Supplement A The Chemistry of Double-Bonded Functional Groups
Edited by Saul Patai
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Supplement A
The chemistry of double-bonded functional groups
Part 2

Edited by

SAUL PATAI

The Hebrew University, Jerusalem

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To
my grand-daughter **Tal** and the
double-bond between us

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Foreword

Most of the originally planned volumes of the series *The Chemistry of the Functional Groups* have appeared already or are in the press. The first two books of the series, *The Chemistry of Alkenes* (1964) and *The Chemistry of the Carbonyl Group* (1966) each had a second volume published in 1970, with chapters not included in the plans of the original volumes and others which were planned but failed to materialize.

This book is the first of a set of supplementary volumes which should include material on more than a single functional group. For these volumes a division into five categories is envisaged, and supplementary volumes in each of these categories will be published as the need arises. These volumes should include 'missing chapters' as well as chapters which give a unified and comparative treatment of several related functional groups together.

The planned division is as follows:

Supplement A: The Chemistry of Double-Bonded Functional Groups ($C{=}C$; $C{=}O$; $C{=}N$; $N{=}N$ etc.).
Supplement B: The Chemistry of Acid Derivatives ($COOH$; $COOR$; $CONH_2$ etc.).
Supplement C: The Chemistry of Triple-Bonded Functional Groups ($C\equiv C$; $C\equiv N$; $-\overset{+}{N}\equiv N$ etc.).
Supplement D: The Chemistry of Halides and Pseudohalides ($-F$; $-Cl$; $-Br$; $-I$; $-N_3$; $-OCN$; $-NCO$ etc.).
Supplement E: Will include material on groups which do not fit any of the previous four categories ($-NH_2$; $-OH$; $-SH$; $-NO_2$ etc.).

In the present volume, as usual, the authors have been asked to write chapters in the nature of essay-reviews not necessarily giving extensive or encyclopaedic coverage of the material. Once more, not all planned chapters materialized, but we hope that additional volumes of Supplement A will appear, when these gaps can be filled together with coverage of new developments in the various fields treated.

Jerusalem, March 1976 SAUL PATAI

The Chemistry of Functional Groups
Preface to the series

The series 'The Chemistry of Functional Groups' is planned to cover in each volume all aspects of the chemistry of one of the important functional groups in organic chemistry. The emphasis is laid on the functional group treated and on the effects which it exerts on the chemical and physical properties, primarily in the immediate vicinity of the group in question, and secondarily on the behaviour of the whole molecule. For instance, the volume *The Chemistry of the Ether Linkage* deals with reactions in which the C—O—C group is involved, as well as with the effects of the C—O—C group on the reactions of alkyl or aryl groups connected to the ether oxygen. It is the purpose of the volume to give a complete coverage of all properties and reactions of ethers in as far as these depend on the presence of the ether group but the primary subject matter is not the whole molecule, but the C—O—C functional group.

A further restriction in the treatment of the various functional groups in these volumes is that material included in easily and generally available secondary or tertiary sources, such as Chemical Reviews, Quarterly Reviews, Organic Reactions, various 'Advances' and 'Progress' series as well as textbooks (i.e. in books which are usually found in the chemical libraries of universities and research institutes) should not, as a rule, be repeated in detail, unless it is necessary for the balanced treatment of the subject. Therefore each of the authors is asked *not* to give an encyclopaedic coverage of his subject, but to concentrate on the most important recent developments and mainly on material that has not been adequately covered by reviews or other secondary sources by the time of writing of the chapter, and to address himself to a reader who is assumed to be at a fairly advanced post-graduate level.

With these restrictions, it is realized that no plan can be devised for a volume that would give a *complete* coverage of the subject with *no* overlap between chapters, while at the same time preserving the readability of the text. The Editor set himself the goal of attaining *reasonable* coverage with *moderate* overlap, with a minimum of cross-references between the chapters of each volume. In this manner, sufficient freedom is given to each author to produce readable quasi-monographic chapters.

The general plan of each volume includes the following main sections:

(a) An introductory chapter dealing with the general and theoretical aspects of the group.

(b) One or more chapters dealing with the formation of the functional group in question, either from groups present in the molecule, or by introducing the new group directly or indirectly.

(c) Chapters describing the characterization and characteristics of the functional groups, i.e. a chapter dealing with qualitative and quantitative methods of determination including chemical and physical methods, ultraviolet, infrared, nuclear magnetic resonance and mass spectra: a chapter dealing with activating and directive effects exerted by the group and/or a chapter on the basicity, acidity or complex-forming ability of the group (if applicable).

(d) Chapters on the reactions, transformations and rearrangements which the functional group can undergo, either alone or in conjunction with other reagents.

(e) Special topics which do not fit any of the above sections, such as photochemistry, radiation chemistry, biochemical formations and reactions. Depending on the nature of each functional group treated, these special topics may include short monographs on related functional groups on which no separate volume is planned (e.g. a chapter on 'Thioketones' is included in the volume *The Chemistry of the Carbonyl Group*, and a chapter on 'Ketenes' is included in the volume *The Chemistry of Alkenes*). In other cases, certain compounds, though containing only the functional group of the title, may have special features so as to be best treated in a separate chapter, as e.g. 'Polyethers' in *The Chemistry of the Ether Linkage*, or 'Tetraaminoethylenes' in *The Chemistry of the Amino Group*.

This plan entails that the breadth, depth and thought-provoking nature of each chapter will differ with the views and inclinations of the author and the presentation will necessarily be somewhat uneven. Moreover, a serious problem is caused by authors who deliver their manuscript late or not at all. In order to overcome this problem at least to some extent, it was decided to publish certain volumes in several parts, without giving consideration to the originally planned logical order of the chapters. If after the appearance of the originally planned parts of a volume it is found that either owing to non-delivery of chapters, or to new developments in the subject, sufficient material has accumulated for publication of a supplementary volume, containing material on related functional groups, this will be done as soon as possible.

The overall plan of the volumes in the series 'The Chemistry of Functional Groups' includes the titles listed below:

The Chemistry of Alkenes (published in two volumes)
The Chemistry of the Carbonyl Group (published in two volumes)
The Chemistry of the Ether Linkage (published)
The Chemistry of the Amino Group (published)
The Chemistry of the Nitro and the Nitroso Group (published in two parts)
The Chemistry of Carboxylic Acids and Esters (published)
The Chemistry of the Carbon–Nitrogen Double Bond (published)
The Chemistry of the Cyano Group (published)
The Chemistry of Amides (published)
The Chemistry of the Hydroxyl Group (published in two parts)
The Chemistry of the Azido Group (published)
The Chemistry of Acyl Halides (published)
The Chemistry of the Carbon–Halogen Bond (published in two parts)
The Chemistry of the Quinonoid Compounds (published in two parts)
The Chemistry of the Thiol Group (published in two parts)
The Chemistry of the Carbon–Carbon Triple Bond (in preparation)
The Chemistry of Amidines and Imidates (published)
The Chemistry of the Hydrazo, Azo and Azoxy Groups (published)
The Chemistry of the Cyanates and their Thio-derivatives (in press)
The Chemistry of the Diazonium and Diazo Groups (in press)
The Chemistry of Cumulenes and Heterocumulenes
Supplement A: The Chemistry of Double-Bonded Functional Groups (published in two parts)
Supplement B: The Chemistry of Acid Derivatives (in preparation)
Supplement C: The Chemistry of Triple-Bonded Functional Groups
Supplement D: The Chemistry of Halides and Pseudo-halides
Supplement E: Other Functional Groups

Advice or criticism regarding the plan and execution of this series will be welcomed by the Editor.

The publication of this series would never have started, let alone continued, without the support of many persons. First and foremost among these is Dr. Arnold Weissberger, whose reassurance and trust encouraged me to tackle this task, and who continues to help and advise me. The efficient and patient cooperation of several staff-members of the Publisher also rendered me invaluable aid (but unfortunately their code of ethics does not allow me to thank them by name). Many of my friends and colleagues in Israel and overseas helped me in the solution of various major and minor matters, and my thanks are due to all of them, especially to Professor Z. Rappoport. Carrying out such a long-range project would be quite impossible without the non-professional but none the less essential participation and partnership of my wife.

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Jerusalem, ISRAEL

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CHAPTER 8

The formation of unsaturated groups by heterolytic fragmentation

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I. INTRODUCTION

Many important methods for the formation of double-bonded functions, such as C=C, C=N and C=O, consist in the removal of hydrogen and an atom or group X from adjacent atoms c and d. The letters c and d symbolize atoms which are able to form double bonds, such as carbon, nitrogen and oxygen[†].

$$\mathrm{B}\!: + \mathrm{H{-}c{-}d{-}X} \longrightarrow \mathrm{BH} + \mathrm{c{=}d} + \mathrm{X}\!: \qquad (1)$$

In the heterolytic variant of this 1,2- or β-elimination reaction[1], a proton is transferred to a base, i.e. hydrogen is removed as an electrofuge[2], since it leaves without the electron pair by which it was bonded to c. On the other hand, X leaves the atom d with the bonding electron pair, i.e. as a nucleofuge[2] (equation 1). Common nucleofugal atoms and groups are halogen (Cl, Br, I), sulphonate ($\mathrm{RSO_3^-}$), the diazonio ($-\overset{+}{\mathrm{N}}{\equiv}\mathrm{N}$), the oxonio ($-\overset{+}{\mathrm{O}}\mathrm{R_2}$), the ammonio ($-\overset{+}{\mathrm{N}}\mathrm{R_3}$) and the sulphonio ($-\overset{+}{\mathrm{S}}\mathrm{R_2}$) groups (Table 1a).

Frequently, the electrofuge is not a single atom, such as hydrogen, but a group of at least two atoms. Since the reacting molecule breaks into three fragments, the process is called a fragmentation reaction[3] (equation 2).

$$\mathrm{a{-}b}\,\vdots\!\mathrm{{-}c{-}d}\,\vdots\!\mathrm{{-}X} \longrightarrow \mathrm{a{-}b} + \mathrm{c{=}d} + \mathrm{X}\!: \qquad (2)$$

Electrofugal groups, designated by the symbols a—b (Table 1b) are readily split off, especially in protic solvents, because they furnish relatively stable cations or neutral molecules. This species will be referred to as the electrofugal fragment. Furthermore, the double-bonded species c=d derived from the middle group —c—d— will be called the unsaturated fragment. Common middle groups and unsaturated fragments are listed in Table 1c. As will be noted, the atomic sequence in the middle groups N—C, N=C and O—C can be reversed to C—N, C=N and C—O depending upon whether the electrofuge is attached to the heteroatom or to carbon.

TABLE 1. $\mathrm{a{-}b{-}c{-}d{-}X} \longrightarrow \mathrm{a{-}b} + \mathrm{c{=}d} + \mathrm{X}$.

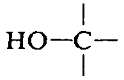
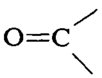
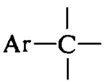
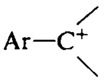
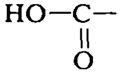
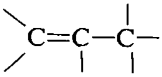
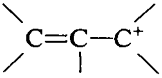
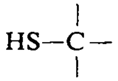
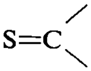
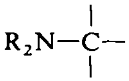
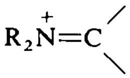
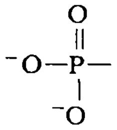
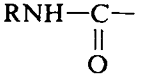
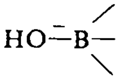
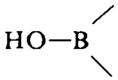
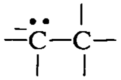
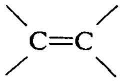
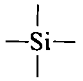
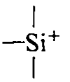
(a) Common nucleofugal groups —X and fragments X:

—X ⟶	X:	—X ⟶	X:
—Cl	$\mathrm{Cl^-}$	$\mathrm{-OH_2^+}$	$\mathrm{H_2O}$
—Br	$\mathrm{Br^-}$	$\mathrm{-NR_3^+}$	$\mathrm{NR_3}$
—I	$\mathrm{I^-}$	$\mathrm{-SR_2^+}$	$\mathrm{SR_2}$
$\mathrm{-OSO_2Ar}$	$\mathrm{^-OSO_2Ar}$	$\mathrm{-N{\equiv}N^+}$	$\mathrm{N_2}$
—OCOR	$\mathrm{^-OCOR}$		

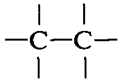
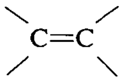
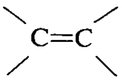
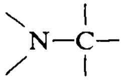
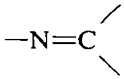
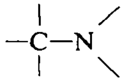
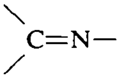
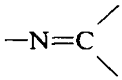
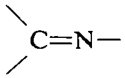
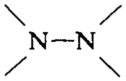
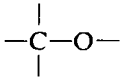
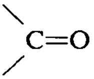
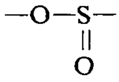
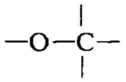
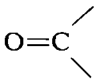
[†] In this volume double-bonded groups are symbolized as X=Y. In this chapter, the letter X will denote the (nucleofugal) leaving group, in keeping with common usage.

TABLE 1 (*continued*)

(b) Common electrofugal groups a—b— and fragments a—b

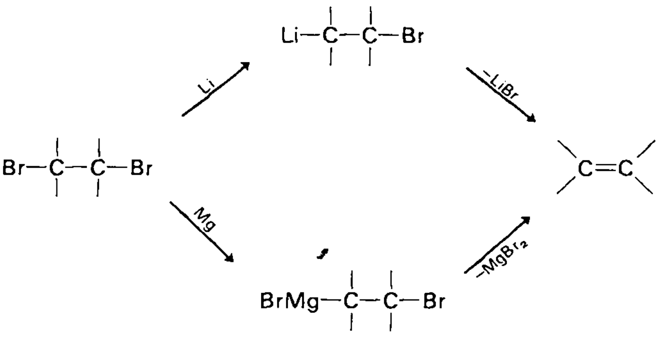
a—b—	$\longrightarrow$ a—b	a—b—	$\longrightarrow$ a—b
 $HO-\overset{\mid}{\underset{\mid}{C}}-$		 $Ar-\overset{\mid}{\underset{\mid}{C}}-$	
 $HO-\underset{\underset{O}{\Vert}}{C}-$	$O=C=O$		
 $HS-\overset{\mid}{\underset{\mid}{C}}-$		H_2N-NH-	$HN=N$
 $R_2N-\overset{\mid}{\underset{\mid}{C}}-$		 $^-O-\overset{\overset{O}{\Vert}}{\underset{\underset{^-O}{\mid}}{P}}-$	$^-OPO_2$
 $RNH-\underset{\underset{O}{\Vert}}{C}-$	$RN=C=O$		
		 $-\overset{\mid}{\underset{\mid}{Si}}-$	 $-\overset{\mid}{\underset{\mid}{Si}}{}^+$

(c) Common middle groups —c—d— and unsaturated fragments c=d

—c—d—	$\longrightarrow$ c=d	—c—d—	$\longrightarrow$ c=d
 $-\overset{\mid}{\underset{\mid}{C}}-\overset{\mid}{\underset{\mid}{C}}-$			$-C\equiv C-$
			
	$N\equiv C-$		$-C\equiv N$
	$-N=N-$	 $-\overset{\mid}{\underset{\mid}{C}}-O-$	
$-N=N-$	N_2	 $-O-\underset{\underset{O}{\Vert}}{S}-$	SO_2
 $-O-\overset{\mid}{\underset{\mid}{C}}-$			

A large number of potentially fragmentable systems a—b—c—d—X are obtained by combination of the electrofugal, middle and nucleofugal groups in Table 1. Some combinations lead to unstable and therefore non-existent molecules. Many others represent well-known types of compounds and new ones are constantly being reported in the literature. The need for a logical system of classification is therefore obvious. The one originally proposed[3c] is based primarily on the nature of the unsaturated fragment c=d, the electrofugal and nucleofugal fragments ranking second and third, respectively.

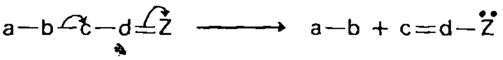
In certain cases this system of classification is somewhat arbitrary. Thus, the formation of an olefin by the reaction of a 1,2-dibromide with lithium (equation 3) can be described as a 1,2-elimination since the electrofuge is a single atom. In the corresponding reaction with magnesium (equation 4) a two-atom fragment, namely $BrMg^+$, is split off. This reaction could therefore be classified as an olefin-forming fragmentation. In this chapter reactions involving organometallic electrofugal fragments are not included.



(3)

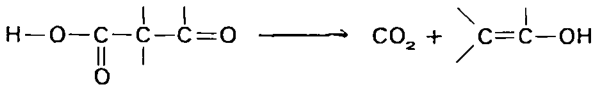
(4)

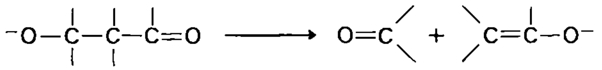
In many cases an electron acceptor, Z, is connected to the atom d by a double bond (equation 5). Despite their resemblance to heterolytic fragmentation, these reactions should not be considered as such.

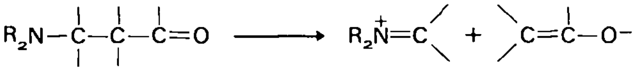


$$\text{a—b—c—d=Z} \longrightarrow \text{a—b} + \text{c=d—}\ddot{\text{Z}} \qquad (5)$$

They lead to two fragments rather than three and are better described as eliminations involving a mesomeric nucleofuge. Well known examples are the decarboxylation of a β-keto acid (equation 6), and the retro-aldol (equation 7), retro-Mannich (equation 8), retro-Claisen (equation 9) and retro-Michael reactions (equation 10). In these cases an enol or a mesomeric enolate ion is liberated as a nucleofuge.


(6)


(7)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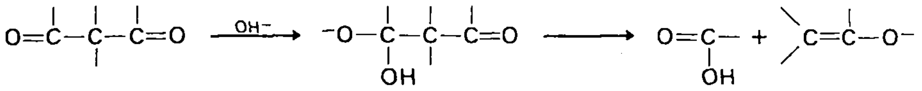
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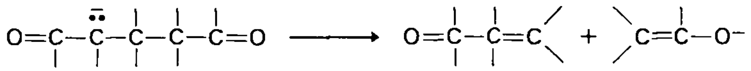
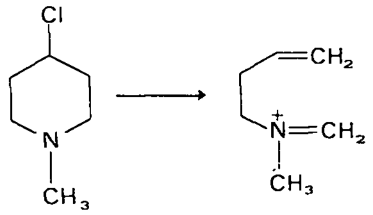
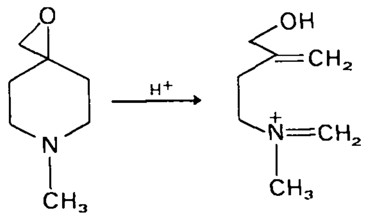

(10)

There are also apparent exceptions to the rule that a reaction must lead to three separate fragments (a—b, c=d and X) in order to qualify as a heterolytic fragmentation. This is the case when two or all three potential fragments are ring members in cyclic reactants as in equations (11) and (12). Nevertheless, these reactions are easily recognized as fragmentations.


(11)


(12)

A few reactions are known which show the characteristic features of heterolytic fragmentation, but which lead to four fragments, as shown in equation (13).

$$\text{a—b—c—d—e—f—X} \longrightarrow \text{a—b} + \text{c}{=}\text{d} + \text{e}{=}\text{f} + \text{X}{:} \qquad (13)$$

Furthermore, the atomic centres d and e can be double-bonded as in equation (14). In this case fragmentation gives rise to three fragments, an electrofugal, a nucleofugal and a doubly unsaturated fragment. Such cases are clearly vinylogues of normal a—b—c—d—X.

$$\text{a—b—c—d}{=}\text{e—f—X} \longrightarrow \text{a—b} + \text{c}{=}\text{d—e}{=}\text{f} + \text{X}{:} \qquad (14)$$

The analogy between fragmentation and 1,2-elimination has already been stressed. Thus, the counterpart of base-induced or bimolecular (E2) elimination (equation 15) is nucleophile-induced fragmentation (equation 16). This involves a nucleophilic displacement on the atom b (other than hydrogen) by the nucleophile Y:, resulting in the liberation of an unsaturated and a nucleofugal fragment.

$$\text{B}{:}\!\curvearrowright\!\text{H—c—d—X} \longrightarrow \text{BH}^{+} + \text{c}{=}\text{d} + \text{X}{:} \qquad (15)$$

$$\text{Y}{:}\!\curvearrowright\!\text{b—c—d—X} \longrightarrow \text{Y—b} + \text{c}{=}\text{d} + \text{X}{:} \qquad (16)$$

Furthermore, the counterpart of α-elimination, which involves the removal of hydrogen and a nucleofuge from the same atom (equation 17), is α-fragmentation shown in equation (18).

$$\text{H—c—X} \xrightarrow{:\text{B}} \text{BH}^{+} + {:}\text{c} + \text{X}{:} \qquad (17)$$

$$\text{a—b—c—X} \longrightarrow \text{a—b} + {:}\text{c} + \text{X}{:} \qquad (18)$$

Since the valency of the atom c is decreased by two, these reactions are only observed when the lower valency state has a certain stability, as with carbon in carbon monoxide or in isocyanides. Equations (16) and (18) will be dealt with in Sections III.H and III.I, respectively.

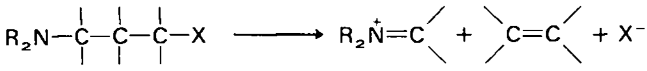
The analogy between fragmentation and 1,2-elimination persists in the area of mechanism since both can occur by three basic mechanisms. These differ with respect to the order in which the fragments are released. Thus, a one-step and two two-step mechanisms can be distinguished depending on whether the electrofuge a—b and the nucleofuge X are released simultaneously from c—d or whether either a—b or X departs ahead of the other. However, mechanism is not an appropriate criterion for the classification of the large variety of fragmentation reactions. Nevertheless, an understanding of mechanism and its stereochemical implications is indispensable for the interpretation of a vast amount of data, as will be discussed in Section II.

Finally, molecular fragmentation resulting from electron impact, as detected by mass spectroscopy, and homolytic fragmentation will not be discussed here since different principles are involved. However, it seems appropriate to point out that the term fragmentation[3a] was introduced as a distinctive name for the class of reactions described in this chapter before the advent of popular mass spectroscopy. Unfortunately, the term is also used rather indiscriminately in other contexts.

II. MECHANISM AND STEREOCHEMISTRY

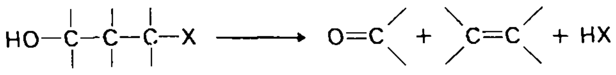
A. Reaction Paths

Of the numerous fragmentations known (a selection is given in Section III), only a few have so far been subjected to detailed mechanistic and stereochemical scrutiny. Among the latter are γ-amino halides and sulphonates (**1**, X = halogen, $-OSO_2R$)[4], γ-hydroxy halides (**2**) and γ-mercapto halides (**3**).



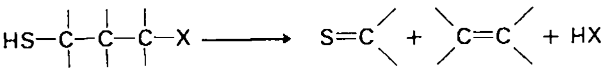
$$R_2N{-}C{-}C{-}C{-}X \longrightarrow R_2\overset{+}{N}{=}C\langle \; + \; \rangle C{=}C\langle \; + \; X^-$$

(1)



$$HO{-}C{-}C{-}C{-}X \longrightarrow O{=}C\langle \; + \; \rangle C{=}C\langle \; + \; HX$$

(2)



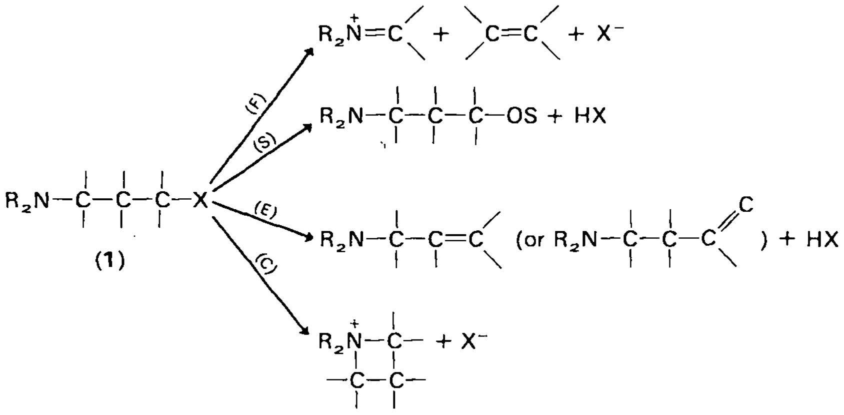
$$HS{-}C{-}C{-}C{-}X \longrightarrow S{=}C\langle \; + \; \rangle C{=}C\langle \; + \; HX$$

(3)

These three types of compounds can undergo olefin-forming fragmentation with release of an electrofugal fragment, namely an immonium ion, a carbonyl and a thione derivative, respectively. The fragmentable chain of atoms may be incorporated in more or less rigid cyclic structures, thus allowing stereochemical and stereoelectronic factors to be studied.

With the proper choice of the nucleofuge X the reactivity under solvolytic conditions, e.g. in 80 vol.-% ethanol, is such that rates can be measured easily, thus facilitating mechanistic investigations.

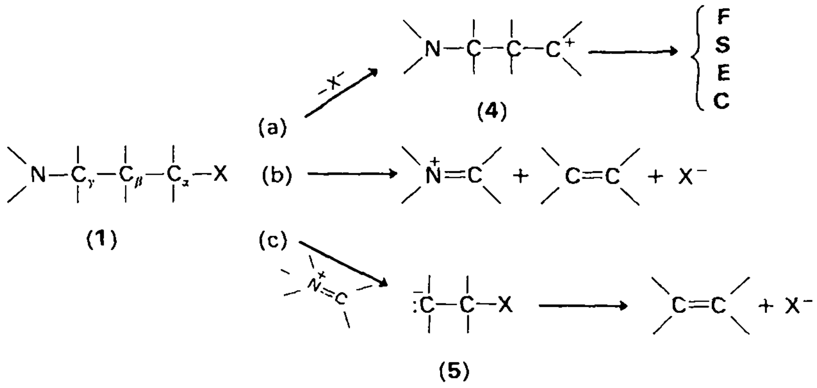
It is opportune to point out that fragmentation is frequently not the only possible reaction path. Given the right structure, configuration and reaction conditions, compounds of the type **1**, **2**, and **3** may undergo nucleophilic substitution, β-elimination or cyclization in addition to, or instead of, fragmentation. Fragmentation is thus intimately connected with other well known nucleophilic reactions. For γ-amino halides in a protic solvent SOH the reactions in Scheme 1 may be envisaged. Fragmentation (F) leads to an immonium ion which is rapidly hydrolysed in aqueous solvents, yielding an amine and a carbonyl compound. Substitution (S) by solvent may be of the S_N1 or S_N2 type depending on the degree of substitution at C_α. Elimination (E) can occur by mechanism E 1 or E 2 and lead to isomeric olefins. Cyclization (C) furnishes an azetidinium ion and will be favoured when C_α is primary or secondary. It is noteworthy that electronic and steric factors may affect the relative rates of these competing reactions in different ways.



SCHEME 1.

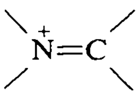
B. The Basic Mechanisms

Although the structural and electronic requirements and the number of bonds broken are the same for all fragmentations, the sequence of bond rupture may be different. Thus the electrofugal and nucleofugal fragments a—b and X may be released simultaneously or successively from —c—d—. For γ-amino halides (**1**) three mechanisms must therefore be considered, i.e. the two-step processes (a) and (c) and the one-step process (b) (Scheme 2), all of which follow the first-order rate law. This also applies to γ-hydroxy and γ-mercapto derivatives (**2** and **3**). Strong bases will, however, convert the latter into their conjugate bases, the overall rate then becoming second-order.



SCHEME 2.

The two-step mechanism of fragmentation of N—C—C—C—X (path a) is initiated by the rate determining loss of the nucleofuge which converts **1** to a γ-amino carbonium ion (**4**). The latter may then undergo cleavage of the $C_\beta—C_\gamma$ bond to form an immonium ion and an olefin, thus completing fragmentation (F). The cationic intermediate **4** may, however, react with a nucleophilic solvent (S), eject a proton (E), or undergo ring closure (C). In the two-step mechanism (a) the amino group is not directly involved in the ionization step. The carbonium ion (**4**) is therefore formed at a 'normal rate', modified only by the inductive effect of the nitrogen atom. Substituents on C_α, which stabilize carbonium ions, will favour this mechanism.

In the one-step or concerted process (b) the electrofugal fragment  $>\overset{+}{N}=C<$ and the nucleofugal fragment X^- leave simultaneously, i.e. in the same transition state. Since ionization is assisted by electron release from the nitrogen atom the concerted mechanism should lead to an increased reaction rate, as compared to the rate of the two-step carbonium ion mechanism (a).

The third mechanism (c) involves a rate-determining ionization yielding the electrofugal immonium ion and a carbanion (**5**). Electron-withdrawing substituents at C_β will therefore favour this process. The carbanion will either eject the nucleofuge X and complete the fragmentation, or accept a proton from the medium. The latter reaction represents a retro-Mannich reaction rather than a fragmentation. The two-step mechanism (a) and the concerted mechanism (b) are frequently observed; mechanism (c), however, is rare.

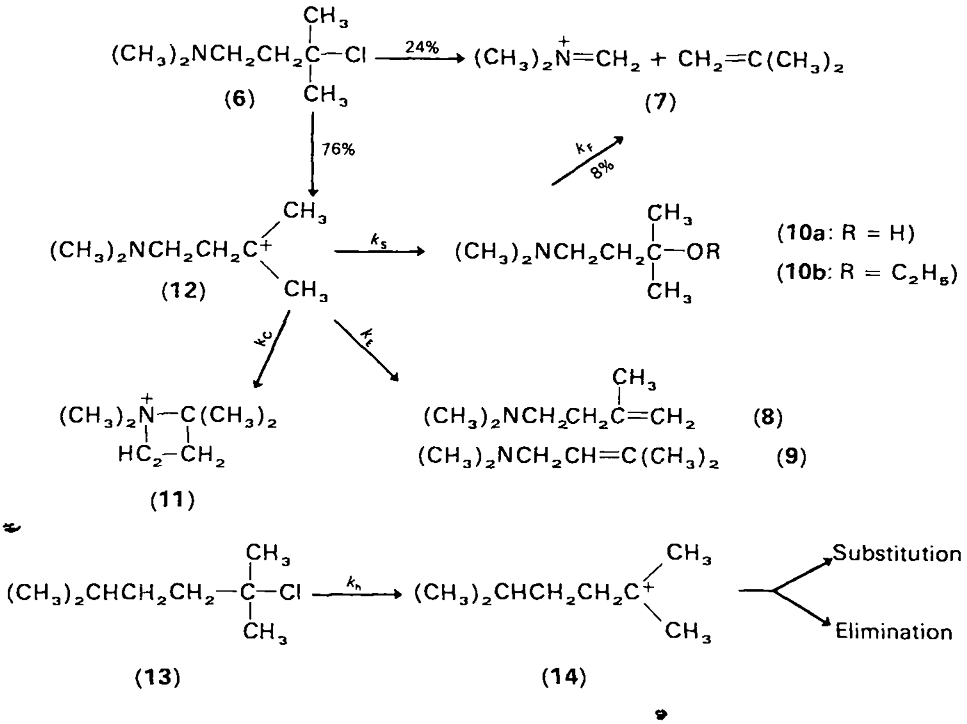
In the following subsections the occurrence and the detection of these basic fragmentation mechanisms will be discussed.

C. The Two-step Carbonium Ion Mechanism

The rate-determining step in this mechanism is the ionization to form a carbonium ion [path (a) in Scheme 2]. It is thus identical with that of unimolecular substitution (S_N1) and elimination (E 1). As in these cases, the tendency to ionize is greatest when a tertiary, and hence particularly stable, carbonium ion is formed. This applies e.g. to 3-chloro-*N*,*N*,3-trimethylbutylamine (**6**) (Scheme 3)[5,6].

The reaction of this compound in 40 vol.-% ethanol leads to 32% fragmentation products, i.e. isobutene together with dimethylamine and formaldehyde, which arise from the hydrolysis of the immonium ion **7**. In addition, 41% of the alcohol **10a** and the ethyl ether **10b** are formed by substitution along with 25% of the amino olefins **8** and **9** by elimination. Finally, 2% of the azetidinium ion **11** are formed by cyclization. In the presence of a carbonium ion trapping reagent, such as sodium azide, the yield of fragmentation products drops from 32% to 24%. Therefore 24% of the 3-chloro amine (**6**) fragment directly by the concerted mechanism b (Scheme 2), whereas 76% ionize to the γ-amino carbonium ion **12**. The latter then undergoes fragmentation (8%), substitution (41%), elimination (25%) and cyclization (2%) in the fast steps k_F, k_S, k_E and k_C. This experiment shows that there are two pathways for the fragmentation of compound **6**.

Further support for this duality of mechanism is provided by the comparison of the rate constant for the 3-chloroamine **6** with that for the sterically equivalent, i.e. homomorphous, chloroalkane **13**. Tertiary halides of the latter type are known to react via carbonium ions **14** under solvolytic conditions. The comparison of the observed rate constant k for **6** and k_h for **13** provides information about the participation of the nitrogen atom in the ionization step. If nitrogen does not participate

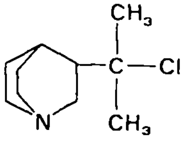


SCHEME 3.

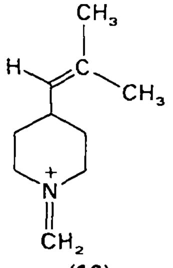
directly, k should be smaller than k_h ($k/k_h < 1$) due to the electron withdrawing inductive effect of nitrogen. If, however, the ionization of the 3-chloroamine **6** is assisted by the nitrogen atom, it should react at a rate comparable to or faster than that of the homomorphous chloroalkane ($k/k_h \gtrsim 1$).

The ratio of the rate constants for the compounds **6** and **13** in 80 vol.-% ethanol increases from 0·5 at 25 °C to 0·9 at 75 °C. Obviously, the contributions of the two fragmentation mechanisms of compound **6** (Scheme 3) also vary with the temperature. In cases where only the two-step carbonium ion mechanism [Scheme 2, path (a)] is possible for stereoelectronic reasons k/k_h ratios as low as 0·12 are observed (Section II.D).

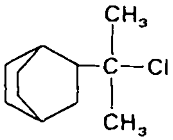
Another example of this duality of mechanism is provided by 3-(1′-chloro-1′-methylethyl)quinuclidine (**15**), which in 80% ethanol reacts to yield 62% the fragmentation product **16** together with 30% substitution products and 6% elimination products[7]. This and the ratio of the rate constants of **15** and the homomorph **17** ($k/k_h = 0{\cdot}64$) indicate concurrent fragmentation by the concerted mechanism and via the γ-amino carbonium ion **18**.



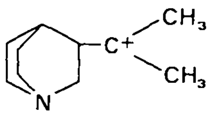
(15)



(16)

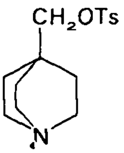


(17)

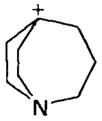


(18)

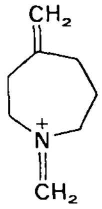
A fragmentable γ-amino carbonium ion can also be produced by rearrangement of an amine with a nucleofugal substituent in the δ-position. Thus the ionization of the *p*-toluenesulphonyl ester **19** is accompanied by a Wagner–Meerwein rearrangement to the bicyclic γ-amino carbenium ion **20**, the precursor of the fragmentation product **21**[8].



(19)

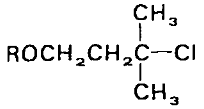


(20)



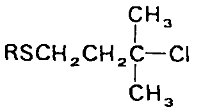
(21)

It is noteworthy that oxygen and sulphur analogues of the 3-chloroamine **6**, i.e. the alcohol **22a** and the thiol **23a**, as well as the corresponding methyl ethers **22b** and **23b**, only undergo substitution and elimination upon reaction in 80% ethanol[9,10]. The products and the rate constants, which are approximately ten-times smaller than the rate constant for the 'homomorphous' tertiary chloride **24**, indicate a S_N1–E 1 mechanism by way of γ-hydroxy, γ-alkoxy and γ-thiocarbonium ions respectively. Evidently the tendency to eliminate oxocarbonium ions **25** and thiocarbonium ions **26** as electrofuge is too low for fragmentation to occur. The conjugate bases of the alcohol **22a** and the thiol **23a**, which are present in basic media, react quite differently, as will be shown in Section II.E.



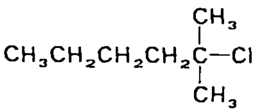
$ROCH_2CH_2\overset{CH_3}{\underset{CH_3}{C}}-Cl$

(22)



$RSCH_2CH_2\overset{CH_3}{\underset{CH_3}{C}}-Cl$

(23)



$CH_3CH_2CH_2CH_2\overset{CH_3}{\underset{CH_3}{C}}-Cl$

(24)

a: R = H
b: R = CH_3

$R\overset{+}{O}=CH_2$

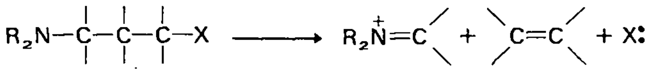
(25)

$R\overset{+}{S}=CH_2$

(26)

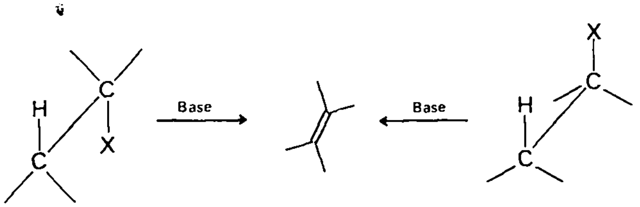
D. The Concerted Mechanism of Fragmentation

At least five atomic centres of a molecule are involved in the transition state of the concerted fragmentation of γ-amino halides and sulphonates (1)[11].



(1)

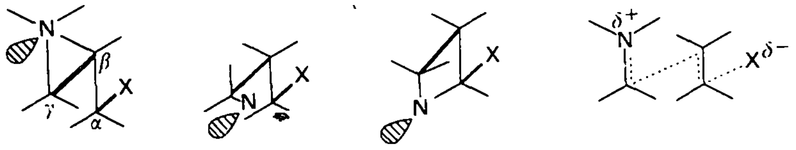
It is, therefore, not surprising that this mechanism is subject to more stringent stereoelectronic conditions than those encountered in bimolecular (E 2) elimination. In the latter case (Scheme 4) an antiplanar orientation of H and X (**27a**, dihedral angle $\Phi = 180°$) leads to faster olefin formation than a synplanar orientation (**27b**, $\Phi = 0$) which, in turn, is more favourable than all intermediate conformations. The reason is that the original C—H and C—X σ-bonds must be coplanar in order to be converted smoothly to p-orbitals of the incipient π double bond[3].



(27a) (27b)

SCHEME 4.

In concerted fragmentation a further electron pair has to become aligned. Extension of the 'principle of maximum overlap of p-orbitals in the transition state' to the fragmentation of 3-haloamines leads to the prediction that the concerted mechanism will only operate if both the C_α—X bond and the orbital of the lone pair of electrons in the nitrogen atom are antiplanar (or antiparallel) with respect to the C_β—C_γ bond (Scheme 5[11], where the antiparallel electron pairs are indicated by heavy lines).

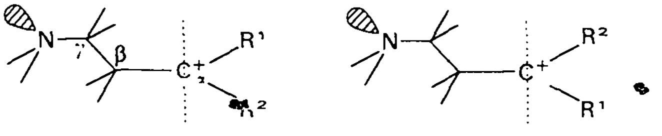


(28a) (28b) (28c) (29)

SCHEME 5.

These conditions are met in the staggered conformation (**28a**) and in all rotamers derived from it by rotation of the amino group around the C_β—C_γ bond, e.g. the skew (**28b**) and the eclipsed conformation (**28c**), two out of an infinite number of rotamers. Only such conformations permit maximum overlap of the p-orbitals of the sp^2-hybridized atoms formed in the unsaturated fragments in the transition state, e.g. **29**. Rotations about the C_α—C_β and C_γ—N bonds, on the other hand, lead to energetically less favourable transition states with the result that the concerted process is suppressed. However, the stereoelectronically favourable conformations are not always the most favourable ones sterically.

It should be pointed out that the stereoelectronic requirements for the fragmentation of γ-amino carbonium ions (**4**) and related intermediates, generated in the two-step mechanism (Scheme 2), are similar but less stringent than for the concerted process. Cleavage of the C_β—C_γ bond will occur readily when the plane through C_α, C_β and C_γ is approximately orthogonal to the second plane described by the three ligands of C_α (Scheme 6)[11].



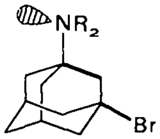
(4a) (4b)

SCHEME 6.

Rotation around the C_α—C_β bond leads to two fragmentable forms **4a** and **4b** which furnish different olefins when the substituents on C_β are different. Since C_α is now the centre of a full positive charge, its greater attraction for the electrons of the C_β—C_γ bond will tend to overcome the disadvantage due to small deviations from orthogonality.

The concerted mechanism is detected mainly on the basis of kinetic criteria. The positive charge formed on the cation in the ionization process is transferred to the relatively stable immonium ion. Therefore N—C—C—C—X systems that undergo concerted fragmentation react more rapidly (rate constant k) than homomorphous compounds without nitrogen (k_h), in which the positive charge remains localized on the C_α atom. A k/k_h ratio greater than unity thus indicates the participation of the amino group, i.e. a concerted process.

Another kinetic criterion for the participation of the amino group is provided by comparison of the rate constants for γ-nucleofugally substituted amines, in which the substituents R on the N atom are varied. Since the amino group acquires the positive charge in the transition state (**29**), the reaction rate must depend on the number and nature of these substituents.



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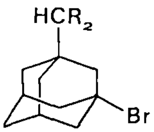

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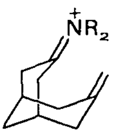

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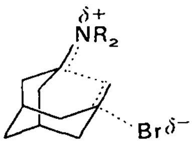
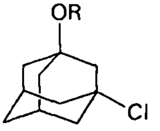


(33)

3-Bromoadamantylamines (**30**, R = H or CH_3) react faster than the homomorphous 1-alkyl-3-bromoadamantanes (**31**, R = H or CH_3), and undergo quantitative fragmentation with formation of the immonium salts (**32**)[12]. As the number of methyl groups on the nitrogen atom is increased, the absolute and relative rates with respect to the homomorphs (**31**) increase. Thus k/k_h is 30 for the primary amine, 222 for the secondary amine, and 520 for the tertiary amine. The increase in the reactivity with the number of *N*-methyl substituents is due to the increasing electromeric effect of the amino group. The atoms taking part in the reaction have the staggered conformation (**28a**) and therefore satisfy the stereoelectronic principles mentioned above. In the transition state (**33**) of this concerted fragmentation the $C_{(3)}$—Br and the $C_{(1)}$—$C_{(2)}$ bonds are cleaved simultaneously.



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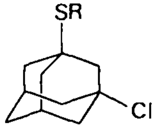
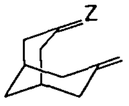


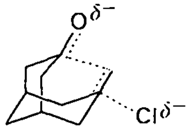
(35)

a: R = H
b: R = C_2H_5



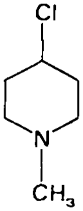
(36)

a: Z = O
b: Z = S



(37)

It is noteworthy that 3-chloroadamantanol (**34a**), 3-chloroadamantanethiol (**35a**) and the corresponding ethyl ethers, **34b** and **35b**, respectively, do not fragment in 80% ethanol although they meet the stereoelectronic requirements. Instead, substitution by solvent via bridgehead carbonium ions takes place[9,13]. On the other hand the conjugate bases of the alcohol **34a** and the thiol **35a** undergo rapid and quantitative fragmentation to the ketone **36a** and the thione **36b**, respectively. A concerted mechanism is implicated by the rate constants which are 3×10^6- and 8×10^4-times larger, respectively, than those of the alcohol **34a** and the thiol **35a**. A negative salt effect is observed in both cases. This points to a transition state such as **37**, in which the negative charge on oxygen (or sulphur) has become dispersed. A comparison of the reactivity of the amino- (**30**), hydroxy- (**34a**) and mercapto- (**35a**) adamantyl halides shows that the electron releasing power of these substituents increases in the order $NH_2 < NHCH_3 < N(CH_3)_2 < S^- < O^-$.



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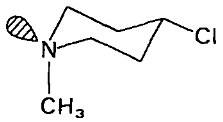
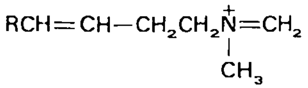
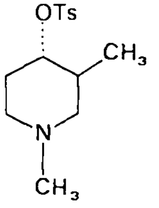


(38a)



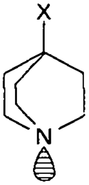
$$RCH{=}CH{-}CH_2CH_2\underset{\displaystyle CH_3}{\overset{+}{N}}{=}CH_2$$

(39)



(40)

The skew conformation (**28b**) of the N—C—C—C—X sequence is present in 4-chloropiperidines, such as the *N*-methyl derivative **38**, provided that the *N*-electron pair occupies the equatorial position at least part of the time, as in **38a**. Indeed, this compound reacts about 100-times faster than chlorocyclohexane with quantitative fragmentation to the immonium ion **39** (R = H)[14]. It is noteworthy that the *p*-toluenesulphonate of 1,3-dimethyl-*trans*-piperidinol-4 (**40**) yields at least 98% of the immonium ion **39** (R = CH_3) containing the more highly substituted double bond[15]. This regiospecificity is reminiscent of the Saytzeff rule, which predicts the same preference in olefin-forming β-elimination[1].



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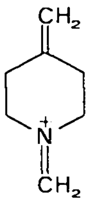

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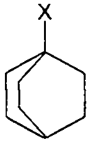
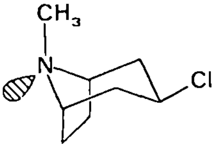


(43)

The eclipsed conformation **28c** is present in the 4-halo- and 4-*p*-toluenesulphonyloxyquinuclidines (**41**, X = halogen or OTs). These compounds undergo quantitative fragmentation, with formation of the 1,4-dimethylenepiperidinium ion (**42**)[16,17]. The reaction rates are extremely high in comparison with those of the homomorphous 1-substituted bicyclo[2.2.2]-octanes (**43**); thus 4-bromoquinuclidine (**41**, X = Br) reacts about 50,000-times faster than 1-bromobicyclo[2.2.2]octane (**43**, X = Br), which is relatively inert in solvolysis[16].

These examples show that systems which satisfy the stereoelectronic conditions undergo concerted fragmentation. This does not, however, prove that these conditions are essential. Such proof can be obtained only by a comparison of the reactivity of two stereoisomers, only one of which satisfies the stereoelectronic conditions. The one that does should fragment by the concerted mechanism, while its stereoisomer should react by the two-step carbonium ion mechanism. In the latter case, fragmentation should be accompanied by conventional reactions, such as substitution, elimination and ring closure, in accordance with path (a) in Scheme 2.



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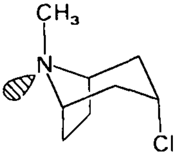

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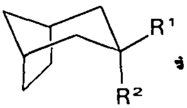

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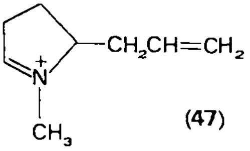
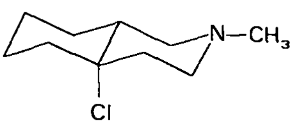


(47)

a: R^1 = Cl, R^2 = H
b: R^1 = H, R^2 = Cl

This hypothesis can be checked with the aid of the stereoisomeric 3-chlorotropanes **44** and **45**[18]. The 3β-chloride (**44**) contains the skew conformation **28b**, and should thus fragment by the concerted mechanism, not however the 3α-chloride (**45**), since its C—Cl bond is not antiparallel to the C_β—C_γ bond. It has in fact been found that the 3β-chloride reacts 13,500-times faster than the homomorphous *exo*-3-chlorobicyclo[3.2.1]-octane (**46a**), and gives only the fragmentation product **47**. The 3α-chloride, on the other hand, does not react appreciably faster than the homomorph **46b**, and gives only substitution and elimination products.



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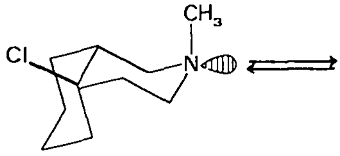
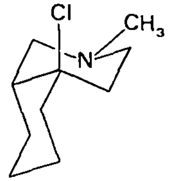
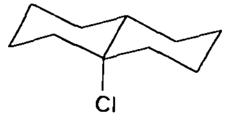


(49a)



(49b)



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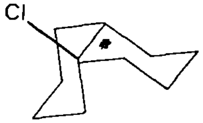

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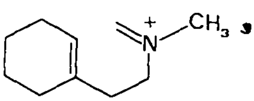

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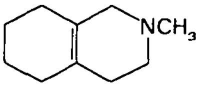

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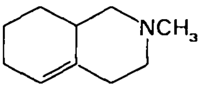

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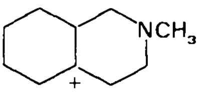

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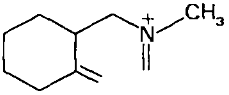
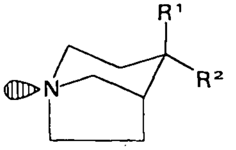


(56)

The influence of configuration on the reaction course is very pronounced in the case of the stereoisomeric 10-chloro-*N*-methyldecahydroisoquinolines **48** and **49**[19]. Whereas the *trans* isomer is fixed in the rigid double-chair conformation **48**, the *cis* isomer is an equilibrium mixture of the conformers **49a** and **49b**. The orientation of the chlorine atom favours concerted fragmentation only in the form **49a**, but not in the conformation **49b** or in the *trans* isomer **48**.

As expected *cis*-10-chloro-*N*-methyldecahydroisoquinoline (**49**) reacts about 128-times faster than the homomorphous *cis*-9-chlorodecalin (**51**), with exclusive fragmentation to give the immonium ion **52**. The reaction of the *trans* isomer **48**, however, is slower by a factor of 4·5 than that of the homomorph **50**, and leads to the immonium salt **52** besides the olefins

53 and 54. (The reasonable assumption is made that the absence of a methyl group on $C_{(3)}$ of the homomorphs 50 and 51 has little or no effect on their reaction rates.) Hence the *cis* isomer **49** must undergo concerted fragmentation, while the *trans* isomer **48** fragments in two steps via the carbonium ion **55**. The fragmentation of **49** shows that 3-haloamines react by the concerted mechanism even when they could give rise to stable tertiary carbonium ions. This example again demonstrates the regioselectivity of concerted fragmentation, since none of the alternative product **56**, which contains a less highly substituted olefinic bond, is obtained.



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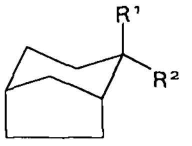

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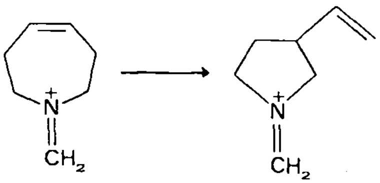
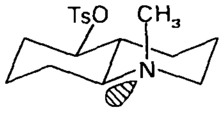


(59) (60)

a: R^1 = H, R^2 = OTs
b: R^1 = OTs, R^2 = H

Another example of the stringent stereoelectronic condition for concerted fragmentation is provided by the *endo* and *exo* isomers of 4-*p*-toluenesulphonyloxy-1-azabicyclo[3.2.1]octane (**57**)[20]. The *endo* isomer **57a** reacts $1{\cdot}47 \times 10^3$-times faster than the homomorphous compound **58a**, yielding the immonium salt of *cis*-azacyclo-4-heptene (**59**). This compound rapidly rearranges to the corresponding salt of 3-vinylpyrrolidine (**60**). Fragmentation again, therefore, produces the olefin with the more highly substituted double bond. This is subsequently converted to the thermodynamically more stable product by a sigmatropic [3,3] rearrangement. On the other hand, the *exo* isomer **57b** does not fulfill the steric requirements, since the axial C_α—OTs is not oriented antiparallel with respect to the C_β—C_γ bond. It therefore reacts by the two-step carbonium ion mechanism, as evidenced by its rate which is 4·4-times lower than that of the homomorph **58b**. In addition, fragmentation is accompanied by substitution and elimination.

The high stereospecificity of concerted fragmentation is even more clearly demonstrated in the case of the three stereoisomeric *N*-methyldecahydroquinol-5-yl *p*-toluenesulphonates **61**, **62** and **63**[21]. Of these only the 5α-*trans* (**61**) and the 5α-*cis* isomer (**62**) with equatorial *p*-toluenesulphonyloxy groups have the required antiparallel arrangement of the electron pairs involved, not however the 5β-*trans* isomer (**63**). The two compounds **61** and **62** do in fact undergo exclusive fragmentation to give the unsaturated ten-membered immonium ions **64** and **65** (or their hydrolysis products). Whereas in the first case the *trans* olefin **64** is formed, the *cis* olefin **65** is obtained in the second. The concerted nature of these processes is apparent from the fact that the reaction rates are higher for the compounds **61** and **62** than for the homomorphous 1-decalyl *p*-toluenesulphonates **68** and **69**.



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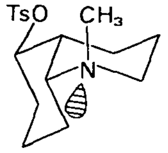

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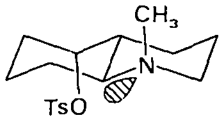

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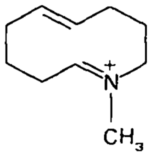

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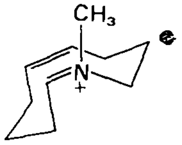

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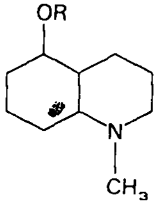

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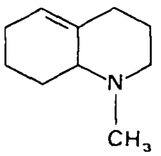

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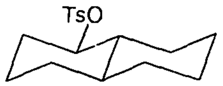

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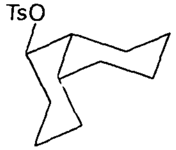

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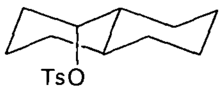
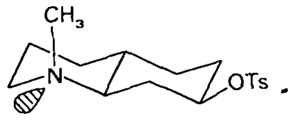


(70)

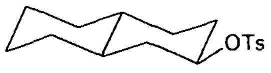
The 5β-*trans* *p*-toluenesulphonate (**63**), on the other hand, reacts more slowly by the factor of about 8 than the homomorphous 1-decalyl *p*-toluenesulphonate **70**, i.e. $k/k_{\mathrm{h}} = 0{\cdot}12$. Since only the substitution and elimination products **66** and **67** are formed, this reaction must proceed by the two-step carbonium ion mechanism.

The steric orientation of the *N*-electron pair has not been considered so far. Instead it has been tacitly assumed that, because of the fast inversion of the nitrogen atom, this electron pair can adopt the antiparallel orientation required for the concerted mechanism. The compounds **61** and **62**, as well as the *N*-methylamines mentioned earlier, were formulated accordingly, although the *N*-methyl group should more often occupy the equatorial position.

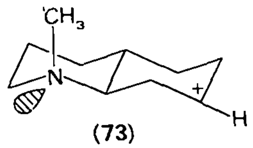
The following study on the 7α- and 7β-*trans*-1-methyldecahydroquinolyl *p*-toluenesulphonates **71** and **72** is of particular interest with respect to the influence of the orientation of the *N*-electron pair[21]. In these compounds the *N*-electron pair, which oscillates in a plane perpendicular to the ring, cannot occupy the orbital antiparallel to the $C_β$—$C_γ$ bond, since this space is taken up by the σ-electron pair of the bond between N and $C_{(2)}$. Thus, in the equatorial 7α-*p*-toluenesulphonate (**71**) fragmentation by the concerted mechanism should not be possible even though the $C_α$—OTs and the $C_β$—$C_γ$ bonds are antiparallel. The two-step fragmentation via the γ-amino carbonium ion (**73**) should also be impossible for the same reason.



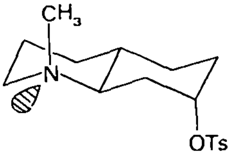
(71)



(74)



(73)



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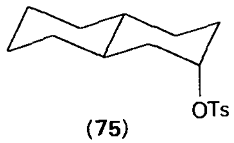
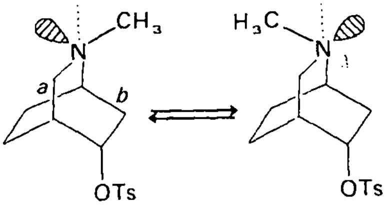
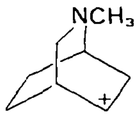


(75)

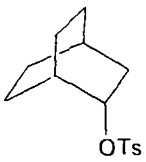
In fact neither the 7α- (**71**) nor the 7β-*p*-toluenesulphonate (**72**) undergo fragmentation. Both compounds exhibit only substitution and elimination via the carbonium ion **73** by the S_N1 and E 1 mechanisms. (In both cases, mixtures of the 7α- or 7β-alcohol and ethyl ether, as well as 1,2,3,4,4a,5,8,8a- and 1,2,3,4,4a,5,6,8a-octahydro-1-methylquinoline are obtained.) The absence of participation of the amino group also follows from the rate constants which are only 0·37 and 0·43 times those of the homomorphous 2-decalyl *p*-toluenesulphonates **74** and **75**. The ionization rates are thus appreciably reduced by the inductive effect of the nitrogen atom. These results show that the orientation of the electron pair on the donor atom is crucial.



(76a) (76b)

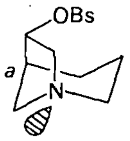


(77)

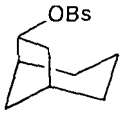


(78)

This is further exemplified by the reaction of *endo*-2-methyl-5-*p*-toluenesulphonyloxy-2-azabicyclo[2.2.2]octane (76)[22] in which the *N*-electron pair rapidly oscillates between the positions indicated in **76a** and **76b**. In these 'invertomers' the C—OTs bond is antiplanar with respect to bond *a*. However, the *N*-electron pair deviates from coplanarity with the bond *a* by approximately 54°. If the electron density in the region marked by the dotted line were appreciable, concerted fragmentation should occur. In fact, only substitution and elimination but no fragmentation products are obtained in 80% ethanol. Since the rate is only one-tenth that of the 'homomorph' **78**, a two-step (S_N1—E 1) mechanism via the carbonium ion **77** is indicated. Fragmentation involving bond *b* is equally prohibited because the C_α—OTs bond is not antiplanar.

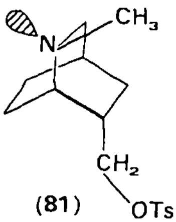


(79)

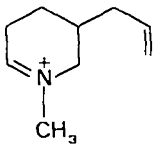


(80)

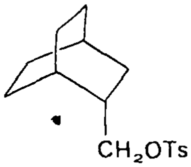
The sensitivity of concerted fragmentation to small deviations from antiplanarity is strikingly illustrated by the behaviour of the *p*-bromobenzenesulphonate of *endo*-1-azabicyclo[3.2.1]octan-6-ol (**79**) in which the C_α—OBs and the *N*-electron appear, at first sight, to be antiparallel to the bond *a*[23]. Actually, small deviations (approx. 20°) are discernible in models, and only little fragmentation, besides substitution and elimination, are observed. The rate, which is only 0·04-times the rate of the homomorph **80**, excludes a concerted process.



(81)



(82)



(83)

This review of concerted fragmentation reactions has thus far been limited to systems with a secondary or tertiary nucleofuge. Moreover, C_α was part of a ring and the geometry of the system therefore largely defined. The question can be raised whether the concerted mechanism still occurs when C_α is primary and rotation around the C_α—C_β bond is possible, as in the *p*-toluenesulphonate of 2-methyl-6-*endo*-hydroxymethylisoquinuclidine (**81**). This compound in fact undergoes quantitative fragmentation to the immonium ion **82** at a rate which is thirteen-times that of the 'homomorph' **83**[22]. Concerted fragmentation therefore occurs although rotation around the C_α—C_β bond is frozen in the transition state.

E. Competitive Concerted Fragmentation

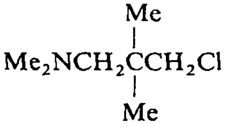
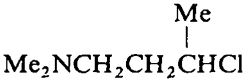
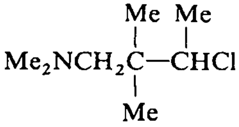
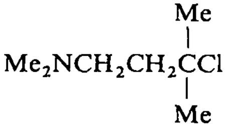
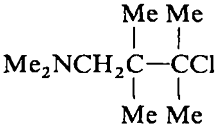
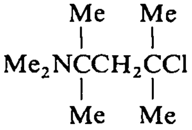
The compounds mentioned in Section II.D which fragment by the concerted mechanism were all cyclic. This is not a coincidence, since the rigidity imparted by their structure favours the concerted process.

On the other hand, open chain, freely-rotating molecules such as 3-chloro-*N*,*N*,3-trimethylbutylamine (**6**) (Section II.C) also react by the two-step carbonium ion mechanism, despite the fact that they can adopt a conformation suitable for concerted fragmentation. The simplest explanation for this behaviour is that, because of thermal motion, the molecules do not remain long enough or often enough in these conformations, i.e. the concerted process is disturbed by rotations around the C_α—C_β and C_γ—N bonds. The formation of the transition state thus involves a loss of freedom of rotation which is unfavourable on entropy grounds. The question may therefore be raised as to whether acyclic, freely-rotating molecules, such as **1**, **2**, and **3** (Section II.A) are capable of undergoing concerted fragmentation.

This question is best answered by discussing the effect of additional methyl substituents in the α, β and γ positions of γ-amino chlorides[4]. Such compounds are listed in Table 2 together with their first-order rate constants and their products in 80%-ethanol. The third column lists the ratios of the rate constants of the γ-amino chlorides and their homomorphs, in which an isopropyl group replaces the dimethylamino group. These k/k_h values reflect the kinetic effect of the nitrogen atom.

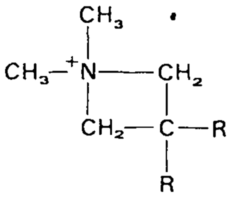
The primary chlorides **84** and **85** cyclize exclusively to an azetidinium ion **90** (R = H or CH_3). The high k/k_h ratios show that ionization is strongly assisted by the amino group and that an intramolecular, anchimerically-assisted nucleophilic displacement reaction occurs. The higher

TABLE 2. Influence of methyl substitution on the reactivity of 3-chloroamines in 80 vol.-% ethanol at 56 °C

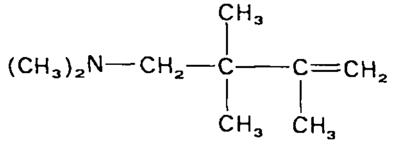
Compound		$k \times 10^5$	k/k_h	Products (%)[a]
$Me_2NCH_2CH_2CH_2Cl$	**(84)**	10·8	$4·3 \times 10^3$	100 C
 $Me_2NCH_2\overset{Me}{\underset{Me}{C}}CH_2Cl$	**(85)**	98	$3·4 \times 10^6$	100 C
 $Me_2NCH_2CH_2\overset{Me}{C}HCl$	**(86)**	1·87	520	100 C
 $Me_2NCH_2\overset{Me}{\underset{Me}{C}}-\overset{Me}{C}HCl$	**(87)**	28·2	4100	72 C, 19 F
 $Me_2NCH_2CH_2\overset{Me}{\underset{Me}{C}}Cl$	(6)	35·5	0·52	38 F, 37 E, 23 S, 2 C
 $Me_2NCH_2\overset{Me}{\underset{Me}{C}}-\overset{Me}{\underset{Me}{C}}Cl$	**(88)**	14,500	125	70 F, 30 E
 $Me_2N\overset{Me}{\underset{Me}{C}}CH_2\overset{Me}{\underset{Me}{C}}Cl$	**(89)**	41,200	24	80 F, 20 E

[a] C = cyclization, F = fragmentation, E = elimination, S = substitution.

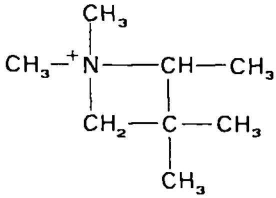
rate of the β-dimethylated chloride (**85**) demonstrates the geminal dialkyl effect, i.e. the β-methyl groups increase the population of the quasi-cyclic conformation which leads to cyclization.



(90)



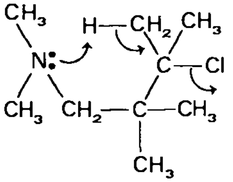
(91)



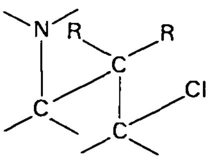
(92)

Cyclization is still the only observable reaction of the secondary chloride **86**, but the rate, and hence k/k_{h}, is lower because of the greater steric hindrance to attack by the amino group at the secondary carbon atom. The introduction of two further methyl groups into the β-position in **87** again increases the reaction rate and the k/k_{h} ratio. However, in this case fragmentation begins to compete with cyclization to **92**, the high k/k_{h} ratio indicating that both processes are assisted by the nitrogen atom. Anchimerically-assisted cyclization is therefore accompanied by concerted fragmentation in the ratio of 4:1.

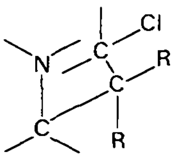
The tertiary chloride **6** was mentioned in Section II.C as an example of a 3-chloroamine which reacts by the two-step carbonium ion mechanism. The k/k_{h} ratio of 0·52 at 25 °C indicates only little participation of the nitrogen atom. A surprising change takes place when two further methyl groups are introduced at C_{β} as in **88**. The k/k_{h} ratio increases by a factor of almost 250, and fragmentation (70 %) and elimination (30 %) to the olefin **91** are the only reactions. Two methyl groups at C_{γ} (**89**) have a similar, but less marked, effect on the k/k_{h} ratio. Again, fragmentation (80 %) and elimination (20 %) are the only reactions observed. In these cases ionization is clearly assisted by the nitrogen atom.



(93)

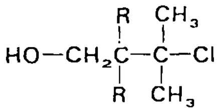


(94a)



(94b)

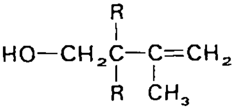
The acyclic γ-amino chlorides **88** and **89** differ from those discussed in Section II.D in that accelerated fragmentation is accompanied by accelerated elimination. The simplest explanation is that concerted fragmentation competes with concerted intramolecular elimination involving the amino group in the cyclic transition state **93**. This type of neighbouring group participation, postulated in 1965[24], has received little attention so far. The geminal methyl groups at C_{β} in compound **88** apparently promote concerted fragmentation by impeding rotation around the C—C and C—N bonds. Furthermore, the preference for the staggered conformation **94a** (with respect to the N and C_{α} atoms) will be less when R is methyl rather than hydrogen. β-Methyl groups will therefore increase the population of skew conformations like **94b**, which lead to anchimerically-assisted elimination (**93**) and cyclization. Similar explanations can be given for the effect of geminal methyl groups at C_γ, as in the γ-amino chloride **89**.



$\mathrm{HO{-}CH_2\overset{R}{\underset{R}{C}}{-}\overset{CH_3}{\underset{CH_3}{C}}{-}Cl}$

(94) R = H

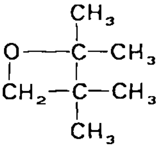
(95) R = CH_3



$\mathrm{HO{-}CH_2\overset{R}{\underset{R}{C}}{-}\underset{CH_3}{C}{=}CH_2}$

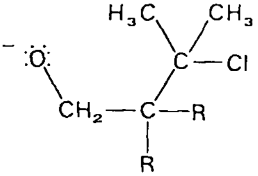
(96) R = H

(97) R = CH_3

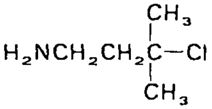


(98)

Competition between concerted fragmentation, elimination and cyclization is also observed with the anions of certain acyclic 3-chloroalcohols[9]. In 80%-ethanol and in the presence of sodium hydroxide, the compounds **94** and **95** react $4{\cdot}4 \times 10^3$- and $1{\cdot}4 \times 10^6$-times faster, respectively, than in the absence of base. The rate of ionization is therefore increased drastically by the negative charge on the oxygen atom. Whereas 73% fragmentation and 27% elimination to **96** take place with the anion of **94**, 61% fragmentation, 37% elimination of **97** and 2% cyclization to **98** occur with the anion from **95**. In these cases a single conformation like **99** would explain all the observed reactions, namely fragmentation, elimination and cyclization.

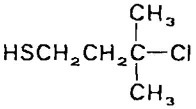


(99)



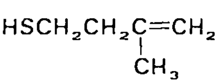
$\mathrm{H_2NCH_2CH_2\overset{CH_3}{\underset{CH_3}{C}}{-}Cl}$

(100)



$\mathrm{HSCH_2CH_2\overset{CH_3}{\underset{CH_3}{C}}{-}Cl}$

(101)



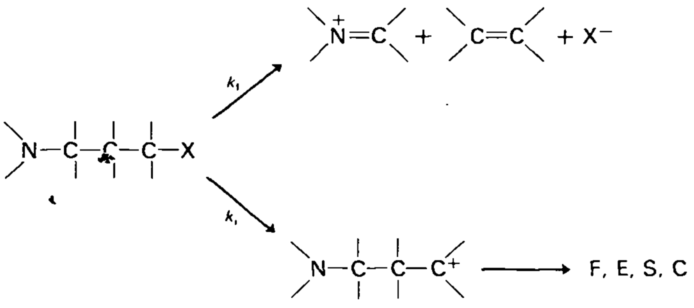
$\mathrm{HSCH_2CH_2\underset{CH_3}{C}{=}CH_2}$

(102)

A comparison of the rates and products of the anion of the 3-chloroalcohol (**94**) with those of the nitrogen analogue (**100**)[5] emphasizes the greater ability of negative oxygen, which has three available electron pairs, to promote concerted fragmentation and intramolecular elimination. On the other hand, the anion of the sulphur analogue **101** only undergoes elimination to the terminal olefin **102**. However since the rate is 10^4-times that of the neutral thiol **101** and no other olefins are found, a concerted intramolecular elimination is indicated[10]. The absence of fragmentation confirms the smaller tendency to form $S{=}CH_2$, as compared to $O{=}CH_2$ and $H_2\overset{+}{N}{=}CH_2$.

F. The Frangomeric Effect

Concerted fragmentation can only occur if the rate constant [illegible] for this process is comparable to, or greater than, the rate constant k_i for ionization to the γ-amino carbonium ion (Scheme 7), i.e. if $k_f \geq k_i$. As shown by the foregoing examples, the concerted process (k_f) always dominates when the stereoelectronic requirements are fulfilled.



SCHEME 7.

For convenience, the increase in ionization rate due to a concerted mechanism is called the ‘frangomeric effect, f’[11,14]. It is defined as the ratio of the rate constants k_f and k_i, i.e. $f = k_f/k_i$.

As a rule k_f and k_i cannot be determined for one and the same compound, since usually only one of the two processes is observed. In order to determine k_i in those cases in which the concerted mechanism predominates, it is necessary to measure the ionization rate k_h of a homomorphous compound. In cases where k_i can be measured directly, it is always smaller than k_h by an inductive factor $i < 1$, i.e. $k_i = k_h \times i$. In the case of γ-amino chlorides (Scheme 7) the $-I$ effect of the nitrogen atoms is responsible for the lowering of the ionization rate k_i.

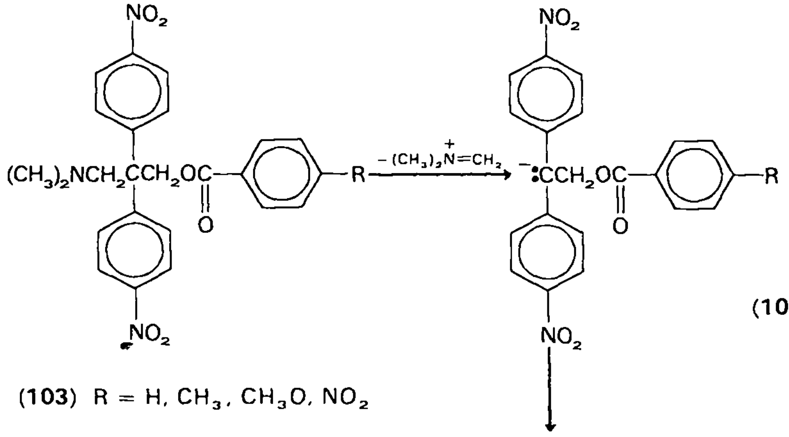
An approximate value for the inductive factor i can be obtained when the rate constant for the two-step carbonium ion mechanism (k_i in Scheme 7) and the rate constant for the corresponding homomorph are known. The i values for compounds **48**, **57b** and **63** (discussed in Section II.D) are 0·22, 0·23, and 0·12, respectively. For γ-amino halides and sulphonates they generally lie between 0·5 and 0·12. They depend on the environment and the orientation of the dipoles as well as on the solvent.

The frangomeric effect can be calculated approximately from the rate of concerted fragmentation k_f, the rate of the homomorph k_h and an estimated inductive factor i, i.e. $f = k_f/k_h \times i$, and the f values vary between 10^1 and 10^5. In comparing them, it should be borne in mind that they are based on a comparison of the rates of two different reactions, namely k_f and k_i in Scheme 7, and that steric effects may affect these reactions in opposite ways. An accurate treatment of the frangomeric effect would therefore require corrections for inductive and steric effects. Nevertheless, an f value larger than unity is a good indication for a concerted fragmentation.

G. The Two-step Carbanion Mechanism

In the cases considered so far, fragmentation was either initiated by release of the nucleofuge X, or it involved the simultaneous release of X and the electrofugal group [path (a) and (b) in Scheme 2]. In the third mechanism [path (c) in Scheme 2] the electrofugal immonium ion is first released yielding an intermediate carbanion. The latter then ejects the nucleofuge X in a subsequent reaction.

This mechanism appears to be extremely rare. It can only occur if the carbanion is stabilized by electron-attracting substituents and if the tendency of X to leave is small.



(104)

(103) R = H, CH_3, CH_3O, NO_2

$(p\text{-}NO_2C_6H_4)_2C{=}CH_2$ (105)

$+\ p\text{-}R{-}C_6H_5COO^-$

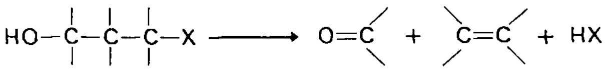
These conditions are satisfied by the benzoates of 3-dimethylamino-2,2-bis(*p*-nitrophenyl)propanol (**103**)[25]. Thus, the first-order rate constants in 80%-ethanol for fragmentation to dimethylamine, formaldehyde and 1,1-bis(*p*-nitrophenyl)ethylene (**105**) are rather insensitive to the *p*-substituent in the benzoate group (the Hammett ρ value is 0·29). This shows that the nucleofuge is not split off in the rate determining step. Moreover, the intermediate carbanion **104** is protonated by the solvent (80%-ethanol) if a less active nucleofugal group than benzoate is used. It is not surprising that no fragmentation occurs when esters of the type **103**, which lack the *p*-nitro groups on the β-substituents, are reacted in 80%-ethanol.

III. THE SCOPE OF HETEROLYTIC FRAGMENTATION

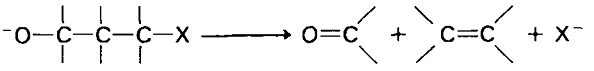
As mentioned in Section I, fragmentation reactions are best classified with respect to the unsaturated fragment c=d. Variation of the electrofugal fragment a—b leads to numerous subdivisions. A review of the large number of cases reported in the literature in terms of this classification would be far beyond the scope of this chapter. Also, little would be gained thereby, since the pertinent moiety invariably consists of the sequence of atoms a—b—c—d—X, regardless of the sometimes-complex structures involved. The examples given in this section were therefore selected primarily to illustrate the scope of heterolytic fragmentation and the general principles involved.

A. Olefin-forming Fragmentation

Probably the most prevalent type of fragmentation occurs with alcohols which contain a nucleofuge in the 3-position (equation 19). Strong bases, such as hydroxide and alkoxide ions, can convert the alcohols to their more reactive anions, as discussed in Section II.E (equation 20).

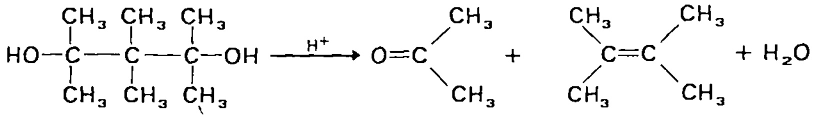


(19)



(20)

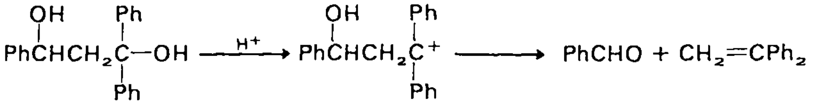
As early as 1907 the fragmentation of tetramethyl-2,4-pentanediol (**106**) into acetone and tetramethylethylene was observed[26].



$$\mathrm{HO{-}C(CH_3)_2{-}C(CH_3)_2{-}C(CH_3)_2{-}OH} \xrightarrow{H^+} \mathrm{O{=}C(CH_3)_2} + \mathrm{(CH_3)_2C{=}C(CH_3)_2} + \mathrm{H_2O}$$

(106)

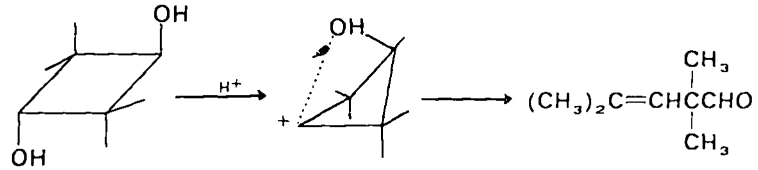
In unsymmetrical 1,3-diols, the nucleofugal fragment is usually the hydroxyl group on the more highly substituted carbon atom. Thus, treatment of 1,1,3-triphenyl-1,3-propanediol (**107**) with acid yields benzaldehyde and 1,1-diphenylethylene. This suggests that the reaction proceeds via the more stable carbonium ion **108**[27].



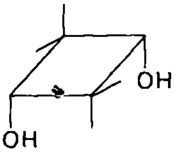
$$\mathrm{PhCH(OH)CH_2C(OH)Ph_2} \xrightarrow{H^+} \mathrm{PhCH(OH)CH_2C^+Ph_2} \longrightarrow \mathrm{PhCHO} + \mathrm{CH_2{=}CPh_2}$$

(107) **(108)**

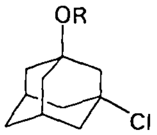
In symmetrical diols, steric factors may determine reactivity. Thus, *trans*-2,2,4,4-tetramethyl-1,3-cyclobutanediol (**109**) fragments in dilute sulphuric acid to the aldehyde **110**, whereas the corresponding *cis* diol **111** is stable even in 20% sulphuric acid[28]. The higher reactivity of the *trans* isomer **109** can be explained by backside solvation of the incipient cationic centre in the puckered carbonium ion **112** by the *trans* hydroxyl group.



(109) **(112)** **(110)**



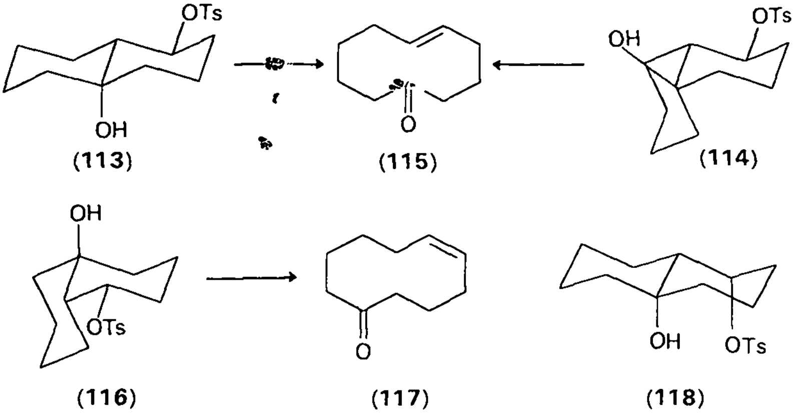
(111)



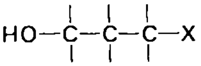
(34)

As a rule alcohols and ethers do not fragment under solvolytic conditions when the carbonium ion is formed irreversibly. This applies even when the stereoelectronic conditions are favourable, as shown for 3-chloroadamantanol (**34**, R = H) and its ethyl ether (**34**, R = C_2H_5) in Section II.D. The reactions of compounds **106**, **107** and **109**, mentioned above, are carried out under acidic conditions. A γ-hydroxy carbonium ion is therefore formed repeatedly, thermodynamic control leading to fragmentation. Under basic conditions, however, the alcoholate anion is present, and the tendency to fragment is therefore much higher (equation 20).

The base-induced fragmentation of 1,3-diol monotosylates is of considerable importance in the synthesis of medium-sized rings[29,30]. Of the four possible stereoisomers of 1-*p*-toluenesulphonyloxydecalol-10, the *trans–trans* **113** and the *cis–cis* isomer (**114**) yield *trans*-cyclodecenone-6 (**115**), whereas the *cis–trans* isomer (**116**) yields the *cis* olefinic ketone **117**. The fourth, *trans–cis* isomer (**118**), leads to less than 6% fragmentation product[29]. All these stereospecific reactions are predictable on the basis of the stereoelectronic rules for concerted fragmentation, as described in Section II.D.



Fragmentation also occurs in the deamination of γ-amino alcohols via diazonium ions (**119**)[31]. However, the nucleofugal group may also be an ammonio (**120**)[32] or an azoxy group (**121**)[33].



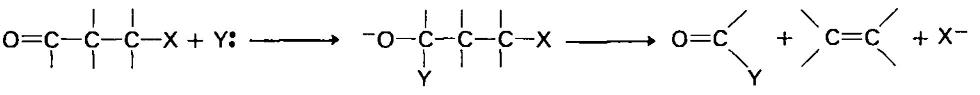
$$\mathrm{HO{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}X}$$

(**119**) $X = -\overset{+}{N}{\equiv}N$

(**120**) $X = -\overset{+}{N}(CH_3)_3$

(**121**) $X = -\underset{\underset{O}{|}}{N}{=}NR$

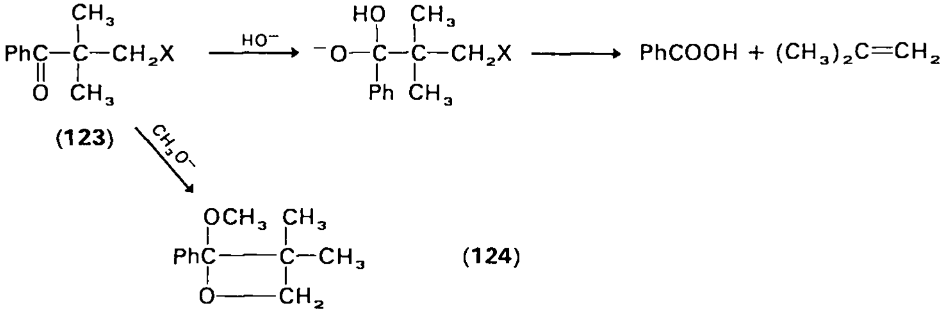
Many fragmentable compounds of the type **122** are generated *in situ* by the addition of a nucleophile Y, such as a Grignard reagent or hydroxide, alkoxide and hydride ions, to a ketone or aldehyde bearing a β-nucleofuge (reaction 21)[34].



(21)

(122)

With hydroxide ion as the nucleophile an acid is formed, especially when the usual 1,2-elimination of HX is difficult or prevented for structural reasons. Thus, ω-substituted pivalophenones (**123**) with sodium hydroxide undergo fragmentation to benzoic acid and isobutene[35]. In this case cyclization to the ketal **124** can compete under certain conditions.



(123)

(124)

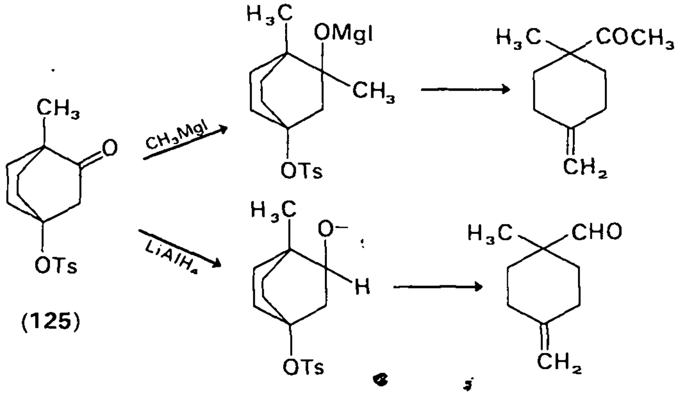
X = Cl, Br, I, OTs

1-Methyl-4-*p*-toluenesulphonyloxybicyclo[2.2.2]octanone-2 (**125**) undergoes fragmentation upon addition of the methyl Grignard reagent or with lithium aluminium hydride[36]. An excess of the nucleophilic reagent converts the products **126** and **127** into a tertiary and a primary alcohol, respectively.

The nucleofuge may be the oxygen atom of an epoxide, as in the reaction of the α,β-epoxyketone **128** with a Grignard reagent[37] or as in the treatment of the α-hydroxy epoxide **129** with acid[38].

In the first case, fragmentation is initiated by the addition of a nucleophile to the carbonyl group of **128**, and in the second by the addition of an electrophile to the epoxide oxygen of **129**.

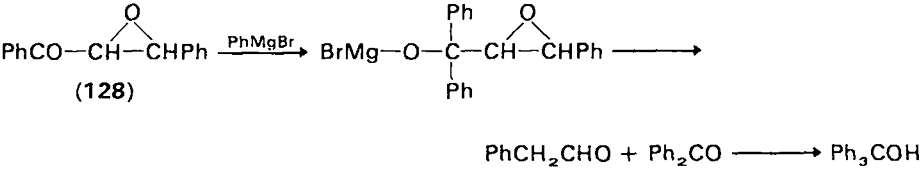
Finally, fragmentable species of the type under discussion may be produced *in situ* by protonation of unsaturated alcohols which are


CH3MgI
LiAlH4
H3C
OMgI
CH3
OTs
COCH3
CH2
O−
H
CHO

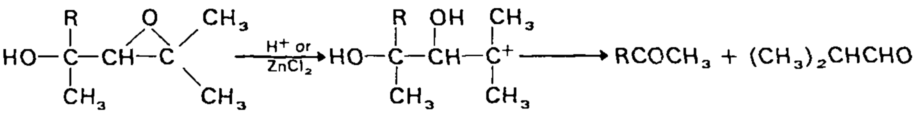
(125)

(126)

(127)

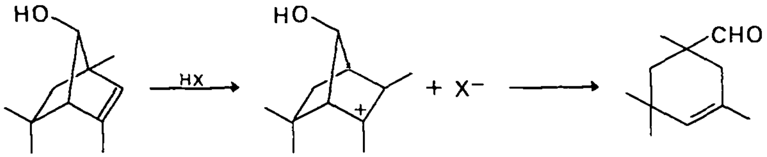

PhCO—CH—CHPh
PhMgBr
BrMg—O—C—CH—CHPh
Ph
PhCH2CHO + Ph2CO → Ph3COH

(128)


H+ or ZnCl2
RCOCH3 + (CH3)2CHCHO

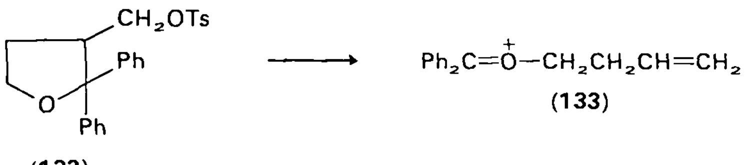
(129)

capable of yielding γ-hydroxycarbonium ions. Thus, *anti*-1,3,5,5-tetramethylbicyclo[2.2.1]hept-2-en-7-ol (**130**) when treated with acid[39] undergoes cleavage via the more stable tertiary carbonium ion **131**.



(130) (131)

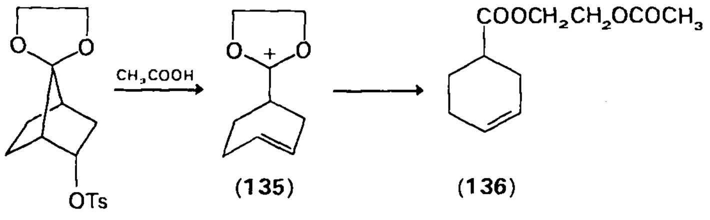
This reaction does not correspond to the definition of fragmentation given in Section I, since the cation **131** is not generated by the departure of a nucleofuge. However **131** may be formally regarded as being derived


CH2OTs
Ph
O
Ph2C=O+—CH2CH2CH=CH2

(132) (133)

from the addition product of **130** with HX, when it would fit the definition.

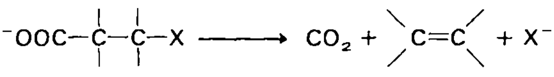
As a rule ethers do not fragment under normal circumstances even when the stereoelectronic conditions are optimal, as shown above for compound **34**. However, this does not apply when an exceptionally stable oxocarbonium ion results. Thus, the cation **133** is obtained upon heating the *p*-toluenesulphonate **132** in dimethyl sulphoxide. Hydrolysis of the former yields benzophenone and 3-buten-1-ol[40].



(134) **(135)** **(136)**

Relatively stable cations are also formed in the fragmentations of acetals and ketals of β-substituted carbonyl compounds, e.g. acetolysis of *endo*-7-ethylenedioxo-2-norbornyl *p*-toluenesulphonate (**134**) yields 57% of the acetate **136** via the dioxocarbonium ion **135**[41].

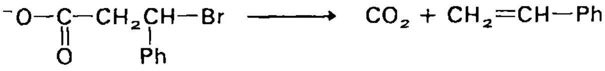
Anions of β-halo-, β-hydroxy- or β-ammonio acids (**137**, X = halogen, OH, R_3N^+) can undergo decarboxylative fragmentation to olefins, often in competition with 1,2-elimination of HX or cyclization to β-lactones (equation 22).



$$^{-}OOC{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}X \longrightarrow CO_2 + \mathrm{>C{=}C<} + X^{-} \qquad (22)$$

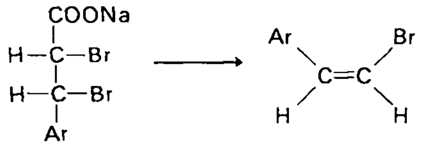
(137)

One of the first examples of this type involves the formation of styrene from a salt of 3-bromo-3-phenylpropionic acid (**138**) in water[42]. In non-polar solvents such as acetone, salts of *erythro*-2,3-dibromo-3-arylpropionic acids (**139**) fragment stereospecifically to (Z)-bromostyrene (**140**), evidently by a concerted mechanism[43].



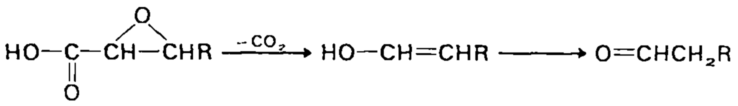
$$^{-}O{-}\underset{\underset{O}{\|}}{C}{-}CH_2\underset{\underset{Ph}{|}}{C}H{-}Br \longrightarrow CO_2 + CH_2{=}CH{-}Ph$$

(138)



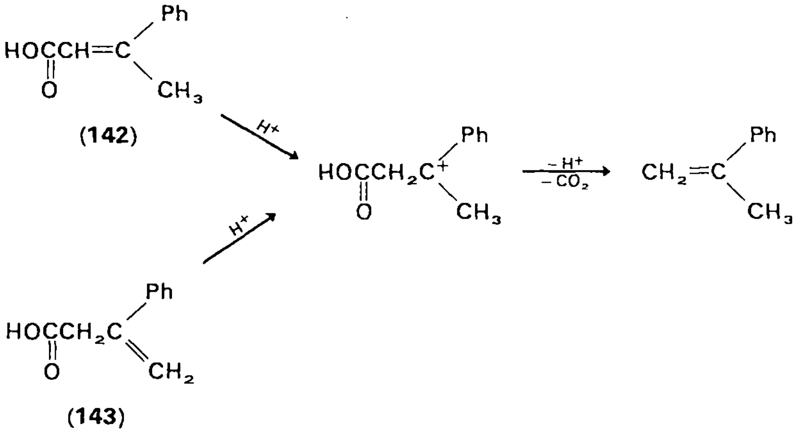
(139) (140)

An interesting variant is the Darzens reaction of α,β-epoxy (glycidic) acids (**141**), yielding the enol form of aldehydes by fragmentation[44].



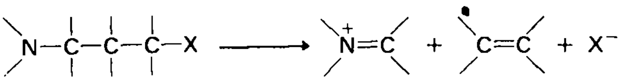
(141)

In principle, any carboxyl group β to a carbonium ion centre can undergo decarboxylation. Such cations are formed from α,β- and β,γ-unsaturated acids, e.g. **142** and **143**, by protonation of the double bond[45].



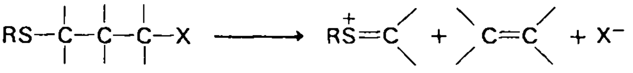
(142) (143)

The fragmentation of amines possessing a nucleofugal group in the 3-position (equation 23) has been discussed in great detail in Section II. Some of these reactions are of use in the degradation of alkaloids and other natural products[46].

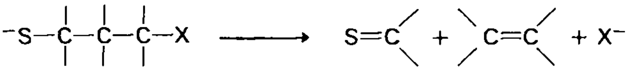


$$>N-\underset{|}{\overset{|}{C}}-\underset{|}{\overset{|}{C}}-\underset{|}{\overset{|}{C}}-X \longrightarrow >\overset{+}{N}=C< \; + \; >C=C< \; + \; X^- \qquad (23)$$

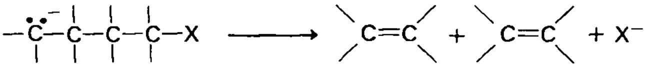
In analogy to 3-substituted alcohols and ethers, the fragmentation of the corresponding thio derivatives (**144**) would not be expected under solvolytic conditions, especially because the tendency for sulphur to form double bonds is smaller than for oxygen (equation 24). However, thiolate ions fragment in favourable cases (equation 25), as discussed in Section II.D.

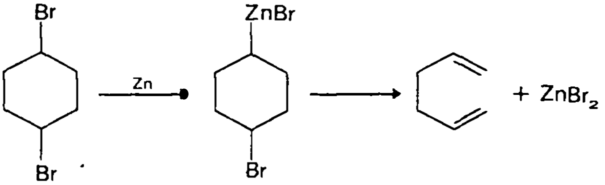

(24)

(144)

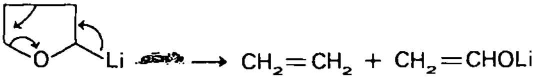

(25)

The electron donor in olefin-forming fragmentations can be carbon when it is present as a carbanion (equation 26). In this case the electrofugal fragment is also an olefin. In practice, the carbanionic centre is often part of an organometallic compound of zinc, magnesium or lithium. Thus, when 1,4-dibromocyclohexane (**145**) fragments to 1,5-hexadiene (**147**) with zinc in dioxane, the zinc compound **146** is probably an intermediate[3a].

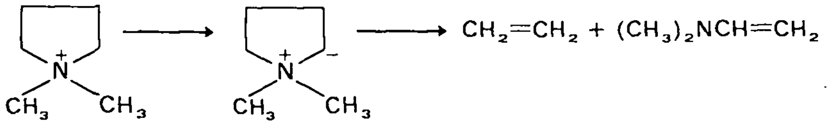

(26)


(145) (146) (147)

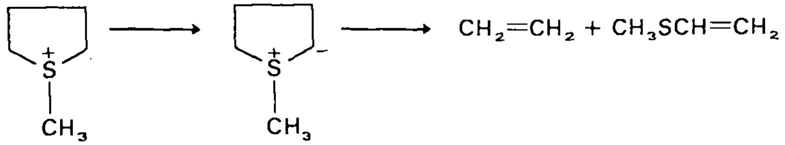
Furthermore, the notorious instability of organolithium compounds in tetrahydrofuran can be explained in this way[47]. Thus, butyllithium converts this solvent into the lithium derivative **148**, which fragments into ethylene and the enolate of acetaldehyde with a half-life of only 10 min at 35 °C.


(148)

Similar reactions occur when the five-membered cyclic ammonium and sulphonium salts **149**[48] and **150**[49] are converted to the respective ylids **151** and **152** by phenyllithium.

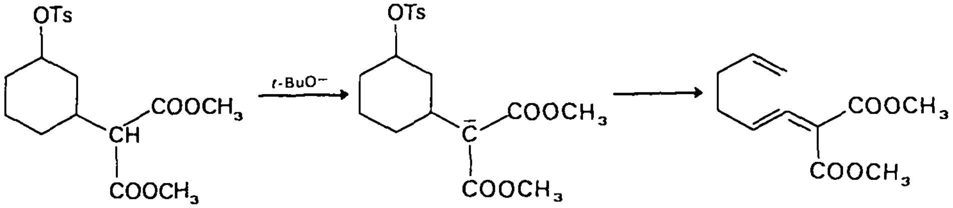

CH₂=CH₂ + (CH₃)₂NCH=CH₂

(149) (151)

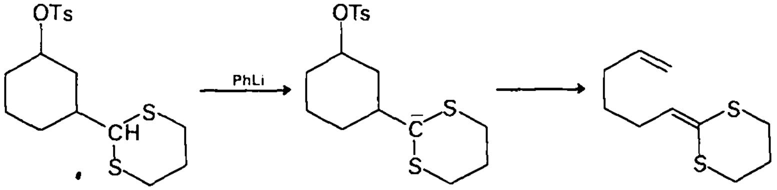

CH₂=CH₂ + CH₃SCH=CH₂

(150) (152)

In many cases a mesomeric carbanion is first generated by a strong base, as illustrated by the fragmentation of the malonic ester derivative (**153**)[50] and of the 1,3-dithiane (**154**)[51].

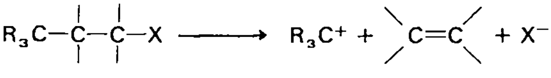

OTs
COOCH₃
CH
COOCH₃
t-BuO⁻
OTs
C
COOCH₃
COOCH₃
COOCH₃
COOCH₃

(153)


OTs
CH
S
S
PhLi
OTs
C
S
S
S
S

(154)

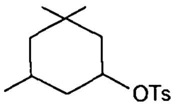
Compounds containing a nucleofuge β to a quaternary carbon atom should yield relatively stable carbonium ions (**155**, R = alkyl or aryl) upon fragmentation (equation 27).



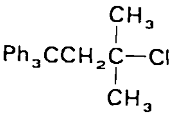
$$R_3C{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}X \longrightarrow R_3C^+ + \;\rangle C{=}C\langle\; + X^- \qquad (27)$$

(155)

In practice, however, the electrofugal activity of ordinary tertiary carbonium ions is not sufficient to permit cleavage under irreversible, solvolytic conditions. Thus, no fragmentation is observed in the solvolysis of *cis*- or *trans*-3,3,5-trimethylcyclohexyl *p*-toluenesulphonate (**156**)^{52}, of 3-chloro-3-methyl-1,1,1-triphenylbutane (**157**)^{53}, or 2-chloropentamethylpentane (**158**)^{53}. However, when the cation derived from **158** is generated by protonation of the olefin **159**, thermodynamically-controlled fragmentation leading to the *t*-butyl cation and 2,3-dimethyl-2-butene takes place. Relief of steric strain certainly contributes to the driving force of this reaction.

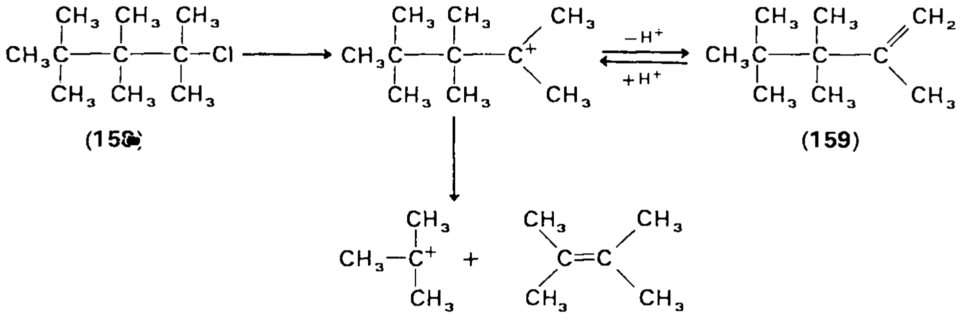


(156)



$$Ph_3CCH_2\overset{CH_3}{\underset{CH_3}{C}}{-}Cl$$

(157)

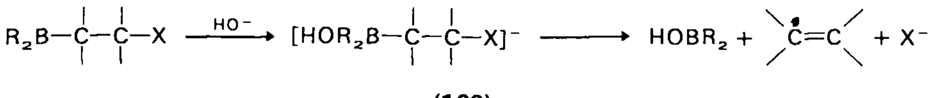


(158)

(159)

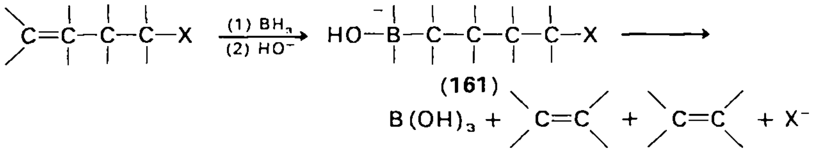
A host of further olefin-forming fragmentations results when electrofugal groups containing boron, nitrogen, silicon or phosphorus, combined with oxygen, are introduced on a carbon atom β to a nucleofugal group.

Thus, β-chloroalkylboron derivatives, which are obtained by hydroboration of vinyl chlorides, are known to decompose easily. Fragmentation is initiated by the addition of a nucleophile, such as hydroxyl ion or even water, yielding the boronate ion **160**^{54}.



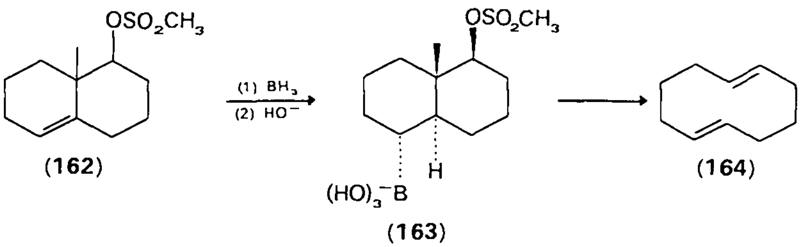
(160)

Boronate fragmentation has been extended to seven atomic centres (equation 28). Boron compounds bearing a nucleofuge in δ-position (**161**) are obtained by hydroboration of suitably substituted olefins. Addition of hydroxyl ion induces fragmentation, leading to two olefinic fragments, provided that the stereoelectronic conditions (Sections II.D) are fulfilled. This applies e.g. to the bicyclic boronate (**163**) obtained from the mesylate (**162**), which yields the cyclodecadiene (**164**) in a stereospecific reaction[55].



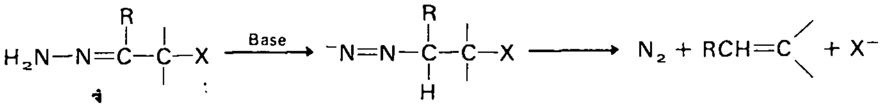
(161)

(28)



(162) **(163)** **(164)**

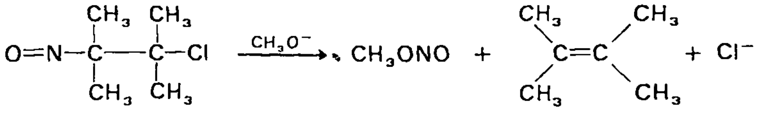
When the hydrazones of aldehydes and ketones bearing a α-nucleofuge (**165**) are treated with strong base under the conditions of the Wolff–Kishner reduction, olefins instead of saturated compounds are formed[56].



(165)

The release of nitrogen as the electrofugal fragment provides the driving force for this reaction, since it proceeds readily even with notoriously poor nucleofuges, such as the hydroxyl and amino groups.

The fragmentation of β-nitroso chlorides, such as **166**, to olefins with methoxide is of no preparative value, since they are prepared from the latter by addition of nitrosyl chloride[57]. However, the reaction is of interest as an example for the possible formation of alkyl nitrite (167) as the electrofugal fragment.



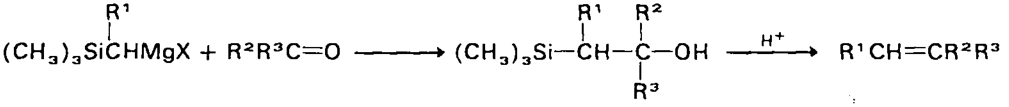
(166) **(167)**

2-Trimethylsilylethyl halides (**168**, R = CH_3, X = Cl, Br) are hydrolysed to trimethylsilanol (**169**) and ethylene[58]. The corresponding alcohol (**168**, R = CH_3, X = OH) undergoes fragmentation in acid solution[59]. The same fragmentation reaction is also observed with trialkoxysilylethyl halides (**168**, R = CH_3O, C_2H_5O)[60]. A synthetic application of this

$$R_3SiCH_2CH_2X \xrightarrow{H_2O} R_3SiOH + CH_2{=}CH_2$$

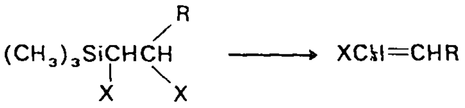
(168) **(169)**

type of fragmentation is the so-called Peterson olefination reaction. In this reaction β-trimethylsilylethanols (**171**), obtained from silylmethyl Grignard reagents (**170**) and ketones, are cleaved, e.g. in acid solution[61].



$$(CH_3)_3Si\overset{R^1}{C}HMgX + R^2R^3C{=}O \longrightarrow (CH_3)_3Si{-}\overset{R^1}{C}H{-}\underset{R^3}{\overset{R^2}{C}}{-}OH \xrightarrow{H^+} R^1CH{=}CR^2R^3$$

(170) **(171)**



(172)

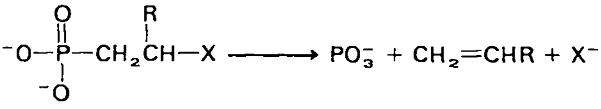
Vinyl halides are obtained stereospecifically by the fragmentation of 1,2-dihaloethylsilanes (**172**, X = Cl, Br)[62].

$$(C_6H_5)_3M{-}CH_2CH_2OH \xrightarrow{H_2O} (C_6H_5)_3M{-}OH + CH_2{=}CH_2$$

(173)

Group IV elements other than silicon can be components of the electrofugal fragment. Thus, the triphenyl germanium, tin and lead derivatives of ethanol (**173**, M = Ge, Sn, Pb) also undergo olefin-forming fragmentation[63].

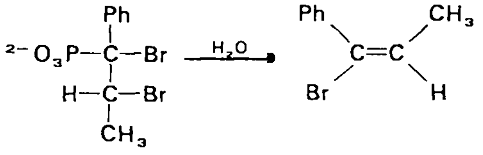
β-Halophosphonic acids (**174**) behave similarly to the β-halocarboxylic acids mentioned above. While relatively stable in neutral media, they fragment rapidly in alkaline solution with the formation of olefins and metaphosphate[64].



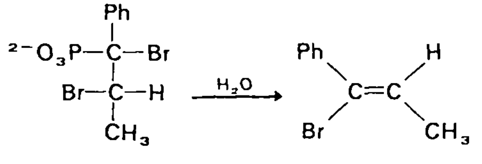
$$^{-}O-\overset{\overset{O}{\|}}{\underset{\underset{^{-}O}{|}}{P}}-CH_2\overset{\overset{R}{|}}{C}H-X \longrightarrow PO_3^{-} + CH_2{=}CHR + X^{-}$$

(174)

As shown by the stereoisomeric 1,2-dibromo-1-phenylpropylphosphonic acids (**175**), the electrofugal and nucleofugal fragments are released in an antiplanar conformation, since the *erythro* form (**175a**) yields (*E*)-1-bromo-1-phenylpropene (**176a**) and the *threo* form (**175b**) the (*Z*) isomer (**176b**) stereospecifically[65].



(175a) **(176a)**



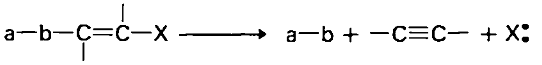
(175b) **(176b)**

Fragmentation also occurs when β-chloroethyl arsenic derivatives such as **177** are treated with base[66].

$$Cl_2AsCH_2CH_2Cl \xrightarrow{NaOH} As_2O_3 + CH_2{=}CH_2 + Cl^{-}$$

(177)

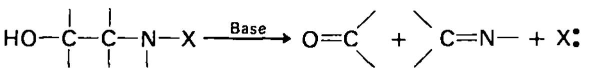
Alkyne-forming fragmentation (equation 29) lies outside the scope of this chapter†. The main electrofugal groups a—b— encountered to date are $^{-}$OC—, $^{-}$OOC—, R_3Si— and —$PO_3{}^{2-}$.



$$\mathrm{a{-}b{-}C{=}C{-}X} \longrightarrow \mathrm{a{-}b} + \mathrm{{-}C{\equiv}C{-}} + \mathrm{X{:}} \qquad (29)$$

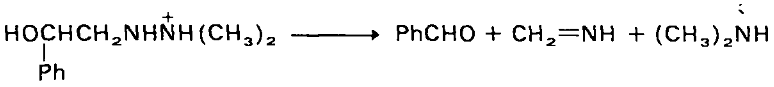
B. Imine-forming Fragmentation

In the reactions discussed so far, the nucleofuge X was attached to a carbon atom. Therefore nucleophilic substitution, 1,2-elimination and cyclization frequently competed with fragmentation. When the nucleofuge is attached to a heteroatom, such as nitrogen or oxygen, nucleophilic substitution is no longer important. However, rearrangement is frequently observed. The stereoelectronic requirements for fragmentation remain the same.



(30)

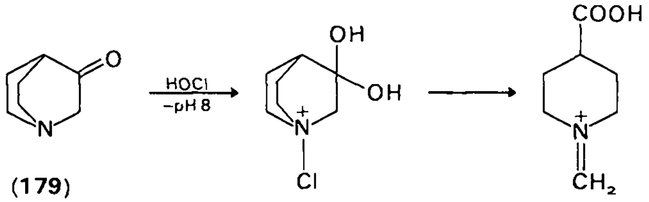
Many imine-forming fragmentations are useful degradation reactions, e.g. for alkaloids. Thus, β-aminoalcohols containing a nucleofuge on the nitrogen atom, undergo fragmentation to imines in the presence of base (equation 30). The nucleofuge X is frequently chlorine[68], because N-chloro amines are readily obtained with N-chlorosuccinimide and other chlorinating agents.



$$\mathrm{HOCH(Ph)CH_2NH\overset{+}{N}H(CH_3)_2} \longrightarrow \mathrm{PhCHO} + \mathrm{CH_2{=}NH} + \mathrm{(CH_3)_2NH}$$

(178)

Acid-catalysed fragmentation is illustrated by the reaction of N,N-dimethyl-N'-(2-hydroxy-2-phenylethyl)hydrazinium ion (**178**), which undergoes N—N bond cleavage[69].



(179)

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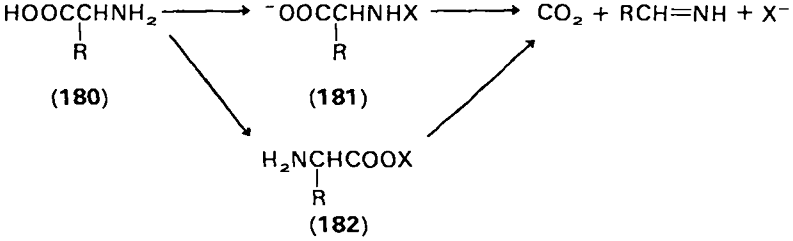
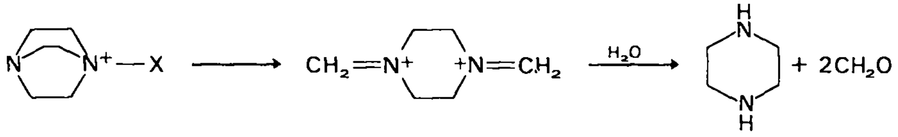
† Some cases are described in a recent monograph[67].

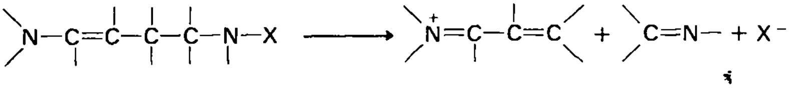
Even α-amino ketones can be cleaved when the amino and carbonyl groups are suitably modified, as in the fragmentation of 3-quinuclidone (**179**) by aqueous hypochlorous acid[70].

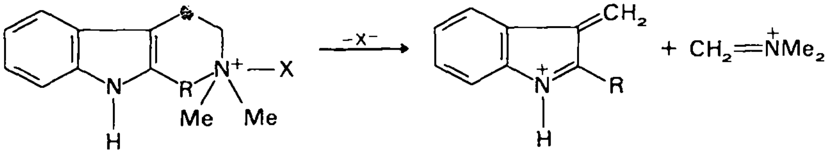

(**180**) (**181**) (**182**)

α-Amino acids (**180**) are decarboxylated by halogenating agents, such as hypochlorite or *N*-bromosuccinimide[71]. *N*-Haloamino acids (**181**) are probable intermediates, but fragmentation via an acyl hypohalite (**182**) cannot be ruled out, since the same products would result.

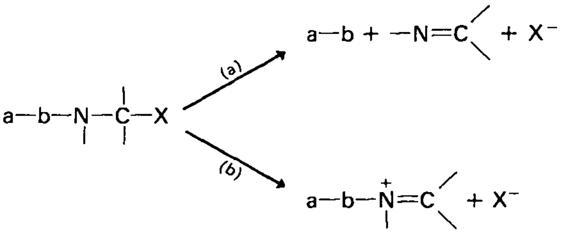
1,2-Diamines are also cleaved, if a nucleofuge can be attached to one of the nitrogen atoms, as in the 1,4-diazabicylo[2.2.2]octane **183**, where X is either benzoate[72] or chlorine[73]. The atomic sequence **184** is the vinylogue of the sequence N—C—C—N—X and should therefore also undergo fragmentation. This is illustrated by the cleavage of the *N*-trifluoroacetate **185a** derived from the *N*-oxide of the tryptamine derivate **185**[74].


(**183**)
X = Cl, OCOPh


(**184**)


(**185**) X = O^-
(**185a**) X = $OCOCF_3$

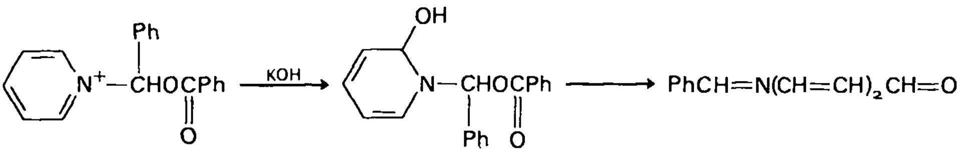
It is interesting to speculate as to whether imine-forming fragmentation would also occur if the nucleofuge were attached to carbon and the electrofuge to nitrogen (Scheme 8, path a). In most cases ionization to the stable immonium ion **186** (or the corresponding imine) should dominate (path b). This would account for the fact that examples of reactions following path (a) are hard to find.



(186)

SCHEME 8.

An example is the fragmentation of *N*-(α-benzoyloxybenzyl)-pyridinium chloride (**187**) with concentrated aqueous potassium hydroxide via the pseudo-base **188**^{75}.

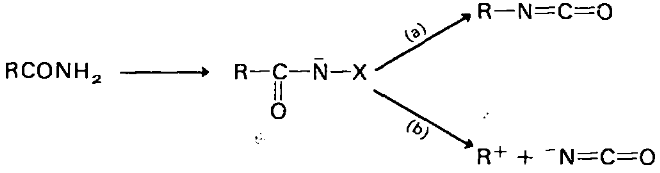


(187) (188)

C. Cyanate-forming Fragmentation

In the Hofmann, Curtius or Lossen degradation of amides, the release of the nucleofuge from the nitrogen atom in the corresponding intermediate **189** is normally accompanied by migration of the group R to form an isocyanate (Scheme 9, path a)^{76}. However, if R is an active electrofugal group, fragmentation (path b) competes with rearrangement.

This applies to amides of α-hydroxy, α-keto and α-amino acids^{77}. Thus, in the Hofmann degradation of α-hydroxy amides (**190**, $R^1 = H$) with sodium hypobromite, no rearranged isocyanate **191** is formed. This suggests that direct fragmentation of the intermediate **192** to the aldehyde

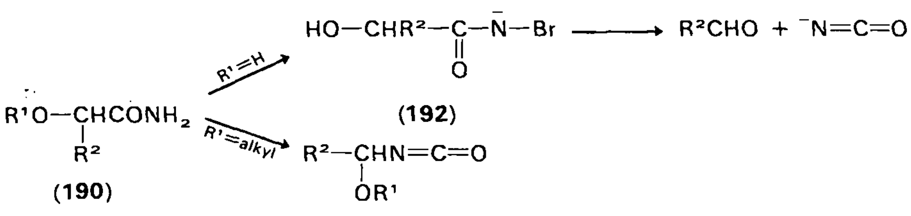


(189)

X = halogen, N_2^+, OCOR

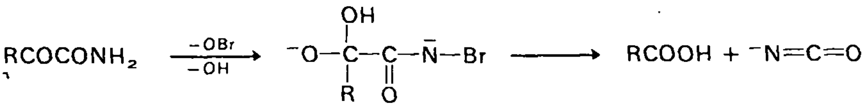
SCHEME 9.

and cyanate ion takes place. By contrast, the corresponding ethers (**190**, R^1 = alkyl) yield the expected rearranged isocyanates **191**[78].



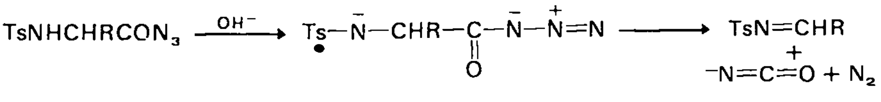
(192) **(190)** **(191)**

The Hofmann degradation of α-ketoamides (**193**) by hypobromite, which leads to carboxylic acids and cyanate ion, can be formulated as a fragmentation of the anion of the *N*-bromo ketone hydrate **194**[79].



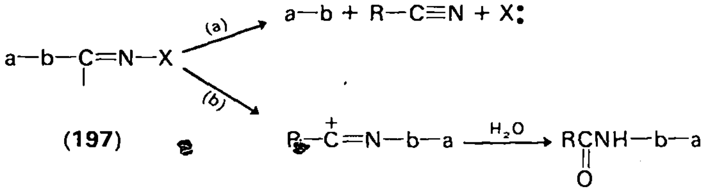
(193) **(194)**

Finally, an interesting reaction of azides of *N*-*p*-toluenesulphonyl-α-aminoacids (**195**) can be rationalized as a cyanate-forming fragmentation. Stable in neutral solution, these compounds decompose when alkali is added, suggesting a fragmentation of their conjugate bases **196**[80].



(195) **(196)**

The unsaturated fragment resulting from heterolytic fragmentation can also be a nitrile. In fact any ketoxime (**197**, X = OH) containing a potentially electrofugal substituent a—b, will undergo fragmentation (Scheme 10, path a) rather than Beckmann rearrangement (path b), when the hydroxyl group is converted into an active nucleofuge, e.g. by protonation or conversion to an ester such as *p*-toluenesulphonate.

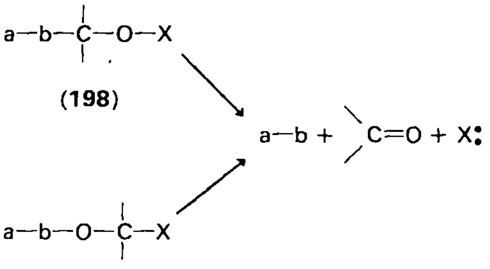


SCHEME 10.

A nitrile is then formed instead of an amide. However, these so-called Beckmann fragmentations[81] are beyond the scope of this chapter, since they involve the formation of a triple-bonded function†.

D. Carbonyl-forming Fragmentation

Carbonyl-forming fragmentations can be subdivided according to the site of the nucleofuge, i.e. on oxygen (**198**) or on carbon (**199**). Furthermore, depending on the nature of the substituents attached to the carbon atom of **198** and **199**, the resulting carbonyl fragment may be an aldehyde, a ketone, a carboxylic acid or even carbon dioxide (equation 31). In most



(31)

cases the nucleofuge is attached to oxygen, as in **198**. This class will therefore be discussed first. Such compounds are frequently derived from hydroperoxides (**200**) which can undergo the Criegee rearrangement to semiacetals or semiketals (**201**) upon protonation or esterification of the hydroxyl group[76,83]. In the case of the Baeyer–Villiger reaction, an intermediate of type **202** is formed which leads to an ester by rearrangement[76,84]. Rearrangement will therefore compete with fragmentation when the electrofugal activity of a—b in **198** is too low to permit fragmentation.

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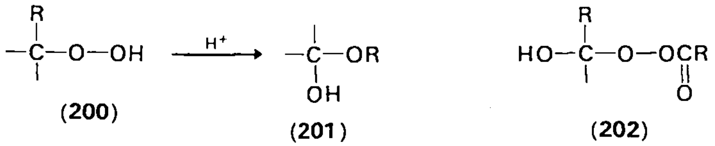
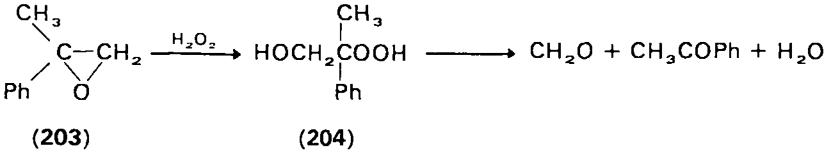
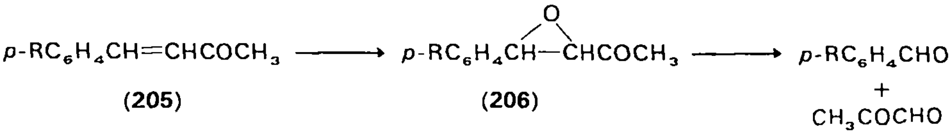
† These reactions have been reviewed recently[3c,82].


(200) (201) (202)

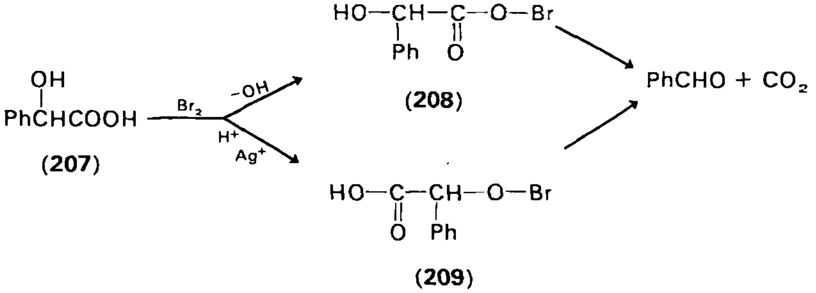
However, fragmentation clearly dominates in systems of the type HO—C—C—O—X, which are formed by ring opening of epoxides with alkaline hydrogen peroxide, e.g. the epoxide **203** yields the isolable hydroperoxide **204**, which undergoes acid and base catalysed or thermal cleavage to acetophenone and formaldehyde[85,86].


(203) (204)

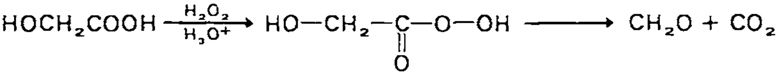
The cleavage of α,β-unsaturated ketones such as **205** with alkaline hydrogen peroxide has been shown to occur in the same manner, i.e. by way of the epoxide **206**[87].


(205) (206)

α-Hydroxy carboxylic acids are decarboxylated by bromine in alkaline or acidic solution with formation of aldehydes. This reaction is analogous to the oxidative decarboxylation of α-amino acids described in Section III.B, in that two fragmentable intermediates could be formed either by attack of bromine on the carboxyl group (**208**) or on the hydroxyl group (**209**). From a detailed study of the oxidation of mandelic acid (**207**) it was concluded that the intermediates are the acylhypobromite (**208**) in alkaline and the α-carboxyhypobromite (**209**) with silver ion in acid solution[88].



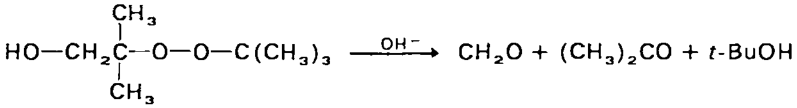
(207) (208) (209)



$$HOCH_2COOH \xrightarrow[H_3O^+]{H_2O_2} HO{-}CH_2{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}O{-}OH \longrightarrow CH_2O + CO_2$$

(210) (211)

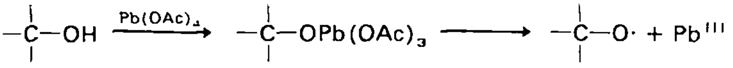
No stable α-hydroxyperacid has been found so far. The simplest case, hydroperoxyacetic acid (**211**), decomposes in acid solution to formaldehyde and carbon dioxide and may be an intermediate in the oxidation of glycolic acid (**210**)[89]



$$HO{-}CH_2\underset{CH_3}{\overset{CH_3}{\underset{|}{\overset{|}{C}}}}{-}O{-}O{-}C(CH_3)_3 \xrightarrow{OH^-} CH_2O + (CH_3)_2CO + t\text{-}BuOH$$

(212)

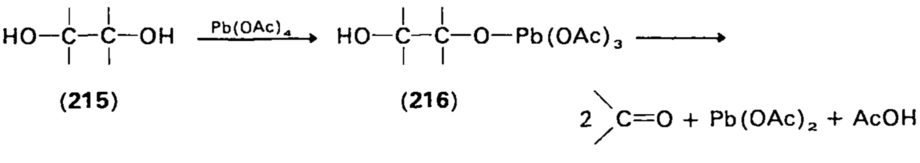
A variant of this type of fragmentation is the base-catalysed cleavage of the β-hydroxy-*t*-butylperoxide **212**, which has been shown to be a heterolytic rather than a homolytic reaction[90].



$$-\underset{|}{\overset{|}{C}}-OH \xrightarrow{Pb(OAc)_4} -\underset{|}{\overset{|}{C}}-OPb(OAc)_3 \longrightarrow -\underset{|}{\overset{|}{C}}-O\cdot + Pb^{III}$$

(213) (214)

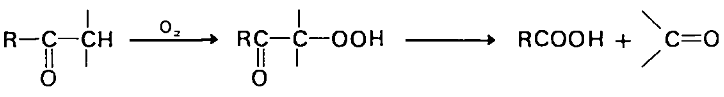
The oxidation of alcohols with lead tetraacetate proceeds via the lead alkoxide **213** and is a homolytic process, as evidenced by the products derived from the intermediate alkoxy radicals **214**[91]. However, the oxidation of 1,2-diols (**215**) by this reagent, leading to carbonyl compounds, is normally a heterolytic reaction, since it is accelerated by acids and bases, but not by peroxides. A carbonyl-forming fragmentation involving the intermediate **216** is therefore indicated†. This reaction is an example of a fragmentation initiated by a nucleofugal metal atom, which can change its oxidation number. In contrast to periodic acid, lead tetraacetate cleaves both *cis* and *trans* diols[92].



$$\mathrm{HO{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}OH} \xrightarrow{\mathrm{Pb(OAc)_4}} \mathrm{HO{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}O{-}Pb(OAc)_3} \longrightarrow 2\,\mathrm{{>}C{=}O} + \mathrm{Pb(OAc)_2} + \mathrm{AcOH}$$

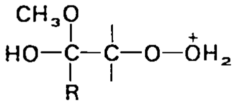
(215) **(216)**

α-Hydroperoxyketones (**217**), which are obtained from enolizable ketones by oxidation with air, are cleaved under acidic or basic conditions to acids and carbonyl compounds[93]. When methanol is the solvent, an ester is obtained which points to the formation of fragmentable intermediates such as **218** and **219**.



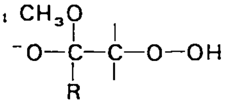
$$\mathrm{R{-}\underset{\underset{O}{\|}}{C}{-}\overset{|}{\underset{|}{C}}H} \xrightarrow{O_2} \mathrm{R\underset{\underset{O}{\|}}{C}{-}\overset{|}{\underset{|}{C}}{-}OOH} \longrightarrow \mathrm{RCOOH} + \mathrm{{>}C{=}O}$$

(217)



$$\mathrm{HO{-}\overset{\overset{CH_3O}{|}}{\underset{\underset{R}{|}}{C}}{-}\overset{|}{\underset{|}{C}}{-}O{-}\overset{+}{O}H_2}$$

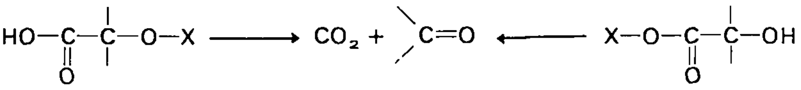
(218)



$$\mathrm{{}^{-}O{-}\overset{\overset{CH_3O}{|}}{\underset{\underset{R}{|}}{C}}{-}\overset{|}{\underset{|}{C}}{-}O{-}OH}$$

(219)

The cleavage of α-hydroxy acids (**220**, X = H) by oxidizing agents, such as lead tetraacetate, is clearly a carbonyl-forming fragmentation[94]. However, it is often difficult to decide whether the nucleofuge becomes attached to the hydroxyl group, as in **220**, or to the carbonyl group, as in **221**.



$$\mathrm{HO{-}\underset{\underset{O}{\|}}{C}{-}\overset{|}{\underset{|}{C}}{-}O{-}X} \longrightarrow \mathrm{CO_2} + \mathrm{{>}C{=}O} \longleftarrow \mathrm{X{-}O{-}\underset{\underset{O}{\|}}{C}{-}\overset{|}{\underset{|}{C}}{-}OH}$$

(220) **(221)**

α-Keto acids are decarboxylated with hydrogen peroxide in alkaline solution, presumably via the intermediate **222**[95]. The carbonyl compound which is formed is a carboxylic acid. The oxidation of oxalic acid (**223**) with a variety of reagents is a carbon-dioxide-forming fragmentation[96].

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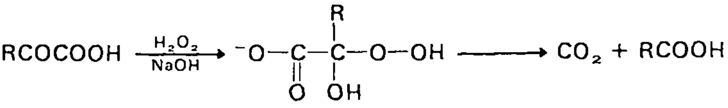
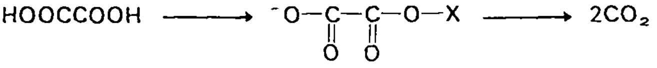
† In this context it is irrelevant whether both electrons are transferred to $\mathrm{Pb^{IV}}$ simultaneously, or one at a time.



$$\mathrm{RCOCOOH} \xrightarrow[\mathrm{NaOH}]{\mathrm{H_2O_2}} {}^{-}\mathrm{O}-\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}-\overset{\overset{\mathrm{R}}{|}}{\underset{\underset{\mathrm{OH}}{|}}{\mathrm{C}}}-\mathrm{O}-\mathrm{OH} \longrightarrow \mathrm{CO_2} + \mathrm{RCOOH}$$

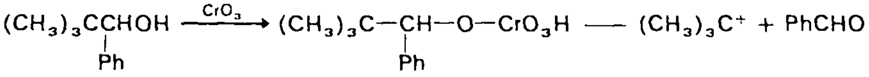
(222)



$$\mathrm{HOOCCOOH} \longrightarrow {}^{-}\mathrm{O}-\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}-\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}-\mathrm{O}-\mathrm{X} \longrightarrow 2\mathrm{CO_2}$$

(223)

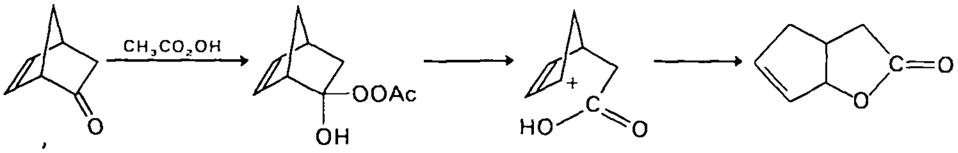
The oxidation of secondary alcohols with chromic acid can lead to varying amounts of fragmentation products in addition to the corresponding ketone if the β-carbon atom is highly substituted[97]. Thus, the oxidation of 2,2-dimethyl-1-phenyl-1-propanol (**224**) yields, via the intermediate **225**, 70% of benzaldehyde and products derived from the *t*-butyl cation[98].



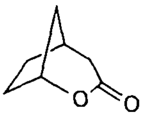
$$(\mathrm{CH_3})_3\underset{\underset{\mathrm{Ph}}{|}}{\mathrm{C}}\mathrm{CHOH} \xrightarrow{\mathrm{CrO_3}} (\mathrm{CH_3})_3\mathrm{C}-\underset{\underset{\mathrm{Ph}}{|}}{\mathrm{CH}}-\mathrm{O}-\mathrm{CrO_3H} \longrightarrow (\mathrm{CH_3})_3\mathrm{C}^{+} + \mathrm{PhCHO}$$

(224) (225)

The Baeyer–Villiger oxidation of ketones to esters can also be superseded by carbonyl-forming fragmentation if the substituent α to the original carbonyl group is an active electrofuge. This is illustrated by the reaction of dehydronorcamphor (**226**) with peracetic acid, which does not furnish the expected lactone **230**. Instead, the intermediate **227** undergoes fragmentation to an allylic cation **228**, which cyclizes to the lactone **229**[99].

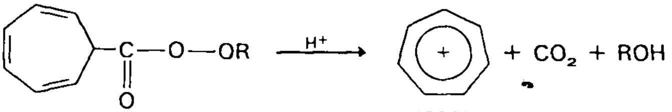


(226) (227) (228) (229)

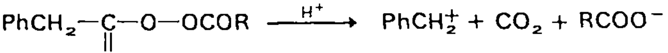


(230)

A number of peresters and acyl peroxides undergo acid-catalysed heterolytic fragmentation instead of homolytic decomposition when stable cations, such as the tropylium ion (**231**)[100], the benzyl cation (**232**)[101] or the cyclopropylmethyl cation (**233**)[102] are formed.

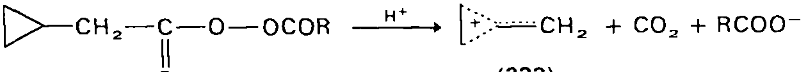

C—O—OR
O
H+
+ CO₂ + ROH

(231)



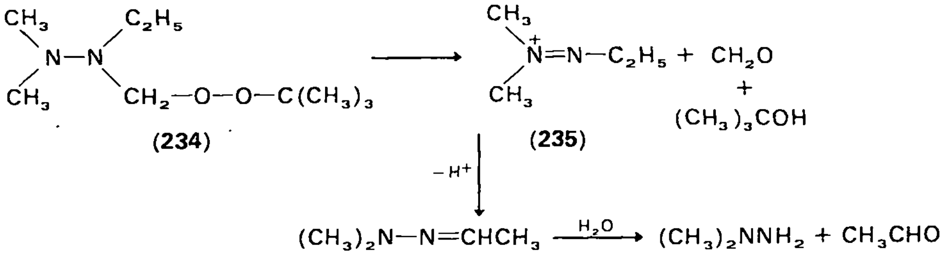
$PhCH_2-\underset{\underset{O}{\|}}{C}-O-OCOR \xrightarrow{H^+} PhCH_2^+ + CO_2 + RCOO^-$

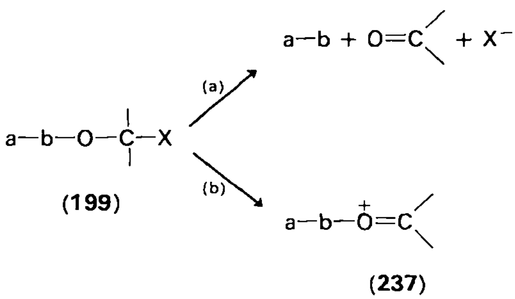
(232)


CH₂—C—O—OCOR
O
H+
CH₂
+ CO₂ + RCOO⁻

(233)

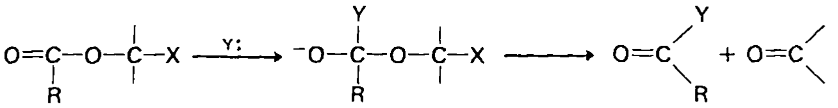
The peroxide **234** is of particular interest, since it yields an unusual electrofugal fragment, namely the cation **235** besides formaldehyde and *t*-butanol[103]. The cation **235** is the conjugate acid of the hydrazone of *N*,*N*-dimethylhydrazine and acetaldehyde (**236**), which are formed upon hydrolysis.


CH₃
C₂H₅
N—N
CH₃
CH₂—O—O—C(CH₃)₃
(234)
CH₃
N=N—C₂H₅ + CH₂O
CH₃
+
(CH₃)₃COH
(235)
−H+
(CH₃)₂N—N=CHCH₃
H₂O
(CH₃)₂NNH₂ + CH₃CHO
(236)


a—b + O=C + X⁻
(a)
a—b—O—C—X
(199)
(b)
a—b—O=C
(237)

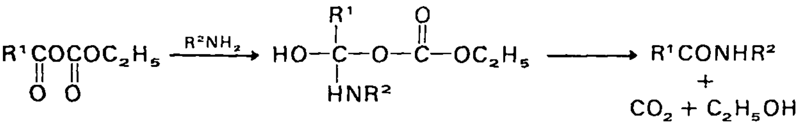
SCHEME 11.

Carbonyl-forming fragmentation (Scheme 11, path a) of compounds of the type **199** are rarer because these are frequently too unstable to be isolated. This is because the nucleofuge is attached to a carbon atom next to oxygen and its departure leads to a relatively stable oxocarbonium ion **237** (path b). It is therefore not surprising that the fragmentable system **199** often has to be generated *in situ* from a stable precursor. Even then simple ionization (path b) has to be taken into account.



(238) **(239)**

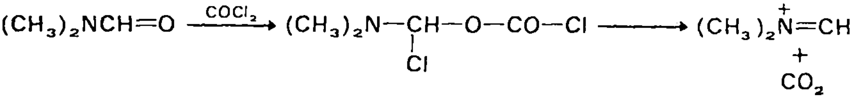
Thus, many fragmentations of this type involve the formation of a fragmentable system **239** through the prior addition of a nucleophile to an α-acyloxy derivative **238**. When the nucleophile Y is hydroxide ion, alkoxide ion or an amine, an acid, an ester or an amide, respectively, is formed beside the carbonyl compound[104].



$$R^1\underset{O}{\overset{}{C}}O\underset{O}{C}OC_2H_5 \xrightarrow{R^2NH_2} HO{-}\overset{R^1}{\underset{HNR^2}{C}}{-}O{-}\overset{O}{C}{-}OC_2H_5 \longrightarrow R^1CONHR^2 + CO_2 + C_2H_5OH$$

(240)

Similarly, mixed anhydrides between a carboxylic acid and carbonic acid (**240**) yield amides and carbon dioxide when treated with amines[105], a reaction widely used in peptide synthesis[106]. These mixed anhydrides are also employed in the acylation of alcohols and thiols[105,107].



$$(CH_3)_2NCH{=}O \xrightarrow{COCl_2} (CH_3)_2N{-}\underset{Cl}{CH}{-}O{-}CO{-}Cl \longrightarrow (CH_3)_2\overset{+}{N}{=}CHCl\ Cl^- + CO_2$$

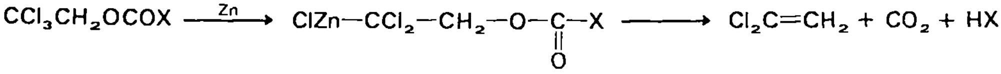
(241)

(242)

The preparation of *N*,*N*-dimethylformamide chloride (**242**), a useful reagent in the Vilsmeier formylation of aromatic compounds, provides a further example for CO_2-forming fragmentation[108]. Dimethylformamide is reacted with phosgene, yielding the fragmentable intermediate **241**.

$$\underset{(243)}{PhCH_2CH_2OCOCH_2SO_2Ph} \xrightarrow{t\text{-BuO}^-} PhCH{=}CH_2 + CO_2 + \underset{(244)}{^-CH_2SO_2Ph}$$

The decomposition of the α-sulphone ester **243** with potassium *t*-butylate is initiated by the removal of a proton from the benzylic carbon atom. In this CO_2-forming fragmentation the mesomeric phenylsulphonylmethide (**244**) assumes the role of the nucleofuge[109].



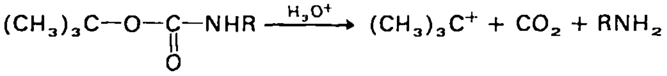
$$CCl_3CH_2OCOX \xrightarrow{Zn} ClZn{-}CCl_2{-}CH_2{-}O{-}\underset{\underset{O}{\|}}{C}{-}X \longrightarrow Cl_2C{=}CH_2 + CO_2 + HX$$

(245)

Trichloroethoxycarbonyl is a general protecting group for amines, alcohols and thiols, as in **245**, X = NHR, OR or SR. It is removed by zinc in a protic solvent[110] or by electrolytic reduction[111].

$$ROH \xrightarrow{COCl_2} \underset{(246)}{R{-}O{-}CO{-}Cl} \xrightarrow{-CO_2} R^+Cl^- \longrightarrow RCl$$

In the conversion of alcohols to alkyl chlorides by phosgene, alkyl chloroformates (**246**) are relatively stable intermediates[112]. Their rates of decomposition parallel the stability of the resulting carbonium ions. The decomposition of **246** is therefore a concerted CO_2-forming fragmentation. The carbonium ions subsequently combine with chloride ions to form alkyl chlorides[113,114].



$$(CH_3)_3C{-}O{-}\underset{\underset{O}{\|}}{C}{-}NHR \xrightarrow{H_3O^+} (CH_3)_3C^+ + CO_2 + RNH_2$$

(247) **(248)**

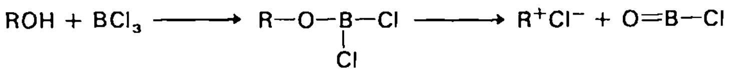
The facile formation of the *t*-butyl cation (**248**) as the electrofugal fragment is the basis for the widespread use of the *t*-butyl group in the temporary protection of functional groups. Thus, *t*-butoxycarbonyl derivatives of amines (**247**) are readily cleaved by acids with the liberation of the amine, CO_2 and the *t*-butyl cation (**248**) which is subsequently converted to isobutene[115].

$$RO^- + \underset{(249)}{:CX_2} \longrightarrow \underset{(250)}{R{-}O{-}\ddot{C}{-}X} \longrightarrow R^+ + \ddot{C}{=}O + X^-$$

The so-called deoxideation of alkoxide ions makes use of a carbon-monoxide-forming fragmentation. In this reaction a haloalkoxy carbene (**250**), formed from the alkoxide ion and a dihalocarbene (**249**, X = Br or Cl) fragments to a highly reactive carbonium ion, carbon monoxide and halide ion[116].

E. Heteroxide-forming Fragmentation

Oxides other than those of carbon can form unsaturated fragments, as shown by the following examples involving boron, sulphur and phosphorus.



$$\mathrm{ROH + BCl_3 \longrightarrow R{-}O{-}\underset{\displaystyle Cl}{\underset{|}{B}}{-}Cl \longrightarrow R^+Cl^- + O{=}B{-}Cl}$$

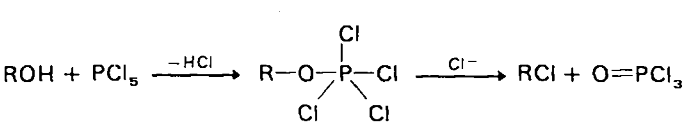
(**251**) (**252**)

Thus, in the preparation of alkyl chlorides from alcohols and boron trichloride, dichloroborinates (**251**) are formed, which fragment to BOCl and an ion pair **252**, the precursor of the alkyl chloride[117].

$$\mathrm{ROH + SOCl_2 \longrightarrow R{-}O{-}SO{-}Cl \xrightarrow{SO_2} R^+Cl^- \longrightarrow RCl}$$

(**253**)

Further, the widespread preparation of alkyl chlorides from alcohols and thionyl chloride involves the fragmentation of the intermediate alkyl chlorosulphite (**253**). In this case the unsaturated fragment is sulphur dioxide[113,118].



$$\mathrm{ROH + PCl_5 \xrightarrow{-HCl} R{-}O{-}\overset{\displaystyle Cl}{\overset{|}{\underset{Cl\quad Cl}{P}}}{-}Cl \xrightarrow{Cl^-} RCl + O{=}PCl_3}$$

(**254**)

In the synthesis of alkyl halides from alcohols (or acyl halides from acids) with phosphorus tri- and pentahalides, a phosphorous ester is first formed, e.g. **254** in the case of PCl_5. The latter then fragments with concomitant formation of a P=O bond[119]. This fragmentation does not yield a free carbonium ion when R is primary, but involves attack by chloride ion at the group R of the ester **254** in a displacement-induced fragmentation (Section III.H).

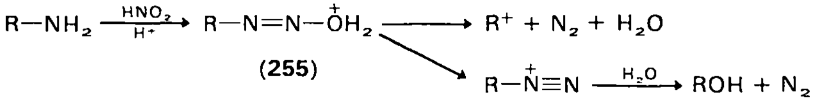
F. Nitrogen-forming Fragmentation

Azo compounds $R^1—N{=}N—R^2$ normally undergo homolytic cleavage with the formation of nitrogen[120]. Only when R^1 and R^2 are electrofugal and nucleofugal groups, respectively, does heterolytic fragmentation dominate (equation 32). However, due to the high energy of formation of molecular nitrogen, fragmentation occurs even when the tendency to form the corresponding electrofugal and nucleofugal fragments is small.

$$a—b—N{=}N—X \longrightarrow a—b + N_2 + X\colon \qquad (32)$$

It is debatable whether this type of fragmentation should be included in a chapter concerned primarily with the formation of double-bonded organic functional groups. However, the liberation of molecular nitrogen as the unsaturated fragment is often accompanied by the formation of unusual electrofugal and nucleofugal fragments. In addition to their use in synthesis, nitrogen-forming fragmentations serve to illustrate further mechanistic principles, and they have not been reviewed recently.

The well-known deamination of primary amines with nitrous acid represents a fragmentation of the intermediate protonated alkyl diazoniumhydroxide (**255**). With secondary and tertiary alkyl substituents its decomposition is concerted and instantaneous. With primary alkyl substituents fragmentation takes place stepwise and diazonium ions (**256**) are true intermediates, as in the case of aryl diazonium salts[116,121].

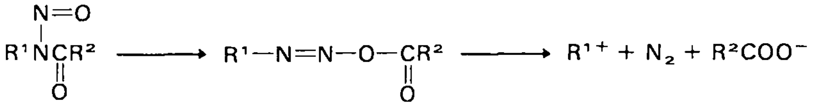


$$R—NH_2 \xrightarrow[H^+]{HNO_2} R—N{=}N—\overset{+}{O}H_2 \longrightarrow R^+ + N_2 + H_2O$$

$$R—N{=}N—\overset{+}{O}H_2 \longrightarrow R—\overset{+}{N}{\equiv}N \xrightarrow{H_2O} ROH + N_2$$

(255) (256)

A carboxylate ion is the nucleofuge in the fragmentation of *N*-nitrosoamides (**257**), which is preceded by rearrangement to diazoacyloxy derivatives **258**[122]. In the fragmentation of triazenes (**259**), which are formed by the coupling of alkylamines and aryldiazonium salts, protonation to **260** is required to generate a nucleofugal arylammonio group[123].

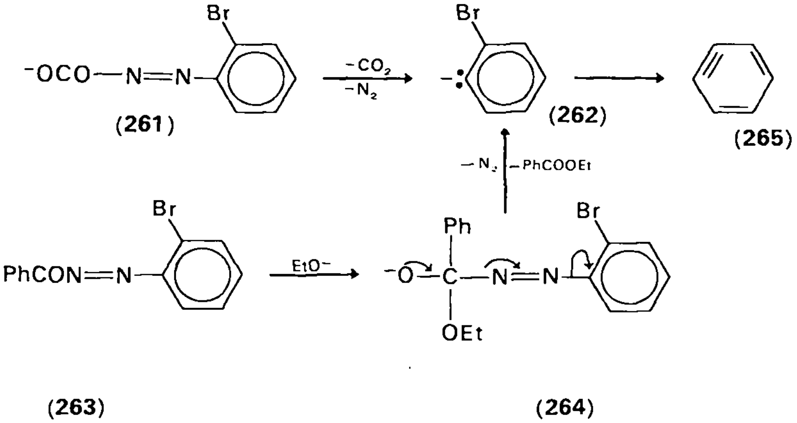


$$R^1\overset{\overset{\displaystyle N=O}{|}}{N}\underset{\underset{\displaystyle O}{\|}}{C}R^2 \longrightarrow R^1—N{=}N—O—\underset{\underset{\displaystyle O}{\|}}{C}R^2 \longrightarrow R^{1+} + N_2 + R^2COO^-$$

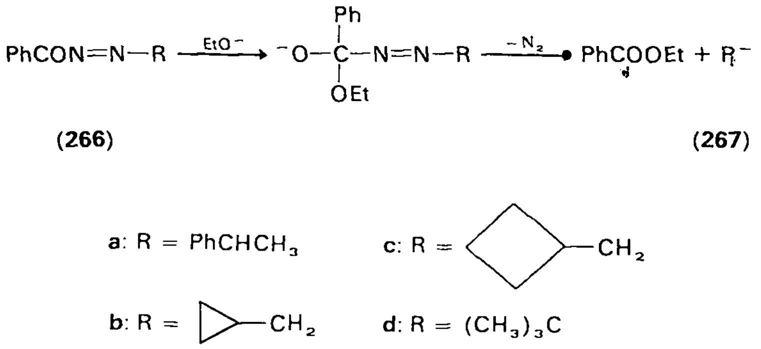
(257) (258)

$$RNH_2 \xrightarrow{ArN_2^+} \underset{(259)}{RNHN{=}NAr} \xrightarrow{H^+} \underset{(260)}{R—N{=}N—\overset{+}{N}H_2Ar} \longrightarrow R^+ + N_2 + ArNH_2$$

The driving force associated with the formation of molecular nitrogen is such that substituents, which do not normally show nucleofugal activity, are released as carbanions, e.g. *o*-bromophenylazocarboxylate (**261**) fragments with liberation of carbon dioxide and nitrogen to *o*-bromobenzene anion (**262**)^{124}. The same anion is formed together with ethyl benzoate when the ketone **263** is treated with sodium ethoxide, evidently by way of the adduct **264**. Under the reaction conditions the aryl anion **262** is protonated. However, some elimination of bromide ion with the formation of benzyne (**265**) also occurs.



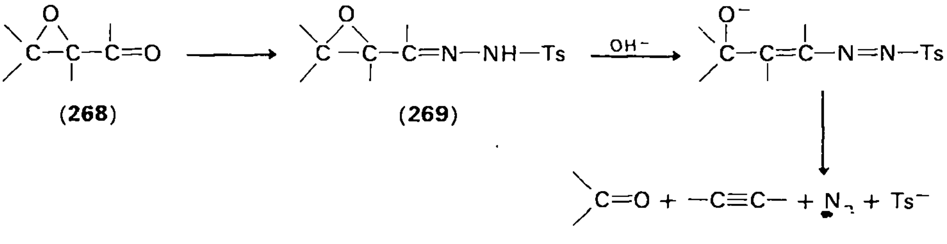
Applied to suitably substituted azoketones **266**, this type of fragmentation can be used to generate carbanions **267**, which are not readily accessible by other routes, such as the α-phenylethyl (**267a**), the cyclopropylmethyl (**267b**), the cyclobutylmethyl (**267c**) and the *t*-butyl anion (**267d**)^{125}.



$$\text{PhCON=N—R} \xrightarrow{\text{EtO}^-} {}^-\text{O—}\underset{\text{OEt}}{\overset{\text{Ph}}{\text{C}}}\text{—N=N—R} \xrightarrow{-N_2} \text{PhCOOEt} + \text{R}^-$$

(266) (267)

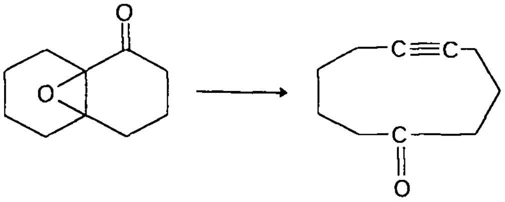
A very useful method for the synthesis of alkynes from α,β-epoxyketones (**268**) also makes use of the driving force associated with nitrogen formation[126]. In this reaction the *p*-toluenesulphonylhydrazone (**269**) of the ketone **268** is converted to the fragmentable anion **270** by removal of a proton with a base. The anion **270** then undergoes fragmentation to a carbonyl compound, an alkyne, nitrogen and *p*-toluenesulphinate.



(268) (269) (270)

(Ts=p-$CH_3C_6H_4SO_2$)

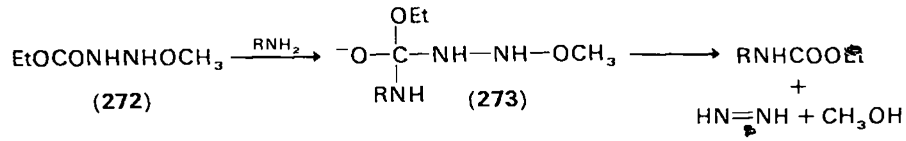
This is another example of a seven-centre fragmentation which leads to four fragments instead of the customary three. The reaction is important in the synthesis of cyclic acetylenic ketones, such as **271**, which would otherwise be almost inaccessible[127].



(271)

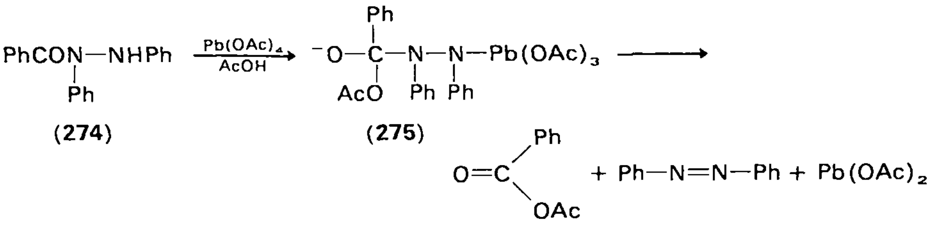
G. Diimide- and Azo-forming Fragmentation

Fragmentation reactions are known which lead to diimide or to an azo compound as the unsaturated fragment. An example of the former reaction is furnished by the ethoxycarbonylhydrazine **272**, which is aminolysed to a urethane, diimide and methanol, presumably via the adduct **273**[128]. Diimide is detected by the reduction of added cyclohexene.



$$\underset{(272)}{EtOCONHNHOCH_3} \xrightarrow{RNH_2} \underset{(273)}{{}^-O-\underset{RNH}{\overset{OEt}{C}}-NH-NH-OCH_3} \longrightarrow RNHCOOEt + HN{=}NH + CH_3OH$$

Finally, oxidation of *N*-benzoyl-*N*,*N'*-diphenylhydrazine (**274**) with lead tetraacetate in the presence of acetic acid yields *trans*-azobenzene (**276**), a reaction which is best rationalized as the fragmentation of the intermediate **275**[129].



(274) (275) (276)

H. Displacement-induced Fragmentation

In the fragmentation reactions discussed so far, inductive or conjugate electron release from the atom 'a' contributed to the stabilization of the electrofugal fragment a—b in equation (33).

$$\overset{\curvearrowright}{\ddot{a}}\!\rightarrow b-c-d-X \longrightarrow \overset{\curvearrowright}{\ddot{a}}\!\rightarrow b + c{=}d + X\colon \qquad (33)$$

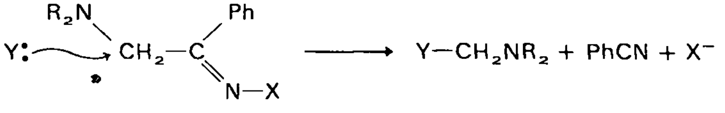
In the following cases the electrons required to break the b—c bond are provided by an external nucleophile Y in a displacement reaction on atom 'b' (equation 34).

$$Y\colon\!\curvearrowright b \frown c \frown d \curvearrowright X \longrightarrow Y-b + c{=}d + X\colon \qquad (34)$$

This process could be concerted, two bonds being formed and two broken in the transition state. Alternatively, the process could take place by a two step mechanism, i.e. displacement of the group c—d—X by Y is followed by the cleavage of the d—X bond (equation 35). Both mechan-

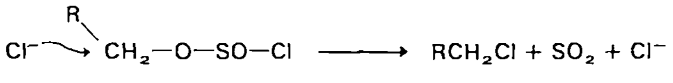
$$Y\colon + b-c-d-X \longrightarrow Y-b + \colon\! c-d-X \longrightarrow c{=}d + X\colon \qquad (35)$$

isms should obey the second-order rate law, if the second step of equation (35) is fast. With rare exceptions[130,132], however, no mechanistic studies have been carried out.



(277)

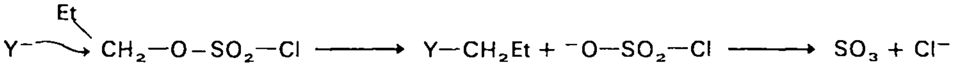
An example of displacement-induced fragmentation is given by *anti*-α-aminoacetophenone oxime derivatives (**277**), which undergo a second order reaction with strong nucleophiles, such as hydroxide or cyanide ion, yielding benzonitrile[130].



$$Cl^- + RCH_2{-}O{-}SO{-}Cl \longrightarrow RCH_2Cl + SO_2 + Cl^-$$

(**278**)

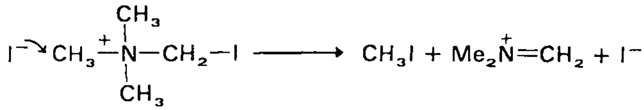
In the reaction of primary (and some secondary) alcohols with thionyl chloride, the intermediate alkyl chlorosulphite (**278**) undergoes nucleophilic substitution at the α-carbon atom by chloride ion with the formation of sulphur dioxide and chloride ion[118,131].



$$Y^- + EtCH_2{-}O{-}SO_2{-}Cl \longrightarrow Y{-}CH_2Et + {}^-O{-}SO_2{-}Cl \longrightarrow SO_3 + Cl^-$$

(**279**) (**280**)

While the above reaction of **278** might be a concerted process, the reaction of *n*-propyl chlorosulphate (**279**) with nucleophiles, such as hydroxide and halide ions in aqueous dioxane, is a two-step process since the relatively stable chlorosulphate ion (**280**) is formed as an intermediate[132]. The latter yields sulphate and chloride ions, presumably via elimination to sulphur trioxide.

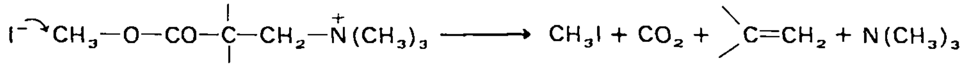


$$I^- + CH_3{-}\overset{+}{N}(CH_3)_2{-}CH_2{-}I \longrightarrow CH_3I + Me_2\overset{+}{N}{=}CH_2 + I^-$$

(**281**) (**282**)

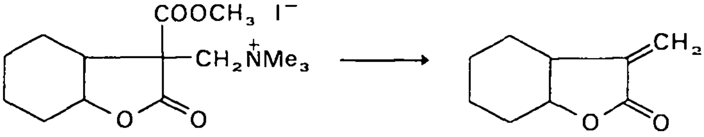
A further example of displacement-induced fragmentation is provided by the iodide-ion-induced cleavage of iodomethyltrimethylammonium ion (**281**), which leads to methyl iodide and dimethylmethyleneammonium iodide (**282**)[133].

Fragmentation can be initiated by cleavage of an ester. Thus, in **283**, attack by iodide ion on the methyl group displaces a β-ammonio carboxylate which undergoes fragmentation. This reaction shows promise as a preparative tool, as in the synthesis of the α-methylene lactone **285** from the ammonium salt **284**[134].



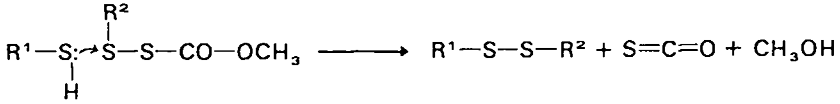
$$I^- + CH_3{-}O{-}CO{-}C{-}CH_2{-}\overset{+}{N}(CH_3)_3 \longrightarrow CH_3I + CO_2 + {>}C{=}CH_2 + N(CH_3)_3$$

(**283**)



(284) (285)

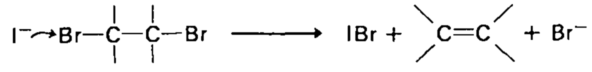
Nucleophilic displacement can take place on atoms other than carbon. Thus, attack by sulphur on sulphur is indicated in the reaction of thiols with sulphenylthiocarbonates (**286**) yielding disulphides (**287**), carbonyl sulphide and methanol, a reaction employed in the synthesis of peptides[135].



$$R^1{-}\underset{H}{S}\!:\rightarrow\overset{R^2}{S}{-}S{-}CO{-}OCH_3 \longrightarrow R^1{-}S{-}S{-}R^2 + S{=}C{=}O + CH_3OH$$

(286) (287)

It is a matter of opinion whether the elimination of halogen from vicinal dihalides by nucleophiles, such as iodide and thiolate ion, phosphites and phosphines, should be regarded as a displacement-induced fragmentation. For example, the reaction of vicinal dibromides (**288**) with potassium iodide is second order and seems to involve nucleophilic attack on bromine by iodide ion, with concomitant formation of iodobromine, an olefin and bromide ion[136].



$$I^-\rightarrow Br{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}Br \longrightarrow IBr + {>}C{=}C{<} + Br^-$$

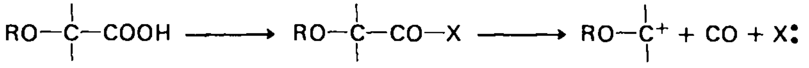
(288)

I. α-Fragmentation

As mentioned in Section I, an electrofugal group a—b and a nucleofugal group X can be released from the same atom ‘c’, when the latter has two available valency states (equation 36).

$$a{-}b\curvearrowright c\curvearrowright X \longrightarrow a{-}b + :c + X \tag{36}$$

The case of most importance to organic chemistry pertains to tetra- and bivalent carbon, as in carbon-monoxide-forming and isocyanide-forming fragmentation[3c].

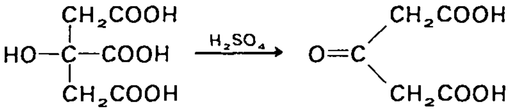


$$\mathrm{RO{-}\overset{|}{\underset{|}{C}}{-}COOH \longrightarrow RO{-}\overset{|}{\underset{|}{C}}{-}CO{-}X \longrightarrow RO{-}\overset{|}{\underset{|}{C}}{}^{+} + CO + X\!:}$$

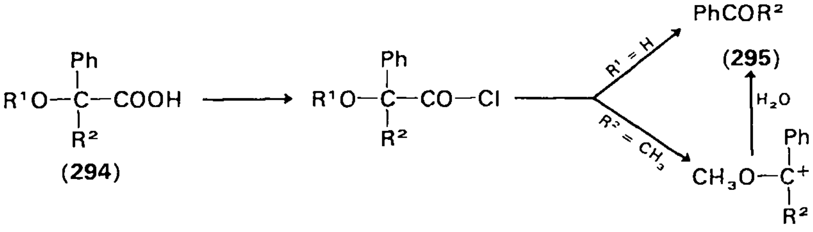
(289) (290) (291)

The former type of fragmentation occurs when α-hydroxy or α-alkoxy acids (289) are protonated (290, X = $\overset{+}{O}H_2$) or converted to the acid chloride (290, X = Cl). The electrofugal fragment is a carbonyl compound when R = H and an alkoxycarbonium ion (291) when R = alkyl.

Thus, citric acid (292) is decarbonylated to acetonedicarboxylic acid (293) with sulphuric acid[137] and α-hydroxyphenylacetic acids (294, R = H) yield ketones 295 when converted to the acid chloride. The same products are obtained from the α-methoxy derivative (294, R = CH_3) when the intermediate oxocarbonium ion 296 is decomposed with water[138].

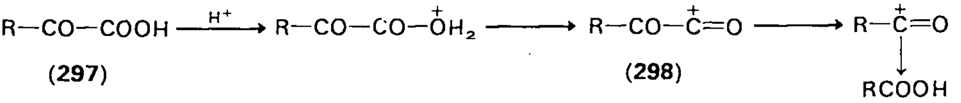


(292) (293)



(296)

α-Keto acids (297) are converted to the next lower acid when treated with mineral acids. This fragmentation proceeds stepwise in the case of phenylglyoxylic acid (297, R = Ph) with formation of the α-ketoacylium cation 298. The latter then decarbonylates to the acylium ion 299, which is converted to benzoic acid by water[139].



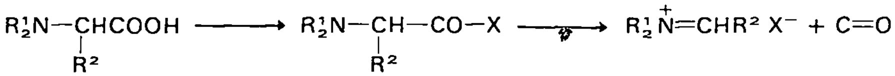
$$\mathrm{R{-}CO{-}COOH \xrightarrow{H^+} R{-}CO{-}CO{-}\overset{+}{O}H_2 \longrightarrow R{-}CO{-}\overset{+}{C}{=}O \longrightarrow \underset{\underset{RCOOH}{\downarrow}}{R{-}\overset{+}{C}{=}O}}$$

(297) (298) (299)

The acid-catalysed decomposition of oxalic acid into carbon monoxide, carbon dioxide and water is an α-fragmentation of the conjugate acid **300**, $X = \overset{+}{O}H_2$. The high electrofugal activity of the carboxyl group is responsible for the instability of the corresponding monochloride (**300**, X = Cl) and monoanhydride (**300**, X = OCOR)[140].

$$HOOC{-}COOH \longrightarrow \underset{(300)}{HO{-}CO{-}CO{-}X} \longrightarrow CO_2 + CO + X$$

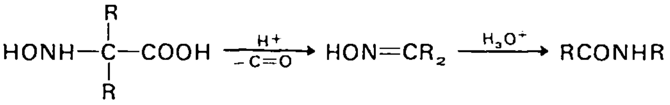
α-(Dialkylamino) acids (**301**) readily undergo decarbonylation to immonium salts when converted to the corresponding acid chloride (**302**, X = Cl)[141]. Mixed anhydrides, e.g. **302**, X = PhCOO, are somewhat more stable.



$$R^1_2N{-}\underset{R^2}{\underset{|}{C}}HCOOH \longrightarrow R^1_2N{-}\underset{R^2}{\underset{|}{C}}H{-}CO{-}X \longrightarrow R^1_2\overset{+}{N}{=}CHR^2\,X^- + C{=}O$$

(301) (302)

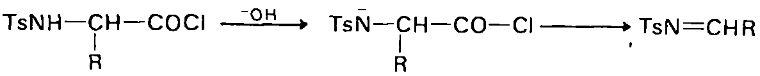
α-(Hydroxylamino) acids (**303**) undergo a similar α-fragmentation when treated with sulphuric acid[142]. The decarbonylation product is an oxime (**304**), which rearranges to an amide under the reaction conditions.



$$HONH{-}\overset{R}{\underset{R}{C}}{-}COOH \xrightarrow[-C=O]{H^+} HON{=}CR_2 \xrightarrow{H_3O^+} RCONHR$$

(303) (304)

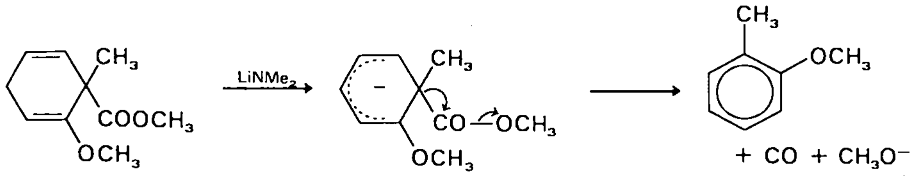
An α-fragmentation accounts for the instability of chlorides of α-(sulphonylamino) acids (**305**, Ts = *p*-$CH_3C_6H_4SO_2$) in the presence of bases. Thus, the phenylalanine derivative **305**, R = CH_2Ph, decarbonylates to the imine **307** via the conjugate base (**306**)[143].



$$TsNH{-}\underset{R}{\underset{|}{C}}H{-}COCl \xrightarrow{^-OH} Ts\overset{-}{N}{-}\underset{R}{\underset{|}{C}}H{-}CO{-}Cl \longrightarrow TsN{=}CHR$$

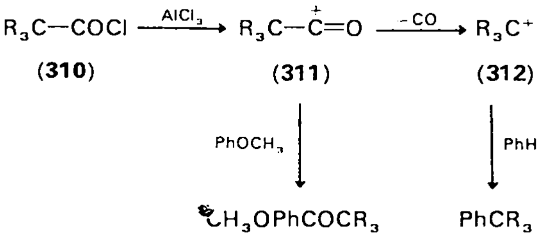
(305) (306) (307)

The conversion of the cyclohexadiene carboxylic ester **308** into *o*-methylanisole by lithium dimethylamide demonstrates the high electrofugal activity of the 'pre-aromatic' anion **309**, which is formed as the intermediate[144].



(308) **(309)**

It is well known that tertiary acid chlorides (**310**) are decarbonylated by Friedel–Craft catalysts, such as aluminium chloride. This α-fragmentation proceeds by way of the acylium ion **311**, which can be intercepted by anisole with the formation of a ketone. When the less reactive benzene is used as the solvent, a reaction takes place only after decarbonylation to the tertiary carbonium ion **312**, leading to an alkylbenzene[145].



$$\begin{tikzcd}[column sep=large] R_3C{-}COCl \arrow[r, "AlCl_3"] & R_3C{-}\overset{+}{C}{=}O \arrow[r, "-CO"] \arrow[d, "PhOCH_3"'] & R_3C^+ \arrow[d, "PhH"] \\ & CH_3OPhCOCR_3 & PhCR_3 \end{tikzcd}$$

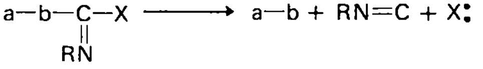
(310) **(311)** **(312)**

A displacement-induced α-fragmentation is indicated in the reaction of chloromethyl chloroformate (**313**) with sodium iodide, which leads to the formation of iodine, formaldehyde and carbon monoxide[146].

$$I^- \quad Cl{-}CH_2{-}O{-}CO{-}Cl \xrightarrow{I^-} I_2 + CH_2O + CO + Cl^-$$

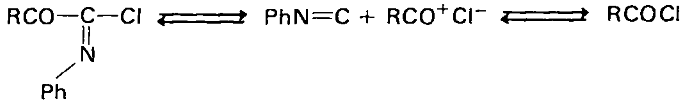
(313)

When an electrofugal and nucleofugal group are present on the carbon atom of an imine, a system results which should undergo an isonitrile-forming α-fragmentation (equation 37).



$$a{-}b{-}\underset{\underset{RN}{\|}}{C}{-}X \longrightarrow a{-}b + RN{=}C + X{:} \qquad (37)$$

Few such cases seem to have been observed so far. An example is the reversible thermal decomposition of acylformimidoyl chlorides (**314**) to acid chlorides and isocyanides. Amines trap the transient acylium ion or the acid chloride with formation of an amide[147].



$$\mathrm{RCO{-}C(=NPh){-}Cl} \rightleftharpoons \mathrm{PhN{=}C + RCO^{+}Cl^{-}} \rightleftharpoons \mathrm{RCOCl}$$

(314)

As an element capable of changing its valency state, sulphur also engages in α-fragmentation with formation of sulphur dioxide (equation 38)[118]. However, the unsaturated fragment is an inorganic molecule and therefore only two cases will be mentioned briefly.

$$\mathrm{a{-}b{-}SO_2{-}X} \longrightarrow \mathrm{a{-}b + SO_2 + X\!:} \qquad (38)$$

Carbonium ions can be generated by heating alkylsulphonyl chlorides (**315**) in dimethylformamide, which reacts to form a strong nucleofugal group in the intermediate **316**[148].

$$\underset{\textbf{(315)}}{\mathrm{RSO_2Cl}} \xrightarrow{\mathrm{DMF}} \underset{\textbf{(316)}}{\mathrm{R{-}SO_2{-}OCH{=}\overset{+}{N}Me_2}} \longrightarrow \mathrm{R^{+} + SO_2 + DMF}$$

$$\underset{\textbf{(317)}}{\mathrm{RSO_2Br + CF_3SO_3Ag}} \longrightarrow \underset{\textbf{(318)}}{\mathrm{R{-}SO_2{-}OSO_2CF_3}} \longrightarrow \mathrm{R^{+} + SO_2 + CF_3SO_3^{-}}$$

A similarly powerful nucleofuge is generated by reaction of the corresponding sulphonyl bromide (**317**) with silver trifluoromethylsulphonate. The rate of fragmentation of the resulting alkylsulphonyl trifluoromethylsulphonate (**318**) parallels the stability of the carbonium ion formed[149] and points to a concerted process.

IV. OUTLOOK

This review, although selective and incomplete, shows that numerous apparently different reactions conform to a common pattern of reactivity if the reactant molecule contains a sequence of potentially electrofugal, unsaturated and nucleofugal fragments. The recognition of this structural feature enables a rational interpretation of a large body of chemical data.

Needless to say, any attempt to reduce a diversity of phenomena to an identical cause can be carried too far and not all decomposition and cleavage reactions belong to the class of heterolytic fragmentation, as defined in Section I. Nevertheless, it is regrettable that, with few exceptions, present textbooks either fail to call attention to fragmentation, or treat it as an appendage of β-elimination, although the latter class is far more restricted.

Hitherto unclassifiable or unexpected reactions frequently turn out to be fragmentations and a study of their nature may help to improve the yield of a desired process. Furthermore, it is still possible to devise new cases of fragmentation by a judicious combination of electrofugal, nucleofugal and middle groups. In fact, such cases are constantly being reported.

Finally, as shown in Section III, fragmentation reactions can be employed in the formation of many functional groups. They are therefore of practical use in synthesis and in degradation. However, these developments are still in their beginnings. In addition many mechanistic questions remain to be answered. Heterolytic fragmentation therefore provides a wide field for future investigations.

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Supplement A The Chemistry of Double-Bonded Functional Groups
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CHAPTER 9

Electrophilic additions to carbon–carbon double bonds

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I. INTRODUCTION

Electrophilic additions to alkenes have been of interest to chemists for many years because of their use as synthetic methods and as tools for mechanistic study. While many similarities exist, the general course of the reaction will depend upon the electrophile, the structure of the alkene and the particular conditions under which the reaction occurs. Among the numerous examples of these reactions are the additions to alkenes of halogens, peroxy acids, organic and mineral acids, sulphenyl halides, selenenyl halides and interhalogens. All electrophilic reagents contain a polar or polarizable bond which is cleaved during the addition in such a way that the rate-determining transition state has a net positive charge.

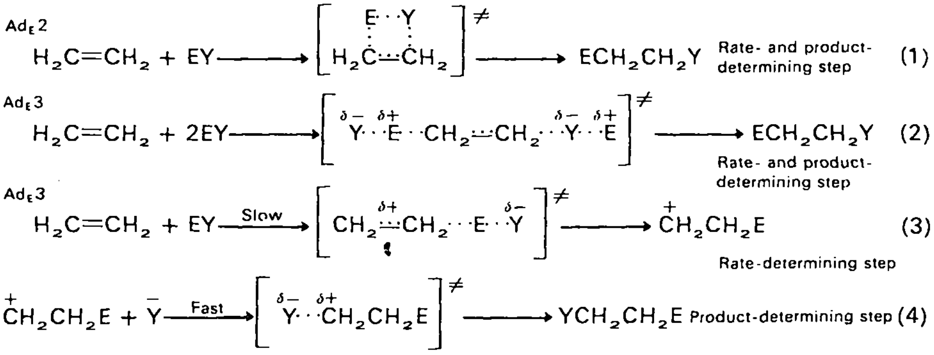
In this review we will examine in detail the addition of a number of these electrophiles to alkenes with the aim of establishing how the alkene structure and reaction conditions affect the rate of addition as well as the regiochemistry[1] and stereochemistry of the addition product(s). From these data we will attempt to describe the mechanism of the various addition reactions.

The mechanisms of electrophilic addition reactions may be classified according to whether the addition products are formed in a one-step process or whether a cationic intermediate is formed on the reaction coordinate between reagents and products.

The simplest one step mechanism is a molecular addition in which the transition state contains both the electrophile and the alkene (equation 1). Using the notation of Ingold[2], this is one example of an Ad_E2 (addition, electrophilic, bimolecular) mechanism. Such a mechanism is symmetry forbidden.

Another single-step mechanism is one in which the two parts of the electrophile are derived from different molecules. The rate-determining transition state for this mechanism contains the alkene and two molecules of electrophile and consequently this is one example of an Ad_E3 (addition, electrophilic, termolecular) mechanism (equation 2). In both the one step Ad_E2 and Ad_E3 mechanisms, the one transition state is both rate determining and product determining.

An important mechanism for reactions in solution is the formation of a cationic intermediate, making the overall addition a multistep process. Nucleophilic attack on the cationic intermediate completes the addition reaction. In the simplest case this mechanism involves two steps. As a result, it is possible that the rate-determining and product-determining steps are different. Thus if the cationic intermediate is formed in a slow step, the transition state leading to this intermediate is then the rate determining one. This transition state can contain the alkene and one, two or more molecules of the electrophile. If the rate determining transition state contains two molecules (one alkene and one electrophile), the mechanism is Ad_E2 (equation 3). While if it contains three molecules (one alkene and two electrophiles), the mechanism is Ad_E3 (equation 5). Rapid capture of the intermediate by a nucleophile is the product-determining step and this transition state is the product-determining one (equation 4). Since the two transition states have different structures, the polar and steric influence of substituents may affect each differently.



$$\mathrm{Ad_E2}\quad H_2C{=}CH_2 + EY \longrightarrow \left[\begin{matrix} E\cdots Y \\ \vdots\quad\vdots \\ H_2\dot{C}\text{---}\dot{C}H_2 \end{matrix}\right]^{\neq} \longrightarrow ECH_2CH_2Y \quad \text{Rate- and product-determining step} \qquad (1)$$

$$\mathrm{Ad_E3}\quad H_2C{=}CH_2 + 2EY \longrightarrow \left[\overset{\delta-}{Y}\cdots\overset{\delta+}{E}\cdots CH_2\text{---}CH_2\cdots\overset{\delta-}{Y}\cdots\overset{\delta+}{E}\right]^{\neq} \longrightarrow ECH_2CH_2Y \quad \text{Rate- and product-determining step} \qquad (2)$$

$$\mathrm{Ad_E3}\quad H_2C{=}CH_2 + EY \xrightarrow{\text{Slow}} \left[\overset{\delta+}{CH_2\text{---}CH_2}\cdots E\cdots\overset{\delta-}{Y}\right]^{\neq} \longrightarrow \overset{+}{C}H_2CH_2E \quad \text{Rate-determining step} \qquad (3)$$

$$\overset{+}{C}H_2CH_2E + \overset{-}{Y} \xrightarrow{\text{Fast}} \left[\overset{\delta-}{Y}\cdots\overset{\delta+}{C}H_2CH_2E\right]^{\neq} \longrightarrow YCH_2CH_2E \quad \text{Product-determining step} \qquad (4)$$

If the cationic intermediate is formed rapidly and reversibly, then a subsequent step will be the slow or rate-determining step. In the simplest case of a two-step mechanism, the second step becomes the slow step and it is both rate and product determining. Rate-determining attack on the cationic intermediate can involve either the nucleophilic part of the electrophilic reagent or a second molecule of electrophile. The former case is still an Ad_E2 mechanism (equation 6) but the latter is an Ad_E3 mechanism (equation 7). Another variant of this mechanism is rate-determining attack on the cationic intermediate by higher molecular aggregates.

$\mathrm{Ad_E3}$

$$\mathrm{H_2C{=}CH_2 + 2EY \xrightarrow[\text{Slow}]{} \left[\overset{\delta+}{C}H_2{-}CH_2\cdots E\cdots \overset{\delta-}{E}Y_2\right]^{\neq} \longrightarrow \overset{+}{C}H_2CH_2E + \overset{-}{E}Y_2} \qquad (5)$$

Rate-determining step

$$\mathrm{\overset{+}{C}H_2CH_2E + \overset{-}{E}Y_2 \xrightarrow[\text{Fast}]{} \left[\overset{\delta-}{E}Y_2\cdots \overset{\delta+}{C}H_2CH_2E\right]^{\neq} \longrightarrow YCH_2CH_2E}$$

Product-determining step

$\mathrm{Ad_E2}$

$$\mathrm{H_2C{=}CH_2 + EY \underset{\text{Fast}}{\overset{\text{Fast}}{\rightleftharpoons}} \overset{+}{C}H_2CH_2E + \overset{-}{Y}} \qquad (6)$$

$$\mathrm{\overset{+}{C}H_2CH_2E + \overset{-}{Y} \xrightarrow[\text{Slow}]{} \left[\overset{\delta-}{Y}\cdots \overset{\delta+}{C}H_2CH_2E\right]^{\neq} \longrightarrow YCH_2CH_2E}$$

Rate- and product-determining step

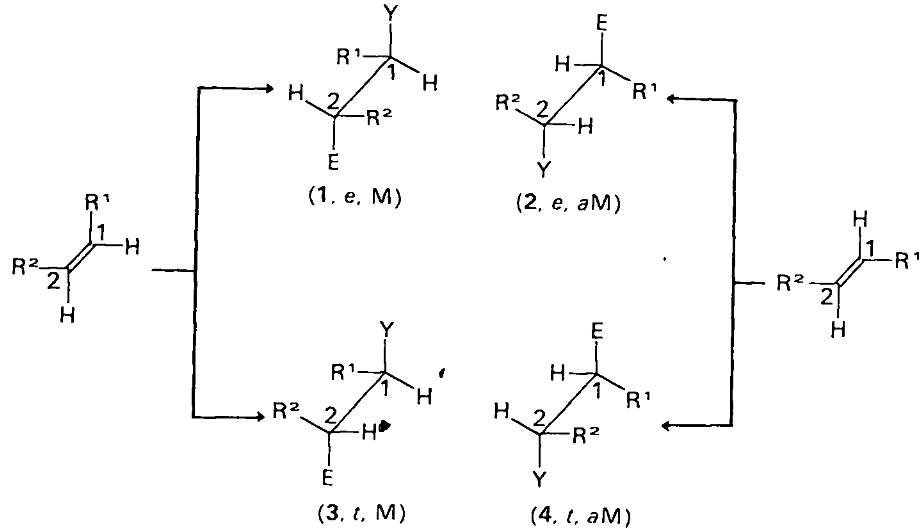
$\mathrm{Ad_E3}$

$$\mathrm{CH_2{=}CH_2 + EY \underset{\text{Fast}}{\overset{\text{Fast}}{\rightleftharpoons}} \overset{+}{C}H_2CH_2E\overset{-}{Y}} \qquad (7)$$

$$\mathrm{\overset{+}{C}H_2CH_2E\overset{-}{Y} + EY \xrightarrow[\text{Slow}]{} \left[\overset{\delta-}{E}{-}\overset{\delta-}{Y}\cdots \overset{\delta+}{C}H_2CH_2E\cdots \overset{\delta-}{Y}\right]^{\neq} \longrightarrow YCH_2CH_2E}$$

Rate- and product-determining step

The addition of unsymmetrical electrophiles to unsymmetrical alkenes can result in the formation of isomeric products. The terminology used in discussing these isomers formed in electrophilic addition reactions is illustrated in Scheme 1. The addition of EY to a pair of isomeric *cis–trans-*

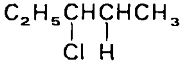


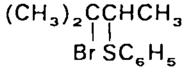
e = *erythro*
t = *threo*
M = Markownikoff
*a*M = *anti*-Markownikoff

SCHEME 1.

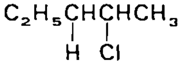
1,2-disubstituted ethylenes can form four stereoisomeric products, **1**–**4**. We can identify each isomer if first we define E as the electrophilic portion of EY and we stipulate that R^1 is more electron donating than R^2. Isomers **1** and **3** which have E attached to $C_{(2)}$ are called the Markownikoff adducts while **2** and **4** which have E attached to $C_{(1)}$ are called the *anti*-Markownikoff adducts. This general definition of the original Markownikoff[3] designation can easily be extended to the adducts of tri- and tetra-substituted ethylenes. Thus the Markownikoff isomer is that one in which the more electrophilic part of the electrophile is attached to the carbon atom whose sum of Taft's inductive substituent constants $\Sigma\sigma^{*4}$, is the more positive.† According to this designation the following are isomeric Markownikoff and *anti*-Markownikoff adducts.

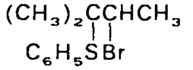
Markownikoff orientation


$\mathrm{C_2H_5}\underset{\mathrm{Cl}}{\mathrm{CH}}\underset{\mathrm{H}}{\mathrm{CH}}\mathrm{CH_3}$


$\mathrm{(CH_3)_2}\underset{\mathrm{Br}}{\mathrm{C}}\underset{\mathrm{SC_6H_5}}{\mathrm{CH}}\mathrm{CH_3}$

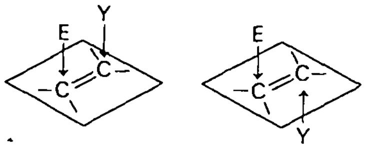
anti-Markownikoff orientation


$\mathrm{C_2H_5}\underset{\mathrm{H}}{\mathrm{CH}}\underset{\mathrm{Cl}}{\mathrm{CH}}\mathrm{CH_3}$


$\mathrm{(CH_3)_2}\underset{\mathrm{C_6H_5S}}{\mathrm{C}}\underset{\mathrm{Br}}{\mathrm{CH}}\mathrm{CH_3}$

Following the terminology of Hassner[1] the predominant formation of either adduct with Markownikoff or *anti*-Markownikoff orientation would be the result of regioselective electrophilic addition. Exclusive formation of either isomer would indicate regiospecific addition. Markownikoff and *anti*-Markownikoff isomers are called regioisomers.

Addition of EY to an alkene can occur in two ways. *Syn* addition occurs when the two parts of the electrophile E and Y are added to the same side of the plane of the carbon–carbon double bond. *Anti* addition occurs when the two parts are added to the opposite sides of the double bond (Figure 1). The adducts **1** and **2** are the result of *syn* addition to a cis alkene while **3** and **4** result by *anti* addition. We can distinguish between these pairs of adducts by using the terms *erythro* and *threo*. These terms are usually



Syn addition *Anti* addition

FIGURE 1. *Syn* and *anti* addition to a carbon–carbon double bond.

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† This definition is applicable only to alkyl-substituted ethylenes.

applied only in the case where $R^1 = R^2$ or $E = Y$ since they refer to the relative stereochemistry of adjacent carbon atoms, each having two identical groups†. However, in this review the adducts formed by *anti* addition to a *trans*-1,2-disubstituted ethylene are designated *erythro* while those resulting from *syn* addition are designated *threo*‡. Thus in Scheme 1 the complete designation for each isomer is as follows:

1: *erythro* Markownikoff;	**2**: *erythro anti*-Markownikoff;
3: *threo* Markownikoff;	**4**: *threo anti*-Markownikoff.

The next step in the sophistication of the description of the mechanism of an electrophilic addition reaction requires some details of the structure of the cationic intermediates and transition states involved in the reaction. Such descriptions lead to certain conclusions regarding the stereochemistry and regiochemistry of the addition product(s). Let us examine this aspect of the mechanisms given in equations 1 to 7.

In the single step Ad_E2 mechanism, both parts of the electrophile add from the same side of the plane of the alkene (*syn* addition). Consequently the products would be the results of stereospecific addition while the nature of the substituents on the double bond would determine the regiochemistry of the addition.

In the case of the single-step Ad_E3 mechanism, *syn* or *anti* addition can occur as illustrated in Figure 2. Depending upon the relative energies of these two transition states, the addition can be either *syn* or *anti* stereospecific. It is even possible that non-stereospecific addition could occur, if the two transition states are of comparable energies.

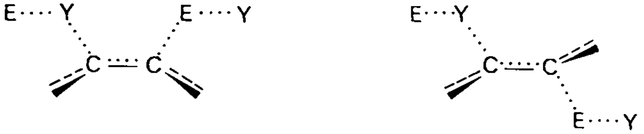


FIGURE 2. *Syn* and *anti* addition by an Ad_E3 mechanism.

The stereochemistry of the products formed by additions involving a multistep Ad_E2 or Ad_E3 mechanism depends very much upon the structure of the product-determining transition state which in turn depends upon the structure of the cationic intermediate immediately preceding it. If this intermediate has an open carbonium ion structure **5** or **6**, nucleophilic attack at either face is possible with the result that both *syn* and *anti* addition products are expected. This is illustrated in Figure 3. Often, however, certain polar, steric or conformational features of the molecule make nucleophilic attack at one face of the carbonium ion more favourable, resulting in preferential *syn* or *anti* addition. In general, additions involving open ions such as **5** are completely regiospecific. The carbon to which the electrophile will bond depends upon the relative stability of the two ions **5** and **6**. Addition occurs to form the more-stable carbonium ion.

---

† When all three groups on adjacent carbons are identical the term *erythro* is replaced by *meso*, and *threo* by *dl*.

‡ For addition to more-highly substituted ethylenes, the terms *erythro* and *threo* are often ambiguous. In such cases the stereochemistry of the adducts is best designated by the *R* and *S* convention[5].

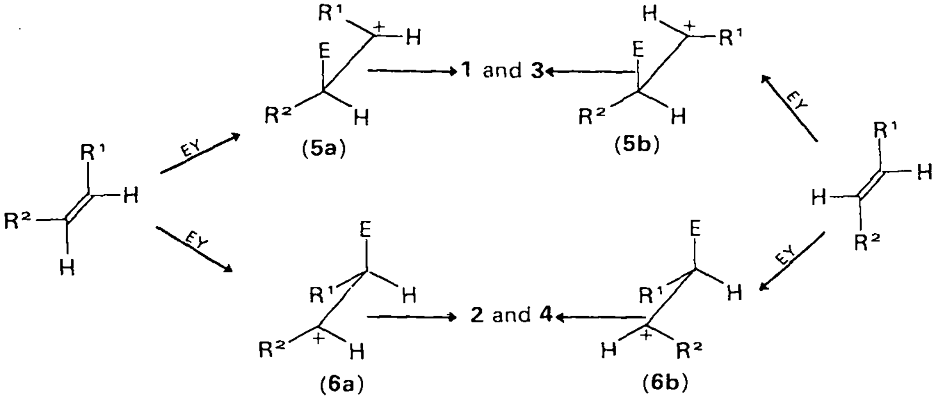


FIGURE 3. Stereochemistry of addition by Ad_E2 mechanism involving an open ion.

If the intermediate has a bridged structure such as 7, nucleophilic attack can occur only on the face opposite to the electrophile. Such backside attack is analogous to the S_N2 mechanism and consequently the product is formed by *anti* stereospecific addition as illustrated in Figure 4. The

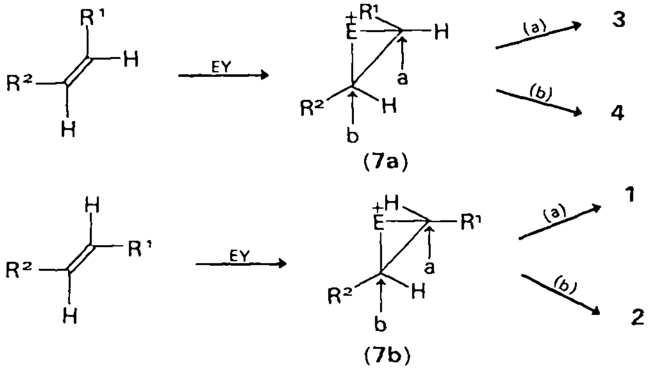


FIGURE 4. Stereochemistry of addition by Ad_E2 mechanism involving a bridged ion.

additions are usually non-regiospecific since attack by the nucleophile can occur at either carbon of the bridged intermediate. Again polar, steric and conformational effects may make attack [illegible] one carbon more favourable resulting in a regioselective addition.

In order to place a particular addition reaction into one of the mechanistic categories, it is necessary to have experimental data about the effect of alkene structure upon the rate of addition and the stereochemistry and regiochemistry of the product(s). By studying the rate of addition and the effect of alkene structure upon the rate, we learn not only the molecularity of the reaction but also the effect of substituents upon the rate-determining transition state. In conjugation with the rate data, a study of the effect of alkene structure upon product stereo- and regiochemistry provides information about the structure of the product-determining transition state. If products of rearrangement are formed, they provide good evidence of a multistep mechanism involving an open carbonium ion.

As more experimental evidence is obtained, it becomes increasingly clear that the mechanistic classification adopted here is an oversimplification. In many addition reactions, molecular complexes are formed rapidly and reversibly between the alkene and the electrophile. Sometimes several cationic intermediates are involved in the reaction, each leading to a different product. Ion pairs can also be important particularly in weakly-ionizing solvents. While these features tend to complicate the mechanism, they do not invalidate the original classification since it focuses attention upon the important features of the mechanism, the molecularity of the rate-determining step, the structures of any cationic intermediates and the structures of the product- and rate-determining steps.

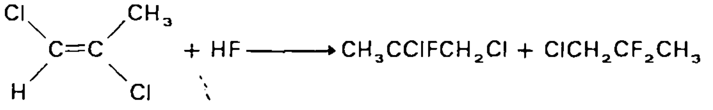
In the following sections we will examine the data on the addition of a number of electrophiles which have been published since the last reviews on this subject[6,7,8].

II. ELECTROPHILIC HYDROGEN

A. *Hydrogen Halides*

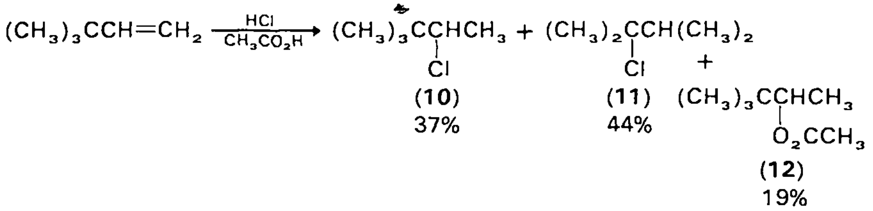
The ionic addition of hydrogen halides to alkenes forms adducts with Markownikoff orientation. Depending upon the structure of the alkene and the reaction conditions, solvent-incorporated and rearranged products can also be formed.

Addition of HF to simple and monochlorinated alkenes occurs readily while di-, tri- and perchloroethylenes react with HF only at elevated temperatures. For example *E*- and *Z*-1,2-dichloropropene react with HF at 120 °C to form the normal addition product **8** as well as the substitution product **9** (equation 8)[8a].



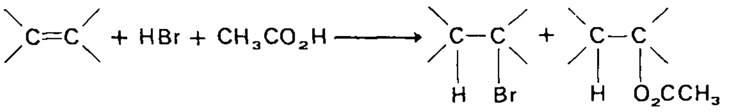
$$\text{ClCH=C(CH}_3\text{)Cl} + HF \longrightarrow \underset{(\mathbf{8})}{CH_3CClFCH_2Cl} + \underset{(\mathbf{9})}{ClCH_2CF_2CH_3} \qquad (8)$$

At those temperatures at which it can be conveniently studied, the equilibrium for the addition of HCl to simple alkenes in the gas phase lies largely towards elimination rather than addition[9]. In organic solvents, addition proceeds smoothly between −80 °C and 80 °C to form rearranged and solvent-incorporated products as well as the normal 1,2-adducts. An example is the addition of HCl to *t*-butylethylene in acetic acid to form **10**, **11** and **12** under conditions of kinetic control (equation 9)[10]. The unrearranged 1,2-adducts, **10** and **12**, are both formed by regiospecific Markownikoff addition.



$$(CH_3)_3CCH{=}CH_2 \xrightarrow[CH_3CO_2H]{HCl} \underset{\substack{(\mathbf{10})\\37\%}}{(CH_3)_3C\underset{Cl}{\underset{|}{C}}HCH_3} + \underset{\substack{(\mathbf{11})\\44\%}}{(CH_3)_2\underset{Cl}{\underset{|}{C}}CH(CH_3)_2} + \underset{\substack{(\mathbf{12})\\19\%}}{(CH_3)_3C\underset{O_2CCH_3}{\underset{|}{C}}HCH_3} \qquad (9)$$

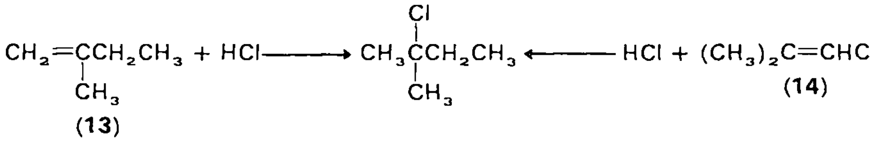
Hydrogen bromide can add to alkenes by either a radical or an electrophilic mechanism. Radical addition is the more facile and its occurrence has been detected even in the presence of radical inhibitors[11]. Usually the presence of products with *anti*-Markownikoff orientation is taken as evidence of a free radical mechanism. Recently Pasto and coworkers[11] have found that a more sensitive probe for radical addition is the occurrence of *cis–trans* isomerization during addition of HBr in acetic acid to either one of the pure isomeric alkenes as reactant. Isomerization caused by bromine atoms is faster than addition. The alkene isomerization reaction could be stopped only when the reaction was carried out in the dark, the HBr–acetic acid solutions were triply freeze-degassed prior to the reaction and the alkene added under argon or helium atmosphere. Under these conditions, alkyl bromides and acetates are formed by the ionic addition of HBr in acetic acid to alkenes (equation 10).



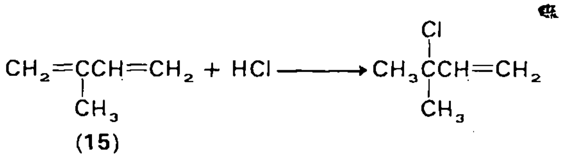
(10)

Our understanding of the mechanism of the addition of HI to alkenes has not advanced significantly since the last reviews of electrophilic addition reactions[6,7].

The addition of HCl to isobutylene in heptane[12], and of HBr to propene in *n*-pentane[13], follows a rate law which is first order in alkene and nearly third order in hydrogen halide. In more-polar solvents, rate laws of lower order have been found. For example Pocker and coworkers have reported the rates and products of addition of HCl to 2-methylbutene-1 (**13**), 2-methylbutene-2 (**14**) and isoprene (**15**) in nitromethane at 25 °C[14]. The product of addition under conditions of kinetic control is 2-chloro-2-methylbutane for both **13** and **14** (equation 11) while the addition to isoprene forms exclusively the 1,2-adduct (equation 12).



$$\underset{\textbf{(13)}}{CH_2{=}\underset{CH_3}{C}CH_2CH_3} + HCl \longrightarrow CH_3\overset{Cl}{\underset{CH_3}{C}}CH_2CH_3 \longleftarrow HCl + \underset{\textbf{(14)}}{(CH_3)_2C{=}CHCH_3} \qquad (11)$$

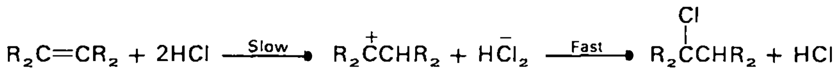


$$\underset{\textbf{(15)}}{CH_2{=}\underset{CH_3}{C}CH{=}CH_2} + HCl \longrightarrow CH_3\overset{Cl}{\underset{CH_3}{C}}CH{=}CH_2 \qquad (12)$$

The rate law is overall third order, first order in alkene and second order in HCl. The addition of tetraethylammonium perchlorate shows no appreciable effect on the rate in contrast to the addition of tetramethylammonium chloride which lowers the rate of addition. This decrease in rate is attributed to the added chloride ions combining with HCl to produce HCl_2^- ions which decreases the concentration of the electrophile. Studies of the infrared, nuclear magnetic resonance spectroscopy and conductance of hydrogen and deuterium chloride solution in nitromethane lead to the conclusion that un-ionized HCl (or DCl) molecules act as the dominant proton donors in this solvent.

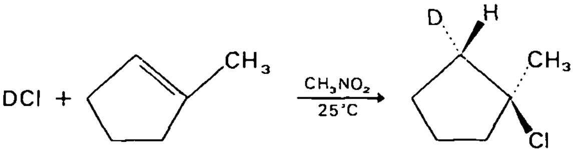
It is concluded that initial proton transfer from HCl to the alkenes is the rate-determining step on the basis of the following three experimental results. Starting with either isomer, there is no interconversion of the two isomeric 2-methylbutenes during the addition. By contrast, under conditions of thermodynamic control an 85:15 equilibrium mixture of 2-methyl-2-butene:2-methyl-1-butene is obtained. Consequently the carbonium ion intermediate is not formed rapidly and reversibly. This conclusion is supported by the lack of incorporation of deuterium into the unreacted alkene in the addition of DCl to either alkene. Finally the formation of only the less-stable 1,2-addition product under kinetic control in the addition to isoprene provides further evidence against a reversible protonation of the alkene. Thus the data are inconsistent with a mechanism in which the reaction of chloride ion with the carbonium ion is rate determining.

An acceptable mechanism is one involving a rate-determining proton transfer from molecular HCl to the alkene with a second molecule of HCl assisting the proton transfer by bonding to the developing chloride ion. This mechanism is illustrated in equation (13).



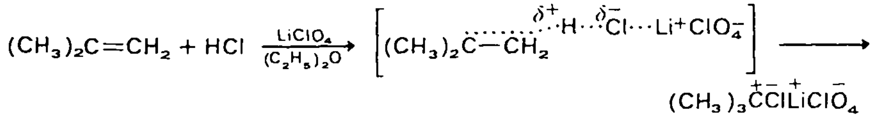
$$R_2C{=}CR_2 + 2HCl \xrightarrow{\text{Slow}} R_2\overset{+}{C}CHR_2 + H\overset{-}{Cl_2} \xrightarrow{\text{Fast}} R_2\overset{\overset{\displaystyle Cl}{|}}{C}CHR_2 + HCl \qquad (13)$$

The stereochemistry of the addition of HCl to 1-methylcyclopentene-2,5,5-d_3 and DCl to 1-methylcyclopentene in nitromethane at 25°C is *anti* stereospecific (equation 14)[15]. This addition obeys the same third-order rate law, first order in alkene and second order in HCl, as the addition to the 2-methylbutenes and isoprene. Under identical conditions, the products of kinetic control of the addition of HCl to 3-methyl-1-butene are only 40% normal 1,2-adduct and 60% rearranged product 2-chloro-2-methylbutane. The fact that rearrangement products are formed concurrently with addition has been taken as evidence against a concerted mechanism and in favour of a mechanism involving a carbonium ion–hydrogen dichloride ion-pair intermediate[15].



(14)

Pocker has found that the rate law for the addition of HCl to methylpropene is third order in diethyl ether; first order in alkene and second order in HCl[16]. At a constant concentration of added $LiClO_4$ the rate law changes to overall second order; first order in both alkene and HCl. The overall rate also depends upon the concentration of $LiClO_4$. The addition of $LiClO_4$ to the reaction does not affect the equilibrium constant between methylpropene and *t*-butyl chloride. It is proposed that $Li^+ClO_4^-$ ion pairs or higher aggregates function as a catalyst by taking over the role of the second HCl in the rate-determining transition state leading to the formation of a quadruple ion intermediate **16** (equation 15).



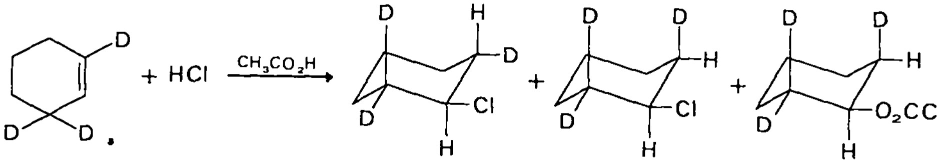
$$(CH_3)_2C{=}CH_2 + HCl \xrightarrow[(C_2H_5)_2O]{LiClO_4} \left[(CH_3)_2C{-}CH_2\cdots\overset{\delta+}{H}\cdots\overset{\delta-}{Cl}\cdots Li^+ClO_4^-\right] \longrightarrow (CH_3)_3\overset{+}{C}\overset{-}{Cl}\overset{+}{Li}\overset{-}{ClO_4} \quad (15)$$

(16)

A similar ion-pair mechanism was proposed by Fahey to account for the rate and product of addition of HCl to *t*-butylethylene and styrene in acetic acid at 25 °C[10]. Unlike the addition in nitromethane or diethylether, the observed rate law for this addition in acetic acid is overall second order, first order in both HCl and alkene. Thus the rate-determining transition state contains only one molecule of HCl. The possibility exists that a molecule of solvent acetic acid replaces the second molecule of HCl needed for the addition in nitromethane as solvent. The observation of a small kinetic isotope effect ($k_H/k_D = 1{\cdot}15 \pm 0{\cdot}07$) is in accord with a mechanism involving a rate limiting protonation of the alkene by HCl to form a carbonium–chloride ion-pair intermediate.

While the addition of tetramethylammonium chloride has little effect upon the addition of HCl to *t*-butylethylene and styrene, it has a marked effect upon both the rate and product composition of addition to cyclohexene. Fahey[17] has found that the rate law for addition of HCl to cyclohexene in acetic acid in the presence of added tetramethylammonium chloride contains two terms: one first order in both HCl and alkene, and another first order in HCl, alkene and chloride ion.

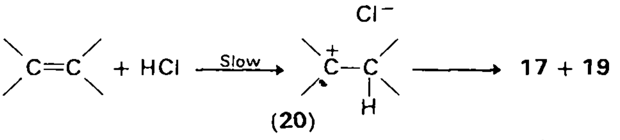
The addition of HCl to cyclohexene-1,3,3-d_3 in acetic acid yields a mixture of the *syn* HCl adduct (**17**), the *anti* HCl adduct (**18**) and the *anti* acetic acid adduct (**19**) (equation 16). In the presence of tetramethylammonium chloride, the product composition changes markedly with changes in the concentration of HCl or added water. Thus by increasing the concentration of HCl, the ratio of **18** to **19** increases while the ratio of **17** to **19** remains essentially unchanged. The effect of tetramethylammonium chloride upon the rate, product composition and stereochemistry is explained by postulating that Ad_E2 and Ad_E3 mechanisms are competing in the reaction. The Ad_E2 mechanism involves the reaction of HCl and alkene to form a carbonium–chloride ion-pair intermediate (**20**) which can either undergo *syn* collapse to form (**17**) or be attacked by acetic



(16)

(17) **(18)** **(19)**

acid on the opposite side to form (**19**) (equation 17). The formation of **18** is postulated to occur by a concerted Ad_E3 mechanism via transition state **21** in which EY represents the nucleophile donor (equation 18). For the formation of **18**, EY is either HCl or tetramethylammonium chloride while for the formation of **19**, EY is a molecule of acetic acid.



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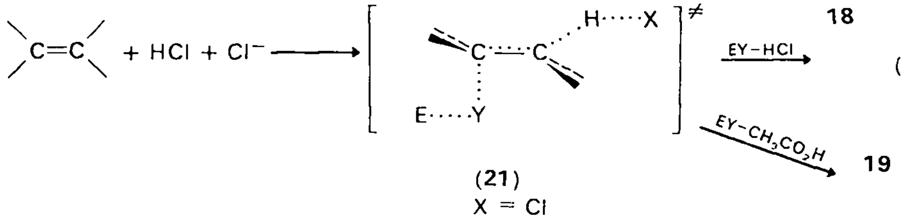


(18)

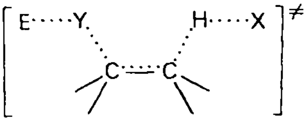
An Ad_E3 mechanism via a transition state similar to **21** is favoured by Fahey[19] to explain the kinetic and stereochemical data of the addition of HBr to cyclohexene and 1-hexene. The results of the addition of HBr in acetic acid to cyclohexene-1,3,3-d_3 are similar to those obtained with HCl. In both reactions addition of HX and also acetic acid occurs with *anti* stereoselectivity. Also the ratio of halide to acetate product is low at low halide ion concentration and increases with increasing halide ion concentration.

Similar *anti* stereoselectivity is found in the addition of DBr in acetic acid-*O-d* to *cis*- and *trans*-2-butene and *cis*- and *trans*-3-hexene while *anti* stereospecific addition is found for cyclopentene[11]. The rate expression for the addition to cyclopentene which best fits the experimental change in HBr concentration and the alkyl bromide/alkyl acetate product ratio is given in equation 19. According to this equation, alkyl bromide is formed

$$-\mathrm{d}[C_5H_8]/\mathrm{d}t = k_{\mathrm{RBr}}[C_5H_8][HBr]^2 + k_{\mathrm{ROAc}}[C_5H_8][HBr] \qquad (19)$$

only from the overall third-order term while alkyl acetate is formed only from the overall pseudo second-order term.

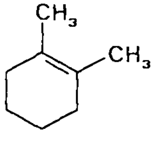
Based upon (i) the kinetic isotope effect ($k_H/k_D = 0{\cdot}48 \pm 0{\cdot}02$ for cyclopentyl bromide and $0{\cdot}63 \pm 0{\cdot}07$ for cyclopentyl acetate), (ii) the increase in the amount of cyclopentyl bromide product with increasing concentrations of added bromide ion, (iii) the lack of change of product stereochemistry with a 100-fold change in initial HBr concentration, (iv) the fact that the alkyl bromide and alkyl acetate formed from a particular alkene have similar stereochemistry, and (v) the lack of formation of rearranged acetates in the addition to *cis*- and *trans*-3-hexene, Pasto and coworkers proposed that the addition of HBr in acetic acid occurs by an Ad_E3 mechanism. One of two such possible mechanisms is a concerted *anti* and



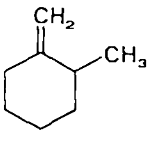
(22, X = Br)

syn Ad_E3 mechanism via transition states **21** and **22**. Alternatively 'a hydrogen bromide–alkene complex may be formed in a pre-rate-determining step equilibrium which leads to polarization of the π-electron system (i.e., development of cationic character on carbon) leading to a reaction with a nucleophile donor in the rate determining step.'[11]

A concerted *anti* Ad_E3 mechanism was originally proposed by Hammond[20] to explain the observation that under conditions of kinetic



(23)



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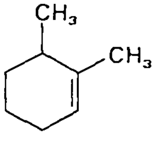
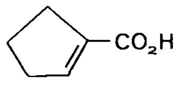


(25)

control 1,2-dimethylcyclohexene (**23**), 2-methylmethylenecyclohexane (**24**) and 1,6-dimethylcyclohexene (**25**) react with HBr to form different proportions of *cis*- and *trans*-1,2-dimethylbromocyclohexane. The data are inconsistent with a mechanism involving a planar carbonium ion intermediate. A similar concerted *anti* Ad_E3 mechanism has been postulated for the reaction of HBr and HCl with **23** and 1,2-dimethylcyclopentene which occur by stereoselective *anti* addition[18,21].

The addition of HCl and HBr to α,β-unsaturated carbonyl compounds has been found to be *anti* stereoselective. Examples include the addition of HCl to **26**[22], **27**[22], **28**[23] and diethyl fumarate (**29**) and maleate (**30**)[24] and the addition of HBr to **31** and **32**[25,26]. The kinetics and stereochemistry of the addition of HCl to **29** and **30** have been recently studied by Fahey[24]. The reactions are stereoselective forming 90% and 67% products of *anti* addition for **29** and **30** respectively taking into account isomerization between **30** and **29**. The rate law is overall third order, first order in alkene and second order in HCl. Additions of DCl in deuterioacetic acid failed to show a detectable kinetic isotope effect. Neither tetramethylammonium chloride nor perchloric acid affected the rate of addition to **29**. These results are interpreted in terms of a mechanism involving 1,4-addition by



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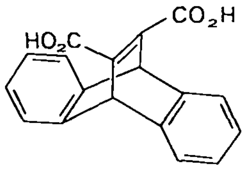
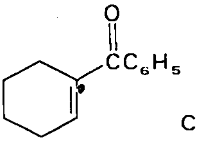
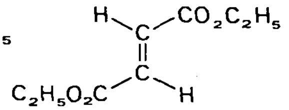


(27)



(28)



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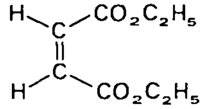

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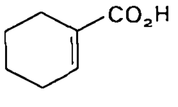
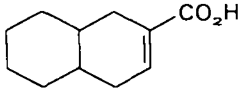
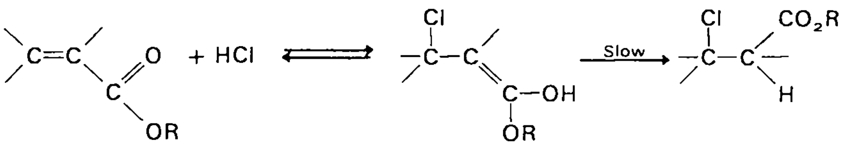


(31)



(32)

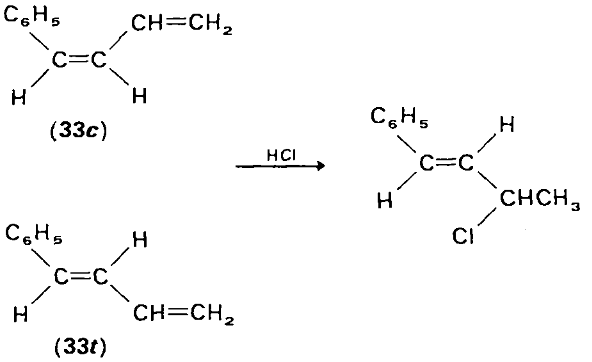
HCl followed by a rate-limiting stereoselective ketonization by HCl (equation 20)[27,28].



(20)

In contrast to the stereoselective *anti* addition to cycloalkenes and α,β-unsaturated carbonyl compounds the addition of DBr and DCl to conjugated alkenes such as acenaphthylene[29], indene[28] and 1-phenylpropene[30] is stereoselectively *syn*. The proposed mechanism of addition involves a carbonium–halide ion tight ion pair intermediate which collapses to form the *syn* addition product. According to this mechanism, *syn* addition should predominate in cases where electrophilic addition to an alkene takes place by means of a carbonium ion intermediate. *Anti* addition will occur whenever any steric effect hinders *syn* collapse of the primary ion pair.

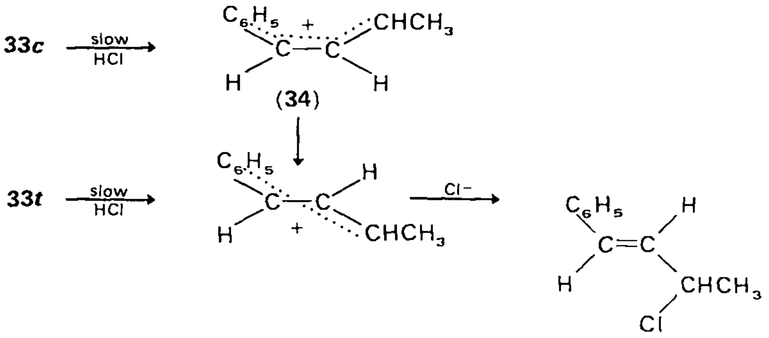
A carbonium ion mechanism has also been suggested for the addition to dienes. The addition of HCl in acetic acid to *cis*- and *trans*-1-phenyl-1,3-butadiene (**33*c*** and **33*t***) has been found to give the same product, *trans*-3-chloro-1-phenyl-1-butene (equation 21)[31]. In the acid concentration range of 0·07 to 0·2 M the reaction is first order in both alkene and HCl. The reaction of **33*c*** with DCl in deuterioacetic acid forms product with deuterium only at the four position indicating that reaction takes place by protonation exclusively at $C_{(4)}$. The rates of addition of DCl in deuterioacetic acid are retarded by a factor of 1·54 and 2·30 for **33*c*** and **33*t*** respectively. A plot of log k_2 for ring-substituted **33*t*** obeys a Hammett type relationship with Brown–Okamoto's σ^{+}[32] giving $\rho^{+} = -2{\cdot}98$.


(33*c*)

(33*t*)

(21)

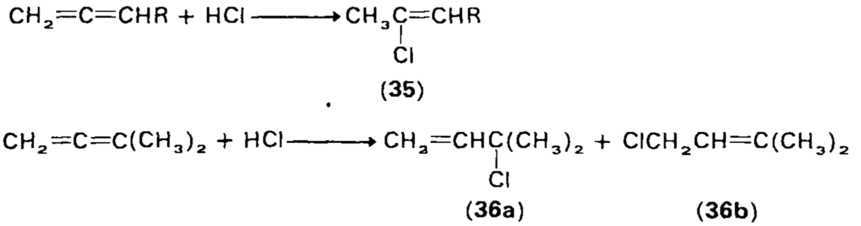
These data are consistent with a mechanism involving rate-determining protonation to form a different allylic cation from each diene in the rate-determining step. Since the same product is formed regardless of the geometry of the initial diene, isomerization to a common allylic ion must occur prior to the product determining step. This indicates that isomerization of the *cis* allylic ion **34** is faster than reaction with chloride ion (equation 22). While some allylic cations have been observed to have high


(34)

(22)

barriers to rotation[33]. The acid-catalysed isomerization of **33*c*** has been observed in aqueous media which provides support for this mechanism[34].

The orientation of the addition of HCl to allenes depends upon the structure of the allene. The additions to allene and monoalkyl allenes occur at the terminal methylene to form vinyl chlorides (**35**) as products while addition to 1,1-dimethylallene occurs at the central carbon to form the allylic chlorides **36a**, **36b**, as products[36] (equation 23).


$$CH_2{=}C{=}CHR + HCl \longrightarrow CH_3\underset{\substack{|\\ Cl}}{C}{=}CHR$$

(35)

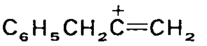
$$CH_2{=}C{=}C(CH_3)_2 + HCl \longrightarrow CH_2{=}CH\underset{\substack{|\\ Cl}}{C}(CH_3)_2 + ClCH_2CH{=}C(CH_3)_2$$

(36a) (36b)

(23)

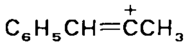
The addition of HCl to phenylallene in glacial acetic acid forms exclusively cinnamyl chloride (equation 24)[37]. This result excludes the possibility of protonation of the terminal carbon atoms of the allene to form either of the vinyl cations **37** and **38**. It cannot however, distinguish between

$$C_6H_5CH{=}C{=}CH_2 + HCl \longrightarrow C_6H_5CH{=}CHCH_2Cl \qquad (24)$$



$C_6H_5CH_2\overset{+}{C}{=}CH_2$

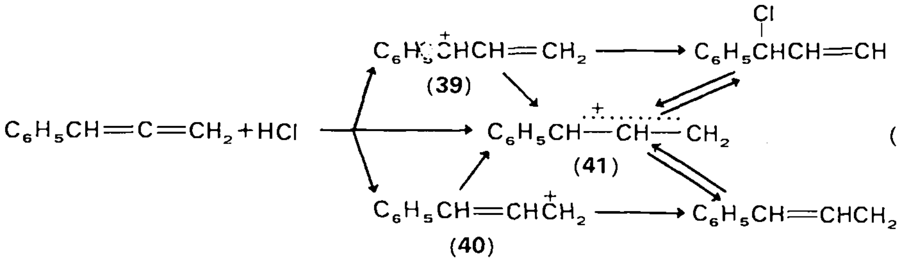
(37)



$C_6H_5CH{=}\overset{+}{C}CH_3$

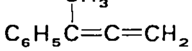
(38)

the three cationic intermediates of the mechanism in equation (25). The structure of the cations **39** and **40** differ from the allylic cation **41** in that the p atomic orbital of the carbonium ion **39** or **40** remains orthogonal to the ethylenic π-bond.



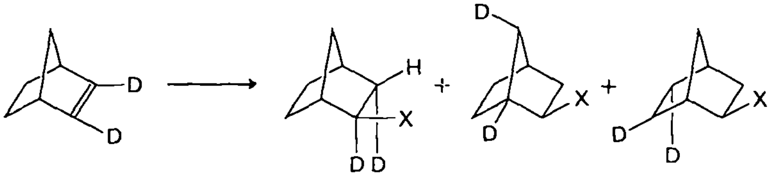
(25)

To establish the structure of the intermediate cation, Okuyama has measured the rate of addition of HCl to a series of substituted allenes[37]. At HCl concentrations between 0·10 and 0·25 M the rate law is overall second order, first order in both alkene and HCl. At higher concentration of HCl(0·64–1·33 M) the order with respect to HCl is second. A plot of log k_3 for several ring substituted phenylallenes obeys the Hammett-type relationship with σ^+ giving $\rho^+ = -4{\cdot}20$ ([HCl] = 0·955 M, 30·4 °C). A plot of log k_2 versus σ^+ gives a value of ρ^+ of $-5{\cdot}0$ ([HCl] = 0·198 M). The relative rates of addition to phenylallene, its α and γ-methyl isomers and *trans*-1-phenylbutadiene-1,3 are

$C_6H_5C{=}C{=}CH_2$	 $C_6H_5\overset{CH_3}{C}{=}C{=}CH_2$	$C_6H_5C{=}C{=}CHCH_3$	$C_6H_5CH{=}CHCH{=}CH$
(42)	(43)	(44)	(45)
1·0	4000	200	1100

The large negative value of ρ^+ is evidence of a positive charge in direct conjugation with the phenyl ring indicating that **39** is the intermediate formed by rate determining protonation. The significantly larger (20 ×) rate increase caused by the α-methyl of **43** as compared with the γ-methyl group of **44** lends support to this view. While **45** reacts only 5·5-times faster than **44**, it is estimated that the conjugated diene **45** is more stable than the allene **44** by at least 10 kcal[38]. This indicates that the rate-determining transition state for addition to **44** is far less stable than that of **45**. Since the mechanism of addition of HCl to **45** involves an allylic ion, it can be concluded that the structure of the rate-determining transition state for the addition to the phenylallenes very closely resembles the orthogonal cation **39**.

Hydrogen or deuterium chloride, bromide and fluoride have been added to a number of bicyclic alkenes under a variety of experimental conditions. The addition of HF, HCl and HBr to 2,3-dideuterionorbornene (**46**) in CH_2Cl_2 forms **47**, **48** and **49** in the percentages indicated in equation (26)[39]. The non-rearranged adduct **47** is formed by *exo–syn* addition in all

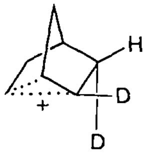


(26)

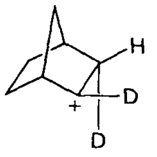
(46) (47) (48) (49)

	(47)	(48)	(49)
HF	22	24	54
HCl	56	42	~2
HBr	54	40	5

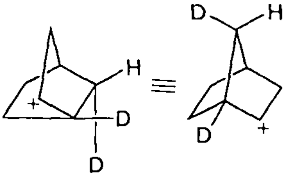
cases. Since **47** and **48** are not formed in equal amounts (especially by addition of HCl and HBr), it is concluded that a non-classical ion **50** is not the sole product-forming intermediate. Protonation must occur initially to form the open ion **51** for if direct protonation to form **50** occurred, then



(50)



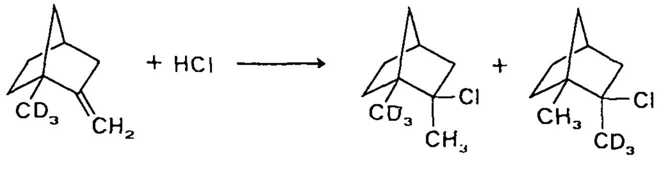
(51)



(52)

equal amounts of product due to capture at $C_{(1)}$ (**48**) and $C_{(2)}$ (**47**), should always be observed. The excess attack at $C_{(2)}$ is consistent with capture of **51** by the nucleophile either before it reaches equilibrium with **52** or before it leaks completely and irreversibly to **50**.

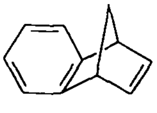
A similar mechanism involving a pair of equilibrating classical ions has been proposed to explain the results of the addition of HCl to 1-methyl-d_3-2-methylenenorbornane (**53**) (equation 27)[40]. Hydrochlorination of **53**



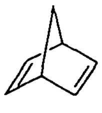
(27)

in diethyl ether or CH_2Cl_2 at 0 °C for only a few minutes produces an adduct with only about 50% scrambling of the CD_3 group. It is concluded that such a result is inconsistent with a non-classical ion intermediate, and it is proposed that a pair of equilibrating classical ions is trapped before complete equilibration has occurred.

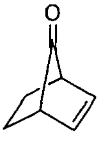
A similar mechanism involving classical ions has been proposed to explain the formation of non-rearranged products by predominantly *exo–syn* addition of hydrogen halides to **54**[41], **55**[42], **56**[43], and **57**[44]. The *exo–syn* addition of HCl to **57** has been taken as evidence against a concerted *syn* Ad_E2 mechanism in the addition to norbornene derivatives.



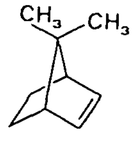
(**54**)



(**55**)



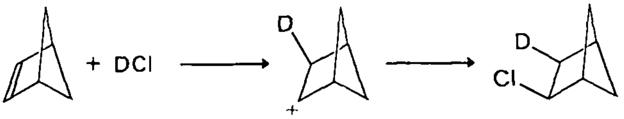
(**56**)



(**57**)

The steric hindrance of the 7,7-dimethyl substituents should prevent *exo–syn* addition. Since this is not observed, such a mechanism is rejected[45].

Stereospecific *syn* addition of DCl in CH_2Cl_2 at −78 °C to bicyclo-[2.1.1]hex-2-ene (**58**) has been observed (equation 28)[46]. Because of its symmetry, the classical cation (**59**), proposed as the intermediate in the



(28)

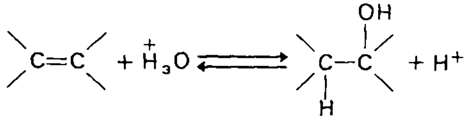
(**58**) (**59**)

addition, lacks the torsional and steric strains invoked to explain the lack of *anti* addition to the norbornyl classical cations[44,47]. The remarkable stereospecificity of the addition to **58**, implies that the factors controlling the stereochemistry of addition to norbornene may not be those governing the *exo*:*endo* ratios in norbornyl solvolysis.

Two different $\mathrm{Ad_E3}$ mechanisms have been postulated to explain the overall third-order, *anti*-stereospecific addition of hydrogen halides to alkenes. One is a mechanism in which the second molecule of hydrogen halide assists in the breaking of the bond of the electrophile in the rate-determining transition state with the subsequent formation of a carbonium ion. The second is one in which the hydrogen and halide are simultaneously delivered by different species to both carbons of the double bond in the rate-determining transition state. Fahey[19] has pointed out that the transition state composition and stereochemical requirements for halide ion promoted elimination[48], and the latter mechanism of addition of HCl to cyclohexenes, are identical which suggests that the two mechanisms (synchronous *anti* $\mathrm{Ad_E3}$ and E2) involve analogous pathways. In such a case, the spectrum of transition states of E2 eliminations[49] could apply to $\mathrm{Ad_E3}$ addition reactions as well. Thus the transition state leading to carbonium–halide ion-pair and the transition state for a synchronous *anti* addition would be at opposite ends of the spectrum. While attractive, experimental evidence is lacking for such an all-inclusive mechanism.

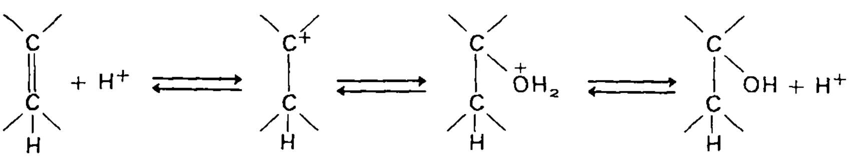
B. Addition of Water, Alcohols, and Carboxylic Acids

Unlike the addition of hydrogen halides, the addition of water, alcohols, and carboxylic acids to alkenes requires acid catalysis. The addition of water, usually referred to as hydration, is reversible (equation 29). The



$$\mathrm{{>}C{=}C{<}} + \mathrm{H_3\overset{+}{O}} \rightleftharpoons \mathrm{{>}\underset{H}{C}{-}\overset{OH}{C}{<}} + \mathrm{H^+} \qquad (29)$$

position of the equilibrium depends upon the structure of the alkene and the experimental conditions. The addition is regiospecific forming products with Markownikoff orientation. Sometimes products of skeletal rearrangement are formed. These observations are consistent with a mechanism involving a carbonium ion intermediate (equation 30)[50].



(30)

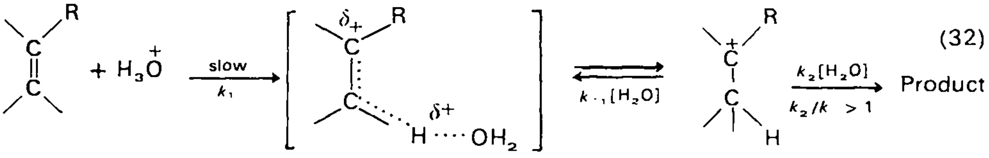
Numerous studies have been carried out to establish the rate-determining step of this mechanism. Only recently has it become clear that proton transfer from the catalyst to the alkene is rate determining. This conclusion is based upon the following experimental evidence.

The rates of hydration show a marked increase with the acidity of the medium. Plots of $\log k_{\text{hyd}}$ versus $-H_0$ (Hammett's acidity function), $-H_0'$[51], and $-H_R$[52] are linear. The hydration of *p*-methoxy-*α*-methylstyrene at 30 °C in formic acid buffer solutions at low and constant ionic strength shows general acid catalysis (equation 31)[53]. A solvent deuterium isotope effect ($k_{H_3^+O}/k_{D_3^+O}$) of between 1 and 6 is found depending upon the alkene and the type and strength of acid used[53,54,55]. Plots of $\log k_{\text{hyd}}$ versus σ^+ are linear with values of $-3{\cdot}58$ and $-3{\cdot}21$ for ρ^+ for styrenes[53] and α-methylstyrenes[56] respectively. Under conditions such that the alcohol formed does not dehydrate appreciably, no exchange between the solvent and the hydrogen of the unreacted alkene is observed[57,58]. The volumes of activation for the acid-catalysed hydration of propene and isobutylene are $-9{\cdot}6 \pm \sim 1{\cdot}0$ cm^3/mol at 100 °C and $-11{\cdot}5 \pm \sim 1{\cdot}0$ cm^3/mol at 35 °C respectively[59].

$$k_{\text{obs}}^{50\,^{\circ}\text{C}} = 0{\cdot}155[\text{H}_3^+\text{O}] + 3{\cdot}00 \times 10^{-4}[\text{HCO}_2\text{H}] \qquad (31)$$

On the basis of these observations, certain conclusions can be reached regarding the rate-determining transition state. The acidity dependence of k_{hyd} requires that the rate-determining transition state contains a proton while general acid catalysis indicates that it also contains a base. The volumes of activation are consistent with a molecule of water bound into the transition state. The primary isotope effect indicates that the proton is undergoing a covalency change and the value of ρ^+ implies a strong demand for electrons from the phenyl ring to the benzylic carbon. The steepness of the plots of acidity versus $\log k_{\text{hyd}}$ indicate that specific hydrogen-bonding solvation of the rate-determining transition state is probably weak. Based upon the rates of hydration of styrene and the rates of dehydration and O^{18} exchange on 1-phenylethanol[60], it is concluded that a symmetrical intermediate is formed after the rate-determining transition state of hydration[53].

The hydration mechanism which most simply fulfils the requirements is one involving rate-determining direct proton transfer to the alkene (equation 32). A number of other mechanisms are inconsistent with the data. Any synchronous *anti* Ad$_E$3 mechanism or one involving rapid and reversible formation of a π-complex intermediate which undergoes



(32)

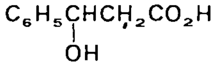
rate-determining collapse to a carbonium ion are ruled out. The key observation which eliminates this latter mechanism is catalysis by general acids. In the last few years, examples of general acid-catalysed hydration of alkenes have become more numerous. Thus hydration of *p*-methoxy-α-methylstyrene[53,62] *m*- and *p*-aminostyrenes[61], *trans*-cyclooctene[63], 2,3-dimethylbutene-2[63], and bicyclo[3.3.1]nonene-1[64] have all been reported to show general acid catalysis.

Another example of this mechanism is the acid-catalysed hydrolysis of vinyl ethers which has been extensively studied by Kresge and coworkers (equation 33). Rate-determining proton transfer to the double bond has

$$H_2C{=}CHOCH_3 + H_2O \xrightarrow{H^+} CH_3CHO + HOCH_3 \qquad (33)$$

been established as the mechanism by the observation of a solvent deuterium isotope effect and general acid catalysis[55,65]. Further evidence that the vinyl ether reacts as an alkene is provided by the fact that the O^{18} does not appear in the saturated alcohol product of hydrolysis conducted in O^{18}-enriched water[66]. The rates of hydrolysis of a number of vinyl ethers in aqueous dioxane show a structure reactivity pattern similar to that of normal electrophilic additions to alkenes[67]. This provides further evidence that rate-determining protonation is to the double bond and not to the ether oxygen. Consequently the mechanism of acid-catalysed hydrolysis of vinyl ethers is the same as that of simple alkenes illustrated in equation 32 (where $R = OCH_3$).

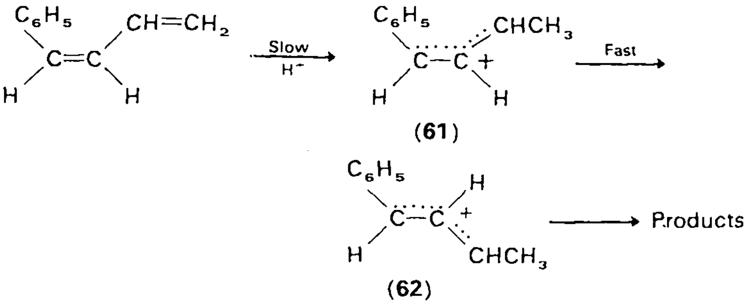
Evidence for a similar mechanism involving rate-determining protonation of a carbon–carbon double bond has been obtained for the acid-catalysed isomerization of *cis*-cinnamic acid[68–70].



$$C_6H_5\underset{\displaystyle OH}{\underset{|}{C}}HCH_2CO_2H$$

(60)

N.m.r. evidence for the presence of the alcohol **(60)** as an intermediate in the isomerization of *cis*-cinnamic acid has been reported[71]. The mechanism of isomerization of *cis*-1-phenyl-1,3-butadiene also involves rate-determining protonation at the terminal site to form the *cis*-carbonium ion (**61**) which rapidly isomerizes to the *trans*-ion (**62**) (equation 33a)[34].

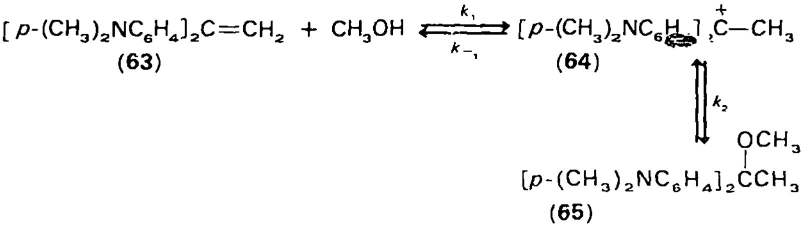


(**61**)

(**62**)

(33a)

The acid-catalysed addition of methanol to 1,1-bis(*p*-dimethylaminophenyl)ethylene (**63**) in 80% methanol–water has been studied by Bernasconi and Boyle (equation 34)[72]. The reaction exhibits slow, general



$$[p\text{-}(CH_3)_2NC_6H_4]_2C{=}CH_2 + CH_3OH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [p\text{-}(CH_3)_2NC_6H_4]_2\overset{+}{C}{-}CH_3 \overset{k_2}{\rightleftharpoons} [p\text{-}(CH_3)_2NC_6H_4]_2\overset{OCH_3}{C}CH_3 \quad (34)$$

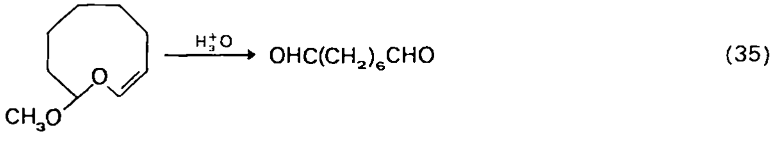
(**63**) (**64**) (**65**)

acid-catalysed protonation at the double bond to form the carbonium ion **64** which is rapidly converted to the methyl ether by reaction with either methoxide ion or methanol. All three species **63**, **64** and **65** can be detected in solution and as a result complete kinetic and equilibrium analysis of the component steps has been accomplished. The rate constant for protonation of **63** (k_1) is 23·1 mol^{-1} s^{-1} while that for deprotonation of **64** (k_{-1}) by solvent is $4{\cdot}8 \times 10^{-2}$ s^{-1}. The ratios of k_2/k_{-1} for methanol and methoxide ion are 1×10^6 and 500 respectively. These data clearly establish that this addition of methanol proceeds by rate-limiting proton transfer; a mechanism similar to that in equation (32).

The rate of acid-catalysed addition of acetic acid to cyclohexene in acetic acid is found to give a linear correlation between log k_{exp} and H_0 (the Hammett acidity function)[73]. The reaction is subject to general acid catalysis and a kinetic isotope effect is observed. A mechanism involving rate-determining protonation analogous to that for alkene hydration (equation 32) is consistent with the data.

The observation that *t*-alcohols undergo ^{18}O exchange only one or two orders of magnitude more rapidly than they dehydrate to alkenes suggests that capture of the carbonium ion by water ($k_2[H_2O]$ in equation 32) is not very much faster than proton loss to regenerate the alkene ($k_{-1}[H_2O]$ in equation 32)[60,74,75]. Therefore changes in the structure of the alkene or the nature of the general acid catalyst might result in $k_{-1}[H_2O]$ becoming larger than $k_2[H_2O]$ which would cause a change in the mechanism of the reaction. The hydrolysis of propiophenone enamines is an example of just such a change in mechanism[76]. In strongly basic solutions (pH $>$ 10) the mechanism is rate-determining proton transfer from the general acid to the enamine, while in weakly acidic solutions (pH $\approx$ 5) uncatalysed water attack becomes rate determining.

Recently the first exception to the mechanism in equation (32) for the hydrolysis of vinyl ethers has been found[77]. The hydrolysis of 9-methoxyoxacyclonon-2-ene (**66**, equation 35) in dilute aqueous hydrochloric acid



(66)

exhibits a large solvent isotope effect. This large maximum[78] solvent isotope is evidence against a mechanism involving a fast pre-equilibrium protonation of oxygen and is consistent with rate determining protonation of the double bond. However, unlike most vinyl ethers, a non-linear relationship is observed between k_{hyd} and buffer acetic acid concentration. This behaviour is explained by postulating a mechanism involving rapid and reversible protonation of the double bond followed by a subsequent rate-determining step.

The acid-catalysed hydration of α,β-unsaturated ketones also seems to occur by two mechanisms. Either protonation of the double bond or attack by water on the carbonium ion can be rate-determining depending upon the structure of the compound. The hydration of 3-buten-2-one occurs by the former mechanism[79] while 4-methoxy-3-buten-2-one occurs by the latter[80].

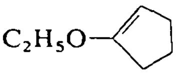
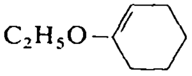
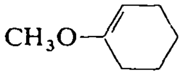
While the results of hydration of enamines, vinyl ethers, and α,β-unsaturated ketones indicate that the mechanism can be changed by varying the alkene structure and/or the experimental conditions, no such evidence is available for a change in mechanism for the hydration of alkenes containing only alkyl or aryl substituents.

Attempts have been made to deduce details of the rate-determining transition state for the hydration of alkenes from the exponent α of the Brønsted relation (equation 36)[81] which correlates catalytic coefficients,

$$k_{\mathrm{HA}} = G(K_{\mathrm{HA}})^{\alpha} \qquad (36)$$

k_{HA}, for a given reaction with the acid dissociation constants of the catalysts, K_{HA}. There is some reason to believe that the exponent α might be related to the degree of proton transfer in the transition state[82]. Consequently Brønsted relations have been constructed for the acid-catalysed hydration of a number of alkenes and vinyl ethers. Because of the slow rate of hydration of most simple alkenes, most data are available for styrene derivatives and vinyl ethers. The data are summarized in Table 1. In

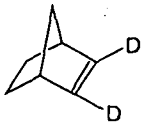
TABLE 1. Brønsted exponents for hydration of alkenes

Alkene	Brønsted exponent	Reference
$C_2H_5OCH{=}C(CH_3)_2$	0·64 ± 0·04	83
	0·63 ± 0·03	83
	0·58 ± 0·03	83
	0·66 ± 0·03	83
$C_6H_5OCH{=}C(CH_3)_2$	0·61 ± 0·03	83
$C_2H_5OCH{=}CH_2$	0·70 ± 0·03	83
$C_6H_5OCH{=}CH_2$	0·84 ± 0·05	83
$4\text{-}CH_3OC_6H_4C(CH_3){=}CH_2$	>0·49	53
$(CH_3)_2C{=}CH_2$	0·85 ± 0·10	54
$4\text{-}(CH_3)_2NC_6H_4CH{=}CH_2$	0·78	61
$4\text{-}NH_2C_6H_4CH{=}CH_2$	0·74	61
$4\text{-}CH_3OC_6H_4CH{=}CH_2$	0·45	62
$4\text{-}CH_3OC_6H_4C(CH_3){=}CH_2$	0·47	62
$3\text{-}CH_3C_6H_4C(CH_3){=}CH_2$	0·61	62
$C_6H_5C(CH_3){=}CH_2$	0·57	62
$4\text{-}ClC_6H_4C(CH_3){=}CH_2$	0·57	62
$3\text{-}ClC_6H_4C(CH_3){=}CH_2$	0·71	62

general the Brønsted exponents are between 0·45 and 0·90. These data have been taken to indicate that in the rate-determining transition state, proton transfer is far advanced (50% or greater). However, a more quantitative interpretation of the data is complicated by deviations from the Brønsted relation[83]. Such deviations, anomalous Brønsted exponents and curved Brønsted plots, together with their implications on certain uses of the Brønsted relation have recently been reviewed by Kresge[84].

While considerable data are available concerning the rate of additon, little is known about the stereochemistry of the addition of water, alcohols and carboxylic acids to simple alkenes. The first attempt was that of Hammond and Collins[85] who studied the hydration of 1,2-dimethylcyclohexene. While the addition was found to be non-stereospecific, the interpretation is clouded by the fact that the starting material contained 15% of 2,3-dimethylcyclohexene which would form the same product upon hydration.

More recently acid-catalysed additions of water, alcohols, and carboxylic acids to a number of bicyclic alkenes have been reported. These additions, like those of the hydrogen halides are predominantly *exo–syn*. For example, *exo–syn* addition, as well as rearranged products, has been reported for the acid-catalysed addition of methanol to **46**[39], perdeuterio acetic acid to **54**[41], and trifluoroacetic-*O-d* and perdeuterio acetic acid to **57**[86] while exclusive *exo–syn* acid-catalysed addition of acetic acid-*O-d* to **58** is found[46]. However special structural features of these bicyclic alkenes make the stereochemical results inapplicable to simple cyclic or acyclic alkenes.



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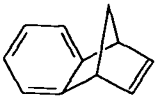

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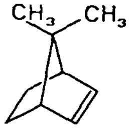

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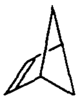
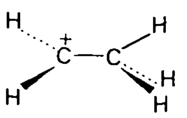


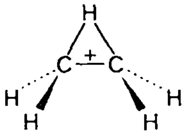
(58)

The addition of hydrogen halides and halogens to alkenes in water, alcohols, and carboxylic acids as solvents results in solvent incorporated products formed by predominantly *anti* addition (see Sections II.A and III). It is postulated that these products are formed either by solvent attack on an ion pair or by a concerted Ad_E3 mechanism. The importance of either of these mechanisms in the acid-catalysed addition of water, alcohols, and carboxylic acids has yet to be demonstrated.

The addition of a proton to ethylene to form the ethyl cation has been the subject of several molecular orbital investigations. Semi-empirical[87–89] calculations predict the classical or open cation (**67**) to be more stable than the bridged ion (**68**). The results of *ab initio* calculations depend upon the basis set used[90–92]. Earlier work confirmed the semi-empirical calculations but the most extensive *ab initio* calculations[92] showed that inclusion of d-functions on the carbon atoms and a p-function on the bridged hydrogen, stabilized the cyclic structure relative to the open ion.



(67)



(68)

From the available data, it can be concluded that the hydration of simple alkenes occurs by a mechanism involving rate-determining transfer of the proton from the catalyst to the substrate. In the rate-determining transition state, the proton is more than halfway transferred. Acid-catalysed *cis–trans* isomerization of alkenes and additions of methanol and acetic acid to alkenes occurs by a similar mechanism. Certain substituted alkenes, such as vinyl ethers, enamines and α,β-unsaturated ketones can undergo hydration by two mechanisms: one like that of simple alkenes and another involving rate-determining water attack on the conjugate acid of the alkene. The stereochemistry of the acid-catalysed addition of water, alcohols, and carboxylic acids is not conclusively established.

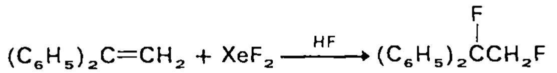
III. HALOGENS

A. Fluorine

Very little has been reported on the addition of molecular fluorine to carbon–carbon double bonds. The reactions are exothermic and are often quite violent. Because of its low bond-dissociation energy (37·7 kcal/mol) reactions of molecular fluorine are often homolytic in nature.

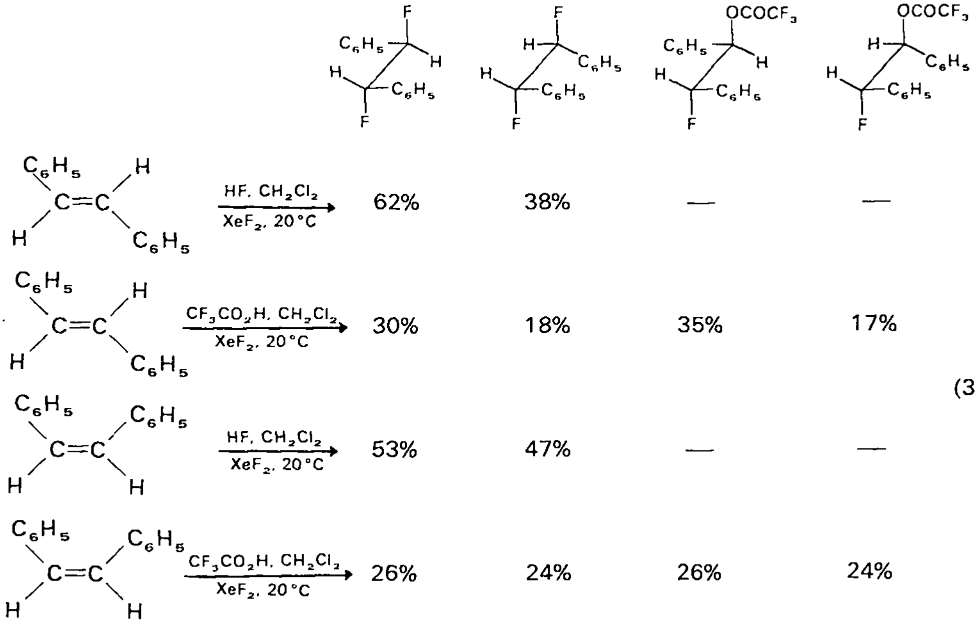
Among the reactions of molecular fluorine which seem to occur by an ionic mechanism are the fluorination of stilbene, indene, acenaphthylene and *cis*- and *trans*-1-phenylpropene at low temperatures in halogenated hydrocarbons[93–95]. Products formed by preferential *syn* addition were found in most cases and were explained by either an open carbonium ion or a four-centre molecular *syn* addition mechanism.

Recently the reaction of xenon difluoride with alkenes in the presence of hydrogen fluoride or trifluoroacetic acid as catalyst to form vicinal difluoro adducts has been reported[96,97]. The reaction of 1,1-diphenylethylene to form 1,2-difluoro-1,1-diphenylethane in nearly quantitative yield is an example of this reaction (equation 37).



$$(C_6H_5)_2C{=}CH_2 + XeF_2 \xrightarrow{HF} (C_6H_5)_2\overset{F}{\overset{|}{C}}CH_2F \qquad (37)$$

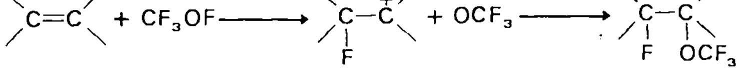
The stereochemistry of the products of the reaction of *cis*- and *trans*-stilbenes with XeF_2 is given in equation (38). While the vicinal difluoro adducts are the only products in the hydrogen fluoride catalysed reactions, the amount of trifluoroacetate product is close to 50% in the trifluoroacetic acid catalysed reaction. From the data in equation (38) it is clear that


F
C6H5
H
H
C6H5
F
F
H
C6H5
H
C6H5
F
OCOCF3
C6H5
H
H
C6H5
F
OCOCF3
H
C6H5
H
C6H5
F
C6H5 H C=C H C6H5
HF, CH2Cl2 XeF2, 20 °C
62%
38%
—
—
C6H5 H C=C H C6H5
CF3CO2H, CH2Cl2 XeF2, 20 °C
30%
18%
35%
17%
C6H5 C6H5 C=C H H
HF, CH2Cl2 XeF2, 20 °C
53%
47%
—
—
C6H5 C6H5 C=C H H
CF3CO2H, CH2Cl2 XeF2, 20 °C
26%
24%
26%
24%

(38)

the products are formed in a non-stereospecific manner. *Trans*-stilbene does form preferentially the adduct by *anti* addition whereas the *cis*-isomer reacts non-stereospecifically to form about equal amounts of the *meso* and *dl* adducts.

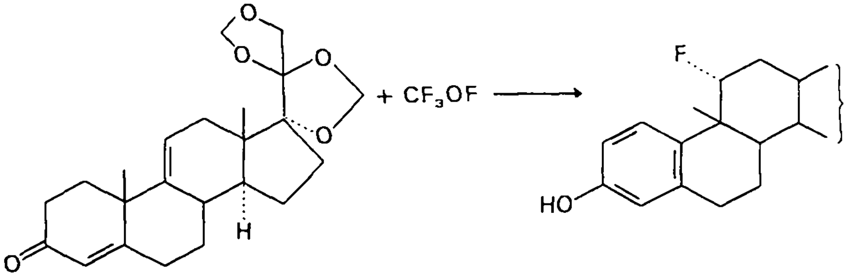
The electrophilic addition of fluoroxy compounds such as fluoroxy trifluoromethane (**69**) and 2-fluoroxy-2-trifluoromethylperfluoropropane to a variety of alkenes has been reported[98]. The addition is postulated to occur by a mechanism involving an α-fluorocarbonium ion (**70**, equation 39). In support of this mechanism, the addition of **69** to alkene **71** results in


C=C
+ CF3OF
C—C
+
F
+ OCF3
−
C—C
F
OCF3

(39)

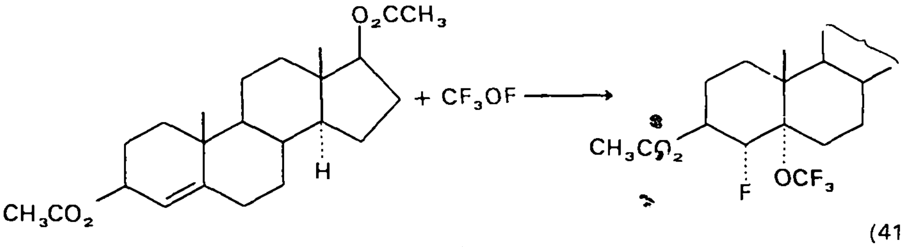
(69) (70)

the formation of the phenol **72** as the major product (equation 40)[99]. Such a rearrangement has precedent and is evidence of a carbonium ion



(71) (69) (72) (40)

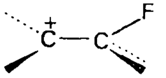
intermediate[100]. The regio- and stereochemistry of the addition was determined by the addition of **69** to **73** which gave **74** as the major product in which the fluorine is *trans*-diequatorial with respect to the acetoxy group (equation 41). Thus the addition forms Markownikoff adducts by



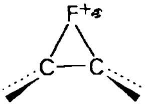
(73) (69) (74) (41)

syn addition which excludes the involvement of a bridged cation in these reactions.

Attempts to use molecular orbital calculations to determine which of the two limiting structures, the α-fluorocarbonium ion (**75**) or the bridged fluoronium ion (**76**) is the more stable have not been very successful. The results depend upon the quality of the basis set used in the calculations. Clark[101] using a 22-sp basis set found that the ion **76** is more stable by 3·58 kcal/mol while Hehre[102], using a 19-sp (STO-3G) basis set found that **76** is more stable by 19·66 kcal/mol. Using the more extensive, (split



(75)



(76)

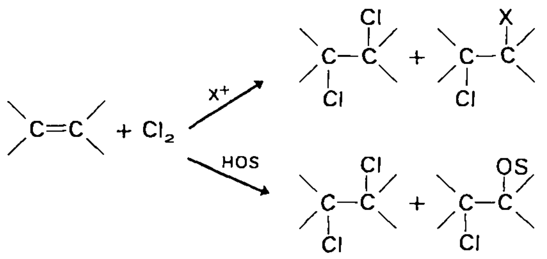
valence shell) 23-sp (4-31G), basis set Hehre found that the open ion **75** is more stable by 11·49 kcal/mol.

Csizmadia and coworkers[103] using a large basis set of Gaussian type functions to optimize the geometries of both ions found that the 2-fluoroethyl carbonium ion (**75**) shows a greater stability than the fluoronium ion (**76**) by about 10 kcal/mol. In keeping with these results Olah and coworkers[104,105] have been unable to observe the fluoronium ion in solutions of SbF_5–SO_2ClF by n.m.r. spectroscopy.

From the data available, it is clear that the ionic addition of fluorine to alkenes occurs non-stereospecifically. A mechanism involving either an open carbonium-ion intermediate prior to the product-determining step similar to that for chlorination and bromination of arenes and/or a four-centre *syn* addition has been proposed to account for the product stereochemistry.

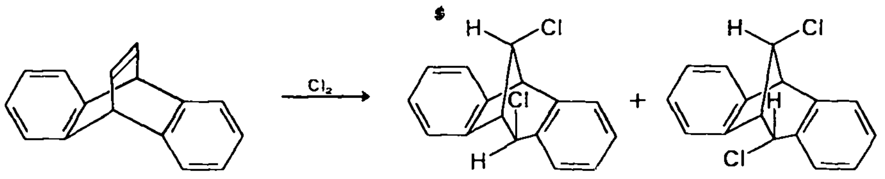
B. Chlorine

Chlorine adds to alkenes to form the expected vicinal dichlorides (**77**). In the presence of added nucleophiles or hydroxylic solvents, addition of chlorine often forms mixed products (equation 42). Skeletal rearrangement (equation 43)[106] and addition–elimination products (equation 44)[107] are sometimes observed as side products. Chlorination, like bromination and iodination, can be carried out in any solvent that does not react with chlorine. In polar and non-polar solvents under oxygen, the addition of

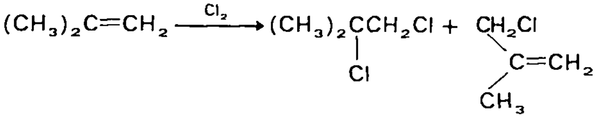


(77)

(42)



(43)



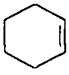
$$(CH_3)_2C{=}CH_2 \xrightarrow{Cl_2} (CH_3)_2\underset{\underset{\textstyle Cl}{|}}{C}CH_2Cl + \begin{array}{l} CH_2Cl \\ \quad \diagdown \\ \qquad C{=}CH_2 \\ \quad \diagup \\ CH_3 \end{array} \qquad (44)$$

chlorine occurs by an ionic mechanism. In the absence of oxygen, even in the dark, chlorination in non-polar solvents can occur spontaneously by a radical mechanism[108].

The rate law for the chlorination of alkenes is second order overall, first order in both alkenes and chlorine[109,110]. Unlike bromination or iodination no terms higher than first order in chlorine have been observed. Catalysis by HCl in acetic acid has been reported to be first order in HCl[111]. Autocatalysis occurs when HCl is spontaneously eliminated from the product during chlorination. Addition of chlorine to 2-bromo, 2-chloro and 2-phenylpropene in CCl_4 is catalysed by HCl. In the presence of excess HCl, the reaction exhibits second order dependence upon HCl[112].

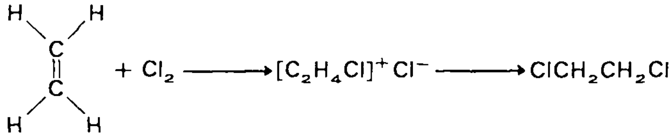
The rates of chlorination are so fast that until recently the only kinetic data available were limited to alkenes containing electron-withdrawing substituents[113]. Even with the latest techniques the rates of chlorination of many alkyl-substituted ethylenes cannot be measured directly and consequently competitive techniques must be used. The relative rates of the alkenes reported in Table 2 were obtained in this way[114]. From the data, it is clear that alkyl groups strongly accelerate the rate while electron-withdrawing substituents greatly depress the rate of chlorination.

TABLE 2. Relative reactivities of alkyl-substituted alkenes with chlorine in neat alkene[114]

Alkene	k_{rel}
$(CH_3)_2C{=}C(CH_3)_2$	$4{\cdot}3 \times 10^5$
$(CH_3)_2C{=}CHCH_3$	$1{\cdot}1 \times 10^4$
$C_2H_5(CH_3)C{=}CH_2$	$1{\cdot}6 \times 10^2$
$(CH_3)_2C{=}CH_2$	58
	50
(*t*) $CH_3CH{=}CHCH_3$	50
(*c*) $CH_3CH{=}CHCH_3$	63
$(CH_3)_3CCH{=}CH_2$	1·15
$C_2H_5CH{=}CH_2$	1·00
$CH_2{=}CHCH_2Cl$	3×10^{-3}
(*c*) $ClCH{=}CHCl$	$>5 \times 10^{-7}$

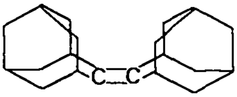
The rates of chlorination in acetic acid of a series of phenyl-substituted cinnamic acids[115] and styrenes[116] have been measured directly and found to follow overall second-order kinetics. Both series of compounds were found to give good Hammett correlations with ρ^+ values of -3.9 for cinnamic acids[115] and -3.22 for styrenes[116].

The simplest mechanism consistent with the rate law as well as the formation of rearranged and solvent-incorporated products is an Ad_E2 mechanism involving a cationic intermediate (equation 45). While spectral



(45)

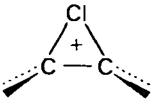
data have been reported for a charge-transfer complex between chlorine and alkenes, there is no firm evidence that this complex is on the reaction coordinate for chlorination[117,118]. The structure of the product of the chlorination of adamantylideneadamantane (**78**) has been assigned a



(**78**)

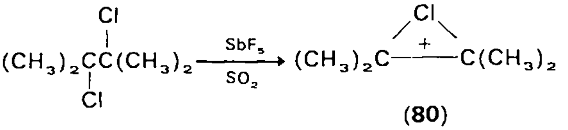
charge-transfer structure on the basis of chemical and spectral data[119,120]. However since **78** does not form a 1,2-dichloride, this does not necessarily provide further evidence as to the intermediacy of charge-transfer complexes in chlorination.

Olah[121] has provided n.m.r. evidence that a cyclic chloronium ion (**79**) is capable of existence. Thus 2,3-dichloro-2,3-dimethylbutane reacts with



(**79**)

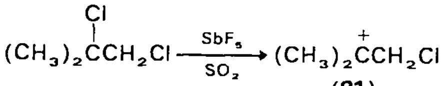
an SbF_5–SO_2 solution to form an ion whose n.m.r. spectrum is best explained by the bridged structure **80** (equation 46). In contrast the similar reaction with 1,2-dichloro-2-methylpropane leads to an ion whose n.m.r.



(46)

(**80**)

spectrum is best explained by the open ion **81** (equation 47)[122]. These results suggest that the energy difference between an open α-chlorocarbonium and a bridged chloronium ion is not very great. Supporting this view is the fact that chlorine is a poor neighbouring group indicating that there is little driving force for the formation of chloronium ions in solvolytic reactions[123]. *Ab initio* calculations on the ethylene–chlorine system, on the other hand, favour the bridged chloronium ion structure by 9·4 kcal/mol[103].



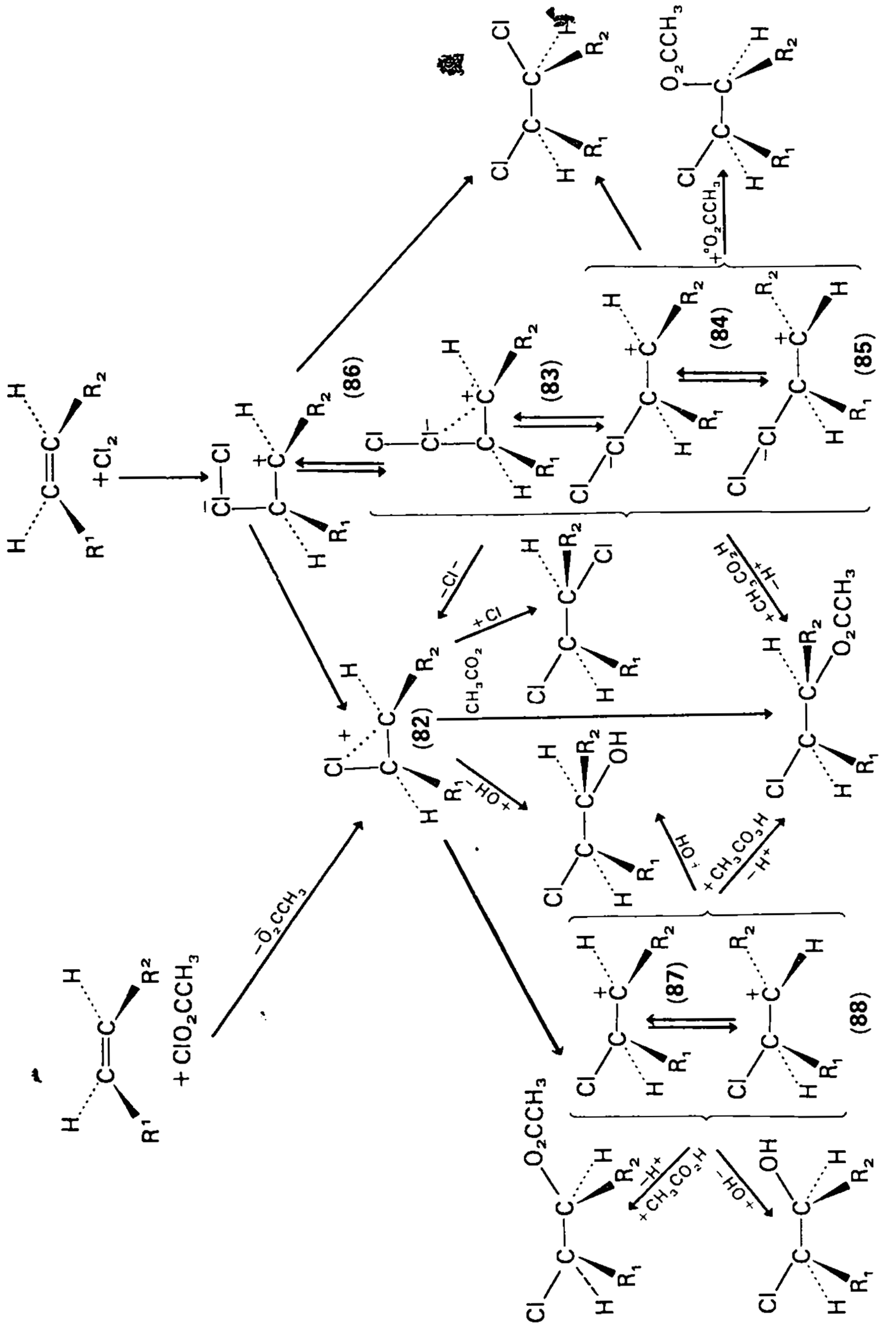
$$(CH_3)_2\overset{\overset{\textstyle Cl}{|}}{C}CH_2Cl \xrightarrow[SO_2]{SbF_5} (CH_3)_2\overset{+}{C}CH_2Cl \qquad (47)$$

(81)

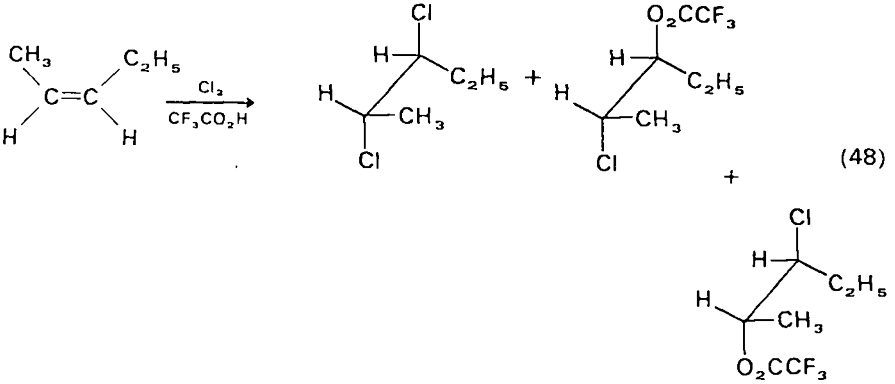
Valuable insight into the importance of these ions in the mechanism of chlorination has been provided by the work of de la Mare[124] who has determined the proportions of diastereoisomeric acetoxy chlorides formed by the addition of chlorine acetate in acetic acid to a number of alkenes. The ratios differ markedly from those of the same products formed by addition of chlorine in acetic acid. Based upon this difference as well as the change in product ratio caused by changes in solvent and added salt, the mechanism in Scheme 2 was proposed which involves several different carbonium ion intermediates. These are a bridged ion (**82**), a bridged zwitterion (**83**), the open zwitterions **84** and **85**, a geometrically different zwitterion (**86**), and the open ions **87** and **88**. A very similar mechanistic scheme has been proposed by Yates and Leung[116]. Depending upon the alkene structure, one or more ions, and consequently one or more reaction paths may be favoured.

From the data of Poutsma, given in Table 2 it can be concluded that the effect of a methyl group on the rate of chlorination is independent of its position on the double bond. The fact that the rates of chlorination of methylpropene and of *cis*- and *trans*-2-butene are almost identical is consistent with a bridged rate-determining transition state in which charge is distributed over both carbons followed by formation of a bridged chloronium ion intermediate similar to **82**. These facts are inconsistent with formation of an open ion intermediate such as **84** which can interconvert to **85**.

Evidence for a bridged product-determining transition state is provided by the exclusive *anti* stereospecificity of the products of chlorination of the *cis*- and *trans*-2-butenes and 2-pentenes. Both the dichlorides and solvent incorporated products are formed by exclusive *anti* addition. Furthermore non-regiospecific solvent-incorporated products are formed (equation 48)[125].


+Cl$_2$
+ClO$_2$CCH$_3$
$-\bar{O}_2$CCH$_3$
(86)
(83)
(84)
(85)
(82)
(87)
(88)
$-$Cl$^-$
+Cl$^-$
CH$_3$CO$_2^-$
$+^-$O$_2$CCH$_3$
+CH$_3$CO$_2$H, $-$H$^+$
+$^-$OH

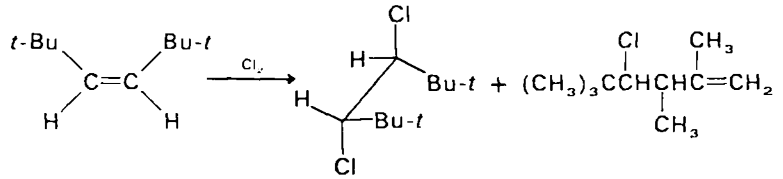
SCHEME 2.



(48)

Similar stereospecific *anti* addition of chlorine[107], $ClOH$[126] and ClO_2CCH_3[124] to cyclohexene has been observed which is consistent with the idea that the mechanism involves only the bridged ion **82**. However, changing the solvent effects the stereochemistry of the addition. Thus the formation of the 1,2-dichloride adduct by the ionic chlorination of *cis*- and *trans*-2-butene in anhydrous HF–NaF solution occurs non-stereospecifically[127]. This suggests that in highly polar solvents open ions are intermediates rather than the bridged ion resulting in open-ion like product-determining transition states. In contrast, chlorination of *trans*-ethylene-d_2 forms >96% *meso*-1,2-dichloroethane-1,2-d_2 by *anti* stereospecific addition. Thus it seems that in this solvent system, the chloronium ion is less stable than a secondary but more stable than a primary α-chloro carbonium ion.

As the number and complexity of the substituents on the double bond increase, there is a general increase in the amounts of products resulting from elimination of HCl. These elimination products are always the allylic rather than the vinyl chlorides (equation 44). Increased amounts of rearranged products are also formed as in the chlorination of *cis*-1,2-di-*t*-butylethylene in CCl_4 which forms 54% of the dichloride (**89**) and 46% of the rearranged product (**90**, equation 49)[128]. Since the dichloride is formed stereospecifically this suggests that the rearrangement occurs directly from



(49)

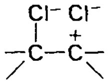
(**89**) (**90**)

the chloronium ion and that an open ion is not formed after the rate-determining transition state.

The chlorination of those alkenes capable of forming resonance-stabilized cations generally results in dichloro products formed by preferential *syn* addition in the absence of external chloride ion. Examples are found in the chlorination of phenanthrene[129], *cis*- and *trans*-stilbenes[130], 1-phenylpropenes[131],β-*t*-butylstyrenes[132] and methyl cinnamates[133]. The solvent-incorporated products, on the other hand are formed predominantly by *anti* addition. These results can be accommodated by the mechanism in Scheme 2. An exception to the above is the chlorination of *cis*- and *trans*-1-3-nitrophenylpropene in methylene chloride which was found to be stereoselective *anti*.

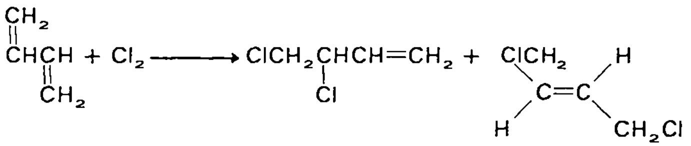
While the mechanism of the chlorination of cyclohexene and simple alkenes in acetic acid involves the path via the bridged intermediate **82**, the data for the chlorination of phenyl-substituted alkenes require the opening of the bridge. Thus forming intermediates **84** and **85** allows formation of both *cis*- and *trans*-acetoxy-chlorides. The *syn* addition of chlorine is postulated to occur via intermediate **86**. Since substantially different product distributions are obtained for the chlorination of methyl *cis*- and *trans*-cinnamates, it is concluded that the two intermediates **84** and **85** do not equilibrate prior to the product forming step[124].

Several authors who have proposed mechanisms similar to that in Scheme 2 prefer an intimate ion pair **91** as the precursor to the *syn* adduct rather than **86**[131,133,116]. The intervention of such an ion pair has been postulated to explain the effect of solvent on the product composition of the chlorination of *cis*- and *trans*-1-phenylpropene[116,131].

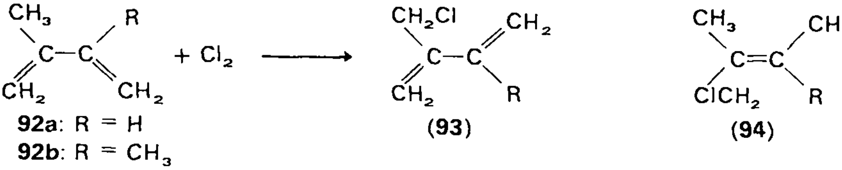


(91)

The chlorination of conjugated dienes forms 1,2- and 1,4-dichloro adducts. For example the ionic chlorination of 1,3-butadiene in non-polar solvents forms a 55:45 mixture of 3,4-dichloro-1-butene and *trans*-1,4,dichloro-2-butene (equation 50)[134,135]. The major products of the ionic chlorination of neat isoprene (**92a**) at 20°C and



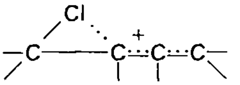
(50)



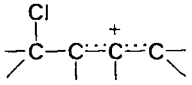
92a: R = H
92b: R = CH$_3$
(**93**)
(**94**)
(51)

2,3-dimethyl-1,3-butadiene (**92b**)[137] are those of substitution (**93a** and **93b** respectively) and 1,4-addition (**94a** and **94b** respectively, equation 51). Minor products include the 1,2-, 3,4- and *cis*-1,4-dichloro adducts. In all of these examples care was taken to ensure that the products were formed by an ionic mechanism.

While the product compositions can be explained by a mechanism involving a cation intermediate, the lack of any data on the product stereochemistry makes it impossible to assign either a bridged (**95**) or an open structure (**96**) to the intermediate.

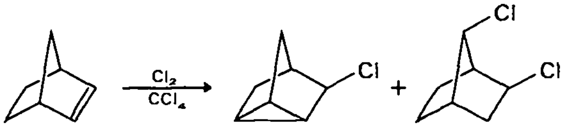


(**95**)



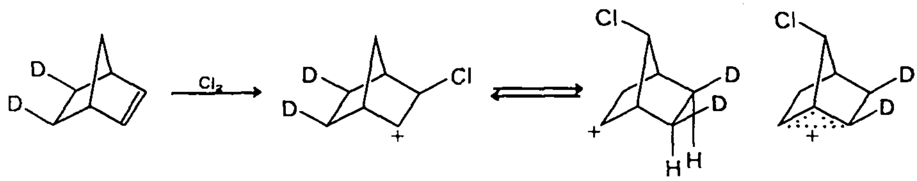
(**96**)

The ionic chlorination of bicyclic alkenes usually forms products of rearrangement and/or elimination of HCl. Thus the addition of chlorine to norbornene in CCl$_4$ forms nortricyclyl chloride (**97**) and *syn*-2,7-dichloronorbornane (**98**) as the main products (equation 52). The nortricyclyl chloride formed by the chlorination of *exo,exo*-5,6- and *endo,endo*-5,6-dideuterionorbornene occurs with proton (deuteron) loss from C$_{(6)}$ with *endo*-stereoselectivity[138]. This result strongly suggests that elimination occurs predominantly from ion **99a** or from the alternate non-classical ion **99b** (equation 53). The major products of the ionic chlorination of



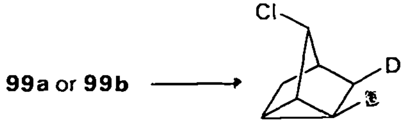
(**97**) (**98**)

(52)

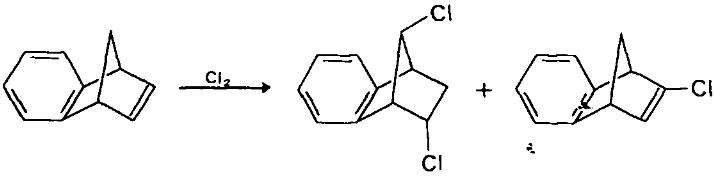


(**99a**) (**99b**)

(53)



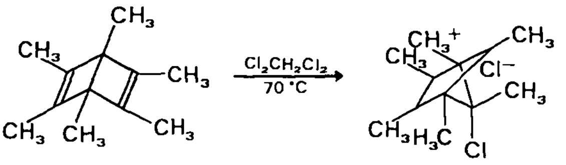
benzonorbornadiene are those of rearrangement (**100**), and elimination of HCl (**101**, equation 54)[139]. The addition of chlorine to hexamethyl Dewar



(54)

(100) **(101)**

benzene (**102**) in methylene chloride at −70 °C is reported to form product **103** which eliminates HCl at temperatures above −20 °C (equation 55)[140].

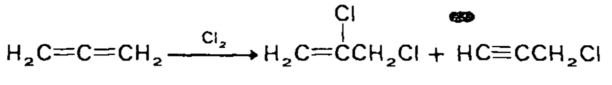


(55)

(102) **(103)**

The data for the chlorination of bicyclic alkenes clearly indicate that an open ion intermediate capable of undergoing rearrangement and elimination is formed prior to the product-determining step.

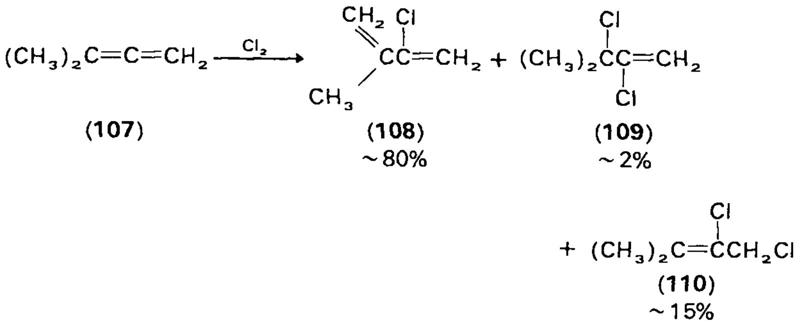
The ionic chlorination of allenes forms dichloro adducts as well as mono chloro dienes or acetylenes formed by the loss of a proton from the cationic intermediate. Thus the chlorination of allene (**104**) under oxygen in inert solvents produces an almost equimolar amount of 2,3-dichloropropene (**105**) and propargyl chloride (**106**) (equation 56) in about 50% yield[141]. The remainder of the products are dimers and polymers resulting from a self-condensation reaction[142]. Chlorination of 1,1-dimethylallene



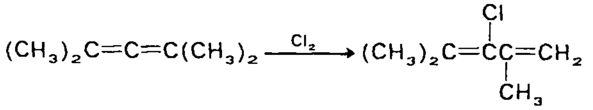
$$H_2C{=}C{=}CH_2 \xrightarrow{Cl_2} H_2C{=}\overset{\overset{Cl}{|}}{C}CH_2Cl + HC{\equiv}CCH_2Cl \qquad (56)$$

(104) **(105)** **(106)**

(**107**) yields predominantly the product of elimination (**108**) with lesser amounts of the two dichloro adducts (**109** and **110**, equation 57)[142].


(107)
(108) ~80%
(109) ~2%
(110) ~15%
(57)

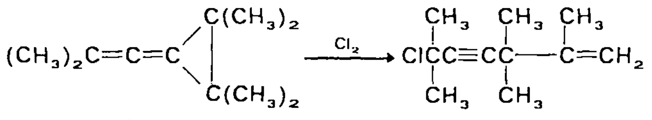
Tetramethylallene (**111**) reacts with chlorine to form only the product of elimination **112** (equation 58)[142] while chlorination of 2-methyl-1-



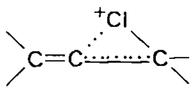
$$(CH_3)_2C{=}C{=}C(CH_3)_2 \xrightarrow{Cl_2} (CH_3)_2C{=}\overset{Cl}{C}\underset{CH_3}{C}{=}CH_2 \qquad (58)$$

(111) (112)

(tetramethylcyclopropylidene)propene (**113**) yields only the chloroacetylene **114** (equation 59)[143].


(113) (114)
(59)

A mechanism involving a cationic intermediate is consistent with the product composition of the ionic chlorination of allene and its derivatives. Because of insufficient data it is impossible to decide which of the three structures **115**, **116**, **117** best represents the electronic structure of the intermediate.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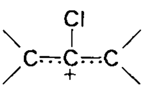
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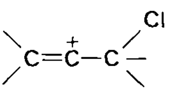
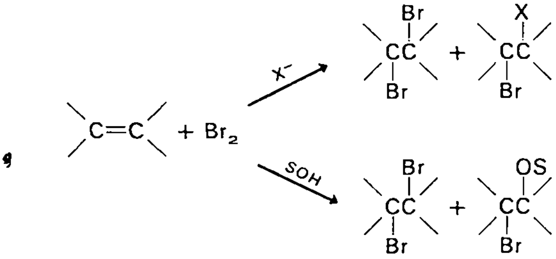

(117)

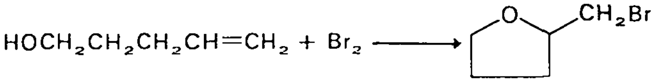
The sum of the evidence for the chlorination of alkenes is consistent with a mechanism involving multiple intermediates all rather close in energy. Under some circumstances, reaction of these intermediates with nucleophiles can occur before they reach their most stable conformation.

C. Bromine

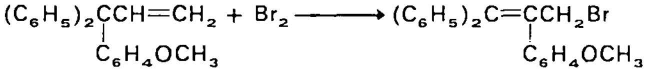
The exothermic addition of bromine to alkenes is a standard text book reaction. While vicinal dibromides are usually formed as products, bromination carried out in the presence of added nucleophiles or in hydroxylic solvents forms mixed products (equation 60). If the alkene contains a nucleophilic substituent in an appropriate position, addition of bromine can form a cyclic product (equation 61)[144]. Bromination of certain alkenes results in products of skeletal rearrangement (equation 62)[145].



(60)



(61)



$$(C_6H_5)_2\underset{\displaystyle C_6H_4OCH_3}{\underset{|}{C}}CH{=}CH_2 + Br_2 \longrightarrow (C_6H_5)_2C{=}\underset{\displaystyle C_6H_4OCH_3}{\underset{|}{C}}CH_2Br \qquad (62)$$

Bromination can be carried out in any solvent that does not react with bromine. In non-polar solvents, bromination usually occurs by a free radical mechanism while in polar solvents an ionic mechanism predominates. The usual brominating agent is elemental bromine. Bromohydrins can be conveniently prepared by reacting *N*-bromosuccinimide with alkenes in moist dimethyl sulphoxide. The bromohydrins are formed stereospecifically and regiospecifically without rearrangement[146].

Depending upon the reaction conditions, the rate law for the ionic bromination of alkenes contains all or part of equation (63)[147]. In sufficiently dilute aqueous or alcoholic solvents, and in the absence of

$$\frac{-\mathrm{d}[\mathrm{Br}_2]}{\mathrm{d}t} = k_2[\mathrm{Br}_2][\mathrm{A}] + k_3[\mathrm{Br}_2]^2[\mathrm{A}] + k'_3[\mathrm{Br}_3^-][\mathrm{A}] \qquad (63)$$

$$[\mathrm{A}] = [\mathrm{Alkene}]$$

Br^-, only the first term is important and the addition follows overall second-order kinetics. By increasing the concentration of bromine, again in the absence of Br^-, the second term becomes dominant and the addition follows overall third-order kinetics. Depending upon the concentration of bromine, its addition in the presence of bromide ion results in a rate law involving all three terms or only the first and third terms of equation (63). By using low concentrations of bromine and relatively high concentrations of bromide ion (0·2 M-Br^-), overall second-order kinetics can be observed[148].

Dubois and coworkers, have used this latter method to study the effect of alkene structure on the rate of bromination. A selection of their results obtained in methanol at 25 °C containing 0·2 M-NaBr is given in Table 3[148].

The rate constant k_g, given in Table 3, is actually a mixture of the first and last terms of equation (63). Under the experimental conditions

$$k_g = \frac{k_2[Br_2] + k'_3[Br_3^-]}{[Br_2 + Br_3^-]}$$

TABLE 3. Rates of bromination of selected alkenes in methanol containing 0·2 M-NaBr at 25 °C[148]

Alkene	k_g
$CH_2{=}CH_2$	30·3
$CH_3CH{=}CH_2$	1840
n-PrCH=CH_2	2090
n-BuCH=CH_2	1990
n-PentCH=CH_2	1970
i-PrCH=CH_2	1700
i-BuCH=CH_2	994
$(CH_3)_2CH(CH_2)_2CH{=}CH_2$	2045
$CH_3CH_2CH(CH_3)CH_2CH{=}CH_2$	926
t-BuCH=CH_2	802
$(CH_3)_2C{=}CH_2$	164,000
i-Pr(CH_3)C=CH_2	97,400
i-Pr(*t*-Bu)C=CH_2	518
(*c*) $CH_3CH{=}CHCH_3$	78,700
(*t*) $CH_3CH{=}CHCH_3$	50,800
(*c*) $C_2H_5CH{=}CHC_2H_5$	87,500
(*t*) $C_2H_5CH{=}CHC_2H_5$	51,500
(*c*) *i*-PrCH=$CHCH_3$	46,400
(*t*) *i*-PrCH=$CHCH_3$	36,000
$(CH_3)_2C{=}CHCH_3$	4,000,000
(*Z*) $C_2H_5(CH_3)C{=}CHCH_3$	2,910,000
(*E*) $C_2H_5(CH_3)C{=}CHCH_3$	2,840,000
$(CH_3)_2C{=}C(CH_3)_2$	55,000,000

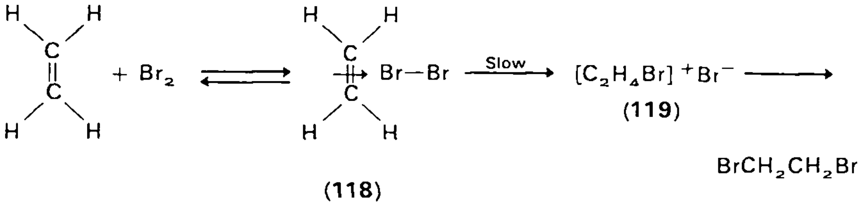
employed the relative values of k_2 and k'_3 ($16 > k_2/k'_3 < \infty$) are such that k_g is a linear function of k_2. Thus the data in Table 3 reflect the effect of alkene structure on the first term in equation (63).

From the data in Table 3, the following conclusions can be drawn: The rate of addition is markedly increased by increasing the number of simple alkyl groups on the double bond; the effect of methyl and ethyl groups is specific, constant and additive[149]; the effect of *n*-alkyl groups larger than *n*-propyl is practically constant; alkyl groups branched at the γ-position show no unusual rate retardation, and introduction of one bulky substituent (e.g., *t*-butyl) causes a minor rate decrease while introduction of a second bulky substituent causes a major rate decrease. In a series of alkenes with the same number of substituents the rate decreases as their complexity increases. *Cis* alkenes react faster than their *trans* isomers. As the number of substituents about the double bond increases this difference in rate between geometric isomers disappears. Attempts to fit the rate of bromination of all the compounds studied by Dubois to a Taft $\rho\sigma^*$ correlation have been unsuccessful although certain subsets of selected compounds can be correlated[150].

The bromination of a number of phenyl-substituted styrenes has been studied by Rolston and Yates under a variety of conditions[152]. The rates were determined at 25 °C in acetic acid with added bromide ion, and the separated rate constants for k_2 and k'_3 were obtained from a study of the dependence of k_{obs} on added bromide ion and measurements of the tribromide ion formation constant. Both sets of rate constants gave better correlations against σ^+ than σ with $\rho^+ = -4{\cdot}2$ and $\rho^+_{\text{Br}^-} = -2{\cdot}0$. Dubois has obtained $\rho = -4{\cdot}3$ from a plot of $\log k_g$ against σ[153]. The rates of bromination under dominant third-order conditions were also obtained in acetic acid at 25 °C[154]. A value for ρ^+ of $-4{\cdot}6$ was obtained which is very similar to that obtained for the k_2 process.

The addition of bromine is *anti* stereospecific only for simple alkenes such as *cis*- and *trans*-2-butene[155]. Addition to *cis*- and *trans* 1-phenylpropene[155] and stilbene[156] is stereoselective, the stereoselectivity depending upon the solvent, temperature and added salts. The product of bromination of simple alkenes in acetic acid is largely the dibromide while styrenes under the same conditions give substantial solvent incorporated products[157]. Bromination of norbornene and 1,2-di-*t*-butylethylene yield rearranged products. Clearly the structure, composition and stereochemistry of the product depends upon the reaction conditions (temperature, solvent, added salts) as well as the alkene structure.

The formation of rearranged and solvent incorporated products clearly indicates that the mechanism of bromination involves at least one cationic intermediate. Evidence for a second intermediate has been presented by Dubois and Garnier[158,159] who studied the charge-transfer spectra of bromine–alkene complexes. They found that the stability of the charge-transfer complex correlates with log k_2 for bromination. Thus the mechanism of bromination can be regarded as involving a rapid reversible formation of a charge-transfer complex (**118**) followed by a rate-limiting ionization to the cationic intermediate (**119**, equation 64).



(118)

(119)

(64)

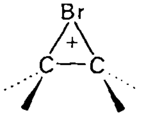
Using the general mechanism of equation (64) attempts have been made to detail the exact mechanism responsible for each term of the general rate expression given in equation (63). The first term ($k_2[A][Br_2]$) represents the reversible formation of the charge-transfer complex followed by rate-determining solvent-assisted bromine–bromine bond cleavage. Evidence for such a specific role of solvent is available from the work of Dubois and coworkers who found a large solvent deuterium-isotope effect for the bromination of 1-pentene in methanol[160]. Furthermore, a plot of the activation energy of bromination in various methanol–water solvent mixtures versus the free energy of solvation of KBr in the same solvent mixtures is linear with a slope of 0·86. From these results it is concluded that hydrogen bonding to the solvent is important in the rate-determining transition state and breaking of the bromine–bromine bond is far advanced. This latter conclusion suggests that the structure of the rate-determining transition state is similar to that of the cationic intermediate.

In solvents incapable of such assistance, the second term ($k_3[A][Br_2]^2$) becomes dominant even at low bromine concentrations. Under such conditions, a bromine molecule may aid the bromine–bromine bond cleavage by forming a charge-dispersed bromide ion. Evidence for this view is provided by the fact that the ρ^+ value for both the overall second- and third-order bromination of phenyl-substituted styrenes is similar[154]. The major difference between these terms is the more negative $\Delta S^{\neq}$ range for k_3. This is consistent with the proposed mechanism since not only is a third molecule involved but also the incipient tribromide ion formation requires a fairly rigid linear arrangement of four bromine atoms.

The mechanistic explanation for the third term ($k'_3[A][Br_3^-]$) is still not entirely settled. The relative reactivities of the reaction of bromine and tribromide ion with a variety of alkenes have been studied by the groups of Bell[161], Kanyaev[162], Yates[163] and Dubois[164] and a number of mechanisms have been proposed. These include (i) catalysis by bromide ion, (ii) electrophilic addition by tribromide ion, and (iii) nucleophilic addition by tribromide ion. Dubois has found that a plot of the ratio k_{Br^-}/k_{Br_2} versus the reactivity of 31 alkenes is curved and has interpreted this result in terms of two competing mechanisms[164]. One involves nucleophilic attack by tribromide ion on the alkene while the other is slow attack by bromide ion on the charge-transfer complex.

Solvents have a great effect upon the bromination of alkenes, and a change in solvent can change the overall rate law. For example, bromination of alkenes at low concentrations ($\sim 10^{-4}$ M) in acetic acid is overall second order while in 1,1,2,2-tetrachloroethane at the same concentrations the reaction is overall third order[165]. In general the more polar the solvent the faster the rate. An exception to this general rule is the slower-than-expected rate of bromination of alkenes in trifluoroacetic acid. To account for these data it is proposed that in this solvent the rate-determining step changes from formation of the cationic intermediate to its capture by solvent[166]. Heublin and Reuscher have used a thermochemical method to probe the effects of solvation of the cationic intermediate in bromination[167]. Stronger solvation was found for cationic intermediates from simple alkenes than for delocalized intermediates formed from phenyl-substituted alkenes.

The electronic structure of the intermediate **119** has been of considerable interest. A bridged structure (**120**) for this intermediate was first proposed by Roberts and Kimball[168]. Recently p.m.r., c.m.r. and electronic absorption spectral data have been reported for such three-member cyclic bromonium ions[169]. The isolation of the stable bromonium ion salt (**121**) in the reaction of adamantylideneadamantane with bromine has also been reported[119]. The addition of the highly-polarized complex BrCN–SbF$_5$ in SO$_2$ as an electrophilic brominating agent to 2,3-dimethylbutene-2, forms



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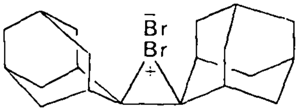
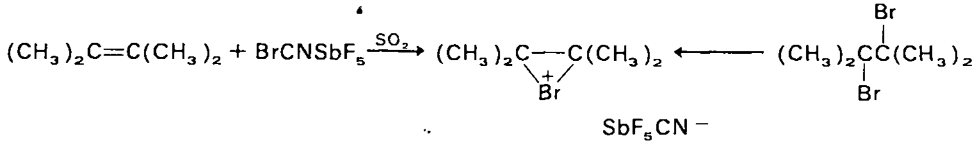


(121)

the bridged ion **122** whose p.m.r. spectrum is identical with the ion prepared by the ionization of 1,2-dibromo precursors (equation 65)[120]. This result is consistent with the idea that the bridged bromonium ion **122** is formed in the bromination of 2,3-dimethylbutene-2.



(122) (65)

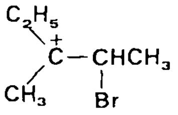
Yates and McDonald[170] have used a thermochemical-kinetic method to probe the structure of the rate-determining transition state. They found that the initial enthalpy difference between pairs of *cis–trans* isomeric alkenes was increased at the bromination transition state. These results were interpreted as evidence for a bridged rate-determining transition state. This interpretation has since been challenged[171].

The results of extended Hückel calculations on the bromine–ethylene system lead to the conclusion that the bromonium ion is more stable than the classical open ethyl carbonium ion[89,172]. However, 'these data strongly suggest that a classical carbonium ion is likely to result only in cases where stabilization is possible through other groups attached directly to the positively charged carbon'[89]. Thus certain structural features in the alkene may cause the electronic structure of the intermediate and the rate-determining step leading to it to resemble an open rather than a bridged ion. To discover what these structural features are, it is necessary to examine in detail the product stereochemistry and rates of bromination of a wide variety of alkenes.

The best evidence for the structure of the rate-determining transition state is available from the work of Dubois[148]. The data are given in Table 4. The alkenes are arranged in groups of three, each one of which contains the same substituents about the carbon–carbon double bond. Only the positions of the substituents are different for the three alkenes in any group. When analysed in this way it is clear that the effect of simple alkyl substituents on the rate of bromination is independent of their position on the carbon–carbon double bond. Such results are in contrast to those of alkene hydration and provide evidence for a bridged rate-determining transition state for simple alkenes.

While the rates of bromination of the isomers are similar, it should be noted that the 1,1-disubstituted ethylene reacts faster than either its *cis* or *trans* isomer in six of the seven examples given in Table 4. This implies that the bromonium ion formed in the addition to the 1,1-disubstituted ethylene is unsymmetrical and that the distribution of charge on the two carbon atoms is unequal.

While the data for the tri- and tetra-substituted alkenes can be analysed in this way, the conclusions are not as clear. The reason is that the difference in energy between **123** and **124** should not be much more than that between bridged ions **125** and **126**. Consequently the similarity in the rates of bromination to the three positionally tri- or tetra-substituted isomeric alkenes does not automatically rule out an open-ion-like, rate-determining transition state.



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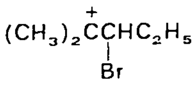
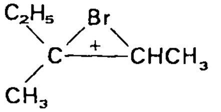


$(CH_3)_2\overset{+}{C}\underset{\substack{|\\ Br}}{C}HC_2H_5$

(124)



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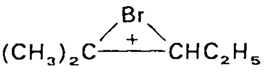


(126)

Data on the stereochemistry of the products of bromination of alkenes are very limited. Yates found that the addition to simple alkenes is *anti*-stereospecific[155] while addition to *trans*-1,2-di-*t*-butylethylene gave rearranged products. The bromination of *Z*- and *E*-3,4-dimethyl-2-pentene is non-stereospecific[285]. For simple alkenes the product stereochemistry is in accord with a bridged product-determining transition state. As the alkene becomes more complex, either by increasing the number of substituents on the double bond or by increasing the complexity of the substituents, the limited data indicate that the products are no longer formed by an *anti*-stereospecific addition. Thus it appears that open ions may be involved in the reaction path prior to the product-determining step of the bromination of these latter compounds.

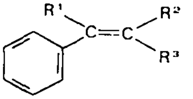
Rolston and Yates[152] have measured the rates of bromination of styrene and its seven, side-chain, methyl-substituted derivatives **127–134** in acetic acid. The results are given in Table 5. The observed rate constants (which are composites of the molecular bromine and tribromide terms) show no simple dependence on the methyl groups attached to the double bond, in contrast to the results of bromination of the ethylene system. It was observed that the α-methyl substitution gives significant rate enhancements whereas β-substitution produces little or no effect. These results, plus the ρ^+ value of $-4{\cdot}21$ for the rate addition of molecular bromine in acetic acid to eight *meta* and *para* styrenes, lead to the conclusion that the rate-determining transition state has an unsymmetrical charge distribution, most of the charge being developed at C_α with little delocalization onto C_β or bromine. This view is supported by the very small (k_H/k_D =

TABLE 4. Rates of bromination of sets of alkenes containing the same substituents

Alkene	$k_g \times 10^4$ [a]	Alkene	$k_g \times 10^4$ [a]
$(CH_3)_2C{=}CH_2$	16·4	*n*-$Pr(CH_3)C{=}CH_2$	16·3
(*c*) $CH_3CH{=}CHCH_3$	7·78	(*c*) *n*-$PrCH{=}CHCH_3$	8·75
(*t*) $CH_3CH{=}CHCH_3$	5·08	(*t*) *n*-$PrCH{=}CHCH_3$	5·15
$C_2H_5(CH_3)C{=}CH_2$	26·8	*n*-$Bu(CH_3)C{=}CH_2$	23·8
(*c*) $C_2H_5CH{=}CHCH_3$	12·6	(*c*) *n*-$BuCH{=}CHCH_3$	14·6
(*t*) $C_2H_5CH{=}CHCH_3$	7·99	(*t*) *n*-$BuCH{=}CHCH_3$	8·42
i-$Pr(CH_3)C{=}CH_2$	9·74	$C_2H_5CH{=}C(CH_3)_2$	600
(*c*) *i*-$PrCH{=}CHCH_3$	4·64	*Z*-$C_2H_5(CH_3)C{=}CHCH_3$	454
(*t*) *i*-$PrCH{=}CHCH_3$	3·60	*E*-$C_2H_5(CH_3)C{=}CHCH_3$	475
t-$Bu(CH_3)C{=}CH_2$	2·94	$CH_3CH{=}C(C_2H_5)_2$	330
(*c*) *t*-$BuCH{=}CHCH_3$	3·90	*Z*-$C_2H_5(CH_3)C{=}CHC_2H_5$	760
(*t*) *t*-$BuCH{=}CHCH_3$	3·60	*E*-$C_2H_5(CH_3)C{=}CHC_2H_5$	660
$(C_2H_5)_2C{=}CH_2$	27	$(C_2H_5)_2C{=}C(CH_3)_2$	940
(*c*) $C_2H_5CH{=}CHC_2H_5$	19·5	*Z*-$C_2H_5(CH_3)C{=}C(CH_3)C_2H_5$	2390
(*t*) $C_2H_5CH{=}CHC_2H_5$	11·1	*E*-$C_2H_5(CH_3)C{=}C(CH_3)C_2H_5$	2200

[a] Rates measured in methanol containing 0·2 M-NaBr at 25 °C[148].

TABLE 5. The rates of bromination of styrene and its side-chain, methyl-substituted derivatives in acetic acid at 25 °C

	R^1	R^2	R^3	k_{obs}(l mol^{-1} s^{-1})
127	H	H	H	11·2 ± 0·1
128	H	H	CH_3	12·3 ± 0·8
129	H	CH_3	H	8·89 ± 0·1
130	CH_3	H	H	680 ± 20
131	H	CH_3	CH_3	14·7 ± 0·2
132	CH_3	CH_3	H	300 ± 20
133	CH_3	H	CH_3	61·7 ± 0·4
134	CH_3	CH_3	CH_3	56·0 ± 0·3

0·98 ± 0·01) secondary isotope effect observed in the bromination of *trans*-1-phenylpropene-α-d_1 in acetic acid[151].

The product distribution and stereochemistry of bromine addition to the styrenes **127**–**134** was also investigated by Rolston and Yates in acetic acid[155]. The data are presented in Table 6.

The styrenes generally form substantial amounts of acetoxy bromides as well as the expected 1,2-dibromides. The acetoxy bromides are the 1-acetoxy-2-bromo compounds with one exception; β,β-dimethylstyrene which gives 5·3% of the 2-acetoxy-1-bromo compound. The additions to the styrenes are non-stereospecific although *anti* addition is favoured. This is in marked contrast to the addition to *cis*- and *trans*-2-butene. Similar product stereochemistry has been observed by Fahey and Schneider for the bromination of 1-phenylpropene and *trans*-anethole in carbon tetrachloride[173]. These results are taken as evidence that the intermediates in the bromination of styrenes resemble a weakly bridged benzylic-like ion (**135**). This leads to the conclusion that the product-determining transition state also has a weakly-bridged structure.

The effect of added salts on the product composition and stereochemistry of bromination of styrenes **127**–**134** provides evidence that more than one intermediate is involved after the rate determining step. The relevant data are presented in Table 7. Added lithium bromide suppresses acetoxy bromide formation and increases the stereospecificity of dibromide formation. Both sodium acetate and lithium perchlorate increase acetoxy bromide formation. Lithium perchlorate markedly decreases the stereospecificity of acetoxy bromide formation from *cis*-1-phenylpropene, but has little effect on the stereochemistry of the dibromide from either *cis*- or *trans*-1-phenylpropene or 2-phenyl-2-butenes. These results are interpreted in terms of a mechanistic scheme involving both intimate and

TABLE 6. Product distribution and stereochemistry of the bromination of styrene and side-chain methyl-substituted styrenes

	Product[a] (%)				
Alkene	1,2-Dibromo	1-acetoxy 2-bromo	2-acetoxy 1-bromo	*anti* 1-acetoxy 2-bromo	*anti* Dibromide
127	79·8	20·2	0	—	—
128	76·6	23·4	0	95	73
129	80·4	19·6	0	95	83
130	98·0	2	0	—	—
131	79·0	15·7	5·3	—	—
132	82	18[b]		—	68
133	88	12[b]		—	63
134	96	4[b]		—	—

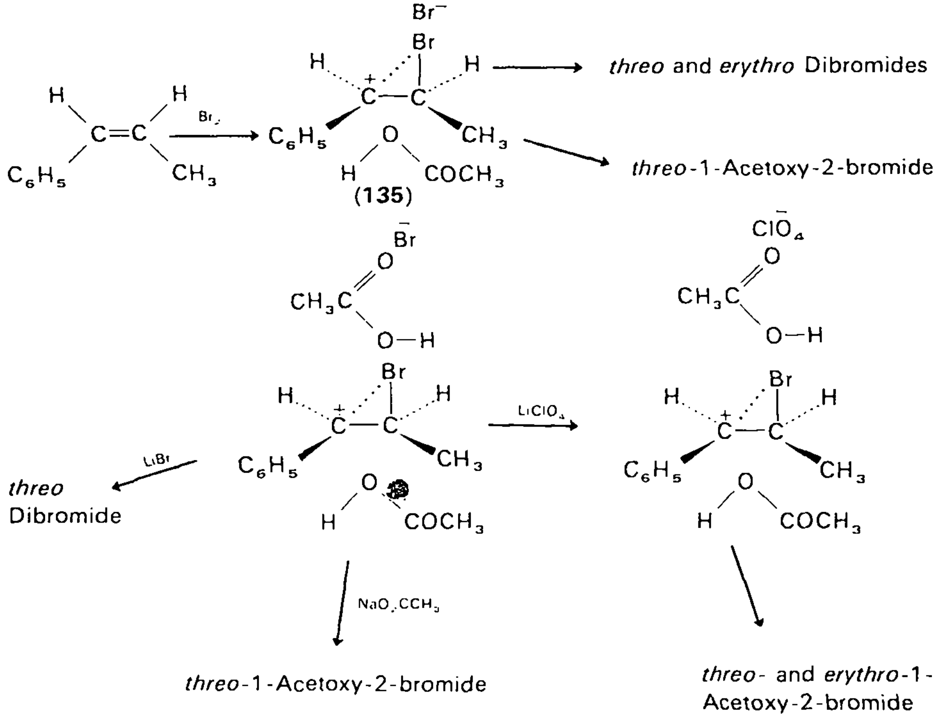
[a] The product distributions reported here were determined under conditions close to those employed for the kinetic measurements.

[b] Structures of acetoxy bromides were not investigated.

TABLE 7. Dependence of stereochemistry and product formation on added salts

Alkene	Added salt (0·1 M)	Acetoxy bromide (%)	*anti* Acetoxy bromide (%)	*anti* Dibromide (%)
127	LiBr	16·5	—	—
127	NaOAc	27·8	—	—
127	$LiClO_4$	32·5	—	—
128	$LiClO_4$	38·7	67	77
128	LiBr	—	—	95
129	$LiClO_4$	36·7	95	86
130	$LiClO_4$	2	—	—
131	$LiClO_4$	33	—	—
132	$LiClO_4$	21	—	71
133	$LiClO_4$	15	—	56
134	$LiClO_4$	16	—	—

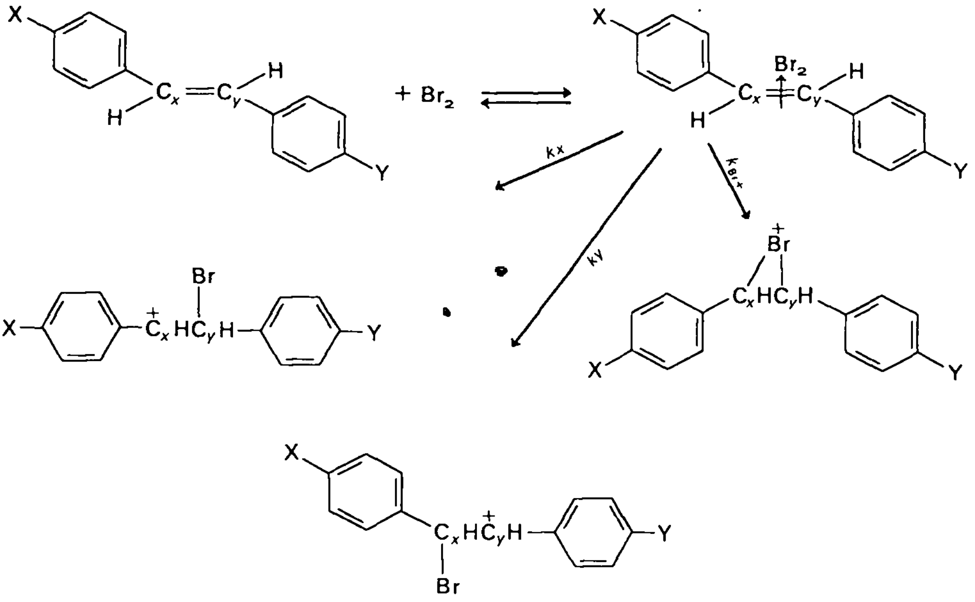
solvent-separated ion pairs in which the cations resemble weakly bridged rather than open benzylic carbonium ions as illustrated in Scheme 3.



Br⁻
Br
H
H
C=C
C₆H₅
CH₃
Br₂
(135)
O
COCH₃
threo and erythro Dibromides
threo-1-Acetoxy-2-bromide
ClO₄⁻
CH₃C
O—H
LiClO₄
LiBr
threo Dibromide
NaO₂CCH₃
threo-1-Acetoxy-2-bromide
threo- and erythro-1-Acetoxy-2-bromide

SCHEME 3.

Ruasse and Dubois have measured the rates of bromination of a large number of *trans*-stilbenes substituted in one or both phenyl rings[171,174,175]. The kinetic data, which span a range of 10^7, are interpreted in terms of the three-path addition mechanism outlined in Scheme 4. The three paths are one involving a bromonium ion k_{Br^+}, one leading to the carbonium ion at C_x, k_x, and one leading to the carbonium ion at C_y, k_y. Depending upon the substituents and the solvent the reaction can take one, two or all three paths. For electron-donating substituents in carbon tetrachloride, a linear free energy relationship is observed (equation 66). This result indicates that



SCHEME 4.

$$\log k/k_0 = \rho \sum \sigma \tag{66}$$

the rate-determining transition state is bridged and that the first charged intermediate is a bromonium ion.

In methanol, no such linear free-energy relationship is found. Rather the relationship shown in equation (67) is obtained by application of the Hammett equation to the carbonium ion pathways. The quantities ρ_α and ρ_β are the reaction constants for aryl substituents α and β to the charge

$$\log\left[(k_x + k_y)/k_0)\right] = \log\left[10^{\rho_\alpha\sigma_x^+ + \rho_\beta\sigma_y} + 10^{\rho_\alpha\sigma_y^+ + \rho_\beta\sigma_x}\right] \tag{67}$$

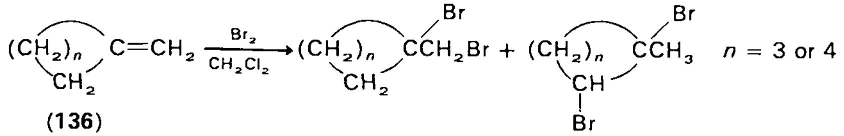
centre respectively. Values of $-5{\cdot}1$ and $-1{\cdot}4$ have been obtained for ρ_α and ρ_β respectively by using sets of compounds for which two of the three pathways can be neglected. Application of these values to compounds for which k_x and k_y are comparable results in reasonable agreement between calculated and experimental reactivities.

From these results it has been concluded that in methanol stilbenes containing strongly electron-donating substituents such as methoxyl groups react by an open carbonium ion path and their rate-determining transition state resembles this open carbonium ion. Stilbenes containing strongly electron-withdrawing substituents such as nitro or trifluoromethyl groups react by a bromonium ion path and their rate-determining transition states are bridged. For other stilbenes reaction occurs by more than one path.

For the monosubstituted stilbenes, the regioselectivity of the products agrees with the calculated relative importance of each pathway[175]. Unfortunately, similar results as well as product stereochemistry have not been reported for any of the disubstituted stilbenes. As a result it is impossible to draw any conclusions regarding the product determining transition state(s) from this work.

The kinetic data for the bromination of cyclic alkenes are given in Table 8. The data of Pritzkow's[176] group are the result of competition experiments and are of limited value since the kinetic order of the reaction cannot be determined. The data of Dubois and Fresnet[177] were obtained by direct kinetic measurements and the rate law is overall second order. From the data we can conclude that cyclohexenes react slightly slower than *cis*-1,2-disubstituted ethylenes. Furthermore substituents in the axial positions at carbons 4 and 5 of the cyclohexene ring can retard the rate of bromination significantly. These results are interpreted in terms of a transannular steric interaction between these substituents and the bromine molecules in the rate-determining transition state.

Anti-stereospecific bromination of cyclohexene to form *trans*-1,2-dibromocyclohexane is well documented[178]. Some cyclic alkenes, like cyclodecene and cyclodecadiene form products of transannular rearrangement[179,180]. The bromination of disubstituted terminal alkenes such as methylenecyclohexane (**136**) gives products in which double bond migration has occurred (equation 68). Thus methylenecyclohexane forms 32%

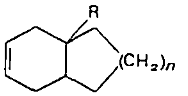
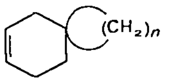


(136)

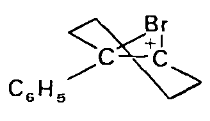
(68)

1,2-dibromo-1-methylcyclohexane and 68% 1-bromo-1-bromomethylcyclohexane[181]. The formation of 1,2-dibromo-1-methylcyclohexane is explained by competing allylic bromination which produces hydrogen bromide. This then converts the terminal alkenes into their more-stable internal isomer which then adds bromine[181].

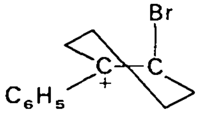
TABLE 8. Rates of bromination of cyclic alkenes in methanol at 25 °C

Alkene	n	R	k_{rel}	$k_2 \times 10^4$ (l mol^{-1} min^{-1})	Reference
Cyclohexene			1·0	68	176, 177
Cyclopentene			3·5	—	176
Cycloheptene			5·7	—	176
Cyclooctene			0·03	—	176
Cyclooctadiene-1,5			0·43	—	176
1-Methylcyclohexene			7·3	—	176
Methylenecyclohexane			8·6	—	176
Vinylcyclohexane			0·039	—	176
cis-2-Butene			1·7	—	176
cis-2-Pentene			2·7	—	176
4,4-Dimethylcyclohexene			0·1	6·8	177
4-Methylcyclohexene			0·84	57	177
4-Ethylcyclohexene			0·94	64	177
4-*t*-Amylcyclohexene			1·3	85	177
Bicyclo[2.2.2.]octene			0·44	30	177
	2	H	0·16	11	177
	3	H	0·53	36	177
	4	H	1·18	80	177
	4	CH_3	0·026	1·8	177
	4		0·10	6·8	177
	5		0·082	5·6	177

The bromination of 1-phenylcyclohexene, like that of *cis*-1-phenylpropene is non-stereospecific although *anti* addition is favoured[182]. Since rotation about the carbon–carbon bond in the intermediates **137** or **138**



(137)

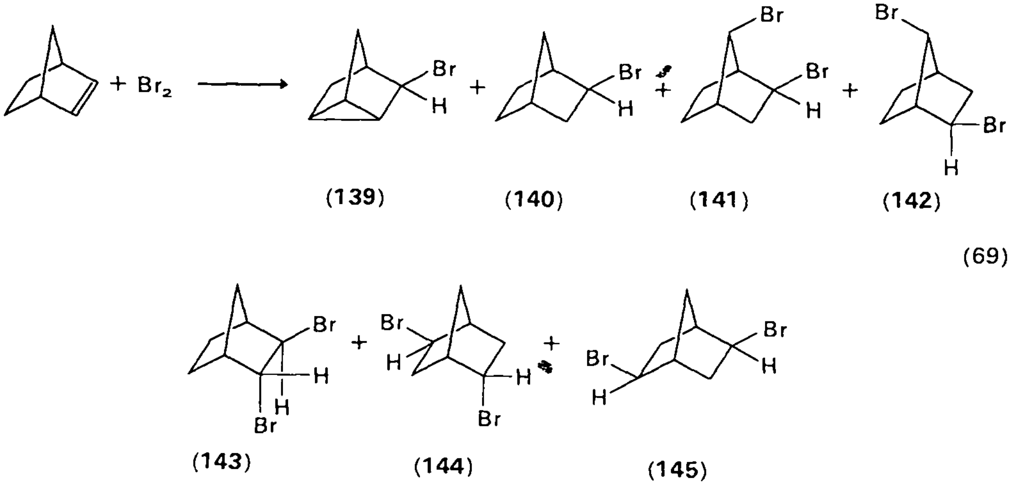


(138)

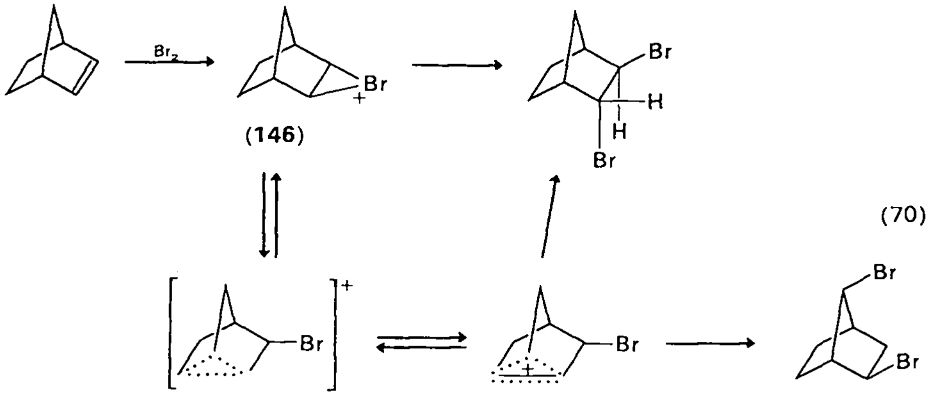
is impossible, this result is evidence that *syn* addition can occur by direct collapse of an intimate ion-pair intermediate.

Despite the limited rate data available for the bromination of cyclic alkenes, it is possible to draw certain conclusions regarding the rate- and product-determining transition states. These conclusions follow from the similarities between the stereochemistry of the product of bromination of cyclic and acyclic alkenes. The *anti*-stereospecific addition observed for cyclohexene and many of its non-conjugated derivatives is identical to that observed for simple acyclic alkenes. It seems reasonable therefore to postulate a bridged rate- and product-determining transition state for both types of alkenes. The non-stereospecific bromination of both 1-phenylcyclohexene and *cis*-1-phenylpropene can be explained by a benzylic-like or a weakly-bridged, benzylic-ion like rate- and product-determining transition state. Further speculation regarding the rate- and product-determining transition states of bromination of other cyclic alkenes is impossible at this time.

The studies carried out on the bromination of norbornene have been more concerned with the nature of the products than with the rates of addition. The reinvestigation of the ionic bromination of norbornene revealed that bromonortricyclene (**139**), 2-*exo*-bromonorbornane (**140**), **141** and **142** are the major products, and **143**, **144** and **145** are the minor products formed under kinetic control (equation 69)^{183}. By the use of



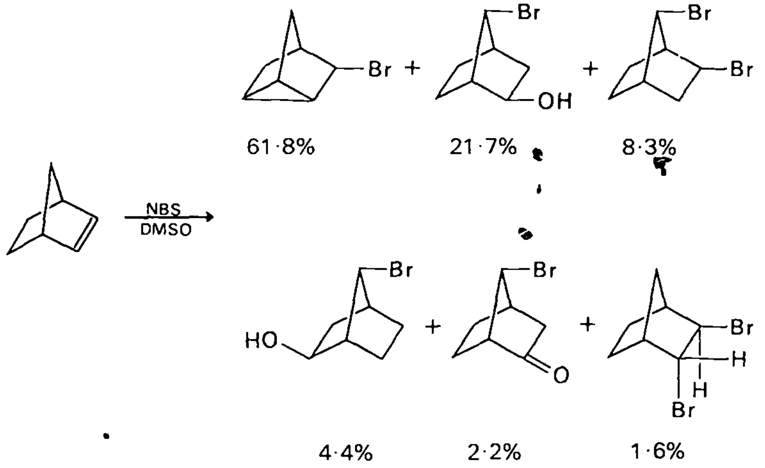
5,6-^{14}C-norbornene it was found that **143** is formed by two ionic pathways: one from the bromonium ion **146** and the other from the cation formed by a 6,1-hydride shift (equation 70). Six products have also been found in the


Br₂
Br
+
Br
H
H
Br
+
Br
Br
Br
Br
Br

(146)

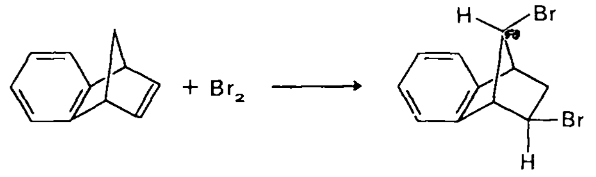
(70)

reaction of norbornene with NBS in moist dimethyl sulphoxide (equation 71)^{184}.


NBS
DMSO
Br
Br
OH
Br
Br
61·8%
21·7%
8·3%
HO
Br
Br
O
Br
H
H
Br
4·4%
2·2%
1·6%

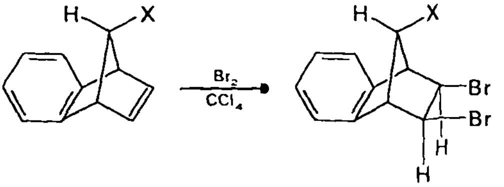
(71)

The stereochemistry of the products of bromination of substituted norbornenes depends greatly upon the nature and position of the substituents. Bromination of benzonorbornadiene (**147**) proceeds with rearrangement to form *exo*-5-*anti*-7-dibromobenzonorbornene (**148**) (equation 72)^{185}. In contrast *anti*-7-bromo (**149a**) and *anti*-7-methoxybenzonorbornadiene (**149b**) add bromine in CCl_4 to form the *syn–exo* adducts **150a** and **150b** respectively without rearrangement (equation 73).



(147) **(148)**

(72)

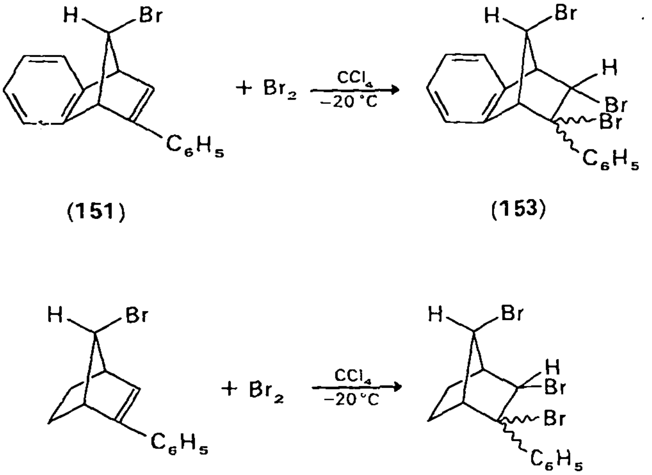

H
X
Br₂
CCl₄
H
X
Br
Br
H
H

(73)

149a: X = Br
149b: X = OCH$_3$

150a: X = Br
150b: X = OCH$_3$

Bromination of *anti*-7-bromo-5-phenylbenzonorbornadiene (**151**) and *syn*-7-bromo-2-phenylnorbornene (**152**) form products **153** and **154** respectively (equation 74)[186]. The *exo* hydrogen on carbon-3 of **154** and


H
Br
C₆H₅
+ Br₂
CCl₄
−20 °C
H
Br
H
Br
Br
C₆H₅
H
Br
C₆H₅
+ Br₂
CCl₄
−20 °C
H
Br
H
Br
Br
C₆H₅

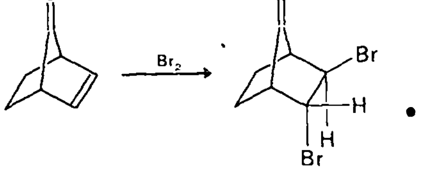
(**151**) (**153**)

(74)

(**152**) (**154**)

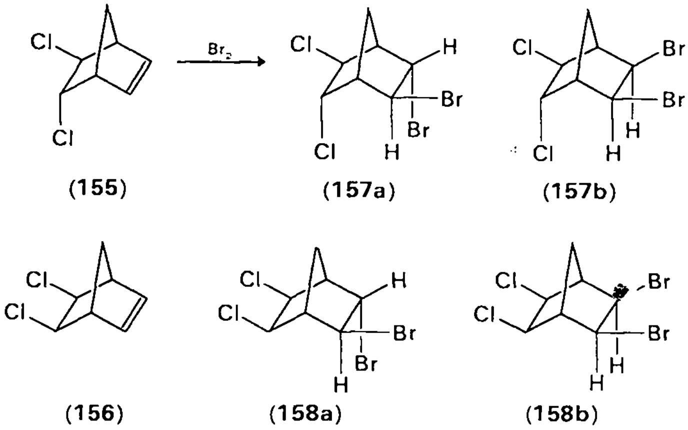
carbon-6 of **153** suggest that initial electrophile approach is *endo*. The presence of a phenyl group on the double bond clearly alters the factors that favour *exo* approach of the electrophile in non-phenyl-substituted norbornenes.

Anti stereospecific addition of bromine to 7-norbornenone has been observed to form *trans*-2,3-dibromo-7-norbornanone (equation 75)[187].

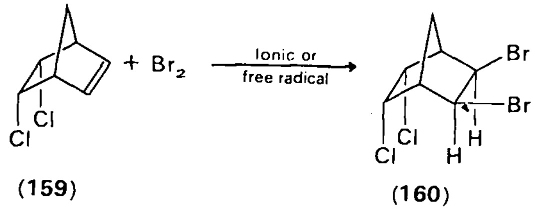

O
Br₂
O
Br
H
H
Br

(75)

Similarly *anti* stereospecific addition occurs to *trans*-(**155**) and *exo–cis*-5,6-dichloronorbornene (**156**) to form **157a** and **158a** respectively (equation 76)[188]. Under free radical conditions, bromination produces substantial amounts of the *cis–exo* dibromo adducts **157b** and **158b**. The results of ionic bromination are consistent with *exo* attack by the bromine and bridged rate- and product-determining transition states. The importance of the steric effect of the *endo* chlorine in the product-determining transition state is evident from the fact that only **157a** is formed. None of the isomeric 2-*endo*-3-*exo*-dibromo-5-*exo*-6-*endo*-dichloronorbornane is formed. This steric effect may be responsible for the fact that 5,6-*cis*-*endo*-dichloronorbornene (**159**) adds bromine *syn–exo* under both free-radical and ionic conditions to form **160** (equation 77)[189].



(76)

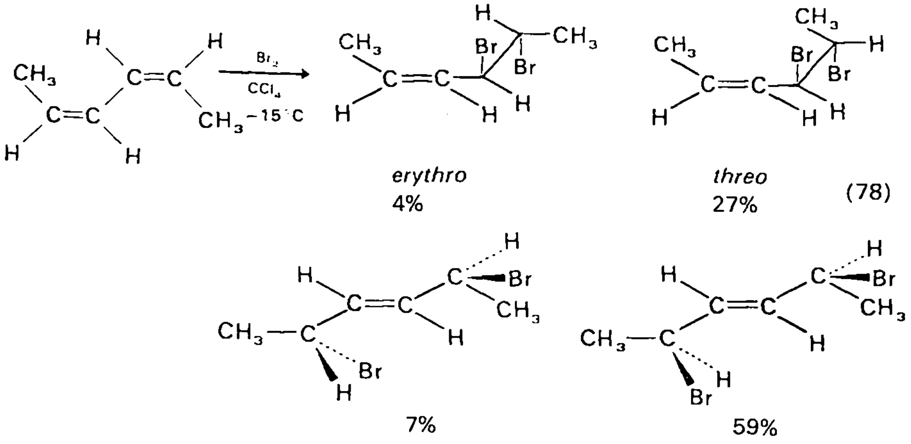


(77)

The experimental results of the bromination of norbornene and its non-conjugated derivatives can be explained by a bridged bromonium ion as the first intermediate to be formed. However, it is not clear what factors govern whether this ion is formed by *exo* or *endo* attack. Further work is also necessary to determine how *exo–syn* addition occurs.

The stereochemistry of the dibromides formed from the bromination of cyclopentadiene, 1,3-cyclohexadiene and (*Z*, *Z*)-, (*E*, *Z*)-, and (*E*, *E*)-2,4-Heasley and coworkers[190]. The stereochemistry of 1,2-addition to the

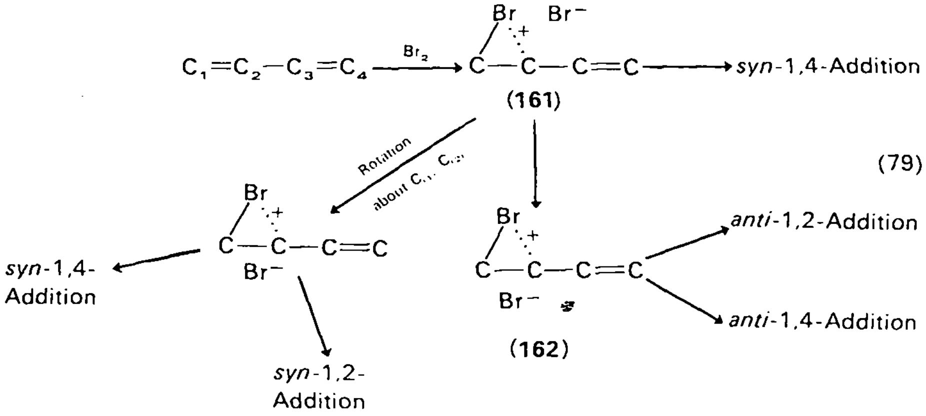
2,4-hexadienes was found to be *anti* stereoselective (69–91 %). The stereochemistry of 1,4-addition was found to be primarily *syn* (equation 78). The



Br_2
CCl_4
−15 °C
erythro
4%
threo
27%
7%
59%

(78)

1,4-dibromides consist predominantly of the *trans* isomer[191]. Heasley has proposed the mechanism in equation (79) to account for these results. In this mechanism a bromine molecule attacks one of the double bonds to form a bromonium ion–bromide ion pair (**161**). Both the 1,2- and 1,4-adducts can arise from this same intermediate. *syn*-1,4-Addition results by



$C_1{=}C_2{-}C_3{=}C_4$
Br_2
syn-1,4-Addition
(161)
Rotation about $C_{1,2}$
anti-1,2-Addition
anti-1,4-Addition
syn-1,4-Addition
syn-1,2-Addition
(162)

(79)

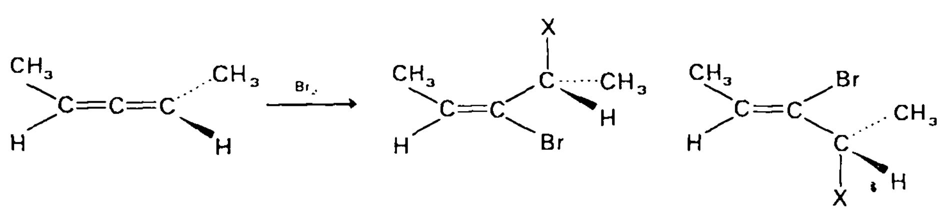
an S_N2' attack on carbon atom 4 while reorientation of the counter ion to form intermediate **162** would result in *anti*-1,2- and 1,4-addition. Rotation about the $C_{(1)}$–$C_{(2)}$ bond or direct *syn* collapse of the ion pair **161** would result in *syn*-1,2-addition. As expected from this mechanism, when the ratio of 1,4- to 1,2-addition is particularly large, as in the case of addition to 1,3-cyclohexadiene and (*Z*,*Z*)-2,4-hexadiene in CCl_4 and CH_2Cl_2, the stereospecificity of 1,4-addition is also high. However in the cases where 1,2-addition is more rapid, the amount of *anti*-1,4-addition product increases.

Stereospecific *anti*-1,2-addition to a conjugated diene has been observed[192]. Thus bromine addition to the 3,4-bond of 1,3-pentadiene is *anti*-stereospecific in contrast to the results with the 2,4-hexadienes. This change in stereochemistry may be due to the extent of charge delocalization into the vinyl group of the intermediate.

While no investigations into the kinetics have been carried out, the bromine concentrations used are in the range in which overall third-order kinetics would be expected. It should be noted that the double bond initially attacked is the one which would be predicted on the basis of the kinetic results of Dubois[148]. Thus the double bond with most electron-releasing substituents reacts the fastest while the *cis* reacts in preference to the *trans* double bond. The products of bromination of conjugated dienes and of 1-phenylpropene are similar in two respects. Both form 1,2-adducts with predominantly *anti* stereochemistry and form acetoxy bromides in acetic acid in a regiospecific Markownikoff manner. The product composition is in accord with a mechanism involving cationic intermediates with unsymmetrically bridged structures which implies that the rate- and product-determining transition states have similar structures.

The treatment of 6,6-diphenylfulvene with 1 molar equivalent of bromine in carbon tetrachloride or cyclohexane forms predominantly *trans*-1,2-dibromo-1,2-dihydro-6,6-diphenylfulvene[192a]. Addition of a second mole of bromine forms *trans,trans,trans*-1,2,3,4-tetrabromo-1,2,3,4-tetrahydro-6,6-diphenylfulvene. The formation of products by *anti* addition of bromine to 6,6-diphenylfulvene is indicative of olefinic rather than aromatic character.

The bromination of 2,3-pentadiene in CCl_4 forms a mixture of 20% *cis*- and 80% *trans*-3,4-dibromo-2-pentene (**163a** and **164a** respectively). In



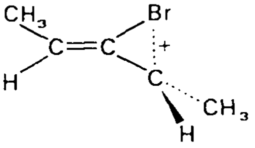
163a: X = Br
163b: X = OCH_3

164a: X = Br
164b: X = OCH_3

(80)

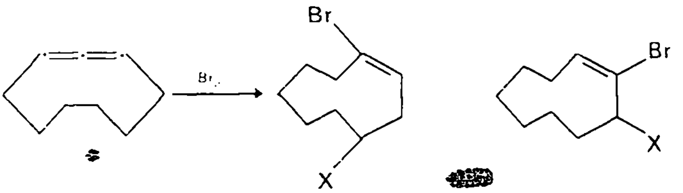
methanol, bromine reacts with 2,3-pentadiene to give 3-bromo-4-methoxy-2-pentene as the major product (85%) formed as a 20:80 *cis–trans* mixture (equation 80). The minor products were the corresponding dibromo products **163a**, **164a**[193]. The orientation of bromine to 2,3-pentadiene is similar to that observed with allene in that the electrophile bonds to the central carbon, and the nucleophile (Br^- or hydroxylic solvent) adds to the terminal carbon[141].

The bromination of optically-active 2,3-pentadiene gives optically-active adducts **163a**, **164a** in CCl_4 and **163b**, **164b** in methanol. The addition is *anti* based upon the configurational relationship between the dissymmetric allene and the asymmetric adducts. These results suggest that the adducts are formed from dissymmetric reaction intermediates such as a bridged bromonium ion **165**.



(165)

The bromination of 1,2-cyclononadiene in CCl_4 at 30°C yields 85% of a 61:39 mixture of *cis*-2,3-(**167a**) and *cis*-1,4-dibromocyclononene (**166a**). The latter compound is formed by 1,5-transannular hydride shift. Bromination in methanol yields 78% of **166b** and **167b** in the ratio of 68:32. Bromination in methanol of partial resolved *R*-(+)-1,2-cyclononadiene yields optically active **167b**, also with the *R* configuration (equation 81)[194]. This result means that bromination in methanol is a stereoselective *anti* addition similar to that found for the bromination of 2,3-pentadiene. The degree of stereoselectivity of the addition could not be determined since the optical purity of the products is not known. These results are consistent with a bridged bromonium ion. It is interesting to note that hydride transfer occurs stereoselectively to form the optically-active products **166a** and **166b** in CCl_4 and methanol respectively.



(81)

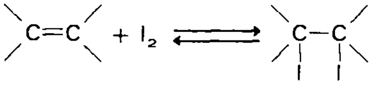
166a: X = Br **167a**: X = Br
166b: X = OCH_3 **167b**: X = OCH_3

The bromination of phenylallene in non-polar solvents such as CS_2 forms primarily 2,3-dibromo-3-phenylpropene which rapidly isomerizes to 2,3-dibromo-1-phenylpropene[292].

In summary, the structure of the intermediates in the mechanism of the addition of bromine to alkenes depends upon the alkene structure. For simple non-conjugated alkenes, the data are consistent with a bridged rate-determining transition state leading to a bromonium ion intermediate. The transition state leading to the 1,2-dibromide product is also bridged. For alkenes capable of forming resonance-stabilized cations, the structure of the intermediate(s) is not as well defined. Rate-determining formation of both open α-bromocarbonium ions and weakly-bridged bromonium ions have been postulated. While many conclusions about the mechanism of bromination can be reached from the available data, many gaps in our knowledge remain to be filled.

D. *Iodine*

The addition of iodine to alkenes in solution to form diiodides (**168**) can occur by either an ionic or a free-radical mechanism[195,196]. The change in free energy for iodination of alkenes is usually small. Consequently an equilibrium is established and incomplete conversion of the alkene to the diiodide is usually observed. The position of the equilibrium depends upon the structure of the alkene, the solvent and the temperature[197].



(168)

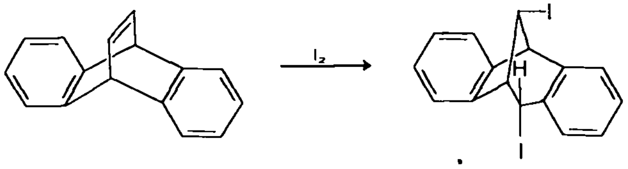
The rate law for the addition of iodine is complex. Terms, second, third and fourth order overall have been identified (equation 82). The overall fourth-order term, first order in alkene and third order in iodine, is important in non-polar solvents such as chlorobenzene, CCl_4 and CS_2 while the overall third-order term is important in acetic acid, isobutyl ether and nitrobenzene[198–201]. The overall second-order term has been reported for the iodination of cyclohexene in a number of solvents[202]. The terms second and third order in iodine have been explained either by electrophilic attack by molecules of iodine complexing together (I_4 or

$$\frac{-\mathrm{d}[\mathrm{I}_2]}{\mathrm{d}t} = (k_2[\mathrm{I}_2] + k_3[\mathrm{I}_2]^2 + k_4[\mathrm{I}_2]^3)[\text{Alkene}] \tag{82}$$

$I_6)^{200-203}$ or by additional molecules of iodine assisting in the breaking of the iodine–iodine bond in the rate-determining transition state[209] to form the known I_3^- and I_5^- ions[204]. Such assistance would be of particular importance in solvents which solvate iodine poorly. Higher order terms in the rate law for bromination are also observed and are explained in a similar manner.

The presence of a charge-transfer complex prior to diiodide formation has been inferred from spectral data[205,206]. The low (sometimes negative) temperature coefficient of iodination is consistent with a reaction in which the formation of a reversible preequilibrium charge-transfer is partially reversed by an increase in temperature.

The limited data available regarding the effect of alkene structure on the rate of iodination are in accord with an electrophilic addition mechanism[197,198]. The observation of a rearranged product in the iodination of 9,10-dihydro-9,10-ethenoanthracene (**169**, equation 83)[207] and a cyclic product from iodination of hex-5-enol-1 (equation 84)[208] are consistent with a mechanism involving a cationic intermediate.



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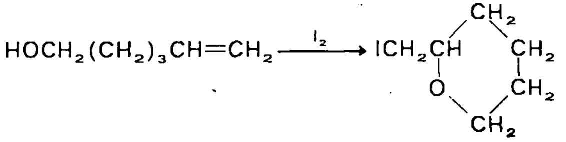
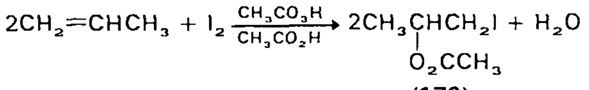


(84)

The reaction of propene with a mixture of iodine and peracetic acid in a mixed solvent of acetic acid and ethyl ether has been found to give 1-iodo-2-acetoxypropane (**170**) in 54–80% yield (equation 85)[209]. The rate

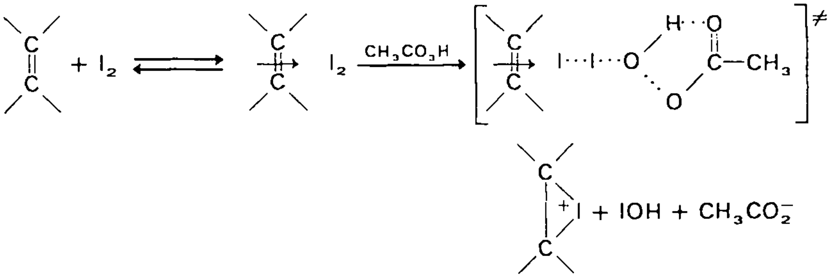


$$2CH_2{=}CHCH_3 + I_2 \xrightarrow[CH_3CO_2H]{CH_3CO_3H} 2\underset{\displaystyle O_2CCH_3}{CH_3\underset{|}{C}HCH_2I} + H_2O \qquad (85)$$

(170)

law of this iodoacyloxylation reaction is overall third order; first order in alkene, iodine and peracetic acid. Under the same conditions the rates of (i) epoxidation of propene by peracetic acid, (ii) addition of iodine in the absence of peracetic acid, and (iii) the reaction of iodine and peracetic acid to form acyl hypoiodite are all slower than the iodoacyloxylation reaction.

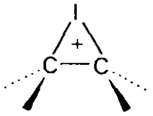
These results rule out mechanisms involving, as intermediates, (i) propylene oxide, (ii) 1,2-diiodopropane, and (iii) acyl hypoiodite. A mechanism involving rate-determining attack by peroxyacetic acid on the charge-transfer complex to form an iodonium ion has been proposed (equation 86).



(86)

Under equivalent conditions cyclohexene reacts to give presumably the *trans*-1-iodo-2-acetoxycyclohexane[210]. The stereochemistry was not, however, unambiguously determined.

A bridged iodonium ion structure (**171**) for the cationic intermediate has often been proposed. The evidence for such a structure is based on limited



(**171**)

data however. Evidence for such a structure in the addition reaction is available from the fact that the iodination of (*R*)-(−)-2,3-pentadiene in methanol[211] yields (−)-*trans*-3-iodo-4*S*-methoxy-2-pentene (plus a small amount of the *cis* isomer) by *anti* addition. While iodonium ions, formed by neighbouring group participation, have been shown to be intermediates in nucleophilic displacement reactions and their existence and bridged structure has been established by n.m.r., their presence on the reaction coordinate of the iodination of most alkenes is not well established.

The situation is complicated by the fact that free-radical iodination forms diiodo adducts by *anti*-stereospecific addition. Thus Skell[212] found that the reaction of iodine with *cis*- and *trans*-2-butene forms *dl*- and *meso*-2,3-diiodobutane respectively when irradiated at −40°C. Similar results have been found by Ayres[213] for the addition of ^{131}I labelled iodine to *cis*- and *trans*-2-pentene. The rate law is fractional order with respect to iodine in the presence of excess alkene (equation 87). Such rate

$$\frac{-\mathrm{d}[\mathrm{I}_2]}{\mathrm{d}t} = k[\mathrm{I}_2]^{3/2} \qquad (87)$$

laws are often found for free-radical reactions and serve to distinguish between the ionic and free-radical mechanisms.

It is interesting to note that Ayers found that the diiodo products did not decompose to the alkene and iodine upon distillation in the dark. This indicates that these compounds, in the absence of iodine, are stable with regard to disproportionation to the alkene and iodine.

The mechanism and stereochemistry of ionic iodination has often been inferred by assuming a similarity between iodination and the additions of iodine halides, iodine isocyanate and other iodine-containing electrophiles. There are insufficient data on the effect of alkene structure on the rate and stereochemistry of the ionic addition of iodine to justify this assumption.

IV. INTERHALOGENS

The variation in electronegativity among the halogens makes possible the combination of one halogen with another to form an interesting series of compounds known as the interhalogens. Whereas the kinetics and mechanism of the reaction of bromine and chlorine with alkenes have received considerable attention, much less is known about the electrophilic addition of the interhalogens. The reaction of ICl and IBr with alkenes has been known for almost a century to yield vicinal iodo chlorides and bromides respectively[214–221]. Based on this reactivity both ICl and IBr have received attention in the analytical determination of carbon–carbon double bonds[222–231].

Of the various possible combinations of binary interhalogens only ClF, ICl and IBr appear to be well defined compounds[232–235]. Chlorine monofluoride may be prepared by the reaction of fluorine with chlorine at 220–250 °C[236–238] or the reaction of chlorine trifluoride with chlorine at 250–350 °C[239,240]. Similarly ICl and IBr are, in general, prepared from equimolar mixtures of the parent halogens.

A. Bromine and Iodine Monofluoride

Bromine monofluoride and iodine monofluoride have not been isolated as pure substances[241–244]. Bromine monofluoride is reportedly stable at low temperatures (≤0 °C) but disproportionates almost completely at 50 °C[244] to bromine and bromine trifluoride. An equilibrium has been shown to exist between bromine, bromine trifluoride and bromine monofluoride.

$$Br_2 + BrF_3 \rightleftharpoons 3BrF$$

Similarly IF readily disproportionates into I_2 and IF_5. Reported additions of these latter to compounds generally assume an *in situ*

$$5IF \rightleftharpoons 2I_2 + IF_5$$

generation of the interhalogen[245–249]. An alternative explanation, which appears more likely, is a mechanism involving attack by a source of electrophilic bromine or iodine followed by nucleophilic fluoride ion attack on the cationic intermediate. Such a mechanism does not require the formation of the interhalogens. The addition of IF to a number of neat perfluoro and fluorochloroalkenes[250] under a nitrogen atmosphere has been described. The source of IF was the iodine–iodine pentafluoride system. Addition was usually carried out in the presence of a catalyst such as AlI_3, $AlBr_3$, $AlCl_3$, AlF_3 and iron-free aluminium. Some product distributions are given in Table 9. There was no discussion of a possible mechanism. Schmidt and Meinert[251] have reported that IF, prepared from AgF and I_2 in acetonitrile at −8 °C, reacts with cyclohexene to give a 60% yield of *trans*-1-fluoro-2-iodocyclohexane. The reaction was postulated to be ionic.

Chambers, Musgrave, and Savory[252] have reported the reaction of a number of perhaloalkenes with mixtures containing BrF_3 and Br_2 or IF_5 and I_2 as effective sources of BrF and IF respectively. Some product distributions are given in Table 10. The regioselectivity was attributed to

TABLE 9. Product distributions from the reaction of IF (I_2–IF_5) with some perfluoro- and fluorochloroalkenes[250]

Alkene	Temperature (°C)	Catalyst	Products	Yield (%)
$CF_2{=}CCl_2$	0	Al/AlI_3	CF_3CCl_2I	80
	20–25	Al/AlI_3	$CF_3CCl_2I/CFCl_2CF_2I$(77/23)	81
$CF_2{=}CFCl$	20–25	Al/AlI_3	CF_2ClCF_2I/CF_3CFClI(50/50)	95
$CF_3CF{=}CF_2$	25	Al/AlI_3	CF_3CFICF_3	34
	62–75	Al/AlI_3	CF_3CFICF_3	52
	125	Al/AlI_3	CF_3CFICF_3	77
$CFCl{=}CFCl$	25	Al	$CF_2ClCFClI$	23
$CF_2{=}CHCl$	25	Al/AlI_3	CF_3CHClI	48
$CF_2{=}CHF$	25	Al/AlI_3	CF_3CHFI	
$CF_2{=}CH_2$	25	Al/AlI_3	CF_3CH_2I	

polarization as given in equation (88). No kinetic investigations have been reported.

$$\overset{\delta+}{\mathrm{I}}-\overset{\delta-}{\mathrm{F}} + \overset{\delta+}{\mathrm{C}}\mathrm{F_2}=\overset{\delta-}{\mathrm{C}}\mathrm{FCF_3} \longrightarrow \mathrm{CF_3CFICF_3} \qquad (88)$$

B. Chlorine, Bromine and Iodine Perfluorides

Although structures of the form XY_n, where X has a greater atomic weight relative to Y and $n = 1,3,5,7$ are known[253–256], little appears to have been reported as to their reactivity with alkenes. Banks and coworkers[257] have reported the reaction of IF_5 (neat) with tetraiodoethylene to give iodopentafluoroethane in 26% yield. The addition was carried out by adding the IF_5 slowly to the alkene at 0 °C. Too rapid an addition of IF_5 leads to an explosion. The reaction was somewhat complicated by reaction of the IF_5 with the silica reaction vessel forming SiF_4, CO_2, perfluoroethylene and an unidentified material.

The gas-phase reaction of IF_5 and ClF_3 with tetrafluoroethylene at temperatures of 450–800 °C has been reported[258]. This reaction is, however, probably entirely radical in nature. Simons and Brice[259] have investigated the reaction of IF_5 and IF_7 with some fluoroolefins at 175–250 °C in the gas phase. The reactions were complicated by further reaction of the vicinal fluoroiodo alkane with molecular fluorine to yield vicinal difluorides and regenerated IF_5 (equation 89). It would appear that, where possible, mixtures of isomers are formed. There exists insufficient detail in the patent to indicate clearly the true nature of the reaction.

TABLE 10. Product distributions from the reaction of BrF, BrCl, and IF with some alkenes using the Br_2–BrF_3, Br_2–Cl_2 and I_2–IF_5 systems respectively[252]

Alkene	System	Products
$CF_2=CF_2$	I_2–IF_5	CF_3CF_2I (86%)
	Br_2–BrF_3	CF_3CF_2Br
	Br_2–Cl_2	CF_2ClCF_2Br
$CF_3CF=CF_2$	I_2–IF_5	CF_3CFICF_3 (99%)
	Br_2–BrF_3	$CF_3CFBrCF_3$ (45·5%)
$CF_2=CH_2$	I_2–IF_5	CF_3CH_2I (86%)
$CF_2=CFCl$	I_2–IF_5	CF_2ICF_2Cl (45%) + CF_3CFClI (37%)
	Br_2–BrF_3	CF_2BrCF_2Cl (73%) + $CF_3CFClBr$ (13%)
	ICl	CF_2ICFCl_2 (29%) + $CF_2ClCFClI$ (57%)
	IBr	$CF_2ICFClBr$ (14%) + $CF_2BrCFClI$ (44%)
cyclo-C_6F_{10}	Br_2–BrF_3	*cyclo*-$C_6F_{11}Br$ (78%)
$CF_2=CCl_2$	I_2–IF_5	CF_3CFCl_2 (25%) + CF_2ICCl_2F (31%) + CF_3CCl_2I (23%)

$$F_2C{=}CF_2 + IF_5 \longrightarrow F_2ClCF_3 + 2F_2$$
$$2F_2 + F_2ClCF_3 \longrightarrow CF_3CF_3 + IF \qquad (89)$$
$$IF + 2F_2 \longrightarrow IF_5$$

Bromine trifluoride reacts violently with any organic compound containing hydrogen[260], and is therefore unsuitable as an addendum except with perhaloalkenes. No reactions appear to have been reported in any detail.

Muray[261] has reported that bromine pentafluoride, BrF_5, reacts with the carbon–carbon double bonds of chlorinated alkenes to yield primarily difluorides and only minor quantities of vicinal bromo fluorides. The reaction is reported to be very similar to that of BrF_3 under similar conditions. No experimental details were given however. McBee and coworkers[262] have described the reaction of BrF_3 with halogenated olefins to be addition of fluorine, bromine, or bromine fluoride to the double bonds. The reaction proceeds smoothly with perhalogenated olefins, but is largely replaced by substitution (addition–elimination) when there is hydrogen present in the molecule. Further, it has been shown that the bromine introduced during the course of the reaction could eventually be replaced by fluorine upon further reaction. The electrophilic nature of these reactions has not been firmly established but is indicated by the slower and milder reactions of olefins with large numbers of electron-withdrawing substituents.

Chlorine trifluoride has received more attention than the bromine and iodine analogues. It is generally considered to be quite reactive and must be prevented from accumulating in the presence of organic material. Devastating explosions have been reported when only quite small amounts were involved[263]. ClF_3 has been reported[264] to add across the double bonds of benzene in CCl_4 at 0 °C in a nitrogen atmosphere to give chlorofluorocyclohexanes, cyclohexenes, and cyclohexadienes. Yields were improved by the use of cobalt(II) fluoride as a catalyst. An increase in the amount of catalyst and solvent, coupled with a decrease in the flow rate of ClF_3, increased the yield of addition products by a factor of three. The catalyst is believed to cause the formation of ClF and F^+ although a transition-state complex between benzene, CoF_2 and ClF_3 may also be involved. An electrophilic mechanism was confirmed by the use of substituted benzenes[265]. It should be noted, however, that substantial proportions of the isolated products are those of substitution. The addition of ClF_3 across non-aromatic and non-conjugate double bonds has been reported in a number of patents[266,267]. No direct proof of the electrophilicity of these reactions has been reported.

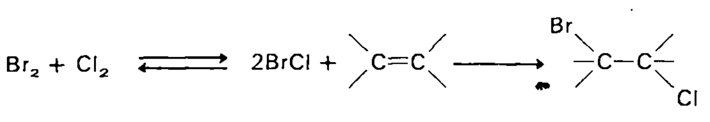
C. Chlorine Monofluoride

Chlorine monofluoride reacts with perhalogenated dienes adding the elements of chlorine and fluorine[268]. The reactions were in general carried out by bubbling ClF into the neat alkene; however, perhalogenated solvents were also used. It was also shown that ClF and ClF_3 gave different product distributions with hexachlorobutadiene under similar conditions. These reactions normally occur at temperatures of 100 °C to 180 °C. With non-halogenated olefins the reactions may be carried out at room temperature under thermostatically controlled conditions and a nitrogen atmosphere. Substitution reactions are found to occur less readily relative to reactions with ClF_3, and BrF_3[269].

Muray has compared the addition of ClF and ClF_3 to 1,2,3,4-tetrachloro-1,3-butadiene. The reactions were carried out at 20 °C in a nickel vessel by bubbling either ClF or ClF_3 diluted with nitrogen into the neat diene. The yields and composition of the chlorofluorobutene adducts varied with the addendum and the extent to which the reaction was carried out. The reaction is complicated by replacement of chlorine and hydrogen by fluorine to form isomeric $C_4Cl_4F_6$ compounds in both cases. Similar observations have been made for chlorinated ethylenes. It was observed that ClF reacts less readily with olefins than does ClF_3. These reactions, however, may be free radical to some extent as pointed out by Muray[270].

D. Bromine Monochloride

Bromine monochloride is usually prepared by the reaction of bromine and chlorine in a suitable solvent such as acetic acid. Addition of an alkene to the equilibrium mixture of bromine, chlorine and bromine monochloride results in the formation of vicinal bromochlorides as the predominant product (equation 90). Evidence that bromine monochloride is

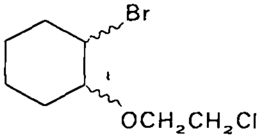


(90)

actually the reactive species is provided by the work of White and Robertson[271] who reported that the rate of addition of BrCl to *cis*-cinnamic acid in acetic acid with constant total halogen, but with different ratios of chlorine and bromine, goes through a maximum when this ratio is unity. Similar results have been reported by Delepine and Ville[272] and by Hanson and James[273]. Hanson and James[273] reported the kinetics of

BrCl additions to be second order, first order in alkene and first order in BrCl in CCl_4 and $CHCl_3$ solvents. The kinetics were measured for cinnamic acid and a number of substituted derivatives and esters at 0 °C. Table 11 gives the results plus those of Br_2 under comparable conditions. Where figures are given in brackets [] the reaction is believed to follow a kinetic order greater than two. White and Robertson[271] have reported that the kinetic form is third order, first order in alkene and second order in BrCl using acetic acid as solvent. Cinnamic and crotonic acids were studied within the concentration range 0·4–0·8 M in BrCl.

The fact that the addition of BrCl is third order in the concentration range 0·4–0·8 M is similar to the results of bromine addition. A bimolecular mechanism at lower concentrations of BrCl in this solvent mixture can not be ruled out. Under comparable conditions BrCl adds 4×10^2 times faster than bromine, and 4×10^6 times faster than iodine, which rules out a mechanism involving initial bromination. A direct comparison with the rate of chlorine addition here is not possible since the rates of addition have not been measured under comparable conditions. However, the reaction of BrCl with a mixture of an alkene and an epoxide to form a β-bromoalkyl β-chloroalkyl ether[274] is evidence against an initial chlorination of the alkene. Thus the reaction of BrCl with a mixture of cyclohexene and ethylene oxide forms the ether **172**. The isomeric ether **173** can be formed



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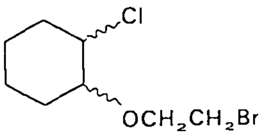

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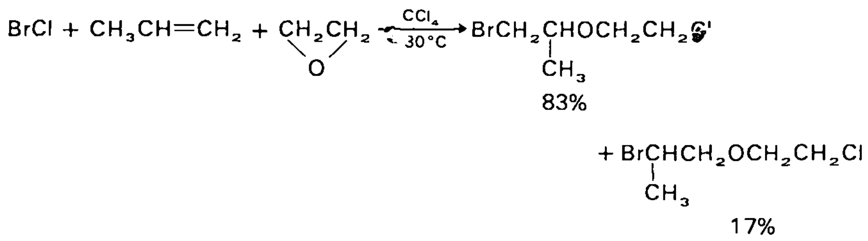
TABLE 11. Specific rate constants for the addition of bromine monochloride and bromine to a series of alkenes

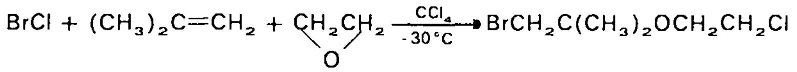
Alkene	Solvent	BrCl k_2(l mol^{-1} s^{-1})	Br_2 k (l mol^{-1} s^{-1})
(*t*) $C_6H_5CH{=}CHCO_2H$	CCl_4	104	0·146
(*E*) $C_6H_5C(CH_3){=}CHCO_2H$	CCl_4	2·51	0·012
(*t*) 2-$CH_3C_6H_4CH{=}CHCO_2CH_3$	CCl_4	2382	[5·47]
(*t*) 2-$CH_3OC_6H_4CH{=}CHCO_2CH_3$	CCl_4	5009	[18·9]
(Z) 2-$CH_3OC_6H_4CBr{=}CHCO_2H$	$CHCl_3$	[59·2]	0·137
(*t*) 3-$CH_3OC_6H_4CH{=}CHCO_2H$	$CHCl_3$	[92·2]	[3·97]
(*t*) 3-$CH_3OC_6H_4CH{=}CHCO_2CH_3$	CCl_4	199	1·09

by adding BrCl to ethylene and cyclohexeneoxide. In this reaction the bromine atom adds to the carbon atom of the alkene while the chlorine atom adds to the carbon atom of the epoxide. No bis(β-chloroalkyl) or bis(β-bromoalkyl) ethers are found. These results are consistent with the view that BrCl is the addendum in this reaction.

The incorporation of an epoxide into the product of BrCl addition to alkene indicates further that the mechanism involves at least two steps with one intermediate which can be trapped by the epoxide. The regiospecificity of the epoxide attack on this intermediate was determined by the following two reactions (equations 91 and 92):



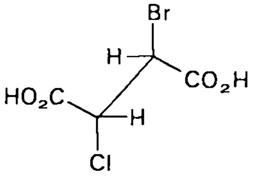
$$\mathrm{BrCl} + \mathrm{CH_3CH{=}CH_2} + \underset{\diagdown\,\mathrm{O}\,\diagup}{\mathrm{CH_2CH_2}} \xrightarrow[-30\,^{\circ}\mathrm{C}]{\mathrm{CCl_4}} \underset{\substack{|\\ \mathrm{CH_3}\\ 83\%}}{\mathrm{BrCH_2CHOCH_2CH_2Cl}} + \underset{\substack{|\\ \mathrm{CH_3}\\ 17\%}}{\mathrm{BrCHCH_2OCH_2CH_2Cl}} \quad (91)$$



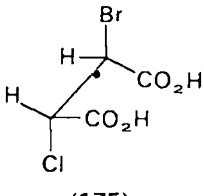
$$\mathrm{BrCl} + \mathrm{(CH_3)_2C{=}CH_2} + \underset{\diagdown\,\mathrm{O}\,\diagup}{\mathrm{CH_2CH_2}} \xrightarrow[-30\,^{\circ}\mathrm{C}]{\mathrm{CCl_4}} \mathrm{BrCH_2C(CH_3)_2OCH_2CH_2Cl} \quad (92)$$

The preferred product in both cases is the one of Markownikoff orientation.

The earliest determination of the stereochemistry of BrCl addition was that of Walden[275], who reacted BrCl with fumaric and maleic acids to yield respectively *meso*(**174**) and *dl*-2-bromo-3-chloro-succinic acid (**175**).



(**174**)



(**175**)

Further work[276] has shown the addition to be *anti* stereospecific to cyclohexene and *trans*-stilbene, but only stereoselective with *cis*-stilbene. The lack of stereospecificity for *cis*-stilbene has been attributed to pre-addition isomerization of *cis*- to *trans*-stilbene.

The product composition of the addition of BrCl to a number of alkenes is given in Table 12. One of the problems of using the available data to deduce the structure of the product-determining transition state is that

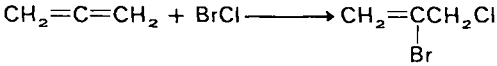
TABLE 12. Product distributions for the addition of bromine monochloride to some alkenes

Alkene	Solvent	Configuration	%M[a]	%aM[a]	Yield (%)	Reference
$CH_3CH{=}CH_2$	aq HCl		54	46	30	279
	aq HCl		58	42	?	214
	Unknown		80	20	?	279
	aq HCl		[100]		?	281
$CH_2{=}CH_2$	CCl_4					277
	aq HCl				?	278
	CH_2Cl_2				39	280, 281
Cyclohexene	$CHCl_3$	*trans*			56	280
$C_6H_5CH{=}CH_2$	$CHCl_3$		100		67	280
(*t*) $C_6H_5CH{=}CHC_6H_5$	$CHCl_3$	*erythro*-BrCl			52	280
		meso-diCl			14	280
(*c*) $C_6H_5CH{=}CHC_6H_5$	$CHCl_3$	*threo*-BrCl			68	280
		erythro-BrCl			5·5	280
(*t*) $C_6H_5CH{=}CHCO_2H$	$CHCl_3$	*erythro*-BrCl	100		31	280
	CH_2Cl_2	*erythro* diCl			73	280
	aq HCl	*erythro* BrCl	100		50	282
	CCl_4	*erythro*/*threo*=1/3	100			
$CH_2{=}CHCH_2OH$	H_2O		36	64		
$CH_2{=}CHCH_2Cl$	H_2O		23	77		
$CH_2{=}CHCH_2Br$	H_2O		22	78		

[a] M = Markownikoff orientation; *a*M = *anti*-Markownikoff orientation.

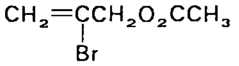
large variations are found in the reported product distributions by various authors[276,283]. An examination of the earlier literature indicates that the question of isomerization between Markownikoff and *anti*-Markownikoff isomers was not necessarily considered, and that little if any attempt was made to show that the product distributions reported conform to those of kinetic control. Qualitatively it can be concluded that Markownikoff addition is generally favoured.

Bromine monochloride adds to allene in chlorinated hydrocarbon solvents to form a 1 :1 adduct in which the bromine is bonded to the central carbon (equation 93)[141]. No propargyl bromide is formed as a product,



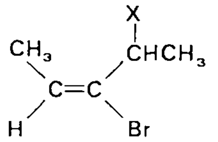
$$CH_2{=}C{=}CH_2 + BrCl \longrightarrow CH_2{=}\underset{\displaystyle Br}{\underset{|}{C}}CH_2Cl \qquad (93)$$

unlike the addition of chlorine to allene where progargyl chloride is the major product. Addition of a second mole of BrCl to form a 2:1 adduct is slow. In acetic acid as solvent, the major product of addition of BrCl to allene is the solvent incorporated product **176a**.

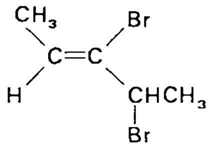


$$CH_2{=}\underset{\displaystyle Br}{\underset{|}{C}}CH_2O_2CCH_3$$

(176a)



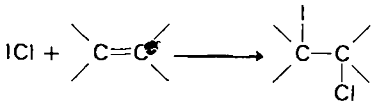
177a: X = Br
177b: X = OCH_3



Bromine monochloride reacts rapidly with 2,3-pentadiene in CCl_4 at 5 °C to give a 28:72 *cis–trans* mixture of **177a**. In methanol as solvent, **177b** is the major product as a 20:80 *cis–trans* mixture. Reaction of BrCl with (*R*)-(−)-2,3-pentadiene gave optically active products. The observed rotation of the bromo ether was found to be the same whether prepared from bromine in methanol or BrCl in methanol. The authors therefore concluded that the stereospecificity of the reaction was the same for both Br_2 and BrCl. From previous work it has been shown that Br_2 adds *anti* to 2,3-pentadiene[193].

E. Iodine Monochloride

Iodine monochloride (ICl) is a relatively stable liquid which reacts with alkenes to form iodochlorides (equation 94).



(94)

The reaction is kinetically complex. White and Robertson[271] established third order kinetics for the addition of ICl to allyl acetate in acetic acid at 25 °C over the concentration range 0·4–0·8 M. The reaction was first order in olefin and second order in ICl. A relative ratio of 10^5 compared to iodine was determined under comparable conditions. The addition of HCl to the solution was found to reduce the rate of addition of ICl considerably. This rate decrease is attributed to the formation of the complex $HICl_2$. An apparent change from a termolecular to a bimolecular mechanism was also observed. The addition to cinnamic acid and 2-methoxycinnamic acid was found to be completely inhibited by the presence of HCl. It is unclear from their results whether the 'bimolecular' reaction was really first order in HCl as well as first order in both alkene and ICl and thus pseudo second order (Ad_E3) or whether it was in fact second order (Ad_E2). Heublein[283] reported that the addition of ICl to *trans*-stilbene in acetic acid, diethyl ether and acetonitrile was bimolecular at a variety of temperatures. These results suggest that ICl additions follow a rate law of the form:

$$\frac{-\mathrm{d}[\mathrm{ICl}]}{\mathrm{d}t} = (k_2[\mathrm{ICl}] + k_3[\mathrm{ICl}]^2 + k_{\mathrm{ICl}_2^-}[\mathrm{ICl}_2^-])[\mathrm{Alkene}]$$

While the stereospecificity of iodine monochloride additions is generally reported to be *anti*, the supporting data are very meagre, in fact several exceptions have been reported. Thus ICl reacts with both *cis*- and *trans*-stilbene to yield exclusively *erythro-dl*-1-chloro-2-iodo-1,2-diphenylethane[283] while addition to 1,1,2-trifluorocyclobutene is reported to occur stereospecifically *syn*[284]. The addition is generally non-regiospecific as illustrated by the data in Table 13[217,218].

The reaction is similar to that of BrCl in that Markownikoff isomers are generally favoured except in the presence of sterically-bulky substituents such as *t*-butyl. The nature of the reaction with perhalogenated olefins is believed to be ionic[284] but has not been studied in sufficient detail. A competitive radical path cannot be ruled out especially under neat, high temperature ($T >$ 180 °C) conditions[287,288].

Iodine monochloride reacts with (*R*)-(−)-2,3-pentadiene[211] in methanol to yield (−)-*trans*-3-iodo-(4*S*)-methoxy-2-pentene as the major product. The *cis* isomer was also formed in 6% yield. Both the iodo ether and the iodo chloro adducts were formed irreversibly in an *anti*-stereospecific manner.

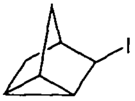
TABLE 13. Product distributions for the addition of iodine monochloride to some alkenes

Alkene	Solvent	Configuration	%M[a]	%aM[a]	Yield (%)	Reference
$CH_3CH=CH_2$	aq.HCl		69			217
	aq.HCl		80			214
	H_2O		71			217
	CH_2Cl_2		65	35		285
$C_6H_5CH=CH_2$	CH_2Cl_2/HCl		≥95	<5		217
$CH_3CH=CHCO_2H$	$CHCl_3$		≥92	<8		217
$CH_2=CHSO_3H$	aq HCl		≥90	<10		217
$CH_2=CHCH_2OH$	H_2O		30	70		217
$CH_2=CHCH_2Cl$	H_2O		15	85		217
t-BuCH=CH_2	CH_2Cl_2		0	100		285
i-PrCH=CH_2	CH_2Cl_2		30	70		285
(*c*) $C_2H_5CH=CHCH_3$	CH_2Cl_2	*threo*	33	67		285
(*t*) $C_2H_5CH=CHCH_3$	CH_2Cl_2	*erythro*	36	64		285
(*c*) *t*-BuCH=$CHCH_3$	CH_2Cl_2	*threo*	0	100		285
(*t*) *t*-BuCH=$CHCH_3$	CH_2Cl_2	*erythro*	0	100		285
(*c*) $C_6H_5CH=CHCH_3$	CH_2Cl_2	*threo*	100	0		285
(*t*) $C_6H_5CH=CHCH_3$	CH_2Cl_2	*erythro*	100	0		285
$F_2C=CFCl$	Neat	$CF_2ClCFClI$	100%			218, 187
	CH_2Cl_2	$CF_2ClCFClI$	70–80%	CF_2ICFCl_2	20–30%	286
$F_2C=CCl_2$	Neat	CF_2ClCCl_2I	≥80%	CCl_3CF_2I	≤20%	286
$CF_3CF=CF_2$	Neat	CF_3CFICF_2Cl	92%	$CF_3CFClCF_2I$	8%	286

[a] M = Markownikoff orientation; *a*M = *anti*-Markownikoff orientation.

Ingold and Smith[218] reported that ICl reacts with 1,3-butadiene at -35 °C in CH_2Cl_2 to yield a 78:22 mixture of the Markownikoff 1,4- and 1,2-adducts respectively. In contrast the reaction with 2,3-dimethyl-1,3-butadiene[289] in CH_2Cl_2 at -78 °C gave polymeric material and 1,2,3,4-tetrachloro-2,3-dimethylbutane; the latter as a 4:1 mixture of the *meso* and *dl* isomers. No mechanism was proposed.

Werstiuk and coworkers[289] have reported that the addition of ICl to norbornene in CH_2Cl_2/pyridine yields **178**, **179** and **180** as 85–90% of the reaction mixture. A comparison of the addition of ICl, bromine, and chlorine to norbornene reveals that the quantity of tricyclic component decreases from 65% in chlorination, to 52% in bromination and 12% in ICl addition, while the reverse trend is established for the *syn–exo* and *exo–endo* dihalides **179** and **180**.



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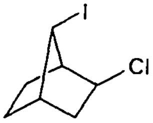

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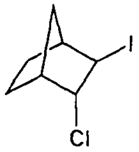
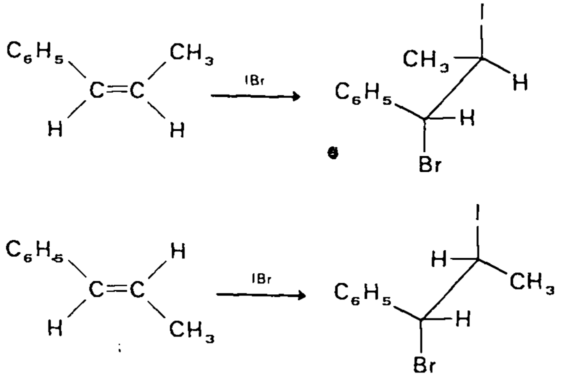


(180)

F. Iodine Monobromide

The addition of iodine monobromide to alkenes is quite facile in solvents such as chloroform, methylene chloride and acetic acid and forms the expected 1,2-iodobromides. In hydroxylic solvents, products of solvent incorporation are readily isolatable.

The regio- and stereochemistry of the addition of IBr to a selected number of alkenes is given in Table 14[285]. The regiospecificity of the kinetically-controlled products is very sensitive to the initial alkene structure. Thus replacing an ethyl group on the alkene by an isopropyl or *t*-butyl group results in the formation of increasing amounts of the *anti*-Markownikoff product. The adducts are generally formed by *anti* addition. Thus *cis*- and *trans*-1-phenylpropene react with IBr to yield *threo* and *erythro*-1-bromo-2-iodo-1-phenylpropane respectively (equation 95). The regio- and stereochemistry of the addition of IBr suggests that the mechanism involves a bridged iodonium ion prior to the product-determining step. An exception is the non-stereospecific addition to *cis*- and *trans*-anethole which implies that in this case, as in the addition of 2,4-dinitrobenzenesulphenyl chloride, an open carbonium ion is formed



(95)

during the reaction. Few kinetic data are available. White and Robertson reported[271] a termolecular process with a relative reactivity of 3 × 10^3 that of iodine and 0·3 that of bromine. Conductivity studies of Spandau

TABLE 14. The regio- and stereochemistry of addition of iodine monobromide to some simple alkenes in methylene chloride at 25 °C[285]

Alkene	Configuration	Percentage distribution[a] M	Percentage distribution[a] *a*M
(*c*) $C_2H_5CH{=}CHCH_3$	*threo*	40	60
(*t*) $C_2H_5CH{=}CHCH_3$	*erythro*	45	55
(*c*) *i*-PrCH=$CHCH_3$	*threo*	≤5	≥95
(*t*) *i*-PrCH=$CHCH_3$	*erythro*	20	80
(*c*) *t*-BuCH=$CHCH_3$	*threo*	0	100
(*t*) *t*-BuCH=$CHCH_3$	*erythro*	0	100
(*c*) *i*-PrCH=CHC_2H_5	*threo*	0	100
(*t*) *i*-PrCH=CHC_2H_5	*erythro*	≤10	≤90
(*c*) *t*-BuCH=CHC_2H_5	*threo*	0	100
(*t*) *t*-BuCH=CHC_2H_5	*erythro*	≃4	≥96
(*c*) $C_6H_5CH{=}CHCH_3$	*threo*	100	0
(*t*) $C_6H_5CH{=}CHCH_3$	*erythro*	100	0
$CH_3CH{=}CH_2$		65	35
$C_2H_5CH{=}CH_2$		45	55
i-PrCH=CH_2		15	85
t-BuCH=CH_2		0	100
$C_6H_5CH{=}CH_2$		100	0
$F_2C{=}CH_2$		100	CF_2BrCH_2I
$ClFC{=}CF_2$		100	$CF_2BrCClFI$

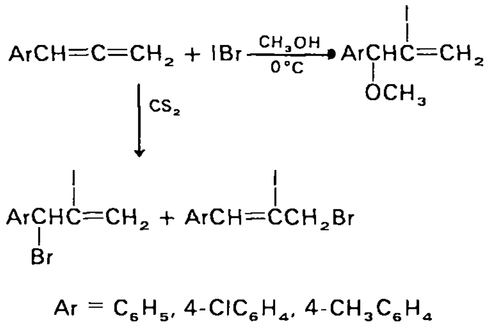
[a] M = Markownikoff orientation; *a*M = *anti*-Markownikoff orientation.

and Gutmann[291] indicate a dissociation of the form:

$$2\mathrm{IBr} \rightleftharpoons \mathrm{I}^+ + \mathrm{IBr}_2^-$$

This suggests that the electrophilic species may be I^+. Further kinetic measurements would be of considerable interest but are lacking.

The reaction of iodine monobromide with (*R*)-(−)-2,3-pentadiene in methanol[211] gives (−)-*trans*-3-iodo-(4*S*)-methoxy-2-pentene in 94% yield compared to a 6% yield of the corresponding *cis* isomer. The products were found to be optically stable in the presence of iodine in methanol, thus ruling out the possibility of racemization of the product after the product-determining step. The optical purity was lower than that found when ICl was used as the electrophile. The addition of IBr to a series of phenylallenes in methanol at 0 °C has been reported[292] to give 2-iodo-3-methoxy-3-aryl-1-propene (equation 96). In CS_2 at 0 °C two products were



(96)

isolated. The results are interpreted in terms of a cyclic iodonium ion intermediate. The reaction occurs primarily at the internal bond.

Reaction of IBr with halogenated alkenes[219,293] such as 1,1-difluoroethylene or chlorotrifluoroethylene in the dark under neat conditions, or in solvents such as CCl_4 and Freon 112, at room temperature give the normal 1,2-adducts.

The limited kinetic and stereochemical data are in accord with an *anti* Ad_E3 mechanism for the addition of IBr to alkenes. In view of the known kinetic complexity of the other interhalogens it is not possible to rule out *a priori* a concurrent Ad_E2 process with a bridged iodonium ion intermediate as is postulated for other species of the general structure IY (e.g., $Y = N_3^-, NCO^-, SCN^-$).

V. PSEUDOHALOGENS

Pseudohalogens are usually defined as 'univalent chemical aggregates, X_2, consisting of more than two electronegative atoms which in the free state resemble the halogens and which give rise to anions resembling the halide ions in their behavior'[294]. Examples of such species are cyanogen $(CN)_2$, thiocyanogen $(SCN)_2$, and selenocyanogen, $(SeCN)_2$. For the purposes of this review we have extended this definition to include compounds of the general structure XY, where X is a halogen, usually iodine but sometimes bromine or chlorine, and Y is either an anionic or cationic species such as ONC^-, OCN^-, N_3^-, $CN^{-/+}$, $SCN^{-/+}$, $SeCN^{-/+}$ or $SCSN_3^-$. The compounds range in general properties from the toxic but comparatively stable cyanides (XCN) to the highly explosive azides (XN_3).

A. Symmetrical Pseudohalogens

The reactions of symmetrical pseudohalogens with alkenes have been reported in numerous reviews[294]. A typical example is the reaction of thiocyanogen with ethylene to give the 1,2-addition product **181** (equation 97).

$$(SCN)_2 + H_2C{=}CH_2 \longrightarrow \underset{(\mathbf{181})}{NCSCH_2CH_2SCN} \qquad (97)$$

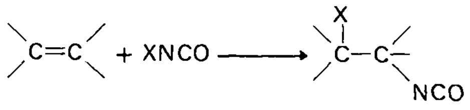
In acetic acid, solvent-incorporated products have been reported[295] in addition to the 1,2-dithiocyanates and the thermodynamically more stable 1-thiocyanate-2-isothiocyanate adducts.

B. Halogen Isocyanates (XNCO)

Halogen isocyanates are usually prepared by the reaction of silver cyanate with chlorine, bromine or iodine in diethyl ether, or a chlorinated hydrocarbon such as ethyl chloride (equation 98)[296–301]. Since they are

$$AgCNO + X_2 \longrightarrow XNCO + AgX\downarrow \qquad (98)$$

explosive, halogen isocyanates are rarely isolated. Rather to effect addition, an alkene is added to the reaction mixture either with or without filtering the silver halide. In either case the major product is the β-haloalkyl isocyanate (equation 99).



(99)

X = Cl, Br, or I

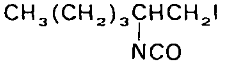
The limited kinetic data for the addition of iodine isocyanate to alkenes are given in Table 15. The rates of addition have been measured essentially in three ways, using both direct and competitive techniques with preformed or *in situ* generated INCO. The *in situ* determination consists of allowing the alkene to react in a stirred heterogeneous system consisting of ether, AgCNO (excess), iodine, the alkene, and INCO. Preformed INCO solutions react extremely rapidly; the rate is at least ten times that observed in the *in situ* reaction method.

The only work which reports the kinetic order of the reaction is a paper by Swern and Rosen[302] who found the addition to be second order overall; first order in alkene and first order in INCO.

The agreement is poor between the kinetic data reported by various workers in Table 15. This lack of agreement is particularly apparent in the relative order of reactivity of *trans*-3-hexene, cyclohexene and cyclopentene. Part of the problem may be that in the studies where INCO is prepared *in situ*, complex formation between the alkene and iodine and/or silver ions competes with INCO addition. Such side reactions would complicate any analysis based upon competition results. Further, the relative reactivities were determined at a variety of temperatures and thus may not be consistent over the ≈ 70 deg C range considered.

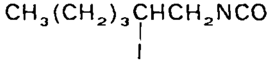
Despite the lack of quantitative agreement, the general trend of the data in Table 15 shows that the rate of addition of INCO increases with an increase in the number of electron-donating alkyl groups on the double bond. This is consistent with an electrophilic addition of INCO. Further speculation regarding the structure of the rate-determining transition state is unwarranted until better and more consistent kinetic data are available.

The stereospecific *anti* addition of INCO to *cis*- and *trans*-2-butene and β-deuteriostyrenes has been reported[303]. Addition to unsymmetrical alkenes is usually non-regiospecific[300,301,303]. Thus 1-hexene reacts with INCO to form a 70:30 mixture of the Markownikoff and *anti*-Markownikoff isomers **182** and **183** respectively. If one substituent on the alkene



$CH_3(CH_2)_3\underset{\substack{|\\NCO}}{C}HCH_2I$

(182)



$CH_3(CH_2)_3\underset{\substack{|\\I}}{C}HCH_2NCO$

(183)

exerts a large steric or polar effect then the addition becomes regiospecific. For example styrene, *t*-butylethylene, and 1-*t*-butyl-2-methylethylene react regiospecifically to form **184**, **185** and **186** respectively. The latter result can be compared to the addition of INCO to *neo*-pentylethylene, in

TABLE 15. Relative rates of the addiction of INCO to alkenes

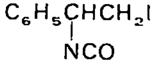
	Method				
	Competitive preformed[a]	Competitive *in situ*[a]	Direct *in situ*[a]		
	25 °C	−20 °C to −30 °C	−47 °C	−22 °C	2 °C
2,3-Dimethyl-2-butene	>3200		3800		
Isopropenyl acetate			3700		
Vinyl acetate			1950		
3-Methyl-1-pentene			1250		
Methyl oleate					570
Methyl elaidate					500
trans-3-Hexene	180	≤7·9		571	
Norbornene				440	
Cycloheptene				430	
Cyclohexene	100	100	100	100	100
1-Hexene					50
Cyclooctene					35
2-Methyl-2-pentene	>1400				
Cyclopentene	>1000	685			221
2,3-Dimethyl-1-butene	140				
1-Octene	44	≤2·7			
Methyl vinyl ketone					0
Vinylidene chloride					0
Methyl methacrylate					0

[a] Competitive preformed: to a solution of INCO in anhydrous ether was added a large molar excess of a mixture of two olefins at 25 °C.

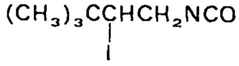
Competitive *in situ*: reactions were run at −20 to −30 °C. AgOCN was added in one portion to a stirred mixture of iodine and the appropriate alkenes. Relative rates taken after 24 h.

Direct *in situ*: as above except only one olefin in solution reaction followed by g.l.p.c.

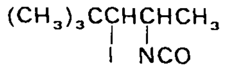
which a 80:20 mixture of Markownikoff–*anti*-Markownikoff adducts is formed, or to methylenecyclohexane which results in a 55:45 mixture of Markownikoff to *anti*-Markownikoff adducts.


$\mathrm{C_6H_5\underset{NCO}{C}HCH_2I}$

(184)

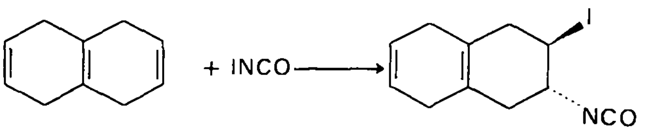

$\mathrm{(CH_3)_3C\underset{I}{C}HCH_2NCO}$

(185)


$\mathrm{(CH_3)_3C\underset{I}{C}H\underset{NCO}{C}HCH_3}$

(186)

Another example of the influence of steric hindrance is found in the addition of INCO to isotetralin (**187**, equation 100) where only the less-substituted double bond was found to react. If the polar effects only were important, reaction with the tetrasubstituted double bond would be expected. These results indicate that both steric and polar effects are important in the product-determining transition state.

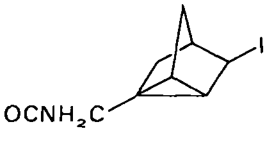


(187)

(100)

The *anti* stereospecific addition of INCO to simple alkenes has led to the use of this reaction for the stereospecific synthesis of *trans*-*N*-(2-iodoalkyl) carbamates[304], aziridines[305], oxazolidones[306], *cis*- and *trans*-2-amino alcohols[304], 1,2-diamines[306], and azepines[307].

The addition of INCO to bicyclic alkenes results in products of rearrangement. Norbornene and α-pinene give complex mixtures while 5-methylenenorbornene, norbornadiene and ethenoanthracene all give the rearranged products **188**, **189** and **190**, respectively, apparently under conditions of kinetic control[303].



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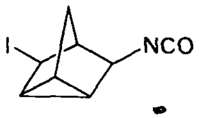

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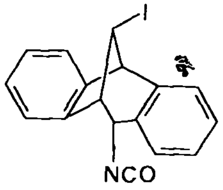


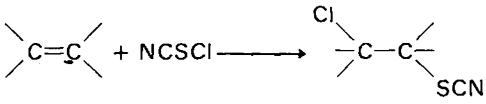
(190)

Reaction of one mole of INCO with conjugated dienes results in the formation of only 1,4-addition products[308]. The addition to non-conjugated dienes is a complicated reaction in which well-characterized products are not readily obtained[308]. Methylallene reacts with INCO to give a 1:1 adduct whose structure was not reported[308].

The limited kinetic and product data are in accord with an $\mathrm{Ad_E2}$ mechanism for the addition of INCO to alkenes. The *anti* addition to simple alkenes supports a bridged structure for the intermediate ion. However, since numerous examples of rearranged products are known, it is impossible to rule out an open ion as an intermediate in certain cases. Clearly more experimental work is needed to clarify the mechanism of this addition.

C. Thiocyanogen Chloride

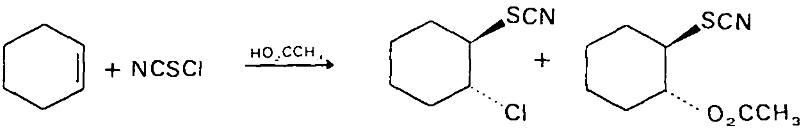
The reaction of thiocyanogen chloride with alkenes in moderately-polar solvents is believed to be an electrophilic addition in which the electrophile is polarized in the manner $\mathrm{NCS^{\delta+}Cl^{\delta-}}$. The reaction of NCSCl with ethylene and cyclohexene in chloroform or toluene at room temperature yields the β-chloroalkyl thiocyanate as product **191** (equation 101)[309,310].



(191)

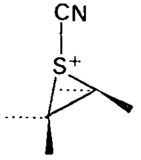
(101)

Guy and Pearson have reported[311,312] the addition of NCSCl to ethylene, *cis-* and *trans-*2-butene, cyclohexene and *trans-*Δ^2-octalin in the presence of a free radical inhibitor in acetic acid in the dark at room temperature. The products are β-chloroalkyl and β-acetoxyalkyl thiocyanates (equation 102). Competition experiments showed the reactions to be rapid in the presence of electron-donating groups and retarded by similarly situated electron-withdrawing groups. Increased reactivity is observed as the solvent polarity is increased. The reaction is stereospecific *anti* and is interpreted (albeit in the absence of kinetic support) in terms of a two-step $\mathrm{Ad_E2}$ mechanism involving an episulphonium ion intermediate **192**.

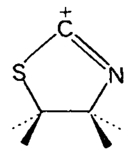


(102)

An episulphonium ion **192** is postulated rather than a thiocyanate bridged intermediate **193** because upon ring opening, the latter

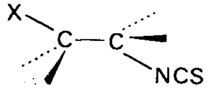


(192)



(193)

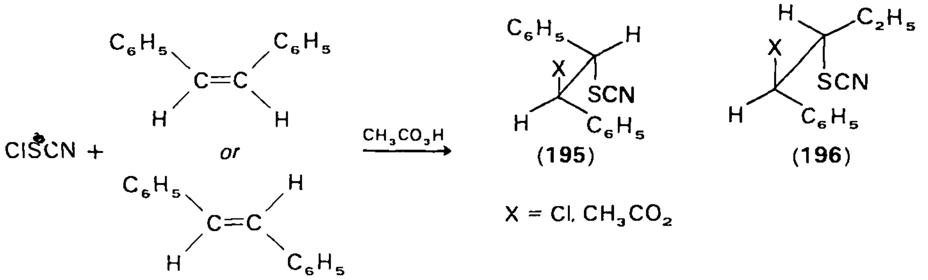
intermediate would lead to the thermodynamically more-stable isothiocyanate isomers **194**, which are not found in the reaction mixture.



X = Cl, CH_3CO_2

(194)

Addition of NCSCl to aryl-substituted alkenes[313] is stereoselective *anti*, indicating that an open ion is formed sometime prior to the product-determining step. Results for *cis*- and *trans*-stilbene are given in Table 16.



(195) (196)

X = Cl, CH_3CO_2

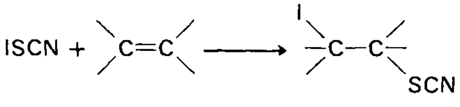
The *anti* stereospecific addition of NCSCl to simple alkyl-substituted alkenes versus only stereoselective addition with aryl-substituted alkenes suggest different transition-state structures in the product-determining step.

TABLE 16. Solvent dependence upon the product ratios of the addition of thiocyanogen chloride to *cis*- and *trans*-stilbene[313]

Stilbene	Solvent	Relative reactivity	**196/195** X = Cl	**196/195** X = O_2CCH_3
cis	CH_3CO_2H	40	75/25	88/12
trans	CH_3CO_2H	13	46/54	10/90
trans	CH_2Cl_2	10	28/72	—
trans	$CHCl_3$	4	8/92	—
trans	C_6H_6	1	37/63	—

D. Iodine Thiocyanate (ISCN)

In contrast to its chlorine and bromine analogues, iodine thiocyanate is generally polarized $I^{\delta+}SCN^{\delta-}$ in ionic media. The addition of ISCN to alkenes yields β-iodoalkyl thiocyanate[197].



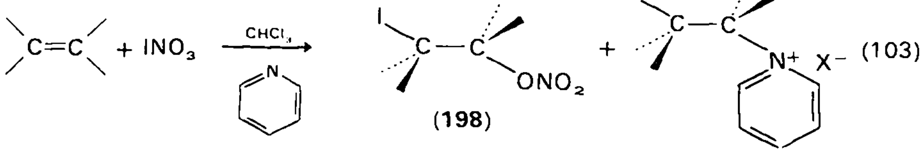
(197)

Pritzkow and coworkers[176] have reported the relative rates of addition of ISCN to a number of alkenes in acetic acid. The reaction is bimolecular, first order in ISCN, and first order in alkene. The relative reactivities of a number of alkenes (cyclohexene = 1·0) are given in Table 17. From the rate data the electrophilicity of the reaction is clearly apparent. Correlation versus Hammett σ and σ^+ values gives $\rho = -3{\cdot}69$, and $\rho^+ = -2{\cdot}59$. The correlation coefficient was somewhat less in the latter case. A correlation of 18 out of the 38 alkyl-substituted alkenes studied with the Taft equation gives $\rho^* = -3{\cdot}42$, $\delta = 0{\cdot}59$. The reason for the truncated basis set in this latter correlation was not discussed. The results are interpreted in terms of a two-step Ad_E2 mechanism involving a bridged iodonium ion intermediate. In view of the absence of stereochemical results there is no clear experimental support for such an assertion.

E. Halogen Nitrates

Stabilized positive halogen compounds such as $[(C_6H_5N)_2X^+NO_3^-]$ (X = Cl, Br, I) and $C_6H_5NI^+NO_3^-$ have been known for some time[314]. Only recently has any attention been paid to their reactivity with alkenes and related organic compounds.

Iodonium nitrate is known to add to alkenes in chloroform–pyridine solutions to form β-iodoalkyl nitrate esters (**198**) and β-iodoalkylpyridinium iodides (**199a**) or nitrates (**199b**) as products (equation 103)[315,316]. In a solution containing at least a two-fold excess of pyridine, the iodonium



(103)

(198)

199a: X = I
199b: X = NO_3

TABLE 17. Specific rate constants and relative reactivities of ISCN addition to a series of alkenes in acetic acid at 30 °C

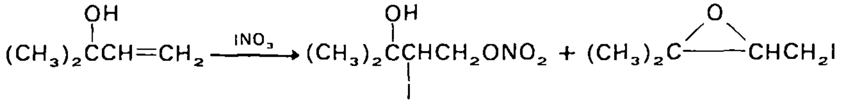
Alkenes	k_{rel}	$k_2 \times 10^3$ (l mol^{-1} s^{-1})
neo-PentCH=CH$_2$	0·039	
t-BuCH=CH$_2$	0·046	
i-PrCH=CH$_2$	0·076	
s-BuCH=CH$_2$	0·068[a]	1·97[a]
i-BuCH=CH$_2$	0·089[a]	3·20[a]
$C_2H_5CH=CH_2$	0·23	
n-BuCH=CH$_2$	0·19[a]	5·00[a]
n-PentCH=CH$_2$	0·26	
n-$C_6H_{13}CH=CH_2$	0·26[a]	7·10[a]
n-$C_{10}H_{21}CH=CH_2$	0·20[a]	6·80[a]
(*c*) $CH_3CH=CHCH_3$	1·5	
(*t*) $CH_3CH=CHCH_3$	0·78	
(*c*) $C_2H_5CH=CHC_2H_5$	1·7	
(*t*) $C_2H_5CH=CHC_2H_5$	0·84	
(*c*) *n*-PrCH=CHPr-*n*	1·3	
(*t*) *n*-PrCH=CHPr-*n*	0·58	
(*c*) *n*-BuCH=CHBu-*n*	1·5	
(*t*) *n*-BuCH=CHBu-*n*	0·74	
$(CH_3)_2C=CH_2$	2·9	
$C_2H_5(CH_3)C=CH_2$	3·5	
n-Pr$(CH_3)C=CH_2$	2·5	
i-Pr$(CH_3)C=CH_2$	2·3	
t-Bu$(CH_3)C=CH_2$	0·99	
$(CH_3)_2C=CHCH_3$	6·1	
$(CH_3)_2C=CHC_2H_5$	7·0	
Cyclobutene	0·89	
Cyclopentene	2·1	
Cyclohexene	1·0	30·0
Cycloheptene	1·9	
Cyclooctene	1·1	
1,5-Cyclooctadiene	1·9	
Norbornene	7·1	
Bicyclo[2.2.2.]octene-2	0.23	
1-Methylcyclopentene	6·4	
1-Methylcyclohexene	3·5	
Methylidenecyclopentene	15·0	
Methylidenecyclohexene	7·2	
Vinylcyclohexane	0·11	
$C_6H_5CH=CH_2$	0·25	

---

[a] Both relative rates by a competitive technique and actual rate constants were measured for these compounds. The agreement between the two methods is quite good.

ion is a stabilized species complexed to two pyridine molecules so that the electrophilic reagent is believed to be $I(C_6H_5N)_2^+$. Evidence for this view comes from the fact that salts such as $I(C_6H_5N)_2^+NO_3^-$, have been isolated[317]. Since the product of the reaction of *trans*-4,4-dimethyl-2-pentene is the same with either $I(C_6H_5N)_2^+NO_3^-$ in anhydrous dimethylsulphoxide or iodonium nitrate in 1:1 pyridine–$CHCl_3$ solution, it is concluded that the same electrophilic species $I(C_6H_5N)_2^+$ is involved in both reactions[318].

The formation of β-iodoalkylpyridinium iodides or nitrates as products as well as a β-iodoalkyl nitrate indicated that the mechanism of the addition involves at least one intermediate. Further evidence for this is the reaction of iodonium nitrate with alkenes containing an internal nucleophile. Thus the reaction of iodonium nitrate and 3-hydroxy-3-methylbutene-1 (**200**) in 2,6-dimethylpyridine–chloroform solution forms the β-iodonitrate (**201**) and the epoxide (**202**) as products (equation 104)[319].



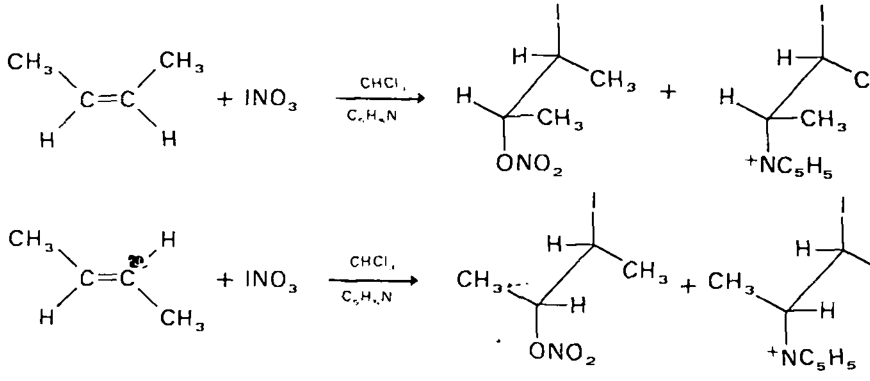
(104)

(200) **(201)** **(202)**

Epoxide formation can be rationalized by internal nucleophilic attack by the oxygen on an intermediate cation.

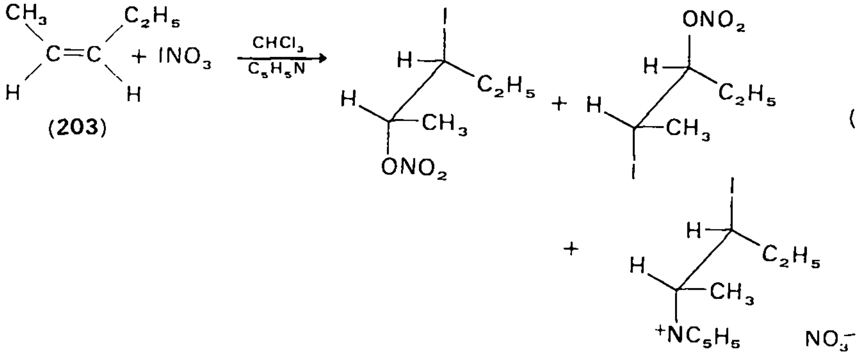
Since kinetic data are not available, no firm conclusions can be reached regarding the rate-determining transition state. However, sufficient data are available to attempt to describe the product-determining transition state.

The addition of iodonium nitrate in chloroform–pyridine occurs in an *anti*-stereospecific manner. Thus *cis*- and *trans*-2-butenes react to give exclusively *threo* and *erythro* products respectively (equation 105).



(105)

Additions to unsymmetrical alkenes such as *cis*-2-pentene (**203**) form both Markownikoff and *anti*-Markownikoff isomers as products (equation 106).

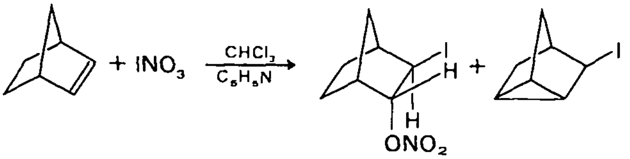


(203)

(106)

The amounts of β-iodoalkyl nitrates and β-iodoalkylpyridinium salts formed by addition to a number of alkyl-substituted ethylenes, as well as their stereochemistry and regiochemistry, are given in Table 18. The fact that the pyridinium group becomes attached to the more-highly substituted carbon on an olefinic bond was established by an X-ray crystallographic study.

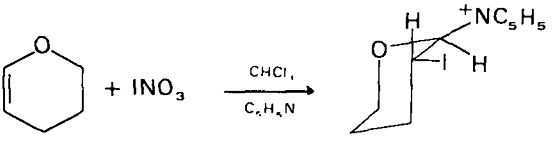
Only limited data are available on the additions to cyclic or bicyclic alkenes. Norbornene adds INO_3 to form the β-iodoalkyl nitrate (**204**) and nortricyclic iodide (**205**, equation 107). No β-iodoalkyl pyridinium salts



(107)

(204) (205)

are formed. In contrast, cyclohexene and cyclopentene form approximately equal amounts of the *trans*-β-iodoalkyl nitrates and β-iodoalkylpyridinium salts, while 2,3-dihydropyran forms only the *trans*-β-iodoalkylpyridinium salt (**206**, equation 108).



(108)

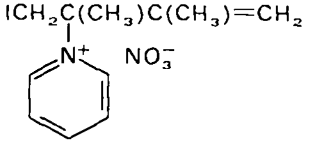
(206)

TABLE 18. Effect of alkene structure on the product composition of the addition of iodonium nitrate in chloroform–pyridine at 25 °C

Alkene	β-Iodoalkyl nitrate (%)[a]			β-Iodoalkyl pyridinium salt (%)[a]			Configuration of products
	Yield	M	*a*M	Yield	M	*a*M	
cis-2-Butene	32			54			*threo*
trans-2-Butene	32			55			*erythro*
cis-2-Pentene	67	30	70	5	0	100	*threo*
trans-2-Pentene	53	45	55	12	0	100	*erythro*
cis-4-Methyl-2-pentene	63	0	100	14	0	100	*threo*
trans-4-Methyl-2-pentene	70	20	80	15	0	100	*erythro*
cis-4,4-Dimethyl-2-pentene	93	0	100	7	0	100	*threo*
trans-4,4-Dimethyl-2-pentene	76	0		5	0	100	*erythro*
Z-3-Methyl-2-pentene				43	100	0	(*RS*, *RS*)
E-3-Methyl-2-pentene				39		0	(*RS*, *SR*)
2-Methyl-2-butene				75		0	—
2,3-Dimethyl-2-butene				47			—
Cyclohexene	60			40			*trans*
Cyclopentene	54			43			*trans*
Styrene	10	100	0	80	100	0	—
cis-Stilbene				83			*threo*
trans-Stilbene				86			*erythro*
Z-2,2-Dimethyl-3-hexene	71	0	100	Trace			*threo*
E-2,2-Dimethyl-3-hexene	51	0	100	Trace			*erythro*
1,4-Cyclohexadiene	27			24			—

[a] M = Markownikoff isomer; *a*M = *anti*-Markownikoff isomer.

Conjugated dienes react with INO_3 in chloroform–pyridine by a 1,2-addition to form only the β-iodoalkylpyridinium salts. Thus 2,3-dimethyl-1,3-butadiene and 2-methyl-1,3-butadiene form only the Markownikoff adducts **207** and **208** respectively.



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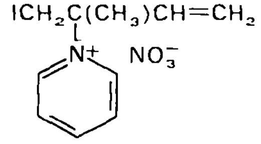
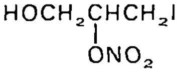


(208)

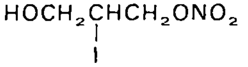
Hydroxyalkenes react with iodonium nitrate in chloroform–pyridine to form both hydroxy β-iodoalkyl nitrates and hydroxy β-iodoalkylpyridinium salts. Compared to an alkene of similar structure without the hydroxyl group, the presence of a hydroxyl group increases the yield of the pyridinium salt as illustrated in Table 19.

By changing the solvent to 2,6-dimethylpyridine–chloroform, the formation of pyridinium salts can be eliminated. Thus, allyl alcohol reacts with INO_3 in chloroform–pyridine to form three products; the isomeric β-iodoalkyl nitrates (**209** and **210**) in 30% yield and a single pyridinium salt (**211**). Changing the solvent to 2,6-dimethylpyridine results in formation of only **209** and **210** in 60% yield.



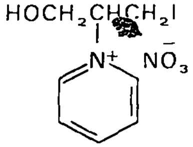
$HOCH_2CH(ONO_2)CH_2I$

(209)



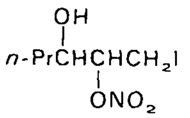
$HOCH_2CH(I)CH_2ONO_2$

(210)



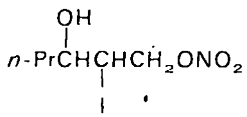
(211)

Changing the solvent to 2,6-dimethylpyridine–chloroform also increases the yield of three-, four- and five-membered cyclic ethers. For example the product of the reaction of hex-1-en-3-ol with INO_3 in pyridine–chloroform is a 50:50 mixture of the isomeric β-iodoalkyl nitrates (**212** and **213**) produced in 34% yield plus **214** produced in 16% yield.



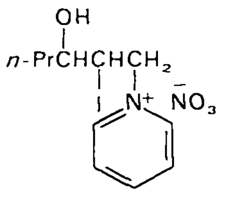
$n\text{-}PrCH(OH)CH(ONO_2)CH_2I$

(212)



$n\text{-}PrCH(OH)CH(I)CH_2ONO_2$

(213)



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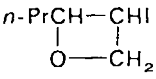


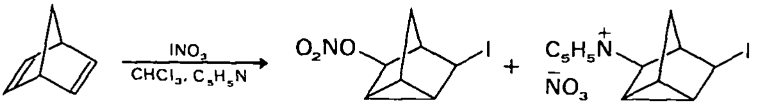
(215)

TABLE 19. Effect of placing a hydroxyl group on an alkene on the product composition of the reaction of iodonium nitrate in chloroform–pyridine

Alkene	Relative yields	
	β-Iodoalkyl nitrate	β-Iodoalkylpyridinium salts
$(CH_3)_2C(OH)CH{=}CH_2$	1	2·0
t-$BuCH{=}CH_2$	1	0·267
$C_2H_5CH(OH)CH_2CH{=}CH_2$	1	2·0
n-$PrCH(OH)CH{=}CH_2$	1	0·47
n-$BuCH{=}CH_2$	1	0
$C_2H_5CH(CH_3)CH(CH_3)CH{=}CH_2$	1	0
Cyclohex-2-enol	1	0·805
Cyclohexene	1	0·66

Reaction in 2,6-dimethylpyridine(*sym*-collidine)–chloroform results in the formation of the oxetane (**215**) in 11% yield and a 53% yield of **212** and **213**. Further data are given in Table 20.

The reaction of INO_3 with norbornadiene gives **216** and **217** in 64% and 10% yields respectively (equation 109). This reaction presumably occurs under conditions of kinetic control.



(109)

(**216**) (**217**)

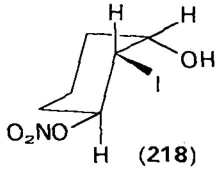
The reaction of INO_3 with cyclohex-2-enol gives 3-hydroxy-2-iodocyclohexyl nitrate (**218**) with the stereochemistry shown in which the

TABLE 20. Effect of solvent and alkene structure on the product distribution of the reaction of INO_3 with some olefinic alcohols

Alkene	Pyridine–$CHCl_3$[a]		2,6-Dimethylpyridine–$CHCl_3$[a]	
	Iodonitrate (%)	Iodopyridinium salts (%)	Iodonitrate (%)	Cyclic ether (%)
$CH_2{=}CHCH_2OH$	30(80% M)	23(100% M)	60(100% M)	
$CH_2{=}C(CH_3)CH_2OH$		75		
$(CH_3)_2C{=}CHCH_2OH$	20(100% M)	40(100% M)	20(100% M)	20
t-$BuCH{=}CH_2$	75(100% M)	20(100% M)		
Hex-1-en-3-ol	34(50% M)	16	53(100% M)	11
Hex-5-en-3-ol	10(75% M)	20	17(100% M)	30
Cyclohex-2-enol	36	29		

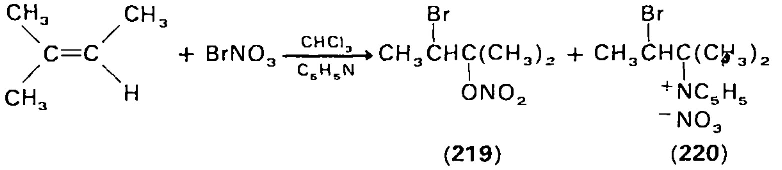
[a] M = Markownikoff isomer.

hydroxyl group is axial. Consideration of the stereochemistry of the two possible intermediates shows that the iodonium ion is formed *cis* to the hydroxyl group.



(218)

The only reported addition of bromonium nitrate $BrNO_3$ is that with 2-methyl-2-butene which gives **219** as the major adduct with only a small yield of the corresponding bromopyridinium nitrate (**220**, equation 110)[320].



$$(CH_3)_2C{=}CHCH_3 + BrNO_3 \xrightarrow[C_6H_5N]{CHCl_3} CH_3\overset{Br}{C}H\underset{ONO_2}{C}(CH_3)_2 + CH_3\overset{Br}{C}H\underset{{}^{+}NC_5H_5\ {}^{-}NO_3}{C}(CH_3)_2 \qquad (110)$$

(219) **(220)**

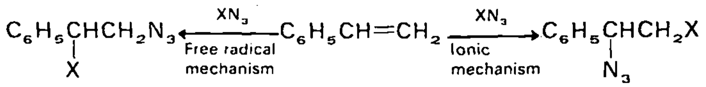
The actual electrophile here is also most likely the complex species: $Br(C_5H_5N)_2^+$.

The data presented appears consistent with a bridged-halonium ion product-determining transition state. Nucleophilic attack on the intermediate halonium ion occurs in general at the least sterically-hindered carbon giving products of *anti*-Markownikoff addition.

F. Halogen Azides

The halogen azides, IN_3, BrN_3 and ClN_3 were first reported and characterized many years ago[321,322]. It is only recently that convenient methods of preparing these unstable compounds in solution have been developed[323,324].

Hassner and coworkers have found that halogen azides can add to alkenes by either an ionic or free-radical mechanism[323,324]. For example in non-polar solvents and in the presence of a radical initiator, chlorine azide reacts with styrene to form the *anti*-Markownikoff isomer **221a**. However, in the presence of air and in a polar solvent in the dark the Markownikoff isomer **222a** is formed. On the basis of the electronegativity trend $I < N_3 < Br < Cl$, it would be expected that the preference for an ionic mechanism would be $IN_3 > BrN_3 > ClN_3$.



$$\underset{\displaystyle X}{C_6H_5\overset{}{C}HCH_2N_3} \xleftarrow[\text{Free radical mechanism}]{XN_3} C_6H_5CH{=}CH_2 \xrightarrow[\text{Ionic mechanism}]{XN_3} \underset{\displaystyle N_3}{C_6H_5CHCH_2X}$$

(221)
a: X = Cl
b: X = Br
c: X = I

(222)
a: X = Cl
b: X = Br
c: X = I

This indeed seems to be the case. Iodine azide reacts almost exclusively by an ionic mechanism, but can, under special conditions, be induced to react via an azide radical mechanism. Table 21 shows the effects of variable solvent and reaction conditions on the addition of XN_3 to styrene at 0 °C. It is apparent that solvents of low polarity, in the presence of light and/or absence of oxygen, enhance the free-radical pathway whereas the ionic pathway is preferred in more-polar solvents in the presence of oxygen. Whereas the nature of the reaction, be it ionic or radical, is readily changed for BrN_3 it can only be accomplished with some difficulty for IN_3 and ClN_3.

The stereo- and regiochemistry of the addition of halogen azides to alkene have been reviewed by Hassner[325]. The mechanistic conclusions can be summarized as follows. The ionic reaction of IN_3 and BrN_3 to alkenes forms non-regiospecific products by *anti* addition. Addition to

TABLE 21. Effect of reaction conditions on the product of addition of halogen azides to styrene at 0°C[323,324]

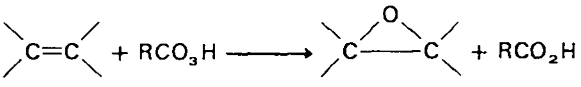
	ClN_3 (%)			BrN_3 (%)			IN_3 (%)	
Conditions	**221a**	**222a**	Other	**221b**	**222b**	Other	**221c**	**222c**
Pentane, air	100	—	—					
Pentane, N_2				100	—	—	39	61
Pentane, O_2							13	87
CH_2Cl_2, air	100	—	—					
CH_2Cl_2, air light				77	23	—		
CH_2Cl_2, air dark				50	50	—		
CH_2Cl_2, N_2				86	14	—	12	88
CH_2Cl_2, O_2				33	67	—		
CH_3CN, O_2	66	14	2	9	50	41	—	100
CH_3NO_2, air H_2SO_4, SO_3	47	47						
CH_3NO_2, O_2	17	48	23	—	100	—		
CH_3NO_2, O_2, dark H_2SO_4, SO_3	—	92	8					
CH_3CN, N_2				35	40	25		
CH_3NO_2, N_2				4	96	—		

certain alkenes, such as benzonorbornadiene results in rearranged products. A mechanism involving a bridged iodonium or bromonium ion intermediate has been postulated to account for the non-regiospecific *anti* addition products. Products of rearrangement or regiospecific and non-stereospecific addition are the result of a mechanism involving an open carbonium ion which in certain cases is more stable than the bridged ion.

VI. COMPOUNDS CONTAINING ELECTROPHILIC OXYGEN, SULPHUR, SELENIUM AND TELLURIUM

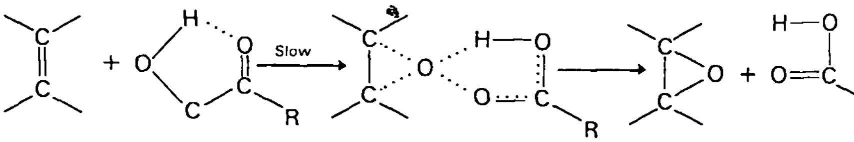
A. Epoxidation by Organic Peroxy Acids

The epoxidation of alkenes is a general reaction which gives oxiranes (**223**) as products in high yield under mild conditions. Consequently it is a reaction that is widely used in synthetic organic chemistry. Organic peroxy acids (**224**) are most commonly used to epoxidize an alkene. Epoxidation by organic peroxy acids has recently been reviewed[326]. Other reagents that are capable of epoxidizing alkenes are covalent peroxides of molybdenum[327], *t*-butyl hydroperoxide in the presence of a catalyst such as molybdenum or vanadium compounds[328], and the silver-metal-catalysed reaction of oxygen[329].



(224) (223)

Epoxidation of alkenes always results in *syn* addition and consequently the stereochemistry of the alkene is maintained in the product. The reaction of organic peroxy acids and alkenes is second order overall; first order in alkene and first order in peroxy acid. Two mechanisms have been proposed for this reaction. The first suggested by Bartlett[330] involves a cyclic, non-ionic, three-membered rate-determining transition state (equation 111). The second suggested by Kwart is a 1,3-dipolar addition of a hydroxyl-substituted carbonyl oxide which involves a five-membered rate-determining transition state (equation 112)[331].



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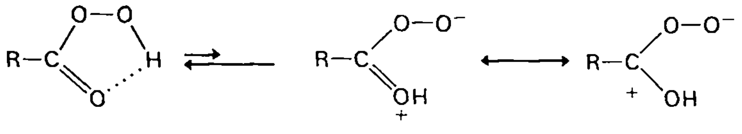

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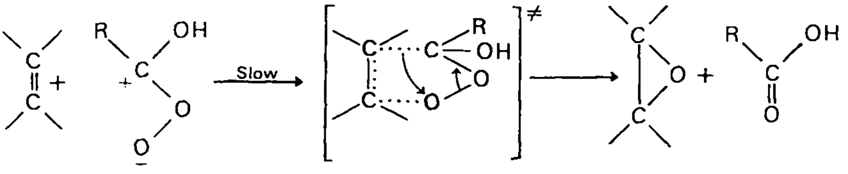


Most of the attempts to distinguish between these two mechanisms have been based upon structure reactivity correlations. By this method, the relative reactivities of specially selected alkenes with reagents known to react by 1,3-dipolar and three-membered cyclic mechanisms are compared with the relative reactivity of the same alkenes toward epoxidation. A similarity in the relative reactivities of epoxidation to one of the two mechanistic models is taken as evidence in support of that mechanism. In Table 22 are listed data which have been used to support the three-membered transition-state mechanism.

From an examination of the data in Table 22 a correlation appears between the size of the cyclic transition state and the relative rates **225**:**226** and **227**:**226**. Reactions whose rate-determining transition state is cyclic and contains five or six atoms have relatively high ratios of **225**:**226** and **227**:**226** while reactions with a three-member, cyclic, rate-determining transition states have low ratios.

To explain these results it has been postulated[332,338] that a considerable part of the strain energy of cyclopentene and norbornene is lost in a four-, five- or six-member, cyclic, rate-determining transition state. As a result cyclopentene and norbornene, which have about 4 kcal/mol and 10 kcal/mol more strain energy respectively than cyclohexene, are more reactive than cyclohexene in diimide reduction, 1,3-dipolar additions, and hydroboration reactions.

For addition reactions that involve a three-member, cyclic rate-determining transition state, the transformation of a double bond into a relatively-strained, three-membered ring would not lead to a significant decrease in the overall strain in the transition state. As a result there is little difference in the relative reactivities of strained and unstrained alkenes for reactions such as the additions of arenesulphenyl chloride and dichlorocarbene, both being examples of reactions involving three-membered, rate-determining transition states. Using this argument, it is

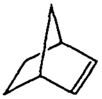
TABLE 22. A comparison of the reactivity of cyclopentene, cyclohexene and norbornene with several reagents

	Cyclopentene (**225**): cyclohexene (226)	Norbornene (227): cyclohexene (**226**)	Size of cyclic transition state	Reference
Diimide reduction	15·5	450	6	332
Diphenylnitrilimine addition	12	280	5	333
Benzonitrile oxide addition	19	1800	5	333
Phenyl azide addition	64	6500	5	333
Hydroboration	110		4	334
Bromination	1·4	13	3	335 176
2,4-Dinitrobenzenesulphenyl chloride	3·3	33	3	176
CBr_2 addition	1·25		3	336
Epoxidation	1·5	1·2		337

concluded that the mechanism of epoxidation involves a cyclic, three-member, rate-determining transition state.

In support of the 1,3-dipolar mechanism, Kwart[339] has pointed out that it cannot be assumed that all 1,3-dipolar addends should react with **225**, **226**, and **227** at vastly different rates. According to Huisgen[340–342] the assumed hydroxylcarbonyl oxide intermediate should not necessarily show large rate differences in reactions with cyclic alkenes like **225**, **226** and **227** because it is a 1,3-dipolar reagent without a double bond in the sextet structure.

The results of the addition of a number of electrophiles to norbornene (**227**) and 7,7-dimethylnorbornene (**57**) which are given in Table 23 substantiate this view.



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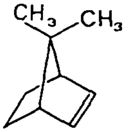


(57)

The data in Table 23 has been used to distinguish between mechanisms involving cyclic and non-cyclic rate-determining transition states. Thus, the relative rates of the free radical addition of PhSH and hydrochlorination to **227** and **57**(k_r) are relatively low; i.e. 2–30. The direction of addition to both **227** and **57** is *exo*. This seems to be characteristic of reactions whose mechanisms involve a non-cyclic rate-determining transition state. For the addition of PhSCl, B_2H_6 and other addenda, whose mechanisms are known to involve a cyclic rate-determining transition state, the ratio k_r is high, i.e. 500–∞ and the direction of addition changes from exclusively *exo* for **227** to predominantly *endo* for **57**.

While these results distinguish between a mechanism involving a cyclic or non-cyclic transition state, they cannot apparently distinguish the actual size of the cycle. Hence, in Table 23 all reactions except diimide addition involving cyclic transition states show a high k_r ratio and a change in product stereochemistry from *exo* for **227** to predominantly *endo* for **57** no matter what their size.

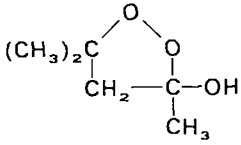
Kwart[339] has demonstrated that the thermolysis (100 °C in deuteriochloroform) of 3-hydroxy-3,5,5-trimethyl-1,2-dioxacyclopentane (**228**, the intermediate formed by the dipolar mechanism from peroxy acetic acid and isobutylene) does produce isobutylene oxide as a minor product. This result establishes that the 1,3-dipolar adduct can decompose to give an epoxide. However the unexpectedly high stability of **228** and the low

TABLE 23. Stereochemistry and relative rates of addition to norbornene and 7,7-dimethylnorbornene

Addendum	% *exo* product[a] (227)	% *exo* product[a] (57)	k_r[b]	Size of cyclic transition state	Reference
B_2H_6	99·5	22		4	344
9-BBN	99·5	3	480	4	343
Peracid	99·5	12	1000		345
PhSCl	~100	4	1820	3	343
N_2H_2	~100	~100	950	6	343
Ag^+	~100	No reaction		3	343
CCl_2	~100	No reaction		3	343
Diphenylnitrilimine	~100	26		5	346
Benzonitrile oxide	~100	34		5	346
HCl	~100	~100	2·2	Non-cyclic	
PhSH	99·5	95	30	Non-cyclic	343

[a] Remainder *endo*

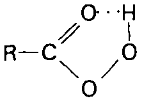
[b] $k_r = k_{exo\text{-}227}/k_{exo\text{-}57}$



(228)

yield of epoxide do not provide convincing evidence for the 1,3-dipolar mechanism. To account for these results it was concluded that **228** never actually forms but that 'the very act of approach to bond formation produces rearrangement to epoxide by virtue of the conformational accommodation that produces O—O bond rupture without intermediate formation of the 1,2-dioxolan (which would be the hypothetical non-planar, stable product of 1,3-dipolar addition)' [339].

The Bartlett mechanism has been used to explain the effect of a change of solvent on the rate of epoxidation[347]. In general, a hydrogen-bonding solvent decreases the rate of epoxidation of an alkene relative to the rate of epoxidation in carbon tetrachloride[347,348]. The effect of the hydrogen bonding solvent is attributed to a disruption of the chelate structure of the peroxy acids (**229**) in favour of an open-chain structure (**230**) involving



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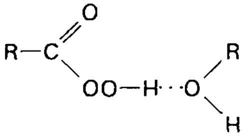


(230)

an intermolecular hydrogen bond between the solvent and the peroxy acid. A shift in the structure of the ground state of the peroxy acid from the chelate structure (in chlorinated solvents) to the open-chain structure (in hydrogen-bonded solvents) requires a desolvation process to take place before the transition state is reached. It is argued that such desolvation increases the activation energy causing the observed increase in the rate of epoxidation[347].

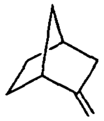
The evidence currently available favours the Bartlett molecular mechanism. However it is not inconceivable that both mechanisms might be important under different conditions of alkene structure and solvent. Only further experiment will provide a definite conclusion.

A large number of studies have been carried out to determine the effect of alkene structure upon the rate of epoxidation. The following general conclusions can be drawn from the available data: (i) The replacement of the hydrogen atoms of ethylene by alkyl groups increases the rate of epoxidation; in fact the effect of successively replacing the hydrogen atoms of ethylene by methyl group produces a cumulative rate increase; thus a plot of $\log k_2$ vs. the number of methyl groups on ethylene is linear[349], suggesting that the rate determining transition state is fairly symmetrical and has been used as support for the Bartlett mechanism[350]; (ii) cycloalkenes react slightly faster than dialkylsubstituted ethylenes; (iii) one double bond of a conjugated diene reacts rapidly with peroxy acids but the second reacts more slowly, presumably because of the proximity of the electron-withdrawing oxirane group; (iv) electron-withdrawing functional groups such as aldehydes, ketones, carboxylic acids and esters adjacent to the double bond greatly depress the rate of epoxidation relative to ethylene; (v) the effect of aryl substituents is variable, sometimes the rate is faster (styrene, 1-phenylpropene) and sometimes slower (stilbene) relative to ethylene, also electron-withdrawing substituents in the phenyl ring decrease the rate while electron donating substituents increase it; (vi) *cis*-alkenes generally react with peroxy acids faster than do their *trans*-isomers; (vii) strained alkenes such as norbornene or methylenecyclobutane epoxidize very rapidly relative to ethylene.

The data supporting these general conclusions has been elegantly summarized by Swern[351].

The reaction of peroxy acids with alkenes can be regarded as the fixing of an oxygen atom across the double bond of the alkene. With simple alkenes, the stereochemistry of the product is identical to that of the alkene. Thus *cis*-alkenes yield *cis*-epoxides and *trans*-alkenes yield *trans*-epoxides. Some cyclic alkenes however can form products with different stereochemistry because of special structural features which make one side of the double bond more susceptible to attack than the other. These structural features usually fall into two classes. In one class the structure of the molecule is such that the bulk of some functional group hinders attack favouring addition *anti* to that group; in the other class, the functional group may attract the electrophile-favouring *syn* addition to itself.

One example of this steric effect has already been discussed, i.e. the change in the stereochemistry of the product of epoxidation of **227**, which is *exo*, to yield predominantly the *endo* isomer for **57**. Similar results are obtained by epoxidation of **231** and **232**. The product of epoxidation of **231** is the *exo* isomer while the *endo* isomer is the major product of epoxidation of **232**[345]. Clearly the presence of the *syn* methyl group exerts a steric effect which hinders *exo* rather than *endo* attack. The effect of the methyl group then falls into the first class. Similar results



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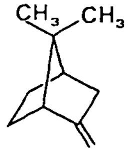

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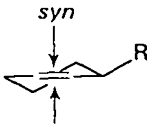
are found in the epoxidation of 3-substituted cyclohexenes **(233)**[352]. When the 3-substituent is a methyl group the *syn*/*anti* ratio is 48:52,



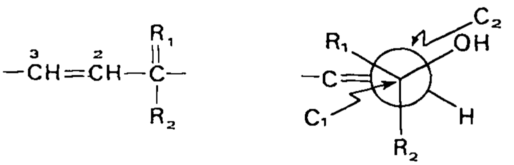
(233)

R =	CH_3	$t\text{-}C_4H_9$	OH	CH_3O	$OCOCH_3$
syn/*anti* ratio =	48:52	10:90	91:9	37:63	43:57

while for a *t*-butyl group the ratio is 10:90. The rate of epoxidation of both of these compounds is slower than that of cyclohexene. These results support the explanation that the steric bulk of the substituent influences both the rate and the direction of attack. Thus the larger the bulk of the group R, the slower the rate of epoxidation and the more *anti* addition.

When a hydroxyl group is placed in the 3-position of cyclohexene the *syn*/*anti* ratio is 91:9 indicating that *syn* addition is preferred[353]. Also its rate of epoxidation is faster than for cyclohexene. Thus an alkyl group and a hydroxyl group have different effects and are examples of the two classes of substituents previously cited. The rate effect of the hydroxyl group is contrary to its usual rate-retarding inductive effect. In addition, the hydroxyl group directs the electrophile *syn* to itself. This stereo-directing influence of a hydroxyl group near the reaction centre seems to be due to the hydrogen of the hydroxyl group, because replacement of the hydroxyl by a methoxy group causes a change in the *syn*/*anti* ratio favouring *anti* addition. The directing effect of the hydroxyl group is believed to be due to hydrogen bonding between the alcohol and the peroxy acid which stabilizes the transition state for *syn* addition, causing not only a rate increase but also directing the electrophile *syn* to itself. Numerous other examples of intramolecular facilitation of epoxidation by hydroxyl groups have been described particularly in the steroid field[354–356].

In contrast to cyclohex-2-enol, the epoxidation of *cis*-cyclooct-2-enol is reported to give the *trans* epoxyalcohol[357], while cyclohept-2-enol forms a mixture of the *cis* and *trans* epoxyalcohols[358]. This apparent anomaly has been resolved by Whitham[359] who has postulated that the preferred conformation of an allylic alcohol in the transition state for epoxidation is close to that depicted in **231**. The peroxy acid is considered to be positioned on the face of the double bond nearest to the hydroxyl



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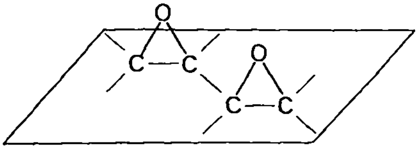
group. By evaluation of the steric interactions in the transition state for epoxidation of cyclic and acyclic allylic alcohols, the kinetic and stereochemical results have been interpreted in a consistent manner.

The stereochemistry of the diepoxidation of conjugated dienes has recently been studied by Heasley and coworkers[190,360] who have prepared and characterized the diepoxides from *trans,trans*-, *cis,cis*-, and *cis,trans*-2,4-hexadienes using *m*-chloroperoxybenzoic acid, peroxybenzoic acid and peroxyacetic acid. The six possible diastereomeric 2,3,4,5-diepoxyhexanes were identified. Each diene gave a mixture of two diepoxides **232** and **233**. Isomers of structure **233** were generally favoured



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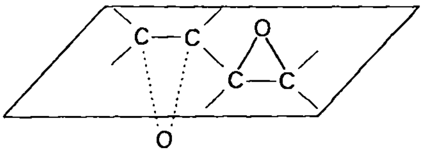

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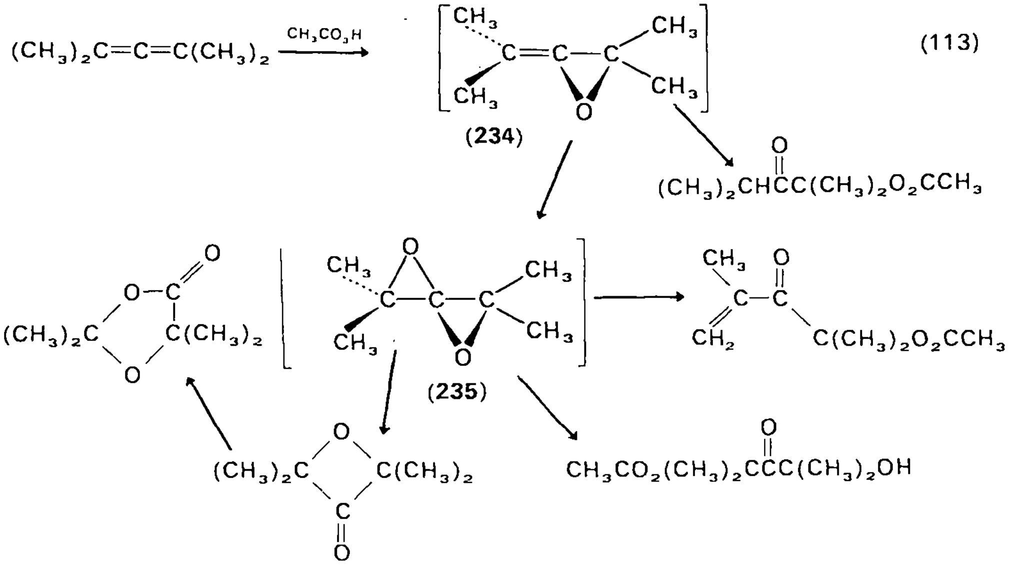
by a factor of two. This result has been explained by assuming that the first-formed epoxide exists in an essentially *s-trans* conformation and that subsequent attack by peroxy acids *anti* to the epoxide oxygen is then sterically favoured over *syn* attack. In agreement with this interpretation is the observation that the monoepoxide of 1,3-cyclohexadiene when reacted with *m*-chloroperoxybenzoic acid yields 95% *trans* and 5% *cis* diepoxide[361].

Much work has been reported on the epoxidation of simple and hindered allenes[362–368].

The peracetic acid oxidation of 2,4-dimethyl-2,3-pentadiene gave the mixture of products[362,367] shown in equation (113) which were attributed to the initial formation of the allene oxide (**234**) and dioxaspiropentane (**235**).



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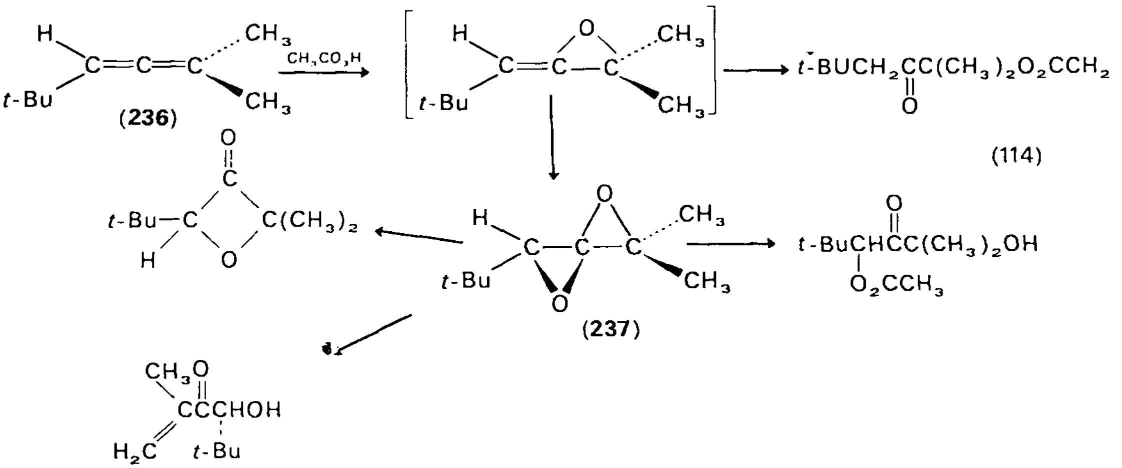
The isolation of 5-*t*-butyl-2,2-dimethyl-1,4-dioxaspiro[2.2]pentane (**237**) from the peracetic acid oxidation of 2,5,5-trimethyl-2,3-hexadiene (**236**, equation 114)[365] is taken as support for this mechanism.



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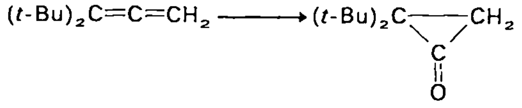
The peroxy acid oxidation of 1,1-di-*t*-butylallene in methylene chloride gave the cyclopropanone **238** (equation 115)[369]. The experimental evidence is, however, insufficient to distinguish between **239** or **240** as the



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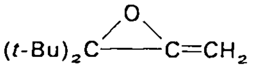
hypothetical precursor to **238**. Evidence in favour of a reaction path via an allene oxide such as **239** or **240** has been provided by Camp and Greene[363]



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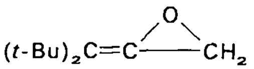

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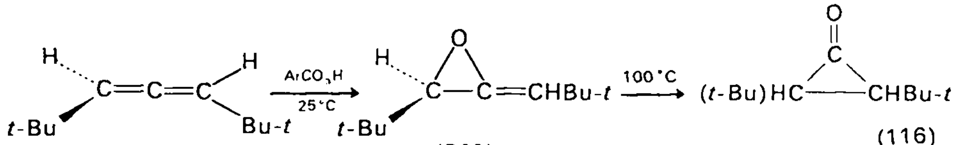
who found that the reaction of excess 1,3-di-*t*-butylallene with *m*-chloroperbenzoic acid in hexane gave **241** (equation 116).



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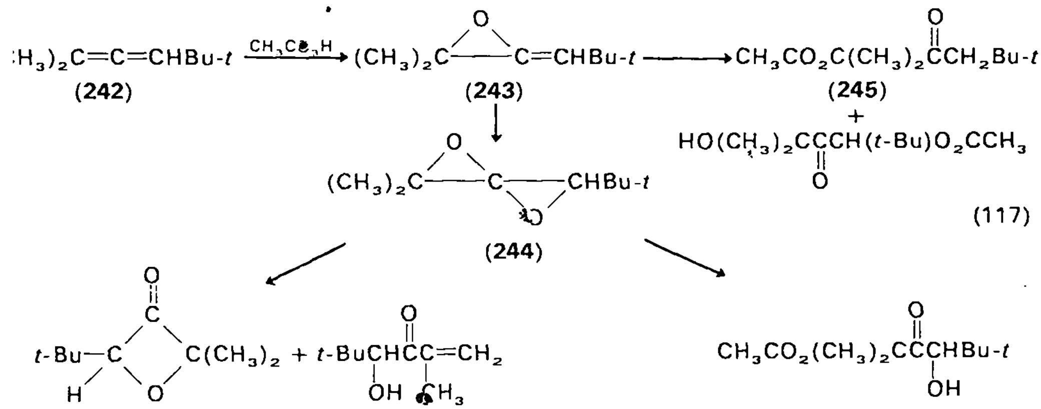
Reaction with a second mole of peroxyacid seems to be faster than the initial monoepoxidation of the allene. Hence an attempt to isolate an allene oxide intermediate (**243**) by the slow addition of one equivalent of peracetic acid to **242** in CH_2Cl_2 led only to a product mixture consisting of **242**, **244**, and a small amount of **245** (equation 117). The isolation of

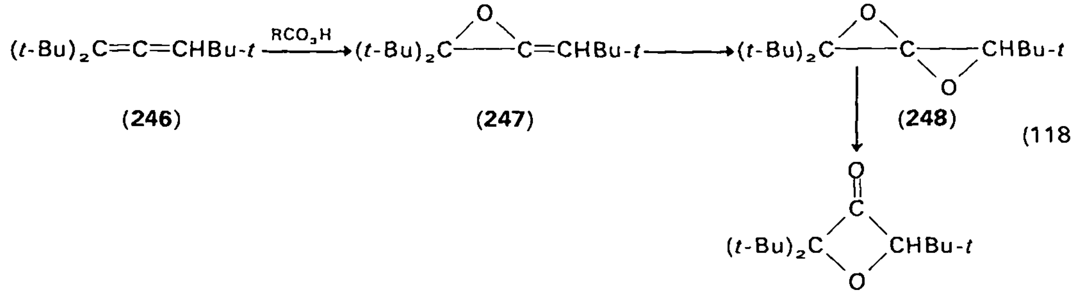


(242) (243) (245) (244)

(117)

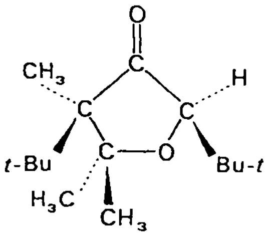
244, however, indicates that **243** is on the reaction coordinate. In contrast tri-*t*-butylallene **246** gave a 9:1 mixture of the *E*-allene oxide **247** and

2,2,4-tri-*t*-butyloxetan-3-one (**249**) with excess *m*-chloroperbenzoic acid in CH_2Cl_2 (equation 118). Treatment of **246** with 4-nitroperbenzoic acid gave *cis*- and *trans*-2,4-di-*t*-butyl-4,5,5-trimethyloxacyclo-pentene-3-one (**250**) and (**251**) respectively as well as **247** and **249**. No evidence was found



(118)

for the isomeric allene oxide (**252**) or the diepoxide (**248**) under conditions of kinetic control. Attempts to isomerize **247** to the corresponding cyclopropanone were unsuccessful. This has been attributed to steric destabilization of the latter in which eclipsed, vicinal *t*-butyl substituents would be present.



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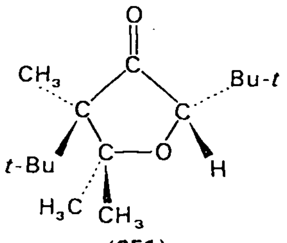

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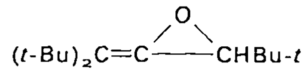

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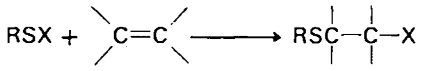
B. Sulphenyl Halides

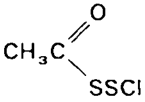
Sulphenyl halides (**253**) react with alkenes to form β-haloalkyl sulphides (**254**) as products (equation 119). Rearranged or solvent-incorporated products are rarely found but sometimes products resulting from the loss of HCl are observed. The halogen of the sulphenyl halide is usually chlorine, sometimes bromine, but rarely iodine or fluorine^{370}. The carbon portion of **253** is usually an alkyl or an aryl group. The most commonly used arenesulphenyl chlorides are 2,4-dinitrobenzene-, 4-chlorobenzene-, 4-toluene- and benzene-sulphenyl chloride while methanesulphenyl



(119)

(253) (254)

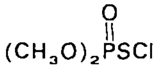
chloride is the most commonly used alkanesulphenyl chloride. Additions to alkenes have also been reported with acetylthiosulphenyl chloride (**255**)[371], dimethylaminosulphenyl chloride (**256**)[372] and *O,O'*-dimethyl-



(255)

$(CH_3)_2NSCl$

(256)



$(CH_3O)_2\overset{O}{\overset{\|}{P}}SCl$

(257)

phosphorylsulphenyl chloride (**257**)[373]. Acetic acid and chlorinated hydrocarbons such as methylene chloride, chloroform and 1,1,2,2,-tetrachloroethane (TCE) have been the solvents most commonly used[374]. Non-polar solvents such as benzene and saturated hydrocarbons can also be used[374] while alcohols or amines react with sulphenyl chlorides and consequently are unsuitable as solvents[375].

Since the last review on this subject, considerable work has been done to clarify many aspects of the mechanism of this reaction[376,377].

The rate law in polar solvents is overall second order; first order in alkene and first order in sulphenyl halide[378–381]. In CCl_4 the rate law becomes more complex and involves additional terms which are second and third order in sulphenyl bromide as well as terms involving the product[382]. The rate of addition is enhanced by polar solvents. In nitrobenzene the rate is five-times faster than in $CHCl_3$. The presence of sodium perchlorate further enhances the rate in acetic acid[379].

Considerable data are available on the rates of addition of arenesulphenyl chlorides to a wide variety of alkenes. Selected data are summarized in Table 24. The data reported in Table 24 are the result of direct kinetic measurements. Relative rates determined by competition experiments have not been included since recent work has shown that these results are often in serious error because thermodynamically-controlled rather than kinetically-controlled product mixtures are often observed under the conditions used[383].

The data in Table 24 clearly establish that electron-donating substituents enhance while electron-withdrawing substituents decrease the rate of addition. Taft correlations are reported for alkyl substituted alkenes with values of $-2{\cdot}88$[384], $-1{\cdot}81$[176] and $-2{\cdot}84$[385] for ρ^*. Hammett ρ values have been obtained for additions of 2,4-dinitrobenzene- and 4-chlorobenzenesulphenyl chloride to ring-substituted styrenes and

TABLE 24. Specific rate constants of addition of arenesulphenyl chlorides to alkenes

Alkene	$4\text{-}ClC_6H_4SCl$ $k_2(\text{l mol}^{-1}\text{ s}^{-1})$		$2,4\text{-}(NO_2)_2C_6H_3SCl$ $k_2(\text{l mol}^{-1}\text{ s}^{-1}) \times 10^3$	
	TCE[a,b]	HOAc[a]	TCE[a]	HOAc[a]
$CH_2{=}CH_2$	65·1			
$CH_3CH{=}CH_2$	205			
$C_2H_5CH{=}CH_2$	248			1·43[c]
i-PrCH=CH$_2$	140			1·12[c]
n-BuCH=CH$_2$	145	33·2[f]		1·42[c] 1·18[d] 1·32[e]
t-BuCH=CH$_2$	95·1			0·755[c] 0·52[d]
$(CH_3)_2C{=}CH_2$	551			4·62[c]
$C_2H_5(CH_3)C{=}CH_2$	611			3·02[c] 2·95[d]
(*c*) $CH_3CH{=}CHCH_3$	1340			26·3[c]
(*t*) $CH_3CH{=}CHCH_3$	434			2·88[c]
(*c*) $CH_3CH{=}CHC_6H_5$	43·0	7·15[g]	0·284[h]	0·45[g]
(*t*) $CH_3CH{=}CHC_6H_5$	118·3	28·6[g]	0·598[h]	1·26[g]
(*c*) *n*-PrCH=CHPr-*n*				10·4[c]
(*t*) *n*-PrCH=CHPr-*n*				1·57[c] 1·55[d]
(*Z*) $C_2H_5(CH_3)C{=}CHCH_3$	4840			
(*E*) $C_2H_5(CH_3)C{=}CHCH_3$	2290			
$(CH_3)_2C{=}C(CH_3)_2$	7700			
$C_6H_5CH{=}CH_2$	62·0	16·0[f]		0·913[c] 0·737[i] 0·741[e]

[a] TCE = 1,1,2,2-tetrachloroethane: HOAc = acetic acid. All additions at 25 °C except for those in reference *c* which are at 30 °C.

[b] Reference 386.

[c] Reference 176.

[d] Reference 385.

[e] Reference 388.

[f] Reference 416.

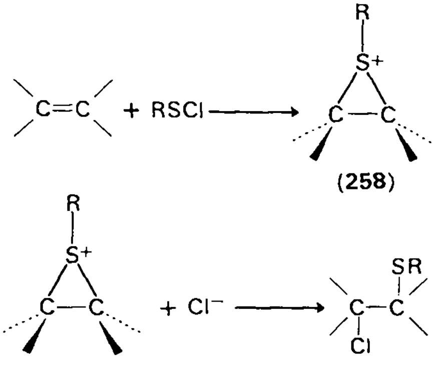
[g] G. H. Schmid and J. W. Gordon, unpublished results.

[h] Reference 410.

[i] Reference 387.

1-phenylpropenes[387–389] and are given in Table 25. These results establish the electrophilic nature of the addition of sulphenyl halides to alkenes.

An Ad_E2 mechanism was first proposed by Kharasch and Buess[390] and is shown in Scheme 5. The first step, equation (120), involves formation of a thiiranium (episulphonium) ion (**258**) which undergoes chloride ion attack in the second step, equation (121).

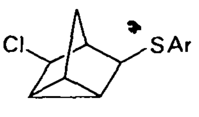


(120)

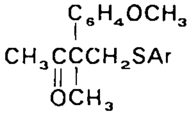
(121)

SCHEME 5.

The usual criteria of a two-step mechanism, solvent-incorporated or rearranged products, are rare in sulphenyl-halide additions. Among the known examples are the addition to norbornadiene[391a] to give **259a** in addition to the normal *trans* 1,2-adduct and the addition to 2-(4-methoxyphenyl)-3-methylbut-3-en-2-ol which forms **259b** by migration of the anisyl group[391b]. The accelerating effect of polar solvents on the rate of addition suggests a rate-determining transition state which is more polar than the starting material in accordance with a two-step mechanism involving a cationic intermediate.



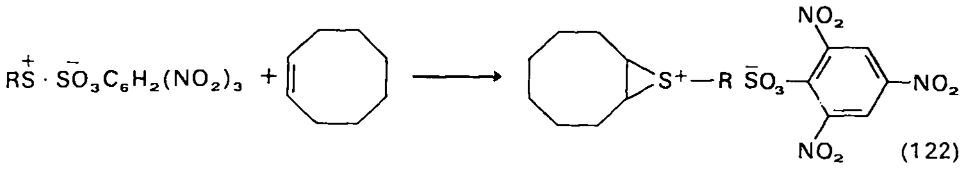
(259a)



$CH_3C(=OCH_3)C(C_6H_4OCH_3)CH_2SAr$

(259b)

A number of stable thiiranium ion salts have been prepared. *S*-Alkyl cyclooctene thiiranium ions have been prepared by the reactions shown in equation (122)[392].



(122)

R = CH_3, C_2H_5, *n*-Pr, *n*-Bu

(260)

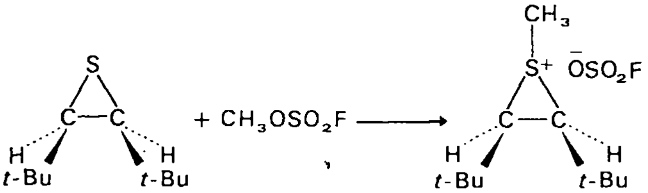
Kellog and coworkers have prepared *cis*-di-*t*-butylethylene methyl episulphonium fluorosulphate from the reaction of methyl fluorosulphate

TABLE 25. Hammett ρ values for the additions of arenesulphenyl chlorides to styrenes and 1-arylpropenes

RSX	Substrate	ρ	ρ^+	Solvent	Reference
2,4-$(NO_2)_2C_6H_3SCl$	$ArCH{=}CH_2$	$-2{\cdot}4$		CH_3CO_2H	387
2,4-$(NO_2)_2C_6H_3SCl$	*cis*-1-$ArCH{=}CHCH_3$	$-2{\cdot}3$	$-1{\cdot}80^a$	CH_3CO_2H	388
2,4-$(NO_2)_2C_6H_3SCl$	*trans*-1-$ArCH{=}CHCH_3$	$-2{\cdot}64$	$-1{\cdot}90^a$	CH_3CO_2H	388
2,4-$(NO_2)_2C_6H_3SCl$	*cis*-1-$ArCH{=}CHCH_3$	$-2{\cdot}79$	$-1{\cdot}97$	TCE	389
2,4-$(NO_2)_2C_6H_3SCl$	*trans*-1-$ArCH{=}CHCH_3$	$-3{\cdot}98$	$-2{\cdot}98$	TCE	389
4-ClC_6H_4SCl	*trans*-1-$ArCH{=}CHCH_3$	$-2{\cdot}41$		TCE	389

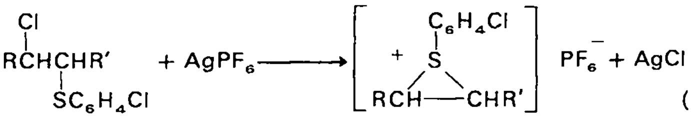
[a] Calculated from data in Reference 388.

with *cis*-di-*t*-butylethylene episulphide in chloroform (equation 123)[393]. Attempts to prepare the corresponding *trans* salt were unsuccessful.



(123)

Recently several thiiranium ions containing different alkyl substituents have been prepared by the reaction of $AgPF_6$ with β-chloroalkyl 4-chlorophenyl sulphide in methylene chloride or nitromethane (equation 124)[285].



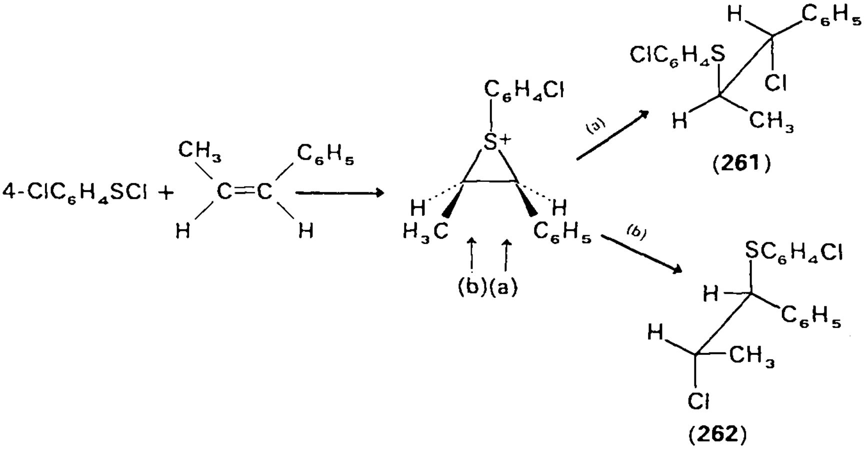
(124)

A number of theoretical calculations of the relative energies of the cyclic and open ions have been reported[89,394,395,396]. The thiiranium ion is the more stable regardless of the type of calculation (semi-empirical or *ab initio*) employed.

Strong evidence in favour of a bridged structure for the cationic intermediate is provided by the almost exclusively *anti* stereospecific addition of sulphenyl chlorides (the few exceptions will be considered later). Thus the addition of 4-chlorobenzenesulphenyl chloride to *cis*- and *trans*-2-butene is 99·98 % *anti* stereospecific over a temperature range of 180 °C[397]. Such a result is inconsistent with a mechanism involving an open-ion intermediate.

The addition of sulphenyl chlorides to unsymmetrical alkenes is non-regiospecific and yields products with both Markownikoff and *anti*-Markownikoff orientation[381,371,398]. Thus the products of addition of 4-chlorobenzenesulphenyl chloride to *cis*-1-phenylpropene are the Markownikoff (**261**) and the *anti*-Markownikoff (**262**) products formed by attack of chloride ion at both carbon atoms of the thiiranium ion (equation 125).

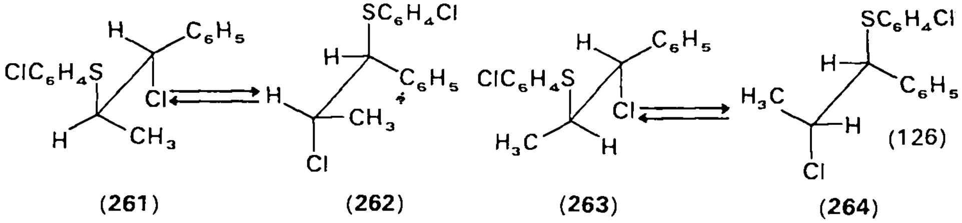
It has also been observed that the reaction of methane-, benzene-, and 4-chlorobenzene sulphenyl chloride with terminal alkenes forms predominantly the *anti*-Markownikoff adduct under kinetic control. These results provide convincing evidence that a thiiranium ion is involved prior to the product determining step.



(125)

Hogg was the first to provide experimental evidence that the first step in Scheme 5 is rate determining[399]. The rates of addition of a series of 4-substituted-2-nitrobenzenesulphenyl bromides and chlorides to cyclohexene were measured. The relative rates of the corresponding bromides and chlorides were found to be essentially constant: $k_{Br}/k_{Cl} = 2{\cdot}4$. Such a result is in accord with a rate-determining first step. If the second step were rate determining, then the relative rates should increase as the thiiranium ion becomes more stable.

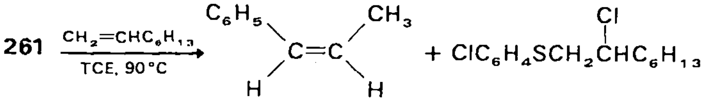
Further experimental data have recently been reported which support this conclusion. In a number of reactions it has been found that the first-formed adduct slowly isomerizes[371,399]. For example, the kinetically-controlled products of the addition of 4-chlorobenzenesulphenyl chloride to *cis-* and *trans*-1-phenylpropene, **261** and **263** respectively, slowly isomerize to **262** and **264** which are the thermodynamically-controlled products (equation 126)[400]. This isomerization is completely stereo-



(126)

specific. The *threo* Markownikoff adduct **261** forms the *threo anti*-Markownikoff adduct **262**. Similarly the *erythro* Markownikoff adduct **263** obtained by addition to *trans*-1-phenylpropene, forms the *erythro* *anti*-Markownikoff adduct **264**. No leakage between the two series has ever been observed.

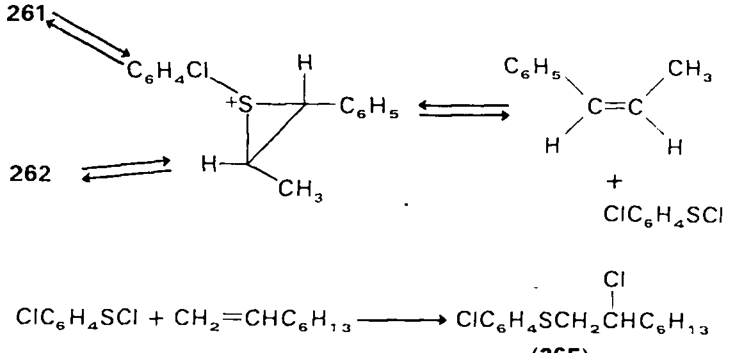
It has been observed in certain systems that the addition of sulphenyl chlorides is a reversible reaction. The reaction of the adduct **261** with excess 1-octene in TCE at 90 °C results in the formation of *cis*-1-phenylpropene and 2-chlorooctyl 4-chlorophenyl sulphide (**265**, equation 127)[401]. This is in effect an exchange of 4-chlorobenzenesulphenyl chloride from *cis*-1-phenylpropene to 1-octene.



(127)

(**265**)

These facts can be explained by a mechanism involving reformation of the thiiranium ion from the adduct **261** which then undergoes attack at three sites: the two non-equivalent carbon atoms and the sulphur atom of the ring (equation 128). The first two sites lead to the Markownikoff–*anti*-Markownikoff isomerization, while the latter leads to the exchange reaction by reforming the arenesulphenyl chloride which can add to 1-octene.



(128)

(**265**)

Evidence for this mechanism is provided by the work of King[402] who found that the rate of diaxial to diequatorial rearrangement of the arenesulphenyl chloride adduct to 5α-cholest-2-ene depends upon the electron-donating ability of the substituent on the phenyl ring. Furthermore, Helmkamp has found that the stable thiiranium salt **260** reacts with nucleophiles, such as chloride ion, at the sulphur to form cyclooctene and methanesulphenyl chloride[403].

The fact that **261** isomerizes to **262** 2·4-times faster than it exchanges to form **265** provides the key to establishing the rate-determining step. The path leading to the thiiranium ion by sulphur neighbouring group participation is the microscopic reverse of that leading to the β-chloroalkyl sulphide product from the thiiranium ion. Since isomerization is faster than the return to starting alkene and arenesulphenyl chloride, the transition state for formation of the thiiranium ion from *cis*-1-phenylpropene and 4-chlorobenzenesulphenyl chloride must be higher in energy than the transition state for isomerization. This clearly establishes that a step prior to forming the thiiranium ion is rate-determining in this system. From the kinetic data available we can draw the reaction coordinate energy diagram shown in Figure 5 for the addition of 4-chlorobenzenesulphenyl chloride to *cis*-1-phenylpropene.

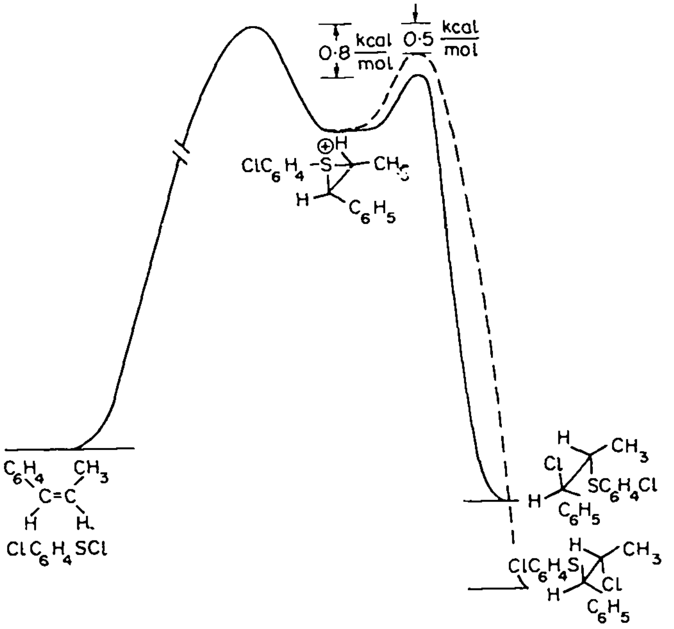
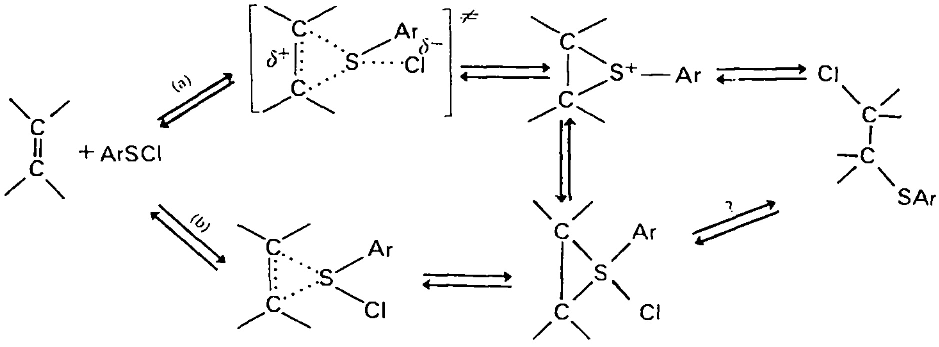


FIGURE 5. Reaction coordinate energy diagram for the addition of 4-chlorobenzenesulphenyl chloride to *cis*-1-phenylpropene in TCE at 25 °C.

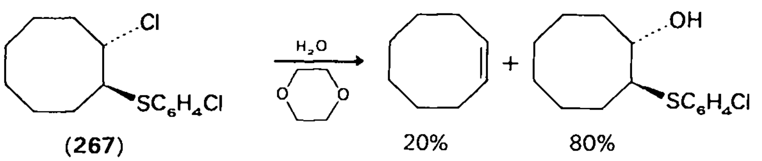
The mechanism in Figure 5, involving one intermediate and two transition states is the simplest. If we regard the reaction of arenesulphenyl chlorides with alkenes as a nucleophilic substitution reaction at sulphur instead of the usual electrophilic addition reaction, we are led to the conclusion that the mechanism in Scheme 5 is only one of a number of possibilities. Two mechanisms which have been proposed for nucleophilic displacements at sulphur are shown in Scheme 6. There is no experimental support for a mechanism involving dissociation of the sulphenyl halide to a sulphenium ion $(RS^+)^{404}$. Path (a), which is the



SCHEME 6.

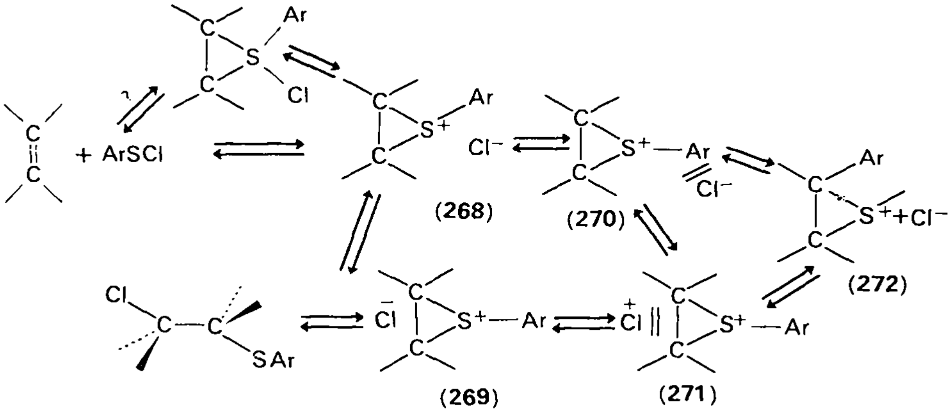
sulphur analogue of the S_N2 mechanism, leads to a single intermediate and is identical to equation (120) in Scheme 5. Path (b) involves formation of a tetravalent sulphur intermediate **266** which may ionize to the thiiranium ion or may proceed directly to the products. While the S_N2 mechanism [path (a)] is favoured by Kice[404], evidence for intermediate **266** has been claimed by Helmkamp[405] and the selenium analogue of **266** has been isolated and characterized[406]. Therefore, there is a possibility that another intermediate may be formed prior to the thiiranium ion. However, conclusive evidence on this point is lacking.

The observation that the isomerization of **261** to **262** (or **263** to **264**) occurs faster than acetolysis suggests that ion pairs are important prior to the product-determining step. Further evidence for the intervention of ion pairs is available from the solvolysis of 2-chlorocyclooctyl 4-chlorophenyl sulphide (**267**) in 80:20% dioxane-water (equation 129)[407].



(267) 20% 80%

The rate of this reaction shows a strong common-ion effect as well as a special salt effect. The products are cyclooctene, 2-(4′-chlorothiophenyl)-cyclooctanol and 4-chlorophenyldisulphide. The presence of cyclooctene is particularly significant since its formation can be explained by nucleophilic attack of water at the sulphur atom of the intermediate thiiranium ion. This reaction then is the solvolytic equivalent of the exchange reaction, equation (127), found in TCE, a non-hydroxylic solvent. This result implies that solvolysis, exchange and isomerization of the β-chloroalkyl arylsulphides are linked by a common mechanism to addition of arenesulphenyl chlorides. Such a common mechanism is shown in Scheme 7.



Scheme 7.

Structures **268** and **269** are intimate ion pairs while **270** and **271** are solvent-separated ion pairs. The difference between these ion pairs is in the location of the counter ion; in **268** and **270** the halide ion is near sulphur while in **269** and **271** the halide is near carbon.

The solvolytic path involving ions **269**, **271** and **272** is the general solvolysis scheme proposed by Winstein[408] and the solvolysis of β-chloroalkyl aryl sulphides meets the requirement for solvolysis by means of any or all of the ions **269**, **271** and **272**. A path involving ions **268** and **270** is consistent with the reaction of thiiranium ion salts with nucleophiles. The exchange reaction (equation 127) indicates that there must be a connection between the two paths either directly between the ion pairs **268–269** and **270–271** or by means of ion **272**.

While the presence of ion pairs in the addition reaction is not yet strongly supported by experimental data, the gross features of the mechanism are well established. However, the structure of the cationic intermediate(s) and the rate- and product-determining step will vary depending upon the structure of the alkene and sulphenyl halide used. Much work has been done recently to establish how the rate- and product-determining transition states vary with alkene structure.

From the data in Table 24, it is clear that increasing the number of alkyl substituents on the double bond causes an increase in the rate of addition. This is due mainly to the polar effect of the alkyl groups. The best example of this is the fact that the progressive substitution of the hydrogens on ethylene by methyl groups has a cumulative effect on the rate[383]. Thus a plot of log k_{rel} versus the number of methyl groups on the double bond is linear. This result indicates a lack of steric hindrance and is consistent with a bridged rate-determining transition state. The exclusive formation of a product of *anti* addition is in accord with a bridged product-determining transition state.

The importance of steric effects in the rate-determining transition state is illustrated by the addition to the *t*-butyl substituted ethylenes[409]. The rate data are given in Table 26. Replacement of one hydrogen on ethylene by a *t*-butyl group results in a small rate enhancement. However, the magnitude of the rate increase, namely a factor of 1·5, is less than that of 3·14 for replacing hydrogen on ethylene by a methyl[383]; which suggests a slight steric retardation by the bulky group. The most remarkable feature of the addition to *t*-butyl-substituted ethylenes is the enormous rate difference of 1·6 × 10^5 between *cis*-1,2-di-*t*-butylethylene and the *trans* isomer. This is by far the greatest acceleration which has been observed for an addition to a *cis/trans* pair of isomeric alkenes. The 1,1-di-*t*-butyl and 1,1,2-tri-*t*-butylethylene show only very modest rate enhancements relative to the *trans*-1,2-di-*t*-butylethylene. The effect of the *t*-butyl groups on the rate of addition can best be explained by steric hindrance to the approach of the electrophile in the rate-determining transition state. It appears that two *trans*-*t*-butyl groups seriously hinder the approach of an electrophile. The arenesulphenyl chloride cannot avoid the bulky *t*-butyl groups in approach to *trans*-1,2-di-*t*-butylethylene. This steric repulsion can be avoided in addition to the *cis* isomer if the arenesulphenyl chloride attacks the double bond off the perpendicular and approaches from the side opposite to the *t*-butyl groups. This explanation seems preferable to one which invokes relief of ground-state steric strain in the rate-determining transition state of the addition to the *cis*-1,2-di-*t*-butylethylene. Such relief of steric strain would be expected to result in formation of an open ion intermediate which would form rearranged and

TABLE 26. Specific rate constants for the addition of 4-chlorobenzenesulphenyl chloride to a series of *t*-butyl-substituted ethylenes at 25°C in 1,1,2,2-tetrachloroethane

Alkene	k_2(l mol^{-1} s^{-1})	k_{rel}
$CH_2{=}CH_2$	65	1
t-$BuCH{=}CH_2$	95	1·5
(*t*-$Bu)_2C{=}CH_2$	0·0317	$4{\cdot}9 \times 10^{-4}$
(*c*) *t*-$BuCH{=}CHBu$-*t*	846	13
(*t*) *t*-$BuCH{=}CHBu$-*t*	0·00536	$8{\cdot}2 \times 10^{-5}$
(*t*-$Bu)_2C{=}CHBu$-*t*	0·00816	$1{\cdot}3 \times 10^{-4}$

non-stereospecific addition products. However, the addition products of kinetic control to *cis* and *trans*-1,2-di-*t*-butylethylene are formed exclusively by *anti* addition in keeping with a thiiranium ion intermediate and a bridged product-determining transition state. The formation of such a bridged intermediate results in very little relief of strain. Yet the *cis* isomer shows greatly enhanced reactivity relative to the *trans* isomer which must be due to some cause other than relief of ground-state steric strain. In keeping with this view is the fact that a methyl episulphonium fluorosulphate salt can be prepared from *cis*-1,2-di-*t*-butylethylene sulphide but not from the *trans* isomers[393].

The effect of alkene configuration on the rate of addition has been investigated[386]. From the data, given in Table 27, it is clear that the rate of addition to a *cis*-alkyl substituted ethylene is always greater than to its *trans* isomer ($k_{cis}/k_{trans} > 1$). There is no correlation between the k_{cis}/k_{trans} ratio and the enthalpies of isomerization for the eleven pairs of isomeric *cis–trans* alkenes studied. Such a result is consistent with the

TABLE 27. The specific rate constants for the addition of 4-chlorobenzenesulphenyl chloride to a series of isomeric *cis-trans* alkenes at 25 °C in 1,1,2,2-tetrachloroethane

Alkene	k_2(l mol^{-1} s^{-1})	k_c/k_t
(*c*) $CH_3CH{=}CHCH_3$	1340	3·12
(*t*) $CH_3CH{=}CHCH_3$	430	
(*c*) $C_2H_5CH{=}CHC_2H_5$	3563	9·18
(*t*) $C_2H_5CH{=}CHC_2H_5$	388	
(*c*) *i*-PrCH=CHPr-*i*	992	9·73
(*t*) *i*-PrCH=CHPr-*i*	102	
(*c*) *t*-BuCH=CHBu-*t*	845	~10^5
(*t*) *t*-BuCH=CHBu-*t*	$5{\cdot}36 \times 10^{-3}$	
(*c*) $CH_3CH{=}CHC_2H_5$	2692	4·79
(*t*) $CH_3CH{=}CHC_2H_5$	568	
(*c*) *i*-PrCH=CHC_2H_5	2769	11·3
(*t*) *i*-PrCH=CHC_2H_5	245	
(*c*) *t*-BuCH=CHC_2H_5	1704	14·1
(*t*) *t*-BuCH=CHC_2H_5	121	
(*c*) *i*-PrCH=$CHCH_3$	2624	8·07
(*t*) *i*-PrCH=$CHCH_3$	325	
(*c*) *t*-BuCH=$CHCH_3$	1209	7·46
(*t*) *t*-BuCH=$CHCH_3$	162	
(*Z*) $CH_3(C_2H_5)C{=}CHCH_3$	4800	2·11
(*E*) $CH_3(C_2H_5)C{=}CHCH_3$	2280	
(*Z*) CH_3(*i*-Pr)C=$CHCH_3$	5900	5·55
(*E*) CH_3(*i*-Pr)C=$CHCH_3$	1063	

view that relief of ground-state steric strain is not important in the rate-determining transition state.

On the basis of the kinetic and product regio- and stereochemistry, it is clear that the evidence is overwhelming in favour of a bridged rate- and product-determining transition states for the addition of sulphenyl chlorides to alkyl-substituted ethylenes.

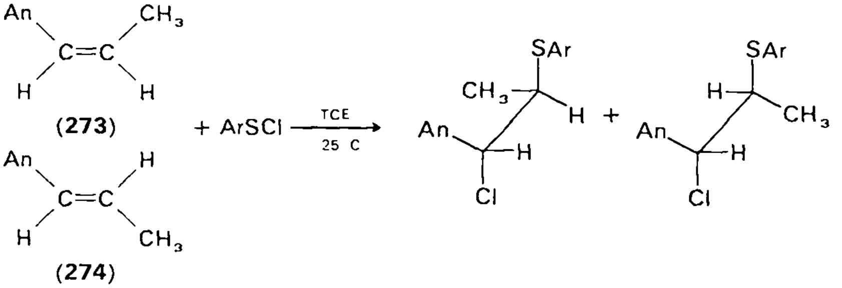
The rates of addition to phenyl-substituted styrenes and their derivatives have been measured by a number of workers. The values of ρ are summarized in Table 25.

All these values of ρ are less negative than those for hydration, bromination and chlorination. This fact has been interpreted as evidence for bridging in the rate-determining transition state. This interpretation is open to question, however, since the ρ for chlorination is less negative than that for bromination of the same series of styrenes under identical experimental conditions. If ρ is a measure of the bridging in the rate-determining transition state the order is reversed. Regardless of the magnitude of ρ, the negative sign indicates development of some positive charge on the α-carbon which implies an unsymmetrical bridged structure for the rate-determining transition state.

The products of addition to *cis*- and *trans*-1-phenylpropene are formed by stereospecific *anti* addition. The kinetically-controlled products of addition to the *cis* alkene are the adducts with Markownikoff and *anti*-Markownikoff orientation while the *trans* isomer forms only the Markownikoff adduct. This result implies that the product-determining transition state for addition to *cis*-1-phenylpropene is more symmetrical (has more sulphur bridging) than the product-determining transition state for addition to the *trans* isomer. This difference has been explained by steric hindrance between the *cis* phenyl and methyl groups which prevents maximum delocalization of the charge on the α-carbon into the phenyl ring[381].

The entire character of this reaction can be changed by placing an electron donating group on the phenyl ring. Thus the products of the addition of 2,4-dinitrobenzenesulphenyl chloride to *cis*- (**273**) and *trans*-anethole (**274**) are formed non-stereospecifically but regiospecifically (equation 130)[410]. This is one of the few examples of a non-stereospecific addition of arenesulphenyl chlorides to alkenes. This result clearly indicates that an open ion is formed prior to the product-determining step. Furthermore the product-determining transition state resembles an open ion rather than a bridged thiiranium-ion-like transition state.

In order to determine whether the rate-determining transition state also resembles an open ion, the rates of addition and product stereochemistry



(273)

(274)

(130)

An = 4-$CH_3OC_6H_4$
Ar = 2, 4-$(NO_2)_2C_6H_3$

Starting alkene	%	%
273	70	30
274	5	95

were determined for the addition of 2,4-dinitrobenzenesulphenyl chloride to a series of *cis*- and *trans*-1-substituted phenylpropenes. The results are given in Figure 6. A linear plot of log k_2 versus σ was obtained for both the *cis* and *trans* series even though the stereochemistry of the addition changed. This result indicates that the electronic demands in the rate-determining transition state are similar throughout the series. The simplest mechanistic explanation is that all the additions in both the *cis* and *trans* series involve a bridged rate-determining transition state. The structure of the product-determining transition state changes however from a bridged one for 4-tolyl and more-electron-withdrawing substituted 1-arylpropenes to an open ion-like one for 1-arylpropenes with substituents which are more electron-donating than methyl[389].

From the data in Figure 6 it can be seen that the ρ value for the addition to the *cis* series is smaller than that for the *trans*. This means that charge delocalization into the phenyl ring is less for the *cis* than for the *trans* series. Such a result is consistent with steric hindrance between the *cis* phenyl and methyl groups which forces the phenyl ring out of the preferred conformation for maximum charge delocalization.

Similar steric effects are found in the addition of 4-chlorobenzenesulphenyl chloride to a series of seven side chain methyl substituted styrenes[411]. Unlike the addition to the corresponding series of methylated ethylenes[383], the effect of the methyl groups is not cumulative. The effect of the methyl group depends upon whether or not the β-methyl group is *cis* to the phenyl. The data are given in Table 28. When it is *cis*, the rate of addition is decreased relative to styrene, and substitution of additional methyl groups has only a small effect on the rate of addition.

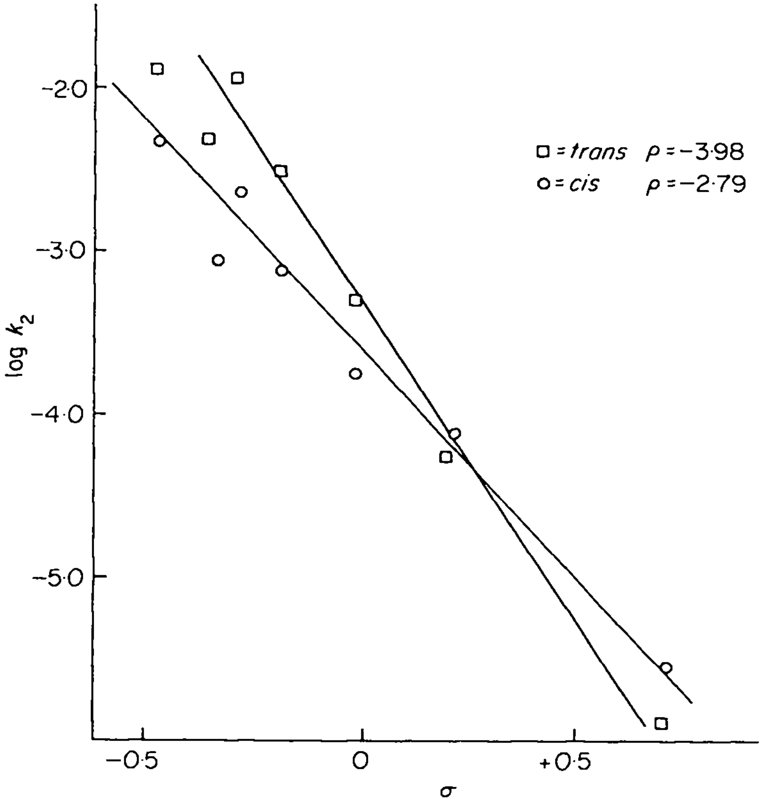
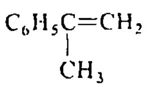
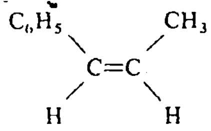
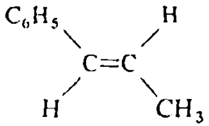
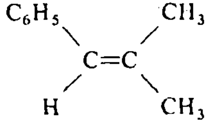
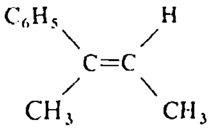
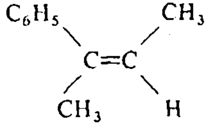
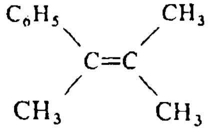


FIGURE 6. Plot of log k_2 versus σ for the addition of 2,4-dinitrobenzenesulphenyl chloride to ring-substituted *cis*- and *trans*-1-phenylpropenes.

In compounds lacking a *cis* β-methyl group the rate of addition more closely resembles that for addition to the methylated ethylenes. Steric hindrance between the *cis* methyl and phenyl groups in the rate-determining transition state is believed to be the cause of this difference between the ethylene and styrene series. On the basis of the products formed, it appears that this effect is carried over into the intermediate thiiranium ion and the product-determining transition state. The larger amount of product with *anti*-Markownikoff orientation formed in the addition to alkenes with *cis* methyl groups can be explained by a similar steric effect.

The progressive substitution of the hydrogens on ethylene by phenyl groups results in a decrease in the rate of addition of 4-chlorobenzenesulphenyl chloride. The data are given in Table 29[285]. Such a decrease in rate is due to the increasing stabilization of the alkene by the larger conjugated system formed as phenyl groups are progressively substituted for hydrogen. Similar results have been found in the bromination[412]

TABLE 28. The kinetic and thermodynamic controlled products of the addition of 4-chlorobenzenesulphenyl chloride to a series of side chain methyl substituted styrenes at 25 °C in 1,1,2,2-tetrachloroethane

Series 1							Series 2						
			Product composition							Product composition			
			KCP^a		TCP^a					KCP^a		TCP^a	
Alkene	k_2(l mol^{-1} s^{-1})	k_{rel}	M^b	aM^b	M^b	aM^b	Alkene	k_2 (l mol^{-1} s^{-1})	k_{rel}	M^b	aM^b	M^b	aM^b
$C_6H_5CH{=}CH_2$	62·0 ± 0·2	1	83	17	100	0	$C_6H_5CH{=}CH_2$	62·0 ± 0·2	1	83	17	100	0
 $C_6H_5\underset{\underset{CH_3}{\vert}}{C}{=}CH_2$	265 ± 3	4·3	87	13	100	0		43·0 ± 0·2	0·69	66	34	30	70
	118·3	1·9	100	0	62	38		26·0 ± 0·8	0·42	37	63	65	35
	442 ± 5	7·1	88	12	94	6		42·0 ± 0·3	0·68	36	64	87	13
								9·05 ± 0·01	0·15	55	45	c	c

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[a] KCP = kinetic controlled product; TCP = thermodynamic controlled product.
[b] M = Markownikoff; aM = *anti*-Markownikoff.
[c] Decomposition and rearrangement.

TABLE 29. The rates and product composition of the addition of 4-chlorobenzenesulphenyl chloride to a series of phenyl substituted ethylenes at 25 °C in 1,1,2,2-tetrachloroethane[285]

Alkene	k_2(l mol^{-1} s^{-1})	Kinetically-controlled product composition	
		M[a]	aM[a]
$C_6H_5CH{=}CH_2$	62·0 ± 0·2	83	17
(*c*) $C_6H_5CH{=}CHC_6H_5$	3·71	*threo*adduct	
(*t*) $C_6H_5CH{=}CHC_6H_5$	8·05	*erythro*adduct	
$(C_6H_5)_2C{=}CH_2$	20·1	$(C_6H_5)_2C{=}CHSC_6H_4Cl$	
$(C_6H_5)_2C{=}CHC_6H_5$	$\sim 5 \times 10^{-4}$	6	94
$(C_6H_5)_2C{=}C(C_6H_5)_2$	$< 10^{-6}$		

[a] M = Markownikoff orientation; aM = *anti*-Markownikoff.

and the addition of chromyl chloride[413] to phenyl substituted ethylenes. Except for 1,1-diphenyl ethylene, which gives a product of elimination of HCl, the adducts are those expected from an *anti* stereospecific addition.

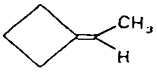
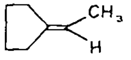
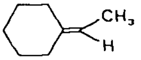
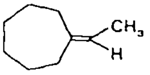
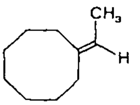
The rate and product stereochemistry of the addition of arenesulphenyl chlorides to most styrenes and stilbenes can best be explained by a bridged structure for both the rate- and product-determining transition states. The exceptions are those alkenes where products of non-stereospecific addition are found. In these cases the evidence is consistent with a mechanism involving a bridged rate-determining transition state followed by formation of an open ion later on the reaction coordinate.

The rate data available for the addition to cyclohexene and its derivatives are all consistent with the proposed Ad_E2 mechanism. The effect of substituents in the 4-position of cyclohexene on the rate of addition of 2,4-dinitrobenzenesulphenyl chloride was studied by Kwart and Miller[384]. The rates could be correlated by means of the Taft equation with $\rho = -2{\cdot}88$. This indicates that the effect of the substituents is almost entirely electronic in nature.

The rate of addition of 4-substituted-2-nitrobenzenesulphenyl chloride to cyclohexene has been found to correlate with σ^+ to give $\rho^+ = -0{\cdot}715$[414]. This result indicates that the sulphur atom also carries an appreciable positive charge in the rate-determining transition state which is in accord with a bridged rather than an open carbonium ion structure for the transition state.

The rate and product composition of the addition of 4-chlorobenzenesulphenyl chloride to a series of ethylidenecycloalkanes is given in Table 30. The rates of addition to the four-, five-, six- and seven-member ring compounds are about three-times faster than would be expected for addition to an acyclic trisubstituted ethylene. In addition to the normal adducts, formed by *anti* stereospecific addition, products from the elimination of HCl are also formed particularly in the case of the six-, seven- and eight-member ring compounds. Similar kinetic results have been obtained by Pritzkow[176].

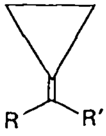
TABLE 30. The rates and product composition of the addition of 4-chlorobenzenesulphenyl chloride to a series of ethylidenecycloalkanes at 25 °C in 1,1,2,2-tetrachloroethane[a]

Alkene	k_2(l mol^{-1} s^{-1})	KCP		TCP	
		%M	%*a*M	%M	%*a*M
	6880	37	63	78	22
	8630	83	17	≥98	≤2
	7670	55	45	≥98	≤2
	7610	≥98	≈2	25[b]	15[b]
	2030	66	34	15[b]	85[b]
$(CH_3)_2C{=}CHCH_3$	3030	35	65	92·0	8·0

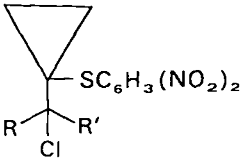
[a] KCP = kinetically controlled product; TCP = thermodynamically controlled product. M = Markownikoff orientation; *a*M = *anti*-Markownikoff orientation.

[b] Product distributions represent relative amounts of M and *a*M isomers. Loss of HCl forming allylic sulphides is favoured under thermodynamic control.

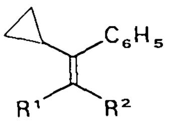
The products of the addition of 2,4-dinitrobenzenesulphenyl chloride to a number of phenyl-substituted methylenecyclopropanes and vinylcyclopropanes have been investigated[415]. The addition to the methylenecyclopropanes **275a** and **275b** in CH_2Cl_2 results in the formation of the normal adducts **276a** and **276b** respectively. In contrast addition to the vinylcyclopropane **277a** and **277b** results in the rearranged products **278a** and **278b** respectively. It is proposed that the presence of the



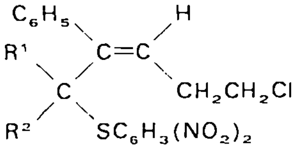
275a: R = R' = C_6H_5
275b: R = C_6H_5; R' = H



276a: R = R' = C_6H_5
276b: R = C_6H_5; R' = H



277a: $R^1 = R^2 = H$
277b: $R^1, R^2 = -CH_2CH_2-$



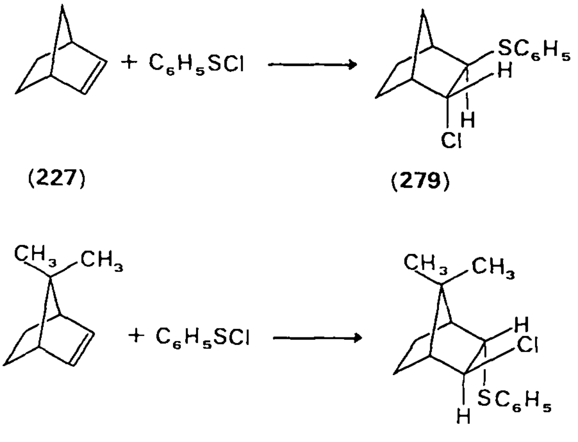
278a: $R^1 = R^2 = H$
278b: $R^1, R^2 = -CH_2CH_2-$

2,4-dinitrophenylthio group on the cyclopropyl ring in the intermediate ion leading to **276a** and **276b** prevents the cyclopropylcarbinyl–homoallylic rearrangement and accounts for the difference in reactivity between these two types of compounds. Consistent with this view is the fact that the methylenecyclopropane of **277b** remains intact in the product while the other cyclopropyl ring undergoes cleavage during the addition. The solvent has a relatively strong influence upon the course of the reaction. Addition in acetic acid forms more rearranged products particularly in the case of **277a**.

It is clear from these results that the addition of 2,4-dinitrobenzenesulphenyl chloride to **275a**, **277a** and **277b** involves formation of open ion intermediates prior to the product-determining step. It is interesting to compare these results with the addition of 4-chlorobenzenesulphenyl chloride to vinylcyclopropane where only normal Markownikoff adducts are observed[416]. Hence in the latter case, the presence of a less-electron-withdrawing substituent (4-ClC_6H_4 vs. $2,4\text{-}(NO_2)_2C_6H_3$) on the sulphur and fewer carbonium-ion-stabilizing substituents on the double bond seems to favour a thiiranium ion over an open carbonium ion path.

The data on the stereochemistry of arenesulphenyl chloride additions to bicyclic alkenes up to 1968 has been reviewed by Fahey[7].

Recently a comparison of the rates and product stereochemistry of the addition of benzenesulphenyl chloride to norbornene (**227**) and 7,7-dimethylnorbornene (**57**) has been made by Brown[345]. The rate of *exo* addition to norbornene is 1820-times faster than to 7,7-dimethylnorbornene. Furthermore, **227** forms the *endo*-chloro-*exo*-thio adduct (**279**) while **57** forms **280** in which the chlorine is *exo* and the arylthio group is *endo* (equation 131). Steric hindrance by the *syn*-7-methyl group of **57** to *exo* approach of the electrophile accounts for the difference in the stereochemistry of the products of addition to **227** and **57**.



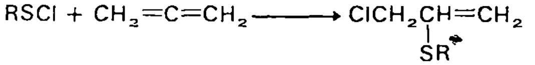
(227) (279)

(57) (280)

(131)

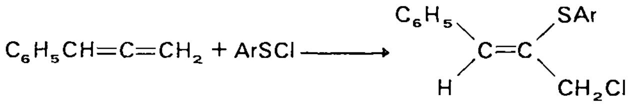
In certain cases products of rearrangement have been isolated from the addition of arenesulphenyl chlorides to bicyclic alkenes. It has not always been established that these are the products of kinetically controlled addition and therefore it is not yet clear if open ions are involved in these cases.

The addition of sulphenyl halides to allenes usually forms a product in which the sulphenyl group is bonded to the central carbon (equation 132)[417]. The carbon to which the chlorine becomes attached depends



$$RSCl + CH_2{=}C{=}CH_2 \longrightarrow ClCH_2\underset{\displaystyle SR}{\underset{|}{C}}H{=}CH_2 \qquad (132)$$

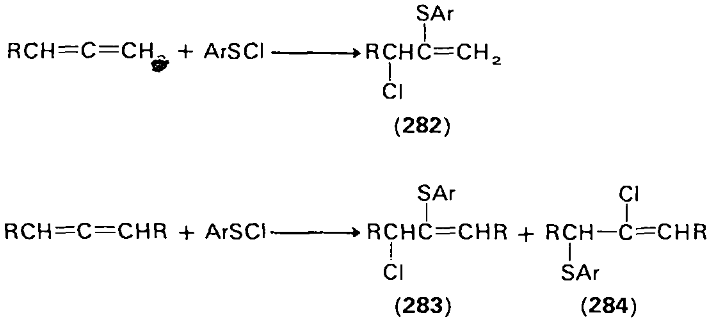
upon the substituents on the allenes. Thus the addition of 2,4-dinitrobenzenesulphenyl chloride to phenylallene forms **281** as the only product (equation 133)[418] while monoalkylsubstituted allenes form **282** as the



(281)

(133)

major product[419]. Addition to 1,3-disubstituted allenes yields mixtures of **283** and **284** as products (equation 134)[420]. In contrast, 1,1-disubstituted



$$RCH{=}C{=}CH_2 + ArSCl \longrightarrow RCH(Cl)C(SAr){=}CH_2$$

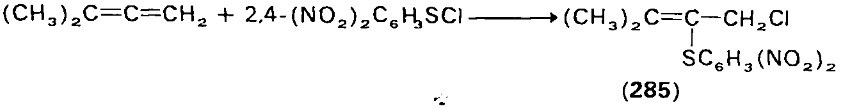
(282)

$$RCH{=}C{=}CHR + ArSCl \longrightarrow RCH(Cl)C(SAr){=}CHR + RCH(SAr){-}C(Cl){=}CHR$$

(283) (284)

(134)

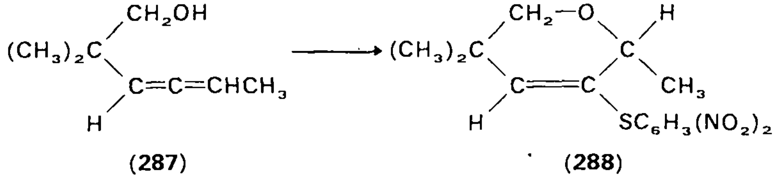
allenes such as 1,1-dimethylallene form the primary chloride **285** (equation 135)[419] by reaction with 2,4-dinitrobenzenesulphenyl chloride.



$$(CH_3)_2C{=}C{=}CH_2 + 2{,}4\text{-}(NO_2)_2C_6H_3SCl \longrightarrow (CH_3)_2C{=}C(SC_6H_3(NO_2)_2){-}CH_2Cl \qquad (135)$$

(285)

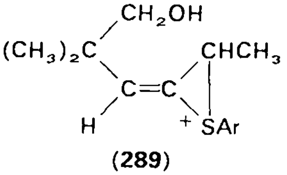
The reaction of 2,4-dinitrobenzenesulphenyl chloride and optically active 2,2-dimethyl-3,4-hexadien-1-ol (**287**) forms the optically active cyclic adduct (**288**) as product (equation 136)[419]. Such a result is consistent



(287) (288)

(136)

with formation during the addition of a dissymmetric intermediate such as the vinylic thiiranium ion **289**. While the limited data are in accord with



(289)

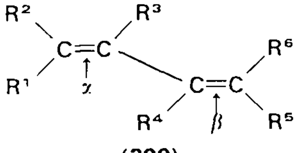
a thiiranium ion intermediate, it is still not clear how substituents affect the direction of addition.

The rate and addition products of 4-chlorobenzenesulphenyl chloride to butadiene-1,3 and eleven of its methylated derivatives have been determined in 1,1,2,2-tetrachloroethane at 25 °C. The rate data are given in Table 31 while the major products are given in Table 32. The rate law is second order, first order in both diene and sulphenyl halide.

TABLE 31. The specific rate constants, k_2, for the addition of 4-chlorobenzenesulphenyl chloride for a series of methyl-substituted 1,3-butadienes in 1,1,2,2-tetrachloroethane as solvent at 25·00 °C ± 0·02

Diene	k_2(l mol^{-1} s^{-1})	k_{rel}
$CH_2{=}CH{-}CH{=}CH_2$	27·75	1·00
$CH_2{=}C(CH_3)CH{=}CH_2$	124·7	4·49
$CH_2{=}C(CH_3)C(CH_3){=}CH_2$	161·4	5·82
Z-$CH_2{=}CH{-}CH{=}CHCH_3$	162·5	5·86
E-$CH_2{=}CH{-}CH{=}CHCH_3$	244	8·79
$CH_2{=}CH{-}CH{=}C(CH_3)_2$	1114	40·1
Z-$CH_2{=}CH{-}C(CH_3){=}CHCH_3$	276·4	9·96
E-$CH_2{=}CH{-}C(CH_3){=}CHCH_3$	475·3	17·1
Z,Z-$CH_3CH{=}CH{-}CH{=}CHCH_3$	670·6	24·2
E,Z-$CH_3CH{=}CH{-}CH{=}CHCH_3$	741·8	26·7
E,E-$CH_3CH{=}CH{-}CH{=}CHCH_3$	767	27·6
E-$CH_2{=}C(CH_3){-}CH{=}CHCH_3$	1264	45·5

These data as well as those results previously reported for the addition of 4-chlorobenzenesulphenyl chloride to alkenes and dienes are in accord with the non-regiospecific but *anti*-stereospecific addition. Somewhat surprising *a priori* is the preferential attack of the sulphenyl chloride on the least-substituted double bond since in electrophilic additions the usual order of reactivity is tetra-substituted > tri-substituted > *cis*-1,2-di-substituted > 1,1-di-substituted ≈ *trans*-1,2-di-substituted > mono-substituted ethylenes. Similar results have, however, been reported for other electrophilic additions to dienes such as bromination[192]. An analysis of the kinetic data in Table 31 shows firstly that substitution of a hydrogen on ethylene (k_2 = 65·1 l mol^{-1} s^{-1}) by a vinyl group leads to a rate decrease in keeping with the expected electron-attracting nature of a vinyl group relative to hydrogen. Substituent effects are somewhat more difficult to analyse for dienes compared to monoalkenes since there exist two possible sites of attack by the electrophile. Thus replacement of a hydrogen by methyl at, for example, R^3 in



(290)

TABLE 32. The major products observed under conditions of kinetic control for the addition of 4-chlorobenzenesulphenyl chloride to a series of methyl-substituted 1,3-butadienes at 25 °C in 1,1,2,2-tetrachloroethane

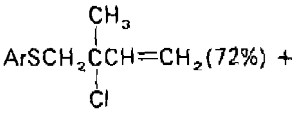
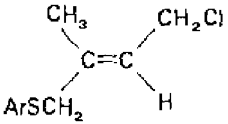
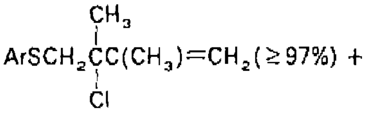
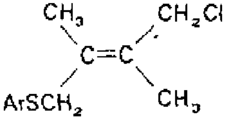
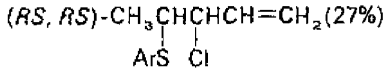
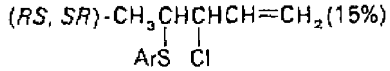
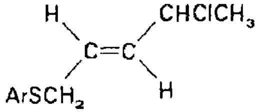
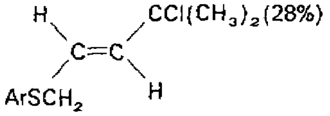
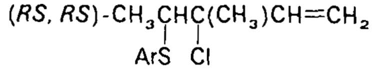
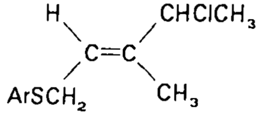
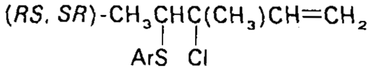
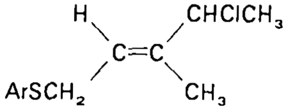
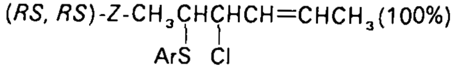
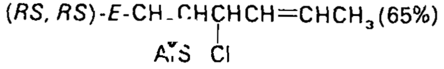
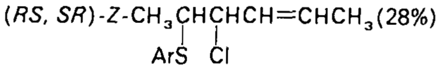
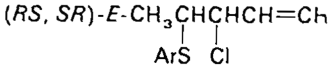
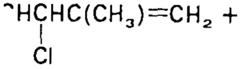
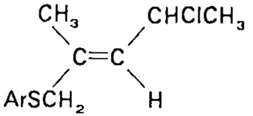
Diene	Product[a]
$CH_2{=}CHCH{=}CH_2$	$ArSCH_2CHClCH{=}CH_2$ (100%)
$CH_2{=}C(CH_3)CH{=}CH_2$	 $ArSCH_2\overset{CH_3}{\underset{Cl}{C}}CH{=}CH_2$ (72%) +  + $ArSCH_2CHClC(CH_3){=}CH_2$
$CH_2{=}C(CH_3)C(CH_3){=}CH_2$	 $ArSCH_2\overset{CH_3}{\underset{Cl}{C}}C(CH_3){=}CH_2$ (≥97%) + 
Z-$CH_2{=}CHCH{=}CHCH_3$	Z-$ArSCH_2CHClCH{=}CHCH_3$ (73%) +  (RS, RS)-$CH_3\underset{ArS}{C}H\underset{Cl}{C}HCH{=}CH_2$ (27%)
E-$CH_2{=}CHCH{=}CHCH_3$	E-$ArSCH_2CHClCH{=}CHCH_3$ (60%) +  (RS, SR)-$CH_3\underset{ArS}{C}H\underset{Cl}{C}HCH{=}CH_2$ (15%) + 
$CH_2{=}CHCH{=}C(CH_3)_2$	$ArSCH_2CHClCH{=}C(CH_3)_2$ (72%) + 

TABLE 32 (*continued*)

Z-$CH_2{=}CHC(CH_3){=}CHCH_3$	*Z*-$ArSCH_2CHClC(CH_3){=}CHCH_3$(63%) + (*RS*, *RS*)- $CH_3\underset{ArS}{C}H\underset{Cl}{C}(CH_3)CH{=}CH_2$ + 
E-$CH_2{=}CHC(CH_3){=}CHCH_3$	*E*-$ArSCH_2CHClC(CH_3){=}CHCH_3$ + (*RS*, *SR*)- $CH_3\underset{ArS}{C}H\underset{Cl}{C}(CH_3)CH{=}CH_2$ + 
Z,*Z*-$CH_3CH{=}CHCH{=}CHCH_3$	 (*RS*, *RS*)-*Z*-$CH_3\underset{ArS}{C}H\underset{Cl}{C}HCH{=}CHCH_3$(100%)
E,*Z*-$CH_3CH{=}CHCH{=}CHCH_3$	 (*RS*, *RS*)-*E*-$CH_3\underset{ArS}{C}H\underset{Cl}{C}HCH{=}CHCH_3$(65%) +  (*RS*, *SR*)-*Z*-$CH_3\underset{ArS}{C}H\underset{Cl}{C}HCH{=}CHCH_3$(28%) (*RS*, *RS*)-*E*-$ArSCH(CH_3)CH{=}CHCHClCH_3$ + (*RS*, *SR*)-*Z*-$ArSCH(CH_3)CH{=}CHCHClCH_3$
E,*E*-$CH_3CH{=}CHCH{=}CHCH_3$	 (*RS*, *SR*)-*E*-$CH_3\underset{ArS}{C}H\underset{Cl}{C}HCH{=}Ch$ + (*RS*, *RS*)-*E*-$ArSCH(CH_3)CH{=}CHCHClCH_3$ + (*RS*, *SR*)-*E*-$ArSCH(CH_3)CH{=}CHCHClCH_3$
E-$CH_2{=}C(CH_3)CH{=}CHCH_3$	*E*-A H. $'{=}CHCH_3$ + (*RS*, *SI*  $\underset{Cl}{HC}HC(CH_3){=}CH_2$ + 

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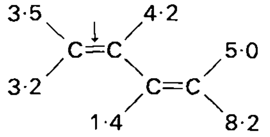
[a]Ar = 4-Chlo ne

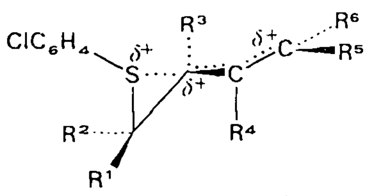
290 will show a different effect if attack occurs at the α double bond than if attack occurs at the β double bond. From both the rates of addition and the kinetically-controlled product composition it is possible to calculate the relative rate increase of replacing a hydrogen by methyl at any of the six possible locations. The rate factors are shown below:



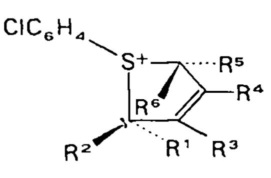
↓ = Position of attack by ClC_6H_4SCl

Thus if R^3 is a methyl group the rate of addition is calculated to be about 4·2 relative to that of butadiene-1,3.

The effects are not strictly multiplicative but are essentially reflective of the effect of substitution. It is seen that k_2 *trans* is somewhat larger than the corresponding k_2 *cis*. This is opposite to what is normally observed for alkyl substituted alkenes where k_2 *cis* $\geq k_2$ *trans* but is similar to cases involving aryl substituted alkenes[381]. A remote *trans*-oriented methyl group (i.e., $R^5 = CH_3$) causes the largest rate increase suggesting extensive charge delocalization where a stabilized resonance contribution can be obtained. The stereospecific *anti* addition, preferential 1,2-Markownikoff regiochemistry, the *trans* orientation of the double bond in the 1,4-adducts and the non-stereospecific formation of the thermodynamically more-stable 1,4-adducts suggests that the rate- and product-determining transition states resemble the well known thiiranium (episulphonium) ion intermediate **291**.



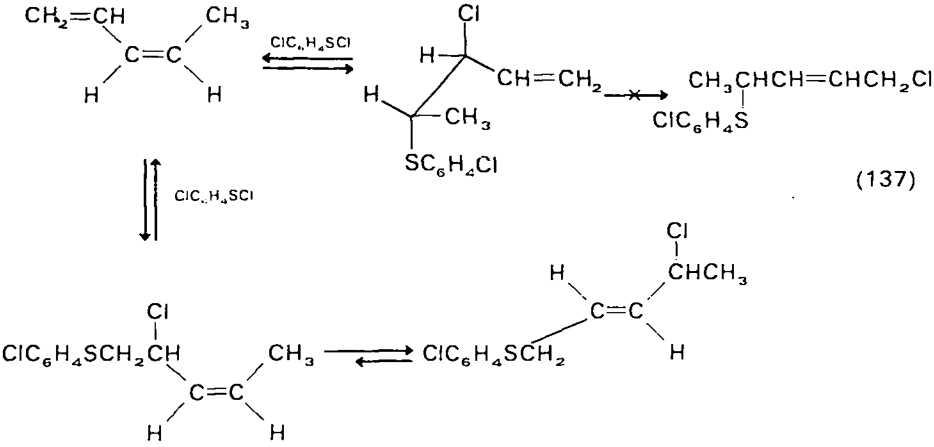
(291)



(292)

The absence of *cis*-oriented 1,4-adducts rules out a substituted tetramethylene sulphonium ion structure (**292**) for a product-determining transition state. The exclusive Markownikoff addition and the presence of 1,4-adducts where R^5 and/or $R^6 = CH_3$ under conditions of kinetic control, further attests to the ability of the vinyl, propenyl and isobutenyl groups to delocalize charge development.

The reaction is reversible. For example, Z-1,3-pentadiene gives, under kinetic control, the adduct from addition to the more-substituted double bond in 27% yield. Under conditions of thermodynamic control this compound disappears giving only the Markownikoff 1,2-adduct following attack on the terminal double bond and the corresponding 1,4-addition product. These reactions are illustrated in equation (137). Further the 1,2-monoadducts from addition to the isomeric 2,4-hexadienes are



(137)

observed to form the respective diadducts under some conditions of thermodynamic control as well as the expected 1,4-addition products.

These results are an extension of the work of Mueller and Butler[422], and of Kresge and Kosbahn[423] and are generally in accord with their findings. The major exception is that under our reaction conditions no *anti*-Markownikoff 1,2-adducts, *cis*-1,4-adducts or substitution products were observed under conditions of kinetic control.

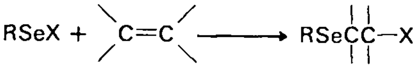
There is overwhelming evidence for bridged rate- and product-determining transition states in the addition of sulphenyl halides to almost all alkenes. Only a few exceptions to this general rule are known and these are found in the additions to alkenes which are capable of forming especially stabilized carbonium ions. Furthermore, in these examples the substituents in the aryl group of the arenesulphenyl chloride used (usually 2,4-dinitro) do not assist in stabilizing a thiiranium ion intermediate. As a result, a product-determining path involving an open rather than a thiiranium ion is favoured. However even in these cases, the rate-determining transition state may still be bridged.

C. Selenium and Tellurium Compounds

1. Divalent selenium

Electrophilic divalent selenium compounds have the general structure RSeX where X is usually a halogen (e.g., chlorine or bromine, rarely fluorine or iodine), acetate, or an anion such as hexafluoro-phosphate or -antimonate. The R group is usually alkyl or aryl.

a. *Selenenyl halides.* The reaction of selenenyl halides (**293**) with alkenes forms β-haloalkyl selenides (**294**) as products[424–434] (equation 138).



(138)

(**293**) (**294**)

Investigations of the scope and mechanism of the addition of arene- and alkane-selenenyl halides are quite sparse compared to the additions of their sulphur analogues. Use of the leitmotif of organic chemistry, i.e. 'like substances react similarly and similar changes in structure produce similar changes in reactivity'[435] has often been invoked despite the lack of available data on the selenenyl vs. sulphenyl halide additions[426,427,432,433].

The selenenyl halides are usually prepared prior to use but an *in situ* generation of methane- and ethane-selenenyl chloride from the corresponding dialkyl diselenide and sulphuryl chloride in methylene chloride has been reported[436].

Rearranged, solvent incorporated products and products resulting from loss of HCl have been reported[285] for a number of alkenes. In general, these products are more common than in the reactions of their sulphenyl halide analogues.

The most common solvents for the addition are methylene chloride, chloroform, carbon tetrachloride, acetic acid, and hydrocarbons such as benzene and hexane. Alcohols and amines readily react with the selenenyl halides and are therefore not suitable[437–440].

The rate law in methylene chloride and acetic acid is overall second order: first order in alkene and first order in selenenyl halide[285]. This contrasts with the third order kinetics previously reported in the addition of benzeneselenenyl chloride to a series of acetylenes[441].

Considerable data are available on the rates of addition of benzeneselenenyl chloride to a wide variety of alkenes. Selected data obtained from direct kinetic measurements are summarized in Table 33. From

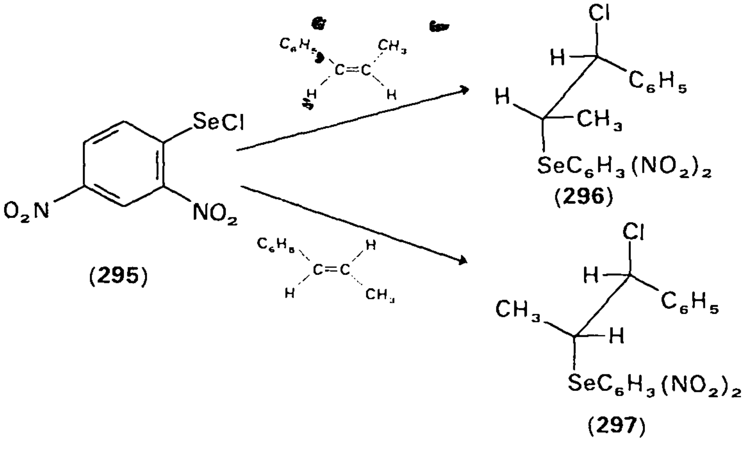
TABLE 33. Specific rate constants for the addition of benzeneselenenyl chloride to alkenes in methylene chloride at 25 °C

Alkene	k_2(l mol^{-1} s^{-1})	k_{cis}/k_{trans}
$CH_2{=}CH_2$	497·7	
$CH_3CH{=}CH_2$	4360	
$C_2H_5CH{=}CH_2$	3320	
$i\text{-}PrCH{=}CH_2$	509	
$t\text{-}BuCH{=}CH_2$	321·2	
$(CH_3)_2C{=}CH_2$	3366	
$C_2H_5C(CH_3){=}CH_2$	1104	
$i\text{-}PrC(CH_3){=}CH_2$	460	
$t\text{-}BuC(CH_3){=}CH_2$	158·5	
$(C_2H_5)_2C{=}CH_2$	615·3	
$i\text{-}PrC(C_2H_5){=}CH_2$	102·5	
$(c)\ CH_3CH{=}CHCH_3$	1868	1·80
$(t)\ CH_3CH{=}CHCH_3$	1036	
$(c)\ CH_3CH{=}CHC_2H_5$	4116	2·22
$(t)\ CH_3CH{=}CHC_2H_5$	1851	
$(c)\ CH_3CH{=}CHPr\text{-}i$	755·1	1·24
$(t)\ CH_3CH{=}CHPr\text{-}i$	609·9	
$(c)\ CH_3CH{=}CHBu\text{-}t$	910	67·4
$(t)\ CH_3CH{=}CHBu\text{-}t$	13·50	
$(c)\ C_2H_5CH{=}CHC_2H_5$	2610	1·87
$(t)\ C_2H_5CH{=}CHC_2H_5$	1390	
$(c)\ C_2H_5CH{=}CHPr\text{-}i$	641·4	1·71
$(t)\ C_2H_5CH{=}CHPr\text{-}i$	375·2	
$(c)\ C_2H_5CH{=}CHBu\text{-}t$	871·8	194
$(t)\ C_2H_5CH{=}CHBu\text{-}t$	4·500	
$(c)\ i\text{-}PrCH{=}CHPr\text{-}i$	18·08	1·19
$(t)\ i\text{-}PrCH{=}CHPr\text{-}i$	15·24	
$(CH_3)_2C{=}CHCH_3$	1875	
$(Z)\ C_2H_5C(CH_3){=}CHCH_3$	1860	1·74
$(E)\ C_2H_5C(CH_3){=}CHCH_3$	1067	
$(Z)\ i\text{-}PrC(CH_3){=}CHCH_3$	278·6	3·11
$(E)\ i\text{-}PrC(CH_3){=}CHCH_3$	89·58	
$(E)\ t\text{-}BuC(CH_3){=}CHCH_3$	0·442	
$(CH_3)_2C{=}C(CH_3)_2$	1227	
$(Z)\ C_2H_5C(CH_3){=}C(CH_3)C_2H_5$	41·91	1·92
$(E)\ C_2H_5C(CH_3){=}C(CH_3)C_2H_5$	21·80	
$c\text{-}PrCH{=}CH_2$	1529	
$c\text{-}PrC(CH_3){=}CH_2$	3993	
$(c\text{-}Pr)_2C{=}CH_2$	13,110	
$C_6H_5CH{=}CH_2$	25	
$C_6H_5C(CH_3){=}CH_2$	47·8	
$C_6H_5C(c\text{-}Pr){=}CH_2$	117·7	
$(c)\ C_6H_5CH{=}CHCH_3$	5·126	0·65
$(t)\ C_6H_5CH{=}CHCH_3$	7·88	

Table 33 it is clear that electron-donating substituents enhance the rate of addition relative to ethylene, but that large steric effects exist when compared to other electrophiles particularly sulphenyl chlorides. The electrophilicity is further substantiated by Hammett ρ values of −3·20, −2·91, −3·13, and ρ^+ values of −2·23, −1·97, and −2·19 for the addition of benzeneselenenyl chloride to ring-substituted styrenes, and *cis*- and *trans*-1-arylpropenes respectively[285].

The additions are usually *anti* stereospecific[426,427,430,432]. For example the addition of 2,4-dinitrobenzeneselenenyl chloride (**295**) to *cis*- and *trans*-1-phenylpropene gives the Markownikoff adducts **296** and **297** respectively by *anti* addition (equation 139). Thus the addition is superficially the same as that of its sulphur analogue[381].

In contrast to the addition of the analogous sulphur compound, the first-formed product of the addition of 4-tolueneselenenyl chloride (**298**) to ethylene is not the β-chloroalkyl selenide (**300**) but the episelenurane 1-chloro-1-(4′-tolyl)selenocyclopropane (**299**)[431]. The subsequent isomerization of **299** gives 2-chloroethyl 4′-tolyl selenide (**300**), the 1,2-adduct (equation 140).



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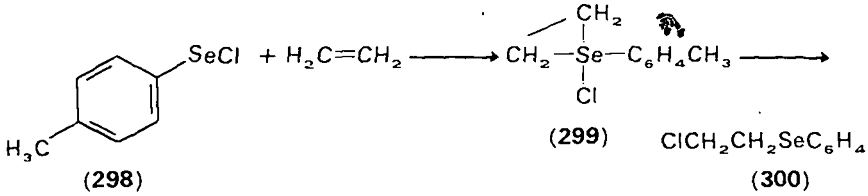


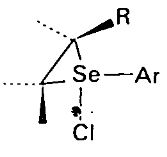
(140)

Semi-empirical molecular orbital calculations performed on an episelenurane related to **299** suggest that the most stable conformation of the episelenurane adducts resembles that of a distorted trigonal bipyramid in which the three-member ring is in an equatorial–apical orientation[442].

The observation of two very distinct methylene carbons in the c.m.r. spectrum of **299** is taken as evidence in support of these calculations. 1-Chloro-1-(4′-tolyl)selenocyclopropane (**299**) is the first reported compound containing selenium(IV) as part of a three-member ring. Other episelenuranes have been isolated with other alkenes when the aryl group of the selenenyl chloride is 4-anisyl, and 3-tolyl^{285}. When the aryl group is phenyl, 4-chlorophenyl, 4-bromophenyl, 4-nitrophenyl, 2,4-dichlorophenyl, or 2,4-dinitrophenyl only the β-chloroalkyl aryl selenide is isolated. No episelenuranes are observed. These reactions were always carried out under a nitrogen atmosphere in solutions which were freeze degassed at least three times. The presence or absence of light does not effect the kinetic product distribution. The episelenuranes are isolatable at room temperature but are in general much more stable at lower temperatures. Characterization by p.m.r., c.m.r., i.r., chemical ionization mass spectra, and chemical reactions readily distinguished these species from the β-chloroalkyl aryl selenides and the known episelenonium salts. The isomerization of the episelenurane is retarded by non-polar solvents and enhanced by more-polar solvents such as methylene chloride, acetic acid, formic acid and nitromethane.

The stability of the episelenurane is very dependent upon the substituents on the original alkene. Thus **299** is stable whereas no episelenuranes have been isolated from the reaction with *cis*- or *trans*-1,2-di-*t*-butylethylene. The stability of the episelenurane formed from addition to substituted alkenes of the form RCH=CHR where R = Me, Et, *i*-Pr, *n*-Pr, *n*-Bu, decreases in the order Me > Et > *n*-Pr > *n*-Bu > *i*-Pr. In general the *trans*-1,2-disubstituted episelenuranes are found to be less stable than the corresponding *cis* isomers.

Two isomeric episelenuranes are formed by the addition to unsymmetrically-substituted alkenes. This result is consistent with the proposed trigonal bipyramid geometry about the selenium atom with the three-member ring spanning apical–equatorial positions. Hence an alkene of the type $\text{RCH}{=}\text{CH}_2$ can form an episelenurane with the R group in either the apical (**301**) or equatorial (**302**) position. In the reaction of 4-tolueneselenenyl chloride (**298**) with simple monosubstituted alkenes,



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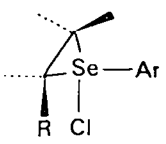


(302)

the two isomeric episelenuranes are not formed in equal amounts. The relative distributions under kinetic and thermodynamic control are given in Table 34. In contrast, the reaction of **298** with 1,1-disubstituted alkenes, usually gives only one isomer, which slowly isomerizes to the Markownikoff β-chloroalkyl selenide. When the two substituents on the 1,1-disubstituted alkene are sterically bulky, the second isomer is also formed which isomerizes to the *anti*-Markownikoff adduct. Thus 1,1-di-*t*-butylethylene forms, under kinetic control, a 2:1 mixture of the normal Markownikoff and *anti*-Markownikoff adducts. The reaction gives initially a white precipitate assumed to be the episelenurane mixture, but the half-life of the solid (only a few seconds in this case) is insufficient to allow unambiguous characterization. This result contrasts sharply with the analogous addition of sulphenyl chlorides to this alkene[409] which gives exclusively the *anti*-Markownikoff adduct under kinetic control.

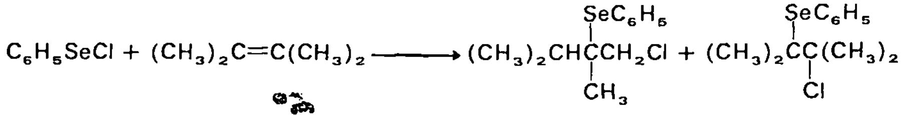
TABLE 34. Kinetic and thermodynamic product distributions of episelenuranes from the reaction of 4-tolueneselenenyl chloride with some monosubstituted alkenes

Alkene	Percentage distribution KCP:TCP[a] Initial	Final
$CH_3CH{=}CH_2$	43:57	0:100
$C_2H_5CH{=}CH_2$	64:36	0:100
i-$PrCH{=}CH_2$	83:17	1:99
t-$BuCH{=}CH_2$	100:0	5:95

[a] KCP = kinetically controlled product: TCP = thermodynamically controlled product.

After 2 months the composition changes to 59% *anti*-Markownikoff, 26% Markownikoff and 15% of a vinyl sulphide product. Further examples of this difference in product composition between additions of arenesulphenyl and areneselenenyl chlorides are given in Table 35.

Episelenurane intermediates have not been isolated from reactions of selenenyl chlorides with either tri- or tetrasubstituted alkenes, although short lived species appear to have been formed in one or two cases[285]. The reactions of areneselenenyl chlorides with these highly substituted alkenes show structural rearrangements which have no direct counterpart in arenesulphenyl halide additions. For example the reaction of benzeneselenenyl chloride with 2,3-dimethyl-2-butene yields the adduct **303** as well as the normal 1,2-addition product (**304**) under conditions of kinetic control (equation 141). This rearrangement can not have occurred



$$C_6H_5SeCl + (CH_3)_2C{=}C(CH_3)_2 \longrightarrow (CH_3)_2CH\overset{SeC_6H_5}{\underset{CH_3}{C}}CH_2Cl + (CH_3)_2\overset{SeC_6H_5}{C}\underset{Cl}{C}(CH_3)_2$$

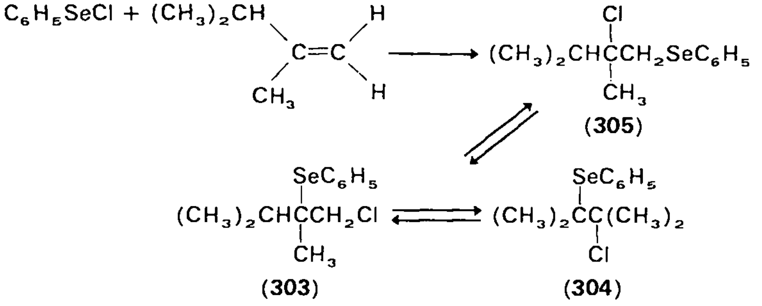
(303) (304) (141)

via isomerization of the starting alkene to 2,3-dimethyl-1-butene followed by addition of the selenenyl chloride because the regiochemistry of **303** from the reaction with 2,3-dimethyl-2-butene is found to be *anti*-Markownikoff, whereas the addition to 2,3-dimethyl-1-butene gives the Markownikoff adduct regiospecifically under kinetic control. Of further interest was the observation that isomerization of **305** to **303** under thermodynamic control also gives rise to some of **304** after a period of about 2 weeks. In all cases studied to date, the rearrangement gives rise to an adduct which would arise *a priori* from addition to a 1,1-disubstituted alkene (equation 142). These data lead to the general conclusion

TABLE 35 Kinetic product distribution for the reactions of benzenesulphenyl and benzeneselenenyl chloride with some alkenes in methylene chloride at 25 °C

Alkene	C_6H_5SCl[a]		C_6H_5SeCl[a]	
	%aM	%M	%aM	%M
$CH_3CH{=}CH_2$	68	32	41	59
$C_2H_5CH{=}CH_2$	75	25	63	37
i-$PrCH{=}CH_2$	100	0	88	12
t-$BuCH{=}CH_2$	100	0	100	0
$(CH_3)_2C{=}CH_2$	86	14	0	100
$C_2H_5C(CH_3){=}CH_2$	57	43	0	100
i-$PrC(CH_3){=}CH_2$	53	47	0	100
t-$BuC(CH_3){=}CH_2$	100	0	0	100
$(C_2H_5)_2C{=}CH_2$	59	41	0	100
i-$PrC(C_2H_5){=}CH_2$	100	0	0	100
(*c*) $CH_3CH{=}CHC_2H_5$	64	36	45	55
(*t*) $CH_3CH{=}CHC_2H_5$	68	32	38	62
(*c*) $CH_3CH{=}CHPr$-*i*	100	0	70	30
(*t*) $CH_3CH{=}CHPr$-*i*	83	17	75	25
(*c*) $CH_3CH{=}CHBu$-*t*	100	0	100	0
(*t*) $CH_3CH{=}CHBu$-*t*	100	0	92	8
(*c*) $C_2H_5CH{=}CHPr$-*i*	90	10	83	17
(*t*) $C_2H_5CH{=}CHPr$-*i*	63	37	89	11
(*c*) $C_2H_5CH{=}CHBu$-*t*	100	0	88	12
(*t*) $C_2H_5CH{=}CHBu$-*t*	100	0	100	0
c-$PrCH{=}CH_2$	0	100	0	100

[a] M = Markownikoff orientation: *a*M = *anti*-Markownikoff orientation.


C6H5SeCl + (CH3)2CH, H, C=C, CH3, H
(CH3)2CHCCH2SeC6H5, Cl, CH3
(305)
(CH3)2CHCCH2Cl, SeC6H5, CH3
(303)
(CH3)2CC(CH3)2, SeC6H5, Cl
(304)

(142)

that the product- and rate-determining transition states resemble the episelenurane intermediate even in those cases where an episelenurane is not *per se* observable. The rearrangements with tri- and tetrasubstituted alkenes appear, therefore, to be the result of a steric barrier towards formation of a tri- or tetrasubstituted episelenurane intermediate. This leads to a 1,3-hydrogen shift to form the thermally-more-stable 1,1-disubstituted episelenurane.

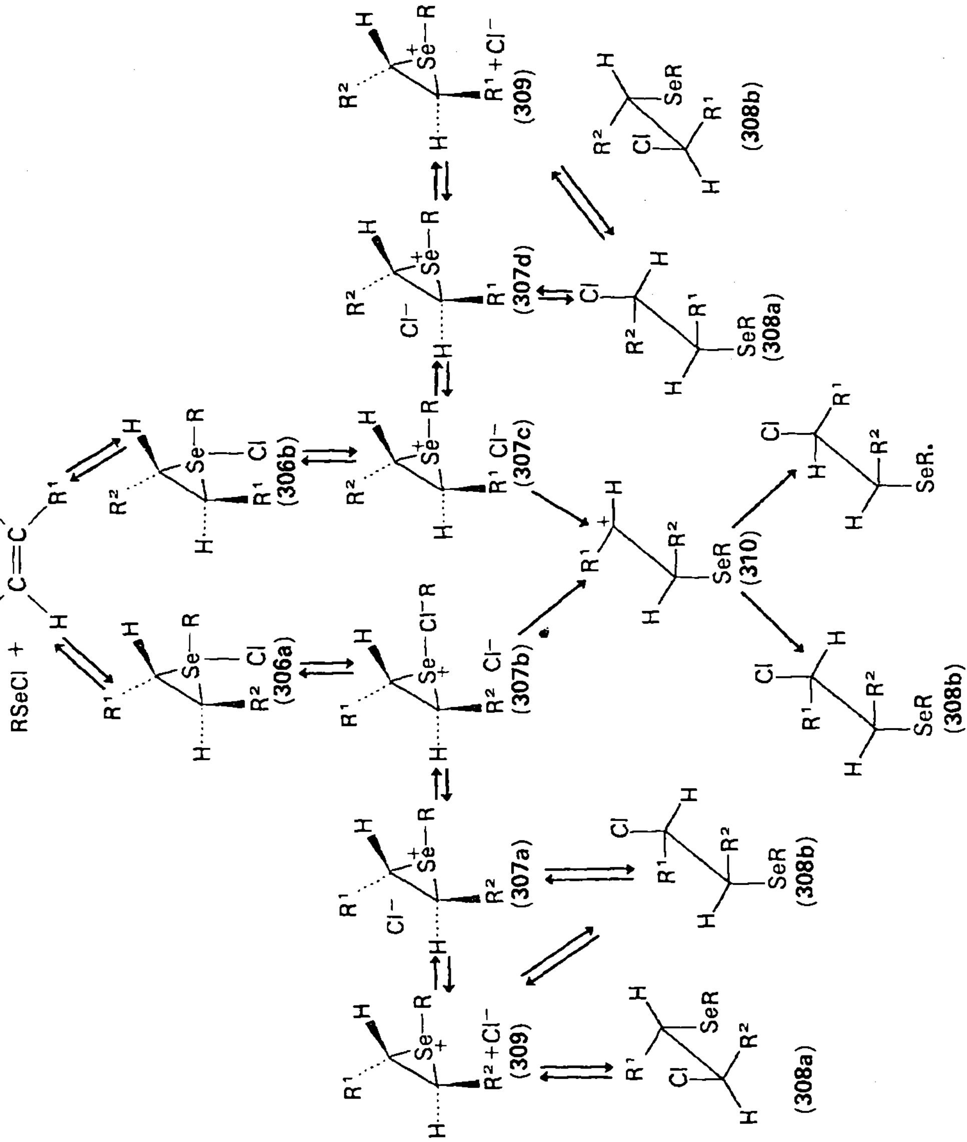
The effect of alkene structure on reactivity is found to be the same for the addition of both benzene- and 4-toluene-seleneny1 chloride within experimental error[285] and hence suggests similar rate-determining transition states for both reactions. This is important since in the first case episelenuranes have never been observed, whereas they are often isolatable from the latter. This result suggests that the structure of the rate-determining transition state very closely resembles that of the episelenurane.

From the data given in Table 33 it is clear that electron-donating groups generally increase the rate, but at the same time the general increase in their steric bulk causes a retardation of the rates. The progressive substitution of hydrogens on ethylene by methyl groups shows a peak at propene followed by a decrease in the order propene > methylpropene > 2-methyl-2-butene > *cis*-2-butene > *trans*-2-butene > 2,3-dimethyl-2-butene > ethylene. This is in contrast to the linear correlation between alkene structure and reactivity found for these same alkenes in the additions of arenesulphenyl chloride, bromine, chlorine and peroxyacids. The relative rates of addition of benzeneselenenyl chloride to vinylcyclopropane and styrene are 61:1, significantly greater than the addition of arenesulphenyl chloride (3·8:1) yet still smaller than bromination ($\geq 10^3$:1) or hydration (996:1)[416]. This is taken as indicative of a rather unsymmetrical transition state for the selenenyl chloride addition yet still a transition state in which full resonance stabilization by the substituents cannot be achieved.

While *anti* stereospecific addition is normally observed[430], non-stereospecific addition occurs under conditions of kinetic control in the addition of benzeneselenenyl chloride to anethole or any 1-arylpropene substituted with an electron-donating substituent better than or comparable to 4-CH_3O[285]. If 4-tolueneselenenyl chloride is used instead, an unstable single episelenurane intermediate can be observed which isomerizes to give a mixture of the *erythro* and *threo* Markownikoff adducts. This latter result indicates that although formation of the intermediate episelenurane occurs stereospecifically, an ion is formed subsequently which no longer resembles the episelenonium ion pair but rather is a relatively open 4-methoxybenzylic carbonium ion. These results coupled with kinetic studies of a series of *cis*- and *trans*-1-arylpropenes which showed a linear correlation of $\log k_2$ versus σ, clearly indicates that under certain conditions the structures of the rate- and product-determining transition states can be different. In this case the rate-determining transition state resembles a cyclic episelenonium ion pair while the product-determining transition state can resemble an open carbonium ion if such an ion is more stable than the bridged one. This behaviour is also observed for the addition of arenesulphenyl chlorides to *cis*- and *trans*-1-arylpropenes[410].

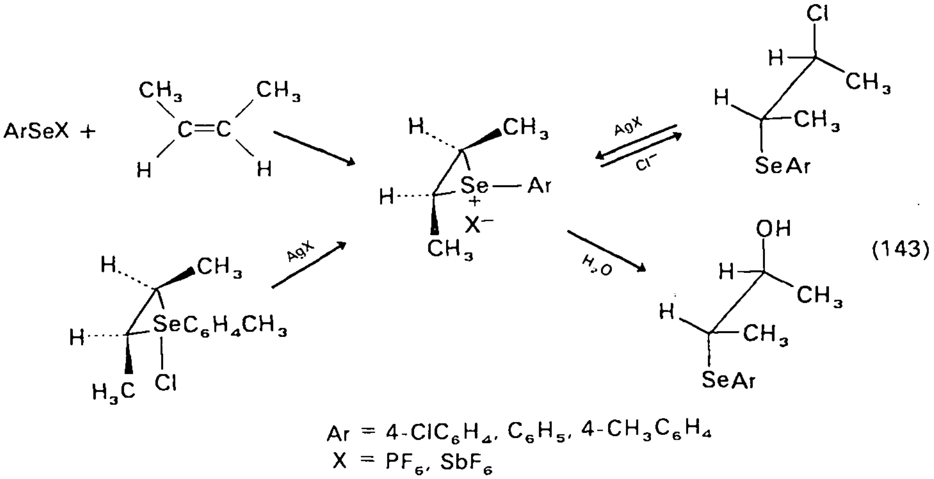
Based on the available data, the mechanism in Scheme 8 can be proposed which involves the formation of two episelenurane intermediates, **306a** and **b**. These intermediates, whose stabilities are dependent upon alkene structure, solvent, and temperature, may ionize via a series of intimate or solvent-separated ion pairs, **307a–d**, to the products of *anti* stereospecific addition **308a** and **b**. In very polar solvents a dissociated episelenonium ion **309** may be preferred and the product distribution then resembles more closely that of the addition of arenesulphenyl chlorides. In rare cases where an open carbonium ion, **310**, of greater stability than the commonly observed bridged species is formed the reaction is regio- but non-stereo-specific. In acetic acid, isomerization of the initially formed episelenuranes is much faster than the formation of solvent-incorporated products. This suggests that ion pairs are important. Furthermore the formation of the episelenurane intermediate occurs with complete retention of the initial alkene configuration and thus results from net *syn* addition. A concerted collapse of this intermediate would yield the product of *syn* addition. This is not observed and therefore requires the hypothesis of some ionic intermediate, **307** or **309**, to allow migration of the chlorine atom from a position adjacent to the selenium atom to one adjacent to, and essentially *trans* coplanar with respect to, selenium.

R¹ more electron donating than R²


RSeCl +
(306a)
(306b)
(307a)
(307b)
(307c)
(307d)
(308a)
(308b)
(309)
(310)

SCHEME 8.

b. *Areneselenenyl hexafluorophosphates and hexafluoroantimonates.* The addition of 4-toluenebenzeneselenenyl hexafluorophosphate to *cis*- and *trans*-2-butene in methylene chloride or nitromethane at 24 °C gives, respectively, *cis*- and *trans*-2-butene episelenonium hexafluorophosphate characterized by p.m.r. and c.m.r., and isolated as colourless solids[285]. These compounds can also be prepared by reacting the corresponding episelenuranes or β-chlor alkyloselenide with $AgPF_6$. Reaction of this salt with halide ions or water gives the product of S_N2 attack at carbon as shown in equation (143).

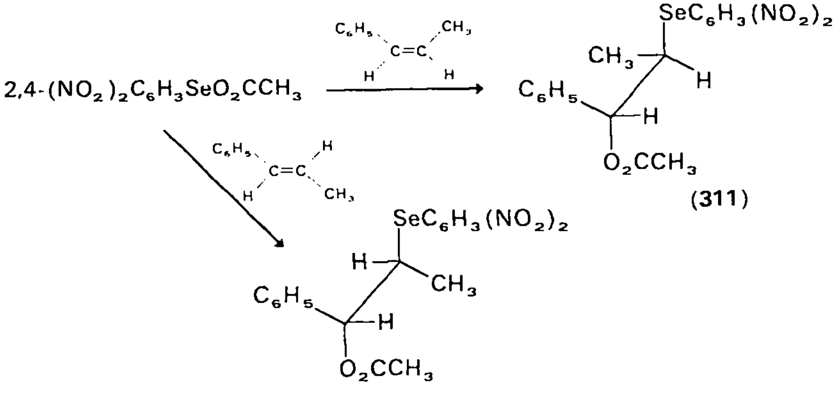


(143)

Even in cases where episelenuranes have not been isolated, episelenonium salts can be formed. For examples, the reactions of 4-chlorobenzene or benzeneselenenyl hexafluorophosphate or hexafluoroantimonate with alkenes form episelenonium hexafluorophosphates or hexafluoroantimonates. These salts can also be prepared by the reaction of a β-chloroalkyl, 4-chlorophenyl, or phenyl, selenide with silver hexafluorophosphate or hexafluoroantimonate.

Similar results were obtained when the selenenyl hexafluoroantimonate was used and the aryl group was changed to phenyl or 4-chlorophenyl.

c. *Areneselenenyl acetates.* The addition of selenenyl acetates to alkenes was first reported in 1953[428]. The stereochemistry of the reaction has been reported to be *anti*, based on the reaction between 2,4-dinitrobenzeneselenenyl acetate and *cis*- and *trans*-1-phenylpropene which gives the Markownikoff adducts **311** and **312** respectively (equation 144)[430]. Markownikoff addition has also been reported for the reaction of 1-anthraquinoneselenenyl acetate with methylpropene and vinyl acetate, and for the reaction of 2-nitrobenzeneselenenyl acetate with styrene and



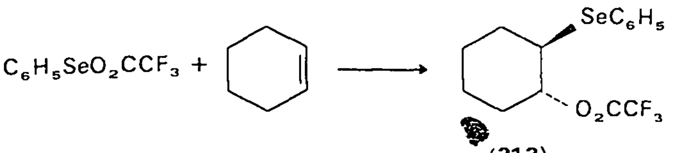
(311)

(312)

(144)

vinyl acetate[429]. The only product isolated in the addition of 1-anthraquinoneselenenyl acetate with 1,3-butadiene was that of 1,4-addition[429].

Reich[427] has recently reported the reaction of benzeneselenenyl trifluoroacetate with a number of alkenes. The addition to cyclohexene is *anti* stereospecific yielding *trans*-2-phenylseleno-1-trifluoroacetoxycyclohexane (**313**, equation 145). The additions were carried out in benzene or methylene chloride. The reaction is not very regioselective. The reaction with styrene gives the Markownikoff isomer exclusively, but 1-methylcyclohexene and methyl acrylate give mixtures in the ratio of 45:55 and 35:65 Markownikoff:*anti*-Markownikoff additions. *Cis*- and *trans*-2-butene are reported to yield diastereoisomers, presumably via *anti* addition. The mechanism of this reaction has been hypothesized to be closely related to that of sulphenyl halides[427]. 1,3-Cyclohexadiene gives predominantly 1,2-additions with some 1,4-products. Non-regiospecific addition has also been reported for the reaction of 2-methyl-2-heptene and 1-dodecene with benzeneselenenyl acetate formed *in situ* from bromine, diphenyl diselenide and anhydrous potassium acetate according to equation 146[426].

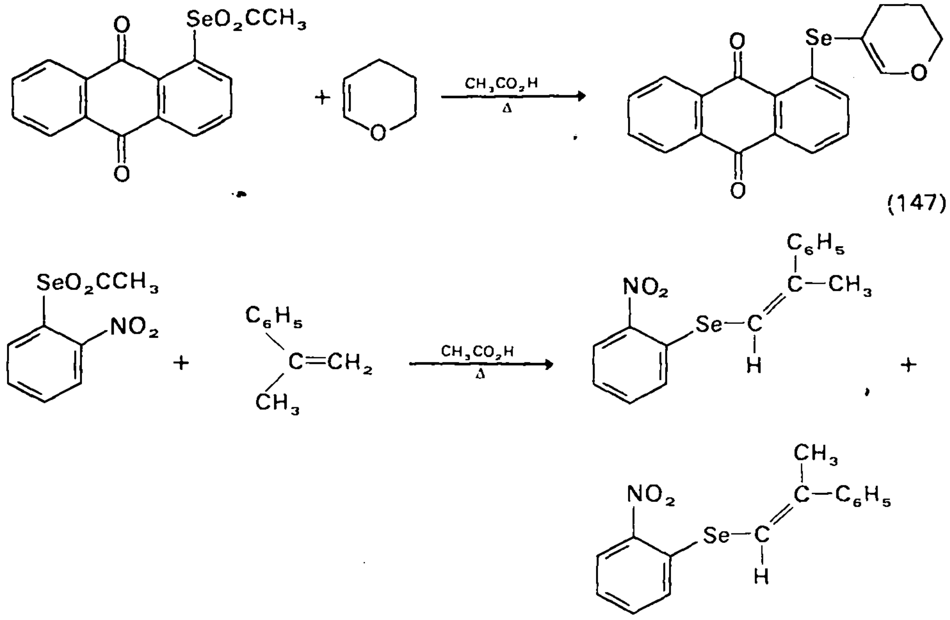


(313)

(145)

$$
\begin{aligned}
C_6H_5SeSeC_6H_5 + Br_2 &\longrightarrow 2\,C_6H_5SeBr \\
C_6H_5SeBr + KOAc &\longrightarrow C_6H_5SeOAc + KBr
\end{aligned}
\qquad (146)
$$

'Substitution' products have been reported in the reaction of 1-anthraquinoneselenenyl and 2-nitrobenzeneselenenyl acetate with 2,3-dihydropyran, 2-phenylpropene and a number of ring-substituted 1,1-diphenylethylenes[429] (equation 147). The reactions were carried out either in acetic acid, carbon tetrachloride, or pyridine. The pyridine was hypothesized to be a catalyst polarizing the Se—OAc bond to give a $ArSeC_5H_5N^+OAc^-$ complex as the electrophile.



(147)

2. Tetravalent selenium and tellurium

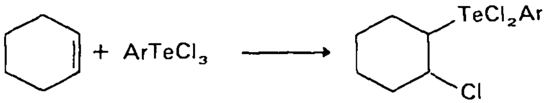
a. *Arylselenium trichlorides.* The addition of arylselenium trichlorides to alkenes to yield β-chloroalkyl aryl selenide dichlorides has received little attention. It has been reported that 2,4-dinitrophenylselenium trichloride reacts with *cis-* and *trans-*1-phenylpropene in a stereospecific *anti* addition in acetic acid, carbon tetrachloride, chloroform and methylene chloride solvents[430]. The addition in this case is non-regiospecific leading to essentially equal proportions of the Markownikoff and *anti*-Markownikoff products. In contrast 4-anisylselenium trichloride reacts to form exclusively the *anti*-Markownikoff adduct by *anti* addition under conditions of kinetic control[285]. Similar results were observed for other unsymmetric 1,2-disubstituted ethylenes. For example the reaction with *cis-* and *trans-*4-methyl-2-pentene gives *threo-* and *erythro-dl-*2-chloro-4-methylpentyl-34′-anisyl selenide dichloride respectively.

The presence of *anti*-Markownikoff adducts from 1-arylpropenes under conditions of kinetic control rules out a carbonium ion intermediate in the product- and rate-determining steps. The enhancement of the rate of addition caused by electron-donating substituents in *trans*-1-arylpropenes, determined by competition experiments, demonstrates the electrophilicity of the reaction[285].

Isomerization to the adduct with Markownikoff orientation is observed in all cases under conditions of thermodynamic control with retention of configuration.

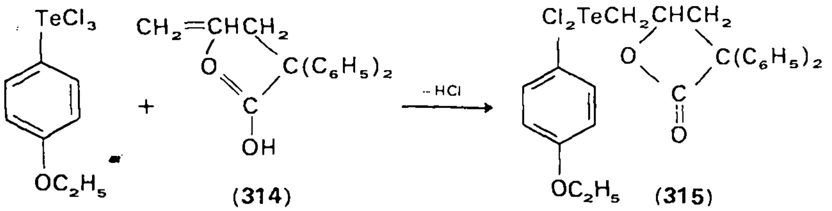
No kinetic results have been reported to date and therefore little is known about the stoichiometry of the rate-determining transition state.

b. *Aryltellurium trichlorides.* The reaction of a number of aryltellurium trichlorides with cyclohexene in refluxing cyclohexene gives 2-chlorocyclohexyl-1-aryl telluride dichlorides[443,444] (equation 148). Attempts to carry out this reaction at room temperature or to react aryltellurium trichlorides with styrene, and 1,4-diphenyl-1,3-butadiene, neat or in solvents such as chloroform and acetic acid gave only starting material.



(148)

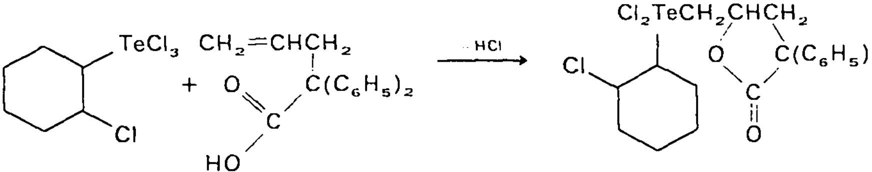
The reaction of 4-ethoxyphenyltellurium trichloride with 4,4-diphenylpenten-4-oic acid in CHCl$_3$ is reported to form 2,2-diphenyl-5-(4′-ethoxyphenyltelluro dichloride)-4-pentanolactone (**315**) with the elimination of HCl (equation 149)[443].



(149)

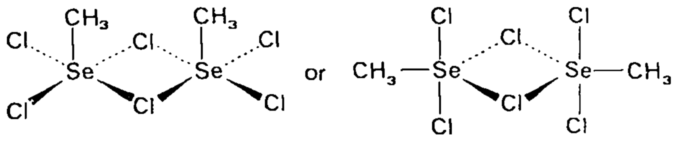
Alkyltellurium trichlorides prepared from the reaction of tellurium tetrachloride and alkenes react further with alkenes to give the bis(β-chloroalkyl) telluride dichloride adducts[445,446]. For example, 2-chlorocyclohexyltellurium trichloride formed from the reaction of cyclohexene and tellurium tetrachloride is stable in excess cyclohexene at room temperature, but will react with **314** to form **316** (equation 150).

No other additions have been reported nor have kinetic results been given to date.



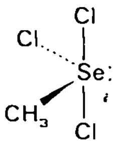
(314) (316) (150)

c. *Alkylselenium trichlorides.* Three alkylselenium trichlorides, $RSeCl_3$, have been reported[447,448] (R = Me, Et, *i*-Pr). Of these only methylselenium trichloride is reasonably stable. Ethylselenium trichloride may be prepared *in situ*. Isopropylselenium trichloride, although apparently formed *in situ*, immediately decomposes to give isopropyl chloride and $SeCl_4$. Methylselenium trichloride has been reported as existing in two forms[448]; one soluble in CH_2Cl_2 the other insoluble. The major difference appears to be that the soluble form, hereafter referred to as the β-form of CH_3SeCl_3 (**317a**), is dimeric in solution whereas the insoluble α-form (**317b**), is believed to be monomeric. The reactivity of these two species is quite distinct[285].



(317a)

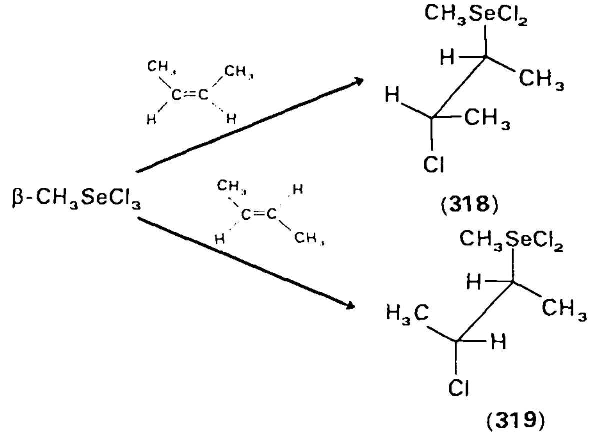
β-CH_3SeCl_3



(317b)

α-CH_3SeCl_3

β-Methylselenium trichloride reacts readily with alkenes to yield β-chloroalkyl methyl selenide dichlorides[285]. Thus *cis*- and *trans*-2-butene give (*RS,RS*)- and (*RS,SR*)-3-chlorobutyl-2 methyl selenide dichloride (**318** and **319**) respectively, via *anti* stereospecific addition (equation 151). Similarly, reactions with *cis*- and *trans*-1-arylpropenes are *anti* stereospecific and regiospecific in the Markownikoff sense when the aryl group is more electron withdrawing than methyl (Ar = 4-CH_3, 4-H, 4-Cl, and 3-NO_2). When the substituent is electron donating (Ar = 4-*i*-C_3H_7O, 4-C_6H_5O, and 4-CH_3O) the addition is non-stereospecific or stereoselective *anti* depending upon the concentration range of methylselenium trichloride used[285]. Preliminary kinetic results indicate that the reaction is essentially second order; first order in alkene, and first order in CH_3SeCl_3 in the concentration range 0·01–0·04 M at 25 °C with methylene chloride or chloroform as solvents. A third order process, first order in alkene and second order in CH_3SeCl_3, is observed in the concentration range 0·2–0·6 M. Under conditions of kinetic control, regiospecific addition to form the Markownikoff adduct occurs irrespective of the concentration range. This latter result contrasts with the previously mentioned regiochemistry of addition of arylselenium trichlorides under equivalent addition conditions[430,285]. The electrophilicity of the reaction is demonstrated by the enhanced reactivity of *cis*- and *trans*-1-arylpropenes substituted with electron-donating substituents when competition experiments are carried out.



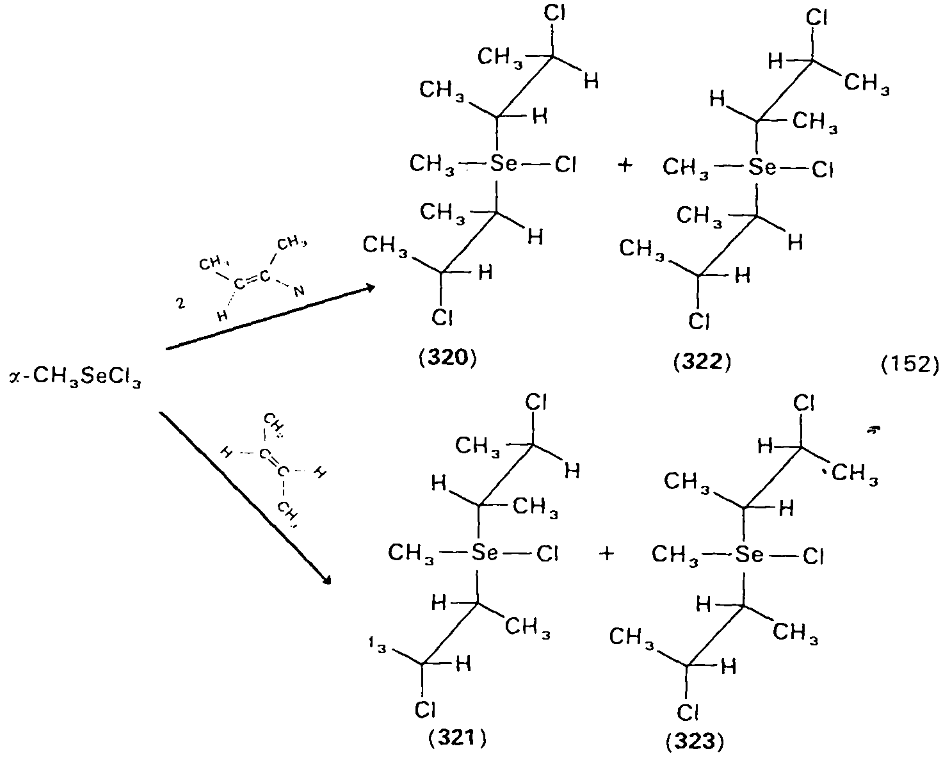
(318)

(319)

(151)

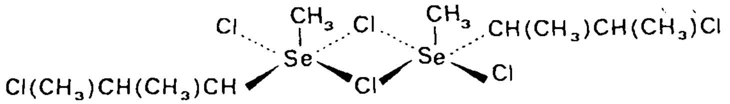
It is clear from the product studies that a change in the structure of the product-determining transition state occurs when the electron-donating ability of the substituent on the phenyl ring is greater than that of a methyl group. The non-stereospecific addition to 1-(4-isopropoxy, 4-phenoxy and 4-methoxyphenyl)propene suggests that an open carbonium ion is involved as an intermediate in these reactions. In the absence of further kinetic data it is impossible to determine whether this change occurs in the rate- or product-determining transition state.

α-Methylselenium trichloride reacts with alkenes to give bis-(β-chloroalkyl) methyl chloro selenuranes[285]. Hence *cis*- and *trans*-2-butene appear to form the bis((2*RS*,3*RS*)-3-chlorobutyl-2) and bis-((2*RS*,3*SR*)-3-chlorobutyl-2) methyl chloro selenurane (**320** and **321**) and the meso compounds (2*RS*,3*RS*)-3-chlorobutyl-2(2′*SR*,3′*SR*)3′-chlorobutyl-2′ and (2*RS*,3*SR*)-3-chlorobutyl-2(2′*SR*,3*RS*)-3′-chlorobutyl-2′ methyl chloro selenurane (**322** and **323**) respectively as determined by p.m.r., c.m.r. and mass spectrometry (equation 152). The reaction is therefore believed to be stereospecific with simple alkyl substituted alkenes. Compounds **318** and **319** are not precursors of **320** and **322**, or of **321** and **323** since they do not add a second molecule of alkene under the reaction conditions. The presence of 2:1 adducts in the addition of α-CH_3SeCl_3 may be attributed



(152)

to its monomeric structure. Under this criterion the 1:1 adducts **318** and **319** from β-CH$_3$SeCl$_3$ may in reality be 2:2 adducts such as **324**. This latter point has yet to be settled.



(324)

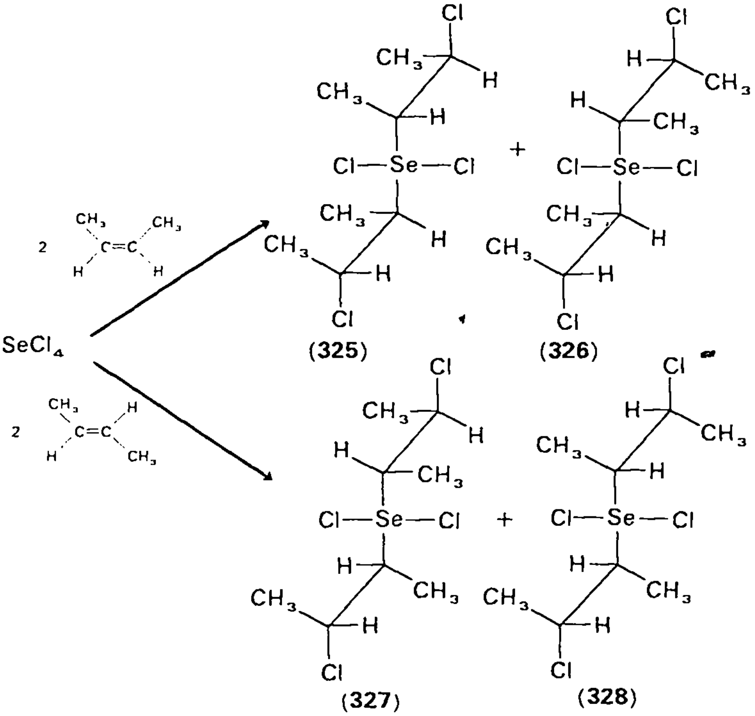
β-Chloroalkylselenium trichlorides formed by the reaction of SeCl$_4$ and alkenes have also been reported[285] to add to alkenes in an *anti* stereospecific but non-regiospecific manner. This reaction is discussed in the next section.

d. *Selenium tetrachloride.* Selenium tetrachloride, SeCl$_4$, reacts with alkenes in a facile manner to yield bis(β-chloroalkyl) selenide dichlorides[449,452,285]. In the earlier literature[428–442] it was often hypothesized that SeCl$_4$ was not well defined in solution and hence existed in equilibrium with related species such as SeCl$_2$, Se$_2$Cl$_2$ and SeOCl$_2$[453–464].

Selenium tetrachloride has since been shown to be well defined. The major problem seemed to be with respect to the nature of the addition product which was sometimes a bis(β-chloroalkyl) selenide or selenoxide as well as the normal selenide dichloride species. Consequently much confusion exists in the interpretation of these reactions from the earlier literature. The reactions with alkenes are usually carried out neat[449] or in solvents such as pentane, hexane or chlorinated solvents[285,449–452]. Hydroxylic solvents react with $SeCl_4$ and therefore cannot be used[465].

Few mechanistic studies have been reported. The electrophilicity of the reaction is demonstrated through competition experiments by the enhanced reactivity of alkenes substituted with electron-donating groups[441], while reactions with chlorinated alkenes are very slow even in the presence of catalysts such as aluminium chloride[450].

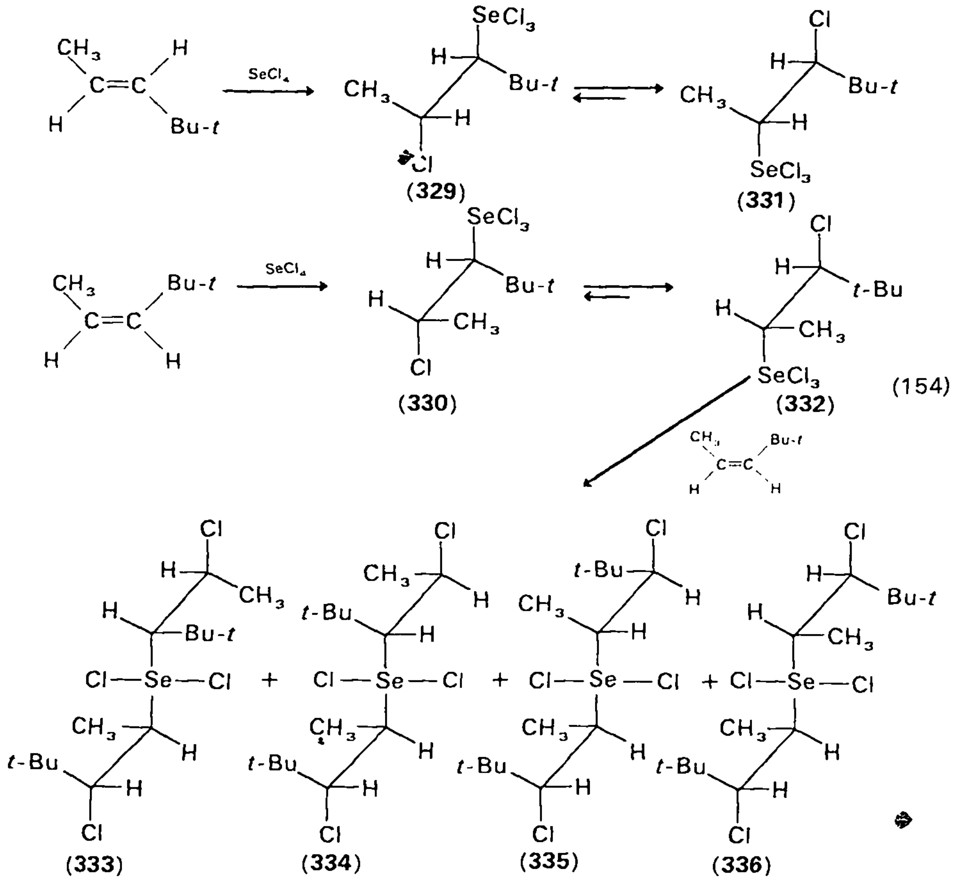
The addition of $SeCl_4$ to *cis*-2-butene at 25 °C in methylene chloride solution appears to be *anti* stereospecific[441], yielding bis-((2*RS*,3*RS*)-3-chlorobutyl-2) selenide dichloride (**325**) and *meso* compound (2*RS*,3*RS*)-3-chlorobutyl-2 (2*SR*,3′*SR*)-3′-chlorobutyl-2′ selenide dichloride (**326**, equation 153). Similarly, addition of $SeCl_4$ to *trans*-2-butene yields a mixture of


(325) **(326)** **(327)** **(328)**

(153)

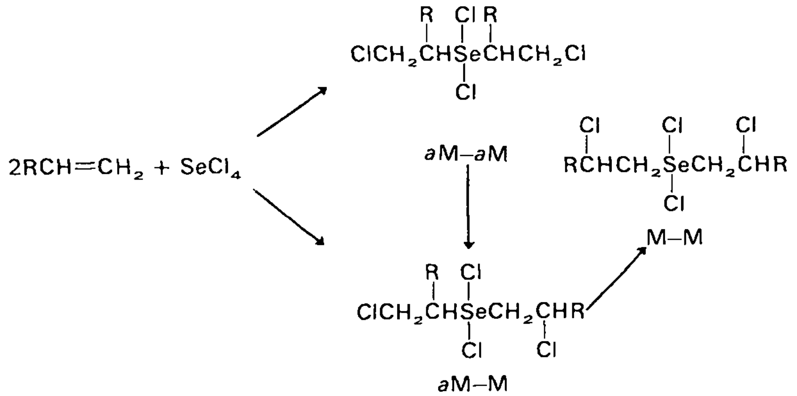
bis-((2*SR*,3*RS*)-3-chlorobutyl-2) selenide dichloride (**327**) and (2*SR*,3*RS*)-3-chlorobutyl-2 (2′*RS*,3′*SR*)-3′-chlorobutyl-2′ selenide dichloride (**328**). The relative configurations of **325** and **326** vs. **327** and **328** were assigned from their respective p.m.r. and c.m.r. spectra.

The reaction of $SeCl_4$ with *cis*- and *trans*-4,4-dimethyl-2-pentene gives the monoadducts **329** and **330** respectively under kinetic control. Subsequent isomerization gives the Markownikoff adducts **331** and **332**. These latter compounds are quite reactive readily adding a second molecule of alkene to yield, in the case of **332**, a mixture of **333**, **334**, **335** and **336** as identified by spectroscopic techniques (equation 154)[285].



(154)

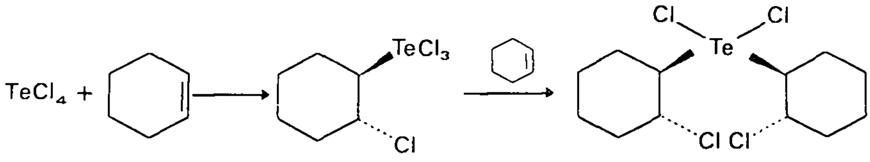
Terminal alkenes, if monosubstituted, yield the *a*M–*a*M isomers and *a*M–M isomers under kinetic control[285]. Subsequent rearrangement, however, allows the isolation of the thermodynamically more-stable M–M adducts (equation 155).


2RCH=CH₂ + SeCl₄
ClCH₂CH(R)Se(Cl)CH(R)CH₂Cl
aM–aM
RCH(Cl)CH₂Se(Cl)CH₂CH(Cl)R
M–M
ClCH₂CH(R)Se(Cl)CH₂CH(Cl)R
aM–M

(155)

No kinetic data are currently available for this reaction. The reactions are quite fast and are generally complete within a few minutes when carried out in methylene chloride at room temperature[285]. The observation that generally only bis adducts are isolated even in cases where an excess of $\mathrm{SeCl_4}$ is employed, indicates that addition of the second molecule of alkene is much faster than the first. This is to be expected since the substitution of an electron-donating alkyl group on $\mathrm{RSeCl_3}$ vs. the electron-withdrawing chlorine in $\mathrm{SeCl_4}$ should tend to stabilize the transition state in the former case relative to the latter. Similar arguments have been used to explain the higher reactivity of areneselenenyl and sulphenyl halides substituted with electron-donating substituents relative to those with electron-withdrawing groups.

e. *Tellurium tetrachloride.* The reaction of tellurium tetrachloride with simple alkenes yields β-chloroalkyltellurium trichlorides and bis(β-chloroalkyl) telluride dichlorides depending upon the relative proportions of alkene and $\mathrm{TeCl_4}$[443–446]. For example the reaction of $\mathrm{TeCl_4}$ with excess cyclohexene[443,444] yields bis(2-chlorocyclohexyl-1) telluride dichloride **338** (equation 156). When less than an equivalent amount of cyclohexene is used[445] 2-chlorocyclohexyltellurium trichloride (**337**) is isolated. The reaction of **337** with excess cyclohexene similarly yields **338**, suggesting that the formation of **338** occurs by two distinct steps. The reaction is claimed to be *anti* stereospecific[444] but no experimental evidence has been presented to substantiate this claim.



(337) (338)

(156)

This reaction is not general since some olefins such as styrene and 1,4-diphenyl-1,3-butadiene do not react either neat or in carbon tetrachloride solvent[444,446]. In these cases elemental tellurium and unidentified halogenated adducts were isolated, suggesting that the telluride dichloride adduct may have formed but decomposed readily under the conditions used. Supporting this view Fisher and Eisner observed[466] the formation of tellurium during the reaction of neat cyclohexene with $TeCl_4$ whereas de Moura Campos and Petragnani[443,444], and later Ogawa[445,446] found that when the reaction is carried out in carbon tetrachloride good yields of the adducts **337** and **338** are obtained.

The regiochemistry is generally believed to be Markownikoff[445,446]. The data supporting this statement are quite weak however, and were not conclusive for either propene or 1-butene, the only cases so far reported.

The effect of solvent on the addition has been investigated. The results are given in Table 36. The reaction is generally faster and the 2:1 adducts were formed preferentially as the dielectric constant of the medium was increased.

TABLE 36. Solvent effects in the addition of tellurium tetrachloride to propene

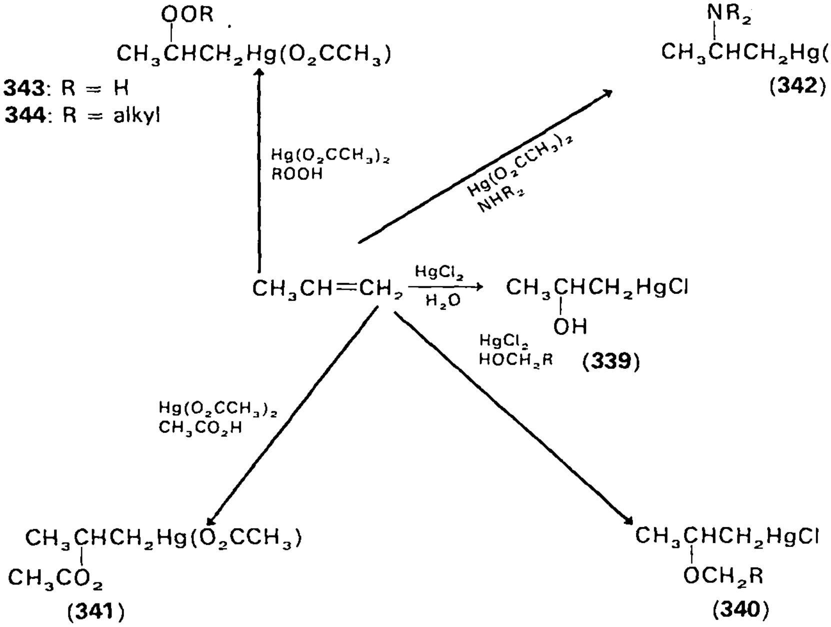
Solvent	Dielectric constant	Product distribution %1:1	%2:1
Ethyl acetate	6·03	98	2
Acetic acid	6·19	83	17
Methylene chloride	8·9	81	19
Acetonitrile	37·5	56	44
Nitromethane	39·0	32	68

VII. ELECTROPHILIC ORGANOMETALLIC COMPOUNDS

A. Mercuration

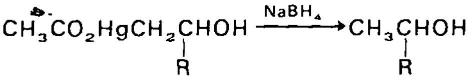
The first example of the addition of mercuric salts to alkenes was reported by Hofmann and Sand in 1900[467]. In this reaction, a mercuric salt, usually the chloride[467] or acetate[468] but sometimes the trifluoroacetate[469], is added to the alkene in the presence of a suitable solvent. The product is a 1:1 adduct whose composition depends upon the solvent and any added nucleophiles. Illustrated in Scheme 9 are a number of adducts formed by mercuration of propene under different reaction conditions. The addition of mercuric chloride to propene in water[470] or in a dioxane–water mixture produces a β-hydroxymercuric adduct **339**. This reaction is often called oxymercuration. Changing the solvent an alcohol, acetic acid or a secondary amine forms the β-alkoxy **340**[471] (alkoxymercuration), β-acetoxy **341**[471] (acetoxymercuration) and β-aminomercuric (aminomercuration) adducts **342**[472], respectively. Reaction of mercuric acetate with an alkene in the presence of hydrogen peroxide or a hydroperoxide forms a β-hydroperoxide **343**[473] and a β-alkylperoxymercuric adduct **344**[474], respectively. The additions are all regiospecific with the Markownikoff isomer formed exclusively.

The synthetic utility of this reaction has been greatly extended by the discovery that reaction of the adducts with $NaBH_4$ results in reductive demercuration[470] (equation 157). Consequently, mercuration–demercuration has become a valuable method for the synthesis of alcohols[470,475],



SCHEME 9.

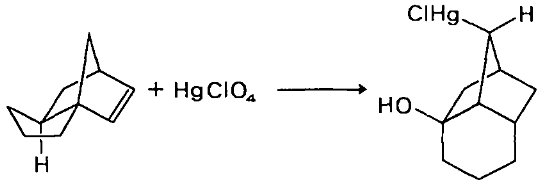
ethers[470], acetates[471], amines[472], hydroperoxides[473] and dialkyl peroxides[474]. Mercuration–demercuration has also been extended to dienes



$$CH_3CO_2HgCH_2\underset{R}{\underset{|}{C}}HOH \xrightarrow{NaBH_4} CH_3\underset{R}{\underset{|}{C}}HOH \qquad (157)$$

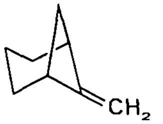
and unsaturated alcohols to form diols, tetrahydrofurans and tetrahydropyrans[476].

While mercuration usually occurs without rearrangement of the carbon skeleton[477], a few exceptions are known. For instance, 4,5-*exo*-trimethylene-2-norbornene (**345**) when treated with aqueous mercuric perchlorate solution produces, after addition of chloride ion, **346** (equation 158)[478]. The mercuration of both 6-methylenebicyclo[3.1.1]heptane (**347**) and 5-methylenebicyclo[2.1.1]hexane (**348**) forms a complex mixture of rearranged products[479].

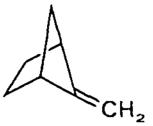


(158)

(345) **(346)**



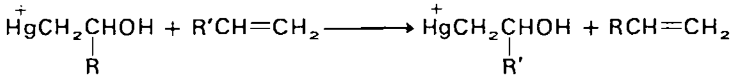
(347)



(348)

Mercuration has been reviewed by Chatt[480], Zefirov[481], Fahey[482] and Kitching[483]. Therefore, only the most recent results bearing directly on the mechanism or the effect of structure on reactivity will be presented here in detail.

A wealth of data is available for the addition of mercuric salts to alkenes, but the details of the mechanism of this reaction are not clear. While the addition has been found to be first order in mercuric salt and first order in alkene[484], these reactions may, in fact, be pseudo second order since the extent of involvement of solvent in the rate-determining step has not been investigated. The reaction is known to be reversible and the details of the deoxymercuration reaction have been extensively studied by Kreevoy[485]. The rate of exchange of oxymercurial ions, formed by the reaction of alkenes with mercuric ion in water, with other alkenes, has been measured (equation 159)[486]. The trend in the rate constants of this deoxymercuration



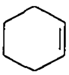
$$\overset{+}{Hg}CH_2\underset{R}{\underset{|}{C}}HOH + R'CH{=}CH_2 \longrightarrow \overset{+}{Hg}CH_2\underset{R'}{\underset{|}{C}}HOH + RCH{=}CH_2 \qquad (159)$$

parallels that of the oxymercuration rate constants previously determined by Halpern[484]; selected examples of which are given in Table 37.

In addition to this work, the effect of alkene structure upon the rate of methoxymercuration has been studied using the competitive reaction technique[487–489]. The data are given in Table 38. With a few exceptions, the results from different workers are in reasonable agreement. In general, the effect of the degree of substitution and the position of the double bond on the rate is as follows: terminal disubstituted > terminal monosubstituted > internal disubstituted > internal trisubstituted > internal tetrasubstituted. The rate is markedly decreased with increasing branching of that alkyl group attached to the double bond. This is true irrespective of whether the branched alkyl group is situated on the carbon which forms the carbon–mercury bond or on the one which forms the carbon–oxygen bond. *Cis* alkenes react faster than their *trans* isomers while inclusion of the double bond into a ring causes a relatively moderate rate increase. Values of $-2{\cdot}25$ (for the plot vs. σ) and $-1{\cdot}59$ (for the plot vs. σ^+) for ρ have been obtained by Pritzkow[487] for the reaction of a series of ring-substituted styrenes with mercuric acetate in methanol. These relatively small negative values of ρ indicate a low demand for electrons at the reaction site.

This variation in rate with structure is very different from that found in the addition of bromine (see Section III.C), chlorine (see Section III.B), peroxy acids (see Section VI.A) and arenesulphenyl chlorides (see Section VI.B) to similarly substituted ethylenes and is more reminiscent of acid-catalysed addition than it is of reactions whose mechanisms involve

TABLE 37. Rate constants for the addition of Hg^{2+} to alkenes in aqueous 0·01 M-$HClO_4$ at 25 °C[484]

Alkene	k^a (l mol^{-1} s^{-1})	k_{rel}
$CH_2{=}CH_2$	$5{\cdot}1 \times 10^3$	1
$CH_3CH{=}CH_2$	$1 \pm 0{\cdot}2 \times 10^5$	20
$C_2H_5CH{=}CH_2$	$8 \pm 2 \times 10^4$	16
$(CH_3)_2C{=}CH_2$	$>10^6$	>200
c-$CH_3CH{=}CHCH_3$	$5{\cdot}8 \times 10^3$	1·2
t-$CH_3CH{=}CHCH_3$	$1{\cdot}7 \times 10^3$	0·3
	$5 \pm 1 \times 10^3$	1
$CH_2{=}CHCH_2Cl$	11	2×10^{-3}
$CH_2{=}CHCH_2CN$	4·3	1×10^{-3}

[a] Ionic strength maintained at 0·10 with $NaClO_4$.

TABLE 38. Effect of alkene structure on the relative rate of methoxymercuration

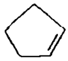
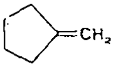
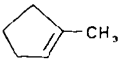
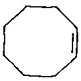
Alkene	k_{rel}^{489}	k_{rel}^{488}	k_{rel}^{490}
$C_2H_5CH=CH_2$	1·00	1·00	1·00
n-$PrCH=CH_2$	6·6		
n-$BuCH=CH_2$	4·8	4·13	
$CH_3(CH_2)_4CH=CH_2$		3·95	
$CH_3(CH_2)_5CH=CH_2$		3·95	7·4
i-$PrCH=CH_2$	2·5		
t-$BuCH=CH_2$	0·15	0·07	0·067
s-$BuCH=CH_2$		1·3	
$(CH_3)_2C=CH_2$		8·7	
$C_2H_5(CH_3)C=CH_2$		7·3	
n-$Pr(CH_3)C=CH_2$	48	5·9	
i-$Pr(CH_3)C=CH_2$		5·2	
neo-$Pent(CH_3)C=CH_2$		0·24	
t-$Bu(CH_3)C=CH_2$			0·54
$(t$-$Bu)_2C=CH_2$			<0·001
$(CH_3)_2C=CHCH_3$		1·57	
$(CH_3)_2C=CHC_2H_5$	1·24	1·05	
$(CH_3)_2C=CHPr$-i		0·056	
$(CH_3)_2C=CHBu$-t	0·020	0·19	
$(C_2H_5)_2C=CHCH_3$		0·08	
$(CH_3)_2C=C(CH_3)_2$	0·061	0·007	
$(c)\ C_2H_5CH=CHCH_3$	0·56		
$(t)\ C_2H_5CH=CHCH_3$	17		
$(c)\ i$-$PrCH=CHCH_3$	0·090		
$(t)\ i$-$PrCH=CHCH_3$	0·026		
$(c)\ C_2H_5CH=CHC_2H_5$		0·25	0·58
$(t)\ C_2H_5CH=CHC_2H_5$		0·04	
$(c)\ n$-$PrCH=CHPr$-n		0·10	0·22
$(t)\ n$-$PrCH=CHPr$-n		0·015	
	0·78		
	59		
	1·86		
	0·002		
Norbornene	3·7		4·6

TABLE 38 (*continued*)

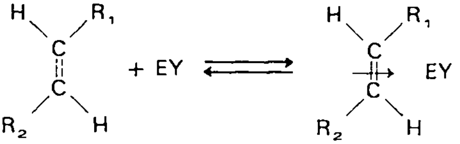
Alkene	k_{rel}[489]	k_{rel}[488]	k_{rel}[490]
Bicyclo[2.2.2]octene	0·01		
$C_6H_5CH{=}CH_2$	0·28		
$C_6H_5(CH_3)C{=}CH_2$	1·18		
cis-$C_6H_5CH{=}CHCH_3$	<0·02		
trans-$C_6H_5CH{=}CHCH_3$	<0·02		
$C_6H_5CH_2CH{=}CH_2$	0·41		
c-PrCH$=CH_2$			700
c-Pr$(CH_3)C{=}CH_2$			350
(*t*) $CH_3CH{=}CHCH_2Cl$		0·027	
$CH_2{=}CHCH_2Cl$		0·06	
(*t*) $CH_3CH{=}CHCH_2OCH_3$		0·11	
$CH_2{=}C(CH_3)CH_2Cl$		0·12	
$CH_2{=}CHCH_2OCH_3$		0·46	
$ClCH_2CH_2CH{=}CH_2$		0·47	
$CH_2{=}C(CH_3)CH_2OCH_3$		1·68	

cyclic 'onium' ions. Yet the composition and stereochemistry of the product is unlike that found for acid-catalysed additions. The stereochemistry of the addition product depends greatly upon the structure of the alkene.

The mercuration of unhindered acyclic alkenes such as the 2-butenes[491], the stilbenes[492], and 1,2-dideuterioethylene[493] has been shown to be *anti*. The configuration of the product obtained by mercuration of cycloalkenes depends upon the size of the ring as well as its geometry. The *anti* addition of mercury salts to cyclohexene is well documented[494,495]. Recently, the stereochemistry of oxymercuration and methoxymercuration of eight stable unsubstituted cycloalkenes from C_4 to C_9 has been studied[496]. The six *cis* cycloalkenes were found to undergo *anti* addition while both *trans*-cyclooctene and *trans*-cyclononene reacted exclusively *syn*. Mercuration of strained bicyclic alkenes such as norbornene[497] and bicyclo[2.1.1]hexene[498] also occurs by *syn* addition.

It is clear that the effect of alkene structure upon the rate and stereochemistry of mercuration is different from that encountered in the addition of other electrophiles. Attempts to apply a mechanism analogous to that of bromination or arenesulphenyl chloride addition to explain the results of mercuration have not been successful. Thus, the effect of alkene structure is inconsistent with a symmetrical bridged structure in the rate-determining transition state. The regiospecificity of the reaction is also inconsistent with a symmetrical bridged structure in the product-determining transition state. Yet, the addition reaction is often stereospecific and rearranged products are not usually formed.

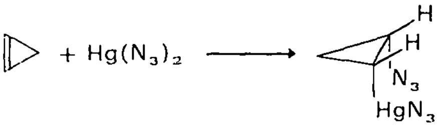
Traylor has recently proposed a mechanism which explains the experimental results[499]. The tendency of certain electrophiles to undergo *syn* addition is a result of their ability simultaneously to bind an alkene and another nucleophile. This occurs by a reversible formation of a molecular complex (**349**) whose structure is more like a π complex than an 'onium' ion. Such molecular complexes are known to form between alkenes and transition metals[500]. The molecular complex **349** is susceptible to *anti* or *syn* attack depending upon the location of the nucleophile. With acyclic unhindered alkenes, attack by external nucleophile occurs on the opposite side resulting in *anti* addition. In other alkenes, certain geometrical restrictions may retard the rate of *anti* addition without affecting the *syn* attack of the nucleophile complexed with the mercury. This results in *syn* addition.



(**349**)

Traylor has identified two such geometrical restrictions. The first is the 'twist–strain' theory whereby a rigid alkene cannot accommodate an antiperiplanar transition state because of strong eclipsing interactions. A second restriction is a complete blockage of one side of the alkene which forces all reagents to approach from the opposite side. This is steric control of the direction of approach.

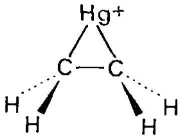
Examples of the first restriction are the mercuration of norbornene and bicyclo[2.1.1] hexene. Both are strained alkenes and form *syn* addition products. The 'twist–strain' theory predicts that only cyclopropene of all the *cis* cycloalkenes should undergo *syn* mercuration because the antiperiplanar transition state for normal addition is prohibited. This prediction has recently been confirmed by Hassner[501] who found that mercuric azide, generated *in situ* from mercuric acetate in tetrahydrofuran and water, adds to cyclopropene forming the *syn* addition product (equation 160).



(160)

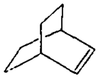
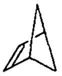
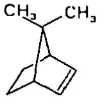
The *syn* addition to both *trans*-cyclooctene and *trans*-cyclononene are examples of steric control. In these ring compounds, one side of the π-bond is completely shielded by the rest of the molecule and, hence, attack by a nucleophile from this direction is difficult. Consequently, additions can only be *syn* to such cycloalkenes. However, as the size of ring of the *trans*-cycloalkene becomes larger and larger, the carbon skeleton becomes less rigid, thereby eliminating ring strain and most of the steric effect. As a result, *trans* addition should once again become favoured with larger *trans* cycloalkenes. This prediction is supported by the observation that *trans*-cyclodecene forms both *syn* and *anti* addition products, while *trans*-cyclododecene forms exclusively the *anti* addition product. Table 39 summarizes the available data on the effect of alkene structure on product stereochemistry.

One of the details of the mechanism of mercuration which remains to be resolved is whether or not intermediates, such as the cyclic mercurinium ion (350) are involved. The cyclic mercurinium ion was proposed originally



(350)

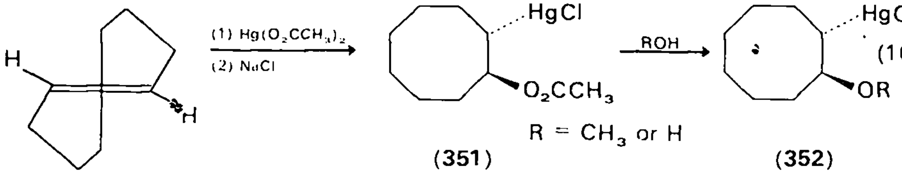
TABLE 39. Effect of alkene structure on the stereochemistry of mercuration

Type	Addition stereochemistry
Unhindered acyclic alkene	*anti*
Cyclopropene	*syn*
cis-$C_{(4)}$–$C_{(8)}$ Cycloalkenes	*anti*
trans-Cyclooctene and *trans*-cyclononene	*syn*
trans-Cyclodecene	*syn* and *anti*
trans-Cyclododecene	*anti*
	*syn* and *anti*
 	*syn* (*exo*)
2,3-Pentadiene	*syn* and *anti*

as an intermediate in the oxymercuration of alkenes in 1939[502]. Spectral evidence has been presented for the existence of such ions in the gas phase[513] and in strong acid media[514]. While there is little doubt that such ions are capable of existence, this does not mean that they must be on the reaction coordinate for the mercuration of alkenes. Evidence has been presented both for and against the involvement of mercurinium ions in the mechanism of mercuration.

The stereochemistry of the products of mercuration of norbornene[505], 1,4,7,7-tetramethylnorbornene[506], *syn*-7-bromonorbornene[506] and 7,7-dimethylnorbornene[507] have all been found to be exclusively *exo–syn*. Comparison of these results with those of the additions of benzenesulphenyl chloride which is known to involve a bridged product-determining transition state provides contrasting results. Thus the stereochemistry of the product of addition of benzenesulphenyl chloride changes from *exo–anti* for norbornene to *endo–anti* for 7,7-dimethylnorbornene. These results indicate that the steric hindrance of the *syn*-7-methyl group changes the direction of attack of the electrophile from *exo* for norbornene to *endo* for 7,7-dimethylnorbornene. Since mercuration does not display this behaviour, Brown[517] has discarded the symmetrical mercurinium ion and prefers a mercury-substituted carbonium ion which reacts rapidly with solvent from whichever direction is the least hindered. Such an ion is believed to have most of its charge on the mercury moiety which accounts for the Markownikoff orientation and the lack of rearrangement usually associated with carbonium ions.

Reutov[508] has prepared the optically active acetoxy adduct **351** by the *syn* addition of mercuric acetate to optically active *trans*-cyclooctene (equation 161). Upon exposure to methanol or aqueous acetone, **351** is converted to **352** which retains some of its optical activity. This result seems to exclude a symmetrical mercurinium ion as a simple intermediate in the transformation of **351** to **352**.



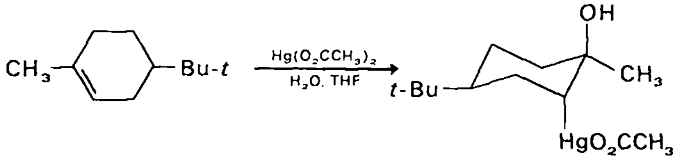
R = CH_3 or H

(351) (352)

(161)

Whitman[509] has studied the oxymercuration of 4-*t*-butylcyclohexene and 1-methyl-4-*t*-butylcyclohexene under neutral and acidic conditions, and has concluded that mercurinium ions are not kinetically important intermediates. This conclusion is based on his failure to trap a mercurinium ion by solvent in the methanolysis of *trans*-2-hydroxylcyclohexylmercuric acetate.

While Whitman[509] and Pasto[468] have both studied the addition of mercuric salts to substituted cyclohexenes, they differ in their interpretation of the results. Both report that oxymercuration of 4-*t*-butylcyclohexene and 1-methyl-4-*t*-butylcyclohexene forms exclusively *trans*-1,4-diaxial products (equation 162). This behaviour is identical to that



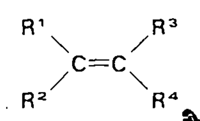
(162)

found in bromination and methoxybromination of the same two alkenes, both of which proceed via cyclic bromonium ions. In contrast, hydrobromination of cyclohexene, which is known to occur by an Ad$_E$3 mechanism, produced a mixture of axial and equatorial bromides. Consequently, Pasto concludes that the oxymercuration of substituted cyclohexenes proceeds via mercurinium ions which are formed in fast, reversible pre-rate-determining equilibria.

Pritzkow[488] has analysed the effect of alkene structure on the rates of methoxymercuration in terms of a multi-parameter Taft equation (equation 163), where σ_1^*, σ_2^*, σ_3^* and σ_4^* are the Taft polar substituent

$$\log k = \log k_0 + \rho_1^*(\sigma_1^* + \sigma_2^*) + \delta_1 \, (E_s^1 + E_s^2) + \rho_2^*(\sigma_3^* + \sigma_4^*) + \delta_2(E_s^3 + E_s^4) \qquad (163)$$

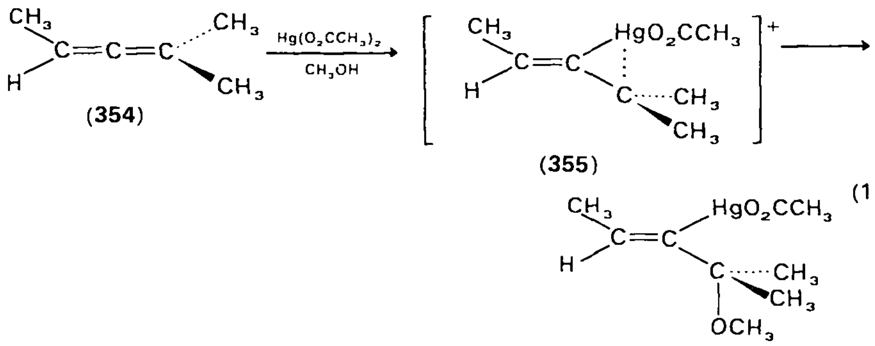
constants and E_s^1, E_s^2, E_s^3 and E_s^4 are the steric substituent constants for the four groups attached to the carbon–carbon double bond of **353**. Values of $-0{\cdot}31 \pm 0{\cdot}44$ and $-1{\cdot}44 \pm 0{\cdot}30$ were obtained for ρ_1^* and ρ_2^*



(353)

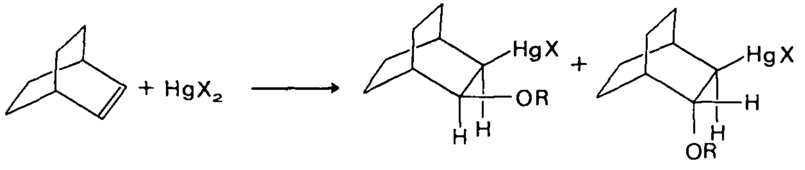
respectively. Since the values of ρ_1^* and ρ_2^* are substantially different, it is concluded that the rate-determining transition state for addition cannot be symmetrical and consequently a dissymmetric, bridged-mercurinium-like transition state is favoured.

Caserio[510] has studied the addition of mercuric salts to optically active 2,3-pentadiene (**354**) while Bach[511] has studied their addition to 1,2-cyclononadiene. A mechanism involving a dissymmetric mercurinium ion **355** has been proposed to account for the stereoselective *anti* addition (equation 164). However Bach[511] has observed that the stereospecificity of the reaction, and hence the importance of dissymmetric intermediates, is dependent upon the mercuric salt used.



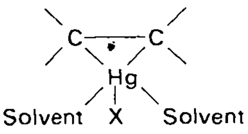
(354) (355) (164)

The influence of different solvents on the stereochemistry of the mercuration of bicyclo[2.2.2]octene has been studied by Bach[512] (equation 165). Selected results are given in Table 40. These data are explained by Bach in terms of a solvated mercurinium ion (**358**). The stereochemistry of the product can change depending upon the solvent shell around the ion and the



(356) (357) (165)

a: R = COCH$_3$
b: R = CH$_3$



(358)

ligand on the mercury atom. Thus, reaction of bicyclo[2.2.2]octene with mercuric acetate in acetic acid forms both *cis* and *trans* adducts **356a** and **357a**. This result is consistent with collapse of an acetate ligand on mercury forming **356a**, while attack by acetic acid solvent forms the *trans* adduct **357a**. Addition of mercuric nitrate in methanol forms a mixture of the *cis* and *trans* adducts **356b** and **357b**. Changing the solvent to methylene chloride with 1 equivalent of methanol added as nucleophile results in the exclusive formation of the *cis* adduct **356b**. Doubling the

TABLE 40. Effect of solvent on the mercuration of bicyclo[2.2.2]octene

Mercuric salt 0·33 M	Nucleophile concentration	Solvent	**356a** (%)	**357a** (%)	**356b** (%)	**357b** (%)
$Hg(O_2CCH_3)_2$		HOAc	64	36		
$Hg(O_2CCH_3)_2$		CH_3OH	7	3	13	77
$Hg(NO_3)_2$		CH_3OH			19	81
$Hg(NO_3)_2$	CH_3OH(0·33 M)	CH_2Cl_2			>99	—
$Hg(NO_3)_2$	CH_3OH(0·66 M)	CH_2Cl_2			79	21
$Hg(NO_3)_2$	CH_3OH(0·66 M)	Dioxane			—	>99
$Hg(O_2CCH_3)_2$		CH_2Cl_2	98	2	—	—
$Hg(O_2CCH_3)_2$	CH_3OH(0·33 M)	CH_2Cl_2	79	4	3	14

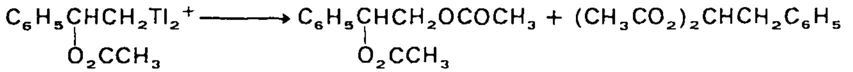
quantity of methanol added results in formation of the *trans* adduct **357b** as well as **356b**. Using dioxane as solvent with 2 equivalents of methanol added, the *trans* adduct **357b** is formed exclusively. 'These data strongly suggest that the mercurinium ion intermediate [**358**] involved in these reactions is solvated by methanol in methylene chloride solvent. Thus, when methanol is present in limiting quantity, collapse of the solvated mercurinium ion from the front side results in exclusive *cis* addition. However, with the donor solvent dioxane, methanol is displaced from the primary solvent shell surrounding the mercurinium ion and exclusive *trans* attack by free methanol in solution on [**358**] prevails'[512].

The mechanism proposed by Bach is very similar to that of Traylor. The major difference is the description of the intermediate: Traylor favours a molecular complex while Bach favours a solvated mercurinium ion. Brown on the other hand prefers a mercury-substituted carbonium ion structure for the intermediate. While the electronic structure of the intermediate is still the subject of debate, there is little doubt that the mechanism of mercuration involves at least two steps. The first is the formation of the intermediate and the second involves its decomposition to products. However, it is not clear which of these steps is rate determining or even if the mechanism is Ad_E2 or Ad_E3. Clearly, more data are needed to resolve these questions.

B. *Thallation*

The products of the addition of thallium(III) salts to alkenes depend upon the salt used and the reaction conditions. Acidic aqueous solutions of thallium(III) sulphate or chloride react with alkenes to form glycols and aldehydes or ketones (equation 166). In acetic acid thallium(III) acetate reacts to form 1,1- and 1,2-diacetate products (equation 167)[513]. Products of skeleton rearrangement are often observed[514]. In acetic acid the products are formed from the β-acetoxyalkyl thallium adduct (**359**) which can be isolated in some cases from the reaction mixture (equation 167)[515,516].

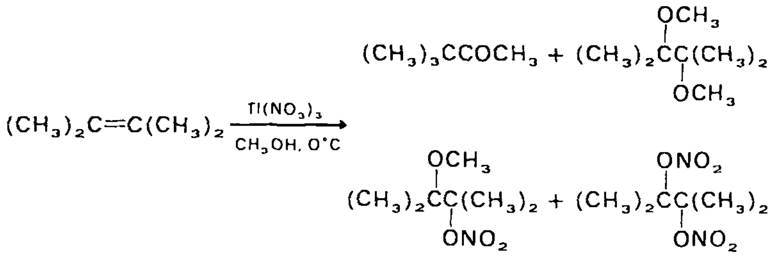
$$2CH_2{=}CH_2 + 2Tl^{3+} + 3H_2O \longrightarrow HOCH_2CH_2OH + CH_3CHO + 2Tl^+ + 4H^+ \qquad (166)$$



$$C_6H_5\underset{O_2CCH_3}{C}HCH_2Tl_2^+ \longrightarrow C_6H_5\underset{O_2CCH_3}{C}HCH_2OCOCH_3 + (CH_3CO_2)_2CHCH_2C_6H_5 \qquad (167)$$

(**359**)

The reaction of thallium(III) nitrate in methanol forms methoxy-nitrates and dinitrates as well as the usual carbonyl compounds and dimethyl glycol ethers (equation 168)[517]. The superiority of thallium(III) nitrate in methanol to other thallium reagents in the synthesis of carbonyl compounds has been discussed by Taylor[518] and McKillop[519].



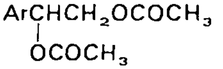
$$(CH_3)_2C{=}C(CH_3)_2 \xrightarrow[CH_3OH,\ 0°C]{Tl(NO_3)_3} \begin{array}{l} (CH_3)_3CCOCH_3 + (CH_3)_2C\overset{OCH_3}{\underset{OCH_3}{C}}(CH_3)_2 \\ \\ (CH_3)_2C\overset{OCH_3}{\underset{ONO_2}{C}}(CH_3)_2 + (CH_3)_2C\overset{ONO_2}{\underset{ONO_2}{C}}(CH_3)_2 \end{array} \qquad (168)$$

Henry has investigated the kinetics of the reaction of thallium(III) with ethylene in aqueous sulphuric, nitric and perchloric acids as well as in mixtures of sodium perchlorate–perchloric acid. The reaction is second order overall: first order in ethylene and in thallium(III) salt[520]. The stoichiometry and the initially-formed products are given in equation (166). The rates and products of thallation of ethylene, propylene and all four butenes were also determined in both acetic and perchloric acid[521,522]. The data are given in Table 41. The effect of alkene structure on the rate establishes the electrophilic nature of the reaction since replacing a hydrogen on ethylene by a methyl group increases the rate.

In acetic acid, thallium(III) exists as an equilibrium mixture of Tl^{3+}, $Tl(OAc)^{2+}$, $Tl(OAc)_2^+$, $Tl(OAc)_3$ and $Tl(OAc)_4^-$. By measuring the pH and the rates of thallation at various free acetate ion concentrations, Henry[522] has concluded that $Tl(OAc)_2^+$ is the electrophile in acetic acid over a wide range of acetate concentrations. At very low acetate concentrations reaction by Tl^{3+} and $Tl(OAc)^{2+}$ is probably important but $Tl(OAc)_3$ and $Tl(OAc)_4^-$ are relatively unreactive.

From the data in Table 41, it is clear that the effect of alkene structure on the rate and product composition is very similar in both perchloric and acetic acids. Hence Tl^{3+} and $Tl(OAc)_2^+$ are similar in their reactivity towards alkenes despite their differences in charge which suggests that in aqueous solutions, strongly solvated Tl^{3+} is the electrophile.

The products and rates of thallation by thallium(III) acetate in acetic acid of six ring substituted styrenes have been determined by Ouellette and coworkers[523]. Two products **360** and **361** are formed with the latter predominating with electron-donating substituents in the phenyl ring. The rate is overall second order, first order in each reactant. A correlation of $\log k_2$ versus σ^+ gives a value of $-2{\cdot}2$ (at 50 °C) for ρ^+.



$$\underset{\displaystyle OCOCH_3}{ArCHCH_2OCOCH_3}$$

(360)

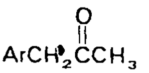
$ArCH_2CH(OCOCH_3)_2$

(361)

A similar study of the products and kinetics of the thallation by thallium(III) nitrate in methanol of a series of phenylethylenes has been carried out by Fliszar and coworkers[524]. Again overall second order kinetics were observed. For thallation of ring-substituted styrenes and α-methylstyrenes, correlations of $\log k_2$ versus σ were superior to σ^+. A value of $-4{\cdot}2$ for ρ was obtained for both series of compounds. Compounds **362**, **363** and **364** are the major products of thallation of styrenes, α-methylstyrenes and 1,1-diphenylethylene respectively.

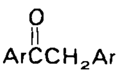
$ArCH_2CH(OCH_3)_2$

(362)



$$ArCH_2\overset{\displaystyle O}{\overset{\|}{C}}CH_3$$

(363)



$$Ar\overset{\displaystyle O}{\overset{\|}{C}}CH_2Ar$$

(364)

The product and kinetic data can be explained by the general mechanism illustrated in Scheme 10. The slow step is formation of the organothallium intermediate **365** which can form products either by phenyl, alkyl, or hydride ion migration or by solvolytic decomposition.

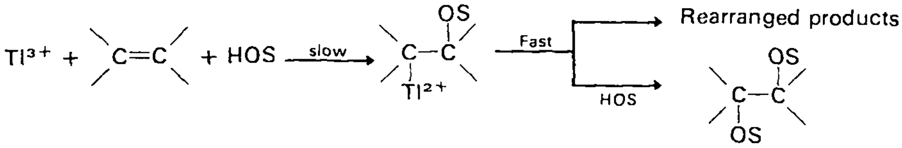
Evidence in support of this mechanism has been provided by Halpern and coworkers, who have studied the rate of thallation of a series of alkenols with thallium(III) perchlorate in aqueous perchloric acid[525].

TABLE 41. Rates and product composition of the reaction of Tl^{3+} and $Tl(OAc)_2^+$ with a series of alkenes

Alkene	k_{rel}		Carbonyl product	Carbonyl product (%)		Glycol product (%)	
	Tl^{3+} [a]	$Tl(OAc)_2^+$ [b]		Tl^{3+} [a]	$Tl(OAc)_2^+$ [b]	Tl^{3+} [a]	$Tl(OAc)_2^+$ [b]
$CH_2{=}CH_2$	1·0	1·0	CH_3CHO	45	45	55	55
$CH_3CH{=}CH_2$	167	152	CH_3COCH_3	75–85	81	15–25	17
$C_2H_5CH{=}CH_2$	162	157	$C_2H_5COCH_3$	45–55	75	15–25	16
(*c*) $CH_3CH{=}CHCH_3$	58	60	$C_2H_5COCH_3$	65–80	85–90	<0·5	—
(*t*) $CH_3CH{=}CHCH_3$	13·6	35	$C_2H_5COCH_3$	65–80	85–90	<0·5	—
$(CH_3)_2C{=}CH_2$	2×10^5	$2{\cdot}3 \times 10^5$	$(CH_3)_2CHCHO$	35–45	37	55–65	52

[a] In aqueous perchloric acid.

[b] In aqueous acetic acid.



365a: S = H
365b: S = OCCH$_3$

SCHEME 10.

The rates which are overall second order, were followed by measuring the increase in the intensity of the band at 212 nm which is due to the thallium(I) product. In three cases the spectral features of the reactions were found to be different. This difference could be explained by the formation and decay of an intermediate which is believed to be the organothallium intermediate **365a**.

The effect of the alkene structure on the rates of thallation and mercuration are given in Table 42. While the rate of mercuration is much faster, the effect of the alkenol structure on the rate of both reactions is very similar. In fact a correlation of log k_2 (for either reaction) versus σ^* gives nearly the same value of $\rho^*(\sim -3{\cdot}2)$. Therefore it is concluded that the step whose rate is being measured is similar in both thallation and mercuration. For mercuration this step is formation of the stable β-hydroxyalkyl mercury compound. By analogy, for thallation it should be formation of the β-hydroxyalkyl thallium intermediate **365a**. The thallation and mercuration of a series of cycloalkenes, 1-methylcycloalkenes and methylenecycloalkanes again show similarities in their rates providing additional support for the general mechanism in Scheme 10[536]. Such similarities between mercuration and thallation are not surprising since thallium(III) is isoelectronic with mercury(II) and lead(IV), both of which are known to react with carbon–carbon double bonds.

The mechanism in Scheme 10 differs from the one originally proposed by Henry[520] in that one intermediate, the precursor of the organothallium adduct **365**, is missing. Structures such as a charge-transfer complex[520] or a cyclic thallanium cation[527] have been proposed for this intermediate. While such an additional intermediate is not ruled out by the data, there is no specific evidence in favour of it. Furthermore so little is known about the stereochemistry of the organothallium adduct **365** that there is no justification even for speculating about the electronic structure of the transition state or of the intermediate preceding it.

The instability of the organothallium adducts **365** is the reason why so little stereochemical data are available. The thallation of both norbornadiene and norbornene by thallium(III) acetate in HCCl$_3$ results in products

TABLE 42. Comparison of the rates of mercuration and thallation of a series of alkenes and alkenols at 25 °C

Alkenol	Thallation[a]		Mercuration[b]		$(k_{Th}/k_{Hg}) \times 10^3$
	k(l mol^{-1} s^{-1})	Reference	k(l mol^{-1} s^{-1})	Reference	
$HOCH_2CH{=}CH_2$	1·21 ± 0·03	525	11·2 × 10^2	526	1·1
$HOCH_2CH_2CH{=}CH_2$	15·0 ± 0·5	525	8·4 × 10^3	526	1·7
$CH_3CHOHCH_2CH{=}CH_2$	12·2 ± 0·6	525	6·1 × 10^3	526	2·0
$CH_2{=}CH_2$	0·45[c]	521	5·1 × 10^3	526	0·1
$CH_3CH{=}CH_2$	0·65	521	1 × 10^5	526	0·7
$CH_3CH_2CH{=}CH_2$	63	521	8 × 10^4	526	0·8

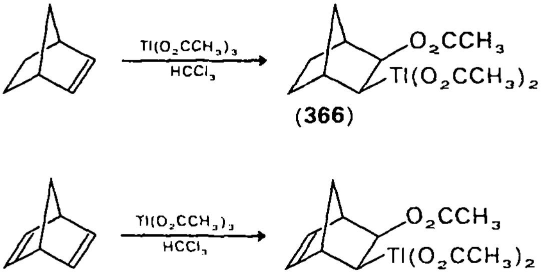
[a] 0·1 M-$HClO_4$ at 25 °C.

[b] 0·01 M-$HClO_4$ at 25 °C.

[c] 0·25 M-$HClO_4$ at 25 °C.

formed by preferential *syn* addition[528–530] (equation 169). Reacting **366** or **367** with acetic acid or carrying out the thallation reaction in acetic acid results in the formation of rearranged diacetate products.

The reaction of optically active 1,2-cyclononadiene with one equivalent of thallium(III) acetate in acetic acid forms an optically active organothallium adduct by *anti* addition[532].



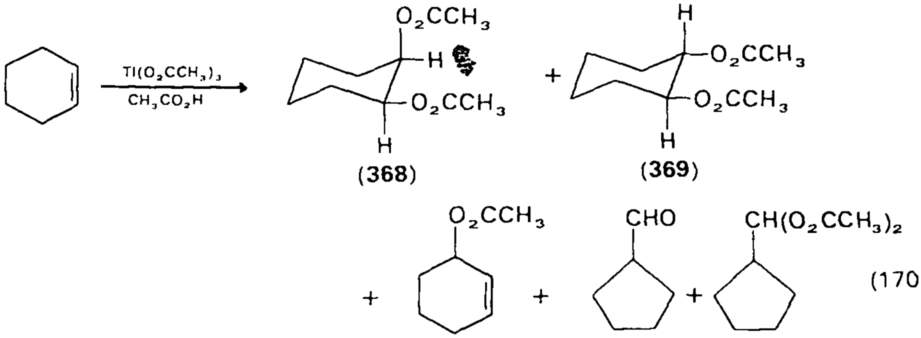
$Tl(O_2CCH_3)_3$
$HCCl_3$
O_2CCH_3
$Tl(O_2CCH_3)_2$
$Tl(O_2CCH_3)_3$
$HCCl_3$
O_2CCH_3
$Tl(O_2CCH_3)_2$

(366)

(169)

(367)

Because the organothallium intermediate **365** can react further by a number of pathways, the final product composition and its stereochemistry is often complex. For example the reaction of thallium(III) acetate in acetic acid with cyclohexene forms compounds **368–372** as products (equation 170)[514]. In anhydrous acetic acid **368**, **369** and **370** are the major products. In acetic acid containing up to 1 mol water, β-hydroxyacetates are also isolated. In anhydrous acetic acid, **369** is formed preferentially (up to 88 % of the diacetates **368** and **369**) while **368** is favoured (up to 80 % of the diacetates **368** and **369**) in aqueous acetic acid. Similarly *cis*-1,2-cyclohexanediol is formed preferentially in the reaction of cyclohexene with thallium(III) sulphate in aqueous sulphuric acid.



$Tl(O_2CCH_3)_3$
CH_3CO_2H
O_2CCH_3
H
O_2CCH_3
H
+
H
O_2CCH_3
O_2CCH_3
H
O_2CCH_3
+
+
CHO
+
$CH(O_2CCH_3)_2$

(368) **(369)**

(170)

(371) **(370)** **(372)**

Several examples of products formed by *anti* stereospecific additions have been reported. The reaction of 4-*t*-butylcyclohexene with thallium(III) sulphate in aqueous sulphuric acid is reported to form the *trans*-1,2-diol[527]. *Cis*- and *trans*-stilbene react with thallium(III) nitrate in methanol at room temperature to form four products: diphenylethanal dimethyl acetal; 1,2-dimethoxy-1,2-diphenylethane (**373**); 1,2-diphenyl-2-methoxy-1-ethylnitrate (**374**), and 1,2-diphenyl-1,2-ethanediol dinitrate (**375**). *Meso*-**373**, *erythro*-**374**, and *meso*-**375**, are formed from *trans*-stilbene while *dl*-**373**, *threo*-**374**, and *dl*-**375** are formed from *cis*-stilbene as expected from *anti* addition[517].

The experimental data obtained so far provide us with only a limited understanding of the mechanism of this reaction. The rate-determining step has been identified and the formation of rearranged products suggests that the transition state leading to these products must have considerable carbonium ion character. However no evidence is available to assist in deducing the structure of the rate-determining transition state. Also we do not know if another intermediate exists prior to the formation of the organothallium intermediate. Clearly more work needs to be done to obtain this information.

VIII. SUMMARY

From the data presented in the preceding sections, it is clear that experimental verification is lacking for all the mechanisms proposed at the beginning of this review. Despite many examples of electrophilic additions to alkenes, reaction mechanisms have been firmly established for relatively few electrophiles. Those reactions for which sufficient data are available to reach some conclusions regarding their mechanisms are summarized in Table 43. From these data, it is clear that mechanisms involving cationic intermediates are more numerous than those involving a single step. However the electronic structures of these intermediates, and the transition states leading to and from them, have not been firmly established in most cases. The major difficulty in obtaining this information is the lack of both kinetic and product data for many reactions. Studies are often carried out either on the rates or product composition of addition of a particular electrophile to an alkene but unfortunately only rarely are both determined under comparable conditions. As a result, bridged transition states and/or intermediates are invoked far too frequently without adequate experimental data.

TABLE 43. Summary of mechanistic class and intermediate structure for the addition of a number of electrophiles to several types of alkenes[a]

Electrophile	Alkyl substituted ethylene	Aryl substituted ethylene	Cyclic	Bicyclic	Dienes	Allenes
HX	o 3	o u	o 2^{b}	o u	o 2 and 3	o 2 and 3
H_2O	o 3	o 3	o u	o u	o u	o u
F_2	c or o u	c or o u	u	u	u	u
Cl_2	b 2	o^{c} 2	b u	o u	u	o u
Br_2	b $2^{d,e}$	b^{c} $2^{d,e}$	b 2	b and o u	b u	b u
I_2	b e	u	u	u	u	u

TABLE 43 (*continued*)

Electrophile	Alkyl substituted ethylene	Aryl substituted ethylene	Cyclic	Bicyclic	Dienes	Allenes
BrCl	b 2 or 3	u	u	u	u	u
ICl	b 2 or 3[d]	u	u	u	u	u
IBr	b 2 or 3	u	u	u	u	u
RCO_3H	b 2	b 2	b 2	b 2	b u	b u
ArSCl	b 2	b 2[c]	b 2	b 2	b 2	b 2
ArSeCl	b 2	b 2	u	u	b 2	u
$RSeCl_3$	b e	u e	u	u	u	u

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[a] o = open structure; b = bridged structure; u = lack of data; c = concerted mechanism; 2 = Ad_E2 mechanism; 3 = Ad_E3 mechanism.

[b] Under certain conditions, concerted termolecular mechanism. See Section II.A.

[c] Bridged ion with electron-withdrawing substituents; open ion with electron-donating substituents.

[d] Termolecular under certain conditions.

[e] Kinetically complex.

TABLE 44. Summary of ρ and ρ^+ values for electrophilic additions to series of ring-substituted styrenes and their side chain alkyl-substituted derivatives

	Parent alkenes									Other systems		
	$C_6H_5CH=CH_2$			c-$C_6H_5CH=CHCH_3$			t-$C_6H_5CH=CHCH_3$					
Electrophile	ρ	ρ^+	Solvent[a]	ρ	ρ^+	Solvent[a]	ρ	ρ^+	Solvent[a]	ρ^+	Solvent[a]	Alkene
H_3O^+		−3·42	H_2O-$HClO_4$							−3·21	H_2O-H_2SO_4	$C_6H_5C(CH_3)=CH_2$
		−3·58	H_2O-$HClO_4$									
		−4·00	H_2O-H_2SO_4									
HCl										−4·20	HOAc	$C_6H_5CH=C=CH_2$
										−2·98	HOAc	t-$C_6H_5CH=CHCH=CH_2$
Cl_2		−3·22	HOAc							−4·46	HOAc	t-$C_6H_5CH=CHCO_2H$
										−3·90	HOAc	t-$C_6H_5CH=CHCO_2H$
										−4·46	HOAc	t-$C_6H_5CH=CHCO_2CH_3$
										−3·59	HOAc	t-$C_6H_5CH=CHCOC_6H_5$
Br_2			HOAc									
	−4·87 k_2		HOAc									
	−4·38 k_3		HOAc									
	−4·20 k_x		HOAc									
ISCN	−3·69	−2·59	HOAc									
$2,4$-$(NO_2)_2C_6H_3SCl$	−2·41		HOAc	−2·3	−1·80	HOAc	−2·64	−1·90	HOAc			
				−2·99	−1·97	TCE	−3·98	−2·89	TCE			
4-ClC_6H_4SCl							−2·41		TCE			
C_6H_5SeCl	−3·20	−2·23	DCM	−2·91	−1·97	DCM	−3·13	−2·19	DCM			
$Hg(OAc)_2$	−2·25	−1·59	HOAc									

[a] DCM = dichloromethane; TCE = 1,1,2,2-tetrachloroethane; HOAc = acetic acid.

Furthermore, general mechanistic conclusions are too often drawn from the data of a reaction of an electrophile with alkenes of only one structural type or from a limited number of compounds. Conclusions based upon such data are often unwarranted. The reactions of chlorine and bromine with alkenes are particularly good examples of this. The structure of the intermediate can be either open or bridged depending upon the alkene structure. Even the mechanism of the addition of arenesulphenyl chlorides which usually involves a bridged ion can be changed by appropriate changes in the structure of the alkene and the sulphenyl halide. Thus important information can be gained by studying the rates and product composition of addition to a wide variety of alkene structural types.

The effect of solvents on the rates and products of electrophilic addition reactions has not been systematically studied. The limited data suggest that certain solvents may play a specific role in the rate-determining transition state. In certain cases, the evidence is consistent with the solvent assisting in the breaking of the bond of the electrophile. Some of the mechanisms in Table 43 which are classified as Ad_E2 may be in fact termolecular. The third molecule in the rate-determining transition state could be a solvent molecule.

Hammett correlations have been made for the addition of a number of electrophiles to ring-substituted styrenes and their derivatives. The values of ρ or ρ^+ from these correlations are collected in Table 44. Attempts have been made to relate the amount of bridging in the rate determining transition state with the value of ρ or ρ^+. Such relationships are based upon the observation that $\rho^{(+)}$ for hydration is approximately -4 while ρ for the addition of arenesulphenylchloride is only about -2. Hence it is predicted that the more negative the value of ρ the more open-ion-like is the structure of the rate-determining transition state. While there seems to be such a trend, there is one important exception. Thus the ρ values for the addition of bromine, chlorine and 2,4-dinitrobenzenesulphenyl chloride to ring-substituted styrenes are $-4{\cdot}87$, $-3{\cdot}22$, and $-2{\cdot}41$ respectively. Based upon these values of ρ one would predict the following order of increasing bridging in the rate-determining transition state: $Br_2 < Cl_2 <$ ArSCl. Such an order is contrary to that deduced from other experimental data. Since the mechanisms of the additions of bromine, chlorine and arenesulphenyl chloride are among the best understood, this inconsistency indicates that a well defined interpretation of the magnitude of ρ and ρ^+ does not yet exist.

Taft correlations appear to hold only with truncated series and thus are of limited use mechanistically. Use of six parameter Taft equations and the establishment of E_s^* values based upon the addition of disiamylborane to alkenes have yet to be proved superior to the original Taft equation[531]. Limited success has been achieved using the truncated set of alkenes comprised of ethylene and its six methyl-substituted derivatives. When $\delta = 0$, linear plots are obtained for chlorine, bromine, peroxy acids, and 4-chlorobenzenesulphenyl chloride, chromic acid, chromyl chloride, and triplet oxygen, sulphur, selenium and bromine. Linear plots are usually obtained where a bridged intermediate is postulated in the rate-determining step. It is interesting to note that as the electrophile is capable of bearing more charge in the rate-determining transition state the value of ρ^* becomes more positive. Thus the value of $|\rho^*|$ decreases in the following order $Cl_2 > Br_2(MeOH) >$ peroxy acid $> CrO_2Cl_2 > Br(4^3P) > H_2CrO_4 > Br_2(F_2ClCCFCl_2) > Se(4^3P) > S(3^3P) > O(2^3P) >$ RSCl as shown in Table 45. The absence of a linear correlation suggests either an open-ion intermediate or steric interactions, i.e. $\delta > 0$, between the alkene and the electrophile.

The one conclusion that can be drawn from the data in this review is that the area of electrophilic addition reactions to carbon–carbon double bonds is still a fertile one for research.

TABLE 45. Summary of Taft correlations of the reaction of several electrophiles with methyl-substituted ethylenes

Electrophile	$\rho^*(\delta = 0)$	Reference
$H_2O/H^{\oplus}$	No correlation	538, 539
Cl_2	−9·5	114
Br_2	−7·0	148, 537
	−4·4	540
RCO_3H	−5·8	349
RSCl	−2·4	383
RSeCl	No correlation	285
Hg^{2+}	No correlation	484, 488
Tl^{3+}	No correlation	521
H_2CrO_4	−4·5	338
CrO_2Cl_2	−5·6	533, 534
$O(2^3P)$	−3·2	536
$S(3^3P)$	−3·5	536
$Se(4^3P)$	−3·8	535, 536
$Br^a(4^3P)$	−5·0	536

[a] Atomic bromine.

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Supplement A The Chemistry of Double-Bonded Functional Groups
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CHAPTER 10

The olefin metathesis reaction*

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* In the present chapter the official IUPAC Nomenclature. described in *J. Polymer Sci.*, 8, 257 (1952), was adopted for polymeric products obtained by cycloolefin metathesis. i.e. the polymerization of *cyclopentene* produces *polypentenamer*.

For the sake of simplicity, in equations involving polymeric materials (equation 11) repeat units are presented bare. eliminating the trivial inclusion of said repeat units in square brackets with subscript '*n*'. Thus, polypentenamer is presented as $-CH_2CH_2CH{=}CHCH_2-$ and not as $[-CH_2CH_2CH{=}CHCH_2-]_n$.

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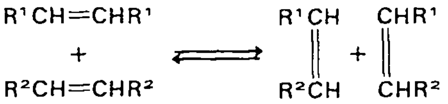
I. INTRODUCTION

Ziegler's classic discovery of low-pressure polymerization of ethylene[1–3], and Natta's subsequent demonstration of the stereoregularity of polypropylene prepared by Ziegler's catalyst[4], gave rise to an unprecedented research activity in transition metal catalysis. Curiously, the lack of a thorough understanding of the intimate electronic transformations occurring on a substrate within the coordination sphere of a metal, did not seem to hamper the experimentalist. A vast number of catalysts, capable of inducing numerous organic reactions, have been developed. Olefin metathesis is a recent addition to the long list of catalytic processes that are promoted by transition metals. Basically, it is a bond reorganization reaction characterized by the fact that the total number and type of chemical bonds remain unchanged during the transformation of reactants into products. As demonstrated later, this unique redistribution reaction proceeds by a net cleavage and reformation of carbon-to-carbon double bonds (equation 1):



$$\begin{array}{c}\mathrm{R^1CH{=}CHR^1}\\ + \\ \mathrm{R^2CH{=}CHR^2}\end{array} \rightleftarrows \begin{array}{c}\mathrm{R^1CH}\\ \| \\ \mathrm{R^2CH}\end{array} + \begin{array}{c}\mathrm{CHR^1}\\ \| \\ \mathrm{CHR^2}\end{array} \qquad (1)$$

In general, no metallic compound can act as a true catalyst unless it can fulfil two prerequisites: (a) it must be able to accommodate an incoming reactant within its coordination sphere, and (b) it should provide an exchange pathway so that an outgoing product can be replaced by an incoming reactant. These are logistic requirements that must be satisfied irrespective of the exact nature of the electronic transformations that occur on the metal. Since the metathesis reaction involves olefinic substrates primarily, it is proper to include herein a brief review on bonding and interchange of olefins on transition metals.

A. Bonding in Olefin–Metal Complexes

It is clear that the bonding of olefins to metal atoms does not involve localized σ bonding. The bonding is attributed to interaction between π

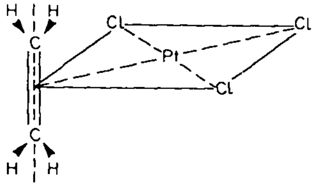


FIGURE 1. Normal π-bond in $K[PtCl_3CH_2{=}CH_2]$

electrons in the unsaturated molecule and a hybrid orbital of the metal. The structure of several stable olefin complexes has been elucidated by X-ray diffraction studies[5,6]. The most widely known is Zeise's salt $K[PtCl_3 \cdot C_2H_4]$, wherein the coordinated double bond is normal to the plane of coordination of the metal as shown in Figure 1. In complexes of unsymmetrical olefins as well as some chelates the double bonds are not necessarily normal to the metal's plane of coordination; hence, the metal atom does not lie exactly along the direction of maximum π-electron density[7]. Dempsey and Baenziger[6], who compared the structures of $[PdCl_2 \cdot C_2H_4]_2$ and $[PdCl_2 \cdot C_6H_5CH{=}CH_2]_2$ concluded that in the styrene complex the π-bond is somewhat distorted so that the palladium atom is closer to the terminal methylidene carbon atom (Figure 2). It is to be emphasized that subtle differences in structures of this type may play an important role in catalysis; in particular, affecting the steric course of a reaction.

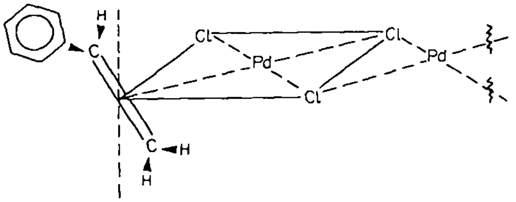


FIGURE 2. Distorted π-bond in $[PdCl_2C_6H_5CH{=}CH_2]_2$

The current metal–olefin bonding concept was developed by Dewar[8] and Chatt and Duncanson[9]. It is illustrated schematically in Figure 3. The bond consists of two parts: (a) a σ-overlap of the π-electron density of the olefin with an unfilled acceptor orbital on the metal, and (b) a 'back donation' of electron density from a filled d_{xy} or other d_π–p_π hybrid orbitals into the π^* antibonding orbitals of the carbon atoms. Measurements of the C—C bond length, which have been carried out in several complexes, are in the 1·40–1·47 Å range compared with 1·34 Å for a typical uncomplexed C=C bond. This supports the contention that an overall weakening of the double bond occurs as a result of coordination.

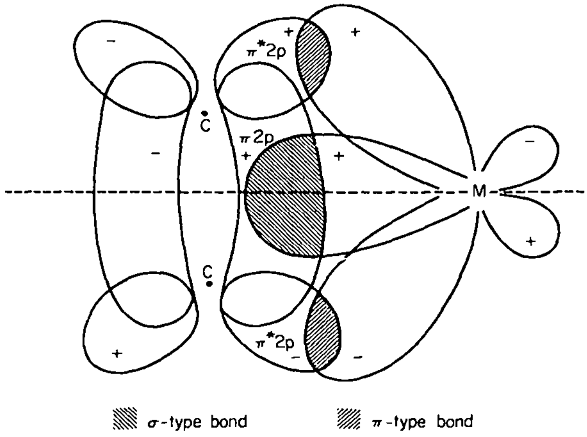
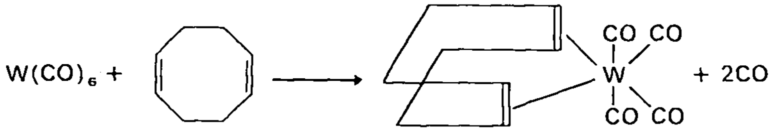
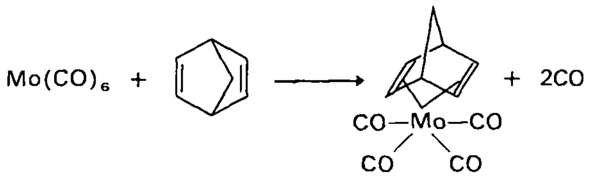


FIGURE 3. Olefin–metal bond in transition metal complexes with olefinic substrates.

The stability of olefin–metal coordination compounds varies substantially. Metals such as Pt, Pd, and Rh do form complexes with simple olefins that are quite stable and these can be isolated and characterized. Metals that form highly effective metathesis catalysts, e.g. W and Mo, are known to form stable π-complexes only with bidentate ligands, and these are limited to zero valent states. Equations 2 and 3 illustrate examples of such complexes:



(2)



(3)

Neither tungsten hexacarbonyl or its molybdenum analogue form stable, isolable, complexes with simple olefins. Tungsten and molybdenum at high oxidation states do not form stable π-complexes with 1,5-cyclooctadiene or norbornadiene.

B. Ligand Exchange in Olefin–Metal Complexes

As stated earlier, as a prerequisite for a metal to be catalytically active it must provide a pathway for the exchange of reactants with products on the reaction site. Early studies regarding olefin displacement reactions were conducted on stable platinum complexes, analogues of Zeise's salt, $K[CH_2{=}CH_2{\cdot}PtCl_3]$[10,11]. Joy and Orchin[11] noted that equilibria are attained in a matter of minutes at room temperature in the reactions:

$$[(1\text{-dodecene})\cdot PtCl_3]^- + XC_6H_4CO{=}CH_2 \rightleftharpoons [(XC_6H_4CH{=}CH_2)\cdot PtCl_3]^- + 1\text{-dodecene} \qquad (4)$$

$$[(CH_2{=}CH_2)\cdot PtCl_3]^- + CD_2{=}CD_2 \rightleftharpoons [(CD_2{=}CD_2)\cdot PtCl_3]^- + CH_2{=}CH_2 \qquad (5)$$

Further studies of this reaction were carried out by Cramer[12,13], who elegantly demonstrated that although certain metal–olefin complexes are thermodynamically stable, their respective olefinic ligands are kinetically labile and subject to a rapid interchange.

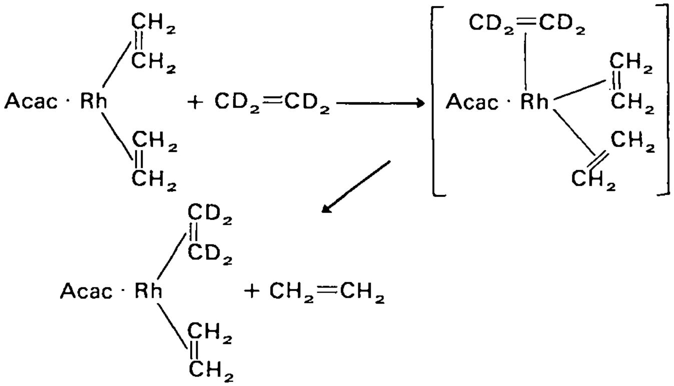
Free ethylene was not detected in the gas phase over a solution of $(C_2H_4)_2{\cdot}Rh{\cdot}Acac$ when heated to 80 °C. However, when the solution of the acetyl acetone complex was treated with C_2D_4 a rapid exchange was observed according to equation 6:

$$(C_2H_4)_2Rh\cdot Acac + C_2D_4 \rightleftharpoons (C_2H_4)(C_2D_4)Rh\cdot Acac + C_2H_4 \qquad (6)$$

Kinetic study of this process revealed that: (a) the exchange rate increased upon addition of ethylene, suggesting a bimolecular reaction; and (b) the average lifetime of a coordinated ethylene molecule on Rh^{I} is less than 10^{-4} sec at 25 °C.

In a corresponding study with the π-cyclopentadienyl complex, $(C_2H_4)_2{\cdot}Rh{\cdot}C_5H_5$, it was found that no exchange of coordinated C_2H_4 and free C_2D_4 occurred in 5 h at 100 °C, conditions far more rigorous than those employed in the acetyl acetonate complex.

Cramer rationalized the marked difference in exchange capability of the two complexes by imposing an S_N2 mechanism for the exchange step. In forming coordination bonds with Rh^{I}, the π-cyclopentadienyl group contributes six electrons and the two ethylene molecules two electrons each. Hence, Rh^{I} ($4s^2$, $4p^6$, $4d^8$) acquires ten electrons and attains the Xe inert gas configuration. On the other hand, the chelated acetyl acetone group and two ethylenes contribute a total of eight electrons—two electrons short of the inert-gas configuration. Thus Rh^{I} in $(C_2H_4)_2{\cdot}Rh{\cdot}Acac$ can accommodate an incoming olefin molecule to form an activated complex for an S_N2 exchange (equation 7), while the analogous cyclopentedienyl complex $(C_2H_4)_2 \cdot Rh \cdot C_5H_5$ cannot exchange olefins by the same mechanism.



(7)

A priori one cannot exclude a dissociative ligand-exchange mechanism prevailing in coordination compounds other than those mentioned above. In fact, Cramer[12] demonstrated that $C_5H_5 \cdot Rh \cdot (CO)_2$ undergoes exchange with ^{14}CO by a dissociative mechanism:

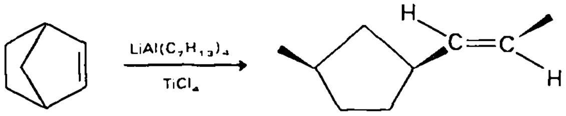
$$\begin{gathered} C_5H_5 \cdot Rh(CO)_2 \longrightarrow [C_5H_5 \cdot Rh \cdot (CO)] + CO \\ [C_5H_5 \cdot Rh \cdot (CO)] + {}^{14}CO \longrightarrow C_5H_5 \cdot Rh \cdot (CO)({}^{14}CO) \end{gathered} \tag{8}$$

Carbon monoxide was found to displace ethylene from $(C_2H_4)_2 \cdot Rh \cdot Acac$ but not from $(C_2H_4)_2 \cdot Rh \cdot C_5H_5$; alternately, ethylene did not displace CO from $C_5H_5 \cdot Rh \cdot (CO)_2$.

The relevance of ligand exchange mechanisms to catalysis in general, and to the olefin metathesis reaction in particular, is clear. While most of the research attention has been directed towards the elucidation of the transition state in the metathesis reaction, little has been focused on the logistics feature of the process. An outstanding feature of certain metathesis catalysts is their capacity to execute the reaction at very low catalyst levels. Extremely fast rates at [olefin/metal] ratios of 1–4 × 10^4 range and higher are quite common with a variety of tungsten-based catalysts. These may reach equilibrium at room temperature in a matter of seconds. Such reaction rates could not be realized if an efficient route did not exist for the exchange of incoming and outgoing olefin molecules on the active catalyst site of the metal.

II. EVOLUTION OF THE METATHESIS CONCEPT

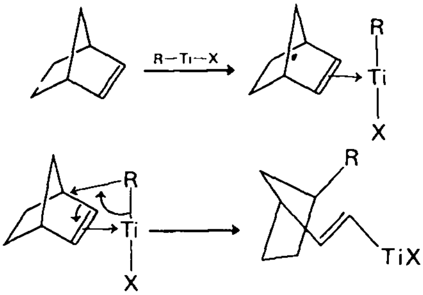
Probably the first citation of a metathesis reaction catalysed by a transition metal dates back to 1955. In a U.S. patent issued to Anderson and Merckling[14], a ring-opening polymerization process of bicyclo[2.2.1]-hept-2-ene using a Ziegler-type catalyst, was disclosed (equation 9):



(9)

Truett and coworkers[15] have subsequently demonstrated that the polymer had an intense band at 10·37 μm suggesting a substantial presence of *trans*-vinylene type of unsaturation. The band disappeared upon reactions with reagents such as perbenzoic acid, performic acid, and bromine. Ozonization of the polymer furnished 1,3-cyclopentane dicarboxylic acid. The spectrum of the di-*p*-bromophenacyl ester derivative of the diacid indicated that the ester groups had a *cis* configuration in relation to the plane of the ring. Hence, Truett and coworkers concluded that the bicyclo[2.2.1]hept-2-ene polymer had a structure comprised of 1,3-*cis* substituted cyclopentane rings which are interconnected by *trans*-vinylene groups (equation 9).

Judging from the mechanism proposed for the polymerization, it is apparent that the early researchers did not recognize the fact that their polymerization proceeds by an entirely new and novel chemistry, namely a ring-opening by cleavage of C=C bonds. Truett postulated a mechanism wherein the active catalyst is a species having titanium in a valence state lower than IV—designated RTiX for simplicity. The proposed process

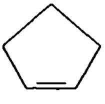


(10)

involves a coordination of the bicyclic monomer with the reduced titanium, followed by a rearrangement step which is thought of as a concerted process (equation 10).

As the cleavage of α carbon-to-carbon bond occurs, the R—Ti bond breaks and a new carbon-to-carbon bond is formed between R and the α carbon. The scheme offers a propagation mode involving a net cleavage and reformation of the single bond adjacent to the double bond. Truett conceded that his scheme does not lend itself to a good understanding of the experimentally established inversion of the hydrogens on the double bond from *cis* to *trans*. However, the proposed mechanism accounted for the *cis*-1,3-stereochemistry of the cyclopentane rings in the polymer.

Expanding on Anderson and Merckling[14], Eleuterio[16] disclosed an additional catalyst combination capable of inducing ring-opening polymerization of a variety of cycloolefins. Using a catalyst prepared from a supported molybdenum oxide on alumina, which was activated by a hydrogen reduction and further reacted with $LiAlH_4$, dicyclopentadiene, dihydrodicyclopentadiene (5,6-trimethylenebicyclo[2.2.1]hept-2-ene), and bicyclo[2.2.1]hept-2-ene were all readily polymerized by a ring-opening route. In addition to these highly strained ring systems, Eleuterio demonstrated that cyclopentene can undergo ring-opening to form the unsaturated high molecular weight polypentenamer:



$$\longrightarrow \quad -CH_2CH_2CH{=}CHCH_2- \qquad (11)$$

The i.r. spectrum of the polypentenamer indicated a mixed *cis* and *trans* vinylene unsaturation. The system was very inefficient yielding 4% product in 6 h at 100 °C.

In a research discipline far removed from polymer chemistry a significant accomplishment was realized. Banks and Bailey[17] reported their results on olefin disproportionation in which linear olefins were converted to homologues of shorter and longer carbon chains. Catalysts for the reaction consisted of $Mo(CO)_6$, $W(CO)_6$, and MoO_3 supported on alumina. The process, as originally described, was conducted at elevated temperatures (*c.* 100–250 °C) by passing the olefin feed over a stationary bed of the activated catalyst. Table 1 presents some typical data on the products distribution of various α-olefins which were disproportionated over $Mo(CO)_6$–alumina catalyst at 120 °C. The data indicate that for the propylene feed the reaction is quite clean; almost equimolar amounts of ethylene and butene are formed according to equation (12):

$$2CH_3CH{=}CH_2 \rightleftarrows CH_2{=}CH_2 + CH_3CH{=}CHCH_3 \tag{12}$$

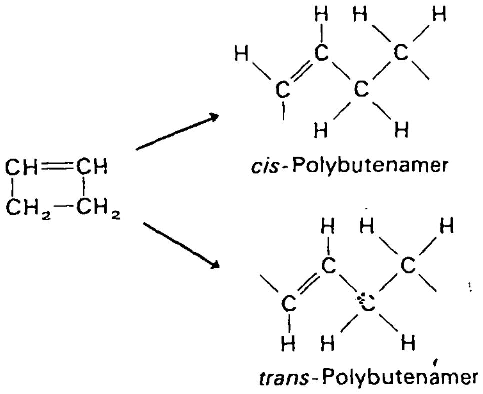
For higher α-olefins the product distributions indicate that, in addition to the redistribution process, a side reaction involving isomerization by double-bond migration takes place. If butene-1 is cleanly disproportionated one should observe only two new products in the effluent stream, namely, ethylene and hexene-3. As shown in Table 1, substantial amounts of propylene and pentenes were observed in addition to the expected ethylene and hexene-3. Banks and Bailey accounted for these results by assuming isomerization by double-bond migration side reaction (equation 13b) occurring concurrently with the redistribution (equations 13a and 13c):

$$2C_2H_5CH{=}CH_2 \rightleftarrows CH_2{=}CH_2 + C_2H_5CH{=}CHC_2H_5 \tag{13a}$$

$$C_2H_5CH{=}CH_2 \rightleftarrows CH_3CH{=}CHCH_3 \tag{13b}$$

$$C_2H_5CH{=}CH_2 + CH_3CH{=}CHCH_3 \rightleftarrows CH_3CH{=}CH_2 + C_2H_5CH{=}CHCH_3 \tag{13c}$$

In the early sixties, Natta and coworkers[18,19] reported the successful ring-opening polymerization of cyclobutene employing Ziegler-type catalysts. By choice of proper catalyst combination and adjustment of reaction conditions, cyclobutene was polymerized to high *cis*- or high *trans*-polybutenamer.



(14)

This work was later expanded to include $RuCl_3$ in polar media catalysts[20]. Table 2 summarizes these polymerization results.

In 1964 Natta's group carried out the ring-opening polymerization of cyclopentene and was able to prepare high *cis*- and high *trans*-polypentenamer[21]. Reasonable yields were obtained at very mild reaction

TABLE 1. Disproportionation of α-olefins over $Mo(CO)_6$–Al_2O_3 catalyst[a]

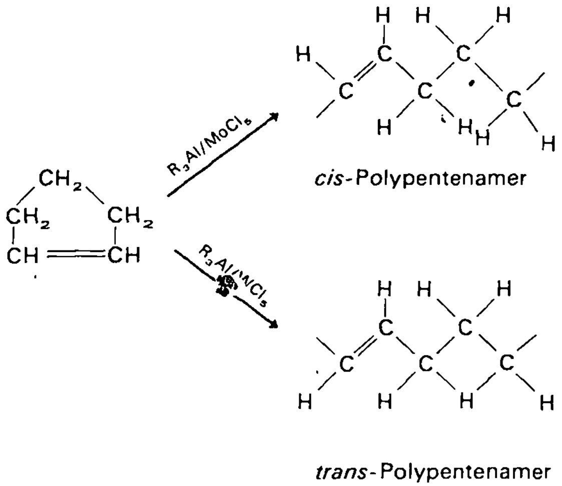
Effluent products distribution (mol-%)	Propylene	Butene-1	Pentene-1	Hexene-1
Ethylene	42	8	2	5
Propylene	—	34	21	13
Butenes	55	—	27	12
Pentenes	2	18	—	15
Hexenes	1	32	27	—
C_7+		8	23	55

[a] Data from Reference 17.

TABLE 2. Cyclobutene polymers by transition metal catalysts

Catalyst system	Polymer structure	Reference
$TiCl_4/Et_3Al/n$-heptane	Predominantly *cis*-polybutenamer	18
$TiCl_4/R_3Al$/toluene	Predominantly *trans*-polybutenamer	19
$MoCl_3/Et_3Al$/toluene	Predominantly *cis*-polybutenamer	19
$RuCl_3/H_2O$	Mixed *cis*- and *trans*-polybutenamer	20
$RuCl_3$/EtOH	*trans*-Polybutenamer	20

conditions, employing catalysts derived from WCl_6 or $MoCl_5$ in combination with organoaluminium compounds.


CH₂
CH₂
CH₂
CH
CH
R₃Al/MoCl₅
R₃Al/WCl₆
H H H
H C C
C C C
H H H H
cis-Polypentenamer
H H H
C C
C C C
H H H H
trans-Polypentenamer

(15)

This disclosure triggered an avalanche of research activity on cycloolefin ring-opening polymerization.

There are no indications that at time of disclosure Banks and Bailey or Natta's group appeared to recognize that their discoveries were indeed special cases of an entirely new metal-catalysed reaction. In fact Natta and coworkers, in their early discussions of the mechanism of ring-opening polymerization, contended that the polymerization proceeds via α-scission; that is, a propagation process wherein the single bond adjacent to the double bond of the cycloolefinic ring undergoes cleavage.

In a U.S. patent application filed in 1966 and in subsequent publications Calderon and coworkers[22–24] reported their results related to the metathesis of acyclic olefins with tungsten-based homogeneous catalysts. When an acyclic olefin was treated with a catalyst derived from WCl_6 (or the product of the reaction of equimolar amounts of WCl_6 and an alcohol) and an organoaluminium compound a unique metathetic transformation occurred (equation 16):

$$2R^1CH{=}CHR^2 \rightleftarrows R^1CH{=}CHR^1 + R^2CH{=}CHR^2 \qquad (16)$$

The reaction proceeded rapidly under mild conditions. No detectable degree of isomerization by double-bond migration was observed. Thus in the metathesis of 2-pentene only two new products were obtained, 2-butene and 3-hexene. The reaction was found to be thermodynamically controlled, and at equilibrium a 1:2:1 molar ratio for 2-butene:2-pentene:3-hexene prevailed. Calderon and coworkers further demonstrated that the reaction proceeds by a transalkylidenation route; in other words, a bond reorganization process consisting of scrambling of alkylidene moieties.

The contribution of this work to the evolution of the olefin metathesis concept was significant. First, it confirmed the notion that the seemingly unrelated olefin disproportionation and cycloolefin polymerization reactions are special cases of an entirely new transition-metal-catalysed reaction. Second, it pointed to the fact that a macrocyclization process accompanies cycloolefin metathesis.

The synthetic applications of olefin metathesis are numerous. The applicability of the reaction in areas such as enhancing the market value of petrochemical streams is obvious. Various cycloolefins can be converted into their respective high molecular weight polymers. These polymers may possess properties ranging from amorphous elastomeric to crystalline plastics. The macrocyclization scheme provides large-ring carbocyclic compounds. By proper selection of reaction conditions (high dilutions) it was shown that the metathesis of cycloolefins affords high yields of macrocyclic compounds[25]. Of special interest is the cyclic dimer of cyclooctene—1,9-cyclohexadecadiene—which is convertible to the respective musk-like ketone. Formation of catenanes has been also demonstrated by the olefin metathesis reaction. Preparation of perfectly alternating copolymers, graft copolymers, and the syntheses of dienes, trienes and other polyenes have all been accomplished by the olefin metathesis reaction. These are to be described in forthcoming sections of this chapter.

III. CATALYSTS FOR OLEFIN METATHESIS

A wide variety of metallic derivatives have been claimed to be active metathesis catalysts. The bulk of these disclosures is contained within the patent literature. It is convenient to classify these catalysts into two main categories: (a) heterogeneous catalysts—transition metal oxides or carbonyls deposited on high surface area supports, and (b) homogeneous catalysts—transition metal salts or coordination compounds in combination with selected organometallic derivatives or Lewis acids. Preparative procedures and optimization of metathesis catalysts vary substantially. Generally, homogeneous catalysts are capable of inducing the reaction under extremely mild conditions, while heterogeneous catalysts are effective at elevated temperatures. The systems complement each other in certain respects. In applications such as olefin interconversions, a solid-bed type catalyst renders itself to a continuous flow type process which is quite common in petrochemical operations. On the other hand in a cycloolefin metathesis, where the product is a high molecular weight material that is adversely affected by exposure to high temperatures, it is advantageous to carry out the reaction in the presence of a diluent and use a homogeneous catalyst which is effective under mild reaction conditions.

Numerous metals have been claimed to exhibit metathesis catalytic activity in either heterogeneous or homogeneous systems. By far the most important ones are tungsten, molybdenum, and rhenium. Most of these disclosures are in the patent literature and have been summarized in a recent review by Bailey[26].

A. Heterogeneous Catalysts

Supported heterogeneous catalysts are comprised of two main components: (a) a high-surface-area refractory material, such as Al_2O_3 or SiO_2, and (b) a promoter, such as WO_3, Re_2O_7, MoO_3, or the respective carbonyls of tungsten and molybdenum. Often, a third component is incorporated for the purpose of minimizing 'coking', improving reactivity, or reducing side reactions. The exact role of each component in a given catalyst is not easily distinguished as most combinations have been developed empirically.

1. Selected heterogeneous systems

A typical heterogeneous catalyst is prepared by impregnating the alumina support with aqueous solution of ammonium meta-tungstate, drying and activating the catalyst at 500–600°C for about 5 h, where the meta-tungstate decomposes to tungsten oxide on the surface of the support. The high-temperature activation can be carried in air or in the presence of an inert gas such as nitrogen. Molybdena–alumina catalysts are prepared similarly by calcination of alumina which is impregnated with ammonium molybdate.

In the early metathesis studies of Banks and Bailey[17], a cobalt molybdate catalyst was employed. A typical $CoO–MoO_3–Al_2O_3$ catalyst had the properties and composition listed in Table 3.

The role of the CoO has been reported as to minimize coking of the catalyst. Bradshaw and coworkers[27], who used a cobalt modified molybdena catalyst in metathesis studies of various olefins, reported a substantial degree of isomerization by double-bond migration. They were able to minimize this side reaction by treating the impregnated catalyst with a solution of sodium bicarbonate prior to activation. It has been claimed that the effectiveness of alkaline ions in improving the reaction selectivity with molybdenum catalysts follows the order: Cs > Rb > K > Na. It has also been reported that treatment of the alumina support with a strong acid, prior to impregnation with the promoter, improved the overall activity of the catalyst.

The catalyst described in Table 3 demonstrated a high efficiency for the disproportionation of propylene at 205 °C. In contrast, WO_3 catalysts

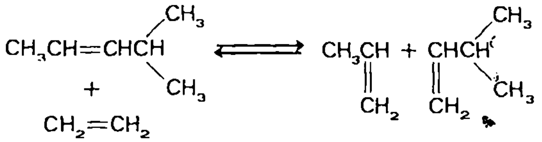
TABLE 3. Properties and composition of $CoO–MoO_3–Al_2O_3$ catalyst[a]

Surface area (m^2/g)	284
Pore diameter (average) (Å)	82
Composition (wt-%)	
CoO	3·4
MoO_3	11·0
Al_2O_3	85·6

[a] Data from Reference 26.

(3% WO_3 on silica) exhibit a high catalytic activity at higher temperatures than the $CoO–MoO_3–Al_2O_3$ combination. Thus the maximum conversion of propylene into ethylene and butene was attained only at 427 °C, but the reaction was found to be highly selective, forming only minor amounts of side reaction products.

Heterogeneous catalysts based on rhenium oxide (1–20% Re_2O_7 on Al_2O_3) have been gaining popularity recently, owing to their high activity at relatively mild reaction conditions, high selectivity, and their resistance to catalytic poisons. Butene-1 is readily converted into ethylene and hexene-3 with a selectivity of 95% at a temperature as low as 25 °C[29]. Rhenium-based catalysts were found very suitable in cross metathesis reactions of ethylene with higher olefins. For example, the preparation of 3-methylbutene-1 and propylene from ethylene and 4-methylpentene-2 is carried out at atmospheric pressure and ~100 °C with an excellent yield and no side reactions[29]:



$$CH_3CH{=}CHCH(CH_3)_2 + CH_2{=}CH_2 \rightleftharpoons CH_3CH{=}CH_2 + CH_2{=}CHCH(CH_3)_2 \quad (17)$$

Olefinic substrates that are prone to electrophilic attack by acidic reagents, e.g. isobutylene, can be metathesized cleanly with Re_2O_7 catalysts.

2. Views regarding the rate-determining step

The dependence of reaction rates on propylene pressure, in its metathesis over $WO_3–SiO_2$ catalyst, led Begley and Wilson[30] to the conclusion that the reaction proceeds by the interaction of an adsorbed propylene molecule with another molecule from the gaseous state (Rideal model), rather than an interaction of two adsorbed molecules on the catalyst surface (Langmuir–Hinshelwood model). The results for the Rideal model suggested that the catalyst surface was saturated at high pressures (20–60 atm) and the rate of reaction at a fixed temperature was determined by the rate at which the reactive molecules struck the surface sites. Davie, Whan, and Kemball[31], who studied the kinetics of propylene metathesis over a supported molybdenum hexacarbonyl on alumina catalyst, concluded that the rate controlling step is a surface reaction between two adjacently adsorbed propylene molecules (Langmuir–Hinshelwood model). The apparently contrasting conclusions of the two kinetic studies could be accommodated if one takes into consideration the fact that the later study was carried out at a temperature range which is considerably lower than Begley and Wilson's.

Davie, Whan, and Kemball[31] conducted spectroscopic studies on their $Mo(CO)_6$–Al_2O_3 catalyst in order to elucidate the nature of the active species. The catalyst, as prepared by impregnation, is simply supported $Mo(CO)_6$. However, during the activation procedure of heating the material under vacuum at an elevated temperature, a loss of carbon monoxide was detected. This was accompanied by a yellow coloration of the solid catalyst. Infrared spectroscopy confirmed a loss of symmetry which is explainable by removal of carbon monoxide. Davie, Whan, and Kemball proposed that the production of a fully active catalyst involves the loss of probably two or more carbonyl groups and their eventual replacement by propylene molecules to form a species of the general formula $Mo(CO)_x(C_3H_6)_{6-x}$, where the value of x is less than 6 and probably 3 or 4. Aside from the observation of CO loss during activation, no solid evidence has been provided for the existence of $Mo(CO)_x(C_3H_6)_{6-x}$.

Quantitative analyses for molybdenum assay in various catalysts, before and after activation, suggested the existence of a saturation point for molybdenum sites on the alumina surface. It was calculated that the apparent area per molybdenum atom at the saturation point is 340 Å^2.

3. Enhancement of catalytic activity

It was mentioned earlier that treatment of the alumina support with a strong acid, prior to impregnation with the promoter, improved the overall activity of the MoO_3–Al_2O_3 catalyst. There have been several reports concerning various techniques on how to modify heterogeneous catalysts in order to enhance their reactivity. Pennella and Banks[32] discovered that by mixing small amounts (1–4 mol-%) of chelating polyenes with the olefinic feed a marked improvement in metathesis efficiency is realized. Figure 4 illustrates this effect for the metathesis of propylene over WO_3–SiO_2 catalyst at 500 °C and atmospheric pressure. The addition of hydrocarbons such as octane or benzene do not affect the efficiency of the process. Dienes such as 1,5-hexadienes and dicyclopentadiene improve the catalyst performance somewhat, while the strongly chelating polyenes, such as 1,4-cyclohexadiene, 1,5,9-cyclododecatriene, 1,3- and 1,5-cyclooctadiene, display a marked enhancement of catalyst efficiency. The role of the chelating polyenes is not well understood. Pennella and Banks speculated

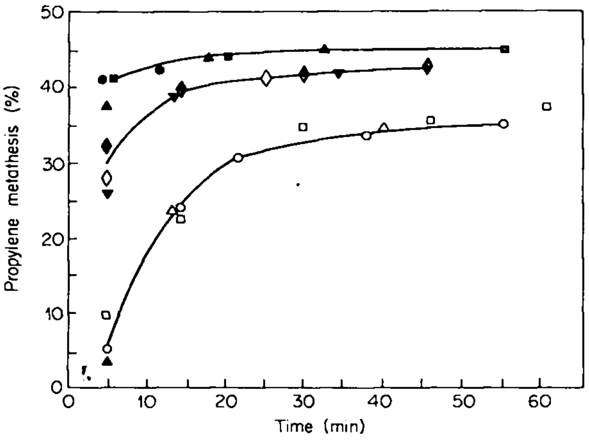


FIGURE 4. Effect of bidentate ligands on propylene metathesis: (○) control; (□) *n*-octane; (△) benzene; (◇) 1,5-hexadiene; (◆) dicyclopentadiene; (●) 1,5-cyclooctadiene; (■) 1,3-cyclooctadiene; (▲) 1,5,9-cyclododecatriene; (▼) 1,4-cyclohexadiene (Reference 32).

that the polyenes bring in additional active metathesis sites by complexation with metallic species which are otherwise inactive. This implies that the polyene is a ligand coordinated to the active site, which raises the question why does not the polyene itself undergo metathesis?

Henrici-Olivé and Olivé[33] conducted a careful study on the effects of O_2 and CO atmospheres during catalyst activation. A catalyst batch was prepared by the usual impregnation of Al_2O_3 with ammonium molybdate and activated at 500 °C for 8 h in an O_2 stream. A second catalyst was prepared as the first but it was subsequently reduced at 500 °C with CO for 3 h and flushed with argon before use. Magnetic measurements carried out on the two catalyst modifications revealed that the oxidized catalyst was diamagnetic while the reduced one was paramagnetic. Evaluation of the magnetic susceptibility data yielded 0·45 unpaired electrons per molybdenum atom, which was interpreted as assuming that 50% of the molybdenum ions were reduced from Mo^{VI} to Mo^{V} by the CO treatment. When the two catalysts were compared in propylene and butene-1 metathesis, under exactly identical reaction conditions, the reduced MoO_3–Al_2O_3 was eight-times more reactive than the oxidized version.

Henrici-Olivé and Olivé prepared a series of Ti–Mo bimetallic catalysts by first impregnating the alumina support with $Ti(OC_4H_9)_4$ and oxidizing it (8 h, 500 °C) in an air stream, followed by a second impregnation with ammonium molybdate, oxidizing, and finally activated by reduction with

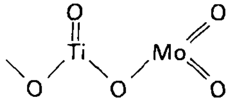
CO as described above. The reduced bimetallic catalysts were paramagnetic and demonstrated an enhanced metathesis activity as compared with catalysts containing either metal alone. Table 4 presents data which demonstrates that for a given concentration of Mo an increase in activity is experienced with increase in Ti concentration, with all other variables constant.

TABLE 4. Bimetallic catalysts in the metathesis of butene-1[a]

Run	$[\text{Mo}]^b \times 10^3$	$\frac{\text{Ti}}{\text{Mo}}$	V^c	Conversion (mol-%)[d]
1	0·1	0	0·24	0·3
2	0·1	1·9	0·24	3·4
3	0·1	9·5	0·24	11·5
4	0·1	19·0	0·24	22·4

[a] Data from Reference 33, carried out at 68 °C
[b] g-atom/g catalyst
[c] Flow rate V in mol of butene-1/(min × g-atom Mo)
[d] Products in effluent other than butene-1.

A comparison of the e.p.r. spectra of the titanium modified and unmodified catalysts reveals different line shapes and g-values of the e.p.r. signals, indicating that the environment of the Mo ions changes when titanium is incorporated in the catalyst. Henrici–Olivé and Olivé concluded that an active site in the bimetallic catalyst is a species having Ti^{IV}–Mo^{V} composite, such as:



(18)

Since TiO_2 is substantially more basic than MoO_3, it was proposed that TiO_2 acts as an electron donor in the bimetallic complex thus increasing the electron density on Mo. This will result in a weakening of the π-bonding of the olefin molecules to the metal which will enhance the rate of exchange of incoming and outgoing olefins on the active site and thus increase the overall reaction rate. It has been proposed[34] that the rate-determining step in olefin metathesis is the exchange step rather than the transalkylidenation step—this will be discussed elsewhere in the chapter.

B. Homogeneous Catalysts

Homogeneous metathesis catalysts are comprised of: (a) tungsten or molybdenum salts or their respective coordination compounds; (b) certain organometallic compounds derived from groups IA, IIA, IIIB, and IVB metals, and optionally a third component (c) which can be an oxygenated compound such as alcohol, ether, organic acid, peroxide, water, and molecular oxygen. In certain combinations Lewis acids have been employed as complete replacements for the organometallic component. In others, a Lewis acid was incorporated in conjunction with the organometallic component. Three main factors govern the reactivity of a homogeneous catalyst towards the metathesis of any given olefinic substrate. First, a selection of a proper combination of catalyst components is necessary. Second, the molar ratio of the respective components ought to be optimized. Third, a suitable catalyst mixing procedure must be established in order to obtain optimum results.

Metathesis by homogeneous catalysts are often conducted in the liquid phase in neat form or in the presence of solvent. Suitable are aliphatic and aromatic hydrocarbons, chlorinated solvents, and any other diluents that do not adversely deactivate the catalyst. Protic solvents, ethers, esters, amines and the like decompose the catalyst and cannot be used as media for olefin metathesis. As a rule, metathesis experiments must be conducted under an inert atmosphere minimizing exposure to air and moisture. Solvents and reactants must be dried rigorously prior to introduction of catalyst. Although oxygen and moisture, in controlled amounts, may act beneficially in rendering an improved catalyst activity, excess amounts of these polar agents may poison the system altogether.

1. Catalyst components and their combinations

Table 5 lists in three classes the various components which have been employed in preparing homogeneous metathesis catalysts. By no means is this list exhaustive. One must appreciate the hard task facing the experimentalist who wishes to define the 'best' catalyst combination for the metathesis of a given olefinic substrate. The number of combinations and permutations is almost endless. Further, for any given three-component combination one must establish an optimum molar ratio of the respective constituents. Are there any guidelines that may shorten this type of a screening programme? Regretfully, no. Consequently, to present a case-by-case review of homogeneous metathesis citations would not contribute to a better understanding of the reaction. Rather, particular cases will be dealt with in order to point out a salient feature of the reaction. Of course, this approach may leave out a substantial number of contributions.

A most suitable catalyst for the metathesis of acyclic internal olefins is $RAlCl_2/WCl_6/C_2H_5OH$ at an Al/W/O molar ratio of 4/1/1. This catalyst

TABLE 5. Catalyst components for homogeneous metathesis

Transition metal derivatives	Organometallics or Lewis acids	Modifiers
WCl_6, WCl_5, WCl_4	RLi, RMgCl, R_2Mg	O_2, H_2O, ROH
$WOCl_4$, WBr_5, WF_6	R_3Al, R_2AlCl, $R_3Al_2Cl_3$	RCOOH, RCOOR, RCOR
$W(CO)_6$, $W(\pi\text{-allyl})_4$	$RAlCl_2$, $AlCl_3$, R_2Zn	RCOH, RSH, RNH_2
$WCl_2(Py)_2(NO)_2$, $MoCl_5$	R_4Sn, R_2Hg	
$MoCl_2(Py)_2(NO)_2$		

is quite sluggish for the metathesis of α-olefins, but works well in cross-metathesis reactions of α-olefins with internal olefins[35]. An extensive discussion on this peculiar behaviour is presented elsewhere in this chapter. The same catalyst is very effective in the polymerization of a variety of cycloolefins, in particular cyclooctene, 1,5-cyclooctadiene, cyclododecene, and 1,5,9-cyclododecatriene. For the polymerization of cyclopentene a slight modification of the catalyst, where a chlorinated alcohol is employed in place of ethanol, leads to a much improved catalytic activity[36]. Suitable homogeneous catalysts for the metathesis of α-olefins are derived from $MoCl_2(Py)_2(NO)_2$ and $WCl_2(Py)_2(NO)_2$ in combinations with organoaluminium halides[37,38]. Best results on the metathesis of terminal olefins were obtained with the molybdenum analogue and organoaluminium sesquihalides. Catalysts derived from $MoCl_5$ have a limited scope of applications. These are essentially inactive on internal or terminal acyclic olefinic substrates. A catalyst derived from $R_3Al/MoCl_5$ demonstrated a fair catalytic activity towards the ring-opening polymerization of cyclobutene and cyclopentene[19,21], but was found completely inactive on seven-membered or larger ring size cycloolefins. The polymer produced from cyclopentene by the $R_3Al/MoCl_5$ catalyst is of high *cis* structure. This is one of a few cases where the metathesis reaction proceeds stereospecifically. An additional combination capable of polymerizing cyclopentene into high *cis*-polypentenamer is R_2AlCl/WF_6[36].

In preparing homogeneous metathesis catalysts, organoaluminium derivatives are generally superior to other organometallic compounds. Thus, $RAlCl_2/WCl_6$ or R_2AlCl/WCl_6 are substantially more active combinations than RLi/WCl_6 or R_2Zn/WCl_6. The performance of the latter systems can be vastly improved by a further addition of $AlCl_3$. The activity of the binary C_4H_9Li/WCl_6 catalyst system[39] was increased by at least 100-fold when an equimolar amount of $AlCl_3$ was added to the reaction (Li/W/Al molar ratio of 2:1:1)[40]. The role of the aluminium component appears to be multipurpose. The organoaluminium compound probably acts as a reducing agent as well as a complexing agent with the transition metal component of the catalyst. It has been shown[40] that WCl_4, obtained by reduction of WCl_6 with H_2 at high temperatures, is not an active metathesis catalyst; however, in combination with $AlCl_3$ (Al:W molar ratio of 2–4/1), a highly active catalyst was obtained. In addition, metathesis catalysts of fair activity are obtainable from $AlCl_3/WCl_6$ and $AlBr_3/WCl_6$ combinations[40,41].

Recent work connected with cyclopentene polymerization reported the substitution of the organoaluminium component with organotin yet maintaining an ultra high active catalyst[42]. In this specific report ether has been used as a catalyst modifier.

2. Procedures for catalyst preparation

A dilute solution of WCl_6 (0·05 M) in an aromatic solvent, e.g. benzene, chlorobenzene, is treated with an equimolar amount of neat ethanol under a N_2 atmosphere. During this step, which presumably affords $WCl_5OC_2H_5$, a colour change from dark violet to red burgundy is observed. The reaction is accompanied by the evolution of a stoichiometric amount of HCl[43]. The moderately stable $WCl_5OC_2H_5$ slowly decomposes into C_2H_5Cl and an orange crystalline precipitate, presumably $WOCl_4$[44].

The organoaluminium component is handled separately as a solution in a hydrocarbon solvent. It is not recommended to preform and store as a single reagent the organoaluminium and the alcohol-modified tungsten hexachloride. When these come in contact, an active metathesis catalyst is formed instantaneously, and the activity decays at a moderate rate[45]. Therefore, it is best to introduce the two components into the reactant mixture consecutively.

By analogy with classical Ziegler–Natta catalysts[46], the following sequence of reactions is postulated:

$$C_2H_5OWCl_5 + C_2H_5AlCl_2 \longrightarrow C_2H_5OWCl_4C_2H_5 + AlCl_3 \qquad (19)$$

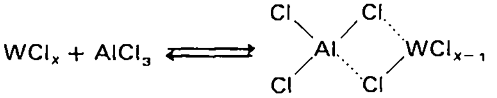
$$C_2H_5OWCl_4C_2H_5 \longrightarrow C_2H_5OWCl_4 + C_2H_5\cdot \qquad (20)$$

$$2C_2H_5\cdot \longrightarrow C_2H_6 + C_2H_4 \qquad (21)$$

$$2C_2H_5\cdot \longrightarrow C_4H_{10} \qquad (22)$$

The formation of ethane and ethylene during the reaction of $C_2H_5OWCl_5$ and $C_2H_5AlCl_2$ has been confirmed experimentally[40]. A similar sequence of reactions as equations 19–22 may reduce the pentavalent tungsten further to form $C_2H_5OWCl_3$. Additionally, pentavalent tungsten may undergo disproportionation into a mixture of hexa- and tetravalent tungsten species.

During the reduction processes described above $AlCl_3$ is being formed. Earlier it was mentioned that $AlCl_3$ displays a co-catalytic activity. One may speculate that the reduced tungsten species may associate via μ-chloride bonding with $AlCl_3$ (equation 23) wherein the aluminium and tungsten are interconnected by bridging chloride ligands, and/or display acid–base type equilibria (equation 24)



(23)

$$WCl_x + AlCl_3 \rightleftharpoons WCl^{+}_{x-1} + AlCl^{-}_4 \qquad (24)$$

The sequence of reactions presented in equation 19–24 suggests that the formation of active sites involves removal of chloride ions from the coordination sphere of the metal, thus providing vacant sites for the incoming olefinic ligands. This can be accomplished either by a reduction sequence (equations 19–20) or by an acid–base equilibrium (equation 24) or both. In either case the role of the aluminium component is important. It may be further speculated that, by association via μ-chloride bonding (equation 23) the aluminium component retards the oligomerization tendencies of reduced tungsten chlorides.

A sequence similar to equations 19–22 was proposed for the reaction of WCl_6 with $(C_2H_5)_4Sn$[42].

$$WCl_6 + (C_2H_5)_4Sn \longrightarrow C_2H_5WCl_5 + (C_2H_5)SnCl \qquad (25)$$

Grahlert and Thiele[47], who studied this reaction at −30 °C, claimed that the green unstable $C_2H_5WCl_5$ intermediate can be stabilized by complexation with strong N-donors, e.g. 2,2'-bipyridine. Pampus and coworkers[42], using n.m.r. spectroscopy (H = 220 MHz) in combination with g.l.c., were able to demonstrate that at −30 °C approximately 50% of the reacted ethyl radicals are bound to tungsten while the rest undergo disproportionation into ethane and ethylene. They further suggested the formation of $C_2H_5WCl_4$ by a synchronous or a step-by-step mechanism. Unlike $C_2H_5WCl_5$, $C_2H_5WCl_4$ can be stabilized by weak donors, especially ethers. In absence of olefinic substrates, solutions of ether-stabilized $C_2H_5WCl_4$ in chlorobenzene are moderately stable (10%

decomposition in 24 h at 18 °C). Introduction of cyclopentene to the solution triggered an immediate evolution of ethyl radicals, suggesting displacement of the ethyl groups by the cycloolefinic ligands. E.s.r. spectra of the mixture showed only one signal at 3920 G, which Pampus and coworkers interpreted as due to a W^{IV}-complex.

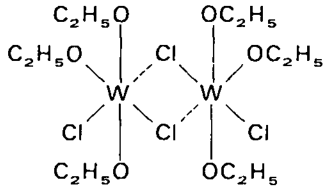
3. The reaction of hydroxy modifiers with WCl_6

The reaction of hydroxy modifiers with WCl_6 was studied by Klejnot[48], Funk and Naumann[49], and more recently in connection with the olefin metathesis catalysts by Hocker and Jones[50]. It was mentioned earlier that the equimolar reaction of WCl_6 with ethanol leads to the eventual formation of $C_2H_5OWCl_5$, which slowly decomposes by the release of C_2H_5Cl. Hocker and Jones, who examined the n.m.r. spectrum of freshly reacted $[WCl_6 + C_2H_5OH]$ and compared it with that of an aged product, concluded that the formation of $C_2H_5OWCl_5$ is in fact a two-step process:

$$WCl_6 + 2C_2H_5OH \longrightarrow (C_2H_5O)_2WCl_4 + 2HCl \qquad (26)$$

$$(C_2H_5O)_2WCl_4 + WCl_6 \longrightarrow 2C_2H_5OWCl_5 \qquad (27)$$

According to Klejnot, when WCl_6 is reacted with a large excess of ethanol, a dimeric pentavalent tungsten compound is being formed which has the structure illustrated in equation (28):



(28)

Funk and Naumann prepared a similar dimeric pentavalent tungsten complex, $[WCl_3(OCH_3)_2]_2$, which was found to be an active metathesis catalyst when reacted further with $C_2H_5AlCl_2$[49].

The highly stable phenoxy-substituted tungsten derivatives, $(C_6H_5O)_4WCl_2$ and $(C_6H_5O)_6W$ exhibit little or no metathesis activity in combinations with organoaluminium compounds.

In summary, the importance of oxygenated modifiers in rendering highly active homogeneous metathesis catalysts is being stressed. Although some experimental results that clarify the nature of the reaction of these modifiers with the transition metal components are available, they do not explain why this modification causes a vast improvement in activity.

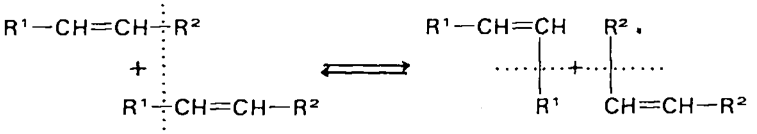
IV. SALIENT FEATURES

A. Redistribution by Transalkylidenation

Metathesis reactions have been classified among redistribution reactions[51]. The term 'redistribution reaction' has been recently applied specifically to reorganization processes involving substituents about a given central atom or moiety[52,53], frequently with the added criterion that these should approach equilibrium. Such reactions are common in organometallic and inorganic chemistry, and methods for evaluating these systems have been established. For hydrocarbons, thermodynamically-controlled redistribution reactions are virtually unknown due to the absence of accessible, low-energy pathways. Notwithstanding the fact that the reorganization process in olefin metathesis does not involve interchange of substituents about a central atom or moiety, nevertheless, the reaction is of special interest since it is thermodynamically controlled and it possesses the basic features of a redistribution reaction.

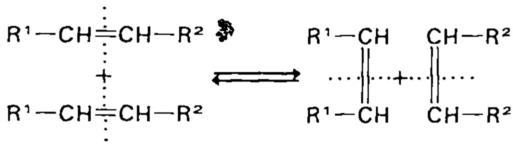
Experiments with deuterated olefins were designed to elucidate the cleavage and reformation scheme in olefin metathesis[22–24]. Table 6 presents the parent mass spectra results of a metathesis reaction between butene-2 and butene-2-d_8. Two schemes were visualized as possible routes for the reaction: (a) a transalkylation scheme, formally involving the interchange of alkyl groups via α-scission (equation 29); and (b) a transalkylidenation scheme involving the cleavage of the double bond itself as a means of redistributing alkylidene species (equation 30).

Transalkylation:



$$\begin{array}{c} R^1\!-\!CH{=}CH\!-\!R^2 \\ + \\ R^1\!-\!CH{=}CH\!-\!R^2 \end{array} \rightleftharpoons \begin{array}{ccc} R^1\!-\!CH{=}CH & & R^2 \\ | & + & | \\ R^1 & & CH{=}CH\!-\!R^2 \end{array} \qquad (29)$$

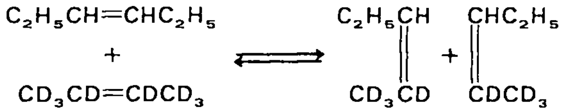
Transalkylidenation:



$$\begin{array}{c} R^1\!-\!CH{=}CH\!-\!R^2 \\ + \\ R^1\!-\!CH{=}CH\!-\!R^2 \end{array} \rightleftharpoons \begin{array}{ccc} R^1\!-\!CH & & CH\!-\!R^2 \\ \| & + & \| \\ R^1\!-\!CH & & CH\!-\!R^2 \end{array} \qquad (30)$$

The transalkylation scheme anticipates formation of $C_4H_6D_2$, $C_4H_5D_3$, $C_4H_3D_5$ and $C_4H_2D_6$, while the transalkylidenation scheme anticipates one and only one new olefin, namely, $C_4H_4D_4$. The data in Table 6 demonstrate that the only new product formed in the metathesis of butene-2 and butene-2-d_8 had a mass of 60, corresponding to $C_4H_4D_4$.

The results positively eliminate a simple transalkylation scheme as being a significant contributor to the olefin metathesis reaction. A further confirmation of the results reported in Table 6 was obtained from the cross metathesis of butene-2-d_8 and hexene-3, where the only new product observed had a mass of 74 corresponding to $C_5H_6D_4$. This can be accounted for by the transalkylidenation equilibrium as depicted in equation (31):



$$\begin{array}{c} \mathrm{C_2H_5CH{=}CHC_2H_5} \\ + \\ \mathrm{CD_3CD{=}CDCD_3} \end{array} \rightleftharpoons \begin{array}{c} \mathrm{C_2H_6CH} \\ \| \\ \mathrm{CD_3CD} \end{array} + \begin{array}{c} \mathrm{CHC_2H_5} \\ \| \\ \mathrm{CDCD_3} \end{array} \qquad (31)$$

TABLE 6. Metathesis of 2-butene with 2-butene-d_8 (76/24)[a]

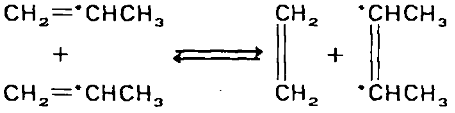
Transalkylation	Transalkylidenation	Mass	Observed intensity[b]	Theory[c]
$CH_3CH{=}CHCH_3$	$CH_3CH{=}CHCH_3$	56	100	100
$CH_3CD{=}CDCH_3$	—	58	<1	0
$CH_3CH{=}CHCD_3$	—	59	<1	0
—	$CH_3CH{=}CDCD_3$	60	61	63
$CH_3CD{=}CDCD_3$	—	61	<1	0
$CD_3CH{=}CHCD_3$	—	62	<1	0
$CD_3CD{=}CDCD_3$	$CD_3CD{=}CDCD_3$	64	11	10

[a] Data from Reference 23.

[b] Values were adjusted by eliminating background spectra of the C_4D_8 and C_4H_8 fragmentation components.

[c] Based on a random distribution of [$CH_3CH{=}$] and [$CD_3CD{=}$] moieties for $C_4H_8/C_4D_8 = 76/24$.

Mol and coworkers[54] carried out an analogous study on the metathesis of propylene over a rhenium oxide/alumina catalyst. Analysis of the ethylene and butene-2 produced by the metathesis of [2-^{14}C]propylene revealed that the ethylene showed no radioactivity while the butene had a specific radioactivity twice as much as that of the starting propylene. The results conform with a double bond cleavage reaction scheme (equation 32):



$$\begin{array}{c} \mathrm{CH_2{=}^{*}CHCH_3} \\ + \\ \mathrm{CH_2{=}^{*}CHCH_3} \end{array} \rightleftharpoons \begin{array}{c} \mathrm{CH_2} \\ \| \\ \mathrm{CH_2} \end{array} + \begin{array}{c} \mathrm{^{*}CHCH_3} \\ \| \\ \mathrm{^{*}CHCH_3} \end{array} \qquad (32)$$

Further experiments with [1-^{14}C]propylene and [3-^{14}C]propylene show that the methyl groups of the respective propylenes retain their identities throughout the metathesis reaction, hence excluding the formation of any π-allylic intermediate at any stage of the reaction. Clark and Cook[56] arrived at similar conclusions using radioactive propylene over CoO–MoO_3–Al_2O_3 catalyst when they carried out the reaction at low enough temperature where isomerization does not take place (<60 °C). At higher temperatures π-allyl complexes are involved specifically in providing a pathway for migration of the double bond along the carbon skeleton of the olefinic substrates.

B. Random and Non-random Distributions of Alkylidene Groups

In the metathesis of acyclic internal olefins of the general formula $R^1CH{=}CHR^2$, the contribution of enthalpy to the free energy of the reaction is negligible ($\Delta H \simeq 0$); thus, the equilibrium distribution of products is virtually random as dictated by entropy considerations. In contrast, the thermodynamic considerations involved in cycloolefin metathesis are quite different: In acyclic olefins, the total number of molecules and the total number and type of chemical bonds is unchanged; in cycloolefins, the total number of molecules drastically decreases as a result of the 'ring-opening' polymerization. In addition, ring-strain energy is released and the high molecular weight, flexible species produced can assume many conformations—a factor that highly influences the entropy change of the system. Hence, since metathesis of cycloolefins are not thermoneutral in general, the distribution of products at equilibrium is not predictable by random statistics.

1. Metathesis of acyclic vinylenic substrates

A series of metathesis experiments on various mixtures of pentene-2 and dodecene-6, in which the relative concentrations of [$CH_3CH{=}$], [$C_2H_5CH{=}$], and [$C_5H_{11}CH{=}$] were varied, demonstrated[24] that the concentrations of the anticipated reaction components are in excellent agreement with those predicted for by a random scrambling of constituents as summarized in Table 7. It was necessary to establish that a true equilibrium was achieved independently of catalyst concentration. The relative constancy of equilibrium constants K_1 and K_2 in Table 7 indicates that an equilibrium was reached in each experiment in which reaction was

TABLE 7. Metathesis of pentene-2 with dodecene-6[a]

Expt. No.	$[WCl_6 + C_2H_5OH]$[b] (M × 10^4)	$[C_5]_0$ (M)	$[C_{12}]_0$ (M)	Mole fraction after reaction f_4	f_5	f_6	f_8	f_9	f_{12}	Equilibrium constants[d] K_1	K_2
1	3·75	0·73	0·25	0·123	0·252	0·138	0·177	0·174	0·0665	0·267	1·83
2	5·00	0·73	0·25	0·115	0·230	0·136	0·167	0·182	0·0645	0·296	2·05
3	6·25	0·73	0·25	0·107	0·227	0·133	0·166	0·187	0·0700	0·276	1·95
4	7·50	0·73	0·25	0·084	0·189	0·116	0·143	0·157	0·0620	0·273	1·91
Theory 1–4				0·138	0·276	0·138	0·190	0·190	0·0655	0·250	2·00
5	3·75	0·485	0·50	No reaction							
6	5·00	0·485	0·50	0·056	0·115	0·064	0·240	0·244	0·256	0·271	1·99
7	6·25	0·485	0·50	0·047	0·097	0·057	0·198	0·219	0·230	0·285	1·94
8	7·50	0·485	0·50	0·052	0·108	0·061	0·213	0·224	0·247	0·272	1·79
Theory 5–8				0·061	0·121	0·061	0·250	0·250	0·258	0·250	2·00
9	3·75	0·24	0·75	No reaction							
10	5·00	0·24	0·75	No reaction							
11	6·25	0·24	0·75	0·015	0·030	0·017	0·171	0·173	0·548	0·283	1·80
12	7·50	0·24	0·75	0·013	0·028	0·016	0·163	0·163	0·531	0·265	1·68
Theory 9–12				0·015	0·030	0·015	0·184	0·184	0·571	0·250	2·00

[a] Data from Reference 23.

[b] Reactions conducted at Al/W/O ratio 4/1/1.

[c] Values of f_i were calculated as the fraction of each olefin to the total initial molar concentration $[C_5]_0 + [C_{12}]_0$.

[d] $K_1 = \dfrac{f_4 f_6}{f_5^2}$; $K_2 = \dfrac{f_8 f_9}{f_5 f_{12}}$

observed. The average values of $K_1 = 0{\cdot}276$ and $K_2 = 1{\cdot}88$ are sufficiently close to their theoretical values (0·25 and 2·00, respectively) to conclude that these reactions are essentially thermoneutral. The data of Table 7 suggests that, in each series of reactions, at the very lowest catalyst level sufficient to trigger the reaction, equilibrium is being established. Further additions of catalyst caused some side reactions. Hence the results from experiments 1, 6, and 11 (the most selective) were compared in Figure 5 with curves which represent the products distribution for the ideal case of random scrambling. The coincidence of the experimental points with theory is excellent.

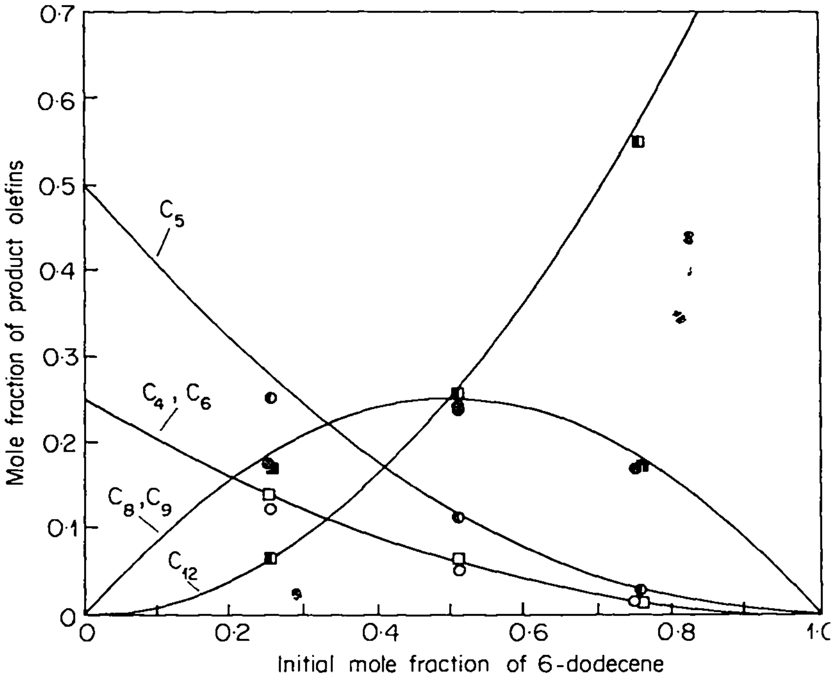
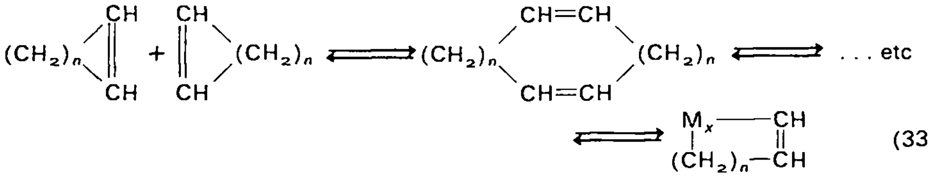


FIGURE 5. Metathesis of pentene-2 with dodecene-6. Solid lines represent theory for ideal random composition: (○) C_4, butene-2; (◐) C_5, pentene-2; (□) C_6, hexene-3; (●) C_8, octene-2; (■) C_9, nonene-3; (◧), dodecene-6. Reprinted with permission from Calderon and coworkers, *J. Amer. Chem. Soc.*, **90**, 4133 (1968). Copyright by the American Chemical Society.

2. Metathesis of cycloolefinic substrates

As mentioned earlier metathesis of cycloolefins need not be thermoneutral processes. It has been argued[56] that the metathesis of cycloolefins, when carried out in the complete absence of acyclic olefins, provides a polymerization via macrocyclization process (equation 33):



(33)

where M = $—(CH_2)_n—CH{=}CH—$, and $x = 0, 1, 2, 3. \ldots$

A general equilibrium for this process can be represented as:

$$R_{x+y} + R_{m+n} \rightleftarrows R_{x+m} + R_{n+y} \tag{34}$$

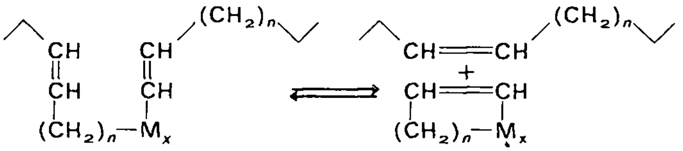
where 'R_i' represents a ring of 'i' repeat units.

The following important implications, which bear directly on the nature of this unique macrocyclization, have precipitated out of the understanding of the basic properties of the olefin metathesis reaction.

(a) A given alkylidene portion of a double bond of a cycloolefin monomer which has undergone metathesis, and thus become an integral part of a higher molecular weight species, remains eligible for further reaction and may participate in additional transalkylidenation steps with other double bonds, which may be constituents of another cycloolefin monomer unit, another macrocycle, or the same macrocycle.

(b) This polymerization possesses the basic features of equilibrium polymerization.

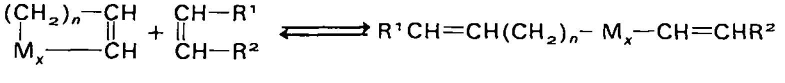
(c) Macrocyclic species, resulting from intermolecular ring enlargement of two smaller rings or from the intramolecular metathesis of two double bonds on the same macromolecule (equation 35) are present in the polymerization mixture at equilibrium.



(35)

(d) The composition of macrocyclic species depends on the spacing between double bonds in the macromolecule (number of $—CH_2—$ groups between neighbouring double bonds).

(e) A metathesis reaction between a macrocycle and an acyclic olefin leads to scission of the ring structure resulting in an open chain polymer as indicated in equation (36).



$$\begin{matrix}(CH_2)_n-CH \\ | \quad\quad\quad \| \\ M_x-\!-\!-CH\end{matrix} + \begin{matrix}CH-R^1 \\ \| \\ CH-R^2\end{matrix} \rightleftharpoons R^1CH{=}CH(CH_2)_n-M_x-CH{=}CHR^2 \qquad (36)$$

Under such conditions a ring-chain equilibrium system is possible as described in equation (37).

$$C_{m+n} \rightleftharpoons C_m + R_n \qquad (37)$$

where C_m is a chain of m repeat units and R_n is a ring of n repeat units.

The quantitative determination of the concentration of each cyclic or open-chain component in an equilibrated cycloolefin metathesized system is experimentally unattainable. Thus, a complete thermodynamic characterization of cycloolefin metathesis is not achievable as is the case for acyclic olefins. Nevertheless, of the vast number of equilibria that can exist in principle in a given system, one was fully characterized, namely, the monomer–polymer equilibrium for cyclopentene–polypentenamer case[57]. Table 8 summarizes the results of a series of cyclopentene polymerization experiments where the equilibrium cyclopentene concentration was determined at various temperatures. Theory predicts the relationship:

$$\ln\,[\mathrm{M}]_e = \frac{\Delta H_p}{RT} - \frac{\Delta S_p^0}{R} \qquad (38)$$

where $[\mathrm{M}]_e$ is the equilibrium monomer concentration, ΔH_p the enthalpy change during polymerization, and ΔS_p^0 the standard entropy change accompanying the polymerization when the monomer concentration is 1 M. Figure 6 illustrates the plot of ln $[\mathrm{M}]_e$ vs. $1/T$ for cyclopentene based on

TABLE 8. Equilibrium cyclopentene concentration vs. temperature[a]

T(°C)	$[\mathrm{M}]_e$ (mol × l^{-1})
0	0·51
10	0·70
20	0·88
30	1·19

[a] Data from Reference 57.

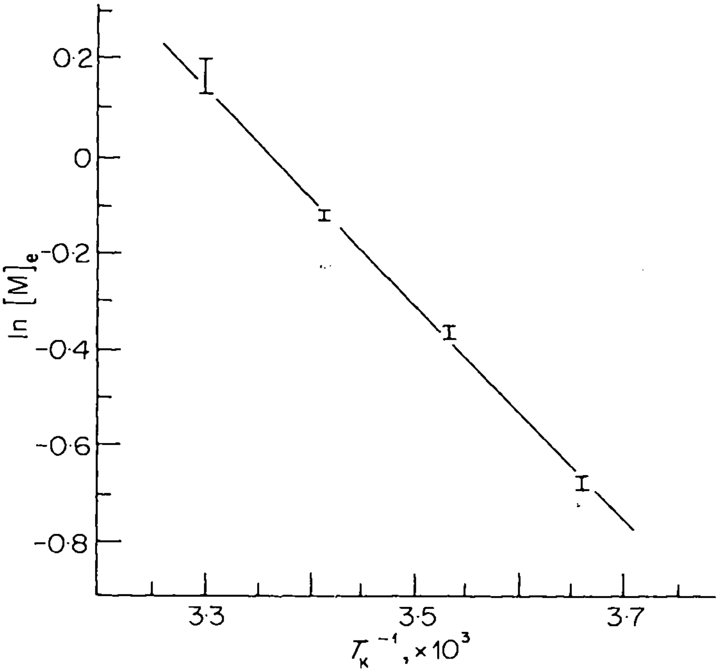
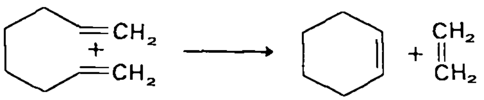


FIGURE 6. Cyclopentene metathesis. Dependence of equilibrium monomer concentration, $[M]_e$, on temperature (Reference 57).

the results of Table 8. From this plot values of $-4{\cdot}4$ kcal/mol and $-14{\cdot}9$ cal/mol deg were calculated for ΔH_p and ΔS_p^0 respectively.

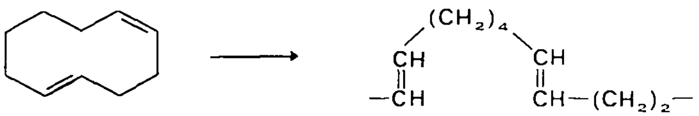
The enthalpy value obtained herein is close to the ring strain energy value for cyclopentene (4·9 kcal/mol) reported by Cox[58]. This is consistent with the contention that in the metathesis of strained-ring cycloolefins the main contribution to ΔH_p is strain energy. The negative entropy value points to the fact that cyclopentene would have been thermodynamically unmetathesizable if it were a strain-free cyclic compound. This indeed is the case for cyclohexene.

Dainton and coworkers[59] who calculated the enthalpies, entropies and free energies for cycloalkanes of various ring sizes, concluded that the entropy change for the virtually strain-free six-membered ring is negative ($\Delta S_p^0 = -2{\cdot}5$ cal/mol deg). Further, as rings grow larger (eight-membered rings and up) their respective entropy values change sign and become positive, thus becoming thermodynamically eligible for ring-opening, regardless of the magnitude of their ring-strain energy. The relatively strain-free 1,9,17-cyclooctatetraeicosatriene (a 24-membered ring) was shown to undergo metathesis readily[57,60]. The six-membered ring 'syndrome' is dramatically demonstrated in the works of Kroll and Doyle[61] and Teyssie[62]. Using a molybdenum-based catalyst on 1,7-octadiene substrate, Kroll and Doyle obtained ethylene and cyclohexene exclusively (99% selectively):



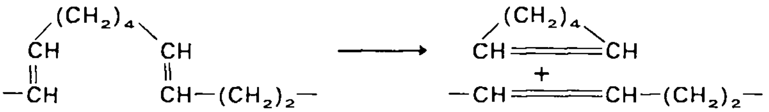
(39)

Teyssie carried out a metathesis experiment on 1,5-cyclodecadiene. At the initial stages of the reaction he obtained a high molecular weight product having the expected structure as indicated in equation (40):



(40)

After allowing the metathesis reaction to proceed further, a sizable amount of cyclohexene was detected and the resulting polymeric structure was equivalent to polybutenamer:



(41)

These examples demonstrate that whenever two double bonds are spaced by a sequence of four methylene groups under metathesis conditions, they will prefer to undergo intramolecular transalkylidenation to yield cyclohexene, since a hexenamer unit is thermodynamically more stable in a ring form than in an open chain form.

C. Geometrical Isomerization in Metathesis Reactions

The steric course of the metathesis reaction of acyclic olefins is generally non-selective. A fully metathesized system provides mixtures of the respective geometrical isomers, and the *cis–trans* composition for each olefin is thermodynamically favoured at equilibrium. There is not any inherent reason for this behaviour. Simply, a stereoselective catalyst for the metathesis of open-chain olefins has [illegible] to be discovered. (In contrast, there are at least two catalyst systems, $R_3Al/MoCl_5$ and R_2AlCl/WF_6, that demonstrate *cis* selectivity in the metathesis of cyclopentene^{21,36}.) An extensive study of the steric course of reaction for pure *trans*- and *cis*-pentene-2, over an entire range of conversions using varied Al/W ratios, was conducted^{24}. The changes in composition of each component vs. conversion for *cis*- and *trans*-pentene-2 are presented in Figures 7 and 8, respectively. The isomer composition of the initially-formed butene-2 and hexene-3 is of particular interest. It is evident that substantial amounts of both *cis* and *trans* isomers of the two product olefins were formed at the outset, whereas the composition of the residual pentene-2 very gradually approached its equilibrium *cis* content. It was also observed that the initially-formed butene and hexene were somewhat higher in *cis* content than the equilibrium values for these olefins, regardless of the structure of the initial pentene. Further, the *cis/trans* isomer ratio of butene-2 was always different from that of hexene-3. Finally, the steric course of the reaction was independent of the Al/W ratio for $1 \leq Al/W \leq 4$.

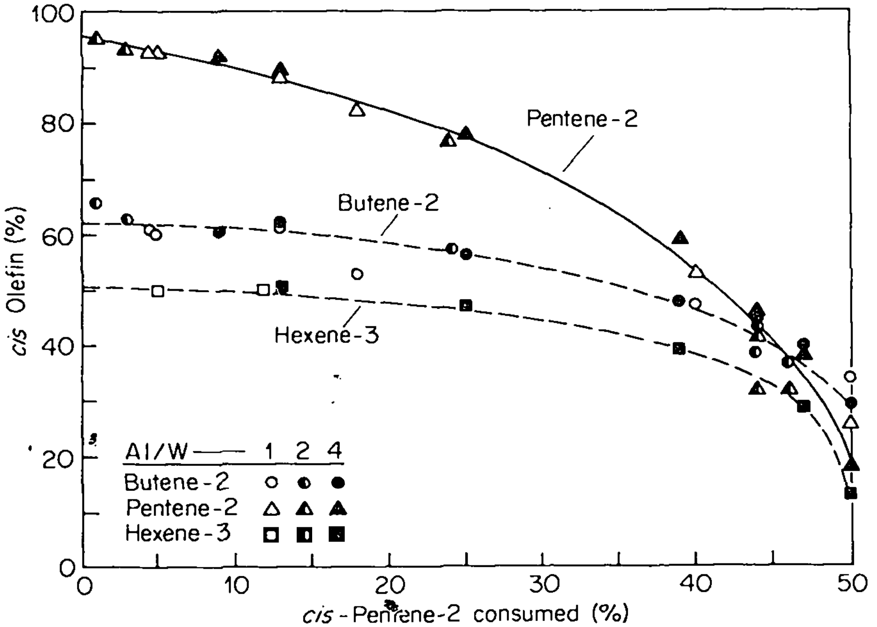


FIGURE 7. Metathesis of *cis*-pentene-2. Effect of conversion on structure. Reprinted with permission from Calderon and coworkers, *J. Amer. Chem. Soc.*, **90**, 4133 (1968). Copyright by the American Chemical Society.

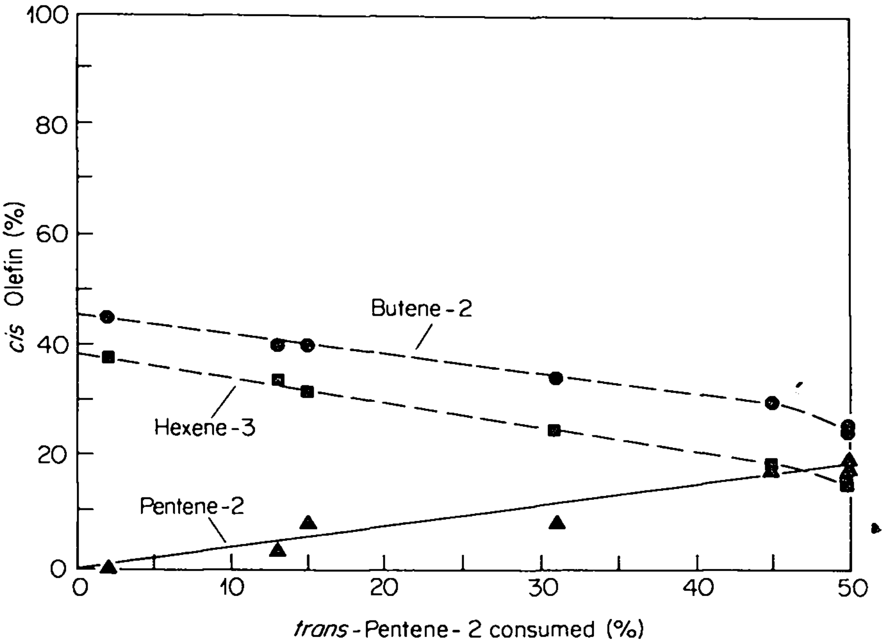


FIGURE 8. Metathesis of *trans*-pentene-2. Effect of conversion on structure. Reprinted with permission from Calderon and coworkers, *J. Amer. Chem. Soc.*, **90**, 4133 (1968). Copyright by the American Chemical Society.

The occurrence of considerable amounts of both geometrical isomers of butene-2 and hexene-3 during the initial stages of reaction, in the absence of extensive isomerization of residual pentene-2 (Figures 7 and 8), demonstrates that the metathesis reaction itself is the principal means of geometrical isomerization.

Table 9 lists the average equilibrium *cis* contents and free energy changes for the *trans*-to-*cis* transformations for several olefins, as obtained in numerous metathesis experiments of a variety of olefinic reactants. These values have a distinct correlation with steric factors in the structure of the olefin as might be expected. Butene-2, having only two methyl substituents on the double bond, has the highest *cis* content at equilibrium and hence the lowest free energy difference between *trans* to *cis*. The 2-alkenes, having one methyl group and one higher *n*-alkyl group as substituents, have a *cis* content of ~21 %, which corresponds to the *trans* isomer being 800 cal/mol more stable than the *cis* isomer. The 3-, 4-, 5-, and 6-alkenes, in which both substituents are high *n*-alkyl groups, have equilibrium *cis* contents of 16 % and a *trans*-to-*cis* free energy difference of about 1000 cal/mol.

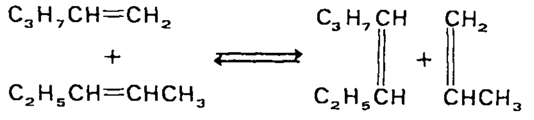
TABLE 9. Equilibrium *cis* content of internal olefins[a]

Olefin	% *cis*[b]	ΔF (cal/mol)[c]
Butene-2	28	560
Pentene-2	21	790
Hexene-2	19	870
Heptene-2	21	790
Octene-2	21	780
Hexene-3	14	1090
Heptene-3	15	1040
Nonene-3	16	1000
Octene-4	17	970
Decene-5	18	930
Dodecene-6	17	940

[a] Data from Reference 24.
[b] Average value to the nearest percent.
[c] ΔF at 25 °C for *trans* ⇄ *cis* in benzene. Average value to the nearest 10 cal/mol.

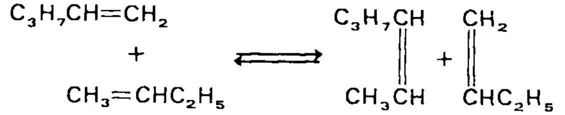
D. Structural Selectivity in Cross-metathesis Reactions

As mentioned earlier the specific catalyst combination $C_2H_5AlCl_2$/WCl_6/C_2H_5OH is very sluggish in α-olefin metathesis. At normal levels, olefin/W molar ratios of 5000–10,000, very little metathesis of pentene-1 was observed; about 1·0 mol-% of ethylene and octene-4 was produced[35]. The lack of apparent metathesis activity of terminal olefins with $C_2H_5ACl_2$/WCl_6/C_2H_5OH could not be rationalized on grounds of steric hindrance that prevents accommodation of α-olefins within the coordination sphere of the metal. When a cross-metathesis reaction of an equimolar mixture of pentene-1 with pentene-2 was attempted employing the same catalyst system, a relative distribution of products as indicated in Table 10 was observed. The self-metathesis of either olefin leads to symmetric products: ethylene and octene-4 from pentene-1, and butene-2 and hexene-3 from pentene-2. The products from the cross-metathesis are unsymmetric. When the ethylidene and the butylidene groups are aligned on opposite sides of the complex one obtains propylene and heptene-3 (equation 42):



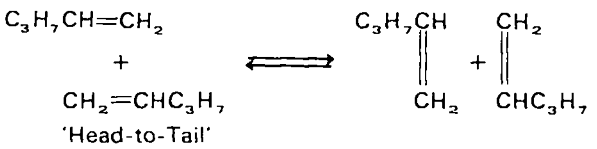
$$\begin{array}{c} C_3H_7CH{=}CH_2 \\ + \\ C_2H_5CH{=}CHCH_3 \end{array} \rightleftarrows \begin{array}{c} C_3H_7CH \\ \| \\ C_2H_5CH \end{array} + \begin{array}{c} CH_2 \\ \| \\ CHCH_3 \end{array} \qquad (42)$$

On the other hand, when the ethylidene is aligned on the same side as the butylidene (equation 43), butene-1 and hexene-2 are produced:



$$\begin{array}{c} C_3H_7CH{=}CH_2 \\ + \\ CH_3{=}CHC_2H_5 \end{array} \rightleftarrows \begin{array}{c} C_3H_7CH \\ \| \\ CH_3CH \end{array} + \begin{array}{c} CH_2 \\ \| \\ CHC_2H_5 \end{array} \qquad (43)$$

The significance of the results in Table 10 lies in the fact that not only does pentene-1 readily undergo cross-metathesis with pentene-2, but it suppresses the self-metathesis of pentene-2. The data suggest that the tendency of pentene-2 to cross-metathesize with pentene-1 is eight-times greater than its tendency to self-metathesize. On first sight, this observation appeared contradictory with the apparent lack of homometathesis activity of pentene-1. One explanation for this dilemma is that terminal olefins, in fact, are more prone to metathesis than internal olefins. Hence, when mixed with internal olefins they 'flood' most of the catalyst sites and inhibit the self-metathesis of the internal olefins. The reason why the reaction products of α-olefin metathesis are not observed is that for some steric reasons, terminal olefins prefer to align 'head-to-tail' (equation 44) and the metathesis of such a configuration yields back the starting material.



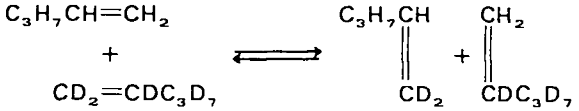
$$\begin{array}{c} C_3H_7CH{=}CH_2 \\ + \\ CH_2{=}CHC_3H_7 \\ \text{'Head-to-Tail'} \end{array} \rightleftarrows \begin{array}{c} C_3H_7CH \\ \| \\ CH_2 \end{array} + \begin{array}{c} CH_2 \\ \| \\ CHC_3H_7 \end{array} \qquad (44)$$

TABLE 10. Cross metathesis of pentene-1 and pentene-2: $C_3H_7CH{=}CH_2 + C_2H_5CH{=}CHCH_3$

Relative concentrations			
Symmetric		Unsymmetric	
$CH_2{=}CH_2$	1	$CH_3CH{=}CH_2$	4
$C_3H_7CH{=}CHC_3H_7$	1	$C_2H_5CH{=}CHC_3H_7$	4
$CH_3CH{=}CHCH_3$	2	$C_2H_5CH{=}CH_2$	12
$C_2H_5CH{=}CHC_2H_5$	2	$CH_3CH{=}CHC_3H_7$	12

Thus, terminal olefins keep spinning their wheels until an internal olefin enters the complex, which after metathesis will yield an unsymmetric cross product.

This hypothesis was confirmed experimentally[35]. A mixture of pentene-1 ($m/e = 70$) and pentene-1-d_{10} ($m/e = 80$) was exposed to the $C_2H_5AlCl_2/WCl_6/C_2H_5OH$ catalyst and a selective scrambling was observed



$$\begin{matrix} C_3H_7CH{=}CH_2 \\ + \\ CD_2{=}CDC_3D_7 \end{matrix} \rightleftharpoons \begin{matrix} C_3H_7CH \\ \| \\ CD_2 \end{matrix} + \begin{matrix} CH_2 \\ \| \\ CDC_3D_7 \end{matrix} \qquad (45)$$

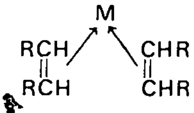
according to equation (45). A distinct formation of species with mass numbers of 72 and 78, corresponding to $C_5H_8D_2$ and $C_5H_2D_8$, was detected with only traces of ethylenes and octenes.

In summary, the observed structural selectivity in the metathesis of terminal with internal olefins results from a higher affinity of terminal olefins to the metathesis catalyst, and a specific geometry of the olefinic substrates on the catalyst site.

V. MECHANISTIC ASPECTS

A. Views Related to the Transition State

Most, but not all, proposed schemes for the transalkylidenation process require the initial formation of a bisolefin–metal entity, bearing two olefinic ligands in a *cis* configuration about the metal:



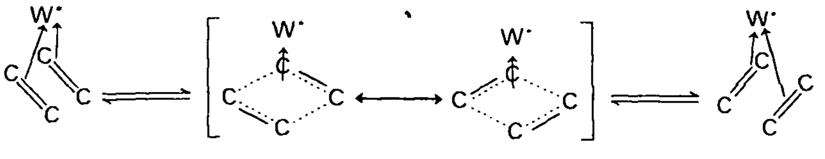
(46)

It is recognized that such a complex has yet to be isolated and characterized for any metathesis catalyst. The complexation process is thought to be a stepwise process as indicated by a kinetics study by Hughes[38].

The nature of the electronic transformation occurring within the coordination sphere of the metal, which provides the actual alkylidene scrambling, is an unresolved aspect of olefin metathesis. Several views regarding this process are presented below, but it is stressed that these must be regarded as highly speculative.

1. Quasicyclobutane transition state

It has been proposed by Bradshaw[27] and subscribed by Calderon and coworkers[24,34] that the transalkylidenation step is a concerted reaction proceeding via a four-centred transition state. Equation (47) illustrates this proposal by symbols of dotted lines and arrows:



(47)

The contention here is that as the transformation progresses along the reaction coordinate, there exists a transition state characterized by having all four carbons equally related to the metal. This transition state has been named 'quasicyclobutane'. If this process is accepted as being a true concerted one, the formation of the quasicyclobutane transition state and its transformation into a bisolefin–metal complex should be considered cycloaddition reactions; hence, the principles of orbital symmetry conservation[63,64] of Woodward and Hoffman ought to be considered here.

When two olefins undergo concerted $[2_s + 2_s]$ bond fusion, a bonding molecular orbital of AS symmetry $(\pi - \pi)$ rises sharply in energy and crosses an antibonding molecular orbital of SA symmetry $(\pi^* + \pi^*)$. A crossing of this kind is characteristic of a symmetry-forbidden reaction, hence, the uncatalysed concerted cycloaddition of two ethylenes is a forbidden process. According to Mango[65–68] certain transition metal complexes can remove these symmetry restrictions and thus convert the symmetry-forbidden to a symmetry-allowed cyclobutanation.

Figure 9 illustrates Mango's forbidden-to-allowed transformation. An injection of a pair of electrons from the d_{zy} metal orbital into the $(\pi^* + \pi^*)$ antibonding molecular orbital, and simultaneously withdrawal of a pair of electrons from the bonding $(\pi - \pi)$ combination by the d_{zx} metal orbital is executed with conservation of orbital symmetry. Recalling that a metal–olefin bond consists of two components, a donor and a back-bonding (see Introduction), the net transformation is:

For the AS combination: $[(\pi - \pi)^2 + d_{zx}] \xrightarrow[\text{donor}]{} [\sigma^* + d^2{}_{zx}]_{\text{back-bonding}}$

For the SA combination: $[(\pi^* + \pi^*) + d^2{}_{zy}] \xrightarrow[\text{back-bonding}]{} [\sigma^2 + d_{zy}]_{\text{donor}}$

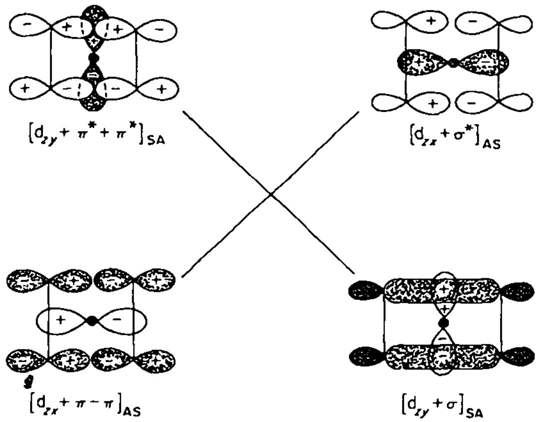

$[d_{zy} + \pi^* + \pi^*]_{SA}$
$[d_{zx} + \sigma^*]_{AS}$
$[d_{zx} + \pi - \pi]_{AS}$
$[d_{zy} + \sigma]_{SA}$

FIGURE 9. Cyclobutanation via Mango's 'forbidden-to-allowed' transformation. Reprinted with permission from Calderon, *Accounts Chem. Res.*, 5, 127 (1972). Copyright by the American Chemical Society.

The net effect on the metal is a spatial relocalization of its valence electrons from $[d_{zx}, d^2_{zy}] \rightarrow [d^2_{zx}, d_{zy}]$. In considering this aspect of the process one must take into account the relative energies of d_{zx} and d_{zy} metal orbitals. If a substantial splitting of the two critical d orbitals exists, an energy barrier will develop which will render the process unworkable. On the other hand if d_{zx} and d_{zy} are degenerate the reaction will proceed smoothly. A factor affecting the relative energies of the d orbitals is the ligand field described by the non-reacting ligands.

In actual olefin metathesis reactions, cyclobutane derivatives have not been detected, therefore raising a doubt as to whether the postulated four-centred transition state is to be considered a cyclobutane. Mango[67] suggested the crucial d orbitals in a metathesis catalyst must be degenerate and the incipient cyclobutane transforms into either of the two possible bisolefin–metal complexes through a molecular vibration along the appropriate reaction coordinate.

2. Tetramethylene–metal complex

Lewandos and Pettit[69] agreed that the transalkylidenation step proceeds in a concerted fashion starting from a bisolefin–metal complex. However, they visualized the process as involving a transition state in which: 'the bonding is most conveniently described as resulting from the interaction of a basic set of metal atomic orbitals and four methylenic units'. Figure 10 illustrates the transformation via the 'tetramethylene–

metal' transition state as suggested by Lewandos and Pettit. Pro and con arguments concerning the conservation of orbital symmetry, involved with rendering an 'allowed' status to the process depicted in Figure 10, have been cited[68,69] but these are not presented here. Suffice it to mention that the important feature of the proposed mechanism is that the transformation of the bisolefin complex into the tetramethylene–metal transition state is accomplished by donation of four electrons from filled ligand orbitals to empty metal orbitals, and back donation of four electrons from filled metal orbitals to empty ligand orbitals. Consequently, the carbon–carbon σ bonds of the initial olefins are ruptured concurrently with the π bonds, so that no genuine cyclobutane molecule is ever formed along the reaction coordinate.

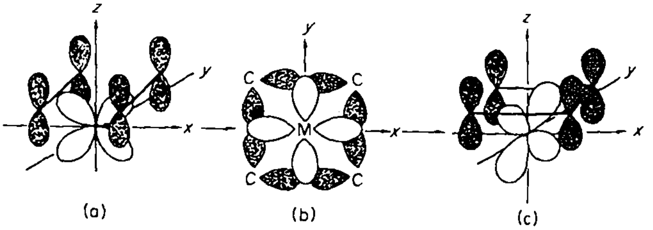
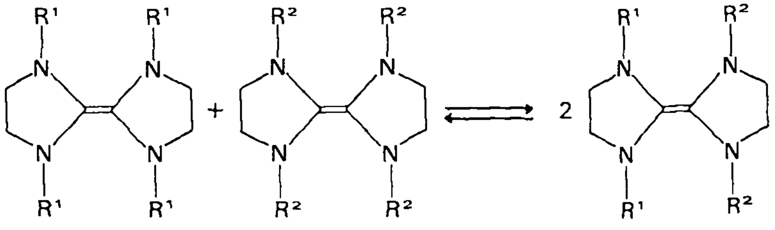


FIGURE 10. Pettit's concept of transalkylidenation via tetramethylene–metal transition state. Reprinted with permission from *Accounts Chem. Res.*, **5**, 127 (1972). Copyright by the American Chemical Society.

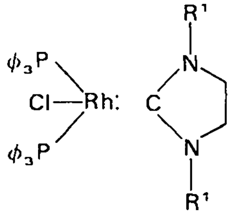
Although Lewandos and Pettit did not use this nomenclature in their proposal, their description obviously alluded to an involvement of carbenes in olefin metathesis. Recently, there have been several experimental disclosures that could be interpreted as supporting evidence for carbene involvement in the reaction. However, none is conclusive to the extent that it can be accepted as a 'proof' to any proposed reaction scheme.

Cardin and coworkers[70] exposed a mixture of unsaturated amines to a rhodium phosphine catalyst and observed some disproportionation:



(48)

As a side product they isolated a complex having one electron-rich alkylidene moiety complexed to Rh^I. They suggested a monocarbene complex as illustrated in equation (49):



(49)

Since rhodium demonstrates no metathetic activity on common olefins, it is not known whether this finding is relevant to the mechanism of olefin metathesis.

O'Neill and Rooney[71] observed that a $CoO-MoO_3$ supported catalyst, which is active in the metathesis of propylene, readily decomposes diazomethane into ethylene and N_2:

$$2CH_2N_2 \longrightarrow CH_2{=}CH_2 + 2N_2 \tag{50}$$

It was suggested that the same sites that are active in metathesis 'also selectively convert adsorbed methylenes into ethylene'. In a subsequent study O'Neill and Rooney[72] demonstrated elegantly that $Mo(CO)_6$ deposited on Al_2O_3 is capable of converting ethylene into propylene directly according to equation (51):

$$3CH_2{=}CH_2 \longrightarrow 2CH_3CH{=}CH_2 \tag{51}$$

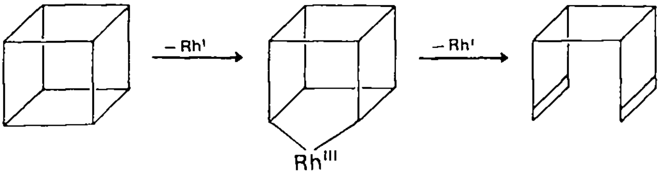
This reaction proceeded slowly at the outset when ethylene was exposed to the catalyst. However, when it was carried out after the catalyst engaged substantially in propylene metathesis, it progresses quite rapidly. Perdeuterated propylene, C_3D_6, was allowed to metathesize at 80 °C until substantial amounts of C_2D_4 and C_4D_8 were formed. A large dose of C_2H_4 was then added. It decreased rapidly with a corresponding large increase in C_3H_6 but not in C_4H_8.

O'Neill and Rooney attempted to outline a mechanism for the direct conversion of ethylene to propylene. They suggested as the most straightforward pathway, a splitting of one ethylene into methylenes, and addition of each of the latter to another ethylene, followed by rearrangement of the resulting trimethylene into propylene. It must be stressed that, although the catalyst for this process is formally a metathesis catalyst, the two reactions are qualitatively distinct. Any conceivable mechanism for the $3C_2 \rightarrow 2C_3$ reaction must involve an eventual migration of hydrogens. As discussed earlier selective olefin metathesis reactions do not involve hydrogen migrations. Hence, a carbene mechanism for $3C_2 \rightarrow 2C_3$ cannot be reasonably 'transplanted' to olefin metathesis.

3. Metallocycle transition state

In 1970 Cassar, Eaton, and Halpern[73] stated that several transition-metal-catalysed cycloadditions, previously considered as concerted processes, are in fact non-concerted involving oxidative addition steps. Olefin metathesis was listed as one of these processes.

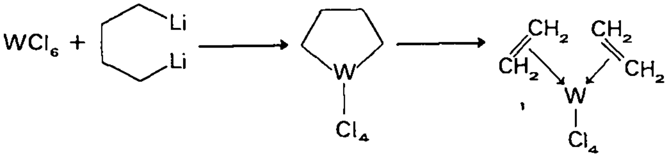
A classic example studied by Cassar, Eaton, and Halpern is the valence isomerization of cubane by a rhodium(I) catalyst:



(52)

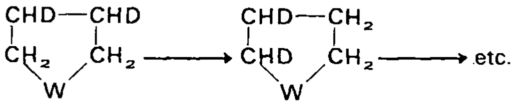
The non-concerted pathway involves the opening of only one σ bond through an oxidative addition ($Rh^{I} \rightarrow Rh^{III}$) forming a metallocycle intermediate. The intermediate rearranges to the corresponding diolefin. A similar mechanism was proposed by Katz and Cerefice[74] for other cycloaddition processes.

Grubbs and Brunck[75] proposed that the reaction products of 1,4-dilithiobutanes with WCl_6 could be well accommodated via a W^{V}-metallocycle intermediate. When an ether solution of the dilithium reagent was reacted with WCl_6 a rapid formation of ethylene was observed. The sequence depicted in equation (53) was postulated:



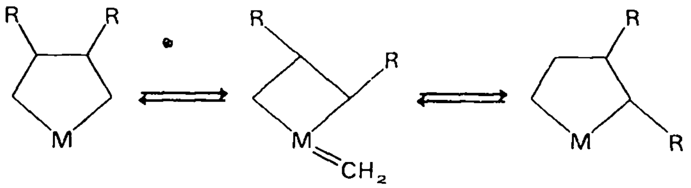
(53)

Extending the investigation further by using deuterium labelling, Grubbs and Brunck concluded that their proposed intermediate can rearrange and thus provide a pathway for alkylidene scrambling. The ethylene mixture produced from Li—CH_2—CHD—CHD—CH_2—Li and WCl_6 contained: CH_2=CHD, CHD=CHD, and CH_2=CH_2. To account for this composition of products it was suggested that the metallocycle undergoes a rearrangement:

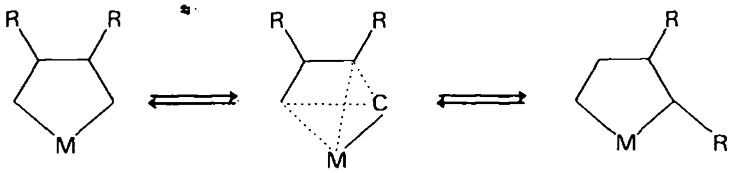


(54)

It is essential that the metal somehow moves from one ring position to another. Grubbs and coworkers[76] proposed two possible routes: equation (55) depicts a carbene–metallocycle route and equation (56) a concerted route for the rearrangement:



(55)



(56)

Mango[67] proposed that this can best be achieved through the extrusion of a cyclobutane ring followed by a second insertion step.

These proposals are considered highly speculative at this stage. They are not supported by any substantial experimental data, and the intimate electronic transformations required to render them feasible have been ignored. Nevertheless, stable metallocycle complexes of Pt and Ir have been prepared and their structures characterized. These have not been reported as active metathesis catalysts. Figure 11 illustrates the structure of Ir(norbornadiene)$_3$acac obtained by Osborn and coworkers[77]. The octahedral Ir^{III} complex has the acetylacetonate and one norbornadiene chelating the metal conventionally, while the remaining two norbornadienes form a five-membered ring metallocycle with the metal.

Heretofore, the bisolefin–metal entity was accepted as the starting intermediate for the transalkylidenation step. Recently, a carbene-type

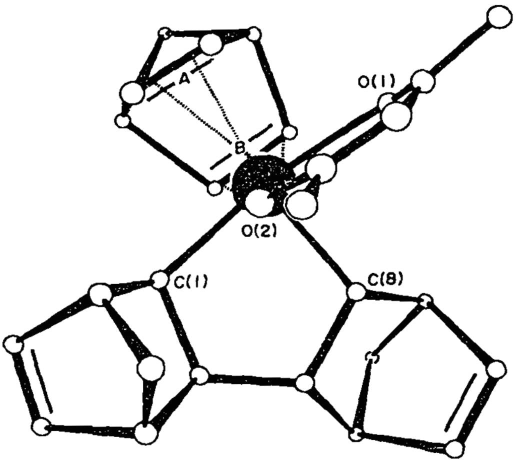
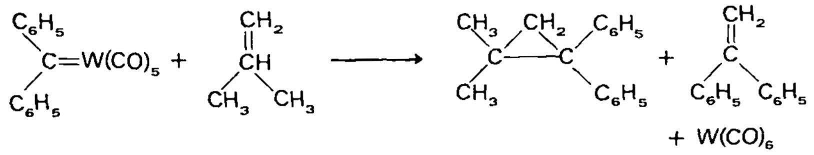


FIGURE 11. Metallocycle structure in Ir(norbornadiene)$_3$acac. Reprinted with permission from Osborn and coworkers, *J. Amer. Chem. Soc.*, **95**, 597 (1973). Copyright by the American Chemical Society.

mechanism was proposed that does not necessarily require the initial formation of a bisolefin–metal complex.

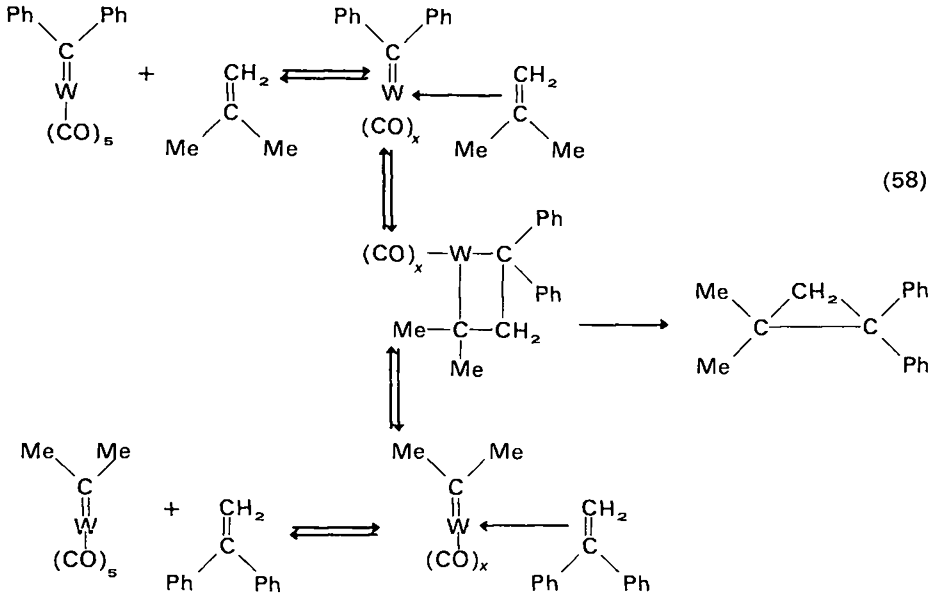
4. Carbene-to-metallocycle

Stable metal–carbene complexes usually require an electron donor heteroatom directly attached to the carbene carbon atom. These complexes have proven to be too stable and unreactive as alkylene transfer agents towards common olefins. Recently, Casey and Burkhardt[78] prepared and isolated $(C_6H_5)_2C:W(CO)_5$, a carbene complex lacking the heteroatom stabilizing effect. Upon heating (100 °C, 2·5 h) this complex with isobutylene, 1,1-diphenylethylene, 1,1-dimethyl-2,2-diphenylcyclopropane and $W(CO)_6$ were obtained[79]:



(57)

The mechanistic scheme proposed for this reaction accommodates both the observed cyclopropanation and the alkylidene transfer from isobutylene to the diphenylcarbene:


(58)

Casey's results are intriguing but one ought to be cautious in accepting these as an ironclad proof for the mechanism of olefin metathesis. There are several points that need to be resolved:

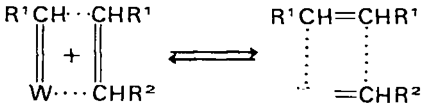
(1) There are no reliable reports that indicate the formation of any cyclopropane derivatives in conventional metathesis experiments.

(2) Casey's experiment is not truly catalytic. The elements of reversibility are lacking. If a true alkylidene scrambling occurred, some ethylene and 2,3-dimethylbutene-2 would have been detected.

(3) How does one generate the original carbene on the metal of a conventional metathesis catalyst?

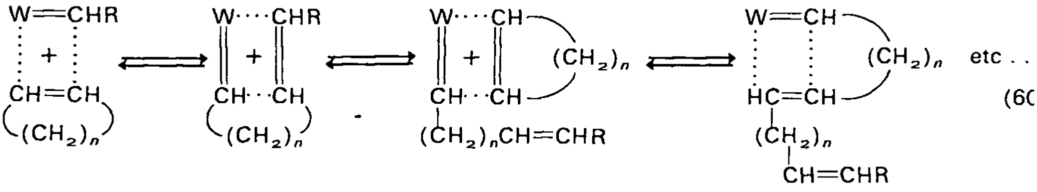
Despite these reservations, Casey's critical experiment ought to be regarded as a valuable contribution to the ongoing attempt to elucidate the mechanism of olefin metathesis.

Herisson and Chauvin[80] proposed essentially the same mechanism in their studies on the cross-metathesis of acyclic with cyclic olefins:



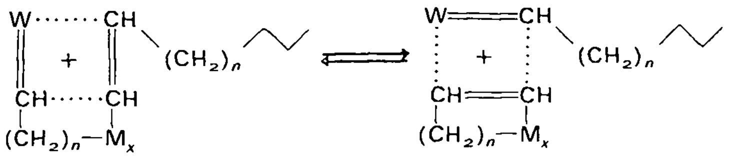
(59)

When applied to cycloolefins, this mechanism does not postulate a polymerization via a macrocyclization pathway; rather, it is consistent with a ring-opening polymerization by chain-end growth:



(6

The formation of macrocyclic oligomers is accomplished by the intramolecular 'back-biting' transalkylidenation of the growing carbene–W chain end with any internal double bond on the same chain, rather than the 'pinching-off' process described earlier in equation (35).



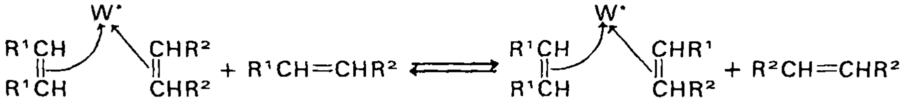
(61)

In summary, four proposed schemes regarding the transalkylidenation mechanism have been presented. The present state of knowledge does not permit a clear-cut selection of a single scheme over the rest. All four proposals involve highly unconventional transition states, which the conservative chemist is reluctant to accept. Ample pro-and-con arguments can be presented for any of the above schemes, and there is no doubt that additional meaningful experiments are badly needed.

B. The Exchange Step

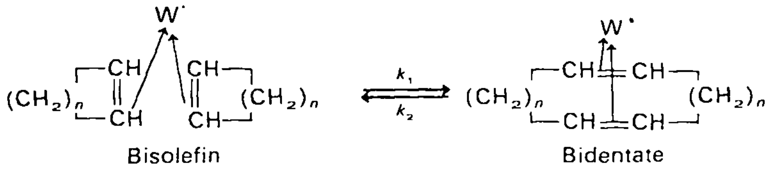
As stated in the introduction, no metallic compound can act as a true catalyst unless it can provide an exchange pathway so that an outgoing product can be replaced by an incoming reactant. To account for the high rates of metathesis reaction, observed at extremely low catalyst levels, a rapid olefin exchange that alternates with the transalkylidenation step is proposed. (The exchange step proposed herein assumes the existence of a bisolefin–metal complex and is hence applicable for any of the top three transalkylidenation schemes discussed in the previous sub-section).

The exchange step (equation 62) implies a nucleophilic displacement; that is, the incoming olefinic ligand is accommodated within the coordination sphere of the metal prior to the disengagement of the leaving ligand.

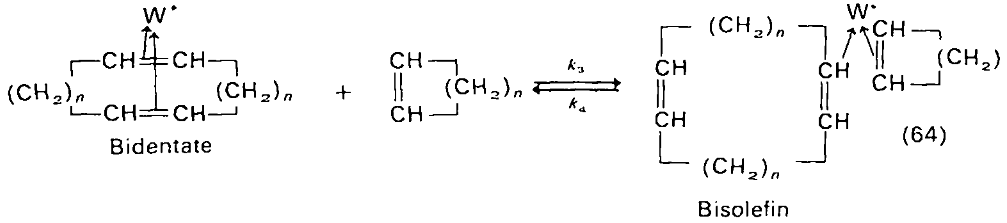

W*
R¹CH
R¹CH
CHR²
CHR²
+ R¹CH=CHR²
W*
R¹CH
R¹CH
CHR¹
CHR²
+ R²CH=CHR²

(62)

From the practical point of view, it appears that a better understanding of this step may be of more importance than the transalkylidenation. A careful analysis of the products obtained during the early stages of cycloolefin metathesis suggests that the exchange step is slower than the transalkylidenation. Assuming that a macrocyclization mechanism dominates cycloolefin metathesis, the propagation process can be represented as follows (equations 63 and 64):


W*
CH
CH
CH
CH
(CH₂)ₙ
(CH₂)ₙ
Bisolefin
k₁
k₂
W*
CH
CH
CH
CH
(CH₂)ₙ
(CH₂)ₙ
Bidentate

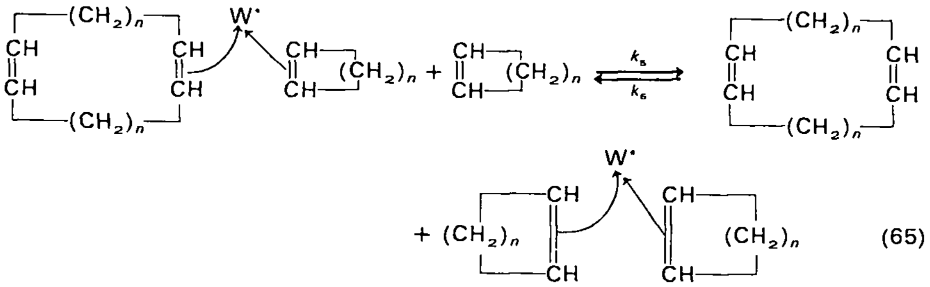
(63)


W*
CH
CH
CH
CH
(CH₂)ₙ
(CH₂)ₙ
Bidentate
+
CH
CH
(CH₂)ₙ
k₃
k₄
(CH₂)ₙ
CH
CH
W*
CH
CH
CH
CH
(CH₂)
(CH₂)ₙ
Bisolefin

(64)

When a bisolefin complex undergoes transalkylidenation (k_1, k_2), the expanded ring is complexed to the metal to form a bidentate complex. Undoubtedly, this is a favoured transformation. In addition to the ring strain energy that may be relieved here, the bidentate complex is much more stable in relation to the bisolefin. When an incoming olefin ligand exchanges with one of the bidentate double bonds (k_3, k_4), a new bisolefin complex is formed. The new bisolefin complex may either undergo transalkylidenation to form the corresponding cyclic trimer and in so doing convert into a bidentate, or undergo a transfer process (k_5, k_6)

involving a further exchange step and produce a free, uncomplexed cyclic dimer (equation 65):


(65)

If the exchange step is much faster than the transalkylidenation step ($k_3 \ldots k_6 \gg k_1, k_2$) the transfer to monomer process would predominate in the early stages of cycloolefin polymerization. This should result in a preponderance of low molecular weight macrocyclic oligomers, with little or no high molecular weight product formed initially. The large build-up of cyclic dimers and trimers at the early stages of cycloolefin metathesis gradually disappears to form higher and higher molecular weight products as reaction progresses. On the other hand, if the transalkylidenation rate is much faster than the exchange step ($k_3 \ldots k_6 \ll k_1, k_2$), every incoming cyclic monomer will metathesize at once and thus incorporate itself into a growing macromolecule. The result will be a high molecular weight product at the outset of cycloolefin metathesis. Table 11 presents typical molecular weight dependence on conversion for cyclooctene metathesis.

The important feature is that very high molecular weight product is produced at the outset of cyclooctene metathesis (inherent viscosity of 3·0–4·0 dl/g corresponds to a polymer having an average molecular weight >200,000). This strongly suggests that the transalkylidenation step is much faster than the ligand exchange and hence cannot be considered as the rate-determining step in cycloolefin metathesis.

VI. SYNTHETIC APPLICATIONS

The great synthetic potential of olefin metathesis rests with its inherent capacity to change the length of the carbon skeleton of hydrocarbons under extremely mild reaction conditions. Its application in areas such as olefin interconversions is obvious. The conversion of propylene into

TABLE 11. Molecular weight dependence on conversion for cyclooctene metathesis with $C_2H_5Al/WCl_6/C_2H_5OH$ catalyst[a]

Conversion (%)	Inherent viscosity (dl/g)
6	3·5
11	3·5
15	3·5
26	4·0
46	4·2
75	4·1

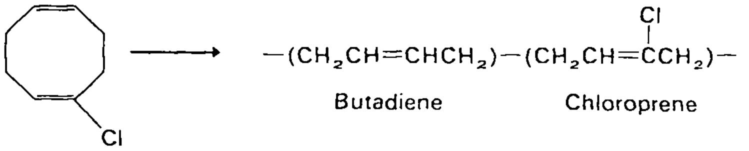
[a] Data from Reference 86.

ethylene and butene reached commercial maturity under the trade name Triolefin Process. The growing demand for 2-methylbutenes, used as starting materials for isoprene synthesis, triggered substantial research and development activity in the cross metathesis of isobutylene with propylene. A case-by-case description of all the reported olefin interconversions was reviewed by Bailey[26].

The effect of substitution on ease of participation in the metathesis reaction is: $[CH_2{=}] > [RCH_2CH{=}] > [R_2CHCH{=}] > [R_2C{=}]$. A limiting factor in expanding the scope of the reaction to unsaturated reactants possessing heteroatom functional groups, has been the catalyst-poisoning effect of polar entities. Chlorine atoms do not act as catalyst deactivators, hence, a chlorine substituent on a carbon far removed from the vinylic site is tolerable, while chlorine substitution at the vinylic site deactivates the double bond toward the metathesis reaction[81]. Recently, the successful metathesis of unsaturated fatty acid esters has been reported using high catalyst levels derived from WCl_6 and $(CH_3)_4Sn$[82]. Thus methyl oleate was metathesized to the corresponding octadecene-9 and the dimethyl ester of octadecene-9-dioic acid.

The synthetic applications of olefin metathesis to polymer chemistry are numerous. A homologous series of linear unsaturated polyalkenamers is provided by the application of the reaction on cycloolefins of the general formula $\overline{[(CH_2)_n{-}CH{=}CH]}$, where $n = 2, 3, 5, 6, \ldots$ and higher, with the exception of cyclohexene. Unsaturated alicyclic monomers having more than one double bond in the ring undergo polymerization, provided that the double bonds are not conjugated[83]. Depending on the structure of the repeat unit and the double bond configuration, these polyalkenamers may display elastomeric or plastic-like properties[84]. A comprehensive review on the preparation of polyalkenamers and their physical properties has been published by Dall'Asta[85].

Substituted cycloolefins can be polymerized to high molecular weight polymers[83], thus providing a route for the preparation of certain perfectly alternating copolymers:



$$-(CH_2CH{=}CHCH_2)-(CH_2CH{=}\overset{Cl}{C}CH_2)- \qquad (66)$$

This aspect of cycloolefin polymerization was studied by Ofstead[81].

By conducting the metathesis reaction of cycloolefins at high dilutions a relatively high yield of macrocyclic compounds is afforded[25]. Of special interest is 1,9-cyclohexadecadiene, the cyclic dimer of cyclooctene, which can be converted to the respective musk-like ketone[87].

Concurrent studies by Wolovsky[88], and Ben-Efraim, Batich, and Wasserman[89] led to the conclusion that interlocked ring systems are present in the macrocyclics mixture of metathesized cyclododecene. The formation of catenanes was accounted for by assuming a concerted intramolecular transalkylidenation of a twisted 'strip', as illustrated in Figure 12.

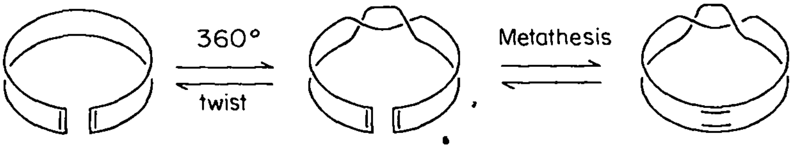


FIGURE 12. Catenane formation. Reprinted with permission from Calderon, *Accounts Chem. Res.*, 5, 127 (1972). Copyright by the American Chemical Society.

The cross metathesis reaction of acyclic with cyclic olefins can be directed towards the formation of liquid polymers, dienes, trienes and other polyenes[37,90], depending on the prevailing ratio of acyclic/cyclic olefins employed. High molecular weight styrene–butadiene copolymers have been shown to undergo exhaustive cleavage when cross-metathesized with large amounts of acyclic olefins[91]. Determination of the resulting fragments was used to elucidate the monomer sequence distribution in the copolymers.

VII. CONCLUSION

Two objectives in olefin metathesis are waiting for a breakthrough. First, hardy catalysts, capable of withstanding polar environments, are needed so that the scope of applications can be expanded into olefins possessing polar functionalities. Second, additional critical experiments are needed that will clarify the mechanism of this remarkable process. Based on experience, it is forecast that the first objective will be realized sooner than the second.

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Supplement A The Chemistry of Double-Bonded Functional Groups
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CHAPTER 11

Oxidation of C=C and C=N groups

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I. INTRODUCTION

The oxidation chemistry of alkenes is much more extensive than that of the various chemical groups which contain the C=N function. For that reason this chapter is considerably lopsided in favour of the former.

The discussion of both will be divided into two main subsections: oxidations by metal ions, and oxidations by non-metallic substances. This seems to be a logical division since most metal-ion catalysed reactions have common mechanistic features. These similarities in mechanism for various metal-ion oxidations will be emphasized in the discussion. In general, the modes of oxidation by non-metallic substances are more diverse and common mechanistic schemes are not normally encountered.

The field of metal-ion catalysed oxidations of alkenes has received considerable study in the last few years because of its industrial importance and to cover it exhaustively would itself require a book. In order to limit the length of the chapter, practically all reactions discussed will be in homogeneous media. This excludes the extensive field of heterogeneous catalysis for which detailed mechanistic knowledge is limited.

As a general rule the oxidation of isolated double bonds will be emphasized but not to the complete exclusion of other systems. Thus some examples of oxidation of both conjugated and unconjugated diene systems will be given. Also some allylic oxidations will be included particularly when the attachment of oxidant to the double bond occurs. The only substances completely excluded will be aromatic substrates.

The definition of oxidation in organic chemistry is a subject which is confusing to many chemists. Since this chapter will be concerned with oxidation of organic compounds it is perhaps appropriate to say a few words on this subject. The inorganic chemist has little trouble in defining oxidation as a loss of electrons or reduction as a gain of electrons since he is dealing with ionizable substances. Hence consider equation (1) in which thallium is obviously reduced in oxidation state by two while mercury increases its oxidation state by two.

$$Tl^{3+} + Hg(O) \longrightarrow Tl^{+} + Hg^{2+} \qquad (1)$$

The organic chemist has no such convenient means of defining oxidation state. In some cases organic oxidation is apparent from change in valence of the oxidant. Consider the oxidation of ethylene by Tl^{3+} to be discussed later. The Tl^{3+} has gained two electrons in going from Tl^{3+} to Tl^{+} so

$$Tl^{3+} + C_2H_4 + H_2O \longrightarrow CH_3CHO + Tl^{+} + 2H^{+} \qquad (2)$$

the organic system must have lost two electrons. However consider the hydration of ethylene in the presence of Tl^{3+}. The Tl^{3+} has not been reduced, so ethylene and ethanol have the same oxidation state while

$$Tl^{3+} + C_2H_4 + H_2O \longrightarrow Tl^{3+} + CH_3CH_2OH \qquad (3)$$

CH_3CHO is in a two-electron-higher oxidation state than ethanol as shown by the following:

$$CH_3CH_2OH + Tl^{3+} \longrightarrow CH_3CHO + Tl^{+} + 2H^{+} \qquad (4)$$

Often it is not so obvious that oxidation has occurred. Thus the bromination of ethylene is an oxidation because bromine goes from a zero oxidation

$$Br_2 + C_2H_4 \longrightarrow BrCH_2CH_2Br \qquad (5)$$

state to a minus one. Another way of putting it is that in Br_2 there are 14 valence electrons while they have a total of 16 in ethylene dibromide. It may be mentioned here that, although halogenation of alkenes is an oxidation, it will not be treated in this chapter because it is a common reaction with a large body of literature that will be discussed elsewhere.

Consider next the hydroxylation of olefins by H_2O_2 to give glycols.

$$C_2H_4 + H_2O_2 \longrightarrow HOCH_2CH_2OH \qquad (6)$$

This can be shown to be a two-electron oxidation because it can also be carried out by the following reaction in equation (7). The hydroxylation

$$C_2H_4 + 2H_2O + Tl^{3+} \longrightarrow HOCH_2CH_2OH + Tl^{+} + 2H^{+} \qquad (7)$$

also is a two-electron oxidation since in H_2O_2, each oxygen is in a -1 oxidation state while in ethylene glycol each is in a -2 state. Consider the hydration of ethylene (equation 3). This is a non-oxidative reaction because the oxygen is in a -2 state in both water and ethylene glycol. Of course a similar type of reasoning is also involved in the oxidation of the C=N group.

II. OXIDATION OF C=C BONDS

A. Metal Ion Oxidants

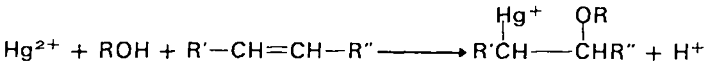
1. Non-transition metal oxidants

a. *General.* With exception of Ce^{IV}, which behaves as a strong one-electron oxidant and has little olefin oxidation chemistry, the only important non-transition metal oxidants are the isoelectronic series: Hg^{II}, Tl^{III} and Pb^{IV}. These oxidants are almost always two-electron oxidants. The oxidation chemistry of these metal ions would not be predicted from their position in the periodic table. Thus in the preceding members of each group the higher oxidation state is the most stable. The sudden change in properties in going from the fifth to the sixth period is called the 'inert pair' effect which refers to the difficulty of removal of the inert $6s^2$ electrons[1]. Thus for Tl^0 the configuration of the valence shell is $6s^2$ 6p from which an electron is readily lost to give Tl^I ($6s^2$). The high Tl^{III}–Tl^I oxidation potential (1·24 V) reflects that Tl^{III} does not readily form because of the inert pair ($6s^2$).

The oxidation potential increases with increasing atomic number. Thus the potentials of the Hg^{II}–Hg^{0}; Tl^{III}–Tl^{I}, and Pb^{IV}–Pb^{II} couples in water are 0·85 V, 1·24 V and 1·69 V respectively. Being isoelectronic the general mode of interaction of these three metal ions might be expected to be similar with the increasing oxidation potentials causing some differences in reactivity. As discussed below, this expectation is realized.

A logical extension of the series discussed above is to Bi^{V}. This oxidation state of bismuth is usually encountered as sodium bismuthate, $NaBiO_3$, which is a powerful oxidant. However its olefin oxidation chemistry has been little studied. A couple of examples of olefin oxidation by bismuth salts will be mentioned below.

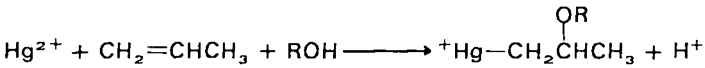
b. *Mercury*(II). Mercury(II), having the lowest oxidation potential, might be expected to be the weakest oxidant of the series and, in fact, its chemistry is dominated by formation of stable adducts with olefins. The most common type of adduct is formed by the oxymercuration reaction (R = H, alkyl, $-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3$ etc) which has been known since about 1900.



$$Hg^{2+} + ROH + R'-CH{=}CH-R'' \longrightarrow R'\overset{\overset{\displaystyle Hg^+}{|}}{C}H-\overset{\overset{\displaystyle OR}{|}}{C}HR'' + H^+ \qquad (8)$$

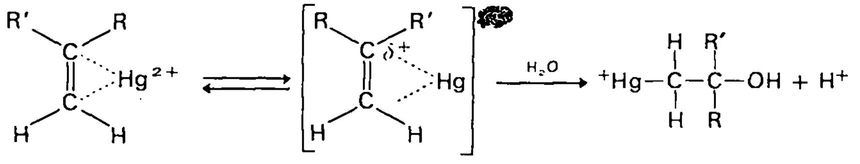
The field was reviewed by Chatt in 1951[2] and more recently by Kitching[3]. The reaction is of some interest in oxidation by metal ions since unstable adducts of this type are believed to be intermediates in oxidations by other metal ions.

Oxymercuration has all the characteristics of an electrophilic reaction. Addition is Markownikoff which means the —OR adds to the most substituted carbon of the double bond. Furthermore electron releasing substituents on the vinylic carbon increase the rate of oxymercuration.



$$Hg^{2+} + CH_2{=}CHCH_3 + ROH \longrightarrow {}^{+}Hg-CH_2\overset{\overset{\displaystyle OR}{|}}{C}HCH_3 + H^+ \qquad (9)$$

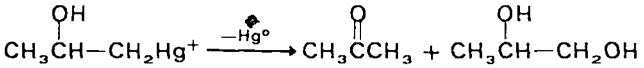
In a kinetic study of the reaction in water Halpern and Tinker[4] found a ρ^* of $-2{\cdot}77$ which is close to that expected for a free carbonium ion in the transition state. The reaction is sometimes pictured as the rearrangement of an intermediate Hg^{II}–π-complex to a transition state with considerable charge on one carbon. However there is no compelling evidence for such intermediate π-complexes and there has been considerable controversy concerning their existence[5–7]. They have been detected in solution under some conditions[8] but not under the conditions of the oxymercuration reaction[4]. The stereochemistry of the



(10)

oxymercuration is *trans* for unstrained olefins but is *cis exo* for strained olefins such as norbornene.

The elimination of Hg^0 from the oxymercuration intermediate might be expected by analogy with other metal ion oxidations to be discussed, to give glycols and carbonyl products as olefin oxidation products. For instance, propylene in water would give acetone and 1,2-propandiol. However with terminal olefins the products have been reported to be

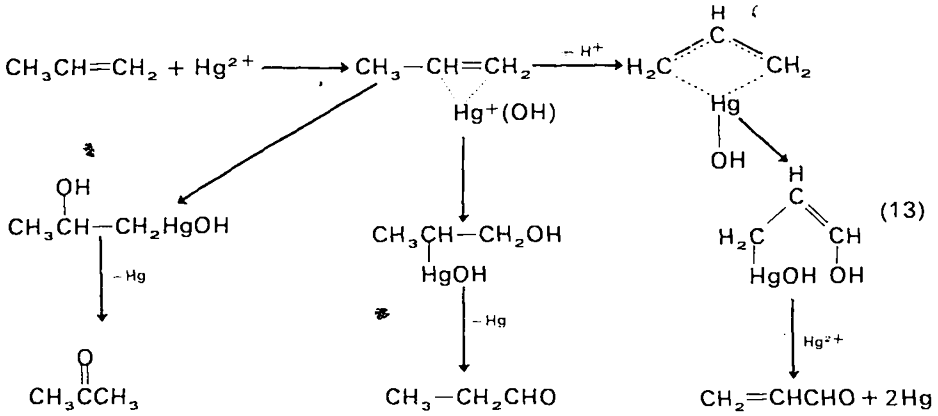


$$CH_3\overset{OH}{C}H-CH_2Hg^+ \xrightarrow{-Hg^0} CH_3\overset{O}{\overset{\|}{C}}CH_3 + CH_3\overset{OH}{C}H-CH_2OH \qquad (11)$$

mainly unsaturated carbonyl compounds in water. Thus, in 1898, Deniges found that propylene was absorbed by aqueous solutions of mercury(II) sulphate or nitrate. Heating these solutions at about 90 °C gave unsaturated carbonyl compounds[10,11] and Hg^I. For instance propylene

$$CH_3CH{=}CH_2 + 4Hg^{II} \xrightarrow{H_2O} CH_2{=}CHCHO + 4Hg^{I} \qquad (12)$$

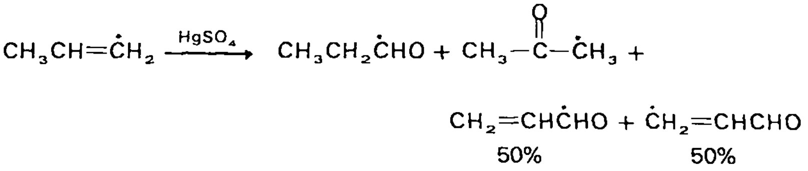
gives acrolein. Later workers, however, disagreed on the product distributions obtained from various mercuric salts in water. Mertz and Dermer[12] found only acrolein in propylene oxidation by $HgSO_4$ as did Fielding and Roberts[13] using $HgSO_4$, $Hg(OOCCF_3)_2$, and $Hg(ClO_4)_2$. Strini and



(13)

Metzger[14], using $HgSO_4$ and $Hg(ClO_4)_2$, found mainly acrolein under most reaction conditions but did detect appreciable (*c.* 10%) yields of acetone and smaller amounts (2–5 %) of propanal. On the basis of mechanistic studies they postulated the mechanism in equation (13)[9,15].

Evidence for this mechanism was provided by ^{14}C-labelling studies[15]. The scrambling of the label in the acrolein product is evidence for a

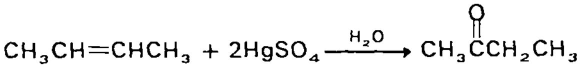


$$CH_3CH{=}\dot{C}H_2 \xrightarrow{HgSO_4} CH_3CH_2\dot{C}HO + CH_3-\overset{O}{\overset{\|}{C}}-\dot{C}H_3 + \underset{50\%}{CH_2{=}CH\dot{C}HO} + \underset{50\%}{\dot{C}H_2{=}CHCHO} \qquad (14)$$

symmetrical intermediate such as the π-allylic intermediate postulated. One problem with the reaction scheme is that the oxidation of propylene to acrolein is a four-electron oxidation and this type of oxidation would not be expected to occur in a single step. Intermediate oxidation products such as allyl alcohol might be expected. Also there is no evidence for Hg^{II}–π-allylic complexes. In addition, the mode of formation of acrolein from the final intermediate is unclear.

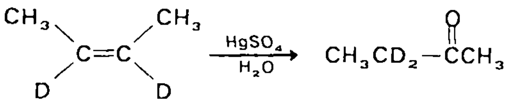
More recent reports of the oxidation of propylene by $Hg(NO_3)_2$ indicate acetone is the only product[16,17]. The reaction was first order in oxymercuration adduct and was not accelerated by free Hg^{2+}. However addition of HNO_3 or salts such as $LiNO_3$, $NaNO_3$, KNO_3 or $NaClO_4$ increased the rate of decomposition of mercurial. This acceleration by salts was similar to that observed in the mercuration of benzene[18] or oxidation of olefins by Tl^{III} [19]. The increasing electrolyte concentration has been postulated to lower the water activity thus desolvating the metal ion, making the metal ion more reactive.

Internal olefins without phenyl substitution give almost exclusively ketones[16], thus 2-butene gives 2-butanone. A deuterium-labelling experi-



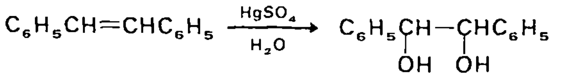
$$CH_3CH{=}CHCH_3 + 2HgSO_4 \xrightarrow{H_2O} CH_3\overset{O}{\overset{\|}{C}}CH_2CH_3 \qquad (15)$$

ment indicates that a hydride shift is involved in the formation of 2-butanone[9]. Phenyl-substituted olefins give glycol type products. Thus



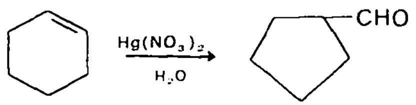
$$\xrightarrow[H_2O]{HgSO_4} CH_3CD_2-\overset{O}{\overset{\|}{C}}CH_3 \qquad (16)$$

stilbene gives 1,2-dihydroxy:1,2-diphenylethane[20]. Sometimes products arising from carbon migration are found. Thus cyclohexene is oxidized to



$$C_6H_5CH{=}CHC_6H_5 \xrightarrow[H_2O]{HgSO_4} C_6H_5\underset{OH}{CH}{-}\underset{OH}{CH}C_6H_5 \qquad (17)$$

cyclopentanecarboxaldehyde by $Hg(NO_3)_2$[20,21].



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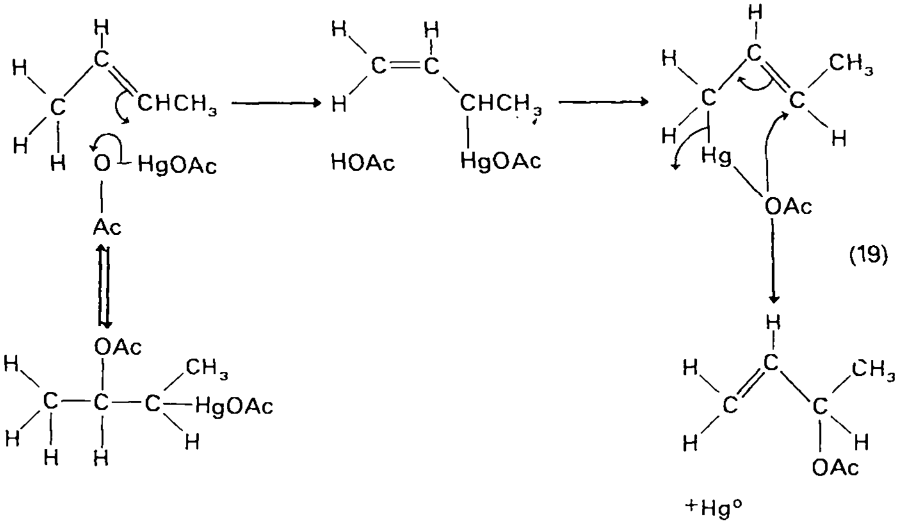
The oxidation of olefins by $Hg(OAc)_2$ in acetic acid gives much less product variety than in water. Thus both terminal and internal olefins are oxidized to allylic acetate in the Treibs reaction[22]. This reaction has been applied to a number of olefins of various structures[22–26]. Oxidation of either 1- or 2-butene gives the same product, 3-acetoxy-1-butene. The mechanism of this reaction has been studied by Rappoport and co-workers[27]. The main features of the scheme are: (i) the olefin is mainly in the form of mercurial but this is in equilibrium with free olefin and $Hg(OAc)_2$; (ii) the free olefin and $Hg(OAc)_2$ can react to give a secondary allylic mercurial; (iii) The secondary mercurial is in rapid equilibrium with the more stable primary allylic mercurial; (iv) The primary mercurial decomposes via an internal attack with elimination of Hg^0 to give the secondary allylic acetate.

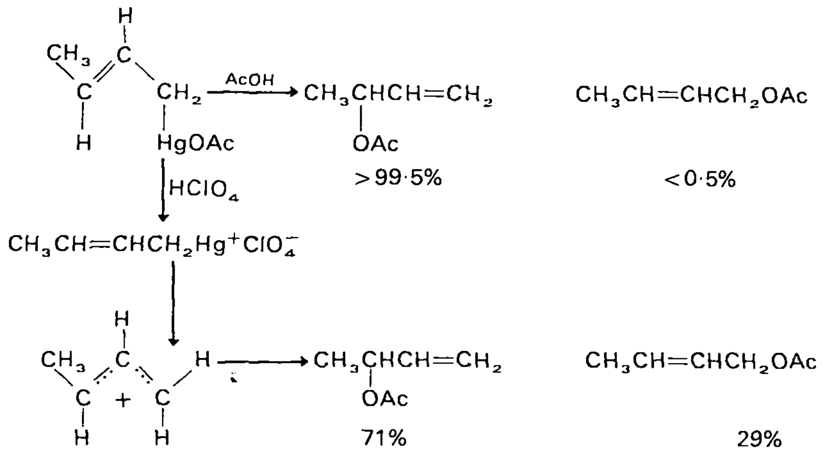


(19)

1-Butene gives the same product since its reaction with mercuric acetate gives the primary allylic acetate directly.

$$CH_3CH_2CH{=}CH_2 + Hg(OAc)_2 \xrightarrow{HOAc} CH_3CH{=}CHCH_2HgOAc + 2HOAc \qquad (20)$$

The same workers studied the decomposition of the preformed primary mercuric acetate and found it did give exclusively the secondary allylic acetate in absence of acid[27,28]. However in the presence of perchloric acid a mixture of primary and secondary allylic acetates were formed in the ratio expected from solvent attack on a crotyl allylic carbonium ion[28]. The rate of the neutral demercuration is increased by addition of $Hg(OAc)_2$, This is believed to result from the change of leaving group from Hg^0 to $(Hg^I)_2$ in the presence of $Hg(OAc)_2$.



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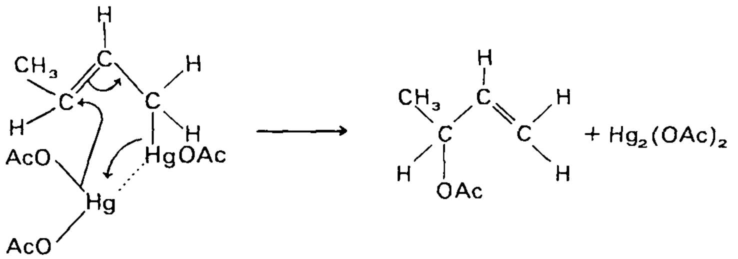

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Monomeric Hg^0 is an unstable species and its formation in the transition state for decomposition would add considerably to the activation energy. This is, no doubt, one of the reasons why mercurials are so stable. However $Hg_2(OAc)_2$ is a stable species and its formation in the transition state would not add appreciably to the activation energy.

Note that the Treibs reaction amounts to a two-electron oxidation corresponding to the formation of allylic alcohols in water. This suggests that perhaps allylic alcohols are the primary products in water but are oxidized rapidly to the unsaturated ketones. Two recent reports indicate this to be the case[29,30]. Thus the mechanism in water could be very similar to that suggested by Rappoport and coworkers[27].

How can the various products observed by different workers be rationalized in terms of known organometallic chemistry of mercury(II)? A very significant study in this regard is the work of Jensen and Ouellette on the solvolysis of organomercurials[31,32]. In acetic acid the solvolysis of cyclohexyl mercuric perchlorate to give cyclohexene and cyclohexyl acetate proceeded at a rate 10^5-times faster than cyclohexyl mercuric acetate[31]. Furthermore the solvolysis of the acetate occurred by prior ionization of the acetate.

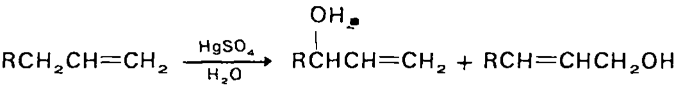
$$\mathrm{RHgOAc} \rightleftharpoons \mathrm{RHg^+ + OAc^-} \tag{23}$$

$$\mathrm{RHg^+} \longrightarrow \mathrm{R^+ + Hg^0} \tag{24}$$

$$\mathrm{R^+ + HOAc} \longrightarrow \mathrm{ROAc + olefin + H^+} \tag{25}$$

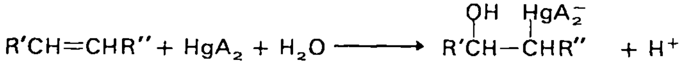
Furthermore there was a marked influence of alkyl structure on the rate[32]. Thus isopropyl mercuric perchlorate solvolysed about 10^4-times faster than ethylmercuric perchlorate. This indicates that there is considerable charge on the carbon attached to the mercury in the transition state.

A recent report by Tinker[30] has shed considerable light on the oxidation of olefins by mercuric salts. He found that the oxidation of terminal olefins such as propylene, 1-butene and 1-hexene by $Hg(SO_4)_2$ gave as primary products the allylic alcohols which were mainly the unsaturated secondary alcohols. The alcohols are rapidly oxidized to unsaturated ketones. However the same terminal olefins were oxidized to saturated



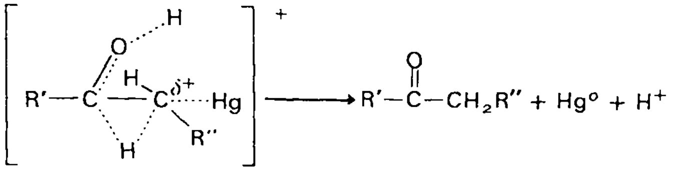
$$\mathrm{RCH_2CH{=}CH_2 \xrightarrow[H_2O]{HgSO_4} R\overset{\displaystyle OH}{\overset{|}{C}}HCH{=}CH_2 + RCH{=}CHCH_2OH} \tag{26}$$

methyl ketones by mercuric nitrate or mercuric perchlorate. Tinker explained these results by the stability of the intermediate oxymercuration adduct. Now if R″ is an alkyl group. the rate of solvolysis would be faster by



$$\mathrm{R'CH{=}CHR'' + HgA_2 + H_2O \longrightarrow R'\overset{\displaystyle OH}{\overset{|}{C}}H{-}\overset{\displaystyle HgA_2^-}{\overset{|}{C}}HR'' + H^+} \tag{27}$$

a factor of at least 10^4-times that if R″ is a hydrogen. according to Jensen and Ouellette[32]. In this case solvolysis proceeds to give a carbonyl product by hydride migration to neutralize the incipient carbonium ion as Hg^0 leaves.

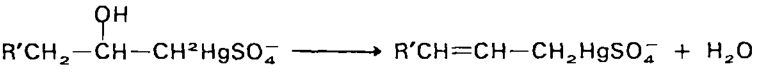


(28)

However if R″ is a hydrogen the adduct is much more stable and the nature of A becomes important. The more strongly complexing is A, the more stable is the oxymetallation adduct to solvolysis. Sulphate is a better complexing agent than either nitrate or perchlorate, so mercuric sulphate does not oxidize terminal olefins to saturated alcohols while mercuric nitrate and mercuric perchlorate do give saturated ketones.

Since the mercuric sulphate oxymercuration adduct is stable to solvolysis it has the opportunity to undergo allylic oxidation. In the case of the Treibs reaction in acetic acid with mercuric acetate the acetate is such a strong complexing agent that saturated products are not formed with either terminal *or* internal olefins. This is in keeping with the results of Jensen and Ouellette who found that cyclohexylmercuric acetate solvolysed about 10^5-times more slowly than the perchlorate salt. Thus even the adduct with mercury attached to a secondary carbon is stable to solvolysis.

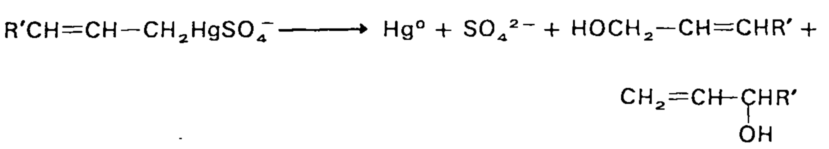
Tinker[30] proposed that the allylic mercurial is formed by dehydration of the oxymercurial rather than by direct attack on the olefin as originally proposed by Rappoport and coworkers[27]. He demonstrated that the



$$R'CH_2-\overset{OH}{CH}-CH^2HgSO_4^- \longrightarrow R'CH{=}CH-CH_2HgSO_4^- + H_2O \qquad (29)$$

corresponding alcohols will dehydrate under the reaction conditions so it is quite reasonable the mercurials would also do so.

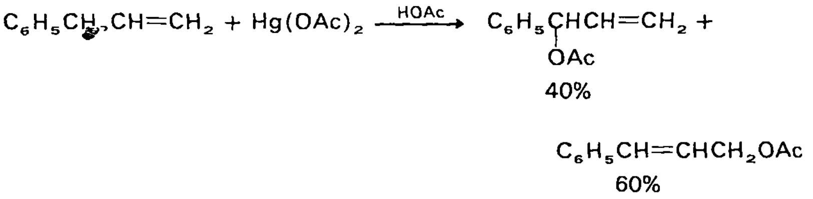
Tinker observed both primary and secondary allylic alcohols in at least one case (1-pentene). This implies an allylic carbonium ion type



$$R'CH{=}CH-CH_2HgSO_4^- \longrightarrow Hg^0 + SO_4^{2-} + HOCH_2-CH{=}CHR' + CH_2{=}CH-\underset{OH}{CHR'} \qquad (30)$$

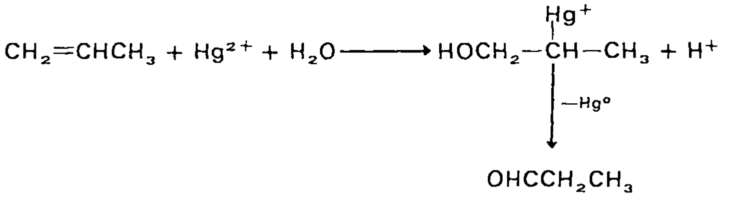
decomposition found for allylic mercuric acetates in the presence of $HClO_4$ (equation 21) rather than the internal rearrangement found in the absence of strong acid (equation 19). This is reasonable since sulphate is a much weaker complexing agent than acetate.

Tinker's proposals are actually rather close to more recent suggestions of Rappoport and coworkers. In a report[33] on the oxidation of allylbenzene in acetic acid by mercuric acetate, published about a year before Tinker's communication, they mentioned the possibility of the allylic mercurial being formed by elimination of HOAc from the oxymercuration adduct in a manner analogous to that suggested by Tinker. In addition Rappoport and coworkers found both primary and secondary allylic acetates as products in the kinetically controlled distribution. At equilibrium the product is almost entirely the primary allylic acetate. To explain these results they suggested an allylic carbonium ion intermediate.



$$C_6H_5CH_2CH{=}CH_2 + Hg(OAc)_2 \xrightarrow{HOAc} \underset{40\%}{C_6H_5\underset{OAc}{CH}CH{=}CH_2} + \underset{60\%}{C_6H_5CH{=}CHCH_2OAc} \quad (31)$$

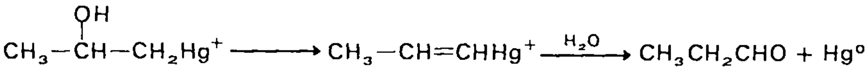
One interesting facet of the dehydration mechanism of Tinker for formation of allylic mercurial is that it offers an explanation of the propionaldehyde product found by Strini and Metzger[13] in the oxidation of propylene. Since oxymercuration is very strongly Markownikoff, the formation of propionaldehyde by anti-Markownikoff oxymercuration



$$CH_2{=}CHCH_3 + Hg^{2+} + H_2O \longrightarrow HOCH_2{-}\overset{Hg^+}{CH}{-}CH_3 + H^+ \quad (32)$$

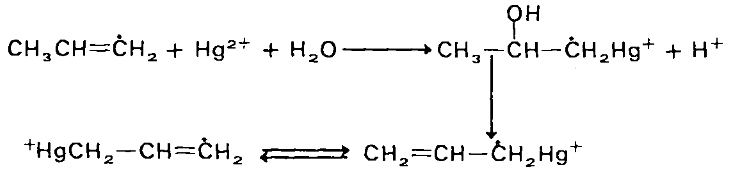
$$HOCH_2{-}\overset{Hg^+}{CH}{-}CH_3 \xrightarrow{-Hg^{\circ}} OHCCH_2CH_3$$

followed by solvolysis does not seem likely. Tinker proposes instead that the mercurial can be dehydrated to a vinyl mercurial which solvolyses to propionaldehyde.



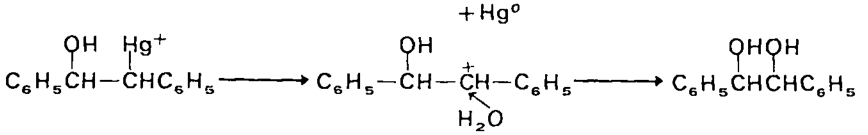
$$CH_3{-}\overset{OH}{CH}{-}CH_2Hg^+ \longrightarrow CH_3{-}CH{=}CHHg^+ \xrightarrow{H_2O} CH_3CH_2CHO + Hg^{\circ} \quad (33)$$

The [13]C-labelling experiments of Strini and Metzger[14], mentioned previously, which suggest a symmetrical species could be satisfied by a rapidly switching pair of allylic mercurials as found in acetic acid, and which is known to occur from n.m.r. spectra[33].



$$CH_3CH{=}\dot{C}H_2 + Hg^{2+} + H_2O \longrightarrow CH_3-\overset{OH}{\overset{|}{C}}H-\dot{C}H_2Hg^+ + H^+$$
$$\big\downarrow$$
$$^+HgCH_2-CH{=}\dot{C}H_2 \rightleftharpoons CH_2{=}CH-\dot{C}H_2Hg^+ \qquad (34)$$

The formation of glycols from phenyl-substituted olefins can be explained by stabilization of the incipient carbonium ion by the phenyl ring, thus allowing attack by solvent. In light of oxidations by Tl^{III}, to be

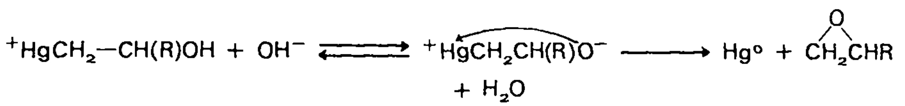


$$C_6H_5\overset{OH}{\overset{|}{C}}H-\overset{Hg^+}{\overset{|}{C}}HC_6H_5 \longrightarrow C_6H_5-\overset{OH}{\overset{|}{C}}H-\underset{H_2O}{\overset{+}{C}}H-C_6H_5 \xrightarrow{+Hg^0} C_6H_5\overset{OH}{\overset{|}{C}}H\overset{OH}{\overset{|}{C}}HC_6H_5 \qquad (35)$$

discussed next, it seems fair to ask if glycols are possible products in the oxidation of non-phenyl-substituted olefins, especially since glycols are difficult to detect. It may be worthwhile taking a closer look for glycol products in, for instance, the propylene oxidation.

Certainly all the factors involved in product distribution have not been elucidated by the previous discussion. In some cases even mercuric perchlorate has been reported to give allylic ketones[13]. An important consideration may be water activity as determined by salt concentration. Thus, as discussed above, Saito and Matsuo[16,17] found that increased salt concentration increased the rate of decomposition of mercurial to saturated ketone. This is a factor not generally recognized which could explain some of the discrepancies in the literature.

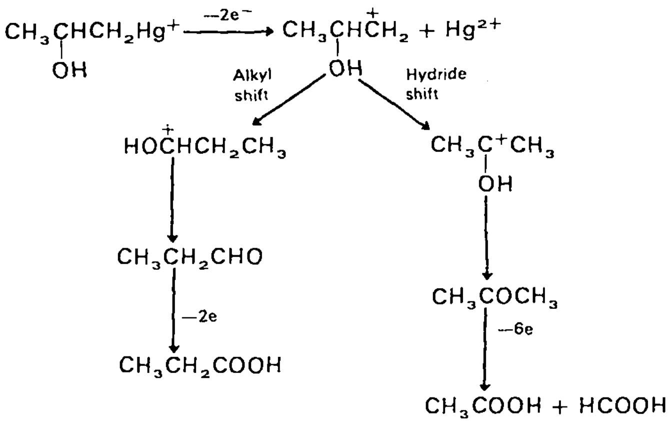
There is one report[34] of the decomposition of hydroxymercuration adducts to give olefin oxides. The mercurial is first formed by introducing the olefin in an aqueous suspension of $HgSO_4$, adjusting the pH to 8–13



$$^+HgCH_2-CH(R)OH + OH^- \rightleftharpoons \underset{+\,H_2O}{{}^+HgCH_2CH(R)O^-} \longrightarrow Hg^0 + \overset{O}{CH_2CHR} \qquad (36)$$

and heating at 70–300°C. The olefin is no doubt formed by neighbouring oxide attack on the Hg^{II}. The pH range is probably a compromise between that range in which appreciable amounts of $^+HgCH_2CH(R)O^-$ are formed and the more basic range in which the very stable $HOHgCH_2CH(R)OH$ is mainly present.

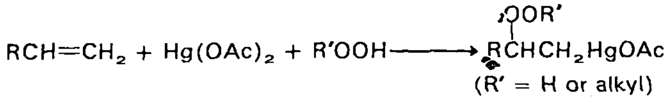
Oxymercuration adducts have also been decomposed electrochemically[35,36]. A variety of products are obtained because the initial products are oxidized further. Thus in aqueous perchloric acid propylene gives acetone, propionaldehyde, formic acid, acetic acid and propionic acid. The product distribution depends to a large extent on electrode potential. The following scheme is used to explain the product distribution with propylene:



$CH_3CHCH_2Hg^+ \xrightarrow{-2e^-} CH_3CH\overset{+}{C}H_2 + Hg^{2+}$
OH
Alkyl shift
Hydride shift
$HO\overset{+}{C}HCH_2CH_3$
$CH_3C^+CH_3$
OH
CH_3CH_2CHO
−2e
CH_3CH_2COOH
CH_3COCH_3
−6e
$CH_3COOH + HCOOH$

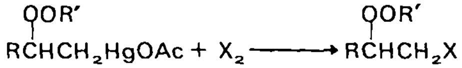
(37)

A novel oxymercuration, which results in eventual net oxidation of the olefin, involves peroxymercuration



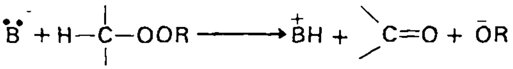
$$RCH{=}CH_2 + Hg(OAc)_2 + R'OOH \longrightarrow \underset{(R' = H \text{ or alkyl})}{R\overset{OOR'}{\overset{|}{C}}HCH_2HgOAc} \qquad (38)$$

The peroxy adduct can be reacted with halogen to give halogen substituted peroxides (X = Br, I) or with a base (B) to give ketones[37]. Reduc-



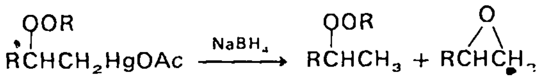
$$R\overset{OOR'}{\overset{|}{C}}HCH_2HgOAc + X_2 \longrightarrow R\overset{OOR'}{\overset{|}{C}}HCH_2X \qquad (39)$$

tion of the adduct with sodium borohydride gives a mixture of peroxide



$$\ddot{B}^- + H{-}\underset{|}{\overset{|}{C}}{-}OOR \longrightarrow \overset{+}{B}H + \gt C{=}O + \bar{O}R \qquad (40)$$

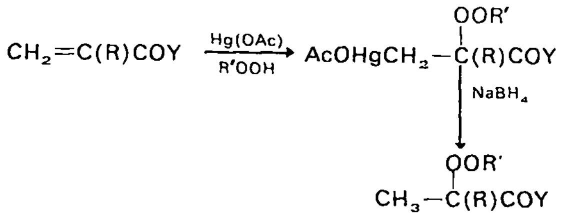
and epoxide[37,38]



$$R\overset{OOR}{\overset{|}{C}}HCH_2HgOAc \xrightarrow{NaBH_4} R\overset{OOR}{\overset{|}{C}}HCH_3 + RCH\overset{O}{-}CH_2 \qquad (41)$$

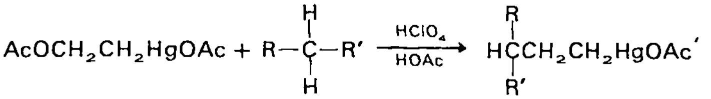
This synthesis has been used to prepare the previously unknown α-carbonyl substituted peroxides[39] ($Y = CH_3$, OCH_3). A by-product (10–30%) was the corresponding epoxide. α,β-Unsaturated esters also gave the corresponding peroxides in high yields[39].

A rather novel oxidation of mercurials involves the reaction of oxymercurials with active methylene compounds followed by the demercura-



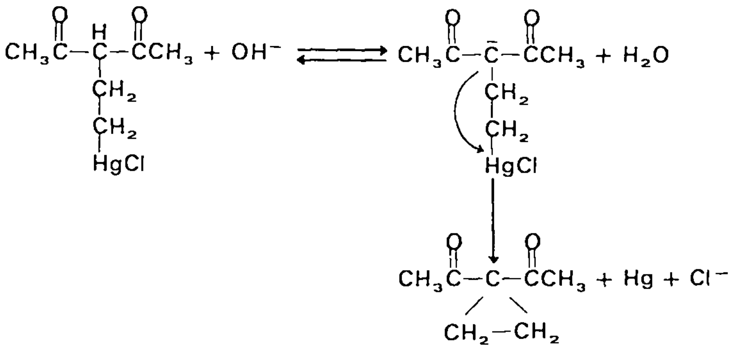
$$CH_2{=}C(R)COY \xrightarrow[R'OOH]{Hg(OAc)_2} AcOHgCH_2{-}\overset{OOR'}{\overset{|}{C}}(R)COY \xrightarrow{NaBH_4} CH_3{-}\overset{OOR'}{\overset{|}{C}}(R)COY \qquad (42)$$

tion of the resulting adducts. The reaction of an acetoxymercurial in acetic acid containing perchloric acid with an active methylene compound such as ethyl acetoacetate results in the introduction of an acetoxymercuriethyl group into the active methylene compound[40]. The scope of the reaction was later studied[41]. It was found to occur between oxy-



$$AcOCH_2CH_2HgOAc + R{-}\underset{H}{\overset{H}{\overset{|}{\underset{|}{C}}}}{-}R' \xrightarrow[HOAc]{HClO_4} H\underset{R'}{\overset{R}{\overset{|}{\underset{|}{C}}}}CH_2CH_2HgOAc' \qquad (43)$$

mercurials of 1-olefins and active methylene compounds which exist mainly in the enol form. These include acetylacetone and benzoylacetone. Acetic acid, methanol, ethanol and 2-propanol have been used as solvents. In aqueous potassium hydroxide, 3,3-diacylpropylmercuric chlorides gave 1,1-diacylcyclopropanes and mercury presumably through an S_N1 mechanism. The same product was obtained in alcohol containing perchloric acid although by a somewhat different type of mechanism.



(44)

c. *Thallium*(III)[42,43]. As opposed to Hg^{II}, oxidation of olefins by Tl^{III} salts is relatively recent. The first report was in 1961 by Grinstead[44] who found that ethylene and 2-hexene were oxidized in water and water–acetic acid media to glycols or their monoesters and carbonyl products. Thus ethylene in water was oxidized to ethylene glycol and acetaldehyde.

$$2C_2H_4 + Tl^{3+} + 2H_2O \longrightarrow CH_3CHO + (CH_2OH)_2 + Tl^{+} + 2H^{+} \qquad (45)$$

TABLE 1. Product distributions for the thallic oxidation of various olefins

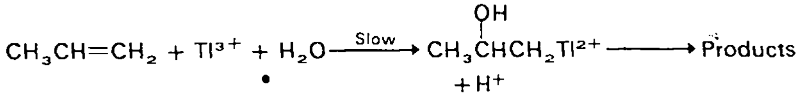
Olefin	Carbonyl product	Carbonyl product (%)	Glycol product (%)
Ethylene	Acetaldehyde	45	55
Propylene	Acetone	75–85	15–25
1-Butene	Methyl ethyl ketone	45–55	15–25
cis-2-Butene	Methyl ethyl ketone	65–80	<0·5
trans-2-Butene	Methyl ethyl ketone	65–80	<0·5
Isobutene	Isobutyraldehyde	37	52

A study[45] of the product distributions from low molecular weight alkenes indicated that both carbonyl and glycol products are formed. With 1-alkenes the only carbonyl product is the ketone rather than the aldehyde. An exception is isobutene which gives isobutyraldehyde as product. Results are listed in Table 1.

The rate of olefin oxidation increased with increasing substitution on one carbon of the double bond[45]. Thus propylene and 1-butene were oxidized 160-times faster than ethylene, and isobutene was oxidized 10^5-times faster than ethylene. This effect of olefin structure is analogous to oxymercuration[4] (see previous section) and in fact the rate expression of $\mathrm{Tl^{III}}$ oxidation is of the same form as that for oxymercuration:

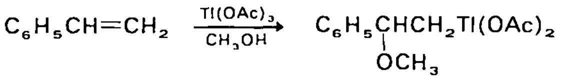
$$\frac{d[\mathrm{Tl}^{3+}]}{dt} = k[\mathrm{Tl}^{3+}][\text{olefin}] \tag{46}$$

These results suggest that an oxythallation adduct is the intermediate. The reaction scheme using propylene as an example would be as follows:



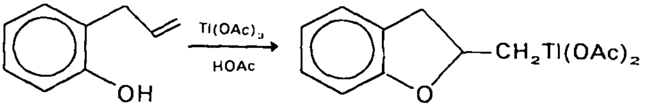
$$\mathrm{CH_3CH{=}CH_2 + Tl^{3+} + H_2O \xrightarrow{Slow} CH_3\underset{}{\overset{OH}{C}}HCH_2Tl^{2+} + H^+ \longrightarrow Products} \tag{47}$$

There is some analogy for the postulated oxythallation intermediate since several adducts have been isolated. They include the reaction product of $\mathrm{Tl(OAc)_3}$ and styrene in methanol[46], the reaction of *o*-allyl phenol with $\mathrm{Tl(OAc)_3}$ in HOAc[47], the reaction product of norbornene



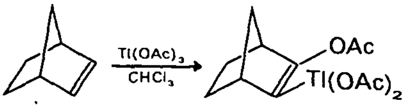
$$\mathrm{C_6H_5CH{=}CH_2 \xrightarrow[CH_3OH]{Tl(OAc)_3} C_6H_5\underset{OCH_3}{C}HCH_2Tl(OAc)_2} \tag{48}$$

with $\mathrm{Tl(OAc)_3}$, in chloroform[48], and the reaction product from isobutene and $\mathrm{Tl(OAc)_3}$ in a mixed solvent containing 80% (v/v) tetrahydrofuran,



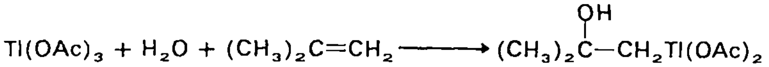
(49)

10 % H_2O and 10 % acetic acid[49]. Note that the stereochemistry of addition



(50)

to norbornene (equation 50) is *cis–exo* analogous to that for oxymercuration. However, it is generally assumed that, as with oxymercuration (see



$$\mathrm{Tl(OAc)_3 + H_2O + (CH_3)_2C{=}CH_2 \longrightarrow (CH_3)_2\overset{\overset{\textstyle OH}{|}}{C}{-}CH_2Tl(OAc)_2} \qquad (51)$$

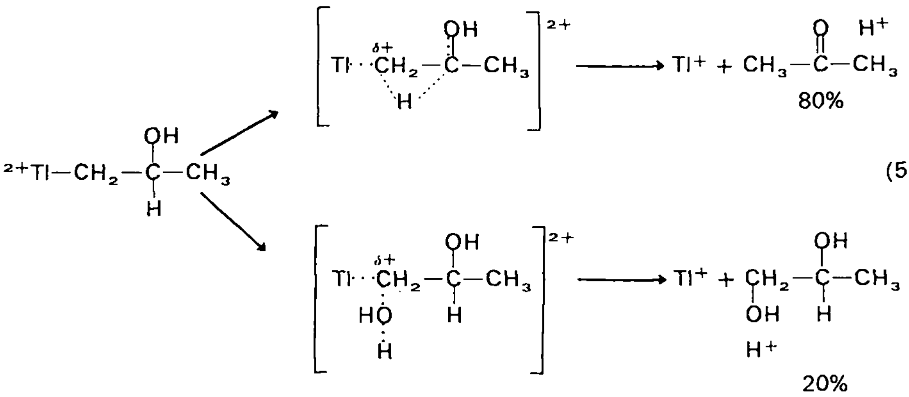
previous section), oxythallation of unstrained olefins is *trans* and stereochemistry of final products can usually be explained on this basis.

The secret to isolating a relatively stable oxythallation adduct is to choose a reaction system in which oxythallation is faster than decomposition. Thus the $\mathrm{Tl^{III}}$ alkyl will be most stable to decomposition when the $\mathrm{Tl^{III}}$ is attached to a primary carbon and is stabilized by complexation to groups such as acetate (see discussion on stability of oxymercuration adducts in previous section). However, in strongly complexing media the oxythallation rate is retarded. To overcome this rate retardation, reactive olefins such as isobutene must be employed, hence in a study of oxidation of the olefins listed in Table 1 in aqueous acetic acid containing acetate ion, it was found that the rate was much slower than in aqueous perchloric acid medium such that the active $\mathrm{Tl^{III}}$ species in the former system is $\mathrm{Tl(OAc)_2{}^+}$ rather than $\mathrm{Tl^{3+}(aq)}$ in the latter system. In the case of isobutene, at high acetate concentration there was evidence that the oxythallation intermediate shown in equation (51) was present in appreciable amounts[50].

Further evidence for intermediate oxythallation adducts in the oxidation of olefins was provided by Byrd and Halpern[51] using stopped-flow techniques. These workers obtained direct spectral evidence for the oxythallation intermediate. They also determined the Taft ρ^* for the reaction and found a value of $-3{\cdot}2$. The similarity of this value to that for hydroxymercuration[4] suggests that a hydroxythallation adduct is an intermediate in the reaction.

The products of the oxidation can be explained if it is assumed that decomposition of the oxythallation product occurs by breaking of the

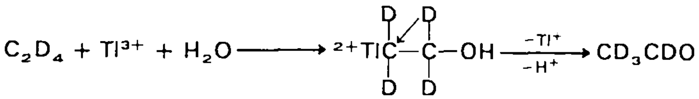
Tl^{III}–carbon bond to give Tl^{I} and an incipient carbonium ion. For the adduct from propylene in water the scheme is as follows:



(52)

Hence, in this particular case the products arise from neutralization of the incipient carbonium ion by hydride shift or attack of water. Note that with propylene in water the product distribution is simpler than in the Hg^{II} oxidation in that allylic oxidation products are not formed. The reason, of course, is that the oxythallation adduct is too reactive to permit the route leading to allylic products to be operative; also note that the carbonyl product is acetone rather than propionaldehyde. This is to be expected since electrophilic additions such as oxythallation are strongly Markownikoff while non-Markownikoff addition followed by decomposition is required to produce propionaldehyde.

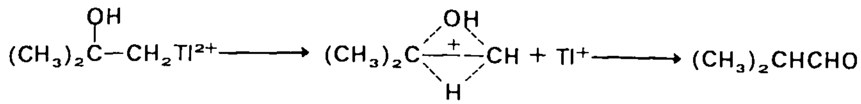
Support for hydride migration in the decomposition of the hydroxythallation adduct comes from deuterium-labelling studies[52]. Ethylene-d_4 is oxidized by Tl^{3+} salts in water to give acetaldehyde-d_4, the product expected from a hydride shift. Furthermore the value of k_H/k_D is 0·8.



$$C_2D_4 + Tl^{3+} + H_2O \longrightarrow {}^{2+}Tl\overset{D}{\underset{D}{C}}-\overset{D}{\underset{D}{C}}-OH \xrightarrow[-H^+]{-Tl^+} CD_3CDO \qquad (53)$$

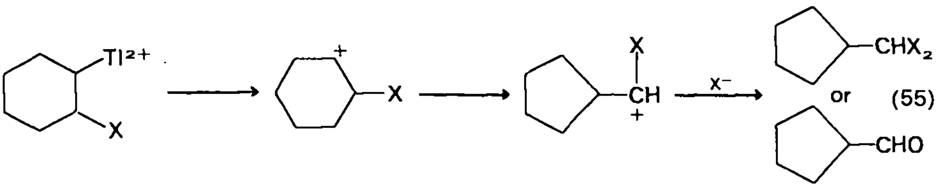
Since it can be shown from other labelling experiments with 1,2-dideuteroethylene that the isotope effect for hydride shift compared to deuteride shift, k_H/k_D is 1·9 the decomposition step must not be rate determining. This is consistent with the scheme represented by equation (47).

With suitable olefin structures, products arising from other means of neutralizing the incipient carbonium ion might be expected. Thus in Table 1 the isobutyraldehyde product obtained from isobutene almost certainly did not arise from the non-Markownikoff addition followed by decomposition but rather by neighbouring hydroxyl participation[50].



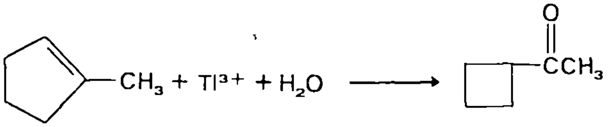
$$(CH_3)_2\overset{OH}{C}-CH_2Tl^{2+} \longrightarrow (CH_3)_2C\overset{+}{-}CH + Tl^{+} \longrightarrow (CH_3)_2CHCHO \qquad (54)$$

Wagner–Meerwein shifts would also be expected and several workers have reported ring-contracted products from cyclohexene in water[53,54], acetic acid[47,55], and methanol[47,56] ($X = OH, OCH_3$ or OAc).



(55)

Cyclobutene[53], cycloheptene[53,57], and cyclooctene[57] also gave ring-contracted products in water and methanol while cyclopentene gave the unrearranged product, cyclopentanone, in water[52]. Apparently the increase in strain in going from a five- to a four-membered ring is great enough to discourage ring contraction. However the 1-methyl-substituted cycloalkenes from butene to heptene all gave ring-contracted products. For instance 1-methylcyclopentene gave cyclobutyl methyl ketone. An interesting ring expansion can also occur; thus methylene cyclopentane in water gave cyclohexanone[53]. The postulated reaction scheme is as follows:



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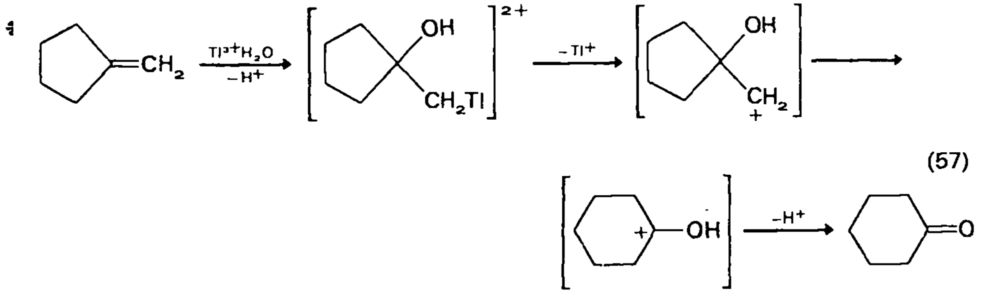
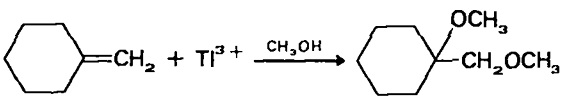


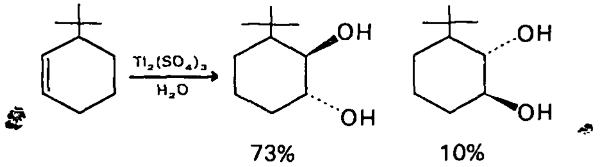
(57)

Other products in the oxidation of these cyclic olefins in water and methanol are 1,2-glycols or their methyl ethers. In many cases these are the major products. Such is the case in the oxidation of methylene cyclohexane in methanol[57].



(58)

In some cases the stereochemistry of the diol products has been determined. The oxidation of 3-*tert*-butylcyclohexene by thallium(III) sulphate in aqueous solution gave the two possible *trans* diols[54]. *Trans* stereochemistry was also found for the diol product in the oxidation of cyclohexene in aqueous solution[53]. This result was interpreted as indicating neighbouring hydroxyl participation in the elimination of Tl$^{\mathrm{I}}$[54]. This is certainly a strong possibility although other possibilities, such as attack



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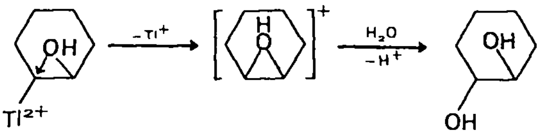
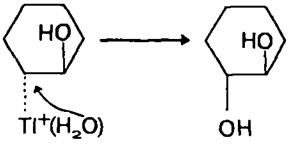


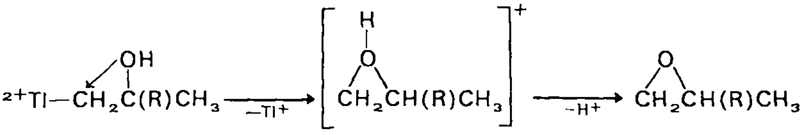
(60)

of water from the coordination sphere of the metal on the incipient carbonium ion as Tl$^{\mathrm{I}}$ leaves, cannot be eliminated. However neighbouring hydroxyl participation has been demonstrated in isobutene oxidation

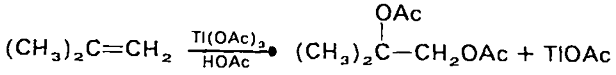


(61)

(equation 54) and in non-nucleophilic media such as 70% (v/v) tetrahydrofuran, 20% water and 10% acetic acid, epoxides are the main products from the oxidation[49]. These could only have arisen from neighbouring hydroxyl participation (R = H or CH_3).

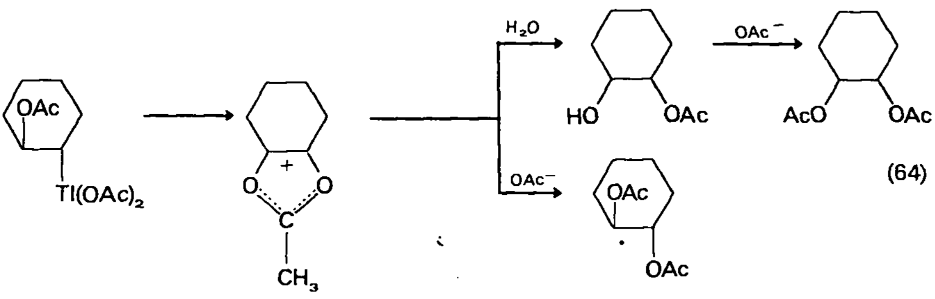

(62)

In acetic acid oxidations by $Tl(OAc)_3$ the major products are 1,2-diacetates. as, e.g. in the oxidation of isobutene[47]. There is evidence

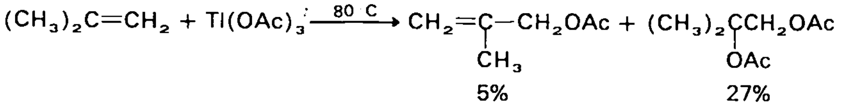


$$(CH_3)_2C{=}CH_2 \xrightarrow[HOAc]{Tl(OAc)_3} (CH_3)_2\overset{OAc}{\overset{|}{C}}{-}CH_2OAc + TlOAc \qquad (63)$$

that these diacetates arise from neighbouring acetate participation. The oxidation of cyclohexene by $Tl(OAc)_3$ in dry HOAc, along with ring-contracted products (equation 55), yields 1,2-diacetate of mainly *trans* (88 % *trans*) stereochemistry. However in wet acetic acid the diacetate is mainly *cis* (81 % *cis*)[55]; similar results were observed by Lee and Price[58]. Since acetate will attack an acetoxonium ion *trans* while water will open it *cis*[59], these results are consistent with the following scheme:

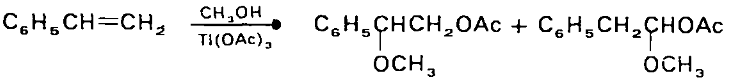

(64)

As mentioned previously one significant difference between Hg^{II} and Tl^{III} oxidations is the much greater importance of allylic oxidation in Hg^{II} oxidations as opposed to Tl^{III} oxidations. In aqueous solution they are usually not found. However in acetic acid $Hg(OAc)_2$ gives almost exclusively allylic acetates, therefore if allylic oxidation products are formed in Tl^{III} oxidations, the $Tl(OAc)_3$ oxidations in acetic acid would be the most likely reaction condition. The oxidation of cyclohexene in acetic acid by $Tl(OAc)_3$ at 25 °C did, in fact, give 2–3 % yield cyclohexen-3-yl acetate: At 95 °C the yield increased to 11 %[54]. The oxidation of isobutene under similar conditions gave 5 % of allylic oxidation product along with a 27 % yield of 1,2-diacetate.



$$(CH_3)_2C{=}CH_2 + Tl(OAc)_3 \xrightarrow{80\ C} \underset{\substack{CH_3\\ 5\%}}{CH_2{=}C{-}CH_2OAc} + \underset{\substack{OAc\\ 27\%}}{(CH_3)_2CCH_2OAc} \qquad (65)$$

The oxidation of styrene might be expected to yield products arising from phenyl migration. Criegee[46] reported that the oxidation of styrene in methanol gave both 1,2- and 1,1-disubstituted phenylethanes. The 1,1-products must have arisen from phenyl migration. Kabbe[47] reported

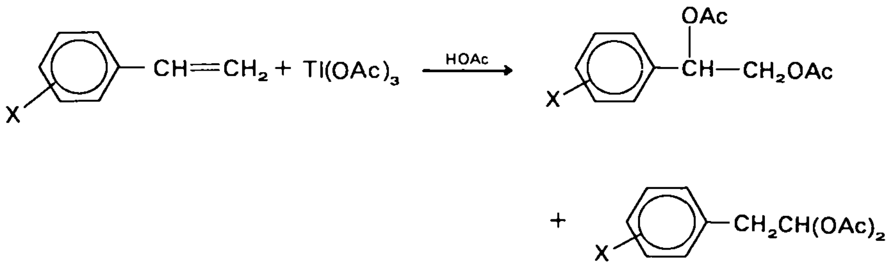


$$C_6H_5CH{=}CH_2 \xrightarrow[Tl(OAc)_3]{CH_3OH} \underset{OCH_3}{C_6H_5CHCH_2OAc} + \underset{OCH_3}{C_6H_5CH_2CHOAc} \qquad (66)$$

similar results in both methanol and acetic acid. He found that methanol gave the largest amounts of rearranged products.

McKillip and coworkers[57] found that $Tl(NO_3)_3$ in methanol gave large amounts of rearranged products. Styrene gave, after workup, 85 % yield of phenylacetaldehyde while α-methylstyrene gave 81 % yield of phenylacetone.

There have been two careful kinetic and product distribution studies on substituted styrenes. Ouellette and coworkers[60] studied the oxidation of styrene and 5-phenyl substituted styrenes by $Tl(OAc)_3$ in HOAc. They found that the rate increased as the electron-releasing ability of X increased (X = p-CH_3O, p-CH_3, m-CH_3, H, p-Cl, m-Cl).



(67)

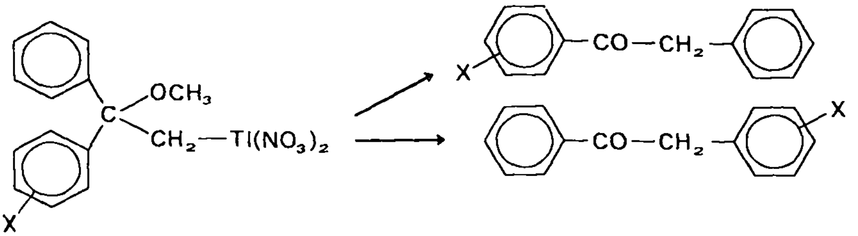
The value ρ^+ is $-2{\cdot}2$. This is similar to the results in water which indicate that oxythallation is the rate-determining step and this addition has considerable carbonium ion character in the transition state.

The ratio of the 1,1-diacetates to 1,2-diacetates also depends strongly on X. When X = p-CH_3O the ratio is 1·80, while when X = m-Cl, the ratio is 0·02. The changes in ratio correlated well with σ^+ giving a ρ^+ of $-1{\cdot}7$. This indicates resonance interaction of the aromatic ring with the positive centre formed as the Tl^I is leaving. The trends are in keeping with migration towards a carbon with positive character.

More recently a similar study employed $Tl(NO_3)_3$ in methanol[61]. The olefinic substrates were styrene and α-methylstyrenes as well as their ring-substituted analogues. In contrast to a previous report[62] they obtained quantitative yields of the dimethylacetals of the corresponding aldehydes from the styrenes. The α-methylstyrenes gave the corresponding phenyl acetones. The Hammett relationship was obeyed for

$$\mathrm{ArCH{=}CH_2 + Tl(NO_3)_3 + 2CH_3OH \longrightarrow ArCH_2CH(OCH_3)_2 + TlNO_3 + 2HNO_3} \qquad (68)$$

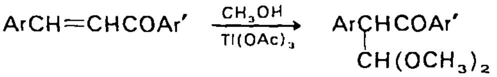
the relative rates of both the various substituted styrenes and α-methylstyrenes to give a ρ of $-4{\cdot}2$. Since no 1,2-disubstituted products were obtained, these workers could not measure the relative migratory ability of the various substituted aromatic groups. Instead they used 1,1-diphenylethylenes with one phenyl group containing a substituent. The ratio of the two products was used as a measure of relative migratory ability. This very interesting study indicated that Brown σ^+ relationship held, giving ρ^+ of



(69)

$-2{\cdot}27$. These results are in agreement with the observations of Ouellette[60]. The higher value of ρ and ρ^+ reflect the more ionic character of $Tl(NO_3)_3$ as compared with $Tl(OAc)_3$.

Another oxidation of olefins involving phenyl migration is the oxidation of chalcones first reported by Ollis and his coworkers[63,64]. When highly activated chalcones ($Ar = 4\text{-}CH_3OC_6H_4$, $Ar' = C_6H_5$) are treated with $Tl(OAc)_3$ in CH_3OH, an acetal is formed. However yields were low and



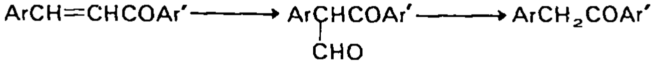
$$\mathrm{ArCH{=}CHCOAr' \xrightarrow[Tl(OAc)_3]{CH_3OH} Ar\underset{\displaystyle CH(OCH_3)_2}{\underset{|}{C}}HCOAr'} \qquad (70)$$

reaction conditions strenuous. This work was extended by McKillop and coworkers[65]. Using the more reactive $Tl(NO_3)_3$ in methanol, these workers were able to conduct the reaction with unsubstituted chalcone ($Ar = Ar' = C_6H_5$) under mild reaction conditions. However, the yields of the acetal were generally low (<20%). These low yields were the result of further reaction of the acetal to give deoxybenzoin, benzoin, and finally benzil. The benzil yield was highest in an aqueous glyme–perchloric acid media and occurred when there were no deactivating

$$\mathrm{Ar{-}CH{=}CH{-}CO{-}Ar'} \longrightarrow \mathrm{Ar{-}CO{-}CO{-}Ar'} \qquad (71)$$

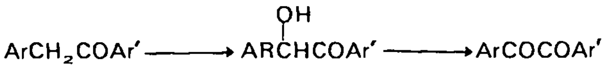
groups on Ar or Ar′. Maximum yield of benzoin occurred when three equivalents of $Tl(NO_3)_3$ were used per equivalent of chalcone.

The initial product is almost certainly 2-benzoylphenylacetaldehyde which undergoes retro-Claisen cleavage to give deoxybenzoin. The



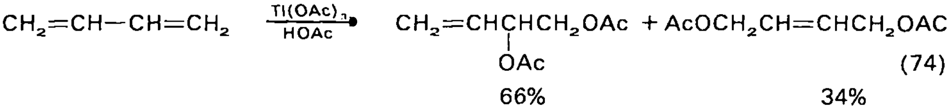
$$\mathrm{ArCH{=}CHCOAr'} \longrightarrow \mathrm{Ar\underset{\displaystyle CHO}{\underset{|}{C}}HCOAr'} \longrightarrow \mathrm{ArCH_2COAr'} \qquad (72)$$

deoxybenzoin is then oxidized to benzoin and finally to benzil. The oxidations probably proceed through the enol forms of the carbonyl groups.



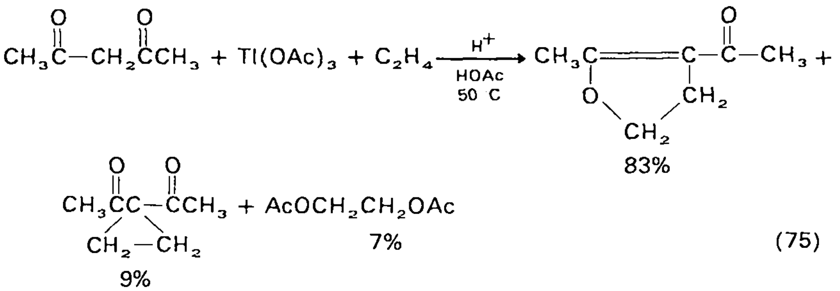
$$\mathrm{ArCH_2COAr'} \longrightarrow \mathrm{AR\overset{\displaystyle OH}{\overset{|}{C}}HCOAr'} \longrightarrow \mathrm{ArCOCOAr'} \qquad (73)$$

The oxidation of 1,3-dienes by $Tl(OAc)_3$ in acetic acid has been reported by Uemura and coworkers[66]. Products arise from both 1,2- and 1,4-addition of $Tl(OAc)_3$. The reaction of butadiene itself gives mainly 1,2-diacetate.



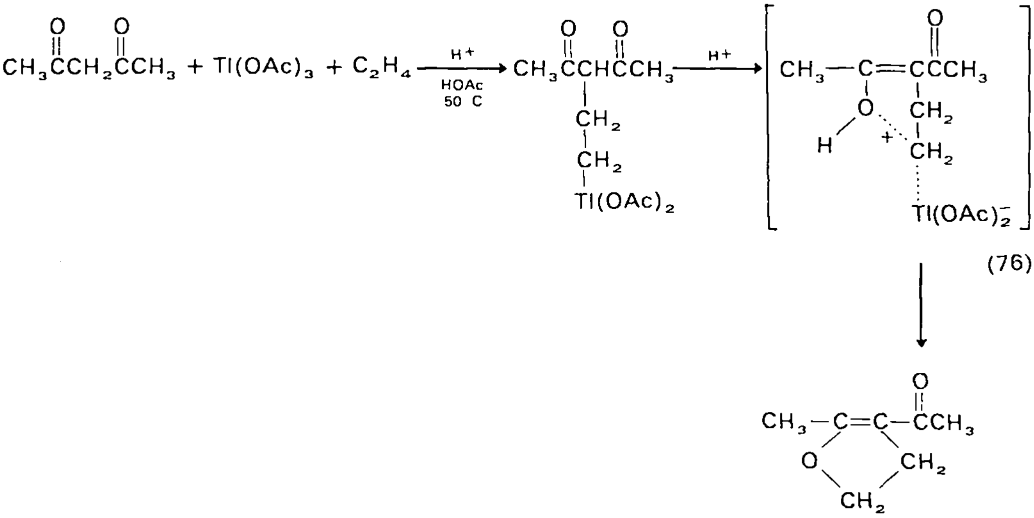
$$\mathrm{CH_2{=}CH{-}CH{=}CH_2} \xrightarrow[\mathrm{HOAc}]{\mathrm{Tl(OAc)_3}} \underset{66\%}{\mathrm{CH_2{=}CH\underset{\displaystyle OAc}{\underset{|}{C}}HCH_2OAc}} + \underset{34\%}{\mathrm{AcOCH_2CH{=}CHCH_2OAC}} \qquad (74)$$

Thallic acetate oxidizes olefins in the presence of active methylene compounds[67] in a manner analogous to that reported for $Hg(OAc)_2$ in the previous section. In this case, however, the main product was a dihydrofuran derivative. The route for formation of the main product must involve hydroxyl participation in the elimination of Tl^I.



(75)

Remote hydroxyl participation in dethallation was also reported by Byrd and Halpern[51]. Thus 1-buten-4-ol and 1-penten-4-ol gave 3-hydroxytetrahydrofuran, and 2-methyl-4-hydroxytetrahydrofuran. The scheme for decomposition of the 1-buten-4-ol adduct would be as follows:



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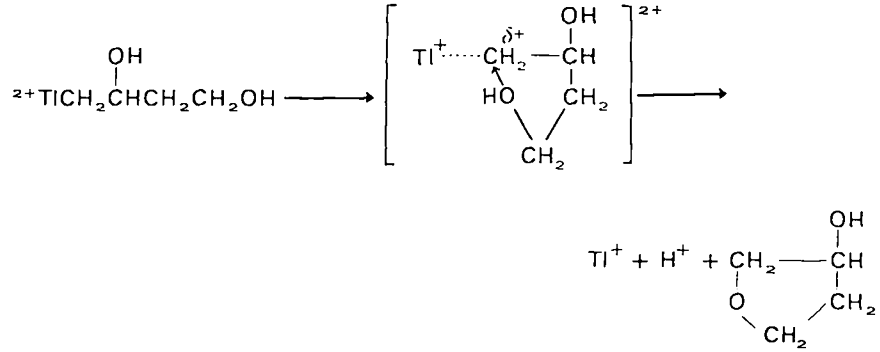
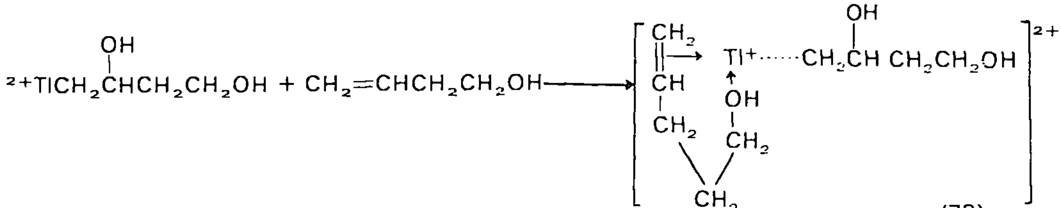


(77)

Another type of hydroxyl + olefin participation was observed by the same workers. Excess 1-penten-5-ol was found to catalyse the decomposition of the oxythallation adduct. The reason for this catalysis was postulated to be stabilization of the leaving Tl^{1+} by coordination to the olefinic alcohol.

There is one report of the use of thallic chloride as a chlorinating agent in CCl_4[68]. However, the main products were the monochlorinated



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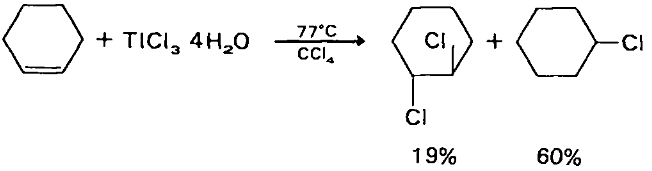
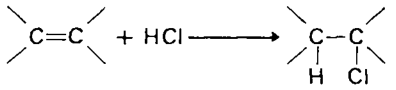
products which must have arisen from the non-oxidative addition of HCl. Thus with cyclohexene, *trans* 1,2-dichlorocyclohexene was the minor and monochlorocyclohexane the major product.



(79)

Phosgene was also detected from oxidation of the solvent. This reaction must be the source of HCl. The reaction could be made slightly catalytic

$$CCl_4 + TlCl_3.4H_2O \longrightarrow COCl_2 + 2HCl + TlCl_3.3H_2O \qquad (80)$$



(81)

by addition of $CuCl_2$ and passing O_2 through the reaction mixture. The $CuCl_2$ reaction gave much higher yields of dichloro products. However, since $CuCl_2$ itself is a better chlorinating agent than $TlCl_3$ (see section on $CuCl_2$ oxidations), it is doubtful that $TlCl_3$ is really the catalyst in this case.

As with Hg^{II} the rate of reaction of Tl^{III} with olefins depends strongly on reaction conditions. Thallic salts with strongly complexing ligands such as acetate or halogen react many times slower than Tl^{III} salts of non-complexing ligands such as perchlorate or nitrate. However, even with free thallic ion in aqueous solution the rate can be increased considerably by addition of non-complexing salts such as sodium perchlorate. For instance, increasing the sodium perchlorate concentration from zero to 5·5 M increases the rate of ethylene oxidation[69] by a factor of over 60. The explanation is that addition of salts causes the water activity to decrease because of hydration of the salts. As the water activity decreases the $Tl^{3+}(aq)$ becomes less solvated and more reactive.

A quantitative study of the effect of acetate ions on the oxidation in aqueous acetic acid has been carried out[70]. In this reaction medium, the values of K_{34} and K_{23} were determined by pH measurements. It was

$$\mathrm{Tl(OAc)_2^+ + OAc^-} \overset{K_{23}}{\rightleftharpoons} \mathrm{Tl(OAc)_3} \tag{82}$$

$$\mathrm{Tl(OAc)_3 + OAc^-} \overset{K_{34}}{\rightleftharpoons} \mathrm{Tl(OAc)_4^-} \tag{83}$$

found that increasing the free acetate concentration strongly retarded the rate of olefin oxidation. Using the values of K_{23} and K_{34} previously determined it could be shown that the active species in the range of acetate concentration studies was $Tl(OAc)_2^+$. $Tl(OAc)_3$ could have some reactivity, but its rate of olefin oxidation was less than 5% of $Tl(OAc)_3$. $Tl(OAc)_4^-$ was completely unreactive. This study did not cover the range at which $Tl(OAc)^{2+}$ was an important species, so its reactivity was not measured. A later, more elaborate study, using the enol form of cyclohexanedione as organic substrate, indicated that $Tl(OAc)^{2+}$ was more reactive than $Tl(OAc)_2^+$[71]. $Tl(OAc)_3$ did have appreciable reactivity in this system, but $Tl(OAc)_2OH$ was more reactive than either $Tl(OAc)_3$ or $Tl(OAc)_2^+$. An interesting point is that all these species were more reactive than Tl^{3+}(aq) itself. The rates were in the order: $Tl(OAc)^{2+} > Tl(OAc)_2OH > TlOH^{2+} > Tl(OAc)_2^+ > Tl(OAc)_3 > Tl^{3+}$(aq).

In the case of halogen complexes TlX^{2+} (X = Cl or Br) is also more reactive than Tl^{3+}(aq) or $TlOH^{2+}$. Higher complexes are unreactive. It is interesting, however, that in the oxidation of styrene, $TlCl^{2+}$ is considerably less reactive than Tl^{3+}(aq)[60].

These studies suggest that the most effective form of Tl^{III} for oxidizing olefins would be a non-complexing salt of Tl^{III} in a poorly solvating solvent. Such a system is $Tl(NO_3)_3$ in methanol which has been used successfully and quite extensively by Taylor, McKillop and coworkers[56,57,61,65].

In comparison with mercury(II), thallium(III) reacts with olefins somewhat slower than mercury(II). The factor is probably over a 100 in most cases. This difference probably reflects the effect of the extra positive charge on Tl^{III} which causes the ligand or solvation shell to be held more strongly. However, in the case of mercury(II), the initial products are usually stable oxymercuration adducts, while the thallium(III) intermediates almost always go directly on to oxidation products.

The reduced form of the oxidant, Tl^{I}, is not reoxidized by air so that the reactions have the disadvantage of not being catalytic. However, a successful electrochemical oxidation of alkenes, using Tl^{III} as catalyst, has been developed[73]. The alkene is oxidized by Tl^{III} to give oxidation products plus Tl^{I}. The Tl^{I} is then regenerated at the anode to Tl^{III}. Relatively

$$\mathrm{Tl^{III}} + \text{Alkene} \longrightarrow \text{Products} + \mathrm{Tl^{I}} \qquad (84)$$

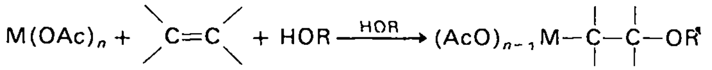
high current efficiencies have been obtained while performing at a con-

$$\mathrm{Tl^{I}} \xrightarrow{\text{anode}} \mathrm{Tl^{III}} \qquad (85)$$

trolled potential. The anode and cathode departments are separated in this process to prevent further oxidation of the initial products.

d. *Lead*(IV)[74–76]. Due to its high redox potential, lead(IV) is unstable in aqueous solution as are its salts of non-complexing anions in almost any solvent. For that reason lead(IV) is almost exclusively used in organic oxidations as lead tetraacetate (LTA). Like $\mathrm{Hg^{II}}$, organic oxidations by LTA have been studied for a number of years. Dimroth and coworkers[77] first used it in 1920. Much of the work on LTA has been carried out by Criegee and his coworkers. Criegee reviewed the field in 1963[74] and 1965[75].

LTA in oxidation potential stands on the other side of $\mathrm{Tl^{III}}$ from $\mathrm{Hg^{II}}$. $\mathrm{Hg^{II}}$ gave considerable amounts of allylic oxidation products because the intermediate oxymercuration did not readily demercurate to give the products expected from this route. $\mathrm{Tl^{III}}$, on the other hand, gave, almost exclusively, products expected from elimination of $\mathrm{Tl^{I}}$ from the intermediate oxythallation adduct to give an incipient carbonium ion. As witnessed by the failure to isolate any LTA oxyplumbation adducts, the intermediates in LTA oxidations are even less stable than those of $\mathrm{Tl^{III}}$. Thus it might be predicted that LTA oxidations might give products arising exclusively from oxyplumbation, followed by elimination of $\mathrm{Pb^{II}}$ from the intermediate. However, LTA oxidations do not follow this simple scheme for two reasons. First LTA is considerably less reactive than $\mathrm{Tl(OAc)_3}$ in the initial reaction to give the intermediate adducts ($\mathrm{M = Pb^{IV}}$ or $\mathrm{Tl^{III}}$). This allows more opportunity for side reactions to

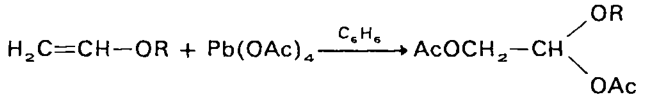


$$\mathrm{M(OAc)}_n + \mathrm{C{=}C} + \mathrm{HOR} \xrightarrow{\mathrm{HOR}} \mathrm{(AcO)}_{n-1}\mathrm{M{-}C{-}C{-}OR'} \qquad (86)$$

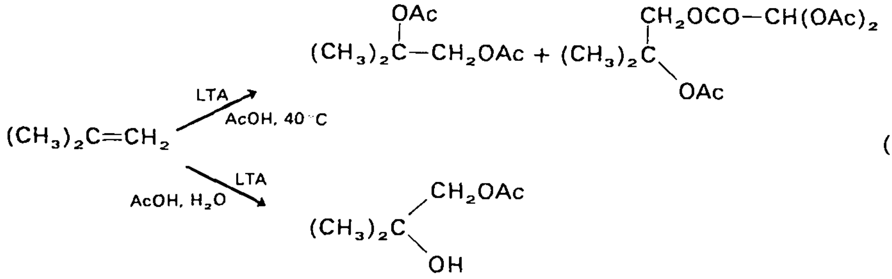
occur. Secondly, LTA is such a powerful oxidant that one-electron oxidations become important. This type of oxidation is generally not present in $\mathrm{Hg^{II}}$ or $\mathrm{Tl^{III}}$ oxidations. Finally, with LTA the initial products are often oxidized to secondary oxidation products.

An indication of the lower reactivity of LTA as compared with $\mathrm{Hg(OAc)_2}$ and $\mathrm{Tl(OAc)_3}$ is the fact it does not react with unactivated olefins such as ethylene. Olefins with activating groups such as enol ethers react much more readily to give diacetate products when benzene is the solvent[78–80].

The reaction of isobutene, also a fairly activated olefin towards electrophilic attack, gives some 1,2-diacetates in dry acetic acid, but the main


(87)

product is a glyoxylic acid derivative. In wet acetic acid the main product is hydroxyacetate. The formation of hydroxyacetate in wet acetic acid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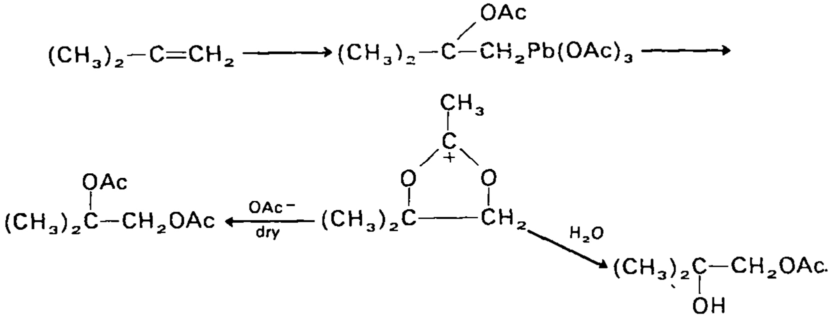
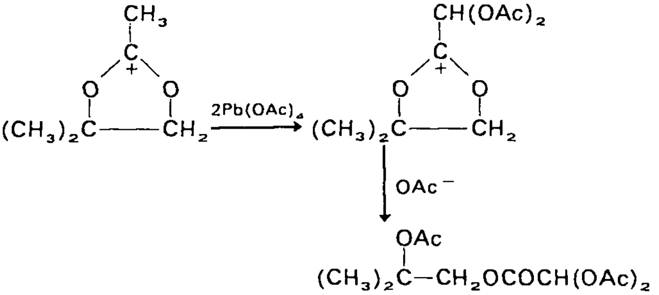
suggests an acetoxonium ion intermediate. It has been suggested that the

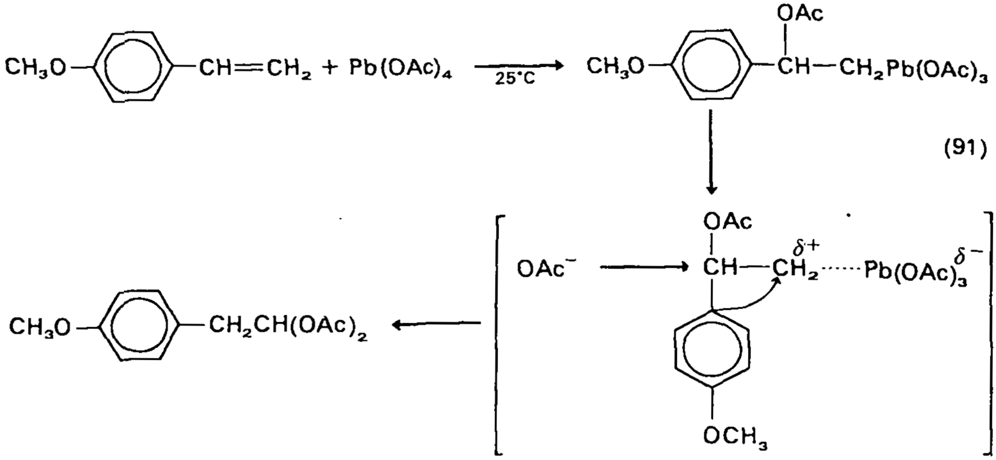

(89)

acetoxonium ion is oxidized followed by attack of acetate to give the glycollic acid derivative[75].


(90)

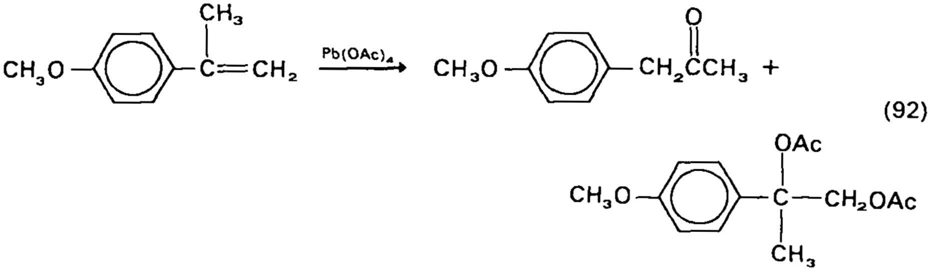
The oxidation of styrene derivatives has received some study. As with $Tl(OAc)_3$ oxidations, phenyl migration is a feature of these oxidations.

Thus *p*-methoxystyrene gives a 90% yield of geminal diacetates[78,82] and ^{14}C-labelling experiments confirmed that phenyl migration occurred[82].


CH₃O
CH=CH₂ + Pb(OAc)₄
25°C
OAc
CH—CH₂Pb(OAc)₃
OAc⁻
δ+
δ−
CH—CH₂······Pb(OAc)₃
OCH₃
CH₂CH(OAc)₂

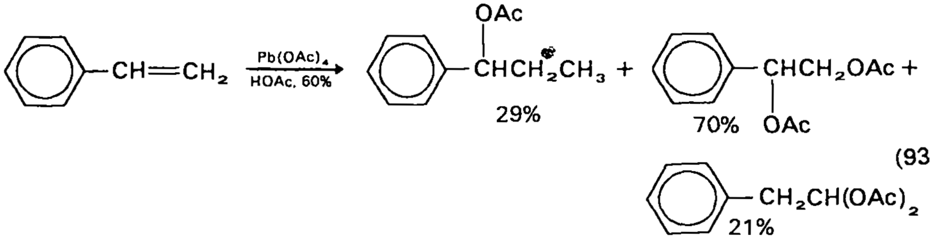
(91)

Oxidation of *p*-methoxy-α-methyl styrene gives, in addition to 1,2-diacetates, *p*-methoxyacetone, which also must have arisen from a phenyl migration[82].


CH₃
CH₃O
C=CH₂
Pb(OAc)₄
O
CH₂CCH₃ +
OAc
C—CH₂OAc
CH₃

(92)

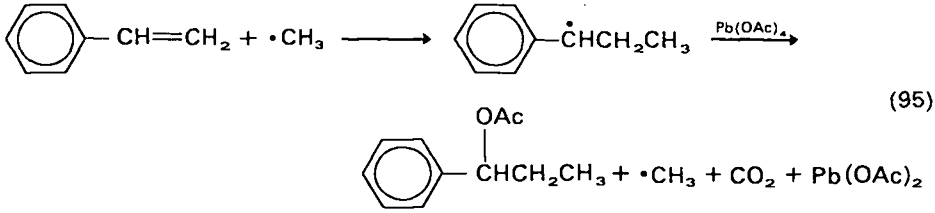
The competition between heterolytic (two electron) and homolytic (radical) pathways has been studied mainly in the styrene series of olefins. Styrene gives the following product distribution at 60 °C in acetic acid (also traces of C_6H_5CHO found)[83]. The major product, which essentially


CH=CH₂
Pb(OAc)₄
HOAc, 60%
OAc
CHCH₂CH₃ +
29%
CHCH₂OAc +
70%
OAc
CH₂CH(OAc)₂
21%

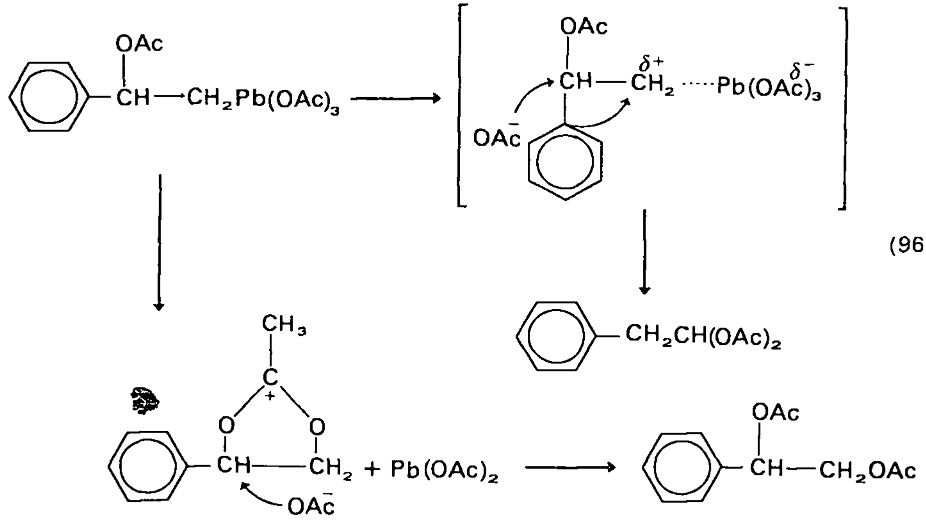
(93)

results from addition of methyl acetate across the double bond, must arise from a radical process since its formation is almost completely inhibited by free-radical scavengers. A plausible route is the following:

$$Pb(OAc)_4 \longrightarrow Pb(OAc)_3^{\bullet} + {}^{\bullet}CH_3 + CO_2 \qquad (94)$$


(95)

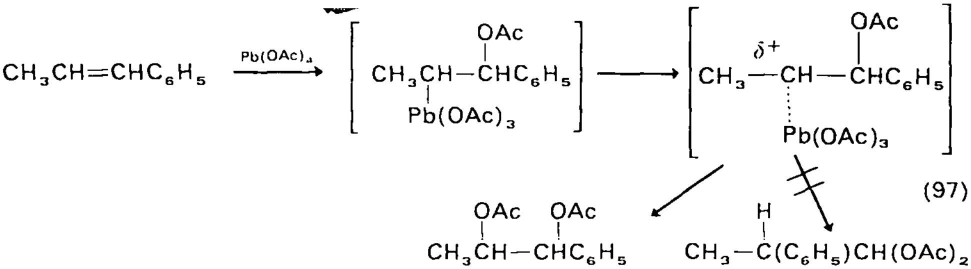
The other products would, of course, arise from oxyplumbation followed by heterolytic splitting of the Pb–carbon bond with phenyl migration or neighbouring acetate participation.


(96)

Increase in temperature favoured the homolytic route, hence at 80 °C the free-radical path accounted for 49 % of the product as opposed to 29 % at 60 °C and 1 % at 45 °C.

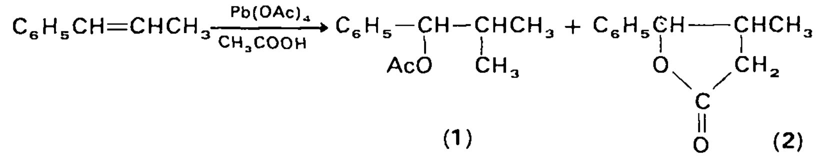
The oxidation of α- and β-methylstyrene was also studied[84]. For α-methylstyrene the relative importance of the heterolytic path compared with the homolytic path was about 19-times greater than it was for styrene. Thus the homolytic path was unimportant for this olefin.

cis- and *trans*-β-Methylstyrene underwent both the heterolytic and homolytic reactions more slowly than styrene. Also, no products arising from phenyl migration are observed. This is in marked contrast to styrene and α-methylstyrene, which give large amounts of rearranged products. The reason for this lack of phenyl participation is probably the fact that in this case lead is leaving from a secondary carbon rather than from a primary carbon as is the case with styrene or α-methyl styrene. The incipient carbonium ion on the secondary carbon is more stabilized than on a primary carbon and there is less need for participation in the decomposition step. The lower rate of reaction of β-methylstyrene as compared with styrene in both homolytic and heterolytic pathways must result from steric hindrance to oxyplumbation and addition of methyl radicals respectively.



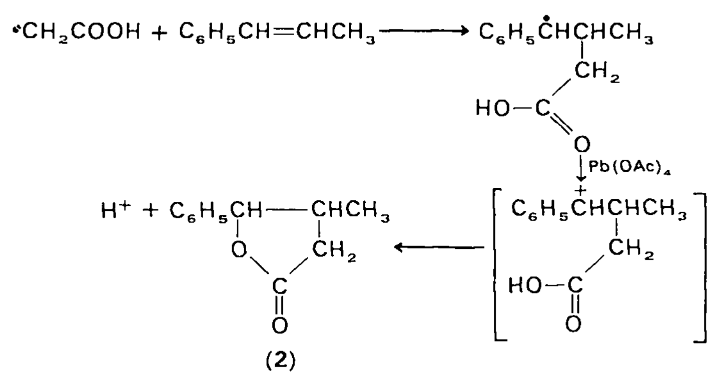
(97)

At higher temperatures a γ-lactone has been found to be another major product formed by a radical route. Heiba and coworkers[85], using potassium acetate to suppress the heterolytic route and to raise the boiling point of acetic acid to 138 °C (which also increases the proportion of homolytic products[83]), found a γ-lactone and the product from addition of methyl acetate to the double bond to be the main products. The latter is known to arise from a radical process (equations 94 and 95). The γ-lactone apparently also is formed by a radical route. The methyl radical formed by



(98)

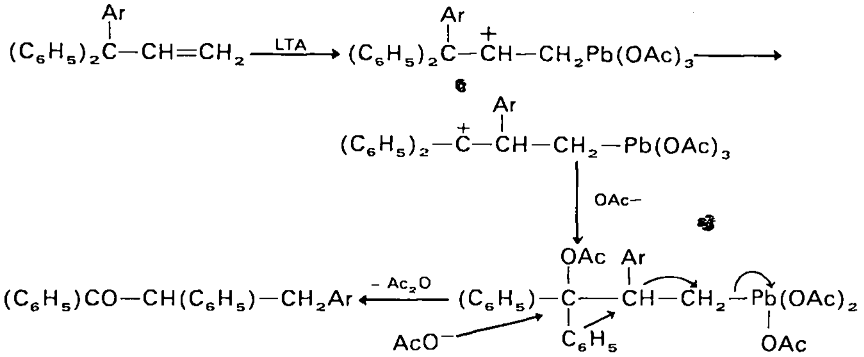
$$\cdot CH_3 + CH_3COOH \longrightarrow \cdot CH_2COOH + CH_4 \qquad (99)$$



(100)

equation (94) can react with acetic acid to give an acetic acid radical which then gives the γ-lactone by the route in equation (99). Since there is competition for the methyl radical between olefin to give **1** and acetic acid eventually to give **2**, the ratio **2**/**1** might be expected to increase as the ratio [HOAc]/[olefin] increases. This relationship is actually found lending support to the proposed mechanism.

An interesting double migration is observed with 3,3,3-triarylpropenes when one of the aryl groups is anisyl[86]. The postulated scheme is as follows (Ar = p-$C_6H_4OCH_3$):

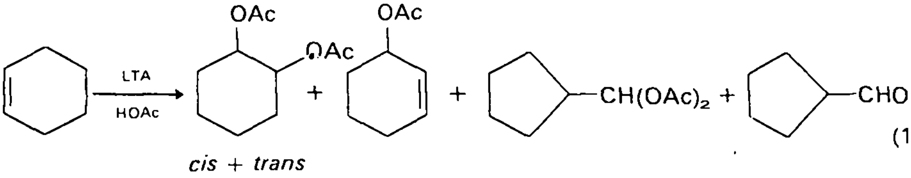


(101)

In most of the oxidations of the acyclic olefins discussed above, allylic oxidation products were found to some extent, and in the oxidation of some olefins such as hexene, 2,3-dimethylpentene-2 and *cis*-octene-4 allylic oxidation products are the only products found in low yield[87,88]. Possible modes of formation of these allylic oxidation products will be considered in the following discussion of the oxidation of cyclic olefins.

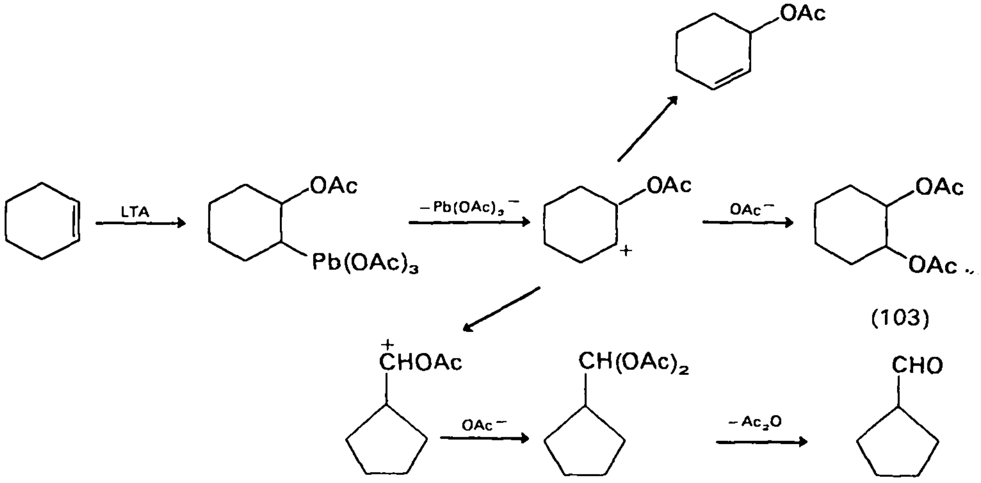
In general, most mechanistic work on LTA acetate oxidations has been carried out on cyclic olefins. One reason, no doubt, is that stereochemistry of 1,2-disubstituted products can be readily determined.

The oxidation of cyclohexene has been studied by several workers[25,47,55,89]. 1,2-Diacetates, allylic acetate and ring-contracted products were formed. The product distribution has been explained by



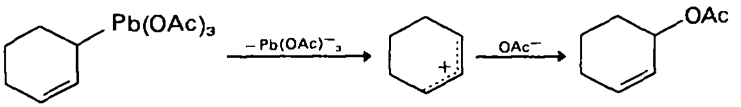
(102)

oxyplumbation followed by elimination of Pb^{II} to give a carbonium ion, although it is doubtful if a free carbonium ion is formed[90]. This heterolytic scheme seems reasonable and is very similar to that postulated for


OAc
LTA
OAc
Pb(OAc)$_3$
− Pb(OAc)$_3^-$
OAc
+
OAc$^-$
OAc
OAc
$\overset{+}{\text{C}}$HOAc
OAc$^-$
CH(OAc)$_2$
− Ac$_2$O
CHO

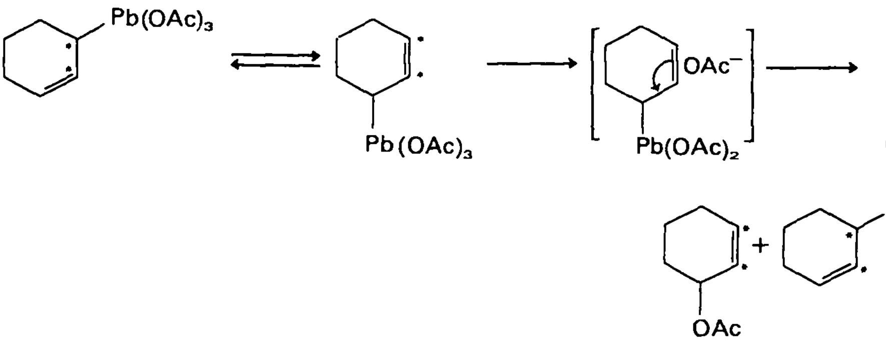
(103)

Tl(OAc)$_3$ oxidations. However the formation of allylic acetate does not appear to occur by this route. ^{13}C-labelling experiments^{25} have indicated that a symmetrical intermediate such as allylic carbonium ion is present. This allylic carbonium ion could arise by elimination of Pb^{II} from an allylic lead(IV) intermediate.


Pb(OAc)$_3$
− Pb(OAc)$^-_3$
+
OAc$^-$
OAc

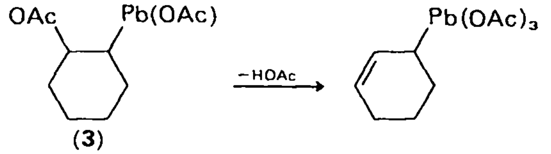
(104)

The elimination could be concerted as was proposed previously for the decomposition of allylic mercurials (equation 19). In this case the ^{13}C-labelling results can be rationalized if the allylic lead(IV) intermediate undergoes allylic rearrangement before decomposition.


Pb(OAc)$_3$
Pb(OAc)$_3$
OAc$^-$
Pb(OAc)$_2$
+
OAc
OAc

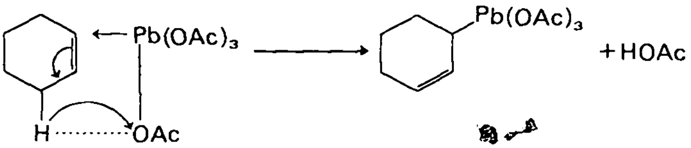
(105)

The mode of formation of the allylic Pb^{IV} intermediate is not obvious. Almost certainly it does not arise from oxyplumbation followed by elimination of HOAc, a route suggested for formation of allylic mercurial[30],


OAc
Pb(OAc)
−HOAc
Pb(OAc)$_3$
(3)

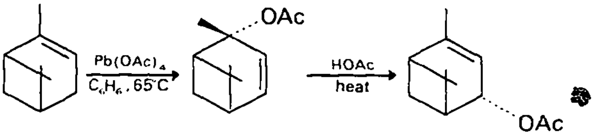
(106)

because the intermediate **3** would be too unstable to oxidative decomposition to permit elimination of HOAc. More likely it is a direct attack analogous to that originally proposed for formation of allylic mercurials[27].


Pb(OAc)$_3$
H
OAc
Pb(OAc)$_3$
+HOAc

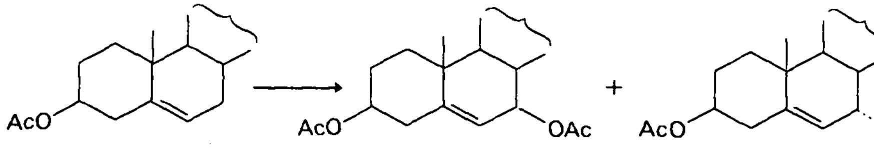
(107)

In many cases the allylic oxidation product is the major product. Pinene in benzene solvent is oxidized to *cis*-2-acetoxypin-3-ene which rearranges in acetic acid to *trans*-verbenyl acetate[91,92], the final product observed in acetic acid.


Pb(OAc)$_4$
C$_6$H$_6$, 65°C
OAc
HOAc
heat
OAc

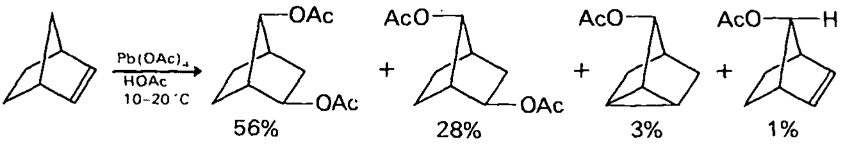
(108)

Allylic oxidation also occurs with 5,6-unsaturated steroids. Cholesteryl acetate gives a 50% yield of a mixture of 7α- and 7β-acetates[93].


AcO
AcO
OAc
+
AcO
OAc

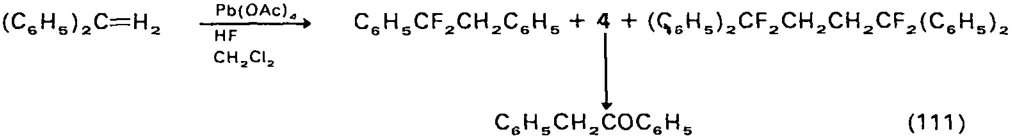
(109)

Alder and coworkers[94] reported that norbornene is oxidized to *syn*-2,7-norbornenediol diacetate. However, in a later study three other products were also detected[95].


Pb(OAc)$_4$
HOAc
10–20°C
OAc
OAc
56%
+
AcO
OAc
28%
+
AcO
3%
+
AcO
H
1%

(110)

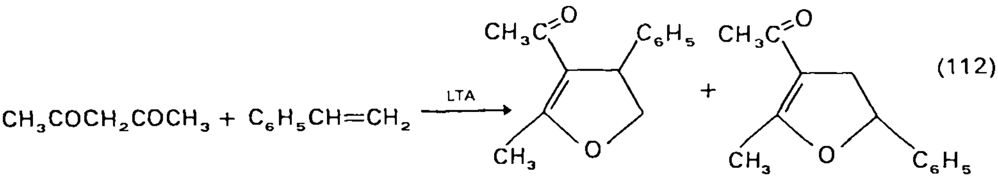
Fluorination of olefins with a mixture of LTA and hydrogen fluoride has been studied by several workers[96–101]. 1,1-Difluoro-1,2-diphenylethane and deoxybenzoin plus smaller amounts of 1,4-difluoro-1,1,4,4-tetraphenylbutane were obtained. The deoxybenzoin was a secondary



$$(C_6H_5)_2C{=}H_2 \xrightarrow[\text{HF}\ \ CH_2Cl_2]{Pb(OAc)_4} C_6H_5CF_2CH_2C_6H_5 + \underset{\underset{C_6H_5CH_2COC_6H_5}{\downarrow}}{4} + (C_6H_5)_2CF_2CH_2CH_2CF_2(C_6H_5)_2 \qquad (111)$$

product formed from a precursor **4**. This precursor has been tentatively assigned the structure $C_6H_5C(OAc)(Y)CH_2C_6H_5$ where Y = F or OAc. Norbornene is oxidized in this system to a wide range of rearranged products containing one or two fluorines or acetates or both. Originally a radical route was suggested for the fluorination reaction, but more recent work[101] indicates that the reaction proceeds by addition of the elements of -F or -OAc plus $-Pb(OAc)_3$ across the double bond followed by heterolytic splitting of the lead(iv) carbon bond.

As with Hg^{II} and Tl^{III}, LTA will also oxidize olefins in the presence of active methylene compounds. Styrene, in the presence of acetylacetone, gives two dihydrofuran derivatives[102].



e. *Bismuth*(v). The writer is aware of only one report of oxidation by bismuth salts. In it was reported that $NaBiO_3$ in HOAc or $ClCH_2CO_2H$ oxidizes olefins, such as propylene, the butenes and cyclohexene, to the diacetoxy and carbonyl derivatives found in the $Pb(OAc)_4$ oxidation and a similar mechanism was proposed[103]. Cyclohexene also gave some adipaldehyde product.

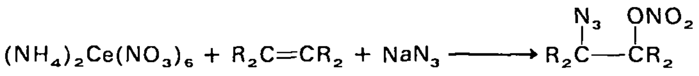
f. *Cerium*(iv). Although an important oxidant for oxygen-containing functional groups, Ce^{IV} is not used to oxidize olefins. One olefin oxidation reported is an indirect oxidation of butadiene in the presence of a bromide ion[104]:

$$Ce^{IV} + Br^- \longrightarrow Ce^{III} + Br\cdot \qquad (113)$$

$$Br\cdot + CH_2{=}CHCH{=}CH_2 \longrightarrow BrCH_2CH{=}CH{-}CH_2\cdot \qquad (114)$$

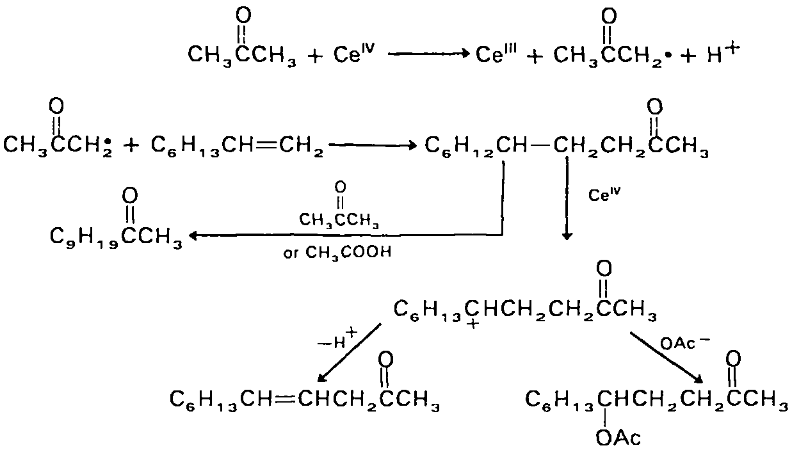
$$2BrCH_2CH{=}CH{-}CH_2\cdot \longrightarrow BrCH_2CH{=}CH{-}CH_2{-}CH_2{-}CH{=}CHCH_2Br \qquad (115)$$

Another apparent indirect oxidation is the formation of α-azido-β-nitroalkanes from olefins[105].



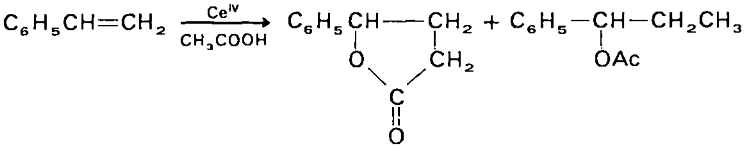
$$(NH_4)_2Ce(NO_3)_6 + R_2C{=}CR_2 + NaN_3 \longrightarrow R_2\overset{N_3}{\overset{|}{C}}-\overset{ONO_2}{\overset{|}{C}}R_2 \qquad (116)$$

Finally reactions analogous to the free radical reactions of $Pb(OAc)_4$ have been reported recently. One example involves addition of acetone to the double bond[106]. Another is the production of γ-lactones and esters



(117)

by radical mechanisms analogous to that postulated for $Pb(OAc)_4$[107] (see equations 94, 95, 99 and 100). One example is the oxidation of styrene in acetic acid.

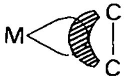


(118)

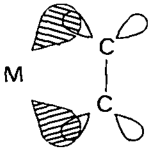
2. Transition metal oxidants

a. *General.* Transition elements are those elements which have an incomplete d shell of electrons or more broadly, for purposes of present discussion, those elements with common oxidation states and unfilled d shells. One immediate result of importance is that since the d electrons are of approximately the same energy, transition elements usually have several oxidation states not differing greatly in energy. This property makes transition elements good catalysts since metal-ion catalysis usually involves the cycling of the metal between two oxidation states.

Another important result of the fact that the d-electrons are in the energy range of bonding orbitals is that transition elements can form non-classical complexes with unsaturated substrates. One particularly important type of compound is the olefin metal π complex which is an important intermediate in many oxidations of olefins by transition metal ions. The first such complex was prepared by Zeise in 1827[108] by heating potassium tetrachloroplatinate(II) in ethanol. The compound, known as Zeise's salt, has the composition $K[C_2H_4PCl_3]$. The accepted bonding scheme in these complexes was advanced by Chatt and Duncanson[109] and by Dewar[110]. The Dewar–Chatt–Duncanson model involves a σ-type bond with empty hybrid orbital on the metal and the filled π orbital of the olefin (**5**) and a π-type bond between the filled d orbital of the metal and the empty π^*-orbital of the olefin (**6**). These intermediates are important in transition metal catalysis of olefins because the olefin in these π-complexes are activated towards nucleophilic attack while uncomplexed olefins tend to undergo electrophilic attack.



(5)



(6)

Since filled d orbitals are required for the π-type bonds, transition elements with partially filled d orbitals of the proper energy tend to be the best catalysts for olefin oxidation. Another way of expressing this fact is in terms of Pearson's hard and soft acid and base terminology[111]. Olefins are soft bases so they will tend to react with soft metals. These metals are at the end of the transition series consisting mainly of the noble metals.

Another classification of the transition elements is in terms of one- and two-electron oxidants. One-electron oxidation requires radical intermediates and non-selective oxidation while two-electron oxidations give more specific reactions. Again the noble metals are generally two-electron oxidants. The one-electron oxidants are not, in any case, good reagents for olefin oxidation but are best for oxygen-containing functional groups.

Another distinction is between oxidations in which metal–carbon σ bonds are formed and those in which they are not. In the latter category are oxidations by Cr^{VI} and OsO_4.

Finally there are oxidations in which the transition metals are not the oxidants but merely catalyse the oxidation by another oxidant. These will be considered separately.

b. *Palladium*(II). No doubt the most extensive type of olefin oxidation is in the field of Pd^{II} catalytic chemistry. Since the disclosure of the Wacker process for manufacturing acetaldehyde from ethylene in 1959[112] there has been a tremendous amount of research on Pd^{II} catalysis in many industrial laboratories throughout the world. The result has been a wealth of new Pd^{II} catalytic chemistry. The reviews in this field are too numerous to list. Most extensive is the two volume treatise by Maitlis[113] which covers the field very well up to the end of 1970. The writer includes a review covering certain aspects of the field in the literature up to the end of 1973[114]. Because of the extent of the field only a few examples will be included with emphasis on newer advances.

(i) Reaction in aqueous solution. No doubt the most studied reaction in Pd^{II} chemistry is the basic reaction of the Wacker process, i.e. the oxidation of ethylene to acetaldehyde by Pd^{II} salts in aqueous solution (equation 119). This reaction had been known for some time but was, of course, of little synthetic utility. However, the discovery by Smidt and coworkers that the Pd^{II} could be regenerated *in situ* by $CuCl_2$ made the reaction commercially feasible (equation 120). Since CuCl is readily oxidized by oxygen to $CuCl_2$ (equation 121) the net reaction (equation 122) is an air oxidation of ethylene to acetaldehyde. The rate expression for the reaction is given by equation (123)[115–118].

$$PdCl_4^{2-} + C_2H_4 + H_2O \longrightarrow CH_3CHO + Pd^0 + 2HCl + 2Cl^- \tag{119}$$

$$2Cl^- + Pd^0 + 2CuCl_2 \longrightarrow PdCl_4^{2-} + 2CuCl \tag{120}$$

$$\underline{2CuCl + \tfrac{1}{2}O_2 + 2HCl \longrightarrow 2CuCl_2 + H_2O} \tag{121}$$

$$C_2H_4 + \tfrac{1}{2}O_2 \longrightarrow CH_3CHO \tag{122}$$

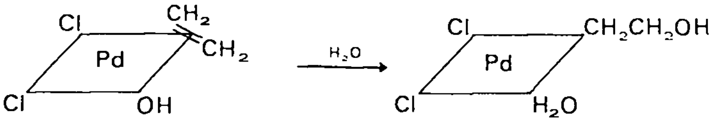
$$-d[C_2H_4]/dt = \frac{k[PdCl_4{}^{2-}][C_2H_4]}{[Cl^-]^2[H^+]} \tag{123}$$

The generally accepted mechanism that obeys this rate expression is given by equations (124–128). The important points are that olefin activation by complexing to Pd^{II} is required and the only organic product

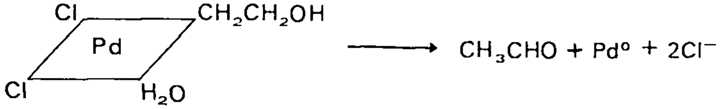
$$PdCl_4^{2-} + C_2H_4 \xrightleftharpoons{K} PdCl_3(C_2H_4)^- + Cl^- \tag{124}$$

$$PdCl_3(C_2H_4)^- + H_2O \rightleftharpoons PdCl_2(H_2O)(C_2H_4) + Cl^- \tag{125}$$

$$H_2O + PdCl_2(H_2O)(C_2H_4) \rightleftharpoons PdCl_2(OH)(C_2H_4) + H_3O^+ \qquad (126)$$



(127)



(128)

is acetaldehyde. Compare this with Tl^{III} where ethylene glycol is also an important product. This means that Pd^{II} is a much more specific oxidant than Tl^{III} (and Hg^{II} or Pb^{IV} for that manner). It means further that the oxypalladation adduct intermediate probably does not decompose by a carbonium ion mechanism or a glycol product would be expected[43]. It is generally true in Pd^{II} oxidation chemistry, at least when a second oxidant is not present, that the products are not those expected from a carbonium ion intermediate but usually those expected from a Pd^{II} induced hydride shift or elimination. It can be shown by isotope studies that the acetaldehyde product in the Wacker reaction arises from a shift of a proton from one carbon of the intermediate to the other carbon. Thus when C_2H_4 is oxidized in D_2O the acetaldehyde produced contains no deuterium[112].

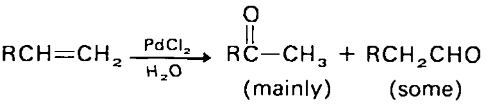
$$^{2-}Cl_3Pd{-}CH_2CH_2{-}OD \xrightarrow{D_2O} Pd^0 + CH_3CHO + DCl + 2Cl^- \qquad (129)$$

At high $CuCl_2$ concentrations another product, 2-chloroethanol, is formed[119]. This is the first example of a rather novel reaction in Pd^{II}

$$C_2H_4 + 2CuCl_2 + H_2O \xrightarrow{PdCl_4^{2-}} ClCH_2CH_2OH + HCl + 2CuCl \qquad (130)$$

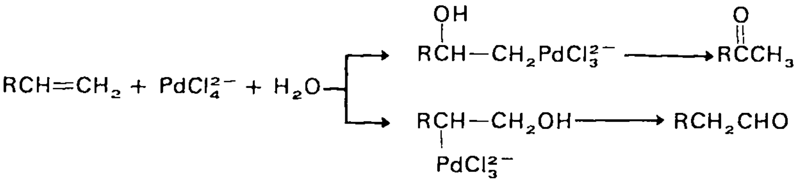
oxidative chemistry in which a second oxidant changes the product of the oxidation. Both Pd^{II} and the second oxidant are required for the oxidation; the second oxidant alone will not give the product. More examples of this reaction will be given in the following section.

As might be expected higher olefins also give carbonyl products[112]. α-Olefins give mainly methyl ketones but some aldehydes are also usually formed[120]. This result suggests that oxypalladation, as opposed to



$$RCH{=}CH_2 \xrightarrow[H_2O]{PdCl_2} \underset{\text{(mainly)}}{R\overset{O}{\overset{\|}{C}}{-}CH_3} + \underset{\text{(some)}}{RCH_2CHO} \qquad (131)$$

oxymercuration and oxythallation, is not strongly Markownikoff. Thus ketone and aldehyde products would arise from different modes of oxypalladation. The lack of specificity in oxypalladation suggests that there is little carbonium ion character in the transition and a comparative kinetic study of the oxidation of ethylene, propylene and the butenes led the writer to propose that the addition is concerted[121].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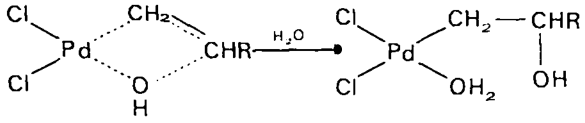
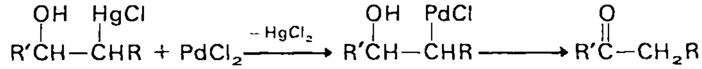

(133)

Often high olefins do not give high yields of the desired olefins in aqueous solution. Clement and Selwitz have devised a convenient method for oxidizing higher olefins using aqueous DMF as solvent[122].

Another means of improving yields of carbonyl products has been described by Rodeheaver and Hunt[123]. These workers prepared the hydroxymercuration adducts and exchanged them with $PdCl_2$ to give the hydroxypalladation adduct which then decomposed in the expected fashion to give ketones. This procedure overcomes the low solubility of the olefin in water and gives much higher yields than direct reaction of aqueous Pd^{II} with olefins, also, since hydroxymercuration occurs exclusively in a Markownikoff fashion, the only carbonyl products are ketones.



$$R'\overset{OH}{\overset{|}{C}}H-\overset{HgCl}{\overset{|}{C}}HR + PdCl_2 \xrightarrow{-HgCl_2} R'\overset{OH}{\overset{|}{C}}H-\overset{PdCl}{\overset{|}{C}}HR \longrightarrow R'\overset{O}{\overset{\|}{C}}-CH_2R \quad (134)$$

There have been several recent studies of the oxidation of allylic alcohols. Allyl alcohol is known to be oxidized to acrolein[112]. Jira[124] has provided evidence that this oxidation proceeds via a β-hydroxypropionaldehyde intermediate which dehydrates to acrolein.

$$CH_2{=}CHCH_2OH \xrightarrow[H_2O]{PdCl_2} OCHCH_2CH_2OH \xrightarrow{-H_2O} OCHCH{=}CH_2 \quad (135)$$

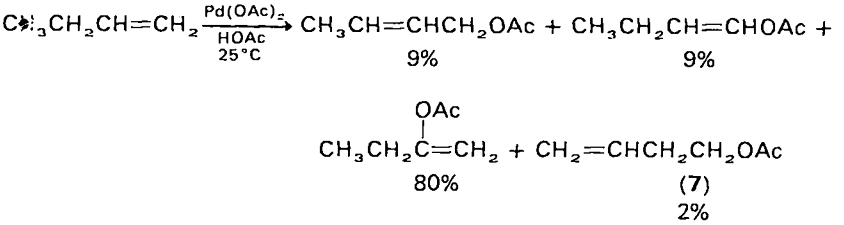
(ii) Reactions in acetic acid. Oxidation in acetic acid has been reported by a number of workers as giving a confusing array of products including vinyl acetate, ethylidene diacetate, acetaldehyde, acetic anhydride, ethylene glycol, mono- and di-acetates and β-chloroethyl acetate[125]. However, at the time that these studies were carried out the importance of added oxidants was not appreciated and many systems contained $CuCl_2$ and other oxidants, hence the discussion will be divided between oxidation in the absence of added oxidant, and in its presence.

In the absence of oxidants the primary product is vinyl acetate. Ethylidene diacetate may also be a primary product, but this does not seem to have been definitely established. At 25°C little ethylidene diacetate is formed but it is reported to be produced at higher temperatures[126], a point which needs further study. The acetaldehyde and acetic anhydride are secondary products from the decomposition of vinyl acetate[127–129].

Almost certainly the vinyl acetate is formed by acetoxypalladation followed by Pd^{II} hydride elimination. The Pd^{II} hydride formed by the

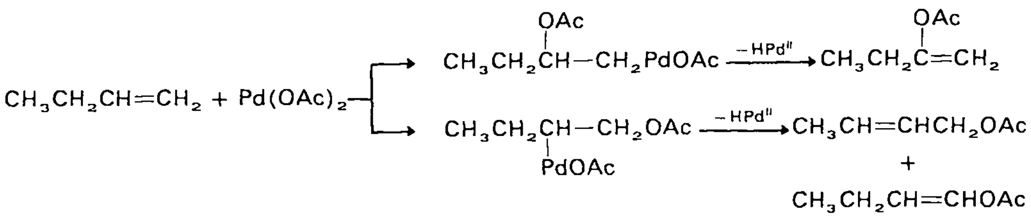
$$Pd^{II}{-}OAc + C_2H_4 \longrightarrow Pd^{II}{-}CH_2CH_2OAc \xrightarrow{-HPd^{II}} CH_2{=}CHOAc \qquad (136)$$

elimination is unstable and decomposes to Pd^0 and H^+. Higher olefins are oxidized to similar products but in this case allylic and vinylic acetate can be formed. Thus 1-butene is oxidized to crotyl acetate and two enol acetates[130]. In addition a small amount of 3-butene-1-yl acetate (7) was



$$CH_3CH_2CH{=}CH_2 \xrightarrow[\text{HOAc},\ 25^\circ C]{Pd(OAc)_2} \underset{9\%}{CH_3CH{=}CHCH_2OAc} + \underset{9\%}{CH_3CH_2CH{=}CHOAc} + \underset{80\%}{CH_3CH_2\overset{\overset{OAc}{|}}{C}{=}CH_2} + \underset{\substack{(7)\\ 2\%}}{CH_2{=}CHCH_2CH_2OAc} \qquad (137)$$

found. The main products can be explained by Markownikoff acetoxypalladation followed by Pd^{II} hydride elimination.



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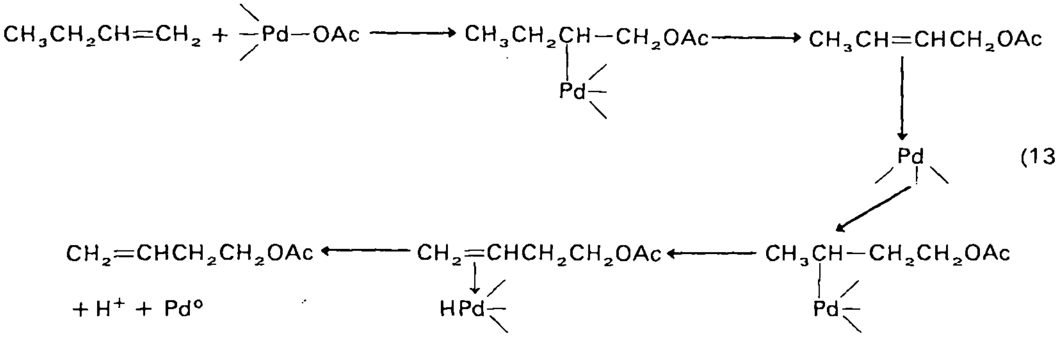
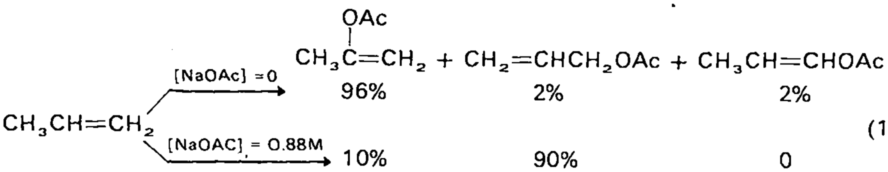


CH₃CH₂CH=CH₂ + Pd–OAc
CH₃CH₂CH–CH₂OAc
Pd
CH₃CH=CHCH₂OAc
Pd
CH₃CH–CH₂CH₂OAc
Pd
CH₂=CHCH₂CH₂OAc
HPd
CH₂=CHCH₂CH₂OAc
+ H⁺ + Pd⁰

(139)

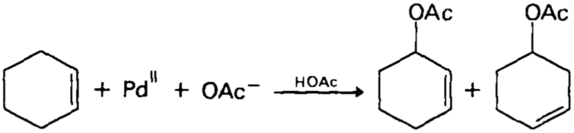
The proportions of products can be changed drastically by addition of sodium acetate[131–134]. Thus propylene is oxidized mainly to isopropenyl acetate in the absence of acetate but gives mainly allyl acetate at a sodium acetate concentration of 0·88 M[134].



OAc
CH₃C=CH₂ + CH₂=CHCH₂OAc + CH₃CH=CHOAc
[NaOAc] = 0
96% 2% 2%
CH₃CH=CH₂
[NaOAC] = 0.88M
10% 90% 0

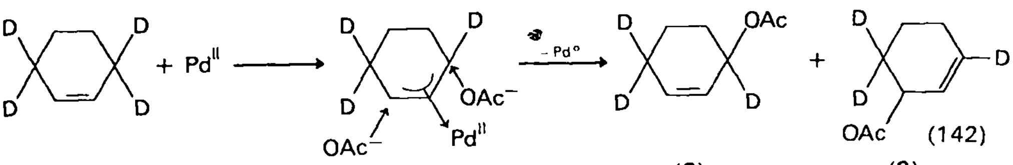
(140)

The oxidation of cyclohexene has been studied to some extent. In the absence of any oxidant to regenerate the Pd⁰, the metal causes disproportionation of the cyclohexene to give benzene[135,136]. In the presence of oxidants, the allylic and homoallylic acetates are formed. Deuterium-labelling experiments[136,137] suggest that the allylic acetate arose from a different mechanism from that proposed for straight chain olefins (equation 138). Thus the oxidation of 3,3,6,6-d_4-cyclohexene gave a 50:50 mixture of the two deuterium-labelled products, **8** and **9**. An acetoxypalladation Pd^{II} hydride elimination mechanism would have given only **9** as a product. Also it was demonstrated that π-allylic Pd^{II} compounds will decompose to allylic acetate[138].



+ Pd^{II} + OAc⁻
HOAc
OAc
OAc
+

(141)

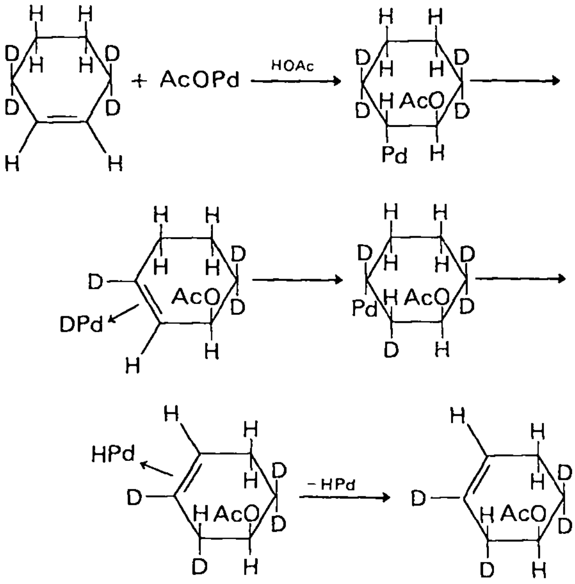


D
D
D
D
+ Pd^{II}
D
D
D
OAc⁻
OAc⁻
Pd^{II}
– Pd⁰
D
OAc
D
D
+
D
D
D
OAc

(142)

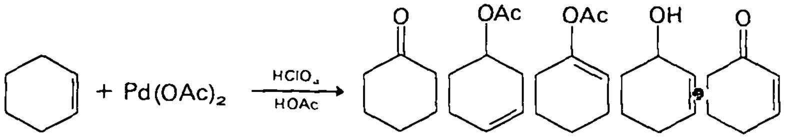
(**8**) (**9**)

The homallylic acetate contained all the deuterium initially present in the deuterated cyclohexene but one of the deuterium atoms has been stereospecifically transferred to an adjacent carbon. The stereochemistry of the product is consistent with *trans* acetoxypalladation and *cis* Pd^{II} hydride elimination and readditions[136,137].



(143)

The oxidation in acetic acid containing perchloric acid gave a variety of products. The cyclohex-2-en-1-ol and cyclohex-2-en-1-one apparently



(144)

arose from free radical processes[135].

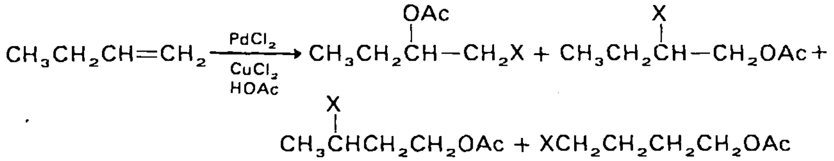
The oxidation of hex-1-ene, hex-*cis*-2-ene and 3,3-dimethylbut-1-ene catalytically under O_2 proved to be complicated[139]. Hex-1-ene gave mainly hex-1-en-2-yl acetate, the product expected from the acetoxypalladation Pd^{II} hydride elimination mechanism. However, hex-*cis*-2-ene gave oxidation via free-radical mechanism. Apparently the internal olefin is too sterically hindered for acetoxypalladation to occur readily, consequently this oxidation path is not important.

As mentioned in the introduction to the last section, the presence of other oxidants caused the product distributions to change. Cupric chloride

$$C_2H_4 + PdCl_2 + CuCl_2 \xrightarrow{HOAc} ClCH_2CH_2OAc + HOCH_2CH_2OAc + (CH_2OAc)_2 \qquad (145$$

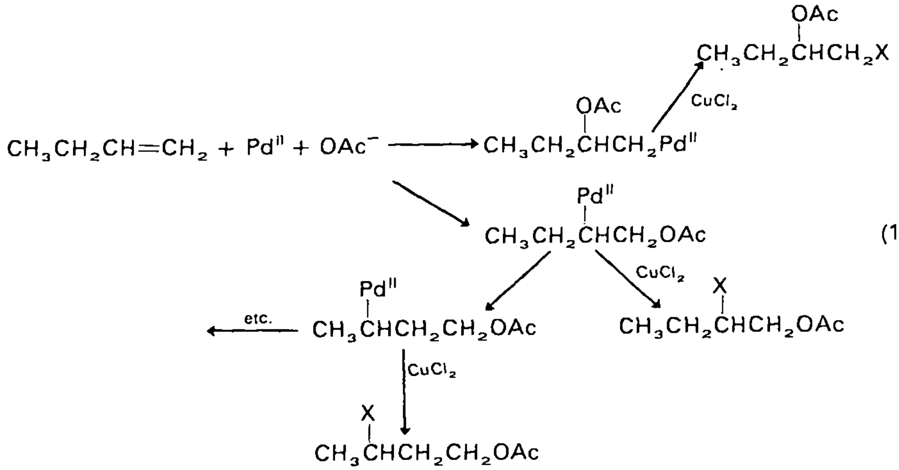
was commonly used to make the reaction catalytic in Pd^{II}. Initially the effect of $CuCl_2$ on product distribution was not recognized. However it has now been demonstrated that the formation of saturated ester product requires the presence of *both* Pd^{II} and $CuCl_2$[140]. It is likely that this route is also responsible for the ethylene diacetate product. Later it was observed that $LiNO_3$ also gave saturated products in the presence of $Pd(OAc)_2$[141]. More recently it has been demonstrated that a number of oxidants will give the reaction[142].

With higher olefins 1,3- and 1,4- as well as 1,2-disubstituted alkanes are formed[140]. The oxidation of 1-butene is an example (X = OAc or Cl).



$$CH_3CH_2CH{=}CH_2 \xrightarrow[CuCl_2,\ HOAc]{PdCl_2} CH_3CH_2\overset{OAc}{\overset{|}{C}}H{-}CH_2X + CH_3CH_2\overset{X}{\overset{|}{C}}H{-}CH_2OAc + CH_3\overset{X}{\overset{|}{C}}HCH_2CH_2OAc + XCH_2CH_2CH_2CH_2OAc \qquad (146)$$

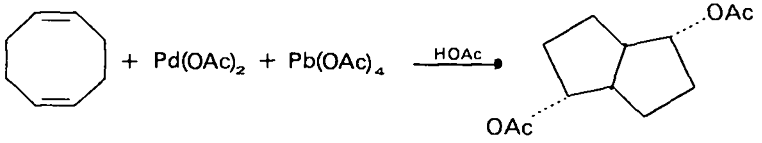
The product distribution can be rationalized by a scheme involving Markownikoff and non-Markownikoff acetoxypalladation followed by reaction with $CuCl_2$ with or without movement of Pd^{II} down the chain. The movement of Pd^{II} down the chain no doubt occurs by Pd^{II} hydride eliminations and readditions as shown in equations (139) and (143).



(147)

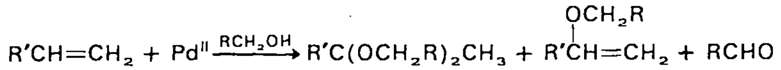
The mechanism of interaction of the oxidant with the acetoxypalladation adduct is uncertain, but a recent study[143] indicates that the route does not involve transfer of alkyl from Pd^{II} to the oxidant.

A novel oxidation of cyclooctadiene by $Pd(OAc)_2$ plus $Pb(OAc)_4$ has recently been reported. The unexpected product was 2,6-diacetoxybicyclo[3,3,0]octane. Moreover only the di-*endo* isomer was obtained[144].



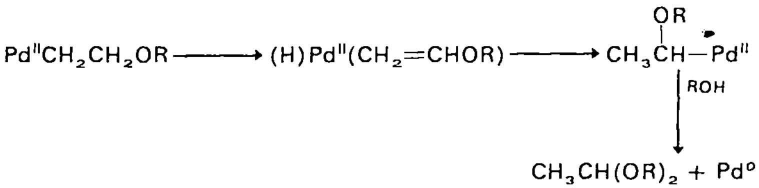
(148)

(iii) Reactions in alcohol. The oxidation of olefins in alcohols gives, in the absence of CO, vinyl ethers, acetals, and aldehydes or ketones from oxidation of the solvent[145]. The vinyl ether must arise from oxypalladation followed by elimination of Pd^{II} hydride. The acetals could arise from addition of alcohol to the vinyl ethers or by a route involving shift of palladium from one carbon to the other followed by elimination of Pd^0. Deuterium isotope studies suggest that the latter is the correct route[146].



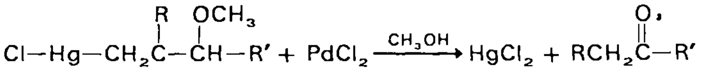
$$R'CH{=}CH_2 + Pd^{II} \xrightarrow{RCH_2OH} R'C(OCH_2R)_2CH_3 + R'\overset{\displaystyle OCH_2R}{\overset{|}{C}}H{=}CH_2 + RCHO \qquad (149)$$

$$Pd^{II} + C_2H_4 + RO^- \longrightarrow PdCH_2CH_2OR \xrightarrow{-HPd} CH_2{=}CHOR \qquad (150)$$

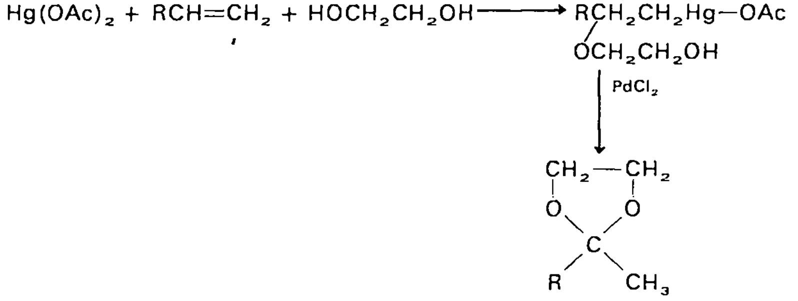


$$\begin{tikzcd} Pd^{II}CH_2CH_2OR \arrow[r] & (H)Pd^{II}(CH_2{=}CHOR) \arrow[r] & CH_3\overset{\displaystyle OR}{\overset{|}{C}}H{-}Pd^{II} \arrow[d, "ROH"] \\ & & CH_3CH(OR)_2 + Pd^0 + H^+ \end{tikzcd} \qquad (151)$$

Hunt and Rodeheaver[147] also used mercurials in methanol to exchange with Pd^{II}. Surprisingly, the ketones rather than the dimethylacetals are obtained. In a 1:1 ethylene glycol–tetrahydrofuran solvent the ethylene ketals are formed[147]. In some cases the rate of olefin oxidation was



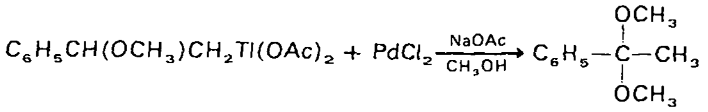
$$Cl{-}Hg{-}CH_2\overset{\displaystyle R}{\overset{|}{C}}{-}\overset{\displaystyle OCH_3}{\overset{|}{C}}H{-}R' + PdCl_2 \xrightarrow{CH_3OH} HgCl_2 + RCH_2\overset{\displaystyle O}{\overset{\|}{C}}{-}R' \qquad (152)$$



(153)

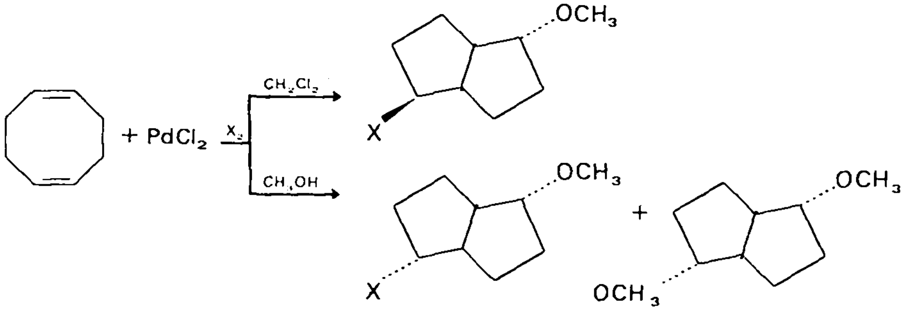
increased considerably by using the mercurial route. Thus, undec-1-ene was not oxidized by $PdCl_2$ alone under the reaction conditions in 2 hours but a 63% yield of oxidation product was obtained in 30 minutes when the mercurial was used.

An analogous reaction was observed with the methoxythallation adduct of styrene[148].

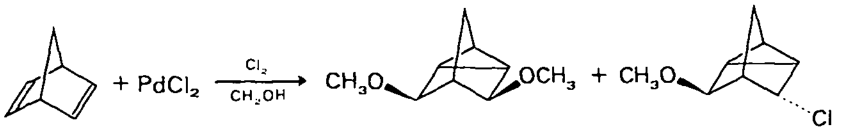


$$C_6H_5CH(OCH_3)CH_2Tl(OAc)_2 + PdCl_2 \xrightarrow[CH_3OH]{NaOAc} C_6H_5-\underset{OCH_3}{\overset{OCH_3}{\underset{|}{\overset{|}{C}}}}-CH_3 \qquad (154)$$

1,5-Cyclooctadiene can also be oxidized to 2,6-disubstituted bicyclo-[3,3,0]octanes in methanol[149]. In this case Cl_2 or Br_2 are used as oxidants. The stereochemistry of the product depends on solvent (X = Cl or Br).



Norbornene gives nortricyclyl derivatives with Cl_2 as second oxidant:



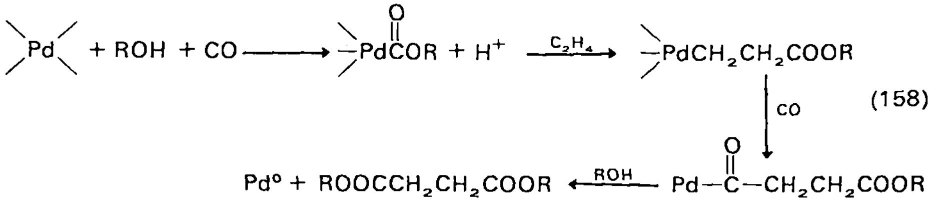
(156)

38% 62% (*endo*/*exo* = 60/40)

In the presence of CO, ethylene is oxidized to acrylic acids, β-substituted acids and dibasic acids depending on reaction conditions[150–152]. The

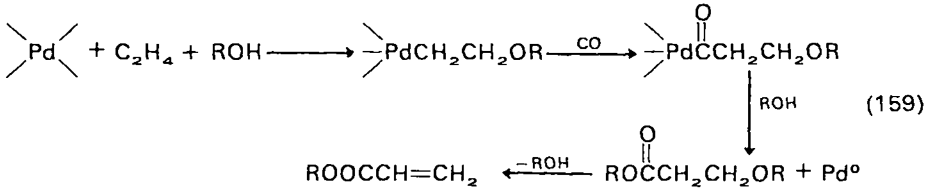
$$C_2H_4 + ROH + CO \xrightarrow{PdCl_2} CH_2{=}CHCOOR + ROCH_2CH_2COOR + (CH_2COOR)_2 \qquad (157)$$

dibasic acid must arise from a triple insertion mechanism.



(158)

The monoacids, on the other hand, must be formed by a double insertion. In this case there are two possibilities, either the CO (equation 159) or ethylene (equation 160) could insert first. The oxidation of cyclopentene gives 1,2- and 1,3-*cis* disubstituted acids[149]. The proposed route is as follows:



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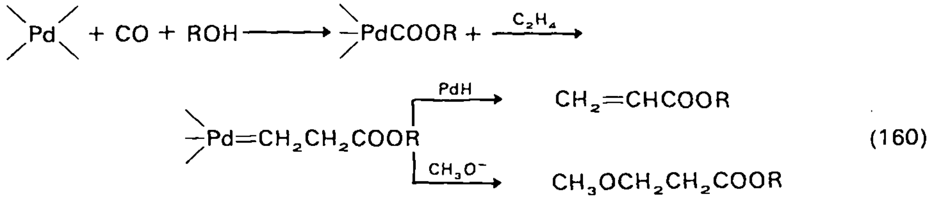

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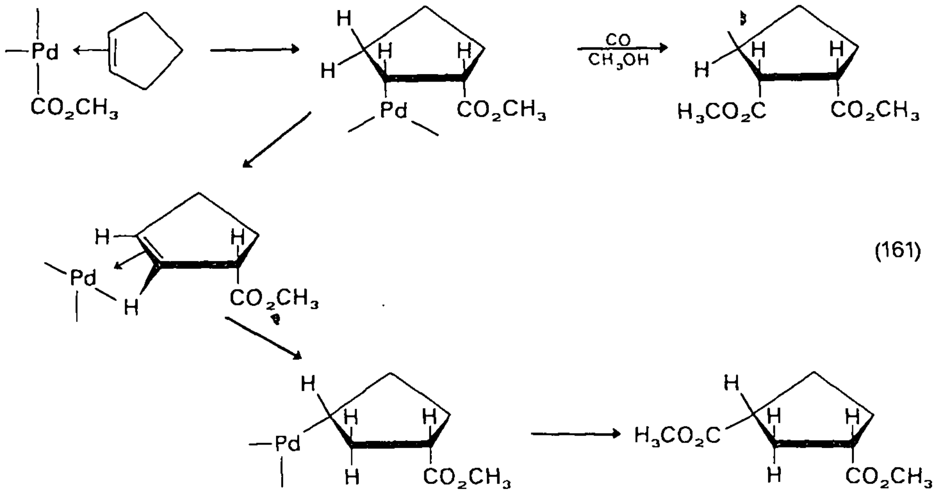
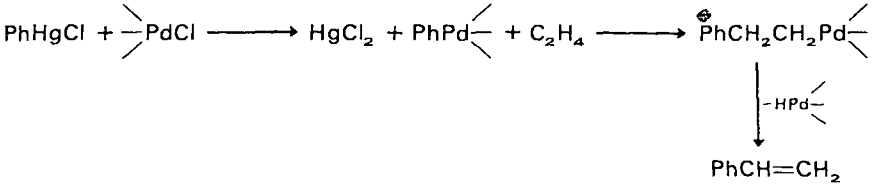


(161)

As might be expected, higher CO pressures favour the 1,2-isomer because the first $\mathrm{Pd^{II}}$ intermediate reacts more readily with CO to give the 1,2-diacid.

(iv) Formation of carbon–carbon bonds[153]. Thus far we have considered olefin oxidations in which the first step is addition of —OH, —OAc or —OR across double bonds. (The one exception is the last example in the previous section: carbonylation to give dibasic acids where the first step is addition of $Pd{-}\overset{\displaystyle O}{\overset{\|}{C}}R$ across double bonds.) The present section will consider oxidations in which Pd—C is added across double bonds in the first step of the oxidation.

The most studied reaction in this area is that in which the carbanoid species is an aromatic group. The aryl Pd^{II} reactant is an unstable species and in the absence of olefin decomposes to coupled aromatics. The reactive intermediate is usually formed by transfer of an aryl groups from Hg^{II} to Pd^{II}. The reaction scheme for formation of styrene is given by equation (162). This reaction has been extensively studied by Heck who has devised a number of variations on the general reaction[154,155].



(162)

In this system the addition of oxidants also gives saturated products. Thus in the presence of CuCl$_2$ the above reaction gives β-phenethyl chloride instead of styrene[156].

$$PhHgCl + PdCl_2 + C_2H_4 \xrightarrow{CuCl_2} PhCH_2CH_2Cl \qquad (163)$$

Mercurials are usually used as source of aryl groups because they can conveniently be prepared by direct mercuration. Other sources used include aromatic sulphinic acids which evolve SO$_2$ in the presence of Pd^{II} to give the desired aryl Pd^{II} intermediate[157]. The arene itself can be used although in this case the reaction is somewhat slower[158].

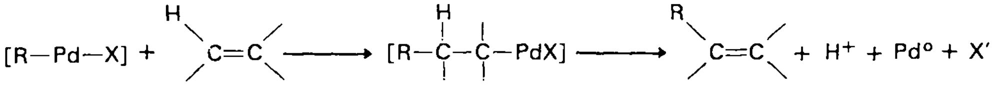
$$ArH + Pd(OAc)_2 + C_2H_4 \longrightarrow ArCH{=}CH_2 + Pd^{0} + 2HOAc \qquad (164)$$

The reaction can be made catalytic in Pd^{II} by using aryl halides. Originally phenyl iodide was used in the presence of potassium acetate[159]; Pd black could be used in place of Pd^{II} salts. Heck also studied this

$$C_6H_5I + C_2H_4 + CH_3COOK \xrightarrow{Pd^{II}} C_6H_5CH{=}CH_2 + CH_3COOH + KI \qquad (165)$$

reaction and proposed that the phenyl palladium was formed by oxidative addition of aryl halide to Pd^0 [160]. The reaction yield and selectivity was

$$RX + Pd \rightleftharpoons [R{-}Pd{-}X] \quad (X = \text{halogen}) \qquad (166)$$



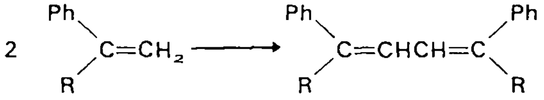
(167)

improved when triphenylphosphine was added to the reaction mixture[161].

The arylation of enol esters was previously found to give a wide range of products including β-aryl carbonyls, arylated enol esters, styrene and stilbene derivatives[162]. The reaction was recently reported to give mainly arylated enol esters if the reactions are carried out with stoichiometric amounts of arylmercuric acetate and palladium acetate in anhydrous acetonitrile or excess enol ester solution[163]. The phenyl group adds to the carbon which does not contain the ester.

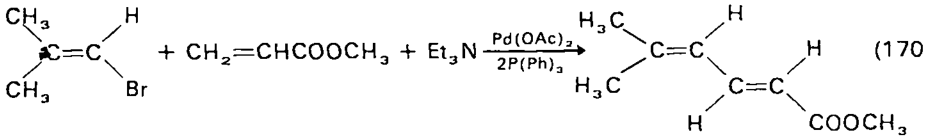
$$C_6H_5{-}HgOAc + Pd(OAc)_2 + CH_2{=}CHOAc \longrightarrow C_6H_5CH{=}CHOAc \qquad (168)$$

The formation of carbon–carbon bonds can also be carried out in the aliphatic series[164]. The first report of this type of reaction was the coupling of α-substituted styrenes[165,166].



(169)

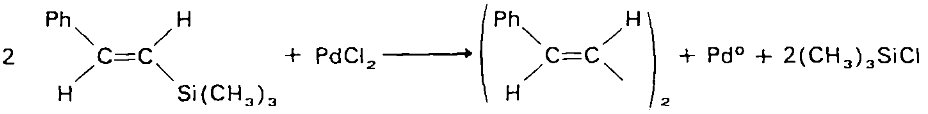
Heck has found that benzyl and vinyl halides can substitute olefinic double bonds[160]. This reaction must involve oxidative addition to Pd^0



(170)

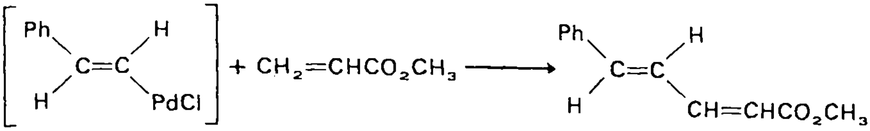
to give vinylic Pd^{II} species in the same fashion as the olefin arylation reaction (equation 166 and 167).

A recent variation on this scheme involves the use of vinyl silanes[167].



(171)

The Pd^{II} must replace the $—Si(CH_3)_3$ group to give a vinyl Pd^{II}. If the reaction is run in the presence of other olefins, unsymmetrically substituted 1,3-butadienes are produced.


(172)

Aliphatic groups without β-hydrogens can also be substituted on double bonds; an example is the neopentyl group. The Pd^{II} alkyl is prepared by exchange with the corresponding mercurial[168].

$$[(CH_3)_3CCH_2Pd^{II}] + CH_2{=}CHCOOCH_3 \longrightarrow (CH_3)_3CCH_2CH{=}CHCOOCH_3 + [HPd^{II}] \quad (173)$$

c. *Platinum*(II), *rhodium*(III), *ruthenium*(III), *osmium*(III), *iridium*(III). Salts of these noble metal ions might be expected to be olefin oxidants and, in fact, they will oxidize ethylene to acetaldehyde in water[112] but none is as effective as Pd^{II}. The oxidation of ethylene to acetaldehyde by Rh^{III} salts has been studied to some extent. In this case the reduced form of the metal is Rh^{I}. In wet dimethylacetamide (DMA) the final Rh^{I} species is an olefin complex[169]. The kinetics suggest a two-step mechanism

$$RhCl_3 . 3H_2O + nC_2H_4 \xrightarrow{DMA} RhCl(C_2H_4)_{n-1} + CH_3CHO + 2Cl^- \quad (174)$$

involving formation of a Rh^{III}–ethylene complex. In fast steps the ethylene

$$Rh^{III}Cl_n \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} Rh^{III}Cl_{n-1} + Cl^- \quad (175)$$

$$RhCl_{n-1} + C_2H_4 \xrightarrow{k_2} \underset{(\mathbf{8})}{[Rh^{III}Cl_{n-1}(C_2H_4)]^{(4-n)+}} \quad (176)$$

complex decomposes to acetaldehyde and Rh^{I} which reacts with ethylene.

$$\mathbf{8} \xrightarrow{H_2O} Rh^{I}Cl_{n-1} + CH_3CHO + 2H^+ \quad (177)$$

$$Rh^{I}Cl_{n-1} + C_2H_4 \longrightarrow \text{Complex} \quad (178)$$

The reaction was also studied in water containing Fe^{III} to regenerate the Rh^{III} from the Rh^{I}[170]. In this case both ethylene-dependent and

$$Rh^{I} + 2Fe^{III} \longrightarrow Rh^{III} + 2Fe^{II} \quad (179)$$

ethylene-independent paths were operative (Rh^{III} = total rhodium concentration). The major contribution to the k_a path involves the rate

$$\frac{-\mathrm{d}[C_2H_4]}{\mathrm{d}t} = k_a[\mathrm{Rh^{III}}] + k_b[\mathrm{Rh^{III}}][C_2H_4] \qquad (180)$$

determining formation of a hydroxo species by elimination of chloride. A

$$RhCl_5(OH)^{3-} + H_2O \longrightarrow RhCl_4(OH)(H_2O)^{2-} + Cl^- \qquad (181)$$

smaller contribution arises from slow formation of an aquo species.

$$RhCl_5(H_2O)^{2-} + H_2O \longrightarrow RhCl_4(H_2O)_2^- + Cl^- \qquad (182)$$

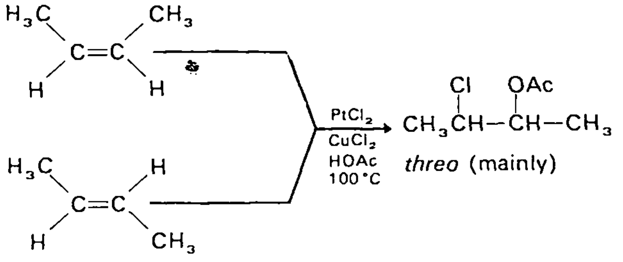
The main contribution to the k_b path is the reaction of $RhCl_5(H_2O)$ with ethylene while there may be a small contribution from a path

$$RhCl_5(H_2O)^{2-} + C_2H_4 \longrightarrow \text{Products} \qquad (183)$$

involving hydroxyl species.

$$RhCl_5(OH)^{3-} + C_2H_4 \longrightarrow \text{Products} \qquad (184)$$

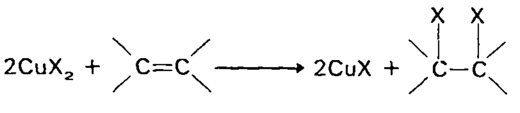
The reactivity of various $\mathrm{Rh^{III}}$ chloride species has been determined[171]. $RhCl_6^{3-}$ is unreactive as are the cationic species $RhCl_2(H_2O)_4^+$, $RhCl(H_2O)_5^{2+}$ and $Rh(H_2O)_6^{3+}$. The last three are unreactive because of their substitution inertness, and the first is unreactive because of the lack of aquo ligands required for the oxidation to occur. $RhCl_4(H_2O)_2^-$ and $RhCl_5(H_2O)^{2-}$ are both reactive with the former being 2–4 times more reactive than the latter. These metal ions were also tested in reaction in acetic acid in the presence of cupric chloride[143] (section I.A.2.a.ii). $RuCl_3$ and $OsCl_3$ were unreactive while $RhCl_3$ and $IrCl_3$ had low reactivity. Surprisingly $PtCl_2$ was more reactive than $PdCl_2$. The reason for this is not known: $PdCl_2$ is generally much more reactive than $PtCl_2$. A striking difference is that $PtCl_2$ produced only 1,2-disubstituted alkanes while $PdCl_2$ gives considerable amounts of 1,3- and 1,4-disubstituted alkanes. Another interesting result is that *both cis-* and *trans*-2-butene gave mainly the *threo* chloroacetate. The reason for this is not apparent but the



(185)

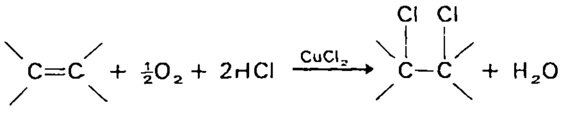
reaction could be of synthetic utility. Certainly the noble metals other than $\mathrm{Pd^{II}}$ deserve more study.

d. *Copper*(II), Copper(II) has a wealth of organic oxidation chemistry[172]. However, although it is important as an oxidant for Pd^{II} relatively little of it involves direct olefin oxidation. Probably the only important olefin oxidation is the halogenation of olefins by cupric halides reported by several workers[173-175]. Since CuCl is readily oxidized by O_2 to $CuCl_2$



(186)

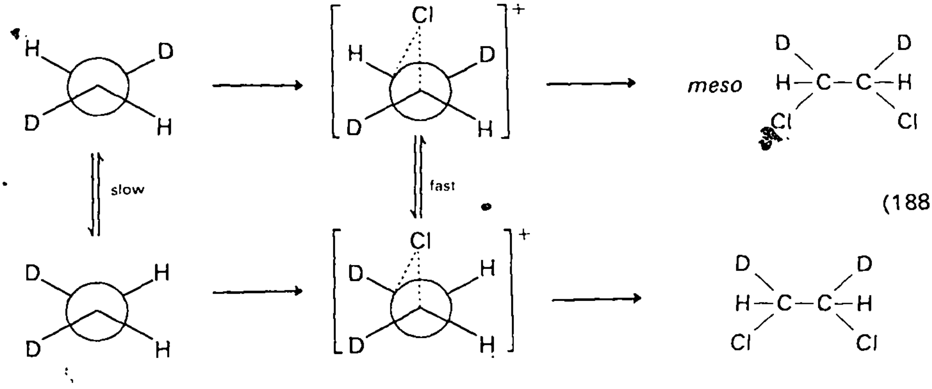
in the presence of HCl (see Wacker reaction, equation 120), this reaction can be made catalytic in $CuCl_2$. In fact this is the basis of the oxychlorination reactions run in the vapour phase at 220–330°C. More recently an aqueous phase process has been developed. These processes have the advantage over chlorination with Cl_2 since HCl is a much cheaper reagent than Cl_2.



(187)

This chlorination is a two-electron oxidation which apparently does not proceed by radical intermediates. Yet, $CuCl_2$ would be expected to be a one-electron oxidant.

The gas-phase reaction gives mainly *trans* addition with *cis*- and *trans*-2-butene but the addition is almost random with 1,2-ethylene-d_2[175]. Chlorinium ion intermediates which easily undergo rotation have been proposed to explain the stereochemical results. However, a path which would seem more in keeping with other transition metal organometallic chemistry would involve intermediates with Cu^{II}–carbon bonds.



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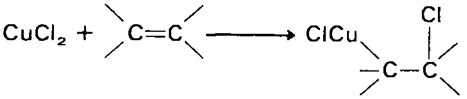
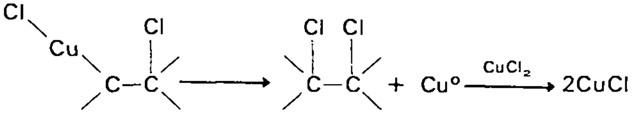


(189)

The intermediate could either decompose to give Cu^0 which would react with $CuCl_2$ or more $CuCl_2$ could aid in the decomposition.



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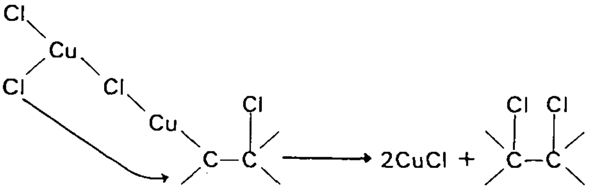
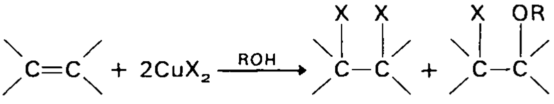


(191)

In alcohol solvents alkoxy halides are produced in addition to the dihalides[176–178].



(9) (10)

(192)

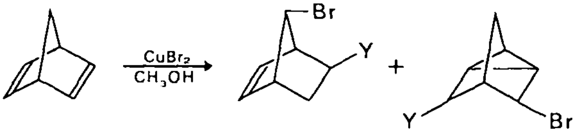
Kinetic studies of the halogenation of olefins with $CuBr_2$ and $CuCl_2$ in methanol indicated that the rate of formation of **9** was greater than first order in CuX_2 while the formation of methoxybromide was 1st order in CuX_2[177,178].

$$\frac{d[\mathbf{9}]}{dt} = k_1[\text{olefin}][CuX_2]^{1\cdot6-2\cdot0} \tag{193}$$

$$\frac{d[\mathbf{10}]}{dt} = k_2[\text{olefin}][CuX_2] \tag{194}$$

In the bromination of the diolefin, norbornadiene, in methanol, products arising from rearrangement of the carbon skeleton were observed[176] (equation 195).

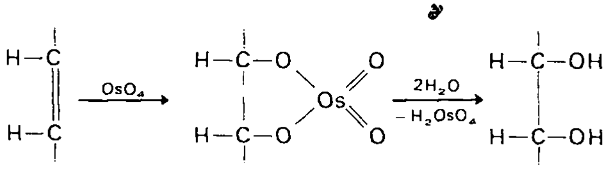
e. *OsO_4, RuO_4 and Re_2O_7*. These oxidants are being considered together since they are all oxides with a high oxidation state and would be expected to behave similarly.



(195)

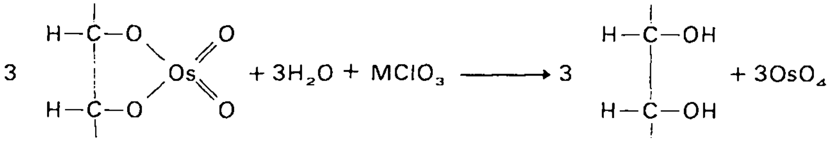
Y = Br(10%) Y = Br(17%)
Y = OCH_3(32%) Y = OCH_3(41%)

The most studied oxidant is OsO_4[179,180] which has been used mainly for hydroxylation of olefins. The glycols have the *cis* configuration and are usually formed in good yields. The first step is formation of an osmate ester followed by decomposition to glycol. The reagents which have been used to cleave the ester include sodium and potassium chlorate, sodium sulphite, alkaline solution of mannitol or formaldehyde and hydrogen sulphite.



(196)

Since OsO_4 is volatile, toxic and expensive, the hydroxylations are usually carried out catalytically with other oxidants which decompose the ester and regenerate OsO_4. Metal chlorates have often been used for this purpose (M = Na, K, Ag)[180].



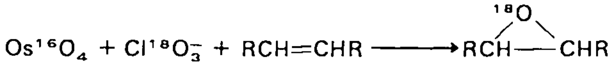
(197)

Barium perchlorate is also used for this purpose. One side reaction is the addition of HOCl to the double bond. This side reaction is avoided when silver chlorate is used since silver catalyses the disproportionation of the hypochlorite[181].

Another oxidant which has been used extensively with OsO_4 is H_2O_2. This reaction is known as the Milas reaction[182,183]. It is not known if H_2O_2 is merely decomposing the ester or whether the mechanism is, in fact, more complicated. In a recent improvement on this procedure potassium osmate, K_2OsO_4 was used in place of OsO_4, the former being much easier to handle than OsO_4[184].

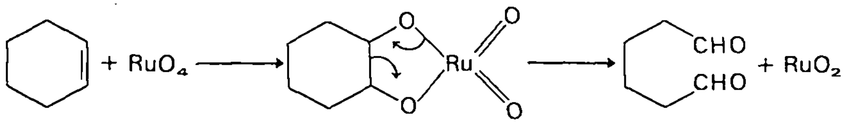
Periodate[185,186] and air[187,188] can also be used but often products other than glycols are formed which is not surprising with periodate since it is a glycol cleaving reagent. OsO_4 plus H_2O_2 also sometimes gives aldehydes or ketones, apparently by direct oxidation rather than secondary oxidation of the glycols[183,189].

In a novel reaction, OsO_4 plus $NaClO_3$ in 50% aqueous HOAc was found to give epoxides[190]. Furthermore, ^{18}O-labelling experiments showed that the epoxide oxygen came from the chlorate.



$$Os^{16}O_4 + Cl^{18}O_3^- + RCH{=}CHR \longrightarrow \overset{^{18}O}{RCH{-}CHR} \qquad (198)$$

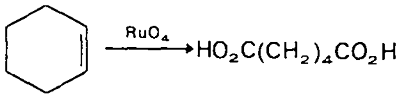
Ruthenium tetroxide olefin oxidation chemistry differs somewhat from OsO_4[191]. These differences arise from the stronger oxidizing power of RuO_4. Thus, while OsO_4 forms diols from olefins RuO_4 cleaves the double bond. In these cleavage reactions RuO_4 may be acting as a rare example of a four-electron oxidant. Thus, cyclohexene has been reported to be oxidized to adipaldehyde[192]. The oxidation may involve oxidative decomposition of a cyclic ester formed initially as in OsO_4 hydroxylations. Evidence that the reaction does not proceed stepwise is in the fact that



(199)

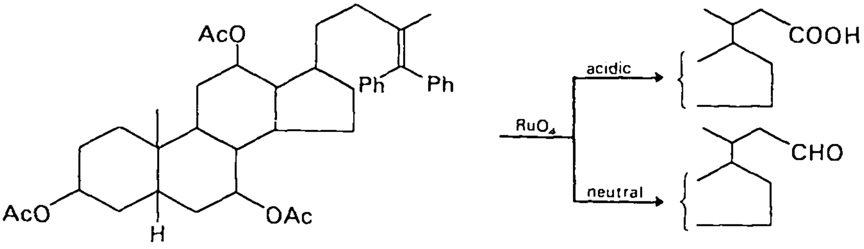
the expected initial oxidation product, 1,2-cyclohexanediol, did not undergo oxidative ring cleavage under the reaction conditions, but gave 1,2-cyclohexanedione.

Under mildly alkaline conditions cyclohexene is oxidized to adipic acid but it was shown that adipaldehyde was an intermediate stage in the oxidation[193].



(200)

Also glycols are sometimes found as minor products, the products being almost always those resulting from the cleavage reaction. Ketones are obtained from tetrasubstituted double bonds and aldehydes or acids as at least one product from less-substituted double bonds[191]. Under alkaline conditions ketones and carboxylic acids are usually found; acidic conditions apparently also favour formation of acids. In a recent report aldehyde was formed in neutral medium and carboxylic acids in acidic medium[194]. The neutral conditions were a 9:1 acetone:water

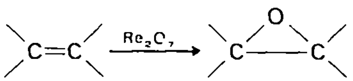


(201)

solution of olefin in contact with a solution of RuO_4 in CCl_4, while the acidic conditions were aqueous acetic acid solution of olefin in contact with RuO_4 in CCl_4.

The reaction has been made catalytic in RuO_4 by using oxidants to regenerate the RuO_4. Sodium metaperiodate has been used[195–198], however, this has the disadvantage that metaperiodate is relatively expensive and is itself an oxidant. An improved procedure has been developed by Wolfe and coworkers using $RuCl_3$ plus hypochlorite in the form of household bleach[193]. The procedure appears to be convenient and inexpensive.

Re_2O_7 has been little studied as an olefin oxidant and certainly appears to deserve more attention. The only reports of olefin oxidant to the writer's knowledge are two patents describing the oxidation of olefins by Re_2O_7 to epoxides[199] and to glycol acetates[200]. The former was produced in an inert solvent while the latter was formed in the presence of carboxylic acid anhydrides.



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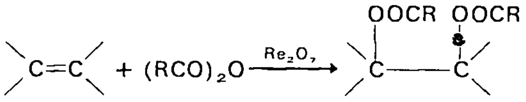
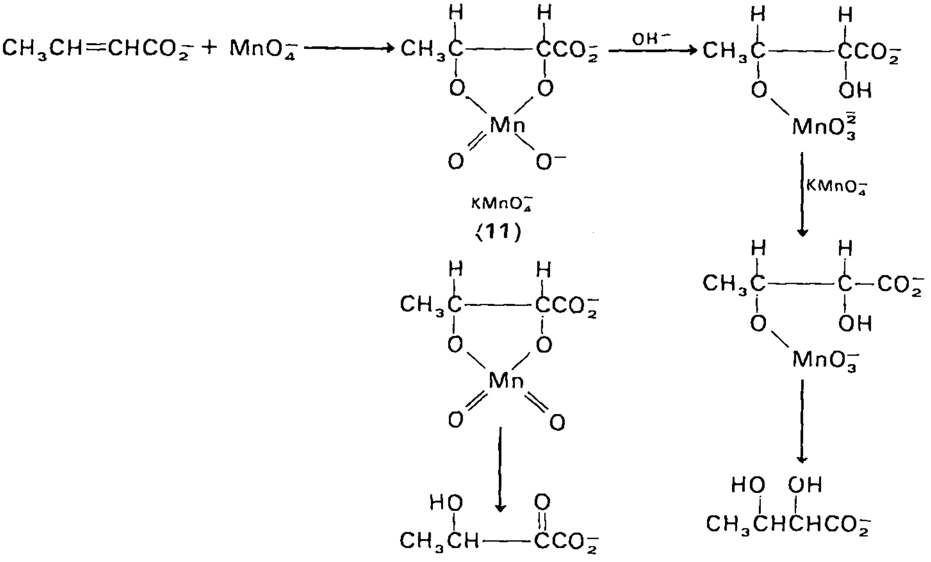


(203)

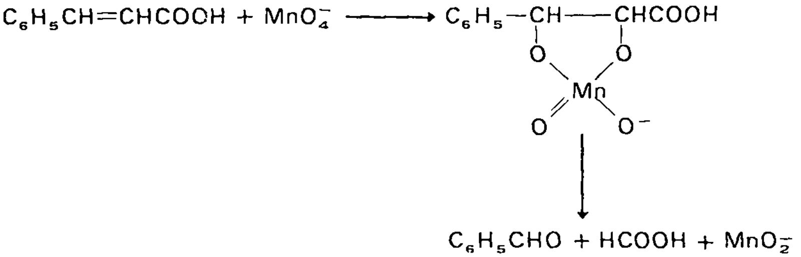
f. *Potassium permanganate*[201]. The use of this reagent for olefin oxidation goes back a number of years. The Baeyer test for unsaturation in organic compounds involves the decoloration of a permanganate solution.

The oxidation products can be glycols, hydroxyketones, diketones, epoxides, or cleavage products. Basic conditions favour the glycol product. Almost certainly the glycol and hydroxyketone arise from a cyclic-ester intermediate similar to that proposed for the OsO_4 and RuO_4 oxidations. Recently spectral evidence for such an intermediate has been reported by two sets of workers[202,203]. Based on the observation of the intermediate plus earlier kinetic results[204]. Wiberg proposed the following scheme (equation 204) for the oxidation of crotonic acid. This scheme is in keeping with earlier results which indicated *cis* stereochemistry for the diol product[205] and oxygen-18 transfer from permanganate to diols[206].



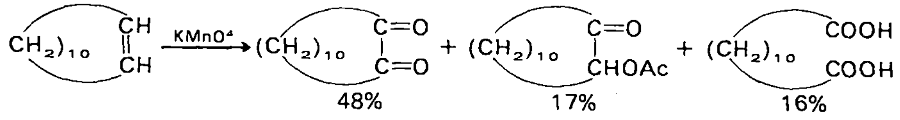
(204)

Lee and Brownridge[202] detected an intermediate which they postulated to be analogous to **11** in their study of the permanganate oxidation of cinnamic acid. However, under their acid conditions the final products were benzaldehyde, formic acid, and Mn^{III}. Thus, in this case Mn^{VII} is behaving as a four-electron oxidant in a fashion very similar to that postulated for RuO_4. It is not certain if cleavage also occurs directly as in this scheme or by secondary oxidation of initial products.



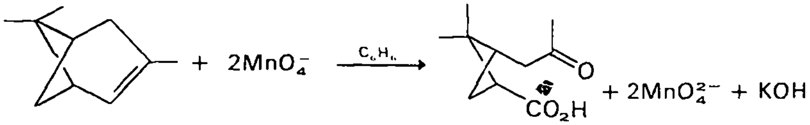
(205)

Sometimes epoxides are products of the oxidation of certain olefins in acetic acid[201]. Recently it has also been reported that α-diketones are major products along with smaller amounts of keto acetates when the oxidation is run in acetic anhydride[207]. Smaller ring cyclic olefins such

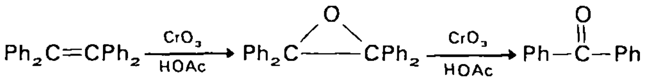

(206)

as cyclohexene do not give α-diketones. Acyclic olefins also gave α-diketones in some cases but often ketoacetates are the main product.

Improved means of carrying out permanganate oxidations have recently been reported. These involve solubilization of permanganate in organic solvents by use of quaternary ammonium salts[208,209] or crown ethers[210]. Oxidations can be carried out under milder conditions with higher yield. Thus, in benzene solution with crown ether and permanganate, α-pinene is oxidized to *cis*-pinonic acid in 90% yield. In aqueous solution yields of 40–60% are obtained.


(207)

g. *Chromium*(VI)[211]. This oxidant is used in the form of chromic acid, chromyl acetate and chromyl chloride. The chromic acid oxidation is carried out either in acetic acid solvent or in aqueous solution. In acetic acid, one of the products that is often found is an epoxide. The other products can often be rationalized in terms of further oxidation of the epoxide to give products at a higher oxidation level. An example is the oxidation of tetraphenyl ethylene[212]: with excess of olefin, epoxide is the main product while an excess of oxidant leads to benzophenone.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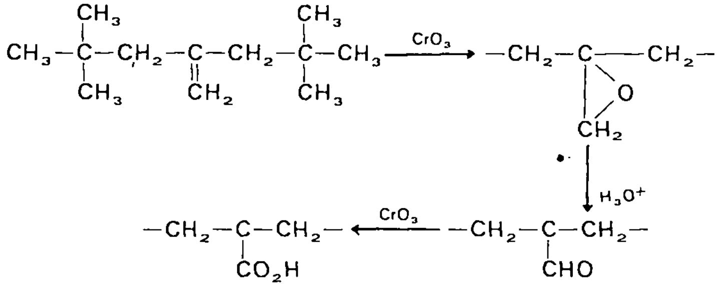
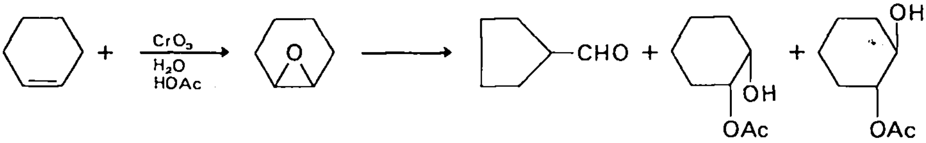
With steroids, allylic oxidation products which could arise from further oxidation of initial epoxide product are found[211].

In aqueous acid medium the product distributions include rearrangement products which could have arisen from an intermediate epoxide.

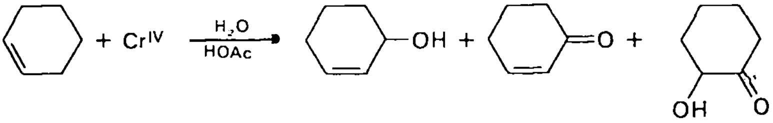

(209)

Thus, 4,4-dimethyl-2-neopentyl-1-pentene is converted to an acid which can be shown to be the further oxidation product from the aldehyde as a result of acid-catalysed rearrangement of a possible initial epoxide product[211]. Recently Rocek and Drozd were able to demonstrate that cyclohexene oxide is an intermediate in the oxidation of cyclohexene in aqueous acetic acid[213]. However, some products, including allylic



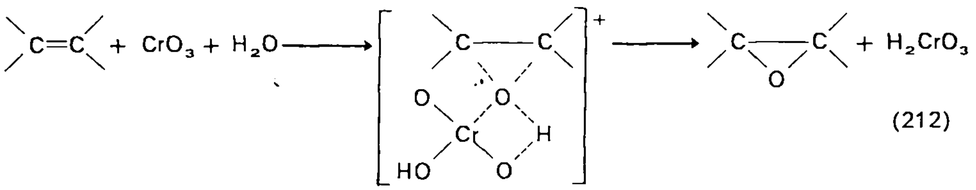
(210)

oxidation products, do not arise from the epoxy intermediate. They are possibly formed by oxidation of cyclohexene by Cr^{IV}.



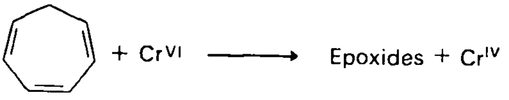
(211)

Based on trends in rates of olefin oxidation with olefin structure Awasthy and Rocek[214] concluded that epoxide formation occurred via a three-member transition state analogous to that for peracid epoxidation or bromination.



(212)

Awasthy and Rocek believe that initial Cr^{VI} oxidation products are always epoxides while the allylic oxidation products arise from oxidation by Cr^{IV} species. This conclusion was reinforced by studies of the chromic acid oxidation of cycloheptatriene[215]: the only isolable initial product was benzaldehyde. Isotope studies suggested a symmetrical intermediate, and the data were most consistent with the following scheme:



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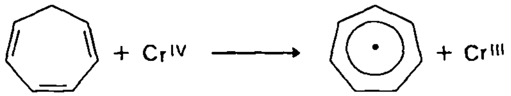

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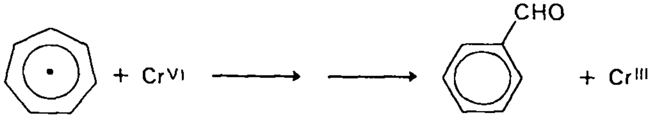
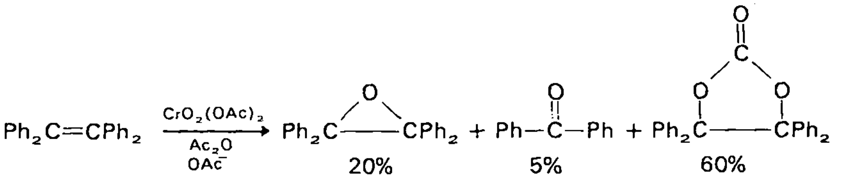


(215)

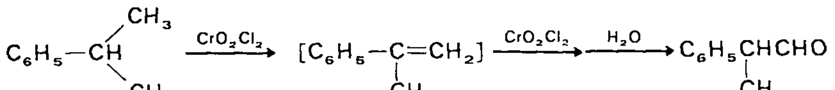
The oxidation of olefins by chromyl acetate gives epoxide as major product with most olefins; cleavage products and allylic oxidation products are also formed. It is possible that most products arise from secondary oxidation of the initial epoxide product but this is not known for certain[211].

In a novel reaction tetraphenylethylene gives mainly a cyclic carbonate as a product[216].



(216)

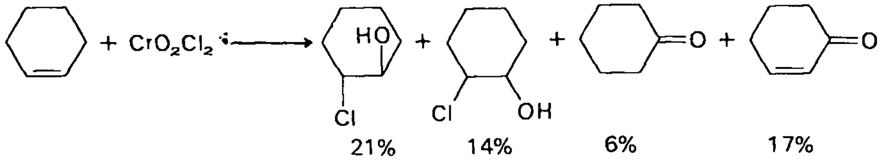
The oxidation of 1,1-disubstituted olefins by chromyl chloride in general gives aldehydes and ketones. The Etard oxidation of aryl alkanes is believed to involve dehydrogenation to the styrene derivative followed by oxidation to the ketone[217].



$$C_6H_5-CH(CH_3)_2 \xrightarrow{CrO_2Cl_2} [C_6H_5-C(CH_3)=CH_2] \xrightarrow{CrO_2Cl_2} \xrightarrow{H_2O} C_6H_5CH(CH_3)CHO$$

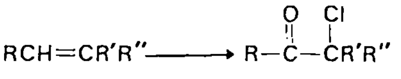
(217)

The oxidation of cyclohexene gives four main identified products[218].



(218)

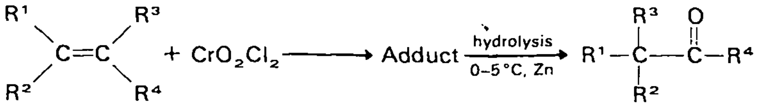
In a recently reported variation of the oxidation, α-chloroketones were obtained directly from olefins in acetone solvent[219].



$$RCH=CR'R'' \longrightarrow R-\overset{O}{\overset{\|}{C}}-\overset{Cl}{\overset{|}{C}}R'R''$$

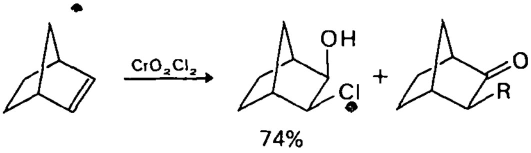
(219)

If high yields of carbonyl products are desired a 1:1 molar ratio of chromyl chloride to alkene is used and the intermediate adduct is reductively hydrolysed with zinc dust to give carbonyl product by alkyl or hydride shifts (R = alkyl or H):



(220)

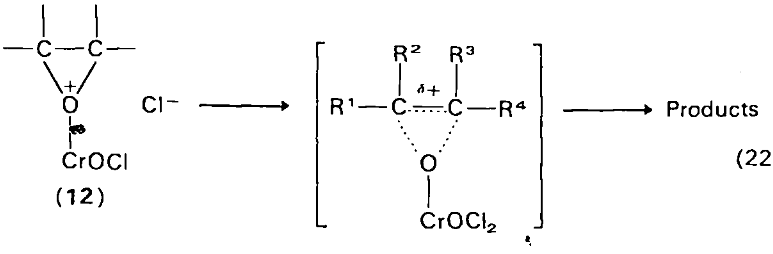
Norbornene was recently reported to be oxidized by chromyl chloride mainly to a chlorohydrin but with smaller amounts of ketone being formed[224]. This was used as evidence against an epoxide intermediate since the chlorohydrin would not have arisen from rearrangement of an



(221)

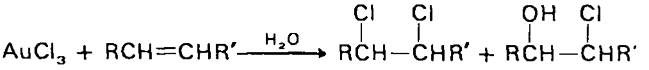
epoxide. However, norbornene adds a number of reagents in a different fashion from unhindered olefins so it may not be too surprising that norbornene has a special mechanism for oxidation.

The intermediate has been postulated as having the structure **12** which decomposes via a highly polar three-membered ring transition state[221–223].



(222)

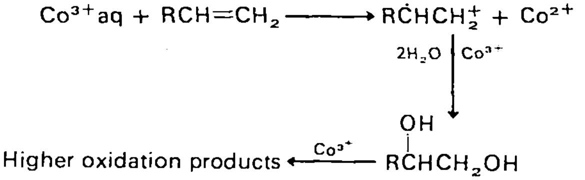
h. *Gold*(III). Gold trichloride has been very little studied in olefin oxidation but there is one report that olefins are oxidized to dichlorides and chlorohydrins by this salt[225].



$$\mathrm{AuCl_3 + RCH{=}CHR' \xrightarrow{H_2O} R\overset{Cl}{\overset{|}{C}}H{-}\overset{Cl}{\overset{|}{C}}HR' + R\overset{OH}{\overset{|}{C}}H{-}\overset{Cl}{\overset{|}{C}}HR'}$$

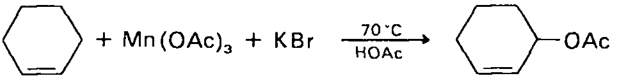
i. *The strong one electron oxidants: cobalt*(III), *manganese*(III), *manganese* (IV) *and vanadium*(V)[226]. The metal ions are called strong one-electron oxidants because of their high redox potential which permits them to oxidize a large number of organic substrates by free radical routes. However, their olefin oxidation chemistry is very limited. V^{V} in aqueous solution is reduced by olefins but the products are unknown. In non-aqueous solvent, $VOCl_3$ plus $POCl_3$ oxidizes cyclohexene to 1,2-dichlorocyclohexane (mainly *trans*)[227].

Co^{III}, on the other hand, does oxidize olefins in aqueous solution by a route probably involving radical cations[228].



$$\begin{tikzcd}
Co^{3+}aq + RCH{=}CH_2 \arrow[r] & R\dot{C}HCH_2^{+} + Co^{2+} \arrow[d, "Co^{3+}", "2H_2O"'] \\
\text{Higher oxidation products} & RCH(OH)CH_2OH \arrow[l, "Co^{3+}"']
\end{tikzcd} \qquad (223)$$

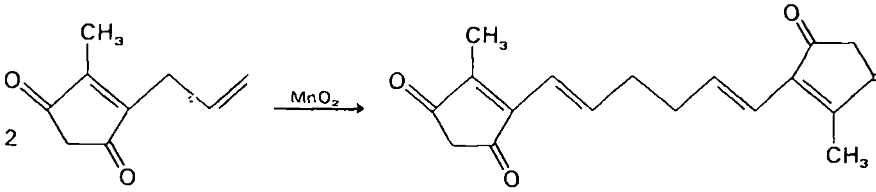
There are two recent reports of allylic oxidation by Mn^{III} which probably involves initial attack on the olefinic double bond. At 70 °C in acetic acid, cyclohexene reacts slowly with manganese acetate but addition of KBr caused a rapid reaction to occur. The main product was cyclohexenyl acetate in 83% yield[229]. $KMnO_4$ at 110 °C could also be used.



(224)

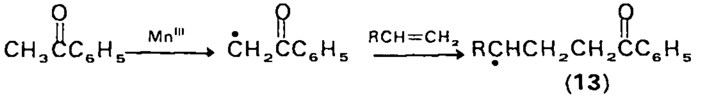
Perhaps bromine radicals are formed which are the actual oxidants.

An oxidative dimerization of compounds related to natural rethrolones with MnO_2 has recently been reported[230]. The dimerization occurs with double bond shift.

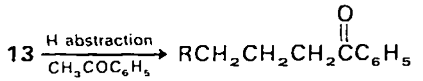


(225)

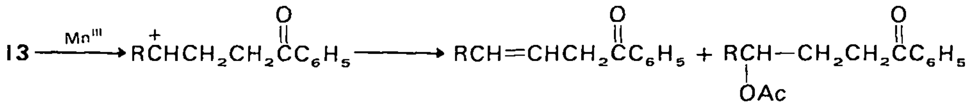
Another oxidation which is definitely indirect is the oxidation of acetone to a radical which will react with olefins[106]. The reaction scheme is identical to that previously reported for Ce^{IV} (equation 117). It has recently been reported that with an aromatic ketone such as acetophenone a fourth product, α-tetralone (**14**), is formed as the predominant product in about 50% yield[231].



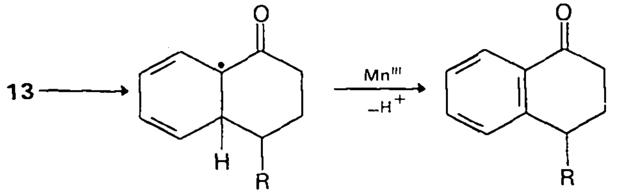
$$CH_3\overset{O}{\overset{\|}{C}}C_6H_5 \xrightarrow{Mn^{III}} \dot{C}H_2\overset{O}{\overset{\|}{C}}C_6H_5 \xrightarrow{RCH=CH_2} \underset{(13)}{R\underset{\bullet}{C}HCH_2CH_2\overset{O}{\overset{\|}{C}}C_6H_5} \qquad (226)$$



$$13 \xrightarrow[CH_3COC_6H_5]{H\ abstraction} RCH_2CH_2CH_2\overset{O}{\overset{\|}{C}}C_6H_5 \qquad (227)$$



$$13 \xrightarrow{Mn^{III}} R\overset{+}{C}HCH_2CH_2\overset{O}{\overset{\|}{C}}C_6H_5 \longrightarrow RCH{=}CHCH_2\overset{O}{\overset{\|}{C}}C_6H_5 + R\underset{OAc}{\underset{|}{C}}H{-}CH_2CH_2\overset{O}{\overset{\|}{C}}C_6H_5 \qquad (228)$$

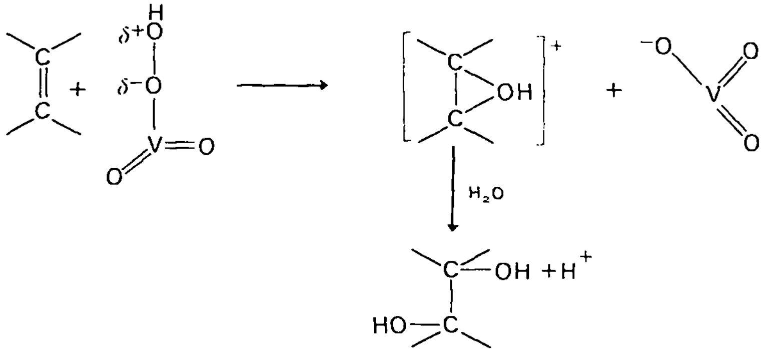


(14)

(229)

3. Oxidations by other reagents catalysed by transition metal ions

a. *Introduction.* Selection of the oxidations which appear in this section is somewhat arbitrary since the mechanism of every oxidation is not known in detail. Thus, OsO_4 plus H_2O_2 (Milas reaction) was included in the OsO_4 section on the assumption that H_2O_2 was merely present to regenerate OsO_4. However, this may not be the case as the mechanism may be more complicated. The same comments apply for $NaClO_3$ or periodate plus OsO_4. Hence, reactions included in this section are those in which the metal *definitely* does not appear to be the oxidant. However, in some cases this assumption may be on shaky ground.

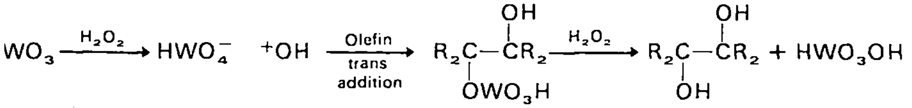


(230)

b. *H_2O_2 or peroxides*[180,182]

(i) Metal oxides plus H_2O_2. Metal oxides which tend to form peracids catalyse the hydroxylation of olefins by H_2O_2. The final products are usually the *trans* diols. The initial product may well be an epoxide which, under the reaction conditions, reacts further to give the diols. With V_2O_5 the scheme would be as in equation (230).

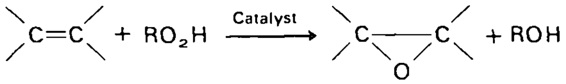
Ta_2O_5, WO_3, SeO_2 and MoO_3 also work in the reaction. One mechanism suggested for the WO_3-catalysed oxidation does not involve epoxide intermediates.



$$WO_3 \xrightarrow{H_2O_2} HWO_4^- \quad {}^+OH \xrightarrow[\text{trans addition}]{\text{Olefin}} R_2\underset{\displaystyle OWO_3H}{C}-\overset{\displaystyle OH}{C}R_2 \xrightarrow{H_2O_2} R_2\underset{\displaystyle OH}{C}-\overset{\displaystyle OH}{C}R_2 + HWO_3OH \qquad (231)$$

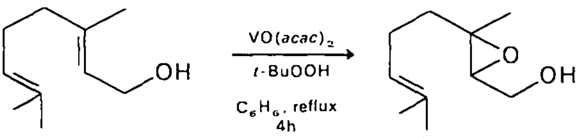
(ii) Epoxidation with hydroperoxides[232]. This field has received considerable study in the last 10 years. In particular there have been several mechanistic studies.

The catalysts for the epoxidation are generally compounds of molybdenum and vanadium although sodium tungstate has some activity[233]. Compounds of Mn^{II} and Mn^{III}, Fe^{II} and Re^{III}, Co^{III}, Rh^{III}, Ni^{II}, Pt^{II}, Cu^{II} and Au^{III} were inactive. A wide variety of molybdenum compounds ranging from molybdenum(VI) peroxy compounds[234] to $Mo(CO)_6$[233] catalyse the reaction. Vanadium is usually used as $VO(acac)_2$ although sodium vanadate has some activity. The reaction is run under anhydrous conditions in organic solvents at temperatures from 0 to 110 °C. The reaction is clean and yields are usually over 75%. Tertiary butylhydroperoxide is generally used as oxygen source.

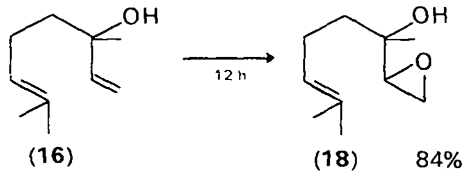


(232)

These reagents have recently been found to exhibit remarkable reactivity towards olefinic alcohols giving selective epoxidations not obtainable with other reagents[235]. Thus, geraniol (**15**) and linalool (**16**) were oxidized to the previously unknown epoxides (**17**) and (**18**).

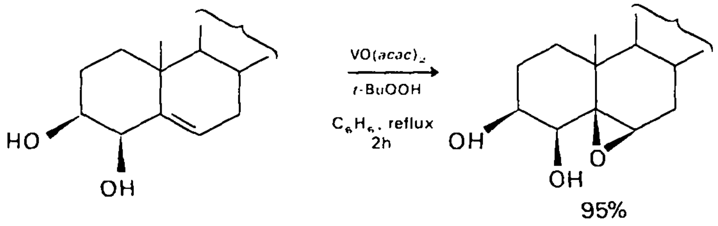


(15) (17) 93% (233)



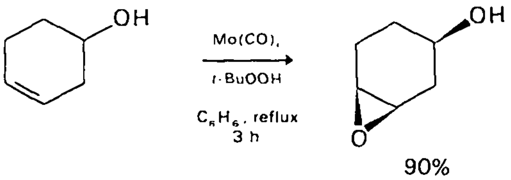
(234)

The stereoselectivity is demonstrated by the following two reactions:



VO(acac)$_2$
t-BuOOH
C_6H_6, reflux
2h
HO
OH
OH
OH
O
95%

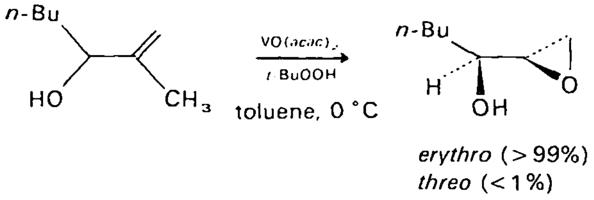
(235)



Mo(CO)$_6$
t-BuOOH
C_6H_6, reflux
3 h
OH
OH
O
90%

(236)

Other examples of stereospecific epoxidation have recently been reported with acyclic olefinic alcohols[236]. Thus, the epoxidation of the allylic alcohol **19** gives the *erythro* epoxy alcohol selectivity.

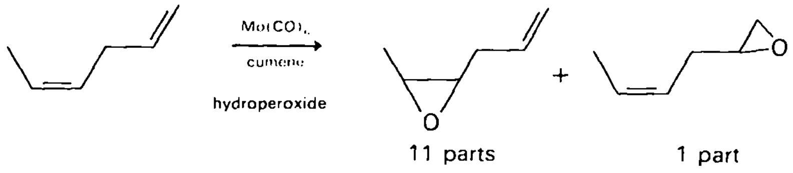


n-Bu
HO
CH_3
VO(acac)$_2$
t BuOOH
toluene, 0 °C
n-Bu
H
OH
O
erythro (> 99%)
threo (< 1 %)

(237)

This stereospecific synthesis was used to prepare the *dl*-C_{18} *cecropia* juvenile hormone from farnesol[236].

Epoxidation of unconjugated diolefins gave mixtures of the two possible epoxides with the internal epoxide predominating. Thus, *cis*-1,4-hexadiene gave an 11 to 1 preference for internal epoxidation, while the *trans* isomer

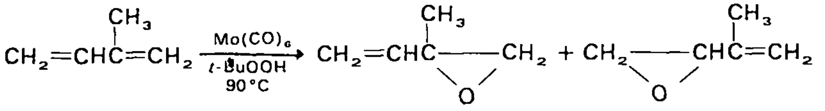


Mo(CO)$_6$
cumene
hydroperoxide
O
+
O
11 parts
1 part

(238)

displayed a 6 to 1 preference for internal epoxidation. These results were obtained using a 2:1 ratio of diene to peroxide. At lower ratios diepoxides are formed in appreciable yield.

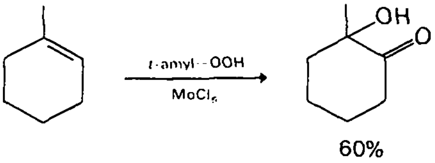
Although a little less reactive than monoolefins, conjugated dienes gave similar results. Isoprene gave the two possible isomers in a 4:1 ratio.



(239)

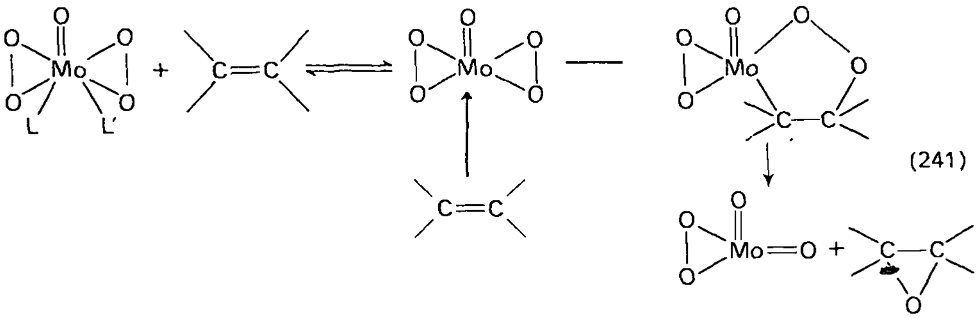
$Mo(CO)_6$ was generally a better catalyst than $VO(acac)_2$ but the latter was superior for the epoxidation of allylic alcohols.

Using an excess of peroxide it has been reported that α-hydroxy ketones can be obtained directly[238].



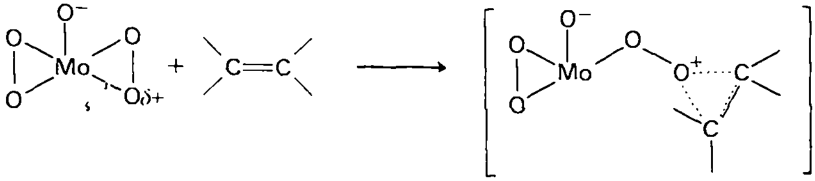
(240)

The mechanism originally suggested for epoxidation by molybdenum(VI) peroxo compounds involved the following sequence[234]:



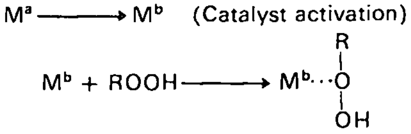
(241)

Results from oxygen-18 labelling experiments were consistent with this



(242)

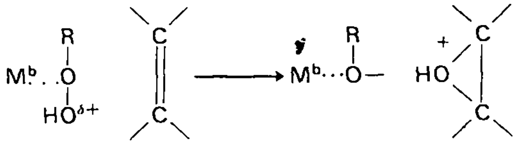
mechanism but other results on relative reactivities of various olefins suggest a three-member transition state[239], which is now generally favoured for these oxidations. In a study of the molybdenum naphthenate-catalysed epoxidation of styrene and some substituted styrenes a ρ of $-1{\cdot}4$ was found[240]. This indicates an electrophilic attack upon the olefin. A general mechanism is as follows:



$$M^a \longrightarrow M^b \quad \text{(Catalyst activation)}$$

$$M^b + ROOH \longrightarrow M^b\cdots\overset{\overset{R}{|}}{\underset{\underset{OH}{|}}{O}}$$

(243)



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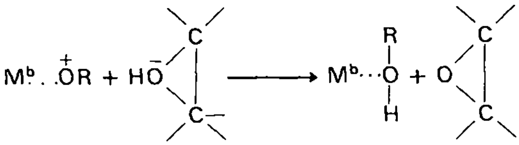
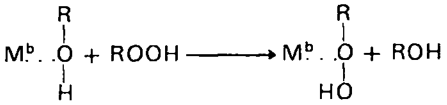
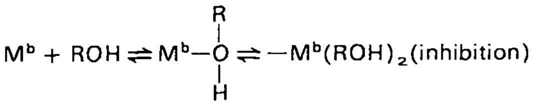


(245)



$$M^b..\overset{\overset{R}{|}}{\underset{\underset{H}{|}}{O}} + ROOH \longrightarrow M^b..\overset{\overset{R}{|}}{\underset{\underset{HO}{|}}{O}} + ROH$$

(246)

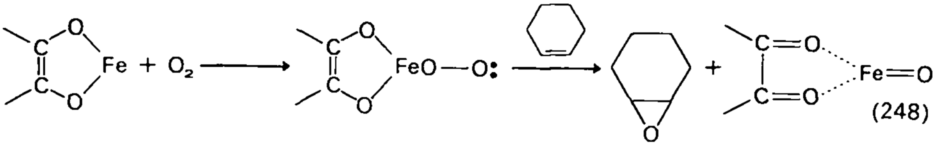


$$M^b + ROH \rightleftharpoons M^b\text{—}\overset{\overset{R}{|}}{\underset{\underset{H}{|}}{O}} \rightleftharpoons \text{—}M^b(ROH)_2\text{(inhibition)}$$

(247)

Evidence for the inhibition step in VO(*acac*)$_2$ catalysis is provided by the fact that *t*-butyl alcohol inhibits the epoxidation by *t*-butyl hydroperoxide[241]. In a recent study of epoxidations by vanadium and molybdenum chelates the rate laws for the vanadium-catalysed system were consistent with attack of olefin on a vanadium(v)–hydroperoxide complex[242]. Epoxidation with MoO$_2$(*acac*)$_2$ was slower and the kinetics were consistent with the formation of molybdenum–olefin, molybdenum–hydroperoxide and a molybdenum–hydroperoxide–olefin complex. Apparently the epoxidation occurs by attack of olefin on the molybdenum–hydroperoxide complex rather than through the ternary complex.

c. *Metal ions plus O_2*. These reactions include both radical and non-radical paths. The non-radical path involves activation of oxygen by Fe^{2+}. The reaction is made catalytic by using ene-diols which are oxidized at the same time as the olefin[243]. The route shown in equation (248) has been suggested; this reaction has been used mainly to hydroxylate olefins[244].



(248)

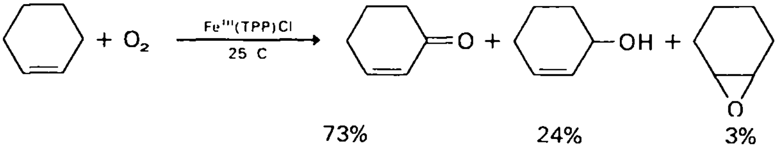
The fact that Ti^{III}, Cu^{I} and Sn^{II} can be used in the aromatic hydroxylation suggests that these metal ions may also be useful for olefin epoxidation. These oxygen activation mechanisms may be similar to those for biological oxidations with oxygenases such as Cu^{I} phenolase, or Fe^{II} pyrocatechase.

The free radical paths no doubt involve chain reactions of O_2 with radicals to give peroxides. The metal ion catalysed the oxidation by decomposing the peroxides to give radicals[245]. The metal ions which

$$M^{n+} + ROOH \longrightarrow M^{(n+x)+} + OH^- + RO\cdot \qquad (249)$$

catalyse autoxidation are Co^{2+}, Fe^{2+}, Cr^{2+}, Cu^{+}, Ce^{3+}, and Mn^{2+}.

Recently it has been reported that metalloporphyrins will also catalyse the free-radical oxidation of olefins[246]. Thus, iron *meso*-tetraphenylporphin chloride, Fe^{III}(TPP)Cl, will catalyse the reaction of oxygen and cyclohexene at 25 °C. Co^{II}(TPP), Rh^{III}(CO)(TPP)Cl and Rh^{III}(TPP)Cl also

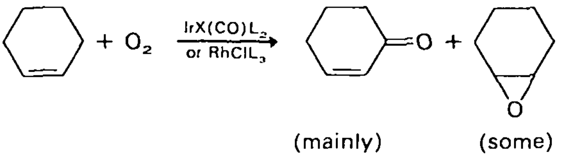


(250)

catalyse the oxidation of cyclohexene. These catalysts also produce cyclohexene hydroxide and in the case of Rh^{III}(CO)(TPP)Cl the hydroperoxide is the only product. Presumably the hydroperoxide is an intermediate in the Fe^{III}(TPP)Cl oxidation since it is decomposed by Fe^{III}(TPP)Cl to the same products as the direct oxidation.

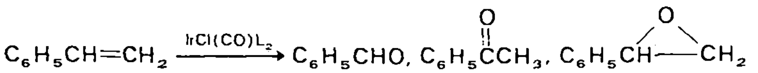
Another olefin oxidation takes place by oxygen-carrying complexes; because of the possibility of novel oxidation pathways, there has been considerable interest in this type of oxidation recently[247]. These complexes are phosphine compounds of Pd^{0}, Pt^{0}, Ir^{I}, Rh^{I}, Ru^{II} and Os^{II} which may also contain carbonyl ligands.

The oxidation products consist of allylic oxidation products, epoxides or cleavage products. The first report[248] of this type of oxidation concerned cyclohexene which gave mainly allylic oxidation (L = PPh_3).



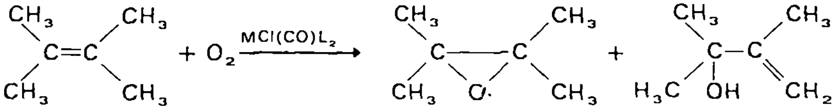
(251)

Styrene, which cannot undergo allylic oxidation, mainly gives cleavage products with some epoxide under certain reaction conditions[249]. Metal complexes of Rh^{I}, Ru^{II} and Os^{II} gave similar results[250] while RhClL$_3$ also



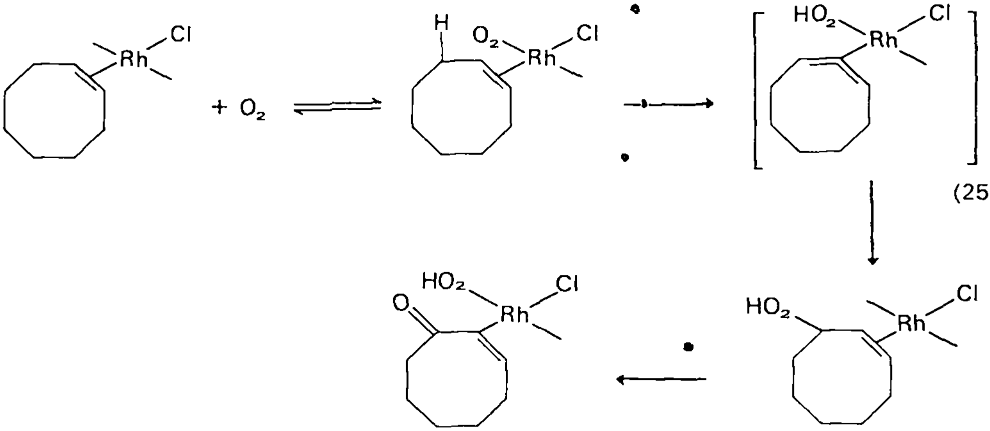
$$C_6H_5CH{=}CH_2 \xrightarrow{IrCl(CO)L_2} C_6H_5CHO,\ C_6H_5\overset{\overset{O}{\|}}{C}CH_3,\ C_6H_5\overset{\overset{O}{\frown}}{CH{-}{-}CH_2} \qquad (252)$$

oxidized substituted styrenes, mainly to give cleavage products[251]. Tetramethylethylene gives epoxide and an allylic alcohol (M = Ir or Rh):



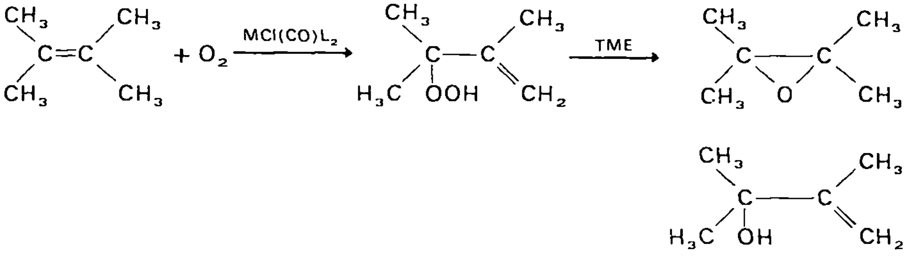
(253)

Originally it was hoped that these oxidations may occur by non-radical oxygen transfer mechanisms analogous to those believed to be operative in oxidations by oxygenases which are metalloenzymes catalysing the direct oxygenation of organic substrates[252]. However most of these reactions are strongly inhibited by radical scavengers which indicates radical pathways. Evidence for allylic hydroperoxide intermediates was provided by James and Ochiai in the Rh^{I}-catalysed oxidation of cyclooctene[253]. They suggested the following route:



(254)

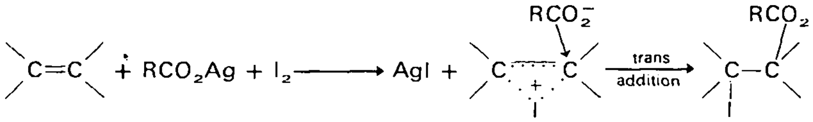
Hydroperoxide intermediates were also found in the oxidation of tetramethylethylene (TME)[254]. Since they could show that peroxides in the presence of catalyst oxidized the olefin to epoxide, they proposed the following path (M = Ir or Rh):



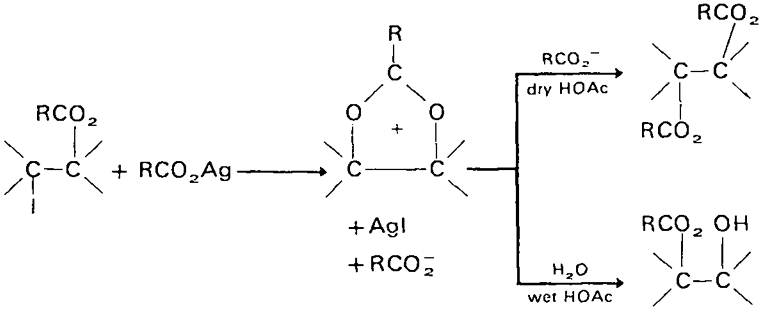
(255)

Since the reaction is inhibited by hydroquinone the hydroperoxide must be formed by a radical chain reaction. It is not clear if the radical chain is initiated by the metal centre or by metal-catalysed decomposition of trace impurities. Similar routes have been suggested for the oxidation of styrene[250]. Certainly more study is required to elucidate completely the mechanisms of these oxidations.

d. *Iodine and silver carboxylate*[255,256]. This reaction, which is called the Prévost reaction[257] in dry acetic acid and Woodward's *cis*-hydroxylation procedure in wet acetic acid[258], is analogous to olefin oxidations by $Tl(OAc)_3$ and $Pb(OAc)_4$ in acetic acid. The reaction almost certainly involves the initial attack of positive halogen and carboxylate on the olefin to give an intermediate adduct. This adduct then reacts again with silver carboxylate to initiate the decomposition of the adduct. The stereochemistry of the product can be explained by neighbouring group partici-



(256)



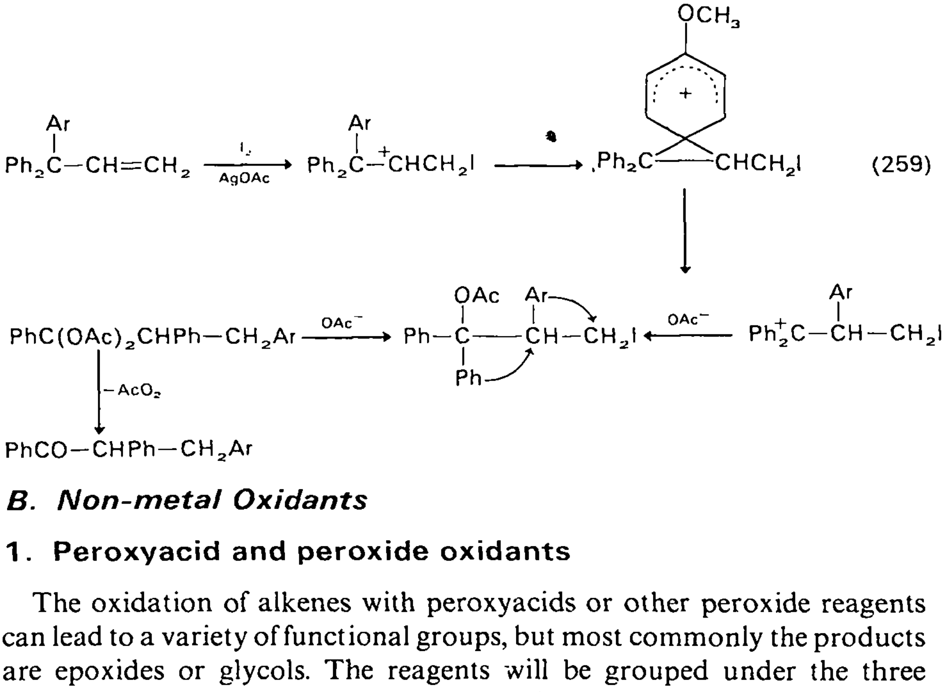
(257)

pation by the carboxylate group. The resulting ion is attacked *trans* by acetate in dry acetic acid or is opened by water in wet acetic acid. Thus, Winstein and Buckles[259] found that α-acetoxy halides were converted to acylated glycols by silver acetate. Retention of configuration occurs in anhydrous acetic acid while inversion occurs in wet acetic acid as shown in the example below (equation 258):

$$\textit{threo}\text{-}CH_3CH(OAc)CHBrCH_3 \begin{cases} \xrightarrow[\text{dry HOAc}]{\text{AgOAc}} \textit{threo}\text{-}CH_3CH(OAc)CH(OAc)CH_3 \\ \xrightarrow[\text{wet HOAc}]{\text{AgOAc}} \textit{erythro}\text{-}CH_3CH(OAc)CH(OAc)CH_3 \end{cases} \qquad (258)$$

These two procedures have been used to prepare *cis*- and *trans*-glycols from a number of cyclic and acyclic olefins. Yields are usually over 60%.

The similarity of the Prévost reaction to lead tetraacetate oxidation of olefins has been discussed[86]. The oxidation of 3,3,3-triaryl propenes indicates carbonium ion character in both addition of iodine and acetate as well as in the decomposition of the adduct (Ar = $-C_6H_5OCH_3$).



(259)

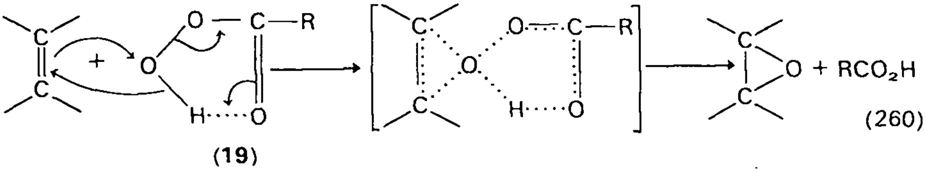
B. Non-metal Oxidants

1. Peroxyacid and peroxide oxidants

The oxidation of alkenes with peroxyacids or other peroxide reagents can lead to a variety of functional groups, but most commonly the products are epoxides or glycols. The reagents will be grouped under the three categories of peroxyacids, hydrogen peroxide and alkyl hydroperoxides.

a. *Peroxyacids.* The reaction of an alkene with a peroxyacid to yield an epoxide (also called an oxirane group) was first discovered by the Russian chemist Prileschajew[260]. A number of reviews on this subject have been published[261–265] including a recent and very extensive coverage by Swern[266]. The mechanism of this epoxidation reaction will be reviewed and then recent examples of the reaction will be discussed to illustrate the variety of peroxyacids and alkene substrates that can be used.

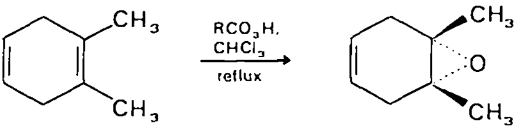
(i) Mechanism of epoxidation. Epoxidation is a second order reaction, first order in alkene and first order in peroxyacid[267]. A high negative entropy of activation suggests a highly ordered transition state[267]. The 'molecular' mechanism (1,1-addition) first proposed by Bartlett[268] (equation 260) involves electrophilic attack by the peroxyacid (**19**) and is consistent with the kinetic data. More recent investigations support this proposal[269,270]. An alternative mechanism involving a 1,3-dipolar



(260)

addition has recently been proposed[271] and criticized[270], while calculations[272] using a semi-empirical method have suggested that both mechanisms are possible with the 'molecular' mechanism being more reasonable in non-polar media and the dipolar mechanism in polar media.

Electron-donating substituents attached to the double bond accelerate the rate and the following relative rates of epoxidation have been determined[273]: $CH_2{=}CH_2 = 1$; $RCH{=}CH_2 \sim 25$; $RCH{=}CHR$, $R_2C{=}CH_2 \sim 500$; $R_2C{=}CHR \sim 6000$; $R_2C{=}CR_2 \gg 6000$. Thus a tetrasubstituted double bond can be selectively epoxidized in the presence of a disubstituted double bond[274] (equation 261). Conversely, an electron-withdrawing substituent such as a carbonyl group retards the rate of

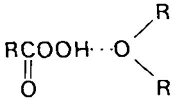


(261)

epoxidation as it decreases the electron density at the double bond undergoing the electrophilic attack. For example, the epoxidation of α,β-unsaturated esters is relatively slow and requires a more active peroxyacid[275] while with α,β-unsaturated ketones or aldehydes a nucleophilic reagent is generally used (see Section II.B.1.b).

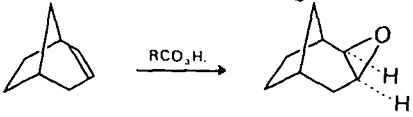
The reactivity of the peroxyacid is also affected by the substituents attached. In general, electron-withdrawing groups enhance the electrophilic character of the oxidant and therefore increase the rate of epoxidation while electron-donating groups decrease it[267,276]. Consequently, trifluoroperoxyacetic acid is a more rapid epoxidation reagent than peroxyacetic acid and *m*-chloroperoxybenzoic acid is more reactive than peroxybenzoic acid.

Solvents can also influence the rate of epoxidation with chlorinated and aromatic solvents affording the higher rates, and ethers, alcohols and carbonyl compounds the lower rates[277,278]. The rate constants decrease with increasing solvent basicity. This is consistent with the fact that the intramolecularly hydrogen-bonded peroxyacid (**19**) is the initial reactive species in epoxidation[272] and any reduction in the effective concentration of this species will decrease the rate. Intermolecular association between the peroxyacid and solvent, to give species such as **20** increases with increasing basicity of the solvent[279]. This intermolecular association necessarily decreases the concentration of **19** and thus the rate of epoxidation.



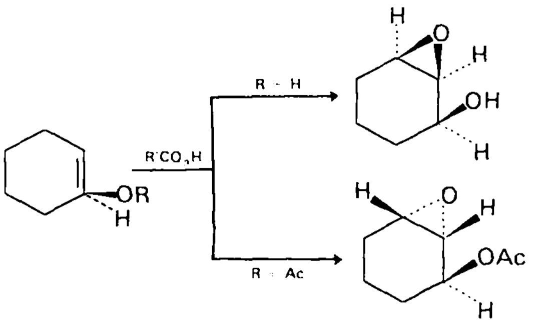
(**20**)

The epoxidation proceeds in a stereospecific *cis* manner with *cis*-alkenes yielding *cis*-epoxides and *trans*-alkenes yielding *trans*-epoxides[267]. The *cis*-alkene is epoxidized about 1·5-times faster than the *trans* isomer with straight chain olefins[273]. The attack of peroxyacid generally occurs from



(262)[280]

the less-hindered side of the alkene to give the less-hindered epoxide (e.g., equation 262), but nearby polar substituents, such as hydroxyl, can both



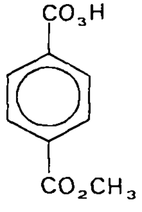
(263)

direct the approach of the peroxyacid and accelerate the rate of the reaction[281] (equation 263). Such is not the case with the related acetoxy compound which gives the expected steric-controlled product.

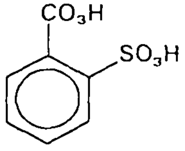
(ii) Preparation and properties of peroxyacids. Peroxyacids are commonly prepared by the reaction of a carboxylic acid (or its anhydride) with hydrogen peroxide (usually 30 %, but sometimes more concentrated) in the presence of a catalytic amount of strong mineral acid[262,266]. Peroxyacids are considerably weaker than the corresponding carboxylic acids, e.g. the pK_a of acetic acid is 4·8, while that of peroxyacetic acid is 8·2[282]. Carboxylic acids exist as dimers in solution, while peroxyacids form intramolecular hydrogen bonds[267] (see **19**) and exist as monomers. As a result, peroxyacids are more volatile than the corresponding carboxylic acids. These contrasting physical properties can often be utilized in the purification of the desired peroxyacid, but frequently it is not necessary to purify the peroxyacid as it is generated *in situ*, that is the hydrogen peroxide and carboxylic acid are combined in the presence of the alkene substrate and the epoxidation is effected directly.

The aliphatic peroxyacids commonly employed in the epoxidation reaction are peroxyformic, peroxyacetic, trifluoroperoxyacetic and monoperoxymaleic acids, the latter two being very powerful oxidants. The most common aromatic epoxidizing reagents are peroxybenzoic, monoperoxyphthalic, *p*-nitroperoxybenzoic and *m*-chloroperoxybenzoic acids, the latter two being the most active. *m*-Chloroperoxybenzoic acid is one of the most convenient peroxyacids because of its high rate of epoxidation, its solubility in a variety of organic solvents, its good stability and its commercial availability as an 85 %-pure crystalline solid[283]. Removal of the major impurity, *m*-chlorobenzoic acid, with an aqueous phosphate buffer gives the peroxyacid in more than 99 % purity.

The preparation of *p*-methoxycarbonylperoxybenzoic acid (**21**) by photooxidation of methyl *p*-formylbenzoate has been described[284]. This peroxyacid is as stable as *m*-chloroperoxybenzoic acid and as reactive as peroxybenzoic acid in epoxidation reactions. Reaction of *o*-sulphobenzoic anhydride with hydrogen peroxide gives in good yield *o*-sulphoperoxybenzoic acid (**22**), a new water-soluble oxidant[285]. If the reaction with an



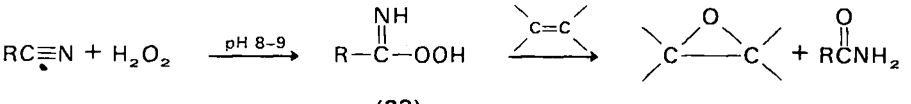
(**21**)



(**22**)

alkene is carried out in buffered solution the major product is an epoxide while in unbuffered solution the strongly acid sulphonic acid opens the epoxide to yield a *trans*-diol.

A novel class of peroxyacids which have not been isolated because of their instability and high reactivity, but which can be generated *in situ* and used for epoxidation reactions, are the peroxycarboximidic acids (**23**). They

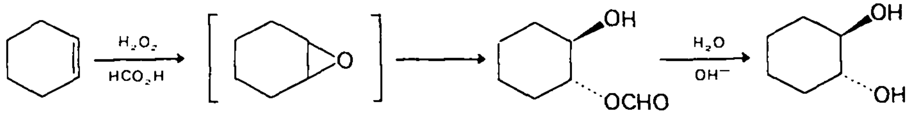


(23)

(264)

are prepared by the reaction of a nitrile with hydrogen peroxide in basic solution[286] (equation 264). These unstable acids readily react with an alkene to give an epoxide in good yield[287]. Note that (**23**) is simply a peroxyacid in which $>$C=O has been replaced by $>$C=NH. Acetonitrile and benzonitrile are commonly used in these preparations with the latter providing the more reactive oxidant, peroxybenzimidic acid (**23**, R = phenyl). The relative reactivities of a number of olefins upon reaction with peroxybenzimidic acid have been examined[288] and it was found that the rate of epoxidation was less dependent on the degree of olefin substitution as compared with the normal peroxyacids. The major advantage of these peroxycarboximic acids is in the epoxidation of acid labile substances such as acetals[289] and carbohydrate derivatives[290].

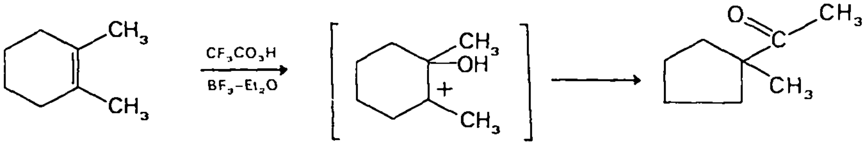
(iii) Examples of epoxidation and related reactions. Epoxides are susceptible to attack by carboxylic acids in the presence of a mineral acid catalyst to yield monoesters of 1,2-diols[262,263] and if the carboxylic acid is sufficiently strong the mineral acid is not necessary. Thus, in some epoxidations the initially formed epoxide reacts further to give a diol monoester. This is particularly true with epoxidations run in formic acid or with those employing trifluoroperoxyacetic acid, which during the course of the reaction is converted to the strongly acidic trifluoroacetic acid (pK_a 0·3). The acid-catalysed opening of the epoxide results in inversion of configuration at the attacked carbon and overall *trans* addition as illustrated in equation (265) for oxidation of cyclohexene[291].



(265)

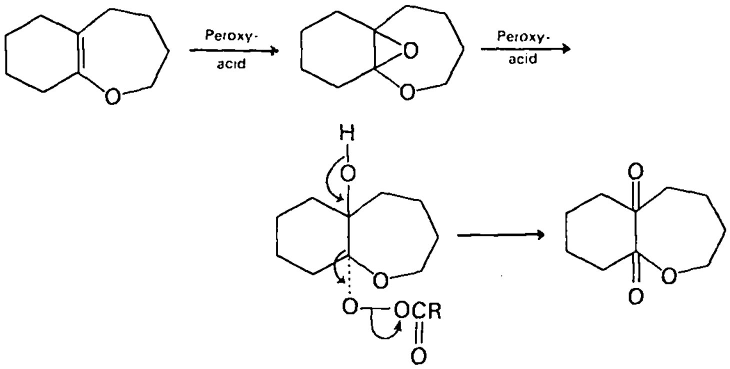
Hydrolysis of the monoester gives a 1,2-*trans*-diol and is an alternative to *trans*-hydroxylation using the Prévost conditions (Section II.A) or *cis*-hydroxylation effected with reagents such as OsO_4 or $KMnO_4$ (Section II.A). This epoxide opening is not a problem when using peroxybenzoic or *m*-chloroperoxybenzoic acid in chloroform, nor is it when using peroxyacetic acid[292] or trifluoroperoxyacetic acid[293] in buffered solution.

Since peroxyacids convert alkenes to epoxides and Lewis acids rearrange epoxides to carbonyl compounds[294], Hart reasoned that a peroxyacid–Lewis acid mixture might convert an alkene directly to an aldehyde or ketone[295,296]. In the fact, treatment of 1,2-dimethylcyclohexene with a mixture of trifluoroperoxyacetic acid and boron trifluoride etherate gave in good yield 1-acetyl-1-methylcyclopentane[295] (equation 266). The product was shown to result from attack of a positive hydroxyl on the double bond followed by a Wagner–Meerwein rearrangement.



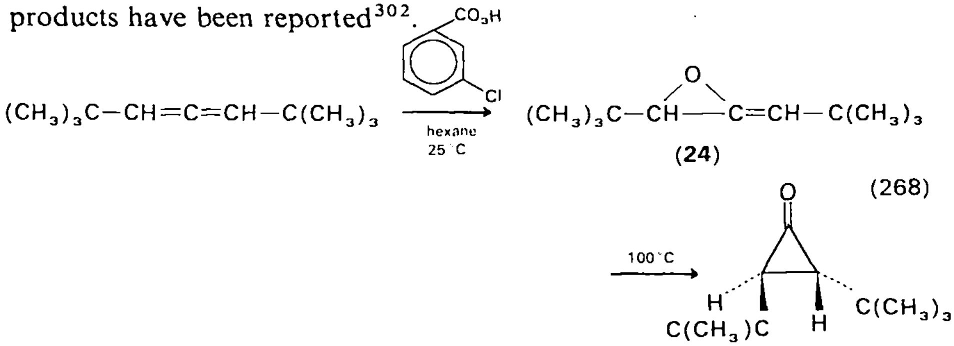
(266)

Enol ethers[297] and enol esters[298] are epoxidized slowly upon reaction with peroxy acids and the resultant epoxides readily rearrange. The epoxidation–rearrangement sequence was utilized in the preparation of a macrocyclic lactone from a bicyclic enol ether[299] as outlined in equation (267).



(267)

Attempts to isolate an allene oxide (e.g., **24**) by epoxidation of one of the double bonds in an allene have been reported[300,301]. Treatment of 1,3-di-*t*-butylallene with *m*-chloroperoxybenzoic acid gave a stable allene oxide (**24**) which, upon heating to 100°C, rearranged to a substituted cyclopropanone[301] as outlined in equation (268). The epoxidation of other substituted and cyclic allenes and the transformations of the resultant products have been reported[302].



(24)

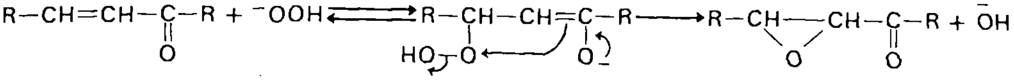
(268)

The reaction of a number of alkenes with optically active peroxyacids (e.g., (+)-peroxycamphoric acid) resulted in asymmetric epoxidation although the optical purity of the products was $<10\%$[303,304].

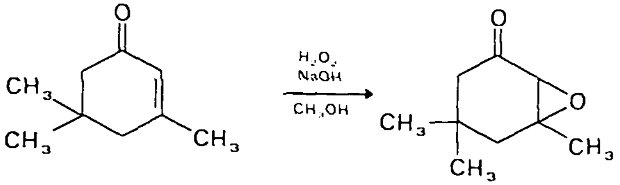
An improved procedure for the preparation of volatile epoxides has been described[305]. After epoxidation of the alkene with *m*-chloroperoxybenzoic acid in a higher boiling solvent such as dioxane or diglyme, the epoxide is distilled directly from the crude reaction mixture. In another report, it was found that unreactive alkenes such as methyl methacrylate could be effectively epoxidized with *m*-chloroperoxybenzoic acid at elevated temperatures (90 °C) if a small amount of a radical inhibitor such as 4,4′-thiobis(6-*t*-butyl-3-methylphenol) was added to the reaction mixture[306]. If the inhibitor is not added, the decomposition of the peroxyacid is more rapid than the epoxidation reaction. A simple procedure for the epoxidation of acid-sensitive olefins with *m*-chloroperoxybenzoic acid has been described[307] which employs a two-phase solvent system consisting of the peroxyacid and the acid-sensitive compound, such as a ketal, in dichloromethane and an aqueous sodium bicarbonate solution. The reactivity of the peroxyacid is slightly diminished in the biphasic medium, but it is still sufficiently reactive to epoxidize monosubstituted double bonds and the yields are comparable to those obtained in a single-solvent procedure.

b. *Hydrogen peroxide oxidation of C=C.* In Section II.A the oxidation of alkenes by hydrogen peroxide in the presence of metal catalysts was described. In this section a few examples of oxidation using hydrogen peroxide and non-metallic catalysts will be outlined.

In Section II.B.1.a it was indicated that epoxidation of α,β-unsaturated aldehydes and ketones by peroxyacids was generally too sluggish to be of use in synthesis. However, if a nucleophilic reagent such as the sodium salt of hydrogen peroxide (NaOOH) is used these carbonyl compounds can be epoxidized readily in high yield. The mechanism is thought to involve nucleophilic addition of the hydroperoxide anion at the beta carbon followed by intramolecular displacement of hydroxide ion[308] as illustrated in equation (269). A typical example[309] of epoxidation employing nucleophilic conditions is given in equation (270).

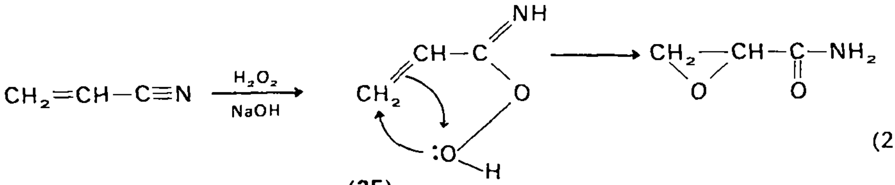


(269)



(270)

The reaction of α,β-unsaturated nitriles with alkaline hydrogen peroxide takes a different course and usually yields epoxyamides. The mechanism as illustrated for acrylonitrile is thought to involve the initial formation of peroxyacrylimidic acid (**25**) which then acts as an electrophilic agent to effect an intramolecular epoxidation[310] as outlined in equation (271).

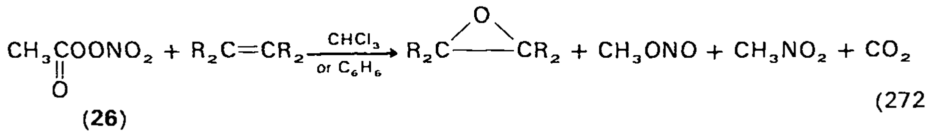


(**25**)

(271)

c. *Alkyl hydroperoxides in oxidation of C=C.* The oxidation of alkenes by hydroperoxides in the presence of metallic catalysts was outlined in Section II.A. α,β-Unsaturated aldehydes and ketones may be epoxidized with *t*-butyl hydroperoxide in the presence of basic catalysts such as sodium hydroxide or Triton B[311,312]. These reactions may be carried out in a completely homogeneous non-polar medium and the yields are comparable to those obtained using the alkaline hydrogen peroxide method. The mechanism is essentially the same as that outlined in equation (269) except that the initial attack at the beta carbon is by an alkyl peroxy anion (ROO^-). The borate-ester-induced decomposition of alkyl hydroperoxides has been shown[313] to generate electrophilic oxygen which reacts with olefins to form epoxides in good yield under relatively mild conditions. The mechanism is non-radical in nature and has many features in common with the epoxidation of alkenes using peroxy acids.

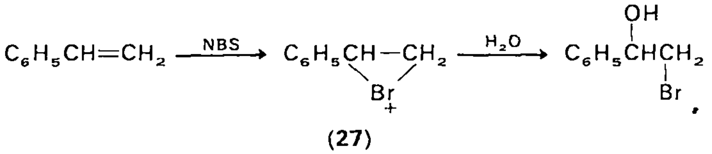
Peroxyacetylnitrate (PAN, **26**) is an important air pollutant in photochemical smog which produces deleterious effects on plants, animals and man. A recent report[314] revealed that PAN is capable of converting alkenes to epoxides (equation 272) and a mechanism for the reaction was proposed.



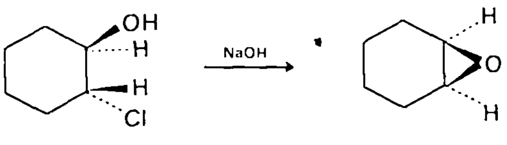
$$\underset{\textbf{(26)}}{CH_3\underset{\underset{O}{\|}}{C}OONO_2} + R_2C{=}CR_2 \xrightarrow[\text{or } C_6H_6]{CHCl_3} R_2C\overset{O}{\frown}CR_2 + CH_3ONO + CH_3NO_2 + CO_2 \qquad (272)$$

2. Hypohalites and related oxidants

The reaction of bromine (or preferably *N*-bromosuccinimide (NBS) or *N*-bromoacetamide[315]) with an alkene in aqueous medium gives a bromohydrin. For example, reaction of styrene with NBS in water yields the bromohydrin indicated in equation (273)[316]. The mechanism involves the initial interaction of the alkene with NBS to give the bromonium ion (**27**) which is then attacked by the nucleophile, water, at the carbon which is best able to stabilize a positive charge. This nucleophilic attack takes place with inversion of configuration and cycloalkenes yield halohydrins with a *trans* geometry. Halohydrins are very useful precursors of epoxides and this *trans* orientation is ideal for the S_N2-type of reaction involved in the epoxide formation as illustrated in equation (274)[317].



$$C_6H_5CH{=}CH_2 \xrightarrow{NBS} \underset{\textbf{(27)}}{C_6H_5CH{-}CH_2 \ (\overset{+}{Br})} \xrightarrow{H_2O} C_6H_5\overset{OH}{\overset{|}{C}}H\underset{\underset{Br}{|}}{C}H_2 \qquad (273)$$

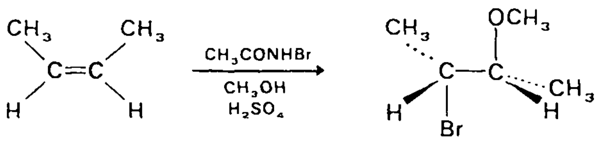


(274)

Chlorohydrins may be prepared by the reaction of alkenes with *N*-chloroamides such as monochlorourea in aqueous acid[318]. Two other methods of preparation involve the use of preformed hypochlorous acid[319] or the generation of hypochlorous acid from calcium hypochlorite in aqueous acid[320]. Iodohydrins may be prepared by the reaction of alkenes with iodine in the presence of an oxidizing agent such as iodic acid[321].

The reaction of *N*-bromosuccinimide with the polyene, squalene, in aqueous glyme resulted in a highly selective reaction to give primarily the terminal bromohydrin[322]. The selectivity was attributed to both steric and conformational effects. In polar solvents such as aqueous glyme it was proposed that the coiling of the non-polar polyene causes shielding of the internal double bonds while the terminal double bonds are more available for reaction. The addition of hypochlorous acid to substituted allenes was shown[323] to lead to the attachment of the chlorine atom on the central carbon and the hydroxyl group on the more substituted end of the allene moiety.

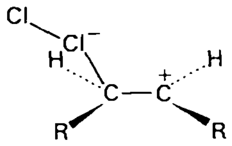
In the preparation of halohydrins, the intermediate halonium ion is attacked by water to give the product, but if water is replaced by some other nucleophile, a variety of halohydrin derivatives may be obtained. Equation (275) shows the preparation of a methoxy bromide with methanol serving as the nucleophile[324].



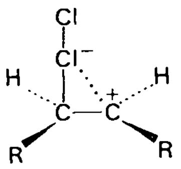
(275)

Polyfluoroalkyl hypochlorites have been reported[325] to add to both unsubstituted and halogen-substituted terminal olefins. The principal products are ethers in which the chlorine atom is bonded to the olefinic carbon bearing the greatest electron density.

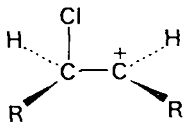
A detailed study of the reactions of a number of alkenes with the reagents chlorine acetate (acetyl hypochlorite) and molecular chlorine in acetic acid revealed significant differences in the stereochemistry of the products[326]. In the chlorine acetate reactions it was concluded that the acetoxy-chloride products were derived largely from attack of the chloronium ion by acetate. In the case of the molecular chlorine reactions to give both acetoxy-chlorides and dichlorides, zwitterionic intermediates (e.g., **28a** and **28b**) were invoked to rationalize the product distributions. With both reagents, varying amounts of *cis* addition products were obtained in addition to the expected *trans* isomers, so 'open' ions such as (**28a**) and (**29**) were suggested as likely precursors of the *cis* products.



(28a)

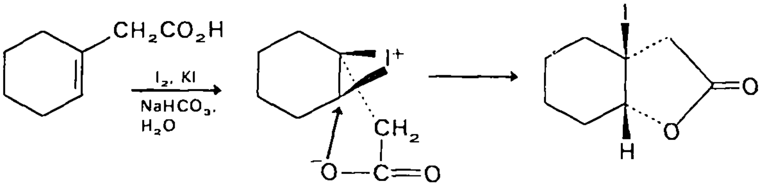


(28b)



(29)

In the halohydrin reactions cited thus far, a nucleophile has attacked the halonium ion in an intermolecular reaction. In the halolactonization reaction[327,328] an iodonium (e.g., **30**) or bromonium ion is attacked by a carboxylate anion to give a halolactone in an intramolecular reaction. Depending on the relative positions of the double bond and the carboxyl group in the starting compound, either a halo-γ-lactone[327] (equation 276) or a halo-δ-lactone[329] may be prepared. With cycloalkenes the cyclization proceeds to give a *cis* ring fusion[329,330].



(30)

(276)

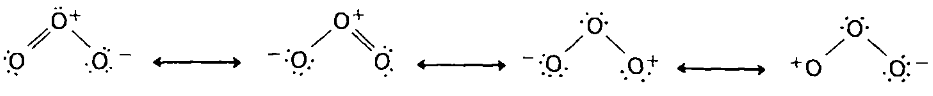
The kinetics and mechanism of iodolactonization of 4-alkenoic acids in the non-polar solvent chloroform have been studied using ^{131}I-labelled iodine[331]. The presence of substituents on the carbon alpha to the carboxyl increase the rate of the iodolactonization reaction[332]. Corey has employed this reaction in the preparation of an intermediate compound in a prostaglandin synthesis[333].

3. Ozone

Ozonolysis is a very effective method of converting an alkene to an aldehyde, a ketone or a carboxylic acid. The reaction may also be used for the quantitative analysis of carbon–carbon unsaturation and for the determination of double bond positions. A number of reviews[334,335,336] have included a discussion of the ozonolysis reaction and several monographs have one or more chapters on this subject[337,338,339].

a. *Properties of ozone.* Ozone is a colourless, highly toxic gas with a characteristic odour. It is commonly prepared from oxygen or air by ultraviolet irradiation or by electric arc discharge, and a laboratory ozonator which uses the latter method is commercially available[340]. The properties, toxicity and reactions of ozone, particularly in biological systems, are the subject of a recent article[341].

Ozone is a non-linear molecule with a bond angle of 116° 49′ and a dipole moment of 0·53 D[342]. From spectral data the oxygen–oxygen bond lengths have been calculated to be 1·278 Å[342]. The molecule is best represented by a resonance hybrid of structures **31a**–**31d**. Thus, ozone can behave as a 1,3-dipole, an electrophile (note that the positive oxygens in **31c** and **31d** have only a sextet of electrons) or a nucleophile. In contrast to

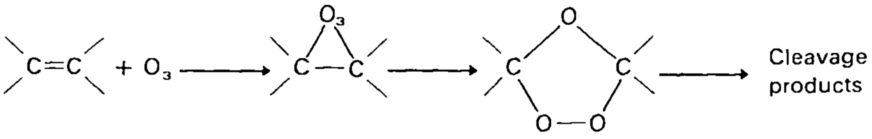


(31a) (31b) (31c) (31d)

molecular oxygen, ozone is not paramagnetic and there is no evidence that it reacts as a radical at room temperature or below.

b. *Mechanism of ozonolysis reaction.* A number of reviews on the mechanism of the reaction between alkenes and ozone have been published[343,344] so this discussion will be concerned primarily with more recent advances in this area.

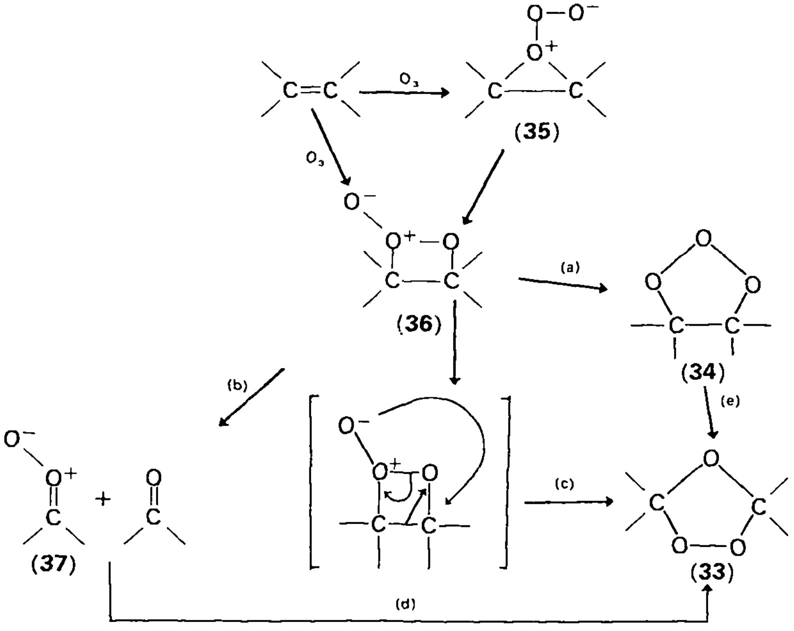
The basic features of the mechanism have long been thought to involve the interaction of ozone with an alkene to give an unstable primary or initial ozonide (**32**), which rearranges to a relatively more stable true ozonide (**33**) with an ether and a peroxy bridge; (**33**) then decomposes to give cleavage products such as aldehydes, ketones and acids. More recent



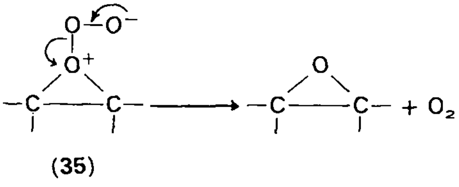
(32) (33)

investigations have been concerned with the precise details of these transformations and the possible existence of other intermediates. Criegee found that ozonolysis of styrene gave no polystyrene[343]. This indicated that the reaction was not free radical in nature and hence the mechanisms to be outlined all involve ionic intermediates.

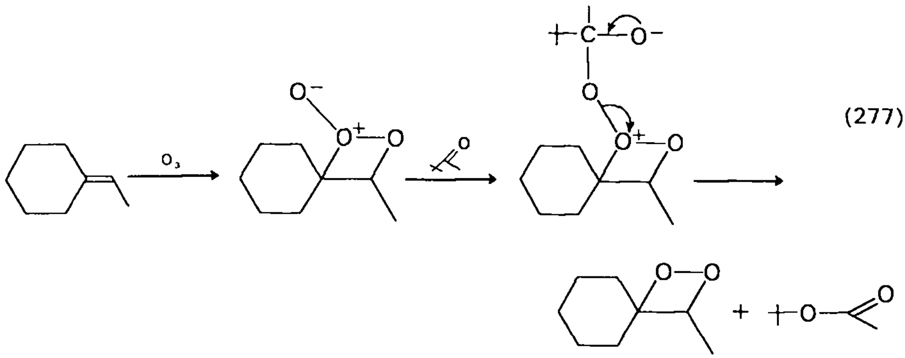
Wibaut suggested[345] that the attack by ozone on the alkene was electrophilic in nature and numerous investigations[346,347,348] since have supported this proposal. Huisgen proposed[349] that the formation of the initial adduct was an example of a 1,3-dipolar cycloaddition reaction leading to the formation of a 1,2,3-trioxolane structure (**34**). Story and coworkers[350] published a unifying concept of the early stages of the ozonolysis reaction which sought to rationalize a number of supposedly contradictory conclusions from previous investigators. He proposed that ozone attacks the alkene to give a σ complex (peroxy epoxide, **35**). The complex then rearranges to the Staudinger molozonide[351] (**36**), or **36** may be formed directly from the alkene via a 1,2-cycloaddition of ozone. The opening of **36** may then lead to three possibilities: (i) formation of a 1,2,3-trioxolane (**34**); (ii) rearrangement in a Baeyer–Villiger fashion to give the normal ozonide (**33**), or (iii) cleavage to the Criegee zwitterion^{343} (**37**) a[illegible] a carbonyl compound. Thus the normal ozonide (**33**) could be formed in at least three different ways, i.e. paths (c), (d) or (e).



The inclusion of all these intermediates in a reaction scheme is supported by the following experimental facts which have been accumulated over a period of years by the efforts of several different research groups. Many hindered olefins, particularly 1-alkenes in which one side of the double bond is heavily substituted, yield upon ozonolysis minor or even major amounts of an epoxide product^{335,344,352,353}. The formation of an epoxide can readily be rationalized by invoking the intermediacy of the σ complex (**35**), which presumably was formed from a π complex of the alkene and ozone^{353}.



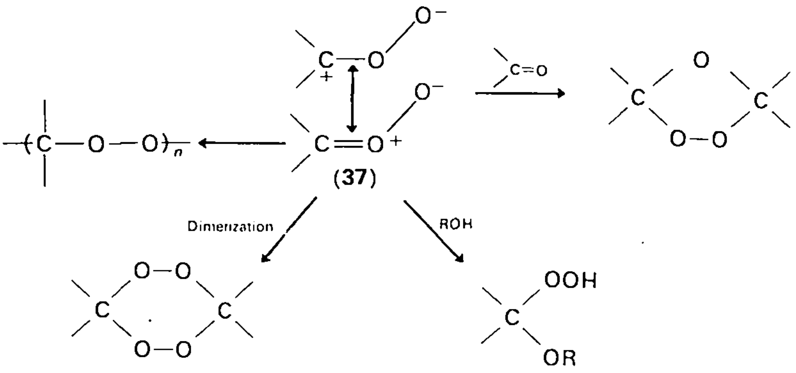
Evidence for the existence of the molozonide (**36**) has recently been presented[354]. Ozonation of ethylidenecyclohexane in the 'Baeyer–Villiger' solvent pinacolone at −45 °C is reported to yield the dioxetane (**38**) plus *t*-butyl acetate as outlined in equation (277). However, doubt has been expressed concerning the existence of intermediates such as **36** in normal ozonolysis reactions as a result of low temperature i.r. studies[355] and the formation of **38** as a product of the ozonolysis reaction has also been questioned[350]. Ozonolysis of a series of simple alkenes at −175 °C revealed the presence of two species, a π complex of the alkene and ozone which reverted to starting materials at higher temperature and a primary ozonide (probably a 1,2,3-trioxolane, **34**) which gave normal ozonolysis products on warming[355]. The authors suggest that any other species, if they exist, must be transitory on the way to the primary ozonide from the π complex or on the way to products from the primary ozonide. A reversible complex as described above has also been invoked to explain the kinetics of a series of olefin–ozone reactions[348].



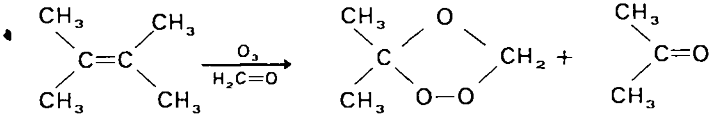
(38)

Evidence concerning the structure of a primary ozonide was provided by Criegee and Schröder[357] who found that reaction of ozone with *trans*-di-*t*-butylethylene at −75 °C gave a crystalline product which could be reduced to a racemic diol. This showed that the initial adduct must have been formed by *cis* addition of ozone and that one of the bonds of the double bond was still intact. Greenwood similarly reported the formation of a primary ozonide from *trans*-alkenes and later from *cis*-alkenes[358], although adducts from the latter are less stable and rearrange more readily to normal ozonides. N.m.r. studies[358,359,360] revealed that, at least with the alkenes examined, the primary ozonide has a 1,2,3-trioxolane structure (**34**). These n.m.r. studies also showed[360] that this primary ozonide (**34**) was the precursor to the normal ozonide (**33**). Fragmentation of an unsymmetrical primary ozonide to give an aldehyde and a zwitterion can occur in two ways and a method of predicting the major cleavage has been reported[361]. It has also been shown that breaking of the C—C bond rather than an O—O bond initiates collapse of the primary ozonide[361].

The so-called Criegee zwitterion (**37**) was postulated[343] as an intermediate in going from the primary ozonide to a normal ozonide. In addition, it satisfactorily explained the formation of ozonolysis side products such as polymeric peroxides, cyclic diperoxides and alkoxyhydroperoxides (when alcohols were used as solvents) as outlined in the following scheme.



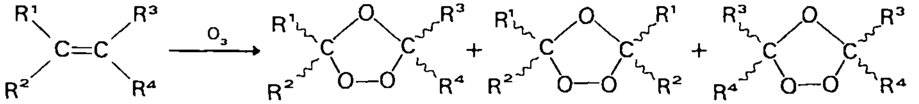
Strong evidence for the intermediacy of (**37**) was obtained by ozonolysis of an alkene in the presence of a 'foreign' aldehyde[343]. The resultant ozonide incorporated the foreign aldehyde and the zwitterion, the latter

 (278)

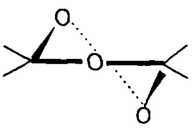
reacting with the more reactive formaldehyde in preference to acetone as illustrated in equation (278).

Ozonides of symmetrical olefins are capable of existing as *cis–trans* isomers[362,363], but contrary to Criegee's prediction[343], ozonolysis of *cis*-1,2-di-*t*-butylethylene gave a 70:30 *cis*:*trans* ozonide mixture and the *trans*-alkene gave 100% *trans*-ozonide[362]. A detailed study[364] of the ozonide stereoisomers obtained from a variety of *cis*- and *trans*-alkenes showed that *cis*-alkenes consistently gave higher yields of ozonides and the size of the substituents had a pronounced effect on the ozonide *cis*:*trans* ratio, e.g. with the *cis*-alkenes, increasing the size of the substituents increased the percentage of *cis*-ozonide. This study was greatly facilitated by the fact that the ozonide mixtures could be analysed by gas phase chromatography[362] and that there were significant spectral differences between the *cis-* and *trans*-ozonides[364]. It was also shown that the ozonide *cis–trans* ratios were influenced by the solvent used in the ozonolysis reaction[365].

The Criegee mechanism[343] predicts that ozonolysis of an unsymmetrical olefin should lead to the formation of two zwitterions and two carbonyl compounds and ultimately to three normal ozonides (as *cis–trans* pairs) with the latter two symmetrical products being referred to as cross-ozonides. Indeed, ozonolysis of methyl oleate[366] or 2-pentene[363] led to the formation of three such pairs of ozonides. In addition, it was found that the ozonide *cis–trans* ratio in cross-ozonides was also a function of the geometry of the starting olefin[367,368]. Ozonolysis of mixtures of olefins would be expected to yield cross-ozonides and in fact ozonolysis of a mixture of 3-hexene and 4-octene gave a good yield of the ozonide of 3-heptene[368], further supporting the intermediacy of the Criegee zwitterion.



As described above, the geometry of the starting olefin is important in determining the *cis–trans* ratio of ozonides, a fact contrary to Criegee's initial postulates[343]. To explain this olefin dependence a number of mechanistic modifications have been advanced. Bailey and coworkers proposed[369] that the Criegee zwitterion could exist as *anti* (from equatorial primary ozonide substituents) or *syn* (from axial substituents) isomers. The *anti* and *syn* zwitterions then react with carbonyl compounds to orient bulky groups *cis* or *trans*, respectively, in the final ozonides. Microwave spectroscopy[370] of the normal ozonides of ethylene (1,2,4-trioxacyclopentane), propylene and *trans*-2-butene showed that all three preferred a half-chair conformation with C_2 symmetry (**39**) as opposed to a half-chair conformation in which the ring carbon atoms are in non-equivalent environments (**40**). Conformation (**39**) is not that predicted from Bailey's rules and revisions to these rules have been proposed[370]. More recently, a theoretical conformational analysis of 12 primary ozonides revealed that several conformers for each compound were approximately equal in stability and hence no one conformer predominates[371]. As there were no clear-cut axial or equatorial positions in many of these conformers, the authors found it difficult to apply Bailey's rules unambiguously to these systems.



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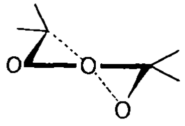
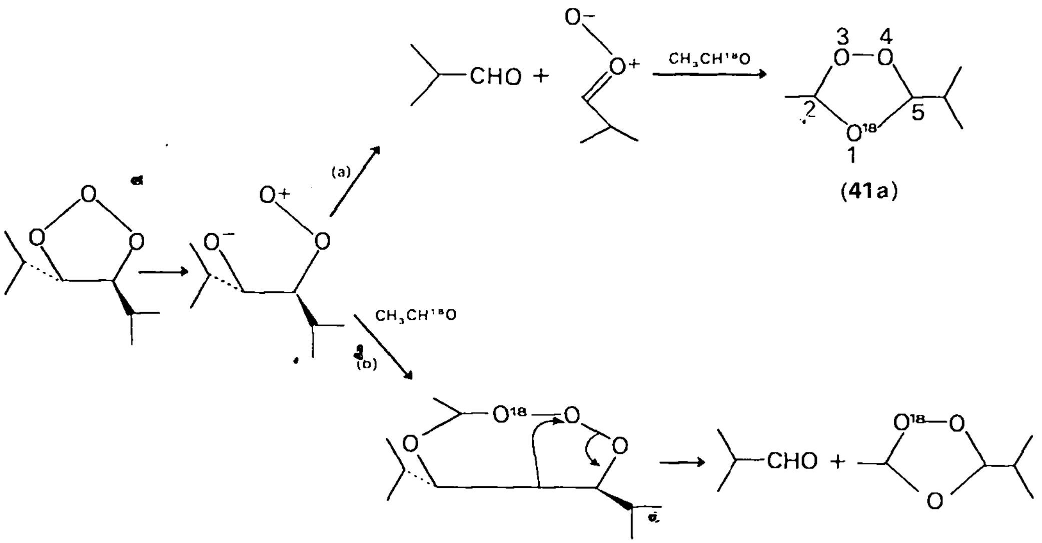


(40)

A considerable body of information concerning the mechanism of ozonolysis has been obtained by conducting ozonolysis reactions in which a 'foreign' aldehyde has been added. Criegee first did such an experiment as outlined in equation (278) to prove the intermediacy of his zwitterion. More recently such experiments have been used to explain why *cis–trans* ratios of cross ozonides were dependent on olefin geometry^{364,367}. Thus, the ozonolysis of *trans*-diisopropylethylene in the presence of acetaldehyde ^{18}O gave ozonide (**41**) in which 32% of ^{18}O was found at position 1, presumably via the Criegee zwitterion [path (a)] and 68% was at position 3, probably formed via the molozonide–aldehyde mechanism [path (b)]. The isomer distribution in adduct (**42**) would then dictate the *cis–trans* ratio of ozonide (**41b**)^{372}. Similarly, ozonolysis of *cis*- and *trans*-diisopropylethylene in the presence of ^{18}O-isobutyraldehyde again showed incorporation of ^{18}O in both the ether bridge and the peroxide bridge of the diisopropylozonide^{373}. The incorporation of ^{18}O in the peroxide bridge was more pronounced at lower temperatures indicating that the



Criegee zwitterion pathway was less important at these temperatures^{373}. The cross ozonide *cis–trans* ratios were also shown to be quite temperature dependent while the normal ozonide *cis–trans* ratios showed smaller effects[373].

On the other hand, microwave and mass spectral studies of the ozonolyses of ethylene, propylene, and *cis-* and *trans*-2-butene with added ^{18}O-formaldehyde or ^{18}O-acetaldehyde at −95 and −126 °C respectively showed that the aldehydic oxygen appears exclusively in the ether bridge of the ozonides[374]. Similarly, Fliszár and Carles[375] found that in the ozonolysis of phenylethylenes in the presence of ^{18}O-benzaldehyde, the ^{18}O label was incorporated exclusively in the ether bridge of the normal ozonides. The authors concluded that, at least for these phenyl-substituted olefins, a refined Criegee mechanism adequately accounted for their results and an additional molozonide–aldehyde pathway was not required. A kinetic study[376] of ozone attack on phenylethylene suggested that at sufficiently high temperatures the ozone–olefin reaction was the rate-determining step while at sufficiently low temperatures the product formation was controlled largely by the decomposition of the primary ozonide.

Obviously more research is still required to elucidate more clearly the effect of substrate structure, reaction temperature and solvent on the mechanism of the ozonolysis reaction.

The decomposition of normal ozonides may be effected by using reductive, oxidative, hydrolytic or thermal conditions. The method used depends upon the structure of the olefin and the products desired. If aldehyde and ketone products are desired then reductive conditions are used, while if carboxylic acids and ketones are desired then oxidative conditions are used.

Reductive decomposition of ozonides can be effected with a wide variety of reagents[377]: hydrogen and catalysts such as Pd, Raney nickel, iodide ion, zinc dust and water or glacial acetic acid as well as other metal–acid combinations, triphenylphosphine and trimethyl phosphite. The use of diborane, sodium borohydride or lithium aluminium hydride normally leads to alcohols as the decomposition products. A lithium aluminium hydride reduction of ^{18}O-labelled ozonides has been reported[378]. Reductive ozonolysis can be effected by conducting the reaction in the presence of an excess of an aldehyde, such as propionaldehyde, to give the expected cleavage products plus propionic acid[379].

Oxidative decomposition of ozonides may be accomplished with a wide variety of oxidizing agents[380] such a chromic acid, permanganate, hydrogen peroxide, Caro's acid and catalytic oxidation. The two most useful reagents are hydrogen peroxide and alkaline permanganate. Hydrolytic decomposition can be effected in high yield by treating the ozonides with water or by steam distillation[381].

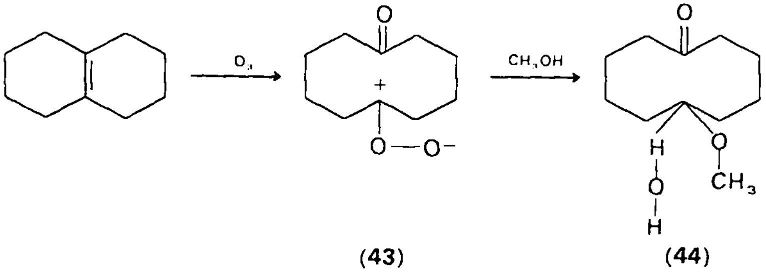
A detailed study of the thermal decomposition of a number of simple ozonides has been reported[382]. The initial step in the thermolysis was shown to be oxygen–oxygen bond homolysis of the peroxide bridge. A number of examples of photochemical decompositions of ozonides have also been reported[383,384].

c. *Special applications of the ozonolysis reaction.* Ozonolysis provides a useful analytical method for determining the position of a double bond in an alkene[377]. Gas chromatographic procedures have been developed for the micro-scale analysis of terpenes[385] and for the specific determination of oleic acid[386]. Chemical modification of the tryptophan residue in a protein with ozone assists in the structure determination of these complex molecules[387].

The reaction of ozone with alkenes can also have deleterious effects as evidenced by the slow degradation of tyres and wire insulation upon exposure to ozone in the atmosphere. The ozonization of polymers containing C=C bonds has been described in a previous volume in this series[388].

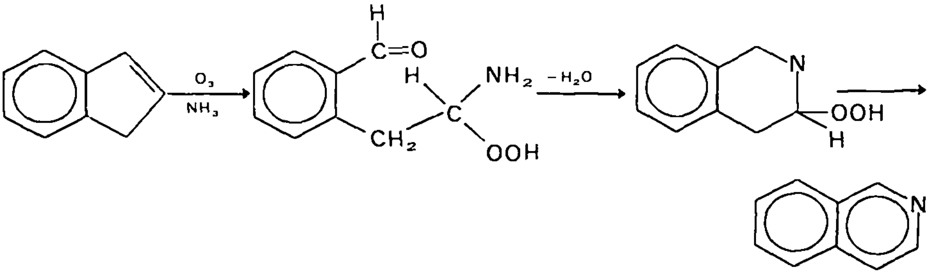
In a number of instances, the addition of pyridine to the ozonolysis reaction mixture was found to give improved yields of the desired products. For example, the selective ozonolysis of an isolated double bond in the presence of an α,β-unsaturated ketone was enhanced by the addition of pyridine[389]. Yields of cleavage products from the ozonolysis of methylenecycloalkanes were also higher in the presence of pyridine[390]. It was originally proposed[389] that pyridine converted the intermediate Criegee zwitterion to a carbonyl compound which in turn was oxidized to pyridine oxide but this mechanism has been questioned[391].

The use of other participating solvents in the ozonolysis reaction can lead to the formation of non-carbonyl functional groups. Ozonolysis of 9,10-octalin in methanol gave a good yield of a methoxyhydroperoxide (44) which was formed by reaction of the intermediate Criegee zwitterion (43) with solvent[392]. Ammozonolysis is a related reaction in which ammonia captures the zwitterion to give an aminohydroperoxide, which

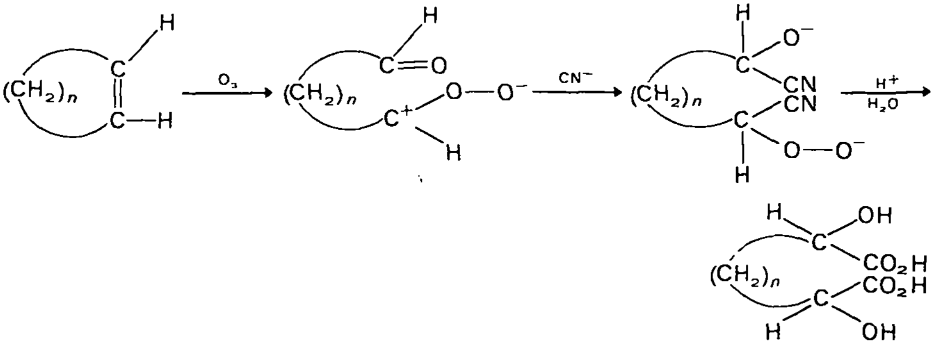


(43) (44)

in turn can react with a neighbouring carbonyl group to give a heterocycle. For example, ammozonolysis of indene gave isoquinoline in 63 % yield[393].

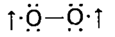


In cyanozonolysis the alkene is ozonized in the presence of hydrogen cyanide, which converts the Criegee zwitterion to a cyanohydroperoxide and the carbonyl group to a cyanohydrin. Hydrolysis of this product then gives a dihydroxy dicarboxylic acid[394].



4. Molecular oxygen

Oxidation of alkenes by molecular oxygen (dioxygen) can be effected by direct reaction with the double bond or by reaction at an allylic position. In the ground state, molecular oxygen normally exists as a triplet diradical ($^3\Sigma_g$) (**45**). The first excited state ($^1\Delta_g$) (**46**) has a half-life of about 10^{-6} sec and is the one normally involved in singlet oxygen reactions with alkenes while the second excited state ($^1\Sigma_g$) (**47**) has a shorter lifetime and rapidly loses energy to form the more stable **46**. The structure of dioxygen has been reviewed in detail[395]. The major portion of this section will be concerned with the reactions of singlet oxygen with alkenes and that will be followed by a more cursory treatment of the oxidation of alkenes by ground state molecular oxygen.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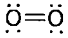
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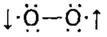
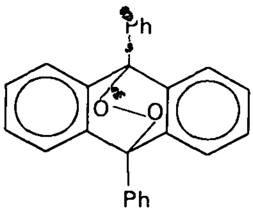

(47)

a. *Singlet oxygen.* Singlet molecular oxygen and its role in alkene oxygenations has been the subject of several reviews[396–400]. 1,4-Cycloaddition reactions of conjugated dienes with singlet oxygen (acting as a dienophile) to give cyclic peroxides have also been reviewed[401].

Singlet oxygen can be generated chemically or photochemically in different ways[395,402]. Chemically it can be formed by the hypochlorite–hydrogen peroxide reaction[403] and by the thermal decomposition of 9,10-diphenylanthracene peroxide (**48**)[404] or a number of ozone–phosphite adducts. For example, the reaction of triphenyl phosphite with ozone at −78 °C yields an adduct (**49**) which decomposes about −35 °C to triphenyl phosphate and singlet oxygen[405]. The adduct of 4-ethyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane and ozone (**50**)[406] is more stable than (**49**) and efficiently produces singlet oxygen at temperatures above 0 °C. A recent report[407] describes the preparation of an even more stable, water-soluble adduct from 1-phospha-2,8,9-trioxaadamantane and ozone (**51**), which readily decomposes to the phosphate and singlet oxygen. A mechanism for the decomposition of phosphite ozonides to phosphate esters and singlet oxygen has been postulated[408].



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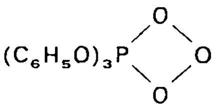

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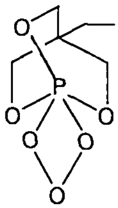

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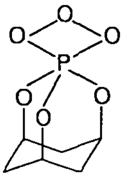
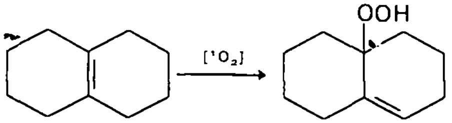


(51)

Singlet oxygen is more commonly generated by photoexcitation of ground state oxygen in a solution containing a photosensitizer such as one of the dyes rose bengal, eosin, methylene blue or a porphyrin derivative. A heterogeneous sensitizer (Ⓟ–Rose Bengal) has recently been prepared by attaching rose bengal to a chloromethylated polystyrene support[409]. The use of this support greatly facilitates the work-up procedure as the sensitizer beads are simply removed by filtration of the reaction mixture through a sintered glass disk. The photosensitization mechanism involves initial conversion of ground state sensitizer to its singlet state followed by intersystem crossing to the triplet state. Energy transfer from the triplet state sensitizer to molecular oxygen then gives singlet oxygen[395].

The reactions of singlet oxygen with alkenes are of three main types: (i) an 'ene' type reaction to form an allylic hydroperoxide (equation 279); (ii) a 1,2-cycloaddition to give a 1,2-dioxetane which cleaves to give two carbonyl groups (equation 280), and (iii) a 1,4-cycloaddition with a conjugated diene to yield a cyclic peroxide (equation 281). Each of these types of oxygenation reactions will be discussed in detail.



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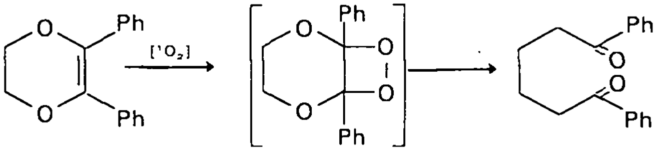

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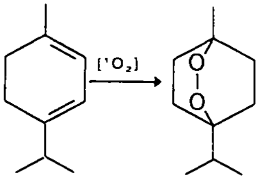

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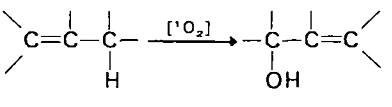
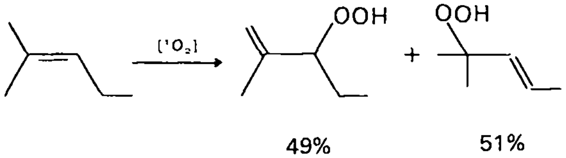
First, some of the pertinent experimental results concerning the reaction of singlet oxygen ($^1O_2$) with an alkene to yield an allylic hydroperoxide (equation 279) will be discussed and on the basis of these facts the mechanistic alternatives will be outlined. The overall reaction can be divided into three parts: (i) introduction of the oxygen molecule at one end of the double bond; (ii) shift of the double bond to the allylic position, and (iii) migration of the allylic hydrogen to the peroxy group. In contrast to autoxidation of alkenes[410], no free radicals appear to be involved in these



$$>C{=}\overset{|}{C}{-}\underset{H}{\overset{|}{C}}{-}\xrightarrow{[^1O_2]}{-}\underset{OH}{\overset{|}{C}}{-}\overset{|}{C}{=}C<$$

oxygenation reactions[411,412]. Alkyl and other electron-donating groups attached to the double bond strongly activate the system while electron-withdrawing substituents such as carbonyl groups deactivate. For example, tetraalkyl-substituted olefins react 20–50-times faster than trisubstituted olefins while disubstituted olefins react even more slowly[396,400].

Cyclohexenes are less reactive than acyclic olefins with the same number of substituents. Equation (282) shows that there is no preference for tertiary over secondary hydroperoxides or for the formation of a more substituted double bond in the product. Equation (283) reveals that migration of the tertiary hydrogen from an isopropyl group to oxygen is an unfavourable process. The hydrogen atom that migrates is the one which is approximately perpendicular (quasi-axial in the case of cyclohexenes) to the original double bond, and further the hydroperoxide group becomes attached to the molecule on that side from which the hydrogen was removed[412]. Both the product distribution and the rate of reaction are very sensitive to steric and conformational effects[396,400]. The solvent effects are similar to those reported for the 'ene reaction'[413]. Finally the ease of abstraction of the hydrogen atom which becomes attached to the



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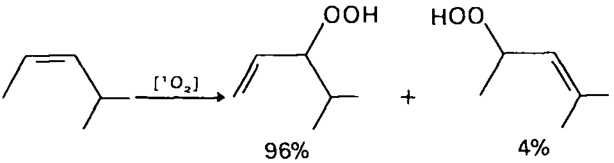
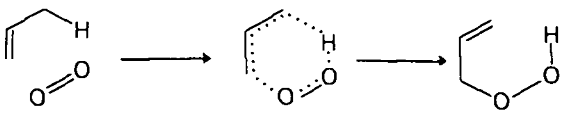


(283)

peroxy group is not inherently related to whether it is primary, secondary or tertiary[395,395,400].

The mechanism which best fits all the experimental facts for the hydroperoxidation of olefins with singlet oxygen is a concerted mechanism proceeding through a six-centre transition state (52). It has been suggested

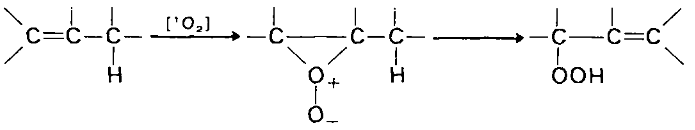


(52)

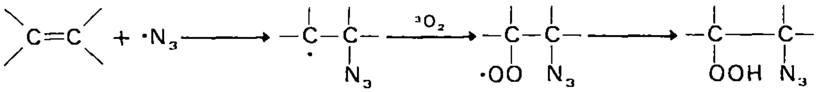
that the geometry of this cyclic transition state has more of the character of the starting olefin than of the final product[412]. This would explain why the thermodynamic stability of the rearranged double bond is not a major driving force in the oxygenation and why there is not a great preference for the abstraction of tertiary hydrogens relative to secondary or primary.

This is also consistent with the low primary deuterium isotope effects that have been found[412].

However, a different mechanism for the hydroperoxidation reaction has also received support. It has been suggested that the reaction of olefin with singlet oxygen yields a perepoxide (**53**) which rearranges with a concurrent proton shift to yield the allylic hydroperoxide[414,415]. In support of this mechanism, it was shown that when the oxygenation was conducted in the presence of azide ion a hydroperoxy azide (**54**) product was isolated. This is consistent only with a reaction path involving an intermediate such as **53** which is susceptible to attack by a suitable nucleophile[415]. These conclusions have been questioned and instead it has been proposed that the hydroperoxy azide was formed by the reaction of olefin with azide radicals to give **55**, which adds triplet oxygen to give **56**, which then abstracts a hydrogen to give the product[416]. In another investigation, a chiral centre was created at the allylic position by the incorporation of one deuterium atom and this optically active olefin was reacted with singlet oxygen. The hydroperoxide products obtained were not consistent with the 'ene mechanism' but were consistent with the perepoxide mechanism[417].



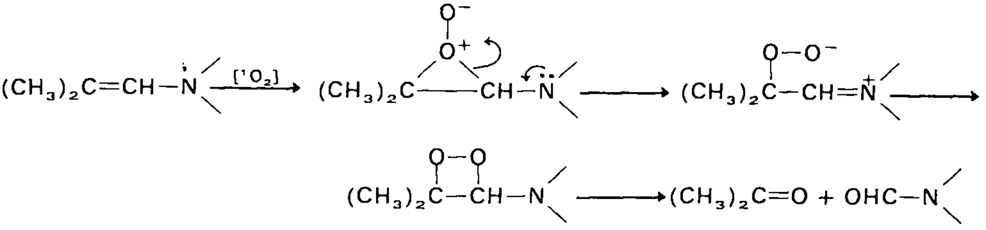
(**53**)



(**55**) (**56**) (**54**)

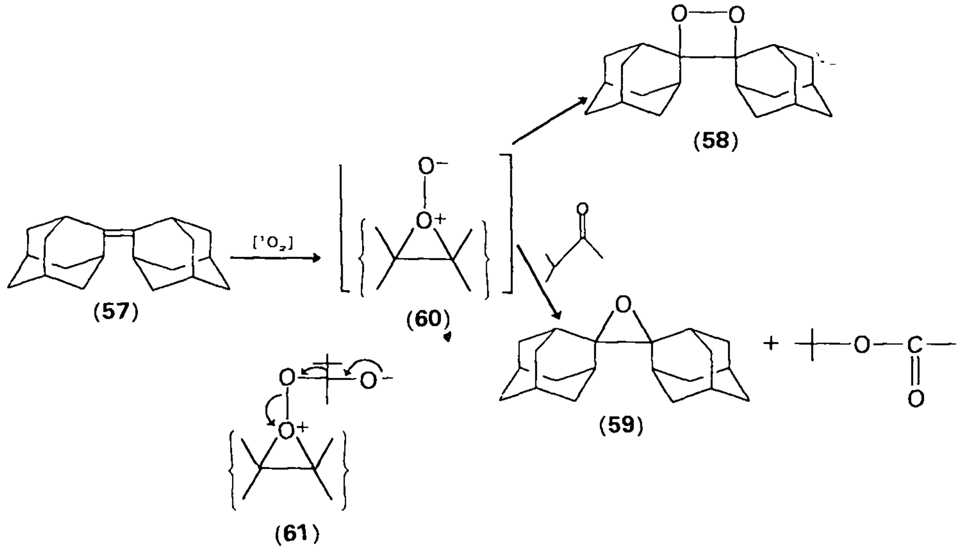
At present one would have to conclude that the body of knowledge supporting the 'ene mechanism' is rather substantial but obviously further research is required before the perepoxide mechanism can be discounted.

The second type of olefin–singlet oxygen reaction to be discussed is the 1,2-cycloaddition which results in the formation of a 1,2-dioxetane (equation 280). This type of intermediate was proposed to account for the fact that carbonyl compounds were formed upon reaction of singlet oxygen with olefins[418]. They have also been considered as possible intermediates in the photooxidation of enamines, with the perepoxide being a precursor of the dioxetane[419]. It was shown that dioxetanes of alkylsubstituted



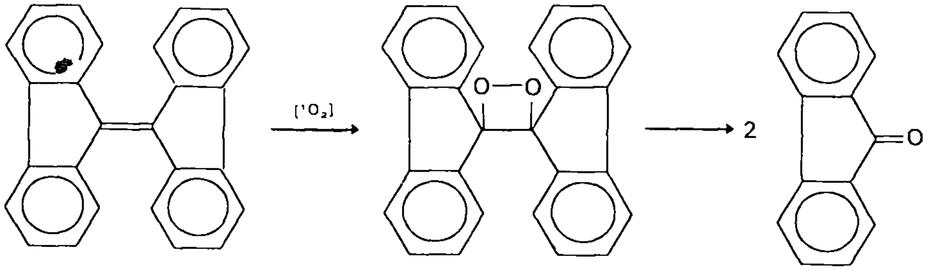
olefins synthesized by cyclization of halohydroperoxides, are relatively stable at room temperature and decompose thermally to yield only carbonyl fragments[420].

Evidence for the inclusion of the perepoxide as an intermediate in these reactions has recently been presented[421]. Photooxidation of adamantylideneadamantane (**57**) yielded the stable, isolable 1,2-dioxetane (**58**). When the photooxidation was carried out in the presence of pinacolone the epoxide (**59**) as well as **58** was isolated. The authors suggest that perepoxide **60** is the logical precursor to both **58** and **59** with **59** being formed via **61** in a Baeyer–Villiger type reaction; however the possibility that **58** is formed directly from **57** cannot yet be excluded.



(58) (57) (60) (59) (61)

The formation of 1,2-dioxetanes upon reaction of olefins with singlet oxygen is favoured by electron-rich olefins such as vinyl ethers[422] (equation 280) or compounds such as 9,9′-bifluorenylidene[423] (equation 284) in which no allylic hydrogens are available. Other systems which have

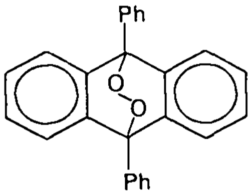


(284)

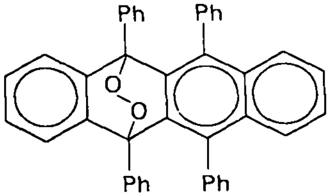
been reported to yield 1,2-dioxetane intermediates are dithioethylenes[424], tetrathioethylenes[424,425] and indenes[418,426] as well as the previously mentioned enamines. Finally, it has been shown that thermal decomposition of 1,2-dioxetanes results in the formation of an electronically-excited carbonyl compound which may either exhibit luminescence[427] or transfer energy to an acceptor[428]. This lends support to the suggestion that one source of bioluminescence is the decomposition of these dioxetanes[429].

The third and last type of olefin–singlet oxygen reaction to be discussed is the 1,4-cycloaddition of $^1O_2$ to a conjugated diene to yield a cyclic peroxide (equation 281). There is general agreement that this is a concerted addition with oxygen serving as a dienophile in a Diels–Alder type reaction. This reaction has been extensively reviewed[395,400,401].

In addition to adding to the typical cyclic or acyclic conjugated dienes, singlet oxygen may also add in a 1,4-manner to reactive aromatic systems such as anthracenes[340], oxazines[404], furans[401], substituted thiophenes[431], and oxygenated aromatic systems[432]. For example, 9,10-diphenylanthracene peroxide (**62**) and rubrene peroxide (**63**) may be prepared conveniently by photolysis of aerated carbon disulphide solutions of the appropriate aromatic compounds[430]. Both of these adducts yield singlet oxygen on thermal decomposition with **62** being the more satisfactory

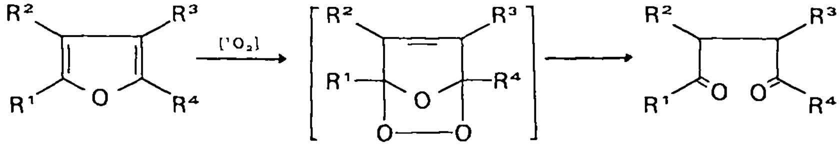


(**62**)

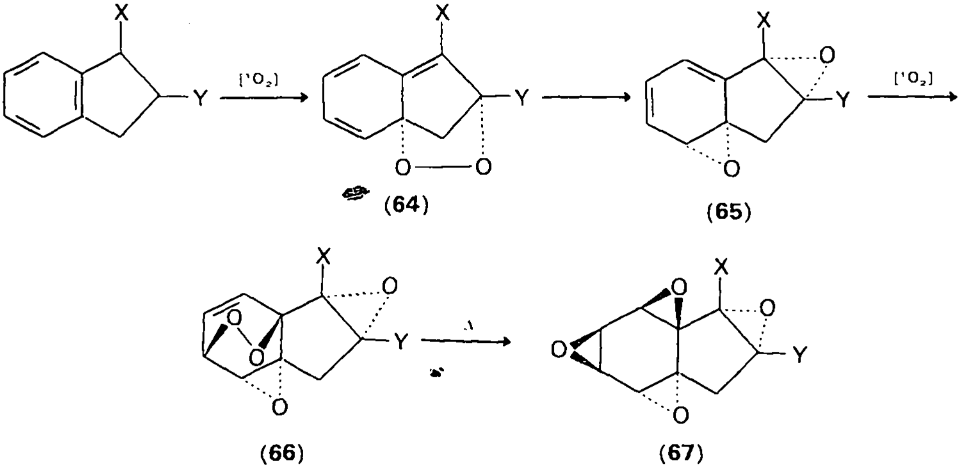


(**63**)

source[404]. Furan and substituted furans react with $^1O_2$ to form ozonides which decompose to give dicarbonyl compounds[401].

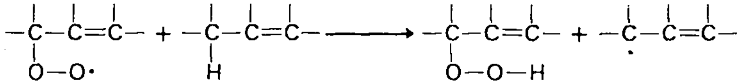


Photooxygenation of indene and certain substituted indenes in acetone at −78 °C is reported to yield initially the 1,4-adducts (**64**), which rearrange to the diepoxides (**65**). 1,4-Cycloaddition of a second molecule of singlet oxygen then gives adduct (**66**) which, upon warming, rearranges to the tetraepoxide (**67**, a benzene trioxide)[433]. Reaction of substituted fulvenes with singlet oxygen yields products which can best be rationalized by assuming an initial 1,4-cycloaddition to the cyclopentadiene moiety[434].

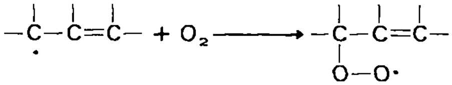


b. *Ground-state molecular oxygen* (*autoxidation*). Autoxidation of alkenes (and other hydrocarbons) is a controlled reaction of molecular oxygen (triplet state) with the substrate to yield a variety of organic oxidation products. The literature related to the autoxidation of alkenes has been extensively reviewed[435–441]. The autoxidation of polymers containing olefinic linkages was discussed in a previous volume in this series[442].

The reactions of alkenes with triplet molecular oxygen have been shown to be free-radical chain reactions which are usually initiated by peroxides. Two general types of mechanisms may be distinguished for these reactions[439]. In the *abstraction* mechanism the initial products are isomeric allylic hydroperoxides which are formed as illustrated in the chain-carrying reactions (285) and (286). Polymerization is a competing reaction

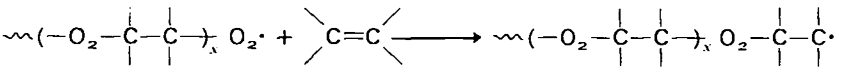


$$-\overset{|}{\underset{\underset{O-O\cdot}{|}}{C}}-\overset{|}{C}=\overset{|}{C}- + -\overset{|}{\underset{\underset{H}{|}}{C}}-\overset{|}{C}=\overset{|}{C}- \longrightarrow -\overset{|}{\underset{\underset{O-O-H}{|}}{C}}-\overset{|}{C}=\overset{|}{C}- + -\overset{|}{\underset{\cdot}{C}}-\overset{|}{C}=\overset{|}{C}- \quad (285)$$

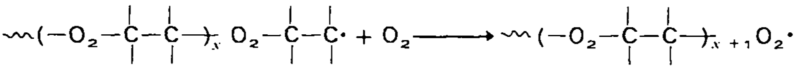


$$-\overset{|}{\underset{\cdot}{C}}-\overset{|}{C}=\overset{|}{C}- + O_2 \longrightarrow -\overset{|}{\underset{\underset{O-O\cdot}{|}}{C}}-\overset{|}{C}=\overset{|}{C}- \quad (286)$$

in which 1:1 alternating polyperoxides are formed by the *addition*



$$\sim\!\!\sim(-O_2-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-)_x\,O_2\cdot + \gt C=C\lt \longrightarrow \sim\!\!\sim(-O_2-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-)_x\,O_2-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}\cdot \quad (287)$$

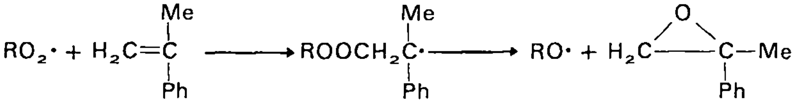


$$\sim\!\!\sim(-O_2-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-)_x\,O_2-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}\cdot + O_2 \longrightarrow \sim\!\!\sim(-O_2-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-)_{x+1}\,O_2\cdot \quad (288)$$

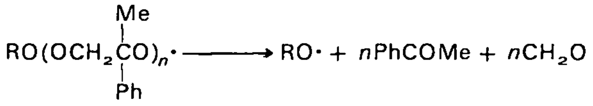
mechanism (equations 287 and 288). Compounds that react primarily by the abstraction mechanism are simple cyclic alkenes and acyclic alkenes containing tertiary allylic hydrogens while those that react by the addition mechanism include conjugated systems, 1-alkenes or alkenes with no allylic hydrogens or unreactive allylic hydrogens[443–445]. Of course, many alkenes give products that can be attributed to both mechanisms. The influence of other factors such as oxygen pressure[439,440,446], reaction temperature[439,440,444,445,446], solvent[446], and concentration of the olefin in both the gas and liquid phases[444] has also been examined.

The abstraction mechanism results in the formation not only of allylic hydroperoxides but also of allylic alcohols, aldehydes, ketones and acids with the same number of carbon atoms[439]. Many of these compounds are secondary products formed as a result of decomposition of the initially formed hydroperoxides. Studies on the thermal decomposition of the hydroperoxides of 2-butene[441] and cyclopentene[444] have been reported. In the latter case the major product of the decomposition was cyclopentenol.

The addition mechanism yields not only polyperoxides but also epoxides, aldehydes and ketones. For example, autoxidation of isobutylene yields acetone and isobutylene in addition to a high boiling residue, which is presumably composed of polyperoxides[444]. Similarly, in the autoxidation of α-methylstyrene at temperatures below 100 °C the principal product was the alternating polyperoxide (**68**) while at higher temperatures the principal products were α-methylstyrene oxide and acetophenone. Equations (289) and (290) indicate possible routes to the formation of the latter two products. In support of equation (290) it was found that (**68**) pyrolyses cleanly to acetophenone and formaldehyde at reduced pressure[445]. The formation of epoxides in the autoxidation of alkenes has been discussed in several review articles[447,448]. The epoxidation of conjugated dienones and diene esters at the γ, δ double bond by molecular oxygen has been reported and a free radical mechanism proposed[449].



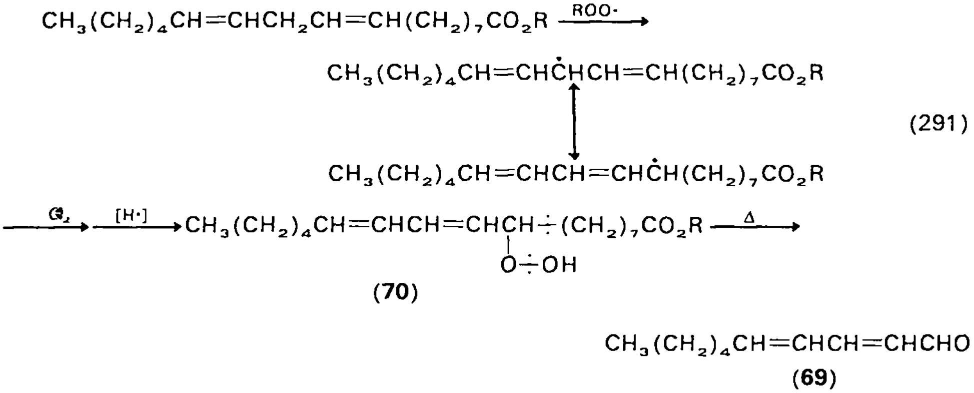
$$RO_2\cdot + H_2C{=}\underset{Ph}{\overset{Me}{C}} \longrightarrow ROOCH_2\underset{Ph}{\overset{Me}{C}}\cdot \longrightarrow RO\cdot + H_2C\overset{O}{\text{———}}\underset{Ph}{C}{-}Me \qquad (289)$$



$$RO(OCH_2\underset{Ph}{\overset{Me}{C}}O)_n\cdot \longrightarrow RO\cdot + nPhCOMe + nCH_2O \qquad (290)$$

(68)

In the autoxidation of methyl oleate (methyl *cis*-9-octadecenoate) a hydrogen atom may be abstracted at either the 8- or 11-position to give two different resonance-stabilized allylic radicals. As a result, four different allylic hydroperoxides were formed[450]. It is believed that the double bonds in the hydroperoxides are predominantly *trans*[451] because the *trans*-allylic radical is thermodynamically more stable than the *cis*. Autoxidation of fats or oils containing linoleate (*cis*, *cis*-9,12-octadecadienoate) results in the formation of significant amounts of 2,4-decadienal (**69**) as well as other aldehydes. This dienal has an extremely potent odour and is thought to be responsible for the 'deep-fried' odour of foods cooked in fats or oils[452]. The precursor of this aldehyde is the conjugated hydroperoxide (**70**), which in turn is formed from linoleate by autoxidation as illustrated in equation (291).



$$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2R \xrightarrow{ROO\cdot}$$

$$CH_3(CH_2)_4CH{=}CH\dot{C}HCH{=}CH(CH_2)_7CO_2R$$

$$\updownarrow \qquad (291)$$

$$CH_3(CH_2)_4CH{=}CHCH{=}CH\dot{C}H(CH_2)_7CO_2R$$

$$\xrightarrow{O_2}\xrightarrow{[H\cdot]} CH_3(CH_2)_4CH{=}CHCH{=}CH\underset{O\div OH}{CH}\div(CH_2)_7CO_2R \xrightarrow{\Delta}$$

(70)

$$CH_3(CH_2)_4CH{=}CHCH{=}CHCHO$$

(69)

The 1,4-addition of singlet oxygen to a conjugated diene was discussed earlier. A recent report describes the Lewis-acid-catalysed oxygenation of a number of steroidal dienes by triplet oxygen and several mechanistic alternatives are suggested[454].

Finally, the commercial importance of drying oils should be mentioned as their behaviour on exposure to air is another example of autoxidation of alkenes. Linseed oil and tung oil are two drying oils which are important constituents of paints and varnishes. These oils have a high content of glycerides derived from acids which contain two or three double bonds (e.g., linoleic and linolenic acids). These glycerides upon reaction with oxygen undergo free-radical polymerization reactions to form tough organic films in the so-called 'drying' process.

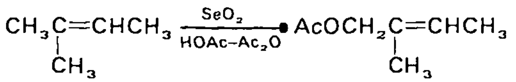
5. Selenium dioxide

Selenium dioxide is another reagent that is effective as an allylic oxidizing agent. However it complements oxidants such as chromium trioxide or air in that it oxidizes at a different allylic position in an unsymmetrically-substituted olefin. If the olefin has no allylic hydrogens then the oxidant may cleave the double bond. A number of comprehensive reviews on selenium dioxide oxidations have been published[455,456].

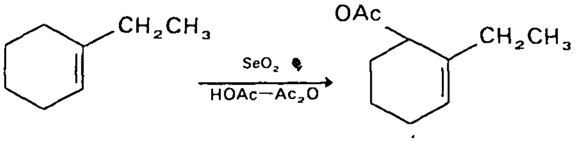
Selenium dioxide exists as selenious acid, $(HO)_2SeO$ in aqueous solutions and as the dialkylselenite ester in alcohol solutions. During the oxidation Se^{IV} is reduced to metallic selenium, an insoluble solid. The nature of the product is influenced by the solvent used for the oxidation as well as by the ratio of oxidant to olefin. In acetic acid or an acetic acid–acetic anhydride mixture allylic acetates are formed; in alcohol solvents ethers are formed, and in aqueous media conjugated carbonyl compounds predominate. In aqueous media, an initially-formed primary or secondary carbinol is susceptible to oxidation particularly if the oxidant-to-olefin ratio is high.

A selenium dioxide–hydrogen peroxide oxidant employing only a catalytic amount of SeO_2 has been used in the allylic oxidation of β-pinene[457] and (+)-limonene[458]. The reagent minimizes the problem of removing selenium from the reaction mixture and in the former case an improved yield of the desired product was obtained. This oxidant is also capable of converting an olefin to the corresponding 1,2-diol[459].

As a result of the systematic investigations of Guillemonat[455,460], the major product from SeO_2 oxidation of a particular olefin may be predicted by employing the following rules: (a) oxidation always occurs alpha to the most substituted end of the double bond (equation 292); (b) when the double bond is in a ring, oxidation occurs within the ring rather than in a side chain (equation 293); (c) the preferred order of reactivity is $CH_2 >$ $CH_3 > CH$, all other factors being equal (equation 294); (d) with a terminal olefin oxidation results in migration of the double bond and formation of a primary alcohol or its derivative (equation 295), and (e) if an allylic position is tertiary, a diene will generally be formed in preference to a tertiary alcohol.



$$CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}{=}CHCH_3 \xrightarrow[HOAc-Ac_2O]{SeO_2} AcOCH_2\underset{\displaystyle CH_3}{\underset{|}{C}}{=}CHCH_3 \qquad (292)$$



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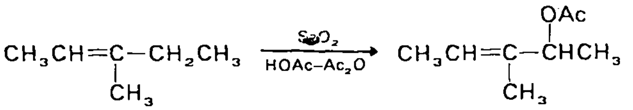
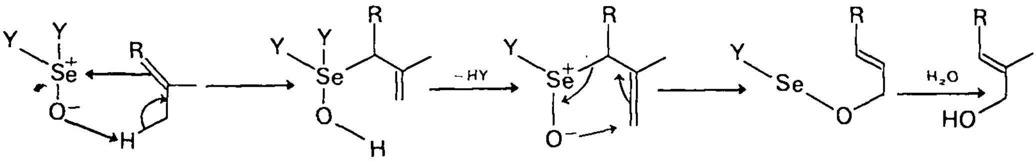


$$CH_3CH{=}\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_2CH_3 \xrightarrow[HOAc-Ac_2O]{SeO_2} CH_3CH{=}\underset{\displaystyle CH_3}{\underset{|}{C}}-\overset{\displaystyle OAc}{\overset{|}{C}}HCH_3 \qquad (294)$$

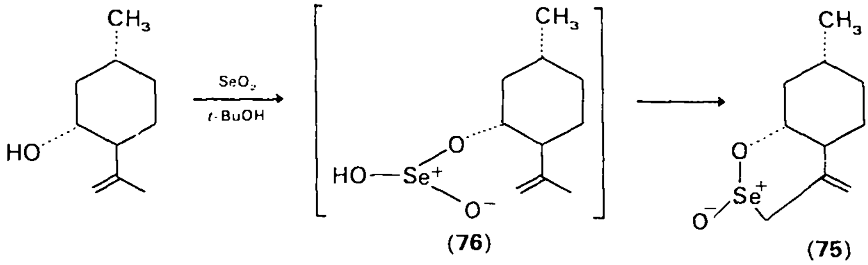
$$RCH_2CH{=}CH_2 \xrightarrow[HOAc-Ac_2O]{SeO_2} RCH{=}CHCH_2OAc \qquad (295)$$

Sharpless and collaborators have provided convincing evidence for a proposed mechanism of the selenium dioxide oxidation of olefins[461,462]. They propose that selenious acid (or a derivative) reacts with the olefin in an ene addition to give **71**, which upon dehydration (or its equivalent) gives an allylselenic acid (**72**). A [2,3] sigmatropic rearrangement of **72** then yields the selenium(II) ester (**73**) which upon hydrolysis gives the allylic alcohol (**74**) or the corresponding aldehyde. In support of this mechanism the



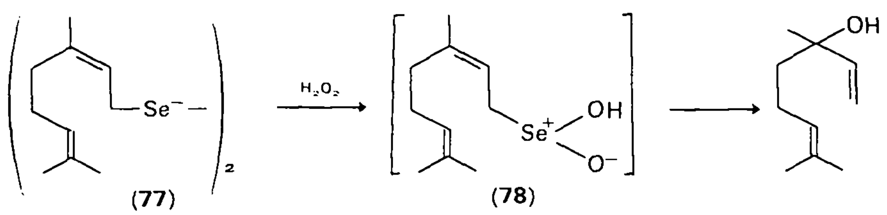
Y = OH, OAc or OR' (71) (72) (73) (74)

proposed allyseleninic acid has been trapped as a seleninolactone (**75**) using a suitable substrate for the oxidation (equation 296)[462]. An intramolecular ene reaction of the selenious acid half-ester (**76**) with the double bond followed by dehydration would give the lactone (**75**). Evidence for the [2,3] sigmatropic rearrangement was provided by the finding that

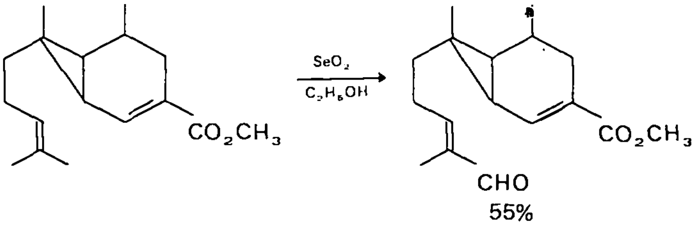


(296)

oxidation of geranyl diselenide (**77**) gave linalool presumably via rearrangement of the intermediate geranylseleninic acid (**78**) followed by hydrolysis[461]. The evidence presented appears convincing enough to replace the mechanistic schemes previously proposed[463,464].



Büchi and Wüest discovered that selenium dioxide oxidation of trisubstituted olefins gave only the (*E*)-alcohol[465]. The mechanism described adequately explains this specificity since sigmatropic rearrangement of **72** must lead stereoselectively to (*E*)-ester (**73**) which upon hydrolysis gives the (*E*)-alcohol (**74**). This selective oxidation has been used to effect a critical step in the synthesis of sirenin (equation 297)[406].



(297)

III. OXIDATION OF C=N BONDS

A. Introduction

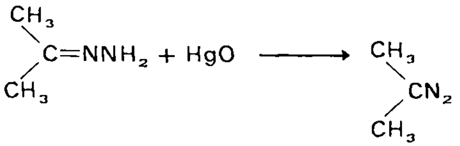
This section will be considerably shorter than that concerned with the oxidation of C=C bonds as the literature is not nearly as extensive. The compounds to be included in this discussion are referred to as imines, azomethines or Schiff bases and have the general structure RR'C=NR'', which also includes oximes and hydrazones.

The oxidants to be discussed will be arranged in the same order as employed in the C=C section but because of the differences in reactivity of C=N, some reagents will be omitted and a few additional ones will be mentioned.

B. Metal Ion Oxidants

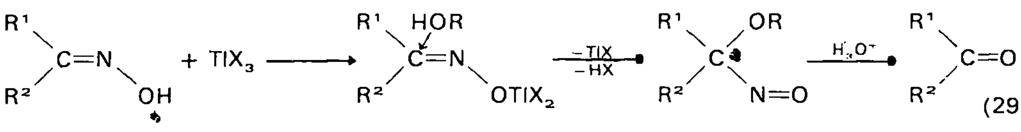
1. Non-transition metal oxidants

a. *Mercury*(II). The only oxidation of C=N with Hg^{II} is the oxidation of hydrazone to give diazo compounds. The oxidation of acetone hydrazone by mercuric oxide to give 2-diazopropane was first described by Staudinger and Gaule[467]. Later Applequist and Babad reported that they could not repeat the procedure[468]. However Day and coworkers have recently reported that the reaction proceeds only if bases such as potassium hydroxide are present[469].



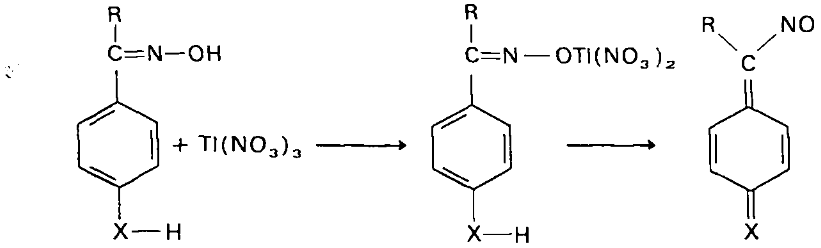
$$(CH_3)_2C{=}NNH_2 + HgO \longrightarrow (CH_3)_2CN_2 \qquad (298)$$

b. *Thallium*(III). The oxidation of oximes, semicarbazones and phenylhydrazones has been reported by Taylor and coworkers[470,471]. The oxidation of oximes provides a convenient conversion of this group to aldehydes or ketones[471]. The proposed reaction scheme is as follows ($X = ONO_2$):



(299)

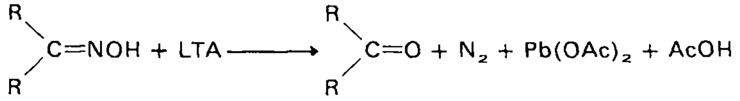
There is evidence that routes involving iminoxy radicals may be operative since this radical was detected by e.s.r. spectroscopy. The reaction does not proceed as rapidly with semicarbazones, is even slower with phenylhydrazone and does not occur at all with 2,4-dinitrophenylhydrazone derivatives. The procedure is unsuccessful when applied to aromatic ketones or aldehydes with *ortho* or *para* OH or NH_2 groups. In this case quinone methides are formed (X = O, NH)[470].



(300)

c. $Pb(OAc)_4$[472–475]. By far the largest amount of literature on oxidation of C=N groups by metal ions concerns $Pb(OAc)_4$. In this field only a few examples of the oxidation of each type of C=N group will be given. The reader is referred to a recent extensive review for more detailed treatment[474].

(i) Oximes. The products of the oxidation of oximes by LTA depend on a number of factors such as substrate structure, temperature, solvent, and ratio of substrate to LTA. At temperatures of about 70 °C, a large number of aldoximes and ketoximes give the parent carbonyl compound and nitrogen[476]. At −78 °C *syn*-aldoximes give nitrile oxides[477,478]. At



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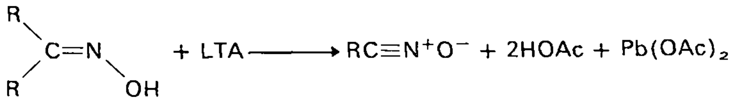
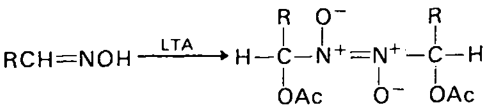
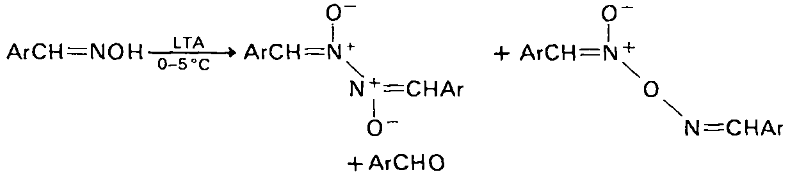


room temperature the main products from the oxidation of aliphatic *anti*- and *syn*-aldoximes are nitrosoacetate dimers[478–480].



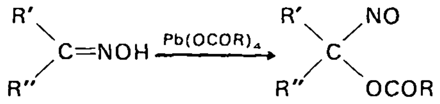
$$RCH{=}NOH \xrightarrow{LTA} H{-}\underset{OAc}{\overset{R}{C}}{-}\overset{O^-}{N^+}{=}\underset{O^-}{N^+}{-}\underset{OAc}{\overset{R}{C}}{-}H \qquad (302)$$

Oxidation of aromatic aldoximes with LTA at 0–5 °C give dimeric type compounds in about 50% yields along with the parent carbonyl compounds[477,481,482].



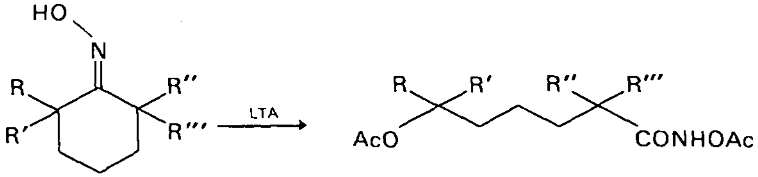
(303)

The $Pb(OCOR)_4$ oxidation of aliphatic and alicyclic ketoximes gives *gem*-nitrosoacetates[479,480,483,484]. The oxidation of sterically hindered



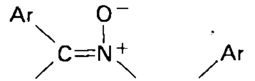
(304)

ketoximes results in C—C bond cleavage rather than nitrosoacetate formation. An example is the oxidation of 2,2,6,6-tetrasubstituted cyclohexanone oximes[478,485].



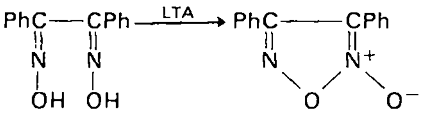
(305)

The oxidation of aromatic ketoximes gave products analogous to those obtained with aromatic aldoximes (equation 303; substitute Ar′ for H) plus azine monoxides (**79**). Aromatic dioximes give a similar reaction



(**79**)

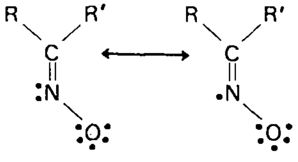
yielding furoxan products[481,482,486]. In acetic acid, nitrogen oxide gases



(306)

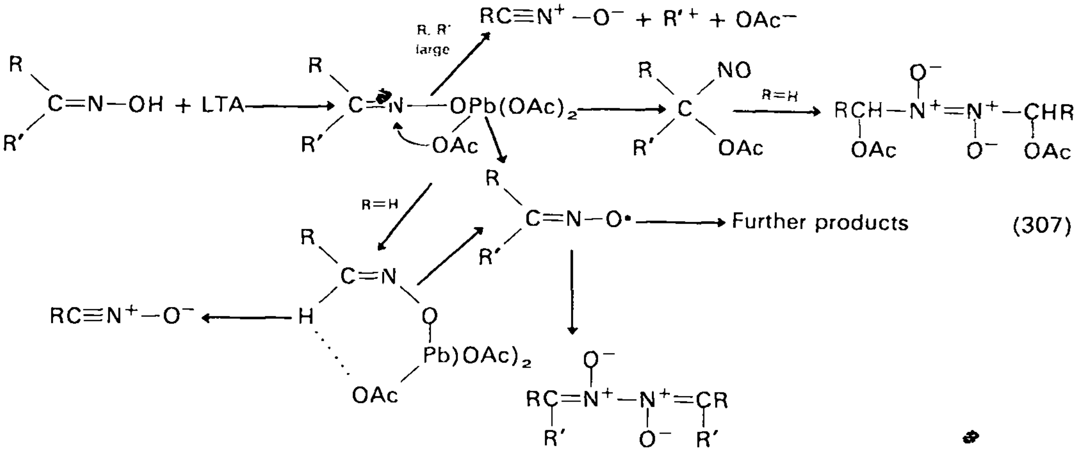
were evolved and a number of secondary products were formed[482].

The mechanisms of these oxidations are very complicated and no doubt involve both two-electron and radical paths. The iminoxy radicals (**80**) have been detected by e.s.r. spectroscopy and are no doubt intermediates in some of the oxidations[483,484]. A number of other radicals have also been



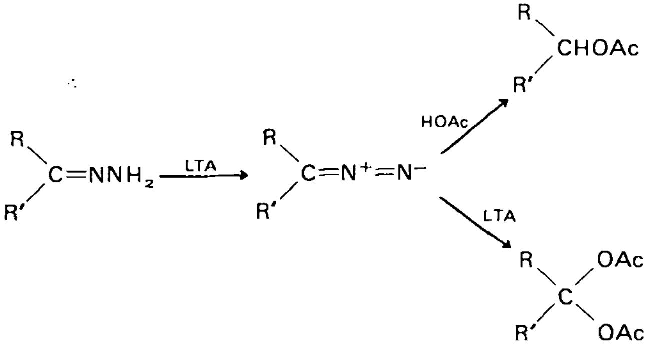
(80)

observed in these oxidations[487–489]. A reasonably coherent mechanism for the oxidations is given by equation (307)[474].



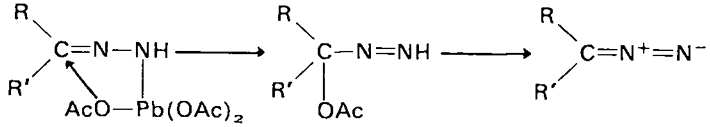
(307)

(ii) Hydrazones. LTA reacts with unsubstituted hydrazones to give a diazoalkane as initial intermediate which reacts either with acetic acid or more LTA[490,491]. The diazoalkane was detected by trapping with

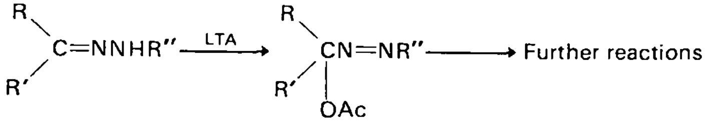


(308)

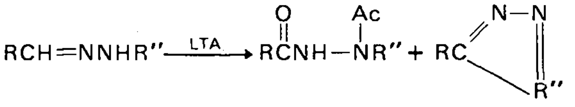
dimethyl acetylenedicarboxylate[490]. When R and R′ are both CF_3[492,493] or CN[494] the diazo compounds are stable. A reasonable mechanism for formation of the diazoalkane is given by equation (309).


(309)

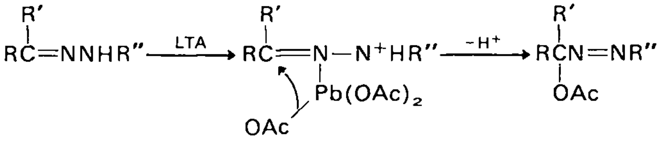
Monosubstituted ketohydrazones yield azoacetates as initial products while aldehyde hydrazones yield acylhydrazines or cyclization products


(310)

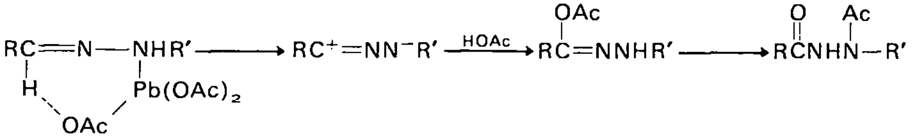
if R″ has a cyclization site. Apparently radical pathways are not involved


(311)

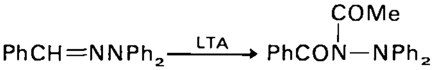
in these reactions. A reasonable path for oxidation of ketohydrazones is given by equation (312) while the aldehyde hydrazone path is given by


(312)

equation (313)[474].

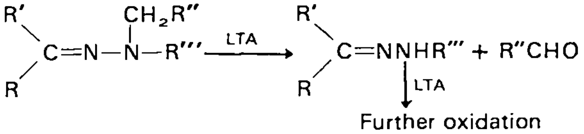

(313

Disubstituted hydrazones react readily with LTA by several pathways, for example, benzaldehyde diphenylhydrazone gives diacylhydrazine[495]. *N*-Alkyl-*N*-arylhydrazones are first dealkylated by LTA followed by the

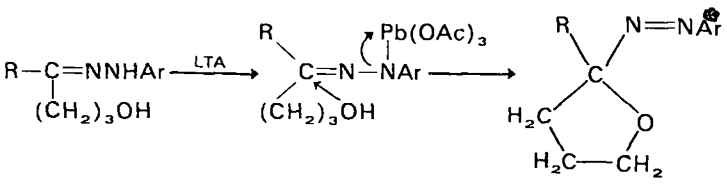


$$\mathrm{PhCH{=}NNPh_2} \xrightarrow{\mathrm{LTA}} \mathrm{PhCO}\overset{\mathrm{COMe}}{\mathrm{N}}\mathrm{{-}NPh_2} \qquad (314)$$

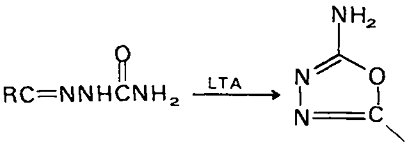
further oxidation of the monosubstituted hydrazone[496,497].


(315)

Cyclization in the oxidation of ketone hydrazones occurs when a suitable cyclization site on the ketone occurs at the fourth or fifth position from the methane carbon[498]. Such groups are carboxylate or hydroxyl as in the example in equation (316). In this case cyclization is usually the major product rather than the azoacetates found in the absence of a cyclization position (equation 310).


(316)

(iii) Semicarbazones[499]. The main products from oxidation of semicarbazones are cyclization products. Thus aldehyde semicarbazones are cyclized to 2-amino-1,3,4-oxadiazolines[500–504] while substituted ketone semicarbazones can be cyclized to oxadiazolines[505]. Recently it has been reported that unsubstituted ketone semicarbazones can be oxidized to 2-amino-Δ^3-1,3,4-oxadiazolines[506].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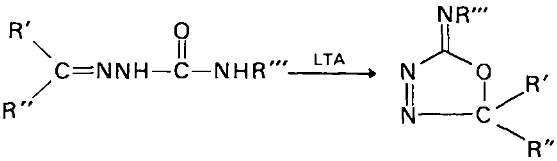
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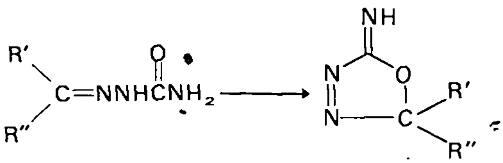
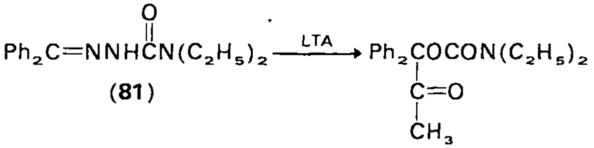
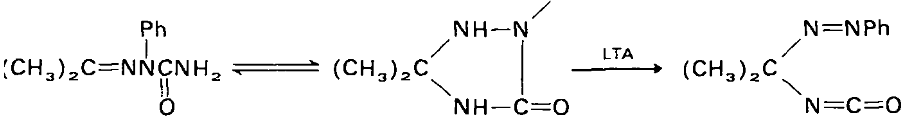

(319)

In some cases cyclization does not occur. Thus the 4,4-substituted semicarbazone, **81**. was not cyclized but instead it lost N_2 to give a carbamate[507]. Likewise the LTA oxidation of the 2-substituted semicarbazone,


$$\mathrm{Ph_2C{=}NNH\overset{O}{\overset{\|}{C}}N(C_2H_5)_2 \xrightarrow{LTA} Ph_2\underset{\substack{|\\ C=O\\ |\\ CH_3}}{C}OCON(C_2H_5)_2}$$
(320)

(81)

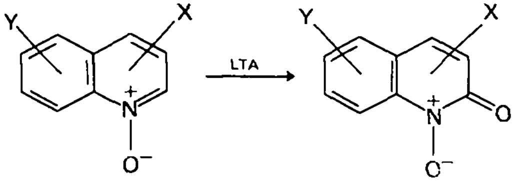
(82), yields an isocyanate, probably by way of the cyclic intermediate, **(83)**[508,509].



(82) **(83)**

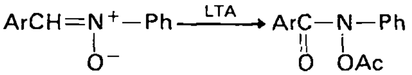
(321

(iv) Nitrones. Relatively little work has been done on the LTA oxidation of this functional group. However, substituted quinoline *N*-oxides will give the corresponding *N*-acetoxycarbostyrile[510–512].



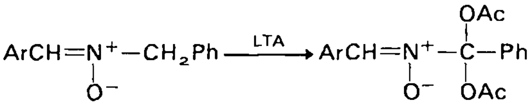
(322)

The oxidation of *N*-arylidene-*N*-phenyl *N*-oxides gave *N*-acetoxy-*N*-aroylaniline[513] while the corresponding *N*-benzyl derivative gave a



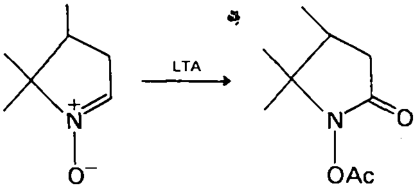
$$\mathrm{ArCH{=}\underset{O^-}{\underset{|}{N^+}}{-}Ph \xrightarrow{LTA} Ar\underset{O}{\underset{\|}{C}}{-}\underset{OAc}{\underset{|}{N}}{-}Ph} \qquad (324)$$

diacetate[514]. The LTA oxidation of 4,5,5-trimethyl-1-pyrroline 1-oxide



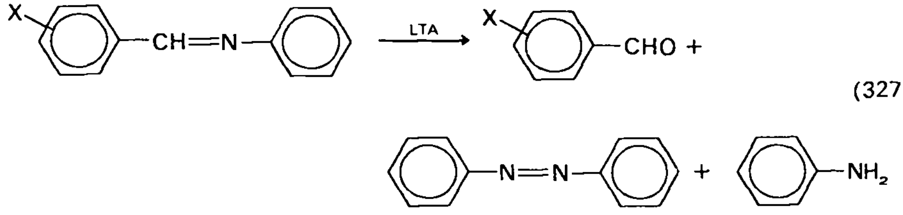
$$\mathrm{ArCH{=}\underset{O^-}{\underset{|}{N^+}}{-}CH_2Ph \xrightarrow{LTA} ArCH{=}\underset{O^-}{\underset{|}{N^+}}{-}\overset{OAc}{\overset{|}{\underset{OAc}{\underset{|}{C}}}}{-}Ph} \qquad (325)$$

gave the 1-acetoxy-2-pyrrolidone[515].



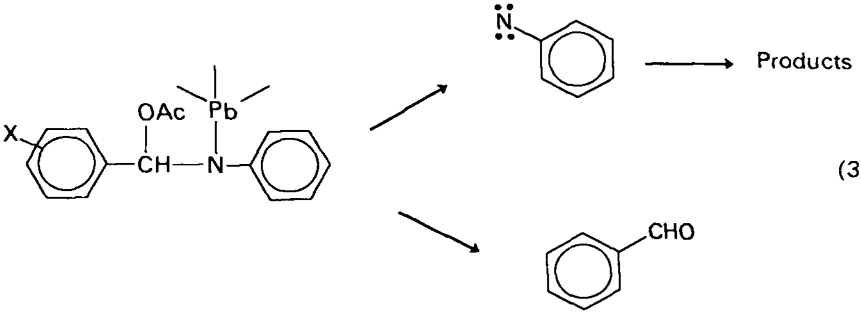
(326)

(v) Schiff bases. The oxidation of benzaldehyde anils has been reported to give azobenzenes, benzaldehydes and anilines[516]. With *p*-methoxybenzaldehyde anil the reaction was faster while *p*-nitrobenzaldehyde anil did not react. The reaction is believed to occur by electrophilic attack of



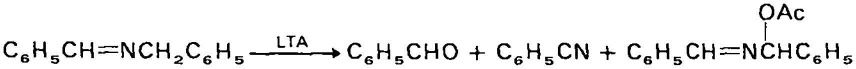
(327)

LTA on the anil to give an intermediate which decomposes to a nitrene.



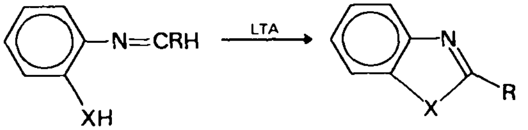
(328)

The corresponding *N*-benzyl Schiff base gives somewhat different products[517] while Schiff bases with NH_2 or OH *ortho* substituents in the



$$C_6H_5CH{=}NCH_2C_6H_5 \xrightarrow{LTA} C_6H_5CHO + C_6H_5CN + C_6H_5CH{=}N\overset{OAc}{C}HC_6H_5 \quad (329)$$

N-aryl ring give cyclization (X = NH or O)[518-520].



(330)

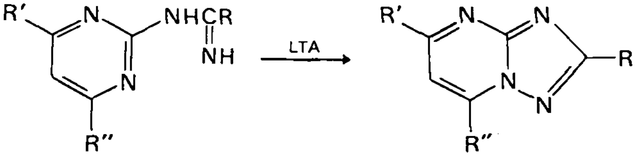
(vi) Imines. The oxidation of imines usually occurs as an intermediate step in the oxidation of primary amines, the first step being the oxidative dehydrogenation to imine. Nitriles are the final products[474]. The amines

$$RCH_2NH_2 \xrightarrow{LTA} (RCH{=}NH) \xrightarrow{LTA} RC{\equiv}N \quad (331)$$

can also be prepared *in situ* by reaction of ammonia with the aldehydes[521,522].

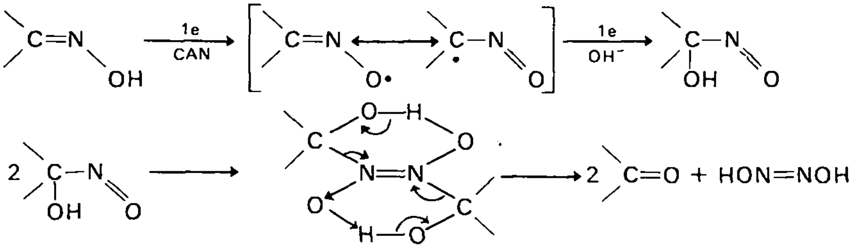
$$RCHO + NH_3 \xrightarrow[\text{benzene}]{0\,^\circ C} (RCH{=}NH) \xrightarrow[0\,^\circ C]{LTA} RC{\equiv}N \quad (332)$$

Amidines undergo oxidative cyclization in the presence of LTA. An example is given in equation (333)[523].


R'
N
NHCR
NH
N
R''
LTA
R'
N
N
R
N
N
R''

(333)

d. *Cerium*(IV). Ceric ammonium nitrate (CAN) has been reported to oxidize oximes and semicarbazones to the parent carbonyl compound in good yield[524]. Semicarbazones in general are less readily oxidized than oximes. The suggested mechanism involves an iminoxy radical. These radicals have been detected by e.s.r. spectroscopy in the CAN oxidation of several oximes[525].

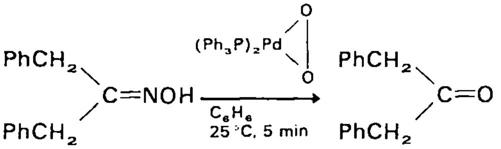

C=N
OH
1e
CAN
C=N
O•
C—N
O
1e
OH⁻
C—N
OH
O
2
C—N
OH
O
C
O—H
O
N=N
O
C
H—O
2 C=O + HON=NOH

(334)

(335)

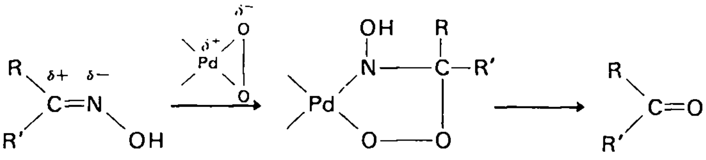
2. Transition metal oxidants

a. *Palladium*(II). In view of the extensive olefin oxidation chemistry of Pd^{II} (see Section II.2.b) it is surprising there was almost no work done in oxidation of C=N bonds. The only study of which the writer is aware involves the oxidative conversion of ketoximes to the corresponding ketones under mild conditions by the dioxygen complex of palladium[526]. Thus dibenzyl ketoxime is converted to the ketone in 98% yield. A cyclo-


PhCH2
PhCH2
C=NOH
(Ph3P)2Pd
O
O
C6H6
25 °C, 5 min
PhCH2
PhCH2
C=O

(336)

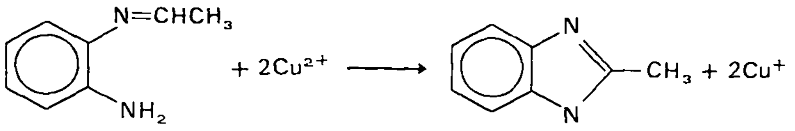
addition mechanism was proposed for the reaction.


R
R'
δ+ δ−
C=N
OH
δ−
O
δ+
Pd
O
OH
R
N
C—R'
Pd
O
O
R
R'
C=O

(337)

b. *Copper*(II). There is a fairly extensive literature on Cu^{II} oxidation of nitrogen-containing compounds[172] but little of it concerns oxidation of C=N functional groups.

One such oxidation involves the cyclization of acetaldehyde *o*-aminoanil to 2-methylbenzimidazole[527]. A free-radical route has been suggested for the reaction.



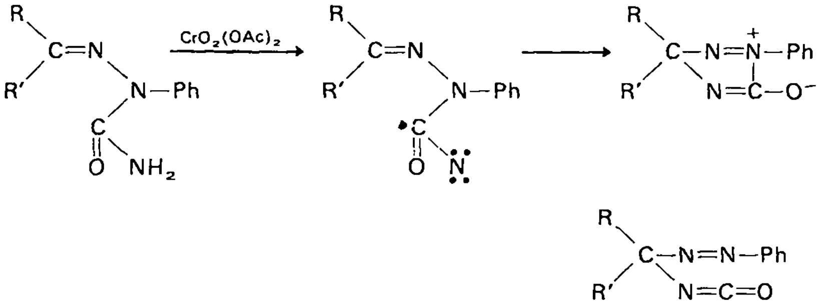
(338)

c. *Silver*(I). Ag_2O has been used in place of HgO in the preparation of diazo compounds from hydrazones (equation 298)[468].

d. *Chromium*(VI). Chromyl acetate has been reported to oxidize hydrazones to the parent carbonyl compounds[509]. When semicarbazones are

$$RR'C{=}NNHR'' \xrightarrow{CrO_2(OAc)_2} N_2 + RR'C{=}O \tag{339}$$

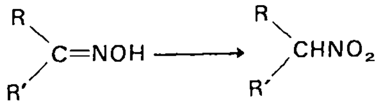
used an isocyanate derivative is formed. The proposed reaction path is as shown in equation (340).



(340)

e. *Manganese*(IV)[528–530]. MnO_2 has been used to a considerable extent in the oxidation of organic nitrogen compounds including C=N groups. Thus, anils are oxidized to ketones while oximes are oxidized to nitro compounds[531].

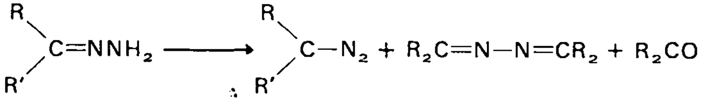
$$R_2C{=}NR' \longrightarrow R_2C{=}O \tag{341}$$



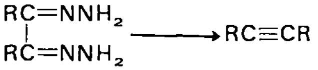
(342)

$$RR'C{=}NOH \longrightarrow RR'CHNO_2$$

Ketohydrazones are oxidized to diazoalkanes, ketazines, and ketones[532–538] (equation 343) while diketohydrazones give alkynes[538,539]



(343)



(344)

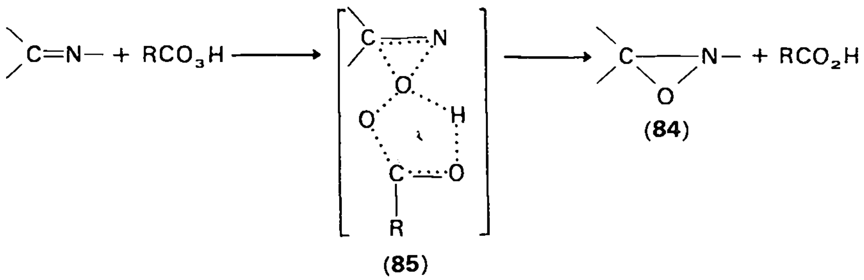
(equation 344). Finally azines are oxidized to ketones[540] (equation 345).

$$R_2C{=}N{-}N{=}CR_2 \longrightarrow 2R_2C{=}O \qquad (345)$$

C. *Non-metal Oxidants*

1. Peroxyacid oxidants

Emmons first discovered that the reaction of an imine with a peroxyacid gave in good yield an oxazirane (oxaziridine) (**84**)[541,542]. The reaction was analogous to that between an olefin and a peracid to give an epoxide. It was suggested[543] that the reaction was mechanistically related either to epoxidation of an olefin (i.e., a concerted electrophilic attack on the C=N via a cyclic transition state (**85**, equation 346)) or to the Baeyer–Villiger oxidation of ketones (i.e., a two-step mechanism proceeding through an intermediate such as **86**, equation 347). Later work agreed with the idea of a concerted mechanism but suggested that the inclusion



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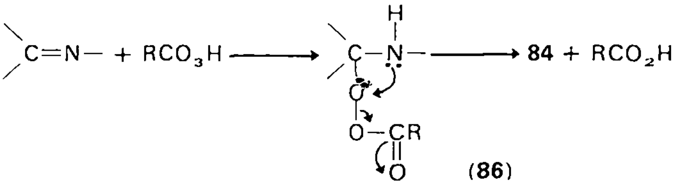
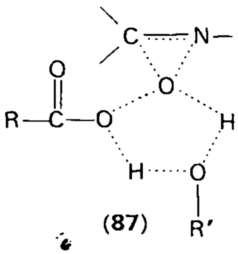


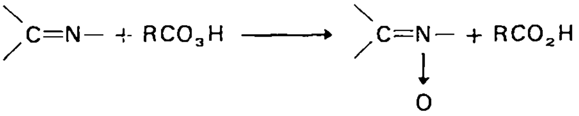
(347)

of a solvent molecule in the transition state (**87**) more adequately accounted for the kinetic data[544]. However the finding that the peroxyacid oxidation of aldimines was not stereospecific and led to a mixture of diastereomers was not consistent with this concerted mechanism[545].



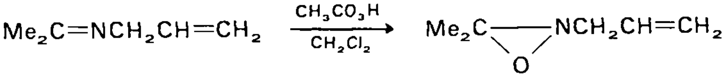
(**87**)

Recent investigations[546,547] concluded that the formation of oxazirane was a two-step process (equation 347) with the acid-catalysed addition of peroxyacid to the imine to give **86** as the rate-determining step for acyclic imines, and with the internal nucleophilic reaction (S_Ni) of adduct **86** being rate determining for cyclic imines. It was also found that an epoxidation-type mechanism with nucleophilic attack by the lone-pair electrons of the nitrogen on the peroxyacid oxygen was possible and resulted in the formation of a nitrone (equation 348)[547]. Nitrone formation was favoured by electron-donating substituents on the imine and by aprotic solvents.



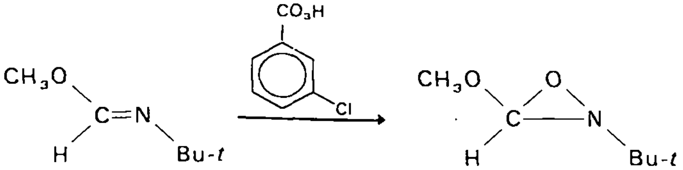
$$\rangle C{=}N{-} + RCO_3H \longrightarrow \rangle C{=}\underset{\downarrow\atop O}{N}{-} + RCO_2H \qquad (348)$$

Early attempts to prepare 3-phenyloxaziranes from the reaction of the appropriate imine with peroxyacid were unsuccessful because of acid-catalysed decomposition of either the imine or the oxazirane[542]. As mentioned earlier (Section II.B.1), the parent carboxylic acids are considerably more acidic than the corresponding peroxyacid. This decomposition problem was circumvented by the use of *m*-chloroperoxybenzoic acid in methylene chloride as the oxidizing solution[548]. The acid product, *m*-chlorobenzoic acid, is insoluble in the solvent and as a result the desired oxazirane may be prepared in good yield. Oxaziranes may be prepared selectively in the presence of carbon–carbon double bonds because of the greater ease of peroxyacid oxidation of the imine (equation 349)[543]. Optically active oxaziranes may be obtained by the reaction of



$$Me_2C{=}NCH_2CH{=}CH_2 \xrightarrow[CH_2Cl_2]{CH_3CO_3H} Me_2\underset{\diagdown O \diagup}{C{-\!\!-}N}CH_2CH{=}CH_2 \qquad (349)$$

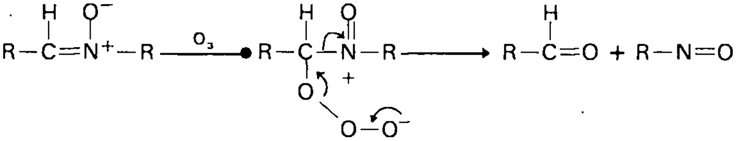
imines with an optically active peroxyacid such as percamphoric acid[549]. The peroxyacid oxidation of imino ethers to give alkoxyoxaziranes has also been reported (equation 350)[550].


(350)

2. Ozone

The reactions of ozone with several classes of compounds containing a carbon–nitrogen double bond have been reported[551]. The compounds studied include Schiff bases[552,553], azines[554,555], nitrones[552,556], hydrazones[553,557] and oximes[553]. The products isolated from the ozonations are oxaziranes, amides and cleavage products such as carbonyl and nitroso compounds.

Early studies indicated that these reactions were initiated by nucleophilic attack of ozone on the carbon of the C=N group[552] but more recent kinetic investigations suggest that the attack is electrophilic[553]. For instance, the proposed mechanisms for ozonation of nitrones[556] and hydrazones[553] are outlined in equations (351) and (352), respectively. Schiff bases react only slowly with ozone and although oxaziranes and amides are probably primary products, kinetic studies are inconclusive and major cleavage products may be formed by secondary processes. It was generally believed that the carbon–carbon double bond was considerably more reactive than the carbon–nitrogen double bond in reactions with ozone[555] but it has been shown that the C=N reactivity is dependent on the group attached to the nitrogen. For instance, *trans*-stilbene and acetophenone dimethyl hydrazone have equivalent rates of ozonation[553].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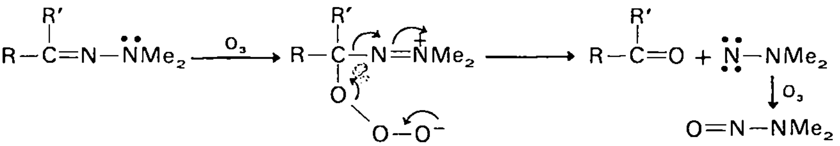
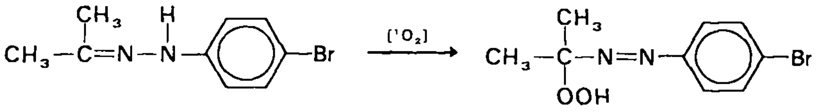

(352)

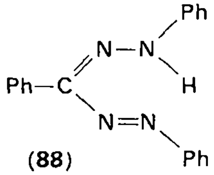
3. Molecular oxygen

In Section II.B.4 the reaction of an olefin with singlet oxygen to yield an allylic hydroperoxide was discussed. The same type of reaction with a phenylhydrazone yields an azohydroperoxide (equation 353)[558]. This reaction is thought to proceed via the 'ene mechanism' as previously outlined for olefins except that in this instance the hydrogen atom is transferred from a nitrogen to give the hydroperoxy group. The oxidation of 1,3,5-triphenylformazan (**88**) with singlet oxygen has been reported



(353)

and an azohydroperoxide intermediate was proposed to account for the products formed[559]. The conversion of aldehyde diphenylhydrazones to

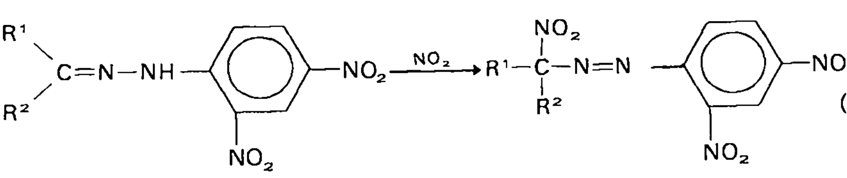


(**88**)

nitriles by photooxidation was reported but no mechanism was proposed for the reaction[560]. Ground state (triplet) oxygen is also capable of converting a phenylhydrazone to the corresponding azohydroperoxide[561] and the reaction is thought to proceed by a free-radical mechanism[562].

4. Nitrogen dioxide and nitrous acid

The oxidation of ketone and aldehyde 2,4-dinitrophenylhydrazones by nitrogen dioxide has been reported[563]. In the oxidation of the keto-hydrazones the nitro-substituted azo compounds (equation 354) are formed in good yields while in the case of the aldohydrazones the azo products rearrange spontaneously to the nitro-substituted hydrazones (equation 355). The mechanism for the oxidation involves an initial



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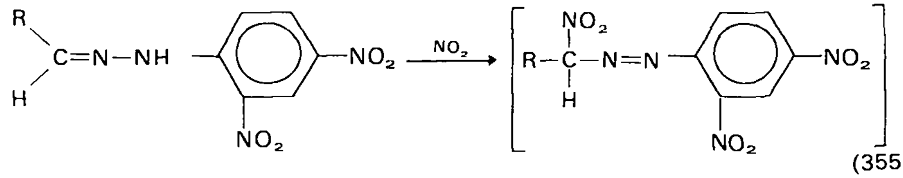

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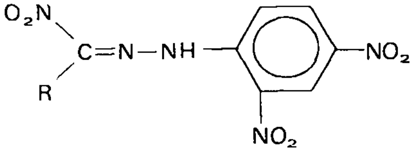

addition of nitrogen dioxide to the carbon atom of the C=N followed by loss of a hydrogen atom from nitrogen to give the azo product. The mechanism is in accordance with the observed kinetic deuterium isotope effect. The oxidation of oximes with nitrogen dioxide has also been reported[564].

The oxidation of oximes with nitrous acid is an effective procedure for the recovery of aldehydes or ketones from the parent oxime. This reaction has been examined using both ^{18}O-enriched nitrous acid[565] and ^{15}N-nitrous acid[576] and mechanisms have been proposed to account for the formation of N_2O, N_2 and NO as well as the carbonyl compound. It was noted that the relative proportions of the gaseous products varied considerably depending on the presence or absence of strong mineral acid[566].

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Supplement A The Chemistry of Double-Bonded Functional Groups
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CHAPTER 12

Transition metal catalysed carbonylation of olefins

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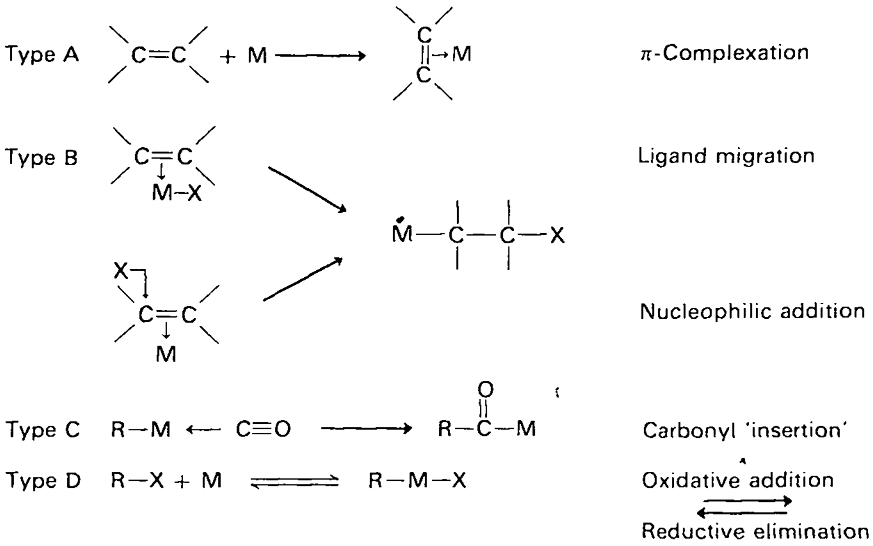
I. INTRODUCTION

The wide variety and unique types of organic reactions which can be carried out by the use of catalytic amounts of transition metal complexes, often under mild conditions, have made this both an intriguing and practical research area. Since in many cases complex organic products can be synthesized from inexpensive simple reagents, this area of chemistry has enjoyed considerable industrial importance. In recent years, our knowledge of the mechanistic details and the scope of transition metal catalysed reactions has expanded rapidly. One such reaction which has experienced considerable attention is the carbonylation of olefins in which a product containing one or more carbonyl groups is obtained by the transition metal catalysed reaction of carbon monoxide and an olefin.

Because of the availability of extensive reviews[1-3] covering the literature on this subject prior to 1970, this chapter will focus on recent synthetic and mechanistic developments in this area.

II. MECHANISM IN HOMOGENEOUS CATALYSIS. THE NATURE OF THE REACTIVE INTERMEDIATES

Homogeneous catalytic reactions can be organized into mechanistically related organometallic transformations[4-14]. Most transition metal catalysed reactions involve a combination of the following transformations:


Type A
π-Complexation
Type B
Ligand migration
Nucleophilic addition
Type C
R—M ← C≡O → R—C(=O)—M
Carbonyl 'insertion'
Type D
R—X + M ⇌ R—M—X
Oxidative addition
Reductive elimination

A. Complexation

1. Metal–olefin π-complexes

Transition metal catalysed reactions of olefins usually involve the formation of a metal–olefin π-complex[15–19]. The currently-accepted explanation of the bonding in olefin–transition metal complexes was proposed in the early 1950's by two independent groups[20,21]. Using a molecular orbital approach, metal–olefin bonding was explained as a combination of σ(olefin → metal)- and π(metal → olefin)-bonding (Figure 1). The σ-bond is formed between the filled olefin π-orbitals and the empty 5d 6s 6p^2 hybrid orbital on the metal. This causes an unfavourable distribution of negative charge on the metal ion; however, the π back-donation from the filled 5d 6p hybrid on the metal to the empty olefin π^*(antibonding)-orbital compensates for this, giving a synergic effect. This bonding scheme requires that the carbon–carbon bond be perpendicular to the plane containing the metal and the remaining ligand atoms, for a square–planar complex.

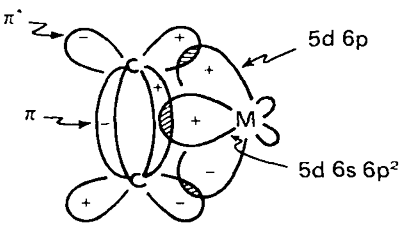


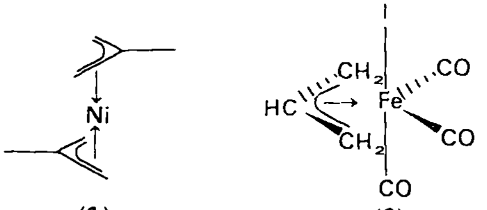
FIGURE 1. Bonding in metal–olefin complexes.

MO calculations have been carried out to determine the electronic structures of various metal–olefin complexes. A semiempirical MO calculation carried out on Zeise's anion, $[Pt(C_2H_4)Cl_3]^-$, suggests that π- and σ-bonding contribute almost equally to platinum–ethylene bonding[22]. More rigorous calculations, however, show that σ-donation is significantly larger than π back-donation, which amounts to a maximum of 25% of the total bonding of ethylene to platinum[23]. Similar results have been obtained from the MO study of a silver(I)–ethylene complex[24].

Carbon-13 magnetic resonance spectroscopy has also been used to study the structure and bonding of metal–olefin complexes[25]. Of particular importance is the substantial upfield coordination shift experienced by olefinic carbon atoms upon complexation (as much as 115 p.p.m. for a norbornadiene–rhodium complex[26]). Representative ^{13}C-chemical shift and $^{13}C—^{1}H$ and ^{13}C-metal coupling constant values are given in Table 1. The strong shielding observed in metal–olefin complexes has been attributed to a change in carbon hybridization[27,28], a net increase in electron density at carbon via metal to ligand π^* back-bonding[29], and to a non-bonding shielding parameter associated with partially filled metal d-orbitals[30]. An investigation of arenechromium(o) complexes[31] suggests, however, that all of these factors can be important in determining the observed ^{13}C-coordination shifts and that none should be considered exclusively.

2. π-Allyl complexes

Transition metal–olefin complexes containing allylic substituents (usually hydrogen, halide, or hydroxyl) can undergo further transformation to π-allyl complexes[37,38]. Two structures are possible for π-allyl functions bound in a transition metal complex (Figure 2). In some cases, such as the bis(allyl)nickel complex **1**[39], the π-allyl group is perpendicular to the metal–ligand bond and all carbon–carbon bond distances in the allyl system are essentially equivalent. On the other hand, in complexes such as **2**[40], the allyl function is contained in the same plane as metal–ligand bonds.



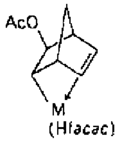
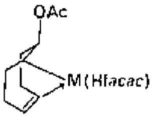
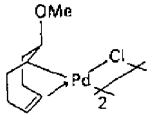
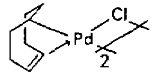
(1) (2)

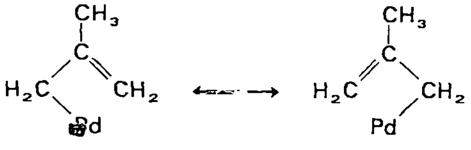
FIGURE 2. Structures of two metal–π-allyl complexes.

The bonding in π-allyl complexes presumably involves the same general considerations as described for olefin complexes. The overlap of filled π- and non-bonding orbitals on the ligand with appropriate empty metal orbitals and back donation to π-ligand orbitals are possible bonding interactions. The results of a ^{13}C-n.m.r. study of chloro(2-methallyl)-(triphenylphosphine)palladium(ii) (structurally similar to **2**) have been interpreted to reveal predominant influence of canonical structures **3a** and **3b** in the overall bonding scheme[41].

The synthesis, synthetic utility, and mechanism of formation of π-allyl complexes have been the subjects of recent attention[42–44]. A study of the formation of π-allyl complexes[45] from various substituted olefins and

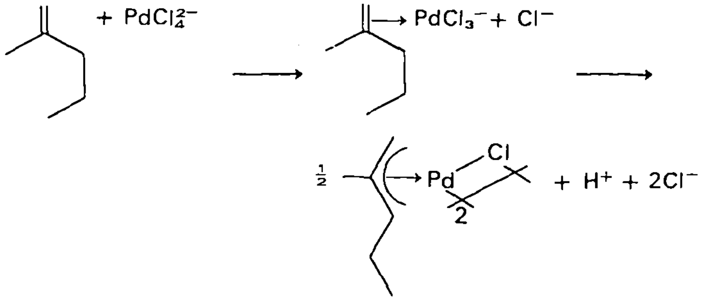
TABLE 1. ^{13}C-n.m.r. data for some organometallic complexes

Compounds		$\delta^{13}C\left(\begin{matrix}C\\ \Vert\longrightarrow M\\ C\end{matrix}\right)$	$\Delta\delta\,^{13}C$	$J(M-^{13}C)$Hz	$J(^{13}C-H)$Hz	$\delta\,^{13}C(C-M)$	$J(M-^{13}C)$Hz	$J(^{13}C-H)$Hz	Reference.
$K[(C_2H_4)PtCl_3]$		67·1	48·2	188					29
$[(1,5\text{-Cyclooctadiene})RhCl]_2$		78·5	49·3	13·9					32
$[(1,5\text{-Cyclooctadiene})PdCl_2]$		116·7	12·1						33
$[(1,5\text{-Cyclooctadiene})PtCl_2]$		100·6	27·2	153					25
$[(\text{Norbornadiene})Cr(CO)_4]$		76·0	68·1						34, 35
$[(\text{Norbornadiene})Rh(C_5H_5)]$		28·7	115·2	10	176				26
	M = Pd	76·4, 105·7			174, 181	25·9		166	36
	M = Pt	61·3, 79·2		132, 296	178, 181	0·3	470	160	
	M = Pd	97·1, 103·5			160, 157	49·0		144	36
	M = Pt	77·9, 82·2		255, 260	157, 154	25·9	730	145	
		102·0, 106·4				52·6			33
		101·0, 105·4	29·2, 24·8		159, 156	57·1		141	33


CH₃
C
H₂C
CH₂
Pd
CH₃
C
H₂C
CH₂
Pd

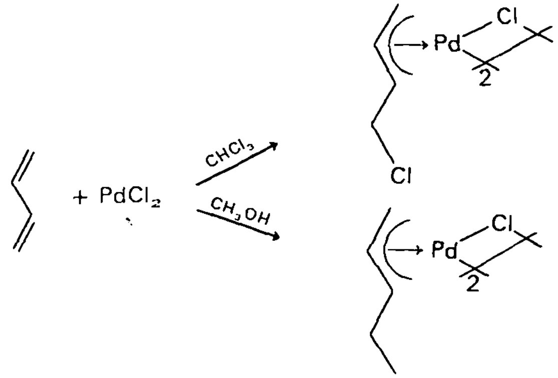
(3a) (3b)

palladium(II) in acetic acid has demonstrated that the tendency for loss of an allylic hydrogen from the initial olefin complex occurred preferentially in the order secondary > primary. This was interpreted as evidence for a hydride abstraction mechanism in which a positive charge is developed on the allylic fragment. The mechanism then requires a two-electron transfer generating a proton, a chloride ion, and the π-allyl complex (equation 1)†.


+ PdCl₄²⁻
PdCl₃⁻ + Cl⁻
½
Pd
Cl
2
+ H⁺ + 2Cl⁻

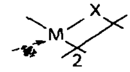
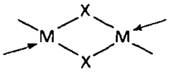
(1)

The formation of π-allyl complexes from conjugated dienes requires the addition of a nucleophile to the diolefin[46] (equation 2). A kinetic study

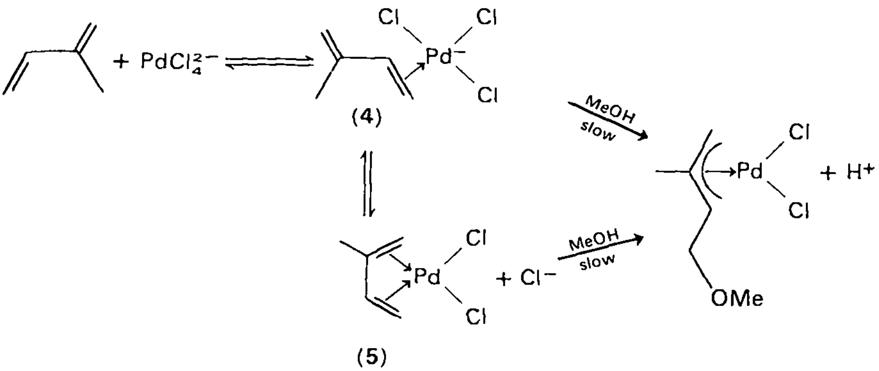

+ PdCl₂
CHCl₃
CH₃OH
Pd
Cl
2
Cl
Pd
Cl
2

(2)

---

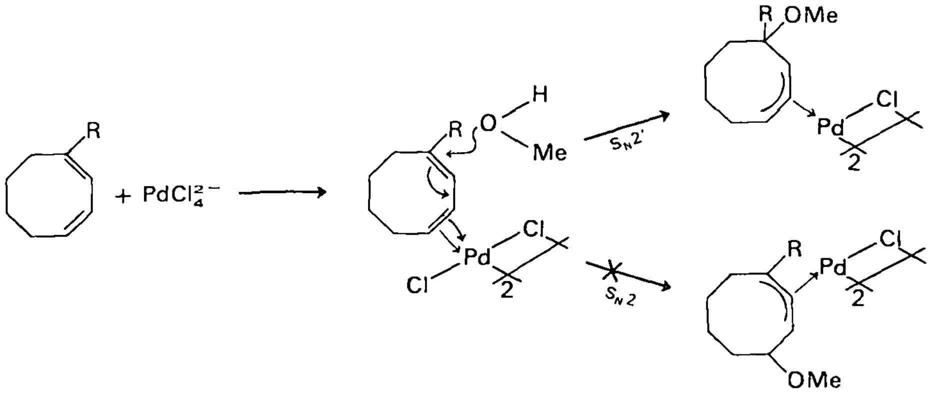
† In this chapter the symbol  is used to represent a bridged dimer of the general structure 

of the reaction of isoprene and palladium(II) chloride in methanol in the presence of lithium chloride has been interpreted in terms of two distinct π-complexes **4** and **5**[47] (Scheme 1). Nucleophilic attack by methanol from outside the coordination sphere of the metal was shown to be the rate-determining step.


+ PdCl$_4^{2-}$
Cl
Cl
Pd$^-$
Cl
(4)
MeOH
slow
Cl
Pd
+ H$^+$
Cl
OMe
Cl
Pd
+ Cl$^-$
MeOH
slow
Cl
(5)

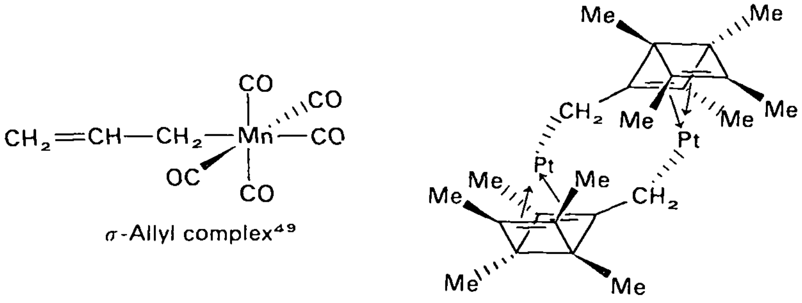
SCHEME 1.

The reaction of 1,3-cyclooctadiene and 1-methyl-1,3-cyclooctadiene with palladium(II) chloride in methanol to form π-allyl complexes has been demonstrated to proceed by an S_N2' process (as opposed to an S_N2 reaction)[48] (Scheme 2).


R OMe
R
+ PdCl$_4^{2-}$
H
R O
Me
S_N2'
Cl
Pd
2
Cl
Pd
Cl
2
S_N2
R
Pd
Cl
2
OMe

SCHEME 2.

In addition, σ-allyl and π-σ-allyl complexes have been reported which contain a localized σ-bond from the metal to an allylic carbon (Figure 3).



σ-Allyl complex[49]

σ-π-Allyl complex[50]

FIGURE 3. Structure of allyl complexes.

B. *Formation of σ-Bonded Intermediates*

The Type B transformation may be regarded as a 1,2-addition of an electrophile M and a nucleophile X across an unsaturated compound. This process generates a carbon–transition metal σ-bond and is a key step in transition metal catalysed reactions of olefins such as polymerization, dimerization, hydrogenation, oxidation, isomerization, and carbonylation. The stereochemistry and the direction of addition to an unsymmetrical olefin is dependent on the nature of the nucleophile or addend[51,52]. Those which are coordinated to the metal and transfer directly from the metal to an olefinic carbon (ligand migration) proceed by *cis* addition in an anti-Markownikoff direction. Those which are solvated but not coordinated and form a bond with an olefinic carbon by external nucleophilic attack proceed by *trans* addition in a Markownikoff direction. A summary of definitive stereochemical studies of the nucleophilic addition in various olefin metallation reactions is given in Table 2.

The *cis*, anti-Markownikoff addition mode can be explained on the basis of steric considerations (see Section III). The metal, because of the smaller steric hindrance it presents with a long carbon–metal bond, becomes attached to the most highly substituted carbon. Attack by uncoordinated nucleophile at the most substituted carbon of the double bond (*trans*, Markownikoff) is observed, however, for electronic reasons. The attacking nucleophile causes polarization of the π olefin–metal bond, shifting the electron density toward the metal atom (Figure 4). Since the incipient positive charge is developed and stabilized by the most substituted carbon of the olefinic ligand, it is the preferential site for nucleophilic attack. This interpretation is consistent with a ^{13}C-n.m.r. study of

TABLE 2. Stereochemistry of nucleophile–metal addition reactions

Nucleophile	Metal	Substrate	Stereochemistry of addition	Reference
Hydride	Rh	Monoolefin	*cis*	53
	Pd	Monoolefin	*cis*	54
	Mo	Monoolefin	*cis*	55
Phenyl	Pd	Diolefin	*cis*	56
	Pd	Monoolefin	*cis*	57
Carboalkoxide	Pd	Monoolefin	*cis*	54, 58
Amine	Pd	Monoolefin	*trans*	59
	Pt	Monoolefin	*trans*	60
Allyl	Pd, Co	Diolefin	*cis*	61, 62
	Pd, Ni	Monoolefin	*cis*	63, 64
Vinyl	Pd	Diolefin	*cis*	65
Chloride	Pd	Diolefin	*trans*	66
	Pd	Monoolefin	*cis* and *trans*	67
Methoxide	Pd, Pt	Diolefin	*trans*	68, 69
	Pd	Monoolefin	*trans*	58
	Ni	Diolefin	*trans*	70
Acetate	Pd	Diolefin	*trans*	71
	Pd	Monoolefin	*trans*	72
Hydroxide	Pd	Diolefin	*trans*	73

^{195}Pt–^{13}C coupling and variations in carbon chemical shifts of *para*-substituted styrene–platinum(II) complexes[74]. The results indicate a

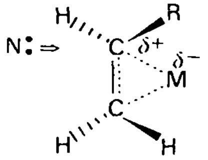


FIGURE 4. Nucleophilic attack of metal–olefin complexes.

polarization of the olefin π-electrons by the *para* substituent; electron-donor groups increase the contribution of valence-bond structures **6b** and **6c** (Figure 5).

Because of the relative ease with which transition metal–carbon σ-bonds are broken, it was widely accepted[75] that this type of bond was inherently weak. The stability of the σ-bonded complexes was proposed to be dependent upon the energy difference (Δ*E*) between the highest occupied electronic level and the lowest unoccupied electronic level of the metal and that the influence of stabilizing ligands was to increase the Δ*E*

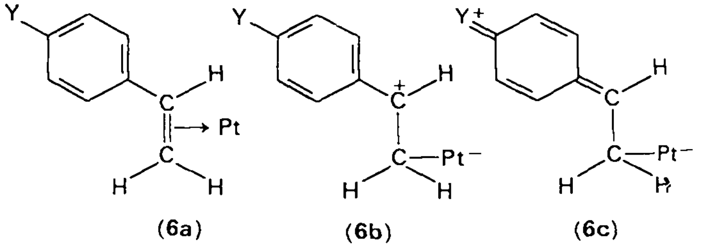


FIGURE 5. Valence-bond structures for a *para*-substituted styrene–platinum complex.

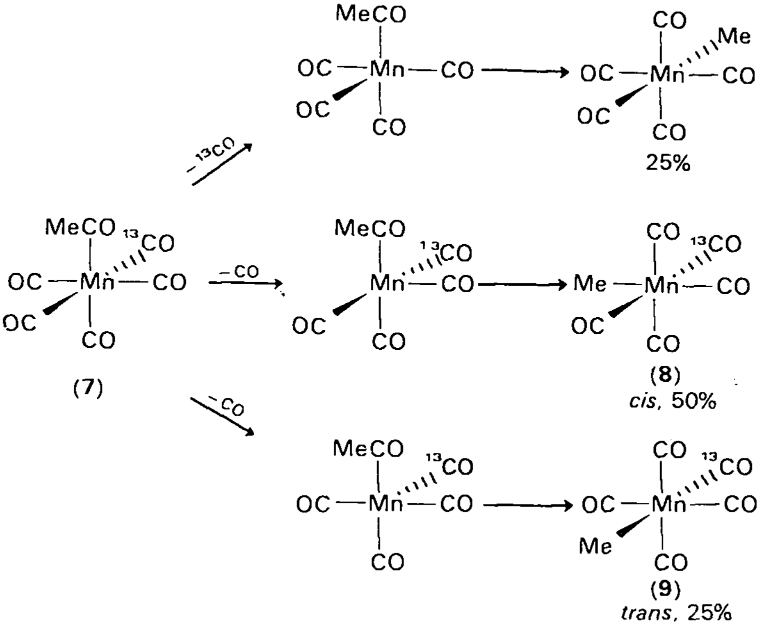
value[76]. The weight of current evidence, however, suggests[76–80] that transition metal–carbon σ-bonds are not intrinsically thermodynamically unstable. The function of the stabilizing ligand is simply to occupy coordination sites necessary for facile, low-energy decomposition pathways (e.g., the reverse of B).

C. Carbon Monoxide Insertion Reactions

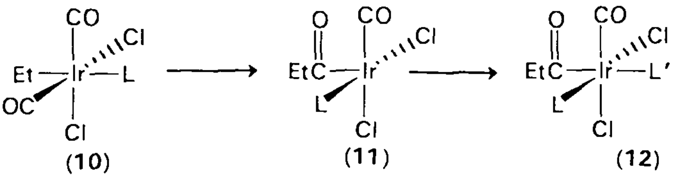
Intramolecular carbon monoxide 'insertion' into a transition metal–carbon σ-bonded complex can be considered to occur by several possible mechanistic pathways[11,81]. An alkyl migration mechanism has been conclusively demonstrated in the decarbonylation (reverse of C) of the acetylmanganese complex **7**[82] (Scheme 3). The decarbonylation of **7** gives the *cis*- and *trans*-methylmanganese complexes, **8** and **9**, in the ratio of 2 to 1. This is consistent only with a methyl migration mechanism, since no *trans* product would be formed by a carbonyl insertion mechanism.

The carbonylation of the alkyliridium complex **10** has been postulated to proceed via a concerted bimolecular mechanism[83] (equation 3). The kinetic product **12** has been proposed to arise from a concerted movement of alkyl and carbonyl to afford five-coordinate **11** which has square pyramidal geometry with the vacant octahedral site *trans* to the acyl ligand.

The stereochemistry of the carbonylation of alkyl–transition metal complexes at carbon has been shown to proceed with retention of configuration when the carbon is σ-bonded to either palladium[71] (see Section III) or iron[84–86]. The decarbonylation of several optically active aldehydes with chlorotris(triphenylphosphine)rhodium(I) occurs with retention of configuration at carbon with high selectivity[87]. These reactions proceed through formation of acylrhodium complexes and their rearrangement to



SCHEME 3.



(3)

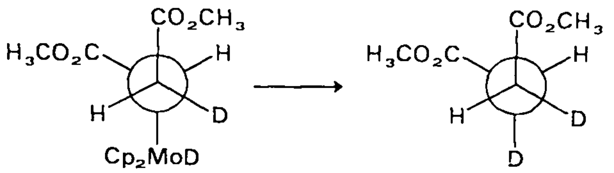
alkylrhodium complexes, followed by reductive elimination to give alkanes[88].

D. Oxidative Addition—Reductive Elimination

The Type D process is the well known oxidative addition reaction of a substrate molecule to a coordinatively unsaturated metal. The transformation takes place with an increase in the formal oxidation state and the coordination number of the transition metal. A wide variety of covalent molecules such as hydrogen, oxygen, halogens, and organic halides can undergo oxidative addition.

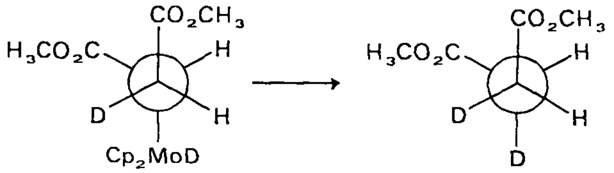
The reverse of oxidative addition, reductive elimination, is often encountered in the transition metal catalysed hydrogenation of olefins.

The reductive elimination of alkanes from alkylmolybdenum deuterides formed by the reaction of olefin and dideuteridobis(π-cyclopentadienyl)-molybdenum (Cp_2MoD_2), has been shown to take place with retention of configuration at the carbon–metal σ-bond[89] (equations 4 and 5).



CO_2CH_3
H_3CO_2C
H
H
D
Cp_2MoD
CO_2CH_3
H_3CO_2C
H
H
D
D

(4)

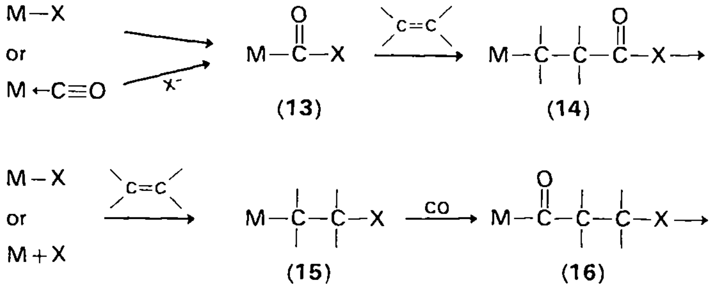


CO_2CH_3
H_3CO_2C
H
D
H
Cp_2MoD
CO_2CH_3
H_3CO_2C
H
D
H
D

(5)

E. Olefin Carbonylation. A Mechanistic Description

Clearly, any transition metal catalysed reaction between an olefin and carbon monoxide in which one or more carbonyl groups are introduced into the organic skeleton will involve several of the organometallic transformations mentioned above. In general, two mechanistic pathways describe generation of an organic carbonyl group in olefin–carbon monoxide reactions (Figure 6). The first sequence involves generation of a



M—X
or
M←C≡O
X⁻
M—C—X
(13)
C=C
M—C—C—C—X
(14)
M−X
or
M+X
C=C
M—C—C—X
(15)
CO
M—C—C—C—X
(16)

FIGURE 6. General mechanisms for transition metal catalysed carbonylation reactions.

metal–acyl derivative **13** which can react by a 1,2-addition mechanism to yield the σ-bonded complex **14**. Alternatively, a σ-bonded complex **15** is formed prior to a carbon monoxide insertion reaction which generates the metal–acyl complex **16**. In each case, further reaction (β-elimination, carbonyl insertion, solvolysis, reductive elimination, etc.) occurs to give the organic products.

In the following sections, mechanistically similar, transition metal catalysed carbonylation reactions have been categorized with respect to two important aspects: (a) the nature of the transformation with regard to the organic product, and (b) the change in oxidation state of the transition metal. Based on these criteria, three organic transformations are defined:

(i) Solvocarbonylation Reactions. In this type of reaction the metal is reduced (generally from the divalent to the zerovalent state) and the reaction is stoichiometric with respect to the metal unless a reoxidant is used. In general, the solvent is incorporated in the organic product.

(ii) Hydrocarbonylation Reactions. These reactions are potentially catalytic with respect to the metal and the change in oxidation state is in the order

$$M^n \xrightarrow{-2e^-} M^{n+2} \xrightarrow{+2e^-} M^n$$

The organic transformation generally involves the addition of a hydrogen and a carbonyl group across the double bond.

(iii) Olefin-coupling Carbonylation Reactions. These reactions are classified strictly on the basis of the organic transformation and without regard to the metallic oxidation change. A π-allyl complex is often involved.

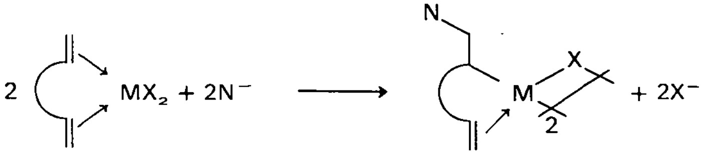
Finally, an important point with regard to this classification is that the oxidative change involved in each reaction type dictates the transition metal catalyst best suited for the particular transformation.

III. SOLVOCARBONYLATION

A. Diolefins

1. Solvometallation reactions

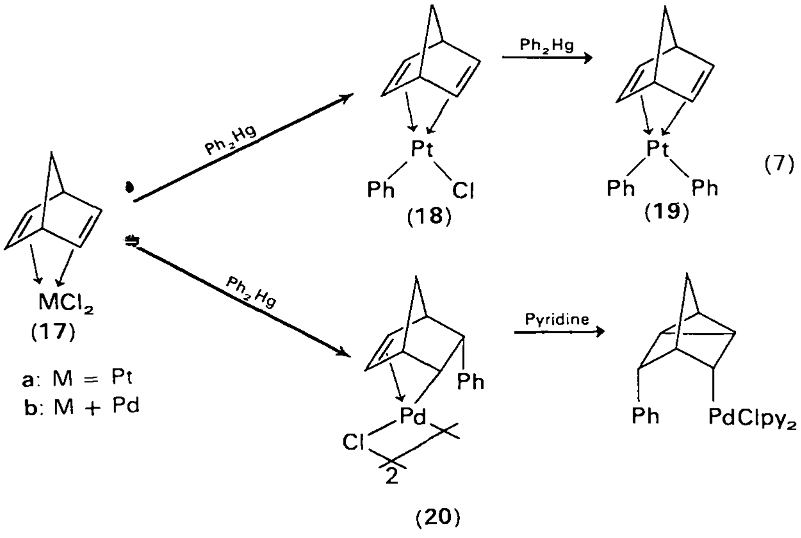
Chelating diolefins coordinated to transition metals readily undergo nucleophilic attack[90–97] to form stable σ-bonded enyl complexes which can be isolated (equation 6). Unfortunately, the suggestion[98] that the Wacker oxidation of olefins[99] involved *cis* stereochemistry in the rate-



(6)

determining hydroxypalladation step was generally accepted and assumed to apply to all similar reactions. The *cis* hydroxypalladation mechanism was based on kinetic results, but the data are also consistent with *trans* stereochemistry for the addition. Thus, the stereochemical path of the methoxypalladation and methoxyplatination of chelating diolefins which was demonstrated to take place *trans* in every case[68,69], was regarded as anomalous. On the basis of an incorrect structural assignment to 1,5-cyclooctadiene oxypalladation product[100], it was even suggested[101] that this addition, contrary to the stereochemical path reported originally[68,69], took place to give the *cis* addition product; X-ray structural determinations have verified the original stereochemical assignments, however[102,103].

In order to explain their assumed anomalous behaviour, it was suggested[101,104,105] that the reaction of bicyclic diolefins followed the *trans* stereochemical path for steric reasons. The *trans* stereochemistry was also attributed to the inability of chelating diolefins to rotate 90° from the position perpendicular to the square plane of the metal complex into a position which would favour *cis* addition by the metal and a ligand attached to it[106]. These explanations evidently are not correct, as is shown by the reactions of dichloro(norbornadiene)platinum(II) and palladium(II), (**17a**, **b**) with diphenyl mercury[56] (equation 7). The platinum complex

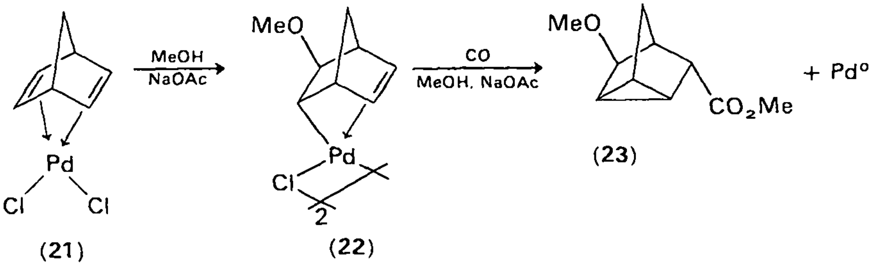


(7)

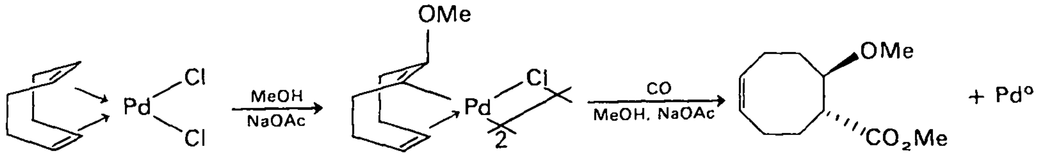
17a reacts with one equivalent of diphenylmercury to afford **18** while two equivalents give **19** by successive chloride displacement reactions. On the other hand, diphenylmercury reacts with the palladium complex **17b** to yield the σ-bonded dimeric enyl complex **20**, in which the palladium and the phenyl moieties are attached *cis-endo* to the bicyclo[2.2.1] skeleton. Thus, the phenyl groups undergo sigma bonding to the metal, and in the case of the more reactive palladium complex, undergo *cis* addition to the coordinated bicyclic olefin. The stability of the platinum analogue to this type of reaction has been demonstrated previously[107,108].

2. Carbonylation of σ-bonded enyl and diolefin complexes

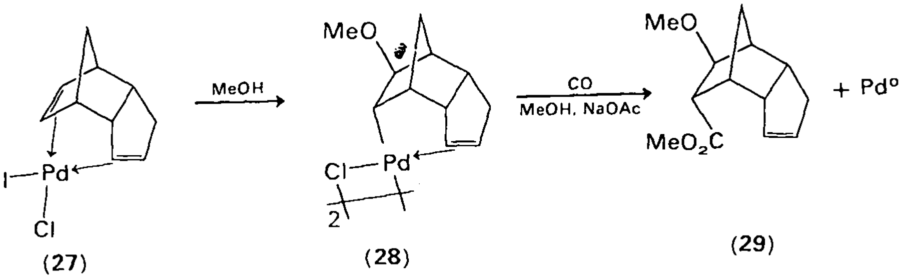
The σ-bonded methoxy enyl complexes **22**, **25**, and **28** react in methanol at room temperature under 1–40 atm of carbon monoxide to afford the methoxy esters **23**, **26** and **29**, respectively[71,109] (equations 8, 9, and 10).


Pd
Cl
Cl
(21)
MeOH
NaOAc
MeO
Pd
Cl
2
(22)
CO
MeOH, NaOAc
MeO
CO₂Me
(23)
+ Pd°

(8)


Pd
Cl
Cl
(24)
MeOH
NaOAc
OMe
Pd
Cl
2
(25)
CO
MeOH, NaOAc
OMe
CO₂Me
(26)
+ Pd°

(9)

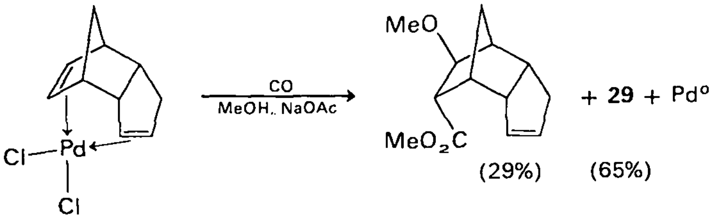

I
Pd
Cl
(27)
MeOH
MeO
Cl
Pd
2
(28)
CO
MeOH, NaOAc
MeO
MeO₂C
(29)
+ Pd°

(10)

The stereochemical assignments of the products are based upon n.m.r. and chemical evidence and show that carbonylation of the palladium–

carbon σ-bond occurs with 100% retention of configuration at carbon.

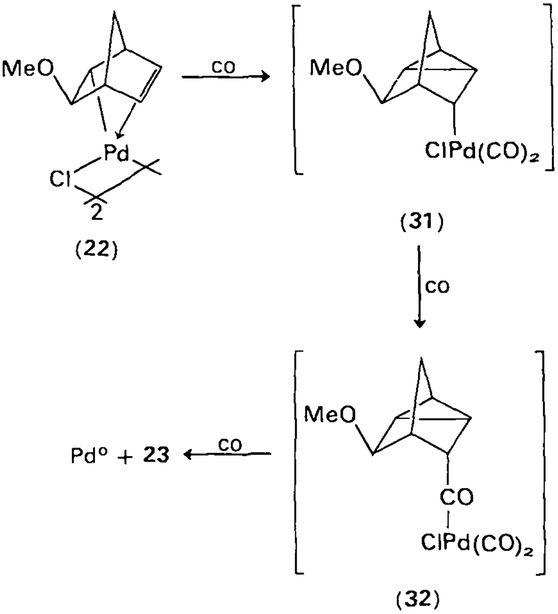
Carbonylations of the corresponding diene complex **21**, **24** and **27**, similarly give the *trans*-methoxy esters **23**, **26**, and **29**. The dicyclopentadiene complex **27**, upon carbonylation in methanolic sodium acetate, affords **29** and a significant amount of the *trans*-acetoxy ester **30** (equation 11). Reaction occurs at the most highly strained double bond of this diolefin.



Cl—Pd
Cl
CO
MeOH, NaOAc
MeO
MeO₂C
+ 29 + Pd°
(29%)
(65%)

(27) (30) (11)

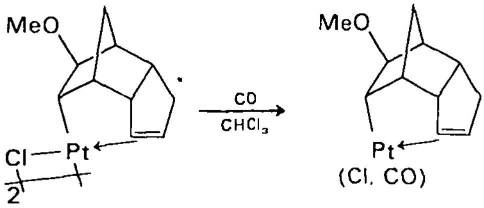
A stepwise mechanism for the carbonylation of the σ-bonded enyl complexes has been proposed (Scheme 4). The first step involves attack on palladium by carbon monoxide with the concomitant homoallyl rearrangement of **22** to the tricyclic structure **31**. The intermediate **31** then undergoes an alkyl–acyl rearrangement to **32** and subsequent solvolysis to products.



MeO
Pd
Cl
2
(22)
CO
MeO
ClPd(CO)₂
(31)
CO
MeO
CO
ClPd(CO)₂
(32)
Pd° + 23
CO

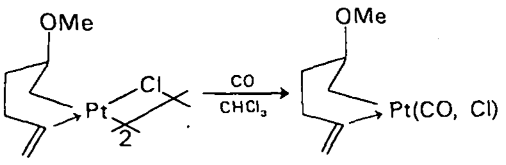
Scheme 4.

Carbonylation of σ-bonded enyl platinum complexes in aprotic solvents has also been reported. Reaction of **33** and **35** with carbon monoxide in chloroform at −20 °C splits the chloro-bridged dimer into monomeric carbonyl complexes **34** and **36**, respectively[110] (equations 12, 13). Carbonylation of **37**, however, promotes the rearrangement from the norbornenyl complex to the tricyclic carbonyl complex **38** (equation 14). It is interesting that the carbonylation of the monomeric phosphine complex **39** results in the generation of the carbonyl insertion derivative **40**[111]. Reaction of **40** with methyl- or phenyllithium reagents yields ketone **41a**, **b** by nucleophilic attack at the carbonyl-metal bond; simultaneous reduction of Pd^{II} to Pd^0 takes place. Reaction with the electrophilic reagents, methyl iodide and hydrogen chloride, yields methyl ketone **41a** and aldehyde **42**, respectively, and the dimeric Pd^{II} complex **43**. The postulated mechanism involves a four-centre bimolecular reaction with a cyclic transition state. However, an oxidative addition–reductive



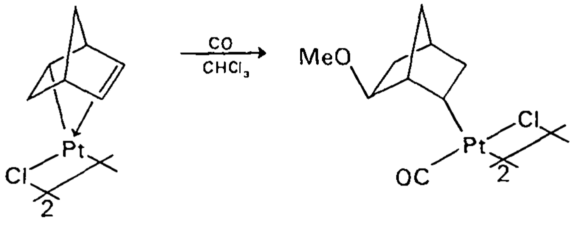
(33) (34)

(12)



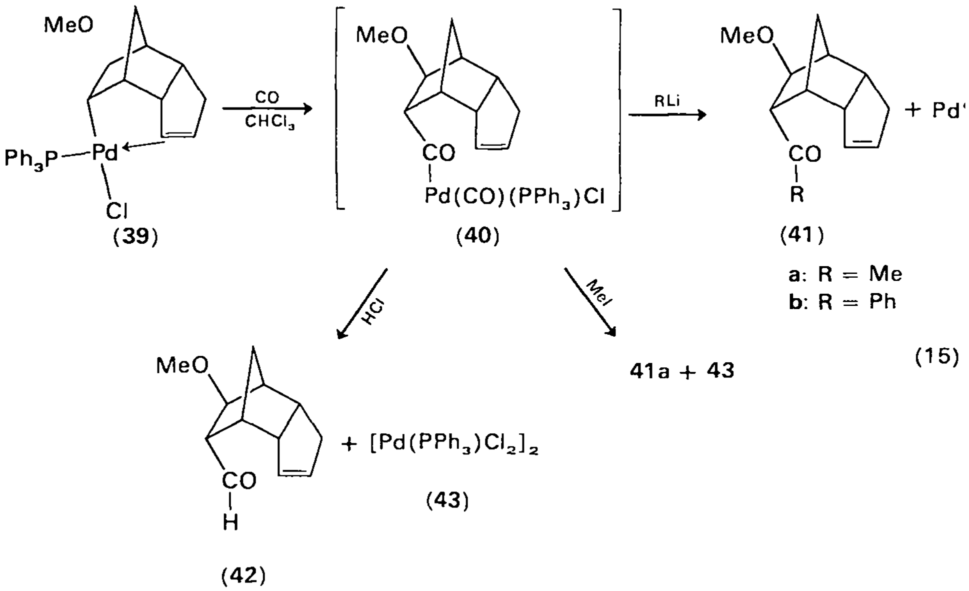
(35) (36)

(13)



(37) (38)

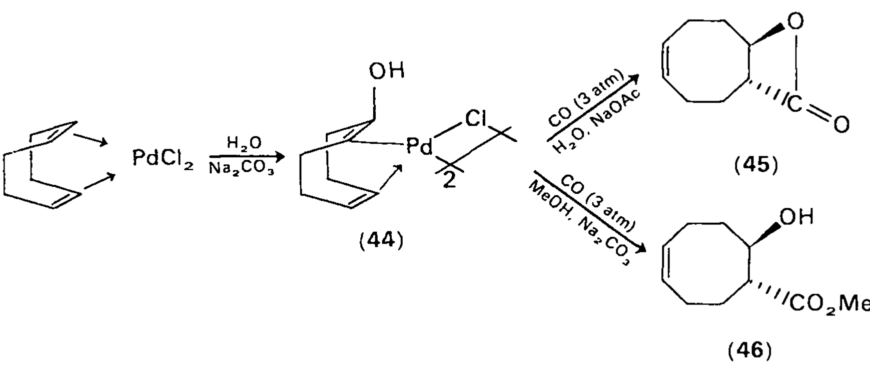
(14)


MeO
Ph3P—Pd
Cl
(39)
CO
CHCl3
MeO
CO
Pd(CO)(PPh3)Cl
(40)
RLi
MeO
CO
R
+ Pd'
(41)
a: R = Me
b: R = Ph
HCl
MeI
41a + 43
MeO
CO
H
(42)
+ [Pd(PPh3)Cl2]2
(43)

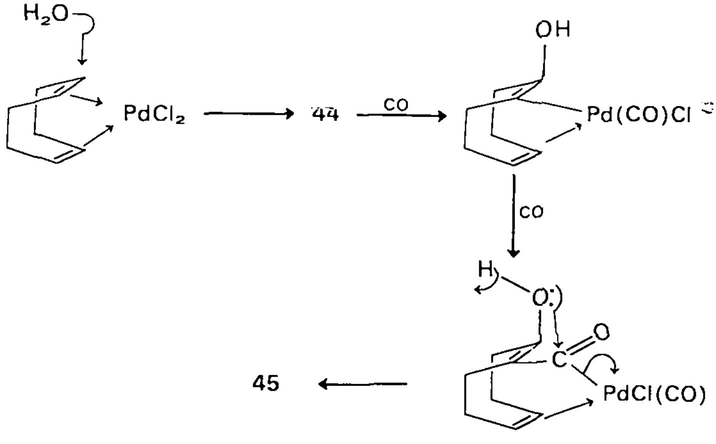
(15)

elimination mechanism generating a Pd^{IV} intermediate[112] is also possible.

The stereochemistry of the hydroxypalladation reaction of 1,5-cyclooctadiene has been demonstrated by the carbonylation of **44** in water in the presence of base[73]. The reaction affords a single organic product, *trans*-2-hydroxycyclooct-5-enecarboxylic acid, β-lactone (**45**) as a result of a *trans* hydroxymetallation reaction followed by carbonylation with retention of configuration at carbon. Carbonylation of **44** in methanol produces the *trans*-hydroxy ester **46**. The mechanism of formation of **45** involves carbon monoxide insertion, probably followed by intramolecular nucleophilic attack by oxygen at the palladium–acyl bond to form the lactone and palladium(0) (Scheme 5).


PdCl2
H2O
Na2CO3
OH
Pd
Cl
2
(44)
CO (3 atm)
H2O, NaOAc
CO (3 atm)
MeOH, Na2CO3
O
C
O
(45)
OH
CO2Me
(46)

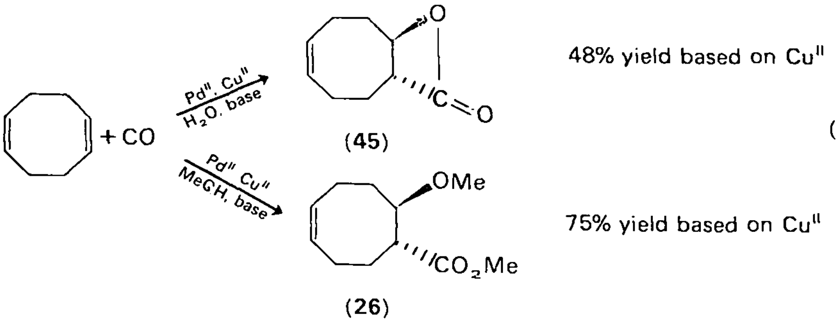
(16)


H₂O
PdCl₂
44
CO
OH
Pd(CO)Cl
CO
H
O
O
C
PdCl(CO)
45

SCHEME 5.

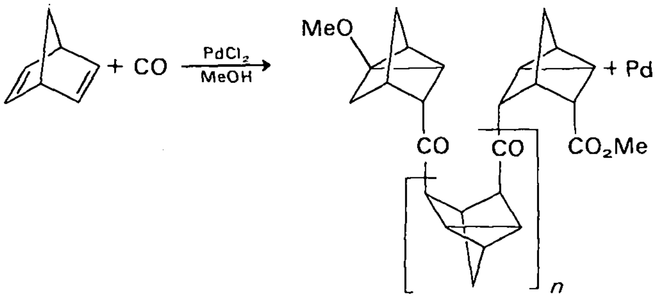
3. Carbonylation of diolefins

Carbonylation of diolefins without prior complex formation has been reported although the reaction mechanism, solvometallation of the diene complex followed by carbonyl insertion, is unchanged. Thus, the β-methoxy ester **26**[71] and the lactone **45**[73] are obtained when 1,5-cyclooctadiene is allowed to react with carbon monoxide in the appropriate solvent in the presence of catalytic amounts of palladium(II) chloride and a copper(II) chloride reoxidant (equation 17).


+CO
Pdᴵᴵ, Cuᴵᴵ
H₂O, base
Pdᴵᴵ Cuᴵᴵ
MeOH, base
O
C
O
(45)
OMe
CO₂Me
(26)
48% yield based on Cuᴵᴵ
75% yield based on Cuᴵᴵ

(17)

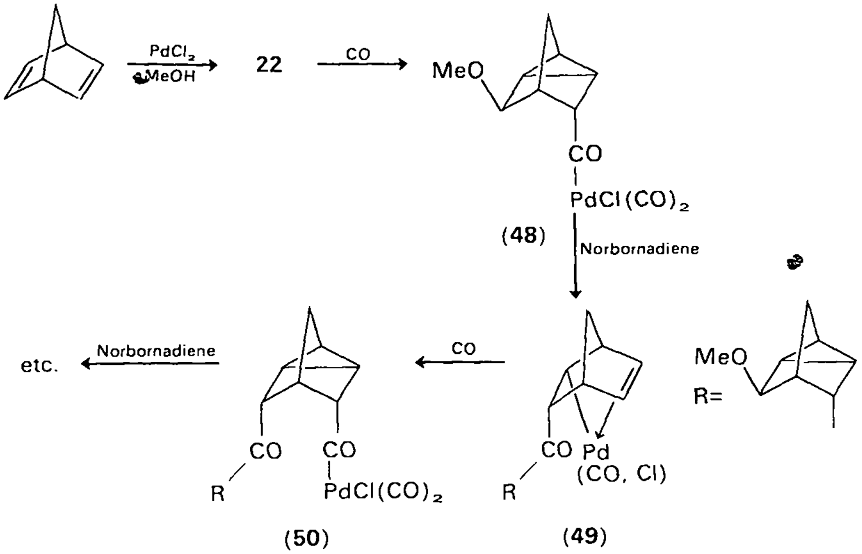
The stoichiometric palladium(II) chloride catalysed carbonylation of either 1,5- or 1,3-cyclooctadiene in methanol gives the β-methoxy ester **26**[113]. A polymeric material, **47**, is produced in the carbonylation of norbornadiene in methanol[114] (equation 18). The reaction mechanism


+ CO
PdCl2
MeOH
MeO
CO
CO
CO2Me
+ Pd
n

(18)

(47)

(Scheme 6) involves initial methoxypalladation to the σ-bonded enyl


PdCl2
MeOH
22
CO
MeO
CO
PdCl(CO)2
(48)
Norbornadiene
etc.
Norbornadiene
CO
CO
CO
R
PdCl(CO)2
CO
Pd
R
(CO, Cl)
MeO
R=
(50)
(49)

SCHEME 6.

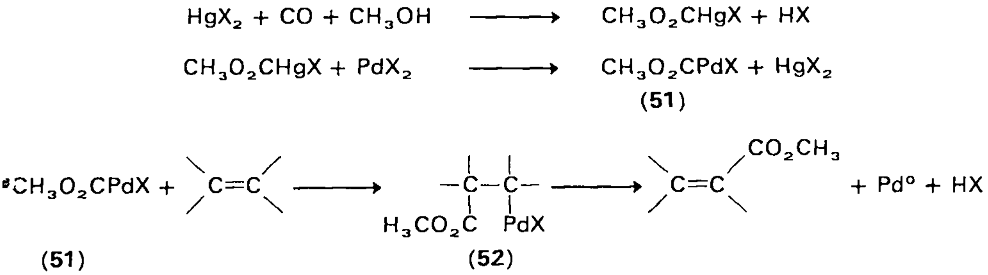
complex **22** followed by carbonylation which promotes the norbornene–nortricyclene rearrangement and forms acyl complex **48**. *Cis*, *endo* addition of the acylpalladium intermediate **48** to norbornadiene forms the σ-bonded enyl complex **49** which rearranges upon carbonylation to form the dimer of **50**. Polymerization continues in this manner. Chain termination takes place by solvolysis of an ensuing acyl–palladium bond, an unfavourable reaction under non-basic conditions.

B. Monoolefins

1. Transmetallation–carbonylation

The organometallic exchange reaction is a generally employed method for the generation of transition metal–carbon σ-bonds[115]. The formation of σ-bonded organopalladium complexes via palladium exchange with organomercurials has been used extensively in the arylation, alkylation and carbonylation of olefins[54,116,117].

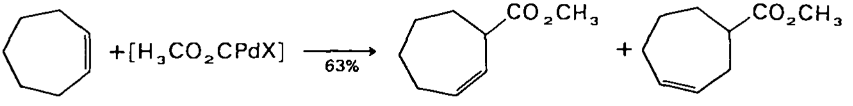
Carboalkoxylation of olefins in the presence of mercury(II) and palladium(II) salts forms α,β-unsaturated esters[116]. The reaction has been proposed to proceed via a highly reactive carboalkoxypalladium intermediate **51**, generated *in situ* by the transmetallation of the mercury salt, CH_3O_2CHgX. Addition of **51** to the olefin gives the intermediate palladium σ-bonded complex **52** (Scheme 7) which decomposes by palladium hydride elimination to the carboalkoxylated olefin product.


HgX₂ + CO + CH₃OH → CH₃O₂CHgX + HX
CH₃O₂CHgX + PdX₂ → CH₃O₂CPdX + HgX₂
(51)
CH₃O₂CPdX +
(51)
H₃CO₂C PdX
(52)
CO₂CH₃
+ Pd° + HX

SCHEME 7.

The direction of addition of palladium and the carboalkoxyl group to unsymmetrical olefins is governed by steric interactions rather than electronic effects[54,117]. The carboalkoxyl group adds to the less substituted carbon atom of the double bond since the relatively long palladium–carbon bond and the square planar geometry about palladium combine to make palladium effectively the smallest part of the organometallic complex. Increasing substitution at the olefinic carbons decreases the reactivity of the olefin. Measurements of competitive reaction rates show the following order (decreasing reaction rates): ethylene > methyl acrylate > propylene > styrene > α-methylstyrene. This order of reactivity is not that expected for radical or ionic additions but is consistent with a concerted *cis* addition in which little charge is generated at carbon.

The carboalkoxylation of cyclic olefins provides mechanistic information in that the reaction with cycloheptene, for example, affords two rearranged products, **53** and **54** (equation 19). A *cis* palladium hydride

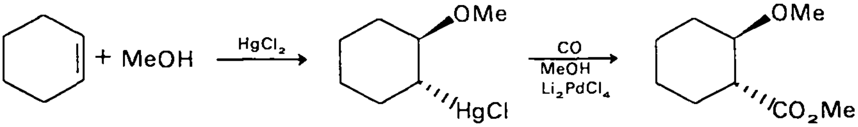

+[H$_3$CO$_2$CPdX]
63%
CO$_2$CH$_3$
+
CO$_2$CH$_3$

(19)

(**53**) (**54**)

elimination–readdition mechanism is consistent with the absence of α,β-unsaturated ester product.

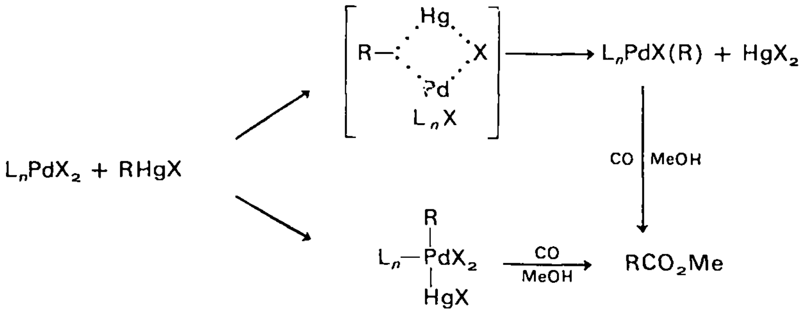
The alkylmercurial compound, **55**, formed by reaction of cyclohexene and mercuric chloride in methanol, has been carbonylated in the presence of a palladium(II) catalyst to afford *trans*-β-methoxy ester (**56**) in a low yield as the only isolated organic product^{118} (equation 20). These results


+ MeOH
HgCl$_2$
OMe
HgCl
CO
MeOH
Li$_2$PdCl$_4$
OMe
CO$_2$Me

(20)

(**55**) (**56**)

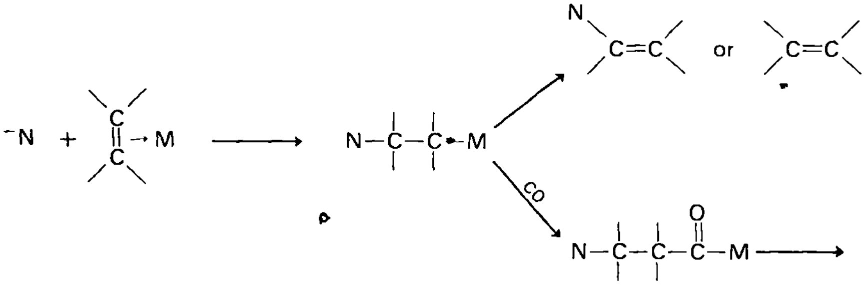
demonstrate that the exchange reaction of palladium for mercury occurs with predominant retention of configuration at carbon. The results are consistent either with a four-centre bimolecular exchange or an oxidative addition of the organomercurial to the palladium(II) species with retention of configuration at carbon (Scheme 8).


Hg
R—
X
Pd
L$_n$X
L$_n$PdX(R) + HgX$_2$
CO
MeOH
L$_n$PdX$_2$ + RHgX
R
L$_n$—PdX$_2$
HgX
CO
MeOH
RCO$_2$Me

SCHEME 8.

2. Solvometallation–carbonylation

The reactions of nucleophiles with monoolefin–transition metal complexes is an important synthetic procedure[119–121]. Whereas the nucleophilic addition to a diolefin complex produces a stable, σ-bonded enyl complex (Section III.A.1), the analogous σ-bonded complex from reaction of a monoolefin is generally unstable and decomposes because of the absence of chelation (Scheme 9). However, in the presence of carbon monoxide, this solvometallation intermediate can be trapped by carbon monoxide insertion. In general, the reaction of an olefin and carbon monoxide in a nucleophilic solvent, catalysed by a transition metal salt, can occur by either of two mechanistic pathways to afford solvometallation derivatives or derivatives of α,β-unsaturated acids and diacids. The relative amounts of each product are quite sensitive to reaction conditions (i.e., the nature of the solvent, olefin, catalyst, etc.). In these carbonylations, reduction of the metal takes place.



Scheme 9.

The carbonylation of ethylene in benzene, catalysed by palladium chloride, gives β-chloropropionyl chloride in a 41% yield based on palladium(II) (equation 21)[122,123]. A variety of olefins can be carbonylated

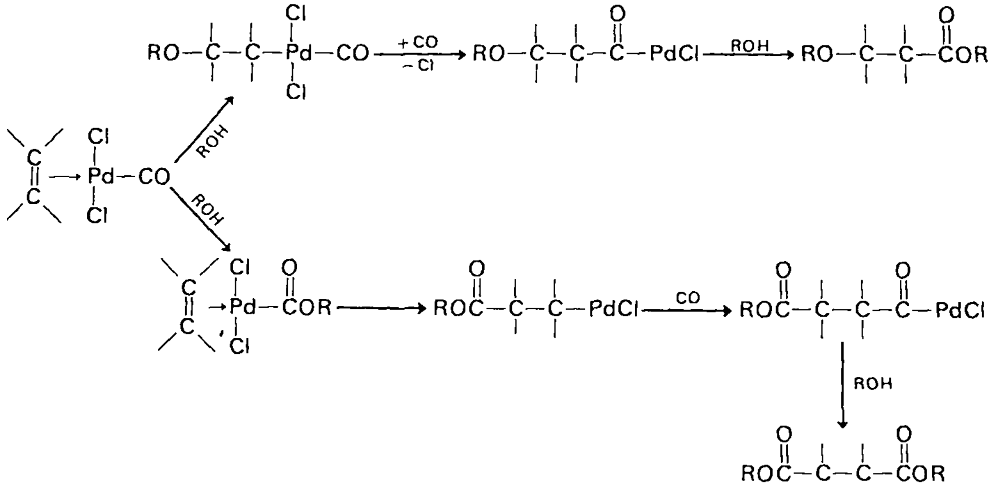
$$CH_2{=}CH_2 + CO + PdCl_2 \xrightarrow[50\ \mathrm{atm}]{\mathrm{Benzene}} ClCH_2CH_2COCl + Pd^0 \qquad (21)$$

under these conditions to give β-chloroacid chlorides.

The carbonylation of olefins in alcohol solutions in the presence of stoichiometric amounts of palladium(II) chloride and mercury(II) chloride gives high yields (based on Pd^{II}) of β-alkoxy esters and diesters[124]. The yields and products of the reaction are dependent upon the structure of the olefin. Carbonylation of 1-hexene gives predominantly the β-methoxy ester, methyl 3-methoxyheptanoate (72%), and a smaller amount (20%)

of the succinic ester, dimethyl 1,2-hexanedicarboxylate. Styrene yields mostly the succinic ester with smaller amounts of the α,β-unsaturated cinnamic ester; the relative amounts are dependent upon the reaction conditions. Cyclopentene yields 36% of the *cis*-1,2-diester and 43% of an unidentified diester, probably the *cis*-1,3-isomer. Although *trans*-3-hexene yields only the *dl*-diester, a product of *cis* addition, *cis*-3-hexene gives both *meso*- and *dl*-diesters as well as β-methoxy ester products. No olefin isomerization could be detected. These results can probably be explained, however, by considering that olefin *cis–trans* isomerization is taking place. Thus, both the *meso* and *dl* esters from *cis*-3-hexene are obtained from a mixture of the *cis*-3-hexene and its isomerization product, *trans*-3-hexene. Only *dl*-diester is detected in the carbonylation of *trans*-3-hexene, since the rate of *cis* carboxylation of *cis*-3-hexene, the isomerization product of *trans*-3-hexene, is relatively slow compared to the rate of addition to the *trans* olefin, and the olefin equilibrium favours the thermodynamically more stable *trans* isomer (*vide infra*).

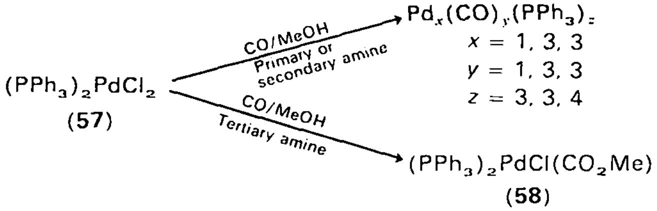
The mechanism proposed for these reactions does not include the role of mercury (Scheme 10). Alkoxy ester is obtained from the alkoxypalladation of the coordinated olefin followed by carbonylation of the



SCHEME 10.

σ-bonded intermediate. The diester product is formed by addition of a carboalkoxypalladium species to the olefin followed by carbon monoxide insertion and solvolysis.

The carboalkoxypalladium adduct is formed through nucleophilic attack by alcohol at the coordinated carbonyl carbon of the palladium complex, and this reaction is a general method for the preparation of inorganic alkoxycarbonyl derivatives[125]. Stable, isolable carboalkoxyl complexes can be prepared from metal salts containing 'stabilizing' phosphine ligands by the reaction of carbon monoxide and alcohol in the presence of a base. Carbonylation of dichlorobis(triphenylphosphine)-palladium(II) (**57**) in the presence of primary or secondary amines affords only palladium(O) carbonyl complexes, while the stable palladium carboxylate **58** is obtained in the presence of tertiary amines[126] (equation 22). A similar carbonylation of dichlorobis(triphenylphosphine)-

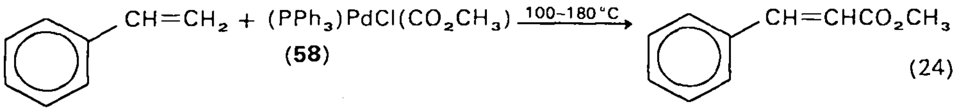


(22)

platinum(II) (**59**) catalysed by methoxide ion generates a stable platinum dicarboxylate **60**[127] (equation 23). As expected, the stable methoxy-

$$\underset{(\mathbf{59})}{(PPh_3)_2PtCl_2} + 2CO + 2MeOH \xrightarrow{OMe^-} \underset{(\mathbf{60})}{(PPh_3)_2Pt(CO_2Me)_2} \qquad (23)$$

carbonyl complex **58** reacts at high temperatures (100–180°C) with olefins to form an unsaturated ester[128] (equation 24).



(24)

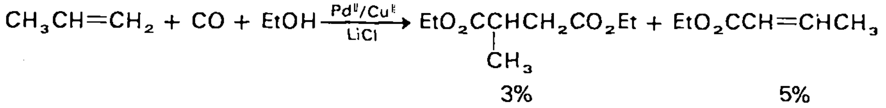
The synthesis of dialkyl succinates by carbonylation of olefins in the presence of a Pd^{II}/Cu^{II}/oxygen or a Pd^{II}/Fe^{III}/oxygen catalyst system proceeds according to the following reaction sequence (for copper)[129]:

$$PdCl_2 + 2CO + CH_2{=}CH_2 + 2ROH \longrightarrow RO_2CCH_2CH_2CO_2R + Pd^0 + 2HCl$$

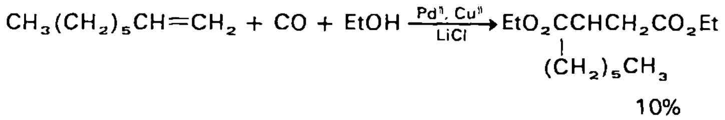
$$2CuCl_2 + Pd^0 \longrightarrow Cu_2Cl_2 + PdCl_2$$

$$Cu_2Cl_2 + 2HCl + \tfrac{1}{2}O_2 \longrightarrow 2CuCl_2 + H_2O$$

The reaction is carried out at 125–150°C with 600–700 psi of carbon monoxide and introduction of oxygen at 10–20 psi increments to give low yields of esters (equation 25, 26).



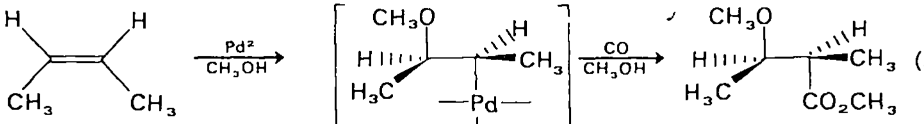
$$CH_3CH{=}CH_2 + CO + EtOH \xrightarrow[LiCl]{Pd^{II}/Cu^{II}} \underset{3\%}{EtO_2C\underset{CH_3}{C}HCH_2CO_2Et} + \underset{5\%}{EtO_2CCH{=}CHCH_3} \qquad (25)$$



$$CH_3(CH_2)_5CH{=}CH_2 + CO + EtOH \xrightarrow[LiCl]{Pd^{II}, Cu^{II}} \underset{10\%}{EtO_2C\underset{(CH_2)_5CH_3}{C}HCH_2CO_2Et} \qquad (26)$$

Water and acid inhibit the production of succinates while substantially increasing the yield of carbon dioxide, the chief by-product. Addition of small amounts of sodium acetate or pyridine increases succinate conversion slightly. The addition of water-scavenging trialkyl orthoformates increases the yield to greater than 90% in the case of ethylene. Succinic esters are also products from the carbonylation of olefins at higher temperatures and pressures in the presence of a $PdCl_2$/alanine/$NiCl_2$ catalytic system[130].

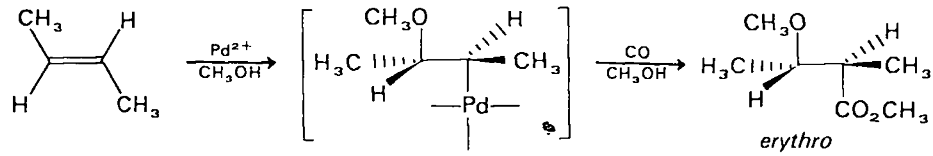
Olefin carbonylation reactions in methanol, utilizing catalytic amounts of $PdCl_2$ and stoichiometric quantities of a $CuCl_2$ reoxidant at room temperature and low carbon monoxide pressure, afford β-methoxy esters or succinic esters depending on the reaction conditions[51,58,131]. Carbonylation of both *cis*- and *trans*-2-butene demonstrates that, as reported for chelating diolefins[68,69], methoxypalladation occurs stereospecifically *trans*. In the initial stages of the reaction, the *threo*- and *erythro*-β-methoxy esters, **61** and **62** respectively, are the exclusive products (equations 27 and 28). In the latter stages of the reaction, as the reaction mixture



(27)

threo

(61)



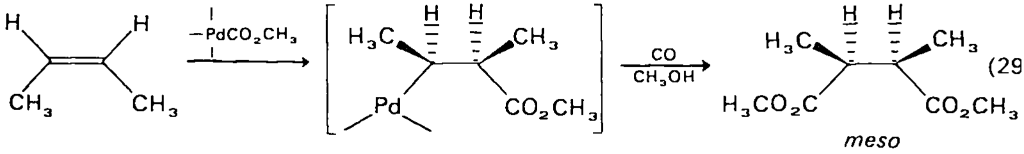
(28)

erythro

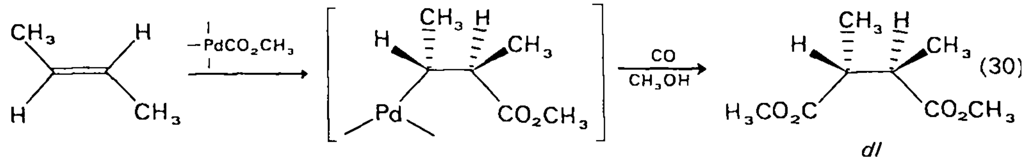
(62)

becomes more acidic, *cis–trans* isomerization of the 2-butenes becomes increasingly important such that *trans* methoxypalladation of the *cis–trans* mixture yields both *erythro* and *threo* products. The acid-catalysed *cis–trans* isomerization reaction reaches equilibrium at 80% *trans*–20% *cis* in each case.

The effect of added base to this system is quite remarkable in that the course of the reaction is completely changed. Equimolar amounts (based on copper(II)) of sodium acetate effectively eliminates methoxy ester production and *cis–trans* isomerization. Dimethyl succinates are the exclusive products. Based upon the stereochemistry of the diester products a *cis* carbomethoxypalladation mechanism has been proposed (equations 29 and 30). The sodium acetate may enhance the formation of the carbomethoxypalladium intermediate by base catalysis[126,127]. Also acetate


H
H
CH$_3$
CH$_3$
–PdCO$_2$CH$_3$
H$_3$C
CH$_3$
Pd
CO$_2$CH$_3$
CO
CH$_3$OH
H$_3$CO$_2$C
meso

(29


CH$_3$
H
–PdCO$_2$CH$_3$
Pd
CO$_2$CH$_3$
CO
CH$_3$OH
H$_3$CO$_2$C
dl

(30)

ion may be coordinated to palladium, thereby changing the structures of the intermediate complexes and thus their activity.

A faster rate of conversion of *cis*-2-butene to β-methoxy ester relative to *trans*-2-butene is consistent with a stereospecific *trans* methoxypalladation mechanism which requires formation of a more stable π-complex for the *cis* isomer[19] and greater relief of steric repulsion in the transition state for the *trans* addition to the *cis* olefin (Figure 7). The

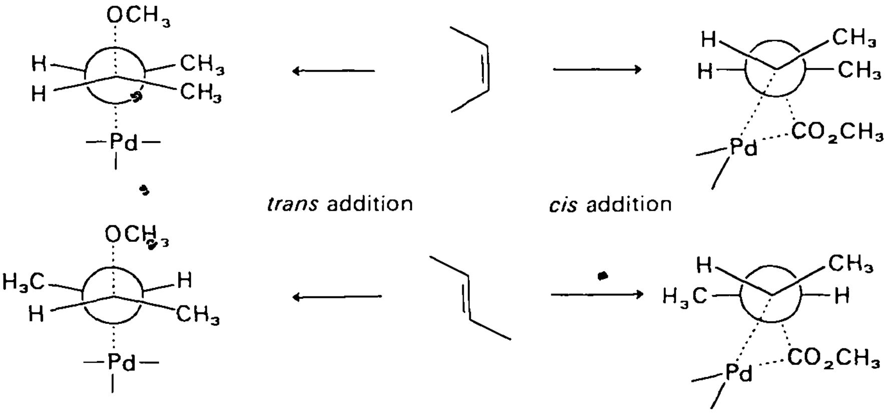
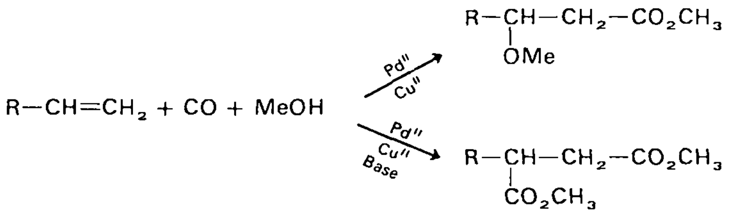

OCH$_3$
CH$_3$
H
–Pd–
trans addition
cis addition
H$_3$C
CO$_2$CH$_3$
Pd

FIGURE 7. Structures of methoxy- and carbomethoxypalladation transition states for *cis*- and *trans*-2-butene.

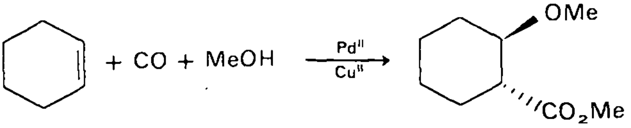
relative rates of diester formation are reversed, however, and *trans*-2-butene is more reactive than *cis*-2-butene. The rate of carbomethoxypalladation is slower for *cis*-2-butene because *cis* addition of coordinated carboxylate ligand and palladium requires greater steric crowding than that observed for the *trans* isomer (Figure 7).

The utility of this reaction has been established by the carbonylation of various cyclic and acyclic olefins[58,131]. While α-olefins are more reactive than the 2-butenes, analogous products, β-methoxy esters and diesters, are obtained (equation 31). Nearly quantitative yields (based on α-olefin) are realized when greater than equivalent amounts of copper(II) are added.



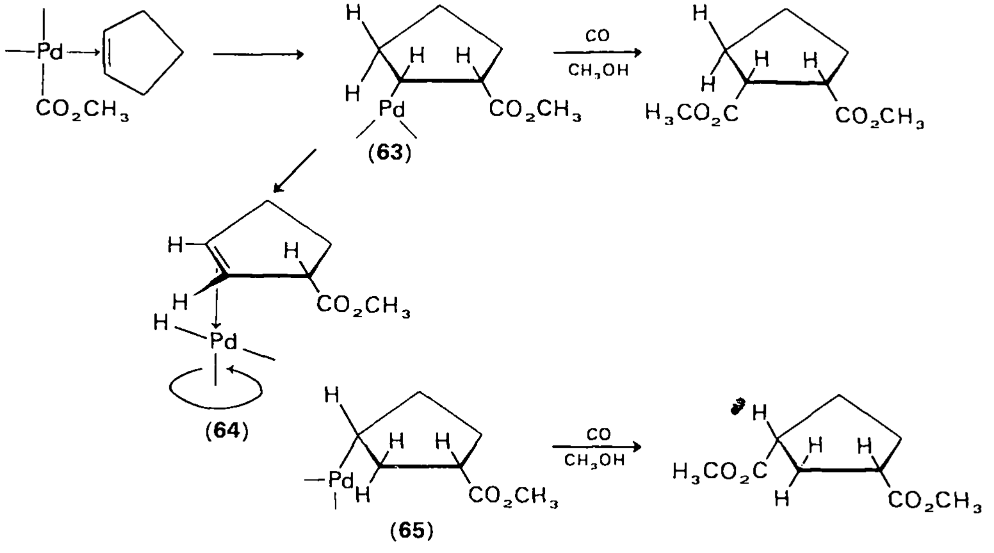
(31)

Carbonylation of cyclic olefins, however, either with or without added base, affords predominantly diester products. The exception is cyclohexene which gives a low yield (17%) of the *trans*-β-methoxy ester (**56**) in the absence of base (equation 32). In each case, the 1,2- and 1,3-cycloalkanedicarboxylic esters obtained are the *cis* isomers. Product distributions and relative rates of reaction are consistent with *cis* addition of a carbomethoxypalladium intermediate to a double bond where the rate of the reaction is determined by the magnitude of the internal strain of the olefin (Scheme 11). The isomerization reaction (**63** → **64** → **65**) can be suppressed and the ratio of the 1,2- to the 1,3-diester can be increased by increasing the carbon monoxide pressure, effectively trapping intermediate **63** before rearrangement can occur. The addition of base or increasing the basic strength of the reaction medium decreases the ratio of 1,2- to 1,3-diesters; palladium-catalysed straight chain olefin isomerization has been shown to require a basic co-catalyst[132].



(56)

(32)



SCHEME 11.

The reaction of 2-, 3-, and 4-methyl-1-pentene affords β-methoxy ester products consistent with Markownikoff methoxypalladation (Table 3)[131]. Steric hindrance to nucleophilic attack of methanol decreases as the methyl substituent becomes increasingly remote from the reactive olefinic carbons.

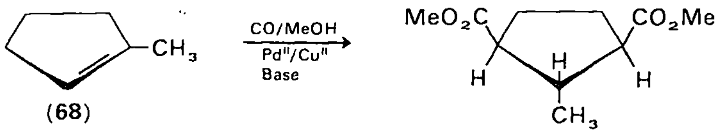
TABLE 3.[131] Carbonylation of methyl-substituted 1-olefins[a]

Olefin	Yield (%)	Product
2-Methyl-1-pentene	2	$CH_3CH_2CH_2C(CH_3)(OCH_3)CH_2CO_2CH_3$
3-Methyl-1-pentene	50	$CH_3CH_2CH(CH_3)CH(OCH_3)CH_2CO_2CH_3$
4-Methyl-1-pentene	57	$(CH_3)_2CHCH_2CH(OCH_3)CH_2CO_2CH_3$

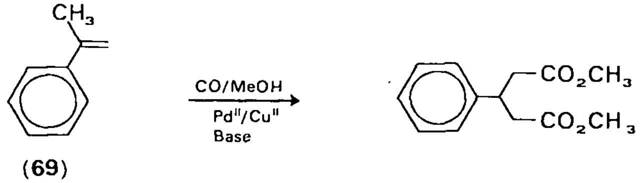
[a] Reaction conditions: 25 mmol olefin, 1·4 mmol $PdCl_2$, 50 mmol $CuCl_2$ and 37·5 ml of methanol at 3 atm carbon monoxide and room temperature.

The reaction of these isomeric olefins in basic media, however, gives several diesters as a result of rearrangement reactions (Table 4). The mechanism for the reaction of 3-methyl-1-pentene is illustrated in Scheme 12. The products and product ratios are consistent with the following observations:

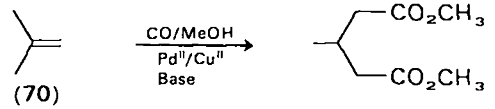
(i) The rate of the hydride abstraction rearrangement process is faster than the rate of carbonylation of a tertiary carbon σ-bonded to palladium. Therefore, no succinic ester product is obtained by reaction of 2-methyl-1-pentene, and carbonylation of intermediate **67** does not take place. Thus, dimethyl glutarates are the exclusive products upon carbonylation of the methyl-substituted olefins **68**, **69** and **70** (equations 33, 34 and 35).


CH3
(68)
CO/MeOH
Pd^{II}/Cu^{II}
Base
MeO2C
CO2Me
H
H
H
CH3

(33)


CH3
(69)
CO/MeOH
Pd^{II}/Cu^{II}
Base
CO2CH3
CO2CH3

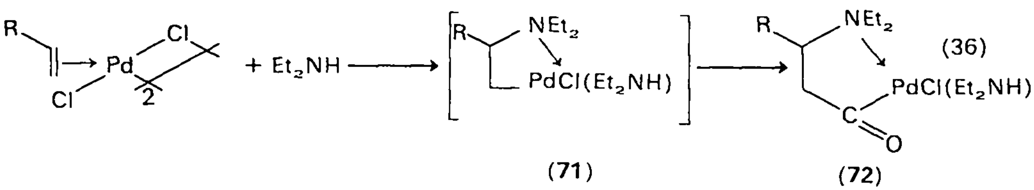
(34)


(70)
CO/MeOH
Pd^{II}/Cu^{II}
Base
CO2CH3
CO2CH3

(35)

(ii) Hydride abstraction from the most highly substituted carbon atom adjacent to a palladium–carbon σ-bond is favoured. Facile abstraction of a tertiary hydrogen is the driving force for palladium migration from the initial σ-bonded complex **66** and therefore accounts for the rearranged diesters from carbonylation of 3-methyl-1-pentene.

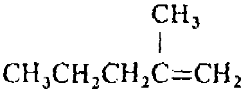
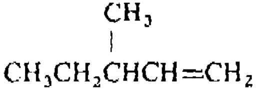
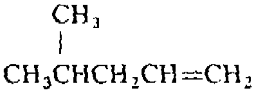
The reaction of olefin–palladium(II) complexes with amines gives unstable σ-bonded palladium complexes as a result of addition of the amine and palladium across the double bond^{59,93,133}. Treatment of **71**, however, with carbon monoxide yields a stable acylpalladium(II) complex **72**^{134} (equation 36). The stability of **72** is attributed to the chelating ability


R
Cl
Pd
Cl
2
+ Et2NH
R
NEt2
PdCl(Et2NH)
(71)
R
NEt2
PdCl(Et2NH)
C
O
(72)

(36)

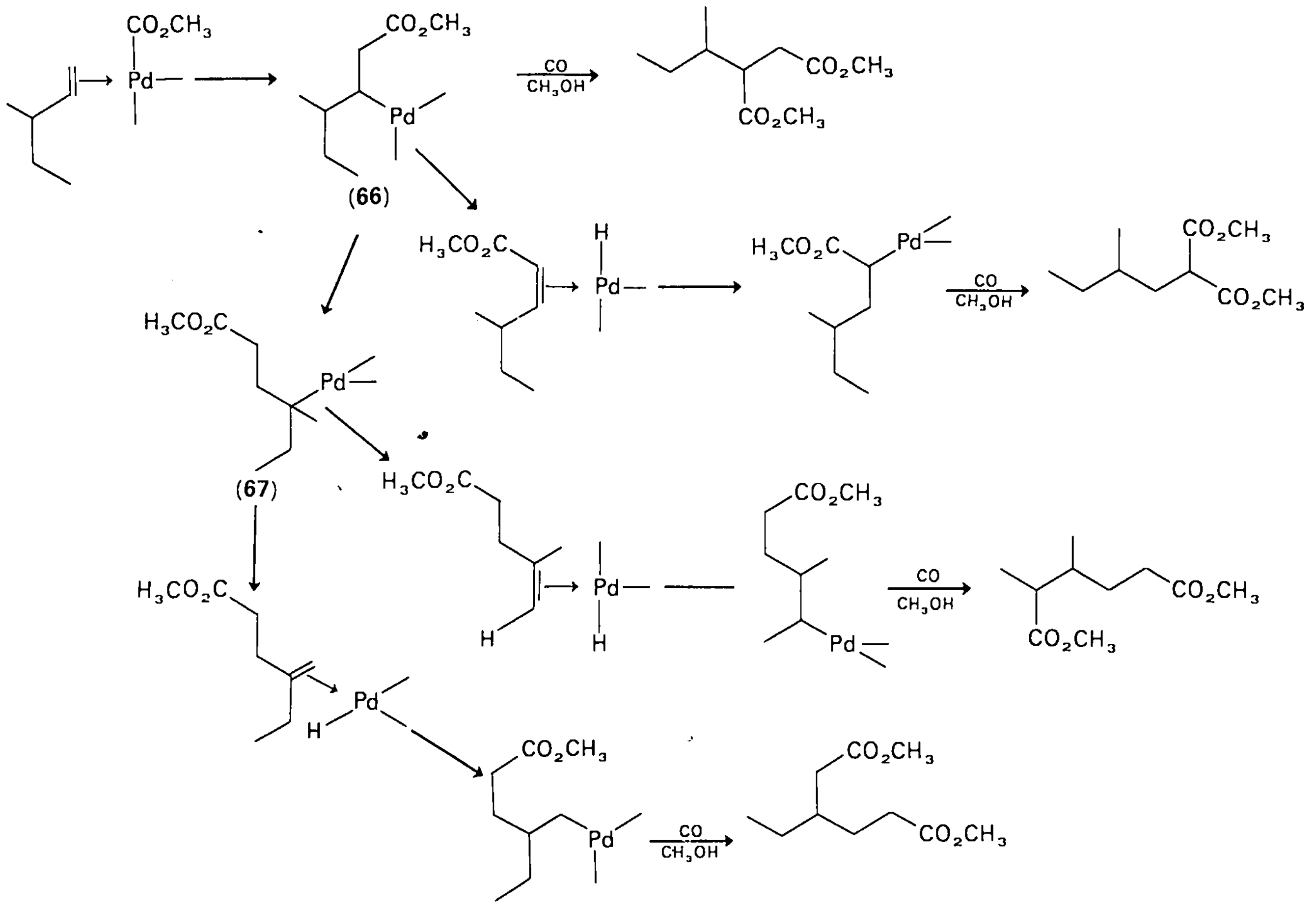
of the acyl-amino ligand and the ring size of the metallocycle.

TABLE 4[131]. Carbonylation of isomeric 1-olefins in the presence of base[a]

Olefin	Yield (%)	Product	(Ratio)
 $CH_3CH_2CH_2\overset{\overset{\displaystyle CH_3}{\vert}}{C}{=}CH_2$	37	$CH_3CH_2CH(CO_2CH_3)CH(CH_3)CH_2CO_3CH^b$ $CH_3CH(CO_2CH_3)CH_2CH(CH_3)CH_2CO_2CH_3{}^b$ $CH_3CH_2CH_2CH(CH_2CO_2CH_3)CH_2CO_2CH_3$ $CH_3CH_2CH_2CH(CH_3)CH(CO_2CH_3)_2$ $CH_3CH_2CH_2C(CH_3){=}CHCO_2CH_3$	(5) (3) (2) (1) (1)
 $CH_3CH_2\overset{\overset{\displaystyle CH_3}{\vert}}{C}HCH{=}CH_2$	39	$CH_3CH_2CH(CH_3)CH(CO_2CH_3)CH_2CO_2CH_3{}^b$ $CH_3CH(CO_2CH_3)CH(CH_3)CH_2CH_2CO_2CH_3{}^b$ $CH_3CH_2CH(CH_2CO_2CH_3)CH_2CH_2CO_2CH_3$ $CH_3CH_2CH(CH_3)CH_2CH(CO_2CH_3)_2$ $CH_3CH_2CH(CH_3)CH{=}CHCO_2CH_3$	(14) (10) (3) (1) (2)
 $CH_3\overset{\overset{\displaystyle CH_3}{\vert}}{C}HCH_2CH{=}CH_2$	69	$CH_3CH(CH_3)CH_2CH(CO_2CH_3)CH_2CO_2CH_3$	

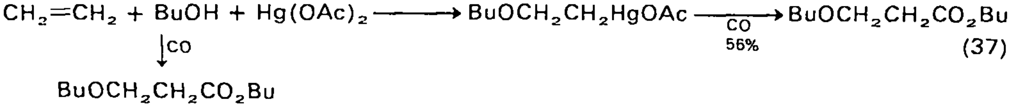
[a] Reaction conditions: 25 mmol olefin, 1·4 mmol $PdCl_2$, 100 mmol $CuCl_2$, 100 mmol NaOAc and 75 ml methanol at 3 atm carbon monoxide pressure and room temperature.

[b] Diastereomeric mixture.


CO_2CH_3
Pd
(66)
CO
CH_3OH
H_3CO_2C
H
(67)

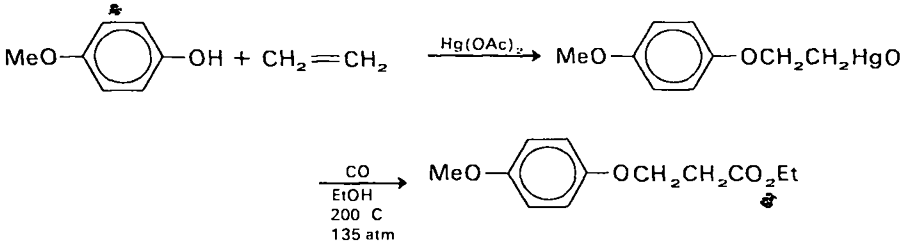
SCHEME 12.

The carbonylation of products obtained from the alkoxymercuration of olefins also gives β-alkoxy esters. The reaction of ethylene with various aliphatic alcohols[135] generates a σ-bonded alkylmercurial which reacts with carbon monoxide at 100 atm and 200°C to yield the appropriate β-alkoxy ester (equation 37). The one-step carbonylation of ethylene in alcohol in the presence of the mercury salt affords low yields of alkoxy ester, however, because of preferential formation of carboalkoxymercury complexes which are unreactive toward the olefin. Carbonylation of 4-substituted phenoxymercuration derivatives of ethylene gives a low yield of ester[136] (equation 38).



$$\begin{tikzcd} CH_2{=}CH_2 + BuOH + Hg(OAc)_2 \arrow[r] \arrow[d, "CO"] & BuOCH_2CH_2HgOAc \arrow[r, "CO"', "56\%"'] & BuOCH_2CH_2CO_2Bu \\ BuOCH_2CH_2CO_2Bu & & \end{tikzcd}$$

(37)

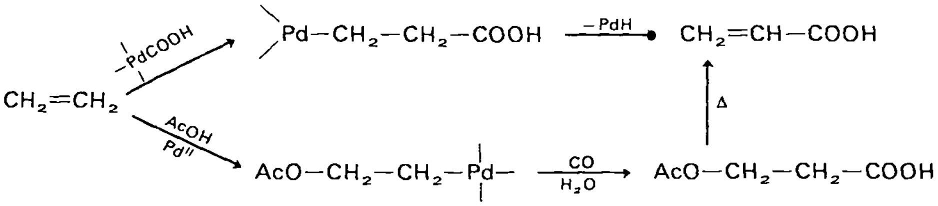


(38)

Ethylene has similarly been carbonylated in methanol at high temperatures and pressures in the presence of $CuCl_2$ to afford methyl 3-methoxypropionate and varying amounts of 1-chloro-2-methoxyethane and 1,2-dichloroethane[173] (equation 39). The yields of β-methoxy ester are 30–60 % based on copper, and optimum conditions are achieved at 170 °C with a CO/C_2H_4 ratio of 1·56. Copper(II) is reduced to copper(I) and copper(0) during the course of the reaction.

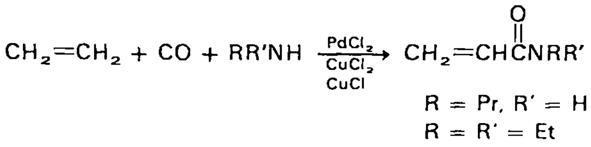
$$CH_2{=}CH_2 + CO + MeOH \xrightarrow{CuCl_2} MeOCH_2CH_2CO_2Me + ClCH_2CH_2OMe + ClCH_2CH_2Cl \qquad (39)$$

The synthesis of acrylic acid and its derivatives by the carbonylation of olefins in acetic acid is a potential industrial process[138,139]. The catalyst system frequently employed is palladium(II) chloride and a copper(II) or iron(III) chloride reoxidant[140–149], although other catalysts have been developed[150–152]. The reaction of ethylene affords two products, acrylic acid and β-acetoxypropionic acid, which can be pyrolysed to acrylic acid. The unsaturated acid is formed by the addition of a carboxypalladium intermediate to the olefin followed by β-hydride elimination[138] (Scheme 13). Yields and product ratios are very sensitive to reaction conditions such as temperature, pressure, solvent systems, catalyst ratios, added drying agents, etc.[138].



SCHEME 13.

Acrylic esters may be obtained from the reaction of olefins in alcohol[150,153] or aldehyde[154] solvents. Carbonylation of ethylene in the presence of amines produces acrylamides[155] (equation 40).



$$CH_2{=}CH_2 + CO + RR'NH \xrightarrow[CuCl_2,\ CuCl]{PdCl_2} CH_2{=}CH\overset{\overset{O}{\|}}{C}NRR' \qquad (40)$$

$R = Pr, R' = H$
$R = R' = Et$

IV. HYDROCARBONYLATION

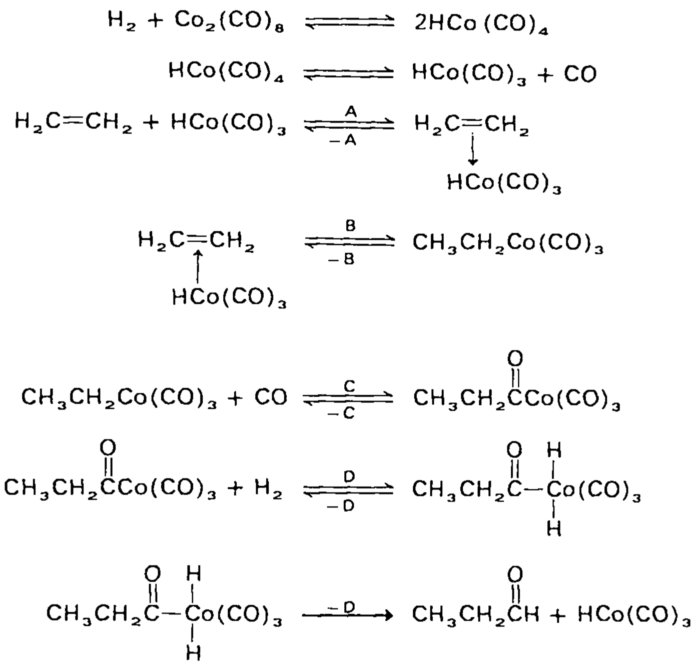
A. Hydroformylation

1. Introduction

The 'oxo' or hydroformylation reaction, the details of which were first disclosed in 1948[156], involves the reaction of an olefin, carbon monoxide, and hydrogen in the presence of a cobalt carbonyl catalyst to produce aldehydes. This was the first homogeneous, transition metal catalysed reaction to become commercially important and thereby provided impetus to the rapid development of the field of homogeneous catalysis. Thus, hydroformylation has been the subject of frequent reviews[157-167], and therefore, only a brief summary of the salient features of this important reaction will be considered in this section.

2. Mechanism and catalysts

The generally accepted mechanism[158,166] of the 'oxo' reaction for the production of aldehydes involves the following organometallic transformations as shown for ethylene (see Section II).



$$H_2 + Co_2(CO)_8 \rightleftharpoons 2HCo(CO)_4$$

$$HCo(CO)_4 \rightleftharpoons HCo(CO)_3 + CO$$

$$H_2C{=}CH_2 + HCo(CO)_3 \underset{-A}{\overset{A}{\rightleftharpoons}} \begin{matrix} H_2C{=}CH_2 \\ \downarrow \\ HCo(CO)_3 \end{matrix}$$

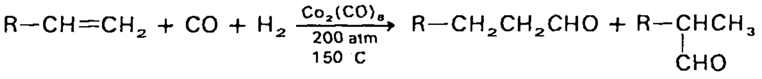
$$\begin{matrix} H_2C{=}CH_2 \\ \uparrow \\ HCo(CO)_3 \end{matrix} \underset{-B}{\overset{B}{\rightleftharpoons}} CH_3CH_2Co(CO)_3$$

$$CH_3CH_2Co(CO)_3 + CO \underset{-C}{\overset{C}{\rightleftharpoons}} CH_3CH_2\overset{\overset{O}{\|}}{C}Co(CO)_3$$

$$CH_3CH_2\overset{\overset{O}{\|}}{C}Co(CO)_3 + H_2 \underset{-D}{\overset{D}{\rightleftharpoons}} CH_3CH_2\overset{\overset{O}{\|}}{C}{-}\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}o(CO)_3$$

$$CH_3CH_2\overset{\overset{O}{\|}}{C}{-}\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}o(CO)_3 \xrightarrow{-D} CH_3CH_2\overset{\overset{O}{\|}}{C}H + HCo(CO)_3$$

The hydroformylation of terminal olefins yields predominantly two aldehyde products (equation 41) and small amounts of products of internal rearrangement. Recently, a mechanism for the hydroformylation



$$R{-}CH{=}CH_2 + CO + H_2 \xrightarrow[\substack{200\ \text{atm} \\ 150\ \text{C}}]{Co_2(CO)_8} R{-}CH_2CH_2CHO + R{-}\underset{\underset{CHO}{|}}{C}HCH_3 \qquad (41)$$

of olefins in the presence of stoichiometric quantities of $HCo(CO)_4$ has been proposed[166] which accounts for the direction of addition and the distribution of products observed for this reaction (Figure 8). The first step of the reaction, π-complexation is followed by reversible metal hydride addition. The anti-Markownikoff addition (73 → 74) is favoured for steric reasons but significant amounts of the Markownikoff addition product (73 → 75) can be formed. When the nucleophilic group is considerably larger than hydride, anti-Markownikoff addition may occur

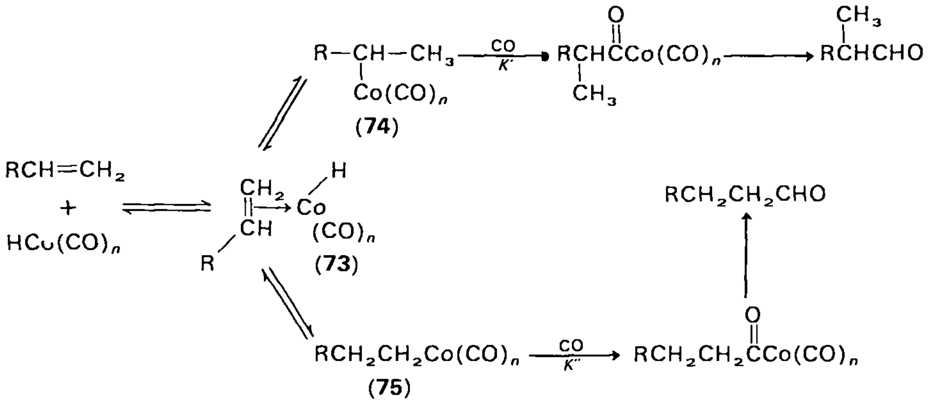


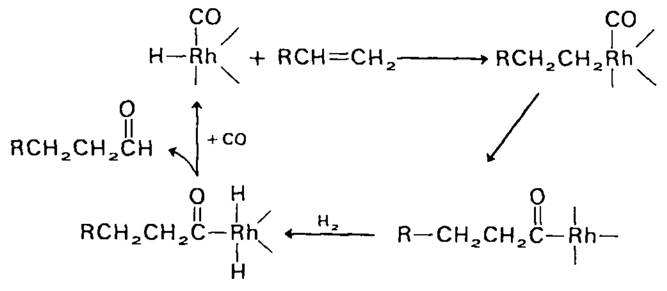
FIGURE 8. Stoichiometric hydroformylation mechanism.

exclusively[54]. The rate of the subsequent step, carbon monoxide insertion into the alkyl–metal bond, might be expected for steric reasons to decrease with alkyl substitution on the carbon bearing the palladium in the order primary > secondary > tertiary (i.e., $K'' > K'$). Any condition which alters the isomerization equilibrium (**74** $\rightleftharpoons$ **73** $\rightleftharpoons$ **75**) or the relative rates of carbonylation (K' vs. K'') influences the isomer ratios.

Catalysts other than $Co_2(CO)_8$ have been developed for the hydroformylation reaction in efforts to obtain systems which produce predominantly *n*-isomers and proceed under less vigorous conditions. Cobalt carbonyl catalysts modified by organophosphine ligands increase the catalytic activity of the metal at reduced temperatures and pressures, and the products from these reactions are generally *n*-alcohols[168–172]. The addition of the phosphine ligands increase the hydrogenation activity of the catalyst while the larger steric requirements of the bulky phosphine ligands(s) increases K'' with respect to K' accounting for the preferred production of *n*-alcohols.

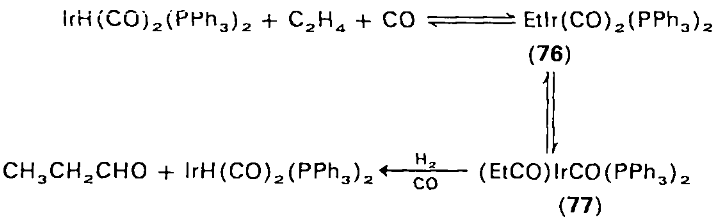
A variety of rhodium carbonyl[173–175] and phosphine[176–185] complexes are also hydroformylation catalysts. The reaction conditions are typically mild, (90–110°C and 10–50 atm) and high selectivity to *n*-aldehydes is observed. The mechanism of the $HRh(CO)_2(PPh_3)_2$-catalysed olefin hydroformylation is similar to the cobalt-catalysed reaction, involving the sequential rhodium hydride addition, carbonyl insertion, and hydrogenolysis steps (Scheme 14)[181,186].

Iridium complexes generally exhibit lower reaction rate and increased olefin hydrogenation as compared to corresponding rhodium and cobalt systems[187]. In a study of the reaction of $IrH(CO)_2(PPh_3)_2$ with carbon



SCHEME 14.

monoxide and ethylene, intermediates **76** and **77** were isolated[188] (Scheme 15). The hydrogenation of acyl complex **77** occurs slowly and is inhibited



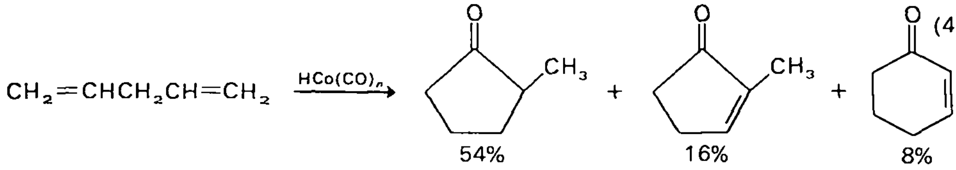
SCHEME 15.

by high carbon monoxide pressure, indicating that oxidative addition of hydrogen occurs after dissociation of a carbonyl ligand. The reaction **76** → **77** is favoured at low temperatures and at high ethylene concentrations. The alkyl–acyl rearrangement is therefore promoted by the coordination of another ligand.

In addition, iron[139-191] and ruthenium[192-194] derivatives are hydroformylation catalysts. Hydroformylation by heterogeneous catalysis has been carried out in which either vapour phase or liquid phase reactions are employed in the presence of transition metal catalysts bound to polymer backbones[195-197] or deposited upon solid supports[198-201].

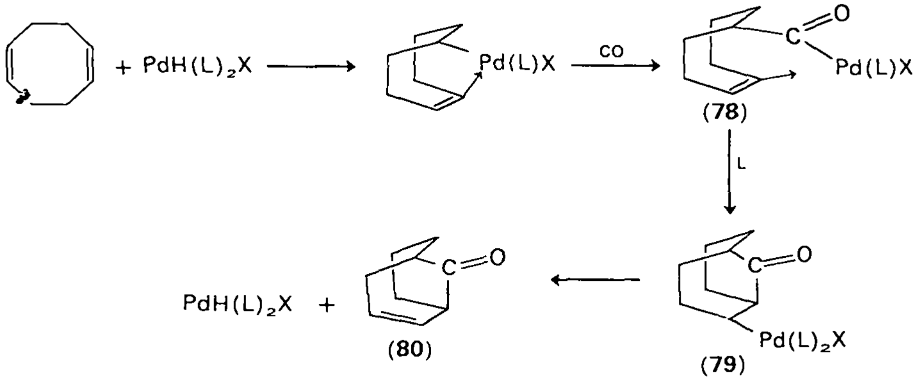
3. Carbonylation with hydroformylation catalysts

The hydroformylation reaction may also be used to synthesize carbonyl compounds other than aldehydes. Hydroformylation of ethylene in the presence of cobalt carbonyl catalysts produces ketones as the major products[202]. 2-Pentanone is synthesized from ethylene and carbon monoxide at high temperatures and pressures utilizing cobalt[203], rhodium[204], and palladium[205] catalysts. Hydrocarbonylation of linear diolefins yields cyclic ketones[206,207] (equation 42). Similarly, the hydro-


CH₂=CHCH₂CH=CH₂
HCo(CO)ₙ
CH₃
CH₃
54%
16%
8%

(42)

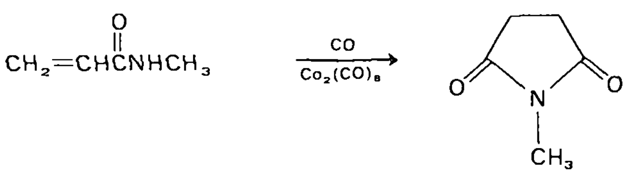
carbonylation of 1,5-cyclooctadiene in the presence of a palladium phosphine catalyst gives the bicyclic ketone **83**[208,209] (Scheme 16).


+ PdH(L)₂X
Pd(L)X
CO
Pd(L)X
(78)
L
PdH(L)₂X +
(80)
Pd(L)₂X
(79)

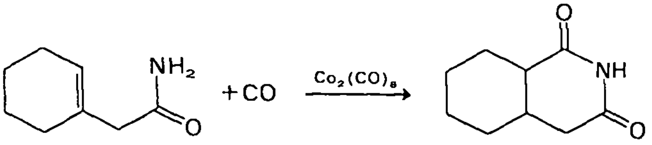
SCHEME 16.

The proposed mechanism requires palladium hydride addition followed by carbon monoxide insertion to produce the acyl complex **78**. Subsequent *cis* addition of the acylpalladium intermediate to the remaining double bond, followed by palladium hydride elimination from the resulting alkyl complex **79**, yields **80**.

When the reacting olefin contains an appropriate nucleophilic substituent, intramolecular lysis of the metal–acyl bond may occur to produce cyclic carboxylic acid derivatives. The hydroformylation of α,β-unsaturated amides takes place with cyclization, as illustrated by the reaction of *N*-methylacrylamide[210] (equation 43). Bicyclic imides are also prepared in this manner[211] (equation 44).

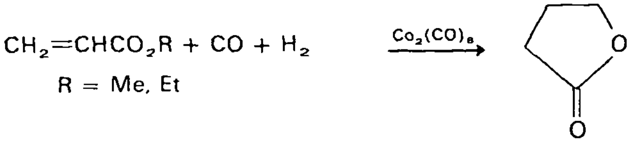

CH₂=CHCNHCH₃
CO
Co₂(CO)₈
O
N
O
CH₃

(43)


NH2
+CO
Co2(CO)8
NH
O
O
O

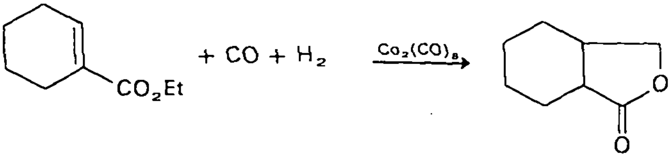
(44)

Unsaturated esters react under hydroformylation conditions to give lactones[212] (equation 45, 46). The mechanism for the formation of cyclic


CH2=CHCO2R + CO + H2
R = Me, Et
Co2(CO)8
O
O

69–88%

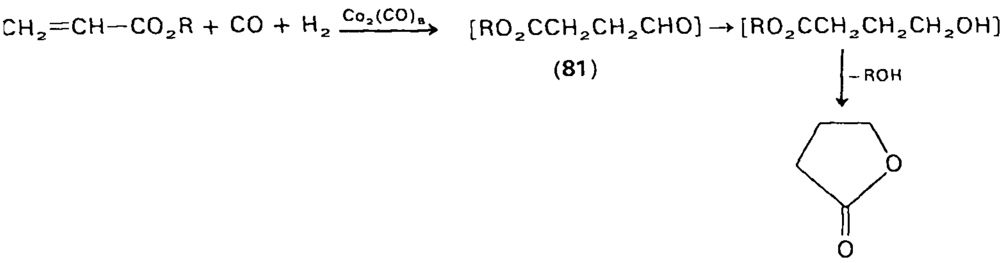
(45)


+ CO + H2
CO2Et
Co2(CO)8
O
O

23%

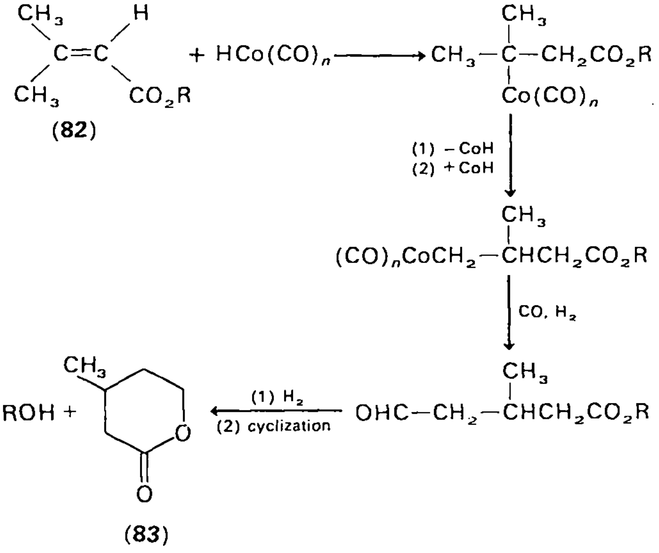
(46)

esters requires initial hydroformylation of the olefinic group to yield the 3-formyl ester **81**, which undergoes hydrogenation followed by transesterification to the lactone (Scheme 17).


CH2=CH—CO2R + CO + H2
Co2(CO)8
[RO2CCH2CH2CHO]
[RO2CCH2CH2CH2OH]
(81)
−ROH
O
O

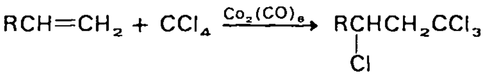
SCHEME 17.

The reaction of methyl 3-methyl-2-butenoate (**82**) does not afford a γ-lactone product, however, since this transformation would require carbonylation of a tertiary carbon. Instead, rearrangement is observed and δ-valerolactone (**83**) is the major product (Scheme 18).



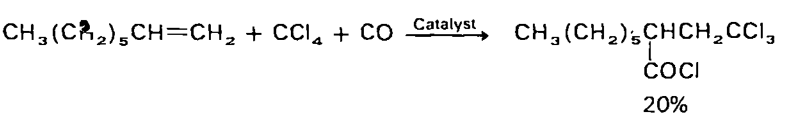
SCHEME 18.

The reaction of carbon tetrachloride and an olefin in the presence of $Co_2(CO)_8$ at 160–180 °C takes place by the addition of the elements of Cl and CCl_3 across the double bond[213] (equation 47). When the reaction

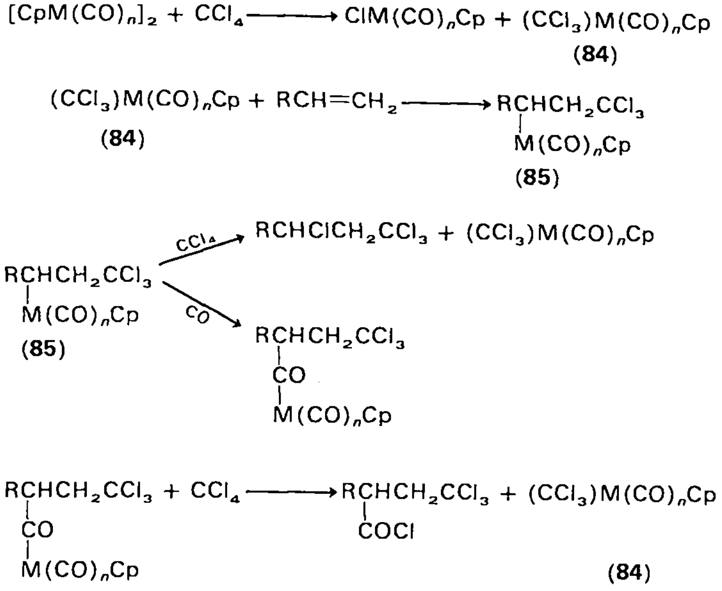


$$RCH{=}CH_2 + CCl_4 \xrightarrow{Co_2(CO)_8} RCH(Cl)CH_2CCl_3 \qquad (47)$$

is carried out using $Co_2(CO)_8$, $[CpFe(CO)_2]_2$ or $[CpMo(CO_3]_2$ (Cp = cyclopentadiene) and carbon monoxide, β-trichloromethyl acid chlorides are the major products (equation 48). Selective formation of the anti-Markownikoff addition product and lack of inhibition by radical scavengers support the mechanism requiring the addition of $Cl_3C{-}M$ to the double bond (Scheme 19). The reaction of CCl_4 with the dinuclear carbonyl catalyst generates the active trichloromethyl complex **84** which undergoes anti-Markownikoff addition across the olefin to generate the



$$CH_3(CH_2)_5CH{=}CH_2 + CCl_4 + CO \xrightarrow{\text{Catalyst}} \underset{20\%}{CH_3(CH_2)_5CH(COCl)CH_2CCl_3} \qquad (48)$$



$$[CpM(CO)_n]_2 + CCl_4 \longrightarrow ClM(CO)_nCp + \underset{(84)}{(CCl_3)M(CO)_nCp}$$

$$\underset{(84)}{(CCl_3)M(CO)_nCp} + RCH{=}CH_2 \longrightarrow \underset{(85)}{R\underset{M(CO)_nCp}{\underset{|}{C}}HCH_2CCl_3}$$

$$\underset{(85)}{R\underset{M(CO)_nCp}{\underset{|}{C}}HCH_2CCl_3} \xrightarrow{CCl_4} RCHClCH_2CCl_3 + (CCl_3)M(CO)_nCp$$

$$\underset{(85)}{R\underset{M(CO)_nCp}{\underset{|}{C}}HCH_2CCl_3} \xrightarrow{CO} R\underset{\underset{M(CO)_nCp}{\underset{|}{CO}}}{\underset{|}{C}}HCH_2CCl_3$$

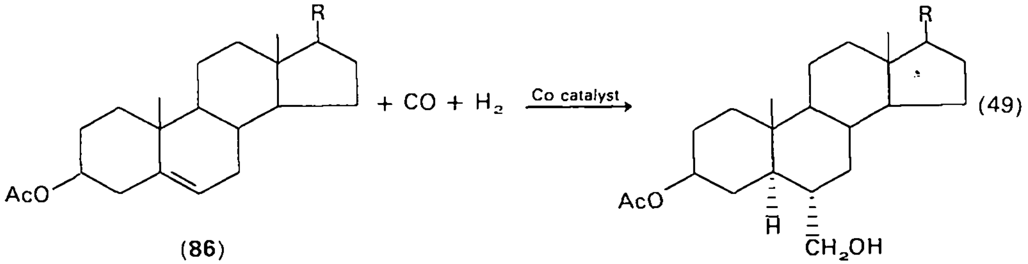
$$R\underset{\underset{M(CO)_nCp}{\underset{|}{CO}}}{\underset{|}{C}}HCH_2CCl_3 + CCl_4 \longrightarrow R\underset{COCl}{\underset{|}{C}}HCH_2CCl_3 + \underset{(84)}{(CCl_3)M(CO)_nCp}$$

SCHEME 19.

alkyl complex **85**. Reaction of **85** with either CCl_4 or CO followed by CCl_4 affords β-trichloromethyl chloride or acyl chloride, respectively, with regeneration of the active complex **84**.

4. Stereochemistry and asymmetric induction

The stereochemistry of addition of H and CO across the double bond of an olefin is *cis* for both cobalt[214-217] and rhodium[53] catalysts. Hydroformylation of steroids **86a** and **b** stereospecifically produces the *cis* addition hydroxymethyl derivatives **87a** and **b**, respectively, in the presence of a cobalt catalyst[214,215] (equation 49). Similarly, *cis* deutero-

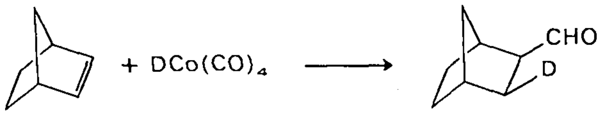


(86)

a: R = —C*H(OH)CH₃
b: R = —COR

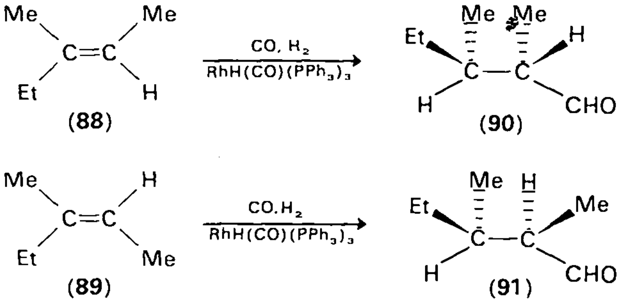
(87a and b)

formylation of norbornene takes place exclusively[217] (equation 50).



(50)

Cis hydroformylation of (*E*)-(**88**)- and (*Z*)-3-methyl-2-pentene (**89**) in the presence of the rhodium catalyst, $RhH(CO)(PPh_3)_3$, affords *threo*-(**90**)- and *erythro*-2,3-dimethylpentanal (**91**) respectively[53] (equation 51).

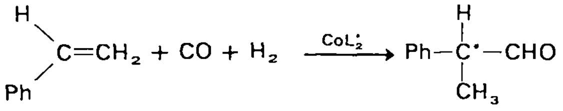


(**88**) (**90**) (**89**) (**91**)

(51)

Thus, initial *cis* addition of the metal hydride complex to the olefin followed by carbon monoxide insertion with retention of configuration at carbon takes place. It is this high stereochemical selectivity in hydroformylation that is the key to asymmetric induction when these reactions are catalysed by transition metals containing chiral ligands. Most asymmetric syntheses utilizing organo-transition metal complexes containing chiral ligands have involved hydrogenation of carbon–carbon double bonds and carbonyl functions[218–223]. The method has been applied to olefin carbonylation reactions only sparingly, however.

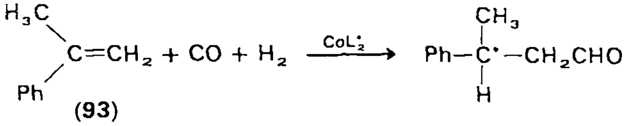
In the first reported syntheses employing this technique[224,225], the hydroformylation of styrene (**92**) and α-methylstyrene (**93**) in the presence of $CoL^*_2[L^* =$ (*S*)-(+)-α-methylbenzylsalicylaldimine (**94**)] afforded (*S*)-2-phenylpropanal and (*S*)-3-phenylbutanal in 0·1–2·9% optical purity (equations 52, 53). Hydroformylation of **92** and **93** catalysed by $Co_2(CO)_8$ in the presence of **94** produced equally low optical yields.



$$\text{H(Ph)C=CH}_2 + \text{CO} + \text{H}_2 \xrightarrow{\text{CoL}^*_2} \text{Ph—C}^*\text{H(CH}_3\text{)—CHO}$$

(**92**)

(52)

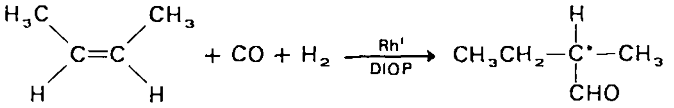

(93)

(53)

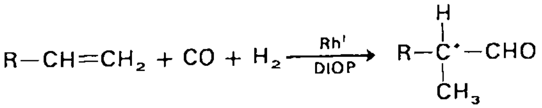
In the presence of RhCl(CO)L*[L* = neomenthylphenylphosphine (**95**)] hydroformylations of styrene, α-ethylstyrene, and phenyl vinyl ether give low optical yields (0·3–2·4%) of aldehydes[226]. Optically active 2-phenylpropanal ([α] = 38·5°), however, is prepared by the reaction of styrene with carbon monoxide and hydrogen in the presence of μ-dichlorobis-(1,5-hexadiene)rhodium(I) and optically active (+)-bensylmethylphenylphosphine (**96**) [metal to ligand ratio = 1 : 10] at 140 °C and 100 atm[227,228] (Figure 9).

Relatively higher optical yields have been obtained with the chelating chiral diphosphine ligand, (−)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane [DIOP][229,230] (**97**). Hydroformylation of styrene in the presence of a rhodium catalyst RhCl(CO)(DIOP) at 70 °C produces (*S*)-2-phenylpropanal in an optical yield of 9%[231]. The same reaction in the presence of a five-fold excess of **97** (relative to the rhodium complex) affords the aldehyde in 16% optical purity.

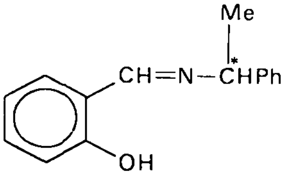
Styrene hydroformylation using $RhH(CO)(PPh_3)_3$ as a catalyst in the presence of **97** (DIOP/Rh complex = 4) produces (*R*)-2-phenylpropanal in 25·2% optical purity[232]. Hydroformylation of *cis*-2-butene at 20°C with this catalyst gives (*S*)-2-methylbutanal in an optical yield of 27% (equation 54), while (*R*)-2-methylpentanal and (*R*)-2-methylbutanal are


(54)

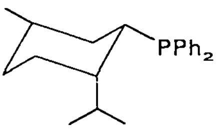
obtained in 19·7% and 18·8% optical purity, respectively, from hydroformylation of 1-pentene and 1-butene at 25°C (equation 55)[233].


$$R{-}CH{=}CH_2 + CO + H_2 \xrightarrow[\text{DIOP}]{\text{Rh}^{\text{I}}} R{-}\overset{H}{\underset{CH_3}{C^{*}}}{-}CHO \qquad (55)$$

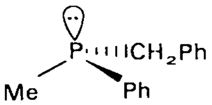
R = Et, Pr



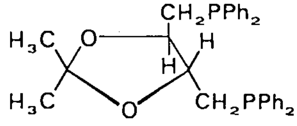
(94)



(95)



(96)



(97)

FIGURE 9. Structures of chiral ligands.

B. Hydrocarbonylation in Protic Solvents

Carbonylation of olefins occurs in the presence of transition metal carbonyl complexes in aprotic solvents with the addition of a hydrogen atom and a formyl group (—CHO) across the double bond (hydroformylation). In protic solvents, such as water or alcohols, the carbonyl group is added rather as a carboxylic acid derivative and the carbonylation of olefins and acetylenes affords aliphatic and acrylic acids[160]. Hydrocarbonylation of long-chain terminal olefins is therefore a method of catalytic synthesis of straight-chain fatty acids. As in the case of hydroformylation, an important consideration (Figure 8) is the direction of addition across the double bond and an important goal of research in this area has been to develop catalytic systems which generate linear products.

Predominantly linear esters are obtained from the $Co_2(CO)_8$ catalysed carbonylation of α-olefins in alcohols in the presence of heterocyclic nitrogen bases[234] (Figure 10). The base reportedly increases the rate of carbonylation and the yields by accelerating alcoholysis of the acylcobalt complexes[235–237]. The structure of the alcohol employed is of particular importance since increasing its length increases the relative amount of linear ester. This suggests that the alcohol is a ligand in these transformations and K'' increases with respect to K' (see Figure 8) as the steric demands of ROH increase.

$$\mathrm{CH_3(CH_2)_5CH{=}CH_2 + CO + ROH}$$

$$\mathrm{Co_2(CO)_8}\Big\downarrow\begin{array}{l}170\,^{\circ}\mathrm{C}\\ 200\ \mathrm{atm}\\ \text{Pyridine}\end{array}$$

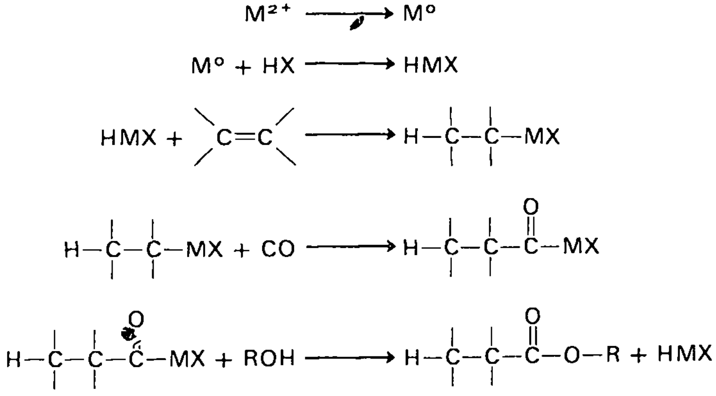
	R = Methyl	R = Ethyl	R = Octyl
% R nonanoate	61·8	82·4	>95
% R α-methyloctanoate	20·1	14·3	—
% R α-ethylheptanoate	9·5	0·8	—
% R α-propylhexanoate	8·6	2·5	—

FIGURE 10. Carbonylation of 1-octene.

The hydrocarbonylation of olefins in methanol with the cobalt salt of a carboxylic acid, cobalt octanoate, and pyridine (base) demonstrates the importance of steric effects in the direction of addition[238]. With these reagents, reaction of 1-decene produces exclusively methyl undecanoate in 80% yield (equation 56). The catalyst is recovered as cobalt undecanoate.

$$\mathrm{CH_3(CH_2)_7CH{=}CH_2 + CO + MeOH} \xrightarrow[\substack{\text{Pyridine}\\ 160\,^{\circ}\mathrm{C},\ 150\ \mathrm{atm}}]{\mathrm{Co[O_2C(CH_2)_6CH_3]_n}} \mathrm{CH_3(CH_2)_8CH_2CO_2Me} \tag{56}$$

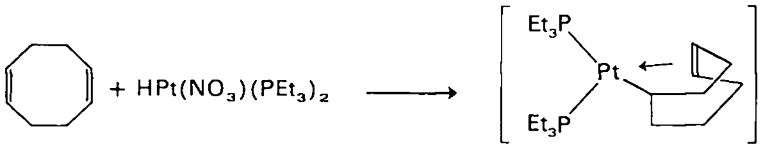
Palladium(II) and platinum(II) phosphine complexes are also active catalysts for olefin hydrocarbonylation reactions and generally give high linear/branched isomer ratios. The proposed reaction mechanism for these transformations[239] requires reduction of the divalent metal under the reaction conditions to the zerovalent state followed by addition of HX to give a hydride complex. Addition of the metal hydride to the olefin, carbonyl insertion, and solvolysis regenerating metal hydride completes the catalytic cycle (Scheme 20).



SCHEME 20.

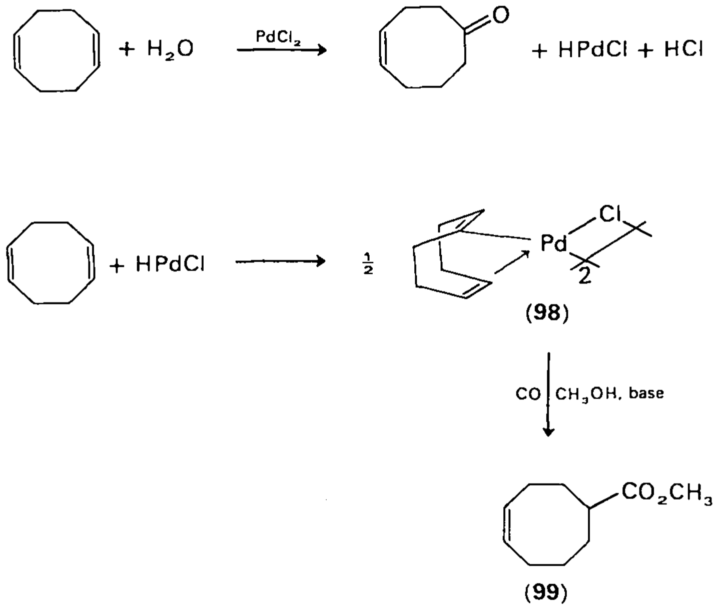
The chemistry of transition metal hydride complexes has been reviewed recently[240,241]. Isolable hydride complexes have been shown to react with olefins to form alkyl complexes[242,243] (equation 57, 58). Recently,

$$CH_2{=}CH_2 + HPtCl(PEt_3)_2 \rightarrow CH_3CH_2PtCl(PEt_3)_2 \qquad (57)$$



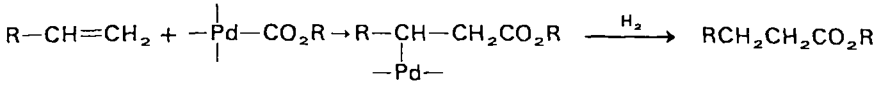
(58)

the dimeric σ-bonded enyl complex **98** was isolated from the reaction of 1,5-cyclooctadiene and $PdCl_2$ in water[73] (Scheme 21). The Wacker oxidation of the diolefin generates Pd^0 and hydrogen chloride (effectively, HPdCl) which reacts with another molecule of cyclooctadiene to form the hydride addition complex. Carbonylation of **98** yields methyl 4-cyclooctenecarboxylate (**99**).



Scheme 21.

Although the metal hydride addition mechanism is well documented, two independent studies of hydrocarbonylation reactions catalysed by palladium–phosphine complexes have indicated that a second mechanism is operative[244,245]. This mechanism involves the initial addition of a carboxy- or carboalkoxypalladium intermediate followed by hydrogenolysis of the β-carboxy- or β-carboalkoxypalladium σ-bonded complex (Scheme 22). The mechanism, however, predicts the exclusive formation



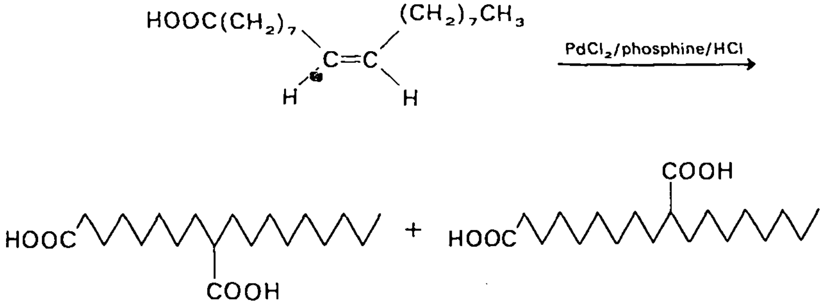
$$\mathrm{R{-}CH{=}CH_2} + -\underset{|}{\overset{|}{\mathrm{Pd}}}-\mathrm{CO_2R} \rightarrow \mathrm{R}-\underset{-\mathrm{Pd}-}{\underset{|}{\mathrm{C}}}\mathrm{H}-\mathrm{CH_2CO_2R} \xrightarrow{H_2} \mathrm{RCH_2CH_2CO_2R}$$

SCHEME 22.

of linear acids and esters on the basis of the steric requirements of the addition reaction. Since the direction of addition in these reactions is not exclusive, this mechanistic pathway cannot be considered to be the only one.

Hydrocarbonylation of olefins utilizing a $\mathrm{Pt^{II}/Sn^{II}}$ catalytic system, in which a $\mathrm{Pt{-}SnCl_3}$ binuclear complex was postulated to be the active catalyst, gives good yields of predominantly linear acids and esters[246]. Other palladium and platinum phosphine[247] and bimetallic[248-251] complexes have been developed which give high yields of α-acids and esters. Iridium phosphine catalyst systems have also been investigated[252-254].

Hydrocarbonylation of oleic acid to 9-(**100**)- and 10-carboxystearic acid (**101**) has been carried out in the presence of a $\mathrm{PdCl_2}$/phosphine/HCl catalyst system[255] (equation 59). C_{15} to C_{18} α-olefins can be carbonylated

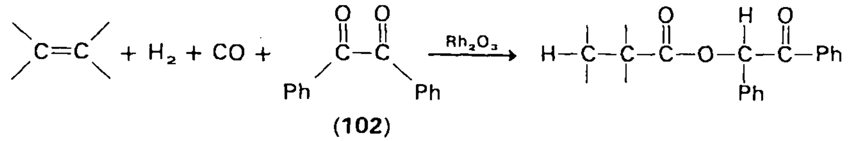


(59)

(**100**) (**101**)

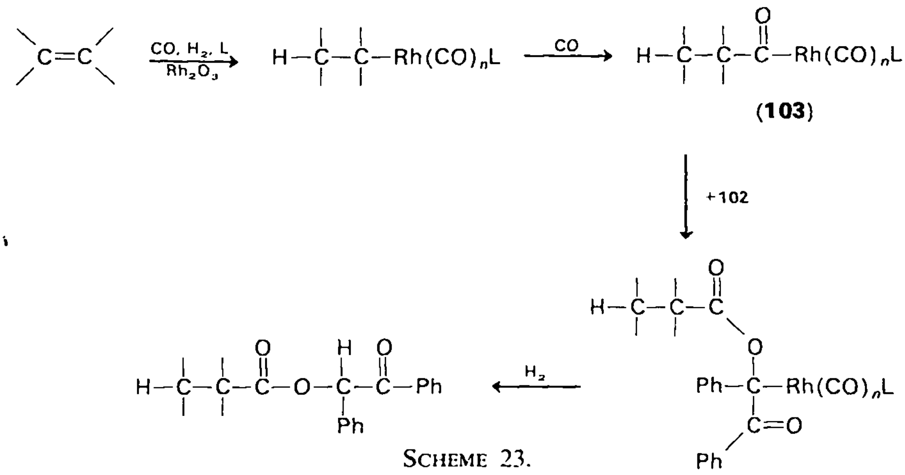
in water in the presence of a $\mathrm{NiI_2}$/pyridine/HI catalyst to afford linear C_{16} to C_{19} fatty acids[256].

Interestingly, benzyl ester derivatives are formed by the low-pressure hydrocarbonylation of olefins in the presence of benzil (**102**) and a rhodium oxide catalyst[257] (equation 60).

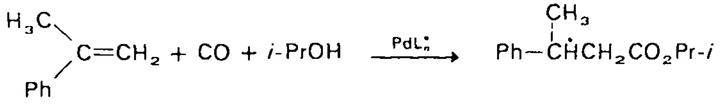

(102)

(60)

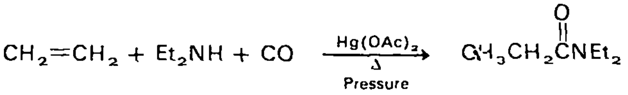
Substantial isomerization occurs during the course of the reaction. For example, 1-octene yields benzyl ester derivatives of nonanoic (46%), 2-methyloctanoic (33%), 2-ethylheptanoic (12%), and 2-propylhexanoic (9%) acids. Isomerization was generally less than that which occurred in the corresponding hydroformylation reaction. The proposed mechanism (Scheme 23) involves initial addition of rhodium hydride and subsequent carbon monoxide insertion to give acyl complex **10**. Addition of the acylrhodium complex to a carbonyl function of **102** forms the ester linkage. Hydrogenolysis completes the reaction.


SCHEME 23.

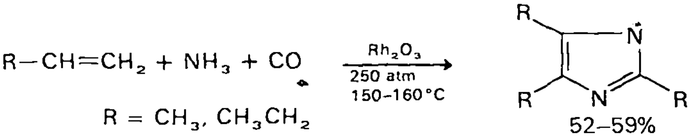
Asymmetric homogeneous hydrocarbonylation with a $PdCl_2$/DIOP (**97**) catalyst in alcohol yields optically active esters[258]. Carbonylation of α-methylstyrene at 100 °C and 300 atm in 2-propanol in the presence of Pd^{II}/DIOP (1:2) gives an 80% yield of isopropyl (*S*)-3-phenylbutanoate (equation 61) in 14·2% optical purity.


(61)

The reaction of ethylene in excess diethylamine containing mercuric acetate at 150–250 °C and 60–75 atm produces the corresponding *N,N*-diethylamide[259] (equation 62). The reaction of α-olefins with ammonia and carbon monoxide in the presence of a rhodium catalyst affords imidazoles in good yields[260] (equation 63).

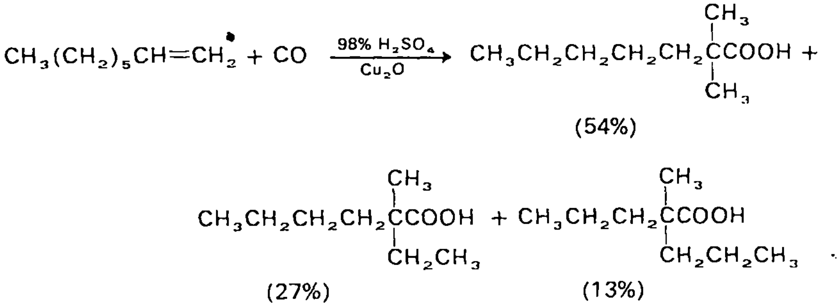


$$CH_2{=}CH_2 + Et_2NH + CO \xrightarrow[\text{Pressure}]{Hg(OAc)_2,\ \Delta} CH_3CH_2\overset{\overset{\large O}{\|}}{C}NEt_2 \qquad (62)$$

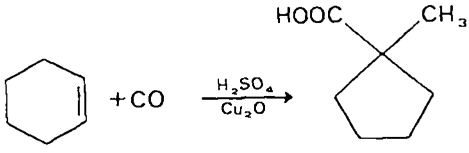


(63)

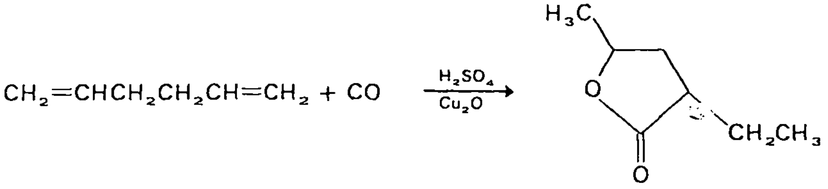
The synthesis of *t*-carboxylic acids from carbon monoxide and olefins in sulphuric acid has been effected by a copper(I) carbonyl catalyst at 20–50 °C and 1 atm of carbon monoxide[261–262]. Catalytic amounts of cuprous oxide are converted to Cu^I carbonyl complexes under the reaction conditions. The reaction of 1-octene gives three *t*-carboxylic acids in 94% total yield (equation 64). Other carbonylation reactions catalysed by copper(I) catalysts are shown below (equations 65, 66, 67).

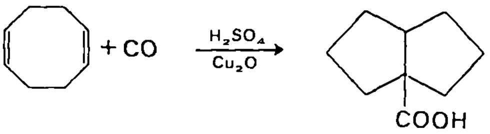


$$CH_3(CH_2)_5CH{=}CH_2 + CO \xrightarrow[Cu_2O]{98\%\ H_2SO_4} \underset{(54\%)}{CH_3CH_2CH_2CH_2CH_2\overset{CH_3}{\underset{CH_3}{C}}COOH} + \underset{(27\%)}{CH_3CH_2CH_2CH_2\overset{CH_3}{\underset{CH_2CH_3}{C}}COOH} + \underset{(13\%)}{CH_3CH_2CH_2\overset{CH_3}{\underset{CH_2CH_2CH_3}{C}}COOH} \qquad (64)$$

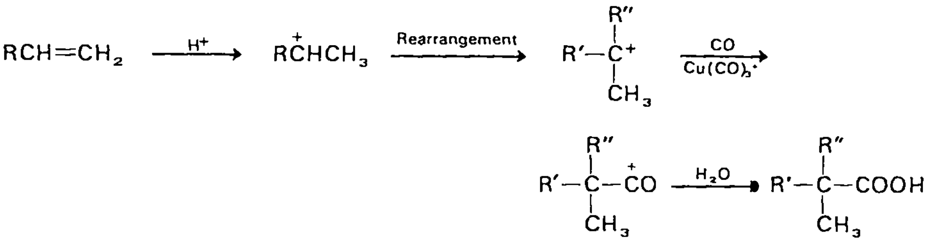


(65)


(66)


(67)

Protonation of the olefin in the acid media and rearrangement to stable tertiary carbonium ions occur in the initial stages of the reaction (Scheme 24). Copper(I) carbonyl assisted carbonylation of the incipient tertiary carbonium ions followed by hydrolysis yields the acid products. A



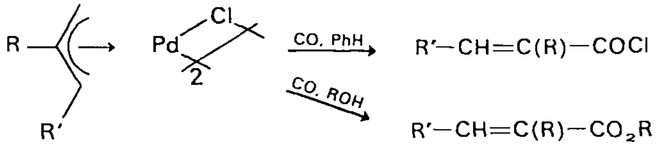
SCHEME 24.

similar transformation of olefins to tertiary esters has been reported using a CO/$SbCl_5$/HCl/alcohol system[263].

V. OLEFIN COUPLING—CARBONYLATION REACTIONS

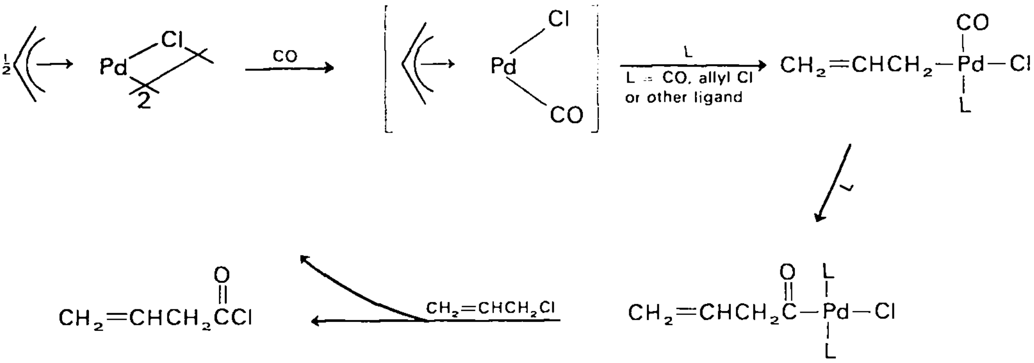
Transition metal catalysed olefin coupling reactions include cyclodimerization[264,265], oligomerization[15], olefin metathesis[266], and polymerization[267,268]. When the coupling reactions are carried out in the presence of carbon monoxide, a carbonyl function may be incorporated into the hydrocarbon skeleton.

Olefin coupling reactions often involve the intermediacy of a π-allyl complex. The reaction of carbon monoxide with π-allylpalladium complexes generally yields β,γ-unsaturated carbonyl derivatives and carbonylation occurs exclusively at the least substituted carbon[239,269,270] (equation 68). The proposed mechanism for the carbonylation of allyl


R
R′
Pd
Cl
2
CO, PhH
CO, ROH
R′—CH=C(R)—COCl
R′—CH=C(R)—CO₂R

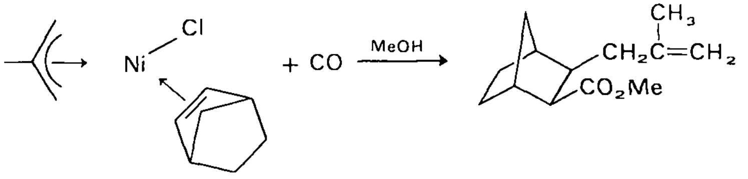
(68)

chloride catalysed by π-allylic palladium complexes[271] involves a π-allyl to σ-allyl conversion followed by a ligand-assisted σ-allyl migration to an adjacent coordinated carbon monoxide molecule (Scheme 25). Reductive elimination yields the butenoyl chloride product and subsequent oxidative addition of another molecule of allyl chloride to the palladium(o) residue regenerates the catalyst.


½
Pd
Cl
2
CO
Pd
Cl
CO
L
L = CO, allyl Cl
or other ligand
CH₂=CHCH₂—Pd—Cl
CO
L
CH₂=CHCH₂C—Pd—Cl
O
L
L
CH₂=CHCH₂Cl
CH₂=CHCH₂CCl
O

SCHEME 25.

The reaction of π-allyl complexes, with olefins and carbon monoxide yields organic carbonyl derivatives. This process is exemplified by the reaction of the nickel complex **104**[64] (equation 69). This general synthetic


Ni
Cl
+ CO
MeOH
CH₃
CH₂C=CH₂
CO₂Me

(69)

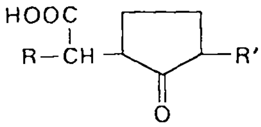
(104)

method can be applied to allyl chloride and ethylene with a nickel carbonyl catalyst system[272] (equation 70). When higher olefins and alkyl substi-

$$H_2{=}CHCH_2Cl + CH_2{=}CH_2 + CO + H_2O \xrightarrow[\substack{30\text{–}50\,^{\circ}C \\ 10\text{–}40\text{ atm}}]{Ni(CO)_4} \underset{45\%}{CH_2{=}CH(CH_2)_3COOH} \qquad (70)$$

tuted allyl halides react, cyclic compounds of the general structure **105** are the predominant products (96–98% of the total) and overall yields are slightly lower than is observed with ethylene[273-275] (equation 71).

$$R{-}CH{=}CHCH_2Cl + R'CH{=}CH_2 + 2CO + H_2O \xrightarrow{Ni(CO)_4} \qquad (71)$$

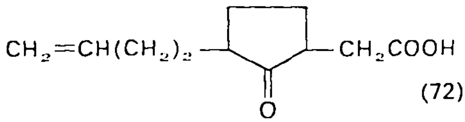


(105)

10–40%

The reaction of allyl chloride and terminal olefins forms only small amounts of **105** (R = H) and the cyclopentanone derivative **106**, formed by the trimerization–carbonylation of allyl chloride, is the major product (equation 72). Similarly, **106** can be prepared by carbonylation of allyl

$$RCH{=}CH_2 + CH_2{=}CHCH_2Cl + CO + H_2O \xrightarrow{Ni(CO)_4}$$



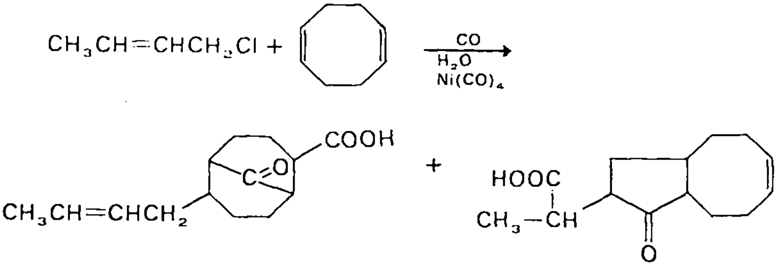
(72)

(106)

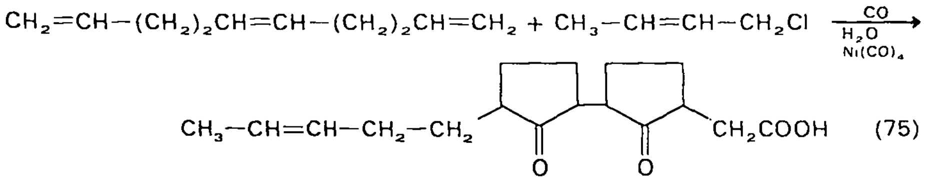
chloride and 1,5-hexadiene (equation 73), since hexadiene is formed by

$$(CH_2{=}CH{-}CH_2{-})_2 + CH_2{=}CHCH_2Cl + CO + H_2O \xrightarrow{Ni(CO)_4} \mathbf{106} \qquad (73)$$

dimerization of allyl chloride (equation 72). This reaction is general for substituted allyl halides and 1,5-dienes and yields can be enhanced by employing modified, cationic nickel complexes. Some interesting syntheses are given in equations (74) and (75).

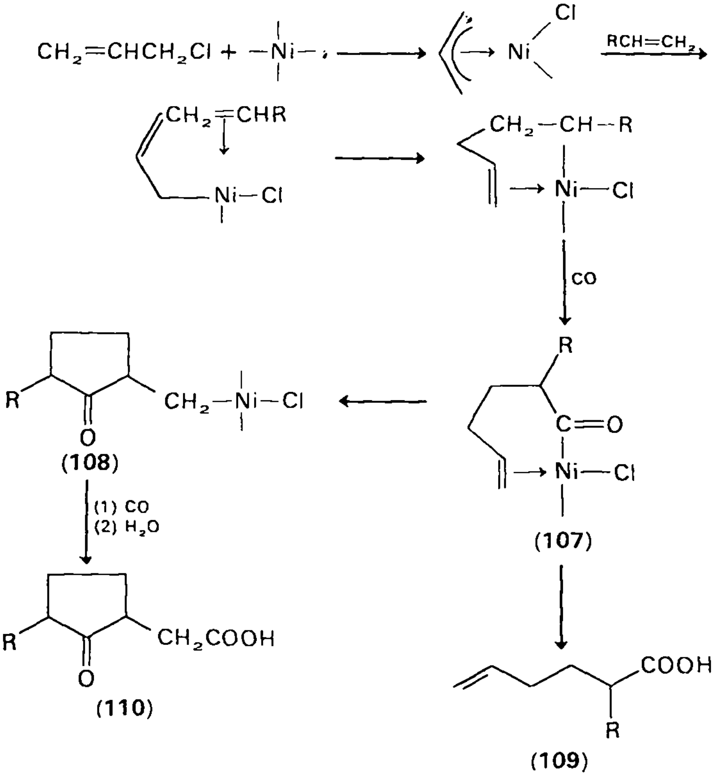

CH₃CH=CHCH₂Cl +
CO
H₂O
Ni(CO)₄
COOH
C=O
CH₃CH=CHCH₂
+
HOOC
CH₃—CH
O

(74)


CH₂=CH—(CH₂)₂CH=CH—(CH₂)₂CH=CH₂ + CH₃—CH=CH—CH₂Cl
CO
H₂O
Ni(CO)₄
CH₃—CH=CH—CH₂—CH₂
CH₂COOH
O
O

(75)

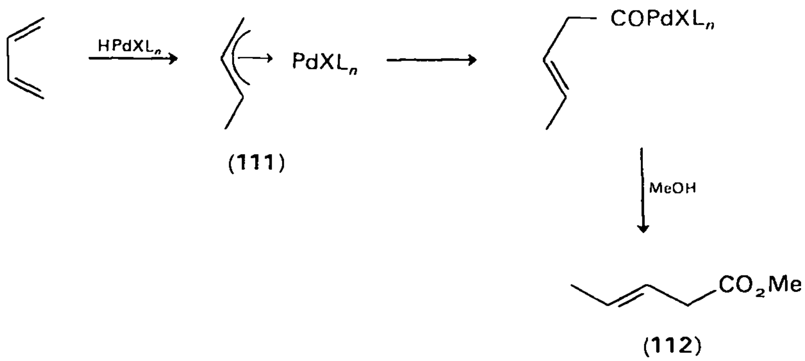
The general mechanism of the reactions given above requires initial oxidative addition of allyl chloride to the nickel catalyst to form a π-allyl complex (Scheme 26). Coordination of the olefin *cis* to the allyl


CH₂=CHCH₂Cl + —Ni—
Cl
Ni
RCH=CH₂
CH₂=CHR
Ni—Cl
CH₂—CH—R
Ni—Cl
CO
R
C=O
Ni—Cl
(107)
R
CH₂—Ni—Cl
O
(108)
(1) CO
(2) H₂O
R
CH₂COOH
O
(110)
COOH
R
(109)

SCHEME 26.

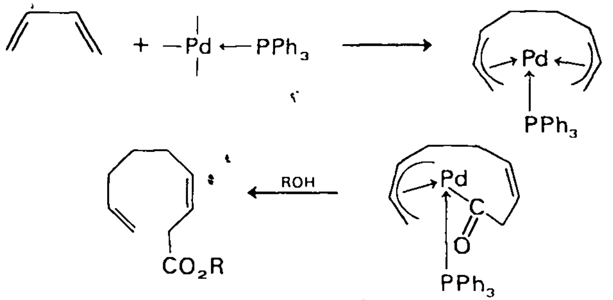
ligand promotes the π-allyl to σ-allyl conversion which is followed by coupling and carbon monoxide insertion. Intramolecular ligand migration (**107** → **108**) or solvolysis (**107** → **109**) of the acylnickel intermediate **107** are competing reactions. Intramolecular carbonylation, which ultimately leads to cyclopentanone product **110** predominates when R ≠ H.

The course of the reaction of carbon monoxide and butadiene is dependent upon the catalyst system used. The carbonylation of butadiene in methanol in the presence of a palladium(II)–phosphine complex under moderate conditions (100°C, < 100 atm) yields methyl 3-pentenoate (**112**)[276]. The mechanism may be considered to be a 1,4-addition of H—CO_2R catalysed by palladium and involves the intermediacy of the π-allyl complex **111** (Scheme 27). Under more severe conditions, **112**



SCHEME 27.

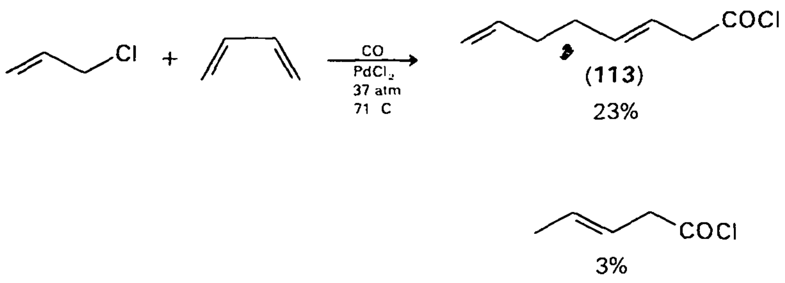
can also be obtained in the presence of a rhodium catalyst[277]. In the presence of halogen-free palladium phosphine catalysts, however, dimerization of butadiene occurs, followed by carbonylation to produce 3,8-nonedienoates[278–280] (Scheme 28). The inability to form the



SCHEME 28.

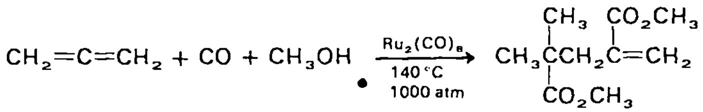
complex **113** when halide occupies a metal coordination site was offered as explanation for the difference in the systems. When acetic acid is the solvent, carbonylation of butadiene in the presence of a Pd^{II}–phosphine complex results in the formation of isomeric nonadienoic acids as well as octatriene and 4-vinylcyclohexene[281].

Carbonylation of butadiene in the presence of allyl chloride catalysed by palladium(II) chloride gives a moderate yield of codimerization product **113**[282] (equation 76).



(113)
23%
3%
(76)

The reaction of allene and carbon monoxide in methanol in the presence of a ruthenium carbonyl catalyst yields predominantly the glutaric ester **114** resulting from dimerization–carbonylation of the cumulative diolefin[283] (equation 77).

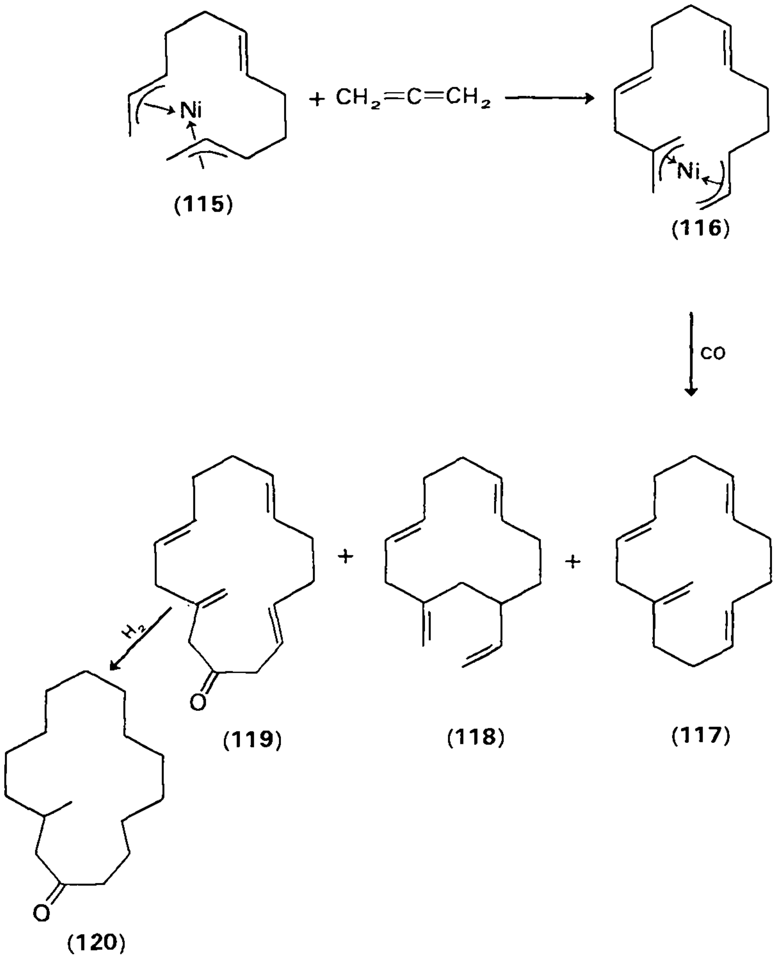


$$CH_2{=}C{=}CH_2 + CO + CH_3OH \xrightarrow[\substack{140\,^{\circ}C \\ 1000\text{ atm}}]{Ru_2(CO)_8} CH_3\overset{\overset{\textstyle CH_3}{|}}{\underset{\underset{\textstyle CO_2CH_3}{|}}{C}}CH_2\overset{\overset{\textstyle CO_2CH_3}{|}}{C}{=}CH_2 \qquad (77)$$

(114)

The dodecatrienylnickel complex **115** reacts with one equivalent of allene to form the bis-π-allyl intermediate **116**[284] (equation 78). Treatment of **116** with carbon monoxide results in cyclization to cyclic hydrocarbons **117** and **118** and the cyclic ketone **119**. Hydrogenation of **119** affords the natural oil, (±)-muscone (**120**).

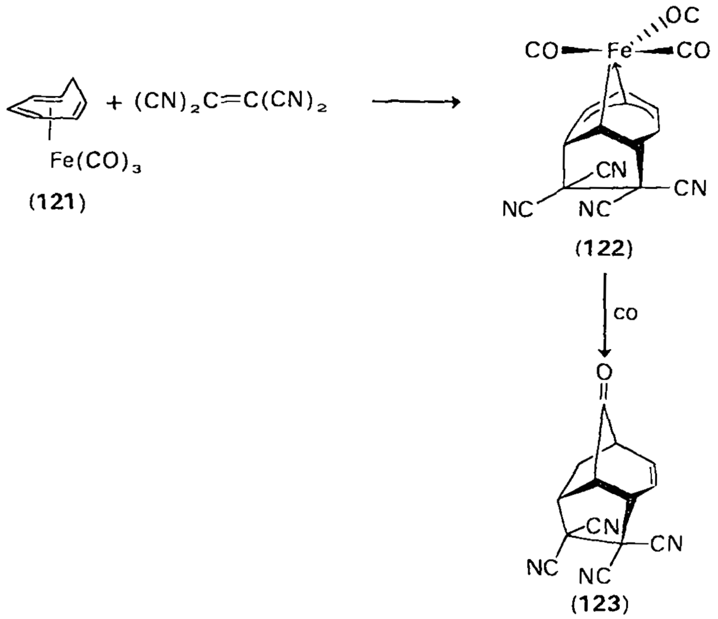
The cycloaddition reaction of cycloheptatriene and electron-deficient olefins is catalysed by iron carbonyl[285]. Reaction of tetracyanoethylene and tricarbonylcyloheptatrieneiron(0) (**121**) at room temperature gives the



(78)

cycloaddition adduct **122**, the structure of which was determined by X-ray analysis[286,287] (equation 79). Reaction of **122** with carbon monoxide yields the tricyclic ketone **123**. The mechanism involves carbonylation of the iron–carbon σ-bond followed by a transannular interaction of the acyliron group with the π-allyl system.

Polycyclic cyclopentanones may be synthesized from the reaction of strained bicyclo[2.2.1] olefin derivatives and carbon monoxide in the presence of an iron carbonyl catalyst[288,289]. For example, benzonorbornadiene (**124**) was either heated or photolysed in the presence of



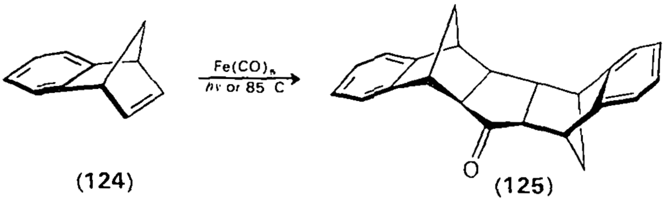
(121)

(122)

(123)

(79)

$Fe(CO)_5$ to produce the cyclopentanone derivative **125**[289] (equation 80).



(124)

(125)

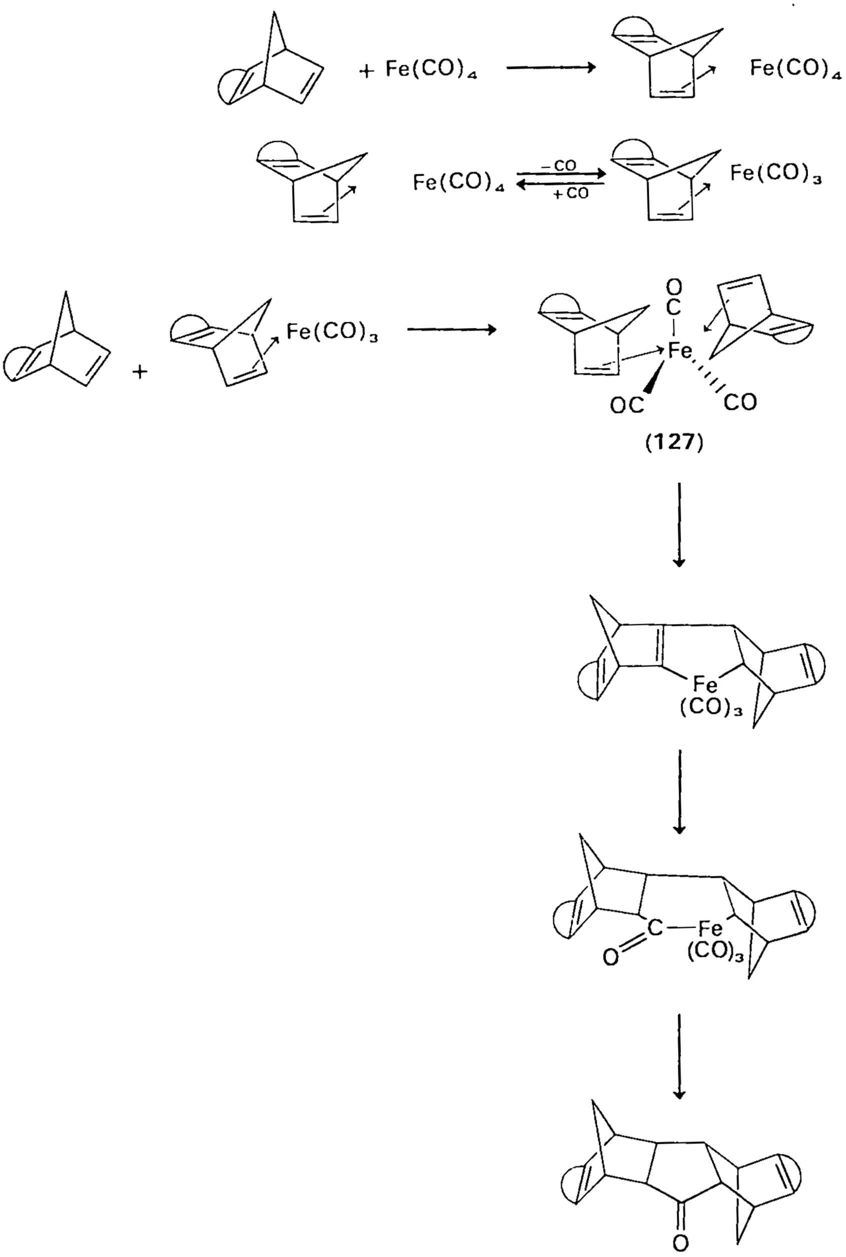
(80)

The stereochemistry of the product is *exo–trans–exo*, regardless of the olefin reactant. The important features of the photochemical transformation (Scheme 29) are initial generation of the very reactive tetracarbonyliron(o) species **126** followed by the stepwise formation of the bisolefin complex **127**. The relative orientation of the olefinic ligands in **127** provides minimum steric repulsion and maximum π overlap necessary for the forthcoming coupling step and determines the stereochemistry of the product.

Reaction of the nortricyclenic palladium complex **128** with bis(*cis*-propenyl)mercury or bis(2-chlorovinyl)mercury followed by carbonylation in methanol results in the formation of the cyclic ketones **129** and **130**, respectively[65] (equation 81). A possible mechanism for the vinyl transfer

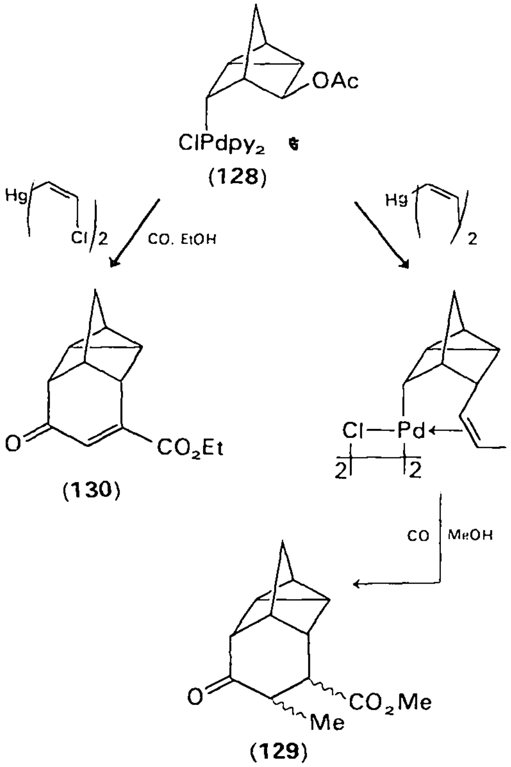
$$Fe(CO)_5 \xrightarrow{h\nu} Fe(CO)_4 + CO$$

(126)


+ Fe(CO)$_4$
Fe(CO)$_4$
Fe(CO)$_4$
−CO
+CO
Fe(CO)$_3$
+
Fe(CO)$_3$
O
C
Fe
OC
CO
Fe
(CO)$_3$
C
Fe
O
(CO)$_3$
O

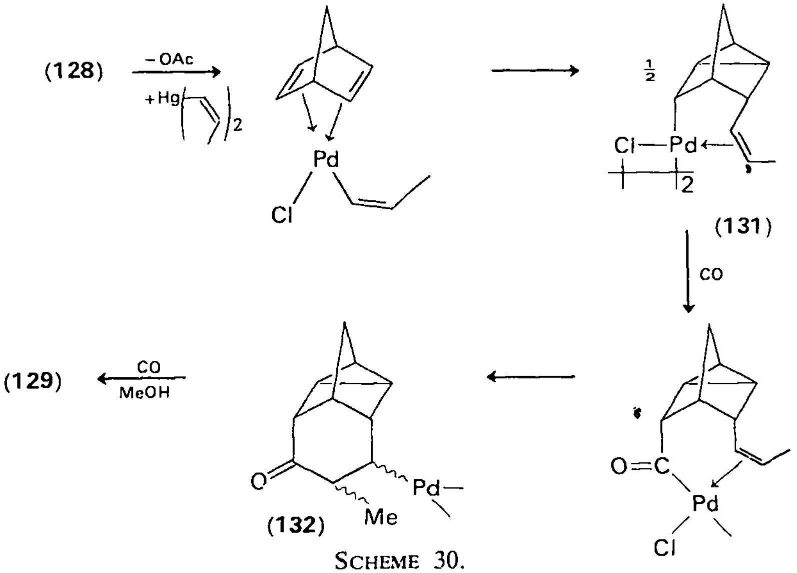
(127)

SCHEME 29.


OAc
ClPdpy$_2$
(128)
Hg
Cl
2
CO, EtOH
Hg
2
O
CO$_2$Et
(130)
Cl—Pd
2
2
CO
MeOH
O
CO$_2$Me
Me
(129)

(81)

reaction requires conversion of **128** to the diene complex upon reaction with the mercurial (Scheme 30). *Cis* addition of vinylpalladium to the


(128)
– OAc
+Hg
2
Pd
Cl
½
Cl—Pd
2
(131)
CO
O=C
Pd
Cl
(129)
CO
MeOH
O
Pd—
Me
(132)

SCHEME 30.

diolefin yields the chelating enyl complex **131**. Carbonylation then proceeds by carbon monoxide insertion followed by intramolecular acylpalladation of the acyclic double bond to generate the alkyl complex **132**. Carbonylation and solvolysis are the final steps to give **129**. The unsaturated keto ester **130** is obtained via elimination of hydrogen chloride from the initially formed product.

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Supplement A The Chemistry of Double-Bonded Functional Groups
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CHAPTER 13

Imidines and diamidides (1,3,5-triazapentadienes)

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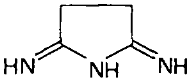
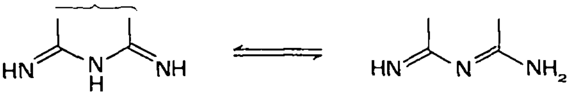
I. INTRODUCTION

In the course of pioneering work on the nature and reactions of imidates[1] derived from nitriles, Pinner encountered[2] the hydrochloride of the tri-nitrogen analogue (**1**) of succinic anhydride. This he named succinimidine hydrochloride. Later he extended[3] the nomenclature to the next higher homologue, glutarimidine.



(1)

The term imidine can therefore be taken as a generic name for those analogues of the cyclic anhydrides of dicarboxylic acids in which nitrogen fully replaces oxygen, so that an imidine is represented by the general formula (2) where the ring may be saturated or unsaturated. Because tautomerism is feasible (equation 1), the name imidine is convenient in that (like the name amidine) it ignores the detail of fine structure, which may not always be relevant or may be difficult to define. Chemically, the



(2)

(1)

special class name imidine appears justified because the compounds defined by 2 have a characteristic set of properties[4]. For example, they are very easily hydrolysed by water and readily undergo displacement reactions with amines and active methylene compounds. However, the term imidine is not recognized in the IUPAC rules on nomenclature[5] and so its use here will be restricted to the generic one. Individual members of the class will be named systematically, for convenience in the diimino tautomeric form (2), unless the substitution fixes the structure in the alternative amino–imino form.

Following the discovery of succinimidine hydrochloride in 1883[2], virtually no further work on this new type of compound was reported until the early 1950's when Bayer Farbenfabriken[6] found that 1,3-diiminoisoindoline (or 1-amino-3-iminoisoindolenine, as they preferred to regard it) was an excellent precursor of metal phthalocyanines, providing for the first time a means of satisfactorily applying these extraordinarily fast pigments to fabrics. One result of this important discovery was the stimulation of interest in the general chemistry of diiminoisoindoline and of other imidines[4,6b,7].

A few homologues of the imidines (2) are known in which *two* of the three nitrogen atoms are parts of ring systems. This annelation can modify the properties especially if one or both of the rings is aromatic.

Some open-chain compounds containing the functional grouping shown at 2 have been described and were called diamidides[8]. Again, the trivial name is convenient for generic designation: individuals are named systematically as 1,3,5-triazapentadienes. One triamidide (a 1,3,5,7-tetraazaheptatriene) has also been prepared[8b]. The main differences from the imidines shown by these acyclic analogues are the apparent absence of easy displacement reactions, the relative inaccessibility of *N*-unsubstituted members, and the absence of members lacking *C*-aryl substituents.

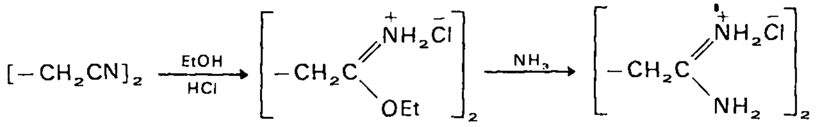
Formally, biurets and biguanides and those compounds derived by addition of amidines to carbodiimides possess the N—C—N—C—N function, but for reasons of their chemistry—the first are ureides and the latter two are guanidines—it would be inappropriate to include such compounds in this Chapter.

II. SYNTHESES OF IMIDINES

The discovery of the first imidine was incidental to other studies[1,2] and the method of synthesis, the cyclization of a diamidine salt (detailed below), has hardly been extended: neither has the related reaction of diimidoates with amines. The most important routes to imidines involve the cycloaddition of ammonia or amines to 1,2- and 1,3-dinitriles. The addition will proceed directly at elevated temperature (*c*. 90–200°C) usually necessarily under pressure but is susceptible to base catalysis (e.g., with alkoxides) and will then proceed in boiling methanol, whilst sodamide or sodio derivatives of amines in molar proportion can be employed under very mild conditions. Amine salts have been little used: they react with dinitriles only at rather high temperatures. The particular importance of 1,3-diiminoisoindoline as a precursor of phthalocyanines has resulted in the investigation of routes to this imidine from substituted (alkoxy, thio, halogeno) 1(*H*)-isoindoles.

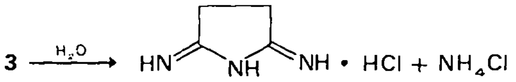
A. Cyclization of Diamidine Salts

This earliest route was an incidental finding of Pinner's in 1883[2], when he attempted to recrystallize succindiamidine dihydrochloride (3) from water in the course of preparing this amidine from succinonitrile by the method shown (equation 2). The gentle heating caused cyclization with elimination of ammonium chloride (equation 3), and succinimidine (2,5-diiminopyrrolidine) hydrochloride crystallized out, being the least soluble salt present. The method was confirmed by I.C.I. Ltd.[9], but remains



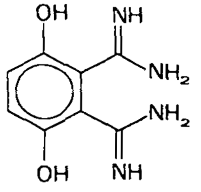
$$[-CH_2CN]_2 \xrightarrow[HCl]{EtOH} \left[-CH_2C\begin{matrix}\overset{+}{N}H_2\overset{-}{Cl}\\ OEt\end{matrix}\right]_2 \xrightarrow{NH_3} \left[-CH_2C\begin{matrix}\overset{+}{N}H_2\overset{-}{Cl}\\ NH_2\end{matrix}\right]_2 \qquad (2)$$

(3)



(3)

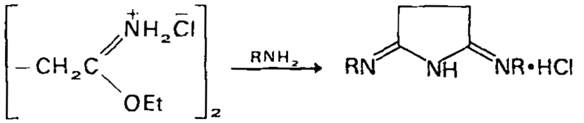
of historical interest, not having been exploited further. This is principally because there are shorter routes from dinitriles to imidines. It appears that diamidines, as free bases, will not necessarily cyclize readily: thus the yellow vicinal diamidine[10] (4) turned black and decomposed above 210°C when heated.



(4)

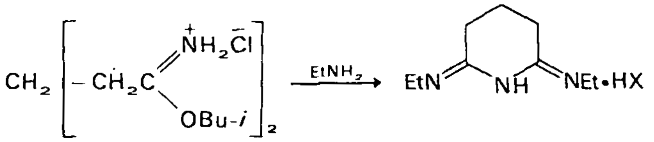
B. Reaction of Diimidoates with Amines

From diethyl succindiimidoate dihydrochloride and methylamine, Pinner[11] obtained the hydrochloride of 2,5-bismethyliminopyrrolidine



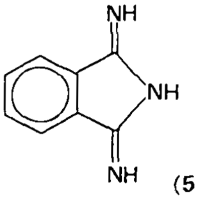
(4)

(equation 4, R = Me). Similarly, from diisobutylglutardiimidoate dihydrochloride and ethylamine he obtained[3] 2,6-bisethyliminopiperidine (equation 5) which was isolated as the platinichloride. More recently, the



(5)

succindiimidoate salt was treated with aniline to provide the hydrochloride of 2,5-bisphenyliminopyrrolidine[9] (equation 4, R = Ph). Also, the diimidoate salt derived from phthalonitrile in chloroform with ethanolic hydrogen chloride was treated with ammonia to give 1,3-diiminoisoindoline (5) as the hydrochloride[4a].

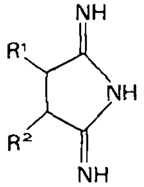


(5)

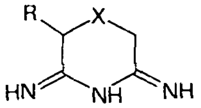
C. Addition of Ammonia or Amines to Dinitriles

1. Uncatalysed addition

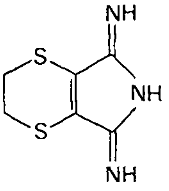
Direct addition of ammonia to dinitriles (equation 6) has frequently proved to be the best method for preparing imidines in quantity. Thus by heating phthalonitrile with an excess of ammonia in methanol at 90–100 °C in a glass-lined autoclave for 4 h, an almost-quantitative yield of 1,3-diiminoisoindoline (**5**) is obtained[4a]. With the temperature and time optimized in each case by trial, the method was used with aliphatic dinitriles to prepare, in the stated yields, 2,5-diiminopyrrolidine (succinimidine)[9] (**6**) (85 %), its 3-methyl homologue[12] (**7**) (73 %), *rac*-2,5-diimino-3,4-dimethylpyrrolidine[13] (**8**) (69 %), 2,6-diiminopiperidine (glutarimidine)[14] (**9**) (45 %), its 3-phenyl derivative[14] (**10**) (52 %), and 4-benzyl-2,6-diiminopiperazine[15] (**11**) (50 %). The imidine (**12**) was also obtained[16] by this route.



(**6**) $R^1 = R^2 = H$
(**7**) $R^1 = Me, R^2 = H$
(**8**) $R^1 = R^2 = Me$

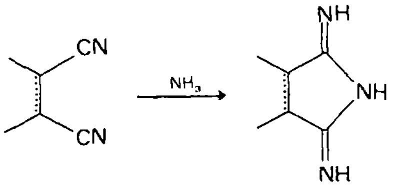


(**9**) $R = H, X = CH_2$
(**10**) $R = Ph, X = CH_2$
(**11**) $R = H, X = NCH_2Ph$



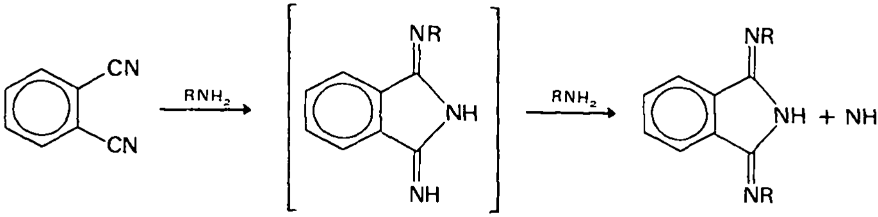
(**12**)

Extension of the reaction (equation 6) to amines has been shown to be feasible. Thus methylamine and ethylamine in ethanol with phthalonitrile at 100°C under pressure gave, respectively, 1,3-bismethylimino- (78 %)

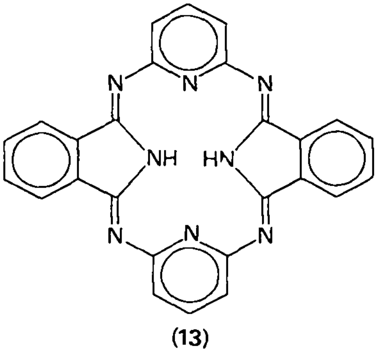


(6)

and -bisethyliminoisoindoline[17] (63 %). Presumably in these cases there is cycloaddition of the amine to the dinitrile followed by substitution with elimination of ammonia, as indicated in equation 7 (although alternatives are possible). In a further extension, aromatic diamines were interacted with phthalonitriles in a high boiling solvent to yield macrocyclic products[18]: for example[18b], 2,6-diaminopyridine and phthalonitrile in boiling chloronaphthalene gave the macrocycle **13**, effectively a disubstituted imidine, which had earlier been made[19] from 1,3-diiminoisoindoline.

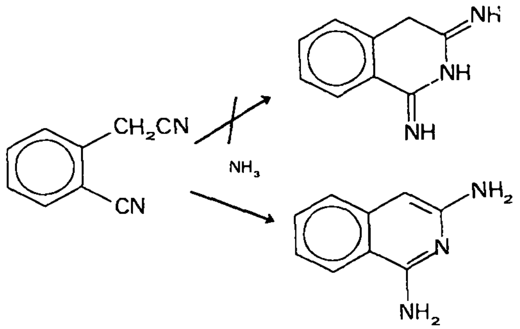


(7)



(13)

The cycloaddition of ammonia to dinitriles (equation 6) does not invariably lead to the formation of imidines. Thus interaction of *o*-cyanobenzyl cyanide with ammonia gave 1,3-diaminoisoquinoline[20] and not the imidine (see equation 8). An imidine of this type might well be

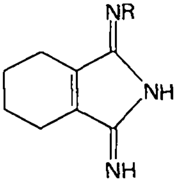


(8)

expected to tautomerize under mild conditions to the resonance-stabilized diaminoazaarene, and so the direct formation of the diaminoisoquinoline rather than the imidine is hardly surprising. Addition of ammonia to 3,6-dihydroxyphthalonitrile in methanol at ordinary temperature occurred without cyclization and so afforded the phthalodiamidine (4)[10]. Attempts to add ammonia to *o*-cyanocinnamonitrile (both *cis* and *trans*) resulted in some addition to the exocyclic double bond and gave 3-amino-3-(*o*-cyanophenyl)propionitrile in very low yield together with much intractable material[21].

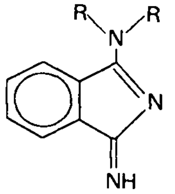
2. Alkoxide catalysed addition

The imidine (**14**) from Δ^1-tetrahydrophthalonitrile was conveniently obtained[22] by passing ammonia through a refluxing solution of the dinitrile in methanol containing a trace of sodium methoxide. The method has also been used[23] for preparing 1,3-diiminoisoindoline (**5**) but the yield was much inferior (43 %)[23a] to that from the addition of ammonia under pressure (method C.1). Further use of the method was recently made to obtain the imidines from 4-nitro- and 4-acetamidophthalonitrile and from 2,3-dicyanopyrazine[23b], the yield in this last case being very high (96·5 %).



(14) R = H
(15) R = Bu
(16) R = Ph

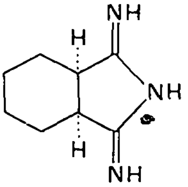
Extensions of the method to amines have been described. Thus the sodium methoxide catalysed cycloaddition of butylamine and of aniline to phthalonitrile in boiling methanol gave **15** and **16**[24]. With the secondary amines, morpholine and diethylamine, and strict control of the reaction time, the rather sensitive 1-amino-3-imino-1(*H*)-isoindoles (**17**) were successfully obtained[17] and characterized as their picrates. Piperidine was similarly added to phthalonitrile[25].



(17) RR = $[CH_2]_2O[CH_2]_2$ or R = Et

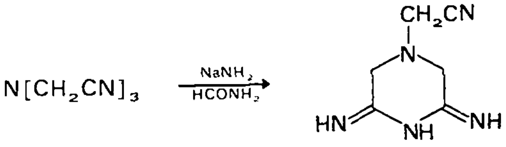
3. Addition effected by sodamide

Bayer Farbenfabriken reported[25] that a 1 molar proportion of sodamide in formamide at ordinary temperatures effected addition of ammonia to phthalonitrile, so affording 1,3-diiminoisoindoline (**5**) which crystallized out. The method worked only moderately well for the preparation from succinonitrile of succinimidine (**1**)[9] which was obtained slightly impure in 47% yield, but was the only effective route by which *cis*-hexahydrophthalonitrile could be converted into the corresponding imidine (**18**)[22].



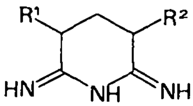
(18)

With the *trans*-hexahydrophthalonitrile, reaction was very slow, and the product was indistinguishable from **18**[22]; that the cycloaddition has been accompanied by a *trans* to *cis* conversion was confirmed by very mild hydrolysis of the imidine product to the *cis*-imide. The sodamide-in-formamide method satisfactorily yielded 3,5-diiminopiperazin-1-ylacetonitrile (**20**)[15] from nitrilotriacetonitrile (**19**), and the imidines (**21**) and



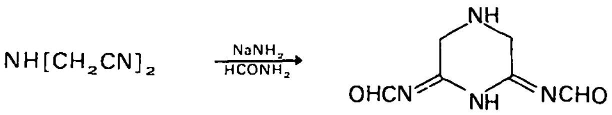
(19) (20)

(**22**) in very high yields from α-methyl- and α,α′-dimethylglutaronitrile, respectively[26]. From *N*-benzyliminodiacetonitrile, the method afforded[15]



(**21**) $R^1 = Me, R^2 = H$
(**22**) $R^1 = R^2 = Me$

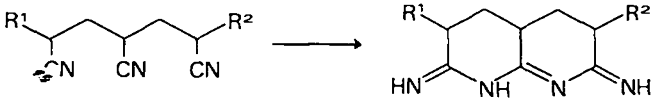
the imidine (**11**) as its formamide solvate. Unexpectedly, iminodiacetonitrile itself (**23**) yielded 2,6-bisformyliminopiperazine (**24**) in a slow reaction[15]. Presumably there is an equilibrium in the reaction medium



(**23**) (**24**)

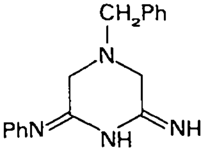
between amide and formamide anion, both of which entities could attack the dinitrile reversibly. Hence the isolation of **24** rather than the expected imidine in this last case is evidently an accident of the lower solubility of the diformyl derivative.

The sodamide–formamide route gave the expected imidines from 4-trimethylsilyl- and 4,5-bistrimethylsilylphthalonitrile[27]. In an interesting further application of the method to the 1,3,5-trinitriles (**25**), the 'extended-imidine' products (**26**) were obtained in excellent yields[26].

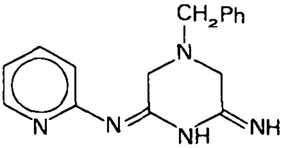


(**25**) (**26**)
$R^1 = R^2 = H$
$R^1 = Me, R^2 = H$
$R^1 = R^2 = Me$

Extension of the sodamide reaction to the use of the sodio derivatives of other amines allowed the preparation of otherwise inaccessible derivatives. Thus treatment of *N*-benzyliminodiacetonitrile with sodio aniline in benzene or in an excess of aniline afforded **27**, whilst with the sodio derivative of 2-aminopyridine in *N*,*N*-dimethylaniline, **28** was obtained[15].



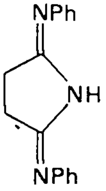
(27)



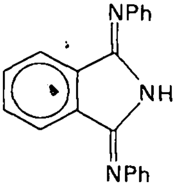
(28)

4. Using amine salts, and related processes

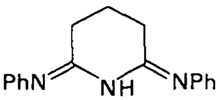
Fusion of succinonitrile with aniline hydrochloride according to Blochmann's method[28] gave an infusible hydrochloride, from which the imidine derivative (**29**) was obtained on basification[9]. Similarly, fusion of aniline hydrochloride with phthalonitrile yielded[9] the yellow hydrochloride of the imidine derivative (**30**) and fusion with glutaronitrile gave[14] the hydrochloride of **31**. The method did not work with α,α′-dimethylsuccinonitrile[13].



(29)



(30)

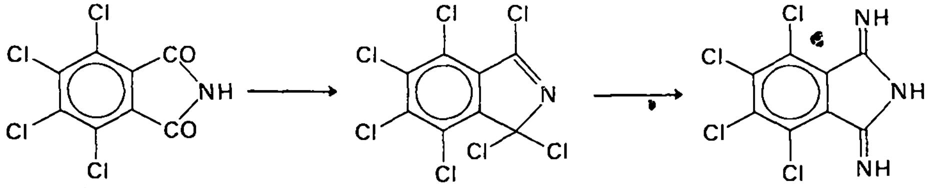


(31)

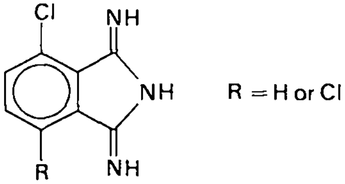
Although the use of ammonium chloride does not appear to have been tried, ammonium nitrate (which sublimes less readily) has been used in a somewhat analogous reaction but starting with imide or anhydride rather than dinitrile. Clearly applicable to the preparation of only the most stable imidines and used so far solely for 1,3-diiminoisoindoline, the method comprised heating phthalimide in nitrobenzene with urea and ammonium nitrate in the presence of ammonium molybdate for 20 h at 150–160°C[6,25,4a]. Alternatively, phthalic anhydride was used both as starting material and solvent and the reaction conducted at 170°C for 8–10 h[6,25]. In each case the imidine was obtained as the nitrate; however, attempts to repeat the directions[6a] for the generation of the base, with aqueous sodium hydroxide and cooling, were quite unsuccessful[4a]. In a related procedure, the amide, toluene-*p*-sulphonamide, was heated with phthalonitrile in molten urea at 150–160°C to give, by cycloaddition, the monotoluenesulphonyl derivative of 1,3-diiminoisoindoline[25].

D. Reactions of Halogen-substituted Precursors with Ammonia

Bayer Farbenfabriken found[29a] that phthalimide and substituted phthalimides such as the 4-phenyl, 4-nitro, 5,6-dinitro, and 3,4,5,6-tetrachloro derivatives underwent reaction with phosphorus pentachloride to give the corresponding 1,1,3-trichloro-1(*H*)-isoindoles which with ammonia then yielded the imidines; for example **32** afforded **33** and thence **34**. Du Pont later used[29b] phosphorus pentachloride in the oxychloride for the first stage, and ammonia in formamide for the second, and thereby prepared the 4-chloro- and 4,7-dichloro-1,3-diiminoisoindolines (**35**).

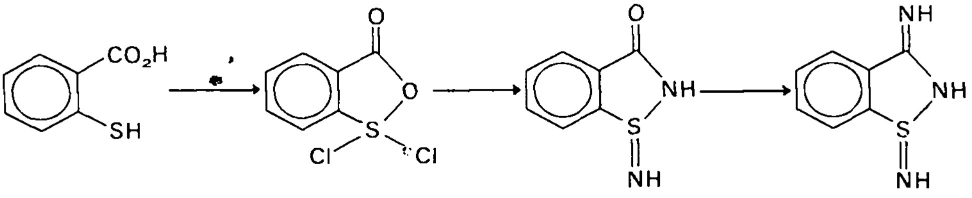


(32) (33) (34)



(35)

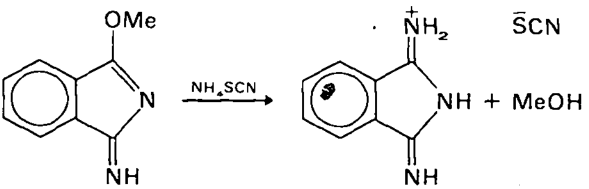
The imidine (**36**), which is also both a sulphimine and a benzoisothiazoline derivative, was prepared from the *S*-dichloro anhydro compound derived from treatment of *o*-carboxybenzenethiol (thiosalicylic acid) with chlorine: first, reaction with ammonia yielded the imide sulphimine, and then fusion with urea in the presence of ammonium molybdate gave the imidine (**36**)[30].



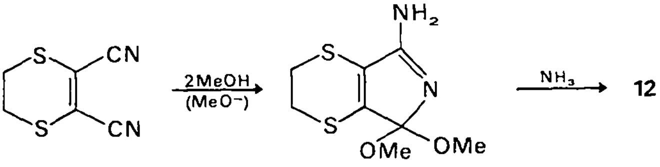
(36)

E. Reactions of Alkoxy- and Thio-substituted Precursors with Ammonia or Amines

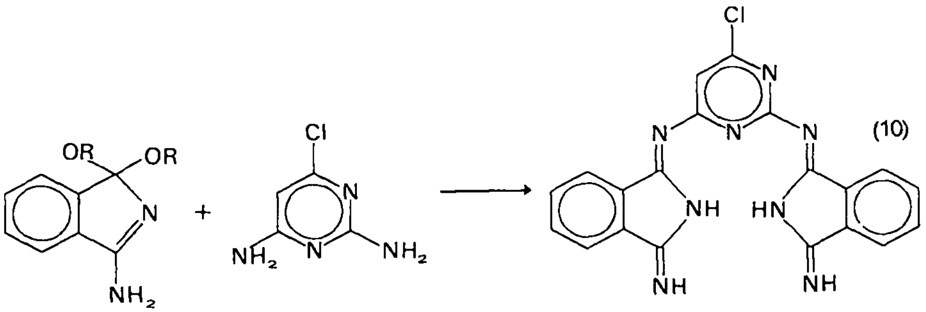
Treatment of phthalonitrile in methanol with one molecular proportion of sodium methoxide gave the cycloaddition product (**37**)[25], or its sodio derivative[31], according to the conditions. Treatment of **37** with ammonium thiocyanate then provided[32] the hydrothiocyanate of 1,3-diiminoisoindoline (equation 9). The dinitrile (**38**) added two molecular proportions of methanol under methoxide catalysis giving **39**[16], which with ammonia in methanol afforded the imidine (**12**). Similar double addition of alcohols or 1,2-glycols to phthalonitrile, with cyclization, was known[6b,25] and the products (**40**) could be converted into imidine derivatives by reaction with amines[25,33,34]; an example[33] is shown in equation (10). Doubtless with similar reactions in mind, the products (**41**) of double addition of thiols to phthalonitrile were prepared[35] using alkoxide as base catalyst.


OMe
N
NH
NH_4SCN
$\overset{+}{N}H_2$
$\bar{S}CN$
NH + MeOH
NH

(37) (9)

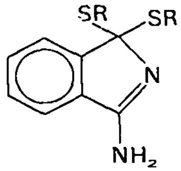

S
CN
S
CN
2MeOH
(MeO⁻)
NH_2
S
N
S
OMe
OMe
NH_3
12

(38) (39)


OR
OR
N
NH_2
+
Cl
N
NH_2
N
NH_2
Cl
N
N
N
N
NH
HN
NH
NH

(10)

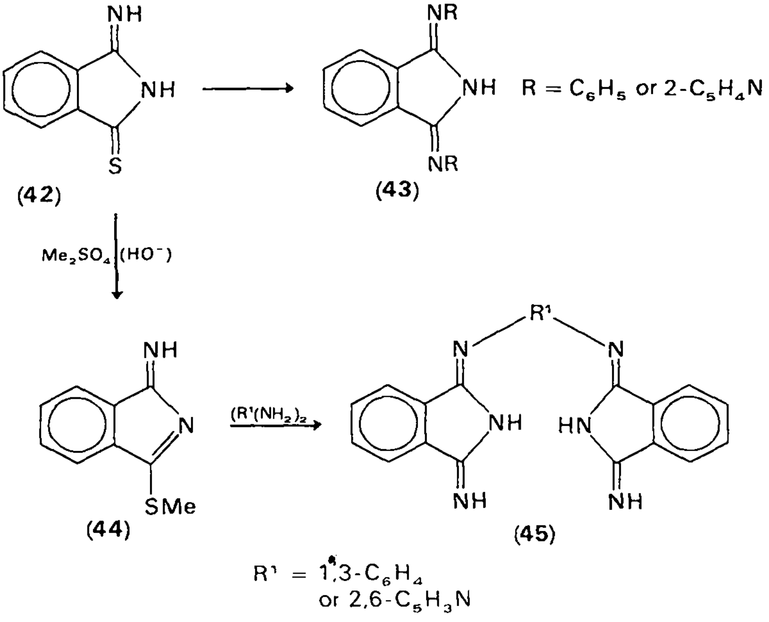
(40)



R = Et or CH_2Ph

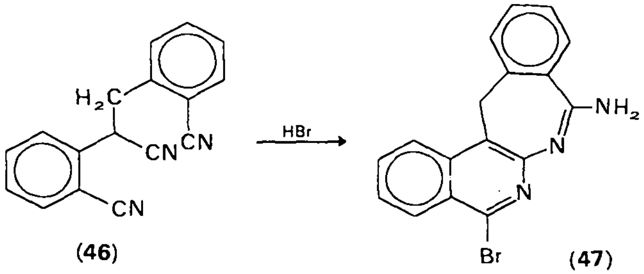
(41)

Addition of hydrogen sulphide to phthalonitrile gave 1-amino-3-thioisoindoline (**42**) which with aniline or 2-aminopyridine in boiling ethanol underwent displacement of both functional groups to give the corresponding disubstituted imidine derivatives (**43**)[36] but this was clearly not a general reaction. With butylamine in the presence of aqueous sodium hydroxide, (**42**) gave the monobutyl-substituted imidine (**15**)[36]. With aniline in the cold the *S*-methyl derivative (**44**) smoothly gave **16**[36], and with *m*-phenylenediamine or 2,6-diaminopyridine yielded the products **45**[36].



F. From the Addition of Hydrogen Bromide to a Trinitrile

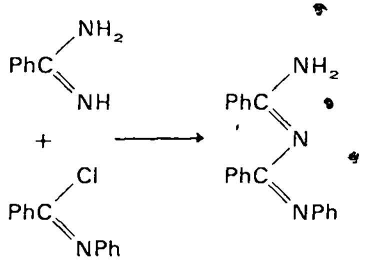
Treatment of the trinitrile (**46**) with dry hydrogen bromide in ether–methylene dichloride effected conversion into the bicyclic imidine derivative (**47**) which, being very sparingly soluble, was characterized as the *N*-diacetyl derivative[37]. Addition of hydrogen bromide to dinitriles[37] does not of course lead direct to imidines, but the reaction of the adducts with ammonia is a possible route. It seems probable that the preparation of the imidine (**12**) from the corresponding dinitrile (**38**) via the tri(hydrogen bromide) complex[16] is an example, although the nature of this complex was not investigated. If so, the preparation should really be classified under II.D above.



(**46**) (**47**)

III. SYNTHESES OF DIAMIDIDES (1,3,5-TRIAZAPENTADIENES)

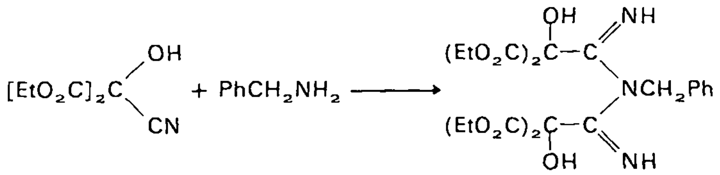
In 1892 Pinner showed[38] that the first few claims to have prepared compounds of this class[39] were incorrect and that the products were triazines. The first authentic preparation of a diamidide was that by Ley and Müller[40] in 1907 of 1,2,4-triphenyl-1,3,5-triazapenta-1,3-diene (**48**) from benzamidine and *N*-phenylbenzimidochloride in ether (equation 11).



(11)

(**48**)

These workers also prepared a guanylamidide. Subsequently, Curtiss and Nickell[41] obtained the very unstable diamidide (**49**) from diethyl cyanotartronate and benzylamine (equation 12). Nothing further was reported until 1951 when the first systematic investigation of diamidides was begun[8].

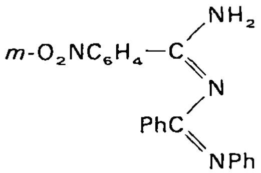


(49)

(12)

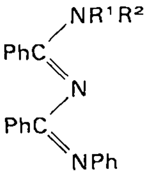
A. Reaction of Benzamidines with Benzimidochlorides

Ley and Müller's preparation of **48** was substantiated by Cooper, Partridge, and Short[8a] who also used the reaction with *m*-nitrobenzamidine, so obtaining **50**. Extension of the reaction (equation 11) to *N*,*N*-



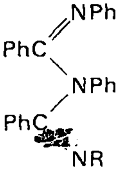
(50)

and *N*,*N'*-disubstituted benzamidines with *N*-substituted benzimidochlorides in benzene then provided, respectively, the conjugated diamidides (**51**) and the unconjugated diamidides (**52**). The latter type was relatively



$R^1 = R^2 = Ph$
or $R^1 = Me$, $R^2 = Ph$

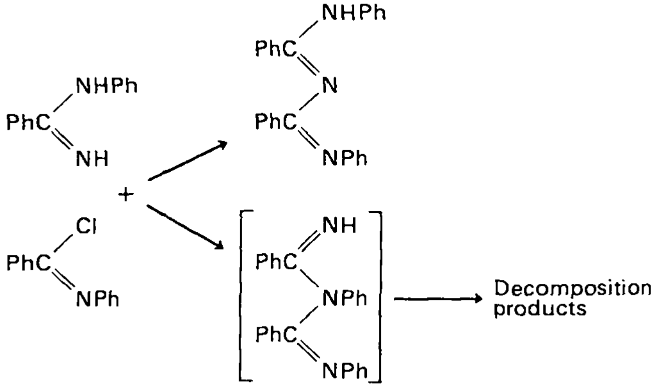
(51)



R = Me, Ph

(52)

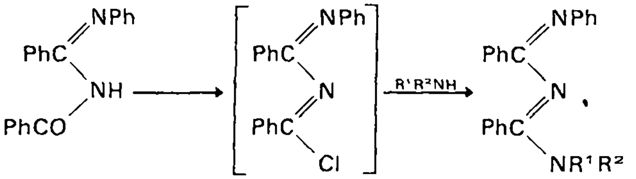
unstable. One reaction capable of giving both types of compound (equation 13) produced only the conjugated diamidide together with decomposition products of the unconjugated diamidide. This was in spite of the fact that, as observed from the yields, the reaction leading to the unconjugated diamidide was the favoured primary process.


PhC
NHPh
NH
+
Cl
PhC
NPh
NHPh
PhC
N
PhC
NPh
NH
PhC
NPh
PhC
NPh
Decomposition products

(13)

B. From N*-Benzoyl-*N′*-phenylbenzamidine and Amines*

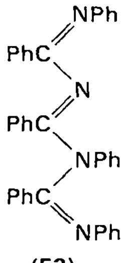
This route[8a], a logical extension of the foregoing, involved the conversion *in situ* of the benzoylamidine into the imidochloride which then reacted with the amine, as in equation (14). *p*-Chloroaniline, aniline, and


NPh
PhC
NH
PhCO
NPh
PhC
N
PhC
Cl
R¹R²NH
NPh
PhC
N
PhC
NR¹R²

(14)

$R^1 = p\text{-}ClC_6H_4$, $R^2 = H$
$R^1 = Ph$, $R^2 = H$
$R^1 = Ph$, $R^2 = Me$

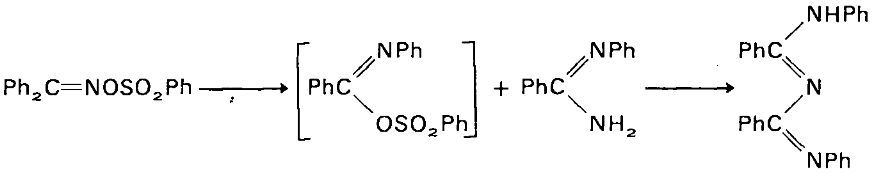
N-methylaniline were used. In a further experiment, employing *N*,*N*′-diphenylbenzamidine as the base, the triamidide (**53**), 1,2,4,5,6,7-hexaphenyl-1,3,5,7-tetra-azahepta-1,3,6-triene, was prepared.



(53)

C. From Imidosulphonates and Amidines

Because the benzenesulphonate of benzophenone oxime undergoes spontaneous Beckmann rearrangement[42] to the imidosulphonate, its treatment with *N*-phenylbenzamidine led[8a] to the diamidide (**54**) (equation 15). More feasibly, imidosulphonates were generated from *N*-substituted amides and sulphonyl chlorides in pyridine. Subsequent addition of an amidine then afforded the diamidide[8a].

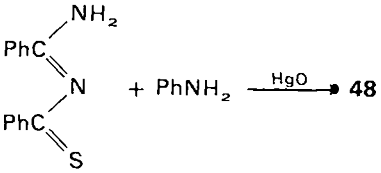


(15)

(54)

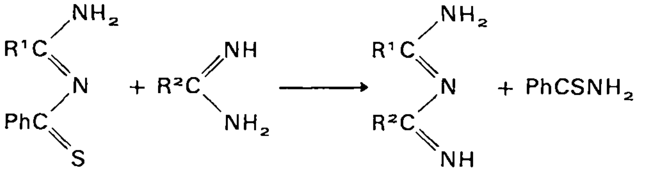
D. From N-Thiobenzoylbenzamidines and Amines

N-Thiobenzoylbenzamidines were prepared from the benzoyl compounds via the imidochloride and treatment with hydrogen sulphide in triethylamine. *N*-Thiobenzoylbenzamidine itself was first treated with aniline in the presence of mercuric oxide and the diamidide (**48**) was thereby obtained[8b] (equation 16).



(16)

A better method[8b] was to treat the thiobenzoyl compound with an amidine, whereby thiobenzamide was eliminated, and in this way (equation 17) several conjugated *N*-unsubstituted diamidides (**55**) were successfully obtained and characterized as their hydrochloride hydrates or hemihydrates.



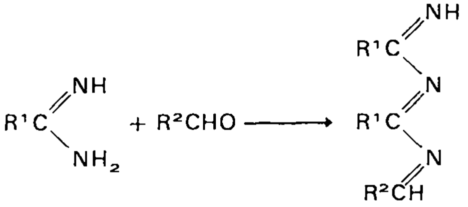
(17)

(**55**)

$R^1 = R^2 = Ph$, $p\text{-}MeOC_6H_4$ or $p\text{-}ClC_6H_4$
$R^1 = p\text{-}MeC_6H_4$, $R^2 = Ph$

E. From Arylamidines and Arylaldehydes

Japanese workers discovered[43] that condensation of aryl aldehydes with arylamidines did not give the simple arylidene–amidines ArCH:N·CAr′:NH as earlier reported[44], but instead led to the diamidide derivatives (**56**) together with substituted triazines.

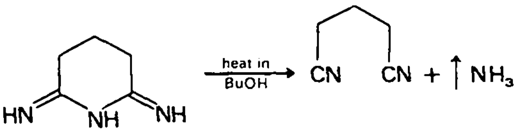


(**56**)

IV. PROPERTIES AND REACTIONS OF IMIDINES

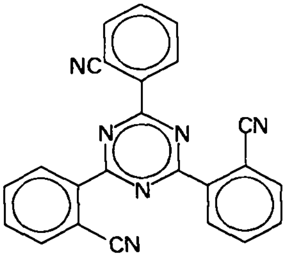
A. General Characteristics

The simple imidines, defined by the structure (**2**) and its tautomers (see Section I) are white crystalline solids, insoluble in hydrocarbons and e.g. diethyl ether and ethyl acetate. They may be crystallized from dry alcohols, formamide, and dimethyl formamide or from mixtures of these with ether or benzene[4a,9,13,14,22]. The imidines (7) and (8) were induced to crystallize by trituration with ethyl acetate[12,13]. On being heated imidines decompose at moderate temperatures, some without melting (see Table 1). Glutarimidine dissociates in boiling butanol to ammonia and the dinitrile[14] (equation 18), as does 1,3-diiminoisoindoline (5) at its melting



(18)

point[45]: in boiling 2-ethoxyethanol, diiminoisoindoline dissociates slowly and affords an appreciable yield of tricyanocyaphenine[45] (57), the trimer of phthalonitrile. Some imidines, e.g. diiminoisoindoline,



(57)

TABLE 1. Melting and decomposition points of some imidines

No	Imidine	Melting or decomposing point	Reference
1	Succinimidine	decomp. 200 °C	9
7	2,5-Diimino-3-methylpyrrolidine	143 °C(decomp.)	12
8	2,5-Diimino-3,4-dimethylpyrrolidine	decomp. 130–140°C	13
9	Glutarimidine	157–158 °C(decomp.)	14
10	2,6-Diimino-3-phenylpiperidine	201–202 °C(decomp.)	14
21	2,6-Diimino-3-methylpiperidine	154–155 °C(decomp.)	82
22	2,6-Diimino-3,5-dimethylpiperidine	209–210 °C(decomp.)	82
20	3,5-Diiminopiperazin-1-ylacetonitrile	180 °C(decomp.)	15
18	1,3-Diimino-*cis*-octahydroisoindole	decomp. 100–125 °C	22
14	Δ^8-Hexahydro-1,3-diiminoisoindole	decomp. 177–180 °C	22
5	1,3-Diiminoisoindoline	196 °C(decomp.)	4a

2,5-diimino-3,4-dimethylpyrrolidine[13] (**8**), and the imidines (**14**) and (**18**) from Δ^1-tetrahydrophthalonitrile and *cis*-hexahydrophthalonitrile give blue products at or near their decomposition points. This is because in the first case traces of phthalocyanine are formed[45] and in the last two cases the corresponding tetrazaporphins[22]. Other imidines, e.g. succinimidine (**1**) and 2,6-diimino-3-phenylpiperidine (**10**) decompose on being heated to give dark, intractable material[14].

The imidines are soluble in water to give basic solutions—some pK_a values are listed in Table 2—but soon undergo hydrolysis to the corresponding iminoimides and thence imides (see Section IV.B). It is not surprising then that imidines are sensitive to atmospheric moisture. Whereas diiminoisoindoline can be stored satisfactorily in tightly-stoppered bottles, succinimidine, glutarimidine and related imidines quickly begin to smell of ammonia (as a result of hydrolysis) unless additionally stored over a desiccant. As bases, the imidines form salts, e.g. hydrochlorides[2,4a], dihydrochlorides[4a,15,22], picrates[13,14,15,22], and platinichlorides[2]; diiminoisoindoline forms a nitrate that is sparingly soluble in water[4a], and so does the imidine (**12**)[16].

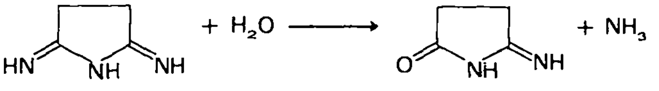
The main chemical reactions of imidines are described in the following sections (IV.B–IV.I). Briefly the imidines readily undergo hydrolysis by water, and substitution by hydroxylamine, primary and secondary amines, and active methylene compounds, with displacement of the exocyclic imino groups as ammonia. Some substitutions with rearrangement have been observed, and also bimolecular reductions. With hydrazine, there may be ring-expansion as well as substitution. Diamines can give macrocyclic products, and through the condensation of imidines with themselves, tetrazaporphin pigments are obtained. Most of the compounds, both acyclic and cyclic, will complex metals (see Section H).

TABLE 2. pK_a Values of some imidines, determined by potentiometric titration of M/800 solutions in 80% methoxyethanol at 20 °C

No.	Imidine	pK_a
1	Succinimidine	10·10
8	2,5-Diimino-3,4-dimethylpyrrolidine	9·63
9	Glutarimidine	9·53
10	2,6-Diimino-3-phenylpiperidine	9·73
18	1,3-Diimino-*cis*-octahydroisoindole	9·21
14	Δ^8-Hexahydro-1,3-diiminoisoindole	7·23
5	1,3-Diiminoisoindoline	7·46

B. Reactions with Water

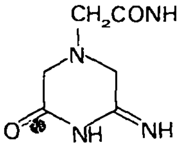
Whilst the hydrochloride of succinimidine appeared to be stable in water[2], the base itself (**1**) was quickly hydrolysed and 5-iminopyrrolid-2-one (**58**) subsequently crystallized out[9] (equation 19). The dimethyl



(1) (58)

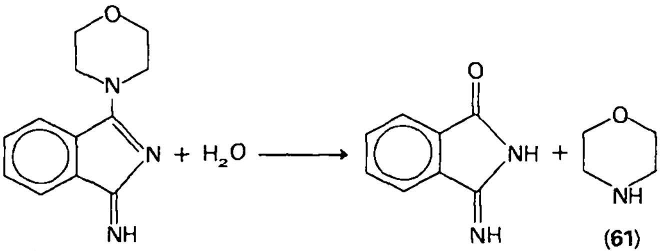
(19)

homologue[13] (**8**), the *cis*-cyclohexanoimidine[22] (**18**), the imidine[16] (**38**), and 4-benzyl-2,6-diiminopiperazine[15] (**11**) all similarly underwent hydrolysis to the corresponding iminoimides: 3,5-diiminopiperazin-1-ylacetonitrile[15] (**20**) suffered hydrolysis of the side-chain nitrile function as well under these mild conditions, to afford the product **59**. The *N*,*N*-

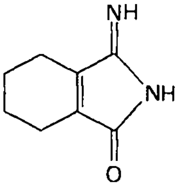


(59)

disubstituted imidine (**60**) in water hydrolysed to the iminoimide (**61**) in good yield, the substituted group being displaced[17]. 1,3-Diiminoisoindoline (**5**) and its tetrahydro analogue (**14**) proved to be more stable so that hydrolyses to the corresponding iminoimides, (**61**) and (**62**), were best carried out by brief boiling with the minimum of water needed to effect dissolution (cf. Ref. 22).

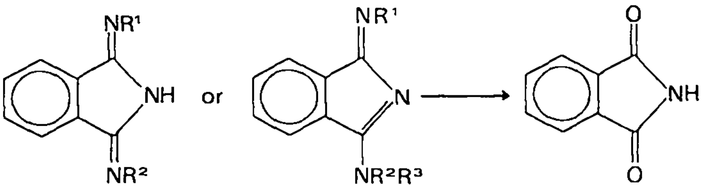


(60) (61)

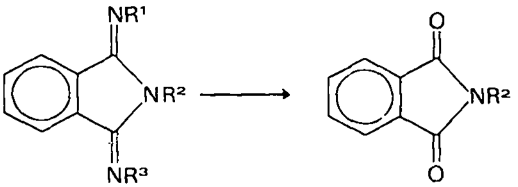


(62)

When imidines or iminoimides were boiled with water for some time, especially in the presence of hydrochloric acid, the corresponding imides were formed in good yield. Boiling aqueous hydrochloric acid hydrolysed $N(1$ or $3)$-substituted diiminoisoindolines to phthalimide (equation 20), or $N_{(2)}$-substituted diiminoisoindolines to N-substituted phthalimides (equation 21) so providing a structurally diagnostic degradation[17]. The method did not appear to be applicable, however, to other imidines.

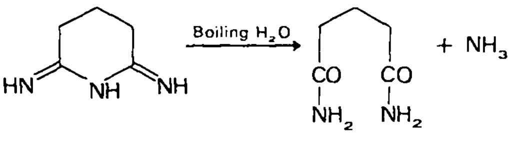


(20)



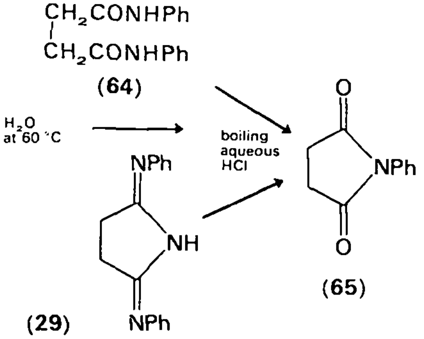
(21)

Glutarimidine with boiling water underwent ring-opening to yield glutaramide[14] (**63**) (equation 22). 2,5-Di(phenylimino)pyrrolidine (**29**) in aqueous methanol at 60–70 °C similarly gave succindianilide[9] (**64**). Under acid conditions the latter cyclized to N-phenylsuccinimide (**65**), so it was hardly surprising to find that the aqueous acid hydrolysis of 2,5-di(phenylimino)pyrrolidine (**29**) gave N-phenylsuccinimide[9] (equation 23).



(22)

(**63**)


CH2CONHPh
CH2CONHPh
H2O at 60 °C
boiling aqueous HCl
NPh
NH
NPh
O
NPh
O

(64)

(29)

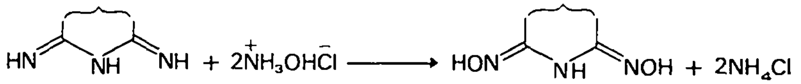
(65)

(23)

C. Reactions with Hydroxylamine

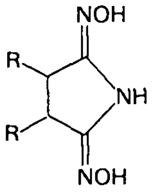
1. Imidine oximes from imidines

An apparently general reaction of imidines is that with two molecular proportions of hydroxylamine hydrochloride in boiling ethanol, whereby the exocyclic imino groups are substituted by the hydroxyimino function with concomitant formation of ammonium chloride (equation 24). By this substitution reaction, the bis-hydroxyimino (dioxime) derivatives

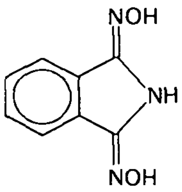

HN
NH
NH + 2$\overset{+}{N}H_3OH\overset{-}{Cl}$
HON
NH
NOH + 2NH_4Cl

(24)

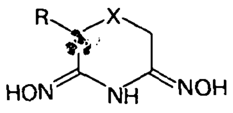
(66)[9], **(68)**[9], **(69)**[14], **(70)**[14], **(73)**[22], **(74)**[22], and **(71)**[15] were obtained. With the imidine (**20**), there was also addition of hydroxylamine to the substituent nitrile function so that the product was the compound (**72**)[15]. Free


NOH
R
R
NH
NOH

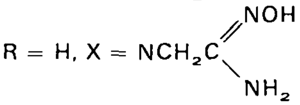
(66) R = H
(67) R = Me

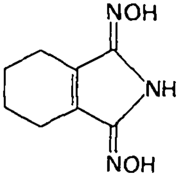


(68)

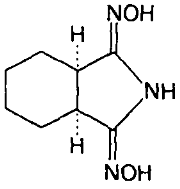

R
X
HON
NH
NOH

(69) R = H, X = CH_2
(70) R = Ph, X = CH_2
(71) R = H, X = NCH_2Ph


(72) R = H, X = $NCH_2C(=NOH)NH_2$

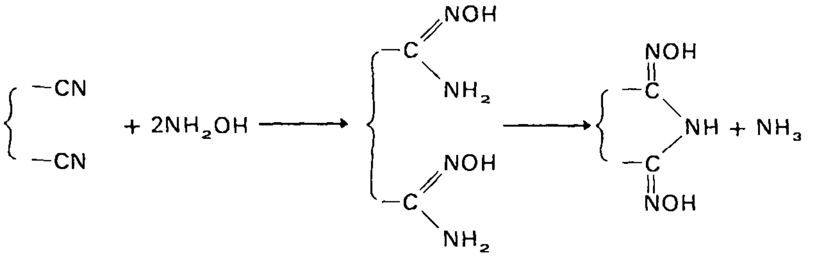


(73)

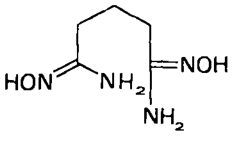


(74)

hydroxylamine was used to convert the diiminopyrrolidine (**8**) into the dioxime (**67**)[13]. In many cases, the dioximes were also obtained by interaction of the appropriate dinitriles with ethanolic hydroxylamine under reflux[9,13,14,15,22], a process evidently involving addition and *then* cyclization (equation 25)[14,15], because under milder conditions the bis-amide oxime, e.g. **75**[14], resulted.

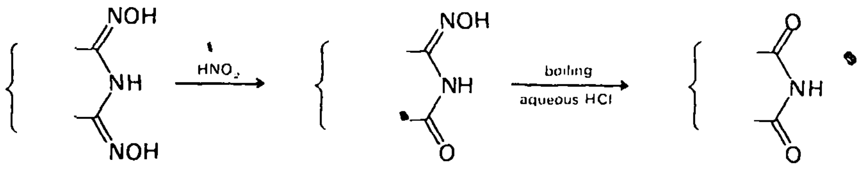


(25)



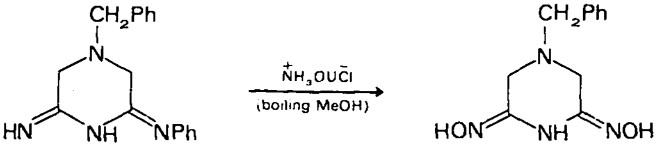
(75)

The imidine dioximes were degraded to monoxime derivatives[9,14,15] (equation 26) by nitrous acid (cf. Ref. 46), or in one instance by mild acid hydrolysis[47]. Acid hydrolysis of the monoxime compounds afforded the corresponding imides[9,14,15].



(26)

When the *N*-phenylimidine (**76**) was heated with hydroxylamine hydrochloride in methanol, both the substituted and unsubstituted imino functions were replaced by hydroxyimino groups (equation 27)[15].

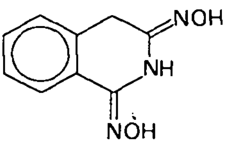


(**76**)

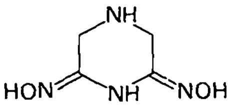
(27)

2. Imidine oximes from dinitriles

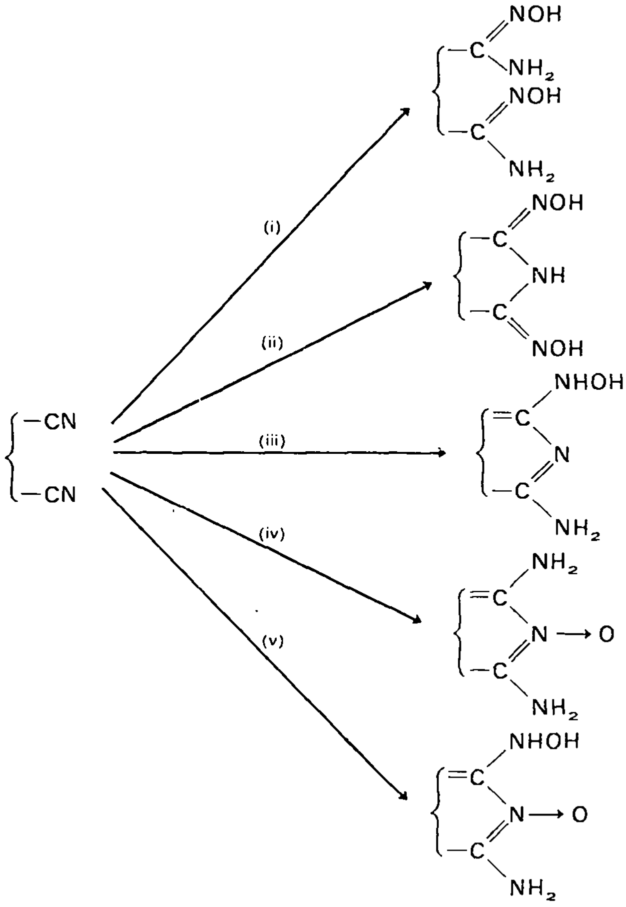
The imidine dioxime derivative (**77**) was obtained by treating *o*-cyanobenzylcyanide with a mixture of hydroxylamine and its hydrochloride in boiling aqueous methanol[48], conditions which were effective[15] for the conversion of glutaronitrile direct to the piperidine dioxime (**69**). For preparing **77** there was no alternative route from an imidine (see Section II.C.1). With hydroxylamine itself in boiling methanol, *o*-cyanobenzylcyanide afforded 1-amino-3-hydroxyaminoisoquinoline[20,48] and not an imidine oxime. *N*,*N*′-Dicyanoamidines and hydroxylamine gave 2,6-diaminotriazine 1-oxides[49], whilst iminodiacetonitrile with a mixture of hydroxylamine and its hydrochloride afforded[48] a mixture of 2-amino-6-hydroxyaminopyrazine 1-oxide and the imidine dioxime (**78**) (which was isolated as a hydrated molecular complex with hydroxylamine hydrochloride). There are then several routes open for the reaction of a dinitrile with hydroxylamine so that the preparation of an imidine dioxime is best carried out from the imidine when this is available. The foregoing products from 1,3-dinitriles correspond to the five possible pathways [shown as (i)–(v) in equation 28] for reaction between a dinitrile and an excess of hydroxylamine. The products of pathways (ii)–(v) correspond to the possible ways in which the bis-amide oxime could cyclize, but it is uncertain[48] that the reactions proceed in that way.



(**77**)



(**78**)

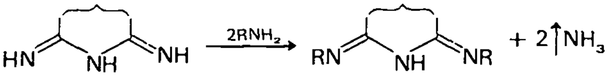


(28)

D. Reactions with Amines

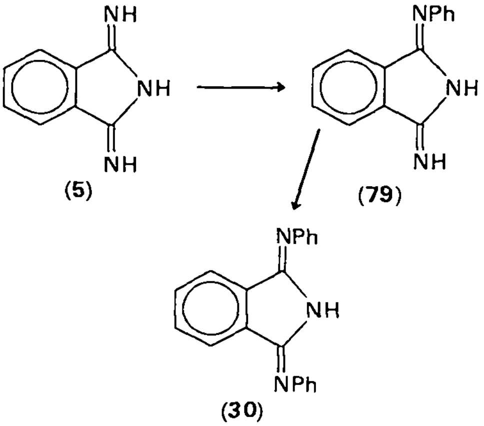
1. Condensations with primary amines

A characteristic reaction of imidines is the replacement of the exocyclic imino groups by amines (equation 29)^4. Thus 1,3-diiminoisoindoline when heated with an excess of an aliphatic or aromatic primary amine such as methylamine, butylamine, benzylamine, aniline, 2-naphthylamine, 2- and 3-aminopyridine, and aminopyrazine, gave the corresponding



(29)

1,3-disubstituted imino derivatives[4a,17,24] with evolution of ammonia. In some cases a stepwise replacement of the exocyclic imino groups could be effected, as exemplified by the behaviour of diiminoisoindoline with aniline[24,50] (equation 30), 3-aminopyridine[24], or 2-naphthylamine[24,50],

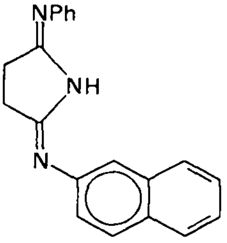


(30)

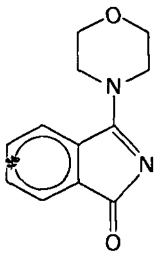
or of succinimidine[9] or 2,6-diimino-3-phenylpiperidine[14] with aniline. It also proved possible to prepare mixed derivatives such as **80**[9] by carrying out the two stages separately with different amines.

2. Reactions with secondary amines

Attempts to react 1,3-diiminoisoindoline with secondary amines such as dimethylamine failed[17] although with morpholine, the part-hydrolysis product (**81**) arose[24]. However. representatives of the amino–imino tautomeric form of the imidine were successfully obtained by alkoxide-catalysed addition of morpholine and of diethylamine to phthalonitrile[17], these reactions providing the imidine compounds (**60**) and (**82**), respectively.

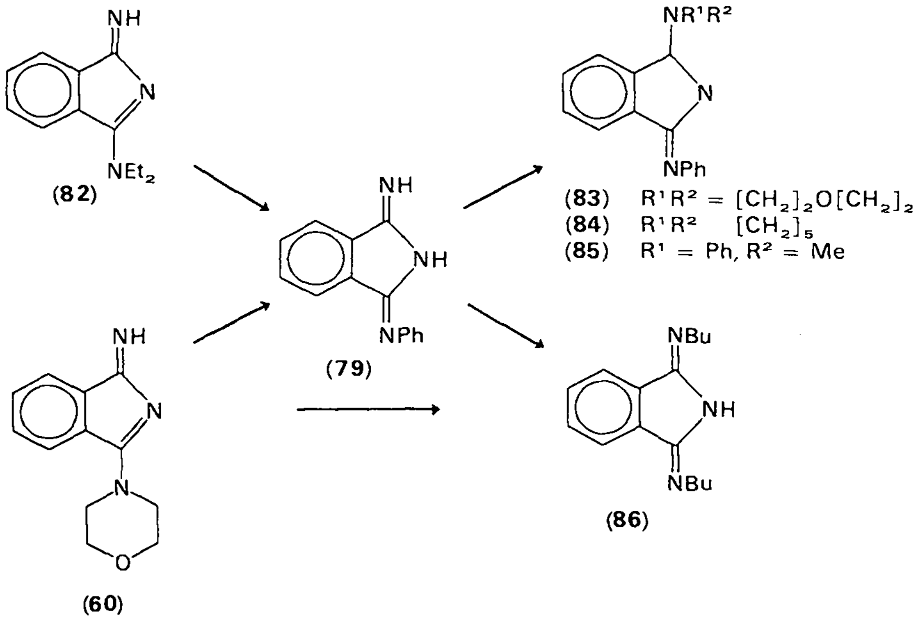


(80)



(81)

An alternative method was to use a secondary amine at the second stage of a two-stage reaction with an imidine (see equation 30). In this way 1-imino-3-phenyliminoisoindoline (**79**) with morpholine, piperidine, or N-methylaniline afforded[24] the amino–imino compounds (**83**), (**84**), and (**85**), the free imino group being replaced in each case.



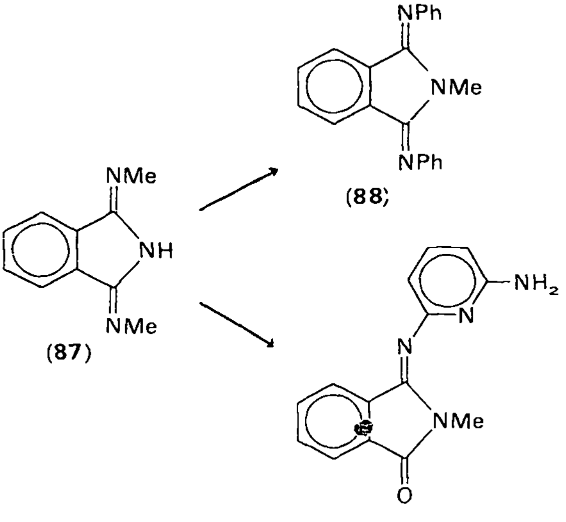
(83) $R^1R^2 = [CH_2]_2O[CH_2]_2$
(84) R^1R^2 $[CH_2]_5$
(85) $R^1 = Ph, R^2 = Me$

3. Replacement of *N*-substituted imidine functions

Sometimes the substituted *N*-functional group of an imidine is displaced preferentially, as was found on treating the imidine derivatives **82** and **60** with aniline in the cold: these reactions afforded 1-imino-3-phenyliminoisoindoline[17] (**79**) only. When refluxed in ethanol with an excess of butylamine both substituted and unsubstituted functions in the imidine derivatives **60** and **82** were displaced—as was then expected—to give 1,3-dibutyliminoisoindoline (**86**)[17]. More surprising, in view of the preparation of the mixed derivative (**80**) above, was the conversion of the monophenylimino compound (**79**) with butylamine in boiling ethanol into the dibutylimino derivative (**86**)[17].

4. Substitution with rearrangement

When either 1-imino-3-methyliminoisoindoline hydriodide or 1,3-dimethyliminoisoindoline (**87**) was heated with aniline, 2-methyl-1,3-diphenyliminoisoindoline (**88**) resulted[17]. The structure of this product, isomeric with that of the compound (**85**) previously encountered, was supported by the results of acid hydrolyses which gave aniline and *N*-methylphthalimide from **88**[17] but a mixture of aniline, *N*-methylaniline, and phthalimide from **85**[24].

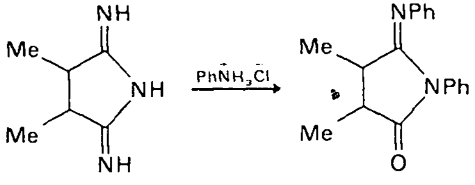


(87)

(88)

(89)

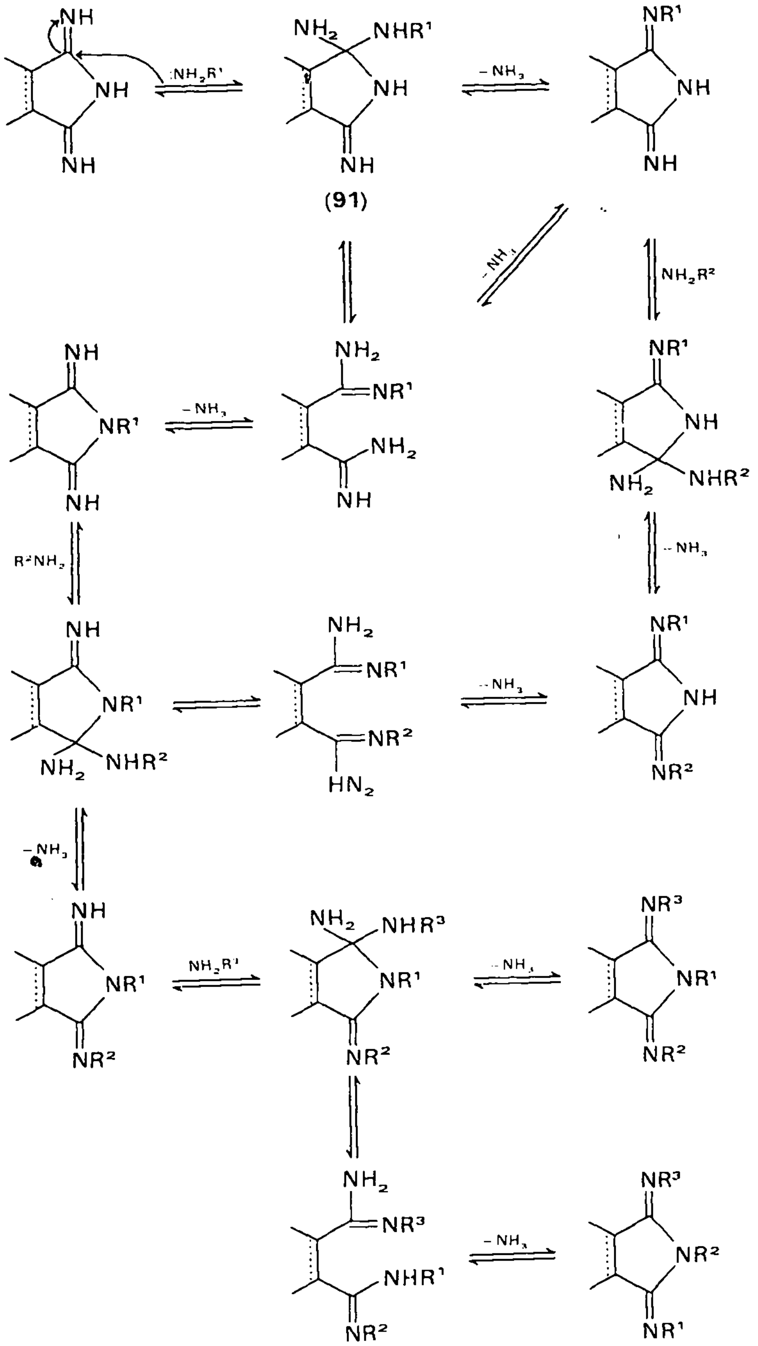
After 1,3-dimethyliminoisoindoline (**87**) had been interacted with 2,6-diaminopyridine in boiling ethyl carbitol, the product (**89**) was isolated. Here, the substitution with rearrangement was slightly complicated by incidental hydrolysis of one of the original exocyclic functions[17]. Somewhat analogous was the behaviour of 2,5-diimino-3,4-dimethylpyrrolidine (**8**) with aniline hydrochloride in boiling propanol which led to 3,4-dimethyl-1-phenyl-5-phenyliminopyrrolid-2-one (**90**)[13].



(8)

(90)

5. Mechanism of amine–imidine substitutions

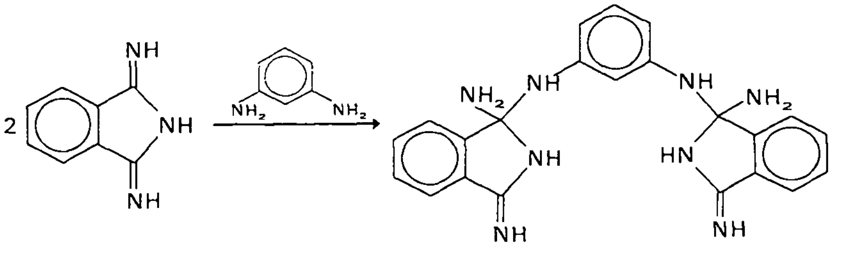

NH
NH
NH
:NH$_2$R^1
NH$_2$
NHR^1
NH
NH
(91)
−NH$_3$
NR^1
NH
NH
−NH$_3$
NH$_2$R^2
NH
NR^1
NH
−NH$_3$
NH$_2$
NR^1
NH$_2$
NH
NR^1
NH
NH$_2$
NHR^2
R^{2}NH$_2$
−NH$_3$
NH
NR^1
NH$_2$
NHR^2
NH$_2$
NR^1
NR^2
HN$_2$
−NH$_3$
NR^1
NH
NR^2
−NH$_3$
NH
NR^1
NR^2
NH$_2$R^3
NH$_2$
NHR^3
NR^1
NR^2
−NH$_3$
NR^3
NR^1
NR^2
NH$_2$
NR^3
NHR^1
NR^2
−NH$_3$
NR^3
NR^2
NR^1

(31)

The preceding experimental results (Sections IV.D.1–4) suggest that amines react with imidines initially by addition (see **91**) and this is followed by an elimination, usually of ammonia. Alternatively, the elimination might take the form of ring-opening to a diamidine derivative in which case reclosure with elimination of ammonia or an amine then follows. After this the product may have a substitution pattern which could not have arisen from the imidine by straightforward addition–elimination. All of the various stages appear to be potentially reversible (equations 31 show many but not all of the possibilities). The nature of the product will depend on a variety of features such as the rates of the possible alternative reactions, the relative stabilities and/or solubilities of intermediates and of alternative products, the relative volatilities of amines, and mass action effects. Prediction of products in particular instances may therefore be difficult.

6. Imidine–diamine adducts

Some tangible evidence for addition being the first step in imidine–amine reactions came from the observation that 1,3-diiminoisoindoline formed a yellow 2:1-adduct (**92**) with *m*-phenylenediamine (equation 32),



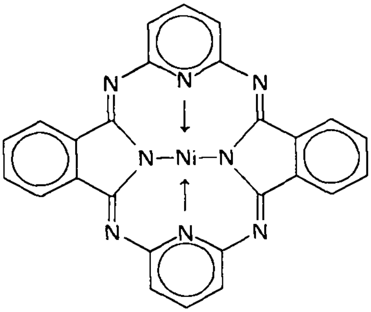
(32)

(**92**)

and analogous adducts with 2,4-diaminotoluene, and 2,6-diaminopyridine[50]. Structures alternative to **92** and its congeners were considered but were rejected on chemical and spectroscopic evidence[50]. The adducts in ethanol solution were labile to picric acid which precipitated diiminoisoindoline picrate almost quantitatively. Towards heat, the phenylenediamine adduct (**92**) was moderately stable, 32% being recovered from boiling ethanol after 1·5 h[50]. However in boiling butanol, ammonia was rapidly evolved and red and yellow compounds were obtained. The nature of these products is described in the next Section.

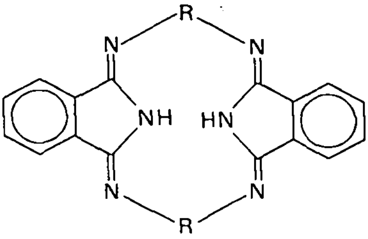
7. Cross-conjugated macrocycles from diamines

Early in the study of the reactions of 1,3-diiminoisoindoline (**5**) with amines, Elvidge and Linstead found[19] that 2,6-diaminopyridine condensed readily with the imidine in boiling butanol to yield the '2,6-pyridine macrocycle' (**13**). This formed scarlet needles, m.p. 344 °C, from hot nitrobenzene and yellow felted needles of a monohydrate from benzyl alcohol (below 100 °C). The structure was indicated by the mode of formation, molecular weight, elementary composition, and the hydrolysis with warm concentrated hydrochloric acid to equimolar amounts of phthalimide and 2,6-diaminopyridine. Final verification of the macrocyclic structure came from X-ray crystallographic analysis[51] of the dark brown nickel derivative (**93**), m.p. 386 °C, which was prepared[19] from the macrocycle (**13**) and nickel acetate in hot benzyl alcohol.

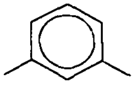


(**93**)

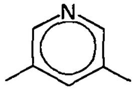
Extension of the macrocycle synthesis to other '*meta*-diamines' was then made. From diiminoisoindoline in boiling butanol with *m*-phenylenediamine, 3,5-diaminopyridine, 2,7-diaminonaphthalene, and 2,8-diaminoacridine, the cross-conjugated macrocycles (**94**–**97**) were readily obtained[52], which have 16-, 20-, and 24-membered inner great rings. All were yellow in colour, high melting and thermally stable. The benzene (**94**) and naphthalene macrocycles (**96**) (obtained in 70% yields) were hydrolysed only by concentrated mineral acid under rather vigorous conditions and then to phthalic acid and the diamine in equal proportions. The new macrocycles all formed orange-red complexes with acetic acid, mineral acids, and various solvents (e.g. formamide). An analogous macrocyclic compound (**98**) was later made by Klyuev and Snegireva[53] from the imidine (**36**) and *m*-phenylenediamine.



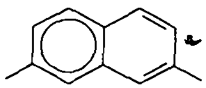
(94) R =



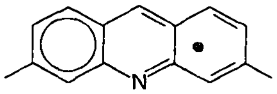
(95) R =



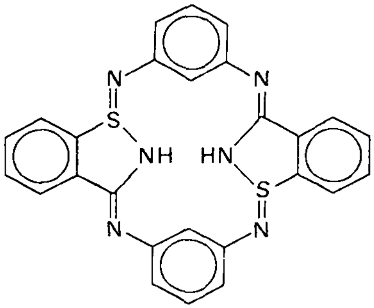
(96) R =



(97) R =

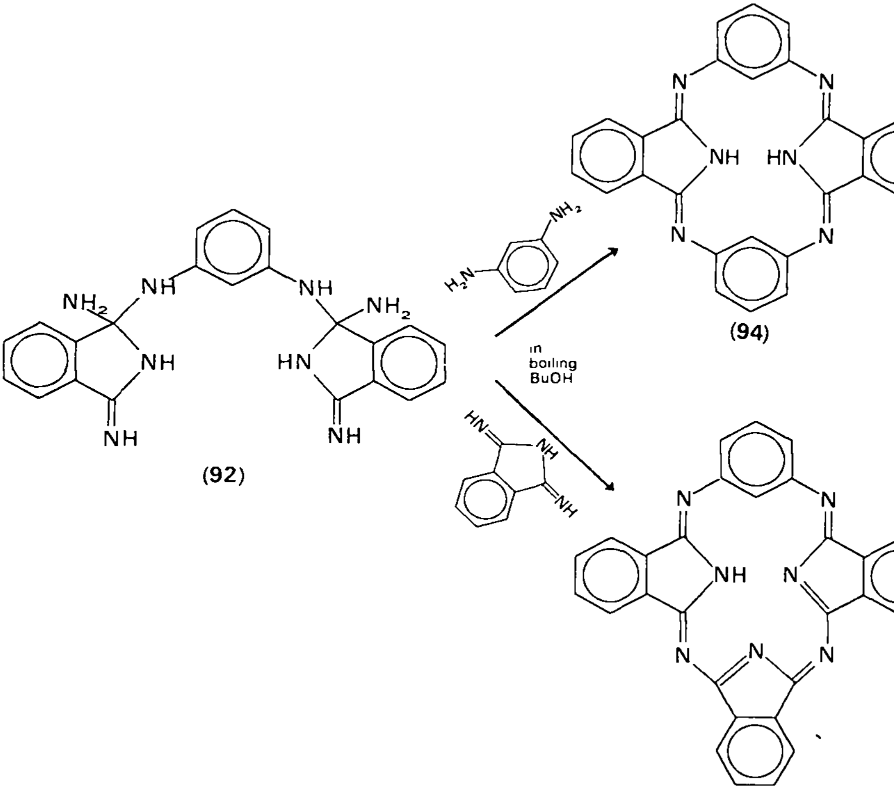


Clark had observed that when the *m*-phenylenediamine-diiminoisoindoline adduct (**92**) was heated in boiling butanol, ammonia was evolved and the yellow benzene macrocycle (**94**) was obtained together with a new red compound (cf. Ref. 50). Heating the adduct (**92**) in butanol with 1 molar proportion of *m*-phenylenediamine gave only the yellow benzene



(98)

macrocycle (**94**)[50]. When instead 1,3-diiminoisoindoline was used then over 70% of the dark red product, $C_{30}H_{17}N_7$, m.p. 353 °C (decomp.) resulted[50]. This was the triisoindole-benzene macrocycle (**99**), evidently formed as indicated (equation 33). Although the new red macrocycle effectively comprised three-quarters of the chromophore of phthalocyanine (λ_{max} 698 nm) and indeed absorbed light up to λ_{max} 507 nm (although not with high intensity), its general properties were very different from that pigment. Thus it was unstable in some solvents, and was readily hydrolysed by aqueous acid to phthalimide and *m*-phenylenediamine (in the proportions 3:1)[50].



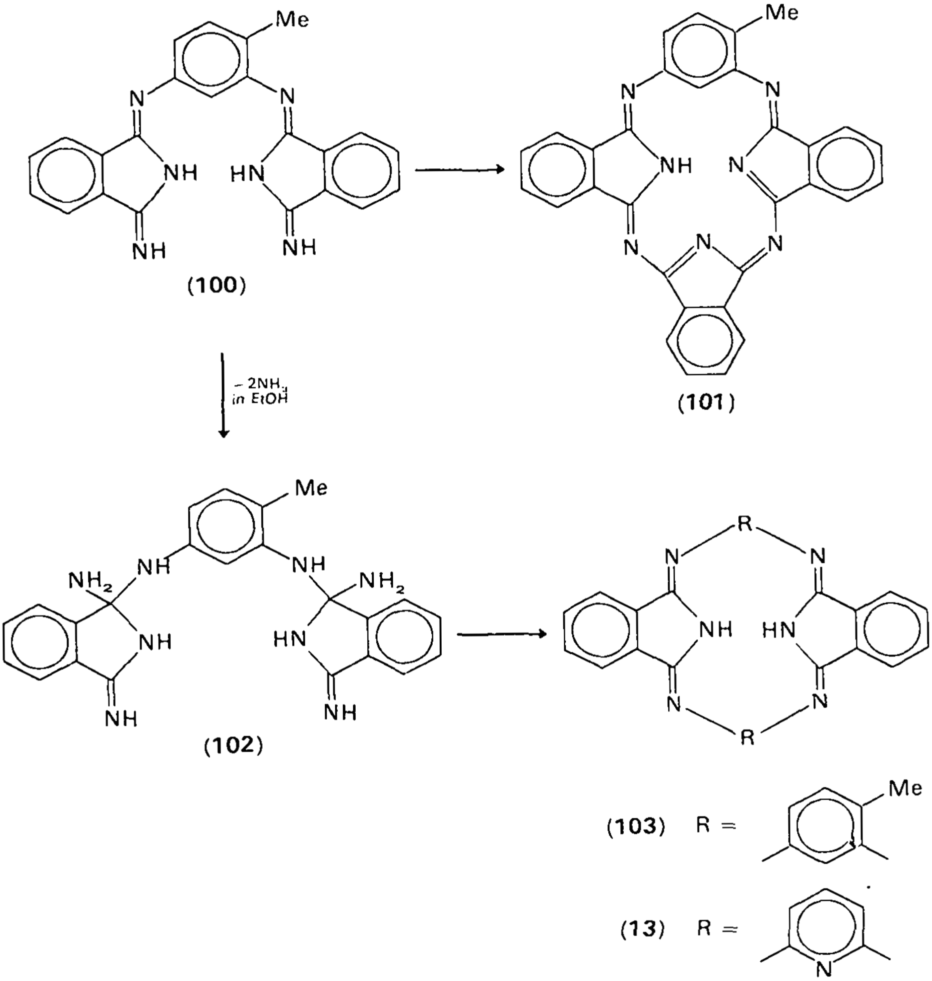
(92)

(94)

(99)

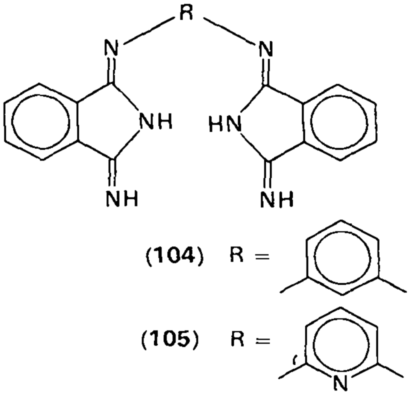
(33)

The analogous 'triisoindole-toluene' macrocycle (**101**) with m.p. 285 °C(decomp.) and λ_{max}542 nm was obtained by condensing the three-unit product (**100**) with diiminoisoindoline in boiling butanol[50]. The starting material (**100**) had arisen slowly from the toluene-2,4-diamine-diiminoisoindoline adduct (**102**) when this was kept in solution[50]. No red macrocycle (**101**) resulted from heating the adduct **102** with or without diiminoisoindoline, and no analogous red macrocycle came from similar experiments with the 2,6-diaminopyridine–diiminoisoindoline adduct. These several experiments gave[50] instead only the thermally stable macrocycles **103** and **13**, respectively, presumably because of dissociation of the adducts in hot solution and recombination of the components to give the most stable products (cf. Section IV.D.5).

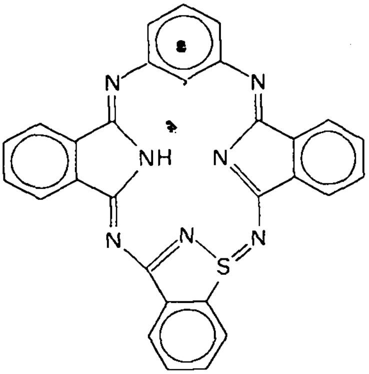


(100) (101) (102) (103) (13)

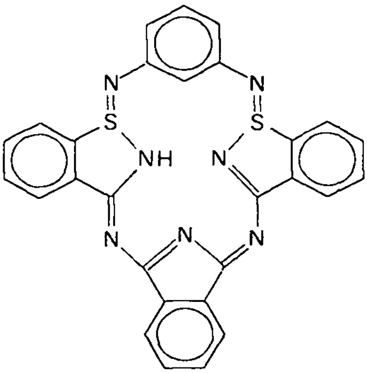
In related experiments[54], the three-unit products **104** and **105** (Section II.E) were used for preparing macrocycles. Compound **104** with *m*-phenylenediamine readily afforded the benzene macrocycle (**94**)


R
N
N
NH
HN
NH
NH
(104) R =
(105) R =
N

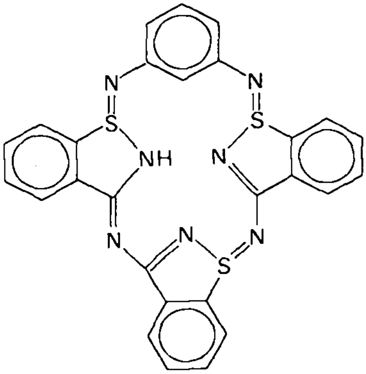
and with diiminoisoindoline yielded the red triisoindole macrocycle (99). The three-unit compound **105** condensed with 2,6-diaminopyridine to give the 2,6-pyridine macrocycle (**13**) but failed to react with diiminoisoindoline even in boiling butanol. Attempts at other mixed condensations



(106a)


N
N
S
S
NH
N
N
N
N

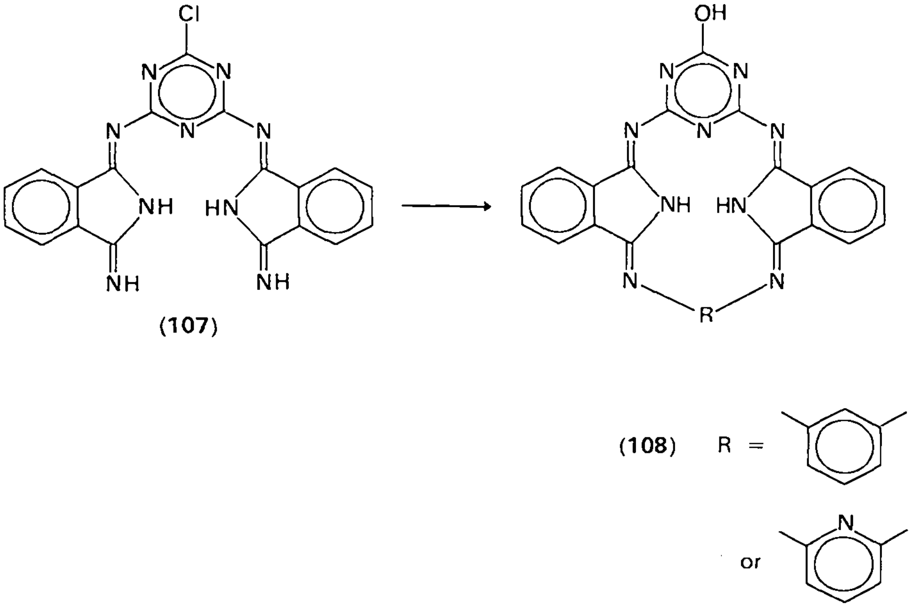
(106b)


N
N
S
S
NH
N
N
N
S
N

(106c)

gave symmetrical products, suggesting again that disproportionations and recombinations occur in imidine–amine interactions (Section IV.D.5).

In extensions of the foregoing work, three-unit products analogous to **104**, derived from substituted *m*-phenylenediamines, were used to prepare the corresponding macrocycles[55a], and the imidine (**36**) was employed for preparing the analogues (**106a**, **b**, and **c**) of the triisoindole type of macrocycle[55b]. Unsymmetrical analogues of the yellow macrocycles were also obtained[55b], for example types (**108**), from condensation of the three-unit compound (**107**) (Section II.E) with *m*-phenylenediamine or 2,6-diaminopyridine. Incidental to the cyclocondensation was hydrolysis of the chloro substituent.

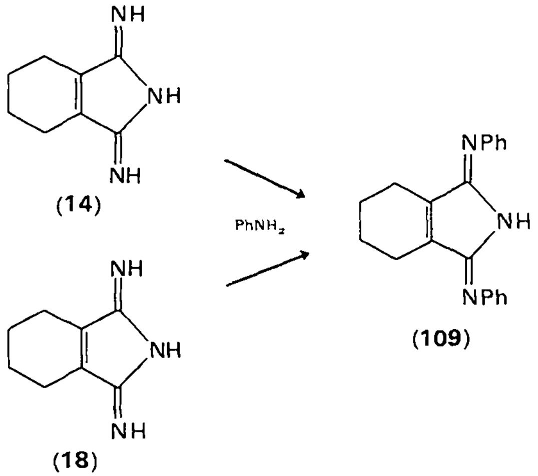


(107)

(108)

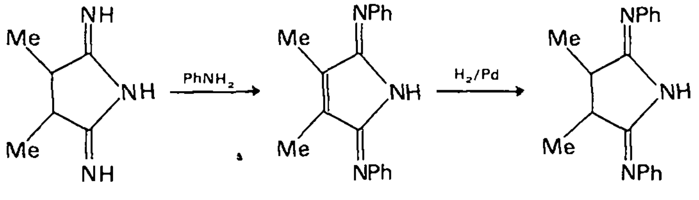
8. Dehydrogenation of imidines in reactions with aniline

When the *cis*-cyclohexano imidine (**18**) was heated with aniline in ethanol, the product isolated was not the expected diphenylimino com-



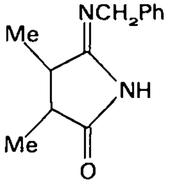
(14) (18) (109)

pound but was the dehydrogenation product[22] (**109**), identical with the product from condensation of the cyclohexeno imidine (**14**) with aniline. 2,5-Diimino-3,4-dimethylpyrrolidine (**8**) similarly interacted with aniline to yield the pyrroline derivative[13] (**110**) and not the expected product. The latter (**111**) was obtained by catalytic hydrogenation of the pyrroline (**110**) and was found not to be particularly sensitive to air. Condensations



(8) (110) (111)

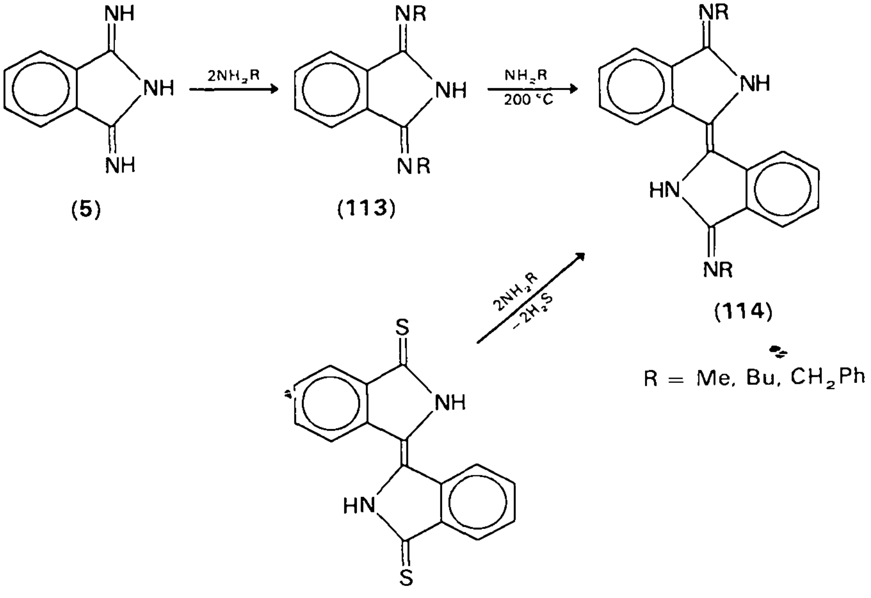
of the imidines (**8**) and (**18**) with hydroxylamine, for example, were not accompanied by dehydrogenation, so that the aniline or an impurity in it seems to be implicated as the oxidant. However, the mechanism of these dehydrogenations remains obscure. In further experiments[13], the dimethylsuccinimidine (**8**) was treated with aniline hydrochloride, and with cyclohexylamine and benzylamine. There was no dehydrogenation, but each of the reactions was accompanied by hydrolysis, e.g. to give **112**, and the first reaction involved also a rearrangement (Section IV.D.4), to give **90**.



(112)

9. Bimolecular reduction of imidines by amines

Whilst treatment of 1,3-diiminoisoindoline with primary amines under mild conditions effects substitution of the exocyclic imino groups as indicated by **113** (see Section IV.D.1), under more vigorous conditions (at up to 200°C) and with methylamine or analogues such as butylamine and benzylamine, there is in addition a bimolecular reductive coupling leading to β-isoindigo derivatives (**114**) as shown (equation 34). The constitution of these orange products was established[56] mainly through their synthesis from dithio-β-isoindigo (**115**) and the particular amines. The nature of the reaction **113** → **114**, as a bimolecular reductive coupling



(5) (113) (114) (115)

R = Me, Bu, CH$_2$Ph

(34)

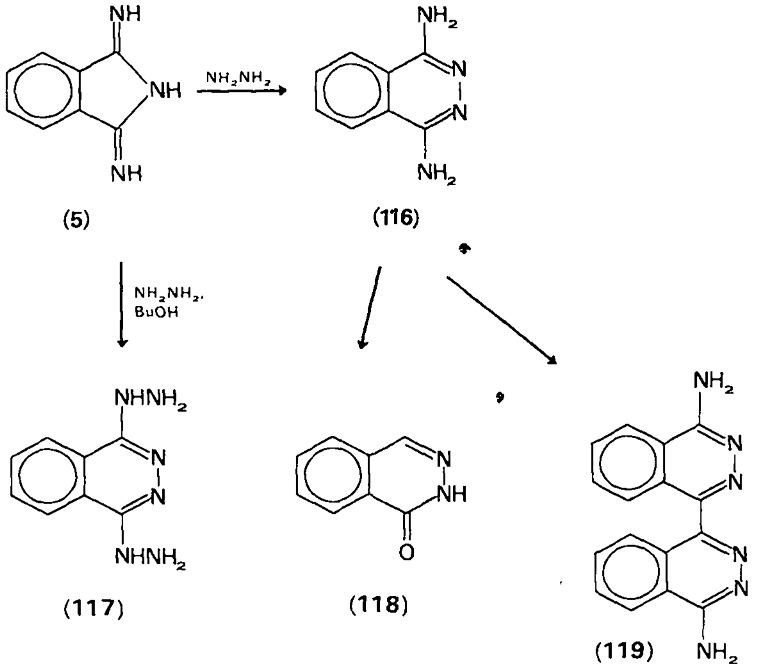
effected by the amine, followed from several observations. The reaction was not effected by ammonia or aniline but only by alkylamines. When 1-imino-3-phenyliminoisoindoline was heated in purified *t*-amyl alcohol with benzylamine and the dibenzylimino-β-isoindigo product was collected and the filtrate treated with 2,4-dinitrophenylhydrazine reagent, almost 2 molar proportions of benzaldehyde were isolated as the derivative. An identical reaction, but omitting the imidine, gave no carbonyl compound. Hence the benzylamine (in this particular case) functions by the process shown (equation 35) at the demand of the imidine. The reductive coupling process is then as indicated (equation 36)[56].

$$PhCH_2NH_2 \longrightarrow 2H\bullet + PhCH{=}NH[\xrightarrow{H_2O} PhCHO] \qquad (35)$$

$$2(\mathbf{113}) + 4H\bullet \longrightarrow (\mathbf{114}) + 2RNH_2 \qquad (36)$$

10. Ring-expansion of imidines by hydrazine

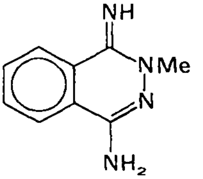
Baumann and colleagues[6b] briefly reported that 1,3-diiminoisoindoline (**5**) underwent ring-expansion with hydrazine, to yield 1,4-diaminophthalazine (**116**). This product is in fact very hygroscopic and is normally isolated as the hydrate[57]. Under more vigorous conditions in boiling



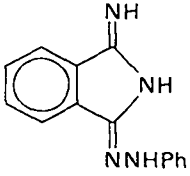
(5) (116) (117) (118) (119)

butanol, diiminoisoindoline and hydrazine yielded[57] 1,4-dihydrazinophthalazine (**117**). At 190°C phthalazin-1(*H*)-one (**118**) was formed, evidently by hydrolytic and reductive deamination of the intermediate diaminophthalazine (**116**) as separate experiments showed. In refluxing hydrazine hydrate, diiminoisoindoline afforded phthalazinone (**118**) together with an orange compound which was identified as the bis-aminophthalazinyl (**119**)[57].

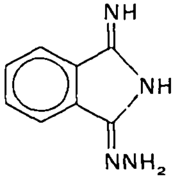
Methylhydrazine effected ring expansion of diiminoisoindoline to the phthalazine derivative (**120**) but phenylhydrazine behaved merely as a somewhat unreactive primary amine (Section IV.D.1) and gave the monosubstituted imidine derivative (**121**) which on acid hydrolysis afforded phthalimide[57]. The corresponding imidine derivative from hydrazine, *viz.* **122**, was obtained by alkoxide-catalysed addition of hydrazine to phthalonitrile. This *N*-amino imidine (**122**) condensed with acetone as expected, yielding **123**, it condensed with hydroxylamine to give the imidine dioxime (**68**), it was degraded by a mixture of nitrous and hydrochloric acids to phthalimide, and underwent ring-expansion in warm ethanol with hydrazine hydrate to 1,4-diaminophthalazine (**116**). Ring expansion of the purified aminoimidine (**122**) was not induced by boiling in ethanol alone, or with added sodium ethoxide or ammonia. Treatment of a solution of the acetone condensation product (**123**) in a minimum of ethanol with hydrazine hydrate caused disproportionation and precipita-



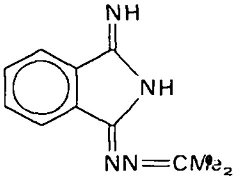
(120)



(121)

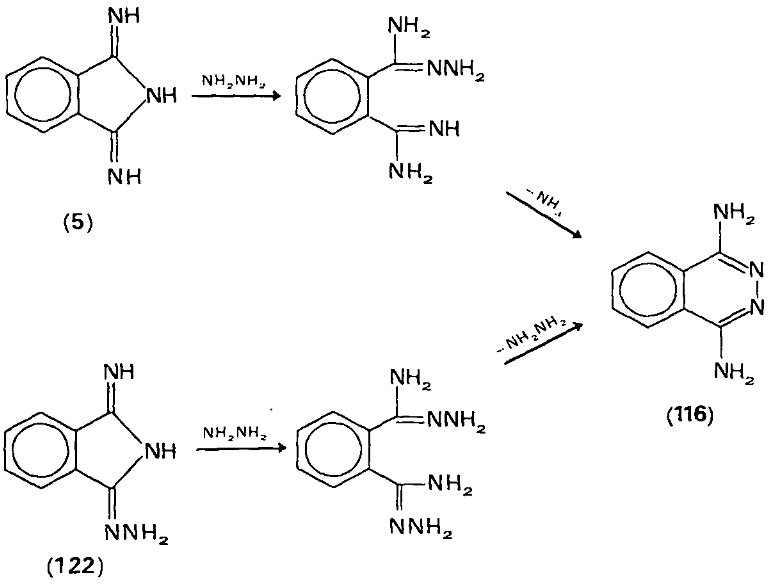


(122)



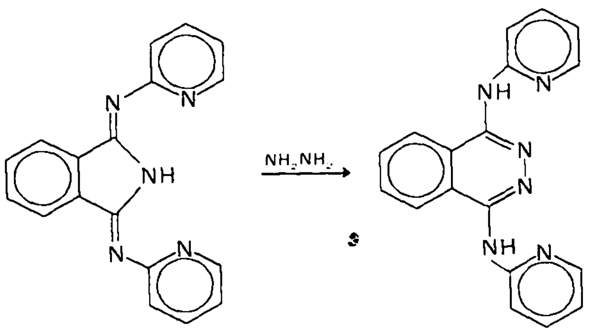
(123)

tion of the sparingly soluble aminoimidine (**122**), ring-expansion having no chance to occur. It appears that ring-expansion of the aminoimidine (**122**) to **116** proceeds through ring-opening to phthalamide dihydrazone and then ring closure with elimination of hydrazine, whilst in the conversion of diiminoisoindoline (**5**) into 1,4-diaminophthalazine (**116**), 2-amidino-benzamide hydrazone would appear to be the intermediate (equation 37)[57].


NH
NH
NH
NH₂NH₂
NH₂
NNH₂
NH
NH₂
(5)
-NH₃
NH₂
N
N
NH₂
(116)
-NH₂NH₂
NH
NH
NNH₂
NH₂NH₂
NH₂
NNH₂
NH₂
NNH₂
(122)

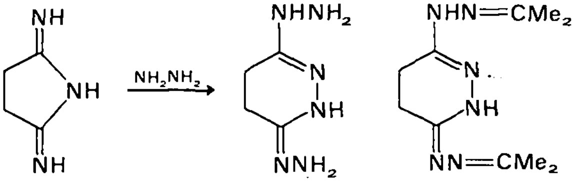
(37)

Other ring-expansions of imidines achieved with hydrazine were the conversion of 1,3-di-2′-pyridyliminoisoindoline (**124**) into the 1,4-di-2′-pyridylaminophthalazine[58] (**125**), and of succinimidine (**1**) to 6-hydrazino-


N
N
NH
N
N
NH₂NH₂
NH
N
N
N
NH
N

(124) (125)

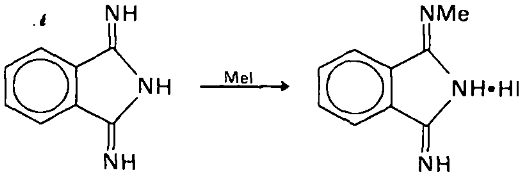
3-hydrazono-2,3,4,5-tetrahydropyridazine[59] (**126**). This particular tautomeric form for the product was strongly indicated by the ^{1}H-n.m.r. spectrum as well as that of the diisopropylidene derivative (**127**) obtained by condensation of **126** with acetone[59].


NH
NH
NH
NH_2NH_2
$NHNH_2$
N
NH
NNH_2
$NHN{=}CMe_2$
N
NH
$NN{=}CMe_2$

(1) (126) (127)

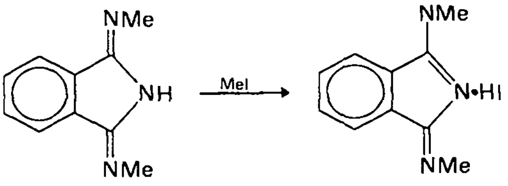
E. Alkylation and Arylation

So far there are few examples of the alkylation or arylation of imidines and their derivatives. In each case, reaction proceeds at an exocyclic nitrogen atom. Thus with methyl iodide at 80°C 1,3-diiminoisoindoline (**5**) yielded[17] the hydriodide of 1-imino-3-methyliminoisoindoline (**128**).


NH
NH
NH
MeI
NMe
NH•HI
NH

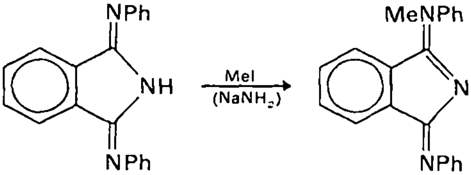
(5) (128)

This formed yellow needles, m.p. 250°C (decomp.). and gave phthalimide on acid hydrolysis. Similar methylation of 1,3-dimethyliminoisoindoline


NMe
NH
NMe
MeI
NMe
N•HI
NMe

(87) (129)

(**87**) yielded the yellow hydroiodide of 3-dimethylamino-1-methylimino-1*H*-isoindole (**129**) which also gave phthalimide on acid hydrolysis[17]. Methylation with methyl iodide of the anion of 1,3-diphenyliminoisoindoline (**30**)—formed with the aid of sodamide—produced[24] 3-*N*-methylanilino-1-phenylimino-1*H*-isoindole (**85**), identical with the product of interaction of 1-imino-3-phenyliminoisoindoline with *N*-methylaniline (Section IV.D.2).

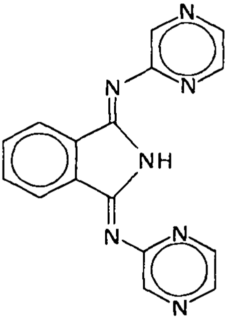


(**30**) (**85**)

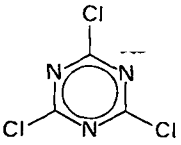
Imidine derivatives bearing pyridyl or pyrazyl substituents such as **124**, **130**, and **95** did not undergo methylation on imidine nitrogen: only quaternization of the aza-arene groups occurred[4a,24,52]. The 2,6-pyridine macrocycle (**13**) appeared not to react with methyl iodide, perhaps because of the inaccessibility of the pyridyl nitrogen atoms[19].

Methylation of the yellow benzene macrocycle (**94**) with methyl iodide yielded[52] an orange-red dimethoiodide in which two of the four peripheral nitrogen atoms had evidently been quaternized. Treatment of this dimethoiodide with warm aqueous sodium hydroxide provided a dimethohydroxide which was easily soluble in methanol. In the air, however, the crystals of the quaternary hydroxide soon effloresced, losing methanol and changing back into the benzene macrocycle (**94**) which is insoluble in methanol. Addition of hydrogen iodide to the methanol solution of the dimethohydroxide precipitated the orange dimethoiodide. The benzene macrocycle dihydriodide, prepared for comparison, was found to be maroon in colour and to have a much higher melting point. Another finding which favoured the foregoing interpretations was that the benzene macrocycle could form a dimethanolate (crystal solvate) and this was sparingly soluble in methanol and stable in the air[52].

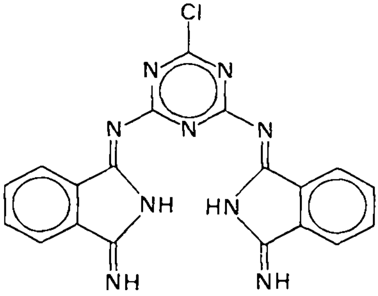
One arylation of 1,3-diiminoisoindoline has been described[33]. This was effected in ethanol with cyanuric chloride (**131**) in acetone and gave the hydrochloride of the three-unit compound (**132**) from which the free base was prepared.



(130)



(131)

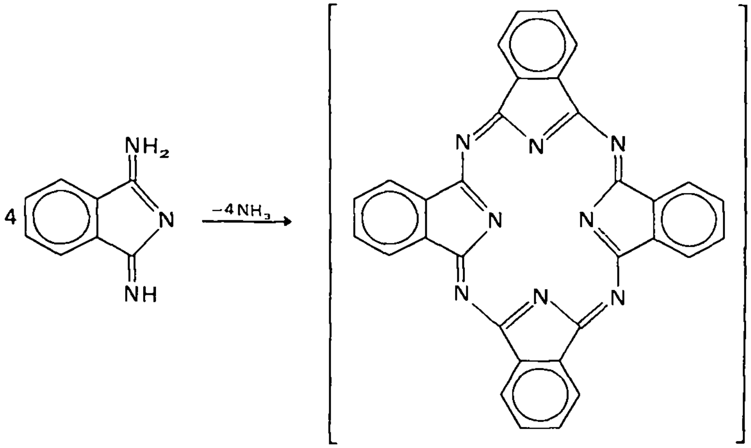


(132)

F. Condensations between Imidines

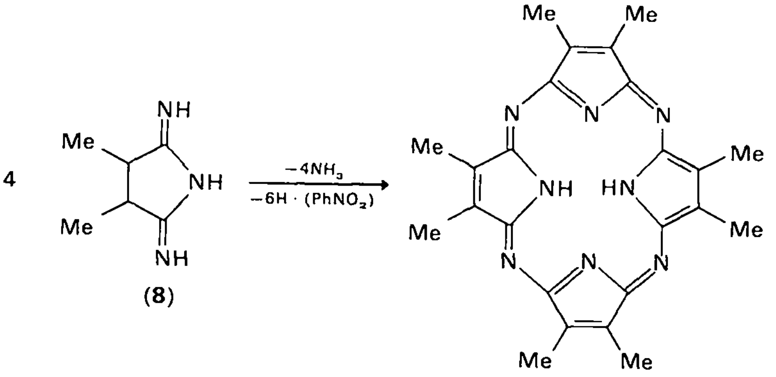
1. Self-condensation

In seeking means of applying the extraordinarily light-fast metal phthalocyanine pigments to cloth, Bayer Farbenfabriken discovered[6] diiminoisoindoline as a precursor. This could be printed on to cloth impregnated with a divalent metal salt and a reducing agent and brief heating then developed the metal phthalocyanine (see Section IV.I.2). Subsequently, Elvidge and Linstead considered the self-condensation of imidines as a means of preparing metal-free tetrazaporphins[45]. For the self-condensation of diiminoisoindoline, as expected, a reducing agent was essential. In theory the self-condensation of 4 molecular proportions of the imidine with elimination of 4 molecular proportions of ammonia could only lead to a structure not known to be capable of existence, namely dehydrophthalocyanine (equation 38). Having a 16π electron conjugated ring this would be antiaromatic: calculation showed that the



(38)

system would be capable of existence only as a di-radical[60]. A source of 2 electrons per cyclization was therefore needed for the self-condensation of diiminoisoindoline to yield phthalocyanine. Indeed when diiminoisoindoline was heated alone in boiling butanol or 2-ethoxyethanol, formation of phthalocyanine was negligible but in boiling tetralin a 45% yield of phthalocyanine resulted, even though at that temperature the dissociation of diiminoisoindoline was far from negligible[45]. In refluxing 2-dimethylaminoethanol diiminoisoindoline and related imidines gave pure phthalocyanine in high yield[23b], the solvent evidently providing an optimum temperature and acting as the necessary reductant. Succinimidine, being a saturated imidine, required (at least in theory)[45] the presence of a dehydrogenating reagent before its self-condensation would lead to tetrazaporphin. A poor yield of this pigment was in any case to be expected (cf. Ref. 61), but in fact no pigment resulted from the use of purely organic reagents[45]. However, in nitrobenzene-2-ethoxyethanol in the presence of magnesium formate, 3% yields of magnesium tetrazaporphin were obtained. Much better was dimethylsuccinimidine (**8**) which when boiled in chlorobenzene in the presence of nitrobenzene afforded octamethyltetrazaporphin (equation 39) in 45% yield[13]. Presumably the required dehydrogenation was effected in these cases by the nitro compound. Methylsuccinimidine likewise gave tetramethyltetrazaporphin when refluxed in butanol with nitrobenzene[12]. Mere heating of the cyclohexano imidine (**18**) gave a blue solid containing tetracyclohexenotetrazaporphin[22], the dehydrogenation in this case evidently proceeding spontaneously.

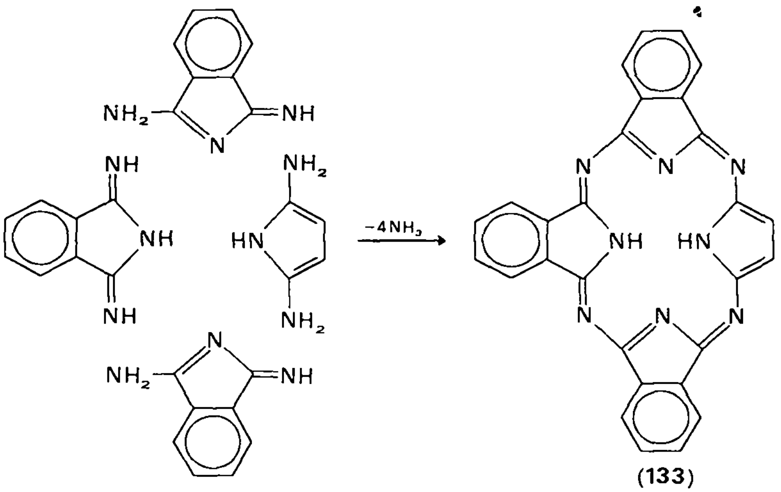

4
NH
Me
NH
Me
NH
−4NH₃
−6H · (PhNO₂)
Me
Me
N
N
N
Me
Me
NH
HN
Me
Me
N
N
N
Me
Me

(8)

(39)

2. Mixed-condensation

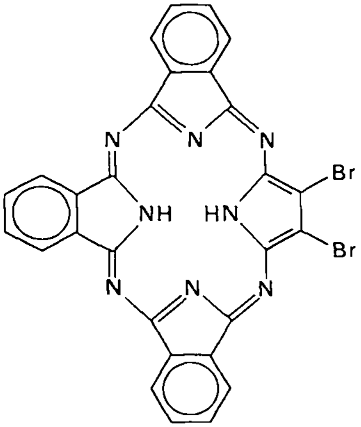
The preceding considerations suggested that satisfactory syntheses of tetrazaporphins might best be achieved through the use of mixtures of imidines at different hydrogenation levels[45,7]. Thus the condensation of 3 molecular proportions of an unsaturated or aromatic imidine with 1 molecular proportion of a saturated imidine (with elimination of ammonia) should provide a tetrazaporphin direct, provided that the first imidine could react in both tautomeric forms and the saturated imidine in the diaminopyrrole form (Equation 40).


NH₂
NH
N
NH
NH₂
NH
HN
NH
NH₂
N
NH₂
NH
−4NH₃
N
N
N
NH
HN
N
N
N

(133)

(40)

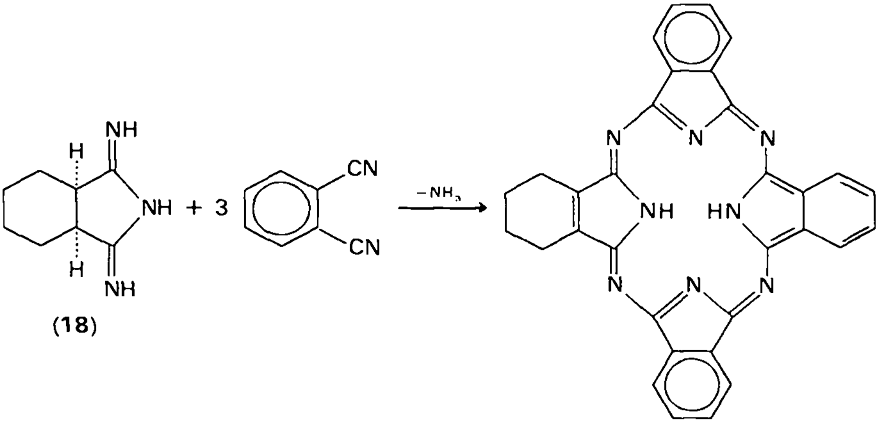
Experiments showed[45] that ammonia was evolved more readily from a mixture of diiminoisoindoline and succinimidine in boiling butanol than from either imidine alone and that a new royal-blue pigment was produced. This was shown to be tribenzotetrazaporphin (**133**) which had been formed as anticipated (equation 40). Subsequently, this new tetrazaporphin pigment was found capable of being readily dibrominated to give the derivative (**134**)[62].



(134)

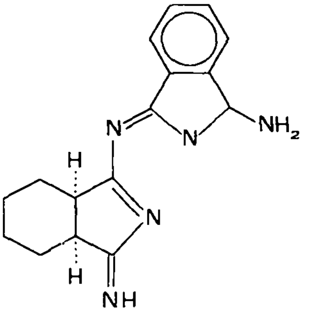
Clearly, the desired condensation reaction (equation 40) was accompanied by other reactions because the crude product contained insoluble charcoal-like material and about 3-times as much phthalocyanine as the required pigment (**133**), which necessitated a tedious extractive and chromatographic separation[45]. The concomitant formation of phthalocyanine suggested that the succinimidine was acting as a hydrogen-donor for the self-condensation of diiminoisoindoline, and indeed the addition of hydrogen acceptors or oxidizing agents suppressed this unwanted reaction[62]. Maleic acid and sodium chlorate were the most effective agents tried. Tribenzotetrazaporphin was then obtained contaminated with less than an equal weight of phthalocyanine so that the separation and purification of **133** was considerably facilitated[62].

Mixed condensations between dimethylsuccinimidine (**8**) and diiminoisoindoline, and between the cyclohexenoimidine (**14**) and diiminoisoindoline appeared more promising[7]. Monocyclohexenotribenzotetrazaporphin (**135**) was obtained[63] by interaction of the *cis*-cyclohexano imidine (**18**) with 3 molecular proportions of phthalonitrile (equation 41).



(18) (135) (41)

In this case, the imidine in its amino–imino form presumably adds the amino function to a molecule of phthalonitrile to give the intermediate **136** which then grows by successive similar additions to phthalonitrile until a four-unit intermediate is reached. The final cyclization will then involve elimination of ammonia between the terminal amino group and the imino group of the original imidine moiety, together with a transfer of 2 H from the imidine residue to two of the four central nitrogens of the large ring, and a redisposition of the π electrons.

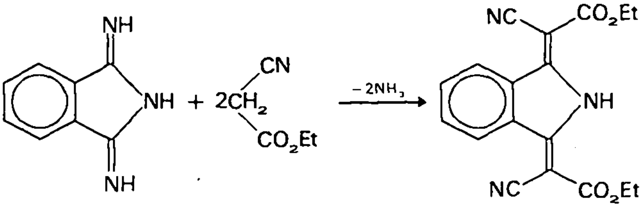


(136)

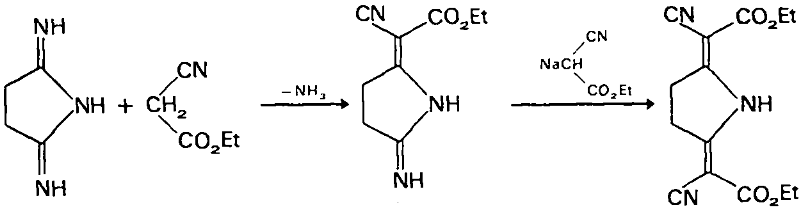
G. Reactions with Active Methylene Compounds

1,3-Diiminoisoindoline (**5**) condensed with the reactive methylene group of ethyl cyanoacetate in boiling ethanol, with elimination of ammonia, to yield the yellow product **137**[64]. Under similar conditions, succinimidine (**1**) condensed with only 1 molecular proportion of ethyl cyanoacetate to give **138**: the further condensation, affording **139**, required the use of ethyl sodiocyanoacetate[64].

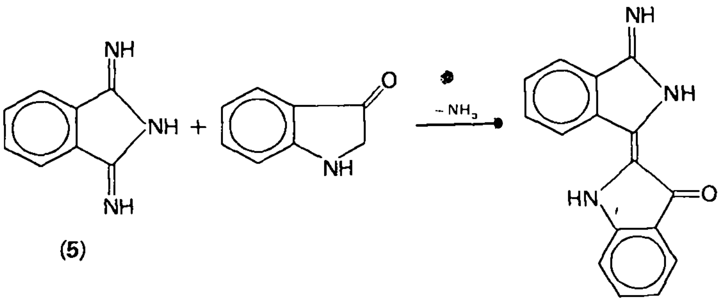
Condensation of diiminoisoindoline with the active methylene group of indoxyl yielded the compound **140** which dyes wool, cotton, etc. in red shades[65]. Yellow, brown and blue dyes (amongst others) were similarly prepared by condensing diiminoisoindoline with barbituric acid, phloroglucinol, and 1-naphthol respectively.


NH
NH
NH
CN
2CH2
CO2Et
− 2NH3
NC
CO2Et
NH
NC
CO2Et

(5) (137)

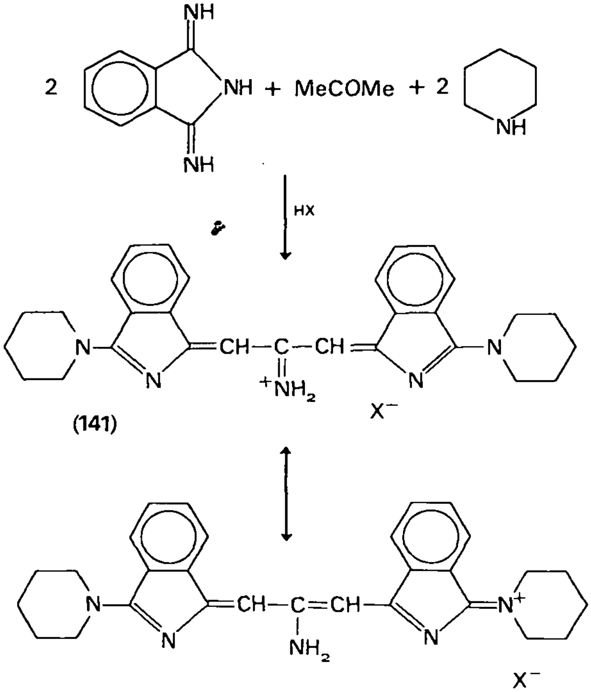

NH
NH
NH
CN
CH2
CO2Et
− NH3
CN
CO2Et
NH
NH
CN
NaCH
CO2Et
CN
CO2Et
NH
CN
CO2Et

(1) (138) (139)


NH
NH
NH
O
NH
− NH3
NH
NH
HN
O

(5) (140)

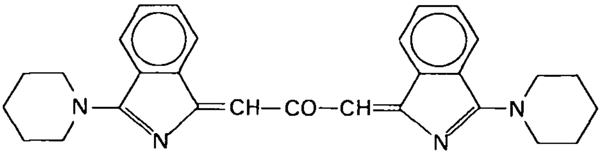
Rather more surprising than the preceding condensations of imidines with active methylene compounds was the finding by Vollmann and Wolf[66] that diiminoisoindoline condensed with both of the methyl groups of acetone in the presence of secondary amines and acid (equation 42).



(141)

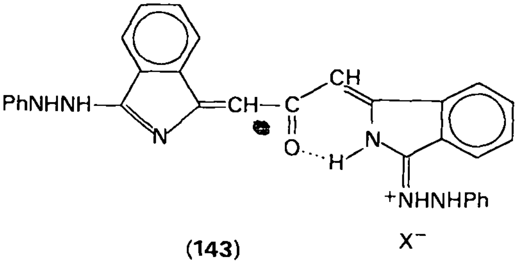
(42)

The products (**141**) are resonance hybrid salts which formally resemble the auramines. Towards aqueous mineral acid at 70–80°C, the products **141** were unstable, the central amino group first undergoing hydrolysis to give **142**. Then in turn each of the terminal nitrogen functions was hydrolysed, these being susceptible to hydrolysis as in imidines.



(142)

A further resemblance was the easy displacement of the terminal amino functions in **142** by phenylhydrazine to give compound **143**[66].



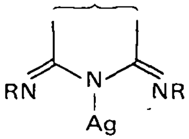
(143)

H. *Metal Derivatives of Imidines and their Substitution Products*

1. Miscellaneous open-chain and macrocyclic chelates

The constitution of imidines and their derivatives is such that the formation of complexes with metal ions can be expected, but few of these complexes have as yet been isolated and characterized.

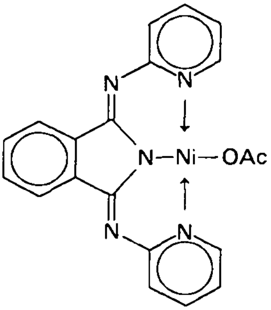
Pinner[2,11] found that succinimidine (**1**) and other imidines in which the central imino group was unsubstituted, such as 2,5-diimino-3,4-dimethylpyrrolidine (**8**), formed insoluble silver derivatives. These he



(144)

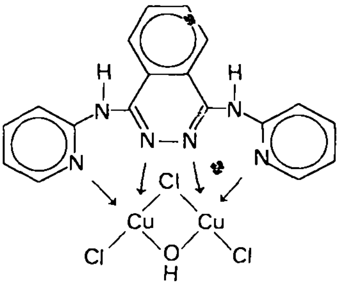
formulated as **144**. The dioxime (**69**) from glutarimidine likewise gave a silver complex[67], but imidine analogues derived from secondary amines, which evidently had a central tertiary nitrogen group $>$N lacking a replaceable hydrogen atom, did not give silver derivatives[11]. The acidity of the central imino group increased markedly when succinimidine was converted into the biscyanomethylene compound (**139**), this then yielding a sparingly soluble potassio derivative[64].

The various dioximes derived from imidines (Section IV.C) behaved like simple oximes and gave red colours with ferric chloride, indicative of complex formation. Copper acetate produced yellow–green colours. Amongst substituted imidines derived from the condensation of an imidine with amines, 1,3-di-2′-pyridyliminoisoindoline (**124**) formed highly crystalline metal derivatives[4a]. Thus with nickel acetate in formamide, the brownish-yellow acetoxynickel(II) derivative (**145**) was obtained of composition (L—H)MOAc together with a sparingly soluble maroon complex



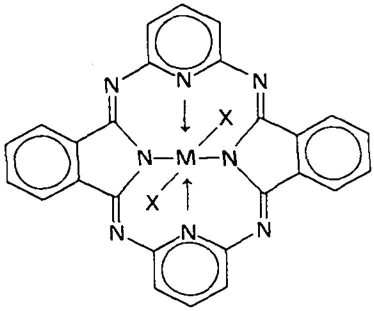
(145)

$C_{36}H_{24}N_{10}Ni$, i.e. $(L—H)_2M$ in which the nickel(II) ion was bound to two dipyridyliminoisoindoline residues[4a]. More recently, these covalent complexes were reprepared, the absence of conductance was checked, and their magnetic susceptibilities were measured[68]: in addition, from nickel, zinc, and other perchlorates a new ionic series of complexes of the composition $L_2M(ClO_4)_2$ was obtained[68]. The related ligand molecule **125**, derived from **124** by expansion of the isoindoline ring with hydrazine (Section IV.D.10), formed a highly insoluble dichromate—therefore probably coordinated—and also a variety of copper derivatives of which the hydrated copper complex, $LCu_2Cl_3(OH)·H_2O$, was shown by X-ray crystallography to have the constitution **146**[58].



(146)

The cross-conjugated macrocyclic compound (**13**) from condensation of 2,6-diaminopyridine with diiminoisoindoline formed a brown, crystalline, thermally-stable square-planar nickel(II) complex (**93**)[19], X-ray analysis of which established the constitution, as already mentioned (Section IV.D.7). The ligand molecule **13** also formed orange complexes with lead(II) and mercury(II) which were much less stable and could be demetallated with hydrogen sulphide in benzyl alcohol[19]. Later, many other metal complexes were prepared from the 2,6-pyridine macrocycle (**13**) which was then rechristened 'hemiporphyrazine'[18b]. These included the tin(II) analogue[69] and also octahedral complexes such as the dichlorotin(IV) complex (**147**)[69], the dihalogenogermanium(IV) compounds (**148**)[18b], and dialkoxysilicon(IV) derivatives (**149**)[69].

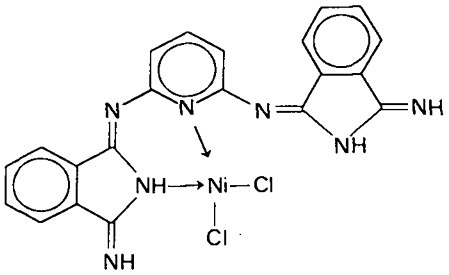


(147) M = Sn, X = Cl
(148) M = Ge, X = F, Cl, Br or I
(149) M = Si, X = OR

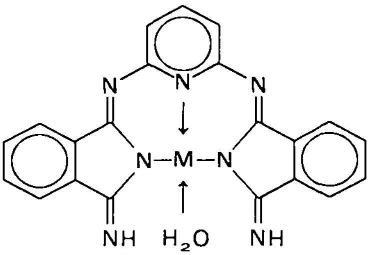
The 3,5-pyridine macrocycle (**95**) which lacks the appropriate central arrangement of four nitrogen atoms, was not at first expected to complex metals, but in fact did so. The products from copper(II) and zinc(II), for example, were brown and yellow amorphous, insoluble, and infusible substances, evidently polymeric in type, presumably with the metal coordinated between peripheral pyridine nitrogen atoms of different ligand molecules[52].

Another macrocycle not at first expected to give metal derivatives was the triisoindole-benzene macrocycle (**99**), but this formed brown products when treated in pyridine with copper(I) cyanide, and the acetates of copper(II) and nickel(II)[50]. Though crystalline, these products were very sparingly soluble and lacked thermal stability so that rigid purification of them was not achieved and their precise composition and nature remains undetermined.

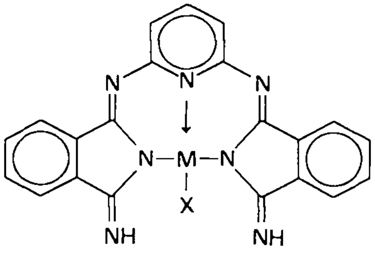
The three-unit compound (**105**) (Section IV.D.7) (also prepared later[70] by the condensation of 2,6-diaminopyridine with 2 molecular proportions of diiminoisoindoline in boiling methanol) behaved as an ambivalent ligand. Towards nickel(II) chloride, it was a bidentate univalent ligand and afforded the complex **150**[71]. Towards copper, nickel, and cobalt, presented as the metal(II) acetates, it behaved as a tridentate divalent ligand, the first two ions giving the brown and red complexes (**151**)[70]. The cobalt(II) salt apparently gave the hydroxycobalt(III) complex (**152**), which was dark red and diamagnetic: an analogous chlorogold(III) complex (**153**) was also prepared[70].



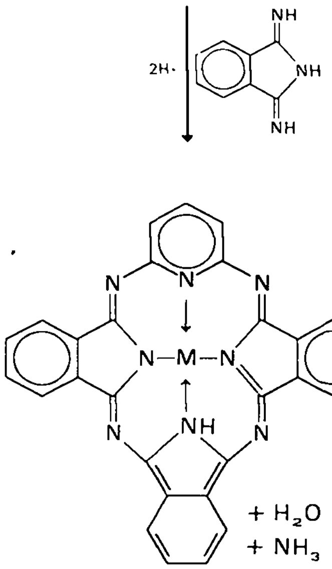
(150)



(151) M = Cu, Ni

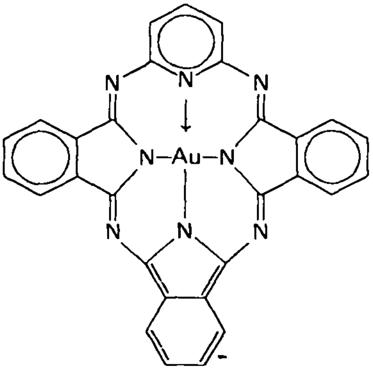


(152) M = Co^{III}, X = OH
(153) M = Au^{III}, X = Cl

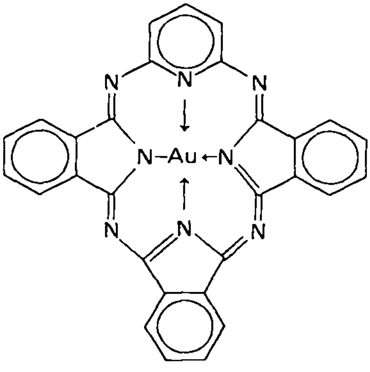


(154)

By heating the preceding copper(II) and nickel(II) complexes (**151**) with diiminoisoindoline in ethoxyethanol or dimethylformamide, Bamfield and Mack[70] achieved a template synthesis of a triisoindole–2,6-pyridine macrocycle as the dark violet metal(II) complexes (**154**). If the structure of these is correct, then the formation reaction is a reductive condensation and the reported effect of hydroquinone in improving the yields becomes understandable. No evidence (such as from mild acid hydrolysis and/or oxidation–reduction titration) was provided to show whether the product from the gold compound (**153**) and diiminoisoindoline was the macrocyclic complex of gold(III) **155**, or of gold (I) **156**.

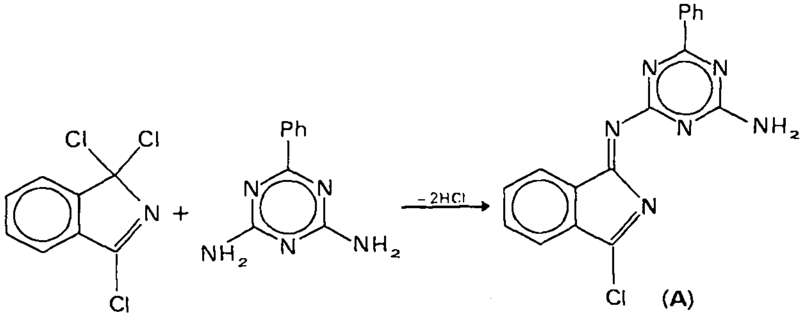


(155)



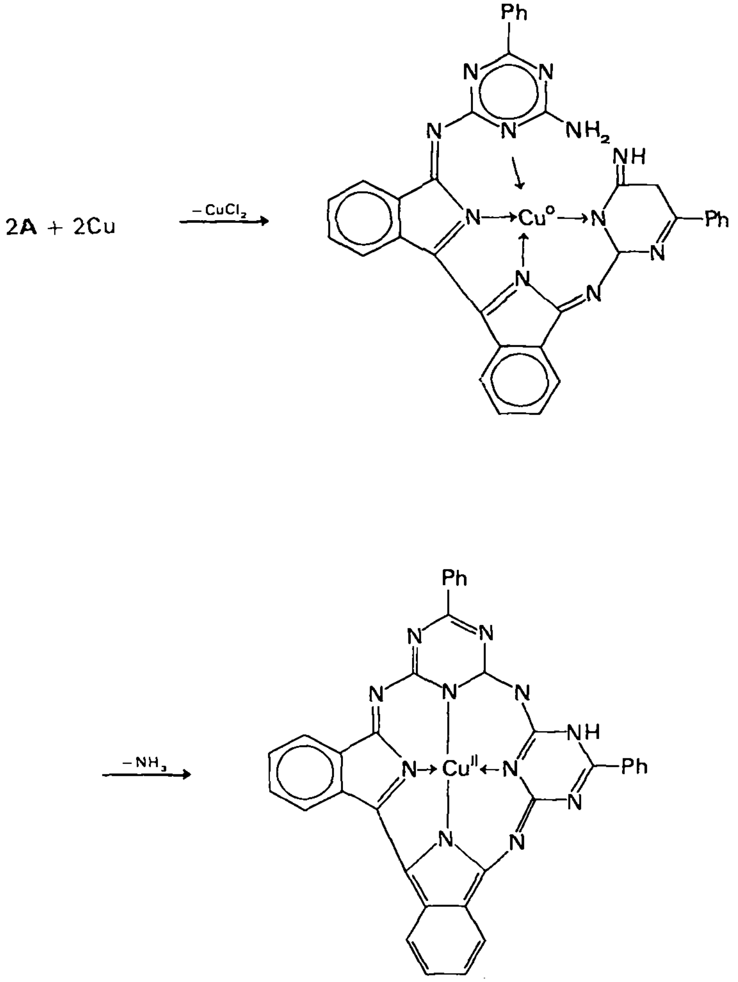
(156)

In the course of the preceding work[70], mass spectral evidence was obtained for the presence of a nickel macrocyclic complex in which there was a direct link (rather than an aza link) between two isoindole rings. A violet macrocyclic copper complex (**158**) having this feature was subsequently isolated[72] from a reaction of the imidine intermediate, 1,3,3-



(157)

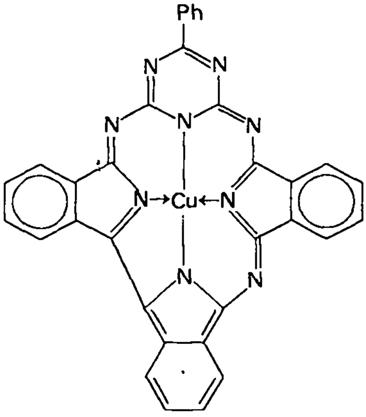
trichloro-1(*H*)-isoindole (**157**) (cf. Section II.D), with 2,4-diamino-6-phenyltriazine in boiling 1-chloronaphthalene in the presence of copper powder or (less satisfactorily) copper acetate. An X-ray investigation substantiated the structure: the compound could have arisen as indicated in equation (43), When copper(II) chloride was used, the yellow–green


2A + 2Cu
−CuCl2
Ph
N
N
N
N
NH2
NH
N
Cu°
N
Ph
N
N
N
−NH3
Ph
N
N
N
N
N
NH
N
Cu^II
N
Ph
N
N
N

(43)

(158)

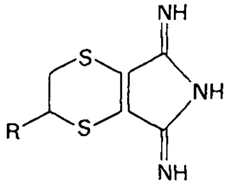
complex (**159**) was obtained instead. Accurate mass measurement of the molecular ion established the composition[72].



(159)

2. Phthalogen compounds

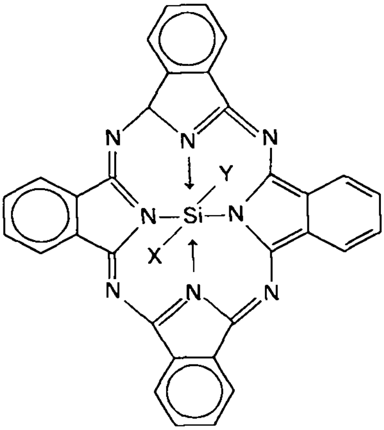
The Phthalogen series of compounds[73], which give rise to the Phthalogen Blue and Green pigments—essentially metal phthalocyanines—constitute a very important commercial discovery by Bayer Farbenfabriken[6] for the printing of fabrics, and for allied uses of these extremely light-fast pigments. There are two main groups of Phthalogen compounds. One comprises simple entities such as 1,3-diiminoisoindoline (**5**)[6,73,74], its 4-phenyl derivative and analogues such as **18** and **160**[16], as well as



(**160**) R = H, Me, Ph, CN

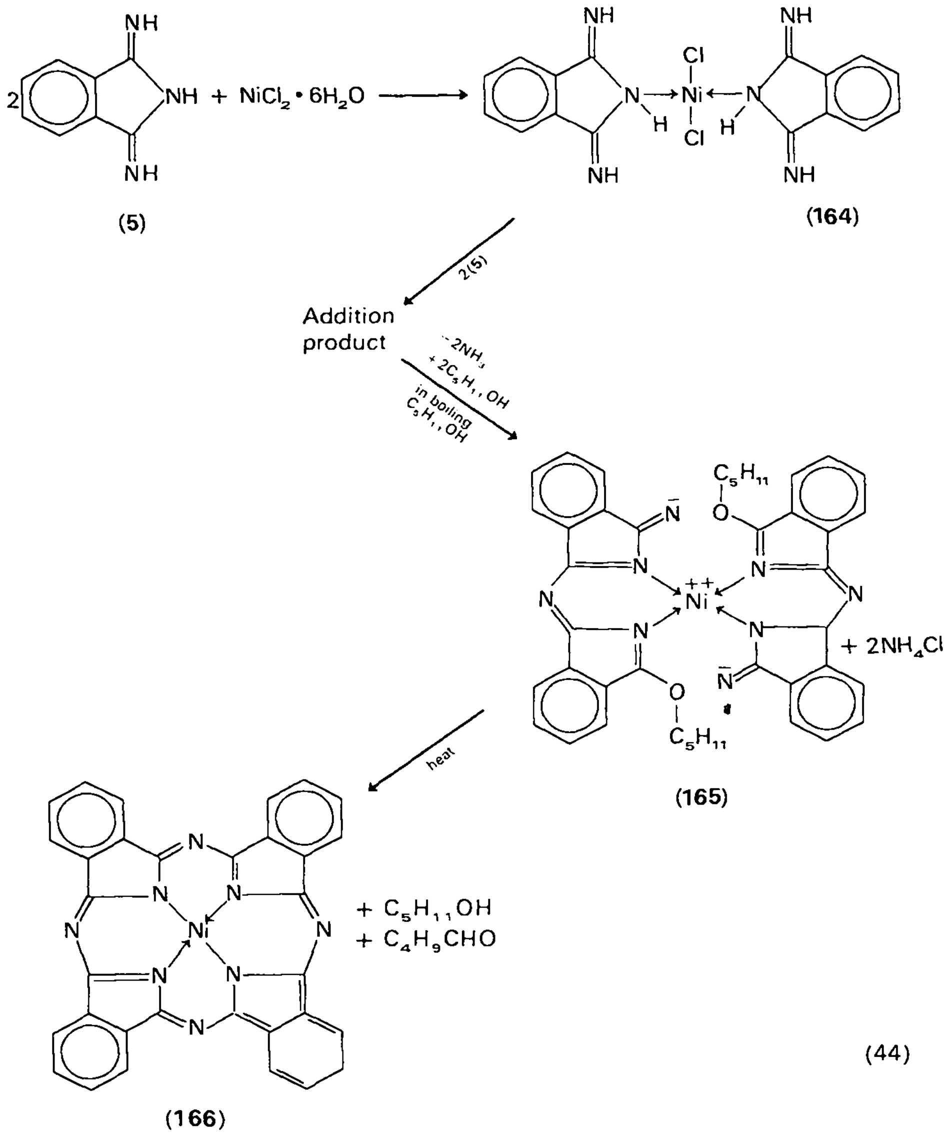
alkoxy[75] and alkylthio[35] derivatives of 1-iminoisoindolines and related compounds (Section II.E) such as **37**, **39**, **40**, **41**, and **44**. These latter are capable of yielding diiminoisoindoline or analogous imidines when heated up to about 140°C with ammonium salts, urea, or other reagents which provide ammonia. Either before or after the printing of cloth with a Phthalogen, it may be treated with metal salts or chelates[76], the other reagents and a mild reducing agent, or the printing might be done with a paste of all necessary components. Then by steaming, metal phthalocyanine pigments are developed right through the fibre and the resulting print, which can incorporate intricate patterns, is permanent to washing[6,16,73–76].

Metal phthalocyanines can be prepared in a pure state direct from 1,3-diiminoisoindoline or its substitution products by heating with powdered metals, e.g. copper, or better with metal salts dissolved in a potentially reducing solvent such as formamide[6,45]. In these ways, the two electrons required per cyclocondensation (see Section IV.F.1) are provided. Use of other reagents has made available novel six coordinate octahedral complexes of phthalocyanine, not obtainable by other routes. For example, from silicon tetrachloride and diiminoisoindoline in boiling quinoline, Kenney and coworkers[23a] prepared dichlorosilicon phthalocyanine (**161**) and thence dialkoxysilicon derivatives (**162**), whilst by using methyl trichlorosilane, the interesting analogue (**163**) was made[77]. These compounds are additionally unusual in having very stable silicon–nitrogen bonds.



(**161**) X = Y = Cl
(**162**) X = Y = OR
(**163**) X = Me, Y = Cl

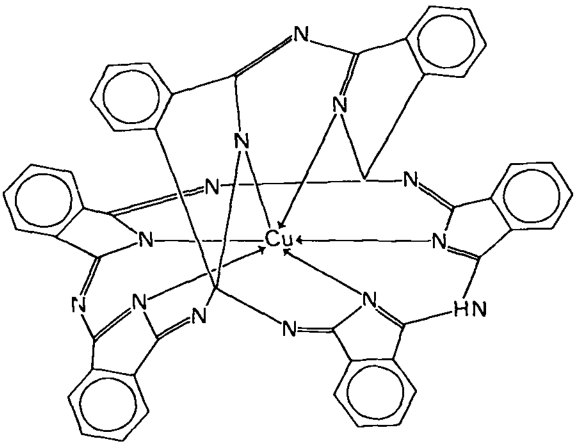
The way in which nickel phthalocyanine is formed from 1,3-diiminoisoindoline and nickel(II) chloride (in a solvent capable of acting as a reducing agent) has been elucidated by Robinson and coworkers[78]. There are three main stages which they were able to carry out separately by using 'artificial' conditions. The mechanism is depicted in equation (44). First, the metal salt chelates two molecules of the imidine to give the


2
NH
+ NiCl2 • 6H2O
(5)
Cl
Ni
(164)
2(5)
Addition product
−2NH3
+2C5H11OH
in boiling C5H11OH
C5H11
Ni++
+ 2NH4Cl
(165)
heat
+ C5H11OH
+ C4H9CHO
(166)

(44)

greenish-tan, square-planar complex (**164**). This then condenses at a higher temperature (e.g., in boiling amyl alcohol) with two more molecules of the imidine and there is concomitant solvolysis of two of the pendant imino groups: a red square-planar complex (**165**) results. By heating this under vacuum, nickel phthalocyanine (**166**) is formed rapidly, quantitatively, together with products from the solvent residues in **165** (in this particular case, amyl alcohol and valeraldehyde, which were characterized by mass spectrometry).

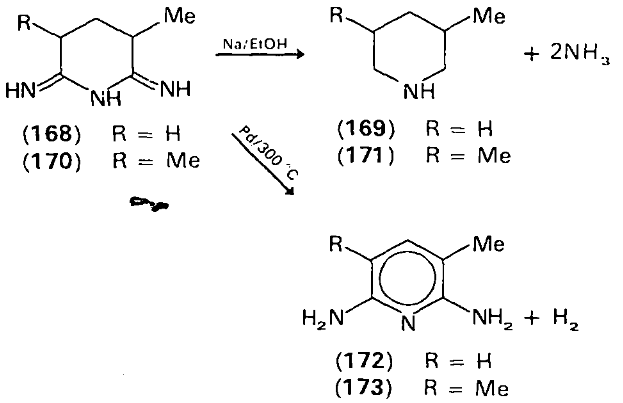
The second group of Phthalogen compounds comprises more complex entities, loosely described as metal polyisoindolines[6,74,79]. Their molecules are built up from six phthalonitrile residues and one metal(II) atom, and are probably as illustrated in (**167**)[80]. They are formed from diiminoisoindoline or analogous imidines and a metal(II) salt in dimethylformamide at 90°C[79,80] or from cobalt (or other metal) phthalocyanine and diiminoisoindoline under mildly oxidative conditions[81]. The metal polyisoindolines, e.g. $C_{48}H_{25}CuN_{13}$, can be isolated as brownish orange crystals, are soluble in acetic acid, and do not hydrolyse readily[80]. The conversion to metal phthalocyanine occurs rapidly on heating in the presence of reducing agents. The printed cloth is therefore padded with hydrosulphite–soda or equivalent agents and then steamed to develop the colour[79,81].



(167)

I. Hydrogenolysis and Dehydrogenation of Glutarimidines

The hydrogenolysis of glutarimidine derivatives to piperidines and ammonia was achieved by Takata[82]. He added portions of the methylglutarimidine (**168**) and sodium alternately to ethanol heated in an oil-bath at 130–140°C and so obtained the piperidine (**169**) in high yield. Similar hydrogenolysis of the dimethylglutarimidine (**170**) afforded 3,5-dimethylpiperidine (**171**). The bicyclic imidine derivatives (**174**) were likewise converted into the decahydro-1,8-naphthyridines (**175**). All of these piperidines were then aromatized by heating with palladium at 230°C.

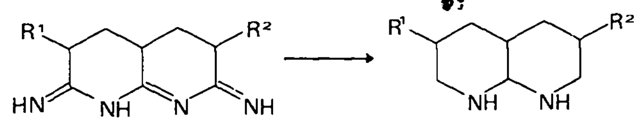


(168) R = H
(170) R = Me

(169) R = H
(171) R = Me

(172) R = H
(173) R = Me

Early attempts to convert glutarimidine derivatives into 2,6-diaminopyridine derivatives by ring-dehydrogenation were unsuccessful[14]: the methods were far too mild. By heating the methylglutarimidine (**168**) in diphenyl ether at 300°C under nitrogen with palladium catalyst for many hours, Takata[82] achieved the dehydrogenation to 2,6-diamino-3-methylpyridine (**172**) in 30% yield. Similarly the dimethylglutarimidine (**170**) gave 2,6-diamino-3,5-dimethylpyridine (**173**).



(175)

(174) $R^1 = R^2 = H$,
$R^1 = Me$, $R^2 = H$, or
$R^1 = R^2 = Me$

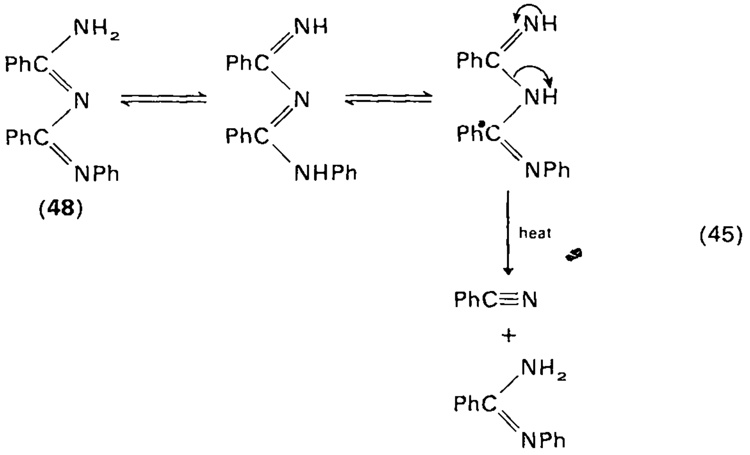
V. PROPERTIES AND REACTIONS OF DIAMIDIDES

A. General Characteristics

The diamidides or 1,3,5-triazapentadienes, e.g. **48**, are the open-chain analogues of the imidines. Few have been described[8,40,41,43], and of these the majority bear only aryl substituents on carbon atoms 2 and 4, and have one or more aryl substituents on nitrogen. Two main classes may be discerned: one comprises those that are conjugated such as **51**, and the other comprises non-conjugated diamidides such as **52**. The former class are yellow and show longest wavelength ultraviolet absorption in the 330–345 nm region[8a]. Non-conjugated diamidides do not absorb beyond about 260 nm and appear colourless or pale yellow[8a].

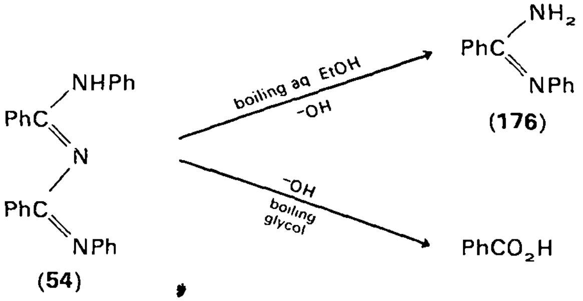
1. Conjugated diamidides

The representatives **50**, **51**, and **54** have surprisingly different chemical properties[8a] from those of the imidines and many of their *N*-substitution products. Conjugated diamidides have moderately high melting points and the poly phenyl-substituted members are thermally stable: thus **54** was recovered in high yield after 1 h at 190–200°C. On the other hand, **48** was degraded to benzonitrile and *N*-phenylbenzamidine (**176**) (equation 45). The poly phenyl-substituted derivatives are also resistant to hydrolysis. 1,2,4,5-Tetraphenyl-1,3,5-triazapenta-1,3-diene (**54**), for example, withstood boiling concentrated hydrochloric acid and suffered little in boiling aqueous ethanolic alkali during 25 h, only 15% being

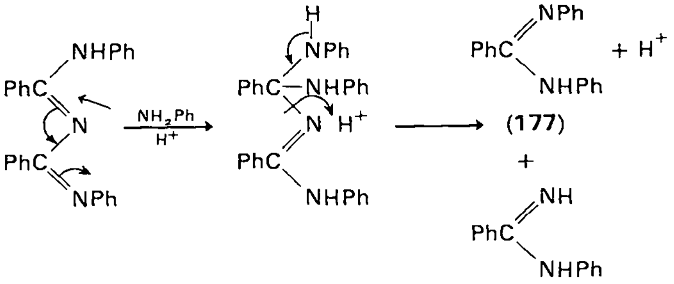


(45)

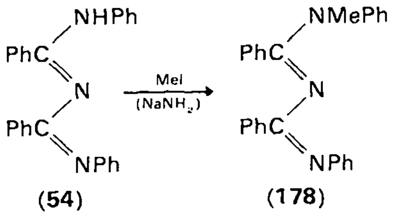
degraded to *N*-phenylbenzamidine (**176**). In boiling glycol with potassium hydroxide, however, the diamidide (**54**) was hydrolysed to benzoic acid.


NHPh
PhC
N
PhC
NPh
(54)
boiling aq EtOH
⁻OH
NH₂
PhC
NPh
(176)
⁻OH
boiling glycol
PhCO₂H

No reaction occurred when the diamidide (**54**) was heated at 100°C with aniline but with anilinium benzenesulphonate in boiling pyridine there was degradation of the diamidide to *N*,*N*′-diphenylbenzamidine (**177**) and *N*-phenylbenzamidine. Evidently there is acid-catalysed 1,4-addition of aniline to the 1,3,5-triazapenta-1,3-diene system, followed by dissociation to the products (equation 46)[8a].

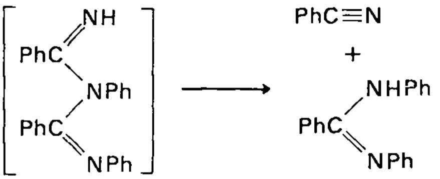
 (46)
NHPh
PhC
N
PhC
NPh
NH₂Ph
H⁺
H
NPh
PhC—NHPh
N H⁺
PhC
NHPh
NPh
PhC
NHPh
+ H⁺
(177)
+
NH
PhC
NHPh

Methylation of the diamidide (**54**) with methyl iodide/sodamide significantly gave only the conjugated product (**178**)[8a].


NHPh
PhC
N
PhC
NPh
(54)
MeI
(NaNH₂)
NMePh
PhC
N
PhC
NPh
(178)

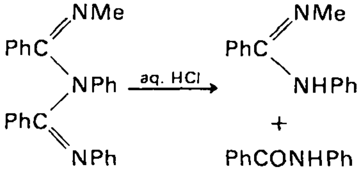
2. Non-conjugated diamidides

Some are evidently too unstable to exist. Thus attempts to obtain the diamidide (**179**) consistently resulted only in the decomposition products shown (equation 47)[8a]. Those which were obtained, e.g. **52**, failed to form crystalline salts with acids and instead were degraded. With hydrochloric acid in aqueous ethanol, the diamidide (**180**) yielded benzanilide and *N*-methyl-*N*′-phenylbenzamidine (equation 48). Even picric acid in benzene degraded this diamidide (**180**), *N*-methyl-*N*′-phenylbenzamidinium picrate and *N*,*N*′-diphenylbenzamidinium picrate being formed. These and related acid degradations may be explained by the reaction sequence shown (equation 49)[8a].


NH
PhC
NPh
PhC
NPh
PhC≡N
+
NHPh
PhC
NPh

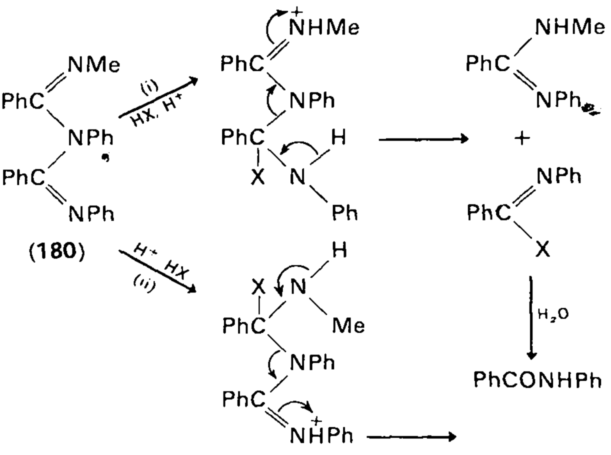
(179)

(47)

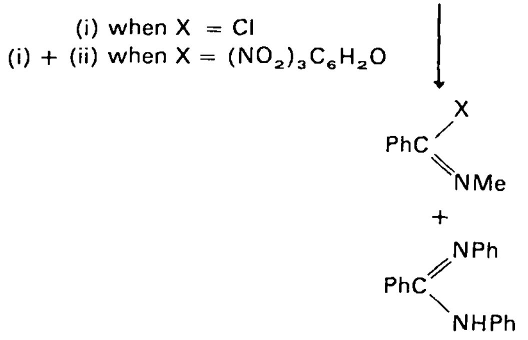

NMe
PhC
NPh
PhC
NPh
aq. HCl
NMe
PhC
NHPh
+
PhCONHPh

(180)

(48)


NMe
PhC
NPh
PhC
NPh
(180)
(i) HX, H+
H+ HX (ii)
NHMe
PhC
NPh
PhC
H
X
N
Ph
H
X
N
PhC
Me
NPh
PhC
NHPh
NHMe
PhC
NPh
+
NPh
PhC
X
H2O
PhCONHPh

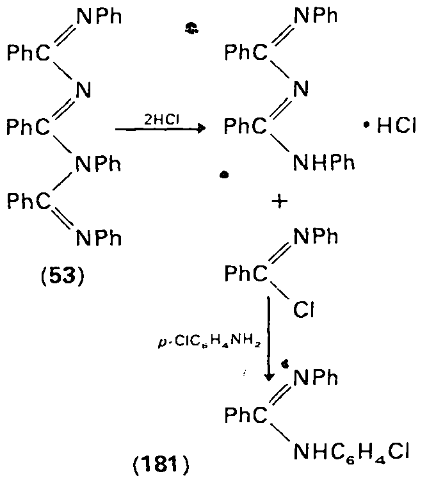
(49)


(i) when X = Cl
(i) + (ii) when X = (NO2)3C6H2O
X
PhC
NMe
+
NPh
PhC
NHPh

(49)

3. A triamidide (53)

This yellow compound combines the structural features of both of the preceding types of diamidide. Whilst it resembled a conjugated diamidide in being thermally stable and resistant to boiling aqueous ethanolic alkali, it did not form crystalline salts[8a]. Acidification of a solution of the triamidide (53) in ethanol with concentrated hydrochloric acid and dilution with water merely precipitated the triamidide (63% recovery). In chloroform with dry hydrogen chloride, the triamidide (53) was degraded to the hydrochloride of 1,2,4,5-tetraphenyl-1,3,5-triazapenta-1,3-diene (**54**). The same result was obtained using benzene as solvent, but in this case, filtration from the diamidide hydrochloride, evaporation of the benzene filtrate, and treatment of the residue with *p*-chloroaniline then afforded *N*-*p*-chlorophenyl-*N'*-phenylbenzamidine (**181**). Acid degradation of the triamidide therefore proceeded analogously to that of the non-conjugated diamidide (**180**), there being addition of hydrogen chloride, followed by dissociation into the diamidide and *N*-phenylbenzimidochloride (equation 50)[8a].

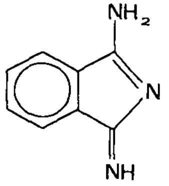

NPh
PhC
N
PhC
NPh
PhC
NPh
(53)
2HCl
NPh
PhC
N
PhC
NHPh
• HCl
+
NPh
PhC
Cl
p-ClC6H4NH2
NPh
PhC
NHC6H4Cl
(181)

(50)

VI. SPECTROSCOPIC EVIDENCE FOR THE FINE STRUCTURE OF IMIDINES

A. Ultraviolet Absorption and N.M.R. Results

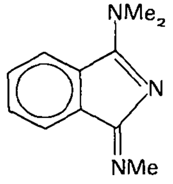
The imidine formally derivable from phthalic anhydride was referred to in the initial description [6a] and subsequent reviews[6b,16] as 1-amino-3-iminoisoindolenine and represented by **182**. However, qualitative light absorption studies[17,24] showed that this potentially tautomeric compound is best regarded as 1,3-diiminoisoindoline (5). Comparison of the light absorptions of tautomeric structures with those of fixed-bond analogues is valid only when the excited states are similar; within such a close group of compounds as the phthalic imidine derivatives this is highly probable. Extensions to other imidines also suggest that the diimino form is preferred. *N*-Substitution may alter the position of tautomeric equilibrium[9,17]. This last conclusion has been challenged[83], though not on a sound basis, as will be explained.



(182)

1. 1,3-Diiminoisoindoline and derivatives

Table 3 gives the principal u.v. light absorption maxima of this imidine and of simple *N*-substituted derivatives which include fixed-bond representatives of both the amino–imino (**182**) and diimino (**5**) tautomeric forms. The 3-dimethylamino-1-methylimino-1*H*-isoindole (**183**) has its



(183)

TABLE 3. Ultraviolet absorption maxima of some phthalic imidines and derivatives in ethanol[a], methanol[b], or acetic acid[c]

No.	Compound	λ_{max}(nm)	$\varepsilon \times 10^{-3}$	Reference
	Fixed-bond structures			
83	3-Morpholino-1-phenylimino-1*H*-isoindole[a]	227	29·1	24
		236	25·6	
		265 280 290	9·6	
		375	11·3	
84	1-Phenylimino-3-piperidino-1*H*-isoindole[a]	264	13·4	24
		280	11·0	
		379	14·5	
85	3-*N*-Methylanilino-1-phenylimino-1*H*-isoindole[a]	258	11·2	24
		268 281 290	12·4	
		368	14·6	
183	3-Dimethylamino-1-methylimino-1*H*-isoindole[b]	279	12·2	17
		348	3·9	
88	2-Methyl-1,3-diphenyliminoisoindoline[b]	227	26·4	17
		258 265	19·9	
		305	9·6	
	Potentially tautomeric structures			
5	1,3-Diiminoisoindoline[a]	251 256	12·5	24
		303	4·6	
185	3-Butylimino-1-iminoisoindoline[a]	251	12·0	24

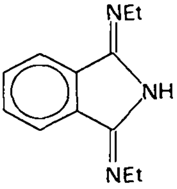
TABLE 3 (*continued*)

No.	Compound	λ_{max}(nm)	$\varepsilon \times 10^{-3}$	Reference
		258 264	13·6	
		304	5·4	
87	1,3-Dimethyliminoisoindoline^b	252	11·1	17
		266	14·0	
		308	7·3	
68	1,3-Dihydroxyiminoisoindoline^a	227	12·7	9
		251	9·0	
		265	12·7	
		297	14·2	
86	1,3-Dibutyliminoisoindoline^a	251	8·0	24
		266	11·0	
		278	8·0	
		304 315	6·0	
184	1,3-Diethyliminoisoindoline^b	265	11·1	17
		312	3·8	
186	3-Benzylimino-1-iminoisoindoline^b	265	15·0	17
		316	4·7	
79	1-Imino-3-phenyliminoisoindoline^a	251 257	14·8	24
		265	16·3	
		280	12·4	
		304 324 330	9·3	
		360	7·3	
187	1-Imino-3,2′-naphthyliminoisoindoline^a	230	55·5	24

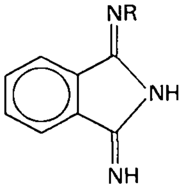
TABLE 3 (*continued*)

No.	Compound	λ_{max}(nm)	$\varepsilon \times 10^{-3}$	Reference
		251	16·8	
		259	21·7	
		266		
		343	7·6	
		367	8·4	
188	1-Imino-3,3′-pyridyliminoisoindoline[a]	268	15·7	24
		280	11·3	
		345	8·9	
30	1,3-Diphenyliminoisoindoline[a]	251	12·2	24
		257		
		264		
		303	8·9	
		328		
		348	7·7	
		365	6·5	
	1,3-Di-2′-naphthyliminoisoindoline[a]	227	63·5	24
		234		
		326	9·1	
		360	10·7	
124	1,3-Di-3′-pyridyliminoisoindoline[a]	235	29·9	24
		257	14·3	
		266	12·5	
		280		
		290		
		304		
		315		
		353	10·7	
189	1,3-Diphenyliminoisoindoline hydrochloride[c]	349	23·2	4a
		398	20·0	

longest wavelength absorption maximum at 348 nm[17] and the 3-*N*,*N*-disubstituted-amino-1-phenylimino-1*H*-isoindoles (**83**), (**84**) and (**85**) all absorb in the 368–379 nm region[24]. On the other hand, the 1,3-diiminoisoindoline derivative (**88**) has its longest wavelength absorption at 305 nm[17]. Because diiminoisoindoline itself absorbs only up to 303 nm[24], it is reasonable to conclude that this imidine exists in the diimino form **5**, and that so do the butyl (**185**) and dimethyl (**87**)[17] derivatives, and also the dioxime (**68**)[9]. Indeed, the last compound gives a dull reddish colour with iron(III) chloride like a simple oxime and not a bluish colour as does 1-amino-3-hydroxylaminoisoquinoline[48]. In addition, there is none of the instability or sensitivity to oxidation normally found with hydroxylamino compounds, so that the dioxime formulation **68** appears certain. The N^1,N^3-dibutyl and -diethyl derivatives of diiminoisoindoline, (**86**) and (**184**), absorb at 315[24] and 312 nm[17] respectively, and the N^1-benzyl substituted compound (**186**) absorbs at 316 nm[17], so it appears that the tautomeric equilibrium for these compounds lies a little towards the amino–imino form. The N^1-aryl (**79**), (**187**) and -heteroaryl (**188**) derivatives

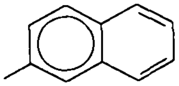


(184)

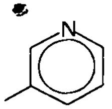


(185) R = Bu
(186) R = CH_2Ph

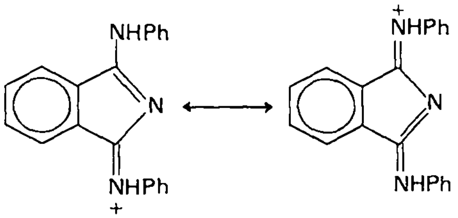
(187) R =



(188) R =

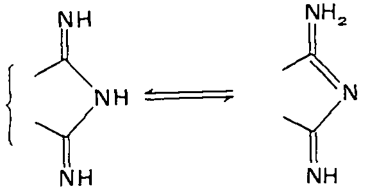


are probably tautomeric mixtures in which the amino–imino forms predominate because these compounds show maxima at up to 360 nm[24]. The corresponding N^1,N^3-disubstituted compounds, e.g. **30** and **124**, absorb around that region, suggesting again that the amino–imino form predominates[24]. Where this form is fixed by trisubstitution as in **83**, **84** and **85** the longest wavelength maximum is shifted bathochromically to 368–379 nm[24] (as already mentioned) and the intensity pattern changes from that of compound **88**[17] in that the longest wavelength maximum intensifies a little and becomes more intense than the maxima immediately to shorter wavelength (see **83**, **84**, **85**, Table 3). The u.v. spectrum of 1,3-diphenyliminoisoindoline hydrochloride shows rather higher intensity absorption (ε 20,000) at the longer wavelength of 398 nm, indicative of the resonance hybrid structure **189**[24].



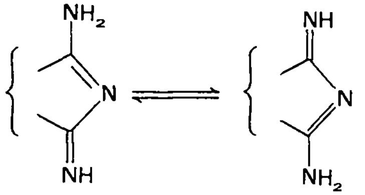
(189)

From ^{1}H-n.m.r. studies of diiminoisoindoline and some of its N-substitution products, it was concluded that all of the potentially tautomeric compounds exist in the diimino form[83]. This conclusion (which is hardly tenable in view of the u.v. absorption evidence) ignores an aspect of n.m.r. spectroscopy. It was observed that the ^{1}H-n.m.r. spectra of diiminoisoindoline and its N^1,N^3-disubstituted derivatives (in which the two substituents were identical) possessed a symmetry indicative of the diimino form. In other words, there was only a single set of resonance signals from the two substituent groups and only two chemical shifts from the isoindole phenylene protons, these giving rise to a symmetrical AA′BB′ pattern. This is a result to be expected if the rate of interchange of tautomers (equation 51) is rapid on the n.m.r. time scale. The n.m.r. spectrum would



(51)

also appear to indicate a symmetrical structure even if the position of this equilibrium were strongly towards the amino–imino form because the proton exchange (equation 52) would make that structure effectively



(52)

symmetrical on the n.m.r. time scale. Illustration of the point seems pertinent. There is detailed i.r. and u.v. spectroscopic evidence[84] to show that phthalhydrazide exists as 4-hydroxyphthalazin-1(2*H*)-one (**190**). Yet the ^{1}H-n.m.r. spectrum in dimethyl sulphoxide shows a symmetrical AA′BB′ pattern from the four protons of the benzene ring (Figure 1),

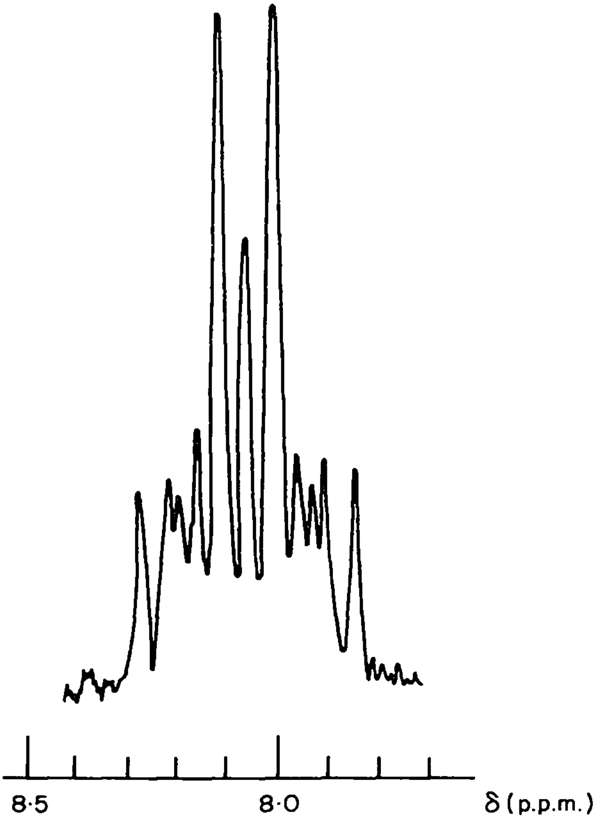
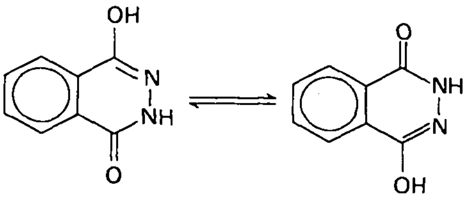


FIGURE 1. ^{1}H-N.m.r. signal from the four phenylene protons of phthalhydrazide (in dimethyl sulphoxide containing TMS, at 60 MHz).

apparently indicative of a symmetrical structure! The explanation is again that the rate of proton transfer between equivalent tautomers (equation 53) is sufficiently rapid on the n.m.r. time scale to average chemical shifts.



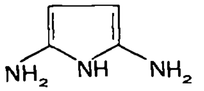
(190)

(53)

Direct observation of the dependence of the ^{1}H-n.m.r. spectrum upon rate of proton transfer was made during investigations of the products from succinimidine and hydrazine[59]. It was found that the complex ^{1}H-n.m.r. spectra of the compounds (**126**) and (**127**), which were consistent with these non-symmetrical structures, collapsed to spectra indicative of symmetrical structures as soon as proton transfer was catalysed by alkali. It is important to note that no change in the u.v. spectra of the compounds (**126**) and (**127**) occurred under the same conditions showing that the species under observation had not changed on addition of the alkali[59].

2. Other imidines

These have not yet been studied quite so extensively, (see Table 4). Succinimidine (**1**) and its dimethyl analogue (**8**) both show maxima at 237 nm, with the corresponding dioximes (**66**) and (**67**) absorbing at 227–228 nm[9,13], suggesting strongly that the imidines exist in the diimino form. Although succinimidine is capable of reacting as if it were 2,5-diaminopyrrole[45], its light absorption differs somewhat from that of simple pyrroles[85] and so it appears that this potential tautomeric form **191** does not contribute to the compound's structure. Indeed, the ^{1}H-n.m.r.



(191)

spectrum[83] is clearly consistent with a succinimidine structure, although not necessarily capable (as claimed) of indicating whether the diimino or amino–imino form is preferred, for a reason as already outlined. Introduction of a double bond between the ββ'-carbons of a succinimidine, as in **14**, produces an expected bathochromic shift of the longest wavelength maximum, to 258 nm[22].

Table 4. Ultraviolet absorption maxima of succinimidine, glutarimidine, some derivatives and analogues in ethanol[a] or methanol[b]

No.	Compound	λ_{max}(nm)	$\varepsilon \times 10^{-3}$	Reference
1	Succinimidine[b]	237	20·0	9
66	2,5-Dihydroxyiminopyrrolidine[b]	227	22·0	9
	2-Imino-5-phenyliminopyrrolidine[b]	240	19·6	9
		251	13·3	
		280	12·6	
29	2,5-Diphenyliminopyrrolidine[b]	227	13·0	9
		280	16·7	
		294	17·4	
8	2,5-Diimino-3,4-dimethylpyrrolidine[a]	237	17·8	13
67	2,5-Dihydroxyimino-3,4-dimethylpyrrolidine[a]	228	17·6	13
111	3,4-Dimethyl-2,5-diphenyliminopyrrolidine[a]	228	14·2	13
		282	16·8	
110	3,4-Dimethyl-2,5-diphenylimino-Δ^3-pyrroline[a]	228		13
		258	15·3	
		266		
		328	7·4	
		348		
14	Δ^8-Hexahydro-1,3-diiminoisoindole[a]	251	15·9	22
		258	14·5	

TABLE 4 (*continued*)

No.	Compound	λ_{max}(nm)	$\varepsilon \times 10^{-3}$	Reference
109	Δ^8-Hexahydro-1,3-diphenyliminoisoindole[a]	228	16·0	22
		251	12·9	
		266	14·5	
		270	9·0	
		280	7·8	
		333	4·2	
9	Glutarimidine[a]	252	17·2	14
69	2,6-Dihydroxyiminopiperidine[a]	234	18·8	14
31	2,6-Diphenyliminopiperidine[a]	228	15·8	14
		291	11·8	
11	4-Benzyl-2,6-diiminopiperazine[a]	250·5	13·8	15
71	4-Benzyl-2,6-dihydroxyiminopiperazine[b]	234	14·9	15
20	3,5-Diiminopiperazin-1-ylacetonitrile[a]	250·5	18·0	15
78	2,6-Dihydroxyiminopiperazine[b]	234	15·8	15
10	2,6-Diimino-3-phenylpiperidine[a]	256	18·0	14
70	2,6-Dihydroxyimino-3-phenylpiperidine[a]	238	19·0	14
	2-Imino-3-phenyl-6-phenyliminopiperidine[a]	258	15·8	14
		290	9·2	
	3-Phenyl-2,6-diphenyliminopiperidine[a]	227	32·8	14
		288	9·75	

Glutarimidine (**9**) absorbs at 252 nm[14] like the piperazine imines (**11**) and (**20**)[15]. The bathochromic shift from 237 nm, the position of the maximum for succinimidine, is evidently a result of the change in ring size and of the resultant effects on the energies of ground and excited states due to the consequential conformational difference[14,86]. Because the dioximes (**69**), (**71**), and (**78**) (which clearly are not hydroxylamino compounds) have maxima at 234 nm[14,15], it is reasonably certain that glutarimidine (**9**) and the analogues (**11**) and (**20**) exist in the diimino form. The same conclusion applies to the phenylglutaric homologue (**10**)[14].

B. Infrared Absorption Results

Because of the solubility characteristics of the imidines (see Section IV.A), their i.r. spectra have been measured only for the solid state[14,15,50]. There is very broad absorption in the NH stretching region, indicative of extensive hydrogen bonding. Under the highest resolution, weak maxima in this region can be detected[50] but no clear-cut information concerning preferred tautomeric forms emerges (see Table 5). However, some interpretations have been attempted for *N*-substituted derivatives of 2,6-diiminopiperazine and thence of glutarimidine[15]. Limited information concerning NH and C=N vibrations has also been obtained.

In the i.r. spectrum of the 3-morpholino-1-phenylimino-1*H*-isoindole (**83**), the highest wavenumber band is at 1641 cm^{-1} (medium intensity) and is attributable to stretching of the exocyclic C=N group. The analogous imine (**60**) shows similar absorption at 1641 cm^{-1} and, in addition, NH stretching at 3165 cm^{-1} and a broadened weaker band at 1694 cm^{-1} (Table 5). The fixed-bond diiminoisoindole derivative (**88**) shows only a slightly broadened strong band at 1640 cm^{-1} from the C=N functions, whilst the compounds **42** and **44** produce sharp strong bands at 1664 and 1653 cm^{-1}, respectively, again attributable to exocyclic C=N, and there is NH stretching at 3135 cm^{-1} [36]. The spectrum of the potentially tautomeric 1,3-diphenyliminoisoindoline (**30**) shows a single NH stretch at 3350 cm^{-1} and strong peaks at 1667 and 1650 cm^{-1}, whilst that of the mono-*N*-substituted diiminoisoindoline (**79**) exhibits NH stretching at 3145 cm^{-1} (as a weak peak in a broad band) and medium absorption at 1686 and 1631 cm^{-1}. Rather more informative was the spectrum in KBr disc of the adduct **92** from *m*-phenylenediamine and diiminoisoindoline. This shows five peaks in the NH region as expected from a compound having one kind of NH_2 group and three kinds of NH group in its structure.

TABLE 5. Infrared absorptions of some imidines and derivatives in Nujol mull[a] or KBr disc[b]

No.	Compound	Maxima (cm^{-1})	Assignment
5	Diiminoisoindoline[a]	3225–2270, 3145vw, 3106vw	NH (bonded)
		1725w, 1680w, 1626, 1597, 1527s	C=N, NH def, Ph
		1304s, 1256s, 1213w, 1170	
		1152s, 1131s, 1075, 1060s, 1005	
9	Glutarimidine[a]	3390–2500, 3185sh	NH (bonded)
		1688br, 1603s, 1559brs	C=N, NH def
		1414, 1332, 1310s, 1217w,	
		1186s, 1145s, 1087br, 1057w	
10	2,6-Diimino-3-phenylpiperidine[a]	3225–2500, 3185sh	NH (bonded)
		1674br, 1600br, 1534brs	C=N, NH def, Ph
		1534w, 1335s, 1292w, 1284,	
		1258, 1220, 1200br	
11	4-Benzyl-2,6-diiminopiperazine[a]	3400–3000	NH
		1690, 1620, 1558s	C=N, NH def, Ph
		1446, 1345s, 1305w, 1207	
		1150, 1105s, 1028w, 934s	
20	3,5-Diiminopiperazin-1-ylacetonitrile[a]	3450–3000	NH
		1668, 1626s, 1570brs	C=N, NH def
		1365s, 1345s, 1315w, 1278	
		1260w, 1200, 1170, 1157s	
27	4-Benzyl-2-imino-6-phenyliminopiperazine[a]	3460s, 3070brs	NH
		1655s, 1648s, 1595w, 1575s	C=N, NH def, Ph
		1493, 1340, 1318s, 1300s,	
		1243, 1205, 1165w, 1115s	
30	1,3-Diphenyliminoisoindoline[a]	3350	NH
		1667s, 1650s	C=N
		1580	Ph

TABLE 5 (*continued*)

No.	Compound	Maxima (cm^{-1})	Assignment
		1330w, 1300, 1220s, 1214s,	
		1190, 1166, 1150, 1126w	
60	3-Morpholino-1-imino-1(*H*)-isoindole[a]	3165	NH
		1694brw, 1645	C=N
		1590, 1562s, 1535s	NH def, Ph
		1362w, 1346, 1325, 1302w,	
		1279brs, 1255, 1182	
79	1-Imino-3-phenyliminoisoindoline[a]	3390–2500, 3145	NH
		1686, 1631, 1592, 1527s	C=N, NH def, Ph
		1324, 1283, 1209s,	
		1157, 1148, 1121s, 1094	
83	3-Morpholino-1-phenylimino-1(*H*)-isoindole[a]	1641	C=N
		1590, 1538brs	Ph
		1337w, 1328, 1302w, 1272s	
88	2-Methyl-1,3-diphenyliminoisoindoline[a]	1640s	C=N
		1585	Ph
		1337, 1244, 1203s, 1152w,	
		1085, 1063, 1040s, 1018	
92	Diiminoisoindoline-*m*-phenylenediamine adduct[b]	3395, 3360, 3225, 3170, 3080	NH$_2$, NH
		1649, 1630, 1610, 1537s	C=N, NH def, Ph
		1493, 1465, 1440s, 1380w,	
		1345, 1326, 1307, 1255s	

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