher ketenes. A preferred catalyst for this application is triethyl thiophosphate, neutralized immediately after the reaction by injection of ammonia. Alternatively, the use of $PS(OEt)_2NEt_2$ as catalyst avoids the use of neutralizing agent.

C. From Malonic Acid Derivatives

Methods of synthesis of ketenes based on malonic acid derivatives may be regarded as an extension of the pyrolysis of carboxylic acids described earlier. There are, however, some experimental features which make it convenient to treat them separately.

Malonic acid itself when heated with phosphorus pentoxide yields a 12% yield of carbon suboxide; better yields may be obtained from the bis(acid chloride)[199] on treatment with heavy metal compounds to combine with the halogen (silver oxide affords a 63% yield).

A common method, due to Staudinger, for the conversion of disubstituted malonic acids into ketenes is the pyrolysis of the anhydrides, obtained by treatment of the acids with acetic anhydride in the presence of sulfuric acid which is subsequently neutralized. Pyrolysis may then be effected by slow heating under reduced pressure to give ketoketenes in good (50–80%) yield[195]. Aldoketenes have not been prepared by the pyrolysis of monosubstituted malonic acid derivatives.



A modification of the above method which has also been developed by Staudinger[224,198], involves the pyrolysis of a mixed substituted malonic–diphenylacetic anhydride prepared by treatment of the appropriate disubstituted malonic acid with the readily available diphenylketene in ether. Decomposition of the mixed anhydride takes place on heating under reduced pressure; isolation may be effected either by distillation for the preparation of the lower molecular weight materials, or, for higher ketenes, by extraction to eliminate the possibility of exchange between diphenylacetic anhydride and the desired ketene that might take place. The route has been applied to a wide

$$R^1R^2C(CO_2H)_2 + 2\ Ph_2C{=}C{=}O \longrightarrow R^1R^2C(CO_2COCHPh_2)_2 \longrightarrow R^1R^2C{=}C{=}O + (Ph_2CHCO)_2O$$

range of dialkyl-, alkylalkenyl-, dialkenyl-, diaryl-, alkylaryl-, and halogen-substituted ketenes. Although allyl-substituted ketenes have been successfully prepared (diallylketene in 80% yield), it has not been possible to prepare propylideneketene ($Me_2C{=}C{=}C{=}O$) in which an extra double bond cumulative to the unsaturation of the ketene grouping would be present[198,223]. The method has failed with certain other substituted ketenes[224,223].

The action of phosphorus pentoxide at 180–200° on the monoethyl ester of α-ethylmalonic acid has given a 23% yield of the corresponding ketene[103]. This is more properly regarded as an example of the pyrolysis of simple carboxylic acids described earlier.

D. *From Acyl Halides with Tertiary Amines*

The dehydrohalogenation of acyl halides by tertiary amines is a well-established route to ketenes which continues to find wide application. The most commonly used procedure is to add slightly more than the equivalent quantity of amine, which may be trimethylamine, triethylamine, pyridine, *etc*., to a solution of the acid chloride in a suitable inert solvent, followed by removal of the amine hydrochloride by filtration and distillation at low pressure.

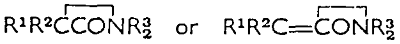
$$R^1R^2CHCOCl + R_3^3N \longrightarrow R^1R^2C{=}C{=}O + R_3^3N{\cdot}HCl$$

Tertiary amines catalyze the dimerization of ketenes, and for this reason the route is unsuitable for the preparation of aldoketenes which readily dimerize. Hill and colleagues[85] have, however, reported the preparation of monomeric ketenes of the type $ROCH{=}C{=}O$ by this method where R is aryl (phenyl, 2,4-dichlorophenyl, *etc.*). The reaction conditions are such as to cause the dimerization of monoalkylketenes and the lower molecular weight disubstituted ketenes[139]; the route is a convenient one for the preparation of aldoketene dimers (see section IV.A). This method has been widely applied to the preparation of diaryl- and alkylarylketenes, *e.g.* diphenylketene (in quantitative yield[192]), phenylmesitylketene and homologs[62,63], alkyl *p*-*t*-butylphenoxyketenes[82,86], *etc.*

Pyridine is reported to be unsuitable for the preparation of dialkylketenes[73]; trimethylamine is most widely used. In some cases, the dehydrochlorination may be effected by heating in the presence of only a catalytic quantity of pyridine. Thus α-mesitylphenylacetyl chloride was converted to the corresponding ketene by refluxing in benzene with a small quantity of pyridine[62]. Newman has described the preparation of the highly hindered ketene $PhCMe_2C(CO_2Et){=}C{=}O$ simply by distillation of the acid chloride under reduced pressure. An even more surprising technique was employed by the same author for the dehydrochlorination of di-*t*-butylacetyl chloride; sodium in liquid ammonia was found suitable in this case and no doubt only the unusual inertness of di-*t*-butylketene allows the use of this powerful reagent[146].

There are reported instances of the reaction being used as a convenient *in situ* method for the generation of ketenes. Thus Opitz and coworkers[151] generated methylketene in this way in their study of the reaction of this ketene and others with enamines. Presumably, this technique could be used only in rapid subsequent reactions when aldoketenes are involved, otherwise the well-known further self-condensation of the liberated ketene will ensue, *e.g.* the reaction of acetyl chloride and pyridine gives dehydroacetic acid; propionyl chloride, butyryl chloride, phenylacetyl chloride, *etc.*, give trisubstituted 4-hydroxy-1,2-pyran-2-ones[cf.182].

According to an early paper by Wedekind and Miller[238], strong tertiary amines such as trimethylamine react with acid chlorides to give 'ketenium compounds' supposedly formed from combination of the ketene first liberated and a molecule of amine and formulated as



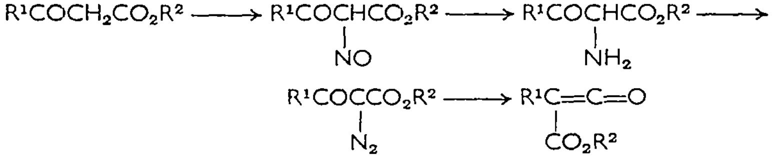
$$R^1R^2CCONR^3_2 \quad \text{or} \quad R^1R^2C{=}CONR^3_2$$

It is now known[139] that the results are explained by the presence of secondary amines in the tertiary amines used with the consequent formation of amides.

E. From Diazoketones

Schroeter first observed the smooth thermal decomposition of the diazoketone $PhCOC(=N_2)Ph$[170,cf.20] to diphenylketene. This method, though of somewhat limited application, is to be valued as the simplest route to diphenylketene; there is little doubt that the existence of this synthetic method has greatly facilitated research into the chemistry of this particular ketene. The diazoketone is readily prepared from the hydrazone of benzil by treatment with mercuric oxide and decomposed without purification by slowly dropping a benzene solution into a flask surrounded by a metal bath at 100 to 110°[175]. The decomposition has also been effected by irradiation but without obvious practical advantage[89,11].

Homologs of diphenylketene have been similarly prepared[65] and a preparation of phenylketene by this route has been described[154]. Several carbalkoxyketenes[207,171] have been prepared from *β*-keto-esters by successive nitrosation, reduction and conversion with nitrous acid to give diazoketones, followed by heating in boiling xylene, *e.g.*



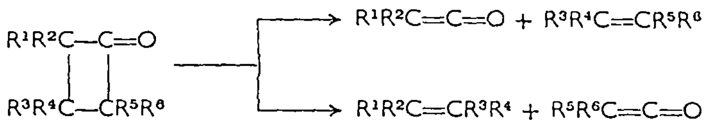
$$R^1COCH_2CO_2R^2 \longrightarrow R^1CO\underset{NO}{C}HCO_2R^2 \longrightarrow R^1CO\underset{NH_2}{C}HCO_2R^2 \longrightarrow$$
$$R^1CO\underset{N_2}{C}CO_2R^2 \longrightarrow R^1\underset{CO_2R^2}{C}{=}C{=}O$$

(**3**, $R^1 = R^2 = Me$;
$R^1 = Ph, R^2 = Me$;
$R^1 = CO_2Et, R^2 = Et$; etc.)

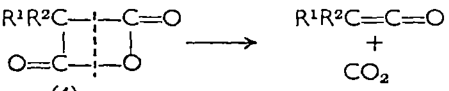
The route was found to be inapplicable to the synthesis of ketenes such as **3**, $R^1 = PhCH{=}CH$, $R^2 = Et$; **3**, $R^1 = MeCH{=}CH$, $R^2 = Et$[207] and acyl-substituted ketenes[171].

F. By Thermal Decomposition of Cyclic Compounds

The decomposition of substituted malonic acid anhydrides described earlier (section II.C) may be regarded as a special case of a more general decomposition reaction of four-membered ring compounds to ketenes and other products. This reaction, which will also be discussed later, may be expressed thus:



The relationship between this reaction and the decomposition of malonic anhydride derivatives **4** can be readily seen. A further example of the decomposition of four-membered rings is the depolymerization of ketene dimers. These compounds (see later) are either cyclobutane-1,3-diones (**5**) or derivatives of methylene-β-propiolactone (**6**), and the thermal decomposition of these compounds in many cases provides a convenient method for the preparation of ketenes in a fairly pure state.



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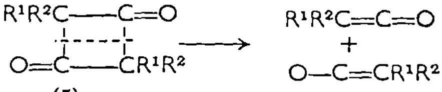

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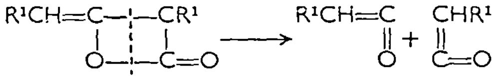
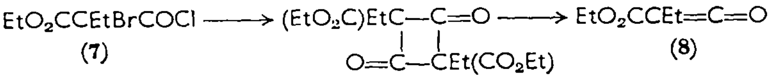


(6)

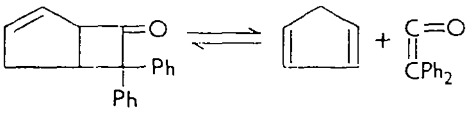
The thermal depolymerization of diketene can be used as a convenient laboratory source of ketene[121,23]; the product is contaminated with allene, carbon dioxide, and other by-products (see section IV.C.1) but can be generated at high rate at 80–85% purity in simple equipment.

The dimers of methylketene and dimethylketene may be converted into the monomers in 80–100% yields by passing through a tube heated to 550–600°c or by decomposition over a hot filament[73,213]. Staudinger found that the dehalogenation of **7** gave the dimer directly, but that thermal depolymerization at 200° *in vacuo* gave ethyl(carbethoxy)ketene (**8**) in 80–90% yield[200].

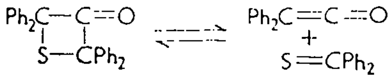


(7) (8)

The depolymerization of the corresponding dimers has also been used for the preparation of $(EtO_2C)_2C{=}C{=}O$[208], $EtO_2CCPh{=}C{=}O$[208,207], $PhCMe{=}C{=}O$[208,222] and $Ph_2C{=}C{=}O$[208,189]. Ketenes combine with olefinic and other unsaturated systems (*e.g.* C=N, C=S, *etc.*) as will be described later and in certain cases the adducts, which consist of four-membered ring compounds, can be smoothly dissociated to the original ketene. Thus the adducts of diphenylketene with cyclopentadiene (**9**) and thiobenzophenone (**10**) respectively give the parent ketene on being heated[189].



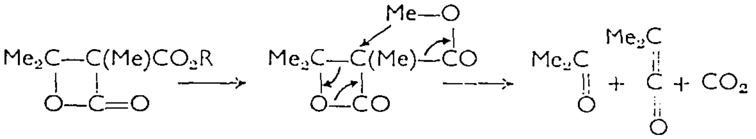
(9)



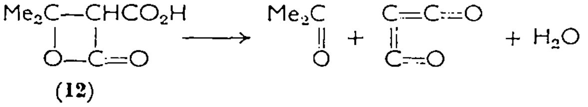
(10)

Certain ketene–amine adducts, in particular those between diphenylketene or diphenyleneketene and quinoline, show the essential reactions of the free ketene, *e.g.* reaction with alcohols, amines, *etc.*, to such a degree that the adducts, which are stable crystalline compounds, must readily dissociate in solution to a certain extent; heating to 120–160° gives dissociation to the parent ketene. These compounds will be described in detail later (section V.C).

The thermal decomposition of *β*-lactones, which may be regarded as adducts of ketene and carbonyl compounds (see section V.A), does not normally give a ketene but an olefin and carbon dioxide. Ott[152] has, however, reported two interesting cases in which *β*-lactones gave ketenes on pyrolysis. Compound **11b** gave dimethylketene but



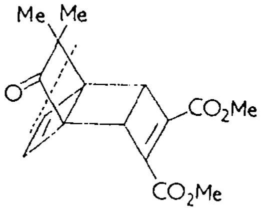
(**11a**, R = H; **11b**, R = Me)



(**12**)

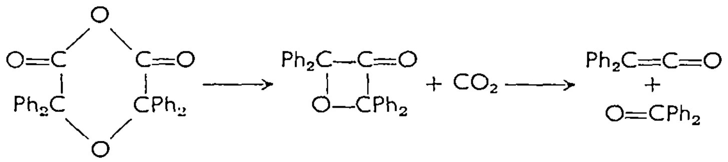
interestingly **11a** did not. Compound **12** gave a small yield of carbon suboxide on pyrolysis. The decomposition of **11b** may be represented as a concerted rearrangement as shown; failure of $MeO_2CCMe{=}C{=}O$ to give dimethylketene on pyrolysis shows that the former is not an intermediate.

The pyrolysis of the complex ring compound **13** *in vacuo* at 500°C gave a high yield (89%) of dimethylketene[2].



(13)

The action of heat upon the cyclic ether anhydride of benzilic acid (**14**) has been elucidated by Staudinger. In the first place, elimination of carbon dioxide gives the four-membered ring compound **15** which then cleaves to give diphenylketene and acetophenone as well as some red polymeric material[191]. The reaction is of little preparative importance.



(14) **(15)**

III. ADDITION REACTIONS TO GIVE CARBOXYLIC ACID DERIVATIVES

A. Reactions with Hydroxyl Groups

Ketenes in general react readily with water to give the corresponding carboxylic acids. Little quantitative work has been done on the

$$R^1R^2C{=}C{=}O + H_2O \longrightarrow R^1R^2CHCO_2H$$

measurements of reaction rates, but clearly there are wide differences between individual ketenes. Ketene itself reacts rather slowly with water, although the addition of acid catalysts greatly accelerates the rate; ketene is readily absorbed by dilute aqueous acetic acid. Carbon suboxide reacts quite slowly with water; Staudinger[182] noted a marked increase in reaction rate from the pale yellow dimethylketene, passing through diethylketene, the orange diphenylketene to the red diphenyleneketene which reacts very rapidly.

There is an extensive literature dealing with the use of ketene to acetylate aliphatic alcohols. Various catalysts are used, *e.g.* sulfuric acid[141], *p*-toluenesulfonic acid[107], *etc.*; acetylation proceeds without catalysts but conversion of the alcohols may be incomplete[52]. With acids such as those mentioned, *t*-butanol may be readily acetylated[141,107]. Basic catalysts have also been used[96].

Variable and generally indifferent results have been reported from attempts to use ketene to acetylate phenols; the reagent has no advantages over the more conventional ones[159,3,107]. Hydroperoxides have, however, been successfully acetylated[13]. The action of ketene upon dialkylhydrogen phosphites in the presence of BF_3, pyridine, *etc.*, has been studied[137,149]; the main reactions yield diethyl 1-acetoxyvinylphosphonate (**16**) and some **17**.

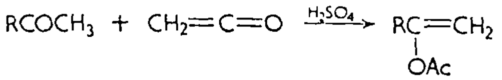
$$(EtO)_2POH + CH_2{=}C{=}O \longrightarrow [CH_2{=}C(OH)PO(OEt)_2] \xrightarrow{CH_2{=}C{=}O} \underset{(16)}{CH_2{=}C(OAc)PO(OEt)_2} + \underset{(17)}{AcPO(OEt)_2}.$$

Ketene has been used for the acetylation of α-nitroalcohols[118].

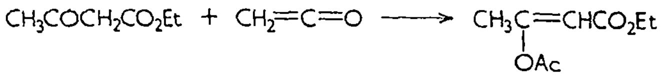
The reaction of other ketenes with alcohols has been less extensively studied. Staudinger has pointed out wide differences in reaction rates between different ketenes; $(C_6H_4)_2 > Ph_2 > PhMe > Me_2$[182]. The reaction is, however, general and is catalyzed by tertiary amines. Primary alcohols react more rapidly than secondary and tertiary alcohols; phenols react very slowly[182].

The reaction of ketene with simple enolizable carbonyl compounds to give enol acetates was first reported twenty years ago; to date, no reports appear to have been published of applications of this reaction to other ketenes. Isopropenyl acetate was obtained in 73% yield from ketene and acetone at 55° in the presence of a small amount of sulfuric acid[44]; a wide variety of other acid catalysts, notably alkyl- and arylsulfonic acids, has been claimed[cf. 121]. The reaction is general, and aliphatic and aromatic ketones capable of enolization can be acetylated. α,β-Unsaturated ketones may also be acetylated with ketene; mesityl oxide gives $Me_2C{=}CHC(OAc){=}CH_2$; the enol acetylation of methyl vinyl ketone and ethylidene acetone has been described[44]. Keto esters such as ethyl acetoacetate and ethyl levulinate, diketones such as acetylacetone may be converted to enol acetates with ketene[45,101]. Acetonylacetone is, however, converted to 2,5-dimethylfuran[101].

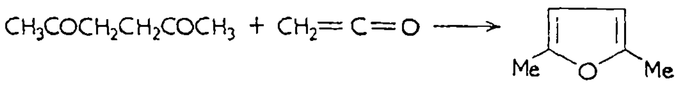
Aldehydes may be enol-acetylated with ketene in the presence of mineral acid catalysts with, however, only poor yields. A side-reaction, which becomes more preponderant with increasing molecular weight of the aldehyde and indeed proceeds with good yields in the



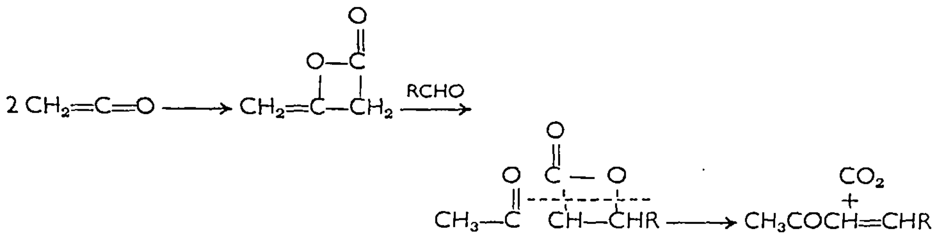
$$RCOCH_3 + CH_2{=}C{=}O \xrightarrow{H_2SO_4} \underset{\displaystyle OAc}{RC}{=}CH_2$$



$$CH_3COCH_2CO_2Et + CH_2{=}C{=}O \longrightarrow CH_3\underset{\displaystyle OAc}{C}{=}CHCO_2Et$$



absence of catalyst, gives α,β-unsaturated ketones and presumably involves the reaction of the aldehyde with diketene formed by the dimerization of ketene[170].



B. Reactions with Thiols

Little work has been carried out on the reactions of ketenes with thiols apart from those of ketene itself. Ketene reacts with hydrogen sulphide to give thioacetic anhydride[242] or in the vapour phase over alumina to give thioacetic acid in good yield[41]. Ethanethiol was treated with ketene at −80° to give a high yield of ethyl thioacetate[109]; catalytic quantities of sulfuric acid have been used in this reaction when conducted at room temperatures[47]. Ketene and *t*-butyl mercaptan react to give the expected thioester[40]. Ketene has been used to acetylate the thiol grouping in cysteine[145] and *N*-acetylcysteamine[119].

C. Reactions with Amines, Amides, Hydrazines, etc.

Ketenes react smoothly with primary amines to give high yields of *N*-acyl derivatives, but wide differences in rate have been reported.

With ketene itself, the reaction with many amines may be carried out in an aqueous medium; amino acids may be readily acetylated as their sodium salts in aqueous solution and some may be so converted even in the absence of alkali[17]. Amino alcohols and phenols undergo exclusively *N*-acylation with ketene[18] under appropriate conditions.

Reaction rate with ketene is a function of the dissociation constant of the base. Whereas aliphatic secondary amines react readily, aromatic secondary amines react slowly. Diphenylamine in ether at 0° reacted slowly to give an indifferent yield of amide[92].

With substituted ketenes, Staudinger[182] observed a higher reaction rate with amines, *e.g.* aniline, than with ethanol. Diphenylketene, for example, reacted with aniline in concentrated solution or without diluent with almost explosive violence. Other ketenes, notably the aliphatic ones, reacted slower. Staudinger also observed a parallel between reaction rate and strength of the base; thus in substituted anilines, the rate followed the order of substitution:

$$\mathrm{H{-}} > m\text{-}\mathrm{NO_2{-}} > p\text{-}\mathrm{NO_2{-}} > o\text{-}\mathrm{NO_2{-}}.$$

Ketene reacts with arylhydrazines to give 1-aryl-2-acetylhydrazines and with methylhydrazine to give NMeAcNHAc[4]. Dimethylketene with methylhydrazine appears to give a similar α,β-diacylhydrazine. Diphenylketene reacts with phenylhydrazine very rapidly to give 1-phenyl-2-(diphenylacetyl)hydrazine and with hydrazides such as PhNHNHAc rather slowly to give 1-phenyl-2-acetyl-2-(diphenylacetyl)hydrazine; with hydrazones and with diazoaminobenzene the secondary amino grouping is acylated[196].

$$\mathrm{PhCH{=}NNHPh \longrightarrow PhCH{=}NN(COCHPh_2)Ph}$$

$$\mathrm{PhN{=}NNHPh \longrightarrow PhN{=}NN(COCHPh_2)Ph}$$

Hydroxylamine reacts readily with ketene to give acetylhydroxamic acid[98]. The acylation of hydroxamic acids (RCONHOH) with ketene involves first *O*-acetylation followed by *N*-acetylation:

$$\mathrm{CH_2{=}C{=}O + NH_2OH \longrightarrow AcNHOH}$$

$$\mathrm{RCONHOH \longrightarrow RCONHOAc \longrightarrow RCONAcOAc}$$

Diphenylketene and hydroxylamine give diphenylacethydroxamic acid[102], $\mathrm{Ph_2CHCONHOH}$.

Ketene reacts slowly with acetamide to give an intermediate, possibly MeC(OAc)=NAc, which on standing gives diacetamide; further treatment with ketene gives triacetamide[153]. Acids catalyze the reaction of ketene with amides[153,173]; imides, such as phthalimide and succinimide, are not attacked by ketene[229].

Monochloroamine gave *N*-chloroacetamide with ketene in good yield. Dibromoamine reacted in an unexpected fashion with ketene to give bromoacetamide in low yield and nitrogen trichloride gave chloroacetamide in 14% yield; in these reactions the *N*-halogen atoms had been replaced by hydrogen[36]. Diphenylketene and nitrogen trichloride in carbon tetrachloride react at −10° and the product, believed to be **18**, after a short period at 40° with aqueous alkali, gave benzophenone and its imine[33,34]. The reactions of diphenylketene with chloroamine and dimethylchloroamine[35] are represented below.

$$\mathrm{Ph_2C{=}C{=}O + NCl_3 \longrightarrow \underset{(\mathbf{18})}{Ph_2CClCONCl_2} \xrightarrow{NaOH} [Ph_2CClNCO] \longrightarrow Ph_2C{=}NH}$$

$$\mathrm{Ph_2C{=}C{=}O + NH_2Cl \longrightarrow Ph_2CClCONH_2} \quad (51\%\ \text{yield})$$

$$\mathrm{Ph_2C{=}C{=}O + NMe_2Cl \longrightarrow Ph_2CClCONMe_2}$$

D. Reactions with Carboxylic Acids

All ketenes react rapidly with carboxylic acids to give acid anhydrides. The reaction proceeds much more rapidly than that with

$$\mathrm{R^1R^2C{=}C{=}O + R^3CO_2H \longrightarrow R^1R^2CO_2COR^3}$$

water, so that, in cases where the anhydride is not rapidly hydrolyzed by water or the water is not present in excess, an aqueous solution of the carboxylic acid will give the anhydride. Thus diphenylacetic acid with diphenylketene in a deficiency of water gave the corresponding anhydride, also formed by shaking the ketene with a suspension of water in an inert hydrocarbon[195].

The reaction of ketene with acetic acid to give acetic anhydride is widely practised industrially. Ketene reacts readily with other carboxylic acids to give mixed anhydrides which may disproportionate to the simple anhydrides[48,99,240]; inert media such as benzene, acetone or ether may be used, and catalysts are not required. The method is a convenient one for the precipitation of the anhydrides of higher carboxylic acids.

$$\mathrm{2\,CH_3CO_2COR \longrightarrow (RCO)_2O + (CH_3CO)_2O}$$

With formic acid[107] and chloroacetic acid[49], the respective mixed anhydrides are formed; that from formic acid is stable to distillation and can be used to acylate amines to *N*-formyl derivatives; the mixed anhydride from chloroacetic acid can also be used to give either acetyl or chloroacetyl derivatives depending upon reaction conditions.

Diphenylketene reacts readily with carboxylic acids and has been used for a particularly convenient synthesis of substituted malonic anhydrides (which are not isolated but are converted direct to ketenes, *cf.* section II.C) from the corresponding acids; the mixed anhydrides $R^1R^2C(CO_2COCHPh_2)$ are first formed and may be isolated[198].

E. Reactions with Halogens and Halogen Compounds

Ketenes characteristically react vigorously with halogens, but the reactions have not been extensively studied in detail. An exception is the reaction of ketene with chlorine. It has been shown recently that the reaction in the vapor phase or in the liquid phase, in media such as carbon tetrachloride, gives in addition to chloroacetyl chloride—the product to be expected from the simple addition reaction—substantial (20–30%) amounts of dichloroacetyl chloride[130,155]. Use of an excess of ketene in the vapor-phase reaction represses the formation of dichloroacetyl chloride. The liquid-phase reaction in ether had been studied some years ago[42] and it has been confirmed that the product so obtained (37% yield) is free from dichloroacetyl chloride. Use of liquid sulfur dioxide at -12 to 24° gives 75% yields[51] and, unexpectedly, use of alkyl acetates as reaction media gives similar yields[129]; in both cases the products were free of dichloroacetyl chloride.

Bromine has been reported to react with ketene[42,129,241]; iodine monochloride has been added to ketene in carbon tetrachloride at -10 to 15° to give iodoacetyl chloride[128].

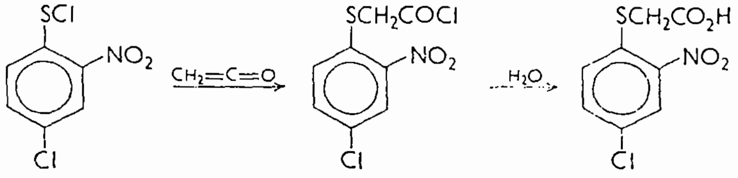
Hydrogen chloride with ketene gives acetyl chloride[242]; the reaction may be conveniently carried out in the vapor phase over a carbon or silica gel catalyst[54]. The analogous reaction with diphenylketene in a hydrocarbon solvent proceeds rapidly to give diphenylacetyl chloride[183]. A variety of other inorganic halogen compounds react with ketenes to give the corresponding acid halide. Thus sulfuryl chloride with ketene[180] and with diphenylketene[205] gives the chloroacid halide and sulfur dioxide. Nitrosyl chloride[245] and ketene gives chloroacetyl chloride; nitryl chloride (NO_2Cl) also gives chloroacetyl chloride and some nitroacetyl chloride (NO_2CH_2COCl)[227] by addition to the ketene olefin linkage. Diphenylketene with phosphorus pentachloride[196] and thionyl chloride[205] gives diphenylchloroacetyl chloride; sulfur and sulfur dioxide are concurrently produced in the latter case.

Sulfur dichloride is claimed[14] to react with ketene at $-20°$ in carbon tetrachloride to give $S(CH_2COCl)_2$. The reactions of thionyl chloride in sulfur dioxide, of sulfur monochloride in chloroform, and of ethylsulfenyl chloride in sulfur dioxide with ketene, followed by treatment of the acid chlorides obtained with an alcohol are represented below[180]. 2-Nitro-4-chlorophenylsulfenyl chloride reacts with ketene to give an acid chloride which, after hydrolysis, gives the acid **19** in 61% yield[163].

$$SOCl_2 \xrightarrow{CH_2=C=O} OS(CH_2COCl)_2 \xrightarrow{MeOH} OS(CH_2CO_2Me)_2$$

$$S_2Cl_2 \xrightarrow{CH_2=C=O} S_2(CH_2COCl)_2 \xrightarrow{MeOH} S_2(CH_2CO_2Me)_2$$

$$EtSCl \xrightarrow{CH_2=C=O} EtSCH_2COCl \xrightarrow{EtOH} EtSCH_2CO_2Et$$



(19)

Staudinger and colleagues[205] studied the reaction of diphenylketene with a variety of acid halides. Oxalyl chloride and bromide reacted readily and smoothly to give diphenylmalonyl halides by addition across the olefinic double bond followed by elimination of carbon monoxide. An analogous reaction takes place with the half ester $ClOCCO_2Et$ to give **20**; phosgene gives the same product as oxalyl chloride although more severe reaction conditions are required.

$$\begin{aligned} Ph_2C{=}C{=}O + (COCl)_2 &\longrightarrow Ph_2C(COCl)COCOCl \\ &\qquad\qquad \downarrow -CO \\ Ph_2C{=}C{=}O + COCl_2 &\longrightarrow Ph_2C(COCl)_2 \\ Ph_2C{=}C{=}O + EtO_2CCOCl &\xrightarrow{-CO} Ph_2C(COCl)CO_2Et \end{aligned}$$

(20)

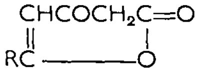
With other acid chlorides, however (*e.g.* acetyl chloride, succinoyl chloride, benzoyl chloride, *etc.*), diphenylketene either gave polymeric material alone or small yields of diphenylacetyl chloride.

Sŏrm, Smrt and coworkers have investigated the reaction of ketene with acid halides. Simple acid chlorides such as benzoyl chloride and propionyl chloride[163] do not react but acid chlorides (RCOCl) with negative substituents decrease in reactivity to ketene in the following order:

R = CH_2Cl, CCl_3, COCl, CO_2Et, $CHCl_2$, COMe, CH_2PH[178,179]

The reactions were generally conducted in chloroform or liquid sulfur dioxide and the acid chlorides (**21**) produced were not isolated but treated with ethanol to give esters. The general reaction below was followed by RCOCl where R = CH_2COCl, CCl_3, $CHCl_2$, CO_2Et and COCl. If R = CCl_3, the acid chloride reacted with a further molecule of ketene to give **22** which, on melting, lost hydrogen chloride to give **23**. A further example of this telomerization process is to be found when R = CO_2Et; the product obtained after treatment with ethanol consisted of both $EtO_2CCOCH_2CO_2Et$ and **23** (R = EtO_2C).

$$\mathrm{RCOCl + CH_2{=}C{=}O \longrightarrow \underset{(\mathbf{21})}{RCOCH_2COCl} \longrightarrow \underset{(\mathbf{22})}{RCOCH_2COCH_2COCl}}$$



(23)

The reaction of more reactive acid chlorides such as malonyl chlorides of the form $R^2R^3C(COCl)_2$ in which R^2 and R^3 are, respectively, H, Ph; H, $PhCH_2$; Cl, Cl; H, $CH_2{=}CHCH_2$, with ketene, followed by esterification with ethanol, gave products of formula $R^1R^2C(CO_2Et)COCH_2CO_2Et$[181].

Benzyl chloride, benzotrichloride, and chloroacetone do not react with ketene. Chlorobenzyl methyl ether[21] condenses with ketene without catalyst at room temperature to give **24**. Chloromethyl ether with ketene in the presence of Friedel–Crafts catalysts, followed by treatment with ethanol, has been claimed to give ethyl 3-methoxypropionate[226]; the use of antimony pentachloride has been claimed to have advantages[57]. A similar reaction with α,β-dichlorodiethyl ether in the presence of 10% of aluminum trichloride, followed by

$$\mathrm{PhCHClOMe \xrightarrow{CH_2=C=O} \underset{(\mathbf{24})}{PhCH(OMe)CH_2COCl}}$$

$$\mathrm{ClCH_2OMe \longrightarrow ClCH_2CH_2COCl \xrightarrow{EtOH} ClCH_2CH_2CO_2Et}$$

$$\mathrm{ClCH_2CHClOEt \longrightarrow ClCH_2CH(OEt)CH_2COCl \longrightarrow \underset{(\mathbf{25})}{ClCH_2CH(OEt)CH_2CO_2Et}}$$

$$\mathrm{Ph_3CCl \longrightarrow Ph_3CCH_2COCl \longrightarrow \underset{(\mathbf{26})}{Ph_3CCH_2CO_2Et}}$$

treatment with ethanol, gives a 43% yield of **25**[21]. Triphenylmethyl chloride requires the use of aluminum trichloride as catalyst to induce the reaction with ketene in benzene, but when nitrobenzene was used no catalyst was required and a good yield of **26** was obtained[21] after esterification of the intermediate acid chloride.

F. Reactions with Hydrogen Cyanide

The reaction of ketene with hydrogen cyanide does not, as might be expected, give acetyl cyanide (**29**) but 1-cyanovinylacetate (**27**)[244] formed by the acetylation of the enol form of acetyl cyanide. The reaction proceeds well at −20 to 10° in solvents such as esters, ethers, *etc.*, acetic anhydride being preferred, with a basic catalyst such as sodium acetate or a tertiary amine[70,112,233]. Improved results are reported at −60 to −70°, for at higher temperatures (10 to 30°), 1,1-dicyanoethyl acetate (**28**), presumably formed by the dimerization of **29**, becomes the chief product. Suitable reaction conditions for the preparation of **28** include[70] the use of a solution of hydrogen cyanide in acetic acid at 0° with sodium acetate as catalyst (it would seem likely that acetic anhydride may be an intermediate under these conditions) or the reaction of ketene and hydrogen cyanide in the vapor phase over activated alumina in the presence of triethylamine[228] or over a carbon catalyst[6].

$$CH_2{=}C{=}O + HCN \longrightarrow CH_3COCN \rightleftharpoons CH_2{=}C(OH)CN$$

$$CH_2{=}C(OH)CN + CH_2{=}C{=}O \longrightarrow \underset{(\mathbf{27})}{CH_2{=}C(CN)O_2CCH_3}$$

$$\underset{(\mathbf{29})}{2\ CH_3COCN} \longrightarrow \underset{(\mathbf{28})}{CH_3C(CN)_2O_2CCH_3}$$

G. Reactions with Ethers, Acetals, etc.

Ketene reacts with acetals in the presence of catalysts such as boron trifluoride etherate to give good yields of 3-alkoxy esters[27,177]. Fox has claimed 90–99% yields from the reaction of ketene with dialkoxymethanes conducted at 10 to 60°[60]. Orthoformic esters react similarly; ketals and tetraethoxymethane do not react with ketene[177].

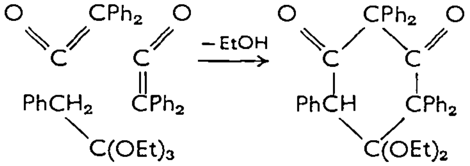
Staudinger and Rathsam[219] have reported the uncatalyzed reaction of diphenylketene with ethyl orthoformate to give the ester **30**.

$$CH_2{=}C{=}O + CH_2(OR)_2 \xrightarrow{BF_3\cdot Et_2O} ROCH_2CH_2CO_2R$$

$$CH_2{=}C{=}O + CH(OR)_3 \longrightarrow (RO)_2CHCH_2CO_2R$$

$$Ph_2C{=}C{=}O + CH(OEt)_3 \longrightarrow \underset{(\mathbf{30})}{(EtO)_2CHCPh_2CO_2Et}$$

The reaction of this ketene with triethyl phenylorthoacetate ($PhCH_2C(OEt)_3$) gave the cyclohexanedione **31**. The same product



was formed between diphenylketene and phenylketene diethylacetal ($PhCH{=}C(OEt)_2$).

Ketenes are generally inert to ethers but, in the presence of boron trifluoride, ketene reacts with tetrahydrofuran to give a small yield of ω-caprolactone[68].

The reaction of ketene with epoxides has recently been studied. In ether or benzene at 5 to 15° with boron trifluoride low yields of γ-lactones ($R\overline{CHCH_2CH_2CO}_2$) have been obtained from ketene with epoxides $R\text{—}\overset{O}{\overline{CH\text{—}CH_2}}$, where R = H, Me, Ph, CH_2Cl[150]. On the other hand, the product from the reaction of diphenylketene and ethylene oxide has been described as $Ph_2C{=}\overline{COCH_2CH_2O}$[69] involving addition to the carbonyl bond of the ketene molecule.

IV. POLYMERIZATION OF KETENES

A. *Dimerization*

With few exceptions, all ketenes dimerize either on standing at room temperature or below, or on being heated for a sufficient period. Aldoketenes polymerize especially rapidly and certain of the low molecular weight members have not been obtained pure for this reason.

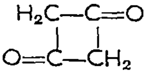
I. Diketene

The first study of the dimerization of ketene to diketene[245,243] followed soon after the first preparation of the monomer. The reaction does not proceed at −80°, at which temperature liquid ketene may be stored, but is rapid at 0°. Ketene does not dimerize in the vapour phase but dimerization takes place initially on points on the vessel surface and then rapidly in droplets of liquid dimer[158]. The reaction is an ionic one with second-order kinetics, proceeding faster in media of higher dielectric constant; the rate is unaffected by addition of peroxides or antioxidants.

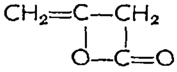
The dimerization of ketene is an important industrial process which is generally carried out at 40 to 50° in a liquid medium of diketene or acetone; yields are claimed to be 90–95%[70]. The dimer may be prepared in the laboratory[240]. Considerable effort has been devoted to the elucidation of the structure of this material. Early suggestions were that diketene had the structure **33** as acetylketene[243] or[244] as cyclobutane-1,3-dione (**34**). Ozonolysis experiments gave formaldehyde and malonic acid[95] and supported the structure **35** as methylene-β-propiolactone, which is now generally accepted.

$CH_3COCH{=}C{=}O$

(**33**)



(**34**)



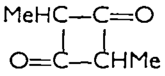
(**35**)

This structure is supported by much chemical evidence, in particular the formation of γ-bromoacetoacetyl bromide from diketene and bromine[243], the formation of $DCH_2COCH_2CO_2Me$ on treatment with CH_3OD[113], the formation of β-butyrolactone on hydrogenation[cf.121], allylic bromination with *N*-bromosuccinimide[20], shown to give a derivative capable with ethanol of giving ethyl α-bromoacetoacetate, and the formation of allene and carbon dioxide as by-products in the thermal decomposition of diketene[59]. In addition, a wealth of physical evidence is also available in support[121]. Diketene is a liquid, which darkens on prolonged standing, with an extremely pungent smell. It is a moderately strong acid (pK 7·1) and can be titrated in an aqueous medium[236].

2. Higher aldoketene dimers

The most convenient method for the preparation of the higher aldoketene dimers is the dehydrohalogenation of acyl halides with tertiary aliphatic amines[165,110,164]. By this technique[73], generally carried out by the addition of triethylamine to a refluxing solution of the acid chloride in ether, a wide range of aliphatic aldoketene dimers has been prepared in good yields. The use of a mixture of two acid chlorides gives rise to mixed ketene dimers in addition to the two simple ketene dimers. Thus a mixture of acetyl and lauroyl chlorides gave, in addition to diketene and decylketene dimer, a small yield of mixed ketene dimer[164].

In his study of the polymerization of methylketene, Staudinger[190] obtained a small yield of a liquid dimer, which had the pungent smell and reactions associated with diketene, and a solid dimer (m.p. 140°)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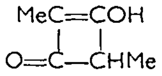
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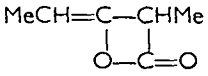
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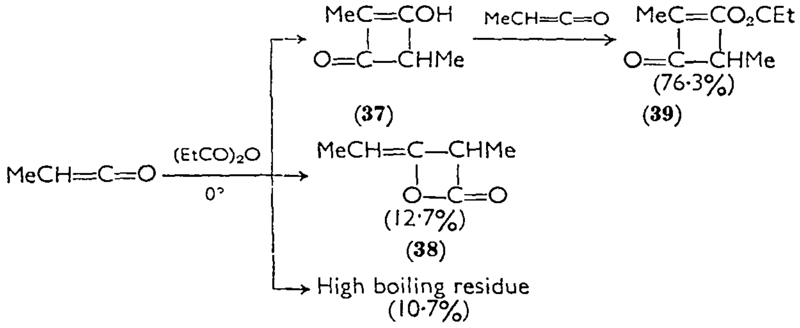
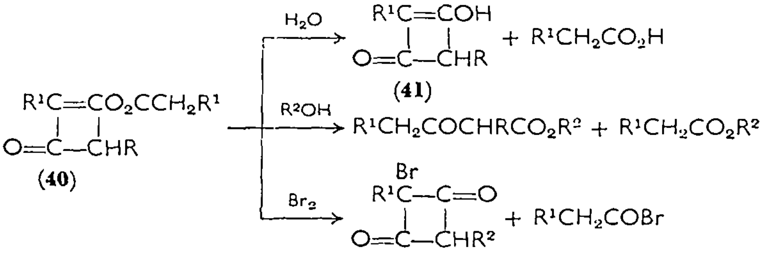
with a pleasant odor. To the liquid dimer he ascribed the cyclobutanedione formula **36** and to the solid dimer the enol structure **37**[182].

A reinvestigation by Woodward and Small[248] has confirmed the enolic structure **37** for the solid dimer. The liquid dimer, however, is now known to have the structure **38**, *i.e.* a homolog of diketene, as shown by spectroscopic evidence[26] and the results of methanolysis with CH_3OD[113]. The liquid dimer, also, is the product of the dehydrochlorination of propionyl chloride with triethylamine and other workers have shown that this general method when applied to the preparation of aldoketene dimers gives methylene-β-propiolactone derivatives and not cyclobutane-1,3-dione homologs. Thus, the ozonolysis of butylketene dimer[95] prepared by this route gave valeric acid, a result consistent only with the β-propiolactone structure. Roberts and coworkers[162] studied the products formed from $Et^{14}COCl$ with $Me(CH_2)_6COCl$ and showed that the distribution of radioactivity on hydrolysis of the ketene dimer was quite inconsistent with the cyclobutanedione structure.

A recent paper by Enk and Spes[50] has shown the dimerization of aldoketenes to be more complex than hitherto believed, but at the same time has resolved certain apparent inconsistencies in the earlier literature. The development of a technique for the continuous production of the lower aldoketenes by the cracking of the corresponding carboxylic acid at 40–100 mm enabled these workers to pass a stream of the desired ketene into an absorption system containing a suitable solvent such as a carboxylic acid ester, a ketone, a carboxylic acid anhydride, or the liquid reaction product itself to give, in addition to minor amounts of a dimer and high boiling residue, a trimer as the main product. The reaction with methylketene is:



Thus at 0° the primary products were the cyclobutenolone **37** with smaller amounts of the β-propiolactone **38**. In the presence of excess methylketene, **37** was acylated to give the trimer **39**. Other aldoketenes reacted similarly to give trimers **40**. The reactions represented below support the formulation made; hydrolysis with dilute alkali or acid gives the enol dimers **41**, and acylation of these compounds with the appropriate aldoketenes gave the trimer as obtained direct, or a 'mixed' trimer if another ketene were employed.



(40)

(41)

If lower temperatures were used for the self-condensation of aldoketenes, a different distribution of products was realized. At −50° methylketene in ethyl acetate gave the enol dimer in 87% yield and the β-propiolactone dimer **38** in 13% yield with no trimer. With increase in temperature, the formation of enol dimer decreased with corresponding increase in trimer formation. Earlier workers who studied the condensation of aldoketenes failed to observe trimer formation because they used either low temperatures or, in batchwise polymerization experiments, did not have an excess of aldoketene present.

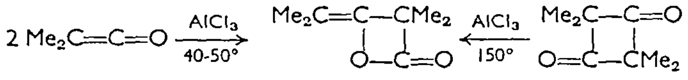
Certain of the results of Reid and Groszos[157] appear in conflict with the above work, but can probably be explained by the formation of trimers which complicated the isolation and identification of the dimers formed.

3. Ketoketene dimers

In general, ketoketenes dimerize at room temperature but at widely different rates[182]. Dimethylketene will dimerize in solution at room temperature within an hour or so; diethylketene requires some weeks to be converted to dimer under these conditions; phenylmethylketene requires some months for complete conversion, and diphenylketene can, in the pure state, be stored for months. Most ketoketenes can, however, be converted to the dimers by heating in a suitable solvent[224]. The simplest ketoketene dimer, that derived from dimethylketene, was first prepared by Wedekind and Weisswange[81] by the dehydrohalogenation of isobutyryl chloride with triethylamine, and shortly after by Staudinger and Klever[59] by the action of zinc on bromoisobutyryl bromide; dimerization of the ketoketene took place rapidly. Unlike the case of aldoketene preparation, where the two general methods of ketene preparation mentioned above give rise to different dimers, for ketoketenes the methods both give the same product.

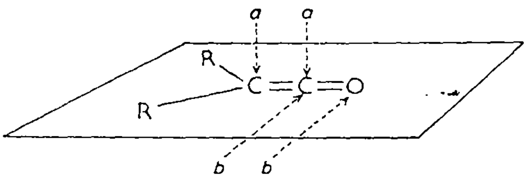
Staudinger's formulation of these compounds as cyclobutane-1,3-diones is generally accepted and it appeared until recently that the dimerization of ketoketenes in all cases gave rise to this general structure. Two exceptions are, however, now known.

Workers led by R. H. Hasek have carried out an intensive study of the reactions of dimethylketene during the last few years and have found that, by passing this ketene into chloroform containing catalytic quantities of aluminum trichloride (at 40 to 70°), a liquid dimer is produced which is clearly distinct from the solid tetramethylcyclobutane-1,3-dione (**42**). The liquid dimer could also be used as a suitable reaction medium and it was also formed by heating of **42** at 150° under reduced pressure with aluminum trichloride and by the thermal depolymerization of the polymer formed by the action of sodium methoxide in ether at room temperature on dimethylketene[74] (see section IV.B). The chemical reactions of the liquid dimer and spectroscopic evidence indicate the β-propiolactone structure **43**.



(**43**) (**42**)

Woodward[248] has pointed out that if the dimerization of ketenes is a four-center reaction, formation of a cyclobutanedione will proceed in the unhindered direction *a–a* at right angles to the plane of both

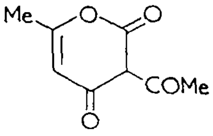


molecules. Formation of the methylene β-propiolactone form, however, requires approach of the two molecules along the path *b–b* which, with bulky substituents as in ketoketenes will be sterically impossible.

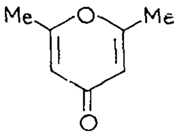
Anet has also recently found that a short period of heating of a benzene solution of diphenylketene with a catalytic quantity of sodium methoxide gave a solid dimer which infrared and nuclear magnetic resonance spectroscopy showed to have the β-propiolactone structure[5]. The cyclobutanedione form of the dimer of diphenylketene was obtained by Staudinger[189] by the prolonged heating of the ketene–quinoline adduct in benzene at 170°.

B. Formation of Higher Molecular Weight Polymers

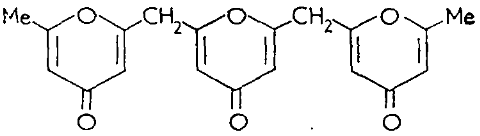
Further polymerization of diketene to higher molecular weight materials, notably dehydroacetic acid, was observed soon after Wilsmore first isolated diketene[244]. The reaction is catalyzed by bases; Boese[25] has shown that the polymerization in boiling benzene gives, in addition to dehydroacetic acid (**44**), 2,6-dimethylpyrone (**45**), and a pyrone derivative formulated as **46**.



(**44**)

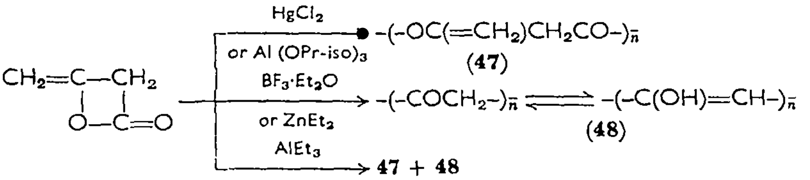


(**45**)

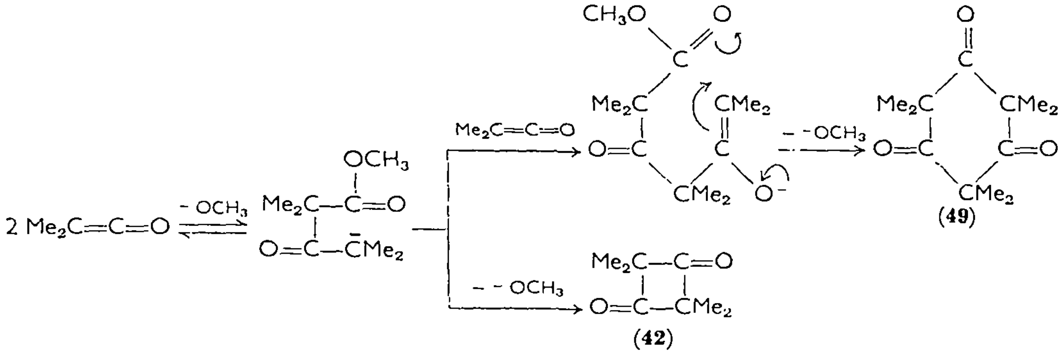


(**46**)

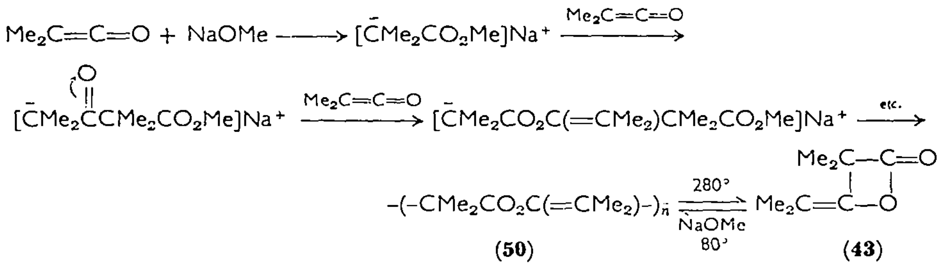
Furukawa and coworkers[61] have found that diketene is converted by treatment in toluene at −5 to 20° with mercuric chloride into a solid polymer formulated as the polyester **47**, whereas other catalysts, *e.g.* $BF_3 \cdot Et_2O$, gave a material formulated as the polyketone **48**.



Little is known about the polymerization of other aldoketenes. Erikson and Kitchens[52] have found that dimethylketene is converted in the presence of sodium methoxide in boiling toluene into a trimer, a cyclohexane-1,3,5-trione **49**, in addition to the dimer **42**. Dimethylketene dimers, both the cyclobutane-1,3-dione and β-lactone forms[75], undergo the same reaction under these conditions. Diphenylketene when heated with sodium methoxide in toluene gives a good yield of a similarly constituted trimer[75]. The mechanism has been formulated as:



Hasek and colleagues[74] found that the action of sodium methoxide on dimethylketene at lower temperatures, *e.g.* in ether, gave a solid polymer which decomposed at about 280° to give a good yield of the liquid β-propiolactone dimer **43**; treatment of the dimer with sodium methoxide in boiling benzene gave the same solid polymer described above which was formulated as the polyester **50** formed by a regular but alternating addition across the C=C and C=O groups of successive monomer molecules. The same polyester was obtained by Natta and coworkers[143] by polymerization of dimethylketene at −60° in the presence of triethylaluminum, whereas the use of aluminum bromide in toluene gave a solid polymer with a polyketone structure, *i.e.* $-(-CMe_2CO-)_n$.

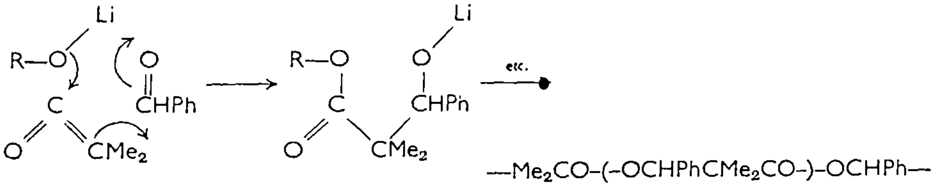


Natta and colleagues have also studied the copolymerization of dimethylketene with carbonyl compounds. Acetone and dimethylketene at −60° in the presence of butyllithium rapidly gave a white solid which x-ray and infrared examination showed to be a highly crystalline, linear polymer[142]. The same material was obtained, irrespective of the proportion of the two reactants. Reduction with lithium aluminum hydride gave $CH_2(OH)CMe_2CH(OH)Me$ and the structure **51** was proposed as a linear polyester formed by addition of the ketene molecule across its carbon–carbon double bond to the carbonyl group of the ketene

$$\begin{gathered} CMe_2{=}C{=}O \qquad O{=}CMe_2 \qquad CMe_2{=}C{=}O \qquad O{=}CMe_2 \\ \Big\downarrow \text{BuLi} \\ -CMe_2-CO-O-CMe_2-CMe_2-CO-O-CMe_2 \end{gathered}$$

(51)

Since the above polymer molecule has no site of asymmetry, it is not possible to ascertain if the process is stereospecific. If, however, acetone is replaced by benzaldehyde or on one of its derivatives, the possibility of stereospecific selectivity exists and Natta has achieved the preparation of alternating crystalline copolymers of such aldehydes with dimethylketene[144]. A variety of catalysts was used and, of these, alkyllithiums or lithium alkoxides gave the most stereoregular alternating copolymers; with naphthylsodium or alkylsodiums, alternating polymers were obtained which were only slightly crystalline or amorphous by x-ray examination. Substituted benzaldehydes, *e.g.* *o*-Cl, *p*-Cl, *p*-MeO, *m*-NO_2, and furfural reacted similarly but more slowly than benzaldehyde. It was demonstrated that since the β-lactone derived from benzaldehyde and dimethylketene was not converted into a polyester in the presence of an alkyllithium, the polymerization did not proceed through the β-lactone. Natta's view of the mechanism is that a lithium alkoxide is the actual polymerization catalyst and that the regular linking of alternate units may be explained by the simultaneous coordination of two monomer units to the lithium alkoxide.



The success with lithium as compared with sodium in the production of a stereoregular polymer was attributed to the smaller ionic radius and coordinating power of the former.

C. Reactions of Ketene Dimers

Ketene dimers can be classified into two general types, namely β-propiolactone derivatives and cyclobutanediones; the latter type is further subdivisible into those derived from aldoketenes which are generally strongly enolized in solution, and ketoketene dimers which cannot exhibit enolic properties. The subdivision is represented in Table 2.

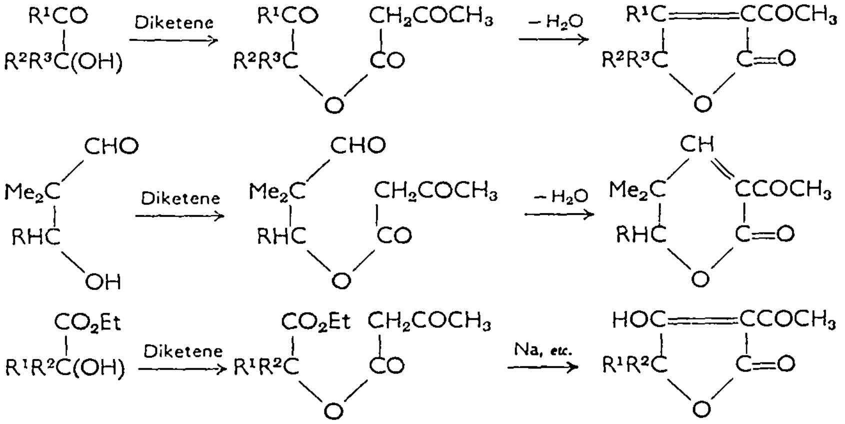
TABLE 2.

Compound	Dimers obtained		
	β-Propiolactone	Non-enolized cyclobutanedione	Cyclobutenolone
Ketene	✓	—	—
Aldoketenes	✓	✓	✓
Ketoketenes	✓	✓	—

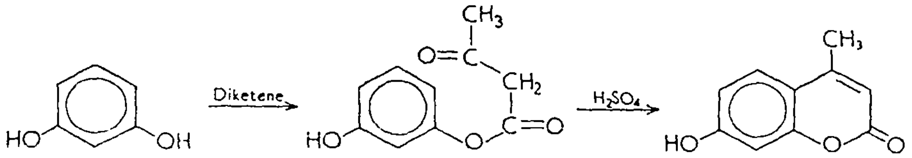
I. β-Propiolactones

a. Diketene. The dimer of ketene itself is the best-known representative of this class; the chemistry of this compound has been recently reviewed[121] and certain of its more important reactions have already been mentioned as structural evidence (section IV.A.1).

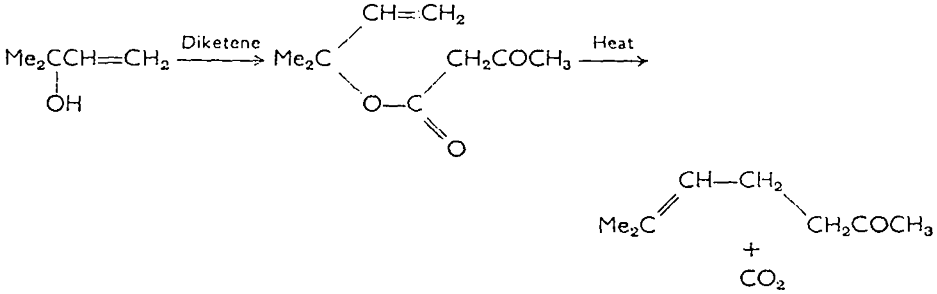
Diketene reacts with water at 50 to 100° in the presence of acidic or basic catalysts and is hydrolyzed to acetone and carbon dioxide with intermediate formation of acetoacetic acid; the reaction in the absence of catalysts even at 100° is quite slow. With alcohols in the presence of catalysts such as sodium alkoxides, tertiary amines or benzenesulfonic acid, diketene gives a wide range of esters of acetoacetic acid. Many esters derived from diketene may not be obtainable by the normal methods for the preparation of acetoacetic esters, and diketene, which may be used to acetoacetylate hydroxy-ketones, -aldehydes and -esters, can be used as a precursor of a variety of heterocyclic compounds as illustrated below[122,124].

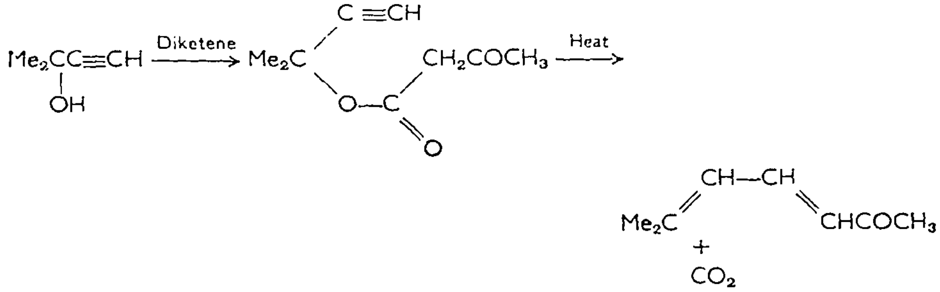


Phenols may be acetoacetylated with diketene and, although phenyl acetoacetates are unstable, several have been obtained as crystalline materials. Appropriately substituted phenyl acetoacetates undergo a Pechmann-type reaction with sulfuric acid to give coumarins, *e.g.*[123]



Diketene makes a wide range of allyl and ethynylcarbinyl acetoacetates readily available. These esters on pyrolysis give, respectively, γ,δ- and $\alpha,\beta;\gamma,\delta$-unsaturated ketones which have proved of considerable value in the synthesis of terpenes, *e.g.*[117,123].

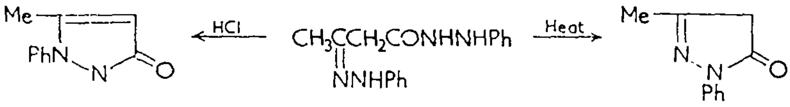




Diketene reacts readily with ammonia and aliphatic primary or secondary amines to give acetoacetamides. Aromatic amines also react rapidly; aniline may be acetoacetylated even in the presence of water but aromatic amines of lower basic strength require inert reaction media and the use of tertiary amines as catalysts.

With phenylhydrazine diketene gives first the phenylhydrazide phenylhydrazone **52** which, on being heated, gives 1-phenyl-3-methyl-5-pyrazolone (**53**), or with strong hydrochloric acid gives the isomeric pyrazolone **54**[132].

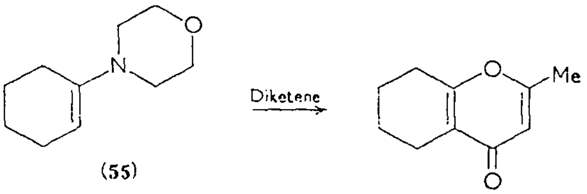
Recently, the reaction of diketenes with certain enamines has been studied. 1-Morpholinocyclohexene (**55**) with diketene gave a tetrahydrochromone **56** with elimination of morpholine[90]; the reaction



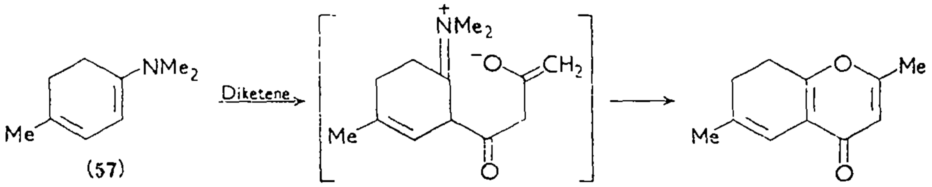
(**54**) (**52**) (**53**)

of 2,3-dihydro-*N*-dimethyl-*p*-toluidine (**57**) with diketene to give the dihydrochromone **58** is analogous[140].

α-Amino acid esters react rapidly with diketene and the products with sodium alkoxide undergo cyclization to α-acetyltetramic acids[127].



(55) (56)

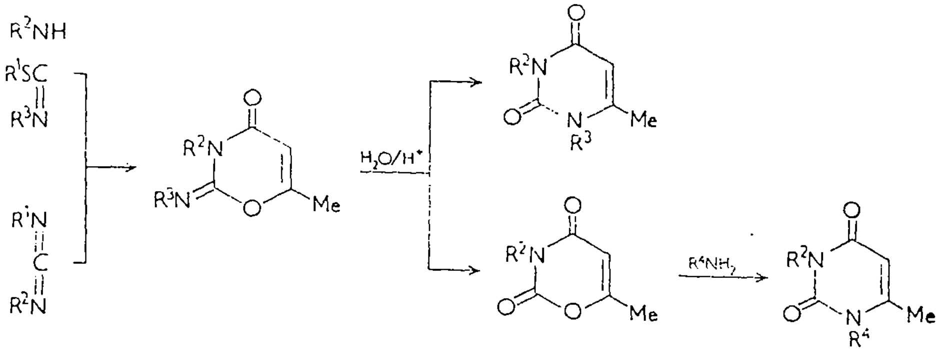


(57) (58)

Diketene reacts with thioureas, ureas, amidines, and guanidines to give the expected substituted pyrimidines[125]. The reactions with *S*-alkylthioureas[126] and carbodiimides[131], however, are of interest as giving 1,3-oxazine derivatives, members of a little-known ring system, as shown on page 1193.

Diketene may be reduced with hydrogen in the presence of a Pd/$BaSO_4$ catalyst at temperatures up to 75° to give a good yield of β-butyrolactone; use of Raney nickel under a variety of conditions, however, gave n-butyric acid[121, *cf*.70].

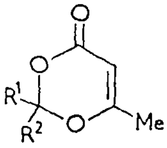
Bromine[244] and chlorine[94] are reported to react with diketene to give the corresponding γ-haloacetoacetyl halides; the products are unstable, and evidence for their formation depends upon their subsequent reaction with alcohols and amines. Similar evidence has been proposed for the formation of $CH_2{=}\underline{C{-}O{-}CO{-}CHBr}$ by the



allylic bromination of diketene with *N*-bromosuccinimide and the corresponding chlorination with 2,4,*N*-trichloroaniline[20]. Dry hydrogen chloride with diketene at low temperatures gives acetoacetyl chloride, which decomposes at ambient temperatures to dehydroacetic acid[104].

The polymerization of diketene has already been described in section IV.B.

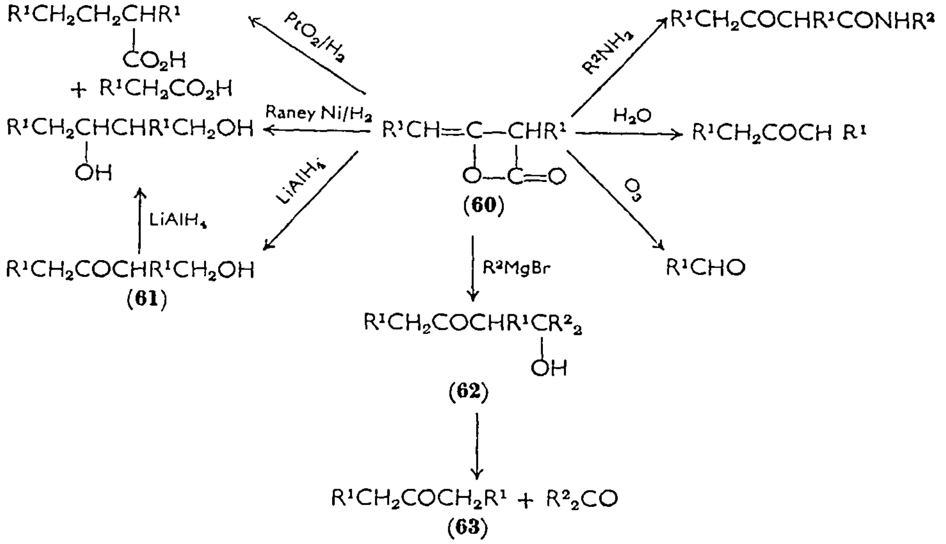
Although normally inert to ketones, diketene reacts with ketones in the presence of acid catalysts to give derivatives of 6-oxo-1,3-diox-4-ene (**59**) which exhibit many of the reactions of diketene[30]. Diketene reacts with acetaldehyde and higher aldehydes[70] to give α,β-unsaturated ketones by the mechanism given earlier (section III.A).



(**59**)

Diketene may be used to prepare *C*-acetoacetyl derivatives in certain cases. In the presence of aluminum trichloride, benzene and other aromatic compounds are acylated with diketene[23]. With pyrrole, diketene gives 2-acetoacetylpyrrole, and substituted pyrroles are acylated in a vacant 2-position if available; 2,5-dimethylpyrrole is attacked in the 3-position[230].

b. Other β-propiolactones. The lower β-propiolactone aldoketene dimers have a pungent smell unlike the cyclobutanedione isomers and tend to resemble diketene in general reactivity. Compound **60** (R = Me or Bu) gives β-keto amides and anilides with ammonia and aniline respectively; hydrolysis with aqueous alkali gave the corresponding ketones (RCH_2COCH_2R)[82]. Hydrogenation with platinum oxide as catalyst gave a mixture of two carboxylic acids, whereas the use of Raney nickel at high pressures gave 1,3-glycols[83].



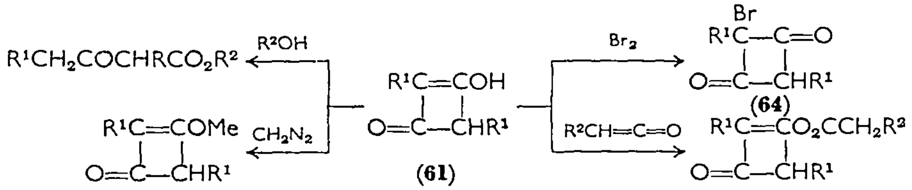
Ozonolysis gave the aldehyde RCHO, thereby providing useful structural evidence[83,95]. Reduction with lithium aluminum hydride gave the keto alcohol **61** which with further reagent gave the 1,3-diol[237]. With ethyl- and methylmagnesium bromides, ketene dimers **60** ($R = n\text{-}C_4H_9$, C_6H_{13}, C_8H_{17}) gave the ketones **63**, arising from the decomposition of the aldol **62**. With phenylmagnesium bromide, the dimers gave substantial yields of the corresponding aldols. Butyllithium with **60** (R = Me) gave diethyl ketone and di-n-butyl ketone[148].

The dimer of dimethylketene is one of the few ketoketene dimers that has been obtained in the methylene-β-propiolactone form and is the sole representative that has been studied in any detail. The reactions of this compound with alcohols and amines are typical of ketene dimers and, although it has not the reactivity of diketene, it is markedly more reactive than the isomeric cyclobutane-1,3-dione form of this ketene dimer. The dimer **43** is reduced by lithium aluminum hydride to $Me_2CHCOCMe_2CH_2OH$[74,75].

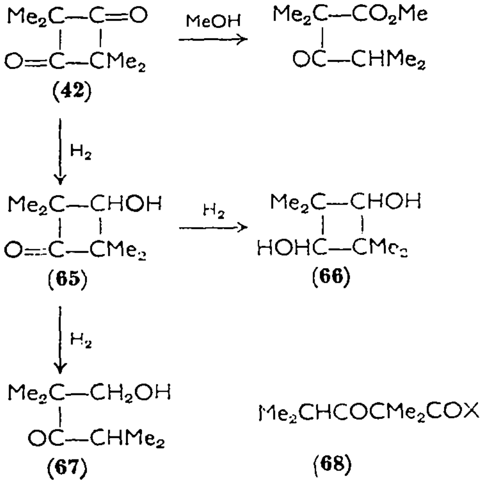
2. Cyclobutanediones

a. Cyclobutanediones from aldoketenes. The reactions of the enolizable cyclobutane-1,3-diones are closely similar to those exhibited by the

2,2,4,4-substituted homologs with the additional properties of a strongly acidic enol, though in the solid state it appears to be in the diketo form. **61** (R^1 = Me) is a stronger acid (pK 2·8) than acetic acid[248]; **61** (R^1 = Et) is only about one-fifth as strong an acid as the methyl homolog[157]. These dimers give bisoximes, are soluble in cold alkali from which after short contact they are recovered unchanged, give intense red colours with ferric chloride, and crystalline monobromides (presumably **64**) with aqueous bromine. They resist catalytic hydrogenation and give ketones RCH_2COCH_2R on hydrolysis. The reaction with alcohols in the presence of basic catalysts gives β-ketoesters. Diazomethane gives the respective enol ether and the enol group may be acylated with a variety of ketenes (*cf.* section IV.A.2)[50,157,248].

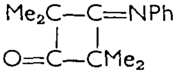


b. Cyclobutanediones from ketoketenes. The best known cyclobutane-1,3-dione, non-enolizable ketoketene dimer is that of dimethylketene. This compound (see section IV.A.3) was early shown to be 2,2,4,4-tetramethylcyclobutane-1,3-dione (**42**)[182]. It may be reduced with hydrogen in the presence of Raney nickel under mild conditions to give the ketol **65**; more severe condition in methanol gave the cyclobutanediol **66** with substantial amounts of the methyl ester derived from methanol and the ketene dimer, and hydrogenolysis products **67**[77].



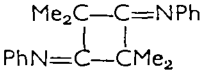
The dimer reacts smoothly in the presence of catalysts to give a variety of derivatives of the β-keto acid **68**, *i.e.* with ethanol in the presence of sodium ethoxide to **68** (X = OEt); *t*-butanol in the presence of sodium hydride to **68** (X = OBu-*t*); phenol to **68** (X = OPh), dodecane-1-thiol to **68** ($X = SC_{12}H_{25}$) in the presence of sodium, *etc.*[77].

Reaction of **42** with ammonia and with primary and secondary aliphatic amines (R^1R^2NH) gave amides **68** ($X = NR^1R^2$) but the reaction with aniline showed marked differences between this dimer and those of the β-propiolactone type in that acid catalysts were necessary to induce reaction and that the products were the mono- and dianils **69** and **70**[76].



$$\begin{array}{l} Me_2C{-}C{=}NPh \\ \;\;\;\;\;|\;\;\;\;\;| \\ O{=}C{-}CMe_2 \end{array}$$

(69)



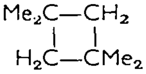
$$\begin{array}{l} \;\;\;\;Me_2C{-}C{=}NPh \\ \;\;\;\;\;\;\;\;\;|\;\;\;\;\;| \\ PhN{=}C{-}CMe_2 \end{array}$$

(70)

The dimer of ethyl(carbethoxy)ketene, however, is reported to react with aniline to give $EtCH(CO_2Et)CONPh$[200].

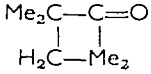
The rearrangement of the dimer **42** to the β-propiolactone form **43** has already been mentioned (section IV.A.3). Unlike the latter isomer, the cyclobutanedione dimer is unaffected by moderate heating with catalytic amounts of sodium methoxide; above 100° disproportionation to a cyclic trimer **49** takes place[75]. The dimer with an equimolar quantity of sodium methoxide gives the anion $Me_2\bar{C}COCMe_2CO_2Me$ which may be alkylated and acylated in the 4-position with a variety of reagents.

The reactions of the above and certain cyclic ketoketene dimers have been studied by Herzog, Walborsky and colleagues[81,235]. Reduction of **42** by the action of sodium in diethylene glycol on the



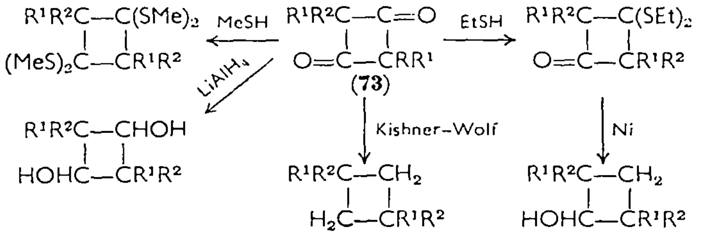
$$\begin{array}{l} Me_2C{-}CH_2 \\ \;\;|\;\;\;\;\;\;| \\ H_2C{-}CMe_2 \end{array}$$

(71)



$$\begin{array}{l} Me_2C{-}C{=}O \\ \;\;|\;\;\;\;\;\;| \\ H_2C{-}Me_2 \end{array}$$

(72)

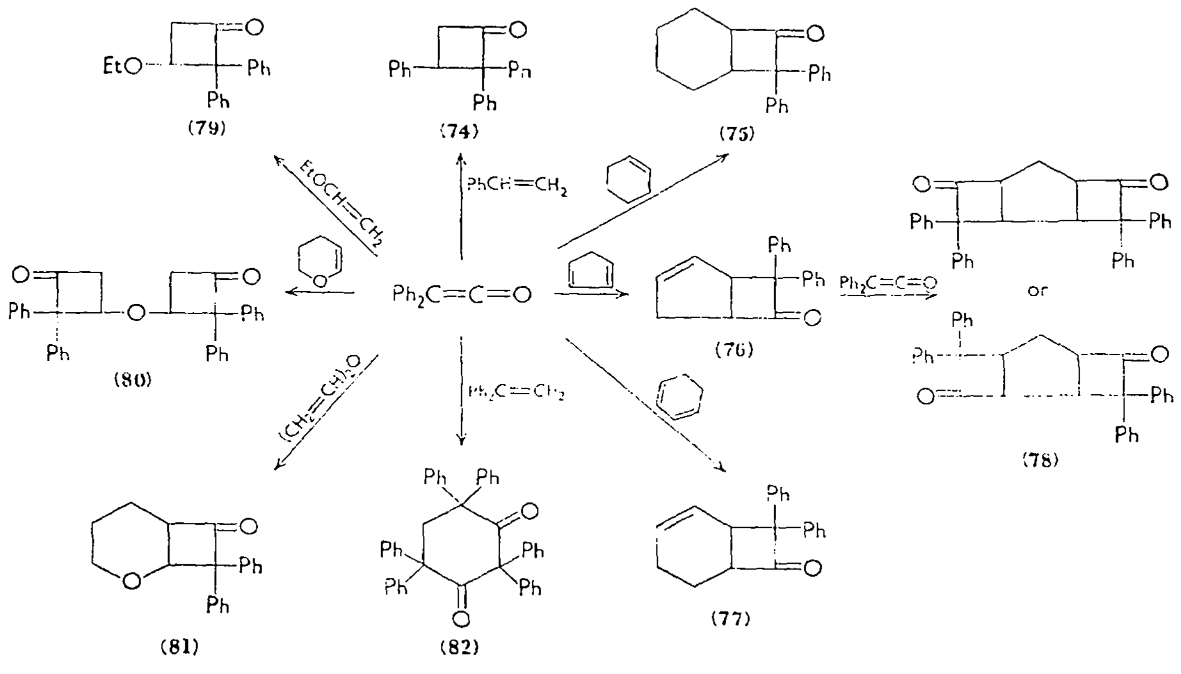


bissemicarbazone gave both the hydrocarbon **71** and the monoketone **72**. Compound **42** formed a bismercaptole with methanethiol which with nickel gave the cyclobutane. Certain of the reactions of **73** ($R^1R^2 = (CH_2)_4$) are shown on the previous page.

V. ADDITION REACTIONS THROUGH CYCLIC TRANSITION STATES

A. Reactions with C=C Bonds

Staudinger and Suter[225] reported an extensive study of the addition of diphenylketene to olefins to give cyclobutanone derivatives. A mixture of styrene and diphenylketene on being heated at 60° for 24 hours gave a crystalline adduct shown[16,221] to be the cyclobutanone derivative **74**; substituted styrenes reacted similarly[225]. Staudinger also studied the reaction of diphenylketene with cyclohexene[225], which combined on being heated for 10 days at 100° to give **75**. Cyclopentadiene and cyclohexadiene combine readily with diphenylketene and the structures of the crystalline products have been proved by degradative studies[55,133] to be **76** and **77** respectively. With an

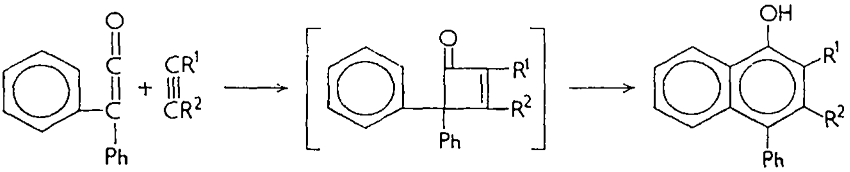


excess of diphenylketene, a further molecule adds to give the equimolar ketene–cyclopentadiene adduct **78**[184]. Ethyl vinyl ether combines similarly[225], and the structure of the product **79** has been established by Hurd and Kimbrough[105]; divinyl ether and dihydropyran combine to give the alkoxy cyclobutanone derivatives **80** and **81**. Farooq and coworkers[56] have studied the reaction of diphenylketene with butadiene and its derivatives. The products are complex and comprise adducts of two moles of ketene to one of diene as well as equimolar adducts. 1,1-Diphenylethylene was shown by Staudinger and Suter[225] in early work to give the cyclohexanedione derivative **82**.

(**83**)

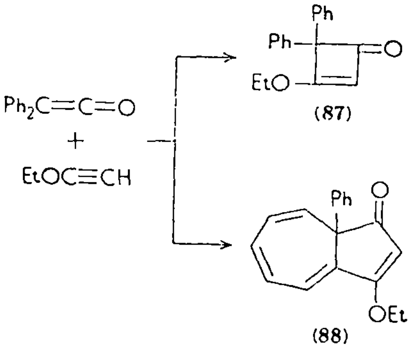
The reaction of olefins with other ketenes has attracted less attention. Brooks and Wilbert[28] found that cyclopentadiene reacted with ketene in toluene at 100° for 1 hour to give a product shown recently[232] to be **83**. Cyclohexadiene gave a cyclobutanone adduct[22] and butadiene reacted with ketene to give a small yield of 3-vinylcyclobutanone[232].

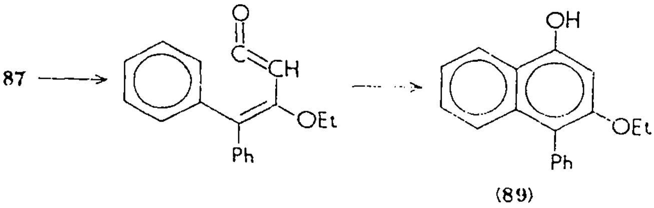
Smith and Hoehn[176] found that diphenylketene reacted with phenylacetylene to give a substituted α-naphthol **84**. The formation of **85** from diphenylketene and *p*-tolylacetylene showed that the fused benzene ring of the product and the phenyl in the 4-position were those derived from the ketene molecule. The failure of $Ph_2CHCOC{\equiv}CPh$ to cyclize to the naphthol showed that this acetylenic ketone was not an intermediate. Diphenylacetylene with diphenylketene at 70 to 80° for three days gave **86**, isolated as the diphenylacetate since the ketene was used in excess. The mechanism proposed involves addition of the ethynyl group to the ketene olefin linkage followed by the rupture of a cyclobutane bond and aromatization.

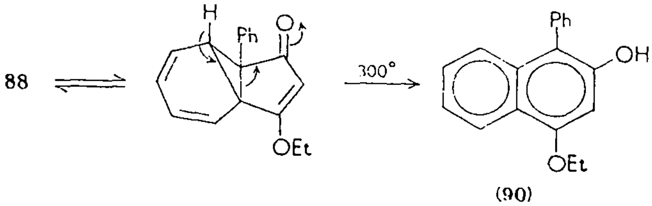


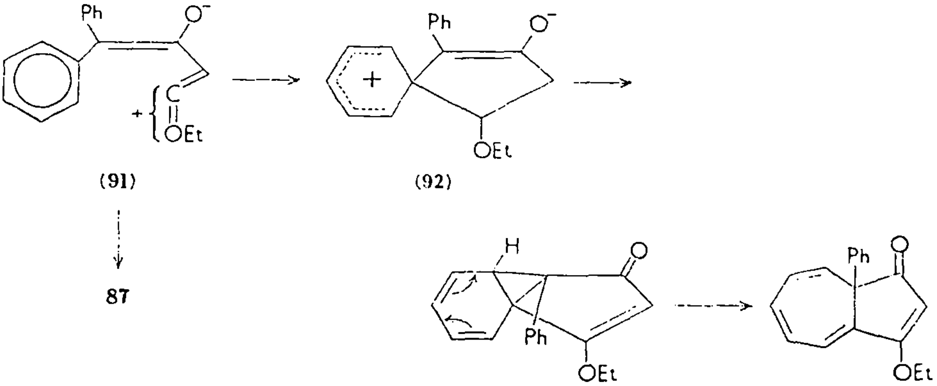
(**84**, R^1 = H, R^2 = Ph; **85**, R^1 = H, R^2 = $p\text{-}MeC_6H_4$; **86**, R^1 = R^2 = Ph.)

The reaction of diphenylketene with ethoxyacetylene shows certain resemblances to the above scheme. Nieuwenhuis and Arens[8,7] first studied the reaction which proceeds readily at −25° in nitromethane solution to give a yellow crystalline compound to which they ascribed



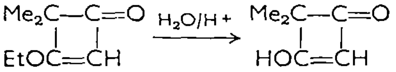






the formula **87** as an ethoxycyclobutenone derivative. It was later realized that this formulation was untenable and subsequent independent work by Barton[12] and by Woodward and coworkers[247] has shown the yellow product to be the azulene derivative **88**. Woodward and his collaborators carried out the addition at $-25°$ in pentane or at $-20°$ in nitromethane with subsequent standing at addition temperatures for several days. They found that roughly equal amounts of the azulene and a further compound shown to be the expected cyclobutenone **87** were formed. The latter readily rearranged on heating in boiling benzene to the α-naphthol **89** in direct analogy with the work of Smith and Hoehn described above. The azulene, however, required heating to 300° to effect rearrangement to the β-naphthol **90**. The postulated mechanism[247] involves first the addition of the ethynyl group to the ketene carbonyl group to give the zwitterion **91**. This may either cyclize to the cyclobutenone or to the spirocarbonium ion **92** which may undergo a norcaradiene–cycloheptatriene rearrangement to give the azulene.

Hasek and Martin[79] have found that ethoxyacetylene combines readily with dimethylketene to give 3-ethoxy-4,4-dimethyl-2-cyclobuten-1-one (**93**) which, unlike the product from diphenylketene, is stable up to 150°. Hydrolysis with dilute acid gives the crystalline hydroxycyclobutenone **94** which can be regarded as the mixed dimer of ketene and dimethylketene and, as such, is a strong acid (pK_a 2·6)



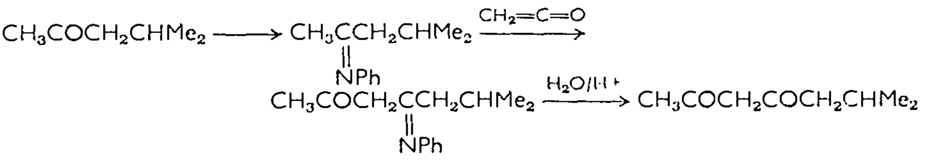
$$\begin{array}{l}Me_2C—C{=}O\\ \;|\quad\;\;|\\ EtOC{=}CH\end{array} \xrightarrow{H_2O/H^+} \begin{array}{l}Me_2C—C{=}O\\ \;|\quad\;\;|\\ HOC{=}CH\end{array}$$

(**93**) (**94**)

Earlier publications contain several references to the reaction of ketene with enamines which could be expressed by the general equation:

$$—N—C{=}C + CH_2{=}C{=}O \longrightarrow —N—C{=}C—CO—CH_3$$

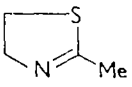
Thus the patent literature[80] reveals that the reaction of Schiff's bases with ketene, either without catalyst or in the presence of aluminum trichloride, zinc chloride, or boron trifluoride, gives an acetyl Schiff's base which, on hydrolysis, was reported to give a 1,3-diketone; a typical example of this reaction is:

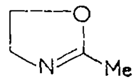


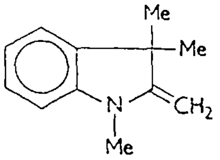
$$CH_3COCH_2CHMe_2 \longrightarrow \underset{\overset{\|}{NPh}}{CH_3C}CH_2CHMe_2 \xrightarrow{CH_2{=}C{=}O} CH_3COCH_2\underset{\overset{\|}{NPh}}{C}CH_2CHMe_2 \xrightarrow{H_2O/H^+} CH_3COCH_2COCH_2CHMe_2$$

Although the above Schiff's base is written in the imino form, Quadbeck[156] has shown that compounds containing the system —N=C—C— react with ketene only if they can rearrange to

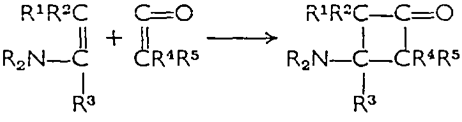
$-N-C=C-$. Thus α-picoline, 2-methylthiazole, *etc.*, do not react, whereas **95** and **96**, in which the double bond is free to move to the enamine form, react readily to give 2-acetonyl derivatives; 2-methylene-1,3,3-trimethylindoline (**97**), which contains an enamine double bond incapable of rearrangement, reacts similarly[32].


(**95**)


(**96**)


(**97**)

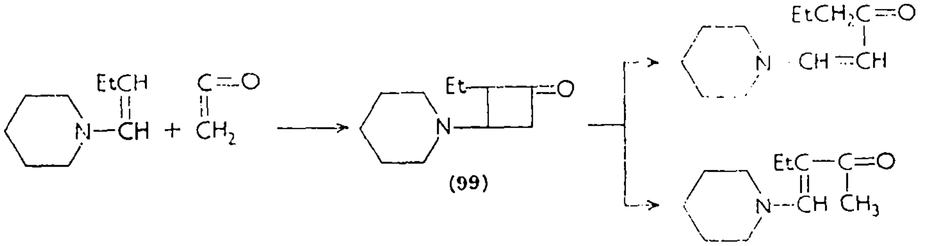
The above observations can now be rationalized by the independent and virtually contemporaneous work of three groups of workers[15,78,151]. It has been found that enamines of the type **97**, *e.g.* 1-morpholinoisobutene, 1-piperidino-2-ethyl-1-butene, *etc.*, react with ketene at or somewhat below room temperature to give the cyclobutanone derivatives **98**. Hasek and Martin[78] additionally prepared similar compounds from dimethylketene and enamines, and Opitz and coworkers[151] extended the scope of the reaction further by the generation of a wide range of aldo- and ketoketenes *in situ*, *e.g.* methylketene, isopropylketene, phenoxyketene, acetoxyketene, chloroketene, *etc.*, by the dropwise addition of an acid chloride $R_2CHCOCl$ to a mixture of triethylamine and the desired enamine. The generalized reaction is:



$$\begin{array}{c} R^1R^2C \\ \| \\ R_2N-C \\ | \\ R^3 \end{array} + \begin{array}{c} C=O \\ \| \\ CR^4R^5 \\ \\ \\ \end{array} \longrightarrow \begin{array}{c} R^1R^2C-C=O \\ |\qquad | \\ R_2N-C-CR^4R^5 \\ | \\ R^3 \end{array}$$

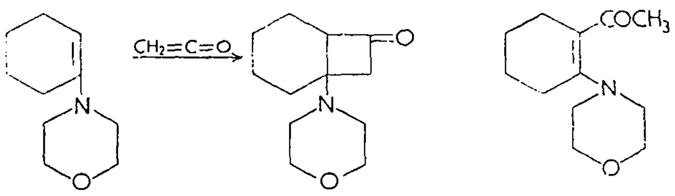
(**97**) (**98**)

The cyclobutanones obtained differ widely in stability. Thus the non-enolizable derivatives (when R^1, R^2, R^4, $R^5 \neq H$), such as the reaction product of dimethylketene and *N*,*N*-dimethylisobutenylamine, are thermally stable. If, however, the cyclobutanone has one or more

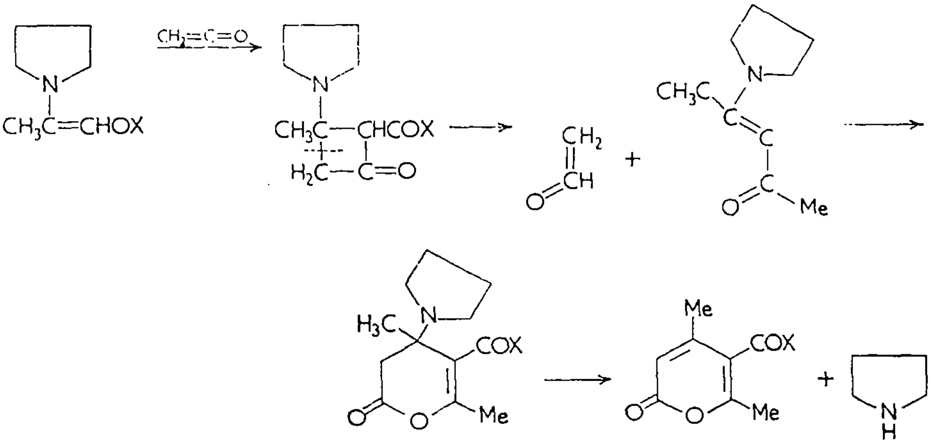


α-hydrogens, the product on distillation, or sometimes simply on standing, undergoes irreversible ring opening to form carboxylic acid amide vinylogs; two products are possible and have in certain cases been observed. Thus ketene and *N*-(1-butenyl)piperidine in hexane at −20° gives the cyclobutanone **99** as shown by the infrared spectrum; rearrangement gave a mixture of two amide vinylogs.

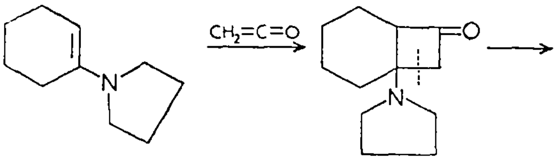
Only one enamine of the general form $R^3 \neq H$ appears to have been examined[151]. This, 1-morpholinocyclohexene, gave only a minor amount of the cyclobutanone, the main product being 1-morpholino-2-acetylcyclohexene formed by cleavage of the unstable primary product.

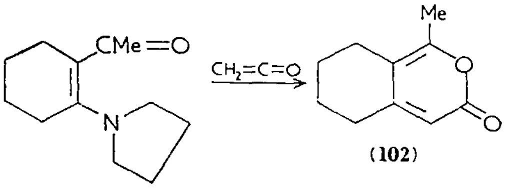


Thus enamines react very readily with ketenes even at low temperatures. The imino derivatives described earlier react less readily and rearrangement to the enamine is probably a necessary first step. Birchtold and coworkers[15] found that 4-*N*-pyrrolidino-3-penten-2-one, 1-*N*-pyrrolidinocyclohexene and ethyl 3-*N*-pyrrolidinocrotonate react at 0° with ketene in excess to give α-pyrone derivatives (**100**, **102**, and **101**, respectively). It is possible that the cyclobutanone derivatives in these cases may be particularly unstable, giving β-aminovinylketones,



(**100**, X = Me; **101**, X = OEt)



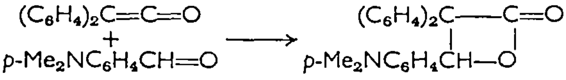


(102)

and that further addition of ketene proceeds in a manner similar to that with vinyl ketones leading, with elimination of tetrahydropyrrole, to α-pyrone derivatives.

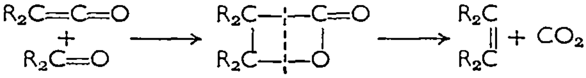
B. Reactions with C=O Bonds

In their early work, Staudinger and his colleagues were well aware of the reaction of ketenes with carbonyl compounds to form β-lactones[182]. They observed that the addition of simple carbonyl compounds to ketenes did not normally proceed unless elevated temperatures were used. Exceptions appeared to exist in the reaction of diphenyleneketene with *p*-dimethylaminobenzaldehyde or benzalacetone from which β-lactones (*e.g.* **103**) were isolated, but as a general rule the reaction conditions were such as to cause the well-known cleavage of the β-lactone initially formed to carbon dioxide and an olefin[187].



$$\begin{array}{c}(C_6H_4)_2C{=}C{=}O\\ +\\ p\text{-}Me_2NC_6H_4CH{=}O\end{array}\longrightarrow\begin{array}{l}(C_6H_4)_2C\text{——}C{=}O\\ \qquad\qquad\quad|\qquad\;|\\ p\text{-}Me_2NC_6H_4CH\text{—}O\end{array}$$

(103)

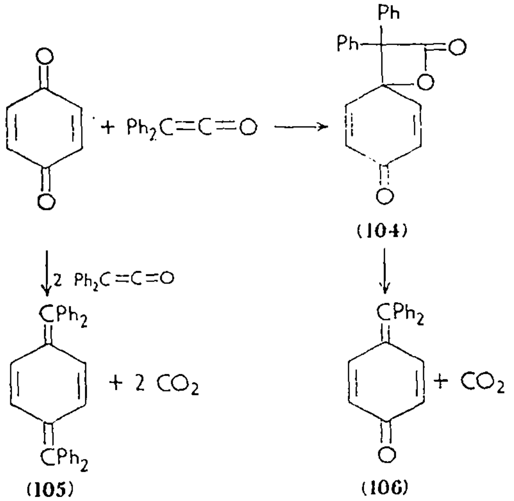


$$\begin{array}{c}R_2C{=}C{=}O\\ +\\ R_2C{=}O\end{array}\longrightarrow\begin{array}{l}R_2C\text{—}C{=}O\\ \;\;|\qquad|\\ R_2C\text{—}O\end{array}\longrightarrow\begin{array}{c}R_2C\\ \|\\ R_2C\end{array}+CO_2$$

Staudinger was unable to bring about the addition of carbonyl linkages to aldoketenes and the simpler ketoketenes, and attempts to increase the severity of the reaction conditions led to polymerization. The bulk of the early work was carried out with diphenylketene[215] and Staudinger reported a series of experiments in which this ketene (as the more stable quinoline adduct, see section V.C) was condensed with a variety of carbonyl compounds at 131° and the rate of reaction followed by measurement of carbon dioxide evolution[182,215,203]. Rates of reaction in carbonyl compounds of the type R^1COR^2 (where R^1 = Ph, PhCH=CH or p-$Me_2NC_6H_4$) declined in the order R^2 = PhCH=CH, H, CN, Ph, Me, NMe_2, OMe, Cl. By means of this reaction, a wide variety of diphenylethylene derivatives has been made. Particularly readily formed are derivatives from diphenylketene with benzoyl cyanide, dibenzylidene acetone, cinnamaldehyde and γ-pyrone[187,188] *e.g.*,

$$(PhCH{=}CH)_2CO + Ph_2C{=}C{=}O \longrightarrow (PhCH{=}CH)_2C{=}CPh_2 + CO_2$$

1,4-Quinones react readily with diphenylketene and the mild conditions required make possible the isolation of β-lactones (**104**)[186,201]. Quinone itself, methylquinone, chloroquinone and 2,6-dichloro-1,4-quinone react readily with diphenylketene in the cold; the carbonyl group remote from substituents reacts preferentially and quinones lacking two unsubstituted adjacent positions react slowly or not at all. Reaction with two moles of the ketene presumably gives a bis-β-lactone, but this is unstable and on decarboxylation gives **105**. The action of heat on the monolactone above its melting point results in disproportionation to quinone and **105**; below the melting point, however, the quinonemethane **106** is formed.



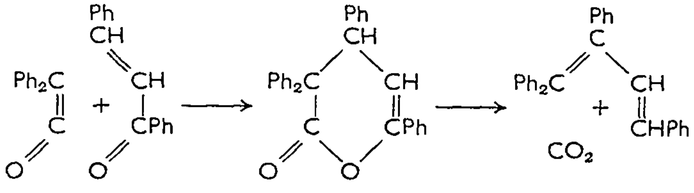
(104)

(105)

(106)

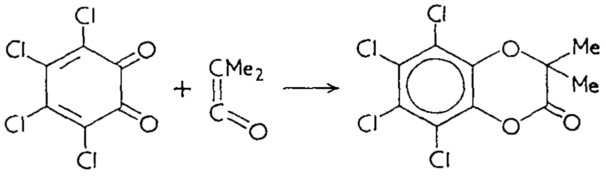
α,β-Unsaturated aromatic ketones react very readily with diphenylketene but the reaction proceeds only partially through the β-lactone to olefin and carbon dioxide. A substantial by-product is the δ-lactone **107** formed by 1,4-addition of the ketene molecule. This reaction proceeds with benzylidene acetophenone and derivatives[158].

The lactones decompose on heating to above 200° giving the same products as obtained on heating the β-lactone that is intermediately formed along with **107.**



(107)

Tetrachloro-1,2-quinone reacts with dimethylketene to give the dioxane derivative **108**[89]. Diphenylketene reacts slowly with phen-



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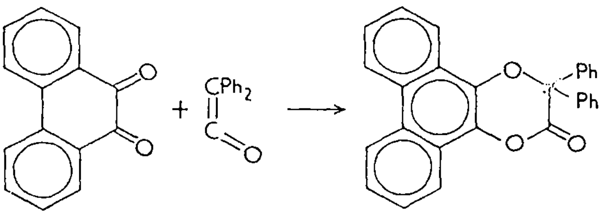
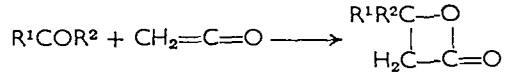


(109)

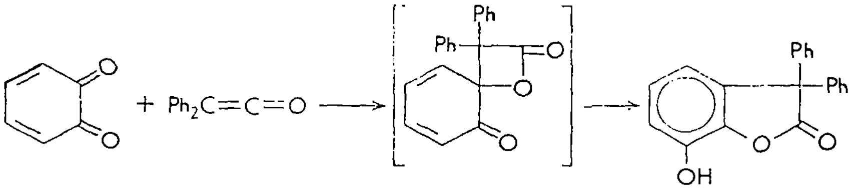
anthraquinone[169] under the influence of sunlight to give a similar compound **109.** With *o*-quinone, however, this ketene reacts[53] in the dark to give the benzofuran derivative **110.** This product might well have arisen from the rearrangement of a β-lactone first formed, since a similar rearrangement to a benzene derivative **111** is reported to occur with the β-lactone derived from diphenylketene and 1,4-quinone[33].

The literature on the reaction of ketene itself with carbonyl compounds to form β-lactones is extensive and of comparatively recent date[70,121,250]. Küng[120] found that, although without catalyst the only observable reaction was the polymerization of the ketene, the reaction of ketenes with aldehydes proceeds smoothly to β-lactones with mild Friedel–Crafts type catalysts in solvents such as ethers or the β-lactone to be formed. With ketones, more powerful catalysts are used without diluents. Temperatures are generally maintained below about 25°[251].



$$R^1COR^2 + CH_2{=}C{=}O \longrightarrow \begin{array}{l} R^1R^2C{-}O \\ \;\;\;| \quad\;\; | \\ H_2C{-}C{=}O \end{array}$$

Ketene may be condensed with keto esters such as pyruvic, levulinic and acetoacetic esters; the products were not in general isolated but were examined by degradative procedures[72]. Diacetyl, acetylacetone and acetonylacetone have been condensed with ketene in the presence of $BF_3 \cdot Et_2O$ to give mono- and di-β-lactones which have been studied by thermal decarboxylation to olefins[70].



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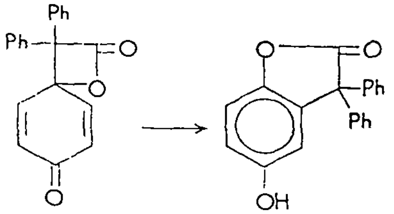
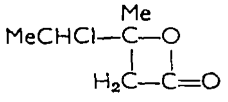


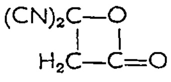
(111)

Cornforth condensed ketene with 3-chlorobutan-2-one and obtained the β-lactone **112** in two stereoisomeric forms[39]. The reaction of ketene with carbonyl cyanide[1] gave the expected product **113**.



$$\begin{array}{r} Me \;\;\;\;\;\; \\ MeCHCl{-}C{-}O \\ |\quad\; | \;\; \\ H_2C{-}C{=}O \end{array}$$

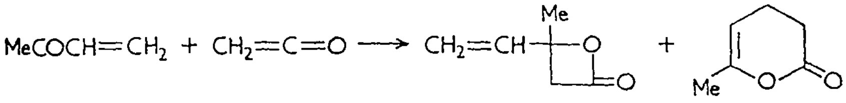
(112)



$$\begin{array}{l} (CN)_2C{-}O \\ \quad\;\;\; | \quad\;\; | \\ \;\; H_2C{-}C{=}O \end{array}$$

(113)

α,β-Unsaturated ketones with an unsubstituted vinyl group, such as methyl vinyl ketone and methyl isopropenyl ketone with ketene in the presence of zinc chloride, give both a β-lactone and a γ,δ-unsaturated δ-lactone; the reaction is indeed analogous to that noted earlier for diphenylketene with α,β-unsaturated ketones[70,71]. Methyl vinyl ketone in the absence of catalyst is reported to react with ketene to give **114** exclusively[88], apparently by a 1,4-addition reaction. Other α,β-unsaturated ketones, however, such as **115** give β,γ-unsaturated lactones **116** with ketene in the presence of $BF_3 \cdot Et_2O$ in high yield[250]. In this case, the first step is probably β-lactone formation followed by ring opening to a diene carboxylic acid and recyclization to **116.**



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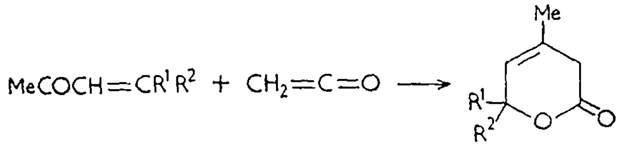


(**115**, $R^1 = R^2 = Me$;
$R^1 = Me, R^2 = H$)

α,β-Unsaturated aldehydes also react with ketene in the presence of catalysts to give mixtures of lactones; crotonaldehyde, for example, gives mainly the β-lactone with some δ-lactone at 0–10°. The condensation of ketene with crotonaldehyde at room temperature in the presence of zinc chloride gives a polymeric hydroxyester which on pyrolysis[70], or treatment with sulfuric acid[24], or with sodium hydroxide[114] gave sorbic acid.

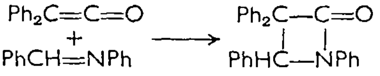
Aromatic aldehydes react with ketene at 0–10° in the presence of boric acid or zinc chloride to give β-lactones which are readily decarboxylated to styrene derivatives[70]. Hurd and Thomas[108] showed that such aldehydes condensed readily with ketene in the presence of potassium acetate to give the mixed anhydride of acetic acid and the α,β-unsaturated acid corresponding to the intermediately formed β-lactone **117.** Similar results were obtained with furfural and cinnamaldehyde[109]. Use of a similar catalyst with acraldehyde at −30° in ether led to 1,3-butadiene-1-carboxylic acid[64].

$$\text{RCHO} + 2\,\text{CH}_2\text{=C=O} \longrightarrow \underset{(\mathbf{117})}{\text{RCH=CHCO}_2\text{COMe}}$$

The extensive chemistry of β-lactones derived from ketene has been reviewed elsewhere[121,250].

C. Reactions with C═N Bonds

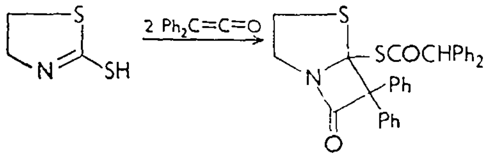
Staudinger in his early investigations showed that diphenylketene and dimethylketene reacted with a wide range of imino compounds, adding across the C=N double bond to give β-lactams. Thus diphenylketene reacts within a few hours at room temperature with benzylidene aniline in light petroleum to give **118** in high yield[182,194,196,215].



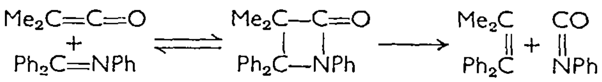
(118)

A wide range of aryl-substituted Schiff's bases has been studied; the rate of addition is increased by phenyl substitution and by conjugation through an olefin group with phenyl as in PhCH=CHCH=NPh. Oxime ethers (*e.g.* PhCH=NOMe) and hydrazones (*e.g.* PhCH=NN(Ph)CH_2Ph), however, do not form adducts with ketenes.

In an extensive reinvestigation of the reaction, Pleger and Jäger[154] showed that, whereas diphenylketene failed to react with $PhCH_2N$=CHPh or isoBuCH=NPh, it reacted readily with a wide variety of amines of the type PhN=CHAr or ArN=CHPh; the rate of addition was hindered by substitution of *o*- , *p*-Cl and *m*- or *p*-NO_2 in either ring of the imine and favoured by substitution with *m*-Cl or *p*-Me_2N. Lewis acid catalysts accelerated the reaction. Similar reactions were observed with phenylketene and ketene but higher reaction temperatures were required (up to 200°). Certain ring compounds containing an imino group were also found to react with diphenylketene, though not with phenylketene or ketene. Thus 2-mercapto-, 2-amino-, and 2-acetamidothiazolidine with diphenylketene gave the expected β-lactams, with concurrent acylation of the mercapto and amino groups in the first two cases, *e.g.*

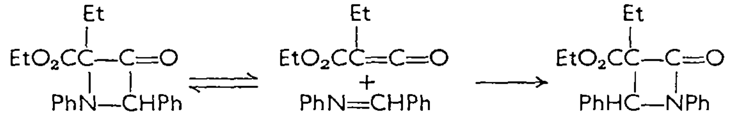


β-Lactams arising from this reaction are often stable compounds and decomposition, which in many cases takes place at only elevated temperatures, can proceed in both possible ways to give, by one, the starting materials and, by the alternative, an olefin and an isocyanate, *e.g.*



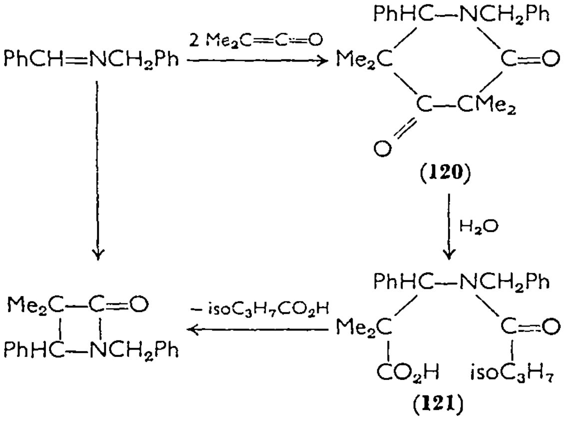
Staudinger pointed out[182] that a substitution on the C=N group which increases the reactivity of the Schiff's base towards ketenes, *e.g.* by Ph, *p*-$Me_2NC_6H_4$, also increases the thermal instability of the β-lactam formed.

Ethyl(carbethoxy)ketene reacts anomalously[182] in that, although a β-lactam is formed at 180° with benzylidene aniline, at −10° another product is formed to which Staudinger ascribed the structure **119** arising from the alternative mode of addition of the starting materials. Compound **119** is thermally unstable and rearranges at 170° to the β-lactam, probably through the starting materials.



(119)

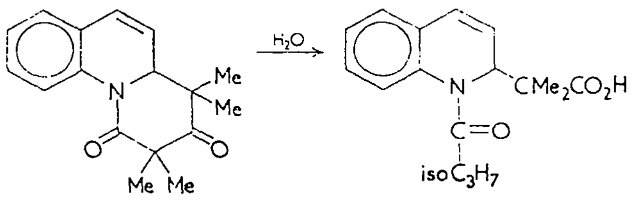
Certain Schiff's bases and aromatic systems containing the grouping C=N—C and not capable of rearranging to enamines give compounds derived from one mole of the base and two of the ketene. Benzylidinebenzylamine with dimethylketene gives, in addition to a small yield of the β-lactam, a diketopiperidine **120** as main product, which as a β-diketone is readily hydrolyzed to the acid amide **121**[214]. The latter on pyrolysis interestingly gives the β-lactam and isobutyric acid.



(120)

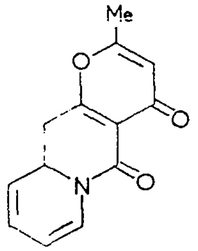
(121)

The diketopiperidine structure is typical also of an interesting group of compounds described by Staudinger as 'ketene bases'. Aliphatic ketoketenes on being allowed to stand with heterocyclic bases such as pyridine, quinoline or acridine, containing the C=N group as part of an aromatic system give thermally stable crystalline derivatives. The dimethylketene–quinoline adduct **122** decomposes only at 250° to give quinoline and the ketene dimer; hydrolysis gives first the acid amide **123** and under more severe conditions, quinoline and isobutyric acid[211,214].



(122) **(123)**

The stability of a ketene base is dependent upon the heterocyclic base employed; that from pyridine and dimethylketene is unstable whereas the base derived from acridine and dimethylketene is very resistant to hydrolysis. The ketene bases derived from diphenylketene and diphenyleneketene[182,196,214], *e.g.* with quinoline, are distinct since, although they are well-defined crystalline materials of quite analogous structure to **122**, they decompose to their constituents at the melting point or even on dissolution in solvents. Molecular-weight determination showed that the diphenylketene–quinoline adduct was completely dissociated in boiling benzene. The crystalline form of



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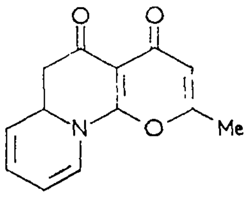
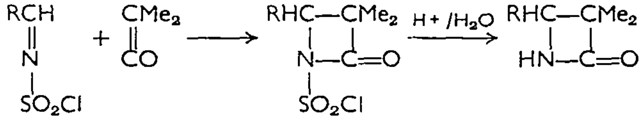


(125)

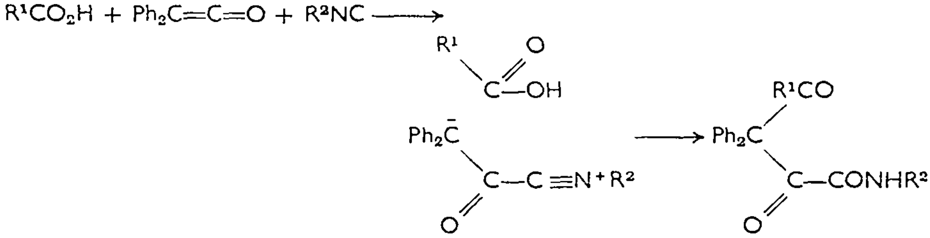
this adduct, however, is stable and not sensitive to the presence of air and moisture. In its reactions at elevated temperatures or in solution with water, alcohols, amines, carbonyl compounds, iminocompounds, oxygen, *etc.*, however, it closely resembles the behavior of the parent ketene. Indeed, despite the limited dissociation of the adduct, certain reactions, such as those with alcohols, proceed more quickly with the adduct than with the free ketene as a result of the catalytic influence of the quinoline liberated. The crystalline adducts of quinoline with diphenylketene and diphenyleneketene represent very useful stable intermediates to be used in place of the oxygen-sensitive free ketenes.

Ketene also reacts with pyridine but the reaction is complex involving the production of tarry products. A yellow compound[246] isolated from the reaction product has been shown to have the structure **124** or **125**[19].

A patent[87] describes the reaction between ketenes, such as dimethylketene, and *N*-alkylidenesulfamyl chlorides; the reaction is of interest as an alternative route to β-lactams bearing no substituent on the nitrogen atom capable of polymerization to polyamides[67].

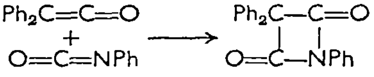


The reaction of diphenylketene with isocyanides and carboxylic acids to α,γ-diketocarbonamides (**126**) is an interesting example of the reaction of a ketene to a carbon–nitrogen unsaturated system[231].



(126)

Staudinger and coworkers (**205**) found that diphenylketene combined with phenyl isocyanate at 220° in a four-center reaction to give the malonimide **127**.

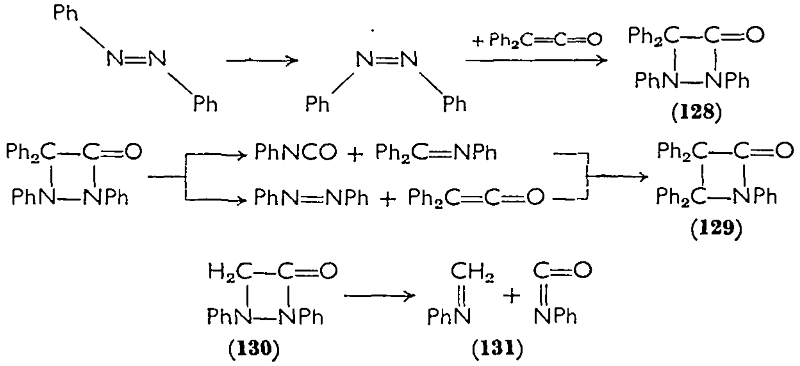


(127)

D. Reactions with Azo Compounds

Staudinger[182] first described the addition of the ketene molecule to an azo linkage. Diphenylketene was found in the earliest work to react with azobenzene at 100° to give the cyclic adduct **128**. In a reinvestigation of the reaction, Cook and Jones[38] showed that, whereas *trans*-azobenzene required heating with diphenylketene at 125–130°

for 42 hours to bring about reaction, the *cis* isomer reacted readily in the cold. Irradiation of the reaction mixture involving the *trans* isomer with light from a mercury lamp induced rapid reaction, and it was concluded that the reaction proceeded through the *cis* form. *o*-, *m*-, and *p*-Azotoluenes reacted similarly[38] but *p*-dimethylaminoazobenzene gave an unstable primary product which decomposed giving a *β*-lactam (see later).

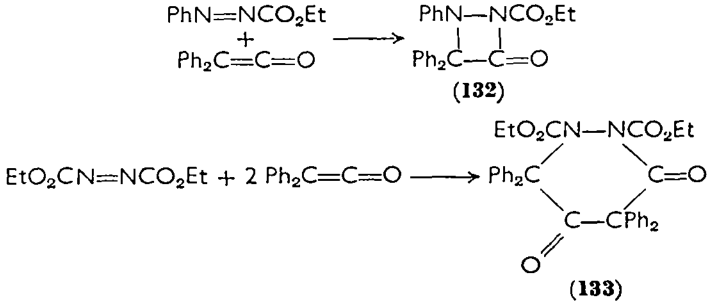

(128)

(129)

(130) **(131)**

The adduct from azobenzene and diphenylketene on pyrolysis gave azobenzene, phenyl isocyanate and the *β*-lactam **129**, the formation of which was ascribed[182] to the combination of diphenylketene and benzophenone anil formed by decomposition according to the two mechanisms shown above. The reaction of ketene with *cis*-azobenzene at 15° with simultaneous irradiation gave the four-membered ring **130**, which in boiling acetone decomposed to phenyl isocyanate and polymers of the Schiff's base (**131**)[167].

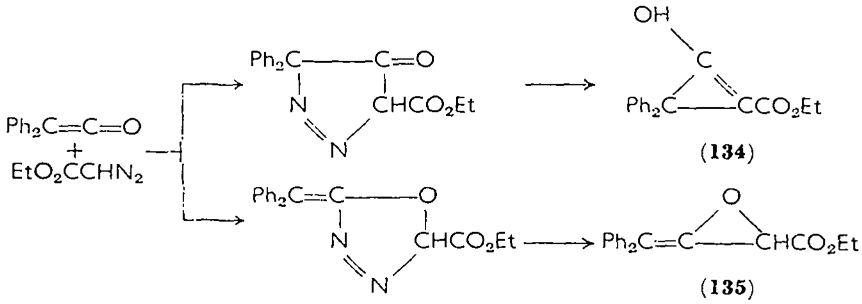
Azo compounds with substituents other than aryl often behave similarly with ketenes. Diphenylketene was shown to react with *cis*- and *trans*-*p*-chlorophenylazocyanide to give a four-membered ring compound[38]. The same ketene reacted with $PhN{=}NCO_2Et$ in the cold to give **132** which showed a marked degree of thermal stability[111].


(132)

(133)

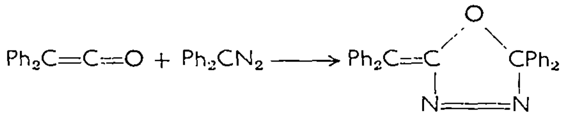
Ethyl azodicarboxylate and diphenylketene, however, gave a compound derived from two moles of the ketene and one of azo compound and formulated by Ingold and Weaver[111] as a hexahydropyrazene derivative **133**. The structure is similar to that of the so-called ketene bases derived from two moles of a ketene and one of a compound with the C=N linkage.

The course of the reaction of ketenes with diazo compounds is more complex. Staudinger and Reber[220] described the formation of two identifiable compounds formulated as a cyclopropanone and an epoxide. The former product (**134**), which showed the properties typical of an enol, was believed to have arisen from this loss of nitrogen of a pyrazolone first formed by addition to the olefin linkage of the ketene. The epoxide (**135**) was held to be formed by the alternative, abnormal addition to the carbonyl group. Reexamination of this reaction would be opportune.



(**134**)

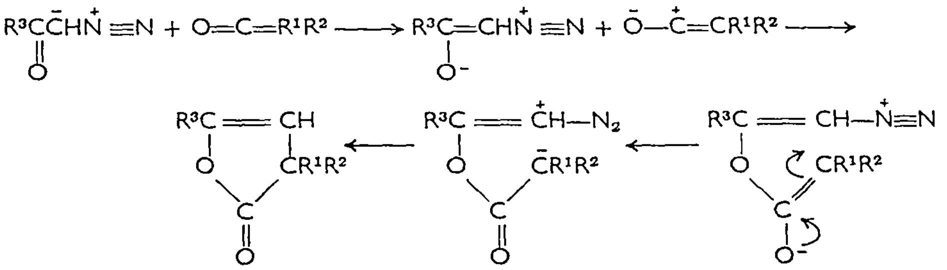
(**135**)



(**136**)

The same authors ascribed the structure **136** to the product of the reaction of diphenylketene and diphenyldiazomethane; **136** evolved nitrogen only on heating to above 150°; diphenylenediazomethane gave a similar product[197,204]. Ketene reacts with diazomethane to give cyclopropanone, which may be isolated as a hydrate in the presence of water or as a hemiacetal with ethanol. Under anhydrous conditions, ring enlargement to give cyclobutanone takes place[115,134,135]. The reaction has been used to prepare labeled cyclobutanone from $^{14}CH_2N_2$[172].

The reaction of ketenes with diazoketones has recently been elucidated[161]. Benzoyldiazomethane reacts with ketene at −60° in xylene and with diphenylketene in ether at room temperature with rapid elimination of nitrogen to give unsaturated γ-lactones of structure **137** ($R^1 = R^2 = H$, $R^3 = Ph$; $R^1 = R^2 = R^3 = Ph$ respectively). A wide range of diazoketones, $R^3 = p\text{-}MeOC_6H_4$, $p\text{-}O_2NC_6H_4$, heptadecyl, 2-furyl, *etc.*, may be successfully used; 2-diazoindanone gives **138** with diphenylketene and the difunctional diazoketone **139** gives a bislactone with ketene. Aliphatic diazoketones react more readily than aryl derivatives and with the latter, the reaction is accelerated by electron releasing substituents, *e.g.* *p*-MeO. The suggested mechanism is illustrated below and represents an instance of addition to the ketene olefinic grouping.



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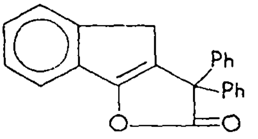

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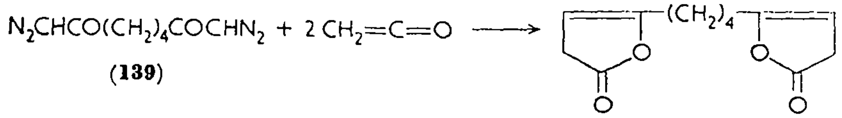
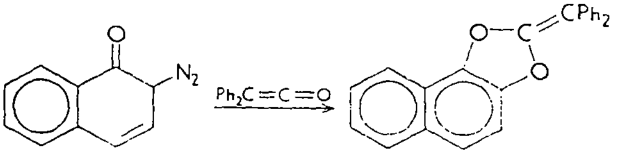


(139)

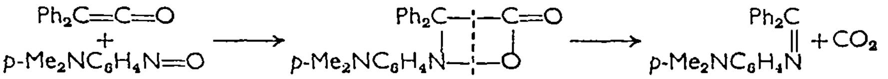
Yates and Robb had earlier found that naphthalene-1,2-diazooxide (**140**) reacted with diphenylketene to give the naphthalene derivative **141**. It may be that in this instance the cyclization of the above intermediate would proceed preferentially to give the more stable naphthalene diether rather than the lactone[249].



(140) **(141)**

E. Reactions with N=O Bonds

The reaction of diphenylketene with *p*-nitroso-*N*,*N'*-dimethylaniline gives the β-lactam **143**. It was asserted by Staudinger that this product arose from the reaction of the two components, which proceeded very rapidly in ether solution, to give first the unstable four-membered heterocyclic compound **142**, decomposition of which gave carbon dioxide and a Schiff's base. Combination of the latter with diphenylketene to give the β-lactam is a known reaction (see section V.C).



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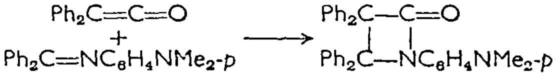
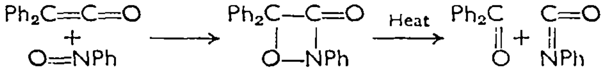


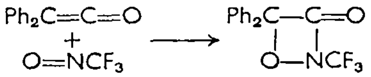
(143)

The reaction of nitrosobenzene with diphenylketene gave only small quantities of benzophenone anil, which, with an excess of the ketene, was converted into the β-lactam **118**. The main product, however, was a crystalline colorless compound which decomposed vigorously on being heated to benzophenone and phenyl isocyanate. The mode of decomposition and independent synthesis led Staudinger to propose the formula **144** for the main reaction product, this being formed by the alternative mode of addition of the N=O group to the olefin linkage in the ketene molecule[209,194]:



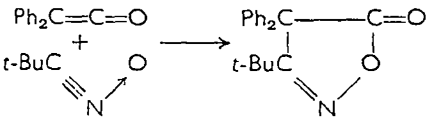
(144)

The above orientation was also observed in the addition of nitrosotrifluoromethane to diphenylketene. The product **145** decomposed at 300° giving, in addition to starting materials, some trifluoromethyl isocyanate[186].



(145)

Little further work has been published on the reaction of ketenes with nitroso compounds. The reaction of diphenylketene with *t*-butyl nitrile oxide, which does not strictly fall under the above heading, may be mentioned as giving the isoxazole derivative **146**[166].

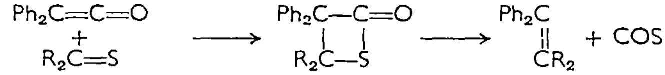


(146)

F. Reactions with C=S Bonds

The action of heat on diphenylketene with carbon disulphide gave large amounts of ketene polymers as well as dimer. Thiobenzophenone and diphenylketene react readily in the cold in dilute solution and afford a crystalline product which undergoes thermal decomposition to the starting materials. The action of aniline gave diphenylacetanilide and $Ph_2C{=}NPh$; Staudinger concluded that the product was not a β-thiolactone but the isomer **147**.

(147)

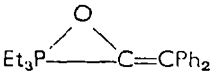


(R = p-$Me_2NC_6H_4$—) **(148)**

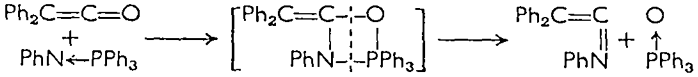
With $(p\text{-}Me_2NC_6H_4)_2CS$, diphenylketene gives the expected decomposition products of the β-thiolactone **148** which, since the reaction proceeds readily in the cold, was inferred to be unstable[193].

G. Reaction with Phosphine Derivatives

Diphenylketene reacts readily with triethylphosphine in ether to give an unstable hygroscopic solid which with water gives triethylphosphine and diphenylacetic acid, and decomposes into the starting materials on being heated[218]. Staudinger formulated the reaction product as:



Ketenes react readily with phosphine imides at low temperatures in inert media. It was claimed that the reaction involves first the formation of a four-ring compound which rapidly decomposes to give a phosphine oxide and a ketene imide[217,206]. Compounds of the latter type, apart from the products derived from ketene itself which polymerize readily, are stable compounds, not affected by water or oxygen.

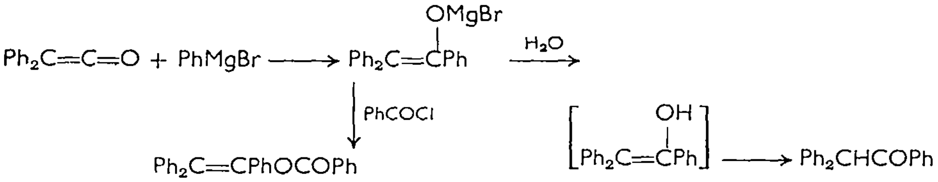


$$\begin{array}{c}Ph_2C{=}C{=}O\\+\\PhN{\leftarrow}PPh_3\end{array} \longrightarrow \left[\begin{array}{c}Ph_2C{=}C-O\\ | \quad\; |\\ PhN-PPh_3\end{array}\right] \longrightarrow \begin{array}{c}Ph_2C{=}C\\ \|\\ PhN\end{array} + \begin{array}{c}O\\ \uparrow\\ PPh_3\end{array}$$

Diphenylketene, dimethylketene, di(ethoxycarbonyl)ketene, and ketene all react with phosphine imides, $R^1N{\leftarrow}PR^2_3$ where R = Me, Et, Ph and R^2 = Et, Ph. It is to be noted that the above suggested mechanism represents an instance of the abnormal addition to the *carbonyl* group of the ketene molecule.

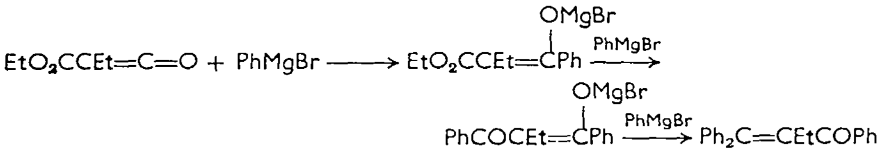
VI. MISCELLANEOUS REACTIONS

Phenylmagnesium bromide reacts readily with diphenylketene to give diphenylacetophenone after hydrolysis of the intermediate[182,185,196]. Staudinger interpreted the reaction as an addition of the Grignard reagent to the olefin bond of the ketene. This, as Gilman and Heckert[66] pointed out, would be an abnormal mode of reaction for the reagent, and these authors found that treatment of the reaction product with benzoyl chloride gave triphenylvinyl benzoate. They concluded that the Grignard reagent had reacted with the carbonyl grouping.



$$\begin{array}{l}Ph_2C{=}C{=}O + PhMgBr \longrightarrow Ph_2C{=}\overset{\overset{\displaystyle OMgBr}{|}}{C}Ph \xrightarrow{H_2O} \left[Ph_2C{=}\overset{\overset{\displaystyle OH}{|}}{C}Ph\right] \longrightarrow Ph_2CHCOPh\\ \qquad\qquad\qquad\qquad\qquad\qquad \big\downarrow PhCOCl\\ \qquad\qquad\qquad\qquad Ph_2C{=}CPhOCOPh\end{array}$$

With ketene itself, ethylmagnesium chloride reacts vigorously to give a 36–37% yield of ethyl methyl ketone; phenylmagnesium bromide gives acetophenone[121]. The work of Hurd and collaborators[103] confirmed that Grignard reagents added to the C=O linkage in ketenes. Phenyl- or ethylmagnesium bromides on addition to ethyl(carbethoxy)-ketene gave the ketones of the general type $RCOCHEtCO_2Et$, but



$$\begin{array}{l}EtO_2CCEt{=}C{=}O + PhMgBr \longrightarrow EtO_2CCEt{=}\overset{\overset{\displaystyle OMgBr}{|}}{C}Ph \xrightarrow{PhMgBr}\\ \qquad\qquad PhCOCEt{=}\overset{\overset{\displaystyle OMgBr}{|}}{C}Ph \xrightarrow{PhMgBr} Ph_2C{=}CEtCOPh\end{array}$$

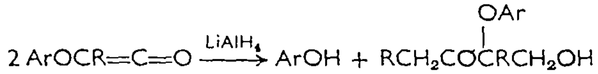
(32)

addition of the ketene to an excess of phenylmagnesium bromide gave **32** as the result of addition of three moles of Grignard reagent.

Diarylketenes bearing heavy substitution, such as (3-bromomesityl)-phenylketene, dimesitylketene *etc.*, reacted with Grignard reagents such as *t*-butyl- and cyclohexylmagnesium chloride, but the ketenes were simply reduced to vinyl alcohols of the general class $R^1R^2C{=}CHOH$[63].

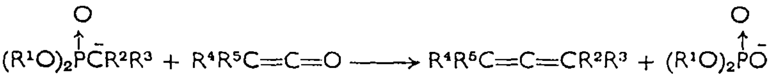
Ketene with diethylzinc gave ethyl methyl ketone. Phenylketene combined in boiling toluene with diphenylmethylpotassium to give a 15% yield of 1,1,3,3-tetraphenylacetone[43].

The reduction of diphenylketene with lithium aluminum hydride in ether gave diphenylacetaldehyde. Since treatment of the intermediate organometallic compound with acetyl chloride gave the enol acetate, it was concluded that the reagent attacks the carbonyl group[138]. The reduction of ketenes of the type $ArOCR{=}C{=}O$, where $Ar = p\text{-}t\text{-}BuC_6H_4$, R = Et, Pr, *etc.*, with lithium aluminum hydride was abnormal and proceeded with elimination of ArOH as shown below[86]. Such ketenes and their dimers also behave abnormally on catalytic hydrogenation[84].



$$2\,ArOCR{=}C{=}O \xrightarrow{LiAlH_4} ArOH + RCH_2CO\overset{OAr}{\overset{|}{C}}RCH_2OH$$

Ketenes react readily with phosphonate anions to give allenes[234]. This reaction would appear worth further examination as a general synthesis of possibly wide application; it represents an unusual instance of a reaction involving only the ketene carbonyl grouping

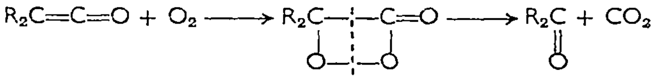


$$(R^1O)_2\overset{O}{\overset{\uparrow}{P}}\bar{C}R^2R^3 + R^4R^5C{=}C{=}O \longrightarrow R^4R^5C{=}C{=}CR^2R^3 + (R^1O)_2\overset{O}{\overset{\uparrow}{P}}\bar{O}$$

VII. OXIDATION OF KETENES

One of the clearest distinctions between aldoketenes and ketoketenes pointed out by Staudinger is the high reactivity of the latter class with oxygen; aldoketenes in contrast are quite stable to oxygen under mild conditions and a study under more vigorous conditions would be complicated by the rapid polymerization of these compounds. Very little work has been reported on the subject of ketene oxidation since the early work by Staudinger[182,202,210]. Since this predates modern work on autoxidation and the development of the free-radical chain mechanism, it would appear opportune to reexamine this topic.

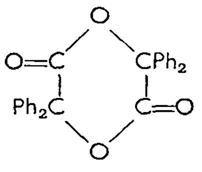
The primary oxidation products derived from the aliphatic ketoketenes are white amorphous powders which decompose with violence in the dry state. The oxidation of dimethyl- and diethylketenes proceeds rapidly in ether solution at −20° to give a suspension of the 'moloxide'—as Staudinger described these materials—represented as **149**. Moloxides liberate iodine from potassium iodide solution and decompose smoothly in ether suspension at room temperature to carbon dioxide and the respective ketone.



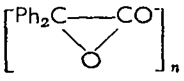
(149)

The oxidation of ketoketenes at room temperature, therefore, gives carbon dioxide and a ketone directly. It was found by Staudinger, however, that, whereas dimethylketene gave a high yield of ketone plus carbon dioxide under these conditions, the extent of moloxide formation fell progressively through diethylketene and phenylmethylketene to diphenylketene with which only 15% of moloxide, as indicated by decomposition products, was observed. With the decrease in oxidation to the moloxide, there was observed an increased formation of a class of compound derived from one mole of ketene with a single atom of oxygen, termed a 'ketene oxide' by Staudinger. The oxidation of diphenylketene is very rapid; the compound is reported to be as sensitive to oxygen as triphenylmethyl. Even at −80°, however, no material of the moloxide type could be isolated and only the formation of some benzophenone and carbon dioxide showed that this compound may be formed to a small extent; the ketene oxide was the main product. On the other hand, no ketene oxide was isolated from the oxidation of dimethylketene; small amounts were obtained from diethylketene and rather more from phenylmethylketene.

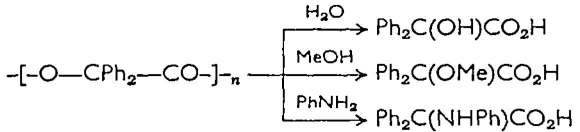
The so-called ketene oxides derived from diphenylketene are mixtures of varying molecular weight, in addition to various amorphous materials some **150** has been isolated. The compounds may be empirically regarded as **151** and probably have the general structure **152** as polyesters. The lower molecular weight fractions are more reactive than the higher melting, higher molecular weight fractions but hydrolysis in all cases leads to benzilic acid; the reaction of methanol and aniline gives methoxy- and *N*-phenylaminodiphenylacetic acid respectively. Evidently in these cases heterolysis occurs by alkyl oxygen fission rather than by the more commonly encountered acyl oxygen fission which would give rise to the methyl ester and anilide of benzilic acid. The Ph_2C group adjacent to the oxygen atom would, however, be expected to promote unimolecular alkyl oxygen heterolysis[116].



(150)

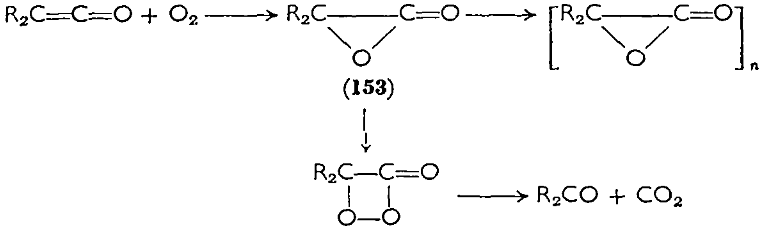


(151)



(152)

Staudinger believed that the first step in the oxidation of ketenes was the formation of an asymmetrical oxygen–ketene adduct, formulated as **153**. This material was supposed to be very unstable and decomposed by either of the two routes shown below to give the moloxide to which a four-membered ring structure was assigned, largely on the basis of the observed decomposition reaction, or the ketene oxide with the loss of an atom of oxygen.



(153)

Ketoketenes containing the ethoxycarbonyl group, *e.g.* $EtC(CO_2Et){=}C{=}O$, $C(CO_2Et)_2{=}C{=}O$, $PhC(CO_2Et){=}C{=}O$, exhibit behavior quite different from that of the simpler ketoketenes. They are substantially colorless and are unattacked by oxygen although they undergo addition and polymerization reactions rapidly[208].

VIII. REFERENCES

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