The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

Supplement C

The chemistry of **triple-bonded functional groups** Part 1

Edited by

SAUL PATAI

and

ZVI RAPPOPORT

The Hebrew University, Jerusalem

1983

JOHN WILEY & SONS

CHICHESTER – NEW YORK – BRISBANE – TORONTO – SINGAPORE

An Interscience ® Publication

Library of Congress Cataloging in Publication Data:

Main entry under title:

The Chemistry of tripled-bonded functional groups.

(The Chemistry of functional groups. Supplement; C)
Includes bibliographical references and indexes.
1. Acetylene compounds. I. Patai, Saul. II. Rappoport,
Zvi. III. Series.
QD305.H8C44 1982 547'.413 82-17355

ISBN 0 471 28032 1 (U.S. : set)
ISBN 0 471 28030 5 (U.S. : v. 1)
ISBN 0 471 28031 3 (U.S. : v. 2)

British Library Cataloguing in Publication Data:

The chemistry of triple-bonded functional groups.
—(The chemistry of functional groups; Supplement C)
1. Chemical elements
I. Patai, Saul II. Rappoport, Zvi III. Series
540 QD181

ISBN 0 471 28032 1
ISBN 0 471 28030 5 v.1
ISBN 0 471 28031 3 v.2

Typeset by Preface Ltd., Salisbury, Wiltshire,
and printed in Great Britain

Contributing Authors

Z. B. Alfassi	Department of Nuclear Engineering, Ben-Gurion University of the Negev, Beer Sheva, Israel 84120
Y. Amiel	The Weizmann Institute of Science, Rehovot, Israel
R. A. Bartsch	Department of Chemistry, Texas Tech University, Lubbock, Texas 79409, U.S.A.
L. Batt	Department of Chemistry, University of Aberdeen, Meston Walk, Old Aberdeen, AB9 2UE, Scotland
G. Bianchi	Institute of Organic Chemistry, University of Pavia, Italy
I. G. Binev	Institute of Organic Chemistry, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria
H. Bock	Chemische Institute der Universität Frankfurt, Niederurseler Hang, D-6000 Frankfurt/Main 50, W. Germany
K. Bott	Hauptlaboratorium der BASF Aktiengesellschaft, D-6700 Ludwigshafen, Federal Republic of Germany
M. Charton	Pratt Institute, Department of Chemistry, Brooklyn, New York 11205, U.S.A.
A. J. Fatiadi	Centre for Analytical Chemistry, National Measurement Laboratory, National Bureau of Standards, Washington, D.C. 20234, U.S.A.
J. P. Ferris	Rensselaer Polytechnic Institute, Troy, N.Y., U.S.A.
K. Friedrich	Chemisches Laboratorium, Albert-Ludwigs-Universität, Albertstrasse 21, 7800 Freiburg 1. Br., Germany
R. Gandolfi	Institute of Organic Chemistry, University of Pavia, Italy
T. L. Gilchrist	Department of Organic Chemistry, University of Liverpool, England
P. Grünanger	Institute of Organic Chemistry, University of Pavia, Italy
F. Hibbert	Department of Chemistry, King's College, Strand, London WC2R 2LS, England
H. Hogeveen	Department of Organic Chemistry, The University, Nijenborgh 16, 9747 AG Groningen, The Netherlands
W. D. Huntsman	Ohio University, Athens, Ohio, U.S.A.
M. G. K. Hutchins	Temple University, Philadelphia, Pennsylvania, U.S.A.
R. O. Hutchins	Drexel University, Philadelphia, Pennsylvania, U.S.A.
I. N. Juchnovski	Institute of Organic Chemistry, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria

C. A. Kingsbury	Department of Chemistry, University of Nebraska, Lincoln, NE 68588, U.S.A.
D. M. Kok	Department of Organic Chemistry, The University, Nijenborgh 16, 9747 AG Groningen, The Netherlands
J. B. Moffat	Department of Chemistry and Guelph-Waterloo Centre for Graduate Work in Chemistry, University of Waterloo, Waterloo, Ontario, Canada
D. G. Morris	Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, U.K.
M. P. Periasamy	Mallinckrodt, Inc., St. Louis, Missouri, U.S.A.
H. C. van der Plas	Laboratory of Organic Chemistry, Landbouwhogeschool, Wageningen, The Netherlands
F. Roeterdink	Laboratory of Organic Chemistry, Landbouwhogeschool, Wageningen, The Netherlands
W. Runge	Organisch-Chemisches Institut der Technischen Universität München, Germany
L. I. Simándi	Central Research Institute for Chemistry, Budapest, Hungary
H. Stafast	Chemische Institute der Universität Frankfurt, Niederurseler Hang D-6000 Frankfurt/Main 50, W. Germany
H. M. Walborsky	Florida State University, Tallahassee, Florida, U.S.A.
K. Yoshida	Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560, Japan
K.-P. Zeller	Institut für Organische Chemie, Universität Tübingen, Auf der Morgenstelle, D-7400 Tübingen, Germany
H. Zollinger	Technisch-Chemisches Laboratorium, Eidgenössische Technische Hochschule (ETH), Zürich, Switzerland

Foreword

The present Supplement C contains material on triple-bonded functional groups, such as carbon–carbon triple bonds, cyano and isocyano groups and diazonium groups. These groups have been treated previously in the Chemistry of Functional Groups Series in the following volumes:

The Chemistry of the Carbon–Carbon Triple Bond (2 parts, 1978);
The Chemistry of Diazonium and Diazo Groups (2 parts, 1978).

Arynes, heteroarynes and isocyanides were treated as triple-bonded compounds, and chapters on them are included in this volume.

Some chapters intended for this supplementary volume did not materialize. These should have treated 'photochemistry of the Cyano Group'; Triple bonds in Cycloadditions', 'Compounds Containing $C(CN)_2$ and Related Groups' and 'Metal Triple-bond Complexes'.

We will be very grateful to readers who would call our attention to omissions or mistakes relating to this and other volumes in the series.

SAUL PATAI
ZVI RAPPOPORT

Jerusalem, June 1982

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 deter-

mination 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 (*two volumes*)
The Chemistry of the Carbonyl Group (*two volumes*)
The Chemistry of the Ether Linkage
The Chemistry of the Amino Group
The Chemistry of the Nitro and Nitroso Groups (*two parts*)
The Chemistry of Carboxylic Acids and Esters
The Chemistry of the Carbon–Nitrogen Double Bond
The Chemistry of the Cyano Group
The Chemistry of Amides
The Chemistry of the Hydroxyl Group (*two parts*)
The Chemistry of the Azido Group
The Chemistry of Acyl Halides
The Chemistry of the Carbon–Halogen Bond (*two parts*)
The Chemistry of Quinonoid Compounds (*two parts*)
The Chemistry of the Thiol Group (*two parts*)
The Chemistry of Amidines and Imidates
The Chemistry of the Hydrazo, Azo and Azoxy Groups (*two parts*)
The Chemistry of Cyanates and their Thio Derivatives (*two parts*)
The Chemistry of Diazonium and Diazo Groups (*two parts*)
The Chemistry of the Carbon–Carbon Triple Bond (*two parts*)
Supplement A: The Chemistry of Double-bonded Functional Groups (*two parts*)

Supplement B: The Chemistry of Acid Derivatives (*two parts*)
Supplement C: The Chemistry of Triple-bonded Functional Groups (*two parts*)
The Chemistry of Ketenes, Allenes and Related Compounds (*two parts*)
Supplement E: The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and their Sulphur Analogues (*two parts*)
The Chemistry of the Sulphonium Group (*two parts*)
Supplement F: The Chemistry of Amino, Nitroso and Nitro Groups and their Derivatives (*two parts*)

Titles in press:

The Chemistry of Peroxides
The Chemistry of Organometallic Compounds
Supplement D: The Chemistry of Halides and Pseudo-halides

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.

The Hebrew University
Jerusalem, ISRAEL

SAUL PATAI

Contents

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 1

Chiroptical properties of compounds containing triple-bonded functional groups

WOLFGANG RUNGE

*Organisch-Chemisches Institut der Technischen Universität München, München, Germany**

*Correspondance address SfS, Werderstrasse 35, D-6900 Heidelberg, Germany.

I. INTRODUCTION

The present chapter is intended to give a review of the chiroptical properties of molecules with triple-bonded functional groups covering the spectral range 589–190 nm, i.e. emphasis is on optical (molecular) rotations, $[\phi]_\lambda^T$ (in particular measured at the wavelength of the sodium D-line, $\lambda = 589$ nm), and circular dichroism (CD), $\Delta\epsilon$, in the near ultraviolet.

Current instruments allow CD measurements to be performed both in the vacuum UV region ($\lambda < 190$ nm) and in the infrared spectral region ('vibrational circular dichroism', VCD). However, no such measurements (which are based on light absorption effects) on triple-bonded molecules have been reported in the literature. Similarly, no 'vibrational Raman optical activity data' (Raman circular intensity differentials referring to light scattering phenomena) of molecules with triple bonds have appeared in the literature.

Furthermore, only a few 'conventional' CD measurements on triple-bonded systems, i.e. measurements of the circular dichroism which is intrinsic to chromophores with triple-bonded subunits, are reported so far. These include CD data for vinylacetylenes, diacetylenes and polyenynes.

Therefore, the main subjects of this chapter are the substituent effects of triple-bonded groups on molar rotations, $[\phi]_D$, and the circular dichroism, $\Delta\epsilon$, of some selected types of molecule or chromophore.

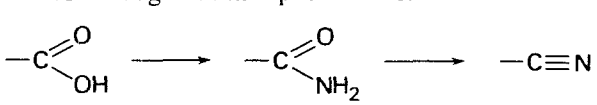
A. The Role of Chiral Acetylenes and Nitriles in Chemistry and Spectroscopy

Among the substituents with triple bonds the ethynyl (—C≡CH) and the cyano groups (—C≡N) are the most important ones.

Chiral acetylenes play fundamental roles in synthetic chemistry, stereochemistry, pharmaceutical chemistry and the chemistry of natural products. In synthetic chemistry, chiral acetylenes are particularly useful, for instance, as intermediates or precursors of chiral allenes[75,82], 1,3-butadienes[18,33], chiral allylic alcohols[90], and propenylamines[67]. In mechanistic studies chiral acetylenes are often used to elucidate the absolute configurations of allenes[75]. Enantiomers of some *N*-(4)*t*-amino-1-methylbutynyl)-substituted succinimides and 2-pyrrolidones, for instance, show strong stereospecificty in motor effects of the muscarinic agent oxotremorine, *N*-(4-pyrrolidino-2-butynyl)-2-pyrrolidine, the pharmaceutical effect being mainly exerted by the (*R*)-(+) isomer[52,65,66]. Numerous chiral acetylenes and polyacetylenes are found in nature[12,13,41]. Chiroptical properties of chiral acetylenes which are important in the above mentioned contexts will be discussed in the present chapter.

Apart from being synthetically important intermediates, molecules with triple-bonded functional groups, such as acetylenes, nitriles and isocyanides, play a key role in the theories of optical rotation, especially rotation of molecules with an asymmetric carbon atom[2,3,43,74]. The significance of such groups for theories of optical rotation will be elaborated in more detail as an important aspect of the present chapter.

A practical reason for the significance of the cyano group in comparing optical activities of various molecular classes is that chiral nitriles may be obtained rather easily through optical resolution of the corresponding carboxylic acids and transformation of these acids into nitriles through routine procedures:



B. Comparison of Triple-bonded Functional Groups with Other Substituents

In order to rationalize the substituent effects of triple-bonded functional groups on optical rotation comparisons will be made with other 'similar' groups. The 'similarity criteria' can be expressed on various levels (corresponding to nominal, interval or even rational scales of measurement).

A qualitative classification of substituents which is of particular importance for optical rotation (Section II.B) is the local symmetry. Referring to this criterion triple-bonded functional groups, such as $-C\equiv CH$, $-C\equiv N$, $-\overset{+}{N}\equiv\overset{-}{C}$, $-\overset{+}{N}\equiv N$, may be compared with other rotationally symmetric groups, such as H, Cl, Br, Me, *t*-Bu or CF_3.

More quantitative similarity criteria involve group increments (and substituent constants) for the calculation of molecular properties or chemical reactivities, respectively. Most relevant in the context of chiroptical properties are the bond refractivity R_D (or bond polarizability α_D), the group parachor P and the group dipole moment $\mu(R)$. In Table 1 a comparison of the numerical values for these last group properties for several groups is presented. It can be seen that the cyano and isocyano groups, in particular, have many of the above properties in common with the halogen atoms Cl and Br and with the triatomic heterocumulenic group $-N_3$ (which is the reason for calling all these radicals 'pseudohalides'). Moreover, referring to resonance form **B** the azido group may be viewed as a substituent with a triple-bonded N≡N subunit:

$$-\overset{-}{N}=\overset{+}{N}=\underset{-}{N}| \longleftrightarrow -\underset{-}{\overset{-}{N}}-\overset{+}{N}\equiv N|$$

(A) **(B)**

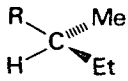
With respect to the polar nature of the triple-bonded groups (as measured by the group dipole moments, electronegativities or polar substituent constants) close similarities with the carboxylic (COOH) or carbomethoxy group (COOMe) are

TABLE 1. Comparison of triple-bonded functional groups with other substituents (R)

Group R	$\mu(R)(D)^a$ for MeR	PhR	$P(cm^{-3})^b$	$R_D(cm^3)^c$	$\chi(R)^d$	$\sigma_I{}^e$	$\sigma_R^0{}^f$
$C\equiv CH$	0.75	0.79	73.5	7.806	3.29	0.30	+0.07
$C\equiv N$	3.92	4.14	64.6	6.106	3.17	0.56	+0.13
$\overset{+}{N}\equiv\overset{-}{C}$	3.83	4.08		7.990		0.67	+0.02
Cl	1.87	1.69	55.2	6.492	3.00	0.46	−0.23
Br	1.81	1.70	68.8	9.389	2.68	0.44	−0.19
$N=\overset{+}{N}=\overset{-}{N}$	2.17	1.44	77[g]	10.048	2.71[g]	0.42	
COOH	1.74	1.73	73.7	6.884	2.84	0.30	+0.14
COOMe	1.72	1.80	118.8	7.002		0.31	+0.16
$HC=CH_2$	0.37	0.13		7.518	2.13	0.01	−0.05

[a] Dipole moment, from Refs. 96 and 97.
[b] Parachor, from Refs. 74 and 88.
[c] Bond refractivity, from Refs. 50 and 74.
[d] Electronegativity, from Ref. 94.
[e] Polar substituent constant, from Ref. 29.
[f] Pi delocalization constant, from Ref. 29.
[g] From Ref. 84.

TABLE 2. Molar rotations $[\phi]_D$ of (*S*) secondary butyl compounds, **1–7**, containing triple-bonded groups R and bond polarizabilities, $\tilde{\alpha}(R)$, of the corresponding groups R[74]



(1–7)

Compound	Group R	$\tilde{\alpha}(R)$ (Å^3)[a]	$[\phi]_D$(EtOH) (deg.)	$[\phi]_D$(S) (deg.)[b]
1	C≡CH	3.095	+38.17	+38.17 (neat)
2	C≡CBr	6.559	+73.90	+78.14 (neat)
3	C≡CCOOH	5.567	+63.60	+63.60 (Et_2O)
4	C≡CC≡CBu-*t*	5.933	+71.85	+71.85 (C_7H_{16})
5	C≡N	2.420	+28.20[c]	+28.27 (neat)
6	N≡C	3.167	+37.97	+40.32 ($CHCl_3$)
7	N=N=N	3.983	+44.49	+46.12 (neat)

[a] $\tilde{\alpha}(R) = 0.3964 R_D$.
[b] S = solvent.
[c] In MeOH.

observed. Regarding their abilities for mesomeric interactions (as expressed by σ_R^0) the C≡CH and C≡N groups are medium–strong mesomeric acceptors, whereas the isocyanide group is a weak mesomeric acceptor. In particular, it is found that significant fractions of the π electron densities in XC≡CH and XC≡N molecules, formally associated with the triple bonds, are actually in the neighbouring bond regions[39,59,62], which accounts for the anomalous strength of single bonds adjacent to triple bonds.

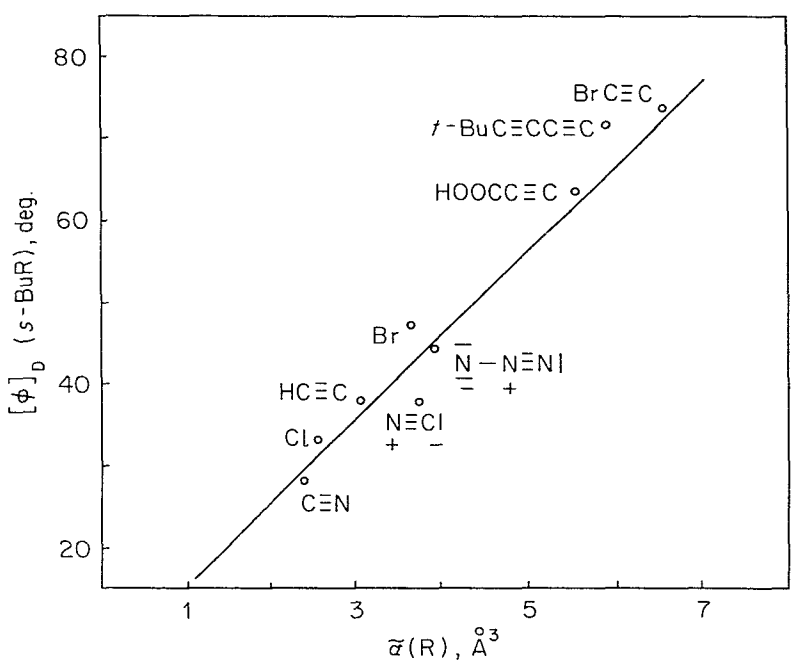


FIGURE 1. Correlation between the molar rotations of secondary butyl compounds *s*-BuR in EtOH and the bond polarizabilities $\tilde{\alpha}(R)$ of the ligands R.

Furthermore, in XC≡CH and XC≡N the charge distribution in the triple-bonded functionality is found to be relatively little affected by the nature of X[62].

The group property being most relevant for optical rotation is polarizability (or refractivity, respectively). In Table 2 a set of molar rotations for secondary butyl compounds *s*-BuR with triple-bonded groups (R) and the bond polarizabilities $\tilde{\alpha}$(R) of the corresponding groups R are summarized[74]. The molar rotations of the (*S*)-(+) molecules (in ethanol as the solvent) fit into the correlation (1) between $[\phi]_D$ and $\tilde{\alpha}$(R) derived by Runge[74] for rotationally symmetric groups with anisotropic polarizabilities $\Delta\alpha$ greater than 1.6 Å^3.

$$[\phi]_D(s\text{-BuR}) = 10.374\,\tilde{\alpha}(R) + 5.108 \quad (1)$$

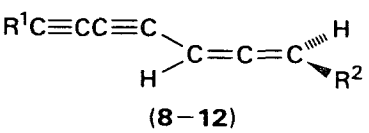
Correlation (1) and the rotations for the secondary butyl compounds of Table 2[74], and *s*-BuCl and *s*-BuBr, are displayed in Figure 1.

II. OPTICAL ROTATION OF MOLECULES WITH TRIPLE-BONDED FUNCTIONAL GROUPS

A. Naturally Occurring Molecules

Acetylenes (and polyacetylenes) are widespread in nature[12,13,41], and for chiral molecules optical rotations are often available. The rotations, however, are mainly used for diagnostic purposes or are only given to complete the set of physical properties which fully characterize the compound. Since the naturally occurring chiral acetylenes are often rather complex, one cannot in most cases easily detect relationships between the signs (or even the orders of magnitude) of the rotations and the structures of the molecules.

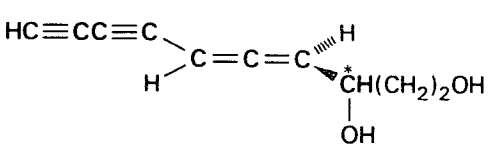
In connection with quantitative structure–property relationships only some naturally occurring chiral diyne-allenes **8–12** are of interest[71,75]. The rotations of these molecules will be discussed in more detail in Section II.B.2.



(8–12)

	R^1	R^2	$[\phi]_D$ (deg.)
8	H	CH_2OH	+448(CH_2Cl_2)
9	H	CH_2CH_2OH	+475(EtOH)
10	H	$(CH_2)_3OH$	+350(EtOH)
11	H	$(CH_2)_4OH$	+288(EtOH)
12	Me	CH_2CH_2OH	+496(EtOH)

The optical rotations of the compounds **8–12** are essentially determined by the axially chiral arrangement of the allenic subunit. This is seen from the rotation of the diyne-allene **13** where the axially chiral allenic subunit and a (centrochiral) asymmetric carbon atom are linked together. **13** exhibits a molar rotation which is comparable to those of the diyne-allenes **8** and **10**, i.e. there is only a small contribution of the asymmetric carbon atom to the overall observed rotation.

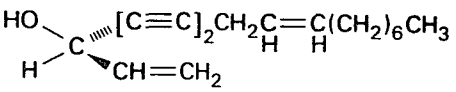


(13)

$[\phi]_D$ + 341°(EtOH)

For illustrative purposes a brief outline of the optical rotations of some other chiral naturally occurring polyacetylenes with an asymmetric carbon atom as the element for the induction of optical activity shall be given. In general, the rotations of these compounds are considerably smaller than those of the diyne-allenes. This is expected, since structural effects of asymmetric carbon atoms on optical rotations in general do not give molar rotations exceeding 100°[74].

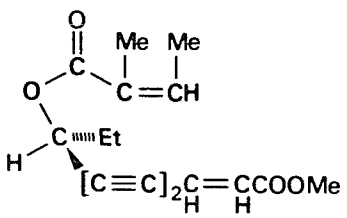
For instance, falcanirol (**14**) of 3-(*R*)-(−) configuration[11,49], and *s-cis* arrangement around the double bond has been obtained with a rotation, $[\alpha]_{578}^{20}$ −22.5° (Et_2O).



(**14**)

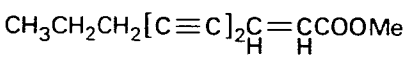
$[\phi]_{578}^{20}$ −55.0°(Et_2O)

Structurally related to **14**, the naturally occurring *cis*-8-hydroxy derivative **15** of lachnophyllum ester **16** of (*S*)-(−) configuration exhibits a larger rotation than expected[9,10]. Irradiation of **15** generates the 2-*trans* isomer which upon saponification



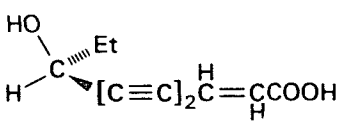
(**15**)

$[\phi]_{578}$ −450°(Et_2O)



(**16**)

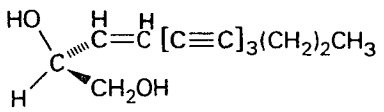
gives the acid **17**. Comparison of the rotations of **14** and **17** with that of **15** indicates that in **15** the two bulky unsaturated groups may be assumed to achieve, due to their steric requirements, a particular chiral conformation and hence be responsible for the observed large rotation.



(**17**)

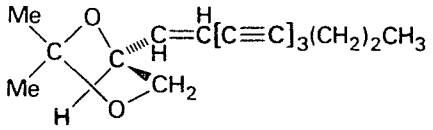
$[\phi]_{578}$ −51.7°(Et_2O)

Some interesting effects of the influence of the double-bond stereochemistry in polyynenes on the optical rotations of allylic asymmetric centres have been observed by Jones and coworkers[1]. For instance, the naturally occurring (2*S*)-tridec-*trans*-3-ene-5,7,9-triyno-1,2-diol (**18**) may be transformed into the acetonide **19** [(4*S*)-2,2-dimethyl-4-(undec-*trans*-1-ene-3,5,7-triynyl)-1,3-dioxolan]. Whereas the *trans* compounds **18** and **19** have rotations of opposite signs the synthetic *cis* compounds **20** and **21** both have negative rotations. The effect of the stereochemistry of the double bond is more pronounced for the acetonides than for the diols as may be seen from the differences between the rotations of **18** and **20** and **19**



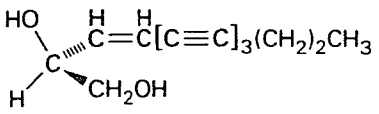
(18)

$[\phi]_D$ −19.9°(EtOH)



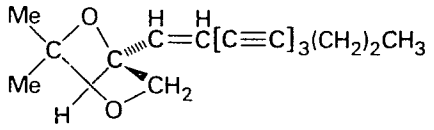
(19)

$[\phi]_D$ +134.5°(EtOH)



(20)

$[\phi]_D$ −76.9°(EtOH)

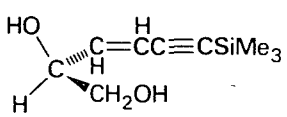


(21)

$[\phi]_D$ −121.2°(EtOH)

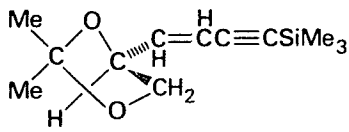
and **21**, respectively. For both the acetonides and the diols the rotations of the *cis* compounds are more negative than those of the *trans* forms.

Similar effects are observed in the rotations of the synthetic trimethylsilylenynes **22–25**[1]. These will be treated in more detail in Section III with their circular dichroism. From the CD it may be concluded that the markedly different rotations of the *cis* and *trans* enynes (or polyynenes, respectively) are due to a twist of the enyne grouping in the *cis* compounds, whereas in the *trans* compounds the enyne grouping may be assumed to be planar. This interpretation seems to be in contradiction to the



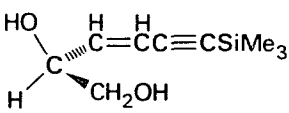
(22)

$[\phi]_D$ −36.9°(EtOH)



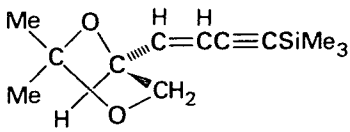
(23)

$[\phi]_D$ +123.4°(EtOH)



(24)

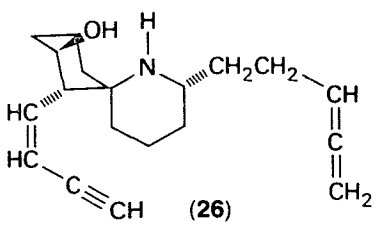
$[\phi]_D$ +35.0°(EtOH)



(25)

$[\phi]_D$ −8.53°(EtOH)

molecular structure determination of the spiro alkaloid dihydroisohistrionicotoxin (**26**) where, by X-ray investigation, the *cis* arrangement of an enyne grouping is found to be planar within 0.003 Å[42]. The findings for **26**, however, do not preclude a skew enyne



(26)

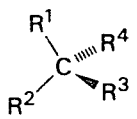
functionality in **25** (or **24**) since **25** (and **24**) has additionally a bulky trimethylsilyl group which may give rise to nonbonded interactions with the dioxolan group or the ligands of the asymmetric carbon atom of the diol, respectively.

B. The Significance of Triple-bonded Functional Groups for Theories of Optical Rotation

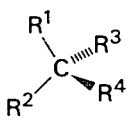
Molecules with triple-bonded functional groups, especially nitriles, have played (and continue to play) a fundamental role in theories of optical rotation, whether empirical, semiempirical or nonempirical in character. The central aim of all these theories is to relate optical rotations to molecular structure.

One of the first approaches, intended to have a large range of applicability for chiral molecules of various kinds, rests on the 'principle of pairwise interactions'[43]. The basic assumption of this empirical approach for the calculation of optical rotation starts from the finding that each pair of groups in an optically active molecule can interact to give rise to a contribution to the optical rotation, i.e. for an optical rotation one has to consider the interactions of at least two groups in a molecule. Thus the principle of pairwise interactions assumes that, to a good approximation, the optical rotation of a molecule may be expressed as the sum of contributions arising from all ways of pairing the groups of the compound, and disturbances of the contribution of a given pair by the remaining groups in the molecule are assumed to be small (and are therefore negligible in the first approximation).

For molecules with an asymmetric carbon atom:



(A)



(B)

the principle of pairwise interactions suggests that the molar rotation (under given standard conditions involving the wavelength of the incident light, the temperature and the solvent) may be expressed according to equation (2).

$$[\phi]_D^T = P(R^1, R^2) + P(R^1, R^3) + P(R^1, R^4) + P(R^2, R^3) + P(R^2, R^4) + P(R^3, R^4) + P(R^1, C) + P(R^2, C) + P(R^3, C) + P(R^4, C) \quad (2)$$

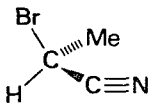
In equation (2) $P(R^1, R^2)$, for instance, is the optical rotation for a hypothetical molecule containing only the two groups R^1 and R^2 in exactly the same relative spatial positions that they would have in the above molecule **A**. Correspondingly, $P(R^1, C)$ is the optical rotation that would be observed if only R^1 and the asymmetric carbon C were present. The next approximation step considers that the group R^3 has some influence on the interaction term $P(R^1, R^2)$, i.e. one takes into account that the interaction between R^1 and R^2 cannot be quite the same as the interaction between these same two groups when R^3 is present. Therefore, defining a 'three-way interaction term' T according to equation (3), the description of the optical rotation is corrected by corresponding triplets (equation 4). If necessary, one can go one step further and introduce 'four-way interaction terms', etc.

The problem of a treatment of optical rotation according to the principle of pairwise interactions, therefore, is to determine how many of these interaction terms must be included in order to obtain a reasonably good quantitative description of optical rotation. Within the 'principle of pairwise interactions' approach it is generally assumed that the three-way terms will be much smaller than the two-way terms.

$$T(R^1, R^2, R^3) = T(R^1R^2, R^3) + T(R^2R^3, R^1) + T(R^1R^3, R^2) \quad (3)$$

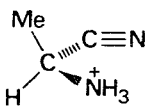
$$\begin{aligned}[\phi]_D^T = {} & P(R^1, R^2) + P(R^1, R^3) + P(R^1, R^4) + P(R^2, R^3) + P(R^2, R^4) + P(R^3, R^4) \\ & + P(R^1, C) + P(R^2, C) + P(R^3, C) + P(R^4, C) \\ & + T(R^1, R^2, R^3) + T(R^1, R^2, R^4) + T(R^1, R^3, R^4) + T(R^2, R^3, R^4) \\ & + T(R^1, R^2, C) + T(R^1, R^3, C) + T(R^1, R^4, C) + T(R^2, R^3, C) + T(R^2, R^4, C) \\ & + T(R^3, R^4, C) \end{aligned} \quad (4)$$

In the examination of the degree to which this principle may be valid in different types of chiral molecules, nitriles, such as (*S*)-α-bromopropionitrile (**27**)[7,74] or the (*S*)-ammoniopropionitrile cation (**28**)[64,74] take on a crucial role for centrochiral molecules with a molecular skeleton of the symmetry T_d ('methane derivatives')[43].



(27)

$[\phi]_D$ −22°(neat)



(28)

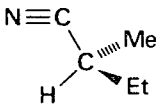
$[\phi]_D$ +18.4°(H_2O)

According to the principle of pairwise interactions the molar rotation of α-bromopropionitrile (**27**), for instance, should be given by equation (5). However, all

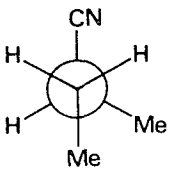
$$\begin{aligned}[\phi]_D^T = {} & P(Br, H) + P(Br, CN) + P(Br, Me) + P(H, CN) + P(H, Me) \\ & + P(CN, Me) + P(Br, C) + P(H, C) + P(CN, C) + P(Me, C) \end{aligned} \quad (5)$$

of these pairwise interactions are identically zero owing to the rotational symmetries of all the groups involved. This means that in **27** all pairwise interactions cancel, since if any two groups are considered apart from the rest of the molecule, a plane of symmetry may be passed through them. Considering that the terms *P* represent the rotation arising from the interactions of two ligands, all the fragments R^iR^j are superimposable on their mirror images and hence can give no contributions to the optical rotation. As a consequence, for any molecule in which all the groups linked to an asymmetric carbon atom have axial symmetry, the contribution of pairwise interactions to the optical rotation must vanish and the rotation must result from at least three-way interactions[43].

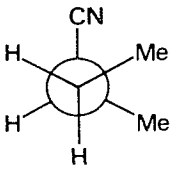
The observation of rotation of the order of 20° for **27** and **28** therefore shows that the assumption of a small (or even negligible) contribution from three-way interactions is either not justified or that special conditions in the above molecules are responsible for the relatively large three-way interactions. Kauzmann and coworkers[43] have attributed the large three-way interactions to the particular character of the molecules, having strongly polar groups in close proximity which are furthermore very susceptible to solvent effects. However, recent investigations[69,74] have shown that the principle of pairwise interactions cannot be applied to molecules with an asymmetric carbon atom and that in general at least triple terms must be used to describe the optical rotations of methane derivatives adequately. If one considers molecules with ligands in which rotation about the bonds attached to the asymmetric carbon atom is possible, such as (*S*)-(+)-*s*-butyl cyanide (**5**) (Table 2), one must consider three rotamers **5a**, **5b**, **5c**. Restricting oneself to a consideration of the fragment CH_3CH_2—C—CN one can see that in the rotamers **5b** and **5c** the conformations of this last fragment are mirror images of one another. Therefore, the pairwise interactions involving the fragment CH_3CH_2—C—CN in the forms **5b** and **5c** are equal in magnitude and opposite in sign, i.e. they cancel. Furthermore, in form **5a** the



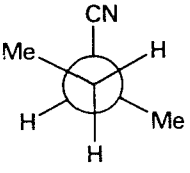
(5)



(5a)



(5b)

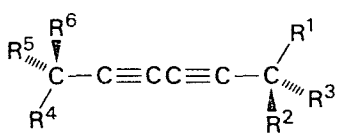


(5c)

CH_3CH_2—C—CN fragment is achiral and therefore the pairwise interactions are identically zero. As a consequence, if *s*-butyl cyanide has an equal population for all its above three rotameric forms the entire rotation must also come from three-way (or higher order) interactions. In allowing the ethyl group in **5** to occupy its three stable conformations to equal extents one has, in effect, attributed to the ethyl group an axis of symmetry about the bond that links it to the asymmetric carbon atom. Any forces which cause the three forms to exist in unequal amounts will tend to influence the optical rotations through involvement of pairwise interactions.

So far, only molecules with one asymmetric carbon atom have been considered. Van't Hoff's theory of the asymmetric carbon atom as a structural condition giving rise to optical activity led him to propose an additivity relationship known as the 'principle of optical superposition'. Acccording to this, in a molecule containing several asymmetric centres each centre contributes to the optical rotation independently of the others. Most of the tests of the superposition principle have been confined to polyalcohols and sugars and as many examples can be cited where the superposition principle fails as where it is obeyed. The complications in applying the rule result largely from the closeness of the asymmetric centres and conformational effects[43]. The superposition principle, however, can be expected to be valid whenever the centres involved are widely enough separated. In this regard the diacetylene skeleton provides an excellent opportunity to test the superposition principle for model compounds obeying the limiting conditions under which the principle may be assumed to be valid.

In diacetylenes, e.g. **29–34**, the ligands attached to the C≡CC≡C skeleton are



(**29** – **34**)

freely rotating, i.e. no conformational preferences for particular rotamers should be observed[25,34,78]. The approximate validity of the superposition principle in case of diacetylenes is demonstrated in Table 3. The alcohols **32–34**, especially, represent good examples for the superposition principle. The hydrocarbons **4** and **29** exhibit some deviations which, however, are within the range of variations which is expected for this principle.

Another useful approach for the estimation of optical rotations of molecules which has been tested using mainly compounds with triple-bonded groups is based on the

TABLE 3. The optical superposition principle demonstrated for various diacetylenes, $R^1R^2R^3CC{\equiv}CC{\equiv}CCR^4R^5R^6$

Compound	R^1	R^2	R^3	R^4	R^5	R^6	Configuration	$[\phi]_D$ (deg.)	Reference
4	Et	Me	H	Me	Me	Me	(*S*)	+67.1[a]	34
29	Et	Me	H	Et	Me	H	(*S*), (*S*)	+151.0[a]	34
30	*t*-Bu	Me	H	Me	Me	Me	(*S*)	+53.8[a]	34
31	*t*-Bu	Me	H	*t*-Bu	Me	H	(*S*), (*S*)	+105.3[a]	34
32	Et	Me	OH	Et	Me	OH	(*S*), (*S*)	−28.4[b]	19
33	Et	Me	OH	Et	Me	OH	(*R*), (*R*)	+26.5[b]	19
34	Et	Me	OH	Et	Me	OH	(*S*), (*R*)	+0.17[b]	19

[a]Neat.
[b]In EtOH.

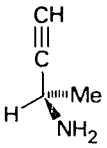
observation that molecules which differ only by the substitution of one ligand by an isosteric one (or almost isosteric one, e.g. C≡N vs. C≡CH) have very similar optical rotations[74]. Since isosteric groups (isoelectronic groups of corresponding symmetries) have similar steric requirements, conformational effects cannot influence the optical rotations of such compounds significantly. However, solvent effects may affect the rotations of isosteric molecules to a different extent. For instance, the different basicity (and polarity) of the C≡N and C≡CH groups may give rise to different solvent effects in solvents capable of hydrogen-bonding. *s*-Butylacetylene (**1**), *s*-butyl cyanide (**5**) and *s*-butyl isocyanide (**6**) (in Table 2) demonstrate the relatively small effects of isosteric substitutions on optical rotations.

Further comparisons of this kind between acetylenes and nitriles (the data being largely from Reference 74) are given in Figure 2. Apart from the phenyl compounds **42**[87] and **43**[6], the ammonium salts **28** and **37** also exhibit fairly large differences between their rotations. These deviations probably result from solvent effects.

Corresponding comparisons between cyanides and isocyanides may be made for the phenyl derivatives **45**[95] and **46**[57] and the diphenylcyclopropanes **47**[89] and **48**[60]. For the isocyanide **45** the given rotation is an estimated value based on the assumption that the densities of the compounds **45** and **46** are identical. Furthermore, the large difference between the rotations of **45** and **46** must come from solvent effects. (*S*)-(+)-*s*-butylbenzene, EtMeCHPh, for instance, shows a marked decrease in rotation when using a solution in ethanol instead of the neat liquid for the measurement: $[\alpha]_{546}$ +33.2°(neat), $[\alpha]_{546}$ +18.7°(EtOH)[45].

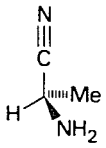
Nitriles have also played a crucial role in strictly theoretical approaches to optical rotation, in particular with respect to the effect of the change in distance of the ligands on the magnitude of the rotation. Regarding this objective the rotations of α-bromopropionitrile (**27**) and 3-methyl-5-bromo-1-cyanoadamantane (**49**) as model compounds with relatively fixed geometries have been compared[2–5]. (**49** is one of the few optically active adamantane derivatives reported so far in the literature.)

As has been shown, in these kinds of T_d molecules the optical rotations must come from three-way and/or higher order interactions (second- and/or third-order contributions in terms of perturbation theory). If r is an 'average' distance between two interacting groups of a chiral molecule the rotations should vary as $1/r^n$ and $n \geq 5$. In the polarizability theory of optical rotations[3], the second- and third-order interactions between polarizable groups vary as $1/r^5$ and $1/r^8$, respectively. A quantum-mechanical theory of optical rotations of tetrahedral molecules (in particular methane derivatives)[37] gives the distance effect as $1/r^7$.



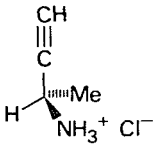
(**35**)

$[\phi]_D$ +15.20°(H_2O)



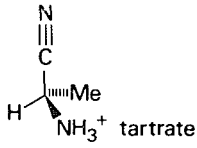
(**36**)

$[\phi]_D$ +18.4°(H_2O)



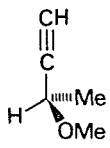
(**37**)

$[\phi]_D$ +9.13°(EtOH)



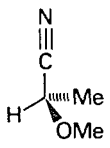
(**28**)

$[\phi]_D$ +18.4°(H_2O)



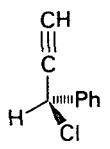
(**38**)

$[\phi]_D$ +109.8°(MeOH)



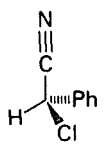
(**39**)

$[\phi]_D$ +100.0°(neat)



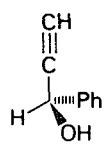
(**40**)

$[\phi]_D$ +82.0°(C_6H_6)



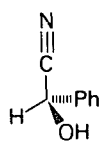
(**41**)

$[\phi]_D$ +67.9°(Me_2CO)



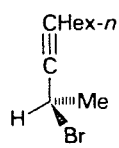
(**42**)

$[\phi]_D$ +35.8°($CHCl_3$)



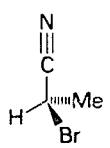
(**43**)

$[\phi]_D$ +64.8°($CHCl_3$)



(**44**)

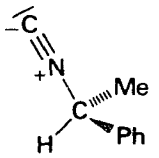
$[\phi]_D$ +23.2°(MeOH)



(**27**)

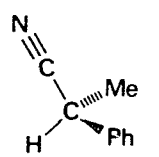
$[\phi]_D$ +20.6°(EtOH)

FIGURE 2. Comparison between the molar rotations of correspondingly substituted acetylenes and nitriles.



(45)

$[\phi]_D$ ~ −54°(neat)



(46)

$[\phi]_D$ −23.50°(EtOH)

(48)

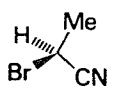
$[\phi]_{546}$ +774°($CHCl_3$)

$[\phi]_D$ +673°($CHCl_3$)

(47)

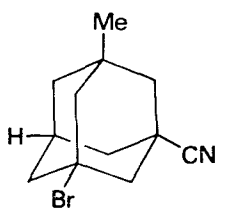
$[\phi]_D$ +723°($CHCl_3$)

By comparing the magnitudes of the rotations of **27** and **49** one sees that the distance effect is a 32-fold decrease. Assuming as a first approximation that the intergroup distances in **27** and **49** increase by a factor of two the second-order contribution would



(27)

$[\phi]_D$ −22°(neat)



(49)

$[\phi]_D$ −0.684°(*cis*-decalin)

fall off by a factor of $2^5 = 32$, which is comparable to the observed effects (the numerical agreement with this rough estimation has to be regarded as fortuitous). This indicates that second-order calculations (involving three-way interactions) can account for the observed rotations of this type of molecule.

The optical rotatory dispersions (ORD) of **27** and **49** (in the range 656–436 nm) fit precisely the one-term Drude dispersion formula (6)[2,8]. This means that the nitriles exhibit plain ORD curves in the transparent region.

$$[\phi]_\lambda = \frac{K}{\lambda^2 - \lambda^2{}_0} \tag{6}$$

$K = -6.143 \times 10^6$ deg. $(nm)^2$; $\lambda_0 = 262$ nm for **27**

$K = -0.205 \times 10^6$ deg. $(nm)^2$; $\lambda_0 = 218$ nm for **49**

The theory of optical rotation relates λ_0 in Drude plots to the wavelengths of electronic transitions whose Cotton effects determine essentially the optical activity[21]. In case of nitriles, however, there is no UV absorption between 200 and 300 nm[8] (cf. also Section II.A). Therefore, in case of the nitriles λ_0 in equation (6) is either of no physical significance or has to be attributed to weak electronic transitions involving the bromine atom (i.e. to the C—Br chromophore). As for instance in α-bromopropionic acid, the n,σ* transition of the C—Br chromophore is observed at 230 nm[55], the ORD of the above bromonitriles seem to be governed by the C—Br subunits.

C. Semiempirical Descriptions of the Optical Rotation of Compounds with Triple-bonded Groups using Chirality Functions

In the preceding section it has been shown that for an adequate description of the optical rotation of molecules with an asymmetric carbon atom (or, more generally, molecules with a skeleton of symmetry T_d) at least three-particle functions (three-way interactions) must be taken into account.

An essentially geometrophysical method, which gives conditions concerning the transformation properties, analytical forms and general restrictions of functions of sufficient generality to describe chirality phenomena for arbitrary molecular classes, has been introduced by the 'Theory of Chirality Functions' of Ruch and Schönhofer[69] and its subsequent modifications[74]. As these methods are underlying the semiempirical descriptions of the optical rotation of various molecules with triple-bonded functional groups (methane derivatives, allenes, spirobiindanes, [2,2]metacyclophanes) to be outlined in the present section, an introductory summary of the relevant features of these methods will be given. (A summary with particular emphasis on allenes has been given recently in this series[71].)

The 'chirality function method' of treating optical activity may take the typical 'substituent effect approach' of organic chemistry, i.e. that properties of molecular systems are related to properties of appropriately selected subsystems. Thus a molecule is dissected (conceptionally) into a skeleton with n ligand sites to which the ligands R are attached. According to Ruch and Schönhofer[69] a function of the ligands or of certain ligand parameters for the description of a chiral property for a class of molecules with a common achiral skeleton is called a 'chirality function'. A chirality function may take many forms. A necessary condition, however, is that the numerical value for a chiral property remains unchanged when the molecule is rotated, but changes its sign when the molecule is replaced by its mirror image.

A restriction to a spatially rigid skeleton (of symmetry G) and an abstraction to a point model for the ligands R which may be characterized by real numbers $\sigma(R)$ allows a systematic treatment of the complex molecular property for 'ideal' molecules on the basis of algebraic arguments. Since for such 'ideal' molecules symmetry operations from G may be represented by permutations of the ligands, the vehicle for a general treatment of optical activity is permutation algebra.

For 'ideal' molecules represented by a fixed arrangement of points in space (with no heteroatoms in their skeleton) the skeletal symmetry G is determined by all the molecules with exclusively n identical ligands. In particular, the point symmetry G defines a class of molecules which may be characterized by a geometrical figure. The individual molecules of the class under consideration are indexed sets where definite numbers are assigned to the sites. In this way, methane derivatives are representatives of a molecular class where the skeleton has the symmetry T_d of a regular tetrahedron. Allenes and spirobiindanes may be viewed as representatives of the molecular class with the skeletal symmetry D_{2d} of an irregular tetrahedron (Figure 3). The restricting conditions imposed by the above model on the treatment of chiral properties of 'real' molecules concerns first the symmetries of the ligands.

If the symmetry arrangement of the ligand sites is not to be influenced by the nature of the ligands or by certain types of ligands (corresponding to a neglect of any interactions between the ligands) the site symmetry has to be retained. This means, that for methane (T_d) derivatives the ligands must have the symmetries C_{3nv} ($n \geq 1$) or $C_{\infty v}$, i.e. the ligands must be rotationally symmetric. Therefore, in contrast to atomic ligands, such as H, Cl, Br, etc., and C_{3v} ligands, such as CH_3, NH_3^+, etc., groups with triple bonds, such as C≡CH, C≡N, N≡C, conform to the conditions required for model-adequate ligands for T_d molecules.

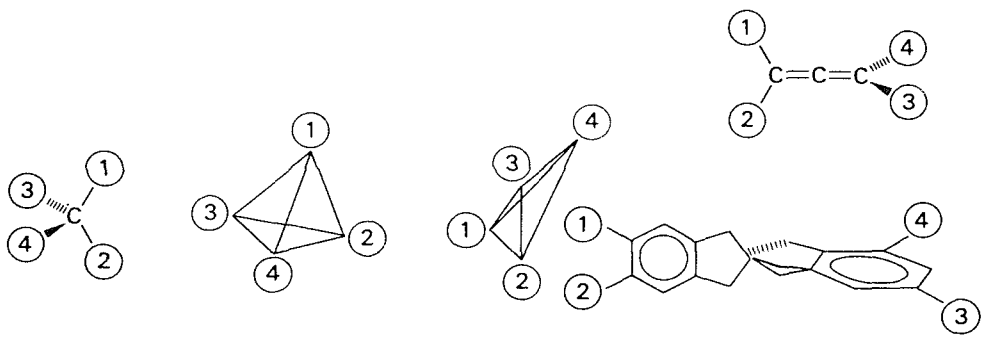


FIGURE 3. Representations of different molecular skeletons by geometrical figures.

In the case of D_{2d} derivatives, however, the ligands must only have a mirror plane identical with that of the D_{2d} skeleton, i.e. the selection of 'permissible' ligands for a treatment of the optical rotation of D_{2d} molecules is less restrictive than for T_d molecules. On the other hand, in relation to the time-scale of experimental investigations of chiroptical properties, freely rotating ligands with a (local) mirror plane symmetry may also become 'permissible' for T_d derivatives (with respect to their time-averaged symmetries or ensemble-averaged symmetries, respectively). Therefore, the model is not as restrictive as one might expect at first glance referring only to the local symmetries of the isolated ligands. Some important groups which exhibit time-averaged rotational symmetries in methane derivatives include the ethyl, methoxy and hydroxy groups[43,74].

Thus, many chemically relevant ligands become permissible if real molecules are investigated by the model theory. The most serious situations which will affect the above-mentioned foundations of the model include deformations of valence and dihedral angles by neighbouring ligands, larger variations of skeleton–ligand bond length and changes of conformation or rotamer population, if certain ligand combinations are present (i.e. certain ligands achieve special arrangements relative to other definitive groups).

Since this approach deals with single, isolated molecules, solvent effects have to be additionally taken into consideration. A first approximation to cope with solvent effects is to compare only measurements which have been performed in the same 'standard' solvent, for instance, ethanol.

Since chiroptical properties are extremely sensitive to small structure changes and to solvent effects, all the above mentioned factors have to be controlled if experimental and calculated optical rotations are to be compared.

For a more general analysis of optical rotations it is advantageous to refer to the 'chirality order' o[69]. This is the maximum number o of identical ligands which may occur in chiral molecules, and hence is characteristic for the chirality phenomenon of a given molecular class with n ligand sites. As an immediate consequence it yields the minimum number of ligands $N = (n - o)$ which, according to their simultaneous contributions, are necessary for the description of a chiral property.

Therefore, in case of tetrahedral T_d molecules, such as methane derivatives or adamantanes ($n = 4$, $o = 1$), at least triple terms have to be taken into account ($N = 4 - 1$) for the description χ (equation 7) of the optical rotation, as has also been shown by a different approach by Kauzmann[43].

$$\chi(R^1, R^2, R^3, R^4) = \sum_{i \neq j \neq k} \omega(R^i, R^j, R^k) \tag{7}$$

On the other hand, in case of four-site D_{2d} molecules (allenes or spirobiindanes) one has $o = 2$ and consequently a chirality function must at least involve pair terms $\omega(R^i, R^j) = \omega(R^j, R^i)$: $N = n - o = 4 - 2$ (equation 8).

$$\chi(R^1, R^2, R^3, R^4) = \sum_{i \neq j} \omega(R^i, R^j) \tag{8}$$

If the pair or triple terms in equations (7) and (8) are factorized the chirality functions involve substituent constants. Assuming that $\omega(R^i, R^j) = \lambda(R^i) \cdot \lambda(R^j)$, the approximation function (9b) for the calculation of optical rotations of D_{2d} systems is obtained from equation (9a).

$$\chi(R^1, R^2, R^3, R^4) = \omega(R^1, R^3) - \omega(R^1, R^4) - \omega(R^2, R^3) + \omega(R^2, R^4) \tag{9a}$$

$$\chi(R^1, R^2, R^3, R^4) = [\lambda(R^1) - \lambda(R^2)][\lambda(R^3) - \lambda(R^4)] \tag{9b}$$

For details of the arguments summarized in this section, the original literature should be consulted[69,71], but for the purposes of the following discussion, this restricted representation suffices.

1. *Methane derivatives*

A semiempirical theory of the molar rotation of molecules with an asymmetric carbon atom (methane derivatives) has been presented by Runge[74]. This treatment covers 'ideal' T_d molecules, but also more complex compounds taking conformational chirality effects[15] into consideration. The general treatment may be viewed as a 'polarizability theory of optical rotation'. In the present section some selected results for ideal T_d molecules with triple-bonded functional groups will be given.

For T_d molecule the molar rotations φ (in ethanol as the standard solvent) may be calculated according to equation (10)[74]. In equation (10) the $\tilde{\alpha}(R^i)$ are bond

$$\varphi(R^1, R^2, R^3, R^4) = \rho(R^1, R^2, R^3, R\pi^4) \cdot \chi'(R^1, R^2, R^3, R^4) \tag{10a}$$

$$\rho(R^1, R^2, R^3, R^4) = \tilde{\alpha}(R^1) \cdot \tilde{\alpha}(R^2) \cdot \tilde{\alpha}(R^3) \cdot \tilde{\alpha}(R^4) \tag{10b}$$

$$\chi'(R^1, R^2, R^3, R^4) = [\mu(R^1) - \mu(R^2)][\mu(R^1) - \mu(R^3)][\mu(R^1) - \mu(R^4)] \times [\mu(R^2) - \mu(R^3)][\mu(R^2) - \mu(R^4)][\mu(R^3) - \mu(R^4)] \tag{10c}$$

polarizabilities of the ligands R attached to the sites i. (For the numbering of the ligand sites see Figure 3). For some groups the $\tilde{\alpha}(R)$ values have been summarized in Table 2. Relevant bond polarizabilities together with the numerical values of the ligand-specific parameters $\mu(R)$ for a wider range of ligands are given in Table 4. The variations of the μ parameters for all the groups with triple bonds are extremely small, amounting to only 2%. With regard to their $\tilde{\alpha}$ and μ values the triple-bonded functional groups may be compared with the halogen atoms Cl and Br.

The interpretation of equation (10) which contains a scalar factor $\rho = \Pi_i \tilde{\alpha}(R^i)$ and a pseudoscalar factor χ' is straightforward: the optical rotation depends simultaneously upon the amount of polarizable matter [reflected by $\tilde{\alpha}(R^i)$] and upon the different ways this matter may be distributed with respect to the given structural (geometrical) situation [which is described by the $\mu(R^i)$]. The parameters $\mu(R^i)$ are related to the distances x_{CR^i} of the centres of polarizability in the C—R^i bond directions from the asymmetric carbon atom C, C being the origin[74].

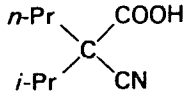
TABLE 4. Bond polarizabilities [$\tilde{\alpha}$(R)] and ligand-specific parameters [μ(R)] for the calculation of optical rotations of methane derivatives[74]

R	$\tilde{\alpha}$(R) (Å^3)	μ(R)
H	0.664	0.6640
C≡CH	3.095	3.5756
C≡CBr	6.559	3.5494
C≡CC≡CBu-*t*	5.933	3.5537
C≡N	2.420	3.6004
$^+$N≡C$^-$	3.167	3.5530
Me	2.509	2.1439
Et	3.125	3.4472
n-Pr	3.125	3.4881
i-Pr	3.745	2.2409
t-Bu	4.365	2.2096
$NH_3^+Cl^-$	2.567	2.1727
NMe_2(=NEt_2)	3.399	2.1742
Cl	2.573	3.5574
Br	3.722	3.5537
OH	1.268	2.0653
NH_2	1.888	2.1211

If in equation (10) three ligands are held constant (e.g. R^2 = H, R^3 = Et, R^4 = Me) it can be shown that equation (10) may be reduced to the linear correlation (1) which relates the optical rotations and the bond polarizabilities[74].

The pseudoscalar factor χ' in equation (10) determines the sign of the optical rotation of the molecule, i.e. the sequence of the μ(R) parameters is relevant. Since the μ(R) and $\tilde{\alpha}$(R) are not generally related to each other, common (empirical or semiempirical) methods for the assignment of the absolute configuration of molecules with an asymmetric carbon atom on the basis of the sense of the screw pattern of the polarisation of the ligands[15] have to be introduced with reservation[74].

The function χ' (10c), first introduced by Crum Brown[23] and Guye[35] and termed 'product of asymmetry', has played a fundamental role in numerous methods of predicting optical rotations[74]. A historically interesting point in connection with a treatment of optical rotations of molecules with triple-bonded functional groups refers to the fact that Guye[35,36] related the parameters μ(R) to the masses of the ligands, whereas Crum Brown thought it to be a function of the composition and the constitution. The proof which is strictest from our current understanding of molecular and electronic structures, that it is not the mass of the ligands which determines the optical rotation was given by Fischer[30]. He showed that *n*-propyl-*i*-propylcyanoacetic acid



(50)

$[\phi]_D$ +19.29°(toluene)

(50) exhibits a considerable optical rotation which should be zero, if Guyes assumptions were correct. The absolute configuration of **50** has not yet been determined.

In Table 5 a comparison between experimental and calculated (equation 10) molar rotations of methane derivatives containing triple-bonded groups is given. In general,

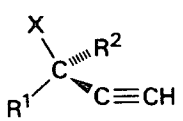
TABLE 5. Calculated (φ, equation 10) and experimental ($[\phi]_D$) molar rotations of methane derivatives, $R^1R^2CR^3R^4$, with triple-bonded functional groups[74]

Compound	R^1	R^2	R^3	R^4	φ(EtOH) (deg.)	$[\phi]_D$ (deg.)
1	C≡CH	H	Et	Me	+43.32	+38.17(neat)
51	C≡CH	H	*i*-Pr	Me	+22.76	+29.20(neat)
52	C≡CH	H	*t*-Bu	Me	+18.02	+13.87(neat)
2	C≡CBr	H	Et	Me	+73.68	+73.90(EtOH), +78.14(neat)
53	C≡CBr	H	*i*-Pr	Me	+47.67	+52.88(EtOH), +55.90(neat)
54	C≡CBr	H	*t*-Bu	Me	+37.77	+34.53(EtOH), +36.50(neat)
5	C≡N	H	Et	Me	+44.31	+28.20(MeOH)
55	C≡N	H	*n*-Pr	Me	+34.00	+30.30(neat)
6	N≡C	H	Et	Me	+38.12	+37.97(EtOH), +40.32($CHCl_3$)
56	Cl	H	C≡N	Me	−11.55	−28.03(neat)
27	Br	H	C≡N	Me	−18.07	−20.61(EtOH)
44[a]	Br	H	C≡CHex-*n*	Me	−10.56	−23.21(MeOH)
57	NEt_2	H	C≡CH	Me	−6.93	−11.14(MeOH)
37	NH_3Cl	H	C≡CH	Me	−4.98	−9.13(EtOH)
58	NH_3Cl	H	C≡CH	Et	+46.27	+17.10(EtOH)
59	NH_3Cl	H	C≡CH	*n*-Pr	+33.02	+25.39(EtOH)
60	NH_3Cl	Me	C≡CH	Et	+0.77	+9.22(EtOH)
28[b]	NH_3X	H	C≡N	Me	−4.06	−18.4(H_2O)
4	C≡CC≡CBu-*t*	H	Et	Me	+71.94	+71.85(heptane)
30	C≡CC≡CBu-*t*	H	*t*-Bu	Me	+35.50	+61.51(heptane)

[a] μ(C≡CHex-*n*) = μ(C≡CH).
[b] X = tartrate.

the agreements are rather satisfying, in particular if the extreme sensitivity of the calculated values towards small changes of the μ parameters is taken into account[74]. Rotations of the phenyl derivatives **40–43**, **45** and **46** cannot be treated by the above chirality function approach, since in the phenyl series the optical rotations reflect not only 'atomic asymmetry', but also conformational chirality effects which result from interactions of the phenyl group with the other groups of the molecule[14,74].

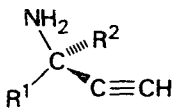
Equation (10) fails to give correct results in case of prop-2-ynyl-1-ols and primary and secondary prop-2-ynylamines:



X = OH,NH_2

R^1,R^2 = alkyl

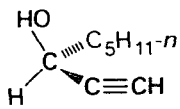
The reason for this failure is assumed[74] to be due to the hydrogen-bonding abilities of the acetylenic functionalities[24,40]. 1-Alkynes behave as proton donors towards Lewis bases and as bases with Brønsted acids. These effects manifest themselves in the extreme solvent dependence of the optical rotations of acetylenic amines and alcohols. For primary acetylenic amines, e.g. **35**, **61**, **62**, even changes in the sign of rotation are observed when measurements on neat liquids or in ethanolic solutions are consi-



	R^1	R^2	$[\phi]_D$(neat) (deg.)	$[\phi]_D$(EtOH) (deg.)
35	H	Me	−36.77	−6.2, −15.20[a]
61	H	Et	−17.38	+11.97
62	H	*n*-Pr	−13.12	+18.65

[a]In H_2O (Ref. 54).

dered[52,65,66,74]. For the propargylic alcohols a typical example of solvent effects which probably involve hydrogen-bonding influences is provided by the rotations of **63** (where the given rotations correspond to a sample of 72.1% optical purity)[16,56].



(63)

$[\phi]_D$ −18.65°(Et_2O)

$[\phi]_D$ −5.04°($CHCl_3$)

Hydrogen-bonding effects may also be responsible for the concentration dependence of the optical rotations of propargylic alcohols. In Figure 4 the specific rotation of (*R*)-(+)-2,2,6,6-tetramethyl-3-heptyn-5-ol (**64**) is displayed[53]. Hydrogen-bonding effects with propargylic alcohols and amines may lead to definite chiral molecular arrangements (chiral clusters) giving additive contributions to the optical rotations which result from the atomic asymmetry of the individual molecules. In the chiral clusters the nature of the alkyl groups seems to play a minor role[74]. Tentatively, one

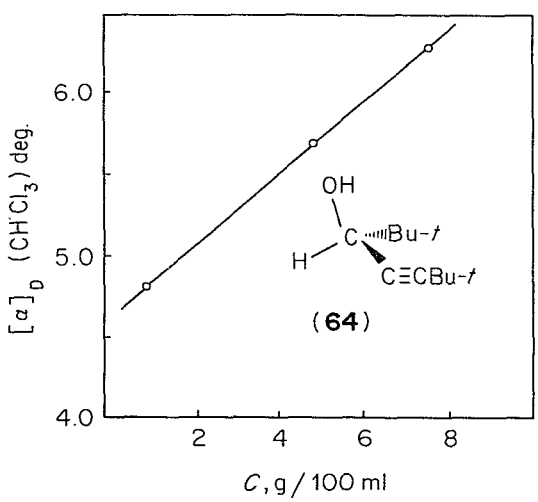
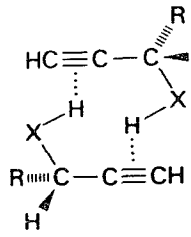


FIGURE 4. Concentration dependence of the specific rotation of (*R*) − (+)-2,2,6,6-tetramethyl-3-heptyn-5-ol (**64**).

may consider dimeric forms, e.g.:



X = O,NH

The above assumptions are suggested by the observation that the molar rotations of alkylated prop-2-yn-1-ols and prop-2-ynylamines may be estimated from equations (11) and (12), respectively. These correspond to calculating the rotations according to equation (10) (the term describing the contribution from the centrochirality of the systems) and subtracting a constant.

$$\varphi' = \rho \cdot \chi' - 45 \quad \text{(for RCH(OH)C}\equiv\text{CH)} \tag{11}$$

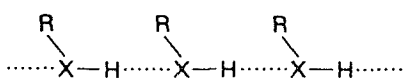
$$\varphi' = \rho \cdot \chi' - 15 \quad \text{(for RCH(NH}_2\text{)C}\equiv\text{CH)} \tag{12}$$

In Table 6 a comparison between experimental and calculated rotations of propargylic alcohols and amines is given. Considering the difficulties in calculating optical rotations in general and, in particular, rotations of amines and alcohols which are extremely sensitive to solvent effects, the calculated values φ' in Table 6 reproduce the experimental values sufficiently.

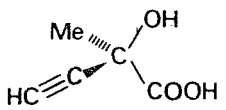
TABLE 6. Calculated (φ', equations 11 and 12) and experimental ($[\phi]_D$) molar rotations of propargylic alcohols and amines, $R^1R^2CR^3R^4$ [74]

Compound	R^1	R^2	R^3	R^4	φ' (deg.)	$[\phi]_D$ (deg.)
65	OH	H	C≡CH	Me	−38.29	−31.40(neat), −36.31(dioxane)
66	OH	H	C≡CH	Et	−20.22	−35.05(Et_2O)
67	OH	H	C≡CH	*n*-Pr	−27.36	−32.23(neat), −31.62(Et_2O)
68	OH	H	C≡CH	*n*-Bu	−29.77	−25.64(Et_2O)
69	OH	H	C≡CH	*i*-Pr	−22.77	−12.35(neat)
70	OH	H	C≡CH	*t*-Bu	−23.65	−19.25(neat)
35	NH_2	H	C≡CH	Me	−11.91	−6.2(EtOH), −15.20(H_2O)
61	NH_2	H	C≡CH	Et	+22.81	+11.97(EtOH)
62	NH_2	H	C≡CH	*n*-Pr	+11.95	+18.65(EtOH)

Linear clustering of the chiral alcohols (or amines) through hydrogen bonding via the heteroatoms:

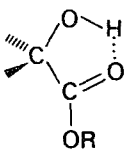


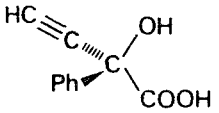
seems to have no significant influence on optical rotation, as the rotations of saturated chiral alcohols measured in the neat liquids differ little from the values observed for ethanolic solutions[74]. The situation for rationalizing optical rotations is more complicated if one considers α-hydroxy acids containing acetylenic groups, such as (*R*)-(−)-



(71)

$[\phi]_D$ −48.72° (neat)



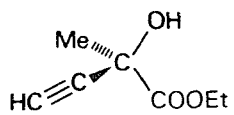


(72)

$[\phi]_D$ −86.33° (Me_2CO)

71[27] and (*R*)-(−)-**72**[28], where inter- and intra-molecular hydrogen bonding may be expected[27]. Furthermore, in the case of **72**, intermolecular hydrogen bonding is not only possible through the acetylenic functionality, but also via the phenyl group.

From **71**, $[\alpha]_D$ − 41° (neat), $[\phi]_D$ − 46.78° (neat), the corresponding ethyl ester **71a** has been obtained with $[\alpha]_D$ − 31.5° (neat)[27]. The optical rotation of **71a** exhibits a

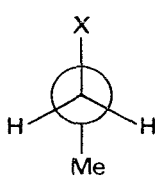


(71a)

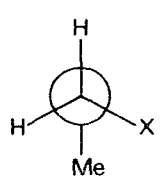
Solvent	$[\alpha]_D^{20}$ (deg.)
CCl_4	−45.4
C_6H_6	−42.8
Neat	−31.5
MeOH	−25.6
MeCOOEt	−21.2
Me_2CO	−17.0

marked solvent dependency[27]. The solvent dependency shows a trend which is expected from the observation that ring-closure brings about a marked increase in the magnitude of the optical rotation[43]. The rotation is greatest in nonpolar solvents where a species with an intramolecular hydrogen bond is largely preferred. The rotation is smallest in polar solvents with hydrogen-bond accepting properties (acetone, ethyl acetate) where intra- and inter-molecular hydrogen bonding with the solvents compete.

Other molecules with triple-bonded functional groups where the chirality function approach is not applicable include the butynyl methyl ether **38** and α-methoxypropionitrile (**39**) (Figure 2) which are both isoelectronic with *s*-butyl cyanide (**5**). Probably conformational effects of the MeO and C≡H groups come into play here[74]. Both propargyl methyl ether ($MeOCH_2C{\equiv}CH$) and methoxyacetonitrile ($MeOCH_2C{\equiv}N$) have been shown to exhibit conformational equilibria between *gauche* and *trans* forms in the gas phase, the former being the more stable form. In both molecules the *gauche* form is exclusively present in the crystalline phase[20]. The greater stability of the *gauche* forms has been attributed to dipolar interactions between the Me



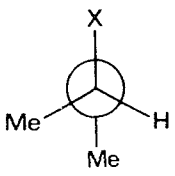
trans



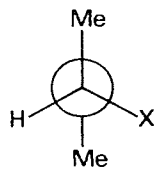
gauche

$MeOCH_2X$

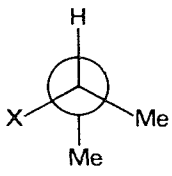
X = C≡CH, C≡N



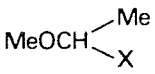
trans



gauche B



gauche A



X = C≡CH, C≡N

and X (X = C≡CH, C≡N) groups[20]. For the chiral systems **38** and **39** one *trans* and two *gauche* forms may be conceived. The rotamer *gauche A* is unfavourable owing to steric crowding. The *trans* form should be considerably less abundant than *gauche B* owing to less favourable Me,X interactions. Therefore, the optical rotations of **38** and **39** must come essentially from only one conformer (*gauche B*).

2. *Allenes and 2,2'-spirobiindanes*

The structures and the analytical forms of the approximation functions for the calculation of molar rotations of arbitrary molecules with a D_{2d} molecular skeleton have been discussed with special emphasis on allenes by Runge[71].

For allenes with the enumeration of the ligand sites given in Figure 3, it has been shown[70,71,75] that the molar rotations χ may be adequately described according to a 'shortened expression' (equation 13), $\lambda(R^i)$ being a ligand-specific parameter for the ligand R at site *i*.

$$\chi(R^1, R^2, R^3, R^4) = [\lambda(R^1) - \lambda(R^2)][\lambda(R^3) - \lambda(R^4)] \qquad (13)$$

With the parameter values given in Table 7 the molar rotations of allenes with triple-bonded functional groups may be calculated. From these values one can see that in the case of the unsaturated (axially chiral) allenes the parameters for the acetylenic and the diacetylenic groups [λ(C≡CH) vs. λ(C≡CC≡CH) or λ(C≡CC≡CMe), respectively] which determine the sign of the rotations differ considerably, whereas for the saturated methane derivatives the corresponding parameters [μ(C≡CH) vs. μ(C≡CC≡CBu-*t*)] have almost identical values. As for methane derivatives the acetylenic and the cyano group exhibit similar overall substituent effects on the optical rotations of allenes, i.e. correspondingly substituted yne-allenes and cyanoallenes should have similar optical rotations. In Table 8 a comparison between calculated and experimental rotations of some naturally occurring diyne-allenes is presented. Until

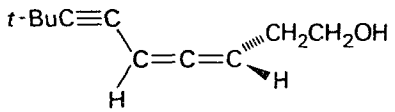
TABLE 7. Parameters for the calculation of the optical rotations of allenes[71]

R	λ(R)	R	λ(R)
H	0	CH_2OH	+9.5
C≡CH	+21.8	$(CH_2)_2OH$	+12.6
C≡N	+19.1	$(CH_2)_3OH$	+9.3
C≡CC≡CH	+37.5	$(CH_2)_4OH$	+7.7
C≡CC≡CMe	+37.5		

TABLE 8. Calculated (χ, equation 13) and experimental ($[\phi]_D$) molar rotations of (*S*)-diyneallenes, $R^1HC{=}C{=}CHR^2$ [71]

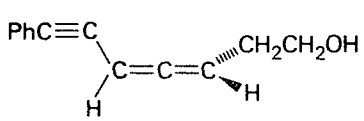
Compound	R^1	R^2	χ (deg.)	$[\phi]_D$ (deg.)
8	C≡CC≡CH	CH_2OH	+366(CH_2Cl_2)	+448(CH_2Cl_2)
9	C≡CC≡CH	$(CH_2)_2OH$	+473(EtOH)	+475(EtOH)
12	C≡CC≡CMe	$(CH_2)_2OH$	+473(EtOH)	+496(EtOH)
10	C≡CC≡CH	$(CH_2)_3OH$	+349(EtOH)	+350(EtOH)
11	C≡CC≡CH	$(CH_2)_4OH$	+289(EtOH)	+288(EtOH)

now no optical rotations of allenes with a cyano group have been reported in the literature[75]. Rotations of two allenylacetylenes **73** and **74** are available[75]. For **73** with $[\phi]_D - 20.53°$ (neat) an optical purity of 7.5% has been calculated[75].



(**73**)

$[\phi]_D$ −20.53° (neat)



(**74**)

$[\phi]_D$ −5.71° (neat)

According to the theory of chirality functions the structures of functions for the calculation of chirality observations only depend upon the number *n* of ligand sites and the symmetry of the molecular skeleton. Therefore, all the arguments given in the discussion of the optical rotations of allenes also apply to 5,5′,6,6′-tetrasubstituted 2,2′-spirobiindanes. Indeed the optical rotations of the latter may be calculated according to equation (14) which corresponds to that used for the allenes (cf. also Figure 3).

$$\chi(R^1, R^2, R^3, R^4) = [\bar{\lambda}(R^1) - \bar{\lambda}(R^2)][\bar{\lambda}(R^3) - \bar{\lambda}(R^4)] \qquad (14)$$

Since in the general theory characteristics of the molecular skeletons are embodied into the corresponding ligand-specific parameters, one cannot expect any relationships between the different parameters (λ vs. $\bar{\lambda}$) which are used for the calculation of the rotations of chemically different types of molecules having skeletons of the same symmetry.

For the (unsaturated) allenes and spirobiindanes, however, it has been shown[73] that there are fair linear correlations between the λ and $\bar{\lambda}$ parameters (equation 15).

$$\lambda(R)(\text{allenes}) = 2.54\bar{\lambda}(\text{spirobiindanes}) - 0.19 \qquad (15a)$$
(for H and σ-inductive alkyl groups)

$$\lambda(R)(\text{allenes}) = 7.13\bar{\lambda}(\text{spirobiindanes}) - 50.16 \qquad (15b)$$
(for mesomeric groups)

In Table 9 some $\bar{\lambda}(R)$ parameters are given. These are used to calculate the molar rotations of the 2,2′-spirobiindanes in Table 10. In unsaturated molecules (allenes, spirobiindanes) the substituent effect of the cyano group on the rotations is comparable with that of other π-acceptor groups, such as COOMe. This is an indication that in unsaturated molecules the substituent effects on the optical rotations may be rational-

TABLE 9. Parameters for the calculation of the optical rotations of 2,2'-spirobiindanes[58]

R	$\bar{\lambda}$(R)	R	$\bar{\lambda}$(R)
H	0	CH=CH$_2$	+11.32
Me	+3.38	CHO	+9.91
Et	+4.39	COMe	+9.52
CN	+9.20	COOMe	+9.34

TABLE 10. Calculated (χ, equation 14) and experimental ([ϕ]$_D$) molar rotations of 2,2'-spirobiindanes in acetone[58] [a]

Compound	R^1	R^3	R^4	χ (deg.)	[ϕ]$_D$ (deg.)
75	CN	COOMe	H	+85.92	+84.6
76	CN	Me	H	+31.57	+31.9
77	CN	Et	CHO	−51.56	−41.9
78	CN	Et	COMe	−47.91	−28.1
79	CN	Et	COOMe	−44.93	−40.8
80	COMe	Et	CN	−47.12	−41.6
81	CN	Et	CN	−46.23	−46.3
82	COOMe	Me	CN	−54.83	−40.9
83	CN	Et	Me	+9.43	+17.0
84	Me	Et	CN	−16.73	−15.5
85	CN	Et	CH=CH$_2$	−63.76	−65.9

[a] R^2 = H.

ized in terms of mesomeric and polar interactions of the ligands with the molecular skeleton.

3. [2,2]*Metacyclophanes*

Another class of aromatic compounds where the optical rotations have been described by the chirality function approach includes the [2.2]metacyclophanes (Figure 5) with a C_{2h} skeletal symmetry.

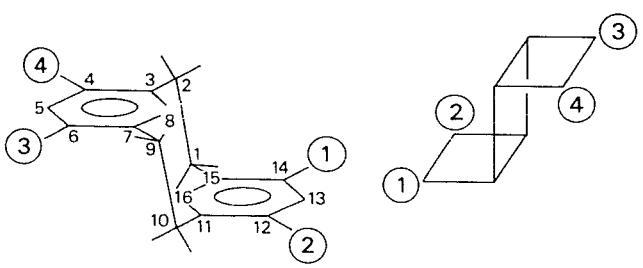
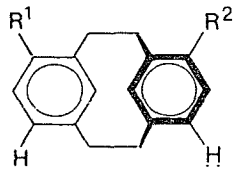


FIGURE 5. The [2.2]metacyclophane molecular skeleton.

For simple disubstituted [2.2]metacyclophanes, e.g. **86–89**, Haase[38] has shown that the optical rotations (in ethanol) may be described approximately by the function (16).

$$\chi'(H, R^1, R^2, H) = -\nu(R^1) - \nu(R^2) - \epsilon.\xi(R^1).\xi(R^2) \qquad (16)$$



(**86** – **89**)

Thus in case of the [2.2]metacyclophanes the description of the optical rotation requires two parameters ν and ξ which are independent of each other. For the ξ values only the absolute magnitudes are known[38]. However, with the following (tentative) values ($\epsilon = -1$) the optical rotations of the 6,12-disubstituted [2.2]metacyclophanes **86–89** may be calculated (Table 11).

R	ν(R)	ξ(R)
H	0	0
Me	+59	0
CN	−88	+8.5
COOMe	−22	+13.0
Br	−181	0

The most interesting aspects of these findings are that there are obviously no correlations between the substituent effects on the optical rotations of [2.2]metacyclophanes and 2,2′-spirobiindanes, though both kinds of molecules are aromatic in character. Furthermore, the substituent effects of the π acceptors CN and COOMe differ considerably on the ν scale, but not so much on the ξ scale.

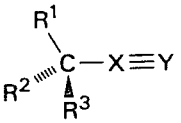
TABLE 11. Calculated (χ', equation 16) and experimental ($[\phi]_D$) molar rotations of [2.2]metacyclophanes **86–89** in ethanol[38]

Compound	R^1	R^2	χ' (deg.)	$[\phi]_D$ (deg.)
86	CN	H	+88	+88
87	CN	CN	+248	+248
88	COOMe	COOMe	+213	+213
89	CN	Br	+269	+274

III. CIRCULAR DICHROISM OF MOLECULES WITH TRIPLE-BONDED FUNCTIONAL GROUPS

Open-chain molecules with triple-bonded functional groups, such as acetylenes or nitriles, contain a rotationally symmetric X≡Y chromophore of local symmetry $C_{\infty v}$, i.e. an 'inherently symmetric chromophore'[21], whose electronic transitions can give rise to optical activity only through perturbation by a chiral molecular environment ('symmetric chromophore in an asymmetric environment').

The simplest (and most frequently observed) case involves the linking of a triple-bonded (or polyyne group to an asymmetric carbon atom:



The extent of induction of optical activity in the electronic bands of the X≡Y chromophore depends upon the juxtaposition of the groups R^i and the forces they exert on the electronic states of the chromophoric system. Within the framework of first-order perturbation theory Schellmann[76] has shown that the extent of induction of optical activity by an electrostatic asymmetric perturbing field (through space) is related to the symmetry of the chromophore. The higher the order of symmetry possessed by a chromophore, the less likely it is to give a static first-order Cotton effect, i.e. the effectiveness of a perturbing electrostatic field diminishes as the number of nodal planes of the chromophore increases. For rotationally symmetric chromophores, such as triple-bonded groups, a perturbing field expressed in terms of a function of the electronic coordinates is therefore expected to be an extremely feeble mechanism for the induction of Cotton effects.

If the potential is Coulombic, the pseudoscalar potential can be directly interpreted in terms of a multipole expansion (involving point charges, dipoles, quadrupoles, etc.). Hence, for a Coulombic interaction, the higher the symmetry of the chromophore, the higher the order of the multipole which is required in the optical activity term and the smaller the anticipated optical activity induced by a given charge distribution.

Therefore, for cylindrically symmetric groups, such as C≡N, C≡CH, C≡CC≡CH, one may expect no first-order contributions from point sources of potential, or only very small contributions. If moderate inductions of optical activity for such molecules are observed, it is likely that second-order perturbations (or quite different mechanisms) have become effective.

The various triple-bonded chromophores exhibit light absorptions in different spectral regions. Isolated carbon–carbon triple bonds produce very weak bands in the range from 240 nm down to 210 nm with a complicated vibrational and rotational structure[22,24,57]. Strong absorptions are observed at wavelengths below 200 nm. The spectrum of HCN is similar to that of acetylene. The bands, however, are shifted considerably to short wavelengths, so that cyanic acid and alkyl cyanides are transparent above 200 nm.

Though accessible to experimental investigations with current instruments (in particular, gas-phase vacuum CD spectrometers) until now no CD spectra of chiral compounds with an isolated triple bond have appeared in the literature. The publication of the magnetic circular dichroism (MCD) spectrum of acetylene by Gedanken[32] demonstrates that the measurements of the optical circular dichroism (CD) of chiral acetylenes should also be possible.

Some CD spectra of molecules are available where the triple-bonded group is conjugated with another mesomeric group, as in diacetylenes, vinylacetylenes, or polyenynes. These will be discussed first, followed by a treatment of the effects of these groups on the circular dichroism of other chromophores. Here one can distinguish two cases. First, the X≡Y group is directly linked to the system whose CD spectrum is being investigated (i.e. X≡Y exerts a mesomeric effect on the chromophore). Second, X≡Y is not directly bonded to the other group and interacts essentially through space with the relevant chromophore (or via secondary effects with the other chromophore, e.g. through changes of the rotamer populations in mono- or poly-cyclic compounds).

A. Circular Dichroism of Chromophores with Triple-bonded Subunits

Conjugation of, for instance, the acetylenic group with a second C≡CH functionality or a vinyl group shifts the electronic bands of HC≡CH into the longer wavelength spectral region. In these cases CD measurements in solution with commercially available instruments monitor that low-energy part of the spectrum which simultaneously determines largely the optical rotations in the transparent region.

A systematization of the electronic (UV and CD) spectroscopy of diacetylenes and vinylacetylenes adopts advantageously a correlative approach, describing the electronic structures in terms of molecular orbitals (MOs). This approach depends on the fact that (1) both types of molecule contain a '4π electron (π_z)' chromophore which corresponds formally to that of 1,3-butadiene, and (2) in both types of molecule the outermost MOs comprise perpendicular π-type orbitals (π_z, π_y). In the parent hydrocarbons the highest occupied (HOMO) and lowest unoccupied (LUMO) MOs of the linear diacetylene molecule (**90**) are doubly degenerate π MOs which split into two components in molecules of lower symmetry, such as vinylacetylene (**91**) of symmetry C_s. The correlation of the symmetry representations of the MOs is given below:

	$D_{\infty h}$	C_s
Unoccupied orbitals	π_u	a′
		a″
Occupied orbitals	π_g	a″
		a′

A schematic orbital diagram for **90** and **91** using only p_y and p_z atomic orbitals (AOs) is displayed in Figure 6. In this particular representation the orbitals correspond simply to the Hückel HOMOs and LUMOs of ethylene and 1,3-butadiene, respectively. The lowest energy electronic excitations which are relevant for the near- and vacuum-ultraviolet absorption are (Figure 6):

$$D_{\infty h}\text{: } \pi_g \rightarrow \pi_u$$

$$C_s\text{: } a'' \rightarrow a' \quad a'' \rightarrow a''$$
$$a' \rightarrow a'' \quad a' \rightarrow a'$$

The (π_g, π_u) MO excitation givs rise to three excited (singlet) states, $^1\Sigma_u^-$, $^1\Delta_u$, $^1\Sigma_u^+$ the ground state being $^1\Sigma_g^+$. Corresponding triplet states are not of interest in the present context.

With reference to the schematic orbital diagrams in Figure 6 'linear' and 'circular' electronic transitions may be distinguished, the former ones being associated with electric transition dipole moments (**μ**), the latter with magnetic transition dipole moments (**m**):

$$\left.\begin{matrix}\pi_z \rightarrow \pi_z^* \\ \pi_y \rightarrow \pi_y^*\end{matrix}\right\} {}^1\Sigma_u^+, {}^1\Sigma_u^- \qquad \left.\begin{matrix}\pi_z \rightarrow \pi_y^* \\ \pi_y \rightarrow \pi_z^*\end{matrix}\right\} {}^1\Delta_u$$

(**μ**) (**m**)

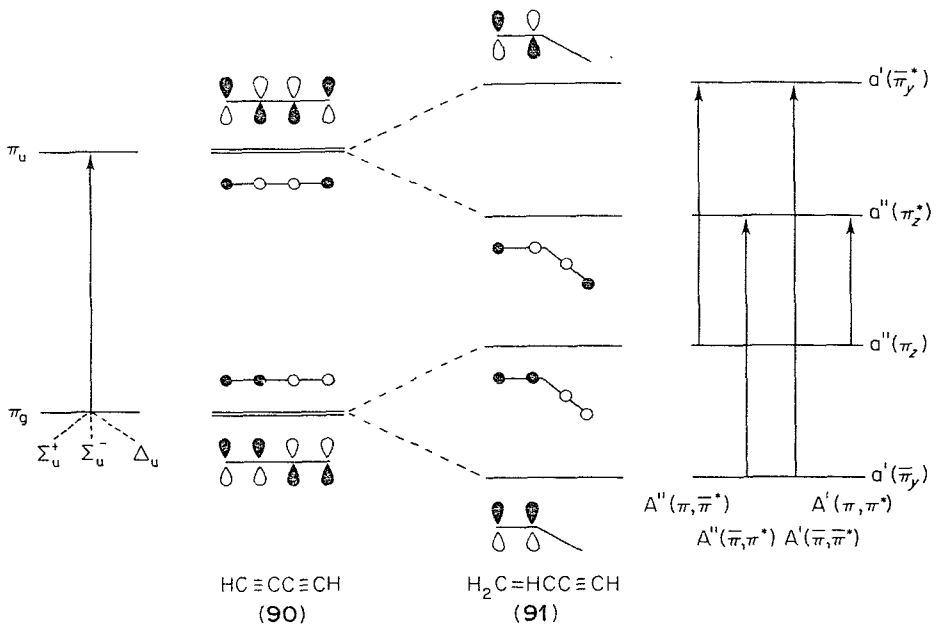
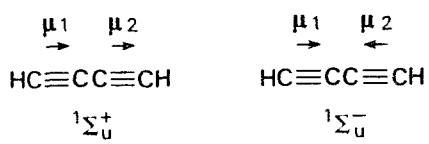


FIGURE 6. Schematic correlative orbital diagrams for diacetylene and vinylacetylene and electronic excitations involving these orbitals.

Using a 'molecules-in-molecules' approach and (more or less) localized excitations in the two acetylenic subunits the in-phase and out-of-phase combination of the pair of linear transitions gives a splitting into a high-energy excited state $^1\Sigma_u^+$ and a low-energy excited state $^1\Sigma_u^-$. As can be seen from the figure below, transitions to the former excited state are strongly electric-dipole allowed ($\boldsymbol{\mu}_1 + \boldsymbol{\mu}_2 \neq 0$) (magnetic dipole forbidden), while to the latter they are electric-dipole forbidden ($\boldsymbol{\mu}_1 + \boldsymbol{\mu}_2 = 0$). Both $^1\Sigma_u$



transitions, however, give rise to electric-dipole allowed, magnetic-dipole forbidden $^1A'$ excited states in vinylacetylene (**91**). The pair of circular ($\pi_z \leftrightarrow \pi_y$) transitions in **90** would remain degenerate, giving an excited state $^1\Delta_u$ of intermediate energy. $^1\Delta_u$ splits into two electric-dipole forbidden, magnetic-dipole allowed $^1A' \rightarrow {}^1A''$ excitations in the C_s molecule vinylacetylene.

The correlations of the excited states of interest in diacetylene (**90**) and vinylacetylene (**91**) are as follows:

Symmetry	Ground state	$\pi \rightarrow \pi^*$	Excited states		
$D_{\infty h}$	$^1\Sigma_g^+$	$^1\Sigma_u^-$	$^1\Delta_u$		$^1\Sigma_u^+$
C_s	$^1A'$	$^1A'$	$^1A''$	$^1A''$	$^1A'$

From the above considerations it is clear that the $^1\Sigma_g^+ \rightarrow {}^1\Sigma_u^-$, $^1\Delta_u$ excitations (in **90**) and the correlated $^1A' \rightarrow {}^1A''$ transitions (in **91**) should be associated with weak electronic absorption bands, where the $^1\Sigma_g^+ \rightarrow {}^1\Sigma_u^+$ and $^1A' \rightarrow {}^1A''$ excitations should be associated with strong electronic bands.

In the $^1\Sigma_u$ states electronic excitation is accompanied by an average displacement of electron density towards the end of the molecule (and the carbon skeleton should remain linear). This would explain predominant progressions of bond-stretching vibrations in the spectrum of both transitions.

From the orbital diagram in Figure 6 one can infer that in vinylacetylene (**91**) the transition densities for the $\pi,\bar{\pi}^*$, $\bar{\pi},\pi^*$ and $\bar{\pi},\bar{\pi}^*$ excitations should be localized essentially in the acetylenic subunit of the molecule, whereas the transition density of the π,π^* transition comprises the whole four-centre orbitals of **91** and hence is similar to the π,π^* transition in 1,3-butadiene.

In Table 12 dichroitic absorptions $\Delta\epsilon$ (and UV absorptions ϵ) of some chiral diacetylenes (**4**, **29–31**), where the diacetylenic chromophore is perturbed either by a *s*-butyl or a 2,2,3-trimethylpropyl group, are given. The 30,000–50,000 cm^{-1} weak absorptions of the diacetylenes have been assigned to the vibrational progressions of the two electric forbidden transitions $^1\Sigma_g \rightarrow {}^1\Sigma_u^-$ and $^1\Sigma_g^+ \rightarrow {}^1\Delta_u$ which overlap each other[47]. Dale[24] has suggested that the $^1\Delta_u$ state is of lowest energy. Both the UV and CD spectra of the diacetylenes are characterized by vibrational fine structures which involve 2100–2200 cm^{-1} progressions, i.e. C≡C stretching modes. In the CD spectra an additional 1300 cm^{-1} progression seems to be present. For all the diacetylenes the UV and CD maxima coincide at about 41,500 cm^{-1}. In the observed spectral range the individual CD bands always have the same signs. For molecules with (*S*) configuration the circular dichroism is positive between 35,000 and 50,000 cm^{-1}. The lack of any observable temperature dependency of the CD bands of the diacetylenes indicates a high conformational homogeneity of the compounds[34]. As is observed with the optical rotations of the diacetylenes (Table 3) the $\Delta\epsilon$ values for the compounds having two identical asymmetric carbon atoms (**29**, **31**) are approximately twice as great as those with only one asymmetric carbon atom (**4**, **30**). As expected, the magnitudes of the $\Delta\epsilon$ values of the diacetylenes are rather small (5×10^{-3} to 2×10^{-1}). The ratio $\Delta\epsilon/\epsilon$ is the order $1\text{–}6 \times 10^{-4}$ which is also a very small value for a magnetic-dipole allowed transition ($^1\Delta_u$), typical values being 10^{-1}–10^{-2}.

In Table 13 the CD data of the *trans*- and *cis*-vinylacetylenes **22–25** are given. The CD spectra of the enynediols **22** and **24** are displayed in Figure 7. The CD spectra of the *trans*- and *cis*-vinylacetylenes differ significantly with respect to the sharpness of the CD bands, the magnitudes and even the signs. The CD spectra of the *cis* forms are more intense and more structured. In all cases the CD and UV spectra seem to be governed by the 'acetylenic' part of the molecule which is manifested by the 1900 cm^{-1} vibrational spacings of the C≡C stretch.

The intense UV maxima of **22–25** near 42,400 cm^{-1} (236 nm) clearly correspond to the π,π^* transitions [excited-state $^1A'$ (π,π^*) in vinylacetylene (**91**)]. The longest wavelength CD bands in the range 38,000–40,000 cm^{-1} (which probably correspond to very weak, nonobservable UV bands) can be thought of as being vibrational progressions of the π–π^* transitions. Alternatively, they can be assigned to separate electronic transitions. If the longest wavelength CD bands in **22–25** correspond (at least) to one additional electronic transition, they should correlate with the (electric forbidden) $^1\Delta_u$ state in diacetylenes, i.e. the longest wavelength weak bands should be associated with $^1A''$ excited states [$^1A'(\bar{\pi},\bar{\pi}^*)$ is allowed and should give a medium strong UV band]. The sign-reversal of the circular dichroism in **22**, **24** and **25** in going from 38,900 cm^{-1} to greater wave numbers and the nature of the vibrational progressions clearly indicate that at least two different electronic excitations (which cannot be

TABLE 12. UV and CD data of some (*S*)-diacetylenes (**4**, **29–31**) in *n*-heptane[34]

$R^1C{\equiv}CC{\equiv}CR^2$

(**4**) R^1 = CHMeEt, R^2 = *t*-Bu
(**29**) R^1 = CHMeEt, R^2 = CHMeEt
(**30**) R^1 = CHMeBu-*t*, R^2 = *t*-Bu
(**31**) R^1 = CHMeBu-*t*, R^2 = CHMeBu-*t*

Compound	$\tilde{\nu}$ (cm^{-1})	ϵ (1 mol^{-1} cm^{-1})	$\tilde{\nu}$ (cm^{-1})	$\Delta\epsilon$ (1 mol^{-1} cm^{-1})
29	35,335	20	36,630	+0.005
	37,735	39		
	39,293	241	39,370	+0.07
	41,494	387	41,494	+0.10
	43,860	362	43,573	+0.09
	46,404	267	45,767	+0.05
			47,393	+0.04
31	35,714	65	35,714	+0.003
	37,950	107	36,765	+0.007
	39,216	287	39,293	+0.14
	41,408	426	41,494	+0.20
	43,764	380	43,573	+0.16
	46,729	431	46,083	+0.11
			47,170	+0.08
4	35,398	22		
	37,736	48	37,037	+0.004
	39,448	254	39,448	+0.05
	41,667	396	41,580	+0.06
	43,860	365	43,573	+0.04
	46,512	330	45,249	+0.03
			46,512	+0.03
30[a]	35,398	20		
	37,736	39	37,175	+0.005
	39,293	241	39,370	+0.06
	41,494	387	41,494	+0.08
	43,860	362	43,573	+0.05
	46,404	267	46,083	+0.05
			47,170	0.0

[a]Ref. 48.

detected by UV spectroscopy) are involved in the light absorptions of the enynes below 50,000 cm^{-1}. Since the electric allowed π,π^* band (with its UV maximum near 42,400 cm^{-1}) involves in-plane C≡C stretching vibrations, no sign-reversal can occur within the corresponding vibronic CD band. If the 1300 cm^{-1} spacings between the two lowest energy bands in **23–25** are assumed to correspond to such bending vibrations as to cause the circular dichroism to reverse its sign, one cannot understand why there is a sign-reversal in **24** and **25** but not in **23**.

Therefore, it is likely that the longest wavelength CD bands in the chiral enynes are associated with a further electronic transition. From analogy with allenes[71] and for energetic reasons the lowest energy $^1A''$ excited state of vinylacetylenes should originate with the π HOMO [excited state $^1A''$ ($\pi,\bar{\pi}^*$)].

Quantum-chemical CNDO/S calculations for vinylacetylene (**91**)[72] give a different pattern for the low-energy excited singlet states. The CNDO/S scheme gives the

TABLE 13. CD data of *trans*- and *cis*-vinylacetylenes (in methanol)[77] [a]

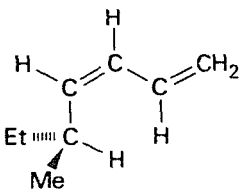
$\tilde{\nu}$ (cm^{-1})	$\Delta\epsilon$ (1 mol^{-1} cm^{-1})	$\tilde{\nu}$ (cm^{-1})	$\Delta\epsilon$(1 mol^{-1} cm^{-1})
trans-(2*S*)-6-Trimethylsilylhex-3-en-5-yne-1,2-diol (**22**)		*cis*-(2*S*)-6-Trimethylsilylhex-3-en-5-yne-1,2-diol (**24**)	
38,911	+0.23	38,911	−3.40
40,984	−0.30	40,161	−4.38
42,735	−0.77	41,322	+2.76
44,643	−0.77	43,290	+6.65
		45,250	+5.67
		46,948	+2.76
51,546	−2.00	51,280	+0.81
trans-(4*S*)-2,2-Dimethyl-4-(-4-trimethylsilylbut-1-en-3-ynyl)-1,3-dioxolan (**23**)		*cis*-(4*S*)-2,2-Dimethyl-4-(-4-trimethylsilylbut-1-en-3-ynyl)-1,3-dioxolan (**25**)	
39,063	+0.38	38,911	−4.00
40,486	+1.01	40,161	−8.70
42,373	+1.01	42,194	−4.97
43,860	+0.57	43,290	+3.04
		45,250	+3.04
		46,950	+1.93
51,282	+0.44	52,080	+3.58

[a] UV data, $\lambda_{max}(\epsilon)$ in ether, are (Ref. 1):
22: 40,650(12,300), 42,373(15,300), 44,250(11,200);
24: 40,984(11,300), 42,735(13,800);
23: 40,650(19,600), 42,550(23,700), 44,250(16,700);
25: 40,486(11,000), 42,373(13,300), 44,050(9300).

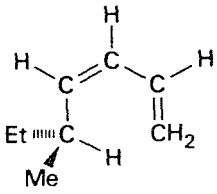
following sequence of excited states: $1^1A''(\bar{\pi},\pi^*) < 1^1A'(\bar{\pi},\bar{\pi}^*) < 2^1A''(\pi,\bar{\pi}^*) < 3^1A''(\bar{\pi},\pi^*) < 2^1A'(\pi,\pi^*)$. The results suggest that the lowest energy excited states of **91** correlate with the lowest energy excited states $^1\Sigma_u^-$ and $^1\Delta_u$ in diacetylene (**90**), which are mixtures of several configurations. For instance, $1^1A'(\bar{\pi},\bar{\pi}^*)$ involves the $(\bar{\pi}_{(1)}, \bar{\pi}_{(-1)})$, $(\pi_{(1)}, \pi_{(-1)})$ and $(\pi_{(1)}, \pi_{(-2)})$ configurations. The calculated energy difference between the three lowest energy excited states amounts to only 0.3 eV. Hence one cannot reliably deduce the sequence of the excited states in vinylacetylene (**91**) from the CNDO/S calculations, which however, reveal that the UV and CD spectra of vinylacetylenes are more complicated than may be anticipated from the shapes of the corresponding electronic spectra.

Consideration of the vinylacetylenes **22–25** starts advantageously with the diotolanenynes **23** and **25**. For comparisons with chiral 1,3-butadienes the π,π^* bands near 42,400 cm^{-1} are of particular interest.

In **23** all the CD bands have the same sign. The π,π^* band of the essentially planar *trans*-enyne **23** (and also the planar *trans*-enyne **22**) have circular dichroisms of the order $\Delta\epsilon_{max} \sim 1$. Such a value is somewhat greater than those observed for the essentially planar open-chain (*cis* and *trans*) 1,3-butadienes, such as *cis*- and *trans*-(*S*)-(+)-5-methyl-1,3-heptadiene (**92**) ($\Delta\epsilon \sim 0.12$–0.30)[26]. In *cis*- and *trans*-**92** one may assume the optical activity to be generated by asymmetric perturbation of the inherently symmetric four-centre butadiene chromophore. The $\Delta\epsilon$ values of the *trans*-vinylacetylene also correspond to the $\Delta\epsilon/2$ values observed for open-chain planar *trans*-dienes with two asymmetric carbon atoms, each linked to a terminal carbon atom of the butadiene functionality ($\Delta\epsilon/2 \sim 1.6$–$2.6$)[33]. Furthermore, the CD values of **22** and **23** are of the same order of magnitude as are observed for planar cyclic *cis*-dienes[17].



(*trans*-**92**)



(*cis*-**92**)

All these findings suggest close similarities between the circular dichroisms of the π,π^* bands in vinylacetylenes and 1,3-butadienes.

Previous research has focused primarily on skew dienes[21], where the chiroptical properties of such nonplanar molecules are characteristic of inherently chiral chromophores which give large CD maxima.

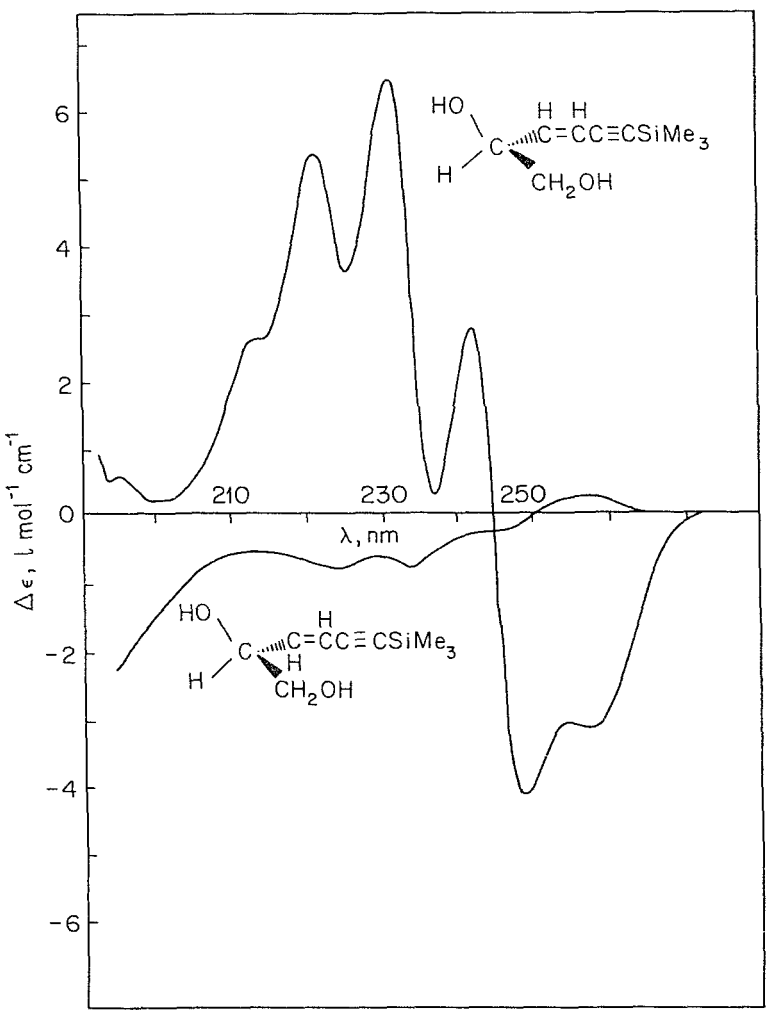


FIGURE 7. CD spectra of *cis*- and *trans*-enyne diols in methanol. Reproduced from Reference 77 by permission of the authors.

Going from the *trans*-enyne **23** to the *cis* form **25** one observes a decrease of the UV intensity of the π,π^* band (Table 13), but no band shift. The decrease in UV intensity is indicative of a distortion of the chromophore from planarity, probably through interactions of the large groups at both ends of the enyne functionality. This manifests itself also in a considerable increase in CD intensity in **25**, $|\Delta\epsilon| \sim 5$, which achieves the characteristic order of magnitude of inherently chiral dienes[21]. This means that in the *cis*-enynes **24** and **25** the elements which induce chirality involve both asymmetric perturbation (nonskew as in the *trans* forms) and inherent chirality (skew element), the last element determining the overall observable circular dichroism.

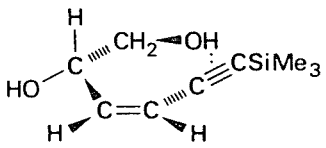
The skew configuration of the enyne grouping induces a helical path for the four 'π electrons' of the C=CC≡C chromophore. Therefore, it is tempting to relate the sign of the circular dichroism of the above enynes to the P or M helicity, respectively, of the chromophore according to the empirical 'helicity rules' for conjugated dienes[21]. However, one has to be aware of some important geometrical and electronical differences between the chromophoric systems in 1,3-butadienes and vinylacetylenes. Firstly, the dienes have a C_{2h} or C_{2v} chromophore made up of two equivalent ethylenic subunits which upon twisting achieves a C_2 rotational symmetry. The enynes having an ethylenic and an acetylenic $2\pi_z$ electron subunit only have C_s symmetries, which upon twisting give asymmetric (C_1) arrangements. Secondly, owing to the availability of σ orbitals ($\bar{\pi}_{(1)}$ and $\bar{\pi}_{(-1)}$) which are close in energies to the π orbitals $\pi_{(1)}$ and $\pi_{(-1)}$ the break-down of the π–σ separability of the orbitals is expected to be more pronounced in the skewed enynes than in skewed dienes.

CNDO/S calculations[72] for vinylacetylene (**91**) which is twisted by an (admittedly very large) angle of $\theta = 20°$ give results pertinent to this discussion. The orbital energies for all the π and the outermost σ orbitals are almost unaffected if planar vinylacetylene (**91**) is twisted by 20°. The energies of the low-energy excited states are also only slightly shifted in **91** with $\theta = 20°$ relative to planar **91**. However, π and $\bar{\pi}$ orbitals are considerably mixed, i.e. there is a breakdown of the π–σ ($\bar{\pi}$) separability. Owing to this breakdown optical activity is generated to a considerable extent by zero-order wave functions. As a further consequence of the breakdown of the π–σ separability the excited states of **91** (with $\theta = 20°$) contain far more electronic configurations in their configuration interaction (CI) expansions.

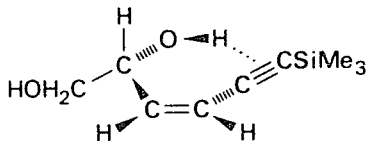
For all these reasons the optical activity of the π,π^* transitions of chiral enynes cannot reasonably be associated with only $2p_z$ electrons arranged on helical paths and it is not possible to establish simple rules which give the directions of electric and magnetic moments for a given transition from which absolute conformations may be deduced. Therefore, it seems that one can neither apply 'helicity rules' for the prediction of the absolute conformations of enynes, nor the qualitative MO procedure proposed by Snatzke[80] for relating signs of CD and conformations to skewed enynes.

For the CD spectra of the *trans*- and *cis*-enyne diols **22** and **24** (Figure 6), one may expect a situation similar to **23** and **25**. However, referring in particular to the CD maxima of the π,π^* transitions near 43,000 cm^{-1} one observes a sign-reversal when comparing the *cis* and *trans* forms, whereas in the case of **23** and **25** the CD maxima of the corresponding transitions are of the same sign, probably due to intramolecular hydrogen-bonding effects. In **22** no hydrogen bonding of a hydroxy group with the acetylenic functionality is possible, while in **24**, intramolecular hydrogen-bonding may play a role, the six-membered ring **24a** being particularly favoured. Such ring-closure would prevent rotation of the group with the asymmetric carbon atom, preventing an equilibrium of several rotamers and thus increasing the optical activity[43]. This would explain the larger CD intensities of the diol **24** relative to those of the dioxolan **25**.

From the CD spectra of the enynes **22**–**25** the optical rotations $[\phi]_D$ in the long wavelength region (Section II.A) may be rationalized qualitatively, since $[\phi]_D$ is essentially determined by the optically active electronic bands with $\lambda_{max} > 190$ nm, and the



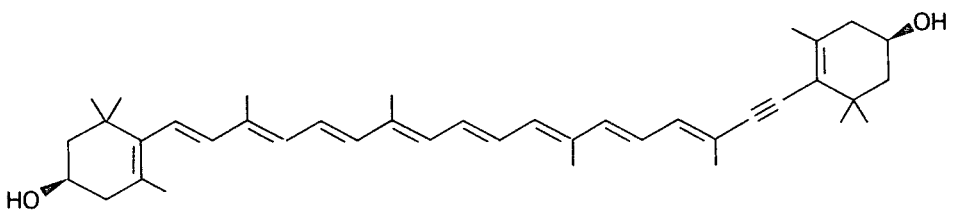
(24a)



(24b)

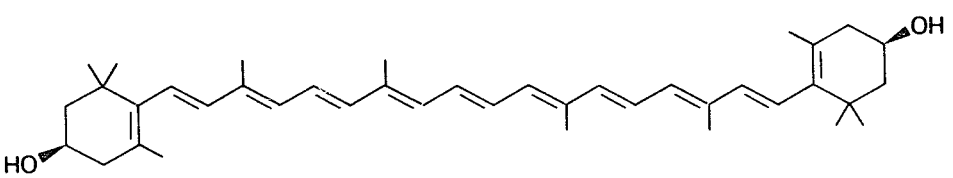
extent to which each CD band contributes to $[\phi]_D$ depends, as a first approximation, on the area under the CD curve. From the CD spectra of **22** and **24** (Figure 7) one can infer that the *trans* diol **22** should have a negative rotation at the wavelength of the sodium D-line. In the *cis* compound **24**, the longest wavelength negative CD band is cancelled by the subsequent stronger positive circular dichroism so that this summation leads to a positive rotation at the sodium D-line. Comparing the areas under the CD bands of **22** and **24** one can expect roughly equal molar rotations with opposite signs.

If the acetylenic group is conjugated with a polyene chain, the CD (and UV) pattern is determined by the polyene part of the chromophore, i.e. the triple bonds may play the roles of formal double bonds. For instance, diatoxanthin (**93**) exhibits almost the same CD pattern as zeaxanthin (**94**)[81]. The CD spectra of the above carotenoids (in the



(93)

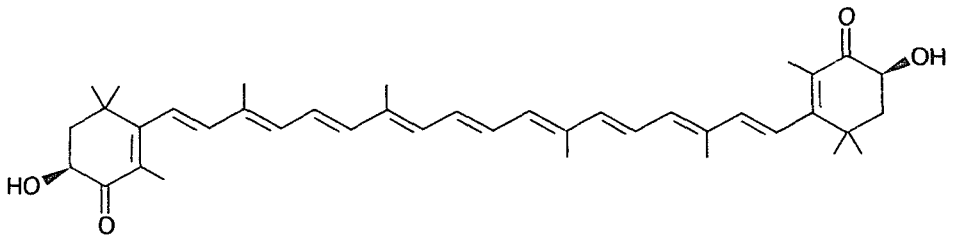
λ(Δε):227(−5.1),250(+4.8),286(−9.2),343(+3.0)



(94)

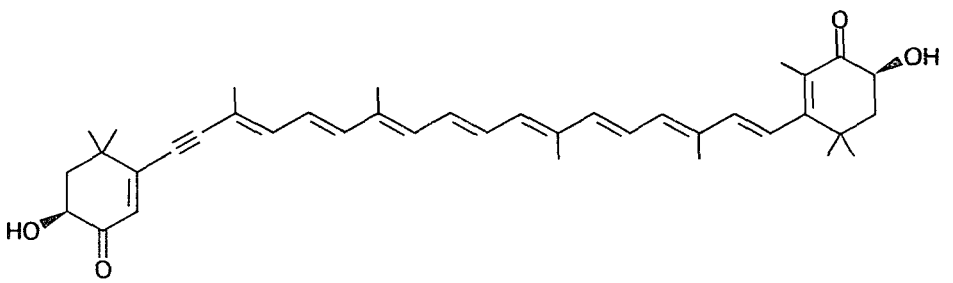
λ(Δε):225(−7.7),251(+8.1),290(−14.6),348(+3.7),490(−2.5)

220–500 nm region) have been classified as essentially 'conservative', showing a sequence of 5–6 relatively sharp Cotton effects of alternating signs, the rotatory strengths adding approximately to zero[81]. In a similar way, the monoacetylenic asterinic acid (**96**) has a CD spectrum which is similar to that of astaxanthin (**95**)[81]. As in **93** and **94**, substitution of an ethylenic group in **95** by an acetylenic group (**96**) leads to a decrease in the CD intensity. On the other hand, much of the structure is lost in the CD spectrum of the diacetylenic asterinic acid (**97**) when compared with that of the pure polyene **95**[81]. The CD spectrum of **97** has been classified as 'intermediate' (close to conservative). If one considers the CD spectrum of alloxanthin (**98**) which is structurally related to zeaxanthin (**94**) the shape of the CD spectrum is considerably changed. **98** exhibits a 'nonconservative' spectrum with $\Delta\epsilon$ having the same sign over the whole spectral region[81].



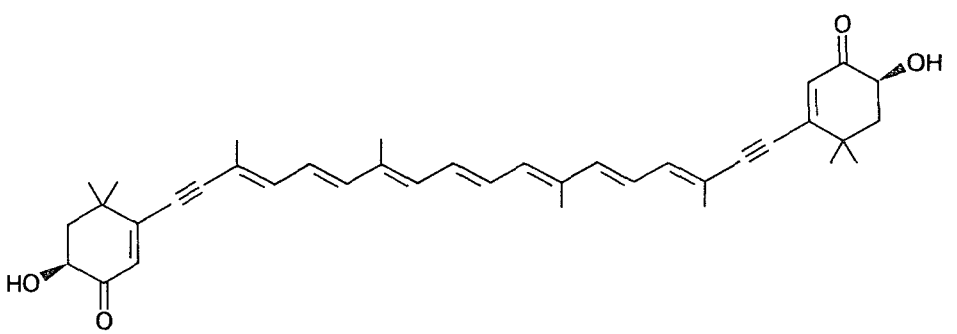
(**95**)

λ(Δε):224(+12.8),249(−14.4),280(+12.5),323(−23.1),384(+6.7),521(−3.2)



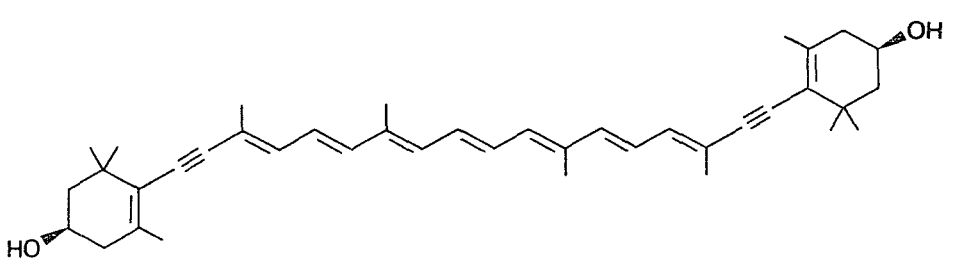
(**96**)

λ(Δε):220(+5),247(−3),276(+4),320(−13),380(+4)



(**97**)

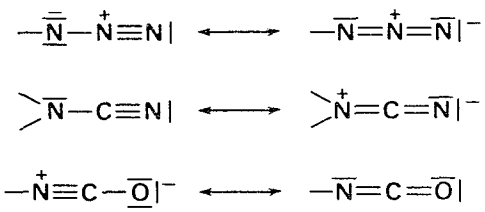
λ(Δε):225(+4.2),260(−2.7), 315(−4.2),360(+1.3),>450(<0)



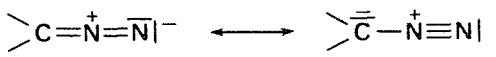
(**98**)

λ(Δε):<230(<0),270(−6),325(−4)

Linking a heteroatom to a triple bond, as in cyanamides, azides, and isocyanates, gives compounds which cannot be compared directly with the original triple-bonded systems, being systems with new bonding situations and characteristics. Typically, these molecules may be described in terms of valence-bond structures which involve cumulated systems.

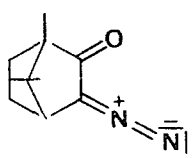


Chiroptical properties of azides, isocyanates, thioisocyanates, cyanamides and thiocyanates have been reviewed by Toniolo[83] and will not be discussed again. However, diazo compounds have not been mentioned by Toniolo[83] and will therefore be considered briefly. The resonance form **B** involving the triple-bonded N≡N functionality is known to contribute essentially to the description of the electronic structure of these compounds.



(A) **(B)**

As early as 1963 Mason reported the circular dichroism of the longest wavelength electronic band of α-diazocamphor (**99**). The CD band of **99** is correlated with the electric-dipole forbidden, magnetic-dipole allowed $\pi,\bar{\pi}^*$ transition in diazomethane (CH_2N_2) [excited state $^1A_2(\pi,\bar{\pi}^*)$ in C_{2v} or $^1A''(\pi,\bar{\pi})$ in C_s, respectively][57].

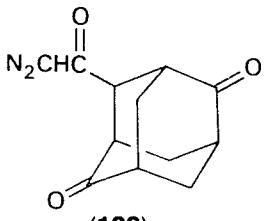


(**99**)

λ_{max}: 407nm

$\epsilon(\Delta\epsilon)$: 19.5(0.255)

Another example of the circular dichroism of the diazo grouping may be found by comparing the CD spectra of (1*R*)-ω-diazo-2-acetyladamantane-4,8-dione (**100**) and (1*R*)-2-methyladamantane-4,8-dione (**101**)[79]. If one subtracts the CD bands of the dione **101** from those of the diazo compound **100**, there remain three CD bands which may be associated with the diazoacetyl grouping CO—CHN_2: $\lambda(\Delta\epsilon)$ = 380(+0.28), 342(+0.19), 250(−3.0). UV bands at 380 nm and 245 nm are also observed for acetyldiazomethane ($MeCOCHN_2$)[63]. The intense UV band of **100** at 250 nm clearly corresponds to the π,π^* transition, whereas the longest wavelength weak UV band should be assigned to the $\pi,\bar{\pi}^*$ band, $\bar{\pi}$ corresponding essentially to the perpendicular N≡N p_y virtual orbital. The other weak UV band at 342 nm is tentatively assigned to the $\bar{\pi},\pi^*$ excitation, where $\bar{\pi}$ is essentially the n_y orbital of the carbonyl group in —CO—CHN_2.

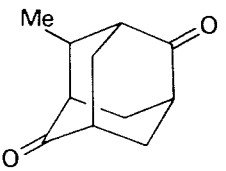


λ(ε):275(7440),250(8940)

(**100**)

λ(Δε):400(0),380(+0.28),342(+0.19),282(0),250(−3.0),227(−2.8)
335(0),328(−0.09),324(0),315(+3.26),304(+2.76),285(+1.02)

λ(Δε):334(0) 313(+0.50),302(+0.74), 293(+0.63)



λ(ε):290(38.8)

(**101**)

B. Substituent Effects of Triple-bonded Groups on the Circular Dichroism of Selected Chromophores

1. [2,2]Cyclophanes

In discussing the substituent effects of triple-bonded groups on the circular dichroism of other chromophores one may distinguish between the cases where X≡Y is directly linked to the relevant chromophore G (hence allowing π conjugative effects between X≡Y and G: G—X≡Y) and when X≡Y and G are not directly bonded.

The circular dichroisms of chromophores with a directly bonded cyano group are, for instance, reported for [2.2]paracyclophanes[31,91,92] and [2.2]metacyclophanes[44].

The observed optical activities of the electronic bands of the cyclophanes correlating with the $^1B_{2u}(^1L_b)$ and $^1B_{1u}(^1L_a)$ bands in benzene have been rationalized on the basis of a 'coupled oscillator' model with almost degenerate electronic states ('exciton model')[91]. This theory involves the triple scalar product of electric transition moments $\boldsymbol{\mu}$ (of electrically allowed, magnetic forbidden electronic transitions) and position vectors as illustrated in Figure 8 for the [2.2]paracyclophanes[91].

The 'exciton model'[21] neglects any electron exchange between the interacting chromophores (e.g. the benzene rings in the [2.2]cyclophanes) and also any skeletal deformations of the interacting groups. Using zero-order wave functions ϕ^A and ϕ^B for two interacting groups A and B, electronic transitions from the ground state 0 into the excited states i (with the transition moments $\boldsymbol{\mu}_{0i}^A$ in A and $\boldsymbol{\mu}_{0i}^B$ in B) give rise to two degenerate excited states which split owing to the Coulombic interaction V of the two transition dipole moments into two exciton states $\Psi^{\pm}$ (equation 17) with energies

$$\Psi^{\pm} = 1/\sqrt{2}(\phi_0^A.\phi_i^B \pm \phi_i^A.\phi_0^B) \tag{17}$$

$E_i \pm V$. This mechanism gives an S-shaped CD curve and the rotational strengths $R^{\pm}$ of the couplet take the forms of equation (18), where $\tilde{\nu}_{0i}$ is the frequency (in cm^{-1}) of the

$$R_{0i}^{\pm} = -i\boldsymbol{\mu}_{0i}^{\pm}\cdot\mathbf{m}_{0i}^{\pm} = \pm 1/2\pi\tilde{\nu}_{0i}\boldsymbol{\mu}_{0i}^{A}\cdot\mathbf{R}^{AB}\times\boldsymbol{\mu}_{0i}^{B} \tag{18}$$

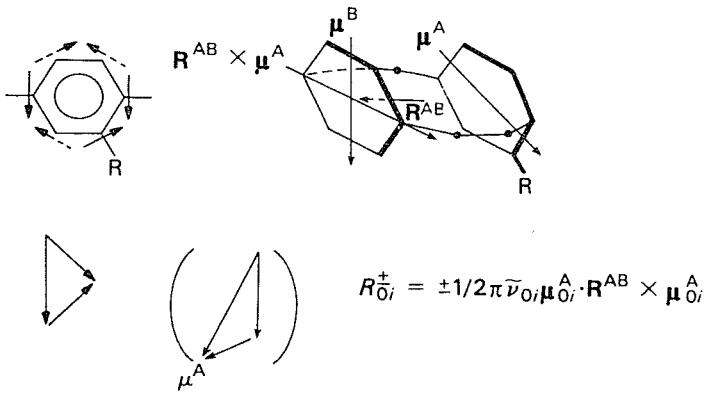
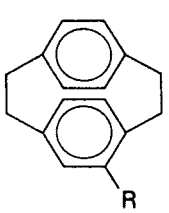


FIGURE 8. Vector constructions relating absolute configurations in ring-substituted paracyclophanes to rotatory strengths. Substituent spectroscopic moments are shown on the left. They contribute to a benzene long-wavelength transition dipole moment $\boldsymbol{\mu}^A$ in a fashion that depends on location of the substituent (full arrow) and the magnitude and sign given to the spectroscopic moment. The net transition vector $\boldsymbol{\mu}^A$ is given for a positive (negative) substituent spectroscopic moment. The vector cross-product on the right is then projected on $\boldsymbol{\mu}^A$ to yield rotatory strengths of a dimer transition couplet. The negative sign refers to the long-wavelength component. Reprinted with permission from O. E. Weigang and M. J. Nugent, *J. Amer. Chem. Soc.*, **91**, 4555 (1969). Copyright [1969] by the American Chemical Society.

zero-order $0 \rightarrow i$ transition in A (or B, respectively) with the electric and magnetic transition moments $\boldsymbol{\mu}_{0i}^{A}$ and $\mathbf{m}_{0i}^{B}$. $\mathbf{R}^{AB}$ is the position vector linking the transition moments $\boldsymbol{\mu}_{0i}^{A}$ and $\boldsymbol{\mu}_{0i}^{B}$. In order to predict absolute configurations of the [2.2]paracyclophanes on the basis of the signs of the CD bands associated with the symmetric or antisymmetric combinations of the benzene $^1B_{2u}(^1L_b)$ (lowest energy) excited states a semiempirical approach has been adopted[91,92]. It relates the transition moments $\boldsymbol{\mu}_{0i}$ to Platt's 'spectroscopic moments' m for the benzene ^1L_b transition[57]. Then the theory suggests that for a given absolute configuration, the sign for the longest wavelength CD band of the transition pair follows (and will be opposite to) that of the signed parameter m, the spectroscopic moment of its substituent.

In Figure 9 the CD spectra of (*R*)-(−)-4-cyano-, (*R*)-(−)-4-carboxy- and (*R*)-(−)-4-ethyl-[2.2]paracyclophane (**102–104**) are displayed[31]. The relevant spectroscopic moments of the considered groups are: m(Et) = +7.0, m(CN) = −18, m(COOH) = −27[57]. Correspondingly, one observes similar shapes for the CD coup-



(102–104)

	R	$[\alpha]_D(CHCl)_3$ (deg.)
102	CN	−175
103	COOH	−164
104	Et	−68

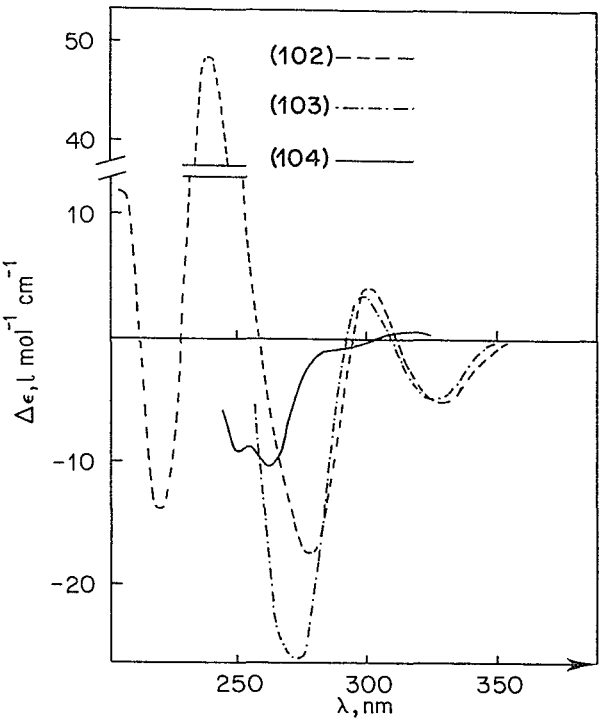


FIGURE 9. CD spectra of optically pure 4-substituted (*R*)-(−)-[2.2]paracyclophanes in ethanol. Reproduced by permission of Pergamon Press from H. Falk, P. Reich-Rohrwig and K. Schlögl, *Tetrahedron*, **26**, 511 (1970).

lets at 310 nm and 290 nm for the compounds **102** and **103** with the CN and COOH groups, but an opposite shape for **104** with an ethyl group. In contrast to the B_{2u} pair the $B_{1u}(^1L_a)$ pair near 250 nm shows the same pattern of CD signs for a given absolute configuration, regardless of the sign of the spectroscopic moment. Falk[31] has attributed this observation to the more pronounced electronic interactions and deformations of the benzene rings associated with the B_{1u} excitation. From the spectroscopic moments of the isocyanide $[m(\overset{+}{N}\equiv\overset{-}{C}) = -6]$ and acetylenic groups $[m(C\equiv CH) = +7]$[61], one may conclude that the acetylenic group will influence the signs of the B_{2u} CD couplets in [2.2]paracyclophanes differently from the other triple-bonded functional groups (—C≡N and—$\overset{+}{N}\equiv\overset{-}{C}$).

The CD spectra of [2.2]metacyclophanes **84–86** and **105** with cyano and carbomethoxy groups, respectively, are displayed in Figure 10[44]. Here it is seen that the high-energy parts of the spectra are rather similar in all molecules with CN or COOMe groups. The disubstituted compounds exhibit 'exciton splittings' of the $^1L_a(^1B_{1u})$ bands near 245 nm, the approximate positions of the maxima of the couplets being indicated by arrows in Figure 10. The low-energy parts of the spectra, however, are different for the cyano and carbomethoxy compounds. In the disubstituted COOMe compound **86** compared with the monosubstituted **105** one observes roughly a doubling of intensity of the negative CD band near 290 nm. On the other hand, the negative CD band near 290 nm in the monosubstituted cyano compound **84** splits into a longer wavelength

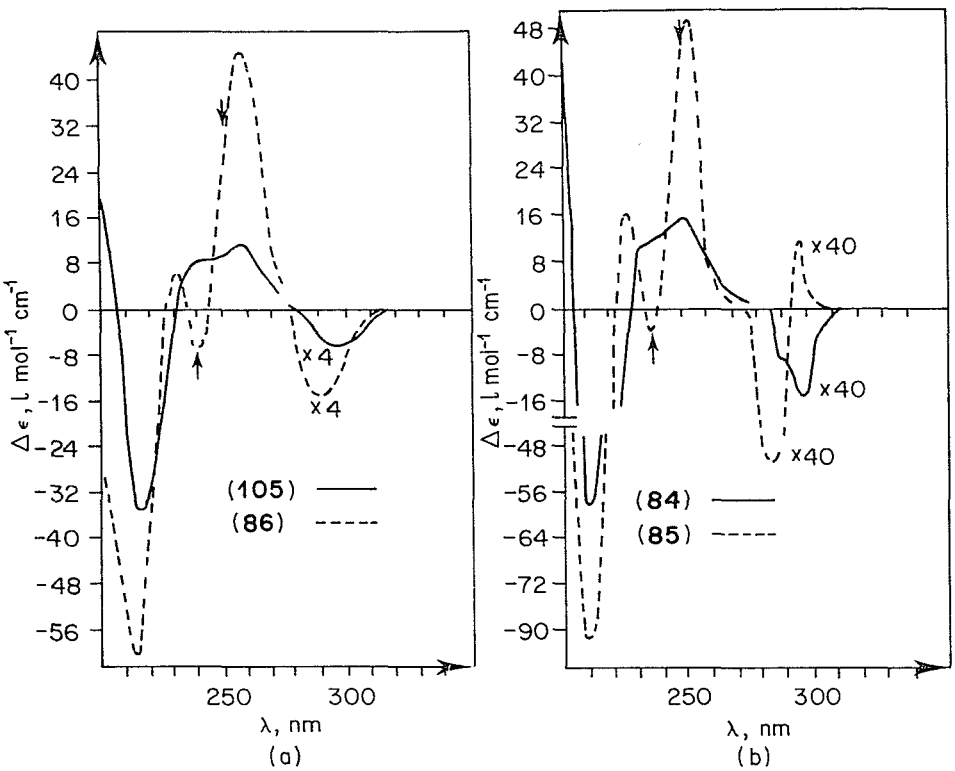
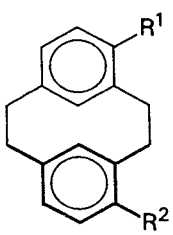


FIGURE 10. CD spectra of (a) carbomethoxy- and (b) cyano-substituted [2.2]metacyclophanes in ethanol. Reproduced by permission of Pergamon Press from H. Keller, C. Krieger, E. Langer, H. Lehner and G. Derflinger from *Tetrahedron*, **34**, 871 (1978).



(84) R^1 = CN, R^2 = H

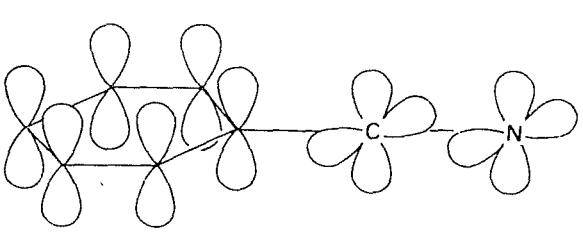
(85) R^1 = CN, R^2 = CN

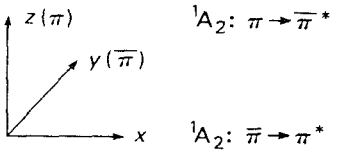
(105) R^1 = COOMe, R^2 = H

(86) R^1 = COOMe, R^2 = COOMe

positive CD band (at 298 nm) and a negative one at 287 nm. The amount of the splitting of these last bands does not depend upon changing the solvent[44]. It cannot be rationalized in terms of exciton theory. Keller[44] has suggested that the splitting may be due to particular vibrational effects. There is, however, another explanation. King[46] has shown that benzonitrile should have two electric forbidden, magnetic allowed $^1A_2$

excited states of energies intermediate between those of the $^1B_2(^1L_b)$ and $^1A_1(^1L_1)$ states. These $^1A_2$ excited states involve transitions mainly localized at the cyano group.



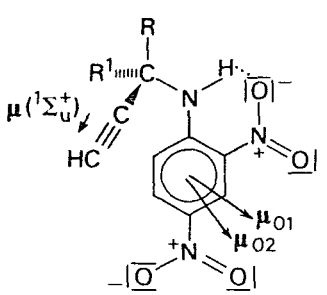


Probably these electronic bands manifest themselves in the low-energy parts of the CD spectra of the cyano-substituted [2.2]metacyclophanes. Owing to overlap with the other bands, however, the $\pi,\bar{\pi}^*$ and $\bar{\pi},\pi^*$ transitions cannot be detected experimentally.

2. N-2,4-Dinitrophenyl and dimedonyl derivatives of 1-alkyl-2-propynylamines

A discussion of the effects of triple-bonded X≡Y groups on the circular dichroism of a second chromophore not directly linked to X≡Y should differentiate chromophoric transitions which are either electric allowed, magnetic forbidden or electric forbidden, magnetic allowed. In general, the magnitude of Cotton effects will depend upon the relative importance of the conformers in equilibrium and on the particular mechanism which is operating to induce the optical activity in the conformer. Therefore, the observed Cotton effects do not necessarily reflect the optical activity of the most abundant conformer, but may originate in one which exhibits the most intense Cotton effect (which in turn is determined by the electronic nature of the interacting groups and their relative orientations).

The induction of optical activity in the (electric allowed) transitions of the 2,4-dinitroaniline chromophore through chiral 1-alkyl-2-propynyl groupings RCHC≡CH, for instance, is essentially via a dipole–dipole coupling through space ('coupled oscillator mechanism') (see **106–109**). In these systems the lowest energy electronic transitions $0 \rightarrow 1$ and $0 \rightarrow 2$ in the aromatic chromophore couple with the electric allowed $^1\Sigma_u^+$ transition of acetylene $[\lambda(^1\Sigma_u^+) \approx 152\ \text{nm}]$[68]. In order that the dipole–dipole coupling should become effective the corresponding transition moments cannot be planar.



(106) – (109)

From ^{1}H-NMR investigations it has been inferred that the preferred conformation of the above aromatic compounds involves an arrangement where the ethynyl group is close enough to the aromatic ring to exert a magnetic anisotropy effect on the H-6 proton of the phenyl ring[68]. This preferred conformation is depicted in **106–109**. The UV spectra of the *N*-dinitrophenyl derivatives exhibit a shoulder near 400 nm which is only little affected by changing the solvent. The corresponding transition moment is μ_{01}. On the other hand, the UV maxima near 328 nm in cyclohexane (transition $0 \rightarrow 2$) are shifted bathochromically to about 343 nm in methanol.

In the molecular arrangement of the aryl and ethynyl groups as depicted in **106–109** the screw of the transition moments $\mu(^1\Sigma_u^+)$ and μ_{01} is left-handed and hence the Cotton effect should be negative for the lowest energy CD bands. This is confirmed by the data given in Table 14 where the UV and CD data of the *N*-2,4-dinitrophenyl derivatives of propynylamines **106–109** are summarized.

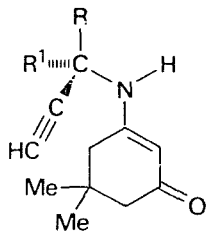
TABLE 14. UV absorption and CD data for *N*-2,4-dinitrophenyl derivatives of chiral (*R*)-propynylamines (**106–109**) in cyclohexane[68]

			UV absorption		Circular dichroism	
Compound	R^1	R	λ (nm)	ϵ (1 mol^{-1} cm^{-1})	λ (nm)	$\Delta\epsilon$ (1 mol^{-1} cm^{-1})
106	H	Me	388	5129	382	−2.48
			325	16,596	316	+3.64
			261	9550	264	−1.21
					224	+6.48
107	H	Et	388	5129	384	−2.18
			327	16,982	317	+3.91
			262	9772	264	−1.03
					224	+6.85
108	H	*n*-Pr	387	5248	386	−2.06
			327	17,783	319	+4.18
			262	10,233	264	−0.94
					223	+7.15
109	Me	Et	396	5129	396	−0.73
			329	17,378	324	+1.58
			264	10,000	264	−0.30
					212	+3.42

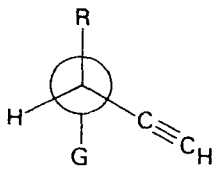
A further example for the induction of optical activity through an acetylenic group involves the dimedonyl derivatives of (*R*)-1-alkyl-2-propynylamines. They exhibit a strong positive Cotton effect at 275 nm which is due to the *trans-s-trans* planar vinylogous amide chromophore G (—COCH=CN<)[67]. UV and CD data for such dimedonyl derivatives (**110–113**) are given in Table 15.

From ^{1}H-NMR chemical shifts it has been concluded that the compounds with R^1 = H (**110–112**) have a preferred conformation **A**, whereas the derivative with R^1 = Me, R = Et (**113**) has a preferred conformation (**B**) with the ethynyl group in the same (or nearly the same) plane as the vinylogous amide chromophore[67].

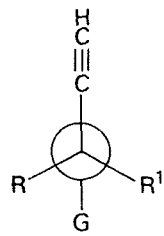
Ringdahl[67] has attributed the considerably smaller Cotton effect of **113** with a quarternary carbon atom when compared with those of **110–112** with tertiary carbon atoms to the greater conformational freedom of **113**, as the rotamer populations may



(110–113)



(A)



(B)

TABLE 15. UV absorption and CD data of dimedonyl derivatives of (*R*)-propynylamines (**110–113**) in dioxane[67]

			UV absorption		Circular dichroism	
Compound	R^1	R	λ (nm)	ε(1 mol^{-1} cm^{-1})	λ (nm)	Δε(1 mol^{-1} cm^{-1})
110	H	Me	275	24,547	274	+9.85
111	H	Et	275	23,988	274	+8.45
112	H	*n*-Pr	276	25,119	274	+7.64
113	Me	Et	276	25,119	276	+0.42

be related to differences in bulk between the R, R^1 and C≡CH groups and the difference between Me and Et is smaller than that between H and an alkyl group.

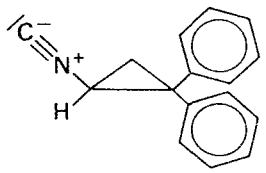
Furthermore, referring to the most abundant conformer it is clear from **A** that in **110–112** a dipole–dipole coupling mechanism, which is known to give strong Cotton effects, may generate the optical activity. On the other hand, in conformation **B** for **113** no such mechanism can operate since the relevant chromophores are (almost) coplanar. Hence, probably a one-electron mechanism, which depends upon the difference of some electronic property of the Me and Et groups, will induce the optical activity. Considering the similar characters of the Me and Et groups one would then expect only a small induction of optical activity in **113**.

The induction of optical activity by an isocyanide group in the electronic bands of another chromophore is exemplified in (*S*)-(+)-2,2-diphenylcyclopropyl isocyanide (**48**)[60]. This induction is somewhat smaller than those observed in other phenyl derivatives of ring compounds with rather fixed conformations and an asymmetric carbon atom in the β-position, such as (1*S*, 2*S*)-(+)-*trans*-2-phenylcyclohexanecarboxylic acid (**114**)[86] or (1*R*, 2*R*)-(−)-*trans*-2-phenylcyclopropanecarboxylic acid (**115**)[85]. The 275–240 nm region of the CD spectrum of **48** is associated with the vibrational progressions of the $^1B_{2u}(^1L_b)$ state and the 234 nm band should correspond to the $^1B_{1u}(^1L_a)$ state or the states correlating with $^1B_{2u}$ and $^1B_{1u}$, respectively.

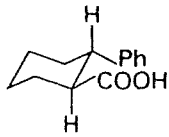
3. *Carbonyl compounds*

The discussion of the substituent effect of triple-bonded groups on the circular dichroism associated with an electric forbidden, magnetic allowed transition will be restricted to the n,π* transition of the carbonyl chromophore and the effects which a cyano group exerts on its circular dichroism.

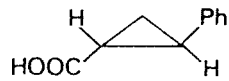
Here one must take into account effects which result from both the steric bulk (affecting rotamer populations or conformations) and the electronic nature of the CN



(48)



(114)



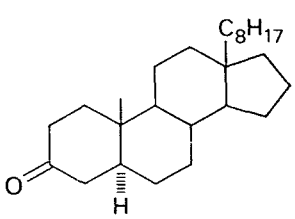
(115)

λ(Δε) : 275(+0.0044),269(+0.0526),265(+0.429)
(MeOH) 261(+0.0569),255(+0.455),250(+0.317),
240(+0.193),
234(+0.342),232(+0.237)

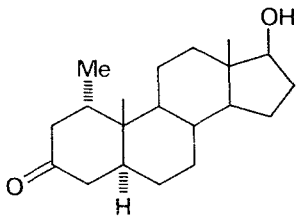
group. On the electronic level carbonyl n,π* Cotton effects are mostly associated with static (Coulombic) forces of the ligands which lead to 'quadrant or octant rules'[21]. As the n,π* CD bands of carbonyl compounds are well removed from other bands the Cotton effects may be discussed in terms of rotatory strengths R^T (at temperature T), R^T (c.g.s.) being defined according to equation (19).

$$R^T \approx 0.23 \times 10^{-38} \int \frac{\Delta\epsilon(\lambda)}{\lambda} \, d\lambda \tag{19}$$

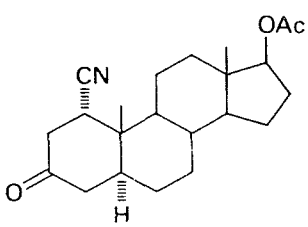
Comparing the circular dichroisms of the n,π* transitions in 5α-cholestan-3-one (**116**) ($R^{25} = +3.31 \times 10^{-40}$ in EPA, $+2.48 \times 10^{-40}$ in decalin and $+2.73 \times 10^{-40}$ c.g.s. in cyclohexane) and 1α-methyl-5-α-dihydrotestosterone (**117**) ($R^{25} = +2.78 \times 10^{-40}$ c.g.s. in EPA) with 1α-cyano-5-α-dihydrotestosterone acetate (**118**) ($R^{25} = +2.29 \times 10^{-40}$, $R^{-192} = +2.26 \times 10^{-40}$ c.g.s. in EPA) and 1β-cyano-5-α-dihydrotestosterone acetate (**119**) ($R^{25} = +3.05 \times 10^{-40}$ c.g.s. in EPA)[93] the following observations are pertinent. In **116**, **118** and **119** the circular dischroism is



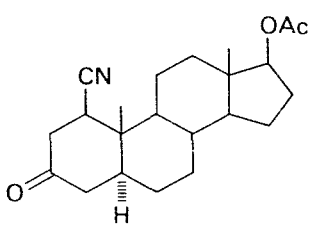
(116)



(117)



(118)



(119)

temperature-independent, which indicates conformational homogeneity (the A-ring of the 5α-keto steroids acting as 'rigid' groups). The substituent effect of the cyano group on the circular dichroism of this type of molecule is hence purely electronic. Relative to the rotational strength of **116** the 1α-cyano group in **118** makes a negative contribution (as expected if **118** exists in a chair conformation)[93]. The 1β-cyano group also shows a somewhat reduced rotational strength compared with that of **116** (as would be expected with ring A in a chair conformation). On the other hand, the temperature dependency of the CD of **117** indicates that in general steric effects have also to be considered when discussing the circular dichroism of such steroids. Since the steric requirements of the cyano group are much smaller than those of a methyl group, the results with **117** indicate that the methyl group exerts a steric effect on the n,π^* CD which is due to a deformation of ring A[93]. Wellman[93] has interpreted the substituent effect of the methyl group in **117** as being largely steric in nature leading to a positively rotating twist conformation of ring A in **117** which minimizes steric interactions between the 1α-methyl group and its surroundings.

IV. ACKNOWLEDGEMENTS

Helpful discussions with Dr. V. Thaller (Oxford, England) and his permission to use his CD data of chiral vinylacetylenes prior to their publication are gratefully acknowledged. Thanks are also due to Prof. L. Lardicci (Pisa, Italy) for bringing the author's attention to his publication on chiral diacetylenes and making additional unpublished material available.

V. REFERENCES

1. M. Ahmed, G. C. Barley, M. T. W. Hearn, Sir E. R. H. Jones, V. Thaller and J. A. Yates, *J. Chem. Soc., Perkin I*, 1981 (1974).
2. J. Applequist, P. Rivers and D. E. Applequist, *J. Amer. Chem. Soc.*, **91**, 5705 (1969).
3. J. Applequist, *J. Chem. Phys.*, **58**, 4251 (1973).
4. J. Applequist, *J. Amer. Chem. Soc.*, **95**, 8255 (1973).
5. J. Applequist, *Accounts Chem. Res.*, **10**, 79 (1977).
6. W. Becker and E. Pfeil, *J. Amer. Chem. Soc.*, **88**, 4299 (1966).
7. K. L. Berry and J. M. Sturtevant, *J. Amer. Chem. Soc.*, **61**, 3583 (1939).
8. K. L. Berry and J. M. Sturtevant, *J. Amer. Chem. Soc.*, **63**, 2679 (1941).
9. F. Bohlmann, K.-M. Kleine and C. Arndt, *Chem. Ber.*, **97**, 3469 (1964).
10. F. Bohlmann and G. Grau, *Chem. Ber.*, **98**, 2608 (1965).
11. F. Bohlmann, U. Niedballa and K.-M. Rode, *Chem. Ber.*, **99**, 3552 (1966).
12. F. Bohlmann, in *Chemistry of Acetylenes* (Ed. H. G. Viehe), Marcel Dekker, New York, 1969, pp. 977–986.
13. F. Bohlmann, T. Burkhardt and C. Zdero, *Naturally Occurring Acetylenes*, Academic Press, London, 1973.
14. J. H. Brewster and J. G. Buta, *J. Amer. Chem. Soc.*, **88**, 2233 (1966).
15. J. H. Brewster, *Top. Stereochem.*, **2**, 1 (1967).
16. R. S. Brinkmeyer and V. M. Kapoor, *J. Amer. Chem. Soc.*, **99**, 8339 (1977).
17. A. W. Burgstahler, D. L. Boger and N. C. Naik, *Tetrahedron*, **32**, 309 (1976).
18. A. M. Caporussi, G. Giacomelli and L. Lardicci, *Gazz. Chim. Ital.*, **106**, 879 (1976).
19. M.-L. Chapmau, W. Chodkiewicz and P. Cadiot, *Tetrahedron Letters*, 1835 (1964).
20. S. W. Charles, F. C. Cullen, G. I. L. Jones and N. L. Owen, *J. Chem. Soc., Faraday II*, 758 (1974).
21. E. Charney, *The Molecular Basis of Optical Activity*, John Wiley and Sons, New York, 1979.
22. K. A. Connors, in *The Chemistry of the Carbon–Carbon Triple Bonds* (Ed. S. Patai), John Wiley and Sons, Chichester, 1978, pp. 137–155.
23. Crum Brown. *Proc. Roy. Soc. Edinburgh*, 181 (1890).
24. J. Dale, in *Chemistry of Acetylenes* (Ed. H. G. Viehe), Marcel Dekker, New York, 1969.

25. J. Dale, *Stereochemie und Konformationsanalyse*, Verlag Chemie, Weinheim, 1978.
26. A. Di Corato, *Gazz. Chim. Ital.*, **98**, 810 (1968).
27. D. Dugat, M. Verny and R. Vessière, *Tetrahedron*, **27**, 1715 (1971).
28. D. Dugat, M. Verny and R. Vessière, *Bull. Soc. Chim. Fr.*, 1903 (1976).
29. O. Exner, in *Correlation Analysis in Chemistry* (Eds. N. B. Chapman and J. Shorter), Plenum Press, New York, 1978, pp. 439–540.
30. E. Fischer and E. Flatau, *Chem. Ber.*, **42**, 2981 (1909).
31. H. Falk, P. Reich-Rohrwig and K. Schlögl, *Tetrahedron*, **26**, 511 (1970).
32. A. Gedanken and O. Schnepp, *Chem. Phys. Letters*, **37**, 373 (1976).
33. G. Giacomelli, L. Lardicci, C. Bertucci and A. M. Caporusso, *Tetrahedron*, **34**, 2015 (1978).
34. G. Giacomelli, C. Bertucci, F. Marcacci and P. Salvadori, *Chim. Ind. (Milano)*, **61**, 471 (1979).
35. P. A. Guye, *Compt. Rend.*, **110**, 714 (1890).
36. P. A. Guye, *Compt. Rend.*, **116**, 1378 (1893).
37. D. Haase and E. Ruch, *Theor. Chim. Acta*, **29**, 189 (1973).
38. D. Haase, *Ber. Bunsenges. Phys. Chem.*, **82**, 436 (1978).
39. W. J. Hehre and J. A. Pople, *J. Amer. Chem. Soc.*, **92**, 2191 (1970).
40. A. C. Hopkinson, in *The Chemistry of the Carbon–Carbon Triple Bond* (Ed. S. Patai), John Wiley and Sons, Chichester, 1978, pp. 75–136.
41. Sir E. R. H. Jones and V. Thaller, in *The Chemistry of the Carbon–Carbon Triple Bond* (Ed. S. Patai), John Wiley and Sons, Chichester, 1978, pp. 621–633.
42. I. L. Karle, *J. Amer. Chem. Soc.*, **95**, 4036 (1973).
43. W. Kauzmann, F. B. Clough and I. Tobias, *Tetrahedron*, **13**, 57 (1961).
44. H. Keller, C. Krieger, E. Langer, H. Lehner and G. Derflinger, *Tetrahedron*, **34**, 871 (1978).
45. J. Kenyon, H. Phillips and V. P. Pittman, *J. Chem. Soc.*, 1072 (1935).
46. G. W. King and A. D. G. Van Putten, *J. Mol. Spectry.*, **42**, 514 (1972).
47. E. Kloster-Jensen, H.-J. Haink and H. Christen, *Helv. Chim. Acta*, **57**, 1731 (1974).
48. L. Lardicci, personal communication, 1980.
49. P. K. Larsen, B. E. Nielsen and J. Lemmich, *Acta Chem. Scand.*, **23**, 2552 (1969).
50. R. J. W. Le Fèvre, *Advan. Phys. Org. Chem.*, **3**, 1 (1965).
51. P. A. Levene, L. A. Mikesa and K. Parsoth, *J. Biol. Chem.*, **88**, 27 (1930).
52. A. Lindquist, B. Ringdahl, U. Svensson and R. Dahlbom, *Acta Chem. Scand.*, **30**, 517 (1976).
53. R. S. Macomber, *J. Amer. Chem. Soc.*, **99**, 3072 (1977).
54. A. Marszak-Fleury, *Ann. Chim. (Paris)*, **13**, 656 (1958).
55. S. F. Mason, *Quart. Rev. (London)*, **17**, 20 (1963).
56. K. Mori and H. Akao, *Tetrahedron*, **36**, 91 (1980).
57. J. N. Murrell, *The Theory of the Electronic Spectra of Organic Molecules*, Methuen, London, 1963.
58. H. Neudeck, B. Richter and K. Schlögl, *Monatsch. Chem.*, **110**, 931 (1979).
59. M. D. Newton and W. N. Lipscomb, *J. Amer. Chem. Soc.*, **89**, 4261 (1967).
60. M. P. Periasamy and H. M. Walborsky, *J. Amer. Chem. Soc.*, **99**, 2631 (1977).
61. J. Petruska, *J. Chem. Phys.*, **34**, 1120 (1961).
62. P. Politzer and S. D. Kasten, *J. Phys. Chem.*, **80**, 283 (1976).
63. M. Regitz, *Diazoalkanes*, Georg Thieme Verlag, Stuttgart, 1977.
64. H. Reihlen, E. Weinbrenner and G. V. Hessling, *Justus Liebigs Ann. Chem.*, **494**, 143 (1932).
65. B. Ringdahl and R. Dahlbom, *Acta Chem. Scand.*, **30**, 812 (1976).
66. B. Ringdahl and R. Dahlbom, *Acta Chem. Scand.*, **30**, 993 (1976).
67. B. Ringdahl and R. Dahlbom, *Chemica Scripta*, **12**, 47 (1978).
68. B. Ringdahl, *Tetrahedron*, **35**, 2413 (1979).
69. E. Ruch and A. Schönhofer, *Theoret. Chim. Acta*, **19**, 225 (1970).
70. W. Runge and G. Kresze, *J. Amer. Chem. Soc.*, **99**, 5597 (1977).
71. W. Runge, in *The Chemistry of Ketenes, Allenes and Related Compounds* (Ed. S. Patai), John Wiley and Sons, Chichester, 1980, pp. 99–154.
72. W. Runge, unpublished results, 1980.
73. W. Runge, *Progr. Phys. Org. Chem.*, **13**, 316 (1981).

74. W. Runge, *J. Amer. Chem. Soc.*, submitted.
75. W. Runge, in *The Chemistry of Allenes* (Ed. S. R. Landor), Academic Press, London, in press, Chap. 6.
76. J. A. Schellmann, *J. Chem. Phys.*, **44**, 55 (1966).
77. P. M. Scopes and V. Thaller, personal communication, 1980.
78. M. Simonetta and A. Gavezzotti, in *The Chemistry of the Carbon–Carbon Triple Bond* (Ed. S. Patai), John Wiley and Sons, Chichester, 1978, pp. 1–56.
79. G. Snatzke, B. Ehrig and H. Klein, *Tetrahedron*, **25**, 5601 (1969).
80. G. Snatzke, in *Optical Activity and Chiral Discrimination* (Ed. S. F. Mason), D. Reidel, Dordrecht, 1979, pp. 43–55.
81. V. Sturzenegger, R. Buchecker and G. Wagnière, *Helv. Chim. Acta*, **63**, 1074 (1980).
82. F. Théron, M. Verny and R. Vessière, in *The Chemistry of the Carbon–Carbon Triple Bond* (Ed. S. Patai), John Wiley and Sons, Chichester, 1978, pp. 381–445.
83. C. Toniolo, in *The Chemistry of Cyanates and their Thio Derivatives* (Ed. S. Patai), John Wiley and Sons, Chichester, 1977, pp. 153–190.
84. A. Treinin in *The Chemistry of the Azido Group* (Ed. S. Patai), John Wiley and Sons, London, 1971, pp. 1–55.
85. L. Verbit and Y. Irwuye, *J. Amer. Chem. Soc.*, **89**, 5717 (1967).
86. L. Verbit and H. C. Price, *J. Amer. Chem. Soc.*, **94**, 5143 (1972).
87. A. Viola, G. F. Dudding and R. J. Proverb, *J. Amer. Chem. Soc.*, **99**, 7390 (1977).
88. A. I. Vogel, *J. Chem. Soc.*, 1833 (1948).
89. H. M. Walborsky and F. M. Hornyak, *J. Amer. Chem. Soc.*, **77**, 6026 (1955).
90. R. Weidmann, A. Schoofs and A. Horeau, *Bull. Soc. Chim. Fr.*, 645 (1976).
91. O. E. Weigang and M. J. Nugent, *J. Amer. Chem. Soc.*, **91**, 4555 (1969).
92. O. E. Weigang and M. J. Nugent, *J. Amer. Chem. Soc.*, **91**, 4556 (1969).
93. K. M. Wellman, W. S. Briggs and C. Djerassi, *J. Amer. Chem. Soc.*, **87**, 73 (1965).
94. P. R. Wells, *Progr. Phys. Org. Chem.*, **6**, 111 (1968).
95. S. Yamada, K. Takashima, T. Sato and S. Terashima, *J. Chem. Soc., Chem. Commun.*, 811 (1969).
96. A. L. McClellan, *Tables of Experimental Diploe Moments*, W. M. Freeman & Co., San Francisco–London, 1963.
97. R. C. Weast (Ed.), *Handbook of Chemistry and Physics*, CRC Press, Cleveland, (Ohio), 1979.

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 2

Thermochemistry of the cyano and isocyano groups

LESLIE BATT
Department of Chemistry, University of Aberdeen, Meston Walk, Old Aberdeen, AB9 2UE, Scotland

I. INTRODUCTION

This review follows the style adopted by Shaw in the thermochemistry chapter of previous volumes in this series[1]. Shaw quoted heats of formation in both calorimetric and S.I. units. We found this too cumbersome previously[2] and opted for calorimetric units. This will be repeated here. Conversion to S.I. units may be made by referring to the relationship that 1 calorie ≡ 4.184 joules. Unlike Shaw we also considered bond dissociation energies because most kineticists, at least, are interested in these values. This has less importance here because for isocyanides the only pyrolysis reaction is isomerization to the more stable nitrile, e.g. equation (1), and for the nitriles the C—N

$$CH_3NC \longrightarrow CH_3CN \qquad (1)$$

bond is so strong (115–130 kcal mol^{-1}) that it never breaks and either the C—C bond breaks or elimination of hydrogen cyanide takes place (equation 2)[3]. In one case the preferred reaction was elimination of hydrogen chloride (equation 3)[4].

For references prior to 1970, heavy reliance was put on the reviews by Benson and coworkers[5], Cox and Pilcher[6] and Stull, Westrum and Sinke[7] all of 1969. From 1970 to the present time, a survey was made in the usual journals with particular emphasis on Russian journals. Because this survey produced so few references and because the

$$CH_3CH(CN)CH_3 \rightarrow CH_3\dot{C}H(CN) + CH_3 \quad (2)$$
$$CH_3CH(CN)CH_3 \rightarrow CH_3CH{=}CH_2 + HCN$$

$$CH_2ClCH_2CN \longrightarrow CH_2{=}CHCN + HCl \quad (3)$$

author was unfamiliar with this field, an on-line computer search was also made from *Chemical Abstracts* over the same time period. Most of the work refers to cyanides rather than isocyanides. Isocyanides have a special significance however, particularly methyl isocyanide, because studies of the pyrolysis of these compounds have led to an advancement in the knowledge of the theory for unimolecular reactions. Apart from the isomerization taking place over both suitable pressure and temperature ranges, the product molecule is so similar in structure to the parent molecule. Most of this work has been carried out by Rabinovitch and coworkers[8]. The results have confirmed the essential correctness of the Rice, Ramsperger, Kassel, Marcus (RRKM) theory as opposed to other theories[9]. Pritchard has also proposed that reaction (1) is very suitable for the testing of thermal explosion theory[10]. Other uses involve unsaturated nitriles for polymer and carbon fibre production and the use of the CN group in organic preparative work and reactions.

Various additivity rules have been used to calculate the thermodynamic properties of compounds[5,6,11–15]; of these three references were inaccessible to us[11,13,14]. We preferred to use the Group Additivity Rules of References 5 and 6. Tabulated values refer to the gas phase. Conversion to the liquid phase may be made by inspection of the original references or by the use of Group Additivity Rules for liquids[16].

II. THERMOCHEMISTRY OF CYANIDES

In two previous reviews, the value recommended for the heat of formation of methyl cyanide was 21.0 kcal mol^{-1} [5,7]. Recently Barnes and Pilcher[17] redetermined its heat

TABLE 1. Thermodynamic data for cyano groups[20]

Group[a]	$\Delta H_f^{0\,b}$	$S_{300}^{0\,c}$	$C_p^{0\,c}$			
			300	500	800	1000
$C(N)_2(C)(CN)$	22.5	40.2	11.1	15.5	19.7	21.3
$C(C)_2(N)(CN)$	25.8	19.8	11.0	14.1	17.3	18.6
$C(C)_3(CN)$	28.2[d]	−2.8				
C_B—(CN)	35.8	20.5	9.8	12.3	14.2	14.9
$C_d(H)(CN)$	40.7[d]					
$C_d(CN)_2$	84.3[d]					
$C_t(CN)$	63.8					

[a] C_B = aromatic C atom; C_d = doubly bonded C atom; C_t = triply bonded C atom.
[b] Units are kcal mol^{-1}.
[c] Units are cal deg^{-1} mol^{-1}. Values are given as a function of temperature in degrees Kelvin.
[d] This work.

TABLE 2. Thermodynamic data for monocyanides

	$\Delta H_f^{0\,a}$	Ref.	$S_{300}^{0\,b}$	Ref.	$C_p^{0\,b}$ 300	500	800	1000	Ref.	D(R—CN)[a]
CH_3CN	17.6 ± 0.2	17	58.3	23	12.6	16.7	21.3	23.6	23	121.8
CH_3CH_2CN	12.3	21	68.5	7	17.3	24.9	50.4	36.1	24	118.2
$CH_3CH_2CH_2CN$	7.5	19	77.9	7	23.3	33.1	43.5	48.2	7	117.5
	8.1	7								
$(CH_3)_2CHCN$	6.0	7	74.9	7	23.1	33.3	43.7	48.4	7	116
	5.4	21								
	5.6	19								
$CH_3(CH_2)_3CN$	2.7	22								116.3
$(CH_3)_3CCN$	−0.8	21	79.6	25						114.9
$CH_3(CH_2)_5CN$	−7.4	11								
$CH_3(CH_2)_6CN$	−12.1 ± 0.4	26								
$CH_3(CH_2)_8CN$	−21.9 ± 0.4	26								
$CH_3(CH_2)_9CN$	−27.1 ± 0.5	26								
$CH_3(CH_2)_{12}CN$	−41.8 ± 0.7	26								
C_6H_5COCN	28.1	27								
$C_6H_5COCH_2CN$	16.8	27								
$C_6H_5COCH_2CH_2CN$	7.2	27								
C_6H_5CN	52.3	19	76.9	28	26.2		52.1		28	130
C_6F_5CN			100.4	29	40.7	52.5	62.1	65.4	29	
p-$CH_3C_6H_4CN$			84.8	30	31.9	47.8	62.8	69.2	30	
CH_2ClCH_2CN			78.1	31	20.0	25.6	35.0	38.3	31	
CH_2BrCH_2CN			79.4	31	21.0	28.1	35.3	38.5	31	

[a]Units are kcal mol^{-1}.
[b]Units are cal deg^{-1} mol^{-1}. Values are given as a function of temperature in degrees Kelvin.

of combustion and found a quite different value of 17.6 ± 0.2 kcal mol^{-1}. This has repercussions for the heat of isomerization of methyl isocyanide to methyl cyanide (equation 1) as noted by Baghal-Vayjooe, Collister and Pritchard[18]. Of two values[7,19] listed for the heat of formation of *n*-propyl cyanide the lower value[19] is taken to be the more reliable as it fits best with that predicted from Group Additivity Rules (Table 1). A mean value of 5.7 kcal mol^{-1} is recommended for ΔH_f^0 (*i*-propyl cyanide) from three determinations[7,19,21]. The comparison made in Hall and Baldt's paper is rather confusing[21]. Neither *n*-butyl cyanide[22] nor *t*-butyl cyanide[21] were considered in previous reviews, but their heats of formation fit very nicely with Group Additivity Rules (Tables 1 and 2). The bond dissociation energies are based upon a value for ΔH_f^0 (CN) of 104 ± 2.5 kcal mol^{-1} [32]. Despite the rather large errors involved, there does appear to be a trend in the R—CN bond dissociation energy as a function of the nature

TABLE 3. Thermodynamic data for polycyanides

					$C_p^{0\,b}$				
	$\Delta H_f^{0\,a}$	Ref.	$S_{300}^{0\,b}$	Ref.	300	500	800	1000	Ref.
$NC(CH_2)_2CN$	50.1 ± 0.16	33	79.1	34	22.2		39.4		34
$NC(CH_2)_3CN$	40.9	7	88.1	35					
$NC(CH_2)_4CN$	35.7	11							
$NCC(CH_3)_2C(CH_3)_2CN$	24.2	11							
$(CH_3)_2C(CN)_2$			83.4	36					
$C(CN)_4$	160.8 ± 2.2	37							
$NCCH_2CN$	63.5 ± 0.5	38	69.2	39	17.4	22.6	27.7	30.0	39

[a]Units are kcal mol^{-1}.
[b]Units are cal deg^{-1} mol^{-1}. Values are given as a function of temperature in degrees Kelvin.

of the alkyl group R. The weakest bond is in the tertiary compound. The bond dissociation energy for methyl cyanide is far higher than for the other primary alkyl compounds. This is in keeping with the usual observations for the first member of a homologous series. However this is less than the value of 206.2 kcal mol^{-1} for cyanogen determined from its head of formation[7] and the above value for ΔH_f^0 (CN). The heats of formation of higher members of the homologous series are also listed in Table 2. These values are also in good agreement with values calculated from group additivity rules. Values for three compounds containing the benzoyl group (PhCO) are listed.

Thermodynamic properties for saturated polycyanides are shown in Table 3. No information is available on the R—CN bond dissociation energies for these compounds but an average C—CN bond dissociation energy for tetracyanomethane may be calculated from reaction (4). This turns out to be 106.5 kcal mol^{-1}, i.e. $\frac{1}{4}\Delta H_4^0$ of

$$C(CN)_4 \longrightarrow C + 4\,CN \qquad (4)$$

(although Barnes, Mortimer and Mayer[37] quote 112 kcal mol^{-1}). This value is certainly much weaker than other values quoted in Table 2. Tables 4 and 5 deal with cyclic and unsaturated compounds respectively.

TABLE 4. Thermodynamic properties of cyclic compounds

	$\Delta H_f^{0\,a}$	Ref.	$S_{300}^{0\,b}$	Ref.	$C_p^{0\,b}$ 300	500	800	1000	Ref.
Cyclopropanecarbonitrile	43.2	21	70.7	40	19.0		37.7		40
Bicyclobutane-1-carbonitrile	72.8	21							
Cyclobutanecarbonitrile	34.2	21							
3-Methylenecyclobutanecarbonnitrile	60.3	21							
Bicyclo[2.1.0]pentane-1-carbonitrile	65.0	21							
Cyclopentanecarbonitrile	10.0	21							
	10.5	41							
Bicyclo[3.1.0]hexane-1-carbonitrile	34.0	21							
Pyridinium dicyanomethylide	125.1 ± 3.0	38							
Cyclohexanecarbonitrile	−1.7	41							
1-Cyclohexene-1-carbonitrile	24.3	41							
2-Cyclohexene-1-carbonitrile	26.2	47							
1-Cyclopentene-1-carbonitrile	37.4	41							
2-Cyclopentene-1-carbonitrile	33.9	41							

[a]Units are kcal mol^{-1}.
[b]Units are cal deg^{-1} mol^{-1}. Values are given as a function of temperature in degrees Kelvin.

III. THERMOCHEMISTRY OF ISOCYANIDES

Thermodynamic data for isocyanides is extremely sparse despite the importance of these compounds in the field of chemical kinetics emphasized earlier. Benson and coworkers[5] only list values for methyl isocyanide. Baghal-Vayjooe, Collister and Pritchard[18] recently measured the heat of isomerization of methyl isocyanide (equation 1) via a controlled calorimetric explosion and found a value for ΔH_1^0 of -23.70 ± 0.14 kcal mol^{-1}.

Using Barnes and Pilcher's value for ΔH_f^0 (CH_3CN)[17] (Table 2) gives a value for ΔH_f^0 (CH_3NC) of 41.32 ± 0.24 kcal mol^{-1}. This compares with the previous value of 35.9 kcal mol^{-1}. Other thermodynamic values listed by Benson and coworkers for methyl isocyanide are $S_{300}^0 = 59.1$ cal deg^{-1} mol^{-1} [51] and $C_p^0 = 12.8$ (300 K), 16.7 (500 K), 21.3 (800 K) and 23.6 (1000 K) cal deg^{-1} mol^{-1} [51]. Baghal-Vayjooe, Collister and Pritchard[18] also determined a value for the heat of isomerization of ethyl isocyanide (equation 5). The value was given by $\Delta H_5^0 = \leqslant 21.5 \pm 1.0$ kcal mol^{-1}.

$$CH_3CH_2NC \longrightarrow CH_3CH_2CN \qquad (5)$$

Using the value in Table 1 for ΔH_f^0 (CH_3CH_2CN) of 12.3 ± 1 kcal mol^{-1}, we arrive at a value for ΔH_f^0 (CH_3CH_2NC) of 33.8 ± 1.4 kcal mol^{-1}. No other thermodynamic data are available at this time for other isocyanides including vinyl isocyanide[52], perfluoromethyl isocyanide[53] and allyl isocyanide[54].

IV. GROUP ADDITIVITY RULES

Thermodynamic properties for various groups are shown in Table 1. The primary use of Group Additivity Rules is for the estimation of thermodynamic properties of

TABLE 5. Thermodynamic properties of unsaturated nitriles

	$\Delta H_t^{0\,a}$	Ref.	$S_{300}^{0\,b}$	Ref.	$C_p^{0\,b}$ 300	500	800	1000	Ref.	D(R—CN)[a]
CH_2=CHCN	43.4	21, 42	65.6	43	15.3	21.0	26.4	28.9	7	127.8
trans-NCCH=CHCN	81.3	38								
cis-CH_3CH=CHCN	32.0	22								
trans-CH_3CH=CHCN	35.8	44	71.4	44	19.7	28.3	37.0	40.3	44	
	33.6	22								
$C_2(CN)_2$	127.5	7	69.4	7	20.6	24.2	27.3	28.6	7	
trans-NCC(Cl)=C(Cl)CN			87.9	45	27.6	33.3			45	
trans-NCC(Br)=C(Br)CN			92.6	45	28.6	33.9			45	
trans-NCC(I)=C(I)CN			96.6	45	29.1	34.2			45	
Br_2C=C(Br)CN			94.2	46	26.5	30.8			46	
I_2C=C(I)CN			100.0	46	27.3	31.3			46	
$(NC)_2$C=CHCN	123.9 ± 1.6	47								
$(NC)_2$(C=C$(CN)_2$	168.5 ± 1.5	47								
$(NC)_2$C=C=O	57.1 ± 0.6	48								
CH_2=CH—CH_2CN	37.7	22								
trans-CH_3CH=C(CH_3)CN	30.0	22								
cis-CH_3CH_2CH=CHCN	27.5	22								
trans-CH_3CH_2CH=CHCN	28.6	22								
CH_3C≡C—C≡N			68.7	49	19.8	25.7	32.0	34.9	48	
NC—C≡C—C≡C—CN			81.0	50	28.0				50	

[a]Units are kcal mol^{-1}.
[b]Units are cal deg^{-1} mol^{-1}. Values are given as a function of temperature in degrees Kelvin.

compounds for which there are no experimental values[1]. Other uses are a check on the validity of experimental values and the determination of 'strain' or 'interaction' energies[20]. Thus the calculated value for the heat of formation of succinonitrile is 45.3 kcal mol^{-1} whereas the measured value is 50.1 ± 0.2 kcal mol^{-1} [33]. The interaction of the two CN groups produces 4.8 kcal mol^{-1} of strain energy. However the insertion of another CH_2 group between the two CN groups reduces this strain energy to almost zero[33]. The strain energies involved with cyclic compounds (Table 4) have already been considered by Benson and coworkers[5] and so will not be dealt with here. Unlike Benson and coworkers[5], we determined the ΔH_f^0 [C_d(CN)(H)] group value (Table 1) from *trans*-dicyanoethylene (Table 5), which is simply half of the value for the heat of formation of *trans*-dicyanoethylene. This brings the calculated value for ΔH_f^0 [NCCH≡C(CH)$_2$] within 1 kcal mol^{-1} of its experimental value and *may* imply an interaction energy of -2 kcal mol^{-1} in *trans*-crotonitrile. However confirmation of the experimental heats of formation involved is needed. Conversion of these heats of formation in the gas phase to the liquid phase may be made by recourse to the very recent review by Ducras, Gruson and Sannier[16].

V. REFERENCES

1. For example, R. Shaw in *The Chemistry of Cyanates and their Thio Derivatives* Part I (Ed. S. Patai), John Wiley and Sons, Chichester, 1977.
2. L. Batt and G. N. Robinson in *The Chemistry of Amino, Nitroso and Nitro Compounds and their Derivatives* (Ed. S. Patai), John Wiley and Sons, Chichester, 1981.
3. K. D. King and R. D. Goddard, *J. Amer. Chem. Soc.*, **97**, 4505 (1975).
4. K. D. King, *J. Chem. Soc., Faraday I*, **74**, 912 (1978).
5. S. W. Benson, F. R. Cruickshank, D. M. Golden, G. R. Haugen, H. E. O'Neal, A. S. Rodgers, R. Shaw and R. Walsh, *Chem. Rev.*, **69**, 279 (1969).
6. J. D. Cox and G. Pilcher, *Thermochemistry of Organic and Organometallic Compounds*, Academic Press, London, 1970.
7. D. R. Stull, E. F. Westrum, Jr. and G. S. Sinke, *The Chemical Thermodynamics of Organic Compounds*, John Wiley and Sons, New York, 1969.
8. S. C. Chan, J. T. Bryant and B. S. Rabinovitch, *J. Phys. Chem.*, **74**, 2055 (1970); S. C. Chan, J. T. Bryant, L. D. Spicer and B. S. Rabinovitch, *J. Phys. Chem.*, **74**, 2058 (1970); F. M. Wang, T. Fujimato and B. S. Rabinovitch, *J. Phys. Chem.*, **76**, 1935 (1972); S. P. Pavlou and B. S. Rabinovitch, *J. Phys. Chem.*, **75**, 1366, 2171 (1971).
9. I. Oref and B. S. Rabinovitch, *Accounts Chem. Res.*, **12**, 166 (1979).
10. H. O. Pritchard and B. J. Tyler, *Can. J. Chem.*, **51**, 4001 (1973); J. L. Collister and H. O. Pritchard, *Can. J. Chem.*, **54**, 2380 (1976); **55**, 3815 (1977); H. O. Pritchard, *Can. J. Chem.*, **57**, 2677 (1979).
11. N. D. Lebedeva and Yu. A. Katin, *Russ. J. Phys. Chem.*, **47**, 922 (1973).
12. J. L. Franklin, *Ind. Eng. Chem.*, **41**, 1070 (1949).
13. H. Lehmann and E. Ruschitzky, *Chem. Tech. (Berlin 21)*, (**4**), 39 (1980).
14. R. Sabbah and A. Julg, *4th Int. Conf. Thermo chim.*, 121 (1975).
15. Y. Yoneda, *Bull. Chem. Soc. Japan*, **52**, 1297 (1979).
16. M. Ducras, J. F. Gruson and H. Sannier, *Thermochim. Acta*, **36**, 39 (1980).
17. D. S. Barnes and G. Pilcher, unpublished work, quoted in Reference 18.
18. M. H. Baghal-Vayjooe, J. L. Collister and H. O. Pritchard, *Can. J. Chem.*, **55**, 2634 (1977).
19. F. W. Evans and H. A. Skinner, *Trans. Faraday Soc.*, **55**, 255 (1959).
20. S. W. Benson, *Thermochemical Kinetics*, 2nd ed., John Wiley and Sons, New York, 1976.
21. H. K. Hall, Jr. and J. H. Baldt, *J. Amer. Chem. Soc.*, **93**, 140 (1971).
22. J. Konicek, M. Prochazka and V. Smisek, *Collect. Czech. Chem. Commun.*, **34**, 2249 (1969).
23. G. A. Crowder and R. R. Cook, *J. Phys. Chem.*, **71**, 914 (1967).
24. N. E. Duncan and G. J. Janz, *J. Chem. Phys.*, **23**, 434 (1955).
25. A. Ribner and E. F. Westrum, Jr., *J. Phys. Chem.*, **71**, 1216 (1967).
26. G. Stridh, S. Sumner and Ch. Svensson, *J. Chem. Thermodynamics*, **9**, 1005 (1977).
27. N. D. Lebedeva, A. S. Dneprovskii and A. Yu. Katin, *Russ. J. Phys. Chem.*, **43**, 1380 (1969).

28. J. S. Green, *Spectrochim. Acta,* **17**, 607 (1961).
29. J. H. S. Green and D. J. Harrison, *Spectrochim. Acta,* **32A**, 1195 (1976).
30. C. L. Chatterjee, P. P. Gang and R. M. P. Jaiswal, *Spectrochim. Acta,* **34A**, 943 (1978).
31. A. Y. Cheung, M. Veljkovic, H. Aleman and J. Lielmezs, *Thermochim. Acta,* **12**, 421 (1975).
32. JANAF Thermochemical Tables, 2nd ed., NSRDS–NBS 37, National Bureau of Standards, Washington, D.C., 1970.
33. N. J. Rapport, E. F. Westrum, Jr. and J. T. S. Andrews, *J. Amer. Chem. Soc.,* **93**, 4363 (1971).
34. C. A. Wulff and E. F. Westrum, Jr., *J. Phys. Chem.,* **67**, 2376 (1963).
35. H. L. Clever, C. A. Wulff and E. E. Westrum, Jr., *J. Phys. Chem.,* **69**, 1983 (1965).
36. A. Ribner and E. F. Westrum, Jr., *J. Phys. Chem.,* **71**, 1208 (1967).
37. D. S. Barnes, C. T. Mortimer and E. Mayer, *J. Chem. Thermodynamics,* **5**, 481 (1973).
38. R. H. Boyd, K. R. Guha and R. Winthrick, *J. Phys. Chem.,* **71**, 2187 (1967).
39. F. Malverson and R. J. Fransel, *J. Chem. Phys.,* **17**, 694 (1949).
40. L. H. Daby and S. E. Wiberly, *J. Mol. Spectry,* **2**, 177 (1958).
41. M. Prochazka, V. Kresianova, J. Konicek and M. Smicek, *Collect. Czech. Chem. Commun.,* **35**, 727 (1970).
42. H. S. Davis and O. F. Wiedman, *Ind. Eng. Chem.,* **37**, 482 (1945).
43. F. Halverson, R. F. Stamm and J. J. Whalen, *J. Chem. Phys.,* **16**, 808 (1948).
44. H. R. Wyss and H. H. Gunthard, *Helv. Chim. Acta,* **44**, 625 (1961).
45. S. B. Lie, P. Klåboe, D. H. Christensen and G. Hagen, *Spectrochim. Acta,* **26A**, 1861 (1970).
46. S. B. Lie, P. Klaboe, E. Kloster-Jensen, G. Hagen and D. H. Christensen, *Spectrochim. Acta,* **26A**, 2077 (1970).
47. R. H. Boyd, *J. Chem. Phys.,* **38**, 2529 (1963).
48. J. B. Moffat, *J. Mol. Struct.,* **62**, 213 (1980).
49. R. Tubino, G. Dellepiane and G. Zerbi, *J. Chem. Phys.,* **50**, 621 (1969).
50. J. B. Moffat and A. J. Knowles, *J. Chem. Eng. Data,* **14**, 215 (1964).
51. M. G. Krishna-Pillai and F. F. Cleveland, *J. Mol. Spectry,* **5**, 212 (1960).
52. H. S. Randhawa, *Ind. J. Pure Appl. Phys.,* **10**, 74 (1972).
53. J. B. Moffat, *Chem. Phys. Letters,* **55**, 125 (1978).
54. M. T. J. Glionna and H. O. Pritchard, *Can. J. Chem.,* **57**, 2482 (1979).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 3

Mass spectra of cyano, isocyano and diazo compounds*

KLAUS-PETER ZELLER
Institut für Organische Chemie, Universität Tübingen, Auf der Morgenstelle, D-7400 Tübingen, Germany

I. INTRODUCTION

In this chapter, a discussion of the mass spectral properties of compounds bearing a cyano, isocyano or diazo group is given. The electron-impact induced fragmentation of compounds with functional groups of these types is rather complex and sometimes

*Strictly, the subject of this chapter should have been triple-bonded groups only, hence, including diazonium compounds. However, almost no material exists on this and it was decided to include in this chapter a treatment of the related diazo compounds.

even surprising. Some of the mechanisms could only be established when highly advanced techniques were applied. It is not intended to describe all these methods in detail. Emphasis is put on the results, in order that the reader may interpret the mass spectra of the title compounds.

Unless otherwise specified the term 'mass spectrum' refers to a 70 eV electron-impact mass spectrum. The abundances of molecular and fragment ions are either quoted as % of the total ion current (% t.i.c.) or as relative intensities (% of the base peak). Fragmentations for which appropriate metastable transitions have been reported are usually characterized by an asterisk.

II. CYANO COMPOUNDS

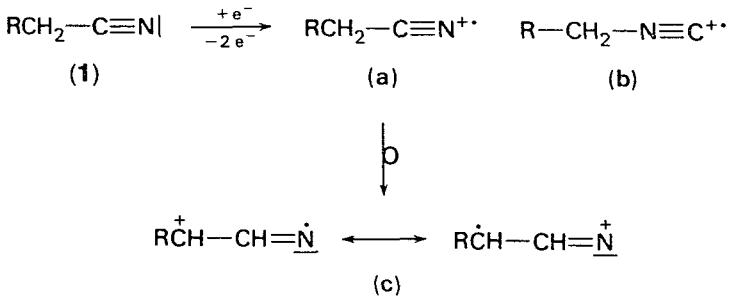
A. Aliphatic Nitriles

The first systematic study on the electron-impact induced fragmentation of aliphatic nitriles was reported by McLafferty[1]. Later, deuterium labelling and high-resolution mass spectrometry were utilized[2–11]. Both techniques allowed the differentiation between isobaric hydrocarbon- and nitrogen-containing fragments and established that aliphatic nitriles decompose by comparatively complex processes.

The molecular ion abundances of aliphatic nitriles (RCN) show a sharp drop from methyl cyanide upwards (Table 1). Although the abundances of the molecular ions are scattered somewhat irregularly, if plotted versus the length of the alkyl chain, they appear to increase again for the largest molecules examined[1]. As pointed out by McLafferty, this may result from a stabilization of the molecular ions by cyclization reactions.

In the case of *n*-propyl, *n*-butyl and *n*-pentyl cyanide no metastable peaks due to a decomposition of molecular ions could be detected in the mass spectra[7]. Furthermore, no fragmentation of $M^{+\cdot}$ ions in the first field-free region of a double-focusing mass spectrometer was observed using the defocusing technique. From this, it may be concluded that any decomposition of the molecular ions of C_3 and higher cyanides is faster than 10^{-6} s[12].

Throughout the mass spectrometric literature it is assumed that the molecular ions of nitriles (**1**) bear the positive charge mainly on the nitrogen atom (**a**). This supposition is substantiated by appearance potential measurements on acetonitrile and halogenated derivatives[13].



(1)

It is interesting to note that the molecular ions of nitriles (**a**) and isocyanides (**b**) possess different structures which are not interconvertible[14] (Section III.A). Deuterium-labelling experiments on nitriles bearing an α-hydrogen have furnished evidence that a part of the molecular ions suffer a hydrogen migration from C(2) to C(1) (**a** → **c**) before they decompose[10,11] (see below). From an ion cyclotron

TABLE 1. High-resolution mass spectra of aliphatic nitriles (R—CN)[a]

		R						
m/e	Fragment	CH_3	C_2H_5	*n*-C_3H_7	*i*-C_3H_7	*n*-C_4H_9	*t*-C_4H_9	*n*-C_5H_{11}
12	C	1.7	1.3	0.3	—	—	—	—
13	CH	1.1	1.3	0.4	0.6	—	—	—
14	CH_2	5.6	2.7	0.9	2.0	0.7	1.0	0.8
15	CH_3	1.2	9.4	2.5	8.5	2.7	7.2	4.0
25	C_2H	1.4	3.6	0.6	0.7	0.4	—	—
26	CN	1.0	1.2	0.3	0.7	—	0.4	—
	C_2H_2	1.2	23.1	6.2	14.5	6.9	3.4	7.9
27	CHN	2.0	2.3	0.7	2.1	0.9	3.1	1.0
	C_2H_3	0.3	20.6	30.8	22.8	39.8	13.3	46.8
28	CH_2N	3.4	26.4	4.5	29.5	5.0	2.1	5.4
	C_2H_4	—	100 $[M - HCN]^+$	3.1	13.5	8.8	0.9	14.7
29	C_2H_5	—	1.0	63.2	1.6	18.2	4.4	55.5
37	C_3H	—	26.0	3.6	6.4	2.2	3.6	2.1
38	C_2N	10.4	2.7	0.9	7.7	0.5	—	—
	C_3H_2	—	1.5	3.4	—	3.4	4.6	3.3
39	C_2H_2N	17.5	2.4	1.3	0.7	0.7	—	0.8
	C_3H_3	—	1.5	9.8	21.0	18.0	22.0	31.1
40	C_2H_2N	50.2	6.0	4.1	1.6	3.4	2.9	4.4
	C_3H_4	—	—	0.7	2.9	1.0	4.6	2.3
41	C_2H_3N	100 $M^{+\cdot}$	2.6	100 ion **n**	5.9	51.8 ion **n**	11.5	58.2 ion **n**
	C_3H_5	—	0.5	8.1	36.4	44.5	100	77.1

TABLE 1. *continued*

		R						
m/e	Fragment	CH_3	C_2H_5	n-C_3H_7	i-C_3H_7	n-C_4H_9	t-C_4H_9	n-C_5H_{11}
42	C_2H_4N	1.1	—	1.6	63.7	1.8	97.4	5.1
	C_3H_6		—	1.0	100 $[M - HCN]^{+\cdot}$	1.4	36.5	16.8
43	C_3H_7		—	—	0.9	100	—	23.3
50	C_3N							
	C_4H_2		2.6	0.6	1.4	2.8	1.2	2.0
51	C_3N							
	C_4H_3		13.1	2.1	8.4	3.0	3.0	3.7
52	C_3H_2N		15.7	3.4	16.3	4.3	6.1	4.5
	C_4H_4				$C_3H_2N^+$			
53	C_3H_3N		10.5	0.8	15.4	3.0	1.2	6.1
	C_4H_5				$C_3H_3N^+$			
54	C_3H_4N		79.7	2.0	39.2 $[M - CH_3]^+$	54.2 $[M - C_2H_5]^+$	1.4	100 $[M - C_3H_7]^+$
	C_4H_6		—	—	—	0.9	—	2.0
55	C_3H_5N		12.2 $M^{+\cdot}$	1.5	—	15.8	—	26.6
	C_4H_7		—	—	—	6.0	1.9	32.1
56	C_3H_6N		2.1	—	—	—	—	—
	C_4H_8			—	—	1.7	1.2	4.2
57	C_4H_9			—	—	—	1.9	32.1
62	C_4N			0.4	—	—	—	—
63	C_4HN			0.8	0.9	—	—	—

64	C_4H_2N / C_5H_4	1.8	2.6	1.2	2.0	1.4
65	C_4H_3N / C_5H_5	0.4	—	—	—	1.2
66	C_4H_4N / C_5H_6	1.1	1.8	1.3	4.4	2.0
67	C_4H_5N / C_5H_7	0.4	1.9	0.5	18.8	2.4
68	C_4H_6N	1.0 $[M - H]^+$	94.6 $[M - H]^+$	2.2	46.5 $[M - CH_3]^+$	40.1 $[M - C_2H_5]^+$
69	C_4H_7N	—	—	—	—	28.7
	C_5H_9	—	—	—	—	2.8
70	C_4H_8N	1.5	2.0	—	—	—
	C_5H_{10}			—	—	7.3
71	C_5H_{11}			—	—	1.7
79	C_5H_5N			—	—	1.6
80	C_5H_6N			—	—	1.3
81	C_5H_7N			—	—	0.8
82	C_5H_8N			3.7 $[M - H]^+$	3.7 $[M - H]^+$	30.5 $[M - CH_3]^+$
84	$C_5H_{10}N$			2.0	0.5	—
96	$C_6H_{10}N$					16.4 $[M - H]^+$
98	$C_6H_{12}N$					2.1

[a] Ion abundances are given in relative intensities (calculated from References 7 and 8 by permission of Heyden and Son Ltd., London). Doubly charged ions and ions due to ^{13}C isotopes have been omitted. The intensities of the $[M + H]^+$ ions are underlined to indicate that these values vary with sample pressure and ion draw-out potential. The values given have been obtained at ca. 10^{-6} Torr. The low-resolution mass spectral data of higher nitriles are tabulated in Reference 1. A number of plotted spectra can be found in References 2, 3 and 6.

resonance study on the proton-transfer reactions of the propionitrile ion-radical it follows that the nonreacting, long-lived molecular ions also rearrange to structure **c**[15].

In most cases a pressure-dependent $[M + H]^+$ ion is observed originating from a specific ion-molecule reaction[16-18]. The analytical use of these 'anomalous ions' for the determination of molecular weights should be kept in mind since their intensities very often exceed those of the molecular ions (Table 1). More than 30 years ago, in the first report on the mass spectral behaviour of nitriles Wertzler and Kinder[16] noted that the abundance of the $[M + 1]^+$ ions of *n*- and *i*-butyronitrile is proportional to the square of the sample pressure and to the ion draw-out potential.

As shown by ion cyclotron double resonance experiments, the $[M + 1]^+$ ions of acetonitrile[19] and propionitrile[15] are formed by proton transfer to a neutral molecule rather than by transfer of a hydrogen atom to a molecular ion. The latter process is assumed to be operative in most other classes of compounds showing the M + 1 phenomenon[20].

The $[M + 1]^+$ ion intensity of α-branched alkyl cyanides is somewhat smaller than in the case of the corrresponding straight-chain compounds. Heerma and de Ridder[8] correlated this observation with the smaller amounts of alkyl and $C_2H_3N^{+\cdot}$ ions produced from α-branched nitriles and suggested these cations to be the proton sources in the formation of the secondary $[M + H]^+$ ions. By comparing the $[M + D]^+$ ion intensity with respect to the $[M + H]^+$ ion intensity in the spectra of partially deuterated alkyl cyanides, the reacting primary ions could be identified. There is clear evidence that the well-known rearranged ion $CH_2{=}C{=}NH^{+\cdot}$ (see below) is mainly involved and that the proton attached to the nitrogen is transferred to the neutral nitrile molecule[9].

At higher nitrile pressures many other secondary ions arising from ion-molecule reactions can be detected[21]. Thus, at 10^{-2} Torr an ion of *m/e* 54 is formed from acetonitrile by the process shown in reaction (2).

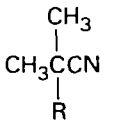
$$^+CH_2CN + CH_3CN \longrightarrow \underset{m/e\ 54}{C_2H_4CN^+} + HCN \qquad (2)$$

The mass spectra of most aliphatic nitriles show peaks formed by loss of a hydrogen atom which are usually slightly more pronounced that the $M^{+\cdot}$ ions. Together with the already discussed M + 1 peaks, the M − 1 peaks allow the determination of molecular weights even in cases where the $M^{+\cdot}$ ions can hardly be recognized. The higher abundances of both the $[M + 1]^+$ and the $[M - 1]^+$ ions reflect the increased stability of even-electron ions over odd-electron species[22].

From the appearance potential of $^+CH_2CN$ formed by loss of hydrogen from acetonitrile and the ionization potential of the $^{\cdot}CH_2CN$ radical Pottie and Lossing[23] calculated a dissociation energy of $D(H{-}CH_2CH) \leq 70$ kcal mol. As this value is nearly identical to that for the bond to allylic hydrogen it seems plausible to represent the $[M - H]^+$ ions of aliphatic nitriles as resonance-stabilized ions of type **d**[1-3]. This

$$\mathbf{a} \xrightarrow{-H^{\cdot}} R\dot{C}H{-}C{\equiv}N^{+\cdot} \longleftrightarrow \underset{(\mathbf{d})}{RCH{=}C{=}N|^+} \qquad (3)$$

assumption seems to be supported by the near absence of hydrogen elimination from 2,2-dimethylpropionitrile (**2c**) and the high $[M - H]^+$ intensity in the mass spectrum of isobutyronitrile (**2a**)[8]. However, deuterium labelling of *n*-hexyl cyanide (**3**) at all carbon atoms[6] reveals that all positions of the alkyl chain contribute to the yield of the $[M - H]^+$ ion. Similarly, in 2,2-d_2-isohexyl cyanide (**4**) only 20% of the label is eliminated in the formation of the $[M - H]^+$ ion[3]. The $[M - H]^+$ ion of isopentyl

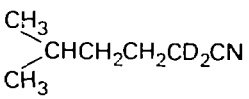


(2)

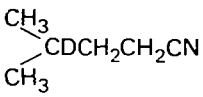
(a) R = H
(b) R = D
(c) R = CH_3

$CH_3CH_2CH_2CH_2CH_2CH_2CN$

(3)



(4)



(5)

cyanide is predominantly formed by loss of the γ-hydrogen as substantiated by study of the deuterium-labelled derivatives **5**[5].

In a thorough investigation applying precise mass measurements and metastable scanning on d_2-labelled propionitrile-2-d_2, Meyerson and Karabatsos[11] were able to clarify the structure and origin of the $[M - H]^+$ ion of propionitrile. They established that not the allylic-like activated hydrogen at C(2) but the more strongly bound hydrogen at C(3) is lost (Figure 1). This seeming inconsistency can be rationalized in terms of a hydrogen migration in the molecular ion **e** (R = D) yielding an allylic rearranged ion (**f**) with increased stability (see below). The driving force for the elimination of a hydrogen atom from C(3) is the formation of a new double bond in conjugation with the preexisting C=N double bond. A similar study on isobutyronitrile-2-d_1 (**2b**)[10] supports this mechanistic interpretation. Furthermore, the

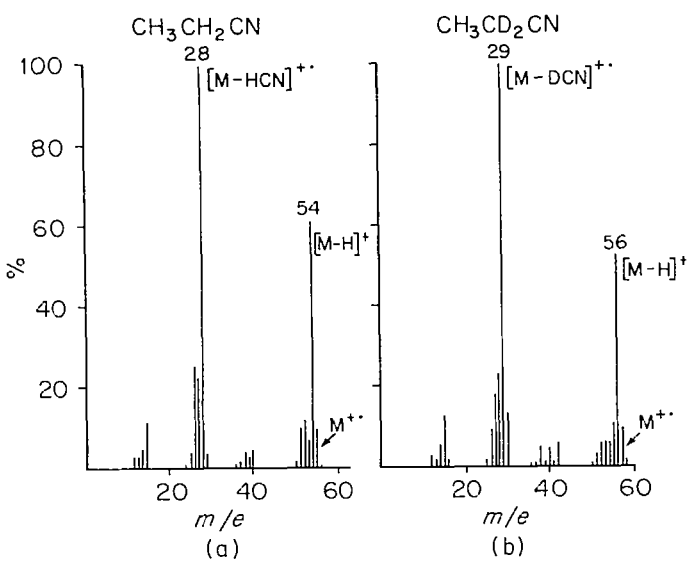
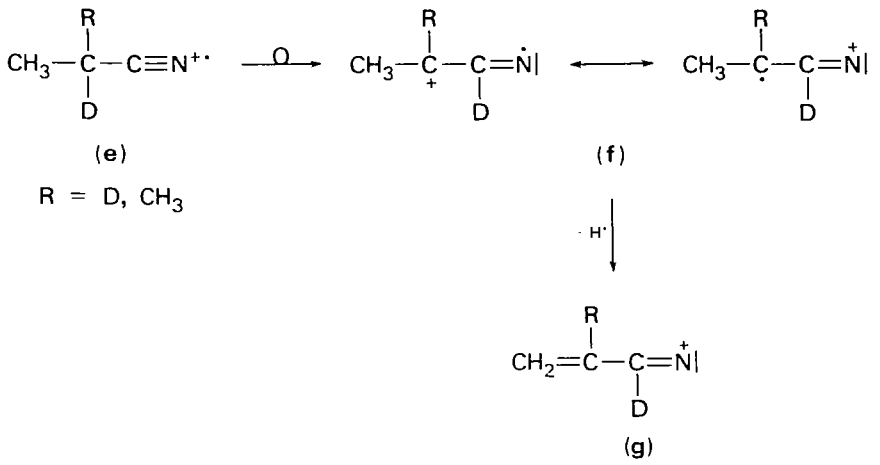


FIGURE 1. Mass spectra of (a) propionitrile and (b) 2,2-d_2-propionitrile. Obtained from tabultated data in S. Meyerson and G. Karabatsos, *Org. Mass Spectrom.*, **8**, 289 (1974), by permission of Heyden and Son Ltd., London.



(e) (f) (g)

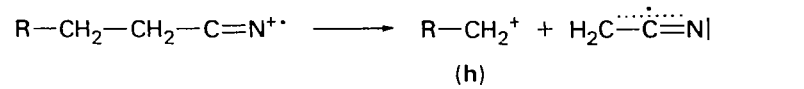
R = D, CH_3

(4)

inability of 2.2-dimethylpropionitrile (**2c**) to eliminate hydrogen to a marked extent can easily be explained by its inability to form a corresponding rearranged molecular ion.

Except for propionitrile and isobutyronitrile, the ions which could result from breaking of the C(1)—C(2) bond ($C_nH_{2n+1}^+$ or CN^+) are not significant. The absence of α-bond cleavage is in sharp contrast to the behaviour of carbonyl compounds and has been attributed to increased stability of the α-bond in nitriles due to hyperconjugation[1].

β-Bond cleavage in the alkyl chain does occur, however, in such a way that the positive charge is preferentially localized in the alkyl fragment (**h**)[7] (Stevenson's rule[24]) (reaction 5).

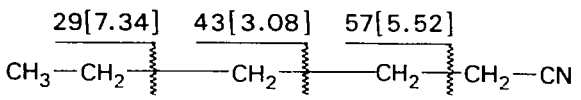


(h) (5)

R	% t.i.c.
CH_3	22.98
C_2H_5	23.28
n-C_3H_7	5.52

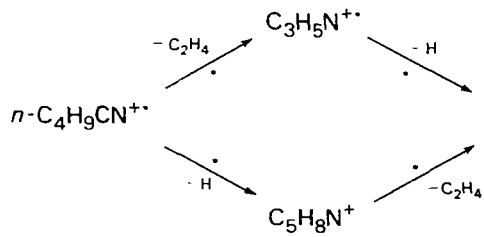
Carbon–carbon bonds more distant from the CN function are also ruptured under formation of alkyl ions. This is depicted in formula **6** for pentyl cyanide which gives the *m/e* [% t.i.c.] values shown. The other hydrocarbon ions in the mass spectra of nitriles are mainly produced by subsequent loss of H_2 and CH_4 from the alkyl ions.

The formal elimination of alkyl radicals from the molecular ions does not usually occur by simple bond ruptures; e.g. the C_2H_5 elimination from ionized n-butyl cyanide



(**6**)

is not a simple cleavage of the C(3)—C(4) bond. As shown by metastable transitions the $[M - C_2H_5]^+$ fragment is formed by two competing ways, both involving a rearrangement process (reaction 6)[7].



(6)

However, in longer chain alkyl nitriles terminal alkyl groups can be eliminated with formation of $[(CH_2)_nCN]^+$ ions. The mass spectrum of undecyl cyanide (7) which shows formation of intensive ions at *m/e* 96 ($n = 5$), *m/e* 110 ($n = 6$), *m/e* 124 ($n = 7$), *m/e* 138 ($n = 8$), *m/e* 152 ($n = 9$) and *m/e* 166 ($n = 10$) may serve as illustration (Figure 2). The prominent contribution of these ions could be due to a

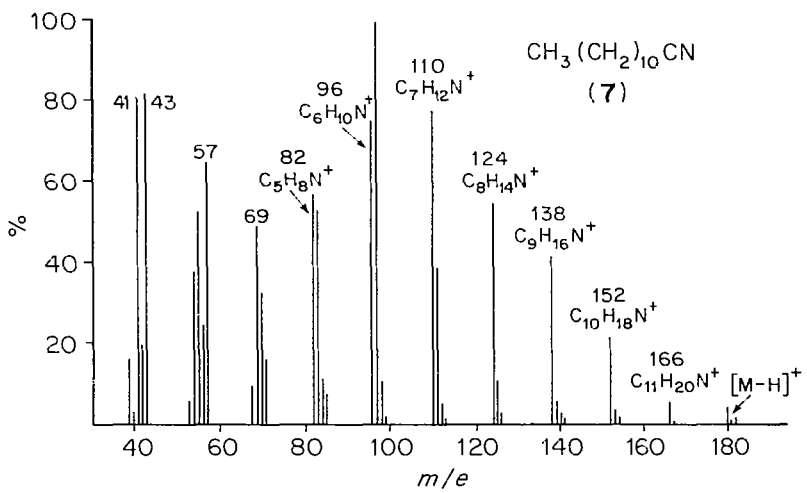
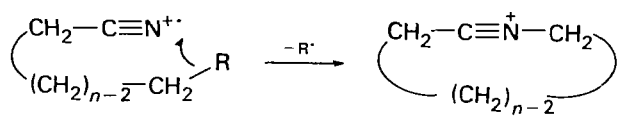


FIGURE 2. Mass spectrum of undecyl cyanide (7). Reproduced from H. Budzikiewicz, C. Djerassi and D. H. Williams, *Interpretation of Mass Spectra of Organic Compounds*, 1967, Chap. 11, by permission of Holden-Day, Inc., San Francisco.

stabilization of such species by cyclization as in structure **j** (reaction 7)[1]. This is reminiscent of the postulated formation of a five-membered ring in the fragmentation of alkyl halides[25]. The sp-hybridization of the cyanide linkage, however, requires a larger ring-size.

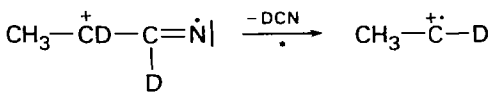


(7)

(j)

$n \geq 5$

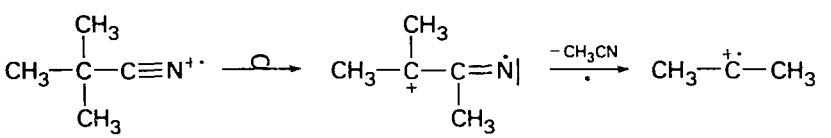
As already mentioned, the loss of a $CN^{\cdot}$ radical is only important for propionitrile and isobutyronitrile. Similarly, both compounds differ from longer-chain nitriles in the facile elimination of HCN[8,10,11]. It could be demonstrated that the bulk of the eliminated HCN contains a hydrogen from C(2) (Figure 1) and that this fragmentation does not proceed stepwise by the loss of $CN^{\cdot}$ and $H^{\cdot}$ in separate steps[11]. The formal 1,1-elimination of HCN can be elegantly rationalized by assuming the intermediacy of the rearranged molecular ions **f**, already discussed when dealing with the hydrogen elimination process (see above) (reaction 8). The similarity in behaviour of propionitrile and isobutyronitrile then follows directly.



(8)

(f) (k)

Loss of CH_3CN from ionized 2,2-dimethylpropionitrile (**2c**), which gives rise to the fourth most intensive ion in its mass spectrum[8,10,11], probably involves an analogous migration of a methyl group from C(2) to C(1) (reaction 9).



(9)

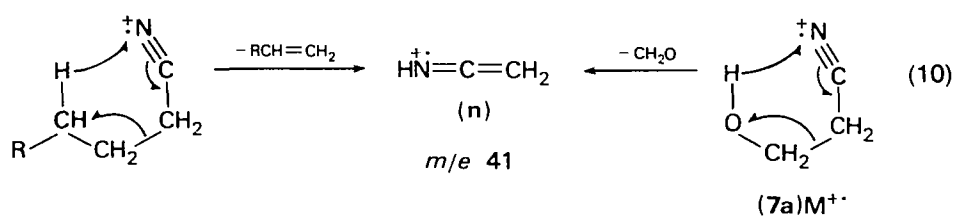
(2c)$M^{+\cdot}$ (l) (m)

The structures of the fragment ions resulting from overall 1,1-elimination of HCN and CH_3CN, respectively, are represented as ionized carbenes (**k**, **m**). Whether this is in fact so or whether the elimination is followed or accompanied by a reorganization to an olefinic structure remains unsettled.

In the mass spectrum of benzyl cyanide the loss of HCN is responsible for the third abundant ion. This extremely complex reaction is discussed in Section II.B.

Some of the principal ions in the mass spectra of alkyl cyanides originate from rearrangement processes. The formation of the $C_2H_3N^{+\cdot}$ ion (**n**, *m/e* 41) is favoured for many alkyl cyanides (reaction 10) and has been explained by a McLafferty rearrangement[1]. Any alternative process yielding a structure corresponding to ionized acetonitrile, $CH_3CN^{+\cdot}$, can be excluded, since the collision-induced fragmentation spectra of the molecular ion of acetonitrile and of the $C_2H_3N^{+\cdot}$ ion derived from C_4 and higher nitriles are different[14].

The coincidence of the $C_2H_3N^{+\cdot}$ ion with the $C_3H_5^+$ ion makes its recognition difficult unless high-resolution instrumentation is employed. Using high-resolution conditions Rol[4] established that passing from propyl cyanide towards cyanides with longer or more branched alkyl chains the $C_3H_5^+$ ion begins to dominate the *m/e* 41



(10)

(7a)$M^{+\cdot}$

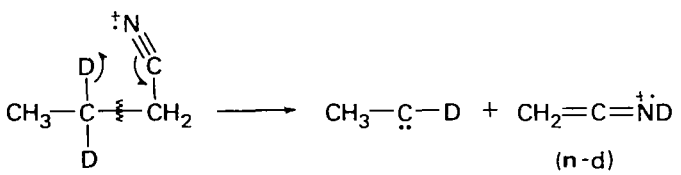
TABLE 2. Composition of the *m/e* 41 peak in the 70 eV mass spectra of alkyl cyanides

Alkyl cyanide	*m/e* 41 peak intensity (% t.i.c.)	Intensity ratio $C_2H_3N^{+\cdot}/C_3H_5^+$
$CH_3(CH_2)_2CN$	58.9	15.67
$CH_3(CH_2)_3CN$	30.3	1.35
$(CH_3)_2CH(CH_2)_2CN$	12.4	0.24
$(CH_3)_2CHCH(CH_3)CH_2CN$	8.4	0.09
$(CH_3)_3CCH_2CN$	12.2	0.21

peak (Table 2). The isobaric $C_3H_5^+$ fragment originates from different sources, e.g. from elimination of H_2 from $C_3H_7^+$. When the energy of the ionizing electrons is lowered to a value just above the ionization potential of the cyanides, the contribution of $C_2H_3N^{+\cdot}$ to the *m/e* 41 peak increases. Thus, in the case of isopentyl cyanide the ratio $C_2H_3N^{+\cdot}/C_3H_5^+$ raises from 0.24 to 5.4 by lowering the nominal electron energy from 70 eV to 12 eV[5]. Apparently, the formation of the rearranged ion **n** requires less energy than that of the hydrocarbon fragment $C_3H_5^+$. The same can be said with respect to other rearranged ions, discussed later, which also coincide with hydrocarbon fragments.

The high intensity of the $C_2H_3N^{+\cdot}$ ion in the spectrum of β-hydroxypropionitrile (**7a**)[1] and the near absence of this ion in the spectrum of β-methoxypropionitrile[1,26] are in line with the assumed γ-hydrogen migration in the formation of the *m/e* 41 fragment **n**. Nitriles with an α-methyl group decompose in the same way, yielding a large peak at *m/e* 55 in place of *m/e* 41.

Further studies with deuterium-labelled alkyl cyanides revealed a substantial contribution of β-[7] and δ-hydrogen[5] to the $C_2H_3N^{+\cdot}$ formation. The ratio of δ- to β-hydrogen transfer in *n*-propyl cyanide was found to be 1.15[7]. It has been suggested that a mechanism involving a five-membered transition state competes with the normal McLafferty rearrangement[7], e.g. reaction (11). The suggestion of the elimination

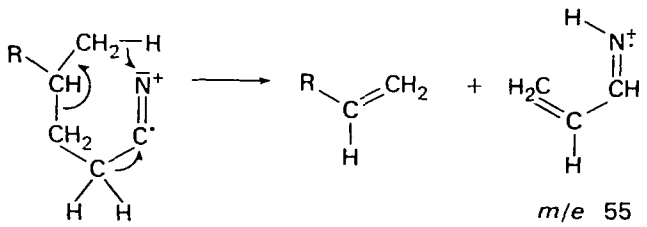


(11)

of methylcarbene as a neutral molecule should be treated with reservation. Alternatively, unknown hydrogen-scrambling processes prior to hydrogen transfer could be responsible for the observed β- and also δ-H participation. It should be noted that similar scrambling reactions in the McLafferty rearrangement of carbonyl compounds have been reported[27].

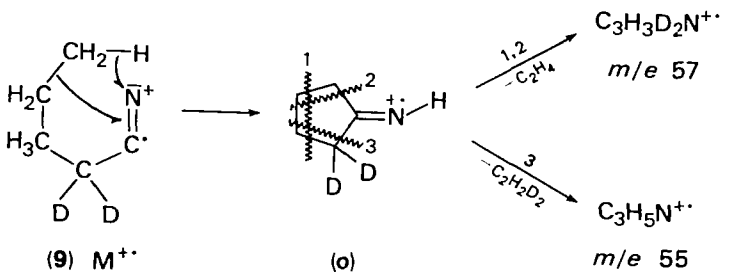
Nitriles with an alkyl chain of four or more carbon atoms (**8**) give a peak at *m/e* 55. As shown by high-resolution measurements the *m/e* 55 peak in the mass spectrum of *n*-butyl cyanide consists of 72% $C_3H_5N^{+\cdot}$ and 28% $C_4H_7^+$ [7]. The latter ion is formed through loss of HCN from the $[M - H]^+$ fragment. The *m/e* 55 peak in the mass spectrum of isopentyl cyanide exhibits a similar composition of the two isobaric fragments[5], whereas in higher cyanides the $C_4H_7^+$ ion becomes dominant[6,7].

The formation of $C_3H_5N^{+\cdot}$ is again a rearrangement process. According to Rol[5], a δ- and an α-hydrogen are transferred to the nitrile group with simultaneous cleavage of



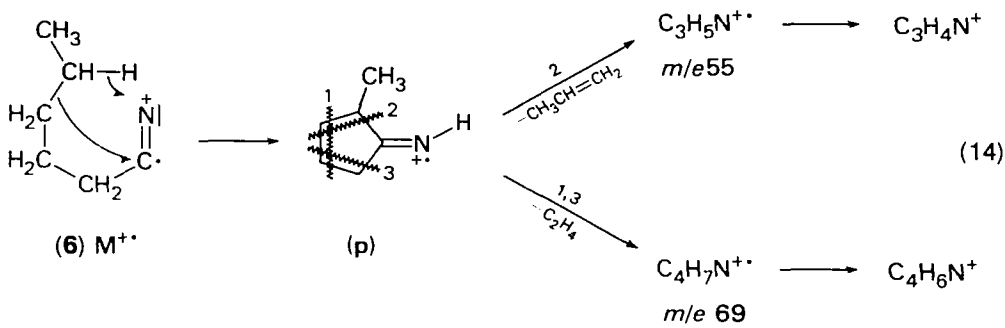
(12)

the γ-bond (reaction 12). However, based on deuterium labelling, Heerma and coworkers[7] suggested that the γ-H transfer is accompanied by the formation of a five-membered ring intermediate (**o**). Their mechanism is represented for the molecule ion of 2,2-d_2-*n*-butyl cyanide (**9**) in reaction (13). As substantiated by the corresponding



(13)

metastable transitions the $C_3H_5N^{+\cdot}$ ion decomposes further by expulsion of a hydrogen atom (see below). The rearrangement ions $C_4H_7N^{+\cdot}$ and $C_3H_5N^{+\cdot}$ in the mass spectrum of *n*-pentyl cyanide (**6**) are explained in the same way via the rearranged ion (**p**) (reaction 14).



(14)

The peak at *m/e* 69 in the spectrum of isohexyl cyanide (**10**) (Figure 3) is made up of $C_4H_7N^{+\cdot}$ and $C_5H_9^+$ ions in the ratio 2.04:1[3]. The genesis of the nitrogen-containing fragment must involve the loss of C_3H_6. From extensive deuterium labelling of the isohexyl group it follows that the terminal isopropyl group is eliminated with back-transfer of one hydrogen. The formation of a propyl cyanide ion-radical (**q**) as suggested by Beugelmans and coworkers[3] is however unlikely (reaction 15), since the molecular ion of propyl cyanide is very unstable[7] and hence cannot represent the intensive rearranged ion $C_4H_7N^{+\cdot}$. Although no satisfying explanation for the formation of the $C_4H_7N^{+\cdot}$ species from isohexyl cyanide and other longer chain cyanides

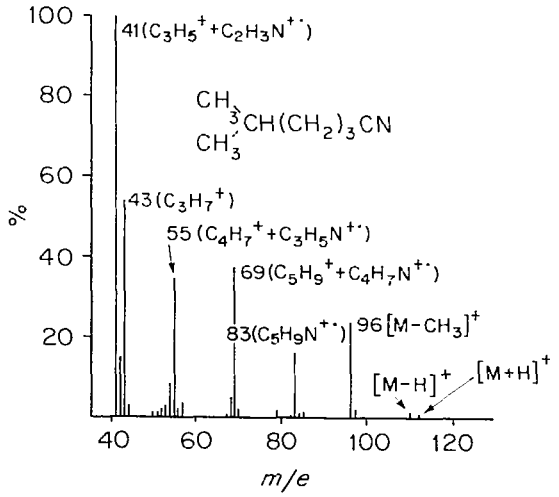
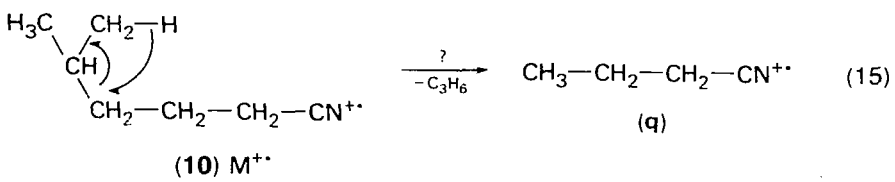
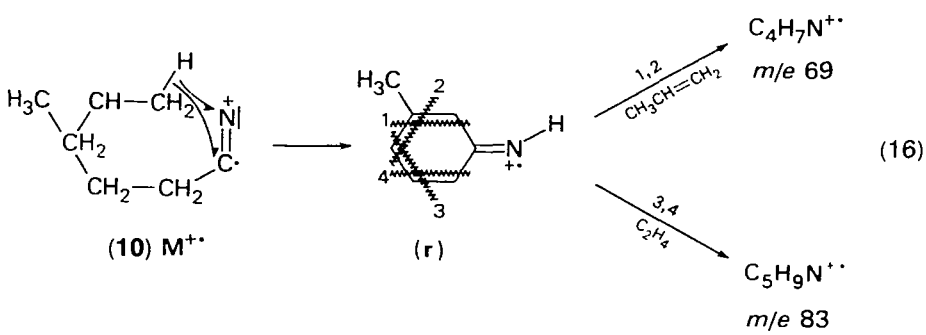


FIGURE 3. Mass spectrum of isohexyl cyanide (**10**). Reproduced with permission from R. Beugelmans, D. H. Williams, H. Budzikiewicz and C. Djerassi, *J. Amer. Chem. Soc.*, **86**, 1386 (1964). Copyright (1964) American Chemical Society.



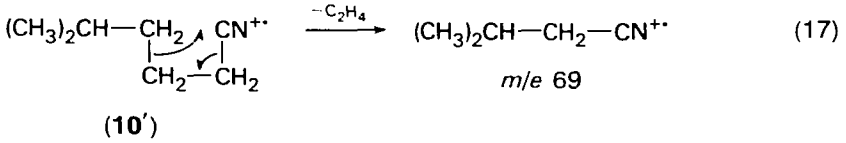
(15)

exists in the literature, it may be formed by transfer of an ε-hydrogen to the nitrile group and the formation of a six-membered intermediate **r** (reaction 16). From inter-

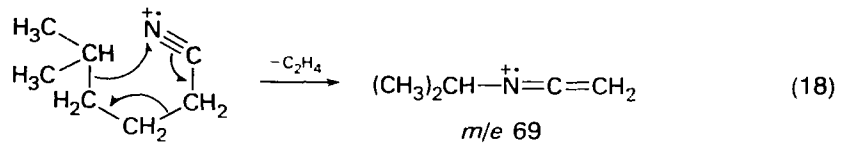


(16)

mediate **r** the $C_4H_7N^{+\cdot}$ ion could originate through loss of C_3H_6 by processes 1 and 2, as well as another intensive fragment, namely $C_5H_9N^{+\cdot}$ at *m/e* 83 by loss of C_2H_4 by processes 3 and 4. All fragmentation processes indicated in formula **r** are in accordance with deuterium labelling results which indicate 22% loss of C(2) and C(3), 78% loss of C(3) and C(4)[3]. In our opinion they provide a more likely explanation than the interpretation given in Reference 3, where two different transition states for the loss of



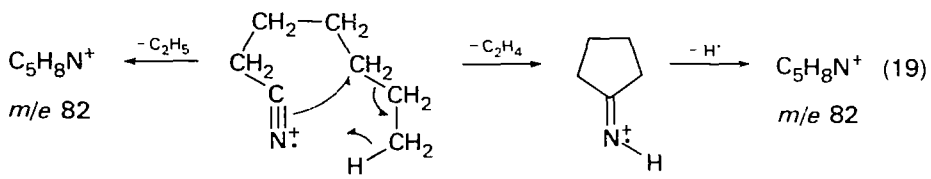
(10′) (17)



(10″) (18)

C_2H_4 have been suggested to account for the deuterium labelling experiments. The four-membered transition state (**10′**) ionized isobutyle cyanide. As already seen, the molecular ions of longer chain nitriles are very unstable and are therefore less likely to describe abundant fragment ions. The six-membered transition state (**10″**) involves the transfer of an isopropyl group which seems to be an improbable process[5].

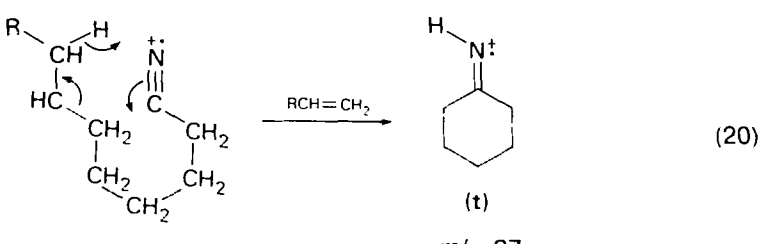
An ion of the composition $C_5H_9N^{+\cdot}$ (*m/e* 83) is present in the spectra of *n*-alkyl cyanides from *n*-hexyl cyanide upwards[6]. For *n*-hexyl cyanide (**3**) it was shown by deuterium labelling [6] that about 75% of the ion results from loss of the two terminal carbon atoms as C_2H_4. Amongst others[6], the mechanism shown in reaction (19) could



(**3**) $M^{+\cdot}$ (**s**) (19)

be operative. The main part of the most abundant peak in the mass spectrum of *n*-hexyl cyanide at *m/e* 82 is formed by loss of a hydrogen atom from **s**. As deduced from the spectrum of the 7,7,7-d_3 derivative, only a maximum of 14% can originate by cleavage of the terminal C_2H_5 group.

In the mass spectra of nitriles with an alkyl chain of seven or more carbon atoms (**11**) a further rearranged ion at *m/e* 97 plays an important role. The driving force for this rearrangement is, according to McLafferty[1], the formation of a stable olefin and the stabilization of the odd-electron ion **t** through cyclization (reaction 20).



(**11**) $M^{+\cdot}$ (20)

Summarizing the discussion on the rearrangement processes occurring in the electron-impact induced fragmentation of nitriles, we may conclude that the presence of ions of the general formula $C_nH_{2n-1}N^{+\cdot}$ (n = 2–6) at m/e 41, 55, 69, 83 and 97 is a characteristic feature of longer chain nitriles. In order to explain their favoured formation, cyclic transition states or intermediates are suggested as mechanistic rationalizations. Primary loss of HCN and H$^{\cdot}$ evidently becomes dominant only when the chain is not long enough to permit easy cyclization.

From a mechanistic point of view it would be desirable to reinvestigate structure and formation of these rearranged ions utilizing the modern tools of mass spectrometry[28] (e.g. metastable ion characteristics, collisional activation, field ionization kinetics etc.).

Finally, the particular fragmentation pattern of the smallest member of the aliphatic nitriles, i.e. acetonitrile[7], should be stressed. The ions in the molecular ion region represent about 85% of the total ion current: $M^{+\cdot}$ (49.3%), $[M - H]^+$ (24.72%), $[M - 2H]^{+\cdot}$ (8.63%), $[M - 3H]^+$ (5.1%). The elimination of HCN yields ionized methylene (2.75%). In a remarkable rearrangement process the $[M - H]^+$ ion ejects a carbon atom (reaction 21) which is proved by a corresponding metastable transition. A metastable peak for the loss of CH from the $M^{+\cdot}$ ion is also observed. According to Seibl[29], however, the metastable peak corresponding to the CH elimination might result from the stepwise loss of H and C in the same field-free region of the instrument.

$$CH_3CN^{+\cdot} \xrightarrow{-H^{\cdot}} C_2H_2N^{+\cdot} \xrightarrow{-C} CH_2N^+ \qquad (21)$$

m/e 28

(1.69% t.i.c.)

A similar carbon expulsion could not be observed in the mass spectra of the homologous nitriles and therefore seems to be unique for acetonitrile. The situation is somewhat reminiscent of charge-separation reactions reported for the doubly charged M^{2+}, $[M - H]^{2+\cdot}$ and $[M - 2H]^{2+}$ ions of malononitrile[30] (reaction 22). However, in

$$\underset{M^{2+}}{C_3H_2N_2^{2+}} \longrightarrow C_2HN_2^+ + CH^+ \qquad (22a)$$

$$\underset{[M - H]^{2+\cdot}}{C_3HN_2^{2+\cdot}} \longrightarrow C_2HN_2^+ + C^{+\cdot} \qquad (22b)$$

$$\underset{[M - 2H]^{2+}}{C_3N_2^{2+}} \longrightarrow C_2N_2^+ + C^{+\cdot} \qquad (22c)$$

this case the eliminated methine fragment or carbon atom bears a positive charge. As shown by ^{13}C labelling, the reaction of the $M^{2+\cdot}$ ion involves the methylene and nitrile carbon atoms in a statistical ratio, while that of $[M - H]^{2+\cdot}$ involves exclusively the CN carbon and that of $[M - 2H]^{2+}$ involves an approximately equal contribution from both carbon sources.

B. Benzyl Cyanide

Usually the mass spectra of benzylic derivatives $C_6H_5CH_2X$ are dominated by the formation of $C_7H_7^+$ ions (m/e 91) originating from loss of a radical $X^{\cdot}$ [31]. However, a

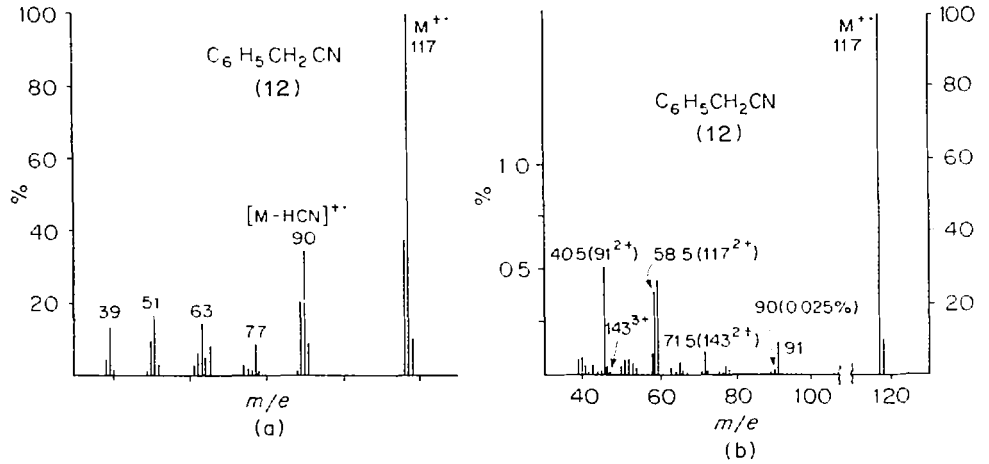


FIGURE 4. (a) Electron impact (EI) and (b) field ionization (FI) mass spectra of benzyl cyanide (**12**). Reproduced from J. van der Graaf, T. A. Molenaar-Langeveld and N. M. M. Nibbering, *Intern. J. Mass Spectrom. Ion Phys.*, **29**, 11 (1979) by permission of Elsevier Scientific Publishing Company, Amsterdam.

benzylic C—CN bond seems to be cleaved only with great difficulty, since the mass spectrum of benzyl cyanide (**12**) exhibits only a very small peak at *m/e* 91[31–33]. A peak of considerable intensity at *m/e* 90 indicates that loss of HCN is preferred over the loss of a $CN^{\cdot}$ radical (Figure 4a).

The elements of HCN are also lost from the intensive $[M - H]^+$ ion. By means of α- and ring-deuterated benzyl cyanides a strong analogy in the generation of the $[M - H]^+$ ions from benzyl cyanide and toluene has been found[32]. In both cases, the hydrogens attached to the ring and benzylic methylene group are partly scrambled before expulsion of a hydrogen atom.

An almost complete randomization of hydrogen and deuterium prior to the electron-impact induced elimination of HCN is observed in benzyl cyanide, specifically labelled in the α, *ortho* and *para* position. The electron impact method provides only a time-integrated view of decompositions occurring within about 10^{-6} s after ionization. Within this time H/D randomization processes are able to compete efficiently with fragmentation reactions. It is obvious that such randomization processes obscure the elucidation of the mechanism for any subsequent fragmentation. However, in the field ionization kinetic method (FIK)[28] decompositions of molecular ions in the first 10^{-11}–10^{-9} s after ionization can be studied. In this extremely short time interval only ions with high internal energy decompose. Due to the small frequency factor of hydrogen randomization, the interference of H/D exchange is considerably reduced in this time interval. Therefore, field ionization mass spectra of deuterated benzyl cyanides should allow conclusions to be drawn about the mechanism of the elimination of HCN.

In the FI spectrum of benzyl cyanide (**12**)[34] doubly and even triply charged ions are present. The ion at *m/e* 71.5 (= 143^{2+}) corresponds to a $[2M - C_7H_7]^{2+}$ species formed in the high field near the emitter[34]. The other ions in the FI spectrum (Figure 4b) are also observed in the EI spectrum. Generally, the abundances of the fragment ions are very low compared to EI measurements. Nevertheless, a reproducibility better than 10% has been reported using multiscan averaging[34].

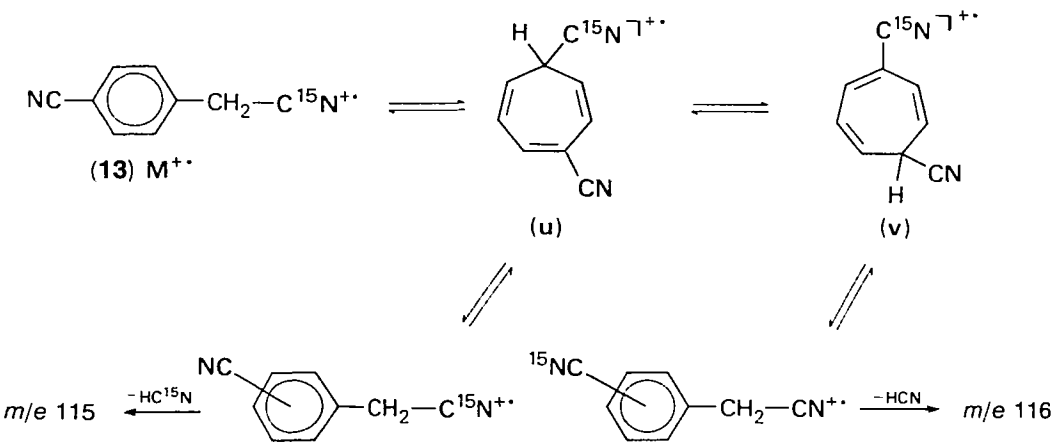
FIK data obtained with ring- and α-deuterated benzyl cyanides demonstrate that at

times $< 10^{-10}$ s the benzylic hydrogens are mainly involved in the elimination of HCN. This suggests formal 1,1-elimination of HCN in competition to hydrogen scrambling. It should be noted that a formal 1,1-elimination of HCN has been found in the molecular ion of propionitrile (Section II.A). The origin of the carbon expelled as HCN has been studied using the ^{13}C-labelled derivatives **12′** and **12″**. As expected, the

$C_6H_5-\overset{\alpha}{C}H_2-{}^{13}\overset{\beta}{C}N$ (**12′**) $C_6H_5-{}^{13}\overset{\alpha}{C}H_2-\overset{\beta}{C}N$ (**12″**)

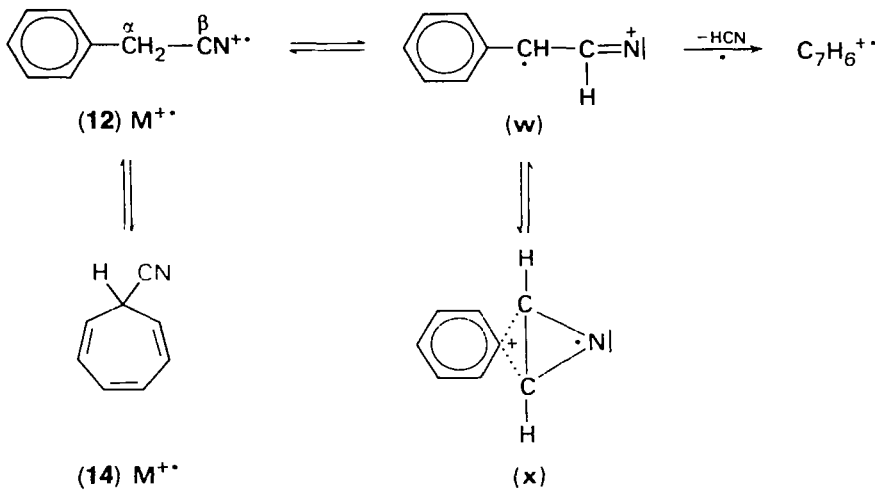
molecular ion of **12′** eliminates only $H^{13}CN$ and that of **12″** only $H^{12}CN$ when decomposing in the ion source. The mass spectrum of the unlabelled compound exhibits a metastable peak at 69.2 for the loss of HCN from $M^{+\cdot}$. In the spectra of **12′** and **12″** this diffuse peak is split up into two peaks at 70.2 and 68.6 corresponding to the loss of $H^{12}CN$ and $H^{13}CN$, respectively. From the relative intensities it follows that only the side-chain carbons are involved. This clearly indicates that in molecular ions of longer lifetimes[35] the positional identity of the α- and β-carbon is partly lost prior to HCN expulsion. The fact that only the side-chain carbon atoms (α, β) are eliminated as HCN means that the randomization of the hydrogen atoms occurs independently of the scrambling of the carbon atoms.

Further insights into the complex processes associated with the expulsion of HCN from benzyl cyanide have been gained from the fragmentation of *o*-, *m*- and *p*-cyanobenzyl cyanide. By means of ^{13}C and ^{15}N labelling it has been demonstrated[33,34] that both cyano groups are eliminated as HCN, the major part originating, however, from the benzylic nitrile function. Furthermore, the kinetic energy release[28] (calculated from the metastable peak width) for the elimination of $HC^{14}N$ and $HC^{15}N$ from **13** are equal within experimental error[34]. Thus, both species should be eliminated from equal or very similar ion structures. This may be explained by a partial interconversion between six- and seven-membered ring-structures, as shown in Scheme 1.



SCHEME 1

The cycloheptatriene species **u** and **v** can interconvert either by a 1,5-hydrogen shift or a series of 1,2-hydrogen shifts. Taking all these facts together, Nibbering and coworkers[33,34] proposed the reaction mechanism shown in Scheme 2 for the elimination of HCN from the molecular ion of benzyl cyanide (**12**). The elimination from the



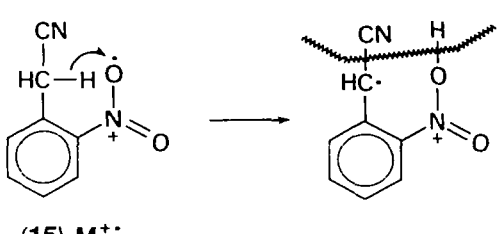
SCHEME 2

ion w competes with scrambling of the hydrogens, which is complete at 10^{-9} s. Judging from the studies with the cyano-substituted benzyl cyanides the interconversion of six- and seven-membered ring-structures should also occur to some extent. Furthermore, from the data obtained with ^{13}C-labelled benzyl cyanides a symmetrical structure must be passed through. Nibbering and coworkers suggested that this is the nonclassical species **x**[34].

The EI spectra of 7-cyanocycloheptatriene (**14**)[32,34,36] and *p*-tolunitrile[34] are very similar to that of **12**. Specifically D- and ^{13}C-labelled analogues revealed the same phenomena as described for benzyl cyanide. Furthermore, kinetic energy release measurements and field ionization kinetics provide evidence that the molecular ions of 7-cyanocycloheptatriene and *p*-tolunitrile isomerize to a benzyl cyanide structure prior to loss of HCN[34].

The elimination of HCN gives rise to one of the most abundant ions in the mass spectrum of *o*-nitrobenzyl cyanide (**15**)[37]. The [M − HCN]$^{+\cdot}$ ion is absent in the mass spectrum of the *para* isomer. From deuterium labelling it follows that the molecular ion of **15** eliminates HCN with exclusive abstraction of one of the benzylic hydrogens. The high site specificity is also observed for the decomposition from the metastable molecular ions. This is in contrast to benzyl cyanide where a complete hydrogen randomization within 10^{-9} s competes with the elimination of HCN.

Mandelbaum and coworkers[37] concluded that loss of HCN from *o*-nitrobenzyl cyanide is a 1,1-elimination only in a formal sense. The benzylic hydrogen atom migrates to a nitro oxygen (*ortho* effect[38]) and from there to the cyano group (reaction 23). The fact that the *para* isomer does not yield a [M − HCN]$^{+\cdot}$ ion supports this interpretation.



(23)

C. Aromatic Nitriles

In aromatic nitriles, the base peak is the molecular ion, in sharp contrast to the behaviour of aliphatic nitriles. The most significant fragment peak at *m/e* 76 in the spectrum of benzonitrile (**16**) is due to the loss of HCN[2] (Figure 5). An intense metastable peak at *m/e* 56.1 corresponds to this process. In 2,4,6-d_3-benzonitrile (**16'**) at an electron beam energy in the range 25–70 eV the *m/e* 76 peak is replaced by peaks at *m/e* 79 and 78 in an approximate ratio of 2:3[39]. The corresponding metastable peaks, found at *m/e* 58.9 and 57.4, also appear in a ratio of 2:3. This indicates a statistical loss of HCN and DCN from molecular ions decomposing in the ion source and in the second field-free region. However, when the electron energy is lowered from 20 eV to 14 eV the $[M - HCN]^{+\cdot}$ peak decreases relative to the $[M - DCN]^{+\cdot}$ peak even though the ratio of the appropriate metastable peaks remains at 2:3. At 14 eV the ratio of the $[M - HCN]^{+\cdot}$:$[M - DCN]^{+\cdot}$ daughter ions is 1:70. At 13 eV only the expulsion of DCN is found in the ion source and the ratio of the metastable peaks corresponding to HCN and DCN elimination is now reduced to ca. 1:3. Thus, at higher electron beam energies, and therefore higher internal energies of the molecular ions, the randomization reaction of hydrogen and deuterium atoms is faster than the elimination reaction under consideration. At lower energies only DCN is eliminated in the ion source pointing to a 1,2-elimination process with the formation of ionized benzyne. The rate of randomization is so reduced at low energies that an insufficient amount of hydrogen atoms reach the *ortho* position to yield a detectable amount of $[M - HCN]^{+\cdot}$ ions. However, as seen from the metastable peak ratio, this rate is still great enough to permit loss of HCN within the time spent by molecular ions decomposing during the travelling from source to collector. The results may be summarized by Scheme 3[39]. Much effort has been concentrated on the elucidation of the structure of the $C_6H_4^{+\cdot}$ ion resulting from fragmentation of benzonitrile by appearance potential

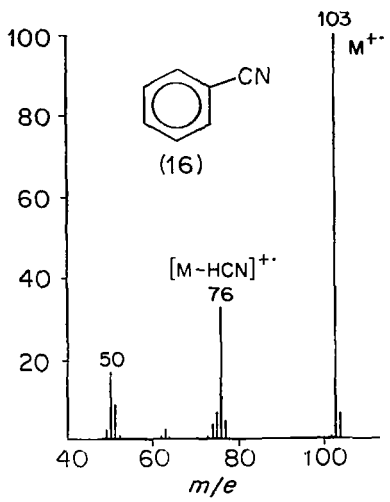
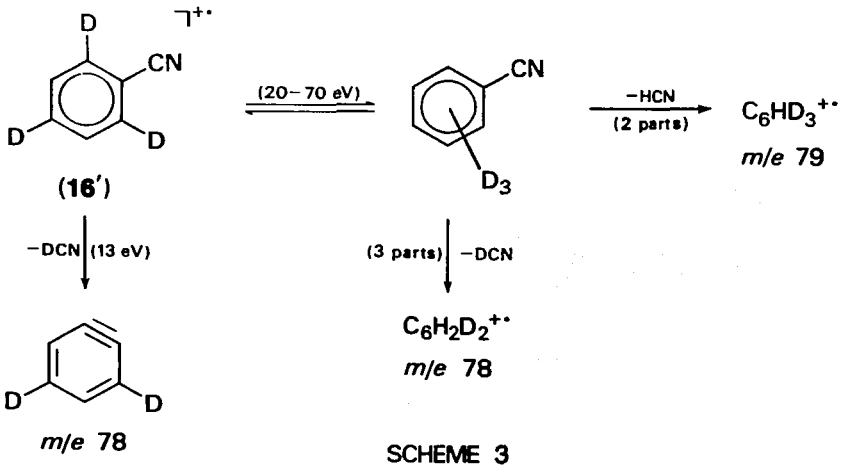


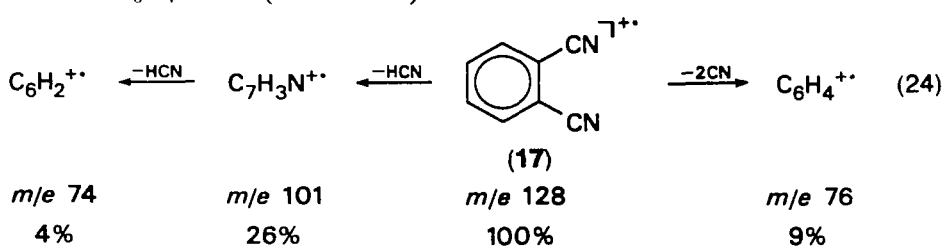
FIGURE 5. Mass spectrum of benzonitrile (**16**). Reproduced from H. Budzikiewicz, C. Djerassi and D. H. Williams, *Interpretation of Mass Spectra of Organic Compounds*, 1967, Chap. 11, by permission of Holden-Day, Inc., San Francisco.



SCHEME 3

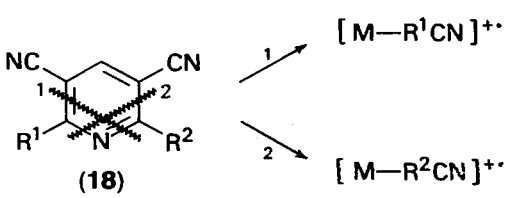
measurements on metastable ions[40–44]. In a recent publication, Baldwin[45] reported a value measured under such conditions that no kinetic shift[46] contributes. From this, the heat of formation of the $C_6H_4^{+\cdot}$ ion was calculated as 1348 kJ/mol, which is consistent with the ion having the benzyne structure.

The three isomeric dicyanobenzenes yield $[M-HCN]^{+\cdot}$ and $[M-2HCN]^{+\cdot}$ ions[47,48]. In addition, 1,2-dicyanobenzene (**17**) fragments by loss of 2 CN with formation of the $C_6H_4^{+\cdot}$ ion[48] (reaction 24).



(24)

In cyano-substituted pyridine derivatives ring-cleavage reactions compete with the elimination of the cyano group as HCN[49,50]. This is shown in reaction (25). Similarly,



(25)

in the fragmentation of other cyano-substituted heterocyclic systems (pyrazine, thiophene, pyrrole, furan) ring-breaking processes are strongly involved[51].

D. Alkyl Cyanoacetates

The mass spectral behaviour of cyanoacetates is unorthodox and therefore warrants separate treatment. The spectra of these compounds contain low-abundance molecular ions and frequently only slightly less intensive $[M+2]^{+\cdot}$ ions[52], in contrast to alkyl cyanides, which exhibit $[M-1]^+$ and $[M+1]^+$ peaks.

The conventional fragmentation processes of ethyl cyanoacetate (**19**) are illustrated

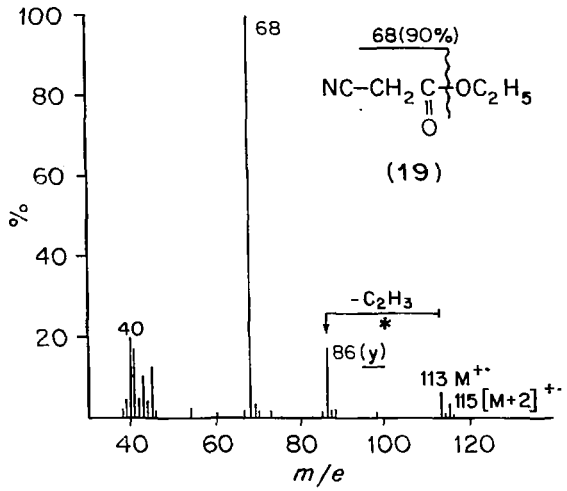
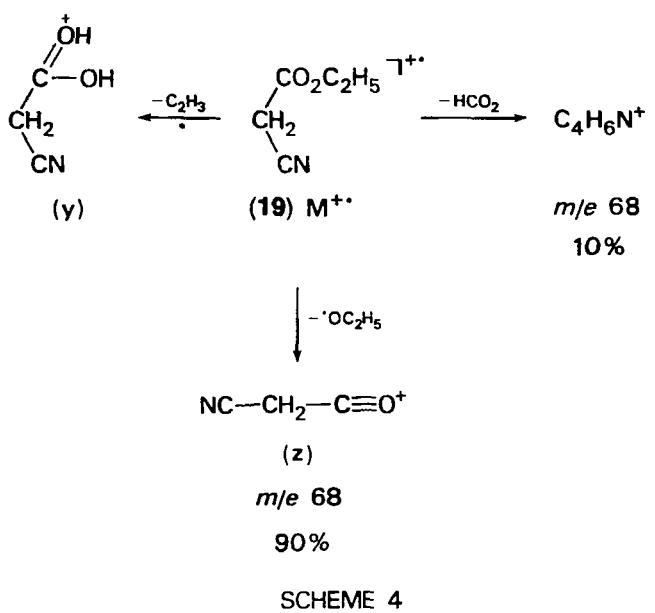


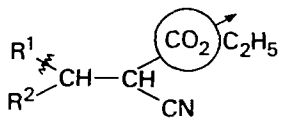
FIGURE 6. Mass spectrum of ethyl cyanoacetate (**19**). Reproduced with permission from J. H. Bowie, R. Grigg, S.-O. Lawesson, P. Madsen, G. Schroll and D. H. Williams, *J. Amer. Chem. Soc.*, **88**, 1699 (1966). Copyright (1966) American Chemical Society.

in Figure 6. The elimination of C_2H_3 from the ethyl group yields a protonated acid ion[53]. Investigation of the *m/e* 68 peak by high-resolution measurements reveals that only 90% of this peak is formed by ethoxy elimination[52]. The remaining 10% with the composition C_4H_6N originates from the very unusual elimination of HCO_2 from the molecular ion (Scheme 4). A similar process in methyl cyanoacetate yields $C_3H_4N^+$ (*m/e* 54). These processes necessitate the migration of an ethyl and methyl group, respectively.



SCHEME 4

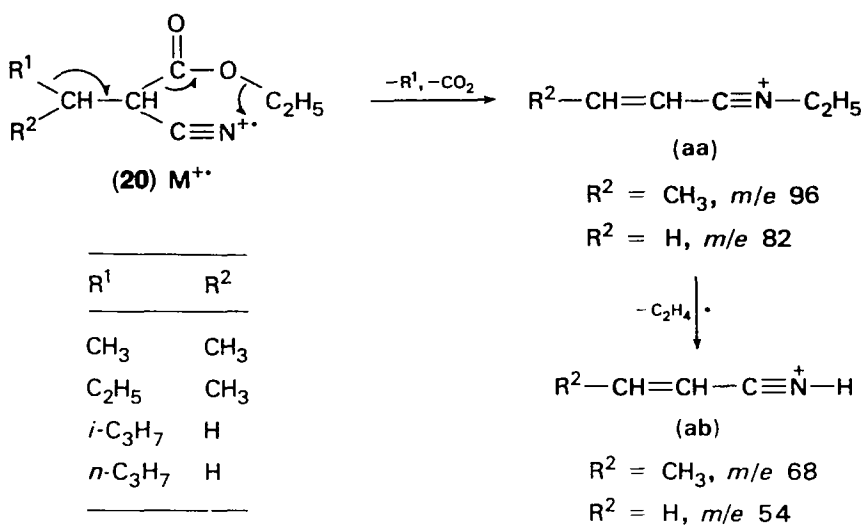
Inspection of the mass spectra of a number of α-alkylated ethyl cyanoacetates of the general formula **20** furnishes evidence that the most pronounced fragmentation pathway involves loss of CO_2 from the ester group and an associated cleavage of the C_α—C_β bond in the alkyl side-chain to eliminate the larger available radical[52]. This breakdown is schematically summarized in formula **20**. Since such processes are not observed in



(20)

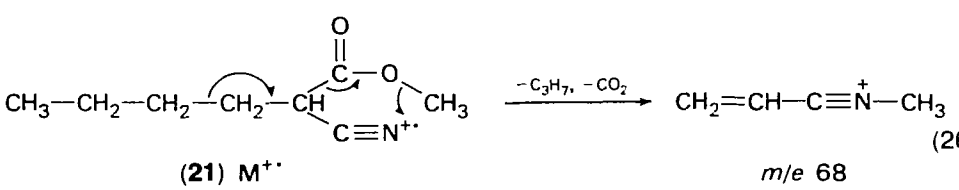
simple esters, it seems most reasonable to implicate the cyano group in the necessary rearrangement step. The mechanism shown in Scheme 5 has been suggested. The mass spectrum of ethyl isopropylcyanoacetate (Figure 7) illustrates the important contribution of this decay sequence.

An analogous methyl migration occurs in the electron-impact induced fragmentation of the corresponding methyl esters[52]. In fact, the base peak in the spectrum of methyl *n*-butylcyanoacetate (**21**) at *m/e* 68 is 75% $C_4H_6N^+$. This fragment originates from loss of $C_3H_7^\cdot$ and CO_2. Moreover, in the spectrum of the methoxy-deuterated ester the isotopic label is retained in the corresponding fragment ion with *m/e* 71, thus unequivocally establishing the methyl migration (reaction 26).



R^1	R^2
CH_3	CH_3
C_2H_5	CH_3
i-C_3H_7	H
n-C_3H_7	H

SCHEME 5



(26)

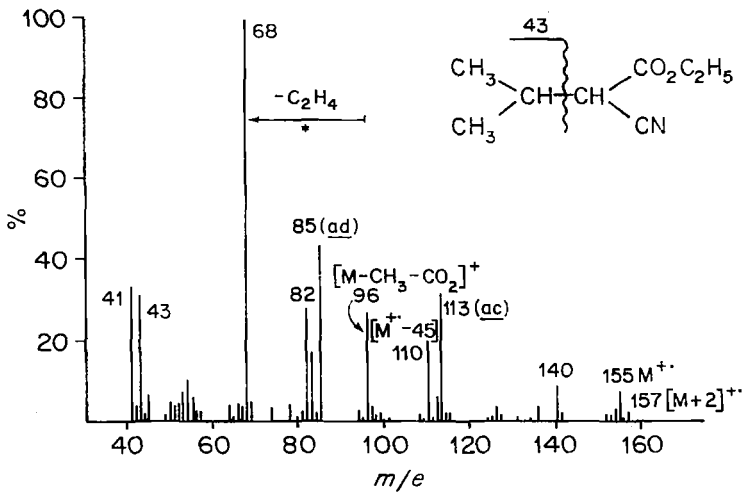
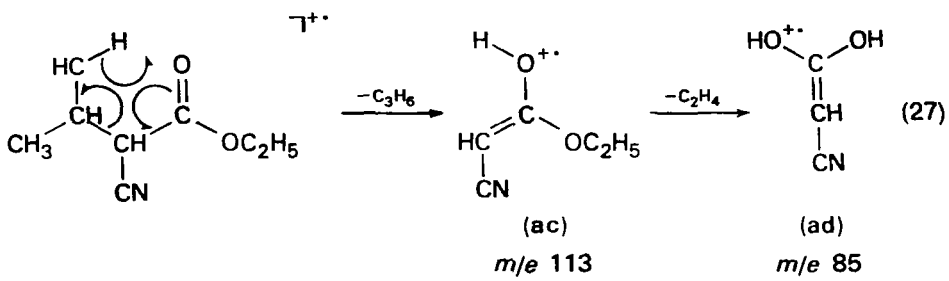


FIGURE 7. Mass spectrum of ethyl isopropylcyanoacetate. Reproduced with permission from J. H. Bowie, R. Grigg, S.-O. Lawesson, P. Madsen, G. Schroll and D. H. Williams, *J. Amer. Chem. Soc.*, **88**, 1699 (1966). Copyright (1966) American Chemical Society.

The spectra of the ethyl esters contain fairly abundant peaks at *m/e* 113 (**ac**) and 85 (**ad**). For their generation, a McLafferty rearrangement, followed by loss of ethylene has been suggested (reaction 27)[52]. The peak at *m/e* 145 (8%) in the spectrum of ethyl

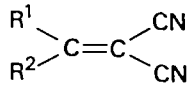


(27)

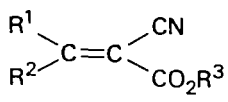
phenylcyanoacetate is formed by expulsion of CO_2 from $M^{+\cdot}$ and can then lose a methyl radical or ethylene to give *m/e* 130 (2%) and *m/e* 117 (100%) respectively[52,54]. The ion at *m/e* 117 may be represented as ionized benzyl cyanide since the fragments below *m/e* 117 and the metastable peaks are very similar to those in the spectrum of benzyl cyanide (Section II.B).

E. α,β-Unsaturated Nitriles

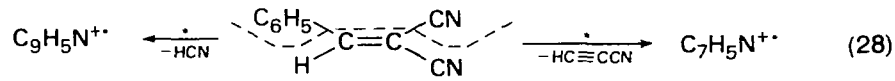
The tendency of nitriles to undergo electron-impact induced skeletal rearrangements is also found in α,β-unsaturated nitriles of types **22** and **23**. In compounds of the general formula **22** containing at least one phenyl group, ions formally equivalent to ionized benzonitrile (or phenyl isocyanide) are frequently observed in the mass spectra[55]. In 1,1-dicyano-2-phenylethylene (**22**, $R^1 = C_6H_5$, $R^2 = H$) the relative intensity of the $C_7H_5N^{+\cdot}$ ion (*m/e* 103) attains 27% (reaction 28). The occurrence of this rearrangement is consistent with the generalization[56] that skeletal rearrangements are facilitated by the proximity of unsaturated groups.



(22)



(23)

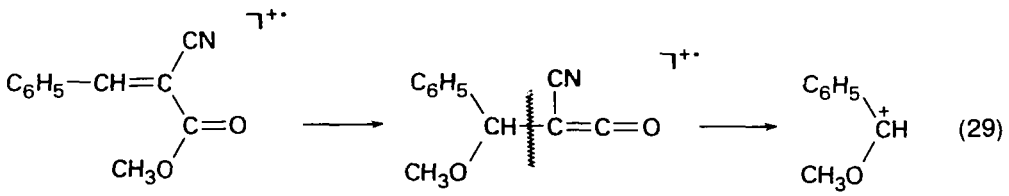


m/e 127 (22) $M^{+\cdot}$ *m/e* 103

45% $R^1 = C_6H_5$, $R^2 = H$ 27%

(28)

In compounds of type **23** and also in other α,β-unsaturated esters a rearrangement that necessitates the migration of an alkoxy group has been observed[55]. The reaction under consideration is probably best represented as a 1,3-alkoxy shift, followed by bond fission to give a benzylic stabilized ion (**ae**), e.g. reaction (29). From comparative



(23) $M^{+\cdot}$ (ae)

$R^1 = C_6H_5$, $R^2 = H$, $R^3 = CH_3$ *m/e* 121

12%

(29)

studies[55] it follows that the β-phenyl substituent on the double bond and hence the benzylic stabilization of the rearranged ion facilitates this process.

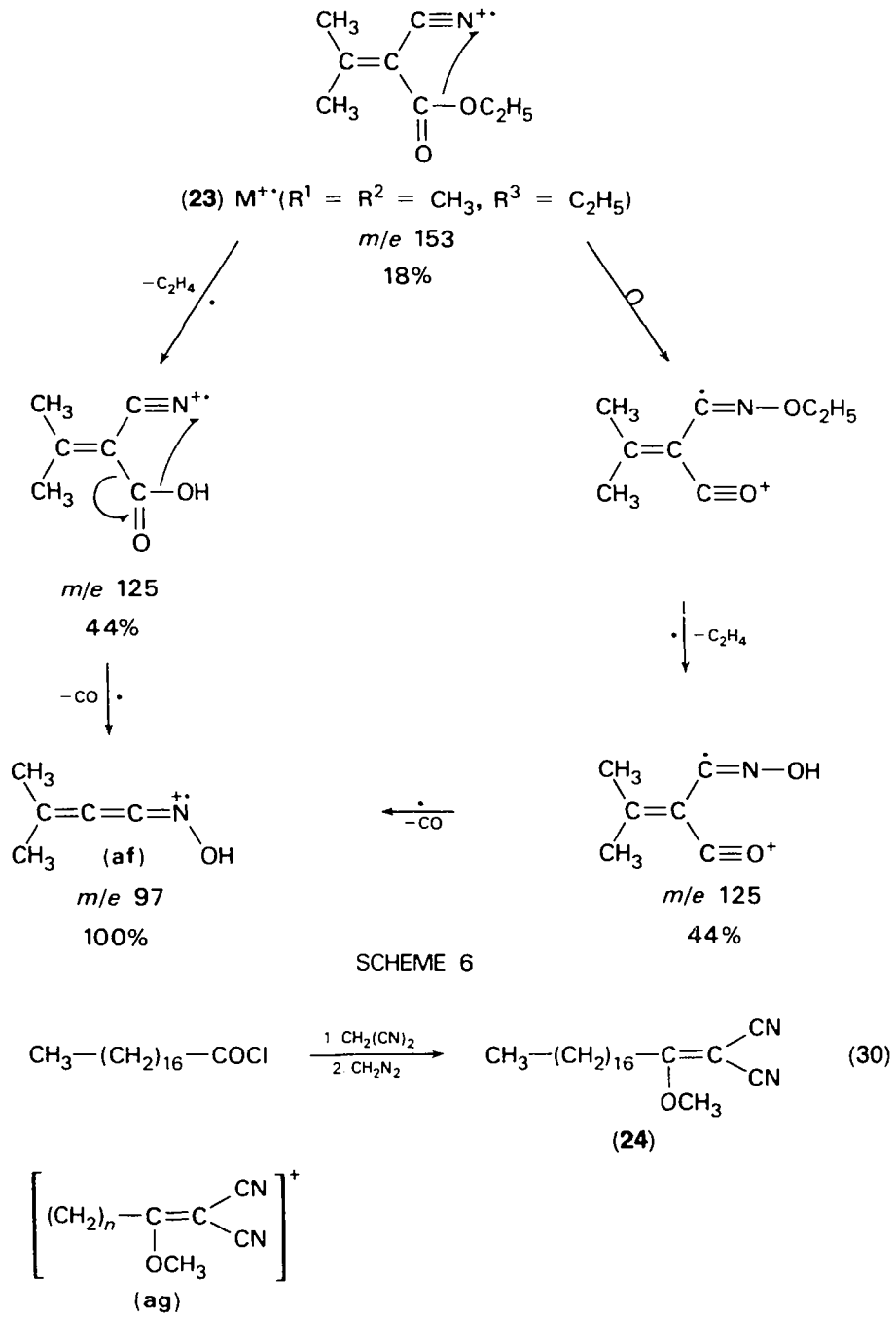
The proximity of the cyano and ethoxycarbonyl group at the same sp^2-hybridized carbon may lead to abundant $[M - C_2H_4—CO]^{+\cdot}$ ions. This sequence is illustrated by reference to the fragmentation of ethyl isopropylidenecyanoacetate (**23**, $R^1 = R^2 = CH_3$, $R^3 = C_2H_5$). Two slightly different interpretations, yielding the same ion structure **af**, are found in the literature[55,57] (Scheme 6).

Dicyanomethylene derivatives of longer chain aliphatic acids have been suggested for the identification and structural elucidation of such molecules[58]. The reaction of stearic acid chloride with malononitrile, using pyridine as catalyst, yields a product, which on treatment with diazomethane gives **24** (reaction 30). The mass spectrum of **24** is characterized by an abundant series of fragment ions of the general formula **ag** extending uniformly to the molecular ion. Similar derivatives of branched fatty acids can be used to advantage in the determination of the branch points since ions arising from bond fission at the branch points are preferentially formed.

III. ISOCYANO COMPOUNDS

A. Aliphatic Isocyanides

The mass spectra of aliphatic isocyanides bear a close resemblance with those of the isomeric nitriles. Thus, the isocyanides also suffer from a drop of the molecular ion abundance from the parent compound upwards, although to a lesser extent than the



SCHEME 6

$$CH_3-(CH_2)_{16}-COCl \xrightarrow[2\ CH_2N_2]{1\ CH_2(CN)_2} CH_3-(CH_2)_{16}-C(CN)_2=C(OCH_3) \quad (30)$$

(24)

$$\left[(CH_2)_n-C(CN)_2=C(OCH_3)\right]^+$$

(ag)

nitriles. Most aliphatic isocyanides yield $[M + H]^+$ and $[M - H]^+$ peaks, which facilitate the molecular weight determination when the $M^{+\cdot}$ peak is very small or absent.

The production of molecular ions from isocyanides requires about 0.6 eV less energy than from nitriles[59]. If it is assumed that the lone-pair orbital represents the

highest occupied orbital, then structure **ah** may be written for the molecular ion (reaction 31).

$$R{-}\overset{+}{N}{\equiv}\bar{C}| \xrightarrow[-2\,e]{+e} R{-}\overset{+}{N}{\equiv}C^{\cdot} \xrightarrow{-CN} R^{+} \qquad (31)$$

(ah)

Before going into details, it should be mentioned that the formation of fragments with the same elemental compositions and similar intensities in the mass spectra of nitriles and isocyanides, respectively, is not caused by partial thermal isomerization of isocyanides in the inlet system. It can be shown by IR spectroscopy that a sample of butyl isocyanide recollected from the hot box inlet system (ca. 100°C) of a AEI MS9 instrument is free of any butyl cyanide[8]. In the case of *t*-butyl isocyanide some thermal decomposition into HCN and isobutene was found in the inlet system.

In contrast to the alkyl cyanides, the α-cleavage process (loss of a $CN^{\cdot}$ radical) yielding the complete alkyl ion R^{+} contributes significantly to the fragmentation pattern[8,59]. Loss of HCN from the molecular ions of isocyanides is also an important fragmentation, even in longer chain compounds. However, concurring fragmentation reactions become more important as the length of the alkyl group increases.

From a thorough discussion of the fragmentation characteristics of methyl isocyanide, clear evidence can be gained that no electron-impact induced isomerization to the corresponding methyl cyanide ion-radical takes place[8]. This is remarkable, since at the first glance the spectra of both compounds show a striking resemblance (compare Tables 1 and 3). Thus, the $M^{+\cdot}$, $[M - H]^{+}$, $[M - 2H]^{+\cdot}$ and $[M - 3H]^{+}$ ions together carry about 85% of the total ion current in both cases. The unique elimination of a carbon atom from $[M - H]^{+}$ and of a CH radical from $M^{+\cdot}$ are also common for

TABLE 3. High-resolution mass spectra of alkyl isocyanides (R—NC)[a]

		R				
m/e	Fragment	CH_3	C_2H_5	*n*-C_3H_7	*n*-C_4H_9	*t*-C_4H_9
12	C	2.6	2.6	0.5	—	—
13	CH	1.3	1.9	0.5	—	—
14	CH_2	4.5	3.5	1.9	0.9	0.7
		$[M - HCN]^{+\cdot}$				
15	CH_3	8.4	6.9	3.8	3.4	7.1
24	C_2	—	1.1	—	—	—
25	C_2H	—	4.9	0.8	0.6	—
26	CN	1.9	2.0	—	—	—
	C_2H_2	0.3	30.8	7.8	8.5	2.9
27	CHN	4.8	6.6	1.1	0.7	5.8
	C_2H_3	0.8	62.2	43.4	54.8	11.9
28	CH_2N	4.7	19.4	19.6	7.5	3.2
	C_2H_4	—	54.6	11.1	23.8	2.7
			$[M - HCN]^{+\cdot}$			
29	C_2H_5	—	100	58.7	24.5	13.7
36	C_3	—	—	0.8	—	—
37	C_3H	—	0.9	3.3	2.3	2.3
38	C_2N	12.1	7.1	1.4	0.7	—
	C_3H_2	—	—	4.1	3.7	7.8
39	C_2HN	19.7	9.8	2.1	1.1	—
	C_3H_3	—	—	16.9	25.1	26.7

TABLE 3. *continued*

		R				
m/e	Fragment	CH_3	C_2H_5	n-C_3H_7	n-C_4H_9	t-C_4H_9
40	C_2H_2N	47.7	34.9	9.2	6.2	3.4
	C_3H_4	—	—	2.0	3.2	3.2
41	C_2H_3N	100 $M^{+\cdot}$	2.0	100 $[M - C_2H_4]^{+\cdot}$	42.5 $[M - C_3H_6]^{+\cdot}$	5.0
	C_3H_5	—	—	21.0	80.6	100
42	C_2H_4N	1.1	1.0	3.7	6.3	20.2
	C_3H_6	—	—	46.4 $[M - HCN]^{+\cdot}$	1.1	8.3
43	C_3H_7		—	9.9	100	1.8
50	C_3N		3.4	—	—	—
	C_4H_2		—	—	2.1	1.6
51	C_3HN		12.7	2.3	1.4	1.5
	C_4H_3		—	—	2.2	1.6
52	C_3H_2N		16.8	4.6	3.8	6.8
	C_4H_4		—	—	0.8	—
53	C_3H_3N		2.5	0.7	0.6	—
	C_4H_5		—	—	3.1	2.1
54	C_3H_4N		32.9	36.9 $[M - CH_3]^+$	16.8	0.9
	C_4H_6		—	—	1.4	0.6
55	C_3H_5N		73.2 $M^{+\cdot}$	—	64.4 $[M - C_2H_4]^{+\cdot}$	—
	C_4H_7		—	—	12.1	4.7
56	C_3H_6N		1.3	—	2.7	—
	C_4H_8		—	—	27.7 $[M - HCN]^{+\cdot}$	9.3
57	C_4H_9			—	2.9	91.4 $[M - CN]^+$
64	C_4H_2N			1.6	1.0	0.9
66	C_4H_4N			1.2	1.4	5.6
67	C_4H_5N			—	—	10.5
68	C_4H_6N			14.9	3.4	85.2 $[M - CH_3]^+$
69	C_4H_7N			9.4 $M^{+\cdot}$	—	—
70	C_4H_8N			0.7	—	—
82	C_5H_8N				4.4	0.6
83	C_5H_9N				— $M^{+\cdot}$	2.9 $M^{+\cdot}$

[a]Ion abundances are given in relative intensities (calculated from Reference 8 by permission of Heyden and Son Ltd., London). Doubly charged ions and ions due to ^{13}C isotopes have been omitted. The intensities of the $[M + H]^+$ ions are underlined to indicate that these values vary with sample pressure and ion draw-out potential.

both spectra. The main difference is found in the intensity of CH_3^+ which in the case of the isocyanide is six times more intensive.

However, by comparing the ratio of the abundances of the daughter ion D^+ and the metastable ion m* for the process $M^{+\cdot} \rightarrow [M - H]^+ + H^\cdot$ (Figure 8), different structures of the two molecular ions are proposed according to McLafferty's criterion[60]. Furthermore, from appearance potential measurements on the metastable and

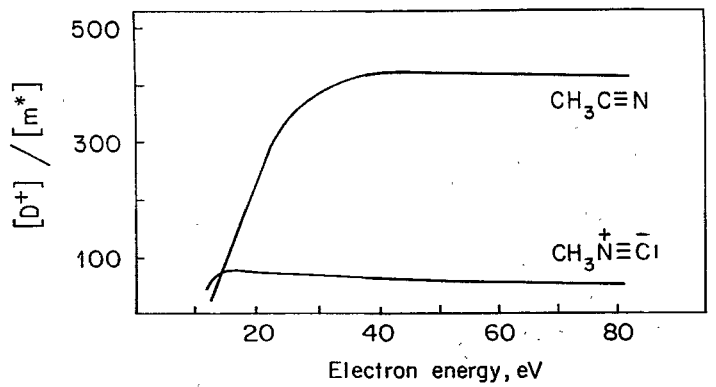
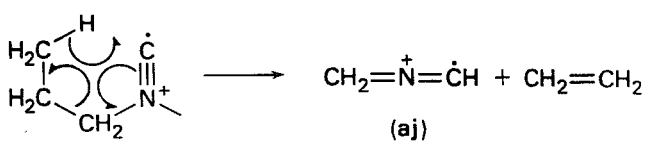


FIGURE 8. Relationship between $[D^+]/[m^*]$ and electron energy (nominal) for the hydrogen elimination process in methyl cyanide and methyl isocyanide. Reproduced from W. Heerma and J. J. de Ridder, *Org. Mass Spectrom.*, **3**, 1439 (1970), by permission of Heyden and Son Ltd., London.

daughter ions, the rough relationships between the rate constants of decomposition and the internal energies of the molecular ions were obtained[8]. From these diag ....s it follows that the activation energy for the decomposition of the cyanide must be less than that of the isocyanide, again pointing to different structures for the corresponding molecular ions. The nonequivalency of the molecular ions originating from the ionization of CH_3CN and CH_3NC was later fully confirmed by CA measurements[14] (Section II.A).

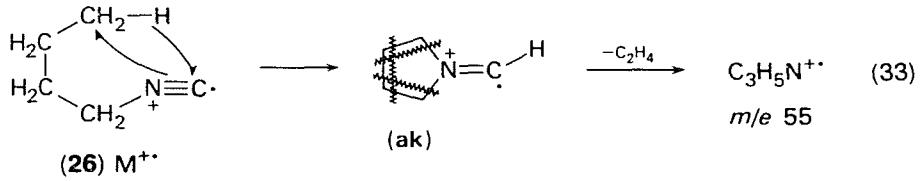
The mass spectrum of ethyl isocyanide[8], given in Table 3, also supports the enhanced stability of isocyanide molecular ions, since the intensity of the $M^{+\cdot}$ peak is about four times larger than that for ethyl cyanide. The weaker α-bond allows the production of $C_2H_5^+$ ions, hampering, however, the concurrent HCN elimination.

From propyl isocyanide upwards rearrangement processes via cyclic transition states or intermediates[8,59] yielding $C_nH_{2n-1}N^{+\cdot}$ ions became important. Thus, in *n*-propyl isocyanide (**25**) $C_2H_3N^{+\cdot}$ (**aj**) represents the most abundant ion. Due to the identical geometry of the cyano and isocyano groups a similar transition state as already discussed for the fragmentation of nitriles (Section II.A) seem most reasonable, e.g. as in reaction (32).



(**25**) $M^{+\cdot}$ (32)

The general resemblance of the spectrum of butyl isocyanide (**26**) to butyl cyanide is more pronounced than in the case of the ethyl and propyl compounds[8]. This is due to the larger alkyl chain which facilitates both the formation of similar hydrocarbon ions and the formation of equivalent cyclic transition states or intermediates necessary for the production of rearranged ions. This explains the high yields of $C_2H_3N^{+\cdot}$ (*m/e* 41) and $C_3H_5N^{+\cdot}$ (*m/e* 55) by loss of propene and ethene, respectively. The $C_3H_5N^{+\cdot}$ ion originates from the molecular ion probably via a five-membered intermediate (**ak**)



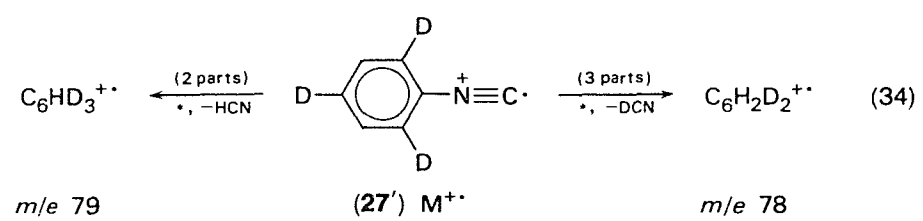
(33)

(reaction 33) of a structure analogous to **o** (Section II.A). Similar to the spectrum of butyl cyanide, the $C_3H_5N^{+\cdot}$ ion is accompanied by a peak at *m/e* 54 ($C_3H_4N^+$). However, as shown by appearance potential measurements, the reactions yielding the $C_3H_4N^+$ ion from *n*-butyl isocyanide and *n*-butyl cyanide respectively are completely different in nature. Whereas in the case of *n*-butyl cyanide the $C_3H_4N^+$ ion is formed via C_2H_4 and $H^\cdot$ elimination (Section II.A), the ion of the same elemental composition but originating from *n*-butyl isocyanide is obtained by direct cleavage of the γ-bond under expulsion of $C_2H_5^\cdot$. The different mechanisms explain the reversed intensity ratios for $C_3H_5N^{+\cdot}/C_3H_4N^+$ in the mass spectra of the isomeric compounds. This ratio is found as 3.83[8] and 0.29[7] for the isocyanide and cyanide, respectively. In butyl cyanide the formation of both ions turned out to be energetically identical rearrangements, resulting in a larger yield of the even-electron ion. When dealing with *n*-butyl isocyanide the $[M - C_2H_4]^{+\cdot}$ and $[M - C_2H_5]^+$ productions are energetically different processes. As rearrangement reactions possess a lower activation energy it is not surprising that the C_2H_4 elimination results in the most abundant ion.

B. Aromatic Isocyanides

The main feature of the fragmentation of aromatic isocyanides is loss of HCN. In phenyl isocyanide (**27**) the molecular ion constitutes the base peak. The relative intensity of the $[M - HCN]^{+\cdot}$ ion is about 40%[61]. A peak at $M^{+\cdot} - 26$ (9%) has been attributed to the loss of a $CN^\cdot$ radical from the molecular ion. However, most probably this ion originates from elimination of C_2H_2 rather than $CN^\cdot$.

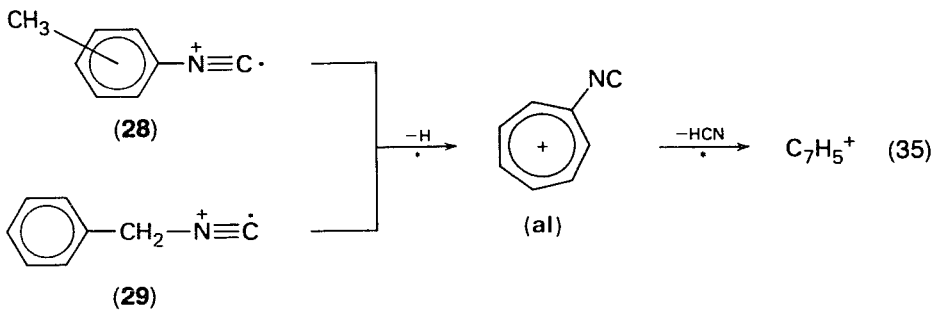
From mass spectrometric studies with 2,4,6-d_3-phenyl isocyanide (**27′**)[62] it follows that all hydrogen atoms of the phenyl ring equally participate in the elimination of HCN (reaction 34). The experimental ratio of $C_6H_2D_2^{+\cdot}$ to $C_6HD_3^{+\cdot}$ is 3:2.2 for both



(34)

the daughter ions produced in the source and the metastable peaks. The slight preference for loss of HCN over the statistical value of 3:2 for a random process may be due to an isotope effect. High-resolution measurements reveal that the $M^{+\cdot} - 28$ and $M^{+\cdot} - 27$ peaks in the spectrum of **27′** are doublets consisting of 86% $[M - DCN]^{+\cdot}$, 14% $[- C_2D_2]^{+\cdot}$ and 86% $[M - HCN]^{+\cdot}$, 14% $[M - C_2HD]^{+\cdot}$, respectively. These data require a correction of the interpretation[61] of the $M^{+\cdot} - 26$ peak in the spectrum of unlabelled phenyl isocyanide.

The three isomeric methylphenyl isocyanides (**28**) and benzyl isocyanide (**29**) exhibit a very similar fragmentation pattern[61] (reaction 35). Elimination of HCN occurs not only from the molecular ion but also from the very strong $[M - H]^{+\cdot}$ ion. A



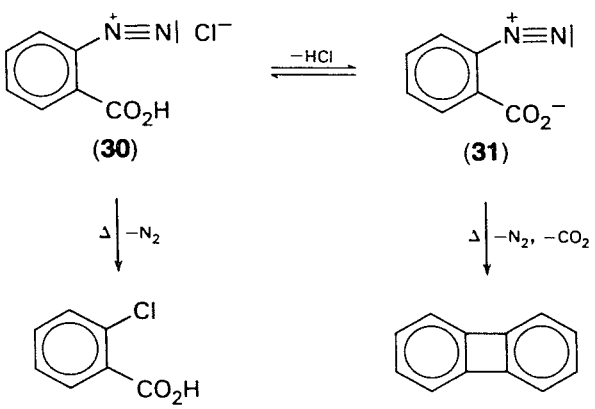
common isocyanotropylium structure (**al**) has been suggested[61] for the $[M - H]^+$ fragment of the four isomers.

In aromatic isocyanides containing two methyl or ethyl groups attached to the phenyl ring loss of HCN is only observed from $[M - H]^+$ and $[M - CH_3]^+$ ions but not from the molecular ions[61]. The elimination of HCN is also suppressed in the molecular ions of methoxyphenyl isocyanides[61]. Whereas the *meta* and *para* compounds decompose by expulsion of CH_2O the major part of the *ortho* isomer fragments by loss of CO and HCO$^{\cdot}$. The expulsion of a formyl radical may be rationalized by a hydrogen transfer to the *ortho* isocyano group (*ortho* effect[38]).

IV. DIAZO COMPOUNDS

A. General Remarks

In order to obtain the electron-impact mass spectrum of a compound a vapour pressure of ca. 10^{-6} Torr is necessary. Diazonium salts cannot be vaporized undecomposed and therefore are not suitable for electron-impact measurements. Thus, diazotized anthranilic acid (**30**) and sulphanilic acid give peaks due to thermal decomposition products when studied in a mass spectrometer[63]. The most important pyrolytic reaction of the hydrochloride of the diazonium carboxylate (**30**) is the formation of chlorobenzoic acid. If the zwitterion (**31**) is introduced into the ion source a peak at *m/e* 152 corresponding to biphenylene is the base peak (Scheme 7).



SCHEME 7

However, diazoalkanes, α-diazocarbonyl compounds and diazo oxides are volatile and allow mass spectrometric investigation. Very often diazo compounds suffer from partial decomposition on the metal surface of the inlet system. Thus, in an early report on the mass spectrum of diazomethane[64] a relative intensity of only 1% was given for the molecular ion peak. This has to be compared with a relative intensity of 96.5% obtained with an all-glass inlet system[65].

A similar situation is found for α-diazoketones. From the mass spectrometric fragmentation pattern and from appearance and ionization potential data, evidence has been gained for the competitive intervention of a mechanism of direct electron impact of the diazo compounds and of the process of ionization of the neutral $[M - N_2]$ fragments obtained by thermal cleavage[66].

From this experience it is not surprising that the reproducibility of mass spectra of diazo compounds and the comparability of measurements on different instruments is lower than with other classes of compounds.

B. Diazoalkanes

The mass spectrum of diazomethane shown in Figure 9 exhibits a strong molecular ion peak and ionized methylene as the base peak[65]. Due to the rapid decomposition of diazomethane in metal inlet systems the correct mass spectrum can only be recorded, when an all-glass system is used. The mass spectrum is similar to that of the cyclic isomer diazirine[65], but the intensities of $N_2^{+\cdot}$ (*m/e* 28) and $M^{+\cdot}$ (*m/e* 42) are larger for diazomethane. Also, doubly charged ions at *m/e* 20, 20.5 and 21 appear in the diazomethane spectrum, but not in that of diazirine.

Paulett and Ettinger[65] reported a value of 9.03 ± 0.05 eV for the ionization potential of diazomethane and 12.3 ± 0.1 eV for the appearance potential of $CH_2^{+\cdot}$. From

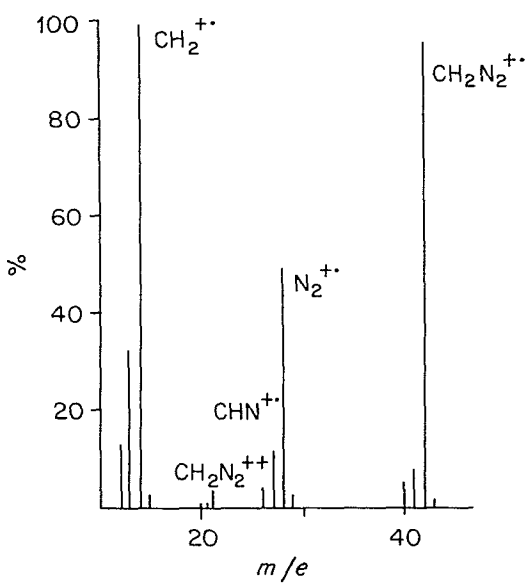


FIGURE 9. Mass spectrum of diazomethane. Obtained from tabulated data in G. S. Paulett and R. Ettinger, *J. Chem. Phys.*, **39**, 825 (1963), by permission of the American Institute of Physics.

these values heats of formation of CH_2N_2 and $CH_2N_2^{+\cdot}$ and the dissociation energy of the CN bond in the neutral and ionized molecule can be calculated by assuming the following processes

(a) $$CH_2N_2 + e \rightarrow CH_2^{+\cdot} + N_2 + 2e$$
$$\Delta H_f(CH_2N_2) = \Delta H_f(CH_2^{+\cdot}) + \Delta H_f(N_2) - AP(CH_2^{+\cdot})$$

Adopting 333 kcal/mol for $\Delta H_f(CH_2^{+\cdot})$[67] it follows:

$$\Delta H_f(CH_2N_2) = 2.14 \text{ eV} = 49.3 \text{ kcal/mol}$$

(b) $$CH_2N_2 + e \rightarrow CH_2N_2^{+\cdot} + 2e$$
$$\Delta H_f(CH_2N_2^{+\cdot}) = IP(CH_2N_2) + \Delta H_f(CH_2N_2)$$
$$\Delta H_f(CH_2N_2^{+\cdot}) = 11.2 \text{ eV} = 257 \text{ kcal/mol}$$

The same treatment yields $\Delta H_f = 314$ kcal/mol for the molecular ion of diazirine. Deviating from literature data[68], this suggests that the molecular ions of the two CH_2N_2 isomers have different structures.

From the appearance potential of $CH_2^{+\cdot}$ in diazomethane and the spectroscopic value for the ionization potential of methylene ($:CH_2$)[67], the CN bond dissociation energy can be estimated as:

$$D(CH_2—N_2) = AP(CH_2^{+\cdot}) - IP(CH_2) = 12.3 - 10.4$$
$$D(CH_2—N_2) = 1.9 \text{ eV}$$

The bond dissociation energy of the molecular ion can be obtained from the expression:

$$D(CH_2N_2^{+\cdot}) = AP(CH_2^{+\cdot}) - IP(CH_2N_2) = 12.3 - 9.0$$
$$D(CH_2N_2^{+\cdot}) = 3.3 \text{ eV}$$

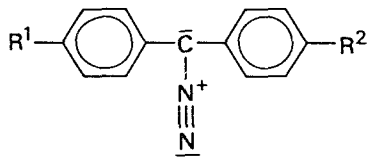
The latter value is appreciably higher than in the neutral molecule. This may be attributed to the removal of an antibonding electron during the ionization process, which stabilizes the resulting molecular ion. The doubly charged species in the mass spectrum of diazomethane also reflects this enhanced stability.

The electron-impact induced fragmentation of diaryldiazomethanes (**32**), 1,4-bis(α-diazobenzyl)benzene (**33**), and the cyclic analogues **34** and **35** has been studied

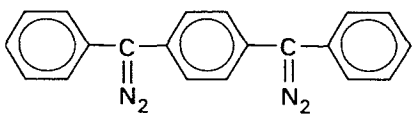
TABLE 4. Mass spectra of diaryldiazomethane derivatives (**32**) and analogous compounds (**33–35**)[a]

Compound	*m/e* (relative intensity)
32a	194 (10) $M^{+\cdot}$, 166 (64), 165 (100), 139 (10), 115 (5), 113 (3)
32b	224 (20) $M^{+\cdot}$, 196 (100), 195 (14), 181 (51), 165 (27), 153 (50), 152 (58), 151 (14), 127 (12), 126 (10), 98 (16)
32c	254 (9) $M^{+\cdot}$, 226 (100), 225 (6), 211 (71), 196 (4), 195 (9), 183 (15), 168 (15), 152 (16), 140 (18), 139 (24), 114 (10), 113 (19)
32d	239 (17) $M^{+\cdot}$, 211 (65), 165 (100), 164 (52), 163 (30), 153 (6), 152 (11), 139 (14), 127 (4), 126 (5), 115 (10), 113 (4), 89 (5), 87 (7)
33	310 (<1) $M^{+\cdot}$, 282 (1), 254 (100), 252 (40), 151 (18)
34	192 (20) $M^{+\cdot}$, 164 (100), 163 (52), 137 (4)
35	218 (7) $M^{+\cdot}$, 190 (68), 189 (100), 188 (14), 187 (16), 163 (8)

[a]Taken from D. Schumann, E. Freese and A. Schönberg, *Chem. Ber.*, **102**, 3192 (1969), by permission of Verlag Chemie GMBH, Weinheim.

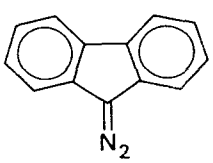


(32)

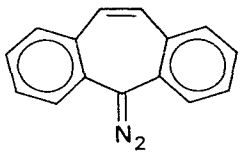


(33)

(a) $R^1 = R^2 = H$
(b) $R^1 = OCH_3$, $R^2 = H$
(c) $R^1 = R^2 = OCH_3$
(d) $R^1 = NO_2$, $R^2 = H$

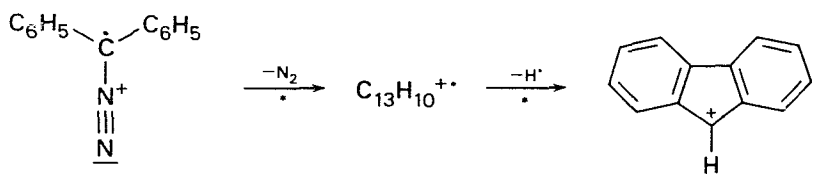


(34)



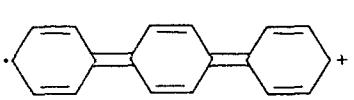
(35)

by Schumann, Freese and Schönberg[69] (Table 4). The fragmentation of the diaryl derivatives yields intensive $[M - N_2]^{+\cdot}$ ions, which in some cases constitute the base peak. The formation of the $[M - N_2]^{+\cdot}$ ions is facilitated by the production of the stable N_2 molecule is the decomposition process. In diphenyldiazomethane (**32a**) the most abundant peak at *m/e* 165 ($C_{13}H_9^+$) is formed by further expulsion of a hydrogen atom from the $[M - N_2]^{+\cdot}$ ion. In the range *m/e* 60–165 the spectrum of **32a** resembles that of fluorene. Therefore, a fluorenyl structure (**am**) is most probable for the $C_{13}H_9^+$ ion (reaction 36). The electron-donating methoxy group stabilizes the $[M - N_2]^{+\cdot}$

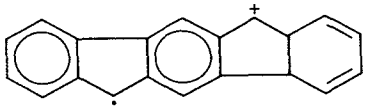


(32a) $M^{+\cdot}$ (am) *m/e* 165 (36)

fragment of **32b** and **32c**, thus lowering the tendency to eliminate hydrogen. The $[M - N_2]^{+\cdot}$ ion of the nitro-substituted compound **32d** preferentially loses the nitro group under formation of the $C_{13}H_9^+$ ion. The mass spectrum of the bisdiazo compound **33** is dominated by the $[M - 2N_2]^{+\cdot}$ and the $[M - 2N_2 - 2H]^{+\cdot}$ ions. Structures



(an) *m/e* 254

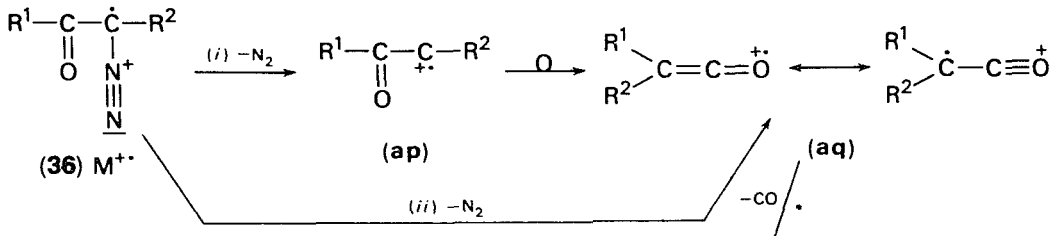


(ao) *m/e* 252

an and **ao** may be written to represent these species. The cyclic diazo compounds **34** and **35** yield abundant $[M - N_2]^{+\cdot}$ and $[M - N_2 - H]^+$ ions.

C. α-Diazocarbonyl Compounds

For α-diazoketones (**36**) the stepwise loss of N_2 and CO, usually substantiated by appropriate metastable peaks, is characteristic[66,70,71] (Scheme 8, Table 5). The loss of



(a) $R^1 = R^2 = H$
(b) $R^1 = C_6H_5$, $R^2 = H$
(c) $R^1 = R^2 = C_6H_5$
(d) $R^1 = CH_3$, $R^2 = C_6H_5$
(e) $R^1 = CH_3OC_6H_4$, $R^2 = CH_3$

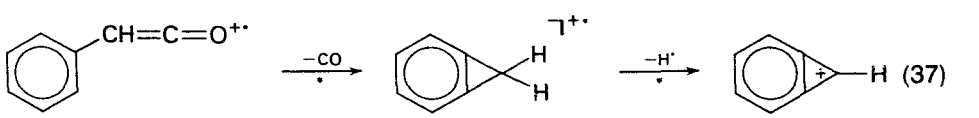
SCHEME 8

CO from the $[M - N_2]^{+\cdot}$ ions of α-diazoketones requires a rearrangement step (electron-impact induced Wolff rearrangement[70,71]).

Two mechanistic rationalizations are possible to explain this fragmentation sequence: (*i*) The elimination of N_2 yields ionized α-oxocarbenes (**ap**) as primary fragments, which then rearrange to the ketene species (**aq**). The subsequent expulsion of carbon monoxide gives the $[M - N_2 - CO]^{+\cdot}$ ions (**ar**). (*ii*) Alternatively, the rearrangement and nitrogen elimination are concerted, thus directly producing ionized ketenes (**aq**).

The relative intensity of the $[M - N_2]^{+\cdot}$ ion from 2-diazoacetophenone (**36b**) increases at lower electron energies compared to that of the benzoyl ion at *m/e* 105. It is assumed that the formation of the *m/e* 105 ion is a direct cleavage process with a high activation energy and a relatively loose activated complex. The observed energy dependence may then be interpreted in the sense that the process yielding the $[M - N_2]^{+\cdot}$ ion involves a rearrangement step with a lower activation energy and tighter transition state geometry[74]. Furthermore, a distinct metastable peak is detected for the N_2 elimination which also suggests a rearrangement process[60,74]. From these considerations the concerted mechanism (*ii*) may be favoured[71].

Very often the CO elimination is followed by loss of a hydrogen atom to produce an even-electron ion. For (**36b**) benzocyclopropene (**as**) and benzocyclopropenyl (**at**) structures have been suggested to represent the $[M - N_2 - CO]^{+\cdot}$ and $[M - N_2 - CO - H]^+$ ions, respectively[71] (reaction 37). The $[M - N_2 - CO]^{+\cdot}$ ions



(37)

(aq) (as) (at)

$R^1 = C_6H_5$, $R^2 = H$

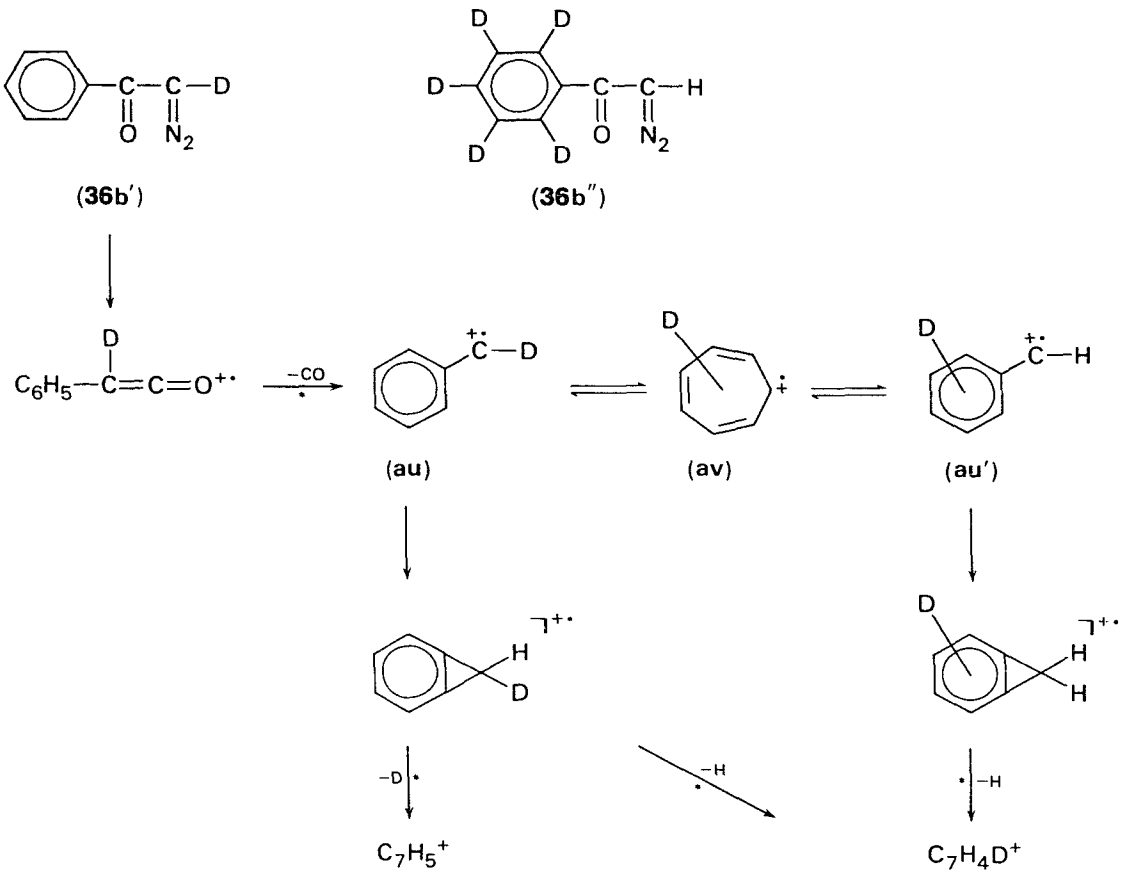
of the labelled compounds **36b′** and **36b″** expel hydrogen and deuterium in the ratio 2.6:1[72] (2:1[71]) and 1:2.7 respectively[72]. This indicates partial scrambling of the hydrogens in the $C_7H_6^{+\cdot}$ ions in competition with hydrogen elimination. The involvement

TABLE 5. Mass spectra of α-diazoketones (**36**)

Compound	R^1	R^2	*m/e* (relative intensity)					Reference
			$M^{+\cdot}$	$[M - N_2]^{+\cdot}$	$[M - N_2 - CO]^{+\cdot}$	$[M - N_2 - CO - H]^+$	Other important fragments	
36a	H	H	70 (100)	42 (51)	14 (79)	13 (17)	29 (40), 41 (28)	72
36b	C_6H_5	H	146 (100)	118 (10)	90 (72)	89 (64)	105 (65), 77 (49)	71
36c	C_6H_5	C_6H_5	221 (1)	194 (66)	166 (58)	165 (100)	164 (10), 163 (10), 139 (10)	70
36d	CH_3	C_6H_5	160 (9)	132 (49)	104 (100)	103 (84)	78 (87), 77 (46)	73

of ionized phenylcarbene (**au**) and the ring-expanded tropylidene species (**av**)[75] may explain the observed partial scrambling (Scheme 9).

In 4-methoxybenzoyldiazoethane (**36e**) the elimination of CO from the $[M - N_2]^{+\cdot}$ ion is followed by loss of $CH_3^{\cdot}$ to produce an abundant ion at *m/e* 119 ($C_8H_7O^+$), which then expels CO under formation of $C_7H_7^+$ (*m/e* 91) (Figure 10a). The same sequence in the mass spectrum of the ^{13}C-labelled derivative **36e'** yields $C_7H_7^+$, $C_8H_7O^+$ and $[M - N_2 - CO]^{+\cdot}$ ions, which still contain ca. 76% of the original ^{13}C enrichment (Figure 10b)[72]. The extensive carbon-scrambling prior to CO elimination, indicated by the carbon labelling experiment, is best rationalized by assuming the intervention of an oxirene intermediate (**aw**) formed by isomerization of the carbene-like fragment **ap** (R^1 = 4-$CH_3OC_6H_4$, R^2 = CH_3). The oxirene pathway[76] competes with the Wolff-analogue rearrangement to the carbonyl-labelled ketene species (**ax**) and is responsible for the formation of the isotopomeric ketene ion-radical (**ax'**). The further breakdown of **ax** gives rise to unlabelled fragments at *m/e* 134, 119 and 91, whereas the fragmentation of **ax'** produces the corresponding ions at *m/e* 135, 120 and 92 (Scheme 10). The loss of identity of the carbonyl and 'diazo' carbon has also been found in the [carbonyl-^{13}C]benzoyldiazomethane molecular ion[72].



SCHEME 9

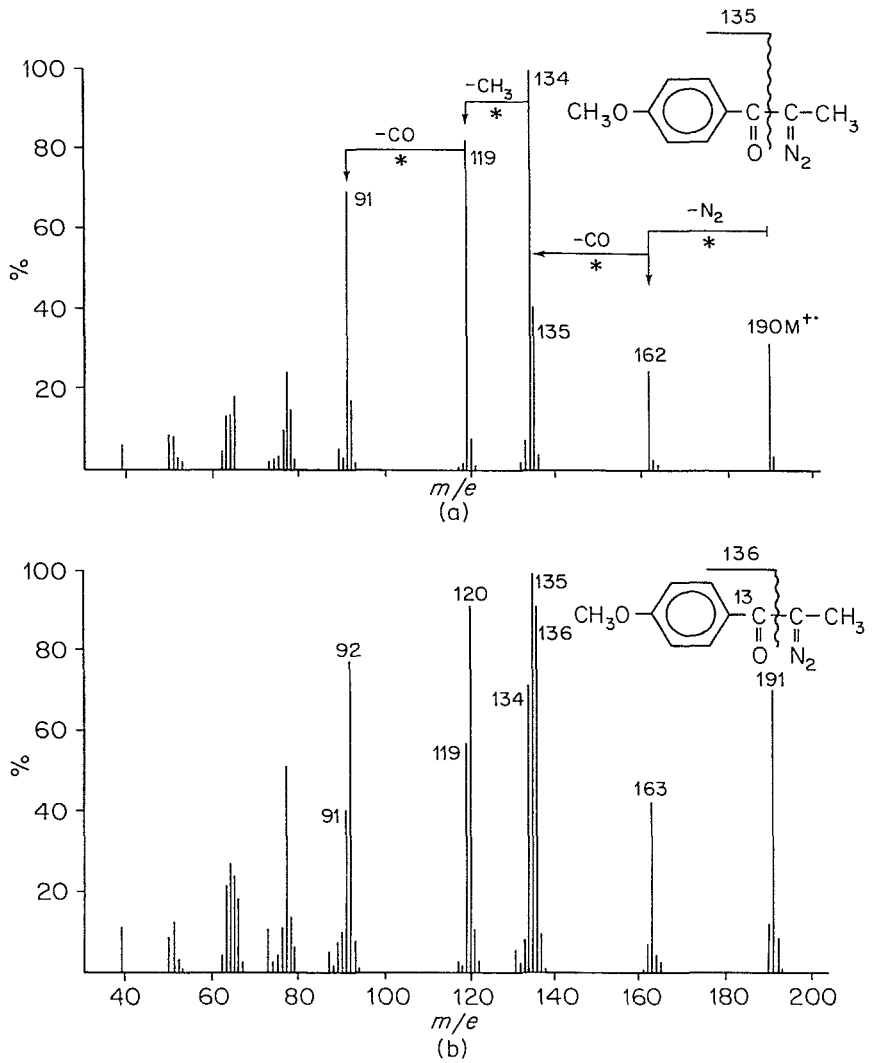
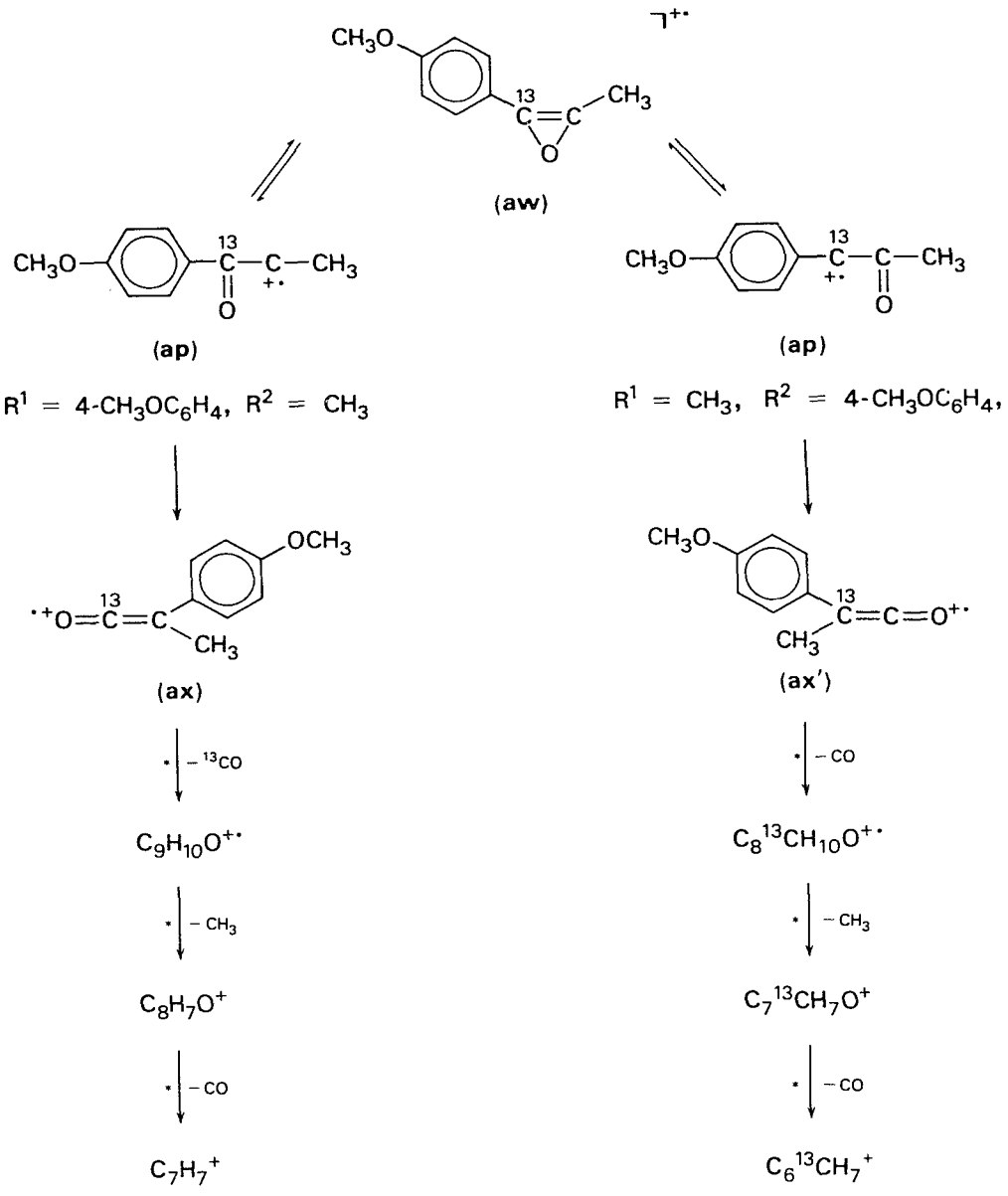


FIGURE 10. Mass spectra of (a) 4-methoxybenzoyldiazoethane and (b) [carbonyl-^{13}C]4-methoxybenzoyldiazoethane.

It should be noted that the above mechanistic rationalization for the $^{12}C/^{13}C$ positional exchange requires the formation of an ionized α-oxocarbene as the primary $[M - N_2]^{+\cdot}$ fragment. This is in contradiction to the concerted process discussed earlier. Furthermore, the above labelling results are in contrast to conclusions drawn on [carbonyl-^{13}C]azibenzil (**36c'**). In the mass spectrum of **36c'** no ^{13}C label is retained in the $[M - N_2 - CO]^{+\cdot}$ ions $(C_{13}H_{10}^{+\cdot})$[77]. This has been interpreted to exclude the intermediate formation of an ionized oxirene. However, the intensity of $M^{+\cdot}$ in the mass spectrum of azibenzil (**36c**) is extremely low (Table 5), which indicates that most of the molecules decompose thermally during introduction into the ion source. The thermal decomposition of azibenzil yields diphenylketene, which then generates the abundant $[M - N_2]^{+\cdot}$ peak by ionization. In this sequence for the formation of ionized



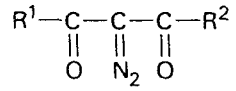
SCHEME 10

ketene, no scrambling of the ^{13}C labelling is possible since it is known that the thermal Wolff rearrangement of azibenzil proceeds without an oxirene participation[77].

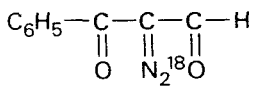
The mass spectra of 2-diazo-1,3-diketones (**37**) also show the subsequent loss of N_2 and CO (Table 6). From the $[M - N_2]^{+\cdot}$ ions of **37b**'[70,78] and **37c**'[70], the labelled and unlabelled carbonyl groups are eliminated in a 1:1 ratio. This is explained by equal migratory aptitudes of hydrogen, methyl and phenyl in the electron-impact induced Wolff rearrangement.

TABLE 6. Mass spectra of 2-diazo-1,3-diketones (**37**)

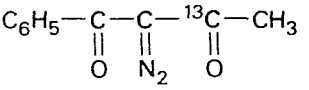
Compound	R^1	R^2	*m/e* (relative intensity) $M^{+\cdot}$	$[M - N_2]^{+\cdot}$	$[M - N_2 - CO]^{+\cdot}$	Other important fragments	Reference
37a	CH_3	CH_3	126 (5)	98 (15)	70 (6)	83 (11) $[M - CH_3CO]^+$, 43 (100) CH_3CO^+, 42 (8) $[70 - CO]^{+\cdot}$	70
37b	C_6H_5	H	174 (1)	146 (88)	118 (5)	105 (100) $C_6H_5CO^+$, 90 (22) $[118 - CO]^{+\cdot}$, 89 (25), 77 (80)	73
37c	C_6H_5	CH_3	188 (2)	160 (36)	132 (15)	118 (33) $[160 - CH_2CO]^{+\cdot}$, 105 (100), $C_6H_5CO^+$, 90 (25) $[118 - CO]^{+\cdot}$, 77 (74)	70
37d	C_6H_5	C_6H_5	250 (2)	222 (16)	194 (1)	105 (100) $C_6H_5CO^+$, 77 (52)	70



(37)

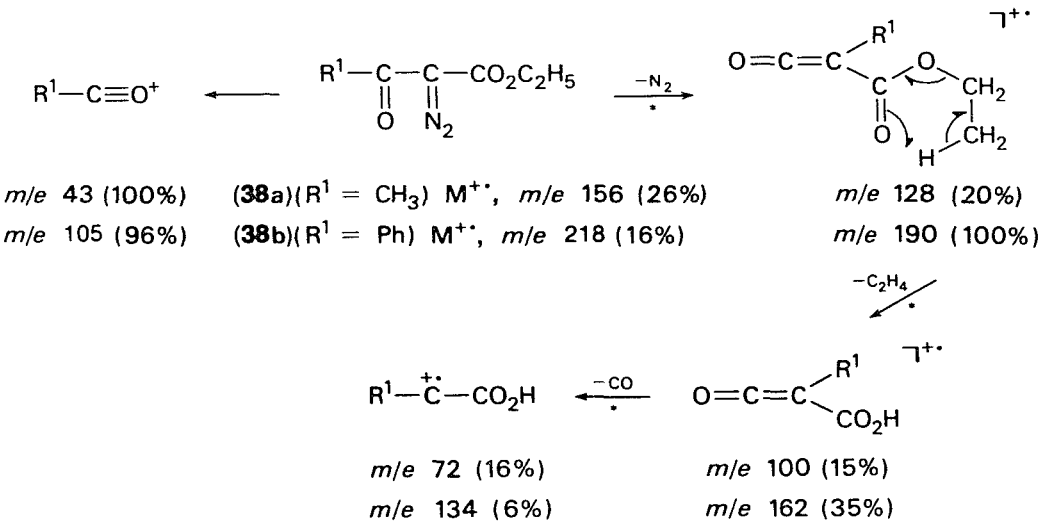


(37b')



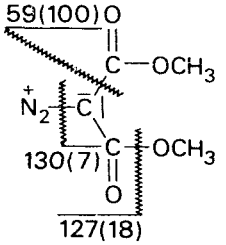
(37c')

The $[M - N_2]^{+\cdot}$ fragments of the ethyl esters of acetyldiazoacetate (**38a**) and the corresponding benzoyl compound (**38b**) do not eliminate CO[70]. By high-resolution measurements it could be shown that the loss of 28 mass units is due to ethylene expulsion. This McLafferty rearrangement is then followed by loss of carbon monoxide. Scheme 11 gives a possible decay sequence.



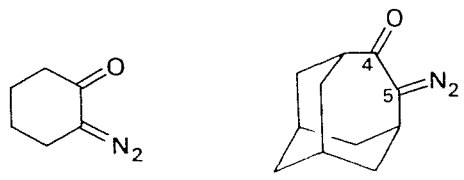
SCHEME 11

In the molecular ion of dimethyl diazomalonate (**39**) the loss of $CH_3O^{\cdot}$ and the α-cleavage process are favoured over the elimination of N_2. This is depicted in formula **39**.



(**39**)

As in open-chain α-diazoketones, the stepwise loss of N_2 and CO is also found in cyclic derivatives. ^{13}C labelling of the carbonyl group revealed that the $[M - N_2]^{+\cdot}$ ion of α-diazocyclohexanone (**40**) not only eliminates carbon monoxide but also ethylene[79]. From the isobaric $[M - N_2 - CO]^{+\cdot}$ and $[M - N_2 - C_2H_4]^{+\cdot}$ ions loss of C_2H_4 and CO, respectively, yields the base peak at *m/e* 40 ($C_3H_4^{+\cdot}$).



(40) (41)

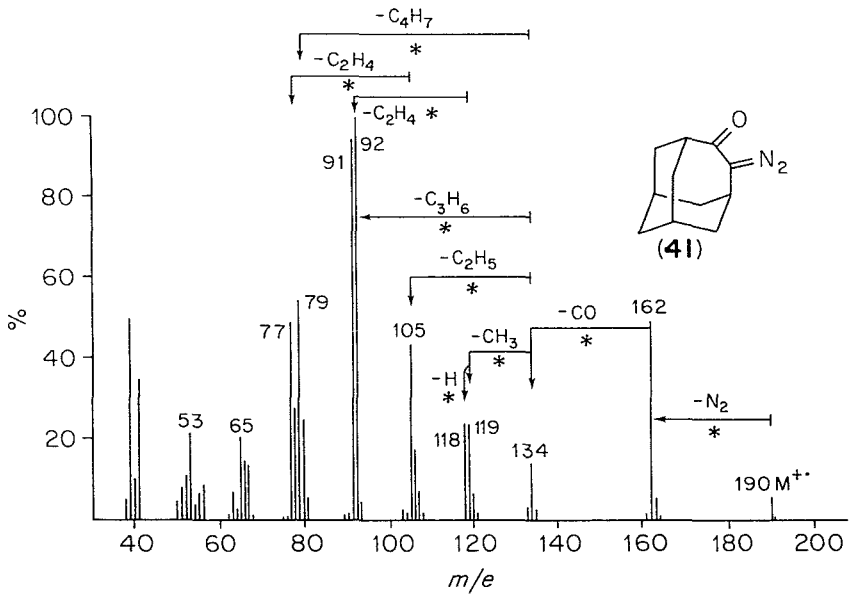


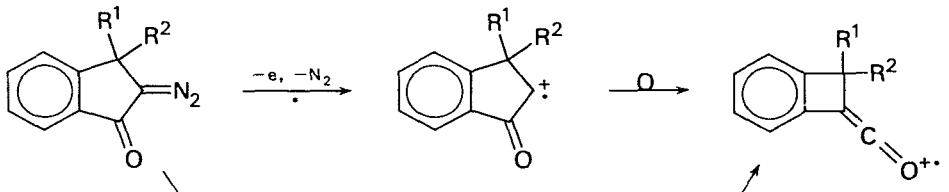
FIGURE 11. Mass spectrum of 5-diazohomoadamantan-5-one (**41**).

In the mass spectrum of 5-diazohomoadamantan-4-one (**41**) (Figure 11), the N_2 and CO expulsion is followed by the formation of a complex series of hydrocarbon fragments[72]. In accordance with the photolytic decomposition[80], the electron-impact induced fragmentation of **41**, labelled at C(5) with ^{13}C, occurs without scrambling of C(4) and C(5). This excludes the formation of a symmetrical oxirene intermediate.

The mass spectra of 3-substituted 2-diazoindan-1-ones (**42**) have been investigated with regard to a possible ring-contraction to strained ring-systems[81]. In fact, the expulsion of CO from the $[M - N_2]^{+\cdot}$ ions of **42a–d** indicates the formation of ring-contracted species **az**, either by simultaneous nitrogen elimination and rearrangement or through the α-oxocarbene ion-radical **ay** (Scheme 12). The heterocyclic systems 3-diazooxindole (**43**) and 3-diazo-2-oxothianaphthane (**44**) behave similarly[81].

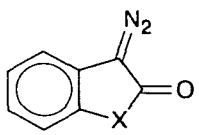
D. Diazo Oxides

The mass spectra of diazocyclohexadien-1-ones (also called diazo oxides or quinone diazides) resemble those described for α-diazoketones. This is exemplified with 6-diazo-2,4-cyclohexadien-1-one (*o*-benzoquinone diazide) (**45**)[63] (Scheme 13). The appearance potential of the $[M - N_2]^{+\cdot}$ ion decreases from 9.5 to 9.1 eV when the

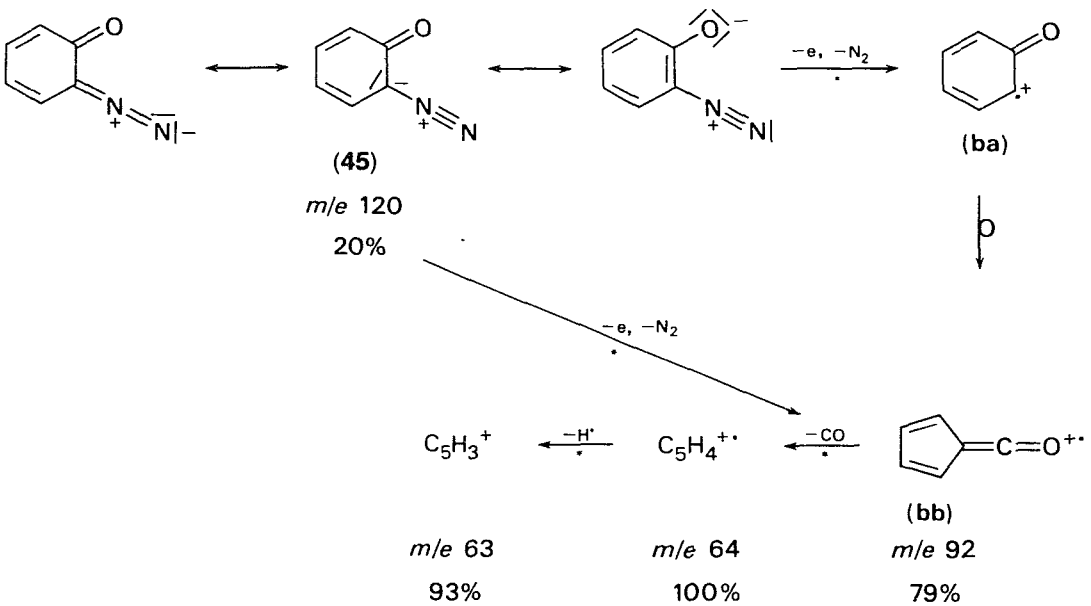


(a) $R^1 = R^2 = H$
(b) $R^1 = H$, $R^2 = CH_3$
(c) $R^1 = H$, $R^2 = C_6H_5$
(d) $R^1 = R^2 = C_6H_5$

SCHEME 12



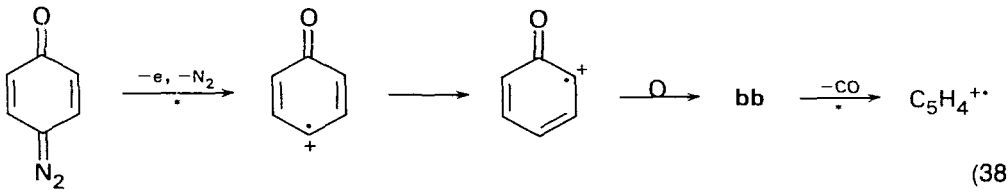
(**43**) X = NH
(**44**) X = S



SCHEME 13

source temperature increases from 50 to 200°C[82]. The value of 9.1 eV is identical with the ionization potential of fulven-6-one (9.05 eV) within experimental error. This is interpreted to mean that at lower temperatures the *m/e* 92 fragment is formed via N_2 elimination from the molecular ion, whereas at higher temperatures the nitrogen is thermally lost with production of fulven-6-one by thermal Wolff rearrangement, followed by electron-impact ionization of the neutral dediazotization product.

The mass spectrum of the *para* isomer (**46**) is qualitatively very similar to that of the *ortho* isomer[63,82]. The expulsion of CO from the $[M - N_2]^{+\cdot}$ ion may be explained by a 1,3-hydrogen shift (**bc** → **ba**) prior to skeletal rearrangement (reaction 38).

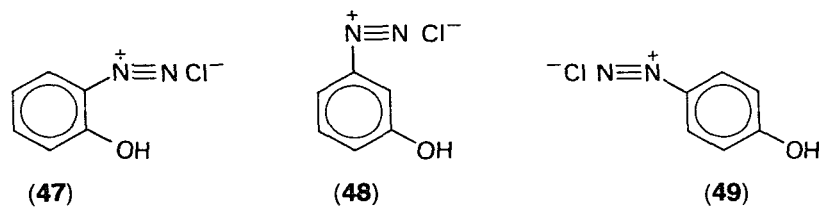


(38)

(**46**) (**bc**) (**ba**)

Both isomers (**45** and **46**) give a peak at *m/e* 94 with the elemental composition of phenol. It is assumed that this peak arises from thermal N_2 elimination followed by hydrogen abstraction at source walls.

The behaviour of the chlorides of the diazotized isomeric aminophenols (**47–49**) shows marked differences[63]. The thermally instable *meta* isomer **48** initially gives the



(**47**) (**48**) (**49**)

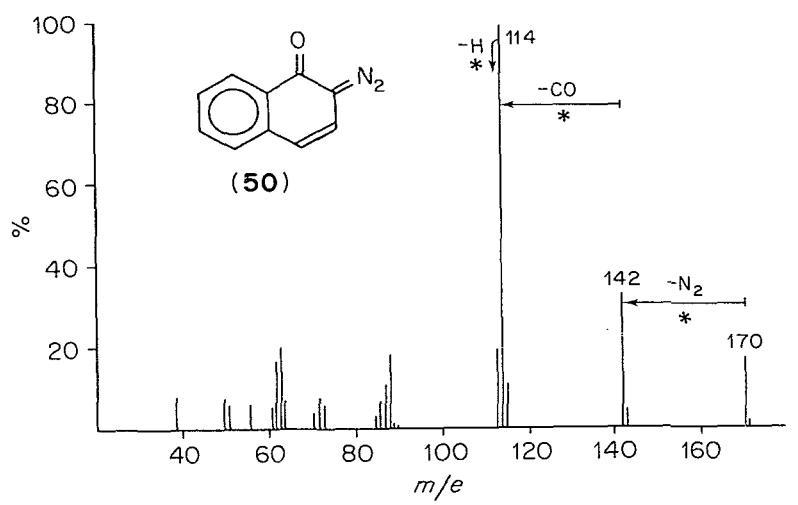
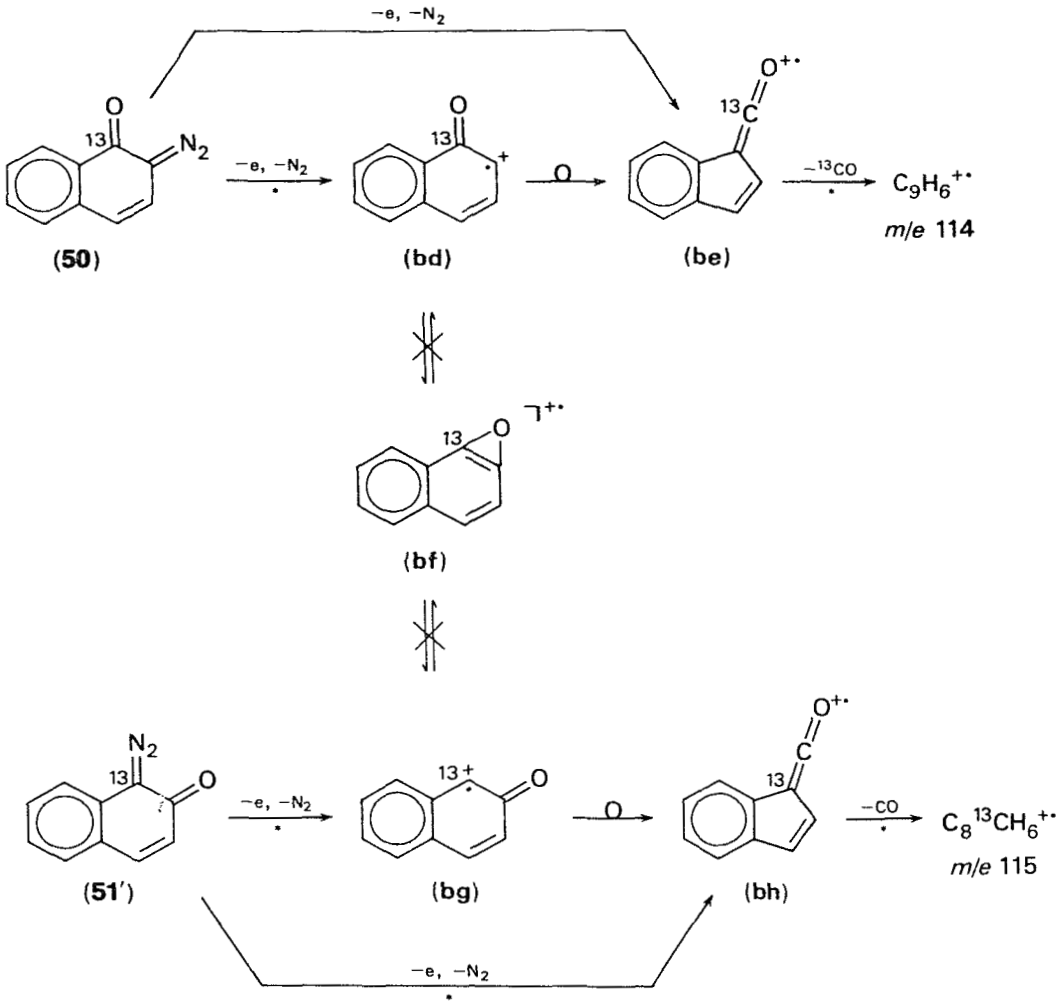
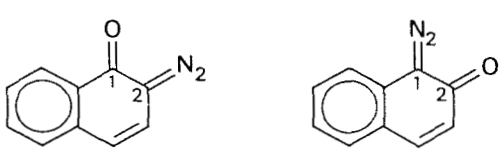


FIGURE 12. Mass spectrum of 2-diazo-1-oxonaphthalene (naphthalene-2, 1-diazoozide) (**50**).



SCHEME 14

spectrum of *m*-chlorophenol (Section IV.A) with peaks gradually appearing at *m/e* 220, 312 and 404. The latter arise from coupling products between chlorophenol and unreacted diazonium salt. In contrast, **47** and **49** give only weak signals due to thermal chloride ion substitution of the diazonium group. The main pyrolytic pathway is loss of HCl with formation of the zwitterions **45** and **46**. Thus, the mass spectra of **47** and **49** are essentially the same as described for **45** and **46**.



(**50**) (**51**)

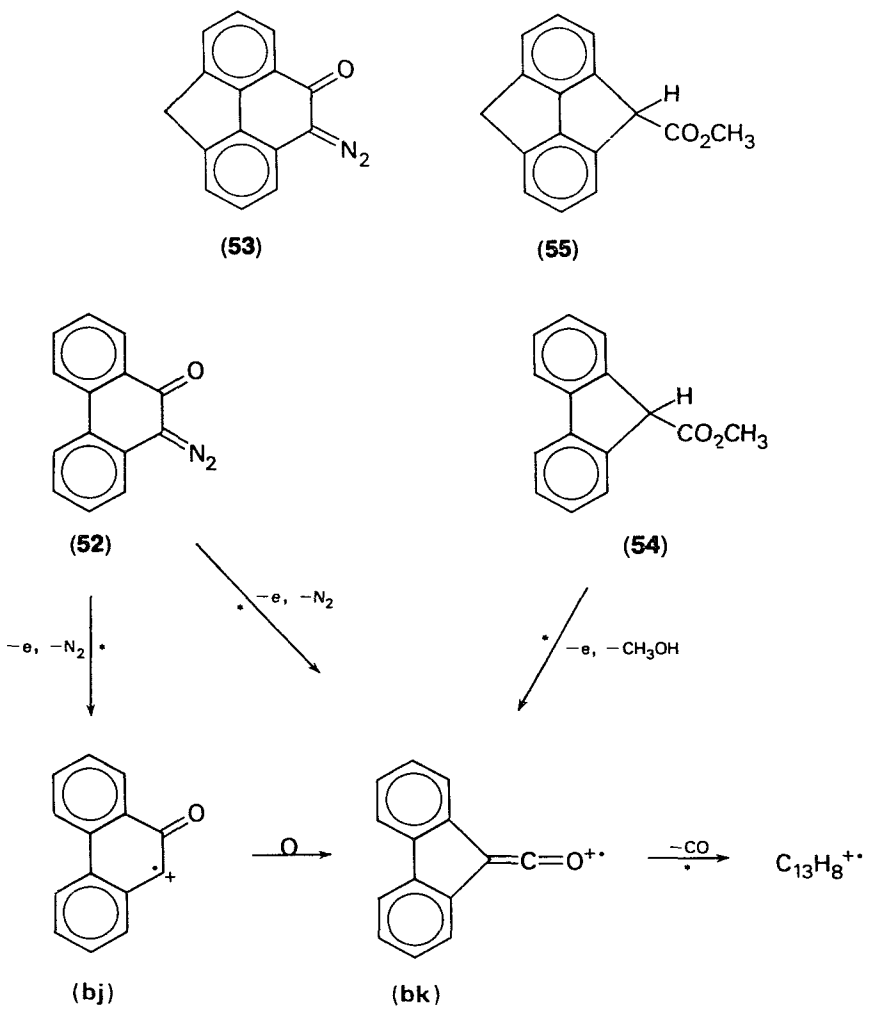
TABLE 7. Mass spectra of 9-diazo-10-oxophenanthrene (**52**) and 9-diazo-10-oxo-4,5-methylenephenanthrene (**53**)[a]

	m/e (relative intensity)					
Compound	$M^{+\cdot}$	$[M - N_2]^{+\cdot}$	$[M - N_2 - CO]^{+\cdot}$	$[M - N_2 - CO]^{++}$	$[M - N_2 - CO - H]^{+}$	$[M - N_2 - CO - C_2H_2]^{+\cdot}$
52	220 (5)	192 (21.5)	164 (100)	82 (22.1)	163 (56.4)	138 (5)
53	232 (23)	204 (87.9)	176 (100)	88 (38.4)	175 (18.5)	150 (16.7)

[a]Reproduced from P. Kinson and B. M. Trost, *Tetrahedron Letters*, 1075 (1969) by permission of Pergamon Press, Oxford.

The electron-impact induced stepwise loss of N_2, CO and $H^{\cdot}$ is repeated in the spectra of the isomeric naphthalene derivatives **50**[83] and **51**[72] (Figure 12). The question of the involvement of the naphthooxirene intermediate (**bf**) has been investigated by means of isotopic derivatives labelled at C(1) with ^{13}C (Scheme 14). The $[M - N_2 - CO]^{+\cdot}$ ion derived from **50'** contains no ^{13}C label, whereas in the same ion produced from **51'** the original label is completely retained. This excludes the formation of an oxirene species (**bf**) from the carbene-like intermediates **bd** and **bg**, respectively[84]. Thus, the behaviour of **50** and **51** is in accordance with that of 5-diazohomoadamantan-4-one (**41**), whereas open-chain α-diazoketones seem to pass through ionized oxirenes under electron-impact (Section IV.C).

Interesting results concerning the mechanism of the electron-impact induced Wolff rearrangement have been obtained with 9-diazo-10-oxophenanthrene (**52**) and 9-diazo-10-oxo-4,5-methylenephenanthrene (**53**)[85]. The main fragments are summarized in Table 7. To investigate the structure of the $[M - N_2]^{+\cdot}$ ions their metastable ion

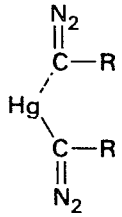


SCHEME 15

characteristics have been compared with those of ketene ion-radicals generated from the esters **54** and **55** by loss of CH_3OH. The metastable peak characteristics (relative peak height and peak width) for the CO elimination step are identical within each ester/diazo oxide pair. This strongly suggests that the $[M - N_2]^{+\cdot}$ ions derived from **52** and **53** have the same structure as the corresponding ions derived from the esters **54** and **55** (**bk**) (Scheme 15). Abundant metastable peaks are found for the transitions involving loss of nitrogen from the molecular ions. This might be suggestive that the nitrogen elimination and the skeletal rearrangement leading to ketene ion-radicals (**bk**) are concerted (Section IV.C)[60,74].

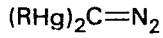
E. Metal-substituted Diazo Compounds

Usually, the intensity of the molecular ion multiplets of diazomercurials[86] are sufficiently high to determine the elemental composition by precise mass measurements. This has been used to advantage in the characterization of the newly synthesized compounds of general formula **56**[87]. The mass spectrum of mercury bis(ethyldiazoacetate) has been reported by Lorberth[88]. The bis(alkylmercury)diazoalkanes **57** give low-abundance molecular ions, which lose nitrogen. The resulting ions undergo cleavage of the Hg—C bonds[88]. The methylmercury diazo compounds **58** and **59** give molecular ions and ions due to loss of N_2[89].



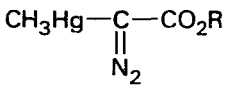
(**56**)

R = CF_3, CN, CO_2R^1



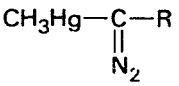
(**57**)

R = CH_3, C_2H_5



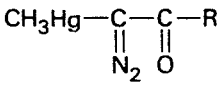
(**58**)

R = CH_3, C_2H_5, *i*-C_3H_7, *t*-C_4H_9, $C_6H_5CH_2$, C_6H_5



(**59**)

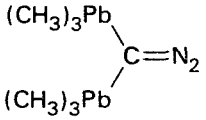
R = CN, C_2H_5



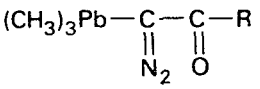
(**60**)

(a) R = CH_3

(b) R = C_6H_5



(**61**)



(**62**)

R = CH_3, C_6H_5

The mercurated diazoketones **60a** and **60b** also show a molecular ion peak[90]. Compound **60b** loses N_2 initially to give the base peak. The $[M - N_2]^{+\cdot}$ ion then expels CO, which is reminiscent of the behaviour of α-diazoketones. The methyl compound **60a** fragments first by loss of either $CH_3^{\cdot}$, N_2 or $CH_3CO^{\cdot}$. The $[M - N_2]^{+\cdot}$ ion eliminates a $CH_3^{\cdot}$ radical before CO is ejected.

The spectra of the lead-substituted diazo compounds **61**[91] and **62**[88,91] exhibit molecular ion peaks and peaks due to loss of methyl radicals and N_2. Ions may be found with masses higher than the molecular weight. This may be due to thermolytic processes during the sample introduction into the ion source.

V. REFERENCES

1. F. W. McLafferty, *Anal. Chem.*, **34**, 261 (1962).
2. H. Budzikiewicz, C. Djerassi and D. H. Williams, *Interpretation of Mass Spectra of Organic Compounds*, Holden-Day, San Francisco, 1967, Chap. 11.
3. R. Beugelmans, D. H. Williams, H. Budzikiewicz and C. Djerassi, *J. Amer. Chem. Soc.*, **86**, 1386 (1964).
4. N. C. Rol, *Rec. Trav. Chim.*, **84**, 413 (1965).
5. N. C. Rol, *Rec. Trav. Chim.*, **87**, 321 (1968).
6. W. Carpenter, Y. M. Sheikh, A. M. Duffield and C. Djerassi, *Org. Mass Spectrom.*, **1**, 3 (1968).
7. W. Heerma, J. J. de Ridder and G. Dijkstra, *Org. Mass Spectrom.*, **2**. 1103 (1969).
8. W. Heerma and J. J. de Ridder, *Org. Mass Spectrom.*, **3**, 1439 (1970).
9. W. Heerma and G. Dijkstra, *Org. Mass Spectrom.*, **3**, 379 (1970).
10. W. Heerma and C. Versluis, *Org. Mass Spectrom.*, **10**, 155 (1975).
11. S. Meyerson and G. Karabatsos, *Org. Mass Spectrom.*, **8**, 289 (1974).
12. R. G. Cooks, I. Howe and D. H. Williams, *Org. Mass Spectrom.*, **2**, 137 (1969).
13. G. P. van der Kelen and P. J. de Bièvre, *Bull. Soc. Chim. Belges*, **69**, 379 (1960).
14. J. van Thuijl, J. J. van Houte, A. Maquestian, R. Flammang and C. DeMeyer, *Org. Mass Spectrom.*, **12**, 196 (1977).
15. C. B. Theissling, N. M. M. Nibbering and S. Meyerson, *Org. Mass Spectrom.*, **11**, 838 (1976).
16. R. Wertzler and J. F. Kinder, CEC Group Report No. 54, Consolidated Engineering Corporation, Pasadena, California, 1948; cited in References 1 and 2.
17. T. W. Martin and C. E. Melton, *J. Chem. Phys.*, **32**, 700 (1960).
18. T. F. Moran and W. H. Hamill, *J. Chem. Phys.*, **39**, 1413 (1963).
19. G. A. Gray, *J. Amer. Chem. Soc.*, **90**, 6002 (1968).
20. G. Spiteller, *Massenspektrometrische Strukturanalyse Organischer Verbindungen*, Verlag Chemie, Weinheim, 1969, p. 54.
21. J. L. Franklin, Y. Wada, P. Natalis and P. M. Hierl, *J. Phys. Chem.*, **70**, 2353 (1966).
22. F. W. McLafferty, *Mass Spectrometry of Organic Ions*, Academic Press, New York, 1963, p. 318.
23. R. F. Pottie and F. P. Lossing, *J. Amer. Chem. Soc.*, **83**, 4737 (1961).
24. D. P. Stevenson, *Disc. Faraday Soc.*, **10**, 35 (1951).
25. Reference 2, Chap. 12.
26. D. Gross and J. Kelm, *Z. Naturforsch.*, **27B**, 327 (1972); in this paper a detailed discussion of the mass spectral behaviour of β-alkoxypropionitriles is given.
27. A. N. H. Yeo and D. H. Williams, *J. Amer. Chem. Soc.*, **92**, 3797 (1970).
28. K. Levsen, *Fundamental Aspects of Organic Mass Spectrometry*, Verlag Chemie, Weinheim, 1978, Chaps. IV and V.
29. J. Seibl, *Helv. Chim. Acta*, **50**, 263 (1967).
30. J. H. Beynon, R. M. Caprioli, R. G. Cooks, N. M. M. Nibbering and T. A. Molenaar-Langeveld, *Org. Mass Spectrom.*, **10**, 824 (1975).
31. K. Biemann, *Mass Spectroscopy*, McGraw-Hill, New York, 1962, p. 137.
32. N. M. M. Nibbering and T. J.de Boer, *Tetrahedron*, **24**, 1435 (1968).
33. T. A. Molenaar-Langeveld, N. M. M. Nibbering and T. J. de Boer, *Org. Mass Spectrom.*, **5**, 725 (1971).

34. J. van der Greef, T. A. Molenaar-Langeveld and N. M. M. Nibbering, *Intern. J. Mass Spectrom. Ion Phys.*, **29**, 11 (1979).
35. Metastable peaks are due to the decomposition of ions in the second field-free region of a double focusing mass spectrometer. Molecular ions reaching this region must have a mean lifetime of ca. 10^{-5} s[28].
36. A. Venema, N. M. M. Nibbering and T. J. de Boer, *Org. Mass Spectrom.*, **6**, 675 (1972).
37. A. Kalir, E. Sali and A. Mandelbaum, *J. Chem. Soc., Perkin Trans. II*, 2262 (1972).
38. H. Schwarz, *Top. Curr. Chem.*, **73**, 231 (1978).
39. R. G. Cooks, R. S. Ward and D. H. Williams, *Chem. Commun.*, 850 (1967).
40. I. Hertel and C. Ottinger, *Z. Naturforsch*, **22A**, 40 (1967).
41. R. G. Cooks, I. Howe and D. H. Williams, *Org. Mass Spectrom.*, **2**, 137 (1969).
42. J. H. Beynon, J. A. Hopkinson and G. R. Lester, *Intern. J. Mass Spectrom. Ion Phys.*, **2**, 291 (1969).
43. P. Brown, *Org. Mass Spectrom.*, **3**, 639 (1970).
44. R. D. Hickling and K. R. Jennings, *Org. Mass Spectrom.*, **3**, 1499 (1970).
45. M. A. Baldwin, *Org. Mass Spectrom.*, **14**, 601 (1979).
46. For the kinetic shift as a source of error in the determination of ΔH_f values see Reference 28, p. 221.
47. A. Cornu and R. Massot, *Compilation of Mass Spectral Data*, Heydon and Son, London, 1966.
48. H. C. Hill and R. I. Reed, *Tetrahedron*, **20**, 1359 (1964).
49. J. Seibl, *Massenspektrometrie*, Akademische Verlagsgesellschaft, Frankfurt am Main, 1970, p. 165.
50. H. Achenbach, K. Wallenfels and P. Neumann, *Chem. Ber.*, **105**, 1640 (1972).
51. G. Holzmann, H. W. Rothkopf, R. Müller and D. Wöhrle, *Org. Mass Spectrom.*, **10**, 97 (1975).
52. J. H. Bowie, R. Grigg, S.-O. Lawesson, P. Madsen, G. Schroll and D. H. Williams, *J. Amer. Chem. Soc.*, **88**, 1699 (1966).
53. A. G. Harrison and E. G. Jones, *Can. J. Chem.*, **43**, 960 (1965).
54. J. H. Bowie, R. Grigg, D. H. Williams, S.-O. Lawesson and G. Schroll, *Chem. Commun.*, 403 (1965).
55. D. H. Williams, R. G. Cooks, J. H. Bowie, P. Madson, G. Schroll and S.-O. Lawesson, *Tetrahedron*, **23**, 3173 (1967).
56. J. H. Bowie, D. H. Williams, P. Madsen, G. Schroll and S.-O. Lawesson, *Tetrahedron*, **23**, 305 (1967).
57. Reference 2, p. 417.
58. R. E. Wolff, J. T. Watson and B. J. Sweetman, *Tetrahedron Letters*, 2719 (1970).
59. R. G. Gillis and J. L. Occolowitz, *J. Org. Chem.*, **28**, 2924 (1963).
60. F. W. McLafferty and R. B. Fairweather, *J. Amer. Chem. Soc.*, **90**, 5915 (1968).
61. B. Zeeh, *Org. Mass Spectrom.*, **1**, 315 (1968).
62. A. N. H. Yeo, R. G. Cooks and D. H. Williams, *Org. Mass Spectrom.*, **1**, 910 (1968).
63. K. Undheim, O. Thorstad and G. Hvistendahl, *Org. Mass Spectrom.*, **5**, 73 (1971).
64. A. Langer, J. A. Hipple and D. P. Stevenson, *J. Chem. Phys.*, **22**, 1836 (1954).
65. G. S. Paulett and R. Ettinger, *J. Chem. Phys.*, **39**, 825 (1963).
66. A. Foffani, S. Pignataro, B. Cantone and F. Grasso, *Nuovo Cimento*, **29**, 918 (1963); *Chem. Abstr.*, **60**, 98h (1964).
67. J. L. Franklin, J. G. Dillard, H. M. Rosenstock, J. T. Herron, K. Draxl and F. H. Field, *Ionization Potentials, Appearance Potentials and Heats of Formation of Gaseous Positive Ions*, National Bureau of Standards, Washington, D.C., 1969, p. 28.
68. Due to an error in the calculations very similar values for the heats of formation of ionized diazomethane and diazirine are reported (159 and 155 kcal/mol, respectively)[65].
69. D. Schumann, E. Freese and A. Schönberg, *Chem. Ber.*, **102**, 3192 (1969).
70. K.-P. Zeller, H. Meier and E. Müller, *Justus Liebigs Ann. Chem.*, **749**, 178 (1971).
71. C. W. Thomas and L. L. Leveson, *Org. Mass Spectrom.*, **13**, 39 (1978).
72. K.-P. Zeller, unpublished results.
73. K.-P. Zeller, *Doctoral Thesis*, University of Tübingen, 1972.
74. Reference 28, pp. 92 and 179.
75. The interconversion of neutral phenylcarbene into tropylidene is a well-documented process; e.g. C. Wentrup, *Top. Curr. Chem.*, **62**, 173 (1976).

76. In the photochemical Wolff rearrangement of α-diazoketones the involvement of oxirenes has also been evidenced; e.g. K.-P. Zeller, *Chem. Ber.*, **112**, 678 (1979).
77. K.-P. Zeller, H. Meier and E. Müller, *Chem. Ber.*, **105**, 1875 (1972).
78. K.-P. Zeller, H. Meier and E. Müller, *Tetrahedron*, **28**, 5831 (1972).
79. U. Timm, *Doctoral Thesis*, University of Tübingen, 1978.
80. K.-P. Zeller, *Z. Naturforsch.*, **31B**, 5861 (1976).
81. D. C. DeJongh, R. Y. van Fossen, L. R. Dusold and M. P. Cava, *Org. Mass Spectrom.*, **3**, 31 (1970).
82. O. Thorstad, K. Undheim and G. Hvistendahl, *Org. Mass Spectrom.*, **9**, 548 (1974).
83. K.-P. Zeller, *Org. Mass Spectrom.*, **10**, 317 (1975).
84. The absence of an oxirene participation could also be demonstrated in the photochemical decomposition of **50** and **51**; K.-P. Zeller, *Chem. Ber.*, **108**, 3566 (1975).
85. P. Kinson and B. M. Trost, *Tetrahedron Letters*, 1075 (1969).
86. Natural mercury is a mixture of the following isotopes: 196 (0.15%), 198 (10.02%), 199 (16.84%), 200 (23.13%), 201 (13.22%), 202 (29.80%), 204 (16.85%). Mercury-containing ions therefore yield characteristic multiplets.
87. T. DoMinh, O. P. Strausz and H. E. Gunning, *Tetrahedron Letters*, 5337 (1968).
88. J. Lorberth, *J. Organomet. Chem.*, **27**, 303 (1971).
89. S. J. Valenty and P. S. Skell, *J. Org. Chem.*, **38**, 3937 (1973).
90. J. Lorberth, F. Schmock and G. Lange, *J. Organomet. Chem.*, **54**, 23 (1973).
91. R. Gruning and J. Lorberth, *J. Organomet. Chem.*, **78**, 221 (1974).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 4

Infrared spectra of cyano and isocyano groups

I. N. JUCHNOVSKI and I. G. BINEV
Institute of Organic Chemistry, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria

I. INTRODUCTION

This chapter deals with the basic relationships of infrared frequencies and intensities of cyano and isocyano groups bonded to carbon atoms, with the structure of the corresponding compounds. Special attention is given to the data on negatively charged ions, as anion-radicals, carbanions and dianions containing nitrile groups, reported mainly after 1970.

At the present time a strict quantitative analysis of the spectrum/structure relationships is possible only for a small number of models. Thus, qualitative interpretations of

the empirical correlations between infrared characteristics and parameters reflecting the molecular structure are presented in most cases.

The integrated intensity data cited here are reported in the so-called 'IUPAC practical units'[1].

II. NITRILES

A. General

The bands corresponding to the nitrile stretching vibration, $\nu(C{\equiv}N)$, can be found in the frequency region of 1900–2400 cm^{-1}; data on $\nu(C{\equiv}N)$ band frequencies and intensities are summarized in monographs[2–4].

The characteristic properties of the $\nu(C{\equiv}N)$ vibration, with respect to both frequency and mode, have been studied by the methods of normal coordinate analysis[5–8]. These studies, together with numerous subsequent works on various compounds containing cyano groups, show that the $\nu(C{\equiv}N)$ vibration mode is characteristic of the whole linear group C—C≡N, not only of the C≡N group, because of the participation of the adjacent bond C—CN; the participation of other internal coordinates in the $\nu(C{\equiv}N)$ mode is not, as a rule, essential. Thus, the $\nu(C{\equiv}N)$ frequency variations are usually determined by the changes in the force constants of both C≡N and C—CN bonds. The values describing $\nu(C{\equiv}N)$ changes caused by variations in the force constants of the group C—CN in the case of acetonitrile [$\nu(C{\equiv}N)$ = 2266 cm^{-1}], for example, are as follows*:

$$\partial\nu(C{\equiv}N)/\partial k(C{\equiv}N) = 55\ mdyn^{-1}cm^{-1}\ Å$$

$$\partial\nu(C{\equiv}N)/\partial k(C{-}CN) = 25\ mdyn^{-1}cm^{-1}\ Å$$

Increasing the mass of the atom X in the group X—C≡N from 12 to 100 atomic units results in a $\nu(C{\equiv}N)$ decrease of 9 cm^{-1} only, i.e. the mass effect of the X atom on $\nu(C{\equiv}N)$ is not dominant. Changes in the chemical nature of the atom X, however, are accompanied by considerable k(X—CN) variations, thus, the effect of these changes on $\nu(C{\equiv}N)$ can be quite large. The relative increases or decreases in $\nu(C{\equiv}N)$ in the latter cases cannot be considered as a measure of the variations in the force constant $k(C{\equiv}N)$. In series of related compounds when X is constant, e.g. aliphatic or aromatic nitriles [cases meeting the condition of relatively small k(C—CN) changes], the $\nu(C{\equiv}N)$ variations follow, as a rule, the corresponding changes in the C≡N bond force constant.

As the $\nu(C{\equiv}N)$ mode is characteristic of the C—C≡N group, the variations in the intensity of the corresponding infrared bands are determined by the polar properties of both the C≡N and the next bond[6]. The infrared data for various nitrile compounds are classified in the present review according to the type of the carbon atom adjacent to the C≡N group.

B. Saturated Aliphatic Nitriles (C_{sp^3}-bonded C≡N Groups)

1. *Frequencies*

It is well known that the $\nu(C{\equiv}N)$ band in the infrared spectra of saturated nitriles is located in a relatively narrow frequency interval, 2230–2280 cm^{-1} (Tables 1 and 2).

*These values were calculated by using the acetonitrile force field given by Dunkan and coworkers[9] and the terms which relate the changes in the characteristic frequencies to the variations in both the force constants and frequency modes[10].

TABLE 1. Apparent fundamental frequencies (cm^{-1}) of CH_3CN, $CH_3C^{15}N$ and CD_3CN in their infrared spectra

	CH_3CN		$CH_3C^{15}N$		CD_3CN	
Assignment	Gas[a]	Liquid[b]	Gas[a]	Liquid[b]	Gas[a]	Matrix isolated[d]
ν_1; $\nu^s(CH_3)$ or (CD_3)	2953.92	2945	2953.76	2945	2127.35	2122.1
ν_2; $\nu(C\equiv N)$	2266.45	2256	2240.30	2225	2277.88	2267.3
ν_3; $\delta^s(CH_3)$ or (CD_3)	1390.0	1378	1390.0	1376	1110.0	1104.7
ν_4; $\nu(C-C)$	919.92	918	911.21	910	831.33	829.1
ν_5; $\nu^{as}(CH_3)$ or (CD_3)	3009.16	3000	3009.16	3000	2256.56	2253.7
ν_6; $\delta^{as}(CH_3)$ or (CD_3)	1448.03	1444	1447.85	1444	1046.45	1040.1
ν_7; $r(CH_3)$ or (CD_3)	1040.79	1040	1040.68	1040	847.11	845.5
ν_8; $\beta(CCN)$	364.71	379	362.10	377[c]	334.80	338.8

[a]Ref. 9.
[b]Ref. 11.
[c]Calculated, see Ref. 11.
[d]Ref. 14.

The vibrational spectrum of acetonitrile is the most studied and best interpreted[9,10] among all spectra of saturated nitriles. Assignments of the fundamental vibrational modes of this molecule and its isotopomers $CH_3C^{15}N$ and CD_3CN are reported in Table 1. The detailed analysis of the infrared spectra of acetonitrile, and D-, ^{15}N- and ^{13}C-labelled acetonitriles shows[9,10] that many of the fundamental frequencies of this molecule are perturbed by Fermi resonances. For example, the ν_2 frequency ($C\equiv N$ stretch) resounds with the combination $\nu_3 + \nu_4$; the latter is present in the spectra of all

TABLE 2. Frequencies (cm^{-1}) of the $\nu(C\equiv N)$ bands of substituted acetonitriles[a]

		Solvent	
Compound	Gas phase	CCl_4	$CHCl_3$
CH_3CN	2267	2255.2[e]	2255.7
CH_3CH_2CN	2265	2249.0	2249.9
$(CH_3)_2CHCN$	2264	2249.2	2246.5
$(CH_3)_3CCN$	2254	2238.8	2235.3
FCH_2CN	2269[b]	2255.7[e]	—
F_3CCN	2274.1[c]	—	—
$ClCH_2CN$	2266	2259.7	—
Cl_2CHCN	2261[d]	—	—
Cl_3CCN	2256[d]	2250.5[f]	2251.5[f]
$BrCH_2CN$	2264[b]	—	—
CH_3OCH_2CN	—	2243[e]	—
$(CH_3)_2NCH_2CN$	—	2232.5	—

[a]Data taken from Ref. 32 unless otherwise stated.
[b]Ref. 33.
[c]Ref. 34.
[d]Ref. 35.
[e]Ref. 29.
[f]Ref. 36.

the isotopomers (except the deuterated compounds) as a moderate band at 2300 ± 6 cm^{-1}. As a result of this coupling the apparent $\nu(C{\equiv}N)$ values are lower than the unperturbed ones. The quantitative estimation of the coupling effects[9] show 2270.6 and 2243.1 cm^{-1} as unperturbed $\nu(C{\equiv}N)$ values of CH_3CN and $CH_3C^{15}N$ (in gas phase), respectively. The frequencies of the six acetonitrile isotopomers, corrected with respect to Fermi resonances and unharmonicities, together with the Coriolis zeta and centrifugal distortion constants, have been used to determine the harmonic force field of acetonitrile[9]. It was found that the C≡N force constant of acetonitrile [$k(C{\equiv}N)$ = 18.40 mdyn $Å^{-1}$] is lower than that of HCN [$k(C{\equiv}N)$ = 18.70 mdyn $Å^{-1}$][12], probably because of the polarizing effect of the methyl group on the π system of the C≡N bond. The empirical force constants of CH_3CN thus obtained are in a fair agreement with those expected on the basis of *ab initio* calculations (see Reference 9 and the data cited therein). The force field suggested by Dunkan and coworkers[9] was refined later[13] without substantial variation.

Complete assignments of the bands in the vibrational spectra have been reported[15–21] for propionitrile[15,21], *n*-butyronitrile[16,17], *i*-butyronitrile[18] and trimethylacetonitrile[15,19,20]. The out-of-plane and in-plane bending vibrations, $\delta(C{-}C{\equiv}N)$, in the saturated nitriles give rise to bands in the 355–400 cm^{-1} and 170–230 cm^{-1} regions[16,17,21]; these bands are sensitive to conformational variations.

Many relationships of more or less general validity were found between the $\nu(C{\equiv}N)$ and the structure of saturated nitriles. Lengthening the alkyl chain or increasing the number of the α-methyl groups results in a fairly smooth decrease in $\nu(C{\equiv}N)$ in the 2255–2238 cm^{-1} region (solvent CCl_4); this decrease has been ascribed mainly to the decrease in the $k(C{\equiv}N)$ force constant[22].

The $\nu(C{\equiv}N)$ were found to increase with the decrease in the dipole moment in a series of aliphatic nitriles[23]; a linear correlation of $\nu(C{\equiv}N)$ with the Taft's σ^* constants was found in a limited series of monosubstituted acetonitriles[24] (equation 1):

$$\nu(C{\equiv}N) = (2250 + 7.4\,\sigma^*)\ cm^{-1} \qquad (1)$$

The decrease in $\nu(C{\equiv}N)$ with increasing the number of methyl groups at the α-carbon atom of acetonitriles and the peculiar $\nu(C{\equiv}N)$ variations of the chlorinated acetonitriles (Table 2) have been ascribed[8] to the inductive effects of the substituents: the positive inductive effect of the methyl groups gradually reduces the C≡N bond order, and in the latter case, because of the reversing of the C≡N bond polarity, the C≡N bond order, and consequently the $\nu(C{\equiv}N)$, increases, reaches a maximum value and decreases again.

It has been found that the $\nu(C{\equiv}N)$ is strongly sensitive to the presence of resonative electron donors bonded to the α-carbon atom[25,26]. The decreases in $\nu(C{\equiv}N)$, caused by α-substituents such as $(CH_3)_2N$, H_2N and CH_3O, are even stronger than those found in benzonitriles with the same substituents in the *para* position (see Section II.C.1). This peculiar frequency effect cannot be found in other characteristic electron-withdrawing groups (e.g. various carbonyl groups); it is not caused by overlap between the free electron pairs of the substituents and the cyano group, but it can be ascribed to *sùi generis* interaction of the substituents with the methylene group[25,26]. This explanation agrees with the structural data for piperidinoacetonitrile[27], with the presence of *trans* rotamers only for aminoacetonitrile[31], and with the fact that the intensities $A(C{\equiv}N)$ in these cases are even lower than that of acetonitrile (cf. Section II.B.2).

The substituent effects on the $\nu(C{\equiv}N)$ of monosubstituted acetonitriles have been studied more recently[28,29] by means of dual-parameter correlation equations, which include inductive and resonance terms. The results confirm the considerable role of

the resonance effects of the α-substituents, showing that they are close to inductive effects in importance. The ν(C≡N) of β-substituted propionitriles lie in a narrow frequency interval, 2249–2258 cm^{-1} in CCl_4, and they depend, in general, on the inductive ability of the substituents[29].

The normal coordinate analysis of mono-halogen-substituted acetonitriles shows that the gradual ν(C≡N) decrease in the order F, Cl, Br, I is due mainly to the lowering of the C≡N force constant[30].

The presence of two geminal cyano groups in malononitrile derivatives results in some ν(C≡N) increase [ν(C≡N) of malononitrile is 2272 cm^{-1}, solvent chloroform][29], which can be related to the mutual inductive influence of these groups. This influence fades away with the increase of n in the compounds $NC(CH_2)_nCN$ and when $n > 4$ ν(C≡N) values practically coincide with those of the aliphatic mononitriles[35]. A mutual inductive influence of cyano groups was found also in the infrared spectra of the model 2,4,6-tricyanoheptane, which showed the same ν(C≡N) as polyacrylonitrile[41]. The normal coordinate analysis of malononitrile and its alkyl and halogen derivatives[23,37–39] showed that the force constants k(C≡N) are in fact higher than those of mononitriles.

In spite of the presence of two geminal C≡N groups in the malonitrile derivatives, the frequencies corresponding to the *syn* phase, ν^s(C≡N), and *anti* phase, ν^a(C≡N), modes practically coincide[39] or their difference is 3–7 cm^{-1} only[38,40]. The mutual inductive influence is further enhanced in tetracyanomethane, and its ν(C≡N) are higher: 2276 cm^{-1} (infrared) and 2288 cm^{-1} (Raman)[42].

Hence, the known data show that the frequency ν(C≡N) of C_{sp^3}-bonded nitrile groups is sensitive to both resonance and inductive effects of the α-substituents. The effects of the β-substituents are mainly inductive; the inductive influence of the substituents fades away with the lengthening of the distance between the nitrile group and the substituents.

2. *Intensities*

Studies on the integrated intensity of the ν(C≡N) band, A(C≡N), of compounds containing C_{sp^3}-bonded nitrile groups have shown that this intensity varies from practically zero to ca. 600 IUPAC units (l mol^{-1} cm^{-2}). Lengthening the alkyl chain is accompanied with a gradual and fading increase in A(C≡N)[35]. Increasing the number of methyl groups at the α-carbon atom also results in a slight A(C≡N) increase[43]. Heteroatomic substituents in the α-position cause, as a rule, strong A(C≡N) decreases[29,35,43,44]. The effects of the same substituents in the β-position are similar, but considerably weaker[29]. A(C≡N) of monohalogenated acetonitriles decreases with increase in the electronegativity of the halogen [substituent, A(C≡N) in l mol^{-1} cm^{-2}]: H, 344; I, 323; Br, 145; Cl, 40; F, 55 (solvent $CHCl_3$)[44]. A(C≡N) of α-alkoxy-[29,45] and alkylammonio-acetonitriles[46] is extremely low; the ν(C≡N) bands in these cases are practically unobservable. A(C≡N) of methoxyacetonitrile was found to increase strongly in the solvents dimethylsulphoxide and *i*-propanol, as well as with the rise in temperature[47].

Substituents of the type ArS— and ArSe— in the α-position do not hinder the registration of the ν(C≡N) band[45]; A(C≡N) of glycidonitriles[48] are close to that of acetonitrile.

A(C≡N) values, taken as log$A$(C≡N), of monosubstituted acetonitriles correlate approximately[49] with Taft's σ^* constants; in the small series of compounds $(CH_3)_nCH_{3-n}CN$ [when n = 0, 1, 2 and 3, A(C≡N) is 88, 112, 125 and 146 l mol^{-1} cm^{-2}] this correlation is satisfactory[43]. A(C≡N) in the series $Cl_nCH_{3-n}CN$ reaches a minimum value at n = 1 [n, A(C≡N) in IUPAC units]: 0, 63; 1, 34; 2, 270; 3, 463

(gas-phase data)[35]. A minimum was also found in the correlation of $A(C{\equiv}N)$ in a series of disubstituted malonitriles with the sum of Taft's constants $\Sigma\sigma^*$ of the α-substituents[50]. This result agrees with the extremely low $A(C{\equiv}N)$ values of monoalkylmalononitriles[51].

By contrast to the corresponding frequencies[29], the statistical treatment of $A(C{\equiv}N)$ of monosubstituted acetonitriles by a dual-parameter equation with inductive and resonance terms gave a poor correlation [substituent, $A(C{\equiv}N)$ in 1 mol^{-1} cm^{-2}]: H, 189, CH_3 456; $(CH_3)_2N$, 44.7; F, 359; Cl, 13.5; CN, 79.5; CO_2CH_3, 54.3 (solvent CCl_4, at infinite dilution)[29].

The qualitative interpretation of the substituent effects on the $A(C{\equiv}N)$ of C_{sp^3}-bonded nitrile groups assumes lowering of both the polarity of the C≡N bond and the dipole moment derivative in presence of electron-withdrawing substituents[35,43,44]; in the case of trichloroacetonitrile this effect causes a C≡N polarity reversal and, hence, an increase in $A(C{\equiv}N)$. The model calculations of dipole moment derivatives of $(CH_3)_nCH_{3-n}CN$ and $Cl_nCH_{3-n}CN$ (n = 0–3), carried out by the Pariser–Parr–Pople (P.P.P.) method, did involve the same assumption: they accounted for the vibrator C≡N only, and the results qualitatively agreed with the experimental data.

On the basis of both valency–optical theory and analysis of the C≡N vibration mode, Roshchupkin and Popov[6b] and Gribov[52] concluded that the $A(C{\equiv}N)$ increase from acetonitrile to trichloroacetonitrile cannot be related to some essential variation in the polar properties of the C≡N group; they attributed the increase to changes in the electrooptical parameters of the C—CN bond, which bond takes an essential part in the $\nu(C{\equiv}N)$ vibration. The $A(C{\equiv}N)$ variations in the series n-$C_nH_{2n+1}CN$ and $NC(CH_2)_nCN$ were also found to be due mainly to changes in the properties of the next bond, C—CN[52].

On the basis of an *ab initio* study of the dipole moment derivatives of chloroacetonitriles $Cl_nCH_{3-n}CN$, Figeys and coworkers[53] concluded (in contrast to the above cited authors[6b,52]) that the $A(C{\equiv}N)$ variations can nevertheless be related to the changes in the C≡N group polar properties. The results, however, are in only partial agreement with the experimental data, predicting a smooth $A(C{\equiv}N)$ increase with the increase in the number of chlorine atoms, while the experimental data (although obtained under different conditions[29,35,43,44]), showed a sharp $A(C{\equiv}N)$ decrease in the case of monochloroacetonitrile. The same study[53] showed that increasing the number of chlorine atoms results in a decrease in the C≡N equilibrium bond moment, but not to its reversal, which is in agreement with Gribov's concept. Thus, the authors[53] criticized the interpretation of Besnainou, Thomas and Bratož[8], who assumed a C≡N polarity reversal in Cl_3CCN and did not account for the contribution of the C—CN bond in the $A(C{\equiv}N)$ variations.

Hence, the variations in $A(C{\equiv}N)$ values of saturated nitriles are not a simple function of the electronic effects of the substituents; they depend on the variations in the polar properties of both C≡N and C—CN bonds, and it seems that the first is playing a more important role.

C. Conjugated Nitriles

1. Frequencies

The frequencies $\nu(C{\equiv}N)$ of conjugated nitriles are, as a rule, lower than those of C_{sp^3}-bonded nitriles; they lie in the 2250–2190 cm^{-1} interval, and in presence of negatively charged substituents the lower limit of this interval is shifted to ca. 2120 cm^{-1}.

The $\nu(C{\equiv}N)$ decrease is due mainly to the decrease in the force constant of the

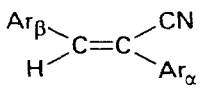
C≡N bond, caused by the conjugation. Further, the increase in the coupling constant k(CN, CC) resulting from the delocalization[54] provokes another ν(C≡N) decrease. On the other hand, the C_{sp^2}—CN bond is shorter than the C_{sp^3}—CN one[54] and, hence, the force constant C_{sp^2}—CN is higher than that of the saturated nitriles. The latter factor should lead to some ν(C≡N) increase. The resulting effect, *viz.* the experimentally found ν(C≡N) decrease, points to the dominating role of the first two factors. According to the comparable results of the normal coordinate analysis of acetonitrile[6a] and acrylonitrile[54], the contribution of the k(C≡N) force constant lowering is the most essential; the lower ν(C≡N) value of acrylonitrile (2232 cm^{-1} in CCl_4) is determined mainly by the k(C≡N) lowering. This conclusion qualitatively agrees with the normal coordinate analysis of benzonitrile[55].

The infrared spectra of certain simple conjugated nitriles, *viz.* acrylonitrile[56], 2-cyanopropene and 2-cyanopropene-d_5[57], 2-chloroacrylonitrile[58], and *trans*- and *cis*-crotononitrile[59] have been well studied and interpreted. ν(C≡N) was found in these cases in the 2227–2242 cm^{-1} region, and ν(C—CN) was found to appear as a band of variable intensity among 860 and 900 cm^{-1} (gas-phase data). The bands corresponding to the in-plane and out-of-plane bending modes of the C—C≡N group in these compounds were detected near 200 and 300 cm^{-1}, respectively[56–59].

The vibrational spectra of benzonitrile[55–60] and substituted benzonitriles[61–64], isomeric dicyanobenzenes[63–65], cyanopyridines[66] and furonitriles[67] have been thoroughly studied and interpreted. The ν(C—CN) bands were found near 1200 cm^{-1}, but this vibration is often coupled with other skeletal modes, similarly to the C—C≡N bendings, whose bands lie under 600 cm^{-1}.

The ν(C≡N) values of conjugated nitriles fall smoothly with the increase in the conjugation between the cyano group and the moiety. Figeys-Fauconnier and coworkers[68] found a correlation between the ν(C≡N) of some polycyclic nitriles and the coefficients of the nonbonding π molecular orbital of the corresponding uneven alternant radicals. The ν(C≡N) in the series S—CH=CH—CN [substituent S, ν(C≡N) in cm^{-1}]: H, 2232; *trans*-Ph, 2222; *trans,trans*-PhCH=CH, 2217; *all-trans*-$Ph(CH{=}CH)_n$, 2215.5; *trans*-CH_2=CH, 2220; *trans*-2-naphthyl, 2221, linearly correlate with both the localization energy of the carbon atom of the corresponding hydrocarbon which is bonded to the cyano group[69] and the C≡N bond order [P(C≡N)], calculated[70] by Hückel's method (HMO). Similar correlations have been found in the case of aromatic polycyclic nitriles [the ν(C≡N) values are listed in Table 3].

It has been found[69,70] that the ν(C≡N)/HMO P(C≡N) correlation for polyenic nitriles does not coincide with that for aromatic nitriles, when the alternation of the bond lengths in the polyenic systems is not taken into account. The ν(C≡N)/HMO P(C≡N) correlation has been used to estimate the steric hindrance in a series of *trans*-α,β-diarylacrylonitriles[72,73] (**1**). Twisting of the substituents Ar_α is accompanied by



(**1**)

Ar_α = Ph, 1-naphthyl, 2-naphthyl

Ar_β = Ph, 1-naphthyl, 2-naphthyl, 1-pyrenyl, 9-anthryl

ν(C≡N) decreases; on the contrary, twisting of Ar_β causes ν(C≡N) increases, both in agreement with the HMO P(C≡N) data[72,73]. The examples given show that in spite of their small variations, ν(C≡N) frequencies of conjugated nitriles without heterosubstituents can be considered as a measure of the moiety/cyano group conjugation.

The substituent effects on ν(C≡N) of substituted benzonitriles have been the subject of a series of investigations (see, for example, References 49, 74–80 and the

TABLE 3. Frequencies (cm^{-1}) and integrated intensities ($l\ mol^{-1}\ cm^{-2}$) of the $\nu(C{\equiv}N)$ bands of some aromatic nitriles (solvent CCl_4)[69,70]

Compound	$\nu(C{\equiv}N)$	$A(C{\equiv}N)$
Benzonitrile	2231	856
3-Cyanobiphenyl	2231.5	—
4-Cyanobiphenyl	2229.5	1780
1-Naphthonitrile	2226	951[b]
2-Naphthonitrile	2230	1430[b]
1-Anthronitrile	2225	1092[b]
2-Anthronitrile	2229	1664[b]
9-Anthronitrile	2218.5	1500[b]
9-Phenanthronitrile	2227	—
1-Pyrenonitrile	2222	2388[b]
2-Pyrenonitrile	2229[a]	—
4-Pyrenonitrile	2227.5	—

[a]The $\nu(C{\equiv}N)$ band is strongly asymmetric[56], hence we estimated the frequency by the spectrum of the ^{15}N-labelled compound which shows a fully symmetric $\nu(C{\equiv}N)$ band, by assuming 27 cm^{-1} isotopic shift.
[b]Ref. 71.

works cited therein); carbon tetrachloride[49,74,77,78], chloroform[74,75], tetrahydrofuran (THF)[79], dimethyl sulphoxide (DMSO) and hexamethylphosphoramide (HMPA)[79,80] were used as solvents. Increasing the accuracy of the $\nu(C{\equiv}N)$ measurements[74,75,77–80], studying large[75,80] or standardized[78–80] series of substituted benzonitriles, and the use of varieties of substituent constants[49,74,77–80] and solvents[79,80] have enabled the authors to estimate objectively the scope and limits of the correlations of $\nu(C{\equiv}N)$ of substi-

TABLE 4. Frequencies (cm^{-1}) and integrated intensities ($10^3\ l\ mol^{-1}\ cm^{-2}$) of the nitrile groups in some substituted benzonitriles[a]

	$\nu(C{\equiv}N)$, solvents			$A(C{\equiv}N) \times 10^{-3}$, solvents		
Substituents	CCl_4[b]	$CHCl_3$[c]	DMSO[d]	CCl_4[b]	$CHCl_3$[c]	DMSO[e]
p-Me_2N	2219.8	2215	2211.5	4.010	6.50	8.68
m-Me_2N	2231.3	2231	2225	1.030	1.76	2.88
H	2232.2	2230.5	2227	0.822	1.23	1.80
p-NO_2	2236.4	2236.5	2233	0.250	0.55	0.75
m-NO_2	2239.1	2239.5	2235.5	0.340	0.65	1.20
p-O^-			2188			19.6
m-O^-			2215			3.5
p-HN^-			2170			31.3
p-NC—HC^-			2181			17.4
m-NC—HC^-			2219			4.0
p-O_2N—HC^-			2211[e]			10.4
p-C_2H_5OOC—HC^-			2184			25.2

[a]Benzonitriles with anionic substituents were obtained by metalation of the corresponding conjugated *C*-, *O*- and *N*-acids with CH_3ONa or CH_3SOCH_2Na[79,80].
[b]Ref. 78, at infinite dilution.
[c]Ref. 75.
[d]Ref. 79.
[e]Ref. 90.

tuted benzonitriles with substituent constants. Selected data on the $\nu(C{\equiv}N)$ of some substituted benzonitriles are collected in Table 4.

The comprehensive study of Exner and Boček[75] (90 compounds, solvent $CHCl_3$) showed a few strong deviations from the $\nu(C{\equiv}N)/\sigma$ correlation line; they are characteristic for the strongest resonative electron donors and could be avoided by using σ^+ instead of σ without worsening the correlation factors[79,80]. Further, the authors emphasized the presence of the so-called '*meta* effect', viz. the $\nu(C{\equiv}N)$ of the *meta*-substituted benzonitriles were found to be higher than predicted by the $\nu(C{\equiv}N)/\sigma$ correlation; these deviations do not depend either on the substituent nature or on molecular symmetry[75]. This effect can be related to some recent CNDO/2 results[81]: the C≡N bond indices [Wiberg's indices, $W(C{\equiv}N)$] of benzonitriles with *meta* substituents, including CN and NO_2, are higher than those of the *para* isomers, so the correlation $\nu(C{\equiv}N)/W(C{\equiv}N)$ of benzonitriles does not show any *meta* effect[81]. The latter result conforms to the concept[75] of the 'electronic' rather than 'vibrational' origin of the *meta* effect. On the other hand, the $\nu(C{\equiv}N)$ of benzonitriles, measured in all the other solvents used[78–80] do not show a similar *meta* effect, which data point to a possible third, solvent, factor in the origin of the *meta* effect.

In studying the substituent effects on the $\nu(C{\equiv}N)$ of benzonitriles with standardized substituents ('basic set', 17 compounds, solvent CCl_4), Deady and colleagues[78] found a perceptible $\nu(C{\equiv}N)$ decrease with the increase in concentration, probably because of formation of multipolar complexes. This phenomenon was observed in CCl_4 only (it can probably be observed in other strictly nonpolar solvents) and in the case of nitriles only (in the spectra of other compounds containing electron-withdrawing characteristic groups with lone electron pairs, e.g. esters, ketones etc., this effect is probably much weaker). So, in order to obtain reliable data in CCl_4, the authors[78] determined $\nu(C{\equiv}N)$ by extrapolation to infinite dilution (Table 4, the first column).

The results of the studies on the correlation of the $\nu(C{\equiv}N)$ of benzonitriles with substituent constants can be summarized as follows:

Among all the single-parameter correlations, these with σ^+ constants (Brown and Okamoto's electrophilic constants[82], equation 2, or its mathematical equivalents) showed best fit, which can be related to the strong electron-withdrawing nature of the indicator cyano group.

$$\nu(C{\equiv}N) = \rho\sigma^+ + b \qquad (2)$$

The results of the statistical treatment of $\nu(C{\equiv}N)$ of benzonitriles in a variety of solvents, according to equation (2), are given in Table 5. As seen there, even the best correlations are not of high accuracy; the use of polar aprotic solvents instead of the common spectroscopic solvents do not cause material changes in the correlation factors.

The correlation of the slopes for *meta*-substituted compounds, $\rho(meta)$, differs from $\rho(para)$[78–80]. This phenomenon was observed in numerous spectroscopic and chemical reactivity series and it is due to the different receptivity of a given indicator group (reaction site) to inductive and resonance effects, when compared to the same in the definition series of the corresponding σ constants[83]. Therefore, the $\nu(C{\equiv}N)/\sigma^+$ correlations in the separate *meta* or *para* series are at times a bit better than those in the joint *meta* + *para* series[78–80].

Much attention was paid to the dual-parameter statistical treatment of the $\nu(C{\equiv}N)$ of benzonitriles, by using the equations of Yukawa and Tsuno[84] and Taft[85] (equations 3 and 4 or their mathematical equivalents). However, the use of these equations[77–80] as well as other dual- and triple-parameter equations[77] does not lead to essential improvement of the correlations; moreover, the equations of type (4) have the disadvantage of requiring obligatory separated treatments of the *meta* and *para* series.

TABLE 5. Correlations of $\nu(C{\equiv}N)^a$ of substituted benzonitriles [joint series, standard substituents: H, CH_3, CH_3O, $(CH_3)_2N$, F, Cl, CF_3, CN and NO_2, all in *meta* and *para* positions, 17 compounds] according to equation (2).

Solvent	ρ^b	b^c	R^d	sd^e
CCl_4	7.0	2232.9	0.957	1.4
$CHCl_3$	8.8	2232.0	0.966	1.5
THF	7.8	2230.2	0.952	1.6
HMPA	8.3	2227.9	0.951	1.8
DMSO	9.0	2228.4	0.961	1.7

[a] $\nu(C{\equiv}N)$ data from Refs. 75, 78–80, statistical treatment from Ref. 80.
[b] Slope.
[c] Intercept, i.e. the statistically expected $\nu(C{\equiv}N)$ of the unsubstituted benzonitrile in the corresponding solvent.
[d] Correlation coefficient.
[e] Standard deviation.

$$\nu(C{\equiv}N) = \rho(\sigma^0 + r'\Delta\sigma_R^+) + b \quad (3)$$

$$\nu(C{\equiv}N) = \rho_I\sigma_I + \rho_R\bar{\sigma}_R + b \quad (4)$$

($\bar{\sigma}_R = \sigma_R^0$, σ_R^-, σ_R^+, and σ_R^{BA}; see Reference 85)

The $\nu(C{\equiv}N)$ of a series of *ortho*-substituted benzonitriles (solvent CCl_4, values in the 2219–2240 cm^{-1} region, at infinite dilution) showed[86] only a general tendency to decrease in the case of electron-releasing substituents; both single- and dual-parameter correlations are poor. Spectra of *o*-amino- and *o*-methoxy-benzonitriles show $\nu(C{\equiv}N)$ splittings, caused probably by Fermi resonances[86].

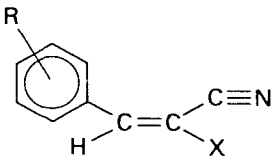
Hence, the approximate correlations found even when using precisely measured $\nu(C{\equiv}N)$, the presence of the '*meta* effect' etc. show that the substituent effects on $\nu(C{\equiv}N)$ have a definite specificity, which cannot be interpreted in detail within the framework of the LFER approach.

Certain MO interpretations[8,87] of the relationship between structure and $\nu(C{\equiv}N)$ of conjugated compounds give results which qualitatively conform to the experimental data. On the basis of PPP semiempirical calculations Besnainou and colleagues[8] found decreases in the force constant $k(C{\equiv}N)$ in conjugated nitriles; the $k(C{\equiv}N)$ and $\nu(C{\equiv}N)$ variations are in good mutual agreement in the case of *o*-, *m*- and *p*-methyl- and amino-benzonitriles[8]. The correlation of the $\nu(C{\equiv}N)$ of substituted benzonitriles with the C≡N π bond order, calculated by a modified HMO method, is satisfactory[87] but it again shows the '*meta* effect' (see above). In fact, these interpretations involve the hypothesis that $\nu(C{\equiv}N)$ is determined only by $k(C{\equiv}N)$ (i.e. by $P(C{\equiv}N)$, which correlates with $k(C{\equiv}N)$, see, for example, Reference 88). The $\nu(C{\equiv}N)$ values, however, depend also on the $k(C{-}CN)$ force constant, and having in mind the inverse proportionality between $k(C{\equiv}N)$ and $k(C{-}CN)$[89], one can conclude that the correlation of $\nu(C{\equiv}N)$ with both substituent constants and C≡N bond indices reflects the proportionality between the elements characterizing the variations in the force field of the whole characteristic group C—C≡N, $k(C{\equiv}N)$ and $k(C{-}CN)$, which follow the molecular structure variations.

The recently reported[79,90] data on $\nu(C{\equiv}N)$ of benzonitriles with negatively charged substituents, such as O^-, $X{-}N^-$, $X{-}HC^-$ etc. (Table 4) show very strong $\nu(C{\equiv}N)$

decreases, due to the very strong resonance interactions of these substituents with the electron-withdrawing C≡N group. These data have been used to obtain a rough estimate of the value of σ^+ of anionic substituents[79]. The effects of positively charged substituents, e.g. $(CH_3)_3N^+$, are not very strong[75].

Lengthening of the conjugated system between substituents and the nitrile group in compounds of type **2** and their higher vinylogues is accompanied[91] by smooth



(2)

X = H, Ph, $COOC_2H_5$ and CN

decreases in ρ in the correlations according to equation (2); the transmission coefficient of one double bond was found to be practically constant, $\pi \approx 0.6$[91].

Relations between structure and ν(C≡N) have also been found[67,92,93] in the series of heteroaromatic nitriles. ν(C≡N) values of β-cyano-substituted pyrrole, thiophene and furan are, by 10–15 cm^{-1}, higher than those of the α-isomers[67,93] and these results are related to the stronger electron-releasing ability of the corresponding heteroatoms in the α-position[93]. The values of ν(C≡N) increase in the order: 2-cyanopyrrole, Fermi doublet at 2229.6 and 2223 cm^{-1}, 2-cyanothiophene, 2225.7 cm^{-1} and 2-cyanofuran, 2236.3 cm^{-1} (solvent CCl_4)[93]. ν(C≡N) of the 5-substituted 2-cyanofurans lie in the 2234–2244 cm^{-1} interval in the same solvent and increase with the increase in the electron-withdrawing ability of the substituents[92], similarly to the case of benzonitriles.

2. *Intensities*

The integrated intensities of the nitrile bands, A(C≡N), are much more sensitive with respect to changes in the molecular structure than the corresponding characteristic frequencies, especially in the cases of conjugated systems. The A(C≡N) of conjugated nitriles vary within very large limits and usually they are higher than those of saturated nitriles. Two approaches have been used to find relationships between the structure and A(C≡N): the empirical approach[94], based on Hammett's LFER concept, and the quantum-chemical one, based on HMO and improved MO methods.

Within the *empirical approach* the substituent-induced A(C≡N) variations are compared to substituent constants by using improved Hammett-type equations (equations 5–7, mathematical equivalents of equations 2–4):

Brown and Okamoto[82]: $$A^{1/2} = \rho\sigma^+ + b \quad (5)$$

Yukawa and Tsuno[84]: $$A^{1/2} = \rho(\sigma^0 + r'\Delta\sigma_R^+) + b \quad (6)$$

Taft[85]: $$A^{1/2} = \rho_I\sigma_I + \rho_R\sigma_R + b \quad (7)$$

The A(C≡N)/sigma correlations have been repeatedly studied[49,75,76,78,80]. It has been firmly established that the best single-parameter correlations of A(C≡N) of benzonitriles are those with σ^+ [49,75,78,80]. These constants are strongly favoured in a variety of solvents; the correlations with all other substituent constants are much worse. The factors of the correlations according to equation (5) for the joint standard series (see the heading of Table 5) of substituted benzonitriles are collected in Table 6.

TABLE 6. Correlations of $A^{1/2}$(C≡N) (A in IUPAC units) of benzonitriles, according to equation (5)[a]

Solvent	ρ	b	R[e]	sd[f]
CCl_4[b]	−18.7	29.6	0.993	1.4
$CHCl_3$[c]	−22.2	39.3	0.986	2.4
HMPA[d]	−24.3	42.8	0.984	2.8
DMSO[d]	−23.6	47.1	0.980	3.2

[a]Statistical treatment: Ref. 80.
[b]A(C≡N) at infinite dilution[78].
[c]A(C≡N) from Ref. 75, converted into IUPAC units.
[d]Ref. 80.
[e]Correlation coefficient.
[f]Standard deviation.

The dual-parameter treatment of the same A(C≡N) data according to equations (6) and (7) led to a further improvement of the correlations (Table 7).

As seen in Tables 6 and 7, the correlations of A(C≡N) of substituted benzonitriles in a variety of solvents with electrophilic-type substituent constants are of high accuracy: their standard deviations are comparable to the experimental errors in the A(C≡N) determination (2–5%). These correlations do not show any *meta* effect (cf. the preceding section); they were tested in comprehensive series (90^{75} and 45^{90} compounds) without showing strong deviations and, hence, they can be used to predict unknown A(C≡N) of benzonitriles with a variety of substituents*.

The high values of the Yukawa–Tsuno coefficient (r' in Table 7) point to the decisive role of the resonance, especially the direct resonance between substituents and nitrile group, in the total electronic effects of the substituents on A(C≡N). The Yukawa–Tsuno coefficient in the ν(C≡N) series of the same benzonitriles shows[80] somewhat lower values, from 1.09 to 1.41 for the five solvents used.

Having in mind the good correlations of the A(C≡N) of benzonitriles with substituent constants, some authors[75,78,86] have suggested that these correlations can be used in the determination of σ^+ substituent constants if the A(C≡N) of the corresponding benzonitriles are known.

In agreement with the concept of the decisive importance of the resonance in the total substituent effect on A(C≡N), the integrated intensities of benzonitriles with extremely strong donors in the *para* position, such as O^-, X—N^-, X—HC^- and other

TABLE 7. Correlations[80] of $A^{1/2}$(C≡N) of benzonitriles, according to equation (6)

Solvent	ρ	r'[a]	b	R	sd
CCl_4	−15.8	1.35	28.4	0.996	1.1
$CHCl_3$	−16.8	1.61	37.1	0.993	1.7
HMPA	−18.8	1.55	40.5	0.998	2.4
DMSO	−17.0	1.71	44.4	0.986	2.6

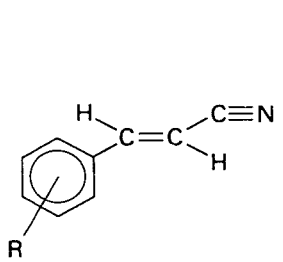
[a]Yukawa–Tsuno coefficient[84]; other headings as in Table 6.

*One must bear in mind that these correlations are valid for the value $A^{1/2}$(C≡N), i.e. the square root of A(C≡N), when the latter is taken in 1 mol^{-1} cm^{-2}.

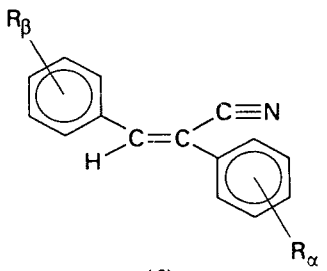
negatively charged substituents, were found to be much higher than those of neutral benzonitriles (Table 4). By using these data and the recently suggested combined approach[90], based on the Yukawa–Tsuno equation, one can estimate σ^+ values of anionic substituents (substituent, σ^+): *p*-O_2N—HC^-, −2.2; *p*-NC—HC^-, −4.7; *p*-EtOOC—HC^-, −5.0; *p*-HN^-, −6.2; *p*-O^-, −4.3; *m*-NC—HC^-, −0.9; *m*-O^-, −1.2 etc.[90].

In spite of the lower A(C≡N) of the *ortho*-substituted benzonitriles, compared to these of the *para* isomers, the authors[86] found a satisfactory $A^{1/2}$(C≡N)/σ^+ correlation in this case too. This result may be due to the absence of considerable steric hindrance between the cyano group and *ortho* substituents.

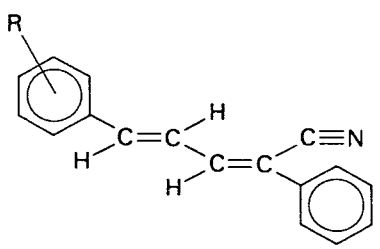
Lengthening of the conjugated system between the substituted benzene ring and the cyano group in the compounds **3**, **4** and **5** results in a smooth decrease in the substituent effects on A(C≡N)[95]. It can be noted that $A^{1/2}$(C≡N) in these cases correlates better with $A^{1/2}$(C≡N) of the corresponding benzonitriles than with σ^+. Hence, in spite of the satisfactory correlations of $A^{1/2}$(C≡N) with substituent constants, these constants reflect only approximately the substituent effects on the integrated intensities of nitrile bands.



(3)



(4)



(5)

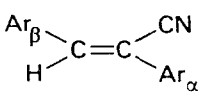
When the substituents are not conjugated with the nitrile group, as in the α-substituted *p*-tolunitriles, the substituent-induced A(C≡N) changes are not essential[29]. Electron-donating groups give rise to increases and electron-withdrawing ones to decreases in A(C≡N) of the 5-substituted 2-furyl cyanides[92], similarly to the case of benzonitriles. The A(C≡N) (in IUPAC units) of 2-cyanopyrrole (3000), 2-cyanothiophene (1430) and 2-cyanofuran (1020) are higher than that of benzonitrile (822) and, according to the authors[93], these results point to a total electron-releasing effect of the heteroatoms with respect to the cyano group. Because of the lower values of the corresponding 3-isomers [A(C≡N) is 1580, 990 and 870 l mol^{-1} cm^{-2}, respectively][93] the authors assumed that the electron-donating effect of the heteroatoms is stronger in the 2-position, as in the frequency case (Section II.C.2). The relative reactivity of the heterocycles has been discussed on the basis of these data[93].

The brief review shows that the nitrile band intensities of various conjugated systems correlate (unlike the corresponding frequencies) very well with the substituent constants. These empirical correlations can be used, for example, as a measure of intramolecular interactions, or to predict the $A(C{\equiv}N)$ of unstudied compounds, or to estimate unknown substituent constants. The use of these correlations, however, is limited within a given conjugated system, e.g. the benzene ring. Thus, it is essential to find methods which can explain, and moreover predict, $A(C{\equiv}N)$ in diverse classes of conjugated nitriles simultaneously.

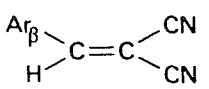
Using the *quantum-chemical approach* the authors have been trying to find correlations between $A^{1/2}(C{\equiv}N)^*$ and calculated values, modelling the dipole moment derivative with respect to either the normal coordinate $(\partial\mu/\partial Q_{CN})$ or the C≡N bond only $(\partial\mu/\partial r_{CN})$. The latter derivatives of a series of polycyclic nitriles have been calculated by Figeys and Nasielski[71] by the HMO method. Comparing these values to $A(C{\equiv}N)$ resulted in the formation of three separate correlations, depending on the number of the *peri*-hydrogen atoms, and this result was related to the varying steric hindrance to cyano group solvation[71]. On the basis of the semiempirical PPP method, Besnainou and coworkers[8] have calculated $(\partial\mu/\partial r_{CN})$ of a few conjugated nitriles, including the isomeric methyl- and amino-benzonitriles, and found a qualitative agreement only between the calculated values and $A^{1/2}(C{\equiv}N)$.

In contrast to the latter studies, the $A(C{\equiv}N)$ variations in a series of 38 conjugated nitriles, including polyenic and polycyclic nitriles as well as substituted benzonitriles, were compared to the values of $(\partial\mu_\pi/\partial Q_{CN})$ calculated by the HMO approximation[96]. These values gave a more precise reflection of the C≡N vibration mode, taking into account the participation of both C≡N and C—CN bonds. Thus, four excellent $A^{1/2}(C{\equiv}N)/(\partial\mu_\pi/\partial Q_{CN})$ correlations were found[96] within four different classes of carbon atoms bonded to the cyano group: class −1, =CH—CN, and classes 0, 1 and 2 according to the classification of Koutecký and colleagues[97]. The splitting of the correlations, similar to that found in Reference 71, was proved to be due to a specific discrepancy of the HMO method[96], not to steric hindrance of the solvation. The $(\partial\mu_\pi/\partial Q_{CN})$ values of compounds with the general structures **6** and **7**, calculated in a similar fashion, showed[73,98] a good agreement with the measured $A(C{\equiv}N)$.

According to both theoretical and experimental data[73,98], the steric hindrance in the case of polycyclic substituents (1-naphthyl, 1-pyrenyl and 9-anthryl) provokes increases (Ar_α) and decreases (Ar_β, structures **6**, **7**) in $A(C{\equiv}N)$. The out-of-plane



(**6**)

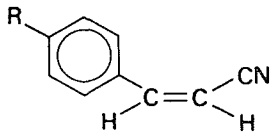


(**7**)

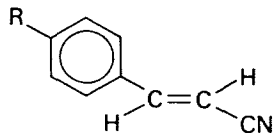
angles of the aryl moieties were estimated in this case on the basis of the $A^{1/2}(C{\equiv}N)/(\partial\mu_\pi/\partial Q_{CN})$ correlations; the values thus obtained[73,98] are in good agreement with those obtained on the basis of $\nu(C{\equiv}N)$ and/or the half-wave potentials of polarographic reduction[99]. The best general (without splitting) correlation of $A(C{\equiv}N)$ in a large series of conjugated nitriles (substituted benzonitriles, cyanopyridines, polycyclic nitriles and substituted acrylonitriles) with $(\partial\mu_\pi/\partial Q_{CN})$ was found[81] when the latter values were calculated by the CNDO/2 method.

The $A(C{\equiv}N)$ of *cis*-cinnamonitriles (**8**) are much lower than those of the corresponding *trans* isomers (**9**). This result can be easily explained[96] bearing in mind that the conjugated system in *cis*-cinnamonitriles, when the $\nu(C{\equiv}N)$ vibration provokes

*$A(C{\equiv}N)$ is proportional to $(\partial\mu/\partial Q_{CN})^2$.



(8)



(9)

R = A(C≡N) in IUPAC units:

$(CH_3)_2N$, 2750	$(CH_3)_2N$, 9500
NO_2, 1170	NO_2, 2000

the appearance of alternating electrical changes, is shorter than that of the *trans* isomers (cf. structures **8** and **9**. At the same time, the ν(C≡N) of **8** are only ca. 2 cm^{-1} lower than those of **9**. The conjugation in the 1-position of both the naphthalene and anthracene rings is stronger and, nevertheless, the A(C≡N) of the 2-cyano-substituted naphthalene and anthracene are higher than those of the 1-isomers (cf. Table 3); this result can be also ascribed to the larger effective length of the conjugated system in the 2-isomers.

gated nitriles are determined mainly by the polarizing influence of the vibrating strong electron-attracting C≡N group on the conjugated system, so that the A(C≡N) depend considerably on the topology of this system.

D. Anion-radicals Containing Cyano Groups

Basic information on the structure of anion-radicals can be obtained by using the ESR method; nevertheless, numerous data on the vibrational spectra of anion-radicals of nitriles have also recently been reported. The vibrational spectra of anion-radicals can give information on changes in the force field of the neutral compounds on their conversion into anion-radicals, and on the distribution of the odd electron over the conjugated system (see the reviews in References 100 and 101). Infrared data for anion-radicals containing cyano groups proved to be a necessary prerequisite for the studies of the reaction of dimerization[102,103], oligomerization and polymerization[104] of some unsaturated nitriles. The highly reactive anion-radicals can be prepared and studied in polar aprotic solvents in the presence of suitable electron donors such as alkali metals and amalgams, other anion-radicals and dianions[105,106], on electro-reduction[107] as well as in the solid state (see, for example, Reference 108).

The conversion of aromatic nitriles into anion-radicals is accompanied, as a rule, by strong ν(C≡N) decreases, toward the 2070–2230 cm^{-1} region[101]. This region is much larger than that of the neutral nitriles, i.e. the effects of the structural variations on ν(C≡N) of anion-radicals are much stronger than in the case of the parent aromatic nitriles (Table 8). Moreover, the absence of correlation between the ν(C≡N) of aromatic nitriles and the ν(C≡N) of their anion-radicals indicates[101] that the effects of the same structural variations are manifested in essentially different ways: while the conventional concepts of inductive and resonance effects give a satisfactory explanation of the variations in the case of neutral conjugated nitriles, the odd-electron distribution over the conjugated system proves to be the dominant factor determining the ν(C≡N) variations in the infrared spectra of the radical-anions of aromatic nitriles[90,101].

The strong ν(C≡N) decreases on the conversion of neutral nitriles into anion-radicals are usually accompanied by strong increases in both the A(C≡N) (1–2

TABLE 8. Frequencies (cm^{-1}) of the $\nu(C{\equiv}N)$ bands of some aromatic nitriles and their anion-radicals[a]

No.	Compound	$\nu(C{\equiv}N)$ of the neutral compound	$\nu(C{\equiv}N)$ of the anion-radicals in various solvents[b]		
			THF	DMSO	HMPA
(10)	Benzonitrile	2230[c,h]	2093 (K^+)[f]	—	2076[e]
(11)	4-Cyanopyridine	2237[d]	—	2094[e]	2095[e]
(12)	1-Naphthonitrile	2224[c]	2210 (Li^+)	2105[e]	2110 (Na^+)
(13)	2-Naphthonitrile	2227[c]	2099 (Li^+) 2092 (Na^+) 2087 (K^+)[f]	2102[e]	2110 (Na^+)
(14)	1-Cyanopyrene	2220[c]	2130 (Li^+)	2132[e,g]	2140[e]
(15)	Terephthalonitrile	2236[c]	2107 and 2140 vw. (Li^+)	2096 and 2141 vw.[e,g]	2101 (Li^+) 2101 (Na^+)
(16)	4-Nitrobenzonitrile	2235[c]	2212 (Li^+)[h]	2193[e]	—
(17)	3-Nitrobenzonitrile	2238[c]	2231 (Li^+)[h]	2224[e]	2223[e]

[a]Data taken from Ref. 101 unless otherwise stated.
[b]Counterions given in parentheses.
[c]Solvent THF. $\nu(C{\equiv}N)$ in DMSO and HMPA are ca. 2–3 cm^{-1} lower.
[d]Solvent DMSO.
[e]$\nu(C{\equiv}N)$ of electrochemically generated anion-radicals, supporting electrolytes: tetraalkylammonium perchlorates.
[f]Ref. 105.
[g]Ref. 109.
[h]Ref. 106.

orders) and the half-width of the $\nu(C{\equiv}N)$ bands[101,105,110]. The $\nu(C{\equiv}N)$ of anion-radicals, studied in dissociating solvents, as DMSO and HMPA, depend very little on the counterions[101]. Anion-radicals do exist as ion pairs in ethereal solvents as THF and dimethoxyethane, therefore the $\nu(C{\equiv}N)$ were found to increase as the cationic radius decreases in the order K^+, Na^+ and Li^+ [101,106].

The $\nu(C{\equiv}N)$ decreases found in the spectra of anion-radicals, compared to those of the parent nitriles, can be ascribed to decreases in the $C{\equiv}N$ bond order and, thus, in the $K(C{\equiv}N)$ force constant, caused by the antibonding character of the odd electron orbitals (antibonding, with respect to the bonds of pronounced double and triple character)[101]. Because of the high energy of the corresponding orbital, the odd-electron distribution over the conjugated system is highly sensitive to variations in bond lengths, thus the $\nu(C{\equiv}N)$ vibration is accompanied by a strong migration of the odd-electron density within this system. Having in mind this effect, one can explain the unusually high $A(C{\equiv}N)$ of most of the anion-radicals. Extending the possibilities of delocalization with the increase in size of the conjugated system in the anion-radicals of polycyclic nitriles leads to relative increases in $\nu(C{\equiv}N)$ (Table 8, compounds **10**, **12–14**). In presence of strong electron-withdrawers, the odd-electron distribution is determined by the competition between the acceptor and the cyano group, thus both the $\nu(C{\equiv}N)$ decreases and $A(C{\equiv}N)$ increases (with respect to the parent compounds) are smaller (Table 8, compound **16**). When the cyano group is not conjugated with the stronger acceptor, the odd electron proves to be practically localized on the stronger acceptor, thus both the frequency decrease and intensity increase (compared to the parent compound) are small (Table 8, compound **17**).

Correlations have been found between the $\nu(C{\equiv}N)$ of the aromatic nitrile anion-

radicals with the C≡N π bond order, P(C≡N), calculated by the HMO[101,106] and PPP MO[111] methods. The ν(C≡N)/P(C≡N) correlation for all the anion-radicals studied [ν(C≡N) in the 2080–2230 cm^{-1} region] is nonlinear[101]. The same correlation has been found to be linear in a series of *meta*- and *para*-substituted benzonitrile anion-radicals, and it has been used to estimate the out-of-plane angles of the anion-radicals of some cyanobiphenyls[101,106].

Conversion of aromatic dinitriles into anion-radicals results in enhancement in the vibrational coupling between the cyano groups[101,106,109]. While the *syn* phase, ν^s(C≡N), and *anti* phase, ν^a(C≡N), frequencies of the two nitrile groups of aromatic dinitriles practically coincide, the spectra of the corresponding anion-radicals show two ν(C≡N) bands with splittings of 30–40 cm^{-1}. Studies of this phenomenon in the asymmetrically ^{15}N-labelled dinitrile anion-radicals as well as theoretical considerations[101,109] have led to the conclusion that the considerable increase in the vibrational coupling is due mainly to the high mobility of the odd electron orbital in the anion-radicals.

Detailed studies of the vibrational spectra and normal coordinate analysis of the anion-radicals of tetracyanoethylene (TCNE)[112–114] and tetracyanoquinodimethane (TCNQ)[115,116] have shown that the addition of the odd electron is accompanied by a decrease in the force constant k(C≡N) and some increase in k(C—CN), in agreement with the MO calculations. Because of the delocalization of the antibonding orbital over the four equivalent nitrile groups in both TCNE and TCNQ, the ν(C≡N) decreases on radicalization, $\Delta\nu$(C≡N), in these cases are considerably smaller than in the above anion-radicals of aromatic nitriles. For example, $\Delta\nu$(C≡N) (calculated with respect to the mean frequency of the infrared doublet) in TCNQ was found to vary from 37 to 41 cm^{-1}, depending on the counterions[112,113]. Considerable increase in A(C≡N) was found in this case too; A(C≡N) of TCNQ is 0.72×10^4 l mol^{-1} cm^{-2} (solvent acetonitrile) and A(C≡N) of the TCNQ anion-radical is 13.2×10^4 (the same units and solvents)[117].

On the basis of the reported data one can conclude that the peculiarities characterizing the infrared spectra of anion-radicals containing cyano groups, i.e., the high ν(C≡N) sensitivity with respect to structural variations, the very high A(C≡N), and the enhanced vibrational interactions are determined mainly by the properties of the antibonding orbital of the odd electron.

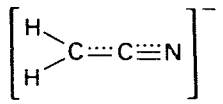
E. Carbanions Containing Cyano Groups

There are numerous infrared data on carbanions containing cyano groups and some of them prove to be of use in structural and mechanistic investigations[90].

It has been suggested[118–120] that the alkali-metal derivatives of acetonitrile exist in various forms, both prototropic and metallotropic. It has been established[121], however, that most of the infrared bands ascribed[120] to different forms of the metalated acetonitrile (bands above 2100 cm^{-1}), actually correspond to products of its further chemical transformations[121]. Thus, it has been reported that the acetonitrile carbanion (solvents THF and HMPA, counterions Li^+, Na^+ and K^+) is characterized by a very strong band of asymmetric or doublet character in the 2049–2072 cm^{-1} region, assigned[121,122] as ν(C≡N). The lower frequency band of the doublet, near 2050 cm^{-1}, was ascribed to the 'free' carbanions; the frequency of the higher frequency band was found to depend on the counterion: increase from 2061 to 2072 cm^{-1} from K^+ to Li^+ (solvent THF), thus, this band was ascribed to the ν(C≡N) of the ion pairs[121,122].

The analysis of both ^{14}N–^{15}N and H–D isotope effects, combined with approximate force-field estimates, obtained by CNDO/2 and normal-coordinate calculations, has led to the conclusion of a planar or practically planar structure for the acetonitrile

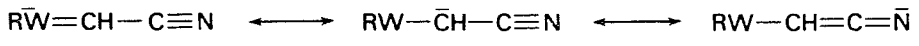
carbanion[122]. The decrease in the C≡N force constant [k(C≡N) = 15.19 mdyn Å^{-1}] and the increase in the C—CN one [k(C—CN) = 6.64 mdyn Å^{-1}] of the acetonitrile carbanion[122], compared to those of the parent acetonitrile [k(C≡N) = 18.40, k(C—CN) = 5.24 mdyn Å^{-1}][9] are also in agreement with the mesomeric structure **18**. All these data qualitatively agree with *ab initio* calculations, which predicted an all but planar structure of **18**, with an out-of-plane angle of 6° [123].



(18)

The high A(C≡N) of [CH_2CN]$^-$ (ca. 26 × 10^3 l mol^{-1} cm^{-2}) is characteristic of cyano groups bonded to carbanionic sites and it qualitatively corresponds to the high ($\partial\mu/\partial Q_{CN}$) value of the acetonitrile carbanion, calculated by the CNDO/2 method[122].

Infrared data on some selected carbanions containing cyano groups are collected in Table 9. As seen there, the ν(C≡N) of carbanions vary within a very broad frequency region, *viz.* 2020–2205 cm^{-1}, much broader than that of the neutral conjugated nitriles (Section II.C.1). The sensitivity of ν(C≡N) with respect to substituent effects should be related to the pronounced conjugation of the lone electron pair of the carbanionic site especially with strong resonance withdrawers (RW in structures **19–21**). Augmentation of the statistical weight of the **19**-type cannonical structures



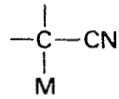
(19) **(20)** **(21)**

determines higher ν(C≡N) frequencies. Alkyl substituents at the carbanionic site cause some ν(C≡N) decrease, mainly because of their positive inductive effects[124,129].

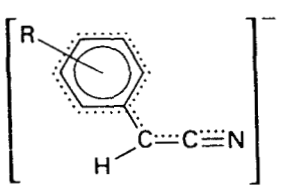
TABLE 9. Cyano group frequencies (cm^{-1}) of some carbanions

Carbanions	ν(C≡N)	Counterions and solvents	Reference
$\bar{C}H_2CN$	2049	K^+, THF	122
	2051, 2061	K^+, HMPA	122
$CH_3\bar{C}HCN$	2040, 2020 (sh.)[a]	K^+, THF	124
$(CH_3)_2\bar{C}CN$	2020	K^+, THF	124
	2026	K^+, HMPA	124
$Ph\bar{C}HCN$	2079, 2068 (sh.)[a]	K^+, THF	124
	2096	K^+, HMPA	124
p-$NO_2C_6H_4\bar{C}HCN$	2151	Na^+, DMSO	125
$R—\bar{C}(CN)_2$	2106, 2158	Na^+, DMSO	126
$EtOOC—\underset{\displaystyle R}{\bar{C}}—CN$	2144–2148	Na^+, DMSO	126
$O_2N—\underset{\displaystyle R}{\bar{C}}—CN$	2193	K^+, DMSO	127
$(O_2N)_2—\bar{C}—CN$	2205	Na^+, DMF[b]	128

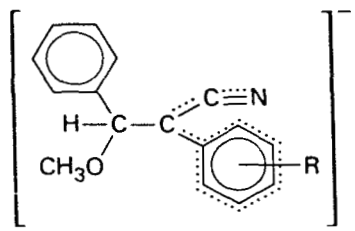
[a]Sh. = approximate frequency of the shoulder on the basic band.
[b]DMF = dimethylformamide.

The infrared spectra of living polyacrylonitrile show bands at 2030–2050 cm^{-1}, assigned as $\nu(C{\equiv}N)$ of carbanionic sites  ($M = Li^+$, Na^+ and K^+) in the end-groups[130,131]. These values, as well as the weak counterion effect (ca. 10 cm^{-1} increase from K^+ to Li^+)[130,131] are in complete agreement with the data for carbanions of saturated nitriles[124], and point to a close analogy in their structures.

The $\nu(C{\equiv}N)$ of carbanions of the type ArCHCN (Ar is phenyl, 2-naphthyl, 1-naphthyl, 1-pyrenyl and 9-anthryl) gradually increase with the increase in conjugation ability of the aryl moiety, from 2080 to 2111 cm^{-1} (solvent DMSO)[125,132], as qualitatively predicted by the HMO C≡N bond orders[133]. $\nu(C{\equiv}N)$ of the carbanions in a series of alkyl- and aryl-acetonitriles were found to correlate with the C≡N π bond orders, calculated by the PPP MO method[121,124]. Correlating the infrared characteristics of carbanions may give some insight into the electronic structure of these important reaction intermediates, and also into the mechanism of transmission of substituent effects through a carbanionic site. The $\nu(C{\equiv}N)$ of the carbanions of *meta*- and *para*-substituted phenylacetonitriles (**22**) lie in the 2070–2150 cm^{-1} region and are found[125,134] to correlate best with the σ^- constants (equation 8 and Figure 1) instead of σ^+ (cf. Section II.C.1). Similar correlations, again with σ^- giving the best fit,



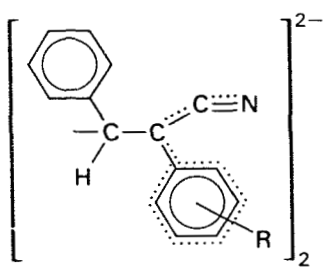
(**22**)



(**23**)

are found for the $\nu(C{\equiv}N)$ of carbanionic derivatives of α-aryl-β-phenylacrylonitriles, *viz*. sodium methoxide adducts (**23**)[135] and dimeric dianions (**24**)[102]. These results point

$$\nu(C{\equiv}N) = (42.3\,\sigma^- + 2085.7)\ cm^{-1} \qquad (8)$$
$$R = 0.973,\ sd = 5.2\ cm^{-1},\ n = 22$$



(**24**)

to a change in the mechanism of the transmission of substituent effects when a carbanionic site is placed between the substituents and the cyano group. In the case of neutral conjugated nitriles the direct resonance between electron-releasing substituents and the nitrile group plays an important role and, thus, the best-fit correlations

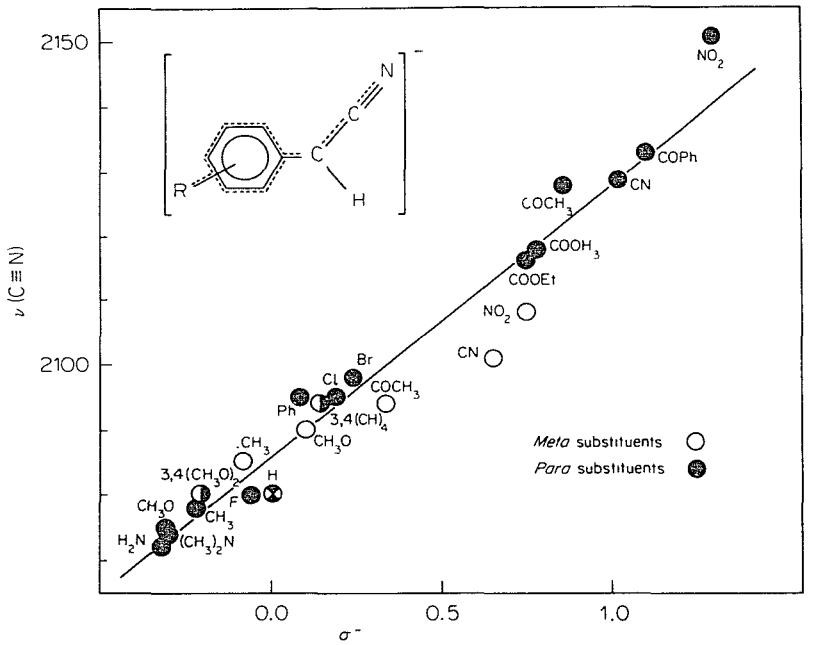


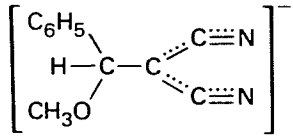
FIGURE 1. Correlation between $\nu(C{\equiv}N)$ and σ^- values of the carbanions of various *meta*- and *para*-substituted phenylacetonitriles.

of $\nu(C{\equiv}N)$ are with σ^+. On the contrary, in the carbanions **22**, **23** and **24** the $\nu(C{\equiv}N)$ variations are determined mainly by the competitive conjugation between the electron-withdrawing substituents and the nitrile group via the carbanionic site; since σ^- are the best reflection of the relative strength of the electron-withdrawers, the best fit of these constants in the $\nu(C{\equiv}N)$ correlations of the carbanions **22**, **23** and **24** appears to be well-grounded. A comparison of the slopes of the $\nu(C{\equiv}N)$/sigma correlations of substituted benzonitriles and of carbanions **22** showed[134] that introduction of a carbanionic site as an additional bridge results in more than three-fold amplification (instead of weakening) of the substituent effects on $\nu(C{\equiv}N)$.

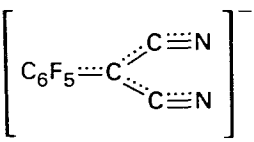
Nitrile groups bonded to carbanionic sites show, as a rule, $\nu(C{\equiv}N)$ bands of high intensity. Because of the high reactivity of the carbanions, precise $A(C{\equiv}N)$ measurements are very difficult; the approximate $A(C{\equiv}N)$ estimates[121,122,125,132], however, showed values up to 65×10^3 l mol^{-1} cm^{-2}. In spite of the strong competitive conjugation in the dinitroacetonitrile carbanion, even its $A(C{\equiv}N)$ is more than twice that of acetonitrile[128]. The high $A(C{\equiv}N)$ values of the carbanions have been related to the strong migration of the carbanionic charge in the $\nu(C{\equiv}N)$ vibration course[102,127,135,136].

The spectra of carbanions containing a dicyanomethide fragment $-\overline{C}(CN)_2$ show two $\nu(C{\equiv}N)$ bands, corresponding to the symmetrical (ν^s) and antisymmetrical (ν^{as}) vibration modes of the two vibrationally coupled cyano groups. Increase in the electron-withdrawing ability of the substituents in the dicyanomethide fragment (structures **25**, **26** and **27**) results in increases in both $\nu^s(C{\equiv}N)$ and $\nu^{as}(C{\equiv}N)$ [carbanion, $\nu^s(C{\equiv}N)$, $\nu^{as}(C{\equiv}N)$ (cm^{-1})]; **25**, 2106, 2158[126]; **26**, 2155, 2185[137]; **27**, 2214, 2221[138] and decreases in the splitting [$\Delta\nu(C{\equiv}N) = \nu^s(C{\equiv}N) - \nu^{as}(C{\equiv}N)$].

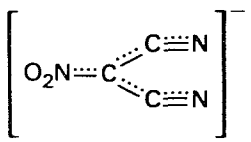
The spectra of ylides containing dicyanomethide fragments (structures **28**, **29** and **30**) do also show doublet $\nu(C{\equiv}N)$ bands[139–141].



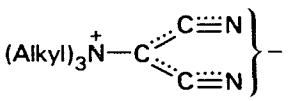
(25)



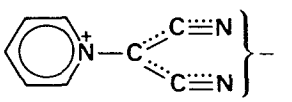
(26)



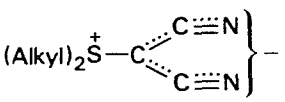
(27)



(28)



(29)



(30)

The normal coordinate analysis of the malononitrile carbanion and its ^{15}N isotopomer shows[89] that the $k(C{\equiv}N)$ force constant of this carbanion is higher than that of the acetonitrile carbanion, and the value of $\nu(C{\equiv}N)$ splitting, $\Delta\nu(C{\equiv}N)$, is determined mainly by the electronic vibrational coupling of the two cyano groups via the carbanionic site.

In spite of the competitive conjugation of the three cyano groups in the tricyanomethide anion $\bar{C}(CN)_3$, its $k(C{\equiv}N)$ value is lower than those of saturated nitriles[142,143], but higher than $k(C{\equiv}N)$ of both malononitrile and acetonitrile carbanions[89]. The two observable $\nu(C{\equiv}N)$ bands of this planar anion of D_{3h} symmetry are somewhat counterion-dependent: 2155–2188 cm^{-1} in the infrared and Raman spectra and 2209–2224 cm^{-1} in the Raman spectrum[144].

F. Di- and Tri-anions Containing Cyano Groups

Adding two or three electrons to conjugated systems containing cyano groups results in further $\nu(C{\equiv}N)$ decreases, because of the antibonding character of the corresponding molecular orbitals with respect to the cyano groups. The $\nu(C{\equiv}N)$ bands of the dianions of aromatic nitriles $[ArCN]^{2-}$ lie in the 2020–2067 cm^{-1} region (solvent THF, counterion K^+); these bands are broader and by an order stronger [$A(C{\equiv}N)$ values of ca. 10^5 l mol^{-1} cm^{-2}] than those of the corresponding anion-radicals[145]. Because of the delocalization of the antibonding orbitals, the $\nu(C{\equiv}N)$ value increases with the enlarging of the conjugated system, from 2020 cm^{-1} (2-cyanonaphthalene dianion) to 2067 cm^{-1} (9-cyanoanthracene dianion).

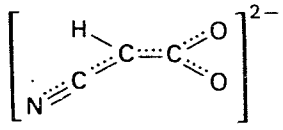
Dianions, derived on metalation of 1,4-bis(cyanomethyl)benzene, 1,4-bis(cyanomethyl)naphthalene and 9,10-bis(cyanomethyl)anthracene, which correspond to the dianions of dicyanoquinodimethane and its polycyclic analogues, show single $\nu(C{\equiv}N)$ bands in the 2040–2050 cm^{-1} interval (solvent THF, counterions Li^+, Na^+ and K^+). and doublet $\nu(C{\equiv}N)$ bands in the 2047–2078 cm^{-1} region (solvent HMPA, the same counterions)[132]. The rise of doublets can be ascribed to the presence of *s-cis* forms of these dianions, probably favoured in the case of the naphthalene derivative[132]. Spectra of the dianion of 1,1-diphenyl-2,2-dicyanoethylene show a doublet, $\nu^{as}(C{\equiv}N)$ and $\nu^{s}(C{\equiv}N)$, at 2085 and 2050 cm^{-1} (solvent DMSO)[146].

The vibrational spectra of the dianions of tetracyanoethylene (TCNE) and tetracyanoquinodimethane (TCNQ) have been interpreted in detail (see References 116 and 117 and the works cited therein). The solid state spectra of $[TCNE]^{2-}$ show two infrared bands at 2086 and 2146 cm^{-1}, and one Raman band at 2068 cm^{-1}; the $\nu(C{\equiv}N)$ values of the trianion $[TCNE]^{3-}$ are still lower, 1980 and 2033 cm^{-1} (infra-

red data)[147], in accordance with the MO predictions. The normal coordinate analysis of TCNE, $[TCNE]^{\cdot-}$, $[TCNE]^{2-}$ and $[TCNE]^{3\cdot-}$ shows a systematic decrease in the k(C≡N) force constant from 17.04 to 12.8 mdyn Å^{-1} and increase in k(C—CN) from 5.32 to 6.34 mdyn Å^{-1}; these variations are parallel to the variations in the C≡N and C—CN π bond orders[147].

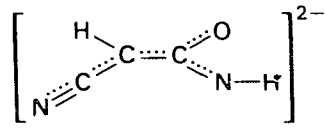
Because of the broader delocalization of the antibonding electron density, the dianion $[TCNQ]^{2-}$ gives higher-frequency ν(C≡N) bands than $[TCNE]^{2-}$: 2096 and 2164 cm^{-1} (infrared), and 2096 and 2196 cm^{-1} (Raman); the ν(C≡N) of the corresponding trianion $[TCNQ]^{3\cdot-}$ are found at 1901 and 2035 cm^{-1} (infrared)[116]. The k(C≡N) force constant is found to decrease from 16.90 to 13.42 mdyn Å^{-1} and k(C—CN) is found to increase on the conversion of TCNQ into the corresponding mono-, di- and tri-anions[116]. The sum of the intensities of the two infrared bands of $[TCNQ]^{2-}$ is 25×10^4 l mol^{-1} cm^{-2} (solvent acetonitrile), i.e. ca. twice higher than that of $[TCNQ]^{\cdot-}$[117]. The (C≡N) band of the dianion of 4,4′-bis(diazocyano)biphenyl at 2090 cm^{-1} (solvent THF) was found to be very strong, A(C≡N) = 87×10^4 l mol^{-1} cm^{-2}, while the intensity of the ν(C≡N) band at 2187 cm^{-1} of the neutral parent compound is only 0.34×10^4 l mol^{-1} cm^{-2} [110].

The high intensities and relatively low frequencies of the ν(C≡N) bands of the aromatic nitrile dianions, compared to those of the parent compounds, make it possible to use their infrared spectra to follow some reactions of electron transfer[145] and vinyl polymerization[104]. Infrared frequencies and their isotopic shifts, combined with CNDO/2, MINDO/3 calculations and normal coordinate analysis were used in a structural study on the dianions of cyanoacetic acid (**31**) and cyanoacetamide (**32**)[148].



(**31**)

ν(C≡N) = 2113 cm^{-1}



(**32**)

ν(C≡N) = 2093.5 cm^{-1}

III. ISOCYANIDES

A. General

Like the C—C≡N group in nitriles, the group C—N≡C in isocyanides is linear; the k(N≡C) force constant in isocyanides is slightly lower than the k(C≡N) in nitriles:

k(C≡N) (mdyn Å^{-1}): HCN, 18.70[12]; CH_3CN, 18.38[149]

k(N≡C) (mdyn Å^{-1}): HNC, 16.40[150]; CH_3NC, 16.67[149]

The isocyanide triple bond is longer than the nitrile one, e.g. r_0(N≡C) in CH_3NC is 1.167 Å[151] compared to r_0(C≡N) = 1.157 Å of CH_3CN[152]. Because of the lower values of the triple-bond force constant, the stretching frequencies of isocyano groups, ν(N≡C), are ca. 100 cm^{-1} lower than the ν(C≡N) of the corresponding nitriles, and they lie in the 2080–2180 cm^{-1} region. Many infrared data on various isocyanides are reported in the monographs in References 2, 3 and 153.

It follows from the normal coordinate analysis of CH_3NC that, by analogy to the nitrile case, the next C—NC bond also takes part in the ν(N≡C) vibration; the participation of the other internal coordinates is weak[9]. Thus, the ν(N≡C) vibration is

characteristic of the whole C—N≡C group, and its frequency variations depend in general on the variations in both N≡C and C—NC bonds.

B. Saturated Isocyanides

The stretching frequencies of C_{sp^3}-bonded isocyano groups lie in the 2130–2170 cm^{-1} region, being usually 20–30 cm^{-1} higher than those of conjugated isocyanides[2,3,153]. The infrared spectrum of the simplest isocyanide, methyl isocyanide, has been studied in detail (see Reference 149 and references therein). The assignment of the observed fundamental frequencies is given in Table 10.

The high-accuracy total harmonic force field of this molecule has been determined by Dunkan and colleagues[9] by using the exact gas-phase infrared frequencies of seven methyl isocyanide isotopomers and the Coriolis coupling constants. The stretching force constants of the C—N≡C group of CH_3NC thus found are: k(C—NC) = 5.448, k(N≡C) = 16.67 mdyn $Å^{-1}$; the same authors reported the following force constants of the isoelectronic compound, CH_3CN: k(C—CN = 5.184; k(C≡N) = 18.38 mdyn $Å^{-1}$ [149]. The much lower value of the (C—N≡C) bending force constant in CH_3NC, compared to its analogue, the (C—C≡N) bending constant, was ascribed to the participation of the canonical structure **34**.

(33) **(34)**

Lengthening the alkyl chain or increasing the number of the methyl groups at the α-carbon atom of alkyl isocyanides results in ν(N≡C) decreases[154,155], similarly to the nitrile case. Precise ν(N≡C) measurements in the series $(CH_3)_nCH_{3-n}NC$ gave the following values [n, ν(N≡C) (cm^{-1})]: 0, 2164.8; 1, 2151.1; 2, 2143.6; 3, 2136.7 (mixed solvent, CCl_4–CD_3CN–tetramethylsilane). The ν(N≡C) lowerings in this series correlate with the $J'(^{14}N-^{13}C)$ coupling constants in their ^{13}C-NMR spectra[155].

Compared to the ν(C≡N) frequencies, which decrease from gas phase to solution, as well as with increase in the solvent polarity[31], ν(N≡C) of isocyanides show a quite different behaviour[156,157]. Precise ν(N≡C) measurements of t-butyl isocyanide in 14 solvents show a 10 cm^{-1} increase from hexane to chloroform. ν(N≡C) values in chloroform (2141.3 cm^{-1}) and other solvents are even higher than in the gas phase (2134 cm^{-1})[157]. This solvent effect on ν(N≡C) can be explained on the basis of the theory of Drickamer and coworkers[158], by assuming a reverse sign for the quantity $(\partial\mu/\partial r_{NC})$ of the ν(N≡C) stretching vibration, compared to that of carbonyl groups which show 'normal' solvent shifts; the qualitative explanation assumes that the more

TABLE 10. Fundamental frequencies (cm^{-1}) in the infrared spectra of CH_3NC and CD_3NC (gas-phase data)[149]

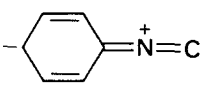
Assignment	CH_3NC	CD_3NC
ν_1; $\nu^s(CH_3)$ or (CD_3)	2963.41	2134.62
ν_2; ν(N≡C)	2166.26	2165.49
ν_3; $\delta^s(CH_3)$ or (CD_3)	1427.40	1118.04
ν_4; ν(C—N)	944.95	876.79
ν_5; $\nu^{as}(CH_3)$ or (CD_3)	3014.58	2262.89
ν_6; $\delta^{as}(CH_3)$ or (CD_3)	1464.32	1058.72
ν_7; $r(CH_3)$ or (CD_3)	1130.34	900.62
ν_8; β(C—N≡C)	262.75	248.87

polar solvents stabilize the more polar extreme structure **33**, and thus favour $\nu(N{\equiv}C)$ increases. Hydrogen-bond formation also favours increases in the statistical weight of **33** and the higher $\nu(N{\equiv}C)$ values of *t*-butyl isocyanide found using alcohols as solvents (2150 cm^{-1}) can be ascribed to this effect[157].

The integrated intensities $A(N{\equiv}C)$ of saturated isocyanides are higher than the $A(C{\equiv}N)$ of the corresponding nitriles[154,156]; for example, $A(N{\equiv}C)$ of *n*-propyl isocyanide is 9.7×10^3 l mol^{-1} cm^{-2}, and $A(C{\equiv}N)$ of *n*-propionitrile is 0.6×10^3 l mol^{-1} cm^{-2} (solvent CCl_4)[156]. The higher values of $A(N{\equiv}C)$ are qualitatively related to the stronger separation of the electron density in the isocyano group[156]. This qualitative explanation, however, seems incomplete, as it neglects the participation[9] of the polar C—NC bond in the $\nu(N{\equiv}C)$ vibration.

C. Conjugated Isocyanides

The complete assignment of the vibrational spectra of vinyl isocyanide (**35**)[159] and phenyl isocyanide (**36**)[160,161] shows a close analogy within the spectra of cyanides and isocyanides; only the bands relating directly to the C—N≡C group are essentially different [compound, $\nu(N{\equiv}C)$[159], (C—NC)[160] (cm^{-1})]: **35**, 2125, 881; **36**, 2130, 1193. As in the nitrile case, the conjugation leads to a 20–30 cm^{-1} decrease in the $\nu(N{\equiv}C)$ of aryl and vinyl isocyanides, compared to that of saturated isocyanides[2,3,153–155]; thus, the $\nu(N{\equiv}C)$ bands of conjugated isocyanides lie in the 2115–2135 cm^{-1} interval. The lower $\nu(N{\equiv}C)$ of conjugated isocyanides can be qualitatively related[153] to a participation of canonical structures like **37** which could provoke decreases in both the multiplicity and force constant of the N≡C bond.



(37)

As in the canonical structure **34**, the isocyano group could act as a resonative electron donor and this possibility has been proved by experimental data[162]. One can expect, therefore, smooth $\nu(N{\equiv}C)$ decreases with increase of conjugation of the isocyano group in conjugated systems without polar substituents. In fact, the $\nu(N{\equiv}C)$ in a small series of aromatic isocyanides, ArNC, were found[163] to decrease with the increase in the conjugation ability of the respective carbon atom of the parent aromatic hydrocarbon, qualitatively reflected by the values of the 'coefficient of conjugation' (Q_L)[164], as follows [Ar, $\nu(N{\equiv}C)$[163], Q_L[164]]: Ph, 2133, 0.315; 2-naphthyl, 2128.5, 0.320; 1-naphthyl, 2126.5 (mean value of a doublet), 0.345; 1-pyrenyl, 2118.5, 0.370. These data point to a close analogy in the conjugation effects on $\nu(N{\equiv}C)$ and $\nu(C{\equiv}N)$ (cf. Section II.C.1), in spite of the contrast in their own resonance effects. The substituent-induced $\nu(N{\equiv}C)$ variations in substituted phenyl isocyanides were found to be very small[2,153]. On the basis of infrared data reported by Ugi and Meyr[154], the authors of several monographs[2,3,153] assumed as one of the peculiar properties of the isocyano group the $\nu(N{\equiv}C)$ decreases in the presence of electron-withdrawing groups, and increases in the presence of electron-releasing substituents; this is exactly opposite to the behaviour of the $\nu(C{\equiv}N)$ of substituted benzonitriles. More precise measurements, however, showed[155] in spite of the small $\nu(N{\equiv}C)$ variations, only partial agreement with the above concept.

The $\nu(N{\equiv}C)$ data[163] of some *para*-substituted phenyl isocyanides [substituent, $\nu(N{\equiv}C)$ in CCl_4, $\nu(N{\equiv}C)$ in $CHCl_3$: NO_2, 2121, 2128; Cl, 2123, 2130; H, 2125.5, 2133; CH_3, 2123.5, 2129; CH_3O, 2123.5, 2129; Et_2N, 2119, 2125.5] showed $\nu(N{\equiv}C)$

lowerings in the case of both electron-withdrawing and electron-releasing substituents, in qualitative agreement with the data in an even smaller series[155]. These results could be related to the ability of the isocyano group to act either as a resonative electron donor or acceptor, depending on the electronic effect of the *para*-substituent[162].

The intensities $A(N{\equiv}C)$ of aromatic isocyanides are higher than those of the saturated ones[154,156]; this intensity enhancement is similar, but much smaller than in the nitrile case. For example, the $A(N{\equiv}C)$ of *n*-propyl isocyanide and phenyl isocyanide were found to be 0.97×10^4 and 1.46×10^4 l mol^{-1} cm^{-2}, respectively (solvent CCl_4)[156]. The $A(N{\equiv}C)$ increase in the case of conjugated isocyanides can be related to the possibility of mesomeric interactions between the isocyano group and the conjugated system (see the canonical structure **37**) which can provoke increases in the $(\partial\mu/\partial Q_{NC})$ value.

Increasing the solvent polarity from CCl_4 to $CHCl_3$ resulted in small (ca. 10%) $A(N{\equiv}C)$ decreases[156] in contrast to the nitrile case (cf. Section II.C.2).

Electron donors cause decreases, and electron acceptors as a rule cause increases, in the $A(N{\equiv}C)$ of substituted phenyl isocyanides[154], in sharp contrast to the nitrile case. The $A(N{\equiv}C)$ changes, however, are relatively smaller [±50% with respect to the $A(N{\equiv}C)$ value of the unsubstituted phenyl isocyanide], compared to the $A(C{\equiv}N)$ variations in the series of substituted benzonitriles. The $A(N{\equiv}C)$ variations can be qualitatively related to decreases or increases in the statistical weight of the polar canonical structure **37**, provoked by electron-donors or electron-acceptors, respectively, in the *para* position.

The CNDO/2 calculations of $(\partial\mu/\partial Q_{NC})$ values[163] of a series of substituted phenyl isocyanides show a qualitative agreement with the experimental data: $(\partial\mu/\partial Q_{NC})$ is decreased by donors and increased by acceptors. Hence, the $A(N{\equiv}C)$ variations are related to variations in the polar properties of the $\overset{\delta+}{C}{-}\overset{\delta+}{N}{\equiv}\overset{\delta-}{C}$ group and to changes in the resonative interactions between the substituent and the isocyano group.

IV. REFERENCES

1. IUPAC, *Comptes Rendus Vingtième Conference*, Munich, Butterworths, London, 1959, p. 187.
2. L. J. Bellamy, *Advances in Infrared Group Frequencies*, Methuen, Bungay, 1968.
3. M. Horak and D. Papoušek, *Infračervena Spectra a Struktura Molekul*, Akademia, Praha, 1976.
4. D. J. Curran and S. Siggia in *The Chemistry of the Cyano Group* (Ed. Z. Rappoport), John Wiley and Sons, London, 1970, p. 194.
5. D. H. Whiffen, *Chem. Ind. (London)*, 193 (1957).
6. (a) E. M. Popov and V. P. Roshchupkin, *Optika i Spektroskopiya, Sb. 2, Mol. Spektr.*, AN SSSR, 1963, p. 166.
   (b) V. P. Roshchupkin and E. M. Popov, *Zh. Opt. Spektr.*, **15**, 202 (1963).
7. J. L. Dunkan, *Spectrochim. Acta*, **20**, 1197 (1964).
8. S. Besnainou, B. Thomas and S. Bratož, *J. Mol. Spectry*, **21**, 113 (1966).
9. J. L. Dunkan, D. C. McKean, F. Tullini, G. D. Nivallini and J. P. Pena, *J. Mol. Spectry*, **69**, 123 (1978).
10. W. T. King and B. Crawford, Jr., *J. Mol. Spectry*, **5**, 421 (1960).
11. A. Parellada, J. Perez-Pena and J. F. Arenas, *J. Mol. Struct.*, **51**, 1 (1979).
12. G. Strey and I. M. Mills, *Mol. Phys.*, **26**, 129 (1973).
13. L. Halonen and I. M. Mills, *J. Mol. Spectry*, **73**, 494 (1978).
14. T. B. Freedman and E. R. Nixon, *Spectrochim. Acta*, **28A**, 1375 (1972).
15. T. Fujiyama, *Bull. Chem. Soc. Japan*, **44**, 89 (1971).
16. T. Fujiyama, *Bull. Chem. Soc. Japan*, **44**, 3317 (1971).
17. S. W. Charles, F. C. Cullen and N. L. Owen, *J. Mol. Struct.*, **34**, 219 (1976).

18. V. M. Baryshev, V. V. Ryabova and R. S. Frenkel', *Zh. Opt. Spektr.*, **35**, 579 (1973).
19. G. A. Crowder, *J. Phys. Chem.*, **75**, 2806 (1971).
20. K. Kumar, *Spectrochim. Acta*, **28A**, 459 (1972).
21. C. J. Wurrey, W. E. Bucy and J. R. Durig, *J. Phys. Chem.*, **80**, 1129 (1976).
22. R. Yamadera and S. Krimm, *Spectrochim. Acta*, **24A**, 1677 (1968).
23. P. Mauret, J. P. Fayet and C. Jehl, *Bull. Soc. Chim. Fr. (II)*, 429 (1976).
24. A. D. Pomogaylo and I. D. Leonov, *Dokl. Akad. Nauk SSSR*, **202**, 1083 (1972).
25. P. P. Shorygin, V. P. Roshchupkin and L. G. Stolyarova, *Zh. Fiz. Khim.*, **39**, 605 (1965).
26. P. P. Shorygin, *Usp. Khim.*, **40**, 695 (1971).
27. L. G. Vorontsova, V. I. Adrianov and B. L. Tarnopol'skiy, *Zh. Strukt. Khim.*, **10**, 873 (1969).
28. R. T. C. Brownlee and R. D. Topsom, *Spectrochim. Acta*, **31A**, 1677 (1975).
29. G. Butt, J. Cilmi, P. M. Hoobin and R. D. Topsom, *Spectrochim. Acta*, **36A**, 521 (1980).
30. G. A. Crowder, *Mol. Phys.*, **23**, 707 (1972).
31. B. Bak, E. L. Hansen, F. M. Nicolaisen and O. F. Nielsen, *Can. J. Chem.*, **53**, 2183 (1976), and references therein.
32. B. H. Thomas and W. J. Orville-Thomas, *J. Mol. Struct.*, **3**, 191 (1969).
33. R. C. Jonas and W. J. Orville-Thomas, *J. Chem. Soc.*, 4635 (1965).
34. H. F. Shurvell and J. A. Faniran, *J. Mol. Spectry*, **33**, 436 (1970).
35. J. P. Jesson and H. W. Thompson, *Spectrochim. Acta*, **13**, 217 (1958).
36. V. E. Borisenko and D. N. Shchepkin, *Zh. Opt. Spektrosk.*, **29**, 845 (1970).
37. B. J. Van Der Veken and H. O. Desseyn, *J. Mol. Struct.*, **23**, 427 (1974).
38. L. Van Haverbeke, H. O. Desseyn, B. J. Van Der Veken and M. A. Herman, *J. Mol. Struct.*, **25**, 53 (1975).
39. S. Bjørklund, E. Augdahl, D. H. Christensen and G. O. Sørensen, *Spectrochim. Acta*, **32A**, 1021 (1976).
40. D. J. Perettie and J. C. Wait, Jr., *J. Mol. Spectry*, **32**, 222 (1969).
41. N. Oi and K. Moriguchi, *Bunseki Kagaku*, **28**, 390 (1979).
42. R. E. Hester, K. M. Lee and E. Mayer, *J. Phys. Chem.*, **74**, 3373 (1970).
43. B. H. Thomas and W. J. Orville-Thomas, *J. Mol. Struct.*, **7**, 123 (1971).
44. P. Sensi and G. G. Gallo, *Gazz. Chim. Ital.*, **85**, 224 (1955).
45. Z. Ejmocki and Z. Ekstein, *Rocz. Chem.*, **45**, 345 (1971).
46. L. A. Kazitsyna, B. V. Lokshin and O. A. Glushkova, *Zh. Obshch. Khim.*, **32**, 1391 (1962).
47. H. Sterk and H. Junek, *Monatsh. Chem.*, **99**, 810 (1968).
48. Z. A. Muldakhmetov, N. S. Kupriyanov, K. Akhmetkarimov and I. I. May, *Izv. Akad. Nauk Kazakhs. SSSR, Ser. Khim.*, **22**, 38 (1972).
49. C. N. R. Rao and R. Venkataraghavan, *Can. J. Chem.*, **39**, 1757 (1961).
50. L. Van Haverbeke and M. A. Herman, *Bull. Soc. Chim. Belg.*, **84**, 439 (1975).
51. N. Latif, N. Mishriky and K. A. Mohsen, *J. Chem. Soc., Perkin Trans. I*, 875 (1974).
52. L. A. Gribov, *Intensity Theory for Infrared Spectra of Polyatomic Molecules*, Consultants Bureau, New York, 1964.
53. H. P. Figeys, P. Grearlings and C. Van Alsenoy, *J. Chem. Soc., Faraday Trans. II*, 542 (1979).
54. E. M. Popov, I. P. Yakovlev, G. A. Kogan and V. V. Zhogina, *Teoret. Eksp. Khim.*, **2**, 464 (1966).
55. A. Kuwae and K. Machida, *Spectrochim. Acta*, **35A**, 841 (1979).
56. A. R. H. Cole and A. A. Green, *J. Mol. Spectry*, **48**, 246 (1973).
57. J. Bragin, K. L. Kizer and J. R. Durig, *J. Mol. Spectry*, **38**, 289 (1971).
58. S. B. Lie and P. Klaboe, *Spectrochim. Acta*, **26A**, 1191 (1970).
59. J. R. Durig, C. K. Tong, C. W. Hawley and J. Bragin, *J. Phys. Chem.*, **75**, 44 (1971).
60. J. H. S. Green and D. J. Harrison, *Spectrochim. Acta*, **32A**, 1279 (1976).
61. C. L. Chatterjee, P. P. Garg and R. M. P. Jaiswal, *Spectrochim. Acta*, **34A**, 943 (1978).
62. P. Ahmad and N. K. Sanyal, *J. Chim. Phys. Phys. Chim. Biol.*, **74**, 1154 (1977).
63. C. G. Barraclough, H. Bissett, Ph. Pitman and P. J. Thistlethwaite, *Australian J. Chem.*, **30**, 753 (1977).
64. P. N. Gates, D. Steele, R. A. R. Pearce and K. Radcliffe, *J. Chem. Soc., Perkin Trans. II*, 1607 (1972).
65. M. C. Castro-Pedrozo and G. W. King, *J. Mol. Spectry*, **73**, 386 (1978).
66. J. H. S. Green and D. J. Harrison, *Spectrochim. Acta*, **33A**, 75 (1977).

67. K. Volka, P. Adamek, I. Stibor and Z. Ksandr, *Spectrochim. Acta*, **32A**, 379 (1976).
68. M. Figeys-Fauconnier, H. Figeys, G. Genskens and J. Nasielski, *Spectrochim. Acta*, **18**, 689 (1962).
69. I. Juchnovski, B. Jordanov and M. Agova, *Mitt. Inst. Org. Chem. Bulg. Acad. Sci.*, **2**, 13 (1965).
70. I. Juchnovski, *Compt. Rend. Acad. Bulgare Sci.*, **19**, 1151 (1966).
71. H. P. Figeys and J. Nasielski, *Spectrochim. Acta*, **22**, 2055 (1966).
72. I. Juchnovski and Z. Popov, *Izv. Otd. Khim. Nauki, Bulg. Acad. Nauk*, **2**, 373 (1969).
73. I. Juchnovski, R. Kuzmanova, J. Tsenov, J. Kaneti and I. Binev, *Z. Naturforsch.*, **33b**, 557 (1978).
74. I. Juchnovski, *Compt. Rend. Acad. Bulgare Sci.*, **19**, 743 (1966).
75. O. Exner and K. Boček, *Tetrahedron Letters*, 1433 (1967); *Collect. Czech. Chem. Commun.*, **38**, 50 (1973).
76. A. R. Katritzky and R. D. Topsom in *Advances in Linear Free Energy Relationships* (Eds. N. B. Chapman and J. Shorter), Plenum Press, London, 1972, p. 119.
77. C. Laurence and B. Wojtkowiak, *Bull. Soc. Chim. Fr.*, 3124, 3833, 3870, 3874 (1971); M. Berthelot, Ch. Laurence and B. Wojtkowiak, *Bull. Soc. Chim. Fr. (II)*, 662 (1973).
78. L. Deady, A. R. Katritzky, R. A. Shanks and R. D. Topsom, *Spectrochim. Acta*, **29A**, 115 (1973).
79. I. Juchnovski and I. Binev, *Tetrahedron*, **33**, 2993 (1977).
80. I. G. Binev, R. B. Kuzmanova, J. Kaneti and I. N. Juchnovski, *Izv. Khim.*, in press.
81. I. Juchnovski and J. Dimitrova, to be published.
82. H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **80**, 4979 (1958).
83. Yu. A. Zhdanov and V. I. Minkin, *Correlation Analysis in Organic Chemistry* (Russ.), Rostov-na-Donu, 1966.
84. Y. Yukawa and Y. Tsuno, *Bull. Chem. Soc. Japan*, **32**, 911, 965 (1959); Y. Yukawa, Y. Tsuno and M. Sawada, *Bull. Chem. Soc. Japan*, **45**, 1198 (1972).
85. R. W. Taft, *J. Amer. Chem. Soc.*, **79**, 1045 (1957); *J. Phys. Chem.*, **64**, 1805 (1960); R. T. C. Brownlee, S. Ehrenson and R. W. Taft, *Progr. Phys. Org. Chem.*, **10** (1973).
86. L. W. Deady, P. M. Harrison and R. D. Topsom, *Spectrochim. Acta*, **31A**, 1665 (1975).
87. Y. Ono, E. Tabuchi and Y. Ueda, *Chem. Pharm. Bull. (Tokyo)*, **22**, 871 (1974).
88. E. M. Popov, G. A. Kogan and V. N. Zheltova, *Teoret. Eksp. Khim.*, **6**, 14 (1970).
89. I. N. Juchnovski, J. S. Dimitrova and J. Kaneti, *Izv. Khim.*, **12**, 97 (1979).
90. I. N. Juchnovski and I. G. Binev in *Organométalliques Fonctionnels*, Recueil des Communications, Colloques Franco-Bulgare, Tryavna, 1980, pp. 144–169, I. G. Binev, R. B. Kuzmanova, J. Kaneti and I. N. Juchnovski, to be published.
91. I. Juchnovski, *Dokl. Akad. Nauk SSSR*, **186**, 878 (1969).
92. F. Povazanec, A. Piklerova, J. Kovač and Š. Kovač, *Chem.. Zvesti*, **29**, 408 (1975).
93. L. W. Deady, R. A. Shanks and R. D. Topsom, *Tetrahedron Letters*, 1881 (1973).
94. A. R. Katritzky and R. D. Topsom, *Chem. Rev.*, **77**, 639 (1977).
95. I. Juchnovski, D. Dumanov and L. Mincheva, *Izv. Otd. Khim. Nauki, Bulg. Acad. Nauk*, **4**, 39 (1971).
96. I. Juchnovski and Ch. Velev, *Izv. Otd. Khim. Nauki, Bulg. Acad. Nauk*, **4**, 333 (1971).
97. J. Koutecký, R. Zahradnik and J. Čižek, *Trans. Faraday Soc.*, **57**, 169 (1961).
98. I. G. Binev, D. M. Vitanov, I. N. Juchnovski and J. Kaneti, *Izv. Khim.*, **12**, 162 (1979).
99. I. N. Juchnovski and Ts. Popov, *Monatsh. Chem.*, **100**, 337 (1970).
100. L. A. Kotorlenko and S. A. Samoylenko, *Usp. Khim.*, **46**, 639 (1977).
101. I. N. Juchnovski, I. G. Binev and J. Kaneti, *Izv. Khim.*, **10**, 554 (1977).
102. I. G. Binev and I. N. Juchnovski, *J. Organometal. Chem.*, **141**, 123 (1977).
103. I. N. Juchnovski and I. G. Binev, *Compt. Rend. Acad. Bulgare Sci.*, **30**, 1419 (1977).
104. I. M. Panayotov, Ch. Tsvetanov and I. N. Juchnovski, *Europ. Polym. J.*, **6**, 1625 (1970).
105. I. Juchnovski, Ch. Tsvetanov and I. Panayotov, *Monatsh. Chem.*, **100**, 1980 (1969).
106. I. N. Juchnovski and I. G. Binev, *J. Mol. Struct.*, **7**, 490 (1971).
107. I. N. Juchnovski and I. G. Binev, *Compt. Rend. Acad. Bulgare Sci.*, **24**, 483 (1971).
108. J. Stanley, D. Smith, B. Lotimer and J. P. Devlin, *J. Phys. Chem.*, **70**, 2011 (1966).
109. I. N. Juchnovski and I. G. Binev, *Chem. Phys. Letters*, **12**, 40 (1971).
110. L. A. Kazitsyna, L. P. Ashkinadze and M. Kh. Shamsutdinova, *Dokl. Akad. Nauk SSSR*, **249**, 390 (1979).
111. I. N. Juchnovski, I. G. Binev, A. F. Nazir and J. A. Tsenov, *Izv. Khim.*, **12**, 500 (1979).

112. J. C. Moore, D. Smith, Y. Youhne and J. P. Devlin, *J. Phys. Chem.*, **75**, 325 (1971).
113. J. J. Hinkel and J. P. Devlin, *J. Chem. Phys.*, **58**, 4750 (1973).
114. Y. Iida, *Bull. Chem. Soc. Japan*, **46**, 423 (1973).
115. R. Bozio, A. Girlando and C. Pecile, *J. Chem. Soc., Faraday Trans. II*, **71**, 1273 (1975).
116. M. S. Khatkale and J. P. Devlin, *J. Chem. Phys.*, **70**, 1851 (1979).
117. V. E. Kampar, S. P. Valtere and O. Ya. Neyland, *Teoret. Eksp. Khim.*, **14**, 369 (1978).
118. C. Krüger, *J. Organometal. Chem.*, **9**, 125 (1967).
119. G. A. Gornowicz and R. West, *J. Amer. Chem. Soc.*, **93**, 1714 (1971).
120. R. Das and C. A. Wilkie, *J. Amer. Chem. Soc.*, **94**, 4555 (1972).
121. I. N. Juchnovski and I. G. Binev, *J. Organometal. Chem.*, **99**, 1 (1975).
122. I. N. Juchnovski, J. S. Dimitrova, I. G. Binev and J. Kaneti, *Tetrahedron*, **34**, 779 (1978).
123. P. J. Mezey, M. A. Robb, K. Yates and I. G. Csizmadia, *Theoret. Chim. Acta*, **49**, 277 (1978).
124. I. N. Juchnovski and I. G. Binev, *Compt. Rend. Acad. Bulgare Sci.*, **26**, 659 (1973).
125. I. G. Binev, I. N. Juchnovski and Ts. M. Kolev, *Izv. Khim.*, **10**, 76 (1977).
126. I. N. Juchnovski and I. G. Binev, *Bull. Soc. Chim. Belg.*, **86**, 793 (1977).
127. Z. I. Demireva, I. G. Binev and I. N. Juchnovski, *Tetrahedron Letters*, 1523 (1976); G. N. Andreev, Z. I. Demireva, I. N. Juchnovski, R. B. Kuzmanova and I. G. Binev, *Izv. Khim.*, **10**, 379 (1977).
128. N. V. Grigor'eva, N. V. Margolis, I. N. Shokhor and I. V. Tselinskiy, *Zh. Strukt. Khim.*, **10**, 943 (1969).
129. G. Albagnac, B. Brun, B. Calas and L. Giral, *Bull. Soc. Chim. Fr. (II)*, 1469 (1974).
130. Ch. Tsvetanov, I. Panayotov and B. Erussalimsky, *Europ. Polym. J.*, **10**, 557 (1974).
131. Ch. Tsvetanov and I. Panayotov, *Europ. Polym. J.*, **11**, 209 (1975).
132. I. N. Juchnovski, V. B. Radomirska, I. G. Binev and E. Grekova, *J. Organometal. Chem.*, **128**, 139 (1977).
133. I. Juchnovski, *Teoret. Eksp. Khim.*, **3**, 410 (1967);
134. I. N. Juchnovski, I. G. Binev and Ts. M. Kolev, *Tetrahedron Letters*, 1519 (1976).
135. I. N. Juchnovski and I. G. Binev, *Tetrahedron Letters*, 3645 (1974); I. G. Binev and I. N. Juchnovski, *Izv. Khim.*, **9**, 33 (1976).
136. I. N. Juchnovski, V. B. Radomirska and I. G. Binev, *Izv. Khim.*, in press.
137. V. M. Vlasov and G. G. Yakobson, *Zh. Org. Khim.*, **7**, 2231 (1971).
138. H. Köhler, B. Eichler and A. Kolbe, *Z. Chem.*, **10**, 154 (1970).
139. Z. Arnold, *Collect. Czech. Chem. Commun.*, **26**, 113 (1961). V. Král and Z. Arnold, *Collect. Czech. Chem. Commun.*, **42**, 3455 (1977); **43**, 1248 (1978). M. Svoboda, M. Synáčková, Z. Samek, P. Fiedler and Z. Arnold, *Collect. Czech. Chem. Commun.*, **43**, 1261 (1978).
140. A. Reiche and P. Dietrich, *Chem. Ber.*, **96**, 3044 (1963).
141. K. Friedrich and J. Kiesel, *Ann. Chem.*, 661 (1976).
142. E. Mayer, D. J. Gardiner and R. E. Hester, *J. Mol. Struct.*, **20**, 127 (1974).
143. I. K. Kireeva, Yu. Ya. Kharitonov, M. A. Knyazeva and Kh. Keller, *Zh. Neorg. Khim.*, **23**, 1183 (1978).
144. Y. A. Pentin, D. I. Makhonkov, L. I. Dyachkova, I. I. Baburin and N. S. Zefirov, *Zh. Obshch. Khim.*, **48**, 1850 (1978).
145. I. Juchnovski, Ch. Tsvetanov and I. Panayotov, *Monatsh. Chem.*, **101**, 1271 (1970).
146. I. N. Juchnovski and I. G. Binev, *Compt. Rend. Acad. Bulgare Sci.*, **31**, 429 (1978).
147. M. S. Khatkale and J. P. Devlin, *J. Phys. Chem.*, **83**, 1636 (1979).
148. J. Kaneti, A. F. Nazir, I. G. Binev, V. B. Radomirska and I. N. Juchnovski, *J. Mol. Struct.*, **68**, 11 (1980).
149. J. L. Dunkan, D. S. McKean, M. W. Mackenzie and J. P. Pena, *J. Mol. Spectry*, **76**, 55 (1979).
150. D. E. Milligan and M. E. Jacox, *J. Chem. Phys.*, **47**, 278 (1967).
151. J. L. Dunkan, D. C. McKean and M. W. Mackenzie, *J. Mol. Struct.*, **42**, 77 (1977).
152. J. L. Dunkan, D. C. McKean and N. D. Michie, *J. Mol. Struct.*, **21**, 405 (1974).
153. L. Malatesta and F. Bonati, *Isocyanide Complexes of Metals*, John Wiley and Sons, London, 1969.
154. I. Ugi and R. Meyr, *Chem. Ber.*, **93**, 239 (1960).
155. R. W. Stephany, M. J. A. de Bie and W. Drenth, *Org. Mag. Res.*, **6**, 46 (1974).

156. R. G. Gillis and J. L. Occolowitz, *Spectrochim. Acta*, **19**, 873 (1963).
157. W. D. Herrocks and R. H. Mann, *Spectrochim. Acta*, **19**, 1375 (1963).
158. A. M. Benson, Jr. and H. G. Drickamer, *J. Chem. Phys.*, **27**, 1164 (1957); R. R. Wiederkehr and H. G. Drickamer, *J. Chem. Phys.*, **28**, 311 (1958).
159. K. Bolton, N. L. Owen and J. Sheridan, *Spectrochim. Acta*, **26**, 909 (1970).
160. B. Bak and C. Kierkgaard, *Acta Chim. Scand.*, **27**, 2531 (1973).
161. R. A. Nalepa and J. D. Laposa, *J. Mol. Spectry*, **50**, 106 (1974).
162. A. R. Katritzky, H. J. Keogh, S. Ohlenrott and R. D. Topsom, *J. Amer. Chem. Soc.*, **92**, 6855 (1970).
163. I. N. Juchnovski, J. Tsenov and V. Juritsyn, to be published.
164. Kh. S. Bagdasaryan, *Theory of Radical Polymerization* (Russ.), Nauka, Moskva, 1966, p. 273.

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 5

Photoelectron spectra of cyano compounds*

H. STAFAST† and H. BOCK§

Chemische Institute der Universität Frankfurt, Niederurseler Hang, D-6000 Frankfurt/Main 50, W. Germany

*Part 98 of *Photoelectron Spectra and Molecular Properties*. For Part 97 cf. H. Bock, W. Ried and U. Stein, *Chem Ber.*, **114**, 673 (1981).
§Author to whom correspondence should be sent.
†Present-address: Physical Chemistry Institute, University of Zürich, Winterthurer Str. 190, CH-8057 Zürich, Switzerland.

Abbreviations

CNDO	Complete Neglect of Differential Overlap
EHMO	Extended Hückel Molecular Orbital
ESCA	Electron Spectroscopy for Chemical Analysis
IE	Ionization Energy
LCBO	Linear Combination of Bond Orbitals
MINDO	Minimum Neglect of Differential Overlap
PE	Photoelectron
PES	Photoelectron Spectroscopy
QMO	Qualitative Molecular Orbital
SCF	Self Consistent Field

I. INTRODUCTION AND SCOPE

Cyano compounds display an impressing variety of interesting chemical and physical properties, and cyano substituents often inflict drastic changes upon parent systems[18,38,40,47,80,89,92].

The smallest derivative, HCN, and its oligomers are well-known precursors in prebiological systems[89]. Acrylonitrile, in contrast to most of the other cyano-substituted ethylenes, polymerizes easily to yield synthetic fibres[110]. Tetracyanoethylene is the prototype electron acceptor[39] and polycyano hydrocarbons are strong C—H acids[76]. On the other hand, neither nitrogen tricyanide nor oxygen dicyanide have been synthesized so far[73]. In spite of the small size of the cyano group, the HNH angle in ammonia opens in cyanamide from 107° to 113.5°; simultaneously the formally single NC bond in $H_2N—CN$ shrinks to a mere 1.34 Å[95,108]. Unexpectedly, many X—C≡N linkages are bent, e.g. in $S(CN)_2$,[81,91].

Photoelectron spectroscopy (PES), a technique developed in the past decade[107], supplies much information on radical cation states generated by photoionization of valence electrons[10,11,20,33,37,49,50,85,107].

Via use of Koopman's theorem, $IE_n = -\varepsilon_j^{SCF}$ [65], which links the experimental ionization potentials IE_n to calculated SCF eigenvalues $-\varepsilon_j^{SCF}$ [20,33,51], this information can be correlated with molecular orbital (MO) models, useful to the chemist for rationalization of molecular properties especially of chemically related compounds[11]. So far photoelectron spectra of some 70 cyano compounds have been recorded and interpreted, which are grouped together in this review as specified in Table 1.

Besides accumulating the PE spectroscopic data for cyano compounds scattered in the literature till the end of 1976 with some extensions to 1981, another purpose of the

TABLE 1. Cyano compounds investigated by PES

Symmetry	R	References
Monocyano compounds, R—C≡N		
$C_{\infty v}$	H—	He(I) 8, 20, 41, 42, 49, 57, 68, 83, 94, 104, 107, 111 and He(II) 41, 83
	D—	3, 107
	F—	He(I) and He(II) 9
	Cl—	29, 52, 58, 69, 106
	Br—	29, 52, 58, 69, 106, 111

TABLE 1. *continued*

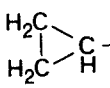
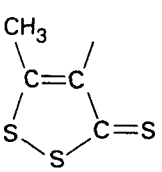
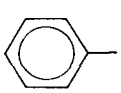
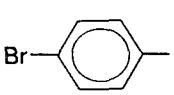
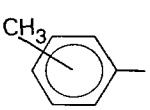
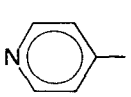
Symmetry	R	References
$C_{\infty v}$	I—	29, 52, 58, 69, 106, 111
	HC≡C—	3, 107
C_{3v}	H_3C—	6, 43, 44, 69, 95, 102, 105, 111
	D_3C—	43, 107
	F_3C—	99
	Cl_3C—	He(I) 69, 90 and He(II) 90
	$(CH_3)_3C$—	99, 102
	H_3Si—	99
	$H_3C\,Hg$—	21
C_{2v}, C_s, C_1	ClH_2CCH_2—	69
	$(H_3C)_2HC$—	6, 69, 102
	ClH_2CCH_2—	102
	$(H_3C)_2HC$—	102
		99, 107
	$H_2C{=}CHCH_2$—	69, 99
	$H_2C{=}CH$—	6, 59, 69, 96
	$H_2C{=}CX$—	59 (X = H, Cl, CH_3, COOR, COCOR)
		46
		47, 62, 87, 107
		4, 62
		*ortho*: 47, 63 *meta*: 63 *para*: 63
		*ortho, meta, para:* 63, 64

TABLE 1. *continued*

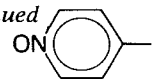
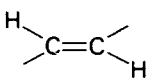
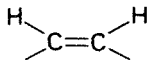
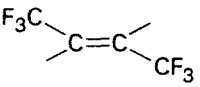
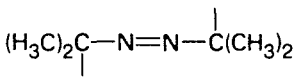
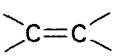
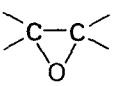
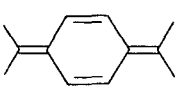
Symmetry	R	References
C_{2v}, C_S, C_1 *continued*		*ortho, meta, para:* 71, 72
	H_2N—	95
	$(H_3C)_2N$—	95
	$(CH_2)_4N$—	99
	ON—	15
	NNN—	5
	F_2P—	27
	$(H_3C)_2P$—	34, 35
	$(F_3C)_2P$—	34, 35
	$(H_3C)_2As$—	35
	H_3CS—	99
Dicyano compounds, R(CN)₂		
$D_{\infty h}$	(NC—CN)	1, 3, 23, 57, 107, 111
	—C≡C—	3, 99
	—Hg—	21
C_{2v}, C_s (geminal)	H_2C	98
	$(H_3C)_2C$	98
	$H_2C{=}C$	59, 96
	$O{=}C$	99, 105, 106
	H_3CP	34, 35
	F_3CP	34, 35
	S	91
	Te	99
C_{2h}, C_{2v}, C_s, C_1	$-H_2C-CH_2-$	100
		14, 59, 96

TABLE 1. *continued*

Symmetry	R	References
C_{2h}, C_{2v}, C_5, C_1 *continued*		14, 59, 96
		59
		60
Polycyano compounds, $R(CN)_n$, n > 2		
T_d		12
D_{2h}		96
C_{2v}		96
D_{2h}		61, 70
C_{3v}		34, 35

following summary is an attempt to improve and to check the often difficult spectroscopic assignment by comparative discussion, e.g. by the use of MO parameters deduced from PES ionization energies. Hopefully, this approach will facilitate and stimulate further investigation of the interesting cyano compounds.

II. INFORMATION FROM, AND ASSIGNMENT OF, THE PHOTOELECTRON SPECTRA OF CYANO COMPOUNDS

Photoelectron spectroscopy[1,33,85,107] deals with the photoionization of a neutral species M to its cation M^+:

$$M + h\nu \rightarrow M^+ + e^- \quad (1)$$

The photon energy $h\nu$ in excess of the ionization energy $IE_n(M)$ is conserved as kinetic energy of the ejected electron:

$$h\nu = IE_n(M) + E_{kin}(e^-) \quad (2)$$

If one chooses, as in most cases, a helium(I) discharge lamp as the source of monochromatic photons with $h\nu$ = 21.21 eV, all ionization potentials up to 21.21 eV

can be measured by counting the emitted electrons of specific kinetic energy. For example, the He(I) PE spectrum (Figure 1) of the 16-valence-electron molecule acetonitrile displays four bands within the He(I) measurement range up to 21.21 eV, due to six of the eight expected ionizations[95].

The ionization energies are energy differences between the ground state of a (closed-shell) molecule M and the ground-state or electronically excited states of its radical cation $M^{\bullet+}$ generated in the photoionization process (equation 1). In general, vibrational and rotational excitations take place simultaneously and therefore equation (2) has to be expanded:

$$IE_n = h\nu - E_{kin}(e^-) - E_{vib} - E_{rot} \tag{3}$$

Further differences between M and $M^{\bullet+}$ states[11,33,85] arise predominantly from the instability of the latter towards changes in structure or spin-orbit coupling in the resulting doublet states with nonzero angular momentum. Although a detailed discussion of the underlying principles, e.g. of Franck-Condon transitions between different potential surfaces[33,85], is beyond the scope of this review, some of the more frequently observed features in He(I) spectra have to be mentioned because they are of importance in spectroscopic assignment. The acetonitrile PE spectrum (Figure 1) shows four different types of bands, which correspond to ionizations (1) + (2), (3), (4) + (5), (6) and which represent partly degenerate radical cation states with a variety of vibrational levels. To begin with, the needle-like band assigned to ionization (3) with some less distinct vibrational satellites of low intensity is typical for the ejection of a 'nonbonding' electron from the nitrogen lone pair, i.e. negligible changes between M and $M^{\bullet+}$ geometries. The distinct progression of peaks in the first band [ionizations (1) + (2)] are caused by $M^{\bullet+}$ vibrations, with, for example, the stretching frequency ν^{+}_{CN} reduced relative to that of M indicating removal of a π_{CN} bonding electron. The broadened third band, which can be deconvoluted into two components (4) and (5), suggests considerable deformation of the acetonitrile geometry in this cation state: a Jahn–Teller distortion removes the threefold molecular axis and thereby the

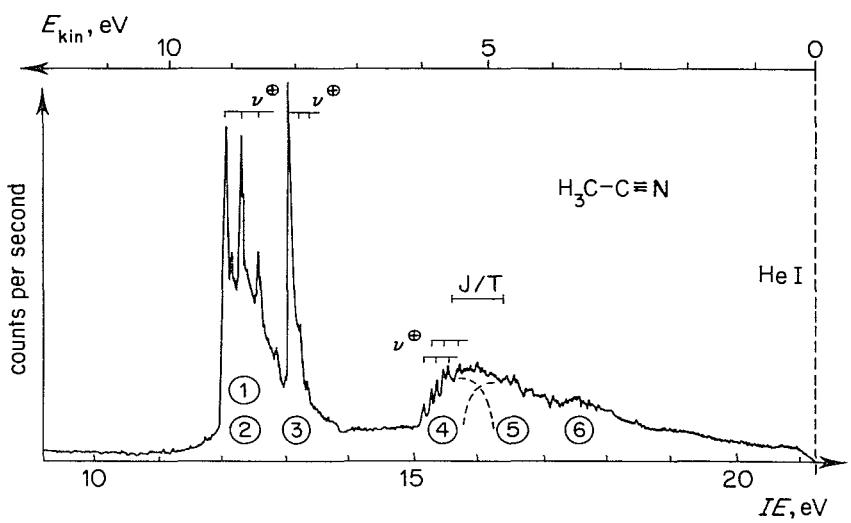


FIGURE 1. He(I)PE spectrum of H_3CCN[95].

degeneracy of the ^2E state, which originates from predominant methyl group ionization. Finally, the fourth band [Figure 1, ionization (6)], which represents one of the remaining $^2\Sigma$ states (π_{CN}, n_N and π_{CH_3} ionizations have already been assigned), exhibits no fine structure at all as is often observed[33] if vibrational spacing is too small to be resolved.

Two other PE spectroscopic peculiarities, which are also helpful in assignment, are illustrated in Figure 2 by bands from cyanogen iodide[52,69] and hydrogen cyanide[33]. Ionization of the p-type iodine lone pairs leads to two $^2\Pi$ states for $ICN^{\bullet+}$, the degeneracy of which is removed by spin-orbit coupling[19,33,55,85,112] to yield $^2\Pi_{3/2}$ and $^2\Pi_{1/2}$ spin states[52,69]. The two needle-like bands (Figure 2a) accompanied by low-intensity vibrational satellites are separated by only 0.53 eV relative to the value ΔIE = 0.942 eV for the iodine cation I^+ (Br^+: 0.458 eV, Cl^+: 0.110 eV; cf. References 19 and 113). Ionization of predominantly C—H bonding electrons of HCN[33] leads to a $^2\Sigma$ state susceptible to (pre)dissociation as confirmed by the abruptly ending vibrational fine structure at 20.3 eV (Figure 2b).

Summarizing, the energy differences between the ground state of a molecule M and the various states of its radical cation $M^{\bullet+}$ measured by PE spectroscopy supply experimental information on the latter. Vibrational frequencies ν^+, band-shape, band-split by Jahn–Teller distortion or by spin-orbit coupling, predissociation and other band patterns characterize individual ionizations and thus establish a basis for spectroscopic assignment. Further advice for assignment can be obtained by recording spectra with different photon sources (Figure 3), or especially by comparing PE spectra of chemically related compounds (Figure 4).

In general, intensity arguments should not be overemphasized in the discussion of PE spectra[20,33]. Nevertheless, as exemplified by the Ne(I), He(I) and He(II) PE spectra of $S(CN)_2$ (Figure 3)[91], cross-section dependent intensity changes[30,83,85,86,90] permit the identification of ionizations, help to deconvolute overlapping bands and give some hints as to how to discriminate between peaks due to electronically and vibrationally excited radical cation states. In the case of $S(CN)_2$, for example, the varying intensity

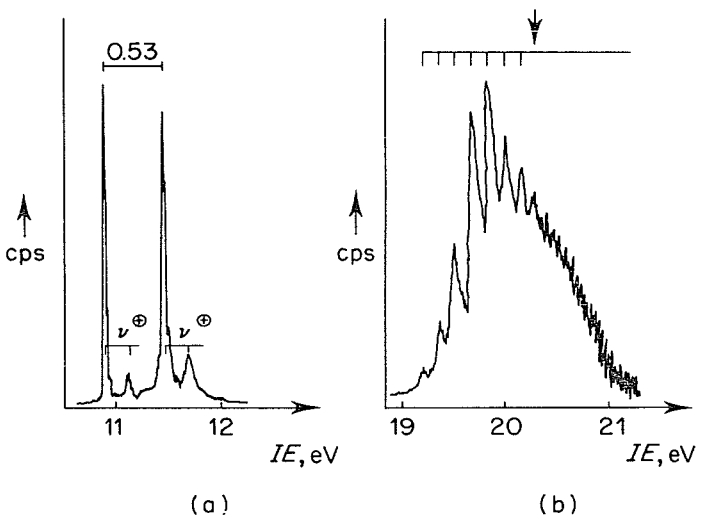


FIGURE 2. (a) First two PE bands of ICN[52,69]; (b) third PE band of HCN.

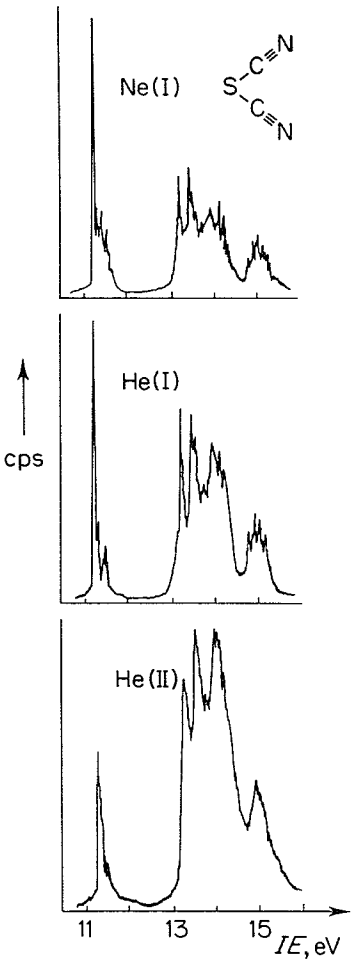


FIGURE 3. PE spectra, 10–14 eV, of $S(CN)_2$ recorded with Ne(I), He(I) and He(II) photon sources.[91]

of the first band at 11.34 eV is due to the different 3p ionization cross-sections of the individual photon sources used and thus further confirms that the sharp peak is due to ionization of the sulphur lone pair[91].

The PE spectroscopic comparison of chemically related compounds often proves to be the most valuable tool in the assignment (cf., for example, References 10 and 11). An excellent example is provided by the diacetylene → cyanogen series[107] (Figure 4): the two diacetylene π ionizations, clearly identified by their vibrational progressions, increase in energy upon isoelectronic exchange CH → N due to the higher effective nuclear charge of nitrogen. In between the π bands the nitrogen lone-pair ionizations appear, being split only in the cyanogen PE spectrum (Figure 4).

Many of the above PE spectroscopic observations are fairly well reproduced by the results of appropriate molecular orbital calculations with the missing link being provided by Koopmans theorem[65]:

$$IE_n^v = -\varepsilon_j^{SCF} \tag{4}$$

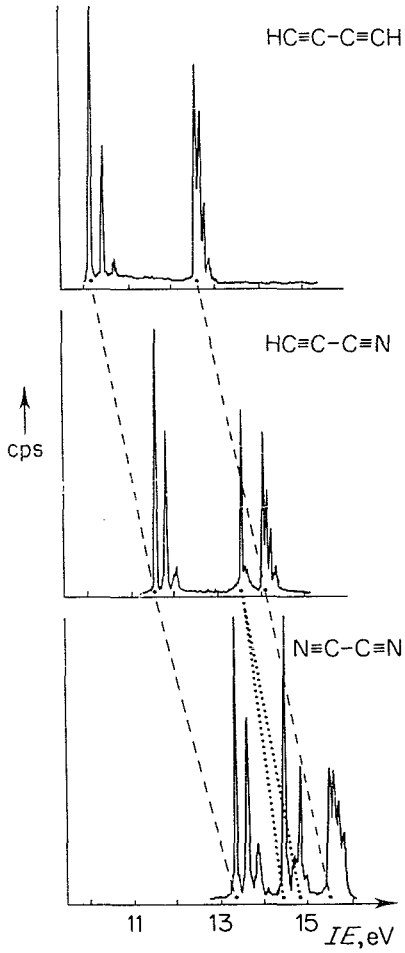


FIGURE 4. He(I) PE spectra, 10–16 eV, of diacetylene, cyanoacetylene, and cyanogen.

which correlates vertical ionization energies IE_n^v with negative eigenvalues $-\varepsilon_J^{SCF}$ of the canonical[67] SCF orbitals calculated for the ground state of the molecule M[20,33,51,85]. Usually the vertical ionization energies[93] are simply assumed to be represented by the PES band maxima. To evaluate the reliability of Koopmans' theorem for cyano compounds, PE spectroscopic ionization potentials and *ab initio* SCF eigenvalues are compared for some smaller molecules in Figure 5. For small cyano compounds, the *ab initio* SCF eigenvalues do not in all cases correlate reasonably with the PE ionization energies: sometimes deviations, e.g. for HCCCN, amount up to 3.3 eV, and repeatedly orbital and radical cation state sequences show a cross-over (Figure 5, ○). The deviations from Koopmans' theorem (equation 4), a detailed discussion of which is far beyond the scope of this review, are due to the assumption of a 'frozen radical cation' neglecting the different electron correlation energies for M and the individual states of $M^{\bullet +}$ as well as electron reorganization upon ionization (cf., for example, References 20, 33, 51 and 85). Quite often the electron ejection is accompanied by considerable structural changes (cf., for example, References 11 and 55). Mispredictions are therefore expected whenever these effects become large and do not cancel out.

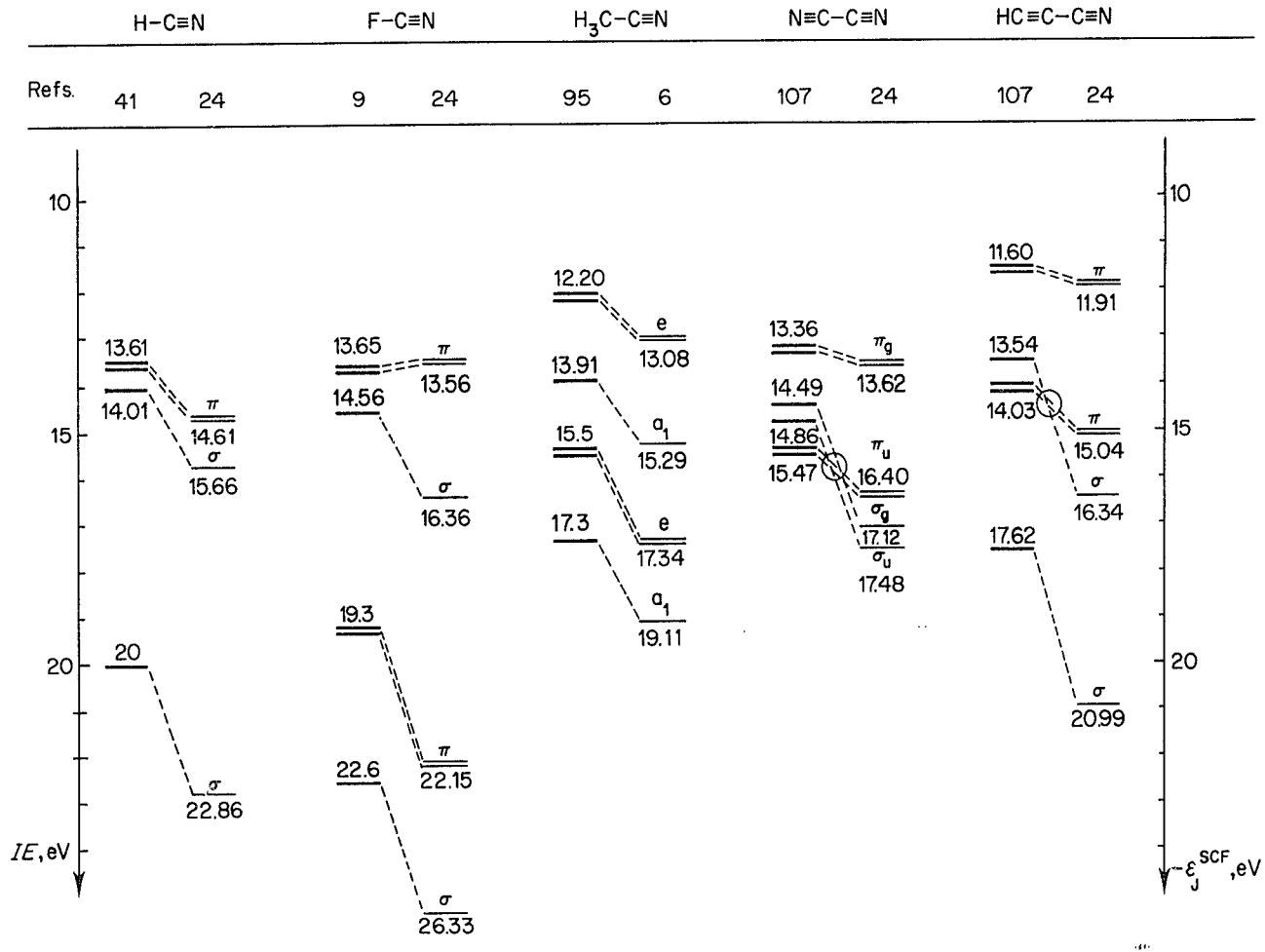


FIGURE 5. Correlation of *ab initio* SCF eigenvalues $-\varepsilon_J^{SCF}$ with PES ionization energies IE_n^v for some cyano compounds (O: sequence deviation).

Nevertheless, failures of Koopmans' theorem are hard to prove and only few are known definitively. It has to be pointed out, that sometimes, and particularly for PE spectra of molecules with numerous overlapping bands and lacking fine structure, molecular orbital calculations are the only means to achieve at least a tentative assignment. In addition, MO models allow to rationalize the vast amount of PES data, to compare chemically related molecules and to correlate other molecular properties as well.

The smaller the changes during ionization to the radical cation state, i.e. the smaller the neglects in the calculation and, especially, if these are performed for the individual radical cation states (cf. Reference, 91) the closer will the results resemble the PE spectroscopic observations. As an example as to what can be achieved by today's quantum mechanics, beyond Koopmans' theorem, the experimental PE spectrum of cyanogen is compared to the one calculated by a Greens' function perturbations approach[23] (Figure 6).

A warning concerning the assignment of PE spectra of cyanogen compounds based on calculations may be summarized as follows: except for radical cation state calculations beyond the Hartree–Fock level[65], caution seems advisable even concerning *ab initio* SCF results. Semiempirical methods are usually not reliable enough to supply more than an idea of what kind of radical-cation states are to be expected (cf., for example, Reference 96). This should be kept in mind, especially for the characteristic π_{CN}/n_{CN} ionization region of cyanogen compounds between 13 eV and 16 eV, where usually numerous PE bands overlap. The most impressive example

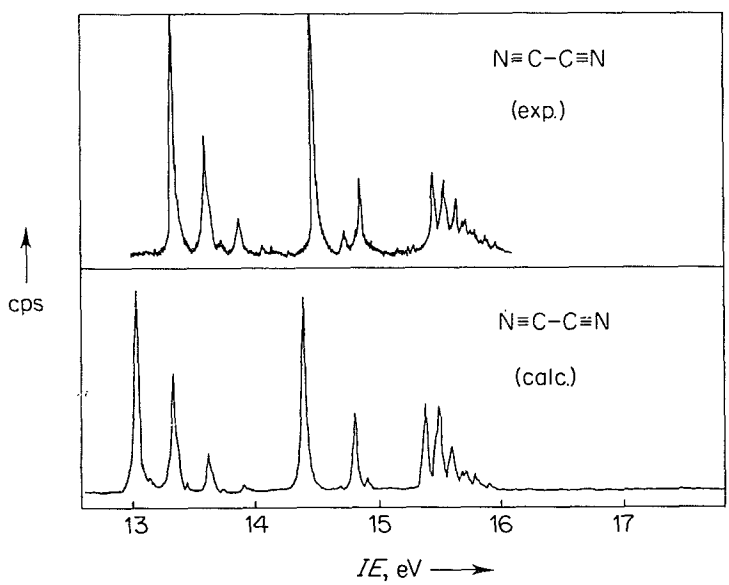


FIGURE 6. PE spectrum of cyanogen and its computer simulation using a Green's function perturbation calculation[23].

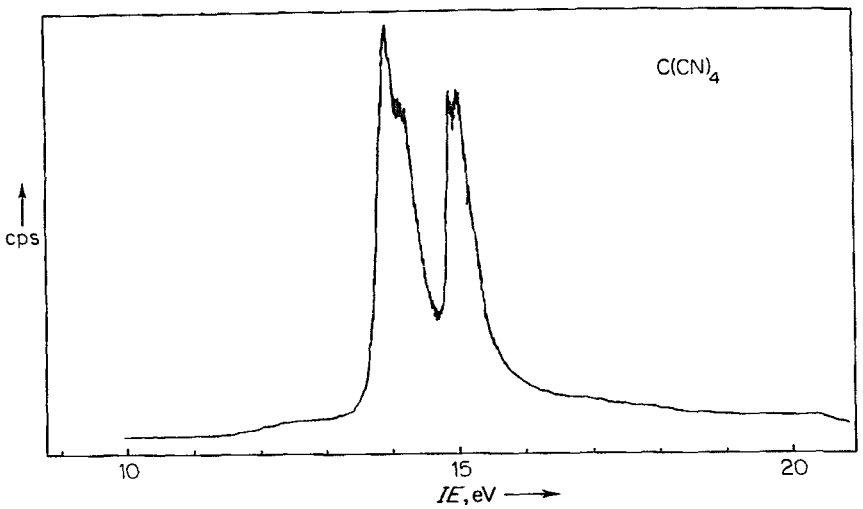


FIGURE 7. He(I) PE spectrum of tetracyanomethane[12].

is supplied by the PE spectrum of tetracyanomethane (Figure 7)[12], exhibiting 12 of its 20 valence electron ionizations within the narrow range of only 1.3 eV.

In those cases where neither spectroscopic arguments nor possibly elusive results of calculations (Figure 5) can provide clues to the assignment of the PE spectra of cyano compounds, the following procedure based on comparison of equivalent radical cation states within series of chemically related compounds (cf., for example, References 10 and 13) has proven to be a good way of gaining insight: starting from symmetry-adapted linear combinations of bond orbitals, the resulting LCBO MO models are easily parametrized using the PE ionization energies. To illustrate the approach, cyanogen may serve as an example (Figure 8).

A model to incorporate the 18 valence electrons of cyanogen needs nine orbitals to occupy, which can be classified in $4\pi_{CN}$, $2n_N$ and $3\sigma_{NCCN}$. Because the He(I) spectrum (Figure 6) shows only six ionizations, the π_{CN} and n_N levels—energetically well separated from the σ levels—may be considered separately in a first approximation. This holds strongly for the $2\pi_g$ and the $2\pi_u$ orbitals, for which one obtains from the PE spectrum a Coulomb integral $\alpha_{CN} = \frac{1}{2}(13.36 - 15.47) = -14.42$ eV and a resonance integral $\beta_{CN/CN} = (13.36 - 14.42) = -1.06$ eV. For the n_N levels, interaction with the σ orbitals of same symmetry has to be incorporated into the model to account for the $\Delta n_N = 0.37$ eV split in the PE spectrum (Figure 6).

Although only occupied orbitals are considered within LCBO MO models, for symmetric cyano compounds a fairly good approximation results because of their relatively high-lying unoccupied orbitals and their large separation of $\pi_{CN} + n_N$ and σ ionizations. The individual parameters obtained are transferable within some limits and, therefore constitute a useful set for spectroscopic assignments[14,96,98,99]. Even in cases where the parameters α and β cannot be adapted, perturbation arguments often supply interesting information. Thus the LCBO MO approach widely used in the following discussions, not only helps to assign PE spectra, but allows some rationalization of bonding within series of cyano compounds.

In summary, cyano compounds, which sometimes exhibit extreme and fascinating molecular properties, give rise also to peculiar and complicated PE spectra.

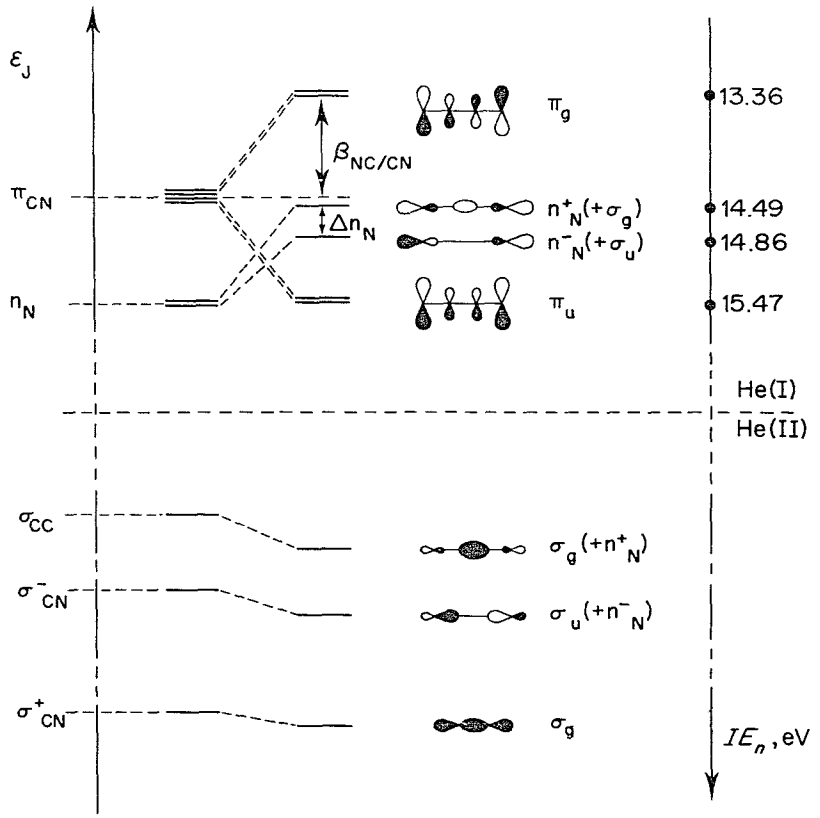


FIGURE 8. LCBO MO models for NC—CN and its π parametrization using PE ionization energies (cf. Figures 5 and 6).

Assignment to individual radical cation states can be based only with reservation on *ab initio* SCF calculations applying Koopmans' theorem, because correlation and relaxation defects may be large, and because numerous ionizations are usually packed into a narrow measurement range. The best approach is, therefore, to rely on information from PE spectroscopic band patterns as well as – guided by simple symmetry-adapted orbital models – on comparison of equivalent radical cation states along series of chemically related molecules.

III. π AND σ INTERACTIONS IN MONOCYANO DERIVATIVES

Most of the cyano compounds investigated so far by PE spectroscopy are monosubstituted derivatives R—C≡N (cf. Table 1). For easier survey, these are subdivided here according to their overall symmetry into those belonging to groups $C_{\infty v}$ and C_{3v}, and those without an ($n \geq 3$)-fold axis. Such a classification advantageously distinguishes between π systems with or without degenerate π_{CN} orbitals. For an illustration of the PE spectroscopic assignment procedure using LCBO MO models to compare radical cation states, the molecules HCN, CH_3CN and NH_2CN form a well-suited series of chemically related compounds (Figure 9)[95].

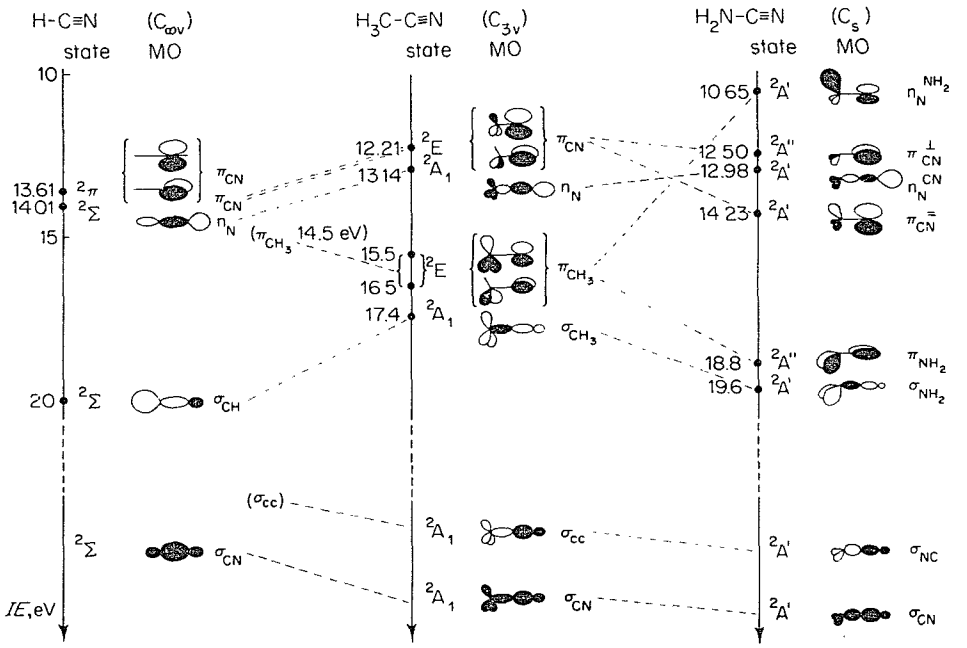


FIGURE 9. LCBO MO models for assignment of PE valence electron ionizations of HCN, CH_3CN and NH_2CN[95].

To interpret the PE spectroscopically observed radical cation states of cyano compounds RCN (R = H, H_3C and H_2N), using qualitative symmetry-adapted LCBO orbitals, one starts advantageously with the 3 $HCN^{\bullet+}$ states (one doubly degenerate), which result from the ionization of the eight valence electrons. They are assigned following the results of *ab initio* calculations (Figure 5) and are denoted according to the predominant orbital contribution. In acetonitrile, the three additional occupied methyl group orbitals π_{CH_3} (e) and σ_{CH_3} (a_1) have to be incorporated via interaction with all other basis orbitals of the same symmetry. This leads in a self-explanatory way to the acetonitrile splitting scheme (Figure 9) in which the mixing of the two e-type orbitals, π_{CN} and π_{CH3}, represents one of the classical examples of hyperconjugation[36]. The molecules $H_3C—C\equiv N$ and $H_2N—C\equiv N$ are isoelectronic: formally one of the CH protons has been 'dislocated' into the nitrogen nucleus. The higher effective nuclear charge raises most ionization potentials, though to different extents. Both π_{CN} ionization energies increase up to 2 eV, while n_N stays almost constant. The orbital correlations between $H_3C—C\equiv N$ and $H_2N—C\equiv N$ are obvious, once the amino lone pair has been generated isoelectronically from a CH bond.

Obviously, LCBO orbitals and their correlation by symmetry and by perturbation arguments, as exemplified for $H—C\equiv N$, $H_3C—C\equiv N$ and $H_2N—C\equiv N$ (Figure 9), are a valuable aid in assigning PE spectra. The corroborated MO models may be used to interpret other molecular properties as well. Therefore, such a simple and useful approach will be preferred for the interpretation of the radical cation states of the monocyano compounds. The individual discussions are based on the quoted literature assignments referred to for details. Whenever possible, unpublished PE spectra[99,100] will be presented in the figures.

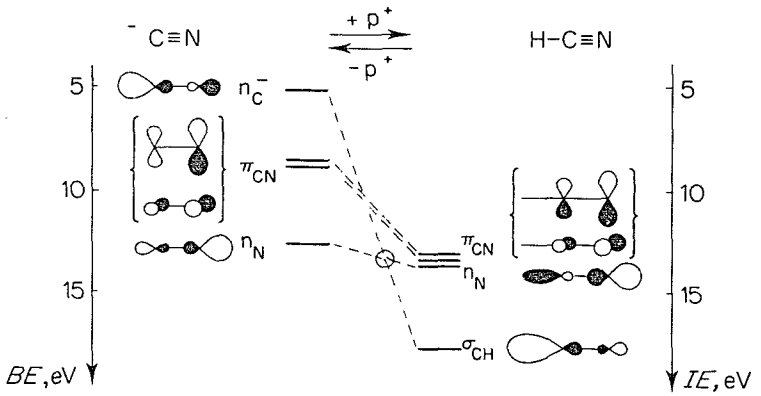


FIGURE 10. Correlation between ESCA binding energies BE_n of ^-CN[78] and PES ionization potentials IE_n of HCN[107].

A. Linear Molecules

Within the series of cyano compounds, there is one purely inductive perturbation[24] of the —C≡N group known: the deprotonation of HCN or, vice versa, the protonation of ^-CN (Figure 10).

Although solid-state ESCA[78] and gas-phase PES data are of limited comparability, obviously the additional p^+ point charge produces the following stabilizations: the most distant nitrogen lone pair is least affected, the π_{CN} ionization energies increase by ~4.6 eV and – neglecting the formal orbital noncrossing (Figure 10, point ○) – formation of the σ_{CH} bond by n_{C^-} protonation expectedly leads to a tremendous change.

From the differences between the isoelectronic species ^-CN/HCN one expects that in linear compounds RCN the substituents R will affect the individual levels in the order $n_N \approx$ constant $\ll \pi_{CN} < \sigma_{RC}$. This is confirmed by the PE spectroscopic comparison of HCN with cyanoacetylene (Figure 5) and the cyanogen halides (Figure 11).

In the derivatives R—C≡N (Figure 11), expansion of the π system as well as of the σ framework leaves the nitrogen lone pair ionization largely unaffected (Figure 11: IE_n = 13.8 ± 0.7 eV; cf. also Figure 2), leads to considerable split of the π ionizations $\Delta IE_\pi > 2.5$ eV and shifts the lowest σ ionization by more than 5 eV between 22.3 eV and 16.7 eV. In detail, comparison between HCN and FCN shows that the π ionizations remain constant – a good example of the 'perfluoro effect'[20,85]. On switching from FCN to ClCN, the sequence of π radical cation states is reversed according to the predominant orbital character. From ClCN to ICN the π and n_N ionizations are shifted nearly parallel to lower ionization energies while increasing spin orbit coupling is observed. Both doubly degenerate $^2\Pi$ states of $BrCN^+$ and ICN^+ are split into $^2\Pi_{3/2}$ and $^2\Pi_{1/2}$ spin states and according to a simple prediction, the sum of the splittings approximately resembles the values $\Delta\Pi_{3/2,1/2}$ found in other cases, e.g. for corresponding methyl halides $H_3C—X$[52] (Table 2).

The X—CN PE spectra exhibit pronounced vibrational fine structures (cf., for example, Figure 2 or 3), the careful analysis of which allows an estimate of bond-length changes Δd, e.g. for the XCN^+ $^2\Pi$ ground state[58] (Table 3). The differences estimated are in accord with qualitative MO considerations. Thus, on removal of a bonding electron, the CN bond is always lengthened, the shortening Δd_{XC}

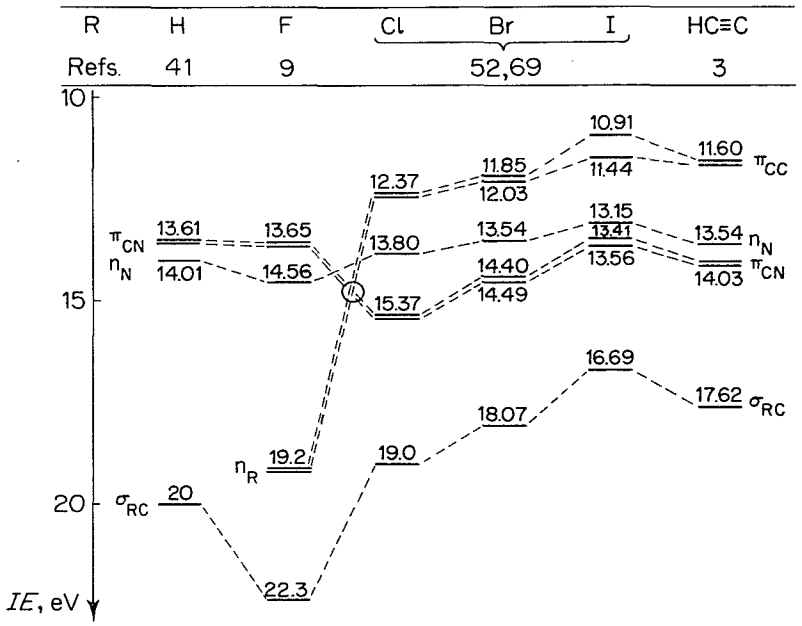


FIGURE 11. Comparison of ionization energies π_{CN}, n_N and σ_{RC} within the series R—C≡N (R = H—, F—, Cl—, Br—, I—, HC≡C—).

in the halides nicely reflects the antibonding X/CN interaction in the highest occupied orbital (cf., for example, Figure 9). Decreasing π interaction with increasing bond length d_{XC} in the order Cl < Br < I also fits into the MO picture.

LCBO MO models (Figure 9) for the compounds RCN in Figure 11 can be parametrized using PE ionization potentials, if an estimate is available for one of the three unknowns α_{CN}, α_π and $\beta_{\pi/CN}$, which have to be determined from two ionization

TABLE 2. PE spectroscopically observed spin-orbit splittings in X—CN and X—CH$_3$[3]

	X—CN			X—CH$_3$
X	$\Delta\Pi^{(1)}_{3/2,\,1/2}$	$\Delta\Pi^{(2)}_{3/2,\,1/2}$	$\Sigma\Delta\Pi_{3/2,\,1/2}$	$\Sigma\Delta\Pi_{3/2,\,1/2}$
Br	−0.18 eV	−0.09 eV	−0.27 eV	−0.30 eV
I	−0.53 eV	−0.15 eV	−0.68 eV	−0.64 eV

TABLE 3. Bond lengths in cyanogen compounds and estimated changes upon ionization[58]

X	d_{XC} (Å)	d_{CN} (Å)	Δd_{XC} (Å)	Δd_{CN} (Å)
H	1.064	1.156	+0.02	+0.06
Cl	1.631	1.159	−0.076	+0.048
Br	1.789	1.158	−0.070	+0.059
I	1.994	1.159	−0.048	+0.013($^2\Pi_{3/2}$)
			−0.060	−0.021 ($^2\Pi_{1/2}$)

potentials. In the case of cyanoacetylene, for instance, an interaction parameter can be transferred from the closely related dicyanoacetylene[107]. From three π ionization energies, that of the radical cation state $^2\Pi_u$ may serve as an intramolecular standard, $\alpha_{CN} = -13.89$ eV (Figure 12) and therefore permit unequivocal evaluation of the parameter $\beta_{CC/2CN}$ as defined by the secular determinant:

$$\begin{vmatrix} \alpha_{CC} - \varepsilon & \beta_{CC/2CN} \\ \beta_{CC/2CN} & \alpha_{CN} - \varepsilon \end{vmatrix} = 0 \qquad (5)$$

with $\varepsilon = -11.81$ eV or -14.95 eV from the PE spectrum of NC—C≡C—CN[99]. Normalization $\beta_{CC/2CN} \cdot 1/\sqrt{2} = \beta_{CC/CN}$ yields the interaction parameter for cyanoacetylene (Figure 12).

Inserting $\beta_{C\equiv C/C\equiv N} = -1.05$ eV into the second-order LCBO MO determinant for cyanoacetylene yields $\Delta\pi = 0.60$ eV, and $\alpha_{CC} = -12.20$ eV as well as $\alpha_{CN} = -13.44$ eV. Comparison of parameters α_{CC} and α_{CN} for acetylene and some linear cyano compounds deduced from their PE spectra[99] (Table 4) reflects the π stabilization due to the larger effective nuclear charge of nitrogen. The general parametrization procedure used above[99] has been applied successfully to numerous other linear compounds like haloacetylenes Hal—(C≡C)—Hal[53] or Hal—$(C\equiv C)_n$—H[48]. Contrary to the near perfect estimate of ionization potentials,

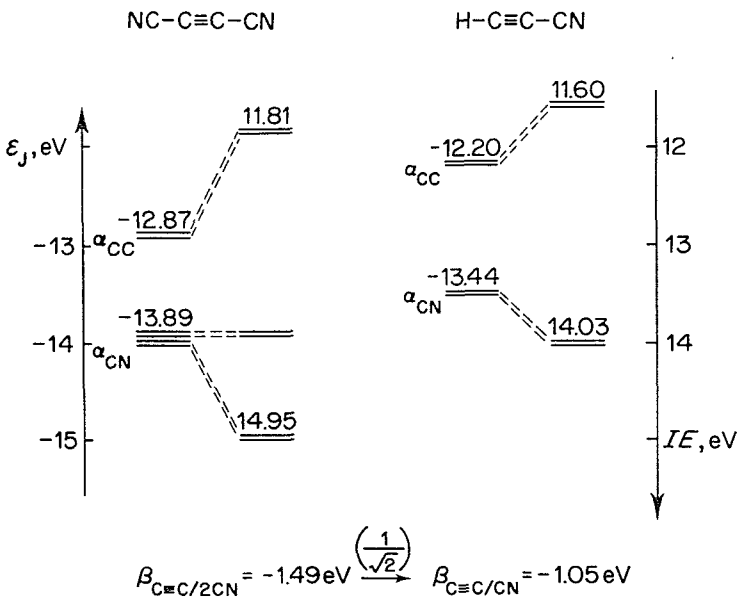


FIGURE 12. LCBO MO models for cyanoacetylenes and their PE spectroscopic parametrization.

TABLE 4. PE spectroscopic parameters for some cyanogen compounds

	H—C≡C—H	H—C≡C—C≡N	H—C≡N	N≡C—C≡C—C≡N	N≡C—C≡N
α_{CC} (eV)	−11.40	−12.20	—	−12.87	—
α_{CN} (eV)	—	−13.44	−13.60	−13.89	−14.42

rather poor wave functions result, and the basis set needs improvement by including antibonding orbitals if phenomena like spin orbit coupling are to be reproduced correctly[53].

B. C_{3v} Molecules

Seven cyano compounds with overall C_{3v} symmetry are listed in Table 1: except for silyl cyanide $H_3Si—C\equiv N$ and the methylmercury compound, they are acetonitrile derivatives $R_3C—C\equiv N$ with R = H, D, F, Cl and CH_3. The PE spectra of H_3SiCN and F_3CCN (Figure 13) have not yet been published[99]. Numerical values for ionization energies are included in the Figures 14 [H_3CCN + H_3SiCN] and 15 [Cl_3CCN + F_3CCN].

As is obvious from the CH_3CN PE spectrum (Figure 1), $^2\Pi$ radical cation states remain doubly degenerate [(1) + (2)] unless Jahn–Teller distortion removes the threefold axis [(4) + (5)]. Starting from the PE spectrum of acetonitrile (Figure 1) and

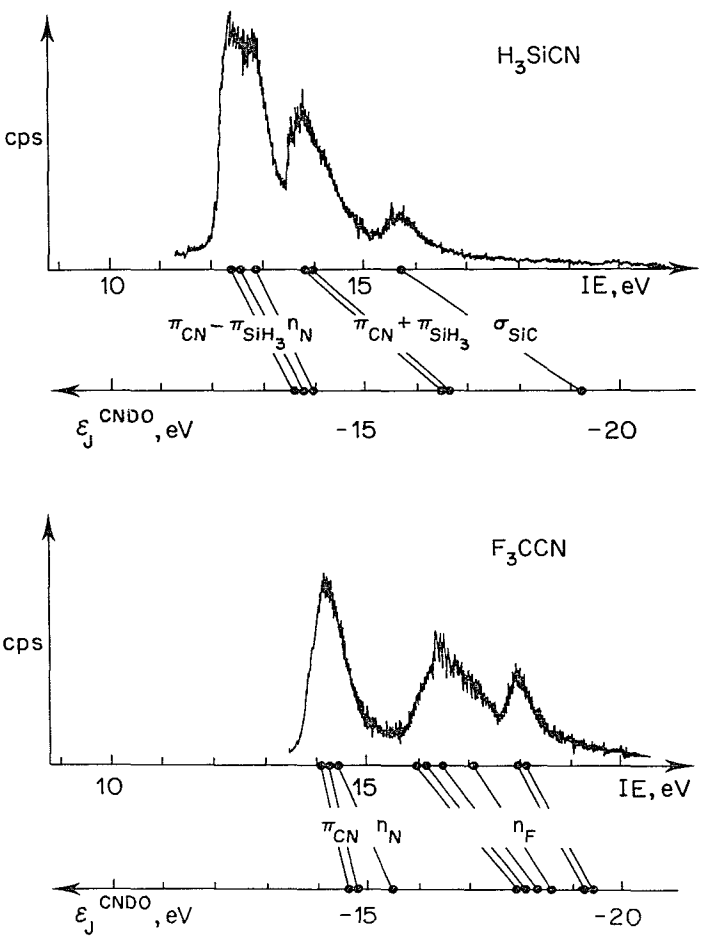


FIGURE 13. He(I) PE spectra of $H_3Si—C\equiv N$ and $F_3C—C\equiv N$ with CNDO assignment (cf. Figures 14 and 15)[99].

TABLE 5. Vibrational frequencies (cm^{-1}) of H_3CCN, D_3CCN and their radical cations

Vibrational mode	ν(H)	ν(D)	$\frac{\nu(H)}{\nu(D)}$	ν^+(H)	ν^+(D)	$\frac{\nu^+(H)}{\nu^+(D)}$
ν_2 (CN stretch)	2249	1990	1.13	2010	1990	1.0
ν_3 (CH_3 def.)	1376	1070	1.29	1430	1070	1.3
ν_4 (CC stretch)	918	810	1.13	810	810	1.0

its MO interpretation (Figure 9), the following radical cation state comparisons will be discussed: (*i*) $H_3C{-}C{\equiv}N$ vs. $D_3C{-}C{\equiv}N$, (*ii*) $H_3C{-}C{\equiv}N$ vs. $H_3Si{-}C{\equiv}N$ and (*iii*) $Cl_3C{-}C{\equiv}N$ vs. $F_3C{-}C{\equiv}N$ – the latter two based largely on results of CNDO calculations.

(*i*) Deuteration of acetonitrile[42,107] expectedly does not change the vertical ionization potentials within a measurement precision of about ±20 meV. However, vibrational fine structure differences help to assign the individual vibrational modes, for instance in the radical cation ground state at IE_1 = 12.21 eV (Table 5). From the ratio $\nu^+(H)/\nu^+(D)$ for ν_3^+, closely resembling the theoretical value, hydrogen involvement in the $CH_3CN^{\cdot+}$ ground state is evident and the increase in $\nu_3(H)$ = 1376 cm^{-1} to $\nu_3^+(H)$ = 1430 cm^{-1} can be interpreted by an antibonding admixture of π_{CH_3} as predicted by the hyperconjugation model for the highest occupied orbital $\pi_{CN} - \pi_{CH_3}$ (cf. Figure 9). This π interaction has been parametrized PE spectroscopically by transferring the resonance integral $\beta_{H3C/CN}$ from dicyanomethane (Section IV) in close analogy to the procedure applied to cyanoacetylene (Figure 12)[99].

(*ii*) C → Si exchange in $H_3C{-}C{\equiv}N/H_3Si{-}C{\equiv}N$ does not change the sequence of radical cation states, which is fully reproduced by the results of modified[66] CNDO calculations with $3d_{Si}$ basis functions. (Figure 14). Although, as usual, no numerical

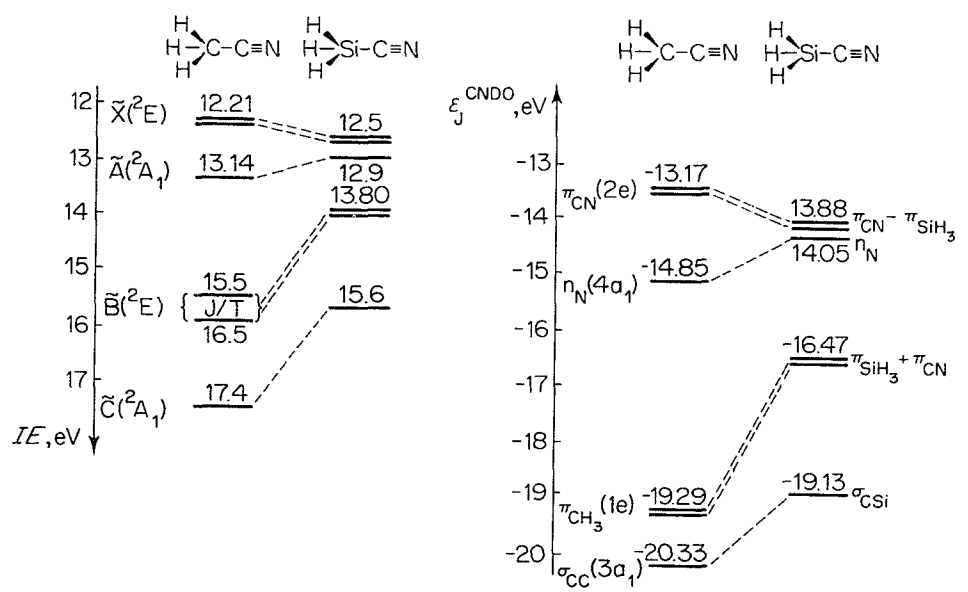
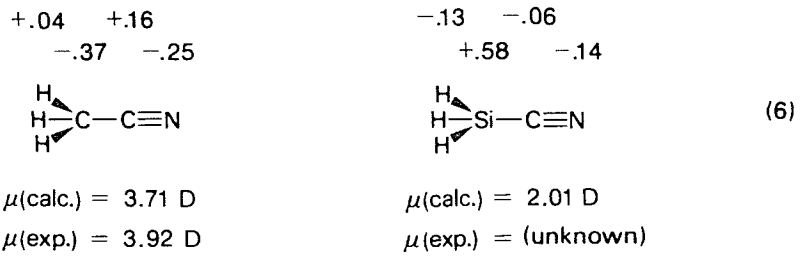


FIGURE 14. Ionization energies IE_j^v of acetonitrile and silyl cyanide together with corresponding CNDO eigenvalues $-\varepsilon_j^{CNDO}$ (basis set including $3d_{Si}$)[99].

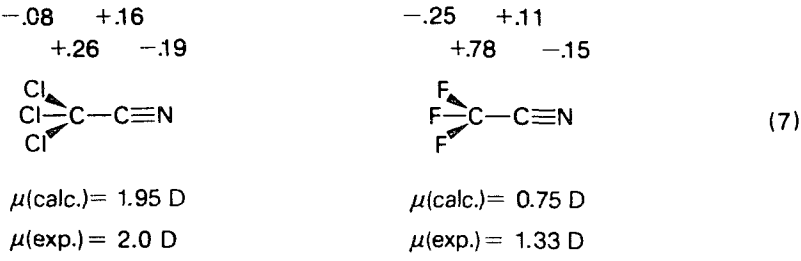
correspondence $IE_{n/-\varepsilon_j}^{CNDO}$ is achieved, the radical cation state correlation lines are fully reflected by the orbital movements. Beginning with the two π states $\tilde{X}(^2E)$ and $\tilde{B}(^2E)$, the hyperconjugative π split is reduced as the bond lengths increase from $d_{CC} = 1.458$ Å to $d_{SiC} = 1.848$ Å[103]; n_N is only slightly shifted upwards corresponding to the decrease in ionization of the $\tilde{A}(^2A_1)$ state, and the lowering of the $\tilde{C}(^2A_1)$ state i.e. the raise of the $\sigma(3a_1)$ orbital can be traced back predominantly to the smaller effective nuclear charge of silicon[36]. Accordingly, the calculated charge distributions differ considerably:



(6)

reversing the nature of the central bond from $—\overset{\delta-}{C}—\overset{\delta+}{C}\equiv$ to $\overset{\delta+}{Si}—\overset{\delta-}{C}\equiv$. Because participation of $3d_{Si}$ polarization functions is somewhat exaggerated in most of the available CNDO versions[36], the dipole moment μ(calc.) = 3.37 D predicted by CNDO without $3d_{Si}$ orbitals in the basis set might be more reliable.

(iii) A comparison of trichloro- and trifluoro-acetonitrile radical-cation states – as examples for larger and more complex molecules – is presented in Figure 15. The assignment of the rather featureless PE spectra (Figure 13) follows the CNDO results in an almost self-explanatory way: orbitals n_{Cl} are above and n_F are below π_{CN} and n_N; both mixing with π_{CN} in a way that the rather small difference of only 0.5 eV between the chloro and the fluoro derivatives can be rationalized immediately. The halogen lone-pair sequence expected from exclusive n_X splitting, $a_2 < e < e < a_1$[13], has to be modified according to the CNDO calculations by taking into account additional interactions with other e- and a_1-type orbitals. The $Cl_3C—C\equiv N$ assignment has been supported by the intensity changes found in the He(II) spectrum[90] (cf. Figure 3). The almost constant π_{CN} and n_N ionizations are in accord with CNDO charge distributions[99]:



(7)

displaying only small differences for the CN groups in both derivatives, but an approximately threefold positive charge of the X_3C carbon due to the fluorine σ acceptor properties.

C. Molecules of Low Symmetry

Most of the monocyano derivatives $R—C\equiv N$, whose PE spectra have been investigated (Table 1), belong to point groups C_{2v}, C_s or C_1, and therefore their main

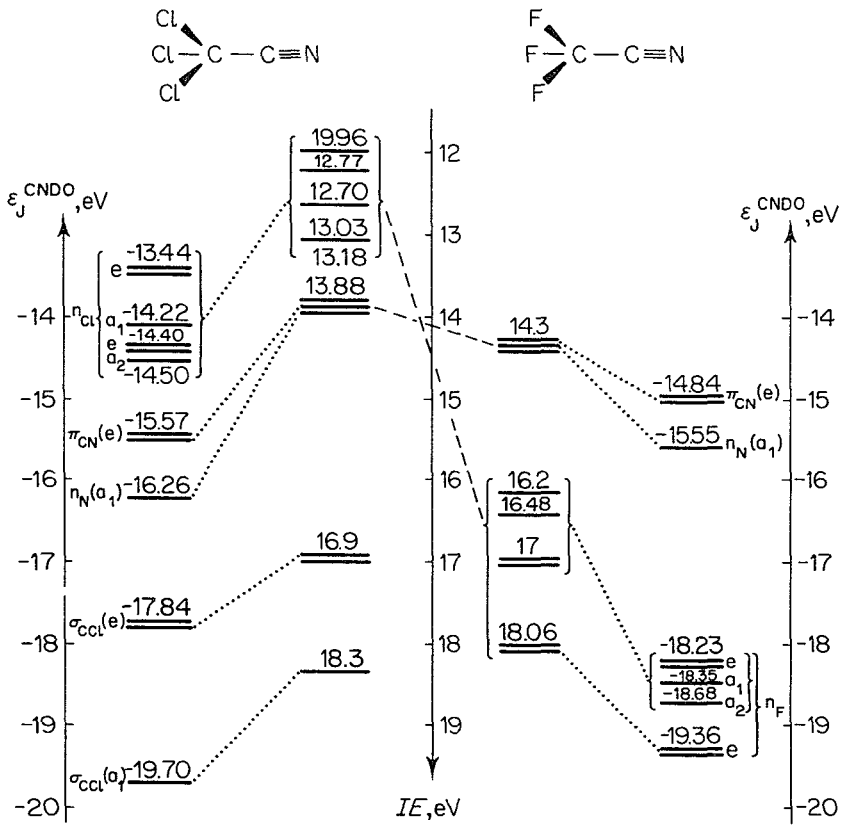


FIGURE 15. Correlation of $Cl_3C—C\equiv N$ and $F_3C—C\equiv N$ ionization energies[69,90,99] (——) and CNDO eigenvalues (. . . . .)[99].

characteristic is the removal of the π_{CN} degeneracy. Correspondingly, the number of bands in the PE spectra increases substantially as illustrated by comparison of the spectra of the linear cyanoacetylene[107] with that of acrylonitrile having low symmetry[96] (Figure 16).

Within an LCBO MO model, two of the four π orbitals of cyanoacetylene remain π in acrylonitrile, which belongs to the point group C_s: the a″-type orbitals π_{CC} and π_{CN}, perpendicular to the molecular plane and inductively shifted, but with nearly constant split. As visualized by the diagrams (Figure 16) all other orbitals are considerably mixed. For instance, the second $\sigma_{CN}(8a')$ orbital results from one of the former doubly degenerate cyanoacetylene π_{CN} orbitals by antibonding admixture of numerous other a′-type orbitals and is accordingly destabilized. The same argument applies to the nitrogen lone-pair orbital $n_N(7a')$. On the other hand, the three σ counterparts can still be recognized as former ethylene σ orbitals (D_{2h}: b_{3g}, a_g and b_{2u}[10]). With an unshifted reference orbital missing, the acrylonitrile LCBO MO model can only be PES-parametrized after extensive radical cation state comparison with the other closely related π and cyano systems[96]. What else can be done to substantiate the PE assignment for acrylonitrile as deduced from radical cation state comparison with cyanoacetylene, based on a LCBO MO model and perturbation arguments? Addi-

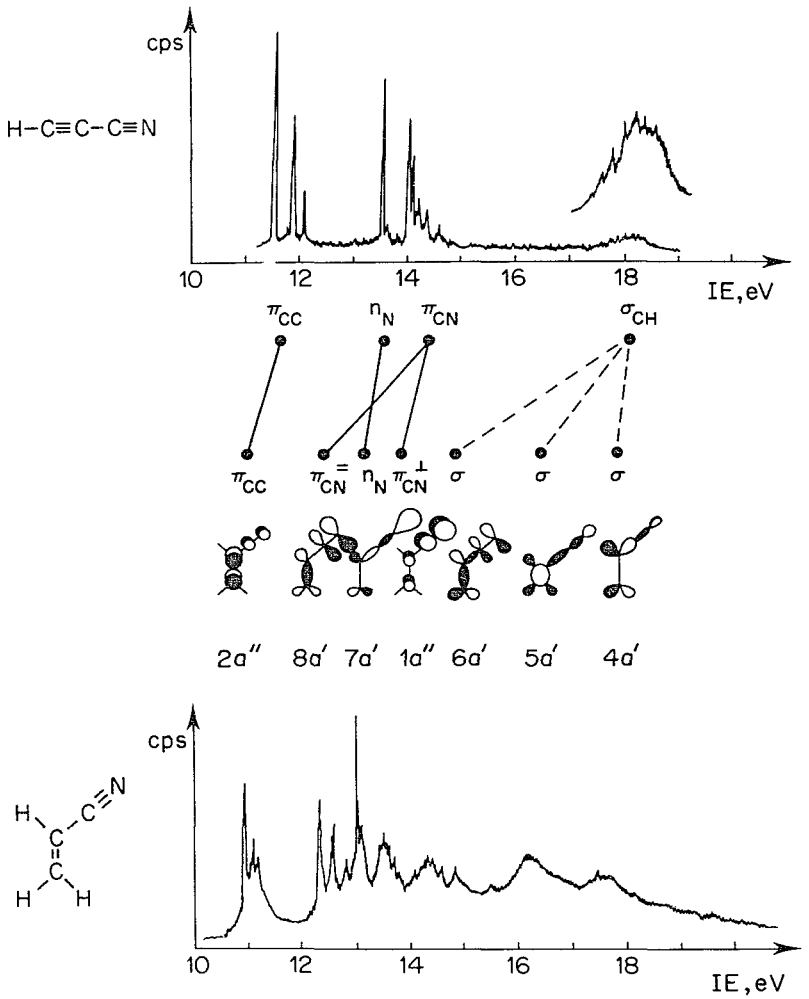


FIGURE 16. He(I) PE spectrum of acrylonitrile[96] and assignment by radical cation state comparison with cyanoacetylene and LCBO MO diagrams.

tional evidence is supplied by the vibrational fine structure in the first three PE bands (Figure 17): the reduced frequencies observed relative to, for example, the ground-state stretching vibrations ν_{CN} = 2239 cm^{-1} and ν_{CC} = 1615 cm^{-1} correspond to ionization of π bonding electrons, whereas the nitrogen lone-pair ionization is accompanied by CC(N) stretching and CH deformation vibrations[96].

Numerous additional radical cation state comparisons can be carried out by designing series of chemically related compounds around acrylonitrile, such as the other cyanoethylenes discussed in Sections IV and V or methyl-substituted derivatives, including also more formally the isomeric allyl cyanide (Figure 18). The first four assigned ionizations in the PE spectra of methyl-substituted acrylonitrile derivatives[60] are more or less lowered relative to the parent compound (Figure 18) as expected from orbital perturbation arguments: both methyl-group effects on *trans* substitution,

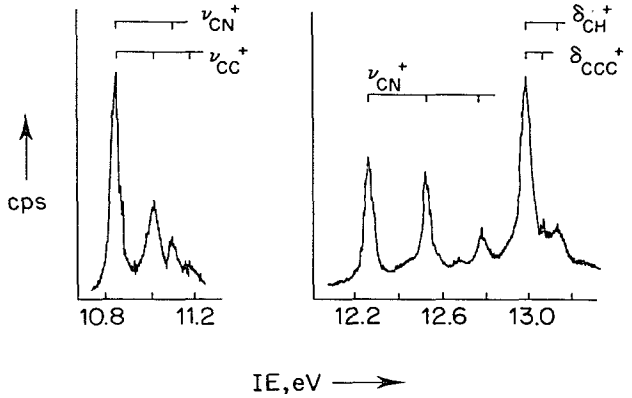


FIGURE 17. Expanded record of the first three PE bands of acrylonitrile with radical cation vibrations ν^+ (cm^{-1})[99].

the larger shift of the upper π_{CC} orbital and the smaller shift of the lower $\pi_{CN}^{\perp}$ orbital can be rationalized by the larger or smaller orbital coefficients at this centre in the butadiene-like C=C—C=N π system[7]. Negligible changes are observed for the in-plane cyano π orbital $\pi_{CN}^{=}$ as well as for the nitrogen lone pair. The ionization energies for allyl cyanide with the π_{CC} and π_{CN} subsystems separated by a methylene group and of probably preferred nonplanar conformation, are nevertheless comparable to those of acrylonitrile itself, suggesting that either $\pi_{CC/CN}$ conjugation is only small or that several counteracting effects almost cancel each other.

The conclusion from the detailed discussion of the PE spectroscopic assignment for acrylonitrile is: for low-symmetry molecules, because of their complex molecular

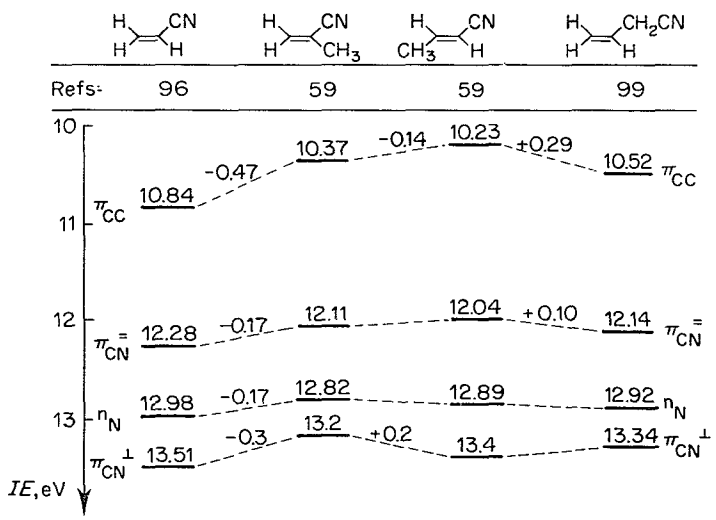


FIGURE 18. Correlation of the four lowest PES ionization energies IE_n^v of some cyano-substituted ethylene derivatives.

orbital interaction schemes, every possible method of PE assignment and consideration has to be applied. The cornerstone will be, in general, the comparison of analogous radical cation states within series of chemically related compounds (cf., for example, Figures 4, 11, 12, 14, 15 or 16). Therefore, improvement of the orbital perturbation models applied is important[54] and, especially for cyano compounds, the 'united atom' approach, e.g. linking corresponding N and CH derivatives[95], may prove useful. Among numerous other contributions, the parametrization of inductive and conjugative CN substituent effects for benzene derivatives[62] as well as for other π[96] and σ systems[98] may be quoted for π perturbation. Band-shape analysis, especially for vibrational fine structures (Figure 2b or 17), often supplies a clue for assignment, e.g. detailed vibrational analysis of the benzonitrile PE spectrum in comparison to that of phenylacetylene leads to a reassignment[47]. Although, as pointed out repeatedly, considerable Koopmans' defects (Figure 5) may arise from neglections in even *ab initio* SCF calculations (cf., for example, References 5, 6 and 74) sometimes simpler semiempirical calculations with reparametrized program versions[66] yield reasonable (although not reliable) results (cf. Figures 14 and 15).

Bearing in mind the preceding restrictive remarks and referring for all details to the literature quoted, the following PE spectroscopic highlights of the essential classes of low-symmetry monocyano compounds (Table 1) are summarized.

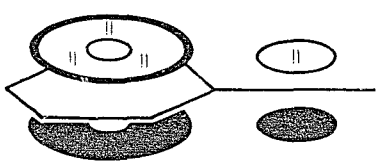
1. *Alkyl cyanides*

No split $\Delta\pi_{CN}$ if observed PE spectroscopically[69,102] although the conformations of ethyl and isopropyl cyanides exhibit at best C_S symmetry. As in acetonitrile (Figures 1 and 14), the first two ionizations are π_{CN} and n_N (Table 6). Increasing methyl substitution causes shifts of $\Delta\pi_{CN} \sim \Delta n_N \sim 0.5$ eV. In the corresponding chloroalkyl derivatives[102], the first ionization potentials are increased to, for example, 13.06 eV for $ClH_2C{-}C{\equiv}N$ and 12.6 eV for $ClH_2C{-}H_2C{-}C{\equiv}N$[102] (cf. also Figure 15).

2. *Benzonitrile and cyanopyridine derivatives*

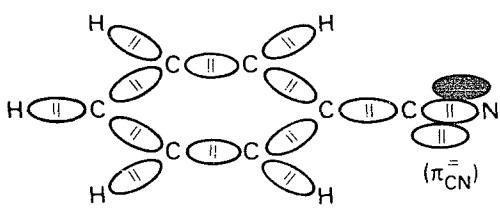
Benzonitrile may serve as a prototype for larger cyano-substituted π systems. The molecule has a total of 38 valence electrons, and from its 19 ionizations about 11 are expected within the He(I) measurement region – those with considerable 2s contribution are usually found outside[10]. From a symmetry-adapted LCBO MO model, the following types of radical cation states are expected:

(C_{2v}) $\quad \Gamma = 9A_1 + 1A_2 + 3B_1 + 6B_2$



π: $\quad (1A_2 + 3B_1)$

(8)



σ: $\quad (9A_1 \qquad\qquad + 6B_2)$

TABLE 6. PES Ionization energies, *IE* (eV), of various alkyl cyanides, RCN

R	$IE(\pi_{CN})$	$IE(n_N)$	Reference
CH_3	12.21	13.14	95
CH_3CH_2	12.11	12.91	69, 102
$(CH_3)_2CH$	12.0[a]	12.7[a]	102
$(CH_3)_3C$	11.7	12.6	102

[a]Estimated from Ref. 102.

Further predictions are: the benzene $\pi(a_2)$ orbital is of unique symmetry type and, therefore, should allow to read off the inductive lowering by the electron-withdrawing cyano group; n_N is expected around 13 eV and the no longer degenerate $\pi_{\overline{CN}}$ (in-plane) and $\pi_{\underline{CN}}$ (perpendicular to the molecular plane) ionizations should split around 12.2 eV (see above).

The PE spectrum of benzonitrile presented together with that of the isoelectronic 4-cyanopyridine in Figure 19, shows most probably 12 ionizations, e.g. two bands overlapping at ~10 eV and five bands between 11.5 eV and 14 eV.

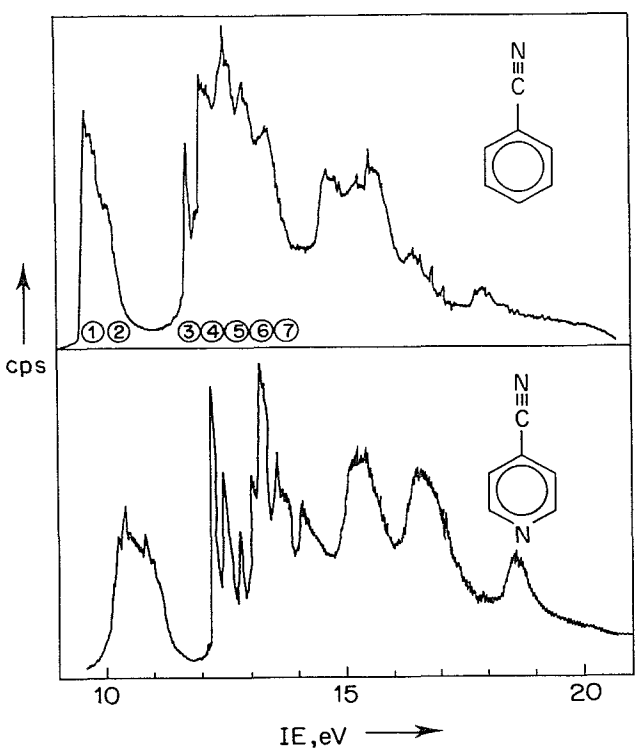


FIGURE 19. He(I) PE spectra of benzonitrile[47] and 4-cyanopyridine[64].

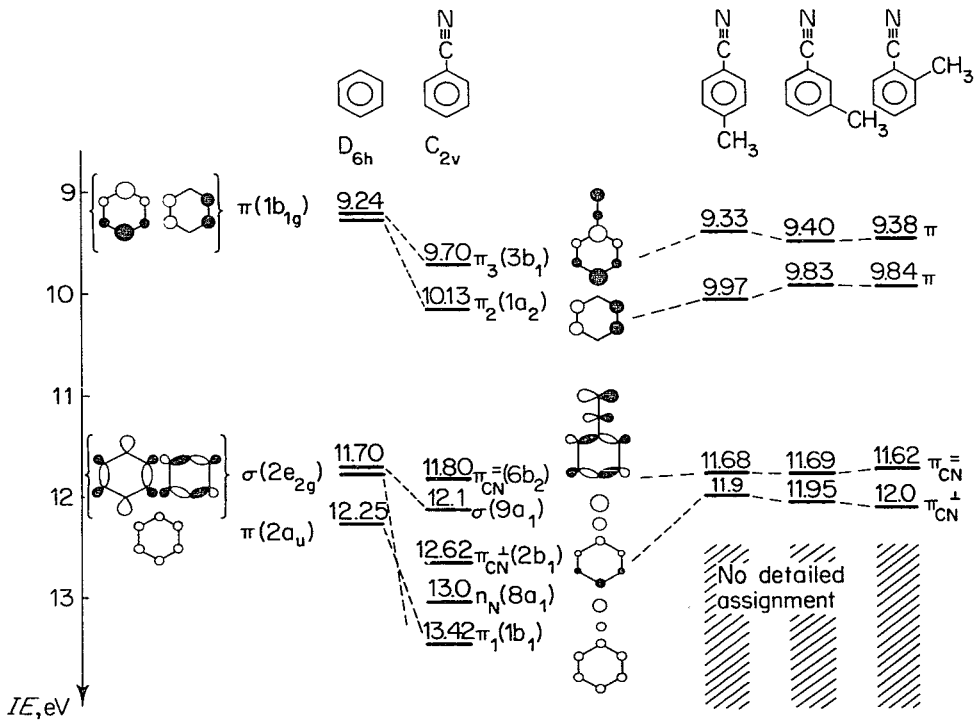


FIGURE 20. Correlation of PE ionization energies, *IE*, of benzene[11], benzonitrile[47] and the isomeric tolunitriles[63] based on π orbital perturbation.

The assignment of the benzonitrile PE spectrum constitutes a transparent example for the application of some cyano perturbation arguments (Figure 20). Starting from the first five benzene radical cation states as well as from the approximate π_{CN} and n_N ionization energies, an obvious sequence proposal develops. From the 0.9 eV increase of $\pi(1a_2)$ an ~1 eV inductive stabilization[62] of all corresponding orbitals is deduced. The $\pi(b_1)$ interaction amounts to ~0.4 eV as gathered from the split between $\pi_1(3b_1)$ and $\pi_2(1a_2)$ as well as from the lowering of $\pi_1(1b_1)$ from 12.25 eV to 13.42 eV caused by the inductive cyano group effect and by π_1/π_{CN} stabilization. In between, the n_N orbital stays at 13 eV (Table 6), and the $\pi_{CN}^{=}/\pi_{CN}^{\perp}$ orbitals with σ and π ring contributions are placed around 12.2 eV. This tentative assignment is in full accord with an elaborate vibrational fine-structure analysis[47] and additionally supported by the methyl substitution effects (Figure 20)[63].

According to the benzene π orbital coefficients (Figure 20), *ortho* and *meta* methyl substitution effects on $\pi_1(3b_1)$ and $\pi_2(1a_2)$ orbitals should be of the same size (Figure 20), whereas in the *para* derivative $\pi_2(1a_2)$ is less perturbed than $\pi_1(3b_1)$. The PE assignment scheme developed (Figure 20) can be applied to all other chemically related compounds, for instance, to rationalize the radical cation state sequences of isoelectronic *o*-, *m*- and *p*-cyanopyridine derivatives (Figure 21)[64].

The pronounced ionization energy shifts between the isomeric cyanopyridines (Figure 21) can be rationalized as follows: relative to benzonitrile, aza substitution increases all ionization potentials due to the higher effective nuclear charge of nitrogen[45] and the largest effect expectedly occurs in 4-cyanopyridine, reducing $\Delta\pi_{3,2}$ to only 0.48 eV. As in pyridine itself, the first ionization then originates from the

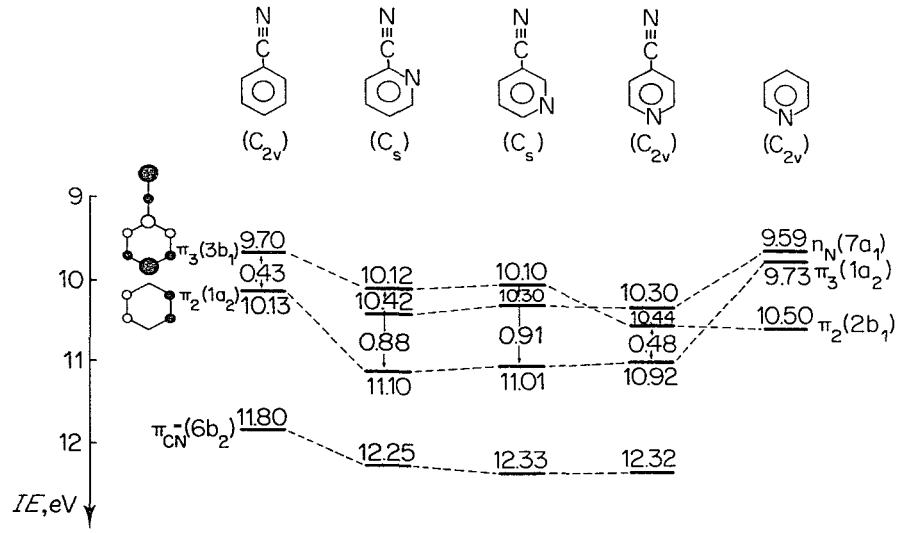


FIGURE 21. Correlation of lower π ionization energies for benzonitrile[47], the cyanopyridines[64] and pyridine[45].

nitrogen lone pair, which in *ortho* and *meta* derivatives is interspersed among the π levels. Independent confirmation of the assignment is supplied by several observed vibrational fine structures[64] as well as by yet another series of chemically related compounds, the *N*-oxide derivatives (Figure 22). Again, the ionization patterns of *ortho* and *meta* derivatives are almost identical, whereas on *para* substitution only a small π split of $\Delta IE_{3,4} = 0.74$ eV results. The latter is due to a considerable inductive

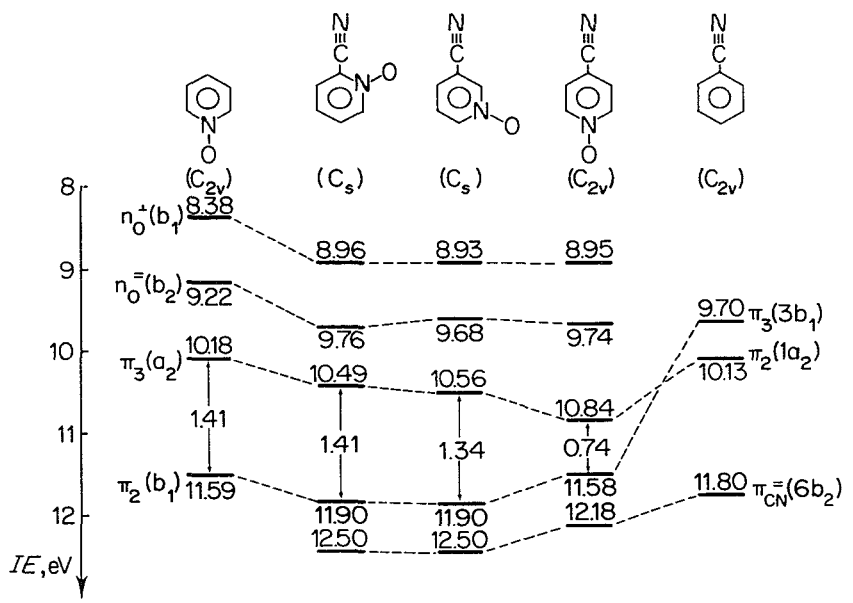


FIGURE 22. Correlation of lower π ionization energies for pyridine-*N*-oxide and its monocyano derivatives[71] and for benzonitrile[47].

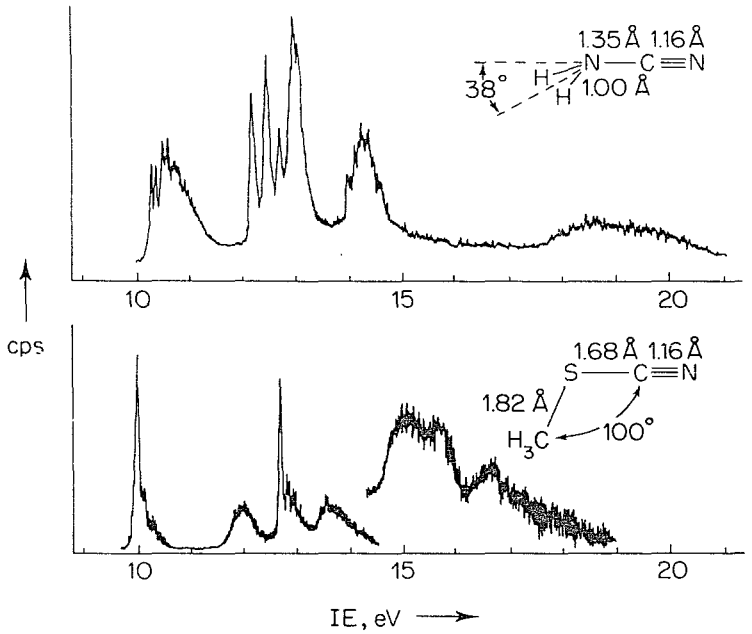


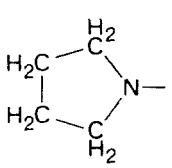
FIGURE 23. He(I) PE spectra of cyanamide[95] and methyl thiocyanate[99], together with some of their structural parameters.

lowering of $\pi_3(b_1)$ of benzonitrile due to the *N*-oxide perturbation and, because the overall symmetry still remains C_{2v} no conjugative lift of the $\pi_2(1a_2)$ level. The PES assignment of the cyanopyridine-*N*-oxides is supported by vibrational fine structures and by MINDO II orbital energies which yield linear regressions $IE^v/-\varepsilon_j^{MINDO}$ with small standard deviations[71].

3. *Group V monocyano compounds R_2E—C≡N*

PE spectra of seven derivatives (Table 1) have so far been recorded; the one of the parent molecule cyanamide[95] is shown in Figure 23 for illustration. Its assignment by

TABLE 7. PES ionization energies, *IE*(eV), for various monocyano compounds, R_2N—C≡N

R_2N—	$IE(n_{NR_2})$	$IE(\pi^{\perp}_{CN})$	$IE(n_{CN})$	$IE(\pi^{\parallel}_{CN})$
H_2N—	10.65	12.50	12.98	14.23
$(H_3C)_2N$—	9.44	11.87	12.55	12.79
	9.05	11.60	12.24	12.65

an isoelectronic 'united atom' perturbation CH → N from acetonitrile has served as an introductory example for the application of LCBO MO models (Figure 9). PES ionization energies have also been recorded for dimethylcyanamide[95] and 1-cyano-pyrrolidine[99] (Table 7).

Cyanamide, unique among other cyano compounds, shows a lower first ionization energy than ammonia (IE_1 = 10.85 eV[107]) and its two π radical cation states, $\pi^{\perp}_{CN}$ and $\pi^{\equiv}_{CN}$ are separated by 1.73 eV, the largest gap for a monocyano compound observed so far. In the dimethyl derivative, obviously considerable differences exist which are also reflected in other molecular properties: in cyanamide, the inversion barrier has been reduced from 5.8 kcal/mol for H_3N to 2 kcal/mol, but dimethylcyanamide is assumed to be planar (cf. Reference[95]). The charge distribution can be satisfactorily reproduced by CNDO calculations[95] [cf. also (6 and (7)]:

+.27 +.27 −.27 −.30	+.25 +.28 −.20 −.33
$(H)_2$—N—C≡N	$(H_3C)_2$—N—C≡N
μ(calc.) = 4.24 D	μ(calc.) = 4.36 D
μ(exp.) = 4.32 D	μ(exp.) = 4.06 D

(9)

PE spectra of cyano-phosphorous and -arsenic compounds are much more difficult to interpret. Parent compounds like H_2NCN are lacking and additional bands overlap with the ionizations π_{CN} and n_N. Tentative assignments[27,34,35] are shown in Table 8. Comparison of the ionization energies of derivatives R_2E—C≡N for E = N, P and As reveals that their radical cation ground-state energies increase contrary to expectation from the effective nuclear charge of the central atom E[35].

4. *Methyl thiocyanate*

H_3C—S—C≡N is the only thiocyanate of which a PE spectrum (Figure 23) has been recorded so far[99]. The two bond distances d_{CS} (Figure 23) differ by 140 pm[28], therefore, the corresponding ionizations with large σ_{CS} contribution are more than 3 eV apart following the assignment based largely on the extensive vibrational fine structures (Table 9). Furthermore, both the n_S and the n_N lone-pair ionizations are easily identified by the needle-like band-shapes (Figure 23), characteristic of ejection of nonbonding electrons. Relative to dimethyl sulphide[109], the n_S radical cation state of H_3CSCN is stabilized by 1.3 eV. The two π_{CN} states are separated by 0.7 eV.

TABLE 8. PES ionization energies, IE(eV), for various cyano compounds X_2E—C≡N

X_2E—	$IE(n_E)$	$IE(\sigma_{XE})$	$IE(n_N)$	$IE(\pi_{CN})$
F_2P—	11.9	(19.2)?	13.5	14.0
$(F_3C)_2P$—	11.72	13.1	13.6	14.0
$(H_3C)_2P$—	9.80	11.85	12.11	12.75
$(H_3C)_2As$—	9.82	11.4	11.99	12.43

TABLE 9. PES assignment for $H_3C—S—C\equiv N$ as based on vibrational fine structure

IE^v (eV)	MO	C_s	ν^+ (cm^{-1})	ν (cm^{-1})[a]	
10.02	n_S	3a″	2000	2173	(C≡N stretch)
			720	705,674	(C—S—C stretch)
12.04	σ_{CS}	8a′	1440	1436,1328	(CH_3 deformation)
12.78	n_N	7a′			
12.93	π_{CN}	6a′	1920	2173	(C≡N stretch)
			640	705,674	(C—S—C stretch)
13.67	π_{CN}	2a″	1280	1436,1328	(CH_3 deformation)
15.1					
15.7					
16.9					

[a]Taken from Ref. 28.

5. *Cyanogen azide and nitroso cyanide*

To conclude this section, the PE spectra of two somewhat unusual monocyano compounds are presented: NNN—C≡N[5] and ON—C≡N[100] (Figure 24).

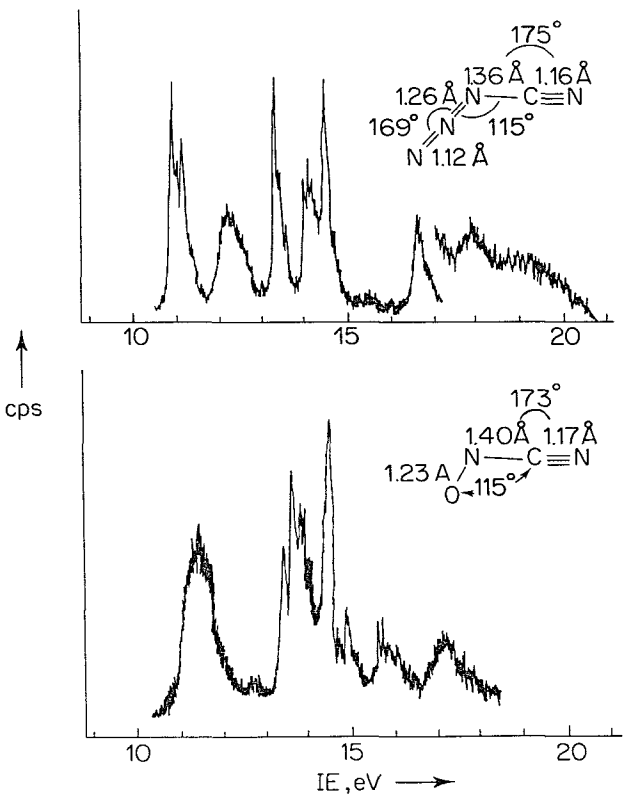


FIGURE 24. He(I) PE spectra of cyanogen azide[5] and nitroso cyanide[100], together with some of their structural parameters.

Both compounds are quite explosive and their structures with bent N—CN groups are well-established by electron diffraction and/or microwave studies[2,26,31].

For N_3—C≡N with its 24 valence electrons, seven (p-type) ionizations are expected and found within the He(I) region up to 21.21 eV (Figure 24). A complete assignment[5] has been achieved based on vibrational fine-structure analysis, intensity changes relative to the Ne(I) PE spectrum, an *ab initio* SCF calculation and radical cation state comparison with HN_3. In simplified orbital notation, the sequence $\pi_3(3a'') < n_{(N_2)N(CN)}(14a') < n_{CN}(12a') < \pi_{\overline{CN}}(13a') < \pi_2(2a'') < n_{N(N_2CN)}(11a'') < \pi_1(1a'')$ results, including another 'breakdown' example of Koopmans' theorem[5].

The He(I) PE spectrum of the 20 valence electron molecule ON—C≡N expectedly displays six separated (p-type) ionizations (Figure 24). The tentative assignment[100] according to an STO-3G *ab initio* calculation yields the sequence $n_0(12a') < \pi_2(2a'') < \pi_{\overline{CN}}(11a') < n_{CN}(10a') < \pi_1(1a'') < \sigma_{NO}(9a') < \sigma_{NO}(8a')$. A CNDO/2 calculation suggests the same radical cation state sequence of increasing energy, and a subsequent configuration interaction almost reproduced the first of the UV absorption maxima reported (exp., 1.69 eV and 5.74 eV[32], calc. 1.79 eV and 7.17 eV) for the blue gas ON—C≡N.

IV. DICYANO COMPOUNDS AND MO PARAMETERS

PE spectra of three linear dicyano compounds NC—CN, NC—C≡C—CN and NC—Hg—CN have been published so far (Table 1). The first two have already been discussed (cf. Figures 4, 5, 8 and 12). The PE spectrum of cyanogen and its assignment has been particularly thoroughly investigated[1,3,23,57,107,111] and achieved by radical cation state comparison along a series of isoelectronic and chemically related molecules (Figure 4), with a highly sophisticated Green-function perturbation calculation (Figure 5) as well as by PE spectroscopic parameterization of symmetry-adapted QMO models (Figure 8).

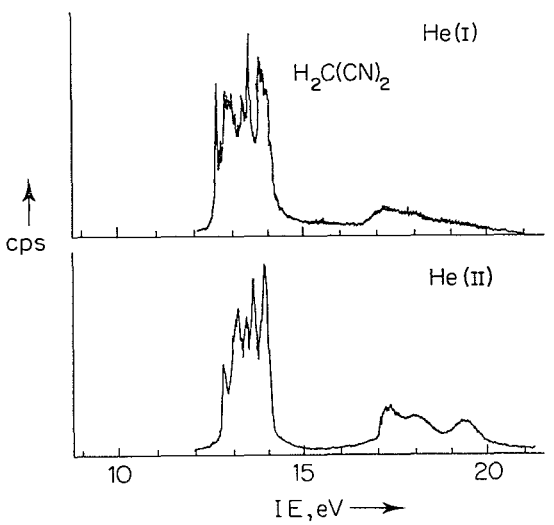


FIGURE 25. He(I) and He(II) PE spectra of dicyanomethane[98,101].

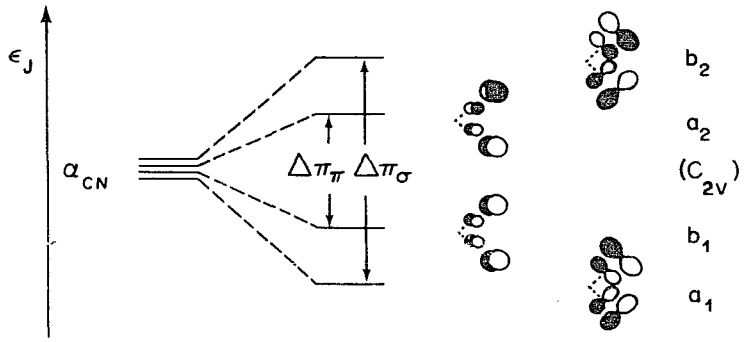


FIGURE 26. Orbital interactions for germinal cyano groups.

Contrary to the relatively simple PE spectra of the linear dicyano compounds, the bent ones exhibit complex PE spectra with partially overlapping bands. In addition, their less simple interaction schemes make it more difficult to obtain PE spectroscopic MO parameters. As a prototype, malononitrile is chosen to demonstrate how its He(I) and He(II) PE spectra (Figure 25) can be assigned by a somewhat shrewd parametrization procedure[98].

In dicyano compounds of C_{2v} symmetry, all degeneracies found in linear molecules are lifted by 'through-space'[56] interactions $\Delta\pi_\pi$ and $\Delta\pi_\sigma$ (Figure 26). The orbital energy splits $\Delta\pi_\pi$ and $\Delta\pi_\sigma$ depend on the NC—X bond distance to the central atom X, and on the bond angle NC—$\hat{X}$—CN. As an approximation, Slater-type orbital overlap integrals yield the angular dependence[99] shown in Figure 27. Increasing angle C$\hat{X}$C decreases orbital separation and the ratio $\Delta\pi_\pi/\Delta\pi_\sigma$ approaches its limit of 1 at 180°. The relatively moderate changes calculated for $\Delta\pi_\pi$ suggest it as a suitable independent variable. Altogether, for the empirical MO parametrization[98], two more parameters are needed than PE data are available. Therefore, the relation $\Delta\pi_\pi/\Delta\pi_\sigma$ evaluated from EHMO overlap calculations has been incorporated as the additional parameter needed.

The additional 'through-bond (tb)'[56] interactions between combinations of the two

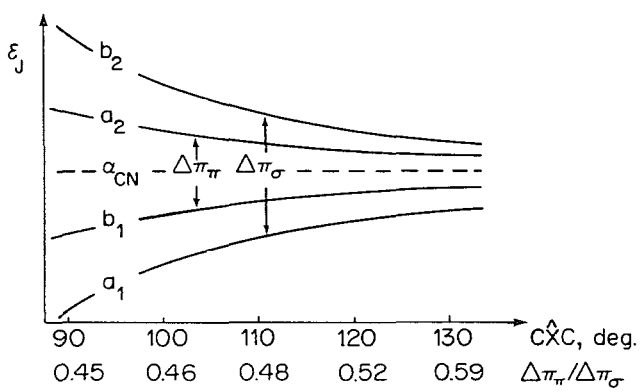


FIGURE 27. Dependence of orbital energy splits $\Delta\pi_\pi$ and $\Delta\pi_\sigma$ on the bond angle NC—$\hat{X}$—CN in dicyano compounds[99].

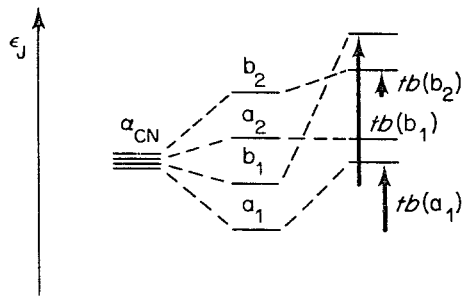


FIGURE 28. Through-bond (tb) interactions between the two geminal CN groups and the molecular skeleton in dicyano compounds.

geminal CN groups and the molecular skeleton are defined in Figure 28. For small dicyano molecules, $\pi_{CN}(a_2)$ is the only occupied orbital of this symmetry and, therefore, can serve as an internal reference. The other π_{CN} orbitals are shifted to an extent which is difficult to estimate. Their relative amounts might be gathered from an EHMO calculation for the still unknown $O(CN)_2$ molecule[99] (Figure 29). From this diagram the order $tb(b_1) > tb(a_1) \geqslant tb(b_2)$ is read off. Furthermore the $tb(b_1)$ and $tb(a_1)$ values approach each other to become identical for linear arrangement. The through-bond interaction term $tb(b_2)$ remains fairly constant up to 120°, decreases and finally vanishes at 180°. Comparison with the splitting scheme above shows that $tb(b_1)$ is the most effective interaction.

Application of the parametrization procedure outlined above[14,95,98,99] together with arguments concerning band-shape or vibrational fine structures and especially radical cation state comparisons within the series of related molecules permitted the assignment of the PE spectra of $H_2C(CN)_2$[98], $H_2C{=}C(CN)_2$[95] and $OC(CN)_2$[99] (Figure 30). In addition, the PE spectrum of $S(CN)_2$ has been recorded with Ne(I), He(I) and He(II) radiation sources, discussed in detail and assigned on the basis of an elaborate *ab initio* calculation[91], dealing also with its rather queer structure, which

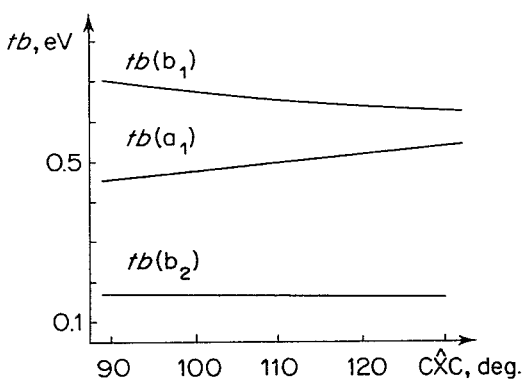
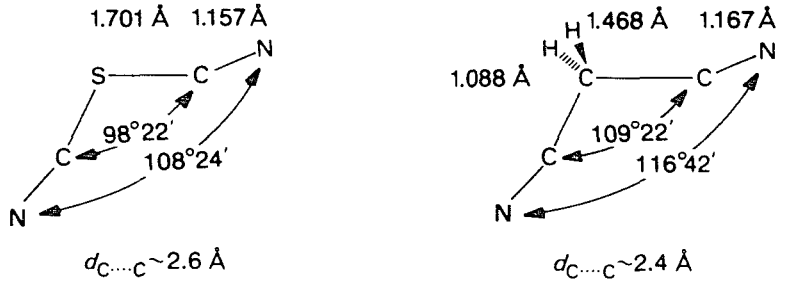


FIGURE 29. EHMO calculation for the unknown $O(CN)_2$ molecule[99].

exhibits, like malononitrile, bent C—C—N linkages[91].



(10)

The comparative PES assignment of the geminal dicyano compounds is displayed in Figure 30; the parameters deduced and used are summarized in Table 10.

As one extracts from the MO parameters (Table 10), large splittings $\Delta\pi_\pi$ and $\Delta\pi_\sigma$ are observed for $H_2C(CN)_2$ with the shortest distance between the cyano groups. In

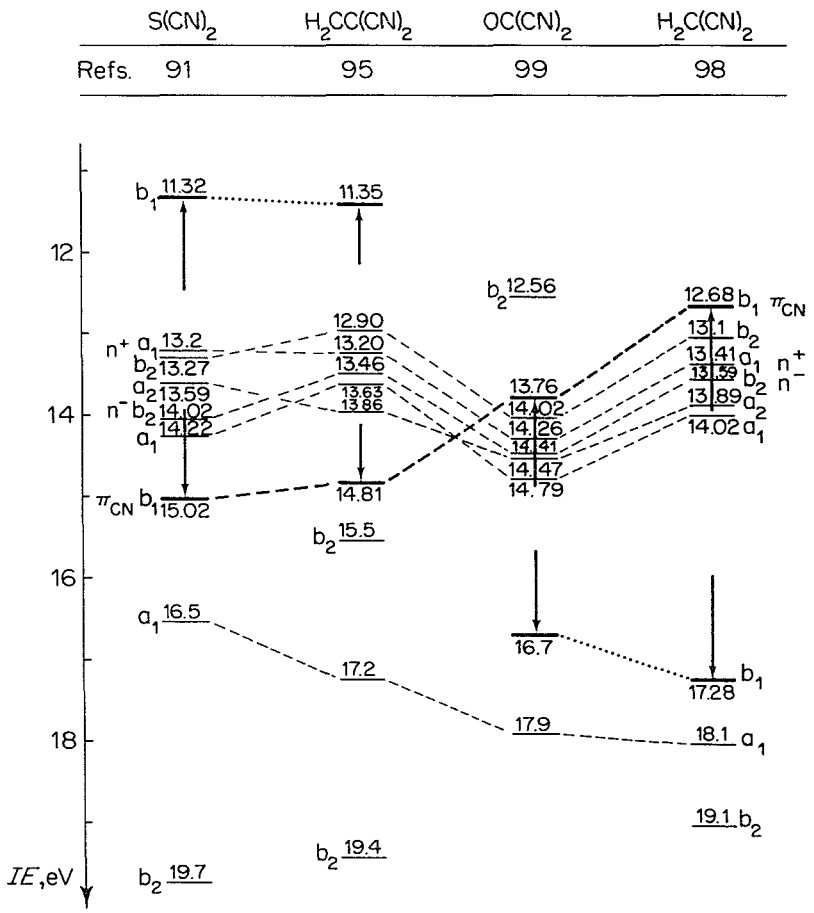


FIGURE 30. Correlation of PE ionization energies, IE_n, of geminal dicyano compounds[99].

TABLE 10. PE spectroscopic MO parameters for geminal dicyano compounds $X(CN)_2$

X	S< >	$H_2C{=}C$< >	O=C< >	H_2C< >
$\Delta\pi_\pi$	0.3	0.3	0.3	0.5
$\Delta\pi_\sigma$	0.7	0.6	0.6	1.0
$tb(a_1)$	0.03	0.7	0.1	0.6
$tb(b_1)$	−1.1	−0.7	1.0	1.7
$tb(b_2)$	0.1	0.8	0.3	0.5
$\beta_{X/2CN}$	−1.8	−1.4	−1.4	−2.2
α_X	−12.5	−12.0	−15.7	−16.4
α_{CN}	−13.7	−14.0	−14.6	−14.1

$H_2CC(CN)_2$ and $OC(CN)_2$ the relatively large angle $C\hat{X}C$ leads to reduced interactions, in $S(CN)_2$ to the large bond distance d_{SC}. For the same reason, interactions $tb(a_1)$ and $tb(b_2)$ are rather small in $S(CN)_2$, whereas $tb(b_1)$ is fairly large – probably due to the diffuseness of the interacting π-type sulphur lone-pair orbital. The smaller values $tb(a_1)$ and $tb(b_2)$ for $OC(CN)_2$ compared to those for $H_2CC(CN)_2$ and $H_2C(CN)_2$ are in accord with the large energy separation between π_{CN} and the π_{CO} and σ orbitals. Another point of view is supplied by the parameters α_{CN} and $\beta_{X/2CN}$, which describe the interaction between the two b_1 orbitals [cf. (5)]:

$$\begin{vmatrix} \alpha_X - \varepsilon & \beta_{X/2CN} \\ \beta_{X/2CN} & \alpha_{CN} - \varepsilon \end{vmatrix} = 0 \qquad (11)$$

The second-order secular determinant also takes into account the energy separation $\alpha_X - \alpha_{CN}$ of the basis orbitals. The results (Table 10) suggest that conjugation π_{CN}/π_{CC} and π_{CN}/π_{CO} are about equal and smaller than π_{CN}/n_S and, above all, as hyperconjugation π_{CN}/π_{CH_2}. The values α_X (Table 10) are lowered by 1.5 eV to 2.2 eV relative to the ones for the parent molecules[107]: $\alpha_{CC} = -10.5$ eV for $H_2C{=}CH_2$, $\alpha_{CO} = -14.1$ eV for $H_2C{=}O$, $\alpha_S = -10.5$ eV for H_2S and $\alpha_{CH} = -14.2$ eV for CH_4 or C_2H_6. The π_{CN} values range between −13.7 eV and −14.6 eV, reflecting the electron-donating or -withdrawing character of the skeleton X, as confirmed by the dipole moments[79,84]:

	$H_2C(CN)_2$	$S(CN)_2$	$OC(CN)_2$
μ(D)	3.74	3.02	1.5

(12)

The correlation diagram of the PES ionization energies of geminal dicyano compounds (Figure 30) reveals an increase in the $\pi_{CN}(b_1)$ orbital from $S(CN)_2$ to $H_2C(CN)_2$, by a sudden change from stabilizing interaction with n_S and π_{CC} to a destabilizing one with π_{CO} or by hyperconjugation.

The n_N ionizations (Figure 30), also observed within the π ionization region, have not been included into the parametrization procedure, because n_N and π_{CN} orbitals are orthogonal to each other, and their mutual interactions are, therefore, only due to perturbations via the molecular skeleton. Finally, estimates of the π_{CN}/n_N interactions show that these are close to the uncertainty limit ±0.1 eV of PE spectroscopically derived MO parameters and, therefore, can be neglected in most cases[96].

For all other recorded PE spectra of geminal dicyano compounds (Table 1), no detailed assignment could be achieved due to strongly overlapping bands. For derivatives $Hal_2C(CN)_2$ with Hal = Cl, Br[99] only a crude subdivision into n_{Hal} and π_{CN}/n_N ionization regions has so far been possible. The $H_3CP(CN)_2$ and $F_3CP(CN)_2$

PE spectra[35] exhibit separate n_P bands at 10.85 eV and 11.81 eV. The $Te(CN)_2$ PE spectrum has also been recorded using a heated inlet system[99], but the only straightforward assignment identifies the 10.3 eV band as due to the lone pair n_{Te} ionization. After only a few runs, the spectrometer used has been heavily contaminated[99].

Other dicyano compounds like *cis*- and *trans*-NC—HC=CH—CN have been discussed in detail on the basis of symmetry-adapted and PES-parametrized MO models[14,96], and will partly be covered in context with other cyanoethylenes in Section V (Figures 31 and 32). In *trans*-$NC(F_3C)C{=}C(CF_3)CN$, the $\pi_{C=C}$ band is shifted by about 0.7 eV to higher energies, while the n_N and π_{CN} bands are shifted by only about 0.4 eV, due to their larger distance to the centre of substitution[59]. No such simple assignments are possible for the PE spectra of $NC—CH_2CH_2—CN$[99] and azoisobutyronitrile[60], for which several conformers are imaginable. The *trans*-$NCCH_2—CH{=}CH—CH_2CN$ PE spectrum closely resembles that of allyl cyanide[99]. Summarizing, for all these molecules the π_{CN} and n_N ionization bands, differently structured and therefore characteristic for the individual cyano compound, are found within the 12–14 eV region.

V. POLYCYANO COMPOUNDS

PE spectra of five polycyano compounds have been reported so far (Table 1), of which those of the prototype molecules tetracyanoethylene (Figure 31) and tetracyanomethane (Figure 7) will be discussed in more detail.

For comparison, the $(NC)_2C{=}C(CN)_2$ PE spectrum is displayed together with the ones of all other cyanoethylenes reported[14,96] in Figure 31. The increase in complexity with increasing molecular size, i.e. increasing number of ionizations from 7 for $H_2C{=}CH—CN$ (cf. Figure 15) to at least 14 for $(NC)_2C{=}C(CN)_2$ is obvious. Most of them are compressed, however, into a relatively small and only slightly shifting region between 11 eV and 16 eV (Figures 31 and 32). In the π_{CN}/n_N region of the TCNE PE spectrum 11 bands are more or less overlapping. The only ionization shifted out of the 1.7 eV area leads to the $^2B_{2u}$ radical cation state and can be rationalized in MO terms by strong conjugation with the $\pi_{CC}(b_{2u})$ orbital[96]. Remaining are three $\pi_{CN}^{\perp}$ perpendicular to the molecular plane, four $\pi_{CN}^{=}$ in the molecular plane and four almost unsplit n_N ionizations (Figure 32). The comparison of the cyanoethylene spectra (Figure 31) clearly demonstrates that the PE spectra represent molecular fingerprints which could be used analytically to identify compounds in the gaseous phase (cf. Section VI.B). The PES assignment is based predominantly on a radical cation state comparison along the series (Figures 33 and 16) supported by PE-parametrized MO model as well as by vibrational fine structure analysis[14,96].

The π_{CN} ionization pattern of TCNE (Figure 32) is squeezed within 1.7 eV and its assignment[96] could only be achieved transferring PE spectroscopic parameters (Table 10) deduced from the spectra of simpler cyano derivatives (cf. Section IV), whereby the parameter $\beta_{CC/2CN} = (\sqrt{2})\ \beta_{CC/CN} = (1/\sqrt{2})\ \beta_{CC/4CN}$ had to be normalized. The parameter sets of cyanoethylenes are summarized in Table 11. Within the parameter sets (Table 11), the inductive lowering of α_{CC} and α_{CN} with increasing numbers of cyano groups is quite remarkable and nonadditive. Compared to the smaller π splits, inductive effects clearly play an important role in cyano substitution.

Tetracyanoethylene oxide (TCNEO) belongs to a lower symmetry group than TCNE and, accordingly, its interaction scheme is more complex. Its PE spectrum[96] could therefore only be assigned by Koopmans' correlation with semiempirical SCF eigenvalues, a procedure which often proved not reliable enough for cyano

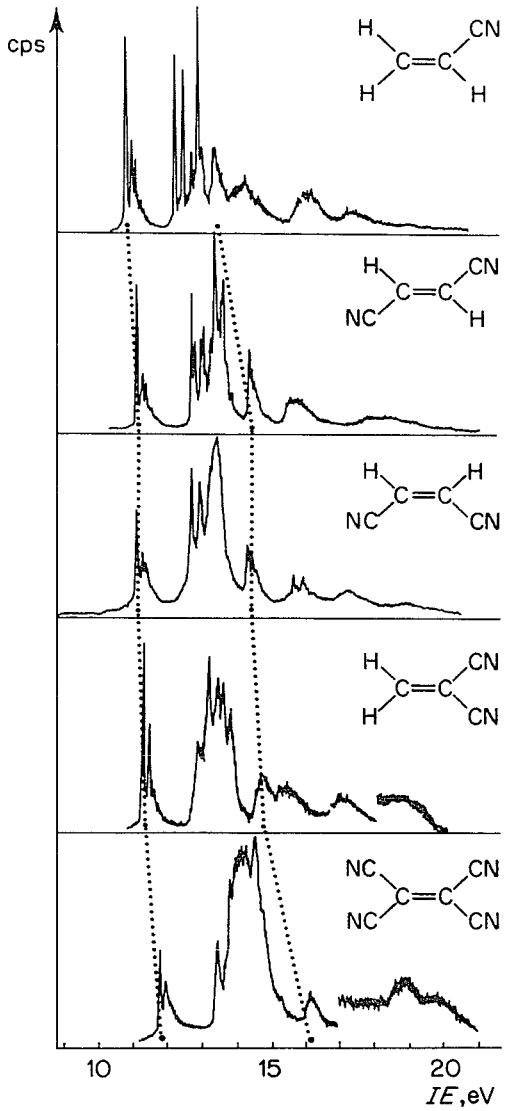


FIGURE 31. Comparison of the PE spectra of cyanoethylenes (dotted lines: π and n_N ionization retion)[96].

compounds[96]. The same reservation holds for the D_{2h} molecule TCNQ (7,7′,8,8′-tetracyano-*p*-quinodimethane) as far as the assignment of its PE spectrum[61,70] is concerned. Both TCNE and TCNQ PE spectra resemble each other to some extent especially in the π_{CN} and n_N part.

An extreme example of a complex PE spectrum is that of tetracyanomethane (Figure 7), hiding 12 ionizations under two PE bands[12]. Its assignment was cumbersome, because many semiempirical and nonempirical SCF MO calculations did

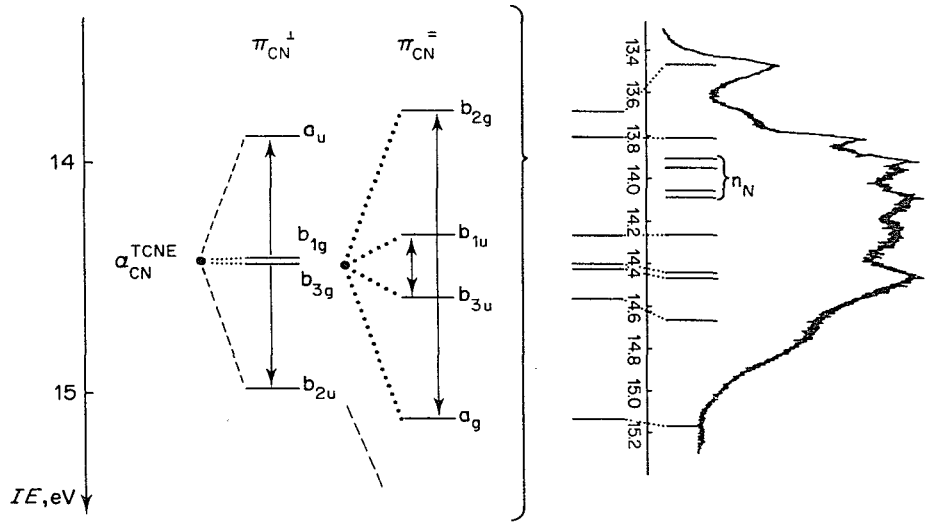


FIGURE 32. PE spectrum (13.5–15.5 eV) of $(NC)_2C{=}C(CN)_2$ showing its π_{CN} and n_N ionization region assignment[96].

not converge except for a modified CNDO version[12]. Finally, a reasonable assignment was achieved by the PE spectroscopic parametrization of a symmetry-adapted LCBO MO model (Figure 34a), which allowed a radical cation state comparison with the chemically related tetrahalogenomethanes (Figure 34b); the extra nitrogen electron gives rise to the additional ionizations t_2 and a_1[12]. All π_{CN} ionizations in $C(CN)_4$ [and also in $P(CN)_3$, the other PE spectroscopically investigated[35] polycyano compound (cf. Table 1)] occur within a narrow energy interval of less than 2 eV.

The calculated CNDO (mod.) atomic charges for $C(CN)_4$:

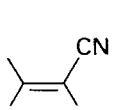
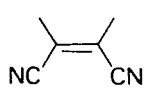
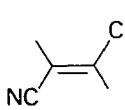
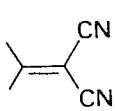
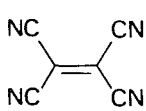
$$\begin{array}{ccccc} +0.13 & & +0.22 & & -0.26 \\ C & \text{———} & C & \text{———} & N \end{array} \qquad (13)$$

especially the considerable positive ones at the cyano carbon atoms, are in accord with the somewhat puzzling reactivity of tetracyanomethane as exemplified by the reaction with LiCl:

$$C(CN)_4 + LiCl \longrightarrow LiC(CN)_3 + ClCN \qquad (14)$$

acting, in more general terms, as if it contains a positive cyano group.

TABLE 11. PE spectroscopic MO parameters (eV) for cyanoethylenes[96]

					
α_{CC}	−11.3	−11.9	−11.9	−12.0	−12.9
α_{CN}	−13.1	−13.7	−13.7	−14.0	−14.5
$\Delta\pi_{\pi}$	—	0.3	0.0	0.3	—
$\Delta\pi_{\sigma}$	—	0.9	0.0	0.6	—
$\Delta\alpha_{CC}$	0.8	1.4	1.4	1.5	2.4

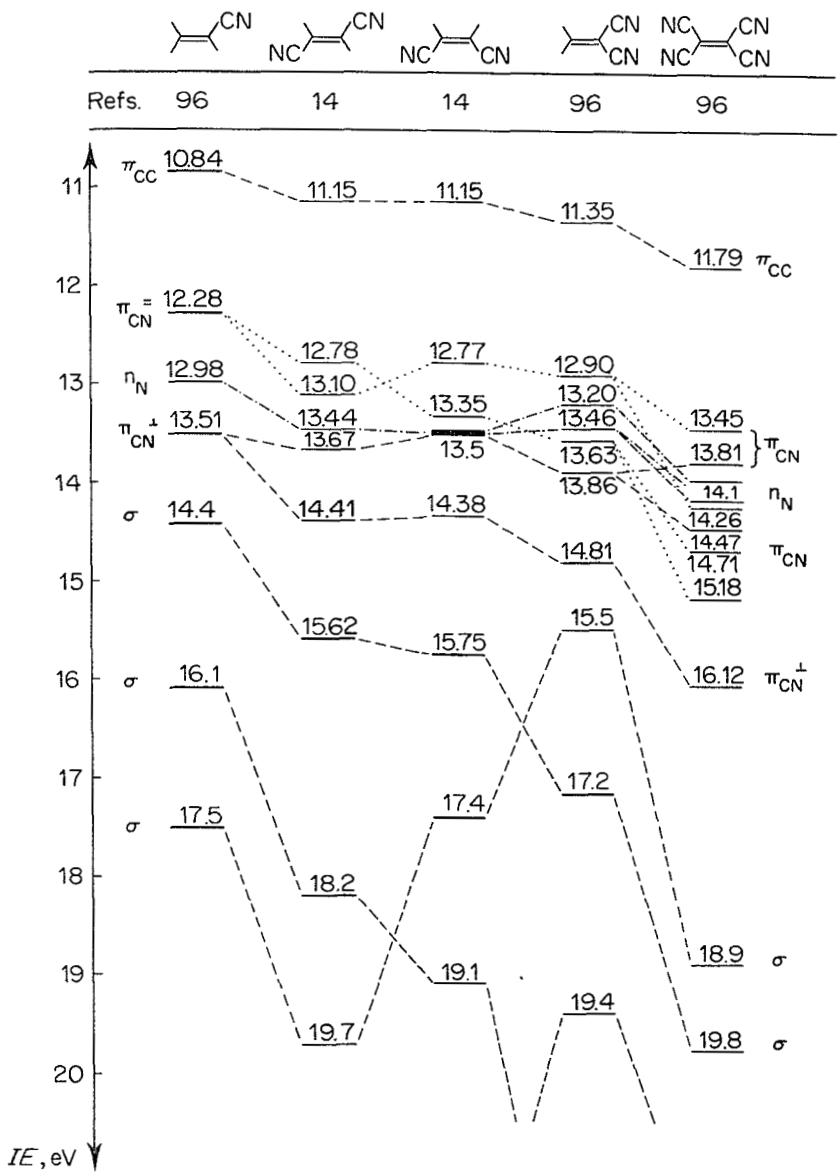


FIGURE 33. PE spectroscopic assignments for the cyanoethylenes (cf. Figures 17 and 31)[96].

VI. CONCLUDING REMARKS

This review summarizes the low-energy photoelectron spectroscopic data of some 70 molecules containing cyano groups. For all classes of compounds investigated, the PE spectra of typical molecules have been represented and their assignment by radical cation state comparison of mutually corresponding compounds, by spectroscopic information like band-shape and vibrational fine structure and by MO

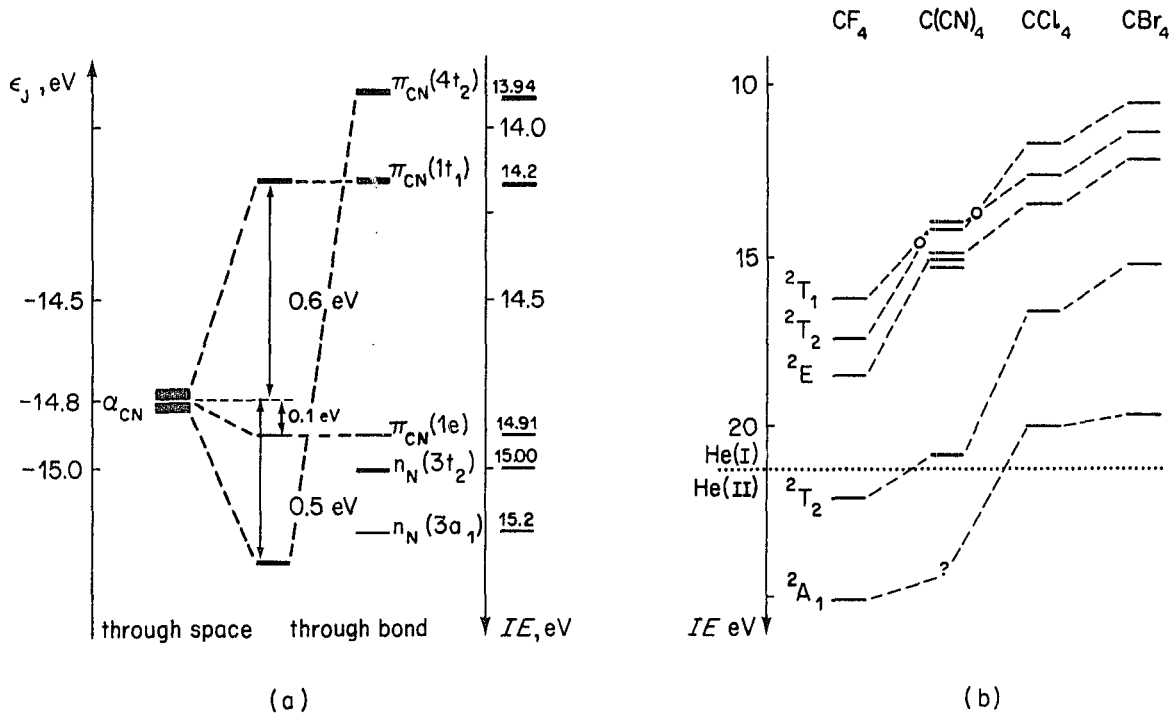


FIGURE 34. (a) MO diagram for $C(CN)_4$ obtained from the interaction of bond orbitals, and (b) comparison of ionization energies for CX_4 species (X = F, CN, Cl, Br).

models has been discussed. Concerning MO theory, calculations for cyano compounds, if they converge at all, proved to be unreliable in many cases, and, therefore, PES-parametrization procedures of symmetry-adapted models have been emphasized.

Considering the present situation in this special research area with most of the prototype molecules investigated, two smaller sections should round off this compilation: a guide for the nonspecialist on available PES information on cyano compounds, and some comments on the analytical applications now possible, especially with regard to the optimization of gas-phase reactions involving molecules with cyano groups.

A. Characteristics of Photoelectron Spectra of Cyano Compounds and Their Interpretation

The results of PE spectroscopic investigations can be summarized in two ways: according to typical ionizations or to classes of compounds as specified by molecular symmetry.

The typical ionizations are advantageously subdivided into those leading to π_{CN} or n_N radical cation states:

π_{CN} Ionizations are found between 11.6 eV (pyrrolidino cyanamide) and 16.1 eV (TCNE). The corresponding radical/cation states can be energetically degenerate, and many either occur within only a narrow energy region even for several CN groups [$C(CN)_4$] or are separated up to 2.7 eV (TCNE). In many cases, π_{CN} ionization bands can be identified by their pronounced vibrational fine structure ($\nu_{CN}^+ \sim 2000\ cm^{-1}$); broad and poorly structured bands (H_3SiCN) are rarely observed. So far no measurable Jahn–Teller distortions following π_{CN} ionization are known.

n_N Ionizations from CN groups normally give rise to one or more sharp band(s) between 12.0 eV (Me_2AsCN) and 15.2 eV [$C(CN)_4$], i.e. within the π_{CN} ionization region. n_N Ionizations from two or more CN groups may be energetically degenerate (*trans*-NCHC=CHCN) or split up to 0.8 eV [$S(CN)_2$].

π_{CN}/n_N Interactions have been proven to be very small. This finding may be explained by their local orthogonality. Within MO terminology, their relatively large orbital energy separation is removed in the PE spectra to a large extent due to different π_{CN} and n_N Koopmans' defects, resulting in a somewhat misleading region of n_N and π_{CN} ionizations.

For a subdivision according to molecular shape, both the number of cyano groups and the molecular symmetry are well suited:

Linear monocyano compounds ($C_{\infty v}$) show degenerate π_{CN} ionizations, which are split by spin-orbit coupling if substituted by heavier halogens. Structural parameters of several cations can be derived from the pronounced vibrational fine structures of the π_{CN} bands. The n_N ionizations display sharp peaks with low-intensity satellites, FCN being an exception.

Monocyano compounds with a threefold axis (C_{3v}) also exhibit degenerate π_{CN} ionizations between 11.7 eV (Me_3CCN) and 14.3 eV (F_3CCN). Their vibrational fine structure may be pronounced (CH_3CN) or unresolved (F_3CCN). Similar behaviour is observed for the cyano nitrogen lone-pair ionization. Contrary to π_{CN} ionizations, Jahn–Teller distortion has been observed (H_3CCN).

Planar monocyano compounds give rise to two π_{CN} ionizations, one from the in-plane π bond $\pi_{CN}^{=}$ and the other from the vertical $\pi_{CN}^{\perp}$ orbital. Their ionization patterns can be rationalized within PE spectroscopically parametrized MO models (H_2C=CHCN) or applying perturbation arguments starting from the parent

π-systems. The benzonitrile PE spectrum with its elaborate vibrational fine structures is a good starting point for the discussion of the tolunitriles, cyanopyridines and cyanopyridine-*N*-oxides. Some smaller molecules like N_3—CN and ON—CN constitute interesting bonding problems with their X—C≡N linkages bent. Some low-symmetry monocyano compounds surprisingly display no measurable π_{CN} band separations [H_3C—CH_2—CN or $(H_3C)_2PCN$], while others show π_{CN} splits up to 1.7 eV (H_2NCN). For several compounds more than one conformer has to be considered, but no complications have been observed in the PE spectra except for band-broadening and vanishing vibrational structures. Unexpectedly, the n_N ionization energy of NH_3 decreases upon CN substitution (severe geometry change) and the n_X ionizations increase in compounds $(H_3C)_2X$—CN in the series from X=N to X=As.

Dicyano compounds of at least C_{2v} or C_{2h} symmetry have been the starting point for PE spectroscopic MO parametrization, providing internal reference ionizations. The difficult PE spectroscopic assignment for geminal dicyano compounds is supported by reports with different irradiation sources, vibrational fine structure and consistency of the final parameter set. Accordingly, π_{CN}/π_{CC} and π_{CN}/π_{CO} interactions in $H_2C{=}C(CN)_2$ and $OC(CN)_2$ are almost equal ($\beta = -1.4$ eV), but smaller than the π_{CN}/n_S interaction in $S(CN)_2$ or the hyperconjugation in $H_2C(CN)_2$ (−2.2 eV). Detailed assignments are also available for $(CN)_2$, $(H_3C)_2C(CN)_2$ and the disubstituted ethylenes and acetylenes.

Polycyano compounds give rise to complex PE spectra characterized by many overlapping bands. Detailed assignment for TCNE or $C(CN)_4$ fits into radical cation state correlations with similar compounds, thus confirming the spectroscopic interpretation.

The main difficulties in interpreting the PE spectra of cyano compounds, together with proposals for their solution, are:

Deconvolution of PE spectra, which is one of the main problems for larger molecules, especially for di- and poly-cyano derivatives.

Cyano substitution effects, which are sometimes hard to predict and unexpected, e.g. the 8.6 eV shift of the σ_{CS} ionization from $S(CH_3)_2$ to $S(CN)_2$ or the decrease in n_N ionization from NH_3 to H_2NCN. Sometimes, large molecular structure changes are observed.

Nonconvergence of MO calculations, which often occurs for cyano compounds. MO calculations can provide, if their reliability can be tested, e.g. by radical cation state comparison, a useful basis for the rationalization of molecular properties. Nevertheless many approximations, at least within the framework of semiempirical procedures, prove to be invalid for the strongly polar CN structures and may produce mispredictions. In addition, high-quality Hartree–Fock calculations often reveal a breakdown of Koopmans' theorem for cyano compounds, i.e. differences between the PE band and Hartree–Fock orbital sequences are registered. Koopmans' defects, i.e. deviations between ionization and orbital energy, may range from −1.65 eV (HCN) to −2.8 eV (HC≡CCN) for n_N ionizations and from +0.09 eV (FCN) to −1.8 eV (H_3CCN) for π_{CN}. They are probably due to large changes in electron correlation upon ionization of the fairly localized cyano group. If, however, correlation is included in the calculation e.g. for HCN or NCCN, satisfactory numerical reproduction of ionization energies is achieved, and the PE spectrum of NCCN has recently been computer-simulated.

PE parametrization of MO models has successfully been applied to cyanogen, cyanoacetylenes, cyanoethylenes, cyanomethanes, and other high-symmetry dicyano compounds. The resulting set of PE spectroscopically evaluated parameters is consistent and the estimated CN substituent effects can be described as strongly

electron-withdrawing (inductive stabilization). Conjugation effects, on the other hand, are relatively small. Changes inflicted by cyano substituents range between the effects for fluorine and chlorine substitution and, although deduced from PE spectra for PE spectroscopic purpose, they have proved to be useful in the discussion of other molecular properties of cyano compounds.

Although many of the inherent difficulties may be hidden behind the more simplified descriptions in this review, the PE spectroscopic and theoretical results on cyano compounds constitute a framework, within which further investigations may be undertaken. There is still a number of interesting compounds awaiting PES investigation. Altogether, the wealth of experimental and theoretical data should improve our chemical intuition about known and, as for instance $N(CN)_3$ (still) unknown cyano compounds.

B. Photoelectron Spectra of Cyano Compounds and Their Analytical Application to the Optimization of Gas-phase Reactions

Photoelectron spectra supply, as repeatedly pointed out (cf., for example, Figure 31) fingerprints of molecules. If, therefore, characteristic PE bands of two molecules do not overlap, both can be detected qualitatively in mixtures as well as quantitatively determined, assuming that band intensity changes are proportional to changes in concentrations. This simple and elegant analytical approach also permits, if starting

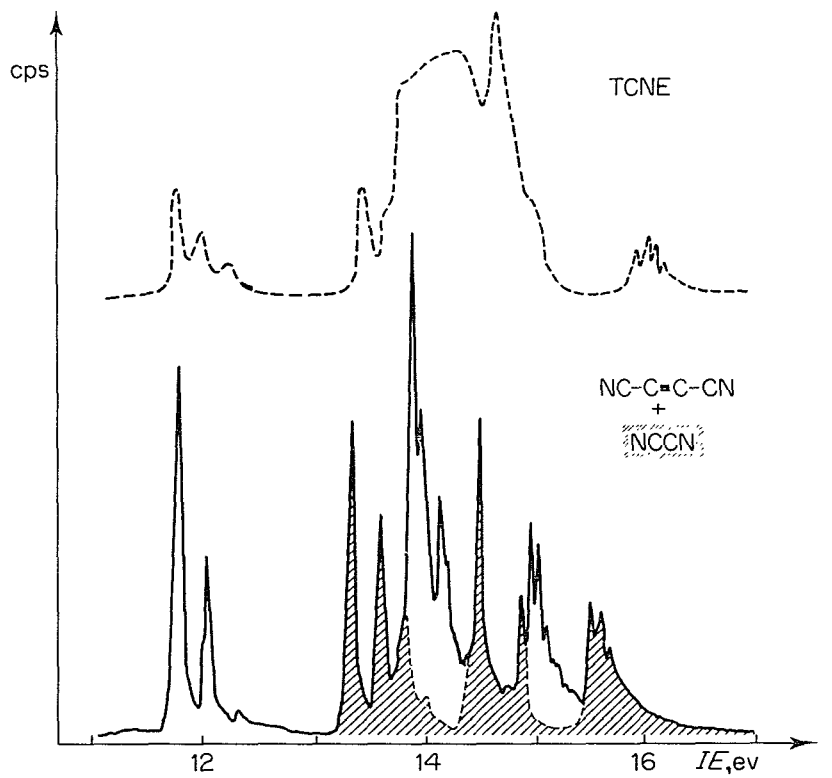


FIGURE 35. TCNE pyrolysis products at 1400 K.

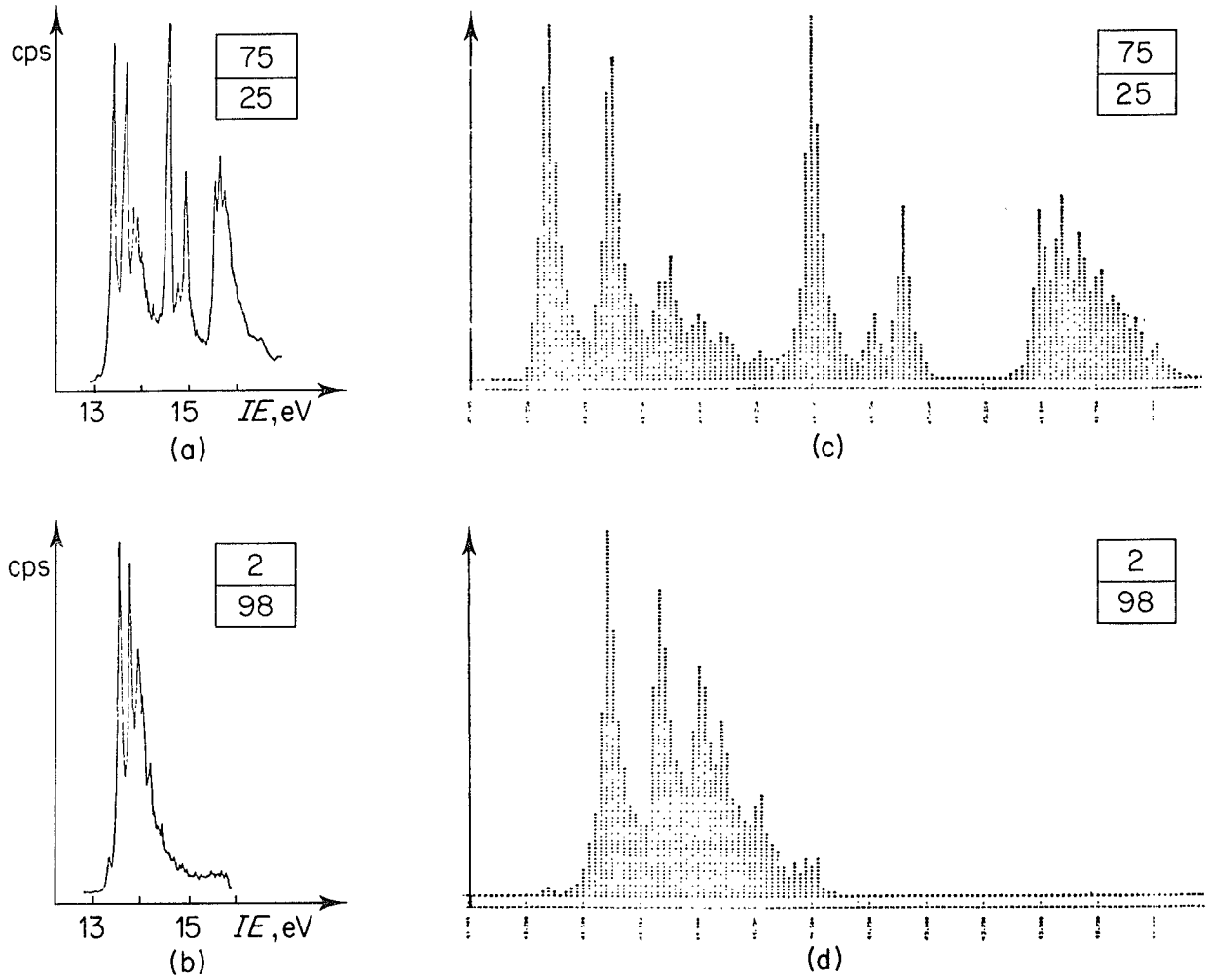
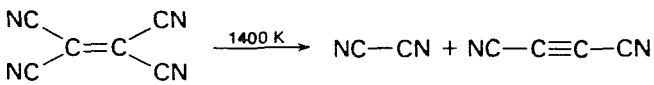


FIGURE 36. PE spectra at 12–17 eV of NCCN/HCN mixtures in various pressure ratios (a, b) and the computer simulation of the same mixtures assuming linear dependence on concentration (e, d).

material and product bands are separated, the follow-up and optimization of gas-phase reactions[15–17]. One example of a thermal decomposition and another of an attempted gas-phase synthesis will illustrate the future potential of PE spectroscopy as an analytical tool especially for poisonous compounds.

Example 1: Pyrolysis of TCNE. Tetracyanoethylene[99] has been found to undergo decomposition at 1300 K, completed at 1400 K[99]. Comparison of the PE spectra of the pyrolysis products (Figure 35) with the one of TCNE (Figure 31) shows that no starting material is present at the end of the reaction. Further comparison with PE spectra of presumable products quickly reveals cyanogen (Figure 6) and dicyanoacetylene (Figure 12). The reaction verified PE spectroscopically:



(15)

has already been reported in the literature[22,25] yielding about 50% dicyanoacetylene.

Example 2: Reaction of XH + NCCN. For oxidations with cyanogen, which

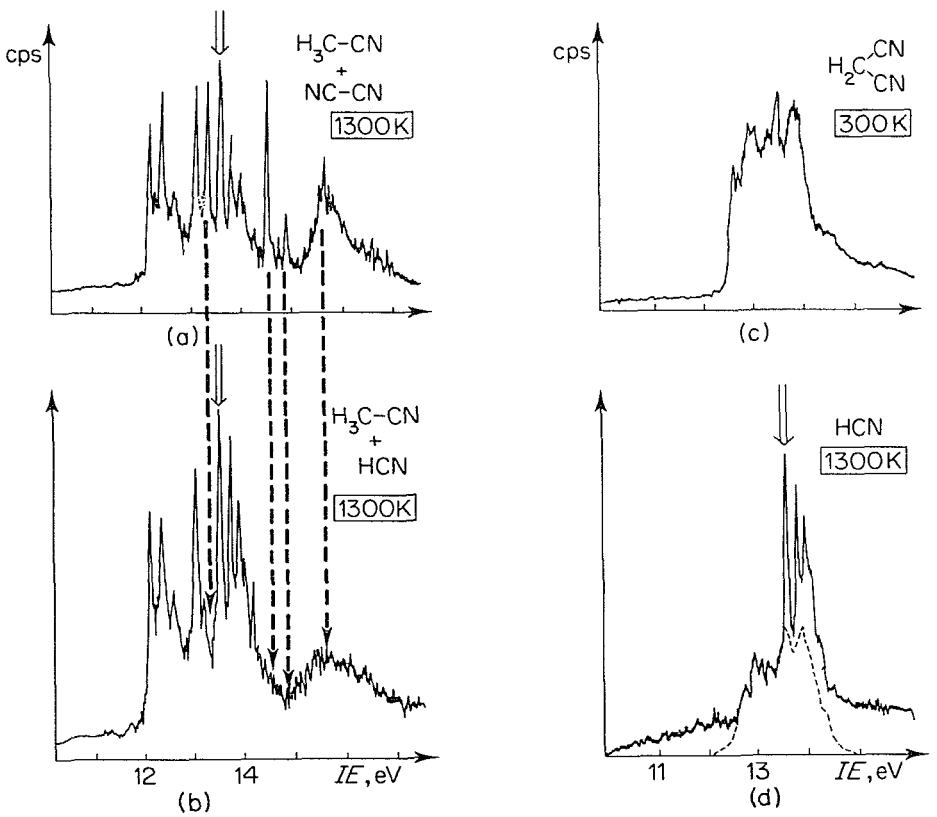


FIGURE 37. PE spectra of CH_3CN/NCCN mixtures heated to 1300 K in the ratio 1 : 1 (a) and 10 : 1 (b), as well as of malononitrile at 300 K (c) and 1300 K (d).

produce hydrogen cyanide:

$$NC{-}CN + XH \longrightarrow X{-}CN + HCN \qquad (16)$$

PE spectroscopy is probably the most convenient method of following the reaction. Calibration of the analytical procedure[16] can either be achieved by PE spectroscopic records of appropriate mixtures (Figure 36a and b) or by computer simulation (Figure 36c and d). As is obvious from Figure 36 the relative intensities of the peaks at 13.3 eV (NCCN) and 13.6 eV (HCN + NCCN) are best suited for analytical comparison, and the ranges of detectability stretch from some 25 HCN in 75 NCCN to 2 NCCN in 98 HCN.

The PES analytical method can be calibrated within about two days and permits an easy screening of many gas-phase reactions[15]. If, for instance, acetonitrile and cyanogen are heated in a flow system[16] to 1300 K, an increase of the 13.6 eV peak is observed[16] indicating the formation of HCN (Figure 37). On tenfold increase of the CH_3CN pressure, the NCCN PE bands disappear completely (Figure 37b) and outside the oven-zone a graphite film forms. According to the PE spectroscopic analysis, the reaction of acetonitrile and cyanogen does not yield any malononitrile under the conditions applied, but rather hydrogen cyanide and elemental carbon:

$$CH_3CN + NCCN \xrightarrow{1300\,K} \begin{cases} CH_2(CN)_2 \\ \downarrow\ 1300\,K \\ HCN + (C) \end{cases} \qquad (17)$$

The malononitrile pyrolysis carried out in addittion (Figure 37c and d) confirms that at the CH_3CN/NCCN reaction temperature of 1300 K decomposition to HCN and carbon already takes place[16].

The future of PE spectroscopy in general, and especially of cyano compounds, may well lie in a predominantly analytical application[15], e.g. the optimization of heterogeneously catalysed reactions such as the cyanation of benzene with cyanogen[17].

VII. REFERENCES

1. As a reference book on PE spectroscopy cf. *Electron Spectroscopy: Theory, Techniques and Applications*, Vols. 1–3 (Eds. A. D. Baker and C. R. Brundle), Academic Press, London, 1977–1989.
2. A. Almenningen, B. Bak, P. Jansen and T. G. Strand, *Acta Chem. Scand.*, **27**, 1531 (1973).
3. C. Baker and D. W. Turner, *Proc. Roy. Soc. (London)*, **A 308**, 19 (1968).
4. A. D. Baker, D. P. May and D. W. Turner, *J. Chem. Soc. (B)*, 22 (1968).
5. B. Bak, P. Jansen and H. Stafast, *Chem. Phys. Letters*, **35**, 247 (1975).
6. V. P. Baybutt, M. F. Guest and I. H. Hillier, *Mol. Phys.*, **25**, 1025 (1973).
7. M. Beez, G. Bieri, H. Bock and E. Heilbronner, *Helv. Chim. Acta*, **56**, 1028 (1973).
8. J. Berkowitz, W. A. Chupka and T. A. Walter, *J. Chem. Phys.*, **50**, 1497 (1969).
9. G. Bieri, *Chem. Phys. Letters* **46**, 107 (1977).
10. H. Bock and B. G. Ramsey, *Angew. Chem.*, **85**, 773 (1973); *Intern. Ed.*, **12**, 734 (1973).
11. H. Bock, *Angew. Chem.*, **89**, 631 (1977); *Intern. Ed.*, **16**, 613 (1977).
12. H. Bock, E. Haselbach, E. Mayer and H. Stafast, *Helv. Chim. Acta*, **59**, 1035 (1976).
13. H. Bock, *Intern. J. Pure Appl. Chem.*, **44**, 343 (1975).
14. H. Bock and H. Stafast, *Chem. Ber.*, **105** 1158 (1972).
15. H. Bock and B. Solouki, *Angew. Chem.*, **93**, 425 (1981); *Intern. Ed.*, **20**, 424 (1981).

16. H. Bock, B. Solouki and J. Wittmann, *Angew. Chem.*, **90**, 985 (1978); *Intern. Ed.*, **17**, 932 (1978).
17. H. Bock, B. Solouki, J. Wittmann and H.-J. Arpe, *Angew. Chem.*, **90**, 986 (1978); *Intern. Ed.*, **17**, 933 (1978).
18. D. Britton, *Perspect. Struct. Chem.*, **1**, 109 (1967).
19. F. Brogli and E. Heilbronner, *Helv. Chim. Acta*, **54**, 1423 (1971).
20. C. R. Brundle and M. B. Robin in *Determination of Organic Structures by Physical Methods*, Vol. 3 (Eds. F. C. Nachod and J. J. Zuckermann), Academic Press, New York, 1971, p. 1.
21. P. Burroughs, S. Evans, A. Hamnett, A. F. Orchard and N. V. Richardson, *J. Chem. Soc., Chem. Commun.*, 921 (1974).
22. T. L. Cairns, R. A. Carboni, D. D. Coffman, V. A. Engelhardt, R. E. Heckert, E. L. Little, E. G. McGeer, B. C. McKusick, W. J. Middleton, R. M. Scribner, C. W. Theobald and H. E. Winberg *J. Amer. Chem. Soc.*, **80**, 2775 (1958).
23. L. S. Cederbaum, W. Domcke and W. von Niessen, *Chem. Phys.*, **10**, 459 (1975).
24. E. Clementi and D. Klint, *J. Chem. Phys.*, **50**, 4899 (1969).
25. E. Ciganek and C. G. Krespan, *J. Org. Chem.*, **33**, 541 (1968).
26. C. C. Costain and H. W. Kroto, *Can. J. Phys.*, **50**, 1453 (1971).
27. S. Cradock and D. W. H. Rankin, *J. Chem. Soc., Faraday Trans. II*, **68**, 940 (1972).
28. G. A. Crowder, *J. Mol. Struct.*, **7**, 147 (1971).
29. R. L. Dekock and D. R. Lloyd, *Advan. Inorg. Chem. Radiochem.*, **16**, 65, 107 (1973).
30. M. J. S. Dewar, A. Komornicki, W. Thiel and A. Schweig, *Chem. Phys. Letters*, **31**, 286 (1975).
31. R. Dickinson, G. W. Kirby, J. G. Sweeny and J. K. Tyler, *J. Chem. Soc., Chem. Commun.*, 241 (1973).
32. E. A. Dorko and L. Buelow, *J. Chem. Phys.*, **62**, 1869 (1975).
33. J. H. D. Eland, *Photoelectron Spectroscopy*, Butterworths, London, 1974.
34. S. Elbel and H. tom Dieck, *Z. Naturforsh.*, **31B**, 178 (1976).
35. S. Elbel, H. tom Dieck and R. Demuth, *Z. Naturforsch.* **31B**, 1472 (1976).
36. W. Ensslin, H. Bock and G. Becker, *J. Amer. Chem. Soc.*, **96**, 2757 (1974).
37. S. Evans and A. F. Orchard, 'Photoelectron spectroscopy' in *Electronic Structure and Magnetism of Inorganic Compounds*, Vol. II, JCS Special Report, Chemical Society, London, 1973.
38. E. Fischer, *Z. Chem.*, **8**, 281 (1968).
39. R. Foster, *Organic Charge-transfer Complexes*, Academic Press, London–New York, 1969.
40. F. Freeman, *Chem. Rev.*, **69**, 592 (1969).
41. C. Fridh and L. Åsbrink, *J. Elec. Spectry Rel. Phenom.*, **7**, 119 (1975).
42. D. C. Frost, S. T. Lee and C. A. McDowell, *Chem. Phys. Letters*, **23**, 472 (1973).
43. D. C. Frost, F. G. Herring, C. A. McDowell and I. A. Stenhouse, *Chem. Phys. Letters*, **1**, 533 (1970).
44. T. Fujikawa, T. Ohta and H. Kuroda, *Chem. Phys. Letters*, **28**, 433 (1974).
45. R. Gleiter, E. Heilbronner and V. Hornung, *Helv. Chim. Acta*, **55**, 255 (1972).
46. D. Gonbeau, C. Guimon, J. Deschamps and G. Pfister-Guillouzo, *J. Elec. Spectry Rel. Phenom.* **6**, 99 (1975).
47. R. Griebel, G. Hohlneicher and F. Dörr, *J. Elec. Spectry Rel. Phenom.*, **4**, 185 (1974).
48. H. J. Haink, E. Heilbronner, V. Hornung and E. Kloster-Jensen, *Helv. Chim. Acta*, **53**, 1073 (1970).
49. A. Hamnet and A. F. Orchard, 'Photoelectron spectroscopy' in *Electronic Structure and Magnetism of Inorganic Compounds*, Vol. I. JCS Special Report, Chemical Society, London, 1972.
50. A. Hamnet and A. F. Orchard, 'Photoelectron spectroscopy' in *Electronic Structure and Magnetism of Inorganic Compounds*, Vol. III, JCS Special Report, Chemical Society, London, 1974.
51. E. Heilbronner, 'Some aspects of UPS' in *The World of Quantum Chemistry* (Eds. R. Daudel and B. Pullmann), D. Reidel, Dordrecht/Holland, 1974.
52. E. Heilbronner, V. Hornung and K. A. Muszkat, *Helv. Chim. Acta*, **53**, 347 (1970).
53. E. Heilbronner, V. Hornung, J. P. Maier and E. Kloster-Jensen, *J. Amer. Chem. Soc.*, **96**, 4252 (1974).

54. Cf., for example, E. Heilbronner and H. Bock, *The HMO Model and its Application*, Vol. 1, Verlag Chemie, Weinheim, 1969 and John Wiley & Sons, London, 1976, Chaps. 6 and 7.
55. G. Herzberg in *Molecular Spectra and Molecular Structure*, Vol. III (*Electronic Spectra and Electronic Structure of Polyatomic Molecules*), van Nostrand, Princeton, New Jersey–Toronto–London–Melbourne, 1967, p. 337.
56. R. Hoffmann, *Acc. Chem. Res.*, **4**, 1 (1971).
57. J. M. Hollas and T. A. Sutherley, *Mol. Phys.*, **24**, 1123 (1972).
58. J. M. Hollas and T. A. Sutherley, *Mol. Phys.*, **22**, 213 (1971).
59. K. N. Houk and L. L. Munchhausen, *J. Amer. Chem. Soc.*, **98**, 937 (1976).
60. K. N. Houk, Y.-M. Chang and P. S. Engel, *J. Amer. Chem. Soc.*, **97**, 1824 (1975).
61. I. Ikemoto, K. Samizo, T. Fujikawa, K. Ishii, T. Ohta and H. Kuroda, *Chem. Letters*, 785 (1974).
62. R. A. W. Johnstone and F. A. Mellon, *J. Chem. Soc., Faraday Trans. II.*, **69**, 36 (1973).
63. T. Kobayashi and S. Nagakura, *Bull. Chem. Soc. Japan* **47**, 2563 (1974).
64. T. Kobayashi and S. Nagakura, *J. Elec. Spectry Rel. Phenom.*, **4**, 207 (1974).
65. T. Koopmans, *Physica*, **1**, 104 (1934).
66. J. Kroner, D. Proch, W. Fuss and H. Bock, *Tetrahedron*, **28**, 1585 (1972).
67. W. Kutzelnigg, *Angew. Chem.*, **85**, 564 (1973); *Internat. Ed.* **12**, 546 (1973).
68. C. Lageot, *J. Chim. Phys. Physicochim. Biol.*, **68**, 214 (1971).
69. R. F. Lake and H. W. Thompson, *Proc. Roy. Soc. (London)*, **A317**, 187 (1970).
70. N. O. Lipari, C. B. Duke, R. Bozio, A. Girlando, C. Pecile and A. Padva, *Chem. Phys. Letters*, **44**, 236 (1976).
71. J. P. Maier and J.-F. Muller *Tetrahedron Letters*, 2987 (1974).
72. J. P. Maier and J.-F. Muller, *J. Chem. Soc., Faraday Trans. II*, 1991 (1974).
73. E. Mayer, *Monatsh. Chem.*, **101**, 846 (1970).
74. A. D. McLean and M. Yoshimine, *Tables of Linear Molecule Wave Functions*, San José Research Laboratory, International Business Machines Corporation, San José, California, 1967.
75. P. C. Meier and W. Simon, in *Molecular Spectroscopy* (Ed. P. Hepple), Institute of Petroleum, London, 1972, p. 53.
76. W. J. Middleton, E. L. Little, D. D. Coffman and V. A. Engelhardt, *J. Amer. Chem. Soc.*, **80**, 2795 (1958).
77. V. Migrdichian, *The Chemistry of Organic Cyanogen Compounds*, Reinhold, New York, 1947.
78. W. H. Morison and D. N. Hendrickson, *Inorg. Chem.*, **11**, 2600 (1972).
79. R. D. Nelson, D. R. Lide, Jr. and A. A. Maryott, *Selected Values of Electric Dipole Moments in the Gas Phase*, NSRDS-NBS 10, National Bureau of Standards, Washington, 1967.
80. S. Petersen in *Houben-Weyl, Methoden der organischen Chemie*, Vol. 8, Georg Thieme-Verlag, Stuttgart, 1968, pp. 278, 304.
81. L. Pierce, R. Nelson and C. Thomas, *J. Chem. Phys.*, **43**, 3423 (1965).
82. A. W. Potts and T. A. Williams, *J. Elec. Spectry Rel. Phenom.*, **3**, 3 (1974).
83. W. C. Price, A. W. Potts and D. G. Streets, in *Electron Spectroscopy* (Ed. D. A. Shirley), North-Holland Publishing Company, Amsterdam–London, 1972, p. 187.
84. M. Puchalik, *Acta Phys. Polon.*, **10**, 89 (1950).
85. J. W. Rabalais, *Principles of Ultraviolet Photoelectron Spectroscopy*, Wiley–Interscience, New York–London–Sydney–Toronto, 1977.
86. J. W. Rabalais, T. P. Debies, J. L. Berkosky, J.-T. J. Huang and F. O. Ellison, *J. Chem. Phys.*, **61**, 516 (1974).
87. J. W. Rabalais and R. J. Colton, *J. Elec. Spectry Rel. Phenom.*, **1**, 83 (1972).
88. C. N. R. Rao, *Tetrahedron*, **32**, 1561 (1976).
89. Z. Rappoport, (Ed.) *The Chemistry of the Cyano Group*, Wiley–Interscience, London–New York–Sydney–Toronto, 1971.
90. M. B. Robin, N. A. Kuebler and C. R. Brundle, in *Electron Spectroscopy* (Ed. D. A. Shirley), North-Holland, Amsterdam–London, 1972, p. 375.
91. P. Rosmus, H. Stafast and H. Bock, *Chem. Phys. Letters*, **34**, 275 (1975) and references therein.
92. J. Sauer, *Angew. Chem.*, **79**, 76 (1967).

93. W. L. Smith, *Mol. Phys.*, **26**, 361 (1973).
94. S. P. So and W. G. Richards, *J. Chem. Soc., Faraday Trans. II*, **71**, 62 (1975).
95. H. Stafast and H. Bock, *Chem. Ber.*, **107**, 1882 (1974).
96. H. Stafast and H. Bock, *Tetrahedron*, **32**, 855 (1976).
97. H. Stafast, Faraday Discussion on 'The photoelectron spectra of molecules', *Faraday Disc. Chem. Soc.*, **54**, 148 (1972).
98. H. Stafast and H. Bock, *Z. Naturforsch.*, **28B**, 746 (1973).
99. H. Stafast, *Ph.D. Thesis*, University of Frankfurt, 1974; cf. also *Master Thesis*, University of Frankfurt, 1971.
100. B. Solouki, H. Bock and P. Rosmus, unpublished results.
101. The He(II) PE spectrum was kindly provided by Dr. H. J. Lempka (Perkin–Elmer Ltd.) and gave rise to a change in the assignment of the 17.28 eV and 18.1 eV bands (Ref. 98) to $\sigma_{CH}(1b_1)$ and $\sigma_{CH}(3a_1)$, respectively. The corresponding MO parameters have been revised accordingly.
102. R. H. Staley, J. E. Kleckner and J. L. Beauchamp, *J. Amer. Chem. Soc.*, **98**, 2081 (1976).
103. *Tables of Interatomic Distances and Configuration in Molecules and Ions*, Supplement 1956–1959, Special Publication No. 18, Chemical Society, London, 1956.
104. W. Thiel and A. Schweig, *Chem. Phys. Letters*, **16**, 409 (1972).
105. R. K. Thomas and H. W. Thompson, *Proc. Roy. Soc. (London)*, **A 327**, 13 (1972).
106. H. W. Thompson in *Molecular Spectroscopy* (Ed. P. Hepple), Institute of Petroleum, London, 1972, p. 3, and previous work quoted.
107. D. W. Turner, C. Baker, A. D. Baker and C. R. Brundle, *Molecular Photoelectron Spectroscopy*, Wiley–Interscience, London–New York–Sydney–Toronto, 1970.
108. J. K. Tyler, J. Sheridan and C. C. Costain, *J. Mol. Spectry*, **43**, 248 (1972).
109. G. Wagner and H. Bock, *Chem. Ber.*, **107**, 68 (1974).
110. O. W. Webster, D. R. Hartter, R. W. Begland, W. A. Sheppard and A. Cairngross, *J. Org. Chem.*, **37**, 4133 (1972).
111. D. S. C. Yee and C. E Brion, *J. Elec. Spectry Rel. Phenom.*, **8**, 313 (1976).
112. K. Wittel, *Thesis*, University of Frankfurt, 1973; cf. *Chem. Phys. Letters*, **15**, 555 (1972).
113. K. Wittel, H. Bock and R. Manne, *Tetrahedron*, **30**, 651 (1974) and literature quoted therein.

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 6

Radiation chemistry of triple-bonded molecules

ZEEV B. ALFASSI
*Department of Nuclear Engineering, Ben-Gurion University of the Negev, Beer Sheva, Israel, 84120**

*Written while the author was a guest at the Institute for Radiochemistry of the Technical University of Munich, FRG. The author is grateful to the Minerva Foundation and Professor W. Gentner for the fellowship which enabled this stay. The author thanks Professor H. Heusinger of the Institute of Radiochemistry for his kind hospitality.

I. INTRODUCTION

Radiation chemistry is the study of the chemical effects produced in a system by the absorption of ionizing radiation. This definition includes the chemical effects due to radiation from radioactive sources, high-energy charged particles and short-wavelength (less than about 400 Å)[1] electromagnetic radiation from accelerators. The principal characteristic of high-energy radiation is that it causes ionization in all materials. This makes the distinction between radiation chemistry and photochemistry[2,3]. Photochemistry deals with longer wavelength electromagnetic radiation which has lower energy (less than about 30 eV). This relatively low energy leads in many cases only to the excitation of the molecules and does not produce ions. Usually, the energy of the particles and photons applied in radiation chemistry is much higher. The whole energy is not absorbed by a single molecule, as in photochemistry, but rather distributed over several molecules, along the track of the ionizing particle or photon. The high-energy photons and particles are not selective and may ionize, excite or dissociate any molecule lying in their path.

The high-energy photons or particles lose energy in successive events and produce primary electrons which produce several secondary electrons with lower energies[4]. The chemical effects of ionizing radiation occur almost exclusively through the secondary electrons most of which have less than 100 eV. These electrons will cause ionization and excitation of the surrounding molecules and will lose energy till they reach thermal energies. In many solvents these thermal electrons polarize the solvent and are bound in a stable quantum state to it; these electrons are called solvated electrons.

The study of radiation chemistry may be divided, from the experimental point of view, into two parts. The first is the study of unstable intermediates which have short lifetimes and thus cannot be studied by the usual chemical methods. The second is the study of the final radiolytic products which can be measured by common chemical techniques.

One way to make the short-lived intermediates amenable to study is to increase their lifetimes, usually by irradiating in the solid state and at very low temperatures. Then, the intermediates can be measured after irradiation by optical absorption spectroscopy or ESR. Another method of making the lifetime longer in the liquid phase, is by adding compounds which upon addition of radicals produce long-lived radicals; this method is called spin trapping[5]. More common in the liquid phase is pulse radiolysis[6,7]. In this technique electron accelerators which can deliver intense pulses of electrons lasting a very short time (nsec up to μsec) are used. Each single pulse can produce concentration of intermediates which are high enough to be studied by methods such as light absorption spectroscopy or electrical conductivity.

The yields of radiolytic products are always expressed by the G value. The G value is defined as the number of particles (molecules, radicals, ions) produced or consumed per 100 eV of energy absorbed in the system. The unit used for the absorbed energy (dose) is the rad, defined as 1 rad = 100 erg g^{-1} = 6.243 × 10^{13} eV g^{-1}.

The radiation chemistry of the three different triple bonds (C≡C, C≡N, N≡N^+) have much in common, in that in all the systems the radicals formed by the radiolysis of the compounds or the solvent add to the triple bonds. In the case of solvated electrons, the electron adds to the triple bond to form the anion radical which now contains a double bond. Although the radiation chemistry of the triple bond is similar to the radiolysis of the olefinic double bond[8], since the main process is addition to the π bonds, it has to be remembered that the triple bonds, both C≡C and C≡N, are less reactive than the C=C double bond. In both acrylonitrile (CH_2=CH—CN) and in vinylacetylene (CH_2=CH—C≡CH) the main reaction is addition to the double bond

and only a very small fraction of the radicals are added to the triple bond[9]. This preference is more prominent in acrylonitrile than in vinylacetylene.

II. RADIOLYSIS OF ALKYNES

A. Radiolysis of Acetylene in the Gaseous Phase

1. General

The radiolysis of several alkyne systems have been studied[10]; however, only acetylene has been studied sufficiently to draw conclusions on the mechanism of the reaction[11] *. The action of ionizing particles on acetylene was first observed in 1874, when on passing a discharge through acetylene, unreactive and insoluble products were observed[12]. Lind and his coworkers[13,14] showed that radiolysis of gaseous acetylene results in the formation of a polymeric substance, cuprene, with the general formula of $(CH)_n$. Mund and Rosenblum[15,16] found that besides cuprene, benzene is also a major product in the radiolysis of gaseous acetylene. These two products, cuprene and benzene, are the only products of importance at moderate conversion and they are formed in a ratio of about 4:1 in terms of C_2H_2 consumed. Little or no extra gaseous products are formed. The G value for acetylene disappearance is about 70 for various radiations, approximately independent of dose, dose rate and acetylene pressure[7,17,18]; the measure of acetylene disappearance was for a time used as a gas-phase dosimeter.

A very interesting finding in the radiolysis of acetylene is that the ratio of the number of molecules consumed to the number of ion pairs produced by the radiolysis (ion-pair yield) is remarkably constant under a variety of experimental conditions. This constancy of the ion-pair yield (~20) was explained by the ion-cluster theory[20,21]. In this theory an ionized acetylene molecule forms a cluster involving 19 neutral acetylene molecules which react to form a polymer. The formation of acetylene ions were shown later by mass spectrometry. Munson has shown that acetylene ions, $C_2H_2^+$, constitute about 75% of the ions in the mass spectrum of acetylene[22]:

$$C_2H_2 \xrightarrow{\sim\sim} C_2H_2^+ + e^-$$

$$C_2H_2^+ + 19\,C_2H_2 \longrightarrow (C_2H_2)_{20}^+$$

$$(C_2H_2)_{20}^+ + e^- \longrightarrow C_{40}H_{40}$$

(The symbol $\xrightarrow{\sim\sim}$ is used to symbolize reactions brought about by the absorption of ionizing radiation.)

Later work has raised objections to the adoption of the ion-cluster theory. Eyring and collaborators[23] calculated that large clusters were theoretically improbable. They drew attention to the possible formation of excited states; both the ions and the excited molecules are capable of giving rise to free radicals which can initiate chain-reactions. However, the later mechanisms which neglect the cluster formation do not give an alternative explanation for the constancy of the ion-pair yield.

*The radiation-induced polymerization of acetylene derivatives, mainly phenylacetylene, was reviewed recently by Chauser and coworkers[19].

2. Benzene formation

The relative extent of formation of cuprene and benzene has been found to be dependent on the pressure, temperature and dose rate. Dorfman and Wahl[24] studied the products of the radiolysis of acetylene in a large excess of helium. In this system only cuprene was formed and no benzene was found. Dorfman and coworkers[17,24] suggested that there are two parallel processes occurring in irradiated acetylene, the one leading to benzene and the other to cuprene. In the case of excess of helium, almost all the energy would be absorbed in helium and thus it could be concluded that the energy transferred led only to the formation of cuprene precursors and not to benzene precursors. Since ionized helium atoms are known to produce acetylene ions it can be concluded that benzene is formed through an excited acetylene molecule and the authors suggested that the acetylene molecule was probably in a triplet state:

$$C_2H_2 \longrightarrow C_2H_2^*$$

$$C_2H_2^* + C_2H_2 \longrightarrow (C_2H_2)_2^* \xrightarrow{C_2H_2} C_6H_6$$

The energy transferred from the ionized and excited states of helium to acetylene does not produce these excited species, and leads only to the ionization of acetylene. It was found that the addition of large excesses of argon, krypton or xenon reduced the ratio of benzene to polymer yields. These experiments showed that while the yield of benzene was the same as expected from the energy absorbed directly by acetylene, the yield of the polymer increased considerably, due to energy transfer from the noble-gas excited atoms and ions[17,24,25]. These results excluded the possibility of formation of benzene via acetylene ions. Further proof was obtained by McLaren[53] who found that the yield of benzene was not affected by large additions of nitrous oxide.

Irradiating acetylene at low pressures decreased sharply the fraction of consumed acetylene which was transformed to benzene[24]. This was explained as being due to the larger number of excited acetylene molecules which were deexcited by collision with the wall of the vessel before they had a chance to react with other molecules. This was further proven by the lower pressure required to show this effect in a spherical vessel compared to a cylindrical irradiation vessel. It was estimated from the pressure and the fraction producing benzene that the lifetime of the benzene precursors is at least 10^{-4} s, which is consistent with the assumption that they are triplet states.

Decreasing the pressure of acetylene in photopolymerization[25,26] led to a decrease in the yields of both benzene and cuprene, maintaining the ratio of benzene to cuprene constant, even at low pressures. Since in this system only excited states of acetylene were formed, the yields of both products decreased with the pressure. This shows that the precursor of benzene is excited acetylene, while cuprene is formed both from excited acetylene and acetylene ions.

However, there is some evidence that benzene formation proceeds, at least in part, by a radical mechanism. Mains and coworkers[27] irradiated an equimolar mixture of C_2H_2 and C_2D_2 and found about 27% of the benzene molecules with an odd number of deuterium atoms (6.6% C_6H_5D, 12% $C_6H_3D_3$ and 8.6% C_6HD_5). The odd number of deuterium atoms can only be produced by a sequence of reactions involving C—H bond ruptures at some step.

The same authors studied the irradiation of mixtures of acetylene with radical scavengers. They found that the addition of oxygen or iodine to acetylene suppressed completely the formation of benzene during irradiation, thus indicating at least one step involving radicals. The authors postulated the formation of $(C_6H_7)^{\cdot}$ which can decompose via cyclization:

$$(C_6H_7)^{\cdot} \longrightarrow C_6H_6 + H^{\cdot}$$

This reaction competed with the recombination of two radicals

$$(C_6H_7)^{\bullet} + R^{\bullet} \longrightarrow \text{products}$$

which explains why benzene formation decreased with increasing dose rate leading to higher radical concentration.

Shida and coworkers[28,29] studied the radiolysis and both the direct photolysis and the mercury-sensitized photolysis of equimolar C_2H_2–C_2D_2 mixtures. They found that the distribution of the various benzene molecules $C_6H_xD_{6-x}$ was independent of pressure and that the same distribution was obtained in radiolysis and in photolysis. These results suggest that benzene is formed through the same mechanism irrespective of the kind of the active rays. Both can be explained by a modified excited-molecule mechanism[29,30] or more favourably by the free-radical mechanism[31,32].

A similar study[33] on the involvement of radicals in benzene formation used a mixture of $^{13}C_2H_2$ with $^{12}C_2H_2$ and led to the result that there was no cleavage of the carbon–carbon triple bond in the production of benzene.

Futrell and Sieck[34] found that neon was the only noble gas which sensitized to any extent the formation of benzene, i.e., the energy absorbed originally in the noble gas led to the formation of benzene. They explained this by the findings that xenon and krypton ions produced, by charge exchange to acetylene, $C_2H_2^+$ ions, neon ions produced C_2H^+ ions and helium ions led to C_2^+ ions. They claimed that only the formation of C_2H^+ ions is accompanied by hydrogen atom formation and suggested that energy transfer from helium led to $C_2 + H_2$ rather than producing hydrogen atoms, which are known to initiate the polymerization of acetylene to benzene[32]:

$$H^{\bullet} + C_2H_2 \longrightarrow (C_2H_3)^{\bullet} \xrightarrow{C_2H_2} (C_4H_5)^{\bullet} \xrightarrow{C_2H_2} (C_6H_7)^{\bullet} \longrightarrow C_6H_6 + H^{\bullet}$$

In conclusion, the radical mechanism seems to be the preferable one and the difference between benzene and polymer formation probably lies in the different precursors which yield the radicals.

3. *Polymer formation*

The polymer formed from acetylene by irradiation or other means is generally referred to as cuprene, although the method of formation influences its properties. Prepared by irradiation, cuprene is a white-yellowish powder insoluble in all common solvents, which neither melts nor sublimes. It is inflammable and will absorb oxygen (up to 25% by weight) when exposed to air. Deuteroacetylene is polymerized at the same rate as acetylene[14,17]. When the polymer is formed under special conditions some crystallinity can be detected; however, as ordinarily produced, the polymer appears amorphous[35].

The studies of Dorfman and coworkers[17,24], Futrell and Sieck[34] and others have shown that energy absorbed by rare gases leads to formation of cuprene. However, no correlation has been found between the sensitization of the polymerization and the yield of $C_2H_2^+$ ions formed by charge transfer from noble-gas ions in mass spectroscopy[34]. In polymerization by γ-radiation krypton was found to be a better sensitizer than xenon or argon, while its efficiency for charge transfer was found to be the lowest one. This led to the conclusion that ions do not play a major role in the polymerization. A similar conclusion that the major polymer forming mechanism is not ionic in character has been reached by Field[18] on the basis of the observed temperature coefficient of the reaction. Thus it has to be concluded that the sensitization occurs through excitation or dissociation of acetylene molecules by noble-gas ions or excited atoms. Benzene, whose ionization potential is below that of acetylene,

was found to retard the polymerization[36]. This indicates that ions play at least a partial role in the polymerization of pure acetylene. Jones[37] has studied the infrared absorption spectrum of cuprene formed by radiolysis (Figure 1). The infrared absorption spectrum was found to be largely characteristic of aromaticity, indicating the cyclization to form aromatic nuclei is not an exclusive property of the reaction path leading to the formation of benzene. Jones suggested that the polymer's lack of colour-depth was also a demonstration of the absence of an extended, conjugated, aliphatic system of multiple bonds (as it is in the carotenoids). The physical properties of cuprene (insolubility, infusibility and non-volatility) appear to be due to a three-dimensional network. Jones suggested that this should be a three-dimensional network of benzenoid rings, probably joined by short, conjugated aliphatic chains and acetylenic linkages, and appended by phenyl and HC≡C— groups. The aliphatic double and triple bonds would account for the large affinity which the polymer showed for oxygen. Jones suggested that aromatization took place at a later stage by a migration of hydrogen atoms. It is interesting to note that the IR spectrum of cuprene is very similar to that of a polymer obtained by irradiation of benzene. Briggs and Back[38] have studied the effect of electric fields applied during the γ-irradiation of acetylene and found two interesting results. The first observation was that while in the absence of the electric field a thin white adherent deposit of cuprene was formed on the bottom surface of the vessel, when a saturation voltage was applied during the irradiation no such deposit of cuprene was observed and a discolouration of the anode suggested formation of a thin film on the surface of the anode. The second finding was that the presence of an electric field had virtually no effect on the rate of disappearance

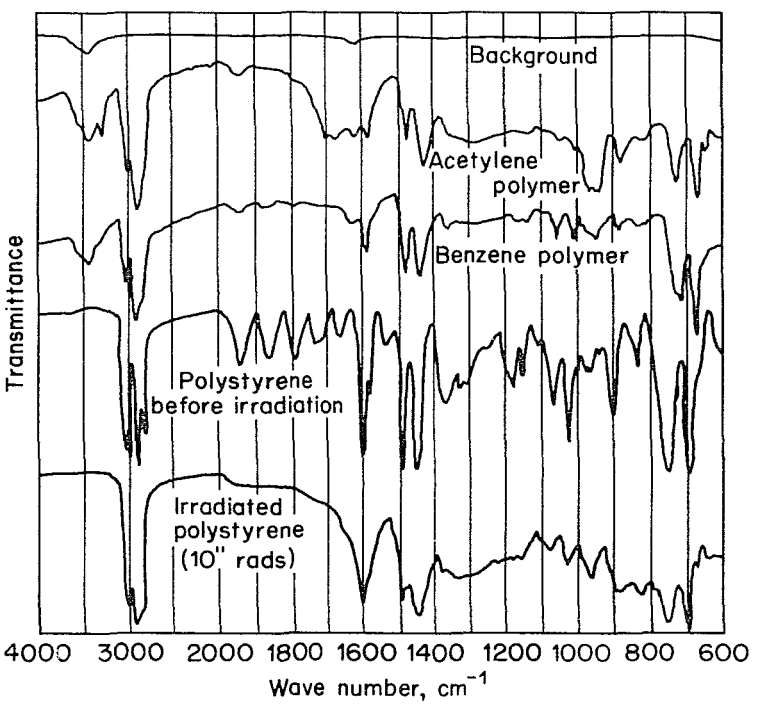


FIGURE 1. Infrared absorption spectrum of cuprene. Reproduced with permission from A. R. Jones, *J. Chem. Phys.*, **23**, 953 (1960).

of acetylene, as reflected by the change in pressure. The second observation indicates a nonionic mechanism of polymer formation, but unfortunately this is not conclusive since the lack of effect of a field on the rate of polymerization is also compatible with a short-chain ionic polymerization in which chains are terminated before the ionic chain carriers can be removed by the field. The observation that electric fields approaching the ion-multiplication region caused no enhancement of the rate of polymerization indicates that low-lying excited states of acetylene do not make an important contribution to the reaction[39]. Electron microscopy photographs[38] of cuprene particles (Figure 2) showed that cuprene was formed in spherical particles, fairly uniform in size, with an average diameter around 300 nm. There were no apparent differences between particles formed in the presence and absence of an electric field.

This indicates that the electric field removes the particles after they have been formed, due to some charges on the polymer molecules. The simplest and most plausible explanation of the effect of the field appears to be a competition between the sedimentation of the particles due to gravity and their horizontal drift in the electric field. Using the average size of the particles and a typical solid hydrocarbon density of 0.7 g cm^{-3} leads to an average particle mass of about 1×10^{-14} g, corresponding to a molecular weight of 6×10^9, and containing 2.3×10^8 molecules of C_2H_2. Using the observed values of $G(-C_2H_2) = 80$ and 25.3 eV/ion pair means that each molecule of cuprene is due to the formation of 10^7 ion pairs. It is unlikely that all these charges are on the cuprene molecule, especially since the discolouration of the anode shows that the cuprene molecule is negatively charged. Lifetime measurements indicated that most of the negative charge carriers in the system were free electrons[23]. The intensity of the electric field needed to obtain saturation was shown to indicate a single charge on the cuprene molecule. Briggs and Back[38] suggested a four-stage mechanism for the polymerization of acetylene without decision between an ionic and a nonionic process.

(1) *Primary polymerization* of acetylene to form polyunsaturated hydrocarbons with molecular weights in the C_4–C_{20} range. Taking a reasonable value of G (chain initiation) = 4, and the observed $G(-C_2H_2) = 80$, this means that each chain initiator

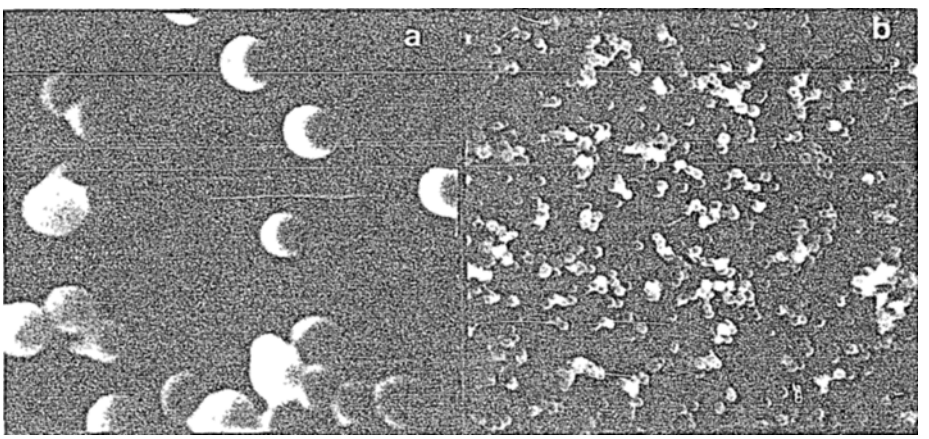


FIGURE 2. Electron microscope photographs of cuprene formed in the radiolysis of acetylene. Magnifications about (a) × 18,000 and (b) × 3500. Reproduced with permission from J. P. Briggs and R. A. Back, *Can. J. Chem.*, **49**, 3789 (1971).

consumes 20 molecules of acetylene. To give low molecular weights of C_4–C_{20} appreciable chain transfer to the C_2H_2 monomer would be required. However, this range of C_4–C_{20} seems arbitrary. The near independence of the polymerization on the dose rate and the pressure indicates self-termination of the chain by cyclization or other rearrangements.

(2) *Secondary polymerization* of the initially formed polyenes. These would tend to be much more reactive than acetylene, and would rapidly attain a low steady-state concentration, with their rate of formation remaining the rate-determining step.

(3) *Physical condensation* of the polymers formed by the primary and secondary polymerization. The spherical shape of the cuprene particles strongly suggests initial condensation as liquid droplets. Condensation as a liquid at room temperature and at the low conversion at which cuprene is observed would require a carbon number of about 20.

(4) *Rapid and extensive polymerization* and cross-linking in the liquid polyene droplets, induced by radiation and leading to the final intractable cuprene product.

It seems possible that in this complex system of processes both ions and free radicals might play a part, although one or the other might be predominant in a particular stage of the reaction.

To further test their suggested mechanism Back and his coworkers[40] studied the radiation chemistry of acetylene at a very high dose-rate from an electron accelerator, yielding 10^{28} eV g^{-1} s^{-1}, compared to previous studies with dose-rates of 10^{16}–10^{18} eV g^{-1} s^{-1}. The high dose-rate should reduce the length of ionic and free-radical chains, which have bimolecular termination steps, but should have a lesser effect on biradical chains which have predominantly unimolecular termination steps. Furthermore, the short lifetime of ions and free radicals at the high dose-rate might reduce the consumption of primary products by these species, enabling the identification of the primary products. The main products observed relative to benzene (1.0) are: diacetylene (5.63), vinylacetylene (2.81), *n*-propylacetylene (0.50), triacetylene (1.25), HC≡C—CH=CH—C≡CH (0.37), HC≡C—CH_2CH_2—C≡CH (0.64), various C_7 compounds (1.28) and some C_8 and C_9 compounds. Conversion to G values can be done by using G(benzene) = 0.31. Irradiation with a dose of 100 Mrad did not lead to formation of observable cuprene-like polymers, in direct contrast to the low dose-rate behaviour where cuprene was seen to settle out after a dose of a few megarads. The yields of all the products examined was found to be independent of the number of the pulses. This implies that no secondary reactions of these products were occurring. Thus the second stage of the mechanism is suppressed and the products observed are from the first stage alone. The average ion lifetimes for such high dose-rates were estimated to be of the order of 3×10^{-8} s which would limit even the primary polymerization process to only a few steps whereas usually the primary polymerization can lead to longer chains. These results support the previously suggested explanation, for the formation of benzene as the sole product of low molecular weight, that it is due to its relative unreactivity toward secondary polymerization. It seems probable that many of the volatile polyunsaturated compounds observed in the high dose-rate studies are transient intermediates in the low-intensity radiolysis. However, the distribution of the primary products might be quite different in the two systems, since the primary polymerization may have been much attenuated at the high intensity. The average radiolytic yield of benzene is very much smaller in the high-intensity system (G = 0.31 compared to 5 ± 1) reflecting the reduced extent of primary polymerization. Willis and coworkers[40] gave also the main ion-molecule sequences which are possible, calculated from high-pressure mass spectrometry studies[41] and the value of 24 eV per ion pair[42] (Table 1). However, these processes do not agree so well with the observed yields of the various products.

TABLE 1. Main ion–molecule sequences in acetylene radiolysis[a]

Yield	Primary event	First stage reaction[b]	Second stage	Third stage
2.96	$C_2H_2^+ + e$	$(1.97)C_4H_3^+ + H \rightarrow$	$C_6H_5^+ \rightarrow$	$C_8H_7^+$
		$(0.99)C_4H_2^+ + 2H \rightarrow$	$C_6H_4^+ \rightarrow$	$C_8H_6^+$
0.48	$C_2H^+ + H + e$	$(0.23)C_4H_2^+ + H \rightarrow$	$C_6H_4^+ \rightarrow$	$C_8H_6^+$
		$(0.16)C_2H_3^+ + C_2 \rightarrow$	$C_3H_3^+ + CH_2 \rightarrow$	$C_5H_3^+ + H_2$
		$(0.09)C_4H^+ + H_2 \rightarrow$	$C_6H_2^+ + H \rightarrow$	$C_8H_4^+$
0.16	$C_2^+ + 2H + e$	$(0.07)C_4H^+ + H \rightarrow$	$C_6H_2^+ + H \rightarrow$	$C_8H_4^+$
		$(0.09)C_3H_2^+ + C \rightarrow$	$C_5H_3^+ + H \rightarrow$	$C_7H_5^+$
0.16	$C^+ + CH_2 + e$	$(0.40)C_3H^+ + H(+H) \rightarrow$	$C_5H_2^+ + H \rightarrow$	$C_7H_4^+$
0.24	$CH^+ + CH + e$			

[a]Reproduced with permission from G. Willis, R. A. Back and R. H. Morris, *Can. J. Chem.*, **55**, 3288 (1977).
[b]Yields are given in parentheses.

B. Radiolysis of Acetylene in the Liquid Phase

In contrast to the gaseous phase, very little work has been done in the liquid phase. Tabata and coworkers[43] found that γ-radiation-induced (~5 Mrad) polymerization of liquid acetylene (−78°C) gives a polymer which is an orange-yellow bulky powder. It is insoluble in benzene, toluene, acetone, pyridine and methanol while soluble in aniline, dimethylformamide and isopropylamine. Larger doses of above 10 Mrad lead to a polymer which is insoluble even in the latter solvents, probably due to the cross-linking of the polyacetylene by further irradiation. Measurement of the intrinsic viscosity showed that it increases with the irradiation dose.

In contrast to the polymer obtained by the gas-phase polymerization, the infrared spectra of the polymer produced in the liquid phase did not show the band of the benzenoid rings. The main absorption is at 770 cm^{-1} which is assigned to the *cis* form of the olefinic linkage. The spectra and the solubilities indicated that the polymer should be a linear polymer, mainly with *cis* structure.

The following two findings showed that this polymerization did not proceed by a radical mechanism:

(1) The initial rate of polymerization was found to be proportional to the dose rate (3.10^4–10^5 rad h^{-1}), while for a homogenous radical mechanism in nonviscous media it is proportional to the square root of the dose-rate.

(2) The addition of radical scavengers such as benzoquinone and diphenyl picryl hydrazide did not reduce the rate of polymerization.

The decision between cationic and anionic mechanisms was made on the basis of the effect of various solvents. Dimethylformamide, which is known to accelerate an ionic polymerizations, was found to retard the γ-induced polymerization of liquid acetylene. On the other hand, methylene chloride was found to accelerate considerably the rate of polymerization. Since it is well known that methylene chloride favours a cationic polymerization, it can be concluded that polymerization of acetylene in the liquid phase proceeds by a cationic mechanism.

Another difference between the gas and the liquid phase is that while about 20% of the consumed acetylene is converted to benzene in the gas phase, no formation of benzene was detected in the liquid phase.

The differences in benzene and polymer formations were explained as due to the fact that while in the gas phase the dominant species are excited states and radicals which can cyclize to form the benzene molecule or benzoid rings with side-chains which continue to polymerize, the active species in the liquid phase are ions which cannot form the benzoid rings by hydrogen transfer.

C. Radiolysis of Acetylene in the Solid Phase

γ-Induced polymerization of solid acetylene at −196°C led to a deep-brown rigid material[43]. The polymer was insoluble in all common solvents, but slightly swelled in dimethylformamide. The infrared spectrum contained neither the benzoid ring band, found in the gas phase, nor the 770 cm^{-1} band appearing in the liquid-phase polymer. Hence, it was suggested that solid-state polymerization led mainly to the *trans* form of polyacetylene. The authors[43] suggested that the mechanism of polymerization at such low temperatures occurs through collective excitation of the monomer crystal, leading to a different structure than do chain-reactions, which govern the formation of the polymer in the liquid phase.

D. Radiolysis of Acetylene in Aqueous Solution

Irradiation of aqueous solutions leads to the formation of hydrated electrons (e^-_{aq}, $G = 2.6$), hydrogen atoms ($G = 0.55$) and hydroxyl radicals ($G = 2.6$) which react with the solutes[44].

Clay and collaborators[45] measured the final products obtained in the γ-irradiation of aqueous solutions of acetylene. Irradiation of water saturated with acetylene (1 atm.) in the absence of oxygen at pH 1.2 yielded a yellow-white solid polymer and several aldehydes: acetaldehyde, crotonaldehyde and glycolaldehyde, each about $G = 0.2$, and a lower yield of formaldehyde. An unidentified additional product which absorbs in the region of 200 nm was suggested to be a conjugated polyenic compound. Irradiation in the presence of oxygen led to the formation of glyoxal as the almost only organic product. The initial yields of glyoxal are strongly dependent on the concentration of acetylene. This dependence, together with the high yields of glyoxal ($G = 14$ at pH 1.2), suggests the existence of chain-reactions for the production of glyoxal.

Neta and Fessenden[46] studied the pulse radiolysis of aqueous solutions of acetylene dicarboxylate ion, followed by ESR spectroscopy. They found that the hydrated electron added to the C≡C triple bond to form an anion radical, which underwent rapid protonation to form a vinyl-type radical, observed in the ESR spectra:

$$^-O_2C{-}C{\equiv}C{-}CO_2^- + e^-_{aq} \longrightarrow {}^-O_2C{-}\bar{C}{=}\dot{C}{-}CO_2^- \xrightarrow{H^+} {}^-O_2C{-}CH{=}\dot{C}{-}CO_2^-$$

The ·OH radicals added to the triple bond to form an enol-type radical which isomerized to the keto form, and the latter was observed in the ESR spectra:

$$^-O_2C{-}C{\equiv}C{-}CO_2^- + OH \longrightarrow {}^-O_2C{-}\overset{OH}{\overset{|}{C}}{=}\dot{C}{-}CO_2^- \longrightarrow {}^-O_2C{-}\overset{O}{\overset{\|}{C}}{-}\dot{C}H{-}CO_2^-$$

The mechanism of the addition of the ·OH radical to the C≡C triple bond in acetylene was studied extensively by Anderson and Schulte-Frohlinde[47] using pulse radiolysis followed by UV absorption spectroscopy. Besides acetylene as a solute they also used N_2O, in order to convert all the hydrated electrons to hydroxyl radicals:

$$e^-_{aq} + N_2O + H_2O \longrightarrow N_2 + OH^- + \cdot OH$$

At low doses and high concentration of acetylene they found the formation of species A with an absorption peak probably below 200 nm. Species A decayed to form species B, which had a maximum absorption at 295 nm. The rate of formation of B was found to be proportional to the concentration of C_2H_2, indicating that B was formed by the reaction of A with one molecule of acetylene. The rate of decay of B was found to be equal to the rate of formation of a new species C which had a maximum absorption at 260 nm, indicating that B decayed to C. Assuming the sequence of the pseudo-first-order reactions:

$$A \xrightarrow{k_1'} B \xrightarrow{k_2'} C$$

and analysing the rate of formation of C for the measurement of k'_2, it was found that k'_2 is proportional to the concentration of acetylene, indicating that C was formed due to the reaction of B with a C_2H_2 molecule. The decay of C was found to follow second-order kinetics indicating the termination of two C molecules together. The scheme of the reactions at low doses and high acetylene concentrations can thus be written as:

$$OH + C_2H_2 \longrightarrow A$$

$$A + C_2H_2 \longrightarrow B$$

$$B + C_2H_2 \longrightarrow C$$

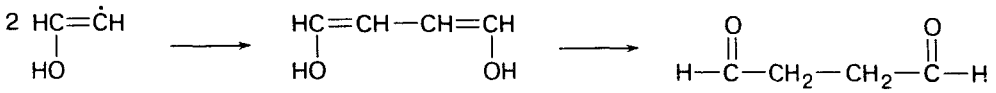
$$C + C \longrightarrow \text{products}$$

A was assumed to be the β-hydroxyvinyl radical HC(OH)=$\dot{C}$H rather than the keto form, the formylmethyl radical O=CH—CH_2, since the spectra did not agree with previous measurements of the latter. B was supposed to be the 1-hydroxy-1,3-butadienyl-4 radical and C was suggested as the 1-hydroxy-1,3,5-hexatrienyl-6 radical. This is supported by the similarity of the UV absorption maximum of C (~260 nm) to that of 1,3,5-hexatriene. The products formed by the recombination of two C radicals are unknown. It is reasonable to assume that they continue to polymerize to form the white polymer found by Clay and coworkers[45].

Since Neta and Fessenden[46] found that at pH 7–14, the radical obtained by the addition of ·OH to acetylenedicarboxylate ion existed mainly in the keto form, the effect of the pH was studied by Anderson and Schulte-Frohlinde[47]. Below pH 6, the spectra of A, B and C were found to be independent of pH and acetylene concentration. On increasing the pH from 8 to 10 the spectra of the transients were changed progressively to that of a new species. Above pH 10 this was found immediately after the pulse, and was the same as found previously for the formylmethyl radical, indicating that OH^- catalyses the isomerization of the β-hydroxyvinyl radical to the keto form:

Studies of solutions containing both acetylene and ethylene glycol showed that the reaction of the formylmethyl radical with acetylene is quite slow, its rate constant being at least a hundred-fold slower than that of the β-hydroxyvinyl radical.

Since species A decays to B by reaction with a molecule of acetylene, this decay can be suppressed by using low C_2H_2 concentrations, thus favouring decay by combination of two A radicals. Another way of doing this, is to increase the dose rate, which leads to higher concentration of the radicals. Studies with low concentrations of acetylene in slightly acidic solution showed the formation of a relatively long-lived transient (several minutes), with a maximum absorption of 240 nm, by a second-order reaction. The latter transient is probably the dimer of A, which rearranges slowly to succinaldehyde, found in considerable yields in solutions of low concentrations of C_2H_2 or at high dose rates[47]:



E. Radiation-induced Cross-linking with Acetylene

Mitsui and collaborators[48–51] found that irradiation of polyethylene with acetylene leads to cross-linking of the polymer. They found that the weight of the polymer increases linearly with the radiation dose. Since the weight of polyethylene irradiated in vacuo remains essentially unaltered, and since bulk polymerization of acetylene hardly occurs at all under their conditions (acetylene pressure 3 kg cm^{-2} and ^{60}Co γ-rays of 1.1×10^5 rad h^{-1}) it seems reasonable that the extra weight is due to the addition of acetylene to the polyethylene, induced by the γ-irradiation. The cross-linking of the polyethylene can be expected to be induced by addition of polymer radicals, resulting from C—H and C—C bond scission by ionizing radiation, to the triple bond of acetylene. $G(-C_2H_2)$ was found to be always larger than G(radicals), especially at the lower temperatures (at 30°C the ratio is 20.7 while at 200°C it is only 1.6), indicating that the addition of acetylene is a chain-reaction.

Irradiation of polyethylene in the presence of acetylene leads to significantly larger gel fraction than irradiation of polyethylene in vacuo. The radiolytic yield of the cross-linking calculated from the gel fraction by Charlesby and Pinner's equation[52] is larger in the presence of acetylene than in vacuo, the effect being larger the lower the temperature in the range 30–200°C. This acceleration of γ-induced cross-linking by acetylene was found to be further increased by the addition of some fluorine-containing monomers[50].

III. RADIOLYSIS OF NITRILES

A. General

Most of the work done on the radiolysis of nitriles has been on acetonitrile (except acrylonitrile, in which the active group is the olefinic double bond and not the CN group). Hence, this section deals mainly with the radiolysis of acetonitrile as a representative of the nitriles, with the radiolysis of benzonitrile given in order to show the effect of the aromatic ring.

The radiation chemistry of aqueous solutions of nitriles is possibly connected to prebiotic chemistry[54,55] and has been studied quite intensively, including cyanide ions and HCN which can be considered as the simplest nitriles.

The radiation chemistry of nitriles is similar to that of acetylenes, in that in both compounds the main reaction of the initial species is addition to the triple bond. However, the final products are very different as can be judged from the observed degree of polymerization (4–5 in acetonitrile compared to above 100 in acetylene and methylacetylene) and the higher G value in acetylene.

B. Radiolysis of Acetonitrile in the Gaseous Phase

The radiolysis of acetonitrile (CH_3CN) in the gaseous phase has not been studied but some of the initial transient species can be deduced from the products of low-energy electron impact on CH_3CN. Sugiura and Arakawa[56] have observed the formation of a negative ion, CH_3CN^-, in a mixture of CH_3CN vapour and various rare gases by electron impact. They ascribed the formation of the ion to the reaction of rare gas atoms (He, Ne, Ar, Kr and Xe) in excited Rydberg states:

$$e^- + A \longrightarrow A^{**} + e^-$$

$$A^{**} + CH_3CN \longrightarrow A^+ + CH_3CN^-$$

where A represents a rare-gas atom. The onsets of the processes is correlated with the ionization potentials of the rare-gas atoms. Similar results were obtained for a CH_3CN/Ar mixture by Stockdale and coworkers[57]. They also observed the production of CH_2CN^- with an intensity of 20 times the CH_3CN^- current. They suggested that this ion was also produced by the excited argon atom in the Rydberg states:

$$Ar^{**} + CH_3CN \longrightarrow CH_2CN^- + ArH^+$$

Electron impact on pure CH_3CN[56–58] led to the formation of CN^-, CH_2CN^- and mass-41 ions ($^{13}CH_2CN^-$ or CH_3CN^-). The peak of CH_2CN^- occurs with 4.0 eV electrons and the mass-41 peak at the same energy can be accounted for in terms of the expected abundance of CH_2CN^- containing one ^{13}C atom. However above ~8 eV the fraction of mass-41 ions is too large by about a factor of 4. About 75% of mass-41 ions are due to CH_3CN^- ions. Sugiura and Arakawa[56] found that the CH_3CN^- intensity exhibited a second-order dependence on the gas pressure, suggesting that these ions are formed by capture of electrons from CH_3CN molecules (or a fragment of them) in highly excited Rydberg states:

$$e^- + CH_3CN \longrightarrow Y^{**} + Z + e^-$$

$$Y^{**} + CH_3CN \longrightarrow Y^+ + CH_3CN^-$$

Shibata and coworkers[59] observed the formation of the highly excited atoms, H^{**}, C^{**} and N^{**} when CH_3CN was bombarded with electrons of 20–100 eV.

CN^- ions are produced with two peaks at ~3 and ~8 eV. Both peaks behave like dissociative attachment:

$$e^- + CH_3CN \longrightarrow CH_3^{\cdot} + CN^-$$

They are proportional to CH_3CN pressure and fall off with delay time between electron beam and ion extraction pulses[57].

The positive ions produced in pure CH_3CN have been studied in several mass spectrometric investigations[60–62]. The main ions produced are CH_3CN^+ (100), CH_2CN^+ (82), CH_3CNH^+ (62), $CHCN^+$ (20) and CCN^+ (11). The numbers in the brackets are the relative intensities and are the average of the results of References 61 and 62.

C. Initial Species Formed in the Radiolysis of Liquid Acetonitrile

Singh and collaborators[63] studied the flash photolysis and pulse radiolysis of solutions of amines in acetonitrile and reported that spectra of solvated electrons with $\lambda_{max} \sim 700$ nm were detected. However, Hayon[64] studied the pulse radiolysis of oxygen-free pure liquid acetonitrile and was unable to detect any transient spectrum in the wavelength range 280–800 nm, appropriate for the solvated electron. Below 280 nm a weak transient was found, probably due to $\cdot CH_2CN$ radical. Hayon[64] determined the yield of electrons (or other forms of reducing agents) in various polar organic liquids by measuring the intensity of the spectra of anthracene anions formed in the solutions of anthracene in these liquids. For liquid acetonitrile he obtained 1.55, and using pyrene instead of anthracene he obtained 1.6. The yield of triplet excited states of the same liquids was determined by using naphthalene as scavanger and the measurement of the triplet spectrum of naphthalene; the yield for liquid acetonitrile was found to be 0.3. Bell and coworkers[65] have measured the pulse radiolysis of liquid acetonitrile under various conditions in order to clarify the character of the reducing species responsible for the formation of the radical anions of anthracene, pyrene,

4-nitrobenzyl compounds[66] and other electron-accepting compounds, in the radiolysis of their solutions in acetonitrile. Pulse radiolysis of pure liquid acetonitrile at room temperature showed the existence of two species. The one with a strong absorption at 1450 nm showed reducing properties, while the other with a very weak absorption below 500 nm had no reducing characteristics and was assigned to the $\cdot CH_2CN$ radical, as was suggested by Hayon[64] for the absorption below 280 nm. The reducing capabilities were proven by the decrease of the initial peak at 1450 nm and by its enhanced rate of decay when the liquid acetonitrile contained electron-acceptor compounds, such as N_2O, O_2, pyrene, biphenyl, *trans*-stilbene and others, subsequently followed by the formation of the known absorption of the radical anions of the solutes. The rate of the decay at 1450 nm and the rate of the formation of the radical anion were equal and showed a linear dependence on the concentration of the solute. This formation of the radical anion competed with the decay of the 1450 nm species by the impurities in the liquid. The study of this competition as a function of the solute concentration led to G(reducing agents) = 1.03, in contrast to Hayon's[64] results of 1.55–1.6, although the same extinction coefficient for the pyrene radical anion was used. Hayon did not consider the impurities in CH_3CN whereas Bell and coworkers[65] did, and hence it was expected that their yields would be higher, in contrast to their reported values. A reasonable explanation for this disagreement may lie in the different methods of dose measurements.

The pulse radiolysis of pure liquid acetonitrile at $-40°C$ showed[65] a reduction in the peak at 1450 nm and a formation of a peak at 550 nm, both species having reducing properties. This trend was inverted at $+62°C$, where the 1450 nm peak was higher and the absorption at 550 nm smaller than at room temperature. The optical absorption at 1450 nm as a function of temperature was found to be a sigmoid shape function which suggested the existence of two reducing species, maintaining an equilibrium. The one favoured at high temperatures, which absorbs at 1450 nm, was designated the R-species, and the other one absorbing at 550 nm was called the Z-species. The dependence of the yield of R on the temperature yields an overall enthalpy change of 8.3 kcal mol^{-1}.

$$R \rightleftharpoons Z \ (-8.3 \text{ kcal mol}^{-1})$$

This assumption of two reducing species in equilibrium also explains the non-Arrhenius behaviour of the rate constant for the decay of the absorption at 1450 nm and the finding that below 20°C the rate of decay of R is not equal to the rate of formation of the radical anion of the solute. The chemical identities of R and Z may be as shown below:

$$R \rightleftharpoons Z$$

$$CH_3CN + e_s^- \rightleftharpoons (CH_3CN)^- \ (-8.3 \text{ kcal mol}^{-1})$$

$$\text{or:} \quad CH_3CN + (CH_3CN)^- \rightleftharpoons (CH_3CN)_2^- \ (-8.3 \text{ kcal mol}^{-1})$$

Bell and coworkers[65] rejected the first possibility on the following grounds:

(1) Low concentration (<1%) of CH_3OH and H_2O in acetonitrile was found to reduce the initial yield of the R species as well as to enhance its rate of decay. This indicates that CH_3OH and H_2O react with R and with its precursor (a quasi-free or epithermal electron) without the formation of any observable products. However, solvated electrons in pure H_2O or CH_3OH are stable (though reactive) entities if they are produced from quasi-free electrons via a physical trapping mechanism. If R is a solvated electron it would be expected that small amounts of H_2O or CH_3OH would cause spectral shifts, but no enhancement of decay. This implies that R is an anion

which can undergo a proton transfer:

$$(CH_3CN)^- + R^1OH \longrightarrow CH_3C{=}NH + R^1O^-$$

(2) The absorption spectrum of R at low concentration (~5%) of CH_3CN in toluene or tetrahydrofuran is identical with that in pure CH_3CN. If R is a solvated electron its spectrum is expected to be influenced by the change of the polarity of the solution, as was found by Baxendale and coworkers[67,68].

Thus Bell and coworkers[65] concluded that there are two reducing entities $(CH_3CN)^-$ and $(CH_3CN)_2^-$ and no solvated electrons are formed. The reducing species, R, decayed following first-order kinetics; however, the rate constants were found to depend on the method of purification of CH_3CN, indicating that the reducing agents mainly reacted with the impurities present in CH_3CN.

Baptista and Burrows[69] detected the absorption of amine radical cations in the pulse radiolysis of solutions of several amines in acetonitrile. This absorption was observed to build up after the electron pulse, following pseudo-first-order kinetics. The pseudo-first-order rate constant was found to be proportional to the concentration of the amine. They suggested that these radicals were formed by an electron transfer to acetonitrile radical cations or cation dimers, which are formed by the radiolysis. They found the yield of these cations to be 0.2. However, Bell and coworkers[65] found that the irradiation of solutions of pyrene or *trans*-stilbene in CH_3CN, containing also 1% nitromethane to remove the anionic species, yielded only very weak absorptions in the region of the aromatic cation bands. The intensities were less than 1% of the absorption intensities in the absence of nitromethane. This shows clearly that the radiation-induced hole in CH_3CN very rapidly loses its ability to oxidize aromatic hydrocarbons. Solutes with a lower oxidation potential, such as the amines, are oxidized by the milder oxidizing species which are present, e.g. $\cdot CH_2CN$.

Mao and Kevan[70] studied the radicals formed during the γ-radiolysis of several liquid-phase aliphatic nitriles, using 'spin trapping' of the radicals by their addition to phenyl *t*-butyl nitrone (PBN) to form radicals stable in solution. The radicals were found to be very stable (they lasted for several days) and their ESR spectra were measured. In CH_3CN solution, only the adduct of $\dot{C}H_2CN$ was detected, but no $\cdot CH_3$ adduct and H adduct were observed. Mao and Kevan believed that their results demonstrated the absence of $\cdot CH_3$ radicals. Similarly they were not able to detect the $C_2H_5\cdot$ adduct from propionitrile. H-adducts were observed in the radiolysis of propionitrile and succinonitrile but the signals were always weak and required high PBN concentrations, indicating a fast reaction of H-atoms. Thus, the absence of H-adducts does not indicate their absence in the radiolysis of CH_3CN. However, Mao and Kevan did not mention the possibility of observing the adduct of CH_3CHN or CH_3CNH produced by the reaction of H-atoms with CH_3CN.

D. Initial Species Formed in the Radiolysis of Solid Acetonitrile

The γ-irradiation of solid CH_3CN at 77 K produces $\cdot CH_2CN$ radicals and a photobleachable species, which on illumination gives $\cdot CH_3$ radicals[71–73]. This paramagnetic photobleachable species was initially referred to as dipole-trapped electrons[74,75]; however, it has been shown[76] that this concept is unnecessary and that the species is better described as a radical anion, as was confirmed later[77]. Later works[78–80] have established that the photobleachable species in γ-irradiated acetonitrile at 77 K differs according to the nature of the crystalline phase. Acetonitrile has two crystalline phases, designated Crystal I and Crystal II with a transition temperature of 216.9 K approximately 12 K below the melting temperature of 229.3 K. Sudden cooling of

liquid acetonitrile to 77 K by immersion in liquid nitrogen results in the formation of Crystal I, the high-temperature phase, metastable indefinitely at 77 K, while slow cooling, allowing the phase transition, produces Crystal II at 77 K. In Crystal I the radiation-induced colour centre ($\lambda_{max} = 510$ nm) is the dimer radical anion $(CH_3CN)_2^-$, whereas in Crystal II the corresponding light-sensitive species ($\lambda_{max} = 430$ nm) is the monomer radical anion CH_3CN^-. Either of these species yields on illumination with visible light methyl radicals and cyanide anions. These dissociations can be reversed by a thermal reaction to regenerate the acetonitrile radical anions[74,75]:

$$(CH_3CN)_2^{-\cdot} \underset{\Delta}{\overset{h\nu}{\rightleftharpoons}} \cdot CH_3 + CN^- + CH_3CN$$

$$CH_3CN^{-\cdot} \underset{\Delta}{\overset{h\nu}{\rightleftharpoons}} \cdot CH_3 + CN^-$$

In both crystalline forms the methyl radicals readily abstract a hydrogen atom from neighbouring acetonitrile molecules to form methane and $\cdot CH_2CN$ radicals[73]:

$$\cdot CH_3 + CH_3CN \longrightarrow CH_4 + \cdot CH_2CN$$

The activation energy for this reaction was found to be 1.4[73,80] or 1.6[81] kcal mol^{-1} in marked contrast to the value of 10 kcal mol^{-1} found in the gas phase at 373–573 K[82]. LeRoy and coworkers[83] have suggested that the low energy of activation at low temperatures is due to quantum-mechanical tunnelling. Sargent and collaborators[81] prepared $\cdot CH_3$ radicals in solid CH_3CN by 185 nm photolysis of acetonitrile at 77 K and found that these radicals did not decay at 77 K and decayed only at higher temperatures (120 K). They suggested that the low activation energy is due to the existence of methyl radicals weakly associated with cyanide ion and not to free methyl radicals. Part of the activation energy of abstraction of an H-atom by $\cdot CH_3$ radicals is due to the conversion of the methyl group from sp^2 in the radical to sp^3 in methane. They assumed that the CH_3—CN^- pair is likely to be intermediate between sp^2 and sp^3. This explanation was seriously criticized by Sprague and coworkers[84]. They found from the ^{13}C splitting of the $\cdot CD_3$ radicals derived from illumination of irradiated $^{13}CD_3CN$ in either of the crystalline forms that the $\cdot CD_3$ radical is a planar one. Besides, ^{13}C splitting showed that the Me···CN^- recoil distance is greater in Crystal I than in Crystal II, while the rate constant for abstraction of hydrogen is much larger (>10) in the case of Crystal I, thus contradicting the effect of CN^- on the reactivity. The main proof for the quantum-mechanical tunnelling is the exceptionally large deuterium isotope effect on the abstraction, which was found to be at least 28,000[85], almost 20 times greater than the maximum effect in the absence of tunnelling. England and Symons[76] have found some evidence for the formation also of $CH_3\dot{C}HN$; this is similar to their findings of the H-adduct $H_2\dot{C}N$ which is the major paramagnetic species in HCN irradiated at 77 K[76].

E. Final Products in the Radiolysis of Liquid Acetonitrile

Cherniak and coworkers[86] irradiated liquid acetonitrile in the presence of ferric chloride and reported a radical yield of about 7.0 radicals/100 eV, suggesting the importance of radicals in the radiation chemistry of acetonitrile. The yields of the final products were studied independently by Bradley and Wilkinson[87] and by Ayscough and collaborators[88] using various scavengers and for various doses and dose-rates. The main product of the radiolysis of acetonitrile at room temperature is a solid short-chain polymer ($G = 4.8$[88] or 6.0[87]). No solid product was deposited until the irradiated acetonitrile was exposed to air[87]; in this process oxygen was absorbed.

This solid product is composed of at least two compounds. Ayscough and coworkers[88] found that only 85% of the polymer was soluble in alcohol. Bradley and Wilkinson[87] eluted, in partition chromatography with 15% methanol in water, only 96% (by weight) of the polymer. The elemental compositions of the alcohol-soluble and insoluble fractions are almost the same, $C_2H_{2.69}N_{1.04}O_{0.14}$ and $C_2H_{2.69}N_{0.96}O_{0.13}$, respectively[88] (overall composition $C_2H_{2.7}NO_{0.14}$), while Bradley and Wilkinson obtained $C_2H_{2.79}NO_{0.01}$. The average molecular weight was measured by cryoscopic measurement in dimethylformamide[87] and in phenol[87,88]. Bradley and Wilkinson reported a molecular weight of 165 while Ayscough and coworkers obtained 185 ± 5; thus the first suggested that the solid is a tetramer of CH_3CN while the second preferred a pentamer, although their molecular weight corresponds to a mixture of pentamers and tetramers (molecular weight CH_3CN = 41).

Other products are hydrogen (G = 0.7) and succinonitrile (0.7 in molecules of CH_3CN). Propionitrile was detected only with high dose rates, G = 0.34 at 10^{18} eV cc^{-1} s^{-1}, while at lower dose rates, 10^{16} eV cc^{-1} s^{-1}, its yield was less than 0.01[87]. On the other hand, the increase of the dose rate decreased the yield of methane (0.78 at 10^{13} eV cc^{-1} s^{-1}, 0.68 at 10^{16} and 0.28 at 10^{18}). No HCN was detected by Bradley and Wilkinson[87] ($G < 0.02$), while Ayscough and coworkers[88] obtained a dose-dependent yield of 0.12–0.36 which increased in the presence of I_2 as a scavenger. Cyanogen was below the limit of detection (0.001) except in the presence of I_2 where G = 0.02 was found[88].

The addition of radical scavengers has a marked influence on the yields of the polymer and of methane. *p*-Benzoquinone was found to eliminate the formation of more than 95% of the solid radiolysis products (mainly polymer and about 10% succinonitrile)[87], and 0.15M I_2 was found to decrease the yield of the polymer from 4.8 to 0.65[88]. I_2 and DPPH[88], quinones and chloranil[87] reduced considerably the yield of methane to 0.12[88]. On the other hand, the yield of hydrogen was reduced by less than 10%. It can be concluded that most of the products are formed by radical processes.

Two possible routes of producing radicals from CH_3CN are by breaking the C—H or the C—C bonds:

$$CH_3CN \longrightarrow \cdot CH_3 + \cdot CN$$

$$CH_3CN \longrightarrow \cdot CH_2CN + H$$

Both radicals were found in the solid state, although $\cdot CH_3$ was formed only by a following illumination, whereas only $\cdot CH_2CN$ was found in the liquid-phase ESR spin-trapping studies. The analysis of the final products showed also that the first reaction has at most a negligible contribution. No evidence for the reaction of ·CN radicals was found. If cyano radicals were contributing to the formation of the solid product, the ratio of nitrogen to carbon in the solid would be greater than in acetonitrile, whereas the experimental results showed the same ratio. Other possible products of ·CN radicals are cyanogen, methyl isocyanide and malononitrile but none of them were found in the irradiated acetonitrile. The yields of HCN are not certain, due to the disagreement between the results of the two groups, but in any case they are very small compared to G(radicals) = 7.0. This supports the findings of Mao and Kevan[70] that only $\cdot CH_2CN$ (no $\cdot CH_3$) could be found in irradiated liquid acetonitrile. This can be expected also from the yields of the radiolysis of liquid ethane, where the intensities of the lines in the ESR spectrum indicate that the methyl radical concentration is 4% of that of the ethyl radicals, corresponding to only 2% C—C bond rupture[89]. In the case of CH_3CN the C—C bond dissociation energy is considerably higher than in ethane[90], while the presence of the CN group weakens the C—H bond

by about 5.5 kcal mol^{-1}, due to resonance stabilization of the $R\dot{C}HCN$ radical[91,92]. Allylic C—H bonds, whose strengths are lower, are less stable to irradiation[93], and the same will be expected for $H—CH_2CN$. The formation of $\cdot CH_2CN$ radicals was also confirmed by the detection of iodoacetonitrile in irradiated solutions of I_2 in acetonitrile[88].

Methane was suggested as being produced by methyl radicals abstracting atoms from CH_3CN molecules, since radical scavengers reduced its yield considerably. The methyl radicals were also considered to be the precursors of propionitrile, by combination of $\cdot CH_3$ and $\cdot CH_2CN$ radicals, supported by the results that propionitrile was formed only at high dose-rates, which would form high concentration of radicals and would favour radical combination, together with reduction in the yield of methane. The existence of $\cdot CH_3$ radicals was also proven by finding CH_3I in the irradiated acetonitrile solutions of iodine.

One of the yet unsolved questions is what happened to the $\cdot CN$ radicals or anions which were formed parallel to these $\cdot CH_3$ radicals. None of the studies solved the material balance of $\cdot CH_3$ and $\cdot CN$. CH_4 ($G = 0.65$) and CH_3CH_2CN ($G = 0.16$)[88] which are derived from $\cdot CH_3$ are not balanced by HCN (0.2). According to Bradley and Wilkinson[87], the imbalance was 0.62–0.78 vs. < 0.02. If the missing $\cdot CN$ would take part in the formation of the polymer, it would make the C:N ratio 1.9 instead of the observed 2.0; a difference much larger than the experimental error. The presence of $\cdot CH_3$ but not $\cdot CN$ radicals was suggested as due to reactions such as

$$R\cdot + CH_3CN \longrightarrow (RCH_3CN)\cdot \longrightarrow RNC + \dot{C}H_3$$

where R is probably $\cdot CH_2CN$. Since malononitrile was not detected, it was suggested[87] that RNC is an unstable volatile isocyanide. The presence of such a product was detected at low doses by gas chromatography[87], but it was not found at high doses.

The formation of the major part of H_2 cannot be explained by radical reactions, since it is also formed in the presence of radical scavengers, and it was suggested to be the product of a molecular elimination process of ions or excited molecules. A similar situation was found in the irradiation of ethane where most of the H_2 molecules came from a single molecule of ethane[94,95]. In ethane irradiated at 1470 and 1295 Å the hydrogen was not only formed from a single molecule, but came preferentially from the same carbon atom of the molecule[96]. Bradley and Wilkinson[87] suggested a neutralization process, such as

$$CH_3CN^+ + CH_3CN \longrightarrow H_2 + \text{products}$$

The relatively low yield of molecular hydrogen indicates that most of the H-atoms, formed together with the $\cdot CH_2CN$ radicals, are not abstracting hydrogen and probably add to the triple C≡N bonds to form $CH_3\dot{C}H{=}N$ or $CH_3\dot{C}{=}NH$. The first of these radicals was identified later in the reaction of H-atoms with CH_3CN in aqueous solution[87]. The presence of radical scavengers reduced $G(H_2)$ from 0.67 to 0.61[88] indicating that the yield of hydrogen atoms reacting by abstraction is 0.06. The total yield of hydrogen atoms produced in the irradiation is about 3.5 (half of the total yield of the radicals), i.e. 2% of hydrogen atoms react by abstracting hydrogen, in good agreement with the value of $3 \pm 1\%$ obtained in aqueous solutions[97,98].

An interesting question is why the increase of the dose-rate led only to enhanced combination of $\cdot CH_3 + \cdot CH_2CN$, and not to $\cdot CH_3 + \cdot CH_3$ or $\cdot CH_2CN + \cdot CH_2CN$. The product of the first reaction, C_2H_6, was not detected at all while the yield of the second product, succinonitrile, increased only very little upon increase of the dose-rate. This seems to indicate a formation of a $\cdot CH_2CN$ radical and a $\cdot CH_3$ radical in close proximity, in a spur.

These results, together with the fact[88] that radical scavengers removed only 40% of the yield of succinonitrile, indicate that a considerable part of the succinonitrile was not formed by combination of two $\cdot CH_2CN$ radicals. Another possible route is that suggested by Bradley and Wilkinson[87] for the formation of molecular H_2:

$$CH_3CN^+ + CH_3CN \longrightarrow (CH_3CN)_2^+$$

where $(CH_3CN)_2^+$ is the dimer cation suggested by Baptista and Burrows[69].

$$(CH_3CN)_2^+ + CH_3CN \longrightarrow (CH_2CN)_2 + H_2 + CH_3CN^+$$

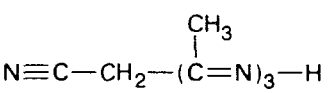
The total yield of radicals was found to be 7.0[86,87] or 6.0[88], in the presence of radical scavengers. Except for propionitrile and succinonitrile, no product was ascribed as arising from radical recombination, and this left at least 5–6 radicals/100 eV to form the polymer. Since G(polymer) is 4.8–6.0, it was suggested[87] that the only combination and dimerization of these free radicals should lead to the formation of the polymer. However, this material balance seems to be fortuitous, since it seems unreasonable to assume only reaction of the radicals between themselves and to neglect their reaction with molecules of the solvent. The yield of the radicals in an unscavenged system can be lower than in a scavenged system due to disproportionation of radicals:

$$CH_3CN \longrightarrow H + \cdot CH_2CN$$

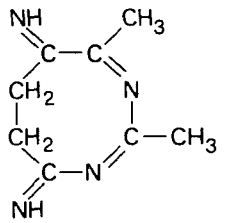
$$H + CH_3CN \longrightarrow CH_3CHN\cdot$$

$$\cdot CH_2CN + CH_3CHN\cdot \longrightarrow 2\,CH_3CN$$

The ultraviolet spectrum of the polymer[87] is consistent with that expected from a conjugated system of carbon and nitrogen atoms with the presence of cyano, imine and amine groups. The infrared spectrum[88] suggests that the main chain has the repeating unit $-C{=}N-C{=}N$ and other absorptions are of $=NH$ stretching and $-CH_2-$ deformation. These observations are compatible with several structures, e.g. **1** and **2**[88].



(1)



(2)

However, these structures do not explain the deficiency in hydrogen found in the elemental analysis, $C_2NH_{2.7}$ or $C_2NH_{2.8}$, while C_2NH_3 would fit these structures, which are oligomers of CH_3CN without any H elimination. The elementary analyses together with the molecular weight indicate a formula $C_8N_4H_{11}$, which is impossible, due to its odd number of electrons. Thus it is reasonable to assume that this tetramer is a mixture of $C_8N_4H_{12}$ and $C_8N_4H_{10}$, of which the first fits the suggested structures. In conclusion, the available data on the radiolysis of liquid acetonitrile are insufficient from both the point of view of material balance and that of the structure of the polymer.

F. Radiolysis of Benzonitrile

Pulse radiolysis of benzonitrile[99] leads to transitory spectra which show the existence of three species: (1) a short-lived species (10 ns half-life) absorbing at 400–600 nm; (2) a 30 ns half-life species absorbing at 380–520 nm; (3) a long-lived absorption dominating the spectrum below 400 nm. No definite identification of the species was made; however, the short-lived species (1) and (2) were suggested to be the benzonitrile ions (anion or cation) and an excited singlet state or excimer of benzonitrile. The long-lived species was suggested to be the triplet state of benzonitrile.

The existence of the suggested various transient species was proven in solutions of benzonitrile in several solvents and in benzonitrile solutions of various solutes. Pulse radiolysis of cyclohexane or methanol solutions of benzonitrile showed the spectra of the benzonitrile anion[99,100] at about 400 nm. In benzene solutions, singlet and triplet excited states of benzonitrile were observed.

Hayon[64] studied the formation of the anthracene anion in benzonitrile solutions and obtained $G(e^-) = 1.40$. He also measured the yield of triplet excited states of liquid benzonitrile by the formation of triplet naphthalene and obtained $G(\text{triplet}) = 1.07$.

Kira and Thomas[99] showed that in benzonitrile solutions of anthracene, both anthracene anions and cations were produced, since ammonia enhanced the absorption near 660 nm and depressed the absorption of the 740 nm peak. From the absorption of benzonitrile solutions of *trans*-stilbene, where only the cation of the solute is formed[101], it was concluded[99] that the yield of benzonitrile cation is 1.4. From the absorption of solutions of pyrene, where the cation exists as the dimer cation, and its absorption does not interfere with that of the anion, and of 1,2-benzanthracene, where only the anion and the triplet excited state exists, it was found that the yield of the reducing agent was 0.5. The finding that anions of anthracene, pyrene, perylene and 1,2-benzanthracene were formed in solutions of benzonitrile, but not the anion of *trans*-stilbene, show that the formation of the solute anion takes place only for solute molecules with high electron affinity. This selectivity implies that the solute anions are formed by the reaction of the solute molecule with benzonitrile anion and not with an electron[99]. This conclusion is confirmed by the fact that the yield of the solute anion was decreased by SF_6 but not by N_2O. If the solute actually scavenged electrons to form the anion, N_2O as well as SF_6 should decrease the yield of the solute anion. The decrease of the yield in the presence of SF_6 but not in the presence of N_2O can be explained by the scavenging of benzonitrile anions by SF_6, which has a large electron affinity.

The yield of singlet excited states of 1,1′-binaphthyl in benzonitrile solutions was found to be 1.4 from which 50% undergo intersystem crossing to triplet excited states. This 0.7 is added to the 1.7 formed directly from the triplet state of benzonitrile. A similar yield, 1.7, was found for a solution of pyrene, in contrast to the 1.1 found by Hayon[64] for anthracene.

The reaction scheme is probably[99]:

$$\text{PhCN} \xrightarrow{\sim\sim} \text{PhCN}^+ + e^-$$

$$\text{PhCN} + e^- \longrightarrow \text{PhCN}^-$$

$$\text{PhCN}^+ + e^- \longrightarrow \text{excited states}$$

$$\text{PhCN}^+ + \text{PhCN}^- \longrightarrow 2\,\text{PhCN}$$

TABLE 2. Radiolytic yields from benzonitrile[102]

Product	$G \times 10^2$
Hydrogen	0.96
Acetylene	0.55
HCN	1.3
Benzene	0.36
Dicyanobenzenes	1.57
Cyanobiphenyls	1.66
Dicyanobiphenyls	8.5

No information exists as to whether the cation and the anion are in monomeric or dimeric forms. The increase of the yield of the anion in the presence of ammonia is probably due to scavenging of benzonitrile cation by ammonia, with formation of a less mobile cation which will neutralize less electrons, thus enhancing the rate of formation of the anions. This also explains the depression of the triplet yield by ammonia since the excited states are formed, at least partly, by the neutralization process.

The sum of the G values for ions and excited states in benzonitrile, 4.5, is close to the G values reported for benzene, benzyl alcohol and toluene.

The final products of the radiolysis of benzonitrile were studied by Knight[102], and are given in Table 2, where for the last three products the yield is the total yield for the various isomers.

As can be seen from this table, the yields are very low compared to those found with acetonitrile. This resembles the behaviour of benzene, which gives much lower yields of products than saturated hydrocarbons or olefins[103], the main product being a polymer[104]. Similarly, a polymer is expected to be the main product in irradiated benzonitrile but its formation was not measured. The main products determined were the various dicyanobiphenyls probably produced by the combination of two $C_6H_4CN\cdot$ radicals, indicating that in benzonitrile also, the main reaction is the rupture of C—H rather than C—CN bonds. However, the formation of dicyanobenzenes and cyanobiphenyls indicates C—CN bond rupture also. The yields of hydrogen and acetylene are about one fourth of those found for benzene[104], indicating some stabilization of the benzenoid ring by the CN group. (The extra HCN is less than the difference in $H_2 + C_2H_2$). Cyanogen and nitrogen were not detected, indicating G values lower than 2×10^{-4} and 4×10^{-5}, respectively. Nitrogen was reported as a product in the radiolysis of all three isomers of tolunitrile[105]; this effect of the methyl group is as yet unexplained.

All the three isomeric dicyanobenzenes were found in the irradiated benzonitrile in the ratio 1:1:1.7 for *ortho*:*meta*:*para* positions. Also, the three isomers of cyanobiphenyl were formed in the ratio of 1.4:1:1.9 for the *ortho*:*meta*:*para* positions. This shows that radiation-induced phenylation of benzonitrile is similar to free-radical phenylation[106] by chemically produced phenyl radicals, in that all positions are attacked and that *ortho*/*para* positions are favoured. However, in 'chemical' phenylation the *ortho*/*para* positions are more favoured (6:1), indicating, possibly, the participation of ions or excited states in radiolysis-induced phenylation.

All the six isomeric dicyanobiphenyls (one cyano group per phenyl ring) were detected as radiolytic products. Their yields do not agree with those calculated for random fragmentation followed by a random substitution, although the calculations predict correctly the most and least favoured isomers.

G. Radiation Chemistry of Aqueous Solutions of Cyanide Anion and HCN Molecule

Radiation-induced chemical changes of cyanide anion and HCN molecule in aqueous solution at low conversions permits the study of the initial products, while at high doses the possible formation of biologically important molecules may be studied.

The irradiation of water[44] leads to the formation of molecular products, H_2 and H_2O_2, and to short-lived transient species – hydrated electron e^-_{aq}, hydrogen atom and a hydroxyl radical, ·OH – which react with the solutes. The radiolytic yields of the transient species are $G(e^-_{aq}) = 2.6$, $G(\cdot OH) = 2.6$ and $G(H) = 0.55$. For the study of the reactions of ·OH alone, the aqueous solutions are saturated with N_2O which yields ·OH radicals on its reaction with e^-_{aq}, thus eliminating e^-_{aq} and doubling the yield of ·OH radicals:

$$e^-_{aq} + NO_2 \longrightarrow NO_2^- \xrightarrow{H_2O} N_2 + OH^- + \cdot OH$$

To study the reactions of e^-_{aq} only, the ·OH radicals are removed by various scavengers such as *t*-butyl alcohol, methanol or formate, which react only with ·OH and not with e^-_{aq}. The reaction of H atoms alone is studied in the radiolysis of solutions at low pH since in these solutions the hydrated electron is protonated to yield hydrogen atom.

$$e^-_{aq} + H_3O^+ \longrightarrow H\cdot + H_2O$$

Ogura and coworkers[107,108] measured the final yields of several products in the radiolysis of CN^- and HCN. They suggested that ·OH radicals react by the same mechanism as has been found for halide anions[109–111] and for SCN^- [112]:

$$\cdot OH + X^- \longrightarrow HOX^{\cdot-} \text{ or } OH^- + X\cdot$$

$$HOX^{\cdot-} + X^- \longrightarrow X_2^{\cdot-} + OH^-$$

This assumption was studied later using steady-state ESR techniques by Behar and Fessenden[113] who could not find any evidence for the formation of ·CN or $(\cdot CN)_2^-$ radicals. This ESR study showed that the reaction of ·OH with CN^- led to the production of a species which had its ESR spectrum characterized by a low *g* value ($g = 2.0015$). Such a low value of the *g* factor is unusual and is often characteristic of σ-electron radicals. The same radical was produced previously by Livingston and Zeldes by photolysis of formamide solutions[114], and identified as the formamide radical $O{=}\dot{C}{-}NH_2$. Radiolytic proof of this identity was found by ESR study of N_2O saturated aqueous solution of formamide[113], for which the same spectra was obtained, by ·OH abstracting an H-atom from the formamide molecule. Livingston and Zeldes[114] showed that the radical obtained was $\dot{C}ONH_2$ and not $HC\dot{O}NH$ by the photolysis of $HCOND_2$ where they found that only the aldehyde hydrogens were abstracted. Thus, unless there is a fast rearrangement, it is reasonable to assume that the radical observed in the ESR was $O{=}\dot{C}{-}NH_2$. The possible enol form of the radical $HO{-}\dot{C}{=}NH$ was rejected by the same authors[114] on the grounds that no proton exchange was observed at 1 M acid.

A reasonable mechanism for the formation of this radical is the addition of ·OH to CN^-:

$$HO\cdot + CN^- \longrightarrow HO{-}\dot{C}{=}N^-$$

followed by protonation and rearrangement:

$$HO{-}\dot{C}{=}N^- + H_2O \longrightarrow HO{-}\dot{C}{=}NH + OH^-$$

$$HO{-}\dot{C}{=}NH \longrightarrow O{=}\dot{C}{-}NH_2$$

At lower pH (4.0 and 2.8), when mainly HCN molecules are present (pK = 9.3), some contribution to the spectrum from the $\cdot CONH_2$ radical was evident, but in addition new lines appeared with a^H = 54.41 G. From the large proton hyperfine constant it is evident that the radical must be HC(OH)=N· with the CH proton producing the large splitting:

$$OH + H{-}C{\equiv}N \longrightarrow H{-}\overset{\displaystyle OH}{\overset{|}{C}}{=}N\cdot$$

The origin of the $\cdot CONH_2$ radical at this acidic pH is not clear, but since the size of its signal was found to be inversely proportional to the flow rate of the system, it must be formed by secondary reactions.

Behar[115] and, later, Büchler and coworkers[116] studied the pulse radiolysis of N_2O-saturated solutions of HCN and CN^- at various pH values. Behar[115] identified three different species. In acid and neutral solution, where only HCN exists, ·OH adds to the HCN triple bond and forms the HC(OH)=N· radical with λ_{max} = 240 nm. The assignment of this formula to the radical, and not HC=N—OH, was based on the ESR findings[113]. This radical disappeared according to a second-order rate law. At pH 10.6 ·OH added to CN^- and after protonation and rearrangement yielded the formamide radical with $\lambda_{max} < 225$ nm. This radical was identified in the ESR study[113] mentioned above. The same spectrum was obtained for $\cdot OH + CN^-$ and for $\cdot OH + HCONH_2$, where ·OH radicals abstracted the aldehyde hydrogen to form $\cdot CONH_2$. The kinetics of the disappearance of this radical obeyed the second-order rate law indicating that two radicals reacted to give a product. At pH 14 ·OH radicals yield the O^- anion which reacts with CN^-. The adduct rearranges in the same way as at lower pH to produce $(\cdot CONH)^-$ with λ_{max} = 245 nm. This radical was also found to follow a second-order decay. Scheme 1, given by Büchler and coworkers[116], summarizes the various reactions of ·OH radicals in solutions of CN^- at various pH values.

The reaction H + HCN was studied by the ESR spectroscopy–radiolysis flow system[113] at pH 2.5. The spectrum observed was characterized by a^H = 87.2, a^N = 10.2 G and g = 2.0028. This is similar to the spectra assigned previously to $H_2C{=}N\cdot$, observed in the solid phase in an argon matrix[117] or in CN^--doped KCl[118]. The same spectrum was observed also at pH 7.0–11.0 indicating that e^-_{aq} produced the same radical as H-atoms:

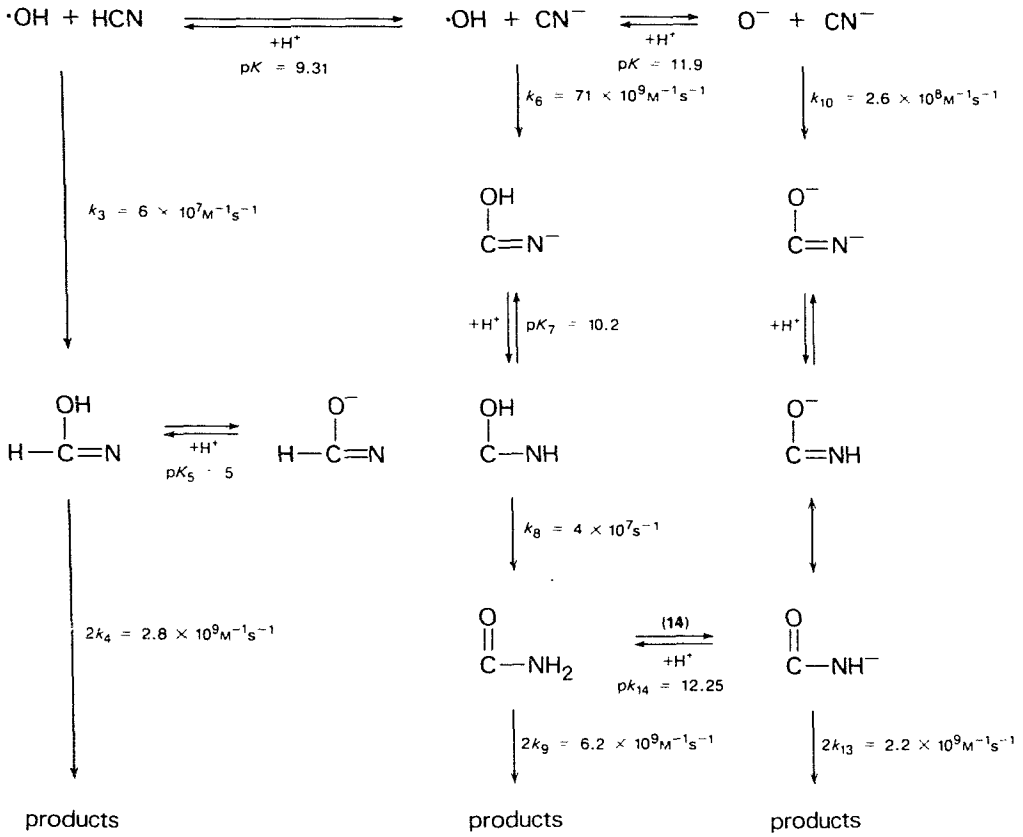
$$H\cdot + H{-}C{\equiv}N \longrightarrow H{-}\overset{\displaystyle H}{\overset{|}{C}}{=}N\cdot$$

$$e^-_{aq} + H{-}C{\equiv}N \longrightarrow [HCN]^-$$

$$[HCN]^- + H_2O \longrightarrow H{-}\overset{\displaystyle H}{\overset{|}{C}}{=}N\cdot$$

At pH 11.8 no ESR signals were detectable, which suggests that e^-_{aq} reacts with HCN but not with CN^-. Studying the radiolysis at very acidic solutions (pH = 1.9) Büchler and coworkers[116] found an absorption band at 275 nm, which was assigned to the H-adduct radical $CH_2{=}\dot{N}$.

Bielski and Allen[119] studied the final products of radiolysis of aqueous solutions of cyanides. In N_2O-saturated solutions, where the only radicals are ·OH (>90%) and H·, the only products of any importance were cyanate and formamide which were



SCHEME 1. The reaction of ·OH with HCN and CN^-. Reprinted with permission from H. Büchler, R. E. Bühler and R. Cooper, *J. Phys. Chem.*, **80**, 1549 (1976). Copyright (1976) American Chemical Society.

produced in equal amounts. These products are probably formed by the disproportionation of two $\cdot CONH_2$ radicals:

$$2\ \dot{C}(=O)-NH_2 \longrightarrow H-C(=O)-NH_2 + H-O-C\equiv N$$

In N_2-saturated solution the main products formed are[119] cyanate (0.65), NH_3 (1.13), formamide (0.83), glycine (0.43), urea (0.10) and insoluble polymer (0.5). The formation of glycine was ascribed to the combination of two $H_2CN\cdot$ radicals, followed by hydrolysis:

$$2\ H_2CN\cdot \longrightarrow (H_4C_2N_2) \xrightarrow{2\,H_2O} NH_3 + H_2NCH_2COOH$$

The γ-irradiation of cyanides in aqueous solutions has been studied also from the point of view of the removal of cyanide ions from wastes, since previous chemical methods such as oxidation with chlorine are quite troublesome. However, it was found[120] that γ-irradiation is effective only for initial concentrations of less than 10 mg ml^{-1} while for higher concentrations very large doses are required.

Irradiated 0.1M solutions of ammonium and sodium cyanide (oxygen free) with doses of megarads showed[121] positive biuret reaction, indicating the formation of peptide bonds. The absorbancies of the biuret reactions increased with the absorbed dose (linearly up to 5–10 M rad). Up to 18% of the nitrogen contained in the mixture of nonvolatile radiolytic products appeared in the peptidic material, Supporting evidence for the presence of peptidic material was provided by IR spectroscopy[122] and by gel chromatography fractionation and enzymatic digestion. The IR spectra of the irradiated sample match in many details that of bovine albumin and the relative intensities increase with the absorbed dose as they do with the biuret absorbancies. Some enzymes, known to cleave peptide bonds unspecifically, gave positive results. After acid hydrolysis of the irradiated products, several amino acids were found; the most abundant ones were glycine, $G = 0.6$ for NH_4CN and 0.24 for NaCN while the sum of the yields of the other amino acids are 0.02 for NH_4CN and 0.05 for NaCN. The other amino acids found were alanine, serine, aspartic acid and a very little glutamic acid and threonine. No amino acids could be detected in the nonhydrolysed irradiated samples ($G < 10^{-4}$).

0.1M aqueous solutions (oxygen free) of HCN[123] were irradiated with up to 16 Mrad γ-rays causing large decompositions up to 90%. Both $G(-HCN)$ and the yield of total nitrogen in the mixture of nonvolatile products, $G(N)$, showed strong dependence on pH and on the dose absorbed. However, the ratio $G(-HCN)/G(N)$ was almost constant, indicating that probably the same reaction mechanisms were operative without dependence on pH and dose. The main small molecules formed were NH_3 and formaldehyde; the G value decreasing with the dose. The yield of NH_3 was higher than that of HCHO, while $G(CO_2)$ corresponds roughly, at the lowest doses, to the excess of free ammonia over aldehyde yields.

Seven amino acids were found in the irradiated solutions: aspartic acid, glycine, histidine, serine, threonine, glutamic acid and alanine (in the order of decreasing yields). Acid hydrolysis of the irradiated solutions increased the yield of the amino acids by more than a factor of 20 ($G = 1.785 \times 10^{-1}$ vs. 8.65×10^{-3}). The same seven amino acids were found after hydrolysis although glycine and threonine became the most abundant ones. The presence of peptidic bonds was proven by positive biuret reaction[123] and IR spectra[122].

H. Radiation Chemistry of Aqueous Solutions of Nitriles

1. *Aliphatic nitriles*

The reaction of e_{aq}^- with organic halides leads to a detachment reaction in which the halide ion is formed. However, due to the high C—CN bond strength and the relatively low solvation energy of the cyanide ions, it was expected[124] that this reaction would not occur in nitriles. It has been suggested[124], therefore, that the initially formed $(RCN)^-$ would subsequently protonate to $RCH{=}\dot{N}$. Neta and Fessenden[97] measured the radiolytic yields of CN^- in aqueous solutions of cyanoacetate ion and acetonitrile and obtained $G = 0.2$ and 0.3, respectively. Thus only about 10% of the electrons form cyanide anion. The formation of the proposed $RCH{=}\dot{N}$:

$$RCN + e^- \longrightarrow (RCN)^-$$

$$(RCN)^- + H_2O \longrightarrow RCH{=}\dot{N} + OH^-$$

was studied by ESR spectroscopy during continuous *in situ* radiolysis of nitrile solutions[97]. The reaction of e_{aq}^- with nitriles led to species which were characterized by

an 80G proton doublet splitting and a 10G nitrogen splitting. The similarity of the proton and nitrogen coupling constants to those of $H_2C{=}N\cdot$ found in the solid state[117,118] indicates that these are radicals of the $RCH{=}N\cdot$ type, as was suggested previously. The primary product of the reaction with e^-_{aq}, $(RCN)^-$, was not observed, probably due to its rapid protonation. A support for the identification of this product, $RCH{=}N\cdot$, is that the same spectrum was obtained at pH = 1, where all e^-_{aq} are converted to H-atoms and the expected reaction would be the addition to the triple bond:

$$H\cdot + R{-}C{\equiv}N \longrightarrow R{-}CH{=}N\cdot$$

The identification of the radicals as $RCH{=}N\cdot$ and not as $R{-}\dot{C}{=}NH$ is due to the large proton splitting which is due to the CH proton[87]. That the H-atoms add to the triple $C{\equiv}N$ bond rather than abstract an hydrogen atom is further proven by the low radiolytic yield of molecular hydrogen found for aqueous solutions of various nitriles at both acid and neutral pH[98,125]. Neta and collaborators[126] suggested that another proof is the relatively high rate constant found for the reaction of H-atoms with acetonitrile, as compared to the rate constant with acetic acid. They suggested that in the case of cyanoacetic acid, addition and hydrogen abstraction take place at similar rates.

Draganic and coworkers[127] have studied the pulse radiolysis of aqueous solutions of some nitriles. The same absorption spectra, for a given RCN, were obtained for acid and neutral solutions, in the presence of OH scavengers. This indicates, as in the ESR studies, the formation of the same radical by e^-_{aq} and by H-atoms in a time-scale of μs, and not only of 0.5 ms as in the ESR studies. These authors suggested that although in the ESR studies only $RCH{=}N\cdot$ was found, it should be possible in pulse radiolysis for $R\dot{C}{=}NH$ to be formed initially and later isomerized. However, since it might be expected that the two radicals would have different spectra and as the spectrum was found to decay in a bimolecular process without the formation of another detectable species, it can be expected that $RCH{=}N\cdot$ is also the product in the short time-scale.

Another proof for the reaction of e^-_{aq} with the CN group and not with the alkyl substituent, R, is the correlation found[125,128] between the rate constant k (e^-_{aq} + RCN) values and Taft σ^* values for various R groups.

The reaction of ·OH radicals with nitriles is different from the reaction of ·OH with HCN. ESR studies of photolytically generated ·OH radicals with nitriles have shown[129] that ·OH radicals react by abstracting hydrogen from the position α to the CN group. More evidence for the abstraction reaction is the fit of the observed rate constant for $\cdot OH + CH_3CN$ to the line plotted for various substituted methanes as a function of the Hammett σ_{para} values[130]. For the other compounds, the abstraction of hydrogen is the only possible route for ·OH radicals, thus indicating that also for acetonitrile this is the main reaction. Neta and Fessenden[97] observed, by ESR steady-state *in situ* radiolysis, the radicals formed by α-hydrogen abstraction from propionitrile, cyanoacetate ion and cyanomethanol, but were not able to detect the $\cdot CH_2CN$ radical from acetonitrile, possibly due to experimental difficulties. Draganic and coworkers believed[125] that ·OH mainly added to the cyano group, and only minor fractions of it abstracted hydrogen. However, there was no experimental support for this argument. For example, in the case of aqueous solutions of cyanamide, they found in pulse radiolysis[125b] that ·OH formed two products in a ratio of 9:1 and assigned the major one to the OH-adduct, but there is no evidence to rule out its being the product from α-hydrogen abstraction.

An interesting question is why both H· and ·OH add to HCN while in the case of RCN, the H-atom adds to the molecule, while ·OH abstracts an α-hydrogen. A possible explanation is that ·OH also adds to the triple bond, but the adduct is

decomposed by elimination of a water molecule in a time shorter than that which can be distinguished in ESR experiments (tenths of ms):

$$R^1R^2CHC{\equiv}N + \cdot OH \longrightarrow R^1R^2CHC(OH){=}N\cdot$$

$$R^1R^2CHC(OH){=}N\cdot \longrightarrow R^1R^2C{=}C{=}N\cdot + H_2O$$

$$\downarrow$$

$$R^1R^2\dot{C}{-}C{\equiv}N$$

although this does not explain the fit to Hammett's line. Pulse radiolysis studies of N_2O-saturated aqueous solutions of some alkyl cyanides[127] have shown that this transient decays following second-order kinetics.

The final products of the radiolysis of aqueous solutions of RCN have been studied by Draganic and coworkers[125] with low absorbed doses (>10 krad) in order to avoid the reaction of the final products with some of the transients. The main products formed were NH_3 and aldehyde in similar yields ($G \sim 1.1$) and very little CO_2. The formation of equal amounts of aldehyde and NH_3 can be explained by the formation of imine, through the disproportionation of two $RCH{=}N\cdot$ radicals:

$$2\ RCH{=}N\cdot \longrightarrow RCN + RCH{=}NH$$

followed by the hydrolysis of the imine:

$$RCH{=}NH + H_2O \longrightarrow RCHO + NH_3$$

This explanation, however, does not fit the results in the presence of O_2 or N_2O where the yields of the aldehyde are higher than those of NH_3 (about 0.8 and 0.3 respectively)[125].

0.1M aqueous oxygen-free solutions of CH_3CN and C_2H_5CN were irradiated with high doses of γ-rays up to 50% conversion (~40 Mrad)[131]. The decomposition of the nitriles led to the formation of nonvolatile nitrogen-containing molecules. The irradiated solutions exhibited a positive biuret reaction, and according to absorbancy

TABLE 3. The radiolytic yields of amino acids (after acidic hydrolysis) in the radiolysis of aqueous solutions of cyanides and nitriles

	Solutes					
Amino acid	NH_4CN	NaCN	HCN	CH_3CN	C_2H_5CN	NH_2CN
Glycine	0.6000	0.2400	0.1400	0.0185	0.0010	
Alanine	0.0040	0.0220	0.0045	0.0020	0.0350	
Glutamic acid	<0.0010	0.0020	0.0005	0.0005	0.0005	
Serine	0.0050	0.0180	0.0020	0.0020	0.0015	
Aspartic acid	0.0100	0.0080	0.0120	0.0030	0.0005	
Threonine	<0.0010	<0.0010	0.0180	—	—	
Histidine	—	—	0.0015	—	—	
Lysine	—	—	—	0.0001	0.0001	
Arginine	—	—	—	—	0.0015	0.06–0.2
Total	0.6190	0.2900	0.1785	0.0261	0.0401	

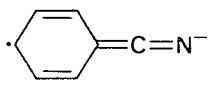
measurements about 10% of the non-volatile nitrogen was in amide groups. Several amino acids were found and their yields increased by a factor of 6–10 upon acid hydrolysis. Glycine and alanine were found to be the most abundant for CH_3CN and C_2H_5CN, respectively. The positive biuret reaction, IR spectra and the release of amino acids on acid hydrolysis show the existence of peptidic material. However, the yields of amino acids after hydrolysis were only one-sixth of the yield of the peptide groups as found by the absorbancy of the biuret reaction product. This is in contrast with the cases of NH_4CN and NaCN where a good agreement was found between the amide group yields and the total yields of natural amino acids released on hydrolysis[121]. The yields of natural amino acids in the radiolysis of cyanides and nitriles after acidic hydrolysis[121,123,131,132] are summarized in Table 3. This includes also cyanamide where no peptidic bond and only one amino acid, arginine, was found[132].

As can be seen from Table 3 the yields of amino acids from organic nitriles are in general much less than from cyanide anion or HCN. A possible explanation might be the formation of amino acids other than the natural ones, which may also account for the disagreement between the peptide-bond yield and the yield of the natural amino acids released on hydrolysis in the case of organic nitriles.

2. *Benzonitrile*

Chutny and Swallow[100] have studied the pulse radiolysis of aqueous solutions of benzonitrile. The e^-_{aq} was found to cause the formation of a species with absorption at 315 and 400 nm, while ·OH radical led to absorption at 343 nm. H-atom reaction led to an absorption spectrum which resembled that of the ·OH reaction except that the maximum now appeared at 348 instead of 343 nm. It is reasonable to assume that ·OH adds to the molecule of benzonitrile but it is not clear whether it adds to the aromatic ring as was found with benzene[133], or to the CN triple bond. Anbar and coworkers[134] have found in a rate study of ·OH with monosubstituted benzene derivatives that ·OH radicals behave like electrophilic reagents. Calculations for electrophilic attack[100] have shown that the most favoured position would be the nitrogen atom; however, the ring would be attacked with almost the same probabilities at the ring-carbon atoms 1, 3 and 5, and thus it would not be possible to expect predominant attack at any particular position.

The species with peaks at 315 and 400 nm, formed by the action of e^-_{aq} in neutral or slightly alkaline solutions of benzonitrile, could be either the anion radical or its protonated form. Going from neutral or alkaline solutions to pH 4 led to a marked change in the absorption spectra. The measured rate constants for the reaction with benzonitrile and with H^+ show that at pH 4 nearly all of the electrons react with benzonitrile and not with H^+, indicating that the change in the spectra is due to protonation of the anion rather than to reaction of H-atoms with benzonitrile. Thus, at neutral or slightly alkaline solutions, the radical anion is observed, whereas at pH 4 the spectrum is that of the protonated form; the pK_a of the protonated form was found to be 7.2. The hydrated electron is a nucleophilic reagent and molecular orbital calculations have shown that the most probable point of attack by nucleophilic agents would be the nitrilic carbon. However, since heteroatoms such as nitrogen have a much larger electron affinity than carbon, it was suggested[100] that the most probable structure of the anion radical would be **3**.



(3)

I. Radiation-induced Production of Nitriles

Radiation-induced production of nitriles can be accomplished by the formation of organic radicals which will react with cyanogen. Knight and coworkers[135] have studied the irradiation of mixtures of various hydrocarbons with cyanogen and proved by IR spectroscopy the formation of nitriles. For a mixture of cyclohexane with cyanogen, they proved the formation of cyclohexyl cyanide with G values of about 7 for doses below 5×10^{20} eV g^{-1}, decreasing to about 5 for a dose of 1.5×10^{21} eV g^{-1}.

The mechanism is probably:

$$RH \xrightarrow{\sim\sim} R\cdot + H\cdot$$

$$R\cdot + (CN)_2 \longrightarrow RCN + \dot{C}N$$

$$\dot{C}N + RH \longrightarrow HCN + R\cdot$$

Another method is the irradiation of short-chain nitriles with ethylene or other double-bond-containing molecules. The ionizing radiation usually leads to abstraction of an H-atom from the nitriles and the produced radical adds to the double bond. Grinevich and collaborators[136] studied the liquid-phase radiolysis of an acetonitrile–ethylene system. They found the formation of straight-chain nitriles having the general formula $H(C_2H_4)_nCH_2CN$ (major product $n = 4$ with $G = 0.6$–1.0) and branched molecules with the general formula $H(C_2H_4)_nCH(C_4H_9)CN$ (major product $n = 3$ with $G = 1.0$–3.0) or with the general formula $H(C_2H_4)_nC(C_4H_9)_2CN$ (major product $n = 5$ with $G = 0.2$–0.4). The formation of normal nitriles occurs by addition of the $\cdot CH_2CN$ radical which is produced by the radiolysis. Branched nitrile formation is due to isomerization of the intermediate radicals with 1,5-migration of a hydrogen atom.

IV. RADIATION CHEMISTRY OF AQUEOUS SOLUTIONS OF DIAZONIUM SALTS

Up to now only a very limited amount of work has been done on the radiation chemistry of diazonium salts. Brede and coworkers[137] have studied the pulse radiolysis of arenediazonium salts in a 50:50 water–*t*-butanol mixture. In this system, only the solvated electrons can react with the diazonium ions since H· and ·OH radicals will react with the large excess of *t*-butanol. They found that the solvated electrons reacted with the arenediazonium ions to produce aryldiazo radicals:

$$e^-_{aq} + ArN_2^+ \longrightarrow ArN_2^\cdot$$

The rate constant for this reaction was found to be 2–3×10^{10} M^{-1} s^{-1}, which is higher than expected for a radical reaction, probably due to the opposite charge attraction.

The aryldiazo radicals undergo both dimerization:

$$2\ ArN_2^\cdot \longrightarrow Ar{-}N{=}N{-}N{=}N{-}Ar$$

and unimolecular decay:

$$ArN_2^\cdot \longrightarrow Ar\cdot + N_2$$

The distribution between these two reactions depends on the nature of the *para*-substituent in the aromatic ring, which influences the stability of the ArN_2 radical.

Using the known G values of the electrons, the rate constants for the dimerization were calculated to be in the region of 5–10×10^{10} M^{-1} s^{-1}, which is almost an order of magnitude higher than for radical recombination. These unusually high apparent rate constants were explained as being caused by the inhomogeneous distribution of the

diazo radicals, which leads to high local radical concentration due to the relatively low diffusion coefficient of the radicals.

V. REFERENCES

1. J. H. O'Donell and D. F. Sangster, *Principles of Radiation Chemistry*, Edward Arnold Publishers, London, 1970.
2. J. W. T. Spinks and R. J. Wood, *An Introduction to Radiation Chemistry*, 2nd Ed., John Wiley and Sons, New York–London, 1976.
3. A. J. Swallow, *Radiation Chemistry – An Introduction*, Longman, London, 1973.
4. A. Mozumder in *Advances in Radiation Chemistry*, Vol. 1, Wiley–Interscience, New York, 1969, p. 1.
5. E. G. Janzen, *Acc. Chem. Res.*, **4**, 31 (1971).
6. P. K. Ludwig in *Advances in Radiation Chemistry*, Vol. 3, Wiley–Interscience, New York, 1972, p. 1.
7. M. S. Matheson and L. M. Dorfman, *Pulse Radiolysis*, M.I.T. Press, Cambridge, Mass., 1969.
8. A. J. Swallow, *Radiation Chemistry of Organic Compounds*, Pergamon Press, Oxford, 1960, p. 79
9. (a) G. V. Buxton, P. G. Ellis and T. F. W. McKillop, *J. Chem. Soc., Faraday Trans. I*, **75**, 1050 (1979).
   (b) N. V. Petrukhin, V. A. Gorbachev, V. M. Bystrov and S. Ya. Pshezhetski, *Polymer Science USSR*, **17**, 2623 (1975).
10. A. Charlesby, *Radiation Res.*, **2**, 96 (1955).
11. S. C. Lind, *Radiation Chemistry of Gases*, Reinhold, New York, 1961.
12. P. Thenard and A. Thenard, *Compt. Rend.*, **78**, 219 (1874).
13. S. C. Lind, D. C. Bardwell and J. H. Perry, *J. Amer. Chem. Soc.*, **48**, 1556 (1926).
14. S. C. Lind, J. C. Jungers and C. H. Schiflett, *J. Amer. Chem. Soc.*, **57**, 1032 (1935).
15. W. Mund and C. Rosenblum, *J. Phys. Chem.*, **41**, 469 (1937).
16. C. Rosenblum, *J. Phys. Chem.*, **52**, 474 (1948).
17. L. M. Dorfman and F. J. Shipko, *J. Amer. Chem. Soc.*, **77**, 4723 (1955).
18. F. H. Field, *J. Phys. Chem.*, **68**, 1039 (1964).
19. M. G. Chauser, Yu. M. Rodinov, V. M. Misin and M. I. Cherkasin, *Russ. Chem. Rev.*, **45**, 348 (1976).
20. S. C. Lind and D. C. Bardwell, *Science*, **62**, 593 (1926).
21. W. Mund, C. Velghe, C. de Vos and M. Vanpee, *Bull. Soc. Chim. Belges*, **48**, 269 (1939).
22. M. S. B. Munson, *J. Phys. Chem.*, **69**, 572 (1965).
23. H. Eyring, J. O. Hirschfelder and H. S. Taylor, *J. Chem. Phys.*, **4**, 479, 570 (1936).
24. L. M. Dorfman and A. C. Wahl, *Radiation Res.*, **10**, 680 (1959).
25. M. Zelikoff and L. M. Aschenbrand, *J. Chem. Phys.*, **24**, 1034 (1956).
26. S. Shida, Z. Kuri and T. Furuoya, *J. Chem. Phys.*, **28**, 131 (1958).
27. G. J. Mains, H. Niki and M. H. J. Winjen, *J. Phys. Chem.*, **67**, 11 (1963).
28. S. Shida, M. Tsukada, N. Fujisaki and T. Oka, *Bull. Chem. Soc. Japan*, **43**, 3314 (1970).
29. S. Shida and M. Tsukada, *Bull. Chem. Soc. Japan*, **43**, 2740 (1970).
30. S. Shida, M. Tsukada and T. Oka, *J. Chem. Phys.*, **45**, 3483 (1966).
31. D. J. Le Roy, *J. Chem. Phys.*, **45**, 3482 (1966).
32. D. J. Le Roy and E. W. R. Steacie, *J. Chem. Phys.*, **12**, 117 (1944).
33. Y. Rousseau and G. J. Mains, *J. Phys. Chem.*, **68**, 3081 (1964).
34. J. H. Futrell and L. W. Sieck, *J. Phys. Chem.*, **69**, 892 (1965).
35. S. C. Lind and C. H. Shiflett, *J. Amer. Chem. Soc.*, **59**, 411 (1937).
36. S. C. Lind and P. S. Rudolph, *J. Chem. Phys.*, **26**, 1768 (1957).
37. A. R. Jones, *J. Chem. Phys.*, **32**, 953 (1960).
38. J. P. Briggs and R. A. Back, *Can. J. Chem.*, **49**, 3789 (1971).
39. H. H. Carmichael, R. Gorden and P. Ausloos, *J. Chem. Phys.*, **42**, 343 (1965).
40. C. Willis, R. A. Back and R. H. Morris, *Can. J. Chem.*, **55**, 3288 (1977).
41. G. A. W. Derwish, A. Galli, A. Giardini-Guidoni and G. G. Volpi, *J. Amer. Chem. Soc.*, **87**, 1159 (1965).

42. L. G. Christophorou, *Atomic and Molecular Radiation Physics*, Wiley–Interscience, New York, 1971, p. 37.
43. Y. Tabata, B. Saito, H. Shibano, H. Sobue and K. Oshima, *Makromol. Chem.*, **76**, 89 (1964).
44. J. K. Thomas in *Advances in Radiation Chemistry* (Eds. M. Burton and J. Magee), Vol. 1, Wiley–Interscience, New York, 1969, p. 103.
45. P. G. Clay, G. R. A. Johnson and J. Weiss, *J. Phys. Chem.*, **63**, 862 (1959).
46. P. Neta and R. W. Fessenden, *J. Phys. Chem.*, **76**, 1957 (1972).
47. R. F. Anderson and D. Schulte-Frohlinde, *J. Phys. Chem.*, **82**, 22 (1978).
48. H. Mitsui, F. Hosoi, M. Hagiwara and T. Kagiya, *J. Polym. Sci., Part A-1*, **6**, 2881 (1968).
49. H. Mitsui, F. Hosoi and T. Kagiya, *J. Polym. Sci., Part A-1*, **7**, 2575 (1969).
50. H. Mitsui, F. Hosoi and T. Kagiya, *Polymer J.*, **3**, 108 (1972).
51. H. Mitsui, F. Hosoi and T. Kagiya, *Polymer J.*, **6**, 20 (1974).
52. A. Chapiro, *Radiation Chemistry of Polymeric Systems*, Interscience, New York, 1962, p. 385.
53. K. G. McLaren, *Intern. J. Radiat. Phys. Chem.*, **2**, 123 (1970).
54. M. Calvin, *Chemical Evolution*, Clarendon Press, Oxford, 1969, pp. 132–141.
55. S. W. Fox and K. Dose, *Molecular Evolution and the Origin of Life*, Freeman, San Francisco, 1972, pp. 178–181.
56. T. Sugiura and A. Arakawa in *Proceedings International Conference on Mass Spectroscopy*, University of Tokyo Press, Tokyo, 1970, p. 848.
57. J. A. Stockdale, F. J. Davis, R. N. Compton and C. E. Klotz, *J. Chem. Phys.*, **60**, 4279 (1974).
58. S. Tsuda, A. Yokohata and T. Umaba, *Bull. Chem. Soc. Japan*, **43**, 3383 (1970).
59. T. Shibata, T. Fukuyama and K. Kuchitsu, *Bull. Chem. Soc. Japan*, **47**, 2573 (1974).
60. T. F. Moran and W. H. Hamill, *J. Chem. Phys.*, **39**, 1413 (1963).
61. J. L. Franklin, Y. Wada, P. Natalis and P. M. Hiere, *J. Phys. Chem.*, **70**, 2353 (1966).
62. G. A. Gray, *J. Amer. Chem. Soc.*, **90**, 6002 (1968).
63. A. Singh, H. D. Gesser and A. R. Scott, *Chem. Phys. Letters*, **2**, 271 (1968).
64. E. Hayon, *J. Chem. Phys.*, **53**, 2353 (1970).
65. I. P. Bell, M. A. J. Rodgers and H. D. Burrows, *J. Chem. Soc., Faraday Trans. I*, **73**, 315 (1977).
66. H. D. Burrows and E. M. Kosower, *J. Phys. Chem.*, **78**, 112 (1974).
67. J. H. Baxendale and E. J. Rasburn, *J. Chem. Soc., Faraday Trans. I*, **70**, 705 (1974).
68. J. H. Baxendale and M. A. J. Rodgers, *J. Phys. Chem.*, **72**, 3849 (1968).
69. J. L. Baptista and H. D. Burrows, *J. Chem. Soc., Faraday Trans. I*, **70**, 2066 (1974).
70. S. W. Mao and L. Kevan, *J. Phys. Chem.*, **80**, 2330 (1976).
71. P. B. Ayscough, R. G. Collins and T. J. Kemp, *J. Phys. Chem.*, **70**, 2220 (1966).
72. M. A. Bonin, K. Tsuji and F. Williams, *Nature*, **218**, 946 (1968).
73. F. P. Sargent, *Can. J. Chem.*, **48**, 1780 (1970).
74. M. A. Bonin, K. Takeda, K. Tsuji and F. Williams, *Chem. Phys. Letters*, **2**, 363 (1968).
75. K. Takeda and F. Williams, *Mol. Phys.*, **17**, 677 (1969).
76. R. J. England and M. C. R. Symons, *J. Chem. Soc. (A)*, 1326 (1970).
77. E. D. Sprague, K. Takeda and F. Williams, *Chem. Phys. Letters*, **10**, 299 (1971).
78. M. A. Bonin, Y. J. Chung, E. D. Sprague, K. Takeda, J. T. Wang and F. Williams, *Nobel Symposium*, **22**, 103 (1973).
79. T. Gilboro and F. Williams, *J. Chem. Soc., Faraday Trans. II*, **70**, 465 (1974).
80. E. D. Sprague and F. Williams, *J. Amer. Chem. Soc.*, **93**, 787 (1971).
81. F. P. Sargent, M. G. Bailey and E. M. Gardy, *Can. J. Chem.*, **52**, 2171 (1974).
82. M. H. J. Winjen, *J. Chem. Phys.*, **22**, 1074 (1954).
83. R. J. LeRoy, E. D. Sprague and F. Williams, *J. Phys. Chem.*, **76**, 546 (1972).
84. E. D. Sprague, K. Takeda, J. T. Wang and F. Williams, *Can. J. Chem.*, **52**, 2840 (1974).
85. E. D. Sprague, *J. Phys. Chem.*, **81**, 516 (1977); **83**, 849 (1979).
86. E. A. Cherniak, E. Collinson, F. S. Dainton and G. M. Meaburn, *Proc. Chem. Soc.*, 54 (1958).
87. D. B. Bradley and J. Wilkinson, *J. Chem. Soc. (A)*, 531 (1967).
88. P. B. Ayscough, H. Drawe and P. Kohler, *Radiation Res.*, **33**, 268 (1968).

89. R. W. Fessenden and R. H. Schuler, *J. Chem. Phys.*, **33**, 935 (1960).
90. H. Okabe and V. H. Dibeler, *J. Chem. Phys.*, **59**, 2430 (1973).
91. K. D. King and R. D. Goddard, *Intern. J. Chem. Kinetics*, **7**, 837; *J. Amer. Chem. Soc.*, **97**, 4504 (1975); *J. Phys. Chem.*, **80**, 546 (1976).
92. Y. Gonen, L. A. Rajbenbach and A. Horowitz, *Intern. J. Chem. Kinetics*, **9**, 361 (1977).
93. Gy. Cserep and G. Foldiak, *Effect of Molecular Structure of the Radiolysis of Alkenes (4th Symposium on Radiation Chemistry)*, (Eds. R. Schiller and P. Hedvig), Akademiai Kiado, Budapest, 1977, p. 147.
94. L. M. Dorfman, *J. Phys. Chem.*, **62**, 29 (1958).
95. L. J. Stief and P. Ausloos, *J. Chem. Phys.*, **36**, 2904 (1962).
96. H. Okabe and J. R. McNesby, *J. Chem. Phys.*, **34**, 668 (1961).
97. P. Neta and R. W. Fessenden, *J. Phys. Chem.*, **74**, 3362 (1970).
98. P. Neta, G. R. Holdern and R. H. Schuler, *J. Phys. Chem.*, **75**, 449 (1971).
99. A. Kira and J. K. Thomas, *J. Phys. Chem.*, **78**, 2094 (1974).
100. B. Chutny and A. J. Swallow, *Trans. Faraday Soc.*, **66**, 2847 (1970).
101. A. Kira, S. Arai and M. Imamura, *Intern. J. Radiat. Phys. Chem.*, **5**, 127 (1973).
102. J. A. Knight, *Radiation Res.*, **65**, 423 (1976).
103. A. J. Swallow, *Radiation Chemistry*, Longman, London, 1973, p. 190.
104. J. Hoigne in *Aspects of Hydrocarbon Radiolysis* (Eds. T. Gaumann and J. Hoigne), Academic Press, New York, 1968, pp. 61–151.
105. J. Weiss, *Radiation Res.*, **45**, 252 (1971).
106. D. H. Hey in *Advances in Free Radical Chemistry* (Ed. G. H. Williams), Academic Press, New York, 1967, pp. 47–86.
107. H. Ogura, *Bull. Chem. Soc. Japan*, **41**, 2871 (1968).
108. H. Ogura, T. Fujimura, S. Murozono, K. Hirano and M. Kundo, *J. Nucl. Sci. Technol.*, **9**, 339 (1972).
109. M. Anbar and J. K. Thomas, *J. Phys. Chem.*, **68**, 3829 (1964).
110. D. Zehavi and J. Rabani, *J. Phys. Chem.*, **76**, 312 (1972).
111. H. Büchler and R. E. Bühler, *Chem. Phys.*, **16**, 9 (1976).
112. D. Behar, P. L. T. Bevan and G. Scholes, *J. Phys. Chem.*, **76**, 1537 (1972).
113. D. Behar and R. W. Fessenden, *J. Phys. Chem.*, **76**, 3495 (1972).
114. R. Livingston and H. Zeldes, *J. Chem. Phys.*, **47**, 4173 (1967).
115. D. Behar, *J. Phys. Chem.*, **78**, 2660 (1974).
116. H. Büchler, R. E. Bühler and R. Cooper, *J. Phys. Chem.*, **80**, 1549 (1976).
117. F. J. Adrian, E. L. Cochran and V. A. Bowers, *J. Chem. Phys.*, **36**, 1938 (1962).
118. J. A. Brivati, K. D. J. Root, M. C. R. Symons and D. J. A. Tinling, *J. Chem. Soc. (A)*, 1942 (1969).
119. B. H. J. Bielski and H. O. Allen, *J. Amer. Chem. Soc.*, **99**, 5931 (1977).
120. G. S. Lian and D. D. Woodbridge, *Bull. Environ. Contamin. Tox.*, **17**, 714 (1977).
121. Z. D. Draganic, I. G. Draganic and V. Niketic, *Radiation Res.*, **69**, 223 (1977).
122. I. G. Draganic, Z. D. Draganic, S. Jovanovic and S. V. Ribnikov, *J. Mol. Evol.*, **19**, 103 (1977).
123. Z. D. Draganic, I. G. Draganic and M. Borovicanin, *Radiation Res.*, **66**, 42 (1976).
124. M. Anbar, *Advan. Phys. Org. Chem.*, **7**, 115 (1969).
125. (a) I. Draganic, Z. Draganic, Lj. Petkovic and A. Nikolic, *J. Amer. Chem. Soc.*, **95**, 7193 (1973).
(b) I. G. Draganic, Z. D. Draganic and K. Schested, *J. Phys. Chem.*, **82**, 757 (1978).
126. P. Neta, R. W. Fessenden and R. H. Schuler, *J. Phys. Chem.*, **75**, 11 (1971).
127. I. G. Draganic, Z. D. Draganic and V. M. Markovic, *Intern. J. Radiat. Phys. Chem.*, **8**, 339 (1976).
128. Z. D. Draganic, I. G. Draganic and S. V. Jovanovic, *Radiation Res.*, **75**, 508 (1978).
129. R. Livingston and H. Zeldes, *J. Mag. Reson.*, **1**, 169 (1969).
130. M. Anbar, D. Meyerstein and P. Neta, *J. Chem. Soc.*, **8**, 742 (1966).
131. I. G. Draganic, Z. D. Draganic and M. J. Shushtarian, *Radiation Res.*, **66**, 54 (1976).
132. Z. D. Draganic, I. G. Draganic and S. V. Jovanovic, *Radiation Res.*, **75**, 508 (1978).
133. L. M. Dorfman, I. A. Taub and R. E. Buhler, *J. Chem. Phys.*, **36**, 3051 (1962).
134. M. Anbar, D. Meyerstein and P. Neta, *J. Phys. Chem.*, **70**, 2660 (1966).

135. J. A. Knight, C. J. Bryan and R. A. Stokes, *Intern. J. Appl. Rad. Isotopes*, **14**, 239 (1963).
136. I. A. Grinevich, P. A. Zagorets, A. G. Shostenko and A. M. Dodonov, *Sov. High Energy Chem.*, **93**, 277 (1973).
137. O. Brede, R. Mehnert, W. Naumann and H. Y. Becker, *Radiochem. Radioanal. Letters*, **39**, 274 (1979).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 7

Electrochemistry of the cyano group

KUNIHISA YOSHIDA
Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560, Japan

Abbreviations

CE	Current Efficiency
CV	Cyclic Voltammetry
HOMO	Highest Occupied Molecular Orbital
LUMO	Lowest Unoccupied Molecular Orbital
SCE	Saturated Calomel Electrode
NHE	Normal Hydrogen Electrode

Glossary

ECE mechanism: The letter *E* symbolizes the electrochemical step and *C* the chemical step. Therefore, *ECE* indicates that the primary electron transfer is followed by a chemical reaction and a second electron transfer at the same electrode potential. Reference electrode Ag/Ag^+ is +0.30 V vs. SCE. Reference electrode SCE is itself +0.24 V vs. NHE at 25°C. The universally accepted standard for electrode potential measurement is the normal hydrogen electrode (NHE).

The electron-withdrawing ability of the cyano group profoundly influences the electrochemical reactions of compounds which contain it. The presence of cyano groups facilitates reduction and hinders oxidation.

I. ELECTROREDUCTIVE FORMATION OF STABLE ANION RADICALS AND DIANIONS

A. Aromatic Nitriles

A report of a detailed investigation of the cathodic reactions of aromatic and aliphatic nitriles has been presented by Rieger and coworkers[187]. Nearly all of the compounds studied undergo one-electron reductions in *N,N*-dimethylformamide (DMF) containing tetra-*n*-propylammonium perchlorate to give anion radicals whose ESR spectra have been recorded. In many cases the anion radicals are stable for long periods of time. Benzonitrile, phthalonitrile, isophthalonitrile, terephthalonitrile, *p*-tolunitrile, pyromellitonitrile (1,2,4,5-tetracyanobenzene), 4-nitrobenzonitrile, 3,5-dinitrobenzonitrile and 4-cyanopyridine are each reduced to their respective anion radicals. 4-Cyanobenzoic acid is reduced in two steps. The first involves reduction of the acidic proton to give the carboxylate, which is yellow-green. The second step leads to the yellow-orange 4-cyanobenzoate dianion radical. 4-Chlorobenzonitrile, 4-anisonitrile and 4-cyanophenol did not yield stable anion radicals. The anion radical of 4-nitrobenzonitrile has previously been studied, but with acetonitrile as solvent, by Maki and Geske[146]. The polarographic reduction of pyromellitonitrile in acetonitrile and the ESR spectrum of its anion radical in dimethoxyethane have also been studied[175,262].

Electrochemical reduction of isomeric mono- and di-cyanopyridines proceeds via

anion-radical intermediates containing the cyclic π-electron septet formed after the uptake of the first electron[235]. These intermediates undergo protonation, dimerization or uptake of a second electron, depending on the position of the cyano group(s), the acidity of the medium and the electrode potential. The ease of reduction of individual neutral isomers is governed by the LUMO energies and can be estimated experimentally by measurements of the solution-phase reduction potential ($E_{1/2}$). There is also a correlation between LUMO energies and $E_{1/2}$ for a series of cyanobenzenes[186].

Ludwig and Adams[142] have used the *in situ* electrochemical generation method in conjunction with the ESR technique in their studies of the electron-transfer reaction between the parent benzonitrile and its anion radical. A bimolecular rate constant of 10^8 M^{-1} s^{-1} can be estimated. Utilizing this method to produce ion-radical–parent mixtures, Kowert and coworkers[120] have determined the rates of homogeneous electron-transfer reactions between aromatic nitriles and their anion radicals (equation 1). The effects of substituents upon the exchange rates of several substituted

$$ArH^{\cdot-} + ArH \rightleftharpoons ArH + ArH^{\cdot-} \quad (1)$$

benzonitriles have been studied and the effect of solvent variation upon the exchange rate of benzonitrile has been determined. Rieger and coworkers[187] have shown that the broadening of the lines in the ESR spectra arises from intermolecular electron exchange between the anion radical and the unreduced material.

The rate constants for the electroreduction of 16 aromatic compounds, including benzonitrile, 4-cyanopyridine, *o*-, *m*- and *p*-tolunitrile, phthalonitrile, terephthalonitrile and *m*-nitrobenzonitrile, at a stationary mercury electrode in DMF have been determined[119]. Heterogeneous electron-transfer rate constants at a platinum–DMF interface have also been calculated from cyclic voltammetric peak separations for the reduction of benzonitrile, 4-cyanopyridine and some aromatic compounds[5].

B. Electron Acceptors

Rieger and coworkers[185] have studied the reduction of several tetracyanoethylene (TCNE) derivatives in DMF and in acetonitrile. TCNE itself is spontaneously reduced to the pale yellow anion radical by dissolving it in DMF. In this case, the small quantity of dimethylamine contained in the DMF would act as electron donor. The half-wave potential for reversible reduction in acetonitrile is −0.2 V vs. Ag/Ag^+. The anion radical produced gives an ESR spectrum identical with that observed from the DMF solution. The anion radical is further reducible to the dianion[241]. Electroreduction of the corresponding saturated compound, 1,1,2,2-tetracyanoethane, at −2.5 V forms the anion radical of TCNE, as indicated by ESR spectroscopy. Reduction of 1,1,2,2-tetracyanocyclopropane (TCNP) in DMF at the half-wave potential of −1.4 V gives a bright red-orange solution, whose ESR spectrum is identical with that found for the TCNE anion radical except that the solution of TCNP yields a spectrum with narrower lines. The narrowness of the lines in the ESR spectrum of the TCNE anion radical obtained by the reduction of TCNE or TCNP undoubtedly arises from the absence of an electron exchange reaction between TCNE anion radical and the unreduced TCNE.

The highly unsaturated compound 7,7,8,8-tetracyanoquinodimethane (TCNQ) is, as a result of conjugation of four cyano groups with the quinoid system, an exceedingly strong electron acceptor[2,156]. It undergoes a reversible one-electron reduction to produce a stable anion radical at +0.127 V vs. SCE in acetonitrile. A second reversible step occurs at −0.291 V, leading to the dianion. Rieger and collaborators[187] found that TCNQ is partly reduced to its anion radical by dissolution in DMF.

2-Alkyl-substituted TCNQ derivatives readily form anion radicals when reduced electrochemically or chemically[65]. 2-Benzhydryl-TCNQ[97], monofluoro-TCNQ

(FTCNQ)[84] and 2,5-difluorotetracyanoquinodimethane (F_2TCNQ)[194] are reduced in acetonitrile in two reversible one-electron steps, being indicative of the formation of anion radical and dianion. The anion radical of 2-benzhydryl-TCNQ can be prepared by controlled-potential electrolysis. Plots of the $E_{1/2}$ values for a homologous series F_nTCNQ (n = 0, 1, 2, 4) vs. Hammett σ values show a linear correlation.

11,11,12,12-Tetracyano-2,6-naphthoquinodimethane (TNAP) shows two one-electron reductions in acetonitrile, the first step giving the negative ion radical $TNAP^{\cdot-}$ and the second step giving the dianion of 2,6-naphthylenedimalononitrile, or an equivalent state of reduction[65]. Using the first reduction potential as a measure of relative π-acid strength[156], TNAP is seen to be a stronger π acid than either TCNQ (+0.127 V) or TCNE (+0.152 V). As expected from its high redox potential as determined by polarography, TNAP readily undergoes chemical reduction to give salts of $TNAP^{\cdot-}$. Mild reducing agents such as iodide ion are suitable. Thus, TNAP reacts with potassium iodide in acetonitrile solution to give $K^+TNAP^{\cdot-}$ as a bright green solid and with sodium iodide in acetonitrile to give $Na^+TNAP^{\cdot}$ as a dark blue solid. These compounds are paramagnetic in solution and in the solid state as determined by ESR spectroscopy.

Another attractive new acceptor would be tetracyanodiphenoquinodimethane (TCNDQ). Attempts to isolate this compound have led only to the formation of a polymeric material, and so the dianion salts of TCNDQ with alkali metal and tetra-alkylammonium counterions have been prepared[3]. Solutions of these dianions undergo two one-electron oxidations at −0.31 and −0.15 V vs. Ag/Ag^+ in DMF. The solution of $TCNDQ^{\cdot-}$ anion radical gives an ESR signal. From the measured potentials using the appropriate form of the Nernst equation, the equilibrium constant of the disproportionation electron-transfer reaction (equation 2) could be calculated. The value

$$2\,TCNDQ^{\cdot-} \underset{}{\overset{K}{\rightleftharpoons}} TCNDQ^{2-} + TCNDQ \qquad (2)$$

of K was 2×10^{-3}. Hence the small potential difference between the successive processes implies that it is not possible to prepare solutions which contain pure $TCNDQ^{\cdot-}$ without $TCNDQ^{2-}$ and/or TCNDQ also present.

The bridged analogue of TCNDQ, 13,13,14,14-tetracyanotetrahydropyrenoquinodimethane (TCNTHPQ), and its corresponding anion radical have been prepared electrochemically from its dianion by a modification of the above procedure[4]. Controlled-potential electrolysis at the second oxidation wave yielded a purple solution of the neutral compound, with no ESR signal. TCNTHPQ can also be prepared chemically[153]. This compound is stable and undergoes reversible reductions to the anion radical and dianion with peak potentials at $E_p^1 = +0.13$ V and $E_p^2 = -0.07$ V vs. SCE.

Besides extending the conjugation of TCNQ, heteroatom substitution has also been used to prepare new acceptors. Haley[92] has reported the synthesis of 2,5-bisdicyanomethylene-2,5-dihydrothiophene, a monosulphur analogue of TCNQ. Cyclic voltammetry (CV) of this compound at a platinum electrode in acetonitrile shows two reversible one-electron reductions at 0.05 V and −0.47 V, supporting the formation of the anion radical. The anion radical has been indeed synthesized in 78% yield by slow addition of the neutral tetracyano compound in methylene chloride to anhydrous lithium iodide in acetonitrile under argon.

A dianionic salt of tetracyanoquinoquinazolinoquinazoline has been prepared and its electrochemical behaviour reported[244]. CV in acetonitrile reveals a one-electron reversible reduction at −1.55 V vs. Ag/Ag^+, which can be assigned to the coupled dianion/trianion radical on the basis of ESR experiments.

Several sulphonyl-*p*-benzoquinones substituted with two cyano groups have been

synthesized and their polarographic reduction potentials have been measured in anhydrous acetonitrile[200]. These compounds are very strong oxidizing agents. 2,3-Dicyano-5-phenylsulphonyl-*p*-benzoquinone is found to have a half-wave reduction potential close to that of the well-known oxidizing reagent 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ). 2,3-Dicyano-5-chloro-6-phenylsulphonyl-*p*-benzoquinone shows the first one-electron reduction wave at +0.62 V vs. SCE on a graphite electrode.

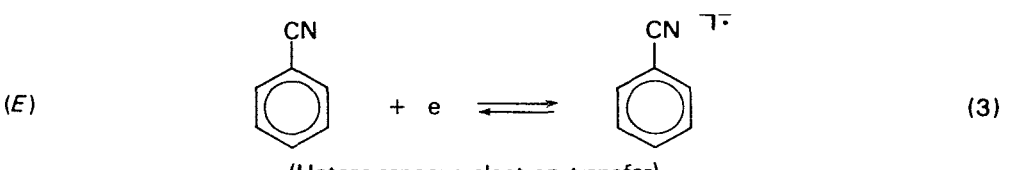
II. ELECTROREDUCTIVE ELIMINATION

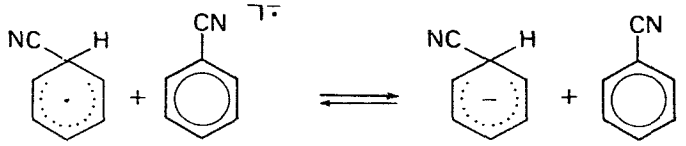
A. Decyanation

Benzonitrile and its homologues undergo reductive cleavage of the C—CN bond. Rieger and coworkers[187] have reported that reduction of phthalonitrile and terephthalonitrile at a potential of the second reduction wave produces benzonitrile anion radical. Three mechanisms have been proposed. Rieger and collaborators have explained the reaction by protonation of the directly generated dianion, followed by C—CN bond fission. On the other hand, Manoušek, Zuman and Exner[150] have studied this reaction in aqueous solution at varying pH values and suggested that the proton transfer occurs prior to the second electron uptake. Chernova and coworkers[53] have claimed that the elimination of cyanide ions occurs at the stage of the formation of the unstable dianions, and not as a result of their protonation.

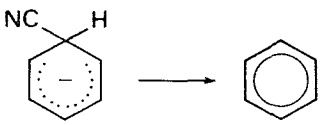
The electrochemical reduction of benzonitrile in an aprotic solvent containing a tetraalkylammonium salt has been studied from a mechanistic point of view.[192] Reduction products are benzene and cyanide ion together with substantial quantities of the alkene and alkylamine. Voltammetry indicates that the first step is a diffusion-controlled, reversible, one-electron transfer leading to the benzonitrile anion radical. The resulting anion radical is relatively stable in the solvent–electrolyte system used and makes possible kinetic studies in homogeneous solution. The anion radical decays according to a first-order kinetic law. The results are interpreted in terms of a mechanism involving slow protonation of the anion radical by the solvent and the acidic ammonium ions, followed by fast dismutation of the resulting neutral radical with the anion radical and elimination of cyanide ions from the anionic species thus formed (equations 3–6). (The letter *E* symbolizes an electrochemical step and *C* a chemical step.)

The dismutation step (equation 5) is closely related to, and in fact should complement, the cathodic reaction. In the cathodic process the anion radical would be near the cathode and the radical resulting from the protonation of the cathodically gener-



(C)  (5)

(Homogeneous electron transfer)

(C)  (6)

ated anion radical would further be reduced to the corresponding carbanion, which should subsequently release a cyanide ion (equation 6).

As to the proton donors enabling the reaction of equation (4), both the solvent and the tetraalkylammonium cations should be taken into consideration. The latter is likely to be involved in a Hofmann degradation with the highly nucleophilic anion radical, as indicated by the presence of substantial amounts of alkene and alkylamine among the reaction products. Such reactions involving tetraalkylammonium cations have been reported previously for electrochemical reductions producing strong bases[87,240].

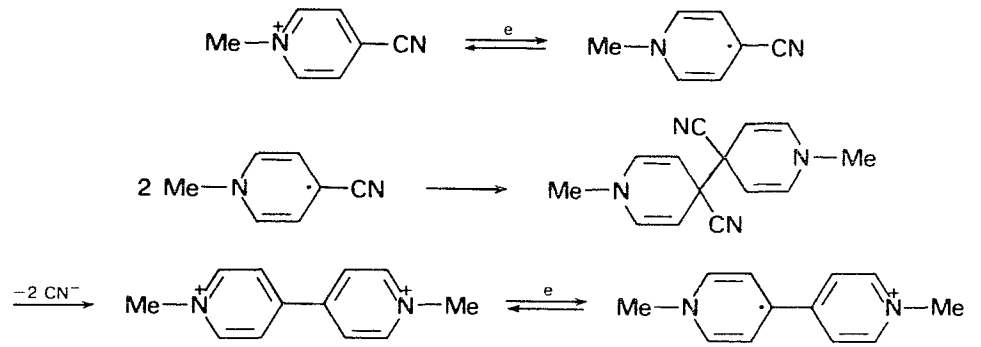
By addition of phenol, elimination of cyanide ion is prevented and the reduction proceeds to the formation of cyclohexene-1-carbonitrile or further to cyclohexanecarbonitrile, depending on the reduction potential (see Section III.C). The rate constant for the proton transfer from phenol to the anion radical is estimated to be 5×10^2 M^{-1} s^{-1}. In the presence of phenol, the anionic species formed in equation (5) undergoes further protonation rather than cyanide ion elimination, which indicates that the cleavage of the C—CN bond is not a very fast process.

The potentiostatic preparative electrode reaction of 4-cyanopyridine in alkaline solution consumes two electrons per molecule, and a fission of the C—CN bond occurs to produce pyridine and cyanide ion in high yield[143]. This reaction has also been confirmed in polarographic reduction[106,232–234].

2-Furonitrile and 2-methyl-5-furonitrile in DMF are reduced electrochemically in an irreversible two-electron step, with detachment of the cyano group[212].

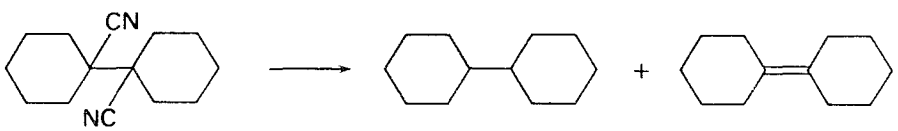
Cyano substituents are also displaced by a *t*-butyl group[127]. A DMF solution containing cyanobenzophenone, *t*-butyl bromide, and supporting electrolyte (Bu_4NI) was reduced by using a mercury pool cathode at the potential region of the first polarographic wave of cyanobenzophenone; 2- and 4-cyanobenzophenone give the corresponding *t*-butylbenzophenones in 40–50% yield. Cyanobenzophenones are reduced at less negative potentials than *t*-butyl bromide ($E_{1/2} = -2.19$ V vs. SCE[128]). Thus, the primary step of this reaction would be the one-electron addition to cyanobenzophenones.

1-Ethyl-4-cyanopyridinium ion exhibits a reversible one-electron wave (first) in both aqueous buffered and acetonitrile solutions[199]. The reduction in the region of the first polarographic wave affords a neutral radical, which then dimerizes with loss of cyanide ion to produce 4,4′-bipyridinium ion. Since 4,4′-bipyridinium ion is more easily reducible than the starting 4-cyanopyridinium ion, it immediately adds another electron to produce the ethylviologen cation radical. 1-Methyl-4-cyanopyridinium ion in alkaline solution behaves similarly[234]. The mechanism shown in Scheme 1 has been proposed for the reductive decyanation reaction.



SCHEME 1

The electrochemical cleavage of nitriles can also be performed in anhydrous amine media, making possible C—CN bond cleavage in aliphatic nitriles[11]. Reductive decyanation of 1,1′-dicyanobicyclohexyl produced bicyclohexyl (80%) and bicyclohexylidene (20%) (equation 7). Decyanation of dehydroabietonitrile, cycloheptyl



(7)

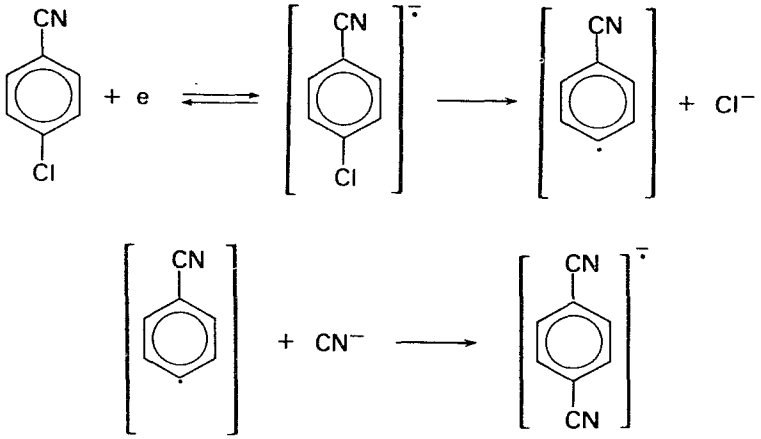
cyanide and *n*-octyl cyanide produced dehydroabietene, cycloheptane and *n*-octane, respectively, in 60–80% yield. This reaction was interpreted as being due to reductive cleavage by solvated electrons. A possible explanation for a reductive decyanation of nitriles to hydrocarbons by solvated electrons generated from chemical sources has been presented[12].

B. Dehalogenation

Bartak and coworkers[32] have studied the electrochemical reduction of a series of chloro-, bromo-, and iodo-benzonitriles in DMF and the subsequent mode of decomposition of the resulting anion radicals. Exhaustive electrolysis of 4-chlorobenzonitrile at a potential between the first and second cathodic waves gives an *n* value of 2. Benzonitrile is formed in 85% yield. Similar voltammetric results have been noted for other halobenzonitriles.

Since reduction of 4-chlorobenzonitrile in the presence of cyanide ion gives rise to a small amount of terephthalonitrile anion radical, the intermediacy of cyanophenyl radicals is suggested (Scheme 2). A pathway consistent with these data involves initial one-electron reduction of the halogenated benzonitrile, rapid loss of halide ion from the anion radical to give the corresponding cyanophenyl radical, and subsequent reduction of the cyanophenyl radical at the electrode surface to cyanophenyl anion (equation 8). Abstraction of a proton from the solvent system by the cyanophenyl anion yields benzonitrile and completes the reaction pathway.

M'Halla and coworkers[157] have investigated the electrochemical reaction of aromatic halides in the absence of added nucleophiles and obtained characteristic rate constants using deuterium-incorporation measurements as a tool. The neutral $Ar^{\bullet}$ radical formed by the carbon–halogen bond-cleavage of the cathodically generated haloaromatic anion radicals (equations 9 and 10) undergoes three concurrent reactions: hydrogen atom abstraction from the solvent SH (equation 11) and electron



SCHEME 2

$$RX + e \rightleftharpoons RX^{\cdot -} \xrightarrow{k} R^{\cdot} + X^{-} \qquad (8)$$

$$R^{\cdot} \xrightarrow{e} R^{-}$$

poration by deuterated water or solvent, a competition between hydrogen-atom and transfer at the electrode and/or from the initial anion radical (equations 12 and 13). The electrode or solution electron-transfer reaction leads to the formation of Ar^- anion followed by protonation (equation 14). By measurements of deuterium incor-

$$ArX + e \rightleftharpoons ArX^{\cdot -} \qquad (9)$$

$$ArX^{\cdot -} \xrightarrow{k_1} Ar^{\cdot} + X^{-} \qquad (10)$$

$$Ar^{\cdot} + SH \xrightarrow{k_2} ArH + S^{\cdot} \qquad (11)$$

$$Ar^{\cdot} + e \longrightarrow Ar^{-} \qquad (12)$$

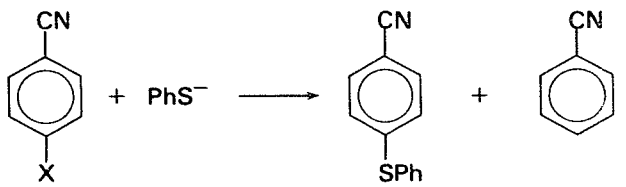
$$Ar^{\cdot} + ArX^{\cdot -} \longrightarrow Ar^{-} + ArX \qquad (13)$$

$$Ar^{-} + \begin{cases} H_2O \text{ (residual)} & \\ SH & \longrightarrow ArH + S^{-} \\ R^1CH_2\overset{+}{N}R^2_3 & \end{cases} \begin{matrix} OH^{-} & (14a) \\ & (14b) \\ R^1\overset{-}{C}H\overset{+}{N}R^2_3 & (14c) \end{matrix}$$

proton transfer could be substituted for the competition between hydrogen-atom transfer (equation 11) and the two types of electron transfer (equations 12 and 13) to the secondary $Ar^{\cdot}$ radical. The method is based upon the determination of the amount of deuterium replacing the hydrogen atom upon electrolysis in the presence of either

10% D_2O in the nondeuterated organic solvent (10% D_2O–CH_3CN) or 10% H_2O in the deuterated solvent (10% H_2O–CD_3CN). Water provides hydrogen ion and no hydrogen atom while the organic solvent acts oppositely. Other proton or hydrogen-atom sources, apart from the solvent and water, such as tetraalkylammonium salts, were avoided. 4-Halobenzonitriles give rise upon electrolysis in the presence of 10% water to an apparent number of electrons practically equal to 2 and a yield of benzonitrile close to 100%. The quantitative kinetic analysis of the competition between hydrogen-atom and electron transfer provides two series of rate data, viz., the cleavage rates of the anion radicals and the rate of hydrogen-atom transfer to the 4-cyanophenyl radical. The rate constants, k_1, for the cleavage of the carbon–halogen bond of the anion radicals of 4-chloro-, 4-bromo-, and 4-iodo-benzonitriles are 5×10^8, 1×10^{10} and $5 \times 10^{10}\ s^{-1}$, respectively. Also, the hydrogen- and deuterium-atom abstraction rate constants are 4×10^7 and $3 \times 10^6\ s^{-1}$, respectively, and consequently the magnitude of the deuterium isotope kinetic effect, k_2^H/k_2^D equals 14. The contribution of the solution electron transfer (equation 13) is negligible in the case of 4-halobenzonitriles (while in the case of 9-chloroanthracene and electrode reduction is negligible).

Pinson and Savéant[181] have also reported the possibility of electrochemically inducing aromatic substitutions of the $S_{RN}1$ type. The chemical aspects of $S_{RN}1$ reactions have been widely investigated and discussed[51]. Reaction was carried out on a mercury pool working electrode by setting up the electrode potential at the reduction level of the substrate in the presence of a nucleophile. With phenylthiolate ion as nucleophile, substitution of halogeno derivatives of benzonitrile occurs electrocatalytically (equation 15) (see Section V.A). Bu_4N^+ salts appear to be better reagents



80% 10% (X = Br)

20% 80% (X = I) (15)

than sodium salts used in conjunction with a crown ether. The bromo derivative leads to strikingly better yields than the iodo. The reaction mechanism (equations 9, 10, 16–18) involves the formation of the anion radical at the electrode and its further decomposition into a neutral electrophilic radical which reacts with the nucleophile

$$ArX + e \rightleftharpoons ArX^{\cdot -} \quad (9)$$

(Standard potential E_1^0)

$$ArX^{\cdot -} \longrightarrow Ar^{\cdot} + X^- \quad (10)$$

$$Ar^{\cdot} + Y^- \longrightarrow ArY^{\cdot -} \quad (16)$$

$$ArY^{\cdot -} - e \rightleftharpoons ArY \quad (17)$$

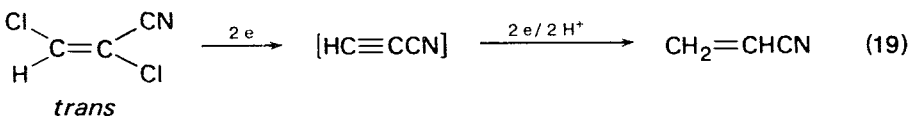
(Standard potential E_2^0)

$$ArY^{\cdot -} + ArX \rightleftharpoons ArY + ArX^{\cdot -} \quad (18)$$

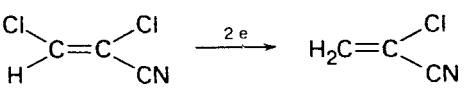
(Equilibrium constant K_d)

yielding the anion radical of the substituted product. Oxidation of the last species may occur by solution electron exchange with the substrate and/or at the electrode. If $E_2^0 < E_1^0$, the equilibrium of equation (18) favours the right-hand side [$(RT/F)\ln K_d = E_1^0 - E_2^0$).

Jura and Gaul[102] have studied the polarographic behaviour of unsymmetrical polyhalogenated propionitriles. Reduction in all cases results in the formation of a double bond. In 30% ethanol containing trimethylammonium iodide, 2,2,3-trichloropropionitrile gives three well-developed waves of equal height. The first wave corresponds to the reductive elimination of adjacent halogens to form a double bond. The resulting 2-chloroacrylonitrile is further reduced to acrylonitrile and finally to propionitrile. 2,3-Dichloropropionitrile is reduced in two steps through acrylonitrile to propionitrile. From the data on these saturated compounds and the mechanism proposed by Elving and Rosenthal[79] for symmetrical structures, it is possible to conclude that reduction proceeds via scission of an α-carbon–halogen bond, formation of a carbanion and simultaneous *trans* elimination of a β-halogen with the formation of a double bond. They have also observed that the *cis* and *trans* isomers of 2,3-dichloroacrylonitrile are reduced to acrylonitrile via different mechanisms. The suggested initial step involves attack at the halogen β to the nitrile. In the case of the *trans* isomer, the formation of the β-carbanion occurs with the simultaneous loss of the α-chlorine atom as chloride (*trans* elimination) and formation of propiolonitrile (2-propynenitrile). The nitrile is immediately reduced to acrylonitrile. The *cis* isomer is incapable of eliminating the second chlorine, consequently the carbanion abstracts a proton from the solvent system to produce 2-chloroacrylonitrile. The reaction sequences are written as shown in equations (19) and (20). It has experimentally been confirmed that



trans (19)

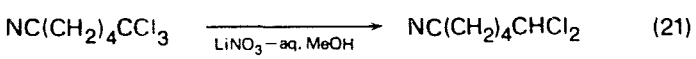


cis (20)

propiolonitrile is reduced at less negative potentials than the *cis–trans* mixture and that it would be reduced at the electrode surface as quickly as it is formed from the reduction of *trans*-2,3-dichloroacrylonitrile. 2,2,3,3-Tetrachloropropionitrile is successively reduced to *trans*-2,3-dichloroacrylonitrile, acrylonitrile and propionitrile.

In polarographic studies, both *cis*- and *trans*-3-chloro-2-phenylacrylonitriles are reduced in two 2-electron steps through atroponitrile (α-cyanostyrene) to the saturated compound[133]. The $E_{1/2}$ of the first reduction step is less negative for the *cis* isomer than for the *trans* isomer. Likewise *cis*- and *trans*-3-chloro-2-(1- and 2-naphthyl)acrylonitriles undergo dechlorination followed by reductive saturation[135].

Nagao and coworkers[162] have presented an electrochemical method for selectively reducing an aliphatic trichloromethyl group to either a chloromethyl or dichloromethyl group. When 1,1,1-trichloro-5-cyanopentane is reduced at the mercury electrode in 90% MeOH—$LiNO_3$ using a divided cell, 1,1-dichloro-5-cyanopentane is formed in good yield (equation 21). On the other hand, 1-chloro-5-cyano-



(21)

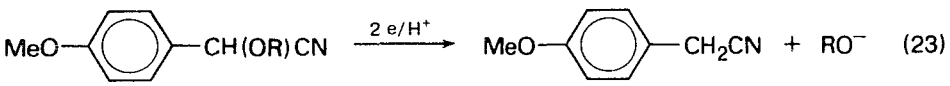
$$NC(CH_2)_4CCl_3 \xrightarrow[Me_4NCl-aq.MeOH]{} NC(CH_2)_5Cl \quad (22)$$

96%

pentane is formed from the trichloro compound when Me_4NCl is used as the supporting electrolyte (equation 22). Since many aliphatic trichloromethyl compounds and their derivatives are readily available by telomerization of olefins with carbon tetrachloride or chloroform, the electroreductive method would open a route to the simple preparation of α,ω-bifunctional aliphatic compounds.

C. Deacyloxylation

Wawzonek and Fredrickson[238] have studied anisaldehyde cyanohydrin and its esters. The large-scale electrolytic reduction of 2-(benzoyloxy)-4-methoxyphenylacetonitrile in 50% dioxane containing Me_4NI gives *p*-methoxyphenylacetonitrile in good yields. 2-(Hydroxy)-, 2-(acetoxy)- and 2-(propionyloxy)-4-methoxyphenylacetonitrile undergo a similar reduction to *p*-methoxyphenylacetonitrile and the corresponding anions (equation 23). On the basis of the ease of reduction and preparation the benzoate is promising as the starting material for the large-scale electrolytic preparation.



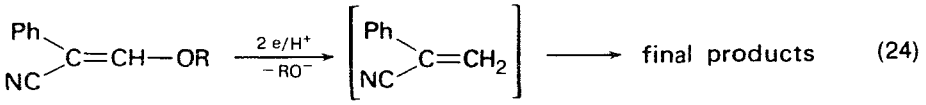
(23)

~65% yield; (R = PhCO)

R = H, MeCO, EtCO, PhCO

D. Dealkoxylation

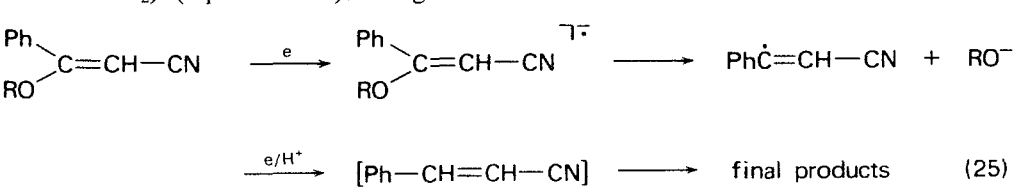
The reduction of *Z*- and *E*-3-alkyl(or aryl)oxyatroponitriles in ethanol, THF or aqueous ethanol proceeds via the intermediate atroponitrile by the elimination of alkoxide ion (equation 24)[136]. The reactions were performed at a potential near the



(24)

first voltammetric wave. At the potential region adopted only organic substrates are reduced to produce an anion-radical intermediate.

Le Guillanton and Cariou[137] have studied the electrochemical reduction of *Z*- and *E*-3-alkyl(or aryl)oxycinnamonitriles, Ph(RO)C=CHCN (R = Me, *n*-Bu, *t*-Bu, Ph and $PhCH_2$) (equation 25), using voltammetries and macroscale reductions with



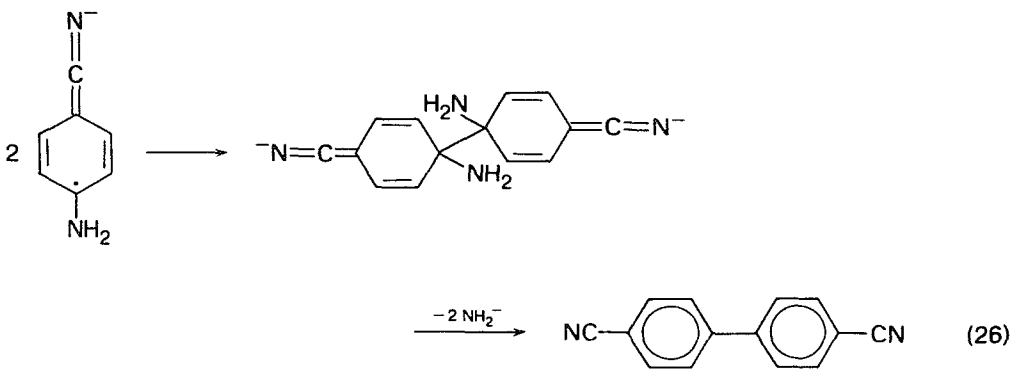
(25)

product identification. Here too, as in the case of atroponitriles, the *Z* isomers are more easily reduced than the *E* isomers. For substrates with substituents having positive Taft σ^* values (R = Ph, $PhCH_2$), the intermediate anion radical loses alkoxide

ion forming cinnamonitrile which is further reduced. For negative σ^* (R = Me, Bu, *t*-Bu), the carbon–carbon double bond is reduced to give saturated nitriles, $Ph(RO)CHCH_2CN$.

E. Deamination

The CV of 4-aminobenzonitrile in DMF suggests a reversible reduction followed by irreversible chemical reaction[187]. The reduction product is the anion radical of 4,4′-dicyanobiphenyl. The reaction has been interpreted by the elimination of amide ion from the cathodically generated anion radical and subsequent dimerization of the resultant 4-cyanophenyl radicals. The dimer is reduced more easily than the starting material, and thus the anion radical of the dimer at the same potential. However, as found by Bartak and coworkers[32], this secondary radical undergoes further reduction to the corresponding anion rather than coupling. Thus, for the reductive formation of 4,4′-dicyanobiphenyl, an alternative mechanism, probably intermolecular coupling at the 4-positions of the primary anion radicals, would function (equation 26).



(26)

Under similar conditions sodium 1,1,3,3-tetracyano-2-dimethylaminopropenide also undergoes deamination to produce the dianion radical of 1,1,3,3-tetracyanopropene.

F. Denitration

Controlled potential reduction of 2-methyl-2-nitropropionitrile ($E_{1/2} = -1.08$ V vs. SCE) has been carried out in acetonitrile at a plateau potential of the first wave of this compound[198]. The coulometric *n* value was found to be 1.3. About 0.7 molar equivalent of nitrite ion was detected in the electrolysed solution, and both isobutyronitrile and tetramethylsuccinonitrile were isolated. The first step of the electrode process is considered to be a one-electron reduction leading to the anion radical which cleaves to nitrite ion and the residual free radical. The resulting free radical abstracts a hydrogen atom from the solvent, dimerizes to the succinonitrile, or is further reduced to the carboanion.

G. Fission of Carbon–Sulphur and Nitrogen–Sulphur Bonds

Wagenknecht and Baizer[237] have investigated the polarographic and macroscale reduction of cyanoalkyldimethylsulphonium ions, $Me_2\dot{S}(CH_2)_nCN$ (n = 1, 2 or 3; **1**, **2** and **3**, respectively), in dimethyl sulphoxide containing Bu_4NBr. $E_{1/2}$s were −1.04, −1.69 and −1.76 V vs. SCE for **1**, **2** and **3**, respectively. The addition of a small

amount (less than 1%) of acetic acid caused the wave height for **1** to increase to twice its original value. Large-scale electrolysis of **1** produced dimethyl sulphide and acetonitrile. The reduction of **1** is most easily understood as a two-electron reduction (equation 27). In the absence of another proton source the cyanomethyl anion abstracts a proton from a second parent sulphonium ion to produce the ylide **4** (equation 28). The net result is that two electrons effectively consume two of the

$$\underset{(\mathbf{1})}{Me_2\overset{+}{S}CH_2CN} \xrightarrow{+2\,e} Me_2S + {}^{-}CH_2CN \qquad (27)$$

$$^{-}CH_2CN + \mathbf{1} \longrightarrow MeCN + \underset{(\mathbf{4})}{Me_2\overset{+}{S}-\bar{C}HCN} \qquad (28)$$

sulphonium ions giving an apparent one-electron reduction. However, when acetic acid is present, the cyanomethyl anions are protonated by the acetic acid and all the sulphonium ions which diffuse to the mercury drop are available for reduction, giving a two-electron reduction wave. The first polarographic waves of **2** and **3** are not effected by the addition of phenol as a proton donor indicating a true one-electron reduction (equation 29). However, the addition of phenol does cause the appearance

$$Me_2\overset{+}{S}(CH_2)_nCN \xrightarrow{e} Me_2S + {}^{\cdot}(CH_2)_nCN \qquad (29)$$
$$n = 2 \text{ or } 3$$

of a second wave. At the potential of the second wave, a two-electron reduction occurs leading to the cyanoalkyl anion (equation 30a or b). In this case the cyanoalkyl anion

$$Me_2\overset{+}{S}(CH_2)_nCN \xrightarrow{e} Me_2S + {}^{\cdot}(CH_2)_nCN$$
$$\text{(a) } 2\,e \qquad \text{(b) } e \qquad (30)$$
$$^{-}(CH_2)_nCN$$

is protonated by phenol, and both waves are observed. In the absence of phenol the second wave does not appear because the cyanoalkyl anion formed reacts with unreduced sulphonium ion (equation 31 or 32) so that two electrons effectively

$$^{-}(CH_2)_nCN + Me_2\overset{+}{S}(CH_2)_nCN \longrightarrow Me_2S + NC(CH_2)_{2n}CN \qquad (31)$$

$$^{-}(CH_2)_nCN + Me_2\overset{+}{S}(CH_2)_nCN \longrightarrow$$

$$Me(CH_2)_{n-1}CN + Me_2\overset{+}{S}-\bar{C}H(CH_2)_{n-1}CN \qquad (32)$$

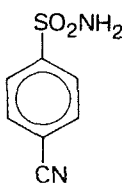
remove two sulphonium ions. This then gives the same wave height as the original one-electron reduction. The products of macroelectrolyses of **2** and **3** at the potential of the first wave were those expected from a one-electron reduction. The primary chemical consequence of the electron transfer is cleavage of the starting material between the sulphonium group and the adjacent carbon. The cyano group influences the fate of the cyanoalkyl fragment. When $n = 1$, further reduction of the initial cyanomethyl radical to the relatively stable cyanomethyl anion is a very favourable process. When $n = 2$ or 3, the cyano group has a much weaker (inductive) stabilizing

influence upon the cyanoalkyl fragment, so that reduction to the cyanoalkyl carbanion is less favoured, and reactions deriving from the initial cyanoalkyl radical predominate.

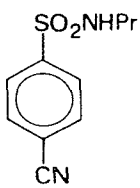
Electroreduction at a mercury cathode of the cyanomethyldimethylsulphonium salt **1** was carried out in aqueous quaternary ammonium electrolytes containing excess acrylonitrile as acceptor of the electrogenerated intermediates at a controlled potential of −0.75 to −1.08 V vs. SCE[25]. The only condensation product isolated was glutaronitrile (CE based on a 2 e process, 20%). Also, 2-phenylthiocinnamonitrile undergoes electrolytic fission to yield thiophenol and cinnamonitrile, and simultaneously the hydrodimer and 3-phenyl-3-(or 2-)phenylthiopropionitrile are generated. In the presence of acrylonitrile, besides the hydrodimer, the products of mixed coupling and 3-phenylthiopropionitrile were obtained.

Polarographic reduction of substituted methyl phenyl sulphones has been investigated[148]. 4-Cyanophenyl methyl sulphone in aqueous alcohol solution gives a two-electron irreversible reduction wave at pH 6–13. Electrolytic cleavage of the sulphur–aryl bond takes place with formation of methanesulphinate anion and benzonitrile. 6-Cyanobenzenesulphonamides in an aqueous borate buffer solution are cleaved not at the S—N but rather at the C—S bond[149]. Such a reduction mode for a sulphonamide is unusual.

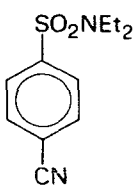
The reduction of three cyanobenzenesulphonamides (**5**–**7**) at a mercury cathode has



(**5**)

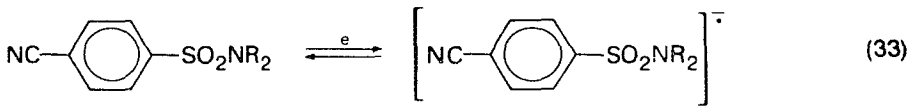


(**6**)

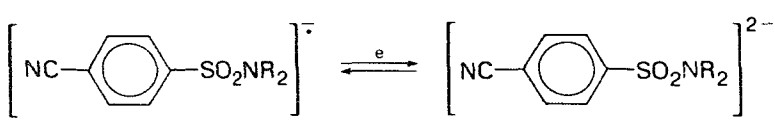


(**7**)

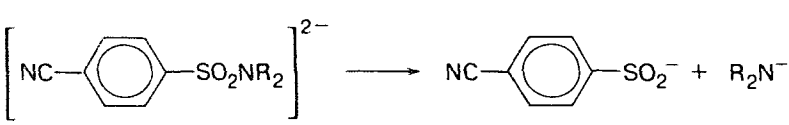
been examined in acetonitrile[60]. CV for each of these exhibits two reduction steps. Controlled-potential electrolyses were performed at the potentials of their second voltammetric peaks. After completion of the initial rapid reaction for which the coulombic n is 1 for **5** and **6** and about 1.4 for **7**, a much slower reaction occurred. Products of these reactions consist of the sulphinate anion and ammonia or amine produced by sulphur–nitrogen cleavage and, in some cases, the deprotonated anion salt of the starting sulphonamide. Equations (33)–(37) represent the rapid stage of



(33)



(34)



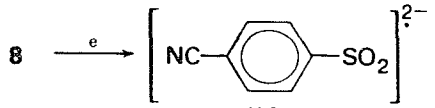
(35)

(**8**) (**9**)

$$\mathbf{9} + MeCN \longrightarrow R_2NH + {}^{-}CH_2CN \quad (36)$$

$${}^{-}CH_2CN + Et_4N^{+} \longrightarrow MeCN + CH_2{=}CH_2 + Et_3N \quad (37)$$

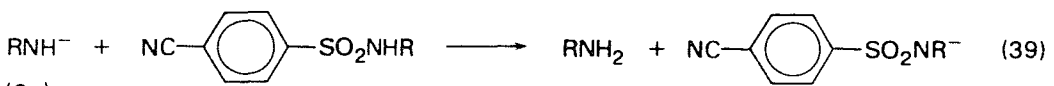
the electroreduction. The rapid reaction, thought to correspond to the first voltammetric peak, would produce the sulphinate and amide ions by virtue of sulphur–nitrogen scission of the intermediate dianion (equation 35). Equation (37) is included because ethylene and triethylamine have also been detected[240]. The second slower stage is identified with formation of the dianion radical **10**, shown in equation (38).



$$\mathbf{8} \xrightarrow{e} \left[\text{NC-C}_6\text{H}_4\text{-SO}_2\right]^{2-\cdot} \quad (38)$$

(10)

This radical has been shown by ESR spectroscopy to be identical with that formed by reduction of 4-cyanobenzenesulphonyl chloride. This would further react with the starting material. On the other hand, when an acidic proton is available on the sulphonamide, the amide ion **9a** reacts as indicated in equation (39), rather than as in



$$RNH^{-} + \text{NC-C}_6\text{H}_4\text{-SO}_2\text{NHR} \longrightarrow RNH_2 + \text{NC-C}_6\text{H}_4\text{-SO}_2\text{NR}^{-} \quad (39)$$

(9a) **(11)**

equations (36) and (37). The resulting sulphonamide anion **11** is not electrochemically active. This accounts for the occurrence of one-electron reactions of **5** and **6** in the absence of proton donors, but of two-electron reactions with a proton donor present.

H. Fission of the Carbon–Phosphorus Bond

Wagenknecht and Baizer[236] have studied the electrochemical reductive cleavage of certain cyanoalkylphosphonium compounds $Ph_3\overset{+}{P}(CH_2)_nCN\ X^{-}$, in which n = 1–4, for the purpose of introducing the cleaved cyanoalkyl moiety to suitable organic acceptors. When n = 2–4, an initial one-electron reduction is observed indicating the initial formation of a phosphoranyl radical. Depending upon the stability of the latter, either it may undergo decomposition at the mercury surface to form 'amalgamated' cyanoalkyl radicals, which at the first polarographic wave rearrange to cyanoalkyl mercurials and at the second wave are reduced to cyanoalkyl anions, or it may migrate away from the cathode before it decomposes, in which case the radicals formed by decomposition enter into reaction with substrates. Bulk electrolyses of the compounds in which n = 2–4 in excess styrene yield $Ph(CH_2)_{n+2}CN$ and biscyanoalkylmercury compounds, $Hg[(CH_2)_nCN]_2$.

For n = 1 in the above phosphonium salts, a direct two-electron reduction to triphenylphosphine and cyanomethyl anion occurs. An overall pseudo-one-electron reduction is actually measured, because the cyanomethyl anion generated exclusively attacks the parent ion to form acetonitrile and $Ph_3P{=}CHCN$, thus engaging two molecules of starting material in reaction with two electrons. Large-scale electrolyses in the presence of styrene yield neither coupled products nor mercurials.

III. HYDROGENATION

A. Cyano Group

For a long time, nitriles were reduced in aqueous or aqueous–ethanolic sulphuric acid at a platinum electrode in a divided cell[6]. Acetonitrile and propionitrile produced the corresponding primary amines together with a considerable amount of ammonia. Benzyl cyanide and benzonitrile yielded β-phenylethylamine and benzylamine, respectively. More recently different experimental conditions have been applied to various types of nitriles. Ohta[169] carried out the reduction of acetonitrile, malononitrile, succinonitrile, adiponitrile, benzyl cyanide, *o*-tolunitrile, 2-cyanoethanol and cyanoacetic acid in aqueous hydrochloric acid using a platinum cathode covered with palladium in a divided cell. In cases where the nitrile was sparingly soluble in aqueous solution, glacial acetic acid was added. Higher aliphatic nitriles, lauronitrile and stearonitrile, were reduced to the corresponding amines in ethanolic sulphuric acid using nickel black over graphite plate as cathode[125]. For benzyl cyanide, copper, lead, mercury, nickel, tin, and copper and nickel covered with palladium were examined as cathodes in aqueous hydrochloric acid containing glacial acetic acid[107]. The last two electrode materials alone were effective under the reaction conditions employed. Palladium black or nickel black deposited on graphite were also efficient cathodes for this compound in ethanolic sulphuric acid and in aqueous ethanolic ammonium sulphate media[124,126].

Polarographic reduction of dicyanobenzenes gives the corresponding aminomethyl compounds in aqueous–organic media or in DMF containing proton donors such as phenol, acetic acid or benzoic acid[53,231]. Substituted benzonitriles bearing electron-withdrawing groups (e.g., acetyl or formyl) *para* to the cyano group are also reduced potentiostatically to benzylic amines in acidic media using a mercury cathode[261]. 4-Cyanopyridine is reduced in the acid region using a mercury electrode to 4-picolylamine[106,234]. Polarographic reduction of *p*-cyanocinnamic acid or its ethyl ester produces the primary amine in acid[49].

The preparative-scale reduction of the cyano group in acrylonitrile has been performed at −1.45 V vs. SCE in aqueous sulphuric acid containing methanol at a lead cathode[166] (equation 40). Allylamine was mainly produced together with a small

$$CH_2{=}CHCN \xrightarrow{e/H^+} CH_2{=}CHCH_2NH_2 \qquad (40)$$

amount of propylamine (CE was 55 and 13%, respectively). The reduction of the carbon bond is reduced more easily than the cyano group of aliphatic nitriles. The reduction was carried out at a lead cathode in 24% phosphoric acid. CE of the dinitrile in a strongly acid solution: a cyano group conjugated with a multiple carbon–carbon bond is reduced more easily than the cyano group of aliphatic nitriles. The reduction was carried out at a lead cathode in 24% phosphoric acid. CE of the aminonitrile was 68%.

The mechanism of the cathodic reduction of nitriles to primary amines depends on the reaction conditions as well as on the reduction potential of the substrate. Electrode material and a pH of the electrolyte solution play an important role in determining the mechanism. Nitriles are reduced in acidic solution to give amines, whereas in neutral or alkaline medium, as mentioned in Section II.A, cleavage of the C—CN bond takes place. In the case of aromatic and conjugated nitriles, the electron transfer occurs at relatively low negative potential. The reduction potential of the corresponding conjugate acid must be lower than that of the parent molecule and, thus, the protonated species would be the electroactive species. With a high hydrogen overvoltage cathode in acidic solution the mechanism of the reduction of nitriles would proceed as shown in equations (41)–(44).

$$Ar{-}C{\equiv}N + H^+ \rightleftharpoons Ar{-}C{\equiv}N/H^+ \quad (41)$$

$$Ar{-}C{\equiv}N/H^+ + e \rightleftharpoons Ar{-}\dot{C}{=}NH \quad (42)$$

$$Ar{-}\dot{C}{=}NH + e + H^+ \longrightarrow Ar{-}CH{=}NH \quad (43)$$

$$Ar{-}CH{=}NH + 2e + 2\,H^+ \longrightarrow ArCH_2NH_2 \quad (44)$$

The electron transfer to unsubstituted alkyl cyanides takes place at a high negative potential. A direct electron transfer would be difficult to achieve under the usual reaction conditions, especially using a low hydrogen overpotential electrode in aqueous solution. Thus, another mechanism, a catalytic hydrogenation, is pertinent.

Imidates (also termed imino ethers, imido esters or imidic acid esters) which are, in the form of their hydrochlorides, available in quantitative yield from nitriles according to the Pinner reaction, can be reduced in 2N aqueous sulphuric acid to primary amines at lead cathodes at 0°C[243]. The yield of amines from aromatic imidates is fairly good but aliphatic ones give lower yields. This reaction may offer an additional route for the electroreduction of nitriles to primary amines in ethanolic sulphuric acid, where the initial reaction would be an acid-catalysed addition of alcohol to the nitrile with formation of a reducible imidate[73]. The details of this reaction have been discussed by Lund[145].

B. Ethylenic Bond

The electroreduction of unsaturated nitriles such as allyl cyanide, methacrylonitrile and crotononitrile in alkaline media at cathodes of tin, zinc and graphite leads to the reduction of the double bond with the formation of monomeric reduction products together with small amounts of the hydrodimer[219]. A zinc cathode is the most effective. At a copper cathode, in addition to reduction of the double bond, reduction of the cyano group takes place with the formation of primary and secondary amines. The reduction of 1-cyano-1,3-butadiene, as a mixture of *cis* and *trans* isomers in aqueous potassium hydroxide solution, gives 2- (23%) and 4-pentenenitrile (6%) and stereoisomeric 2,2′-dicyanobicyclobutyls (9% yield)[104]. Lead, zinc, graphite coated with mercury or thallium, and tin were tried as cathodes. The electrode material has no substantial effect on the proportions of the monomeric and dimeric products. 1,4-Dicyano-1-butene, as a mixture of *cis* and *trans* isomers, is reduced to adiponitrile in neutral solutions of dipotassium hydrogen phosphate at a zinc or amalgamated lead cathode[208]. A small amount of the hydrodimer, 4,5-di(cyanomethyl)suberonitrile, is also formed as a by-product.

Cyano groups conjugated with a carbon–carbon double bond are polarographically active. Sevast'yanova and Tomilov[202] have studied the reduction of a homologous series of α,β-unsaturated nitriles. In DMF solutions these nitriles are reduced at less negative potentials than in aqueous solutions. The positional influence of methyl and cyano substituents on the half-wave reduction potentials has been discussed briefly.

1-Cyclohexene-1-carbonitrile has been potentiostatically reduced in DMF containing phenol as a proton donor at a potential negative enough to cause the reduction of the substrate to produce cyclohexanecarbonitrile in good yield[192].

Preparative-scale reductions of cinnamonitrile derivatives Ph(R)C=C(X)CN (R = *t*-Bu or Ph; X = CN or COOEt) have been carried out at mercury, vitreous carbon or lead cathodes potentiostatically[15] (equation 45). Acetic acid was used as

$$\text{Ph(R)C=C(X)CN} \xrightarrow{2\,e/2\,H^+} \text{Ph(R)CHCH(X)CN} \qquad (45)$$

R = Ph, X = CN or COOEt; R = *t*-Bu, X = CN

proton donor, the solvents being either 4-methyl-1,3-dioxolan-2-one or DMF. The authors expected that optically active reduction products would result from induction of asymmetry by protonation with optically active proton donors. 2-Cyano-3-*t*-butylcinnamonitrile is particularly suitable for such a study because it can be reduced at a potential at which alkaloid salts as proton donors are not discharged and the expected product [Ph(*t*-Bu)CHCH$(CN)_2$] can exist as enantiomers. Controlled-potential preparative-scale reduction of this compound, in DMF and in the presence of (−)-ephedrin hydrochloride or (+)-quinidine sulphate, gave a racemic product with high CE, which implies that protonation is not the stereochemistry-determining step. Mixtures of stereoisomeric cyclic hydrodimers were the only products of similar reductions of compounds with R = H or Me and X = CN.

CV and ESR studies of cinnamonitrile derivatives with R = H, Me, *t*-Bu or Ph and X = CN or COOEt in aprotic solvents have been carried out by the same workers[14]. Except for R = H or Me, reversible one-electron reduction to an anion radical occurred, followed by irreversible reduction to a dianion at more cathodic potentials. In the presence of an added proton donor like acetic acid, two-electron reduction interposed by protonation was observed in the region of the first reduction peak potential. The effects of different proton donors on the reversibility of the first reduction peak have been assessed. For compounds with R = H or Me irreversible one-electron reduction to the anion radicals followed by rapid radical dimerization was observed even with an added proton donor.

The electrochemical reduction of *Z*- and *E*-3-alkyl(or aryl)oxycinnamonitriles, Ph(RO)C=CHCN (R = Me, Bu, *t*-Bu, Ph and $PhCH_2$), has been studied by polarographic and cyclic voltammetry and macroscale electrolyses with product identification[136]. In aqueous organic media, *Z* isomers are more easily reduced than *E* isomers, whereas in anhydrous acetonitrile, differences between half-wave potentials of the *E* and *Z* isomers are small or nil. For compounds which contain substituents having negative Taft σ^* values, the carbon–carbon double bond is reduced to give saturated nitriles, Ph(RO)$CHCH_2CN$.

Atroponitrile (α-cyanostyrene) generated by reductive dechlorination (Section II.B) of 3-chloro-2-phenylacrylonitrile readily undergoes reduction of the carbon–carbon double bond under the conditions used[133,135]. The olefinic group in 2-(1- and 2-naphthyl)acrylonitriles can be reduced likewise.

C. Benzene Nucleus

Heterocyclic and homocyclic nuclei are often reduced with relative ease at high overvoltage cathodes such as mercury and lead or specially activated cathodes like platinized platinum.

Benzonitrile in DMF containing Bu_4NI and varied amounts of water as proton donor is reduced to a mixture of cyclohexadienecarbonitriles[203]. Benzonitrile forms a single one-electron wave, the height and shape of which are unchanged by the addition of proton donors, indicating the absence of protonation in the electroreductive process. The benzene nucleus of benzonitrile also undergoes reduction in DMF in the presence of a relatively strong proton donor such as phenol[192]. Exhaustive electroreduction at −2.1 V vs. Ag/Ag^+, with a phenol concentration sufficient to make the polarographic wave bielectronic, yields 1-cyclohexene-1-carbonitrile ($E_{1/2}$ = −2.30 V) as a main reduction product. If reduction is carried out at a potential negative

enough to cause further reduction, the final product is cyclohexanecarbonitrile. 1-Cyclohexene-1-carbonitrile might be the product of isomerization of other cyclohexenecarbonitriles, since the protonation on the intermediate anion radical is likely to take place on the aromatic carbon atom bound to the cyano substituent (see Section II.A, equation 4).

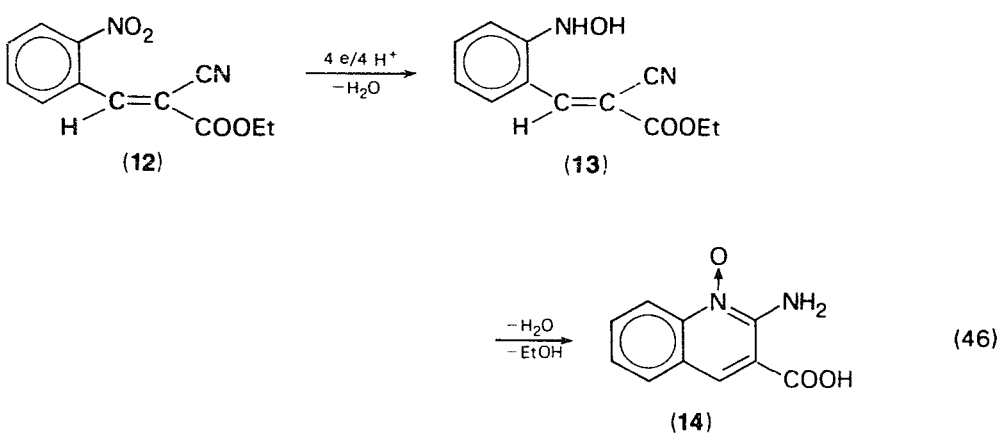
D. Carbonyl Group

The carbonyl moiety is reducible competitively in a nitrile molecule. Controlled-potential electrolysis of 2,2-dimethyl-3-oxopropanecarbonitrile ($E_{1/2} = -1.75$ V vs. SCE) in 75% dioxane containing LiCl as supporting electrolyte at a mercury cathode gives reduction of the aldehyde function[109]. No cleavage of the C—CN bond has been found. 1-Methyl-2-oxocyclohexanecarbonitrile behaves similarly.

Daver and Le Guillanton[63] have reported the electrochemical reduction of some enolizable β-ketonitriles. The preparative-scale electroreduction of aroylacetonitriles, $ArCOCH_2CN$ (R = Ph, *p*-BrC_6H_4, furyl), occurs exclusively at the carbonyl group of these compounds in the β-oxo form. The reduction of α-arylacylacetonitriles, RCOCH(Ar)CN (R = H, Me; Ar = Ph, 1- and 2-naphthyl) in 10% aqueous ethanol gave 50–90% of the corresponding β-hydroxynitriles RCH(OH)CH(Ar)CN, however the compound with R = H and Ar = 2-naphthyl, was not reduced under the conditions employed[134].

E. Nitro Group

Ethyl 2-cyano-3-(2-nitrophenyl)-2-propenoate (ethyl α-cyano-*o*-nitrocinnamate, **12**) gives three or four polarographic waves, depending on pH[144]. The first wave is a four-electron reduction of the nitro group to the hydroxylamino group. Controlled-potential reduction of **12** in 70% ethanol containing 1.0M hydrochloric acid at the plateau of the first wave (−0.2 V vs. SCE) produced 2-amino-3-carboxyquinoline-1-oxide (**14**, 90% yield). The reduction consumed 4.2 F mol^{-1}. The reaction can be formulated as equation (46), where the hydroxylamino group attacks the cyano group



(12) (13) (14) (46)

with ring-closure to **14**. The cyclization reaction is so slow that it does not influence the polarographic curve of **12**. Compound **13** has not been isolated.

IV. ELECTROHYDRODIMERIZATION

A. Self-coupling

Following the reductive coupling of acrylonitrile[114,115] and other derivatives of α,β-unsaturated nitriles[113,116] to 'hydrodimers' upon treatment with alkali metal amalgams in strong mineral acid (equation 47), Baizer and coworkers[16–21] developed a

$$2\ CH_2{=}CHY \xrightarrow{2\ e/2\ H^+} +CH_2{-}CH_2Y)_2 \qquad (47)$$

useful electrochemical coupling of a variety of olefinic compounds to hydrodimers. A similar type of reaction is widely known with carbonyl type compounds and results in pinacolization (equation 48)[7,189]. The term hydrodimerization was introduced by Knunyants and Gambaryan[112].

$$2\ R^1CR^2{=}O \xrightarrow{2\ e/2\ H^+} (R^1\underset{|}{C}R^2{-}OH)_2 \qquad (48)$$

Though hydrodimerization of acrylonitrile itself or mixed reductive coupling with other activated olefins can also be conducted in comparable yield with sodium amalgam combined with certain catalysts[151], the electrochemical method has proved much superior for the dimerization of other α,β-unsaturated nitriles: e.g. methacrylonitrile and 3,3-dimethylacrylonitrile yield no dimer in the amalgam process, while the electrochemical process gives 75% and 87–93% yields, respectively[16,19]. Most extensively studied and optimized to nearly quantitative yield and CE is the electrohydrodimerization of acrylonitrile to adiponitrile, a key Nylon 66 intermediate. The preferred conditions require the electroreduction of a concentrated solution of the olefin in a mildly alkaline *hydrotrope* (or *hydrotropic solvent*), that is, a concentrated aqueous solution of a certain hydrotropic salt that is quite a good solvent for organic compounds [e.g. a concentrated aqueous solution of a tetraalkylammonium *p*-toluenesulphonate (R_4NOTs)], sometimes with the aid of an organic cosolvent, at lead or mercury cathodes[17,18]. If the catholyte has acrylonitrile concentrations much below 10% or contains alkali metal cations, increasing quantities of propionitrile appear as by-products. The nature of the electroreduction products of acrylonitrile in aqueous quaternary ammonium salts under mildly alkaline conditions also depends on the quantity of water in the catholyte[22].

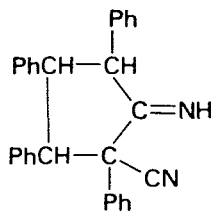
A number of α,β-unsaturated nitriles, having a variety of structural features, were successfully hydrodimerized electrochemically[19]. In most cases, the products obtained are those to be expected from coupling at the β positions and addition of hydrogen to the α positions. α-Methyleneglutaronitrile yields 1,3,6,8-tetracyanooctane, mainly as one diastereoisomer[23]. Although dimerization of crotononitrile (equation 49) and methacrylonitrile (equation 50) occurs largely through the β position, small amounts (8–11%) of dimers also arise through the α position[101].

$$MeCH{=}CHCN \longrightarrow \beta{-}\beta + \alpha{-}\beta \qquad (49)$$

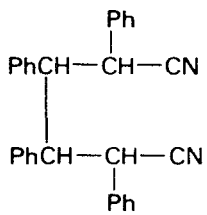
$$CH_2{=}\underset{|}{\overset{Me}{C}}CN \longrightarrow \beta{-}\beta + \alpha{-}\beta \qquad (50)$$

The electroreductive coupling at the first polarographic wave of β-substituted acrylonitrile has been studied[178]. Both symmetrical and unsymmetrical hydrodimers were observed together with dihydro monomers. For example, cinnamonitrile afforded

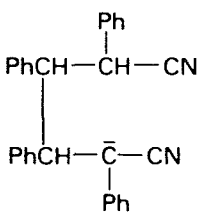
four isomers on hydrodimerization: 3,4-diphenyladiponitrile (16%), 2-benzyl-3-phenylglutaronitrile (42%), a substance which was probably 2,3-dibenzylsuccinonitrile (7%) and an unidentified isomer (9%). These products were obtained in the presence of tetraalkylammonium ions, while in the presence of lithium ions almost exclusively 3,4-diphenyladiponitrile was formed[179]. α-Phenylcinnamonitrile afforded dimer **15** together with a small amount of dimer **16** in the prsence of the Et_4N^+ ion, while, with sodium as the counterion, about equal amounts of these two isomers were obtained. In the case of the lithium ion the main product was **16**. These results illustrate the differences between the hydrated alkali metal cations and the hydrophobic quaternary ammonium cations. As shown in Section IV.C, these reactions involve the final intermediate **17**. In the former case **17** is immediately hydrated to **16**, whereas in the latter case **17** escapes hydration long enough to be able to engage in the intramolecular reaction leading to **15**.



(15)



(16)



(17)

Allyl cyanide gives a quantitative yield of a single isomer of 3,4-dimethyladiponitrile previously obtained from crotononitrile[170]. The base-catalysed equilibration of β,γ–α,β-unsaturated systems is known extensively.

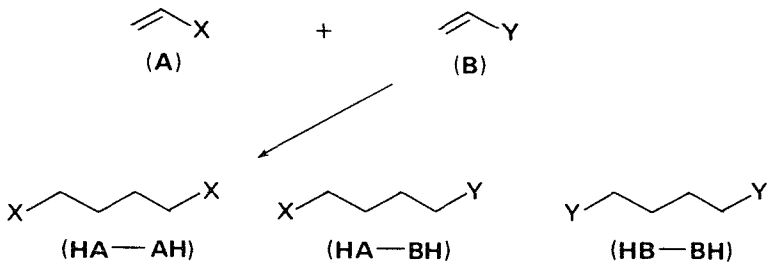
In the dimerization of activated dienes coupling may occur at the β or δ positions, and so, neglecting stereochemistry, three possible products (β—β and δ—δ by self-coupling and β—δ by cross-coupling) can arise. Hydrodimerization of 1-cyano-1,3-butadiene in aqueous R_4NOTs yields mainly the product of δ—δ coupling, 1,8-dicyano-octa-2,6-diene[20]. After catalytic hydrogenation of the intermediate products, a small amount of saturated β—β coupling product, 3,4-diethyladiponitrile, was found as by-product.

Electroreductive coupling has been extended to intramolecular reactions capable of yielding a wide variety of cyclic compounds. 1,6-Dicyanohexa-1,5-diene undergoes 'electrohydrocyclization' to form the cyclobutane in a low yield[9,176].

Independently of Baizer, Tomilov and coworkers[219] studied the electrohydrodimerization of allyl cyanide, crotononitrile and methacrylonitrile in aqueous solutions of sodium hydroxide with different cathode materials. The greatest yield of hydrodimer (57%) was obtained from crotononitrile, the maximum yield of hydrodimer from methacrylonitrile was considerably lower (13%), while allyl cyanide formed no hydrodimer at all. A graphite cathode is the most effective for the purpose under consideration. In neutral solutions of potassium phosphate the electroreduction of 1,4-dicyano-1-butene produced a small amount of the hydrodimer, γ,δ-di(cyanomethyl)-suberonitrile, along with the main dihydro product[208].

B. Cross-coupling

Baizer[18] has considerably enhanced the synthetic usefulness of the hydrodimerization reaction through the introduction of the concept of mixed reductive coupling of two different activated olefins A and B. Previously, the literature on electrochemical mixed coupling was restricted to the preparation of mixed pinacols in



SCHEME 3

acid medium from a mixture of ketones[8]. The reaction proceeds via an addition of cathodically generated anionic species to polarized (but not reduced) counterpart molecules. In principle, such reactions can afford three different products (Scheme 3). However, if A is easier to reduce than B by at least 0.2 V and reaction is carried out at the reduction potential of A, then, neglecting a homogeneous exchange electron transfer with the partner, only HA—AH and HA—BH are formed. The yield of HA—BH relative to HA—AH can be enhanced by employing B in large excess. The ratio of cross-coupled to self-coupled product also increases substantially as the controlled cathode potential is made more negative without reducing B[27]. This is exemplified by mixed coupling of the pairs diethyl maleate and acrylonitrile or *trans*-ethyl 3-cyanoacrylate and acrylonitrile. Even under the latter conditions, however, if the reduction potentials of A and B are more than ca. 0.4 V apart, HA—AH is formed along with very little, if any, HA—BH[178]. When the reduction is carried out at the cathode potential negative enough to reduce B, CEs of the mixed products increase and couplings which fail at the less negative potential can occur[29].

A variety of activated mono- and di-olefins such as ethyl acrylate, diethyl maleate, diethyl fumarate, methyl α-acetamidoacrylate, 1-cyano-1,3-butadiene[18], *N,N*-dimethyl-β-carbethoxyacrylamide, ethyl β-cyanoacrylate[178], 9-benzalfluorene, 8,8-diphenylbenzofulvene[21], α-methyleneglutaronitrile[23], styrene and 1,1-diphenylethylene[29], coupled with acrylonitrile to yield cross-coupled products. The catholyte occasionally contained DMF or acetonitrile as cosolvent in order to ensure homogeneity. Mixed coupling products have also been obtained with benzalacetone or mesityl oxide and acrylonitrile[24,34]. With these α,β-unsaturated ketones, the carbonyl moiety remains intact.

Sugino and Nonaka[213,214] found that acetone could be cross-coupled with acrylonitrile in aqueous sulphuric acid at a mercury cathode. At the potential region adopted (−1.2 V vs. SCE) only acetone is discharged. This reaction is also applicable to other aliphatic ketones. In Et_4NOTs, the reaction occurs at −1.90 V. The yield of the cross-coupled product decreases. The half-wave potentials of acrylonitrile and acetone in this electrolyte system are −1.9 and −2.4 V, respectively. The authors have suggested that acetone reduces to a carbanion which adds to an acrylonitrile molecule with subsequent protonation to yield γ-hydroxy-γ-methylvaleronitrile (equation 51). On

$$Me_2CO \xrightarrow{2\,e/H^+} Me_2\bar{C}OH \xrightarrow{CH_2=CHCN} Me_2C(OH)CH_2\bar{C}HCN \xrightarrow{H^+} \text{product} \qquad (51)$$

the other hand, Brown and Lister[50] have proposed a radical mechanism (equation 52). A primary electron transfer occurs to an adsorbed acetone molecule, with protonation, yielding an adsorbed radical which is the common precursor of the

$$Me_2CO \xrightarrow{e/H^+} Me_2\dot{C}OH \xrightarrow{CH_2=CHCN} Me_2C(OH)CH_2\dot{C}HCN \xrightarrow{e/H^+} \text{product} \quad (52)$$

diverse products of acetone reduction alone and of the coupled products obtained in the presence of acrylonitrile.

Acrylonitrile can reductively couple with acetone, benzophenone and benzaldehyde in aqueous Et_4NOTs in the presence or absence of DMF[29]. In this electrolyte system, the ketone acts as an acceptor. Mixed coupling only occurs beyond the electrode potentials required for the reduction of acrylonitrile. However, benzaldehyde couples reductively with acrylonitrile even at a potential sufficient to reduce only benzaldehyde.

Reduction of benzalaniline in the presence of excess acrylonitrile gives, among other products, 1,5-diphenyl-2-pyrrolidone[26].

C. Mechanism

Originally, Baizer[16,17] proposed that in hydrodimerization of derivatives of α,β-unsaturated nitriles (using acrylonitrile as an example), the dianion, which is probably formed in two successive one-electron steps through the anion radical, or its α-protonated form, engaged in nucleophilic attack. The β-position of the dianion or carbanion would attack the β-position of another molecule of polarized (but not reduced) starting material to yield the coupled carbanion. Beck[33], based on an analysis of current–potential curves for the reduction of acrylonitrile, proposed a rate-determining step involving one electron and one water molecule to form a neutral radical, which is immediately reduced further to the protonated carbanion. However, Figeys[85] showed that according to the atom localization energies calculated by the LCAO method the site of protonation of acrylonitrile anion radical and the position of attack on the neutral molecule is not the α but the β position. If so, the resultant products would be branched-chain dimers rather than the linear dimers that are mainly observed. These results lead to the conclusion that a major pathway to the cathodic formation of dimeric products at the first reduction wave is the nucleophilic attack of the intermediate anion radical on the starting material (equation 53), rather than protonation of the anion radical followed by reduction to an anion and subsequent attack on the olefin.

Another possible mechanism is an *EC* mechanism, viz. radical dimerization of two anion radicals followed by the reaction of the resulting dicarbanion with water or other proton donors (equation 54).

Petrovich, Baizer and Ort attempted to distinguish experimentally these two possibilities using CV[177] and product analyses[178] and concluded tha a major pathway to the cathodic formation of dimeric products is an *ECE* mechanism (equation 53). This

$$CH_2=CHCN \xrightarrow[(E)]{e} CH_2=CHCN^{\cdot-} \xrightarrow[(C)]{CH_2=CHCN} NC\dot{C}HCH_2-CH_2\bar{C}HCN \xrightarrow[(E)]{e/2\,H^+} \text{hydrodimer} \quad (53)$$

conclusion is based on the use of the tetraalkylammonium cation in DMF solutions. Petrovich and Baizer[179] also favoured an *EC* mechanism (equation 54) by using alkali metal cations.

$$2\,CH_2=CHCN^{\cdot-} \xrightarrow[(C)]{} NC\bar{C}H-CH_2-CH_2-\bar{C}HCN \xrightarrow{H^+} \text{hydrodimer} \quad (54)$$

The mechanism of electrohydrodimerizations of activated olefins and related substances has more recently been the subject of numerous investigations. The mechanism which has emerged, based on chronoamperometric[55], rotating ring-disc electrode[183,184], ESR spectroscopic[90], linear scan voltammetric[129,130], chronopotentiometric[190] and a.c. polarographic[98] studies, is one in which the predominant pathway of the electrohydrodimerization reaction for reduction at the first wave is an initial one-electron transfer at an electrode, followed by a second-order radical dimerization of the electrogenerated ion radicals (*EC* mechanism) to a dicarbanion and subsequent protonation, rather than reaction of the anion radical with parent and subsequent electron transfer (*ECE*) or initial formation of a dianion (*EE*).

Rate constants for anion-radical dimerizations determined by rotating ring-disc electrodes were found to be 110 (dimethyl fumarate), 880 (cinnamonitrile), and 7×10^5 (fumaronitrile) $M^{-1}\,s^{-1}$ [183]. Rate constants obtained by ESR agree with those determined as above and with other electrochemical measurements[90].

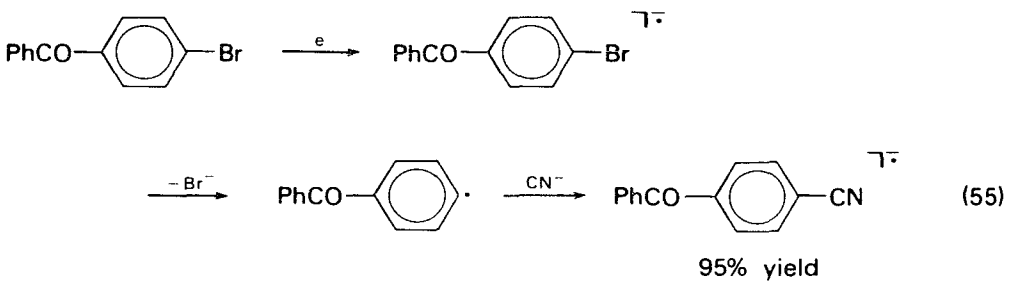
The effect of alkali metal ions on rates of dimerization in DMF has been studied by chronoamperometric and chronocoulometric techniques[99]. The addition of alkali metal ions (M^+) greatly increases the rate of dimerization of anion radicals ($R^{\cdot-}$) and a mechanism based on formation of the ion pair ($M^+R^{\cdot-}$) followed by reaction of $M^+R^{\cdot-}$ with $R^{\cdot-}$ or coupling of two $M^+R^{\cdot-}$ species has been proposed based on an analysis of the kinetic data.

V. ELECTROREDUCTIVE NITRILE FORMATION

A. Cyanation

Electroreduction can be used to induce aromatic nucleophilic substitutions by setting up the electrode potential at the reduction level of the substrate in the presence of a nucleophile[181]. Controlled-potential reduction of 4-bromobenzophenone in acetonitrile at −1.7 V vs. Ag/Ag^+ in the presence of Et_4NCN formed the 4-cyanobenzophenone anion radical. When cyanide, unlike thiolate, is used as nucleophile, the process is not entirely electrocatalytic since the anion radical of the cyano-substituted product is electrochemically stable toward the electrode at the reduction potential of the starting material and also toward the starting halogeno compound itself as far as solution electron exchange ($ArCN^{\cdot-} + ArBr \rightleftarrows ArCN + ArBr^{\cdot-}$) is concerned; a part of the desired product has to be obtained from further separate oxidation of its anion radical (see equations 9, 10, 16–18 in Section II.B).

Air oxidation gives a good yield of the final substitution product (equation 55).



(55)

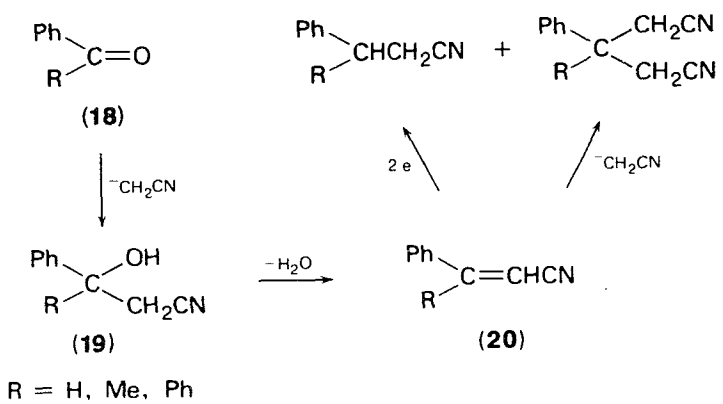
95% yield

Electrochemical reoxidation, either shifting the potential to −1.4 V after reductive production of the anion radical, or carrying out the experiment in an undivided cell with a platinum anode, also leads to 4-cyanobenzophenone, although in a somewhat smaller yield. The reaction mechanism involves the formation of the anion radical at

the electrode and its further decomposition into a neutral electrophilic radical which reacts with the nucleophile yielding the anion radical of the substituted product. In the case of 1-bromonaphthalene, practically no substitution product was found in preparative-scale electrolysis. As described in Section II.B, the potentiostatic reduction of 4-chlorobenzonitrile in DMF in the presence of cyanide ion gives rise to a small amount of terephthalonitrile anion radical[32].

B. Cyanoalkylation

Abbot, Bellamy and Kerr[1] have reported that electroreduction of acetophenone at a mercury cathode (−3.0 V vs. Ag/Ag^+) in dry acetonitrile gives a mixture of 3-phenylbutyronitrile (30%) and 3-methyl-3-phenylglutaronitrile (35–40%). Related carbonyl compounds, e.g. benzaldehyde and benzophenone, give similar products. By analogy with the known chemical reactions of the conjugate base of acetonitrile with carbonyl compounds[105,229], they have suggested that the first step in the formation of these products (Scheme 4) involves the addition of the cyanomethyl anion [generated by proton abstraction from the solvent by the strong bases present (anion radicals and/or dianions formed by a direct 2 e process or via disproportionation electron transfer of anion radicals), which would be formed by electron addition to either the starting carbonyl compound **18** or the intermediate α,β-unsaturated nitrile **20**] to the carbonyl group to form a hydroxynitrile **19**. They have presented voltammetric evidence which supports their reaction mechanism and which indicates that the addition is fast[40,41]. In the presence of either an aromatic carbonyl compound or the corresponding α,β-unsaturated nitrile, the nucleophile ($^-CH_2CN$) is electrogenerated indirectly, or directly, in two ways, (*a*) by reduction of azobenzene in acetonitrile and (*b*) by reduction of cyanomethyltriphenylphosphonium and arsonium cations in DMF. The reduction of azobenzene in acetonitrile is known to involve two one-electron transfer steps, the anion radical being stable but the dianion being rapidly protonated by the solvent to give the conjugate base of hydrazobenzene and the cyanomethyl anion[47]. The reduction of the cyanomethyltriphenylphosphonium cation also involves the transfer of two electrons at the first reduction peak, generating triphenylphosphine and the cyanomethyl anion (see Section II.G and II.H). The electrochemical behaviour of the cyanomethyltriphenylarsonium cation has been found to be similar to that of the phosphorus analogue.



SCHEME 4

The carbonyl groups of *p*-phenylthioacetophenone[230] and isobutyraldehyde[35] are attacked by cyanomethyl anions derived from solvent acetonitrile. This anion is also able to add to acetonitrile and subsequently the adduct undergoes protonation leading to 3-iminobutyronitrile (70% CE)[35].

Kistenbruegger and coworkers[111] have reported the analogous condensation reactions of acetonitrile using cathodically generated bases. The electroreduction of alkyl benzoates in dry acetonitrile near their peak potentials yields benzoylacetonitrile, together with benzoic acid and alcohol, and occasionally, hydrocarbon. When the reaction is performed in propionitrile, α-benzoylpropionitrile is obtained. The electrochemical reduction of methyl phenylglyoxalate gives methyl 3-cyano-2-hydroxy-2-phenylpropionate together with phenylglyoxalic acid and methyl mandelate under the same conditions. Analogously, β-(dialkylamino)cinnamonitriles (10–36% yield) can be obtained from *N,N*-dialkylthiobenzamides. *N*-Methylthiobenzanilide did not produce the corresponding aminocinnamonitrile, but gave *N*-methylaniline and *trans*-stilbene together with a trace of benzoylacetonitrile. The reaction proceeds through an initial electron transfer from the substrate. Cathodically generated bases abstract a proton from residual water and solvent acetonitrile to produce hydroxide ions and cyanomethyl anions, respectively. These anions react with the substrate to form alcohol, carboxylate and enolate anions, and the latter give the observed products upon treatment with water or acid. While the electron transfer to *N,N*-dimethylbenzamide occurs at a very high negative potential ($E_{1/2} < -2.4$ V), the reduction of this compound was performed in the presence of azobenzene, as in Bellamy's studies.

Takahashi and coworkers[217] have reported that electrolyses of trialkylboranes in aliphatic nitriles containing tetraalkylammonium halides at platinum electrodes form nitriles. The reaction was carried out in acetonitrile nonpotentiostatically in an undivided cell. Trihexylborane gave octanenitrile in 52% yield. With solvent propionitrile 2-methyloctanenitrile was obtained in 27% yield. Electrolyte anions such as bromide and iodide were effective. When using a divided cell, nitriles were not found but alkyl halide was mainly obtained in the anode compartment. The reaction is interpretable as nucleophilic attack of the cathodically generated cyanoalkyl anion on the alkyl halide produced anodically. When acetone was used instead of organoboranes, 3-hydroxy-3-methylbutanenitrile was produced.

In accordance with the above coupled reaction mechanism, the nonpotentiostatic reduction of bromoalkanes such as *n*-pentyl and *n*-hexyl bromide in aliphatic nitriles at platinum electrodes has been carried out with the formation of cyanoalkylated products in 67–89% yield[31].

The electrochemical reduction of α,β-unsaturated nitriles in aqueous alkaline solution at a tin cathode gives organotin compounds[103]. Tetrakis-2-cyanoethyltin and tetrakis-2-cyanopropyltin have been obtained by the reduction of acrylonitrile and methacrylonitrile, respectively. The structure of the organotin compound produced from 1-cyano-1,3-butadiene has not yet been identified.

The cathodic reduction of organic halides has been used for the preparation of organometallic compounds. Electroreduction of 3-iodopropionitrile in 0.5N sulphuric acid or in neutral sodium sulphate solution yields hexakis(2-cyanoethyl)ditin (12%), tetrakis(2-cyanoethyl)lead (13%), bis(2-cyanoethyl)mercury (46%), 2-cyanoethylmercuric iodide (4%) and bis(2-cyanoethyl)thallium iodide (5%)[220]. These organometallic compounds are probably formed by reaction of the cathode material with the cyanoethyl radical formed in the first stage of the reduction of 3-iodopropionitrile (equations 56 and 57). The formation of 2-cyanoethylmercuric iodide occurs only in the electrolysis of neutral solutions, and probably arises from the reaction of iodopropionitrile with the sodium amalgam formed at the cathode. In acid medium this

$$NCCH_2CH_2I \xrightarrow{e} NCCH_2CH_2^{\cdot} + I^- \quad (56)$$

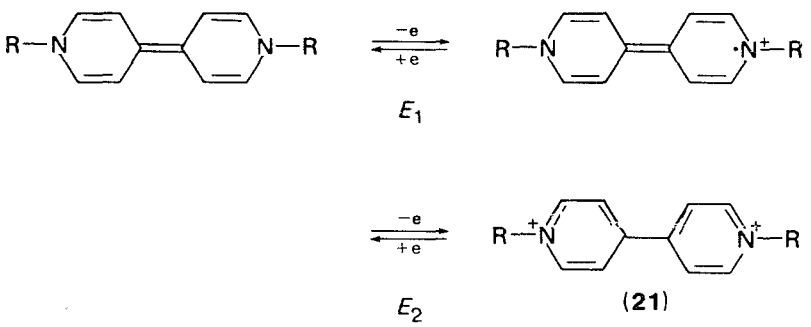
$$NCCH_2CH_2^{\cdot} + M \longrightarrow NCCH_2CH_2M \quad (57)$$

organomercuric halide is not formed. The nature of the reactions leading to the formation of bis(2-cyanoethyl)thallium iodide has not been elucidated.

Electrolyses of cyanoalkylsulphonium[237] and phosphonium[236] ions at a mercury electrode have yielded, together with other products, bis(cyanoalkyl)mercury, $Hg[(CH_2)_nCN]_2$.

VI. MISCELLANEOUS REDUCTIONS

Hünig and coworkers[100] continue to study the redox chemistry of violenes. Violenes are cation radicals derived from conjugated systems of the type $X—(CH=CH)_n—X$, in which n may be zero and X may be NR_2, SR or OR. Voltammetry of the *N*-substituted 4,4′-bipyridyls [**21**, where R = CH(CN)COOEt, $\bar{C}$(CN)COOEt, $\bar{C}(CN)_2$] yields



(58)

reversible two-step electron transfers. The difference between the redox potentials E_1 and E_2, which can be correlated with the Taft substituent constants σ^*, decreases if potentials become more positive. The first redox potentials (E_1) have been correlated with the absorption maxima of the radical cations.

The cathodic reduction and anodic oxidation of mono- and bis-hydrazyls of the *N,N*-diphenyl-*N′*-(2,4,6-tricyanophenyl)hydrazyl type have been studied[188]. For example, the polarographic curves of the monohydrazyls such as 3,5-difluoro (or dichloro)-2,4,6-tricyanophenyl(*N′,N′*-diphenylhydrazine) and *N,N*-diphenyl-*N′*-picrylhydrazyl (DPPH) in benzonitrile show a single reversible one-electron anodic wave and a single reversible one-electron cathodic wave of equal height. The d.c. polarograms of the bishydrazyls such as 5-phenoxy-2,4,6-tricyano-1,3-phenylenebis-(*N′,N′*-diphenylhydrazine) give four waves of equal height. The oxidation occurs in two reversible one-electron waves. The first reduction wave is reversible, the second one pseudo-reversible, each corresponding to one-electron addition. A linear relationship exists between the half-wave potentials and the inductive effects of the substituents of the tricyanobenzene ring.

Preparative-scale electroreduction of ethyl 2-cyano-3-cyclopropyl-2-butenoate in DMF containing both water and acetic acid gives ring-cleavage products, ethyl 2-cyano-3-*n*-propyl-2-butenoate and ethyl 2-cyano-3-*n*-propylbutanoate in a ratio of 5:1[28]. The reduction of the unsaturated product under the same conditions yields the saturated derivative. Thus the cyclopropyl group of the starting vinylcyclopropane undergoes selective reductive ring-cleavage leaving the double bond intact, with the electroanalytical data indicating that the cleavage occurs at the anion-radical stage.

The controlled-potential reduction of 1-cyclopropylethylidenemalononitriles in acetonitrile also gives the ring-cleaved products[42]. In the presence of phenol as an effective proton donor, these cleaved products are further electroreduced to the saturated malononitrile derivatives. Linear sweep voltammetry indicates that the reduction mechanism involves the sequence: electron transfer at the electrode, ring-cleavage, electron transfer in solution (the resultant ring-opened anion radical is reduced by the initial anion radical), rather than at the electrode, and protonation (by the substrate or during work-up).

Anion radicals of acrylonitrile and methacrylonitrile generated at a mercury cathode under anhydrous conditions react rapidly with carbon dioxide[228]. Further reduction of the resultant radical carboxylate intermediate and subsequent carboxylation results in the formation of substituted succinic acid derivatives (equation 59). When the reduction potential of the olefin approaches that of carbon dioxide ($E_{1/2} = -2.3$ V vs. SCE), it becomes less clear whether reduced carbon dioxide (i.e. $CO_2^{\cdot-}$) or the anion

$$\begin{aligned} CH_2{=}CHCN &\xrightarrow{e} [CH_2{=}CHCN]^{\cdot-} \xrightarrow{CO_2} {}^{-}O_2CCH_2\dot{C}HCN \\ &\xrightarrow{e} {}^{-}O_2CCH_2\bar{C}HCN \xrightarrow{CO_2} {}^{-}O_2CCH_2CH(CN)CO_2^{-} \qquad (59) \\ & \qquad\qquad\qquad\qquad\qquad\qquad 41\%\ CE \end{aligned}$$

radical of the olefin is the primary electrode product which participates in the subsequent chemical reactions. Monocarboxylation is realized by adding water at low levels (2.8M) to an aprotic solvent. For example, acrylonitrile is converted to 3-cyanopropionic acid.

Acetic anhydride, like carbon dioxide and proton donors such as phenol, may serve as a trapping agent for anionic electrode intermediates[62,89]. The potentiostatic reduction of crotononitrile and cinnamonitrile in anhydrous acetonitrile containing the acylating agent and a supporting electrolyte, using carbon-rod electrodes in a divided cell, gives the product RCH(Ac)CH_2CN (51% yield for R = Me, 76% yield for R = Ph)[205].

Controlled-potential electrolysis of β-bromo-β-nitrostyrene at a mercury cathode (−0.4 V vs. SCE) in 80% aqueous dioxane containing 0.3M sulphuric acid yields benzyl cyanide (80%) and benzaldehyde (10%)[13,59]. When the reduction is performed in aqueous methanol, some mandelonitrile methyl ether is formed in addition to the preceding products. The reduction mechanism has not been fully elucidated.

VII. ELECTROOXIDATIVE NITRILE FORMATION

A. Anodic Cyanation

Anodic oxidation of aromatic compounds in solutions containing cyanide ions gives nitriles. Three different solvent systems are available for this cyanation. First, a protic solvent such as methanol can dissolve alkali metal and mercuric salts as well as tetraalkylammonium salts and is favourable from the voltammetric point of view, viz. as a solvent–electrolyte system with wide anodic limits. A methanol solvent system was first examined by Tsutsumi, Koyama, and Yoshida[121,245], and independently by Parker and Burgert[172]. However, the use of this nucleophilic solvent in early studies, led to the competitive formation of methoxylated products which were often predominant over the cyanation products. In those days, the oxidation potential of cyanide ions was thought to be considerably lower than that of common organic compounds[70,172,197]. If this was the case, cyanide ion would not survive the potential

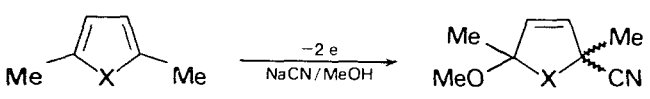
necessary to oxidize the reactant. Yoshida investigated this solvent system and found that the background current with the MeOH/NaCN system was negligible up to 1.4 V vs. SCE at platinum anode[246,248]. The relatively wide anodic limit for this solvent–electrode couple should permit the electrochemical method to work successfully, because, as described later, anodic cyanation commences with the discharge not from cyanide ion but from the organic substrate. CAUTION: *A methanolic sodium cyanide solution must be handled in a well-ventilated room as it contains hydrogen cyanide as a result of the equilibrium between CN^- and the solvent methanol!*

A second system is the adoption of a polar aprotic organic solvent. Tetraalkylammonium and tetraphenylarsonium cyanide are soluble in acetonitrile and DMF. As mentioned below, acetonitrile is suitable for replacement of aromatic methoxy by cyano groups and for the introduction of a cyano group into an α position of tertiary amines[10]. For replacement of aromatic hydrogen, however, a cyanide salt in methanol is the preferred medium. This system is less satisfactory from other points of view, e.g. by giving low CE due to concurrent discharge of cyanide ion at the potentials where the oxidation is efficiently conducted. Acetonitrile used in conjunction with a crown ether could be a promising solvent system, since, for example, potassium cyanide dissolves in acetonitrile in the presence of 18-crown-6, but such systems have not yet been studied!

A third possibility is to use an emulsion system with the aid of phase-transfer agents. The system consists of a substrate, methylene chloride, aqueous sodium cyanide and a phase-transfer agent (Bu_4N^+ ion as the sulphate)[74]. The Bu_4N^+ ion extracts CN^- ion almost quantitatively from water to methylene chloride, and emulsification is achieved by use of a special high-speed stirrer. One advantage of using emulsified systems is the relatively high conductivity of the electrolytic solutions, while the phase-transfer agent ensures that the electrode process takes place in the organic phase.

By 1968, anodic oxidation of a variety of benzenoid compounds and some olefins in MeOH–NaCN had been carried out, which included benzene, toluene, ethylbenzene, isopropylbenzene, *t*-butylbenzene, mesitylene, tetralin, anisole, chlorobenzene, methyl benzoate, biphenyl, naphthalene, anthracene and 1,3-butadiene[70,122,173,215]. The CE of the resultant nitriles was very low (e.g. 12% in the case of anisole). Substrates with higher oxidation potentials underwent no cyanation. Alkylbenzenes gave the side-chain methoxylation products predominantly. With MeOH–KCN, *p*-xylene gave *p*-(methoxymethyl)toluene along with smaller amounts of 2,5-dimethylbenzonitrile[10].

Synthetically successful cyanations in solvent methanol were first reported by the writer[246,248,257]. 2,5-Dimethylfuran underwent a mixed anodic 1,4-addition of one cyano and one methoxy group with the formation of a 2:1 mixture of *cis*- and *trans*-2,5-dihydro-5-methoxy-2,5-dimethyl-2-furonitrile in about 60% CE, together with small amounts of methoxylation products (equation 60). The electrooxidation was

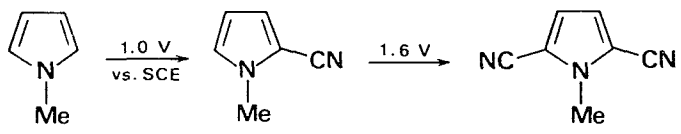


X = O, S (60)

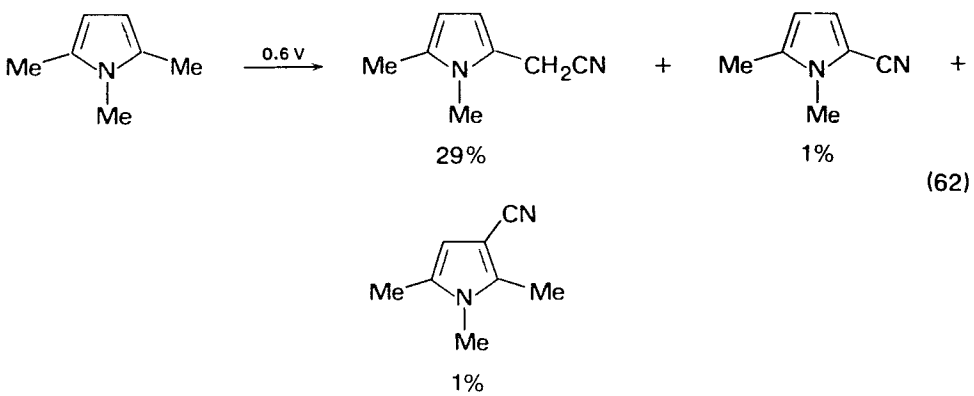
performed under both potentiostatic and nonpotentiostatic conditions using a divided cell. When the reaction was conducted in an undivided cell, the yield decreased considerably. The reactions involve initial electron loss from the organic substrate and are sterically controlled by the electrode. Similar cyanomethoxylation occurred in the case of 2,5-dimethylthiophene[249].

This reaction has been extended to aromatic five-membered nitrogen heterocycles.

In the case of pyrroles, no reduction to 3-pyrrolines occurs and substitution products are exclusively formed[256,258,259]. The substitution occurs preferentially at the 2 (and 5)-position. When the substituent is attached to the 2-position, further substitution of the pyrrole ring occurs at a free 5-position irrespective of the nature of the substituent already present. For example, 1-methylpyrrole is converted to 1-methylpyrrole-2-carbonitrile, which can subsequently undergo anodic oxidation to afford 1-methylpyrrole-2,5-dicarbonitrile (equation 61). On the other hand, use of 2,5-dimethyl compounds leads to the formation of side-chain substitution products (equation 62). This is the first successful example of the direct anodic formation of a benzylic cyanide.



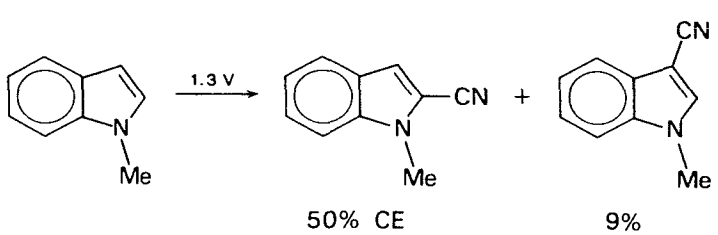
(61)



(62)

In the past, numerous attempts to get benzylic cyanides resulted in failure: the resulting products were frequently methoxylation products. Methyl displacement by the cyano group occurs slightly in some cases. The product yields from 1-phenylpyrroles are superior to those from 1-methylpyrroles. The methyl or phenyl group at the 1-position is not attacked.

Cyanation of indoles predominantly takes place at the 2-position (equation 63).



(63)

A similar preference has been observed in certain photochemical additions where electron transfer is believed to be involved[152,195]. Electrophilic substitution usually occurs at the 3-position of indoles, whereas radical reactions proceed less selectively to give mixture of 1-, 2-, 3-, 4- and 6-substituted indoles. Side-chain displacement of methylindoles has not been observed.

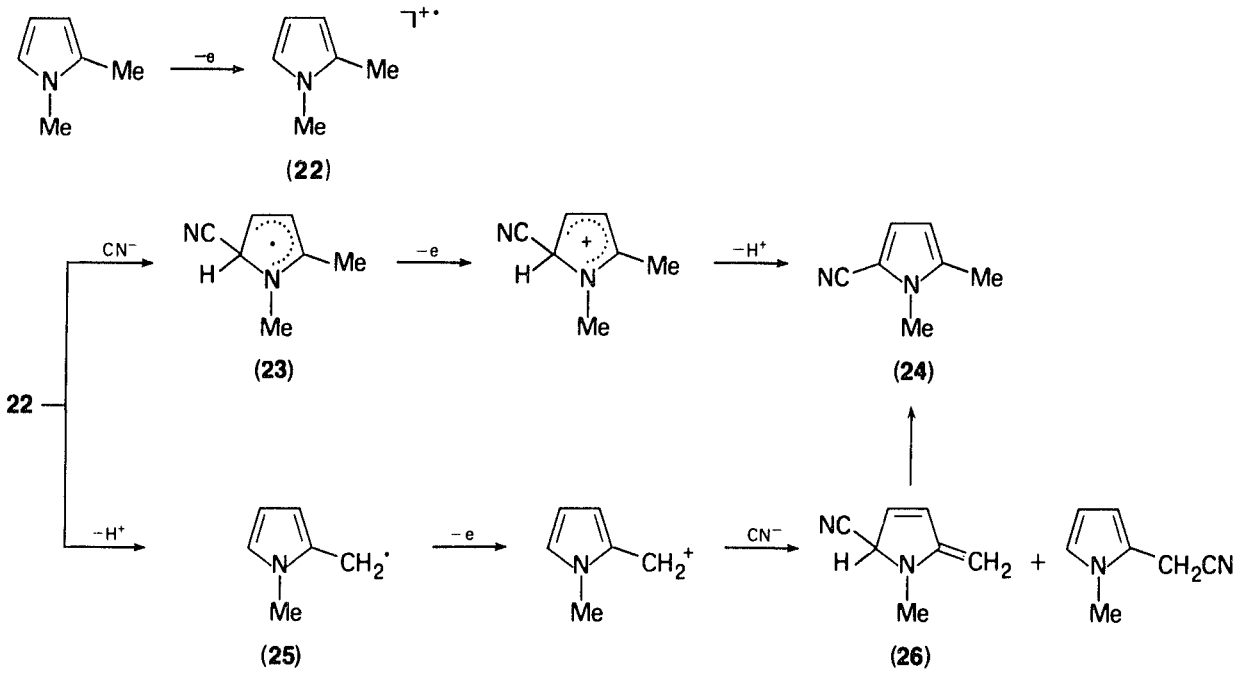
Consideration of the voltammetric characteristics, coulometry and a preferential attack on the 2-position of the indole molecule leads to the initial formation of a cation radical. The propriety of the proposal that anodic cyanation involves initial cation-radical formation is also proved by comparison with the photosensitized electron-transfer reaction in the same solvent system. The latter reaction proceeds via a free cation-radical intermediate. The unsymmetric 1,3-dimethylpyrrole and once again 1-methylindole were chosen as model compounds in order to study the orientation of the substitution products. The isomer distribution of the products coincided in both the anodic cyanation and photosensitized reactions. Net charge distribution calculated by the ω technique supports the observed reactivity of these cation radicals as well.

In the anodic substitution of 1,2-dimethylpyrrole, two competitive pathways are conceivable for the cation radical (Scheme 5). Firstly, the anodically generated cation radical **22** is attacked by the cyanide ion to produce the radical **23**, followed by further anodic oxidation and successive proton release, thus leading to the nuclear cyanation product **24**. Alternatively, **22** could undergo deprotonation to afford an analogue of a benzylic radical intermediate **25**, which would subsequently undergo anodic oxidation to give a cation, followed by nucleophilic attack by cyanide ion to give 5-methylene-1-methyl-3-pyrroline-2-carbonitrile (**26**), which should be eventually aromatized in protic solvents. To distinguish between these two possibilities, anodic oxidation of 1,2-dimethylpyrrole was examined in a CH_3OD solution of sodium cyanide. No incorporation of deuterium in the 2-methyl group of compound **24**, was observed, while trace amounts of 1-methylpyrrole-2-acetonitrile were detected. Therefore, the second (deprotonation) mechanism is not important for aromatic substitution. Analogous results were obtained in the anodic cyanation of 1,3-dimethylindole in CH_3OD. In this case, 1-methylindole-3-acetonitrile could not be detected.

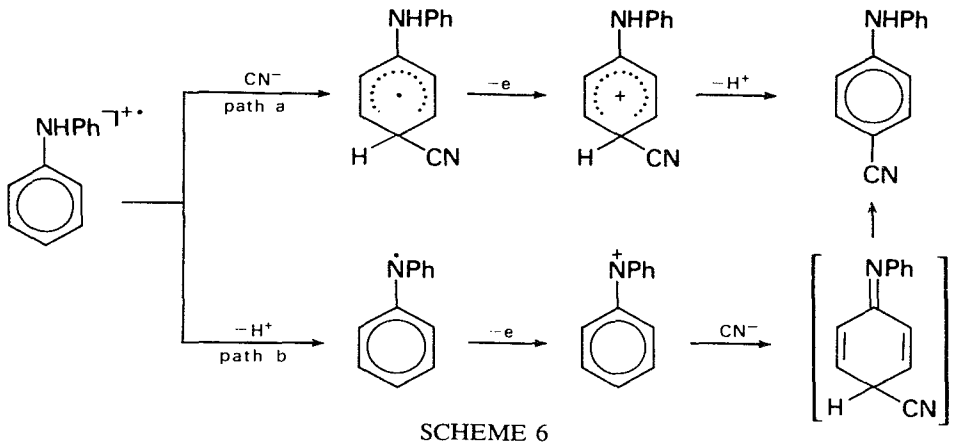
Certain arylpyrroles appear to yield 3-pyrrolines under cyanation conditions. When 1,2,3,5-tetraphenylpyrrole in MeCN–Et_4NCN was oxidized at a potential on the plateau of the first wave, 1,2,3,5-tetraphenyl-2,5-dicyano-3-pyrroline was obtained[141]. The yield was not reported.

When diphenylamine and its monosubstituted derivatives in MeOH–NaCN were electrooxidized at an anode potential between 0.3 and 0.6 V vs. SCE, nuclear cyanation products were obtained in good yields[250]. The nuclear substitution reaction of diphenylamines is uncommon[254]. With diphenylamines containing a methoxy or methyl group in the *ortho* or *meta* position as well as with unsubstituted diphenylamine, substitution occurred at the *para* position. *p*-Cyanodiphenylamine gave *p,p'*-dicyanodiphenylamine, but *p*-methoxydiphenylamine remained almost intact under these conditions even though it discharged practically. This phenomenon is ascribed to the regeneration of aromatic amine by electron transfer between the anodically generated cation radicals and the cyanide ion, as has already been indicated by using very stable cation radicals such as tri-*p*-anisylamine, tri-*p*-tolylamine and 9,10-diphenylanthracene in acetonitrile[171].

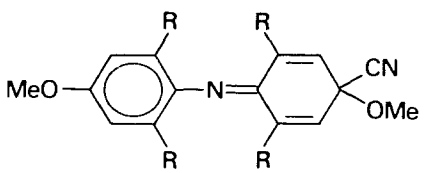
Since the applied potentials were too low to permit oxidation of cyanide ion, the reaction must involve the initial oxidation of the amine substrate to give a cation radical. The subsequent steps include addition of cyanide ion, transfer of a second electron and loss of a proton, but the timing of the attack by the cyanide ion is not clear. In addition to a direct nucleophilic attack on cation radicals, an alternative mechanism, although disproven experimentally for nuclear substitution of methylpyrroles, may remain valid in this case. The latter mechanism (path b in Scheme 6) was proposed by Serve[201] on the basis of the isolation of the quinoneimine cyanohydrin methyl ethers **27** from electrooxidation of di-*p*-anisylamines in MeCN–Et_4NCN. These products have been explained by the addition of cyanide ion to the electrogenerated nitrenium ion. However, direct addition of cyanide ion to the cation radicals can also


Me
N
Me
−e
Me
N
Me
⁻|⁺·
(22)
22
CN⁻
NC
H
N
Me
Me
(23)
−e
NC
H
N
Me
Me
−H⁺
NC
N
Me
Me
(24)
−H⁺
N
CH₂·
Me
(25)
−e
N
CH₂⁺
Me
CN⁻
NC
H
N
CH₂
Me
(26)
+
N
CH₂CN
Me

SCHEME 5



SCHEME 6



(27)

R = MeO, Me

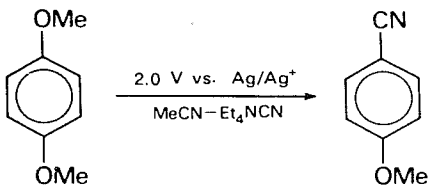
explain the formation of the adducts. Conclusive evidence as to a key intermediate has not yet been obtained.

Yoshida and coworkers have investigated in detail the anodic oxidation of a variety of methyl aromatic compounds in MeOH–NaCN and have clarified the factors controlling the competition between nuclear and side-chain substitution[249,252] and the orientation in nuclear substitution[248,259,260] involving the study of an MO reactivity index for the cation radicals. They have demonstrated that factors governing the competition are ascribable to reactivities of the cation radicals themselves (e.g. the degree of positive charge localized on the aromatic carbon atoms in the cation radicals and the relative stability of the initially formed cation radical and the benzylic radical produced by deprotonation) as well as to the nucleophilicity of the attacking agents.

They have used the results for the purpose of developing synthetically useful substitution reactions. In order to lower the oxidation potential of alkyl aromatic compounds and simultaneously to increase the positive charge localized on the aromatic carbon atoms in their cation radicals, a methoxy group was put on the aromatic ring[252]. In the case of *ortho*- and *meta*-substituted methylanisoles, substitution of an aromatic hydrogen by cyanide became the main reaction. With *p*-methylanisole, side-chain methoxylation surpassed nuclear cyanation. Net positive charge distributions calculated for methylanisole cation radicals show much the same distribution pattern as that of the substitution products of aromatic hydrogens by cyanide ions. Moreover, the relative degree of positive charge on the aromatic carbon atoms with hydrogen attached in the *p*-methylanisole cation radical is less than that in *o*- and *m*-methylanisole cation radicals. Therefore, the anodic oxidation of *o*- and *m*-methylanisoles occurs almost exclusively on the aromatic nucleus, whereas in the *p*-methylanisole

cation radical, a possible proton loss competes with nuclear attack. Aromatic substitution of methylpyrroles also belongs to this category. In this case the nitrogen atom plays a role as a suitable substituent. Condensed bicyclic aromatic compounds, e.g. methylnaphthalenes, could also be used as suitable model compounds. As expected, aromatic substitution with cyanide ion occurred preferentially and in good yields at the free α position in all the molecules investigated[260]. In this case, positional reactivities are rationalized in terms of the LUMO electron densities (i.e. charge-transfer interaction) rather than net positive charge distributions (i.e. electrostatic interaction).

Andreades and Zahnow[10] have developed the MeCN–Et_4NCN system. Two types of aromatic cyanation reactions are observed. One type is replacement of an aromatic methoxy group by cyanide ion. With di- and tri-methoxybenzenes, direct replacement occurs only when methoxy groups are situated in *ortho* and *para* positions. *p*-Dimethoxybenzene (equation 64), veratrole and 1,2,3-trimethoxybenzene give



(64)

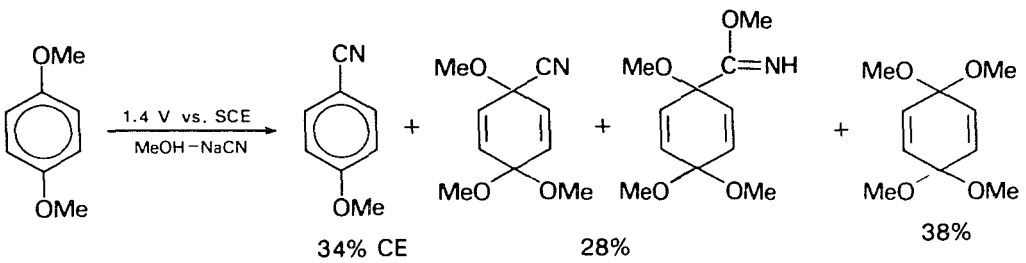
95% yield, 20% CE

anisonitrile, *o*-methoxybenzonitrile and 2,6-dimethoxybenzonitrile, respectively. Yields are generally >90% with CE of ~30%. With anisole and *m*-dimethoxybenzene, substitution of aromatic hydrogen occurs generally in much lower yields. Dicyanation is observed in the case of anthracene to give 9,10-dicyanoanthracene in 54% CE.

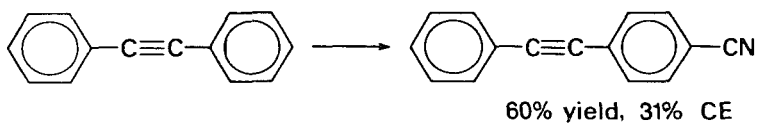
Replacement of aromatic methoxy by cyanide ion can be observed in other systems. Anodic cyanation of *o*- and *p*-methoxydiphenylacetylene in methanol affords cyanodiphenylacetylenes in 10–15% yield (based on current)[251]. Similarly, methylanisoles in methanol produce the corresponding methoxy displacement products together with other products[252]. The use of acetonitrile as solvent increases yields of methylbenzonitriles at the expense of hydrogen displacement. Replacement of methoxy by cyano groups was used to synthesize 4-alkoxy-4′-cyanobiphenyl, a class of liquid crystals. The oxidation of 4,4′-dibutoxy- and 4,4′-dioctyloxy-biphenyl in an emulsion system gave the desired products with good yield and with low CE, together with minor amounts of products originating from 1,4-addition of two cyano groups, hydrogen substitution and aromatic coupling[76].

The anodic cyanation of di- and tri-methoxybenzenes has also been studied in an emulsified aqueous–organic system, consisting of aqueous NaCN–CH_2Cl_2-substrate-phase-transfer reagent[75]. Substitution of both methoxy and hydrogen takes place, as was found by Andreades and Zahnow[10], and dicyanation also occurs to some extent. With methanol as solvent, *p*-dimethoxybenzene undergoes the addition of one cyano and one methoxy group across the aromatic nucleus in competition with methoxy displacement[242,253] (equation 65). Such a 1,4-mixed addition has been observed in furan and thiophene derivatives as described earlier. The CE of anisonitrile and of quinone diketal are highly potential-dependent, while the CE of 3-cyano-3,6,6-trimethoxy-1,4-cyclohexadiene taken together with its base-catalysed methanolysis product is found to be independent of potential. A similar trend appears on changing the concentration of cyanide ion in the bulk solution. Total CE is about 100%.

Anodic cyanation of diphenylacetylene (equation 66) and methoxydiphenylacetylenes in methanol occurs on the aromatic nucleus and not on the acetylenic triple



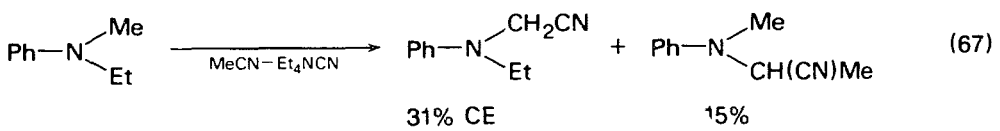
(65)



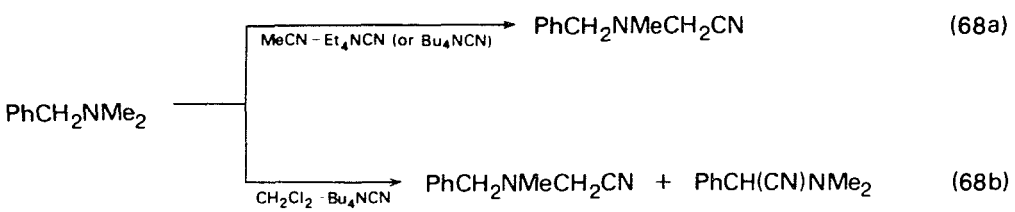
(66)

bond[247,251]. Methoxy displacement has been mentioned above. Nuclear substitution also takes place in competition with substitution of olefinic hydrogen in the anodic cyanation of *trans*-stilbene using an emulsion system[77].

Electrochemical oxidation of tertiary aromatic and aliphatic amines in MeCN–Et_4NCN effects introduction of a cyano group into an α position of an alkyl group[10]. Nuclear cyanation is not observed. In mixed amines, e.g. *N*-methyl-*n*-ethylaniline, cyanation occurs preferentially at a primary position (equation 67). Furthermore, benzyldimethylamine gives exclusive cyanation at a methyl group rather than at a benzyl position (20% CE) (equation 68a). Cyanation of the latter amine has also been



(67)



(68a)

(68b)

studied in an emulsion system using methylene chloride as the organic solvent component and CH_2Cl_2–Bu_4NCN[75]. About 50:50 mixtures of methylene and methyl substitution product are obtained (equation 68b). With *N*-methyldiphenylamine in methanol, cyanation at a methyl group supplants nuclear substitution[250]. Cyanation of tertiary aliphatic and heterocyclic amines in aq. MeOH–NaCN occurs exclusively at the α position of the aliphatic chain[54]. From the relative ratio of the isomers obtained from unsymmetric amines, the order of ease of substitution has been estimated.

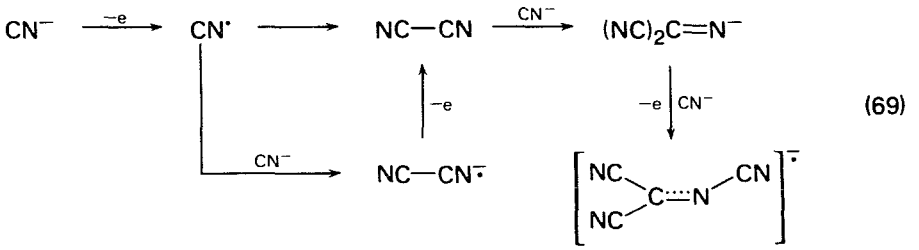
Anodic aromatic addition and substitution reactions are used for the synthesis of some chemically and biologically important nitriles. Substitution of olefinic hydrogen of uracil in MeOH–KCN gives 5-cyanouracil in 95% isolated yield[155]. The results of anodic substitution of simple alkyl-substituted phenol ethers have been utilized for the

cyanation of estrone methyl ether. 3-Methyl-estra-1,3,5(10)-triene-17-one in MeOH–NaCN gives the addition product, 10β-cyanoestra-1,4-diene-3,17-dione, in about 60% yield, together with minor amounts of two ring *A* substitution products and some methoxylation products[182]. Zinc-octaethylporphyrin in DMF–Et_4NCN–Et_4NClO_4 at the potential range of the first oxidation wave give quantitatively *meso*-monocyano-octaethylporphyrin[52]. At higher potentials and on adjusting the concentration of cyanide, di-, tri-, and tetra-cyanated porphyrins have been obtained with good selectivity and yields.

Anodic oxidation of organic substrates in the presence of cyanide ions occasionally results in isocyanation. Anodic isocyanation is an unusual reaction even though isocyanides of unknown structure have been detected in the product mixtures[122,215]. Two examples of the generation of isocyanides have been reported: 1,4-addition to 9,10-dialkylanthracenes[174] and the formation of 3-isocyanocyclohexene (2–6% yield) and isocyanocyclohexane (0.1–0.7% yield) from cyclohexene[255]. In the former case the exact structure and yields of isocyanides were not given.

Anodic aromatic cyanation has been compared with photoinduced nucleophilic substitution of aromatic compounds in the presence of cyanide ion. These photochemical reactions include direct excitation of the substrate[64,165] and the use of a sensitizer such as acetone[64] or an electron-accepting sensitizer such as 1-cyanonaphthalene or 1,4-dicyanobenzene[258,259] and appear to proceed via solution-phase cation-radical intermediates. Den Heijer and coworkers[64] used aqueous *t*-butanol as a solvent to keep similar reaction conditions with the corresponding photochemical reaction.

Under the anodic cyanation conditions, especially at relatively high potentials, frequently a reaction may give a high material yield while its CE is very low. Possibly, the cyanide ion (and its conjugate bases as result of the equilibrium between CN^- and protic solvents) discharges together with the organic substrate to produce a cyano radical, which does not enter into organic products but, as found by Andreades and Zahnow[10], will attack the cyanide ion to form cyanogen anion radical or dimerize to cyanogen (equation 69). The excess current would thus be consumed by inorganic electrode processes as well as by the regeneration of the substrate by homogeneous electron transfer as mentioned in the case of *p*-methoxydiphenylamine[250].



(69)

Finally, the combination between electrogenerated cation radicals and cyanide anions has to be discussed. Reduction of and addition to the cation radical have reciprocal effects on each. This problem has been treated using methylnaphthalene cation radicals in MO calculations[260]. Evidence of electron transfer is suggested by the quantitative regeneration of the anodically oxidized starting material and by the appearance of the anodic catalytic currents in the cyclic voltammogram of the reactant in the absence and presence of different concentrations of cyanide ion. The redox reaction between tri-*p*-anisylamine cation radical and cyanide ion in acetonitrile is rapid and gives a value of about 10^5 M^{-1} s^{-1} as the second-order rate constant[46,171]. The rate constant[81] of the reaction of the cation radical of 9,10-diphenylanthracene

with cyanide ion in acetonitrile is 6×10^6 M^{-1} s^{-1}, with the cyanide ion behaving as a reductant. The second-order rate constant[82] for the addition reaction of perylene cation radical with cyanide ion in methanol is found to be equal to 4.6×10^5 M^{-1} s^{-1}.

B. Anodic Formation of CN Group

Anodic oxidation of an α-amino acid produces the corresponding nitrile. Leucine produces isovaleronitrile in 30% yield together with isovaleraldehyde in dilute sulphuric acid[158]. The oxidation of isonicotinic thioamide in alkaline solution at a mercury electrode yields 4-cyanopyridine and mercury sulphide[143]. Polarographic oxidation of *o*-phenylenediamine in the presence of proton acceptor shows an abnormally high wave. This has been ascribed to the formation of *o*-quinonediimine which is further oxidized to muconononitrile[239] since such a reaction is reported to take place in the chemical oxidation of the diamine[163].

Primary aliphatic amines having a methylene group adjacent to the amino group such as *n*-propylamine, *n*-butylamine, isobutylamine and benzylamine are rapidly oxidized using a silver electrode in aqueous alkali (strictly speaking, a silver oxide electrode under the electrolysis conditions used) to give the corresponding nitrile and aldehyde[95]. Under suitable conditions, the CE is over 90%. There are two competing reactions for the intermediate imine; it may be oxidized to the nitrile (equation 71a) or hydrolysed to the aldehyde (equation 71b). Oximes are oxidized to the corresponding nitriles under the experimental conditions employed. The cleavage of the carbon–nitrogen bond known previously[30] is less favoured at a silver oxide anode than at a

$$RCH_2NH_2 \xrightarrow{-e} RCH_2NH_2^{+\bullet} \xrightarrow{-2\,H^+/-e} RCH{=}NH \qquad (70)$$

$$RCH{=}NH \xrightarrow{-e} RCH{=}NH^{+\bullet} \xrightarrow{-2\,H^+/-e} RC{\equiv}N \qquad (71a)$$

$$RCH{=}NH \xrightarrow{H_2O} RCHO + NH_3 \qquad (71b)$$

platinum anode. Hampson and coworkers[96] have further studied the anodic oxidation of secondary amines at silver oxide electrodes. In addition to nitriles and aldehydes, products derived from carbenium ions have been found. Thus for example di-*n*-butylamine yields *n*-butyl alcohol in addition to butyronitrile and butyraldehyde. The most susceptible C—N bond undergoes fission.

Keene and coworkers[108] have reported the oxidative dehydrogenation of primary amines bound to bis(2,2′-bipyridine)ruthenium(II). CV of the complexes $[Ru(bpy)_2(NH_2CH_2R)_2]^{2+}$ (R = phenyl, vinyl, *n*-propyl) shows reversible, one-electron oxidations in acetonitrile with $E_{1/2}$ = 1.03–1.04 V vs SSCE (the saturated sodium chloride calomel electrode). For the bis(benzylamine) complex, $[Ru(bpy)_2(NH_2CH_2Ph)_2]^{2+}$, the electrooxidation was monitored in detail using CV. The cyclic voltammogram following electrooxidation at 1.15 V until n = 2.0 (the number of electrons passed per mole of complex) indicates that there are in solution equal amounts of the starting complex, and a four-electron oxidation product with $E_{1/2}$ = 1.29 V. After complete electrooxidation at 1.15 V (n = 4.0), only the four-electron oxidation product remains in solution. The ^{1}H-NMR spectrum of the oxidation product of the bis(allylamine) complex shows that the four-electron oxidation

product is the amine–nitrile complex $[Ru(bpy)_2(NH_2CH_2CH{=}CH_2)(NCCH{=}CH_2)]^{2+}$ and not the bis(monoimine) complex $[Ru(bpy)_2(NH{=}CHCH{=}CH_2)_2]^{2+}$, and, consequently, that the four-electron oxidation of $[Ru(bpy)_2(NH_2CH_2R)_2]^{2+}$ is described satisfactorily by equation (72). A further oxidation process occurs past the $n = 4.0$

$$[Ru(bpy)_2(NH_2CH_2R)_2]^{2+} \xrightarrow{-4\,e} [Ru(bpy)_2(NH_2CH_2R)(N{\equiv}CR)]^{2+} + 4\,H^+ \qquad (72)$$

stage. If continued electrooxidation on the diffusion plateau of the $E_{1/2} = 1.29$ V wave (at 1.35 V) is stopped at $n = 2.0$ ($n_{total} = 6.0$ based on $[Ru(bpy)_2(NH_2CH_2Ph)_2]^{2+}$ as the starting complex) equal amounts of an unreacted $[Ru(bpy)_2(NH_2CH_2Ph)(N{\equiv}CPh)]^{2+}$ and a $n = 4.0$ ($n_{total} = 8.0$) oxidation product are obtained. Exhaustive electrooxidation on the diffusion plateau of the $E_{1/2} = 1.29$ V wave gave $n_{total} = 8.0$, and the complex with $E_{1/2} = 1.52$ V as the sole product (equation 73). The reactions appear to

$$[Ru(bpy)_2(NH_2CH_2R)(N{\equiv}CR)]^{2+} \xrightarrow{-4\,e} [Ru(bpy)_2(N{\equiv}CR)_2]^{2+} + 4\,H^+ \qquad (73)$$

proceed by initial oxidation of Ru(II) to Ru(III), followed by a series of stepwise dehydrogenation reactions which occur via imine intermediates.

VIII. REACTION OF NITRILE SOLVENT WITH ANODICALLY GENERATED CATIONIC SPECIES

A. Electrochemical Ritter Reaction

The Ritter reaction is a method for the preparation of *N*-substituted amides by the addition of nitriles to a wide variety of compounds capable of forming a carbenium ion in the presence of sulphuric acid, such as alkenes or alcohols, described first by Ritter in 1948[123,191]. Eberson and Nyberg[67] have reported an electrochemical analogue of the Ritter reaction. When trimethylacetic acid is electrolysed in acetonitrile containing a few percent of water, *N*-*t*-butylacetamide can be isolated in 40% yield, with no sign of formation of any Kolbe coupled product (equation 74;

$$RCOO^- \xrightarrow{-2\,e/-CO_2} R^+ \xrightarrow{MeCN} R{-}N{=}\overset{+}{C}{-}Me \xrightarrow{H_2O} R{-}NHCOMe \qquad (74)$$

R = *t*-Bu). This reaction involves the electrophilic attack of an electrogenerated carbenium ion on a free electron pair of the solvent acetonitrile and subsequent hydrolysis. A similar study has been published by Kernprobst and coworkers[110]. The reaction is influenced by the nature of the anode material and the structure of the carboxylic acid used[161,218].

Similar reactions also occur with alkylbenzenes. When durene was electrooxidized at an anode potential of 1.0 V vs. SCE in MeCN–$NaClO_4$, the product obtained after hydrolysis was 2,4,5-trimethylbenzylacetamide (38% yield). Hexamethylbenzene oxidized in similar fashion at an anode potential of 0.8 V gave pentamethylbenzylacetamide in 42% yield[68]. The anodic limit of the MeCN–$NaClO_4$ system far exceeds the anodic potentials that were applied in these two experiments, and it was concluded that electron transfer occurs from the substrate. The anodically generated cation radical undergoes deprotonation to afford a benzylic radical, which subsequently undergoes anodic oxidation to give a benzylic cation. Nucleophilic attack by the solvent acetonitrile gives a nitrilium ion, which can produce an acetamide upon aqueous work-up (equation 75)[43,72]. The *N*-substituted acetonitrilium ion can be trapped by use of a cation-exchange resin carrying sulphonic acid groups[44].

The electrochemical Ritter reaction is applicable to a wide variety of compounds

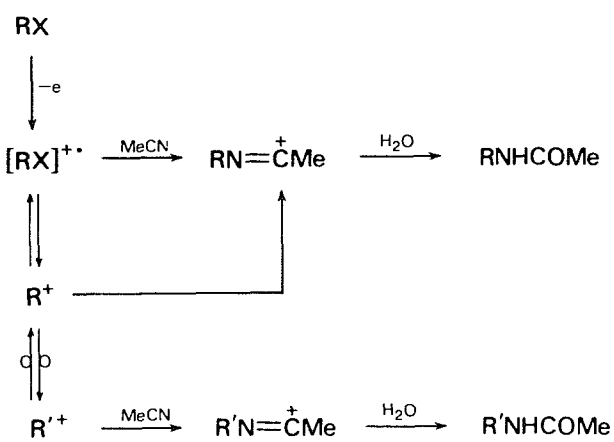
$$ArCH_3 \xrightarrow{-1\,e} ArCH_3^{+\cdot} \xrightarrow{-H^+} ArCH_2^{\cdot} \xrightarrow{-1\,e} ArCH_2^{+} \xrightarrow{MeCN}$$

$$ArCH_2N{=}\overset{+}{C}Me \xrightarrow{H_2O} ArCH_2NHCOMe \qquad (75)$$

capable of producing a carbenium ion via anodic oxidation, e.g. allylic olefins like cyclohexene and propylene[56,83,86], adamantane and a series of 1-substituted adamantanes[78,117], linear[57] and branched[206] aliphatic hydrocarbons, α-branched aliphatic ketones[37], ketones without α-branching[36,91,94], benzylic ethers[48,139,154] and acyclic esters[160]. The relevant cation radicals can lose a proton and be further oxidized, or, according to the structure of the substrate, split at a carbon–carbon bond; in each case carbenium ions are formed, which react with the acetonitrile directly or after skeletal rearrangement.

The case of alkyl halides is different (Scheme 7). The formation of carbenium ions from anodic oxidation of alkyl iodides in acetonitrile was first recognized by Miller and Hoffman[159]. Later, Laurent and coworkers[132] gained evidence that an S_N2-type displacement on an initially formed cation radical is involved in primary alkyl iodide oxidations in acetonitrile. Both mechanisms are feasible. Likewise, an anodically generated alkyl or alicyclic bromide cation radical is thought to undergo attack by the nucleophilic solvent acetonitrile and/or undergo carbon–halogen bond-breaking to generate the carbenium ion[38,39].

Acetamidation can also take place on an aromatic ring. It was successful only under stringently dry conditions for anthracene[93] and for several aromatic carbonyl compounds[210]. Preparative-scale oxidation of anthracene in acetonitrile–trifluoroacetic anhydride (25:1) resulted in the formation of *N*-(9-anthranyl)acetamide, in 82% isolated yield. Amidation of aromatic carbonyl compounds PhCOR (R = Me, *n*-Pr, EtO, OH) occurs in good yield at the *ortho* (mainly) and *para* positions at the controlled potential of 2.3–2.4 V vs. Ag/Ag^+ in MeCN/0.1 M Et_4NBF_4 (or $LiClO_4$) using a divided cell. The overall two-electron mechanism of aromatic acetamidation is similar to that proposed for cyanation, which involves direct one-electron oxidation of the aromatic compound, nucleophilic attack by acetonitrile on a cation radical, followed by a second electron transfer and finally proton loss.



SCHEME 7

B. Reactions of Nitrile Solvent with Anodically Generated Radicals, Cation Radicals and Cations

Unsubstituted alkyl cyanides are quite difficult to oxidize electrochemically, and consequently they are commonly used as solvents in anodic studies[147]. Neutral radicals (e.g. chlorine dioxide[193] and hydroxy radicals[131]) or cation radicals of aliphatic amides[167] generated at the anode abstract a hydrogen atom from alkyl cyanide solvents to form cyanoalkyl radicals. The fate of the latter depends on the environmental conditions. In the absence of a suitable trapping substrate, the cyanomethyl radical ($\dot{C}H_2—C\equiv N| \leftrightarrow CH_2=C=\dot{N}|$) would couple head-to-head to form succinonitrile[167] or head-to-tail[66,69] to form *N*-cyanomethylketenimine which would further react with the residual water. Isopropylcyanomethyl radical from isobutyronitrile undergoes disproportionation to methacrylonitrile and isobutyronitrile[167]. In the presence of nortropane, the cyanomethyl radical can couple with the anodically generated amino radical of nortropane[131].

Cation radicals of trialkyl phosphites react with solvents such as propionitrile and butyronitrile in different modes[88]. The reaction could be deprotonation or addition, followed by rapid removal of the radical products. Anodic oxidation of disulphides in acetonitrile in the presence of an olefin gives acetamidosulphides[45] (equation 76).

$$RSSR^{+\cdot} \xrightarrow{MeCN} RS—N=\overset{+}{C}Me \xrightarrow{\text{olefin}} RS—\overset{|}{\underset{|}{C}}—\overset{|}{\underset{|}{C}}—\overset{+}{N}=CMe \qquad (76)$$

The product of controlled potential 2e oxidation of dimanganese decacarbonyl $Mn_2(CO)_{10}$ in MeCN–Bu_4NBF_4 has been identified as the cation $Mn(CO)_5—N=\dot{C}Me$ by IR spectroscopy[180].

Preparative-scale anodic oxidation of 2,4,6-tri-*t*-butylphenol in MeCN–$NaClO_4$ at 1.0 V vs. Ag/Ag^+ gives 3-methyl-5,7-di-*t*-butyl-1,2-benzisoxazole in 69% yield (68% CE)[216]. This compound would be produced by attack of the nitrogen atom of the solvent acetonitrile at the oxygen atom of the phenonium ion generated by anodic 2e oxidation.

IX. MISCELLANEOUS OXIDATIONS

The cyano group is used as an electron-withdrawing group which is not itself oxidized under the conditions used. Substituent effects on the coupling rate of mono-*para*-substituted triphenylamine cation radicals have been studied[61,164]. The strong enhancement of benzidine coupling is clear with the cyano derivative.

Koenig and coworkers[118] have investigated the electrochemical Ritter reactions of *para*-substituted phenyl alkyl ketones in comparison with photoelectron spectra. *p*-Cyanovalerophenone gives the Ritter amide indicating intramolecular abstraction of the γ hydrogen atom, typical of the n_0 ionic states.

Preparative-scale electrooxidation of 3-hydroxyatroponitrile in aqueous THF at the potential of the first wave produces a mixture of diastereoisomers of 2,3-diphenylsuccinonitrile[138]. Homologous enol ethers have also been examined. The reaction proceeds via the radical coupling of cation radicals.

The electrolysis of ω-cyanobutyric acid in methanol produces the Kolbe dimer, suberonitrile, in 41% yield[168]. On the other hand, α-cyanocarboxylic acids give two types of coupling products, a normal Kolbe dimer and an abnormal carbon-to-nitrogen coupling product[66,69,71] (see Section VIII.B).

When using 1,2-dichloroethane containing 10% trifluoroacetic acid as a solvent, even deactivated aromatic compounds such as benzonitrile and nitrobenzene undergo anodic iodination at the *meta* position[140].

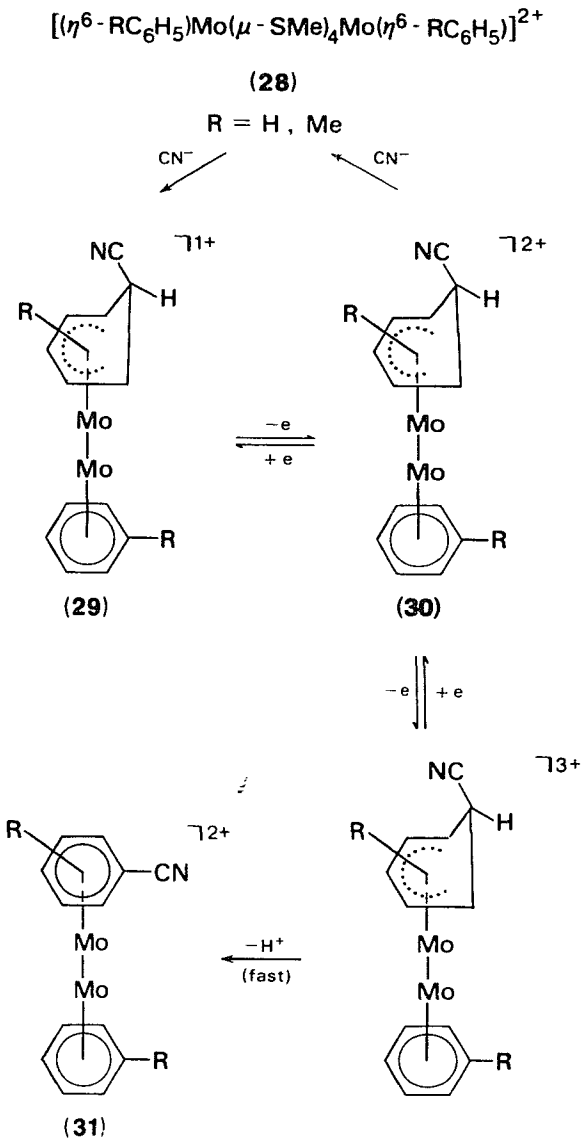
The anodic oxidation of dihydrocyano derivatives of azines, obtained by the reaction of quaternary azinium salts with potassium cyanide in aqueous media, proceeds via deprotonation from the cation radicals[211].

Silverthorn[207] has reported the conversion of a cyanocyclohexadienyl ligand in the cation **29** (R = H, Me) into a π-cyanoarene ligand (Scheme 8), together with electrochemical evidence for a two-electron oxidation/proton elimination mechanism. The starting substrate **29** can be prepared in essentially quantitative yield by the addition of cyanide ion (as the sodium salt) to the cation **28** in acetonitrile solution. The CV of **29** (R = H) at a platinum electrode in propylene carbonate with Et_4NPF_6 as supporting electrolyte shows two oxidation waves with $E_{1/2}$ (1st) at +1.17 V and $E_{1/2}$ (2nd) at +1.9 V vs. SCE. The first one-electron oxidation wave is reversible and a second one-electron step is partially reversible. Exhaustive electrooxidation at a potential held in the range of the first voltammetric peak gives the oxidation product **30**, which on standing for several hours reverts back spontaneously to the starting substrate **28** with the formation of ~0.5 equiv. of hydrogen cyanide. Exhaustive electrooxidation at the potential of the second voltammetric peak produces the π-cyanobenzene complex **31** which is obtained in ~90% yield. The reaction appears to involve the fairly rapid elimination of a proton from the cyanocyclohexadienyl ligand in the cation $[(\eta^5\text{-}RC_6H_5CN)Mo(\mu\text{-}SMe)_4Mo(\eta^6\text{-}RC_6H_5)]^{3+}$ yielding the π-cyanoarene complex directly. This type of reaction would be useful for the synthesis of substituted π-arene complexes not obtainable by conventional methods and might lead to a synthetic method of free, substituted arenes.

Electrochemical oxidation of isocyanide complexes of transition metals began with the investigation of the effects of substitution by the isocyanide of ligand groups attached to the metal on $E_{1/2}$, i.e. the ease of oxidation. The ease of oxidation increased by about 0.4 V on decreasing carbonyl substitution (i.e. increasing values of n) in the series $[Mn(CO)_{6-n}(CNMe)_n]PF_6$[222]. Molecular orbital calculations show that the $E_{1/2}$ value is linearly related to the HOMO energies in these complexes[196]. Also, the $E_{1/2}$ values measured for the isomeric complexes of manganese(I) carbonyl methyl isocyanide correlate with the HOMO energies[225]. The ease of oxidation also depends on the choice of isocyanide. Oxidation of hexakisphenyl (or other aryl) isocyanide manganese(I) complexes is more difficult than is oxidation of the corresponding methyl species. Among the aryl isocyanide complexes there are smaller, though still substantial, differences in oxidation potentials depending on the nature of the *meta* or *para* substituent[221,226]. Electron-donating groups predictably increase the ease of oxidation, electron-withdrawing groups decrease the ease of oxidation. The same trend toward oxidation is observed in the hexakisaryl isocyanide chromium(0) species[80,221]. For each complex, a one-electron oxidation is observed. The lower potential when compared to the isoelectronic manganese species is anticipated due to the lower valency of chromium in these oxidations. Hexakisisocyanide manganese(I) complexes are observed to undergo a second one-electron oxidation at considerably higher potential. Presumably this represents an oxidation to the manganese(III) species. The second oxidation was observed for the analogous chromium complexes. The isoelectronic iron(II) species $[Fe(CNMe)_6]^{2+}$ gives neither a clean electrochemical oxidation nor a reduction.

$Mn(CNPh)_5X$ (X = Cl, Br) complexes undergo a one-electron oxidation at ~0.3 V vs. SCE[223]. The oxidation potential of several phenyl isocyanide complexes of cyclopentadienyliron and manganese carbonyl halides has been measured using CV and the ease of electrochemical oxidation correlated with the reactivity for several chemical oxidants.

Moreover, the $E_{1/2}$ values of $[Mn(p\text{-}MeC_6H_4NC)_4(CO)(L)]PF_6$ (L = MeNC, *t*-BuNC, *p*-MeC_6H_4NC, pyridine, *o*-toluidine) compounds correlate with carbonyl



SCHEME 8

vibrational frequencies[224]. Connor and coworkers[58] have previously noted correlations of $E_{1/2}$ with the A_1 carbonyl stretching frequency of metal carbonyl isocyanide complexes of the type $M(CO)_{6-n}(CNR)_n$ (M = Cr, Mo, W; n = 1–3). Also, Sarapu and Fenske[196] have noted a similar correlation of carbonyl force constants and stretching frequencies with $E_{1/2}$ values for the complexes $Mn(CO)_{5-n}(CNMe)_nBr$ (n = 0–4) and $Mn(CO)_{6-n}(CNMe)_n^+$ (n = 1–6).

CV of the cyclopentadienyliron complexes of arylisocyanides, $Fe(C_5H_5)(CNAr)_2Br$, shows a single reversible one-electron oxidation wave in acetonitrile[227]. Oxidation

$$Fe(C_5H_5)(p\text{-}CNC_6H_4F)_2Br \xrightarrow{-1e} [Fe(C_5H_5)(p\text{-}CNC_6H_4F)_2Br]^+$$

$$\longrightarrow 2\ p\text{-}CNC_6H_4F + [C_5H_5FeBr]^+$$

$$Fe(C_5H_5)(p\text{-}CNC_6H_4F)_2Br + p\text{-}CNC_6H_4F$$

$$\longrightarrow [Fe(C_5H_5)(p\text{-}CNC_6H_4F)_3]Br$$

SCHEME 9

potentials are in the range of 0.45–0.63 V vs. SCE. The required potentials for oxidation correlate well with Hammett σ_p and σ_m constants for substituents on the aryl rings. A similar correlation has been found for oxidations of $Cr(CNC_6H_4R)_4$[80] and $[Mn(CNC_6H_4R)_6]PF_6$[226], as discussed above. A controlled-potential oxidation of $Fe(C_5H_5)(p\text{-}CNC_6H_4F)_2Br$ has been carried out in acetonitrile at a potential of 0.60 V, slightly above the measured $E_{1/2}$ value for this compound. Work-up of the resultant solution gives only $[Fe(C_5H_5)(p\text{-}CNC_6H_4F)_3]Br$ in 36% yield based on iron. The reaction proceeds as shown in Scheme 9. The anodically generated one-electron oxidation product is unstable and ejects isocyanide into solution. Voltammetric behaviour has also been investigated for the cationic compounds $[Fe(C_5H_5)(CO)_{3-n}(CNR)_n]PF_6$ (n = 2, 3; R = p-C_6H_4F, Me).

In all these electrooxidation reactions, the isocyanides themselves remain intact owing to their high resistance to oxidation.

If forcing conditions such as heating the anolyte during the electrooxidation were employed, isocyanides might be oxidized. In boiling methanol, cyclohexyl isocyanide undergoes methoxylation nonpotentiostatically[204]. Seven products have been isolated, with a total yield of about 20%. It is not clear what chemical species is discharged, substrate, solvent, electrolyte anion or all.

X. REFERENCES

1. E. M. Abbot, A. J. Bellamy and J. Kerr, *Chem. Ind. (London)*, 828 (1974).
2. D. S. Acker and W. R. Hertler, *J. Amer. Chem. Soc.*, **84**, 3370 (1962).
3. A. W. Addison, N. S. Dalal, Y. Hoyano, S. Huizinga and L. Weiler, *Can. J. Chem.*, **55**, 4191 (1977).
4. E. Aharon-Shalom, J. Y. Becker and I. Agranat, *Nouv. J. Chim.*, **3**, 643 (1979).
5. E. Ahlberg, B. Svensmark and V. D. Parker, *Acta Chem. Scand.*, **34B**, 53 (1980).
6. F. B. Ahrens, *Z. Elektrochem.*, **5**, 99 (1896).
7. M. J. Allen, *Organic Electrode Processes*, Reinhold, New York, 1958, p. 61.
8. M. J. Allen, J. A. Siragusa and W. Pierson, *J. Chem. Soc.*, 1045 (1960).
9. J. D. Anderson, M. M. Baizer and J. P. Petrovich, *J. Org. Chem.*, **31**, 3890 (1966).
10. S. Andreades and E. W. Zahnow, *J. Amer. Chem. Soc.*, **91**, 4181 (1969).
11. P. G. Arapakos and M. K. Scott, *Tetrahedron Letters*, 1975 (1968).
12. P. G. Arapakos, M. K. Scott and F. E. Huber, Jr., *J. Amer. Chem. Soc.*, **91**, 2059 (1969).
13. J. Armand and O. Convert, *Collect. Czech. Chem. Commun.*, **36**, 351 (1971).
14. L. A. Avaca and J. H. P. Utley, *J. Chem. Soc., Perkin Trans.*, **2**, 161 (1975).
15. L. A. Avaca and J. H. P. Utley, *J. Chem. Soc., Perkin Trans.*, **1**, 971 (1975).
16. M. M. Baizer, *Tetrahedron Letters*, 973 (1963).
17. M. M. Baizer, *J. Electrochem. Soc.*, **111**, 215 (1964).
18. M. M. Baizer, *J. Org. Chem.*, **29**, 1670 (1964).
19. M. M. Baizer and J. D. Anderson, *J. Electrochem. Soc.*, **111**, 223 (1964).
20. M. M. Baizer and J. D. Anderson, *J. Electrochem. Soc.*, **111**, 226 (1964).
21. M. M. Baizer and J. D. Anderson, *J. Org. Chem.*, **30**, 1348 (1965).
22. M. M. Baizer and J. D. Anderson, *J. Org. Chem.*, **30**, 1351 (1965).

23. M. M. Baizer and J. D. Anderson, *J. Org. Chem.*, **30**, 1357 (1965).
24. M. M. Baizer and J. D. Anderson, *J. Org. Chem.*, **30**, 3138 (1965).
25. M. M. Baizer, *J. Org. Chem.*, **31**, 3847 (1966).
26. M. M. Baizer, J. D. Anderson, J. H. Wagenknecht, M. R. Ort and J. P. Petrovich, *Electrochim. Acta*, **12**, 1377 (1967).
27. M. M. Baizer, J. P. Petrovich and D. A. Tyssee, *J. Electrochem. Soc.*, **117**, 173 (1970).
28. M. M. Baizer, J. L. Chruma and P. A. Berger, *J. Org. Chem.*, **35**, 3569 (1970).
29. M. M. Baizer and J. L. Chruma, *J. Electrochem. Soc.*, **118**, 450 (1971).
30. K. K. Barnes and C. K. Mann, *J. Org. Chem.*, **32**, 1474 (1967).
31. G. C. Barrett and T. J. Grattan, *Tetrahedron Letters*, 4237 (1979).
32. D. E. Bartak, K. J. Houser, B. C. Rudy and M. D. Hawley, *J. Amer. Chem. Soc.*, **94**, 7526 (1972).
33. F. Beck, *Chem.-Ing.-Tech.*, **37**, 607 (1965).
34. F. Beck, *Ber. Bunsenges. Phys. Chem.*, **72**, 379 (1968).
35. B. F. Becker and H. P. Fritz, *Justus Liebigs Ann. Chem.*, 1015 (1976).
36. J. Y. Becker, L. R. Byrd, L. L. Miller and Y.-H. So, *J. Amer. Chem. Soc.*, **97**, 853 (1975).
37. J. Y. Becker, L. L. Miller and T. M. Siegel, *J. Amer. Chem. Soc.*, **97**, 849 (1975).
38. J. Y. Becker, *J. Org. Chem.*, **42**, 3997 (1977).
39. J. Y. Becker and D. Zemach, *J. Chem. Soc., Perkin Trans. 2*, 914 (1979).
40. A. J. Bellamy, *J. Chem. Soc., Chem. Commun.*, 944 (1975).
41. A. J. Bellamy, G. Howat and I. S. MacKirdy, *J. Chem. Soc., Perkin Trans. 2*, 786 (1978).
42. A. J. Bellamy and J. B. Kerr, *Acta Chem. Scand.*, **33B**, 370 (1979).
43. A. Bewick, G. J. Edwards, J. M. Mellor and S. Pons, *J. Chem. Soc., Perkin Trans. 2*, 1952 (1977).
44. A. Bewick, J. M. Mellor and B. S. Pons, *J. Chem. Soc., Chem. Commun.*, 738 (1978).
45. A. Bewick, D. E. Coe, J. M. Mellor and D. J. Walton, *J. Chem. Soc., Chem. Commun.*, 51 (1980).
46. H. N. Blount, N. Winograd and T. Kuwana, *J. Phys. Chem.*, **74**, 3231 (1970).
47. K. G. Boto and F. G. Thomas, *Australian J. Chem.*, **26**, 1251 (1973).
48. J. W. Boyd, P. W. Schmalzl and L. L. Miller, *J. Amer. Chem. Soc.*, **102**, 3856 (1980).
49. M. J. D. Brand and B. Fleet, *J. Electroanal. Chem.*, **19**, 157 (1968).
50. O. R. Brown and K. Lister, *Discuss. Faraday Soc.*, **45**, 106 (1968).
51. J. F. Bunnett, *Acc. Chem. Res.*, **11**, 413 (1978).
52. H. J. Callot, A. Louati and M. Gross, *Tetrahedron Letters*, **21**, 3281 (1980).
53. V. A. Chernova, A. A. Pozdeeva, V. Z. Latypova, Yu. M. Kargin and S. I. Zhdanov, *J. Gen. Chem. USSR (Engl. Transl.)*, **49**, 2039 (1979).
54. T. Chiba and Y. Takata, *J. Org. Chem.*, **42**, 2973 (1977).
55. W. V. Childs, J. T. Maloy, C. P. Keszthelyi and A. J. Bard, *J. Electrochem. Soc.*, **118**, 874 (1971).
56. D. Clark, M. Fleischmann and D. Pletcher, *J. Electroanal. Chem.*, **36**, 137 (1972).
57. D. B. Clark, M. Fleischmann and D. Pletcher, *J. Chem. Soc., Perkin Trans. 2*, 1578 (1973).
58. J. A. Connor, E. M. Jones, G. K. McEwen, M. K. Lloyd and J. A. McCleverty, *J. Chem. Soc., Dalton Trans.*, 1246 (1972).
59. O. Convert and J. Armand, *Compt. Rend. Ser. C*, **265**, 1486 (1967).
60. P. T. Cottrell and C. K. Mann, *J. Amer. Chem. Soc.*, **93**, 3579 (1971).
61. S. C. Creason, J. Wheeler and R. F. Nelson, *J. Org. Chem.*, **37**, 4440 (1972).
62. T. J. Curphey, C. W. Amelotti, T. P. Layloff, R. L. McCartney and J. H. Williams, *J. Amer. Chem. Soc.*, **91**, 2817 (1969).
63. A. Daver and G. Le Guillanton, *Bull. Soc. Chim. Fr.*, 312 (1971).
64. J. Den Heijer, O. B. Shadid, J. Cornelisse and E. Havinga, *Tetrahedron*, **33**, 779 (1977).
65. J. Diekmann, W. R. Hertler and R. E. Benson, *J. Org. Chem.*, **28**, 2719 (1963).
66. L. Eberson, *J. Org. Chem.*, **27**, 2329 (1962).
67. L. Eberson and K. Nyberg, *Acta Chem. Scand.*, **18**, 1567 (1964).
68. L. Eberson and K. Nyberg, *Tetrahedron Letters*, 2389 (1966).
69. L. Eberson, *Electrochim. Acta*, **12**, 1473 (1967).
70. L. Eberson and S. Nilsson, *Discuss. Faraday Soc.*, **45**, 242 (1968).
71. L. Eberson and S. Nilsson, *Acta Chem. Scand.*, **22**, 2453 (1968).
72. L. Eberson and B. Olofsson, *Acta Chem. Scand.*, **23**, 2355 (1969).

73. L. Eberson in *Organic Electrochemistry: An Introduction and a Guide* (Ed. M. M. Baizer), Marcel Dekker, New York, 1973, pp. 413–428.
74. L. Eberson and B. Helgée, *Chem. Scripta*, **5**, 47 (1974).
75. L. Eberson and B. Helgée, *Acta Chem. Scand.*, **29B**, 451 (1975).
76. L. Eberson and B. Helgée, *Acta Chem. Scand.*, **31B**, 813 (1977).
77. L. Eberson and B. Helgée, *Acta Chem. Scand.*, **32B**, 313 (1978).
78. G. J. Edwards, S. R. Jones and J. M. Mellor, *J. Chem. Soc., Perkin Trans. 2*, 505 (1977).
79. P. J. Elving and I. Rosenthal, *J. Amer. Chem. Soc.*, **73**, 1880 (1951).
80. G. J. Essenmacher and P. M. Treichel, *Inorg. Chem.*, **16**, 800 (1977).
81. J. F. Evans and H. N. Blount, *J. Amer. Chem. Soc.*, **100**, 4191 (1978).
82. T. R. Evans and L. F. Hurysz, *Tetrahedron Letters*, 3103 (1977).
83. G. Faita, M. Fleischmann and D. Pletcher, *J. Electroanal. Chem.*, **25**, 455 (1970).
84. J. P. Ferraris and G. Saito, *J. Chem. Soc., Chem. Commun.*, 992 (1978).
85. M. Figeys, *Tetrahedron Letters*, 2237 (1967).
86. M. Fleischmann and D. Pletcher, *Chem.-Ing.-Tech.*, **44**, 187 (1972).
87. A. J. Fry and R. G. Reed, *J. Amer. Chem. Soc.*, **94**, 8475 (1972).
88. W. B. Gara and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 2*, 150 (1978).
89. P. H. Given and M. E. Peover, *J. Chem. Soc.*, 465 (1960).
90. I. B. Goldberg, D. Boyd, R. Hirasawa and A. J. Bard, *J. Phys. Chem.*, **78**, 295 (1974).
91. M. M. Green, G. J. Mayotte, L. Meites and D. Forsyth, *J. Amer. Chem. Soc.*, **102**, 1464 (1980).
92. N. F. Haley, *J. Chem. Soc., Chem. Commun.*, 1030 (1979).
93. O. Hammerich and V. D. Parker, *J. Chem. Soc., Chem. Commun.*, 245 (1974).
94. S. Hammerum and O. Hammerich, *Tetrahedron Letters*, 5027 (1979).
95. N. A. Hampson, J. B. Lee, J. R. Morley and B. Scanlon, *Can. J. Chem.*, **47**, 3729 (1969).
96. N. A. Hampson, J. B. Lee, J. R. Morley, K. I. MacDonald and B. Scanlon, *Tetrahedron*, **26**, 1109 (1970).
97. H. D. Hartzler, *J. Org. Chem.*, **30**, 2456 (1965).
98. J. W. Hayes, I. Ružić, D. E. Smith, G. L. Booman and J. R. Delmastro, *J. Electroanal. Chem.*, **51**, 269 (1974).
99. M. J. Hazelrigg, Jr. and A. J. Bard, *J. Electrochem. Soc.*, **122**, 211 (1975).
100. S. Hünig and W. Schenk, *Justus Liebigs Ann. Chem.*, 1523 (1979).
101. G. C. Jones and T. H. Ledford, *Tetrahedron Letters*, 615 (1967).
102. W. H. Jura and R. J. Gaul, *J. Amer. Chem. Soc.*, **80**, 5402 (1958).
103. L. V. Kaabak and A. P. Tomilov, *J. Gen. Chem. USSR (Engl. Transl.)*, **33**, 2734 (1963).
104. L. V. Kaabak, A. P. Tomilov and S. L. Varshavskii, *J. Gen. Chem. USSR (Eng. Transl.)*, **34**, 2121 (1964).
105. E. M. Kaiser and C. R. Hauser, *J. Org. Chem.*, **33**, 3402 (1968).
106. A. M. Kardos, P. Valenta and J. Volke, *J. Electroanal. Chem.*, **12**, 84 (1966).
107. F. Kawamura and S. Suzuki, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, **55**, 476 (1952).
108. F. R. Keene, D. J. Salmon and T. J. Meyer, *J. Amer. Chem. Soc.*, **98**, 1884 (1976).
109. J. M. Kern and P. Federlin, *Bull. Soc. Chim. Fr.*, 4383 (1972).
110. J. M. Kernprobst, A. Laurent and E. Laurent-Dieuzeide, *Bull. Soc. Chim. Fr.*, 3657 (1968).
111. L. Kistenbruegger, P. Mischke, J. Voss and G. Wiegand, *Justus Liebigs Ann. Chem.*, 461 (1980).
112. I. L. Knunyants and N. P. Gambaryan, *Usp. Khim.*, **23**, 781 (1954); *Chem. Abstr.*, **49**, 6090h (1955).
113. I. L. Knunyants and N. S. Vyazankin, *Trudy Chetvertogo Soveshchaniya po Elektrokhimii, Moscow*, 227 (1956); *Chem. Abstr.*, **54**, 9811b (1960).
114. I. L. Knunyants and N. S. Vyazankin, *Izv. Akad. Nauk SSSR, Otdl. Khim. Nauk*, 238 (1957).
115. I. L. Knunyants and N. S. Vyazankin, *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)*, 253 (1957).
116. I. L. Knunyants and N. S. Vyazankin, *Dokl. Akad. Nauk SSSR*, **113**, 112 (1957).
117. V. R. Koch and L. L. Miller, *J. Amer. Chem. Soc.*, **95**, 8631 (1973).
118. T. Koenig, R. Wielesek, L. L. Miller and Y.-H. So, *J. Amer. Chem. Soc.*, **99**, 7061 (1977).
119. H. Kojima and A. J. Bard, *J. Amer. Chem. Soc.*, **97**, 6317 (1975).

120. B. A. Kowert, L. Marcoux and A. J. Bard, *J. Amer. Chem. Soc.*, **94**, 5538 (1972).
121. K. Koyama, T. Susuki and S. Tsutsumi, *Tetrahedron Letters*, 627 (1965).
122. K. Koyama, T. Susuki and S. Tsutsumi, *Tetrahedron*, **23**, 2675 (1967).
123. L. I. Krimen and D. J. Cota, *Org. Reactions*, **17**, 213 (1969).
124. V. Krishnan, A. Muthukumaran, K. Ragupathy and H. V. K. Udupa, *Trans. SAEST*, **13**, 161 (1978); *Chem. Abstr.*, **91**, 46346z (1979).
125. V. Krishnan, N. Mahalingam and H. V. K. Udupa, *J. Chem. Tech. Biotechnol.*, **29**, 703 (1979).
126. V. Krishnan, A. Muthukumaran, K. Ragupathy and H. V. K. Udupa, *J. Chem. Technol. Biotechnol.*, **29**, 163 (1979).
127. L. H. Kristensen and H. Lund, *Acta Chem. Scand.*, **33B**, 735 (1979).
128. F. L. Lambert and K. Kobayashi, *J. Amer. Chem. Soc.*, **82**, 5342 (1960).
129. E. Lamy, L. Nadjo and J. M. Savéant, *J. Electroanal. Chem.*, **42**, 189 (1973).
130. E. Lamy, L. Nadjo and J. M. Savéant, *J. Electroanal. Chem.*, **50**, 141 (1974).
131. B. L. Laube, M. R. Asirvatham and C. K. Mann, *J. Org. Chem.*, **42**, 670 (1977).
132. A. Laurent, E. Laurent and R. Tardivel, *Tetrahedron Letters*, 4861 (1973).
133. G. Le Guillanton and A. Daver, *Compt. Rend., Ser. C*, **272**, 421 (1971).
134. G. Le Guillanton, *Bull. Soc. Chim. Fr.*, 3458 (1973).
135. G. Le Guillanton and A. Daver, *Bull. Soc. Chim. Fr.*, 724 (1973).
136. G. Le Guillanton, M. Cariou and A. Lebouc, *Bull. Soc. Chim. Fr.*, 2980 (1974).
137. G. Le Guillanton and M. Cariou, *Electrochim. Acta*, **22**, 619 (1977).
138. G. Le Guillanton and M. A. Le Moing, *Electrochim. Acta*, **24**, 1203 (1979).
139. R. Lines and J. H. P. Utley, *J. Chem. Soc., Perkin Trans. 2*, 803 (1977).
140. R. Lines and V. D. Parker, *Acta Chem. Scand.*, **34B**, 47 (1980).
141. S. Longchamp, C. Caullet and M. Libert, *Bull. Soc. Chim. Fr.*, 353 (1974).
142. P. Ludwig and R. N. Adams, *J. Chem. Phys.*, **37**, 828 (1962).
143. H. Lund, *Acta Chem. Scand.*, **17**, 2325 (1963).
144. H. Lund and L. G. Feoktistov, *Acta Chem. Scand.*, **23**, 3482 (1969).
145. H. Lund in *The Chemistry of Amidines and Imidates* (Ed. S. Patai), Wiley–Interscience, London, 1975, pp. 241–253.
146. A. H. Maki and D. H. Geske, *J. Amer. Chem. Soc.*, **83**, 1852 (1961).
147. C. K. Mann in *Electroanalytical Chemistry*, Vol. 3 (Ed. A. J. Bard), Marcel Dekker, New York, 1969, pp. 57–134.
148. O. Manoušek, O. Exner and P. Zuman, *Collect. Czech. Chem. Commun.*, **33**, 3988 (1968).
149. O. Manoušek, O. Exner and P. Zuman, *Collect. Czech. Chem. Commun.*, **33**, 4000 (1968).
150. O. Manoušek, P. Zuman and O. Exner, *Collect. Czech. Chem. Commun.*, **33**, 3979 (1968).
151. F. Matsuda, *Tetrahedron Letters*, 6193 (1966).
152. T. Matsuo, S. Mihara and I. Ueda, *Tetrahedron Letters*, 4581 (1976).
153. M. Maxfield, D. O. Cowan, A. N. Bloch and T. O. Poehler, *Nouv. J. Chim.*, **3**, 647 (1979).
154. E. A. Mayeda, L. L. Miller and J. F. Wolf, *J. Amer. Chem. Soc.*, **94**, 6812 (1972).
155. H. Meinert and D. Cech, *Z. Chem.*, **12**, 291 (1972).
156. L. R. Melby, R. J. Harder, W. R. Hertler, W. Mahler, R. E. Benson and W. E. Mochel, *J. Amer. Chem. Soc.*, **84**, 3374 (1962).
157. F. M'Halla, J. Pinson and J. M. Savéant, *J. Amer. Chem. Soc.*, **102**, 4120 (1980).
158. S. Miduno and Y. Takayama, *Bull. Chem. Soc. Japan*, **17**, 136 (1942).
159. L. L. Miller and A. K. Hoffmann, *J. Amer. Chem. Soc.*, **89**, 593 (1967).
160. L. L. Miller and V. Ramachandran, *J. Org. Chem.*, **39**, 369 (1974).
161. D. L. Muck and E. R. Wilson, *J. Electrochem. Soc.*, **117**, 1358 (1970).
162. M. Nagao, N. Sato, T. Akashi and T. Yoshida, *J. Amer. Chem. Soc.*, **88**, 3447 (1966).
163. K. Nakagawa and H. Onoue, *Chem. Commun.*, 396 (1965).
164. R. F. Nelson and R. N. Adams, *J. Amer. Chem. Soc.*, **90**, 3925 (1968).
165. S. Nilsson, *Acta Chem. Scand.*, **27**, 329 (1973).
166. T. Nonaka and K. Sugino, *J. Electrochem. Soc.*, **114**, 1255 (1967).
167. J. F. O'Donnell and C. K. Mann, *J. Electroanal. Chem.*, **13**, 157 (1967).
168. H. A. Offe, *Z. Naturforsch.*, **2B**, 185 (1947).
169. M. Ohta, *Bull. Chem. Soc. Japan*, **17**, 485 (1942).
170. M. R. Ort and M. M. Baizer, *J. Org. Chem.*, **31**, 1646 (1966).
171. L. Papouchado, R. N. Adams and S. W. Feldberg, *J. Electroanal. Chem.*, **21**, 408 (1969).

172. V. D. Parker and B. E. Burgert, *Tetrahedron Letters*, 4065 (1965).
173. V. D. Parker and B. E. Burgert, *Tetrahedron Letters*, 2415 (1968).
174. V. D. Parker and L. Eberson, *J. Chem. Soc., Chem. Commun.*, 441 (1972).
175. M. E. Peover, *Trans. Faraday Soc.*, **58**, 2370 (1962).
176. J. P. Petrovich, J. D. Anderson and M. M. Baizer, *J. Org. Chem.*, **31**, 3897 (1966).
177. J. P. Petrovich, M. M. Baizer and M. R. Ort, *J. Electrochem. Soc.*, **116**, 743 (1969).
178. J. P. Petrovich, M. M. Baizer and M. R. Ort, *J. Electrochem. Soc.*, **116**, 749 (1969).
179. J. P. Petrovich and M. M. Baizer, *J. Electrochem. Soc.*, **118**, 447 (1971).
180. C. J. Pickett and D. Pletcher, *J. Chem. Soc., Chem. Commun.*, 660 (1974).
181. J. Pinson and J.-M. Savéant, *J. Amer. Chem. Soc.*, **100**, 1506 (1978).
182. K. Ponsold and H. Kasch, *Tetrahedron Letters*, 4465 (1979).
183. V. J. Puglisi and A. J. Bard, *J. Electrochem. Soc.*, **119**, 829 (1972).
184. V. J. Puglisi and A. J. Bard, *J. Electrochem. Soc.*, **120**, 748 (1973).
185. P. H. Rieger, I. Bernal and G. K. Fraenkel, *J. Amer. Chem. Soc.*, **83**, 3918 (1961).
186. P. H. Rieger and G. K. Fraenkel, *J. Chem. Phys.*, **37**, 2795 (1962).
187. P. H. Rieger, I. Bernal, W. H. Reinmuth and G. K. Fraenkel, *J. Amer. Chem. Soc.*, **85**, 683 (1963).
188. J. Rieser, G. Abou-Elenien, K. Wallenfels and H. Baumgärtel, *Tetrahedron Letters*, 2363 (1976).
189. M. R. Rifi in *Technique of Electroorganic Synthesis*, Part 2 (Ed. N. L. Weinberg), in *Techniques of Chemistry Series* (Ed. A. Weissberger), Wiley, New York, 1975, pp. 83–267.
190. S. C. Rifkin and D. H. Evans, *J. Electrochem. Soc.*, **121**, 769 (1974).
191. J. J. Ritter and P. P. Minieri, *J. Amer. Chem. Soc.*, **70**, 4045 (1948).
192. A. M. Romanin, A. Gennaro and E. Vianello, *J. Electroanal. Chem.*, **88**, 175 (1978).
193. D. C. Russell, *Anal. Chem.*, **35**, 1291 (1963).
194. G. Saito and J. P. Ferraris, *J. Chem. Soc., Chem. Commun.*, 1027 (1979).
195. I. Saito, S. Ito and T. Matsuura, *J. Amer. Chem. Soc.*, **100**, 2901 (1978).
196. A. C. Sarapu and R. F. Fenske, *Inorg. Chem.*, **14**, 247 (1975).
197. D. T. Sawyer and R. J. Day, *J. Electroanal. Chem.*, **5**, 195 (1963).
198. H. Sayo, Y. Tsukitani and M. Masui, *Tetrahedron*, **24**, 1717 (1968).
199. W. M. Schwarz, E. M. Kosower and I. Shain, *J. Amer. Chem. Soc.*, **83**, 3164 (1961).
200. R. M. Scribner, *J. Org. Chem.*, **31**, 3671 (1966).
201. D. Serve, *J. Amer. Chem. Soc.*, **97**, 432 (1975).
202. I. G. Sevast'yanova and A. P. Tomilov, *J. Gen. Chem. USSR (Engl. Transl.)*, **33** 2741 (1963).
203. I. G. Sevast'yanova and A. P. Tomilov, *Soviet Electrochemistry (Engl. Transl.)*, **3**, 494 (1967).
204. T. Shono and Y. Matsumura, *J. Amer. Chem. Soc.*, **90**, 5937 (1968).
205. T. Shono, I. Nishiguchi and H. Ohmizu, *J. Amer. Chem. Soc.*, **99**, 7396 (1977).
206. T. M. Siegel, L. L. Miller and J. Y. Becker, *J. Chem. Soc. Chem. Commun.*, 341 (1974).
207. W. E. Silverthorn, *J. Amer. Chem. Soc.*, **102**, 842 (1980).
208. Yu. D. Smirnov, S. K. Smirnov and A. P. Tomilov, *J. Org. Chem. USSR (Engl. Transl.)*, **4**, 208 (1968).
209. Yu. D. Smirnov and A. P. Tomilov, *J. Org. Chem. USSR (Engl. Transl.)*, **5**, 850 (1969).
210. Y.-H. So, J. Y. Becker and L. L. Miller, *J. Chem. Soc., Chem. Commun.*, 262 (1975).
211. I. M. Sosonkin, O. N. Chupakhin and A. I. Matern, *J. Org. Chem. USSR (Engl. Transl.)*, **15**, 1785 (1979).
212. J. Stradins, V. Kadis, R. Gavars, L. Krumina and V. A. Slavinskaya, *Vses. Nauchn. Konf. Khim. Tekhnol. Furanovykh Soedin.*, [*Tezisy Dokl.*], *3rd*, 130 (1978); *Chem. Abstr.*, **92**, 188123u (1980).
213. K. Sugino and T. Nonaka, *J. Electrochem. Soc.*, **112**, 1241 (1965).
214. K. Sugino and T. Nonaka, *Electrochim. Acta*, **13**, 613 (1968).
215. T. Susuki, K. Koyama, A. Omori and S. Tsutsumi, *Bull. Chem. Soc. Japan*, **41**, 2663 (1968).
216. A. B. Suttie, *Tetrahedron Letters*, 953 (1969).
217. Y. Takahashi, M. Tokuda, M. Itoh and A. Suzuki, *Chem. Letters*, 523 (1975).
218. H. G. Thomas, *Angew. Chem. (Intern. Ed. Engl.)*, **10**, 557 (1971).
219. A. P. Tomilov, L. V. Kaabak and S. L. Varshavskii, *J. Gen. Chem. USSR (Engl. Transl.)*, **33**, 2737 (1963).

220. A. P. Tomilov, Yu. D. Smirnov and S. L. Varshavskii, *J. Gen. Chem. USSR (Engl. Transl.)*, **35**, 390 (1965).
221. P. M. Treichel and G. E. Dirreen, *J. Organometal. Chem.*, **39**, C20 (1972).
222. P. M. Treichel, G. E. Dirreen and H. J. Mueh, *J. Organometal. Chem.*, **44**, 339 (1972).
223. P. M. Treichel, K. P. Wagner and H. J. Mueh, *J. Organometal. Chem.*, **86**, C13 (1975).
224. P. M. Treichel and H. J. Mueh, *J. Organometal. Chem.*, **122**, 229 (1976).
225. P. M. Treichel, H. J. Mueh and B. E. Bursten, *J. Organometal. Chem.*, **110**, C49 (1976).
226. P. M. Treichel and H. J. Mueh, *Inorg. Chem.*, **16**, 1167 (1977).
227. P. M. Treichel and D. C. Molzahn, *J. Organometal. Chem.*, **179**, 275 (1979).
228. D. A. Tyssee and M. M. Baizer, *J. Org. Chem.*, **39**, 2819 (1974).
229. A. Uchida, S. Saito and S. Matsuda, *Bull. Chem. Soc. Japan*, **42**, 2989 (1969).
230. W. J. M. Van Tilborg, C. J. Smit and J. J. Scheele, *Tetrahedron Letters*, 2113 (1977).
231. L. V. Vesheva, T. B. Argova, L. S. Reishakhrit and T. V. Forsova, *J. Gen. Chem. USSR (Engl. Transl.)*, **40**, 1912 (1970).
232. J. Volke, R. Kubíček and F. Šantavý, *Collect. Czech. Chem. Commun.*, **25**, 1510 (1960).
233. J. Volke and J. Holubek, *Collect. Czech. Chem. Commun.*, **28**, 1597 (1963).
234. J. Volke and A. M. Kardos, *Collect. Czech. Chem. Commun.*, **33**, 2560 (1968).
235. J. Volke and V. Skála, *J. Electroanal. Chem.*, **36**, 383 (1972).
236. J. H. Wagenknecht and M. M. Baizer, *J. Org. Chem.*, **31**, 3885 (1966).
237. J. H. Wagenknecht and M. M. Baizer, *J. Electrochem. Soc.*, **114**, 1095 (1967).
238. S. Wawzonek and J. D. Fredrickson, *J. Electrochem. Soc.*, **106**, 325 (1959).
239. S. Wawzonek and T. W. McIntyre, *J. Electrochem. Soc.*, **114**, 1025 (1967).
240. J. L. Webb, C. K. Mann and H. M. Walborsky, *J. Amer. Chem. Soc.*, **92**, 2042 (1970).
241. O. W. Webster, W. Mahler and R. E. Benson, *J. Amer. Chem. Soc.*, **84**, 3678 (1962).
242. N. L. Weinberg, D. H. Marr and C. N. Wu, *J. Amer. Chem. Soc.*, **97**, 1499 (1975).
243. H. Wenker, *J. Amer. Chem. Soc.*, **57**, 772 (1935).
244. F. Wudl, M. L. Kaplan, B. K. Teo and J. Marshall, *J. Org. Chem.*, **42**, 1666 (1977).
245. K. Yoshida and S. Tsutsumi, *Tetrahedron Letters*, 2501 (1966).
246. K. Yoshida and T. Fueno, *Bull. Chem. Soc. Japan*, **42**, 2411 (1969).
247. K. Yoshida and T. Fueno, *Chem. Commun.*, 711 (1970).
248. K. Yoshida and T. Fueno, *J. Org. Chem.*, **36**, 1523 (1971).
249. K. Yoshida, T. Saeki and T. Fueno, *J. Org. Chem.*, **36**, 3673 (1971).
250. K. Yoshida and T. Fueno, *J. Org. Chem.*, **37**, 4145 (1972).
251. K. Yoshida and T. Fueno, *J. Org. Chem.*, **38**, 1045 (1973).
252. K. Yoshida, M. Shigi and T. Fueno, *J. Org. Chem.*, **40**, 63 (1975).
253. K. Yoshida, *J. Amer. Chem. Soc.*, **98**, 254 (1976).
254. K. Yoshida and T. Fueno, *J. Org. Chem.*, **41**, 731 (1976).
255. K. Yoshida, T. Kanbe and T. Fueno, *J. Org. Chem.*, **42**, 2313 (1977).
256. K. Yoshida, *J. Amer. Chem. Soc.*, **99**, 6111 (1977).
257. K. Yoshida, *J. Chem. Soc., Chem. Commun.*, 20 (1978).
258. K. Yoshida, *J. Chem. Soc., Chem. Commun.*, 1108 (1978).
259. K. Yoshida, *J. Amer. Chem. Soc.*, **101**, 2116 (1979).
260. K. Yoshida and S. Nagase, *J. Amer. Chem. Soc.*, **101**, 4268 (1979).
261. P. Zuman and O. Manoušek, *Collect. Czech. Chem. Commun.*, **34**, 1580 (1969).
262. A. Zweig, J. E. Lehnsen, W. G. Hodgson and W. H. Jura, *J. Amer. Chem. Soc.*, **85**, 3937 (1963).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 8

The directing and activating effects of triply bonded groups

MARVIN CHARTON
Pratt Institute, Department of Chemistry, Brooklyn, New York 11205, U.S.A.

Abbreviations*

X	Substituent
Y	Active site
G	Skeletal group
Ak	Alkyl
pfAk	Perfluoroalkyl
Vi	Vinyl
1-Vn	$CH_2{=}C\lesssim$, vinylidene
2-Vn	—CH=CH—, vinylene
3-Pn	*m*-Phenylene
4-Pn	*p*-Phenylene
c	Cyclo, thus cHx is cyclohexyl
Hx	Hexyl
Hp	Heptyl
Dc	Decyl
OTr	Tresylate
El	Electrophile
f	Over a partial bond in a transition state indicates bond-formation
b	Over a partial bond in a transition state indicates bond-breaking
PRDDO	Partial Retention of Diatomic Differential Overlap

I. TRIPLY BONDED GROUPS

A. Introduction

The first step in discussing the directing and activating effects of triply bonded groups is to determine what groups fall into this category. We shall define triply bonded groups as those which contain two atoms that are joined by a combination of one σ and two π bonding orbitals; thus these atoms formally share six bonding electrons and the bond resulting has a bond order greater than two. Triply bonded groups are conveniently divided into two classes: those which are ionic and those which are not. It must be noted at this point that this discussion will be restricted to

*Only abbreviations not used by *Chemical Abstracts* are given here.

TABLE 1. Uncommon triply bonded groups, $-M^1 \equiv M^2$

M^1	M^2	Species reported	References
C	P	$HC \equiv P$	1–5
		$MeC \equiv P$	
		$FC \equiv P$	
S	N	$F_3S \equiv N$	6–8
		$FS \equiv N$	
		$HOS \equiv N$	
		$ClS \equiv N$	
		$N \equiv SF_2NSF_2$	
		$N \equiv SF_2SOF_2$	
		$N \equiv SF_2NSO_2F^-$	
P	N	–	
B	N	–	
N	B	–	

those groups in which one of the triply bonded atoms is bonded to the rest of the system of interest. Thus the 1-propynyl group, $MeC \equiv C-$, will be discussed whereas the propargyl group, $HC \equiv C-CH_2-$, will not.

B. Neutral Triply Bonded Groups

The largest and most frequently encountered type of neutral triply bonded group is $-C \equiv C-Z$, where Z is any atom or group of atoms. The cyano group, $-C \equiv N$, is also very commonly studied. The isocyano group, $-\overset{+}{N} \equiv \bar{C}$ (written also as $-NC$) has not received nearly as much attention. No studies of the substituent effect of the nitrile oxide group, $-C \equiv \overset{+}{N}-\bar{O}$, are extant. Some other triply bonded groups which have been reported but have received little or no attention from organic chemists are given in Table 1 with examples of species in which the bond is said to exist. Also listed are several possible triply bonded groups of which there are no known examples.

C. Ionic Triply Bonded Groups

Three triply bonded ionic groups are frequently encountered; the diazonium, N_2^+, the acylium, $-CO^+$, and the acetylide, C_2^-, groups. Others are possible but have not been reported. The formation and some reactions of acylium ions have been reviewed[9].

II. SUBSTITUENT EFFECTS IN XGY SYSTEMS

A. Introduction

The directing and activating effects of all groups are dependent on the substituent effects of the groups. In order to properly discuss direction and activation it is first necessary to review the nature of substituent effects. For our discussion of these effects we shall make use of the methodology of correlation analysis (linear free energy relationships)[10,11]. In solution the overall effect of a substituent can be described in terms of its electrical and steric components. In the gas phase it is sometimes necessary to consider the polarizability of the substituent as well.

Each of these contributions is represented in the correlation equation by an appropriate substituent constant. The most familiar of these correlation equations is the Hammett equation:

$$Q = \rho\sigma_X + h \tag{1}$$

which has been used for many years to quantify substituent effects on the reactivity and physical properties of benzene derivatives. In this equation Q is the quantity to be correlated, σ_X is the substituent constant for the X substituent, and ρ, the slope, is a function of those factors held constant throughout the data set studied such as the medium, temperature, pressure, skeletal group and quantity correlated, and the type of active site at which the phenomenon studied takes place. The intercept, h, is equal to the calculated value of Q for the unsubstituted member of the set.

B. Electrical Effects

It is convenient to divide the electrical effect of a substituent into two contributions: the localized effect and the delocalized effect.

1. *The localized effect*

This effect is also referred to as the 'inductive' effect. This is a misnomer, because the most probable mode of transmission of electrical effects is through space (field effect) rather than through bonds (inductive effect)[12,13]. This mode of transmission is true of the entire electrical effect. The localized effect is so-called because it involves the most localized electrons (other than core electrons) in the species. Let us consider a set of chemical species of the form XGY where X is the substituent, Y the active site (at which the measurable phenomenon takes place) and G the skeletal group to which X and Y are bonded. The localized effect is the only effect observed when X is bonded to a G consisting only of sp^3-hybridized carbon atoms.

The localized effect is best described by the σ_I constants[14]. These constants are based on reference systems in which the substituent X is bonded to a rigid skeletal group G containing only sp^3-hybridized carbon atoms. The distance between the active site Y and the substituent X is sufficiently large to preclude the existence of steric effects, and the rigidity of G removes the possibility of conformational equilibria. Available values of σ_I for triply bonded groups are given in Table 2.

2. *The delocalized effect*

This effect, also known as the resonance effect, is due to electrons in π and n orbitals. (The n orbitals referred to are lone pairs on the atom of the substituent which is bonded to G in an XGY system or to Y in an XY system.) These electrons are the most extensively delocalized in a species. When a group X is bonded to a carbon atom hybridized sp^n with $n \leq 2$ the group can exert both localized and delocalized electrical effects. Ehrenson, Brownlee and Taft[21] have shown that four different types of delocalized effect parameter are required for XGY reactions in solution. When a species can form a lowest energy molecular orbital (LEMO) which involves n and/or π electrons on X, G and Y the type of delocalized effect parameter, σ_D, depends on the nature of Y. If Y is a strong delocalized effect acceptor, Y^+, such as $Ak_2\dot{C}$—, or —C≡$\dot{O}$, the σ_R^+ constants are required. If Y is a strong delocalized effect donor, Y^-, such as NH_2 or O^-, the σ_R^- constants are required. If Y is neither a strong donor nor strong acceptor, the σ_R constants are required. When XGY is incapable of forming a

TABLE 2. Values of substituent constants for neutral triply bonded groups, X[a]

	X											
Constant	HC≡C—	MeC≡C—	EtC≡C—	ViC≡C—	HC≡C—C≡C—	MeC≡C—C≡C—	PhC≡C—	PhC≡C—C≡C—	NC—	CN—	P≡C—	$F_3CC\equiv C$—
σ_I	0.29	0.30	0.30[c]	0.35	0.39[c]	0.39	0.33	0.41[c]	0.57	0.63	0.36[c]	0.42[d]
(E)	U[b]	0.014	U[c]	0.014	U[c]	0.014	0.014	U[c]	0.008	0.015	S	U
σ_R	−0.04	−0.27					−0.21		0.08			0.03[d]
(E)	U[b]	0.034					U		0.008			U
σ_R^0	−0.04[e]	−0.27[e]					−0.21[e]		0.08[e]			0.03[e]
(E)	U	U					U		0.008			U
σ_R^+	−0.12[f]				−0.17[f]				0.08[e]			
(E)	U				U				0.008			
σ_R^-	0.13[g]				0.19[g]				0.26			
(E)	U				U				0.030			
υ	0.58	0.58	0.58	0.58	0.58	0.58	0.58	0.58	0.40	0.40[h]	0.5[i]	0.58
α	0.085	0.131	0.178[h]		0.170[h]	0.216[h]	0.322	0.407[h]	0.053	0.053[j]	0.137[k]	0.125[h]
$\sigma_R^\dagger$	−0.45								−0.10		−0.39[c]	
(E)	0.019								0.022		S	
σ_p	0.25	0.03					0.26		0.65			0.45
(E)									0.0019			U
σ_m	0.29	0.21					0.12		0.61			0.43
(E)									0.0053			U

[a]Values of σ_I, σ_R, σ_R^+, σ_R^0, σ_R^- are from Reference 14 unless otherwise noted, values of υ from Reference 15 and values of $\sigma_R^\dagger$ from Reference 16. The σ constants reported are based on chemical reactivity data, except for $\sigma_R^\dagger$. Abbreviations: E, error; U, uncertain; S, speculative.

[b]Electrical effect substituent constants for the C_2H group are suspect due to the possibility of variation with the medium as a result of hydrogen bonding.

[c]Obtained as described in text.

[d]Calculated from the pK_as for 3- and 4-$F_3CC\equiv CPnCO_2H$ of 5.08 and 4.93 respectively in 44.1 w/w % aq. EtOH at 25°C reported in Reference 17. The calculations were made using equations (177) and (179) in Reference 14. The L_p, D_p and h_p values required are from set 4 of Table 26 in Reference 14. The L_m, D_m and h_m values used are −1.74, −0.438 and 5.82 respectively. They were obtained from a correlation of pK_as of 3-$XPnCO_2H$ in 44.1 w/w % aq. EtOH with the LD equation (equation 4). The data correlated are from References 18–20.

[e]σ_R^0 and σ_R^+ for these groups are probably equal to σ_R; see Reference 14.

[f]Estimated from k_{rel} for protodetrisilylation in MeOH–aq. $HClO_4$ of 4-substituted phenyltrimethylsilanes.

[g]Estimated from k_{rel} for the hydroxide-ion-catalysed cleavage of 4-substituted benzyltrimethylsilanes in aq. MeOH.

[h]Estimated assuming additivity.

[i]r_V for an atom seems to depend on its hybridization state and to decrease with decreasing p character. For P, r_V = 1.80; for CN, r_V = 1.60. A value of 0.5 for υ seems reasonable.

[j]Assumed identical to α for —C≡N.

[k]Sum of α_C calculated from $(\alpha_{C\equiv CH} - \alpha_H)/2$ and the average value of α_P calculated from $\alpha_{PX_2} = 2\alpha_X$ with X = H, F, Cl, Me.

LEMO involving n and/or π electrons, the σ_R^0 constants are required. Systems of this type are $XG'CH_2Y$ and $XG'CH_2CH_2Y$.

It has recently been shown that for reactions involving Y^+ in the gas phase, and for ionization potentials, it is necessary to have a fifth type of delocalized effect parameter, σ_R^+ [16]. These constants have been shown to be a function of σ_R^+ and of a polarizability parameter, α, which will be described below. These results suggest that gas-phase data for systems with Y^- and electron affinity might possibly require a sixth set of delocalized effect constants $\sigma_R^‡$, related to σ_R^- and α.

If the overall electrical effect of a substituent is represented by the composite substituent constant σ_X, then we may write, based on the discussion above

$$\sigma_X = \lambda\sigma_{IX} + \delta\sigma_{DX} \tag{2}$$

where λ and δ are coefficients. Then substituting equation (2) into equation (1) results in the expression

$$Q_X = \rho\lambda\sigma_{IX} + \rho\delta\sigma_{DX} + h \tag{3}$$

$$= L\sigma_{IX} + D\sigma_{DX} + h \tag{4}$$

We shall refer to this equation throughout this work as the LD equation, and in general, we shall designate correlation equations by the coefficients of those substituent constants which are present in the correlation equation. Thus, the correlation equation

$$Q_X = L\sigma_{IX} + D\sigma_{DX} + Sv_X + A\alpha_X + h \tag{5}$$

which includes not only the electrical effect constants, σ_I and σ_D, but also the steric effect constant, v, and the polarizability constant, α, will be referred to as the LDSA equation; while the equation

$$Q_X = L\sigma_{IX} + D\sigma_{DX} + Sv_X + h \tag{6}$$

will be designated the LDS equation.

Available values of all of the above types of delocalized electrical effect substituent constants for triply bonded groups are reported in Table 2. Electrical effect substituent constants for ionic groups can only be considered as highly uncertain estimates as the electrical effect of these groups is very strongly dependent upon the medium (solvent and ionic strength)[14]. Substituents which contain an OH group, and in particular OH itself, are also highly dependent on the medium where the electrical effect is concerned[14]. This is due to hydrogen bonding involving the hydrogen atom of the OH group. Substituent constants for these groups can also be considered only as approximations and *must be used with caution*. The oxygen atom in the OH group has an electronegativity of 3.5. Jaffé and Hinze[22–24] give a value of 3.28 for the electronegativity of sp-hybridized carbon. It therefore seems quite possible that the ethynyl group can behave, at least to some extent, like an OH group and that the electrical effect substituent constants for the ethynyl group are also best considered to be approximations. In support of this proposal, two lines of evidence may be presented:

(*i*) The ethynyl hydrogen atom has been shown to form hydrogen bonds[22].

(*ii*) The ethynyl group deviates from the correlation line in some correlations of chemical reactivity with the LD and LDS equations.

Examples are the pK_a values for $XC{\equiv}CCO_2H$ in water at 25°C (in this set the value for X = H represents the ethynyl group[25]) and log k_r for the basic hydrolysis of XCO_2Et in water at 25°C[26].

3. *The relationship between the electrical effects of different types of triply bonded groups*

A frequently used method for describing the electrical effects in heterocyclic compounds is based on the concept of 'replacement' substituent constants[27]. In this method the effect of replacing one or two carbon atoms in a benzene ring by a heteroatom is considered to be equivalent to the introduction of a substituent. A substituent constant for this replacement by a heteroatom can be determined in the same way as for the introduction of a substituent. Thus, replacement constants have been calculated for the replacement of CH by N (resulting in a pyridine ring) at the 2-, 3- and 4-positions. Replacement of CH in benzene by N is equivalent to the introduction of a strong electron acceptor group, the effect being greater at the 2- than at the 4-position. The same type of treatment can be applied using the ethynyl group as the reference group. As can be seen from the σ_I constants in Table 2, the introduction of the nitrogen atom at position 1 (isocyano group) is somewhat more effective than at position 2 (cyano group) and in both cases it is equivalent to a strong electron-withdrawing substituent.

No experimentally determined delocalized effect value based on chemical reactivity is available for the isocyano group. The σ_R value for the cyano group again shows that the introduction of nitrogen at position 2 results in an electron-withdrawing delocalized effect. As replacement substituent constants are roughly additive we may predict that the N_2^+ group should be very strongly electron-withdrawing by both localized and delocalized effects.

This view is supported by σ_p ($\sigma_p = \sigma_I + \sigma_R$) values reported for $N_2^+ BF_4^-$ of 3.43 and 3.04[28,29]. Although as was noted above, σ constants for ionic groups are only approximate, the enormous σ_p values observed above clearly indicate a strong electron-withdrawing effect.

We can further predict that the delocalized effect of the isocyano group should be very weakly electron-withdrawing. Some support for this view comes from a value of σ_R^0 for CN— of 0.02 obtained from ^{19}F-NMR chemical shift measurements[28]. A value of −0.15 for σ_R can be estimated from a correlation of q_π, the total π charge donated to the benzene ring by a substituent, based on *ab initio* quantum calculations[29] with σ_R constants. The correlation equation obtained is

$$q_\pi = 0.162\,\sigma_R + 0.00565 \tag{7}$$

The very large replacement constants reported for 3- and 4-pyranyl suggest that the $-C\equiv\overset{+}{O}$ group should also be very strongly electron-withdrawing by both localized and delocalized effects[27]. A further argument in support of this conclusion is that $-C\equiv\overset{+}{O}$ and $-\overset{+}{N}\equiv N$ are isoelectronic.

4. *The estimation of σ_I and σ_D for triply bonded groups*

It has been shown that for many functional groups of the type ZW— where W = NH, O, S, CH_2, C=O, SO_2, and in particular, 4-Pn and 2-Vn, relationships can be obtained of the type

$$\sigma_{ZW} = L\sigma_{IZ} + D\sigma_{DZ} + h \tag{8}$$

and

$$\sigma_{ZW} = \rho_n\sigma_{nZ} + h' \tag{9}$$

where σ_{ZW} may be $\sigma_{I,ZW}$ or $\sigma_{D,ZW}$ and σ_n is a composite substituent constant[14]. These equations are useful in the estimation of $\sigma_{I,ZW}$ and $\sigma_{D,ZW}$ for groups for which no

experimentally determined values are available. It would be very helpful to have such relationships for ZC≡C— groups (ZW with W = —C≡C—). Unfortunately only four reliable $\sigma_{I,ZW}$ values are available. Correlation of these with equation (4) did not give significant results.

Correlation with the equation

$$\sigma_{I,ZW} = L\sigma_{IZ} + h \tag{10}$$

did give significant results with $r = 0.9673$, $S_{est} = 0.0119$, $L = 0.316$, $h = 0.300$, $F = 42.97$, $100R^2 = 93.47$.

The set of $\sigma_{I,ZW}$ values studied has little variation in substituent type, in fact, the mean of the σ_R values is -0.17 with a standard deviation, S, of 0.07. It is uncertain, therefore, whether or not equation (6) can be applied to groups Z for which σ_R is greater than S, or at most $2S$. That equation (10) is of use in estimating σ_I values for Z—C≡C— when σ_{RZ} is within $\pm S$ of the mean σ_R value of -0.17 is supported by the following observation. A value of σ_I of 0.41 for the PhC≡C—C≡C— group may be estimated from equation (5). A value of σ_I of 0.40 can be estimated for this group from the pK_a in water at 25°C of $HNMe_2CH_2C{\equiv}C{-}C{\equiv}C{-}Ph$[30] and the relationship

$$pK_a(X) = -6.91\,\sigma_{IX} + 9.56 \tag{11}$$

As equation (11) is uncertain, the close agreement between the two estimates of σ_I is probably fortuitous. Estimates of $\sigma_{I,EtC{\equiv}C-}$ by the two methods give σ_I values of 0.30 and 0.23 respectively.

We may use equation (6) to obtain $\sigma_{I,repl}$ (repl = replacement constants) for the substitution of C by N at positions 1 and 2 of the ethynyl group. The values are obtained from the σ_I values for —CN and —NC. The $\sigma_{I,repl}$ constants for N^1 and N^2 are 1.14 and 0.93 respectively.

Wepster and coworkers[29] have provided further evidence for the failure of the Hammett and Taft equations when ionic groups are used. They have proposed that at zero ionic strength the effect of an ionic group can be represented by the equation

$$\sigma = \sigma^L + \delta_B \tag{12}$$

where σ^L is that part of the electrical effect which is transmitted by the inductive mode and δ_B that part transmitted by the field mode. We should like to avoid designating the mode of transmission of the electrical effect, and suggest that the electrical effect of an ionic group X_i could be modelled on equation (8):

$$\sigma_{T,X_i} = \sigma_{I,X_i} + \sigma_{D,X_i} + \sigma_{q,X_i} \tag{13}$$

where σ_T is the overall electrical effect, σ_I and σ_D the localized and delocalized electrical effects that the group would exert if it were uncharged, and σ_q the electrical effect due to the charge. Then, the observed σ_I for an ionic group in a system free of delocalized effects is given by

$$\sigma_{I,obs} = \sigma_{I,X_i} + \sigma_{q,X_i} \tag{14}$$

If we assume that $\sigma_{I,X_i} \simeq \sigma_{I,X_m}$ where X_m is a suitable uncharged model group whose structure is similar to that of X_i we can then estimate values of σ_{q,X_i}. Such estimates are reported in Table 3.

We can now make use of our replacement constants. Assuming that they are additive and using equation (7) we can calculate a value of σ_{IX_i,N_2^+} of 0.90. Then assuming $\sigma_{q,N_2^+} \simeq \sigma_{q,NMe_3^+}$ we estimate $\sigma_{I,obs}$ from equation (14) to be about 1.8. Values of 0.30 and 0.29 for σ_{R,N_2^+} have been obtained from infrared spectroscopy data[31]. A σ_R value of 0.65 has been reported from ^{19}F-NMR chemical shifts[32]. These values combined with our estimate of $\sigma_{I,obs}$ give $\sigma_p = 2.1$–2.5. This is in reasonable

TABLE 3. Composition of σ_I values for ionic groups, X_i[a]

X_i	$\sigma_{I,obs}$	X_m	σ_{I,X_i}	σ_q
Me_3N^+	1.07	Me_2N	0.17	0.90
Bu_3P^+	0.60	H_2P	0.18	0.42
Me_2S^+	0.90	MeS	0.30	0.60
N_2^+	1.80[b]		0.90[c]	0.90[d]
CO_2^-	−0.19	CO_2Me	0.32	−0.51
SO_3^-	0.15	SO_2CF_3	0.71	−0.56
C_2^-	−0.2[b]	C_2H	0.31[e]	−0.5[f]

[a]It is vital to note that substituent constants for ionic groups are very strongly medium-dependent. They should be used only in the medium in which they were determined.
[b]Calculated from equation (14).
[c]Calculated from $\sigma_{I,N}{}^1$(repl) and $\sigma_{I,N}{}^2$(repl) assuming additivity and equation (10).
[d]Assumed equal to σ_q for NMe_3^+.
[e]Calculated from equation (10).
[f]Assumed equal to the mean of the σ_q values for CO_2^- and SO_3^-.

agreement with the experimental values cited above. Equation (9) also permits us to estimate $\sigma_{I,obs}$ for the acetylide group, C_2^-, with C_2H as X_m and assuming that $\sigma_{Iq} \leqslant -0.5$, we obtain $\sigma_{I,obs} \leqslant -0.2$. The group will be a strong donor by the localized effect. Since the ethynyl group has a weak electron donor delocalized effect, the C_2^- group can be expected to exert an overall electron donor effect.

Landgrebe and Rynbrandt[33] have attempted to determine a σ_p^+ constant for the ethynyl group from the rate of solvolysis of the substituted benzyl chloride in 50% v/v aqueous ethanol using the correlation equation obtained for some very much earlier data of Olivier[34]. The Olivier data for 4-substituted benzyl chlorides are not well correlated by the LD equation using the σ_R^+ constants. The results of Landgrebe and Rynbrandt for σ_p^+ are therefore not useful and no confidence can be placed in their conclusion that the ethynyl group has a very small acceptor delocalized electrical effect. Eaborn and his coworkers[35–39] have reported relative rate constants (k_{rel}) for the protodetrimethylsilylation of 4-substituted phenyltrimethylsilanes in methanol–aqueous perchloric acid. From their data[40,41] values of σ_R^+ can be estimated for the ethynyl and butadiynyl groups. As the medium in which k_{rel} for C_2H and C_2C_2H were determined is slightly different from that in which the other members of the data set were studied, these σ_R^+ values have uncertain errors. They are probably fairly good estimates, however. As would be expected, the ethynyl and butadiynyl groups are capable of stabilizing a positive active site in an XGY system by delocalization. Their σ_R^+ values are comparable to those observed for the phenyl and vinyl groups (−0.17 and −0.15, respectively).

Eaborn and Parker[42] have also studied the base-catalysed cleavage of 4-substituted benzyltrimethylsilanes in aqueous methanol. From their data values of σ_R^- can be estimated. As the medium in which k_{rel} for the ethynyl and butadiynyl derivatives was determined is again slightly different from that in which the remainder of the data set was studied these values are uncertain. They are probably at the right order of magnitude however, and show that the ethynyl and butadiynyl groups are capable of stabilizing Y^- in XGY by delocalization. The σ_R^+ and σ_R^- values estimated for the ethynyl and butadiynyl groups are reported in Table 2.

Finally, we may speculate about the value for σ_I for the —C≡P group based on the following arguments: We have shown elsewhere[26] that the σ_I value of a group WZ_n is given by the equation

$$\sigma_{I,WZ_n} = a_{11}\chi_W + a_{12}n_Z + a_{10} \quad (15)^*$$

where χ_W is the Allred–Rochow electronegativity[43] of W and n_Z is the number of Z groups. We have also shown that

$$\sigma_{I,CH_2X} = a_{21}\sigma_{IX} + a_{20} \quad (16)$$

where X = WZ_n. Combining equations (15) and (16) gives

$$\sigma_{I,CH_2X} = b_{11}\chi_W + b_{12}n_Z + b_{10} \quad (17)$$

Similarly, from equations (15) and (10),

$$\sigma_{I,XC\equiv C} = b_{21}\chi_W + b_{22}n_Z + b_{20} \quad (18)$$

The definition of σ_I replacement constants is based on the idea that the replacement of C(2) in the ethynyl group by some other atom, M, is equivalent to the introduction of a substituent. This substituent would have no Z groups attached and therefore

$$\sigma_{I,-C\equiv M} = b_{31}\chi_M + b_{30} \quad (19)$$

We must presumably use χ_M values for sp-hybridized M. Such values are available from the work of Jaffé and Hinze[22–24] for C and N. We have calculated a value of 3.74 for χ of sp-hybridized P from the equation

$$\chi_P = d_1 P_p + d_0 \quad (20)$$

where P_p is the percent p character of the hybridized orbital. From equation (19) we obtain a value of 0.36 for $\sigma_{I,-C\equiv P}$ (Table 2). This value is probably within ±0.1 of the correct value.

There is no way to calculate σ_R, σ_R^+ or σ_R^- for —C≡P. The correlation of dipole moments of substituted cyano compounds with the LD equation using the $\sigma_R^\dagger$ constants is given by

$$\mu_X = -3.91\,\sigma_I - 3.53\,\sigma_R^\dagger + 2.80 \quad (21)$$

From the correlation equation, the value of μ reported for P≡C—C≡N and the above estimate of σ_I, we may calculate a $\sigma_R^\dagger$ value of −0.39[1].

C. Steric Effects

Steric effects are defined here as resulting from electronic repulsions between nonbonded atoms. The steric effect of a group X can be represented by a function of its van der Waals' radius, r_{VX}. Thus, the steric parameter υ is defined[15,25] as

$$\upsilon_X = r_{VX} - r_{VH} = r_{VX} - 1.20 \quad (22)$$

Triply bonded groups are linear at least as far as the triple bond is concerned and are cylindrically symmetric to the group axis (Figure 1). The radius of interest is that perpendicular to the group axis. Steric parameters for triply bonded groups which can be calculated or estimated are also given in Table 2.

*a_{11}, a_{12} etc. are regression coefficients, determined by correlating the data with the equation by multiple linear regression analysis. The b coefficients (equations 17–19) are combinations of the a coefficients.

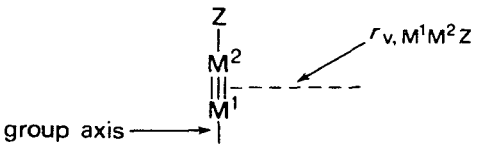


FIGURE 1

No data are available from which the steric effects of ionic substituents can be calculated. It is possible to make some estimates based on reasonable assumptions however. For the diazonium group the van der Waals' radius of nitrogen, 1.55 Å, can be taken as the basis for an υ value of 0.35. For the acylium ion the υ value can be assumed to be approximately equal to that of the cyano group, 0.40, as the van der Waals' radii of N and O differ by only 0.03 Å. The acetylide ion should have the same υ value as any —C≡CZ group, i.e. 0.58.

D. Polarizability

Some examples of chemical reactivity in the gas phase are known; these are best correlated by equations which in addition to electrical and/or steric effect terms, also include a polarizability term. The polarizability of a group X is conveniently represented by the parameter α, defined by the equation

$$\alpha = (MR_X - MR_H)/100 \tag{23}$$

where MR_X and MR_H are the molar refractivities of X and H respectively. Values of α for triply bonded groups are given in Table 2. The MR_X values from which they were calculated are from the compilation of Hansch and coworkers[44].

III. SUBSTITUENT EFFECTS IN XY SYSTEMS

A. Introduction

Of particular importance in determining the directing or activating effect of a substituent is its behaviour when it is directly bonded to an active site. Electrical effect substituent constants are generally determined in XGY systems where the substituent X and the active site Y are joined to a skeletal group G. Proper choice of G excludes the possibility of steric effects and is therefore a powerful reason for the use of XGY systems in defining electrical effect substituent constants. It is important to note, however, that the effect of a substituent in XGY is not necessarily identical with its effect in XY. We have remarked that the available evidence suggests that the major mode of transmission for the localized electrical effect in XGY is via the field effect although this is clearly not always the case. When G is methylene, *o*-phenylene or vinylidene the field effect model breaks down. In XY, however, no intervening bonds separate substituent and active site. It follows then that in this type of system the inductive effect can and should be of major importance.

The delocalized effect of X in XY may also differ from that of X in XGY. Let G be a π-bonded skeletal group such that both the X and the Y groups can interact with G to form a lowest energy molecular orbital encompassing the entire system. Then the delocalized effect of X is due to its perturbation of the interaction of G with Y. Thus, X acts by increasing or decreasing the electron density in the π orbital of G. In an XY system, X interacts directly with Y. It is instructive to consider the interaction of a

triply bonded group M^1M^2 with three special cases of Y – the carbenium ion, $^+CH_2$, the radical $^\cdot CH_2$ and the carbanion $:CH_2^-$ by means of valence bond theory and of qualitative MO theory.

Valence bond theory gives for the major contributing structures of the three species:

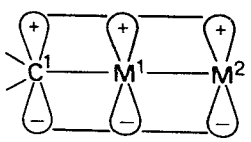
(*i*) $\overset{+}{C}-M^1\equiv M^2 \longleftrightarrow C=M^1=\overset{+}{M}^2$

(*ii*) $\dot{C}-M^1\equiv M^2 \longleftrightarrow C=M^1=\dot{M}^2$

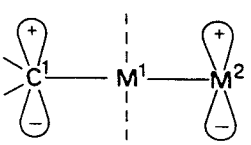
(*iii*) $\ddot{C}-M^1\equiv M^2 \longleftrightarrow C=M^1=\ddot{M}^2$

while qualitative MO theory gives the orbitals and the correlation diagrams shown in Figure 2.

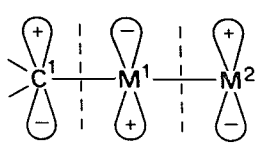
Clearly, this qualitative discussion shows that any $M^1\equiv M^2$ group is capable of stabilizing to some extent carbenium ions, radicals and carbanions, as in each of these cases either the charge or the unpaired electron is distributed between the C^1 and M^2 atoms.



$$1\pi = a_1P_{C^1} + a_2P_{M^1} + a_3P_{M^2}$$



$$1n = a_1P_{C^1} + a_3P_{M^2}$$



$$1\pi^* = a_1P_{C^1} - a_2P_{M^1} + a_3P_{M^2}$$

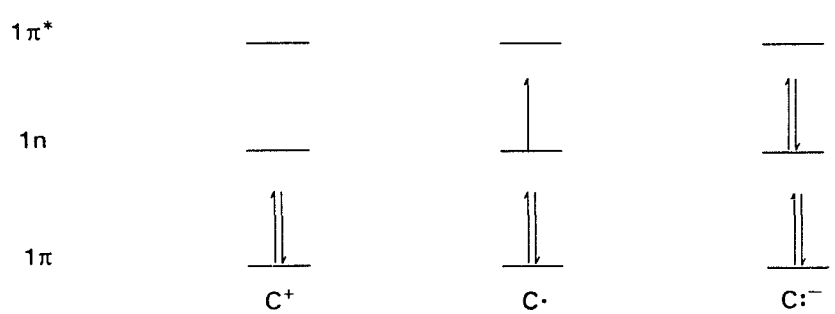


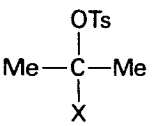
FIGURE 2

B. Carbenium Ion Stabilization

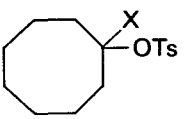
Recent reports show that the cyano group is indeed capable of stabilizing a carbenium ion by the delocalized effect. Thus, Gassman and Talley[45,46] have reported that for the solvolysis of 2-substituted 2-propyl and 1-substituted 1-cyclooctyl tosylates (**1** and **2**) in CF_3CO_2H at 25°C, the k_{rel} values are much smaller than those predicted from the localized electrical effect of the CN group and smaller even than that observed for the β-cyano system, **3** (Lg = leaving group). The k_{rel} are defined by equation (24).

$$k_{rel} \equiv k_H/k_X \tag{24}$$

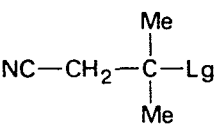
Values of k_{rel} for **1** and **2** are 3500 and 1900 respectively. The k_{rel} value of 200 observed[46] for **4** supports this conclusion. *Ab initio* and PRDDO calculations provide



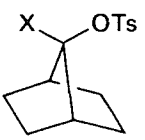
(1)



(2)

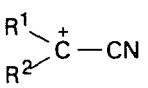


(3)



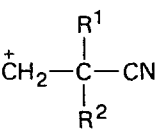
(4)

further theoretical support for the ability of the CN group to delocalize positive charge when bonded to a carbenium ion[47]. Calculations have been carried out on acetonitrile, **5**, and a number of α- and β-cyanocarbenium ions (**6** and **7**). Values of the bond order



(6)

(a) $R^1 = R^2 = H$
(b) R^1 = Me, $R^2 = H$
(c) $R^1 = R^2$ = Me
(d) R^1 = *t*-Bu, R^2 = Me



(7)

(a) $R^1 = R^2 = H$
(b) $R^1 = R^2$ = Me

and in some cases the localized molecular orbital (LMO) electron density are given in Table 4. The bond orders for the CN bond and for the C—C bond to which it is attached are essentially the same in **7a** and **7b** as in **5**. In **6a–6d** the CN bond order is significantly decreased and the C—C bond order significantly increased. Interestingly, as hydrogen is replaced by the methyl group on the carbenium carbon atom, the CN bond order increases and the C—C bond order decreases. The methyl group is a delocalized electrical effect (resonance) donor and presumably decreases the charge on the carbenium carbon atom and therefore the need for delocalizing it.

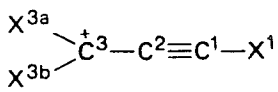
TABLE 4. Results of quantum-chemical calculations

(a) Bond orders and electron densities for acetonitrile and some carbenium ions[35–39 a]

Compound	C^3—C^2	C^2—N^1	C^3	C^2	N^1
5	1.038	2.939			
6a	1.418	2.522	0.33	1.15	0.52
6b	1.310	2.627	0.25	1.15	0.60
6c	1.232	2.707	0.17	1.10	0.72
6d	1.234	2.705			
7a	0.977	2.925			
7b	0.979	2.927			

[a]The numbered atoms refer to the structural fragment N^1—C^2—C^3 common to all of the species studied.

(b) Charge distributions in propargyl cations[48]



			Charge (10^{-3} electron)		
X^{3a}	X^{3b}	X^1	C^3	C^2	C^1
H	H	H	357	29	250
H	H	Me	333	−14	292
Me	H	Me	399	−7	215
H	H	NH_2	284	79	448
H	H	F	375	−12	573
F	H	H	666	−23	265
Me	H	Me	378	−51	262
Me	Me	H	422	−36	187
F	H	F	691	−71	602
F	F	H	952	−39	290

Olah and his coworkers[49] have prepared the stable carbenium ion Ph_2CCN^+ by reacting $Ph_2C(OH)CN$ with FSO_3H in SO_2ClF at −78°C. The NMR spectrum is believed to show delocalization of positive charge by the cyano group as well as the phenyl groups.

Koshy and Tidwell[50] have reported that the CF_3 group in **1** (X = CF_3) is, as expected, very strongly rate-decelerating with $k_{rel} = 1.1 \times 10^5$, and that in fact CF_3 is the most strongly known deactivating group. As the CF_3 group is a strong localized effect electron acceptor, and as it cannot stabilize a positive charge by delocalization, this is not surprising. As a result of this difference in behaviour, in an XGY system with Y = C^+, the CN is a stronger electron acceptor overall than is CF_3. In an XY system with Y = C^+, this order is reversed.

The XGY order is clearly demonstrated by inspection of the σ_{60}^+ values for CF_3 and CN. Charton has pointed out that composite substituent constants, σ_n, may be

defined by the equation

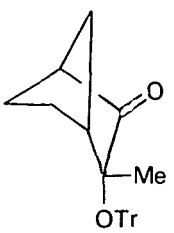
$$\sigma_n^d \equiv \sigma_I + \left(\frac{P_D}{100 - P_D}\right)\sigma_D \tag{25}$$

In this equation d indicates the type of σ_D (nothing, 0, +, −, for σ_R, σ_R^0, σ_R^+, σ_R^-, respectively), and P_D, the percent delocalized effect is given by

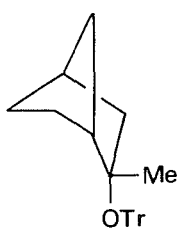
$$P_D = \frac{\delta \cdot 100}{\lambda + \delta} \tag{26}$$

The subscript n is equal to P_D. Values of σ_{50}, σ_{60}^+ and σ_{50}^- for some groups are given in Table 5, together with $\log k_{rel}$ values where available. The σ_{60}^+ and σ_{50}^- values were chosen because they have about the same electrical substituent effect composition as the σ_p^+ and σ_p^- values.

Creary has studied the formation of α-acyl carbenium ions[51]. His results suggest the possibility of some charge delocalization by the carbonyl group as would be expected from the above qualitative valence bond and MO treatments of $M^1 \equiv M^2$ groups. Clearly the same arguments can be applied to $M^1 = M^2$ groups as well. Unfortunately, none of the systems studied by Creary is directly comparable to those described above. Thus the rate of solvolysis of compound **8** was determined in acetic acid at 25°C and that of **9** estimated. The ratio k_9/k_8 is a measure of the effect of replacing CH_2 by C=O, however, and not of replacing H by X as is the case for the k_{rel} values described above.

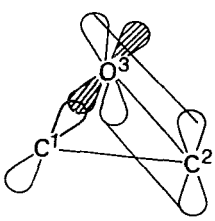


(8)

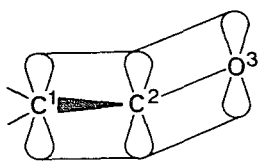


(9)

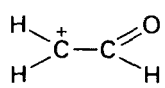
The formation and properties of α-acylcarbenium ions has been reviewed[52]. Two possible structures for the α-acylcarbenium ion have been proposed, **10** and **11**. Structure **11** is analogous to that described above for $C—M^1 \equiv M^2$ systems. In structure **10** the n_O orbital on oxygen (shaded) interacts with the empty orbital on C^1. *Ab initio* calculations on the ion **12** give conflicting results. The use of the STO-3G basis set indicates that when $C^1C^2O^3$ is 68° **10** is about 16 kcal mol^{-1} more stable than **11**, the use of a larger basis set suggests that **11** is 6–8 kcal mol^{-1} more stable than **10**.



(10)



(11)



(12)

Houk and his coworkers[53] have carried out *ab initio* quantum-chemical calculations on ions of the type $^+CH_2X$ with X equal to CN, CHO, CF_3 and NH_3^+ using a 4-31G

basis set. They found ΔE values (kcal mol^{-1}) of -9.9, -6.1, -37.3 and -156.9 respectively. This places the CN, CHO and CF_3 groups in the order $CF_3 < CN < CHO$ in terms of their ability to delocalize the charge on a carbenium ion.

Available solvolysis data[54] show that the ethynyl and propynyl groups can indeed stabilize a carbenium ion by delocalization of the positive charge. The $\log k_{rel}$ values show that as is expected from the greater electronegativity of sp vs. sp^2 carbon, the ethynyl group is less effective than the vinyl group in the stabilization of carbenium ions. The propynyl group is much more effective, as is expected from its σ_{60}^+ value. Other alkynyl (AkC≡C—) groups have $\log k_{rel}$ values comparable to that of propynyl.

Ab initio calculations on the structure and charge distribution of some alkynyl carbenium ions have been carried out using the STO-3G basis set[48]. The results are in agreement with the qualitative discussion above, and with the calculations for α-cyano carbenium ions. The charge distributions are summarized in Table 4.

Taft, Martin and Lampe[55] have measured ΔA_X values for the difference in appearance potential between XCH_2^+ and CH_3^+ in the gas-phase reaction

$$XCH_3 + e \longrightarrow XCH_2^+ + H^+ + 2\,e$$

These ΔA_X values are considered to measure the effect of X on stabilizing the carbenium ion. Values for typical groups are given in Table 5. Clearly, the ethynyl group is as effective as the vinyl group in stabilizing the carbenium ion. Although the cyano group destabilizes the carbenium ion, the magnitude of ΔA_{CN} is much less than might have otherwise been expected. The nitro group, which can be described by the same type of qualitative MO treatment as that used for M^1≡M^2 groups is surprisingly effective at stabilizing the carbenium ion. If the nitro group is excluded, the ΔA_X values are fairly well correlated by the LD equation using the σ_R^+ constants (Section II.B.2). Since the σ_R^+ constants were defined from ionization potentials for the lowest energy π orbital in monosubstituted benzenes which is an XY system, this result is not surprising. Whether σ_R^+ constants are equally effective in the correlation of chemical reactivities *in solution* for systems with electronically deficient Y is not yet known.

No data are available for the isocyano group, —N≡C. The electronegativities of sp-hybridized N and C are 5.07 and 3.29 respectively[22–24]. Clearly, we would expect the carbon atom in the isocyano group to bear a positive charge much more readily than the nitrogen atom in the cyano group. Thus, the isocyano group should be much more effective than the cyano group in stabilizing a positive charge and of course much less effective in stabilizing a negative charge by π delocalization. Data are also unavailable for the —C≡P group.

We have previously calculated a value of 3.75 for the electronegativity of sp-hybridized phosphorus. The —C≡P group should therefore also be capable of delocalizing a positive charge, although the effect of the more diffuse 3p orbital on phosphorus must also be considered. Neglecting the difference in p orbitals it should be more effective than a cyano group and less so than an ethynyl group.

C. Radical Stabilization

Gleicher and his coworkers[67] have determined the Hammett ρ value for the reaction of 3- or 4-substituted phenylacetonitriles with trichloromethyl radicals to be 0.55. It had been shown elsewhere that for the reaction

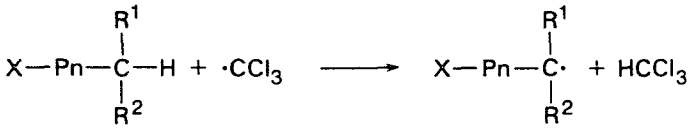


TABLE 5. Substituent effects on carbenium ions, carbon radicals and carbanions

X	σ_{50} [a]	σ_{60}^{+} [b]	σ_{50}^{-} [c]	$\log k_{rel}$	ΔA_X [d]	$\log k_{rel}$ [e]	$\log k_{rel}$ [f]
CN	0.65	0.69	0.83	3.54[g]	0.4	−8.23	
CF_3	0.51	0.63	0.58	5.04[g]			
Ac	0.50	0.39	0.71				
CO_2Et	0.41	0.47	0.61				
NO_2	0.77	0.82	1.04		−2.35		
SO_2Me	0.70	0.70	0.94				
H	0	0	0	0[h,i]	0	0	0
HC≡C	0.25	0.11	0.42	−2.09[h]	−2.4	−9.71	
				−1.72[i]			
MeC≡C	0.03	(−0.11)[j]		−5.43[h]			−2.21
				−3.73[i]			
PhC≡C	0.22	(0.01)					−2.53
H_2C=CH	−0.04	−0.12		−6.02[h]	−2.35	−9.70	
MeCH=CH	−0.09	(−0.17)					−3.10
PhCH=CH	(0.03)	(−0.02)					−3.20
Ph	0.01	−0.14	0.08		−2.4	−9.36	−2.47
Me	−0.17	−0.25	−0.10		−1.5	−2.75	
Cl	0.22	0.16	0.17		−1.4		
OMe	−0.28	−0.70	−0.21		−3.0		

X	Δ_X [k]	ΔH_D^0 [l]	pK_a [m]	pK_a [n]	pK_a [o]	pK_a [p]	Δ_X [q]	$\sigma_R^{\ominus}$ [r]
CN	0.148	86	31.3	11.1	4.93	−6.22	9.85	0.22
CF_3					7.40			
Ac	0.162[s]	92	26.8[t]	13.6				0.53
CO_2Et	0.072[u]			15.7[v]		0.98[v]	2.65[v]	
NO_2			17.2		3.63	0.14	3.49	0.35
SO_2Me			31.4[t]	15.0				
H	0	104	~65	~65	10.23	3.63	0	0
HC≡C		93.9						
MeC≡C								
PhC≡C								

TABLE 5 *continued*

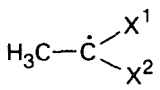
X	σ_{50} [a]	σ_{60}^{+} [b]	σ_{50}^{-} [c]	$\log k_{rel}$	ΔA_X [d]	$\log k_{rel}$ [e]	$\log k_{rel}$ [f]
$H_2C{=}CH$		85					
MeCH=CH							
PhCH=CH							
Ph		85	~44	32.2	3.89		0.28
Me	0.081	98		8.60	5.30	−1.67	−0.03
Cl		101.7		7.20	3.53	0.10	
OMe	0.172[w]	93.3					−0.38

[a]These constants are equivalent to σ_p.
[b]These constants are approximately equivalent to σ_p^+ in composition.
[c]These constants are approximately equivalent to σ_p^-.
[d]From Reference 55. Values are in eV, error ±0.1 eV.
[e]From the thermolysis of **14**; Reference 72.
[f]From the thermolysis of **15**; References 73 and 74.
[g]From the solvolysis of **1**.
[h]From the solvolysis of Me_2CXCl in 80% aq. EtOH at 25°C.
[i]From the solvolysis of Me_2CXCl in HCO_2H at 15°C.
[j]Substituent constants in parentheses are estimates and therefore uncertain.
[k]From References 70 and 71.
[l]From References 56 and 57.
[m]pK_a of MeX in DMSO at 25°C; References 58–64.
[n]pK_a of CH_2X_2 in DMSO at 25°C; References 58–64.
[o]pK_a of XCH_2NO_2 in water at 20°C; References 65 and 66.
[p]pK_a of $XCH(NO_2)_2$ in water at 20°C; References 65 and 66.
[q]Δ_X values from equation (32).
[r]$\sigma_R^{\ominus}$ substituent constants defined or derived from pK_as of XCH_2Z in DMSO (Z = CN, $PhSO_2$).
[s]Value is for Et—C=O.
[t]Includes statistical factor of 2.
[u]Value is for CO_2R.
[v]Value is for CO_2Me.
[w]Value is for OEt.

ρ as a function of R^1 and R^2 can be calculated from the equation

$$\rho_{R^1R^2} = -0.606\Sigma\sigma_p^+ + 0.195\Sigma E_S - 1.063 \quad (27)$$

The ρ value calculated for the reaction of the phenylacetonitriles is -0.98 to -1.10 depending on the choice of the E_S value (Taft steric parameter) for CN. The difference is thought to be due to a special radical-stabilizing capacity of the cyano group. In a study of the reaction of chloro- and dichloro-acetonitrile with cyclohexyl radicals it was observed that replacement of Cl or H by CN decreases E_{Cl}, the chlorine-transfer activation energy, by about 15.5 and 31.8 kJ mol^{-1} respectively. This difference has been ascribed to stabilization of the transition state by a π delocalized effect of the cyano group[68]. Further evidence comes from electron spin resonance spectroscopy. It has been shown that the splitting a_H^{Me}, caused by β protons of the radical **13**, is



(13)

proportional to the spin density, ρ_α, at the atom α to the radical carbon atom[69]. Thus

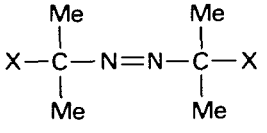
$$a_H^{Me} = Q_H^{Me}\rho_\alpha \quad (28)$$

where Q_H^{Me} is constant. Fischer[70,71] has shown that ρ_α can be calculated from the equation

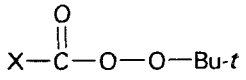
$$\rho_\alpha = \prod_{i=1}^{3}(1 - \Delta_X i) \quad (29)$$

where Δ_X is a constant characteristic of the spin-withdrawing (electron-withdrawing) effect of the substituent X. The Δ_X constant is also presumably a measure of the ability of the X group to delocalize the unpaired electron. Values of Δ_X are given in Table 5. They clearly demonstrate the ability of the cyano group to stabilize a radical. Clearly, the localized electrical effect is not the major factor in determining Δ. The Me and CO_2R groups have about the same value of Δ. Their σ_I values are -0.01 and 0.30 respectively. The CO_2Et and COEt groups have the same σ_I value, 0.30, but Δ for the former is about half that of the latter. The major factor in determining the value of Δ is probably indeed the ability to delocalize an electron.

Timberlake and his coworkers[72] have collected values for the relative rate of thermolysis of the substituted azopropanes, **14**. Values of $\log k_{rel}$ (equation 24) are given in Table 5. The results show that propynyl, ethynyl and cyano groups are all very effective at stabilizing radicals, the cyano group being about an order of magnitude less so than the others. Martin and Sanders[73] have examined the thermolysis of substituted *t*-butyl peresters, **15**. Their results show that the propynyl and phenylethynyl groups are slightly less effective than the propenyl and styryl groups. Values



(14)



(15)

of $\log k_{rel}$ calculated from their data in *p*-cymene and the data of Bartlett and Hiatt[74] in chlorobenzene are given in Table 5.

The cyano group has been reported to stabilize the biradical intermediate formed in the thermolysis of cyano-, *E*- or *Z*-dicyano-, and 1-cyano-3-methylenecyclobutanes by 6–10 kcal mol^{-1} [75]. Other examples of radical stabilization in thermolysis have been reported[76,77].

Additional evidence is provided by the C—H bond dissociation enthalpies ΔH_D^0 for the reaction

$$XCH_2H \longrightarrow XCH_2^{\cdot} + H^{\cdot}$$

at 25°C in the gas phase[56,57]. Values of ΔH_D^0 are also reported in Table 5.

The experimental results described above clearly support our conclusions based on the valence bond and qualitative MO treatments. All triply bonded groups can be expected to stabilize carbon radicals by delocalizing the unpaired electron.

D. Carbanion Stabilization

Bordwell and his group[58–64] have carried out an extensive series of investigations of structural effects on carbanion formation. Values of pK_a in dimethyl sulphoxide (DMSO) are given in Table 5 for XMe and X_2CH_2. The values for XMe show that while the cyano group is capable of stabilizing a carbanion, it is nowhere near as effective as a nitro group, and is significantly less effective than an acetyl group.

We can define a set of $\sigma_R^{\ominus}$ constants which are applicable to XY systems with a lone pair on the atom of Y which is bonded to X from an appropriate data set. Such a data set should be for systems which (*i*) are free of steric effects, (*ii*) are free of conformational effects, (*iii*) have a high sensitivity to electrical effects and (*iv*) encompass a range of substituent types. The pK_a values of substituted acetonitriles in DMSO, measured by Bordwell and his coworkers[58–64,78] are very suitable for this purpose. The cyano group, with a value of the steric parameter, υ, of 0.40, has one of the smallest of group steric effects. The carbanion which forms is apparently planar[78,79] and therefore free of conformational effects. While the number of substituents X for which pK_as have been determined is not as great as could be wished, there is an acceptable range of substituent types. Correlation of pK_as with the LD equation (equation 4) using σ_R^- constants, and including only those groups for which the substituent effect in XGY is not greatly different from that in XY gave significant results (X = Me, H, PhO, PhS, CN, CO_2Et) with $L = -26.9$, $D = -22.7$. Clearly, a very high sensitivity to electrical effects is present in this system. Using these L and D values to properly scale $\sigma_R^{\ominus}$, and the experimentally observed pK_a for X = H as h, we may define $\sigma_R^{\ominus}$ from the equation

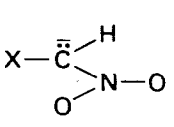
$$\sigma_{RX}^{\ominus} \equiv [pK_a(X) - L\sigma_{IX} - h]/D \tag{30}$$

Further values of $\sigma_R^{\ominus}$ have been obtained from pK_as for XCH_2SO_2Ph. The correlation obtained for these pK_as with the LD equation using the $\sigma_R^{\ominus}$ values defined in equation (30) suggests that little or no steric effect is present in the XCH_2SO_2Ph. The carbanion obtained for this system is thought to be planar[78], and therefore no conformational problem should exist. $\sigma_R^{\ominus}$ values have also been estimated from pK_as in DMSO for XCH_2NO_2 and XCH_2Bz. These values are much more uncertain. Steric effects on the pK_as of $AkCH_2NO_2$ have been observed. If steric effects exist in XCH_2NO_2 they must also exist in XCH_2Bz. The success of the pK_a correlations with the LD equation is probably due to the small size of the steric effect.

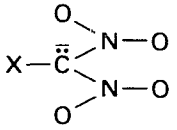
The $\sigma_R^{\ominus}$ values show that the cyano group can stabilize a carbanion effectively by π delocalization. It is less effective in this regard than the acetyl, benzoyl and nitro groups and about as effective as the phenyl and phenylsulphonyl groups. No $\sigma_R^{\ominus}$ values are available for the ethynyl group or for any substituted ethynyl groups. As

both the ethyl and butadiynyl groups have positive $\sigma_R^{\ominus}$ values, and as the phenyl, vinyl and 2-naphthyl groups all have positive $\sigma_R^{\ominus}$ values, we may conclude that substituted ethynyl groups will generally have positive $\sigma_R^{\ominus}$ values and will be effective in stabilizing carbanions by delocalization of the charge.

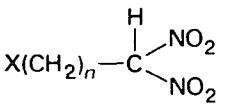
The values of pK_a for X_2CH_2 show an inversion in the effectiveness of the acetyl and cyano groups. The pK_a values[65,66] for XCH_2NO_2 and $XCH(NO_2)_2$ given in Table 5 also show a change in behaviour; the cyano group is almost as effective as the nitro group in stabilizing the carbanion, **16**, and is six orders of magnitude more effective at stabilizing the carbanion **17**. This is seen even more clearly in the pK_a values for the



(16)



(17)



(18)

terminally substituted alkyldinitromethanes, **18**, given in Table 6. The quantity $\Delta_{0,1}$, given by

$$\Delta_{0,1} = pK_a(X)^1 - pK_a(X)^0 \tag{31}$$

where the superscripts 0 and 1 indicate the number of methylene groups between the substituent X and the carbanion carbon atom is useful for making comparisons. It is far greater for the cyano group than for any of the planar π-bonded (Pπ) groups such as nitro, carboxamido or carbomethoxy. The order of carbanion stabilization is inverted from that observed in XMe. Additional support for this conclusion comes from consideration of the Δ_X values given by

$$\Delta_X = pK_a(H) - pK_a(X) \tag{32}$$

which are reported in Table 5. The most likely reason for this behaviour is that when X in **16** and **17** is a Pπ group, it is sterically hindered and cannot be coplanar with the carbanion carbon. This will result in a decrease in the effective π delocalization. The cyano group by contrast will be unaffected by this type of steric effect due to its cylindrical symmetry and small size. The same arguments apply to substituted ethynyl groups and presumably to the —C≡P group as well.

Finally, correlations of pK_as for alkyl-substituted nitro- and dinitro-methanes with the branching equation[80–82]

$$Q_X = \sum_{i=0}^{m} a_m n_m \tag{33}$$

TABLE 6. pK_a values for $X(CH_2)_n—CH(NO_2)_2$

	pK_a[a]					
X	$n = 4$	3	2	1	0	$\Delta_{0,1}$[b]
CN	5.00	4.34	3.50	2.34	−6.22	8.56
NO_2			3.37		0.14	<3
CO_2Me			4.43	3.08	0.98	2.10
$CONH_2$		4.75	4.49	3.41	1.30	2.11

[a] References 65 and 66.
[b] $\Delta_{0,1}$ from equation (31). This quantity is equivalent to $\log(k_a^0X/k_a^1X)_n$. n is the number of CH_2 groups between X and $CH(NO)_2$.

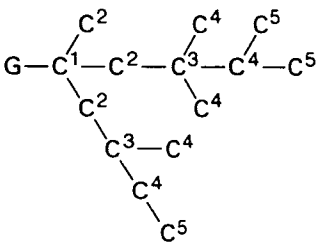


FIGURE 3

show that the steric effect due to branching at the first carbon atom of the alkyl group is greater for the latter than for the former. This is in agreement with a steric origin for the difference in the observed effects of the cyano group and the Pπ groups in the two systems.

The branching equation is an essentially topological relationship which accounts for steric effects by counting the number of branches at each atom of an alkyl group. Consider the alkyl group shown attached to a skeletal group G in Figure 3. The atoms are numbered in sequence starting from the atom bonded to G. The number of branching atoms attached to the ith atoms is equal to the number of atoms designated $i + 1$. Thus, in general, $n_i = \Sigma C^{i+1}$. In the example given in Figure 3, $n_0 = 1$, $n_1 = 3$, $n_2 = 2$, $n_3 = 5$, $n_4 = 3$. This type of equation has the advantage that there is no experimental uncertainty in the substituent parameters. The a_m are simply coefficients which are normally determined by multiple regression analysis.

E. An Overview of the Delocalized Electrical Effect

It is both interesting and instructive to arrange the various types of delocalized electrical effect substituent constants in order of decreasing electron demand of the active site, Y. This has been done in Table 7. We may *assign* values of a parameter η which is a measure of the relative electronic demand of the active site in each type of system used to define σ_D values. The σ_D constants may now be correlated with the η values by means of the equation

$$\sigma_{DY} = \xi\eta_Y + \xi^0 \tag{34}$$

TABLE 7. Electron demand as a function of Y

Y type[a]	Defining system	σ_D type	m[b]
$Y^{>+}$	XY^+	$R^\dagger$	3
Y^+	XGY^+	R^+	2
$Y^{\delta+}$	$XGY^{\delta+}$	R	1
Y^0	XG^1G^2Y[c]	R^0	0
$Y^{\delta-}$	$XGY^{\delta-}$	none	−1
Y^-	XGY^-	R^-	−2
$Y^{>-}$	XY^-	$R^\ominus$	−3

[a] In order of decreasing electronic demand.
[b] Arbitrary measure of electronic demand of Y.
[c] G^1 is 1,4-phenylene, G^2 is CH_2. 'Through' π delocalization between X and Y is minimal.

The slope, ξ, is a measure of the sensitivity of the delocalized electrical effect of a given group X to the electronic demand of an active site Y. The intercept, ξ^0, is equivalent to a calculated value of $\sigma_R{}^0$. Although it is likely that the $\sigma_R{}^+$ constants include a polarizability factor as well as a delocalized effect, they have been used here as a replacement for the as yet undefined $\sigma_R{}^\oplus$ constants. Most substituents give significant correlation with equation (34). The ξ values for some typical groups are reported in Table 8. With the exception of F, all of the groups studied give negative values of ξ. As would be expected, then, σ_D becomes more positive (increases) as the electron demand of Y decreases. The most sensitive groups ($\xi > 0.09$) are Ac, Bz, Vi, Ph, SMe, NH_2 and C≡CH. The ethynyl group is therefore comparable to vinyl and phenyl in its sensitivity to the electronic demand of the active site. From equation (34), a value of about 0.3 can be estimated for $\sigma_R{}^\ominus$ in accord with the discussion above. The least sensitive groups ($\xi \leq 0.03$) are Cl, Br and CF_3. Groups with intermediate sensitivity ($0.03 < \xi < 0.09$) include CO_2Et, $CONH_2$, NO_2, CN, Ak, OMe, OPh and cPr. The cyano group is comparable in its sensitivity to the methoxy, cyclopropyl and carboxamido groups.

It is convenient to classify substituents into three types with regard to their delocalized electrical effects. For the first type, σ_D is always negative no matter what the electronic demand of the active site happens to be. This type of group is always an electron donor. For the second type of group, σ_D is positive in at least one type of system. This group exhibits variable behaviour; it can function as a donor in some systems and an acceptor in others depending on the electronic demand of the active site. Examples of donors are halogens and alkyl, alkoxy and alkylamino groups. Examples of variable groups are vinyl, phenyl, substituted carbonyl, ethynyl, cyano, nitro and alkylthio groups. A few groups belong to the third type in which σ_D is always either positive or 0. These groups are acceptors; examples are the formyl and trifluoromethyl groups.

The variation in ξ from one substituent to another shows clearly why no one set of delocalized electrical effect substituent constants can correlate data for all possible types of Y. If ξ were the same for all groups then a single σ_D constant would be

TABLE 8. Values of ξ for some typical groups

X	Group type[a]	$-\xi$	X	Group type	$-\xi$
Me	d	0.030	SO_2Me	(v)	~0.03
cPr	v	0.050	$SiMe_3$	v	~0.08
Vi	v	0.12	Ph	v	0.12
C≡CH	v	0.10	CF_3	a	~0.03
Ac	v	0.088	F	d	−0.039
Bz	v	0.10	Cl	d	~0.02
CHO	a	0.091	Br	d	~0.02
CO_2Et	v	0.081	$CONH_2$	v	0.049
CN	v	0.050	CH_2Ph	v	0.031
NO_2	v	0.070	CH_2Cl	(v)	~0.03
H	–	0	CH_2OMe	(v)	~0.04
NH_2	d	0.13	CH_2CN	(v)	~0.02
OMe	d	0.062	OPh	d	0.039
SMe	d	0.091			

[a]d indicates a donor, a an acceptor and v a variable group. When in parentheses, the group type is uncertain.

sufficient. It follows then that to determine the extent of the electron demand of a given Y it is necessary to study a set of X with a range of ξ values.

IV. DIRECTING EFFECTS ON PRODUCT FORMATION

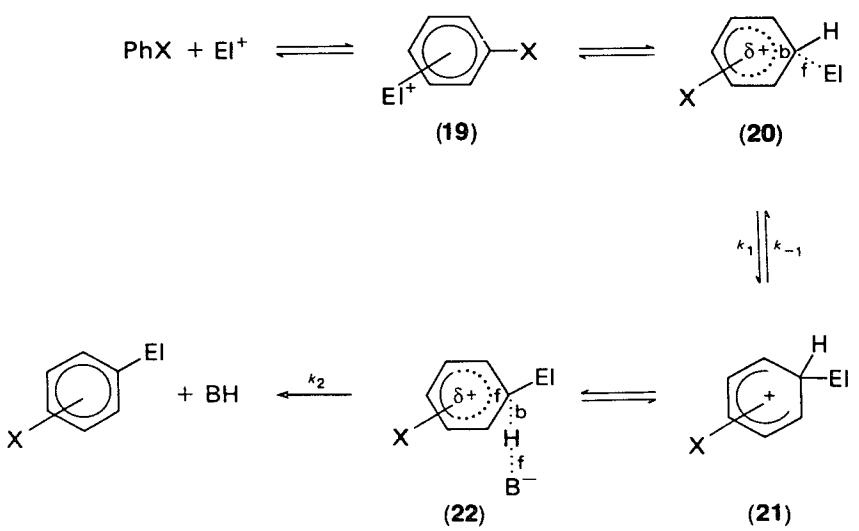
A. Introduction

In many organic reactions the products include two or more structural isomers. Generally the composition of the reaction mixture is determined by the electrical and steric effects of those groups present in the reactant before the reaction occurs.

The effect of substituents upon product composition has been variously termed the directing effect, the orientation or the regioselectivity, depending upon the author and the reaction being discussed. We shall use the term orientation as it is the simplest single word. It would be most difficult, and furthermore unnecessary, to be encyclopedic and to attempt to consider orientation in every reaction in which it can occur. We shall limit this discussion to some of the best known examples and to cases of some special or unusual interest.

B. Electrophilic Aromatic Substitution

The reaction which has been examined most intensively in this regard is electrophilic aromatic substitution. It seems clear now that in the most commonly encountered reactions of this type, such as sulphonation, nitration, halogenation, alkylation and acylation, the mechanism in the case of a monosubstituted benzene derivative, PhX, can be written as shown in Scheme 1; **19** is a charge-transfer complex, between PhX and the electrophile El^+, **20** is the first transition state (dotted lines labelled f or b indicate bonds being formed and/or broken) and $\delta+$ indicates a partial positive charge. Structure **21** is the carbenium ion (Wheland) intermediate and **22** is the second transition state. In general $k_1 \ll k_{-1}$ and k_2 and is therefore rate-determining. Partial



SCHEME 1

rate factors for *ortho*, *meta* and *para* substitution can be calculated from the expression[83]

$$f_{iX} = \frac{k_X P_{iX} \times 6}{k_H n_i} \tag{35}$$

where k_X and k_H are the rate constants for PhX and PhH respectively, P_i is the percent of the total product which underwent substitution at the ith position and n_i is the number of equivalent ith positions in the ring. If we consider *meta* versus *para* substitution, we can write

$$\frac{P_{3X}}{2P_{4X}} = \frac{f_{3X}}{f_{4X}} \equiv r_{3,4X} \tag{36}$$

and applying the LD equation, we have

$$\log r_{3,4X} = \log f_{3X} - \log f_{4X} \tag{37}$$

$$= L_3\sigma_{IX} + D_3\sigma_{DX} + h - L_4\sigma_{IX} - D_4\sigma_{DX} - h \tag{38}$$

$$= (L_3 - L_4)\sigma_{IX} + (D_3 - D_4)\sigma_{DX} \tag{39}$$

$$= L'\sigma_{IX} + D'\sigma_{DX} \tag{40}$$

Clearly, the directing effect of the X group must depend upon its electrical effect. Similarly, for *ortho* versus *para* substitution[84,85]

$$\frac{P_{2X}}{2P_{4X}} = \frac{f_{2X}}{f_{4X}} \equiv r_{2,4X} \tag{41}$$

and from the LD and LDS equations

$$\log r_{2,4X} = \log f_{2X} - \log f_{4X} \tag{42}$$

$$= L_2\sigma_{IX} + D_2\sigma_{DX} + S_2\upsilon_X + h - L_4\sigma_{IX} - D_4\sigma_{DX} - h \tag{43}$$

$$= L''\sigma_{IX} + D''\sigma_{DX} + S_2\upsilon_X \tag{44}$$

and the directing effect of X should be a function of its electrical and steric effects. Although this treatment ignores the possibility of *ipso* substitution followed by rearrangement it should in most cases be a reasonable approximation.

A field effect calculation (Kirkwood–Westheimer equation)[86] of the ratio L_3/L_4 gives a value of 1.2. It is well known that the delocalized effect is much greater in the 4-position than in the 3-position. From the composition of σ_m and σ_p constants, $D_3/D_4 \simeq 0.3$. Then from equation (39)

$$\log r_{3,4X} = \log\left(\frac{P_{3X}}{2P_{4X}}\right) = (1.2L_4 - L_4)\sigma_{IX} + (0.3D_4 - D_4)\sigma_{DX} \tag{45}$$

The appropriate type of σ_D constant for electrophilic aromatic substitution is σ_R^+. Then

$$\log r_{3,4X} + \log\left(\frac{P_{3X}}{2P_{4X}}\right) = 0.2L_4\sigma_{IX} - 0.7D_4\sigma_{RX}^+ \tag{46}$$

As generally $D_4 > L_4$ in this reaction the amount of *meta* substitution relative to *para* substitution is determined largely by the delocalized electrical effect of X. It is difficult to provide extensive tests of this conclusion as well-characterized data sets with a wide range of substituent type are not generally available for electrophilic aromatic substitution. Such a data set would include substituents of all possible types. In some types of electrophilic aromatic substitution, such as Friedel–Crafts alkylation and acylation, such a data set is unobtainable as substituents which are localized and

TABLE 9. Partial rate factors and orientation ratios for the electrophilic fluorination of PhX in CCl_3F at $-78°C$[87]

	Partial rate factors			Orientation ratios	
	f_2	f_3	f_4	$r_{2,4}$[a]	$r_{3,4}$[b]
Me	8.46	1.55	8.2	1.03	0.190
CN	0.0178	0.041	0.017	1.04	2.38
NO_2	0.00459	0.041	0.011	0.409	3.64
CF_3	0.0144	0.058	0.036	0.400	1.60
OMe	123.	0.81	76.1	1.62	0.0106
Br	0.0828	0.061	0.43	0.192	0.142
Cl	0.192	0.077	0.44	0.435	0.174
F	0.264	0.16	1.56	0.169	0.100
H	1	1	1	1	1

[a] $r_{2,4} = P_o/2P_p$.
[b] $r_{3,4} = P_m/2P_p$.

delocalized effect electron acceptors cannot be included in the data set. Recently a report has appeared on the fluorination of PhX in CCl_3F at $-78°C$[87]. The data set is reasonably well characterized (see Table 9) and fits equation (47) very well as L' is not significant. Thus, the validity of equation (39) is supported.

$$\log r_{3,4} = \log\left(\frac{P_{3X}}{2P_{4X}}\right) = D'\sigma_R^+ \tag{47}$$

That the steric effect is an important factor in determining orientation in the 2-position is clearly shown by an examination of the data obtained by Wepster and Baas[88–91] for the nitration of alkylbenzenes and of Cerfontain and Schaasberg–Nienhuis[92] on their sulphonation. Although there has been considerable discussion over the last twenty years with regard to the electrical effect of alkyl groups it seems likely that the localized electrical effect of alkyl groups is both constant and not significantly different from zero. Although the delocalized effect is significantly different from zero, for all but the $\sigma_R^\ominus$ values it is also constant[93–98]. Alkyl groups are therefore an admirable probe for steric effects. Values of $r_{2,4}$ have been successfully correlated with both the branching equation (equation 33) and the modified Taft equation

$$Q_X = S\upsilon_X + h \tag{48}$$

These results are in agreement with equation (44).

Correlations with equation (44) of $r_{2,4}$ for nitration in nitromethane and chlorination in CCl_4–$HClO_4$–$AgClO_4$ provide some further support for the validity of this equation. The major factor in determining orientation again appears to be the delocalized electrical effect.

Clearly, if the correlation equation for $r_{2,4}$ or $r_{3,4}$ is known and the appropriate substituent constants are available, the orientation can be predicted.

C. Free Radical Addition to Olefins

When a radical adds to an unsymmetrically substituted olefin there are two possible products:

$$\cdot CZ^1Z^2Z^3 + X^1X^2C{=}CX^3X^4 \longrightarrow Z^1Z^2Z^3C{-}CX^1X^2{-}\dot{C}X^3X^4$$

(23)

$$+$$

$$Z^1Z^2Z^3C{-}CX^3X^4{-}\dot{C}X^1X^2$$

(24)

Orientation is a function of structural effects in the radical and in the olefin. The problem has received considerable study, particularly by Tedder and his co-workers[99–102]. We shall designate the carbon atom of the double bond with the greatest value of Σv_X as C^1 and the other carbon atom of the double bond as C^2. We may define the orientation ratio r_{21} as the percent of radical attack at C^2 divided by the percent at C^1

$$r_{21} \equiv \frac{P_2}{P_1} = \frac{k_2}{k_1} \tag{49}$$

Let us first consider the effect of structural variation in the radical. For the rate constant k_1 for attack by the radical at C^1 we may write the LDS equation as

$$\log k_1 = L_1\Sigma\sigma_{IZ} + D_1\Sigma\sigma_{DZ} + S_1 v_{CZ^1Z^2Z^3} + h_1 \tag{50}$$

In this equation two assumptions are made: (*i*) the electrical effects of Z are additive, and (*ii*) in the transition state the radical $CZ^1Z^2Z^3$ will resemble the group $CZ^1Z^2Z^3$ and therefore its steric effect will be proportional to that of the $CZ^1Z^2Z^3$ group. An analogous equation can be written for k_2:

$$\log k_2 = L_2\Sigma\sigma_{IZ} + D_2\Sigma\sigma_{DZ} + S_2 v_{CZ^1Z^2Z^3} + h_2 \tag{51}$$

Then subtracting equation (50) from equation (51) and combining with equation (49),

$$\log r_{21} = L'\Sigma\sigma_{IZ} + D'\Sigma\sigma_{DZ} + S'\Sigma v_{CZ^1Z^2Z^3} + h' \tag{52}$$

Obviously this treatment is analogous to that used for electrophilic aromatic substitution. Some of the data collected by Tedder and Walton[99,100] have been correlated with equation (52) giving significant results. The data are shown in Table 10. Unfortunately, in the data set available, the variables are not well separated. Thus

$$\Sigma\sigma_{IZ} = a_{12}\Sigma\sigma_{DZ} + a_{13}v_{CZ^1Z^2Z^3} + a_{10} \tag{53}$$

$$\Sigma\sigma_{DZ} = a_{21}\Sigma\sigma_{IZ} + a_{23}v_{CZ^1Z^2Z^3} + a_{20} \tag{54}$$

$$v_Z = a_{31}\Sigma\sigma_{IZ} + a_{32}\Sigma\sigma_{DZ} + a_{30} \tag{55}$$

The σ_R^+ constants were used as the σ_D parameter in the correlations as they were defined from ionization potentials of PhX involving electron loss from a π orbital. This results in the formation of a radical cation and as was noted above the system is an XY system.

That orientation as a function of radical structure is dependent on the electrical and/or steric effects is further shown by consideration of the data reviewed by Tedder and Walton[100] for perfluoroalkyl radicals. These results are also summarized in Table 10. What few data are available suggest that for perfluoroalkyl (pfAk) groups,

$$\sigma_{I,pfAk} = \text{constant} \tag{56}$$

$$\sigma_{D,pfAk} = \text{constant} \tag{57}$$

TABLE 10. Orientation in homolytic addition values of r_{21}[99,100]

(1) Substituted ethylenes + $Me^{\bullet}$
H, 1; Me, 6.7; F, 5; CF_3, 3; Vi, 100
(2) Substituted ethylenes + $CF_3^{\bullet}$
H, 1; Me, 10; F, 11.1; CF_3, 50
(3) Substituted ethylenes + $CCl_3^{\bullet}$
H, 1; Me, 14.3; F, 12.5
(4) Vinyl fluoride + $^{\bullet}CZ^1Z^2Z^3$
CH_3, 5.00; CH_2F, 3.33; CHF_2, 5.26; CF_3, 11.1; CH_2Cl, 5.56; CCl_3, 14.3; $CHBr_2$, 16.7; CBr_3, 25.0; $C(CF_3)_3$, 200
(5) Vinylidene fluoride + $^{\bullet}CZ^1Z^2Z^3$
CH_2F, 2.27; CHF_2, 6.07; CF_3, 33.3; CH_2Cl, 7.14; CCl_3, 100
(6) Trifluoroethylene + $^{\bullet}CZ^1Z^2Z^3$
CH_3, 0.476; CH_2F, 0.490; CHF_2, 1.05; CF_3, 2.00; CH_2Cl, 0.471; CCl_3, 3.45; $CHBr_2$, 3.23; CBr_3, 4.17
(7) Vinyl fluoride + $^{\bullet}C_mF_{2m+1}$
CF_3, 11.1; CF_3CF_2, 18.5; $(CF_3)_2CF$, 50.0; $(CF_3)_3C$, 200; $CF_3(CF_2)_2$, 20.0; $CF_3(CF_2)_3$, 20.0; $CF_3(CF_2)_6$, 20.4; $CF_3(CF_2)_7$, 23.3
(8) Vinylidene fluoride + $^{\bullet}C_mF_{2m+1}$
CF_3, 33.3; CF_3CF_2, 90.9; $(CF_3)_2CF$, 1000; $CF_3(CF_2)_2$, 111; $CF_3(CF_2)_3$, 143; $CF_3(CF_2)_6$, 143; $CF_3(CF_2)_7$, 167
(9) Trifluoroethylene + $^{\bullet}C_mF_{2m+1}$
CF_3, 2.00; CF_3CF_2, 3.45; $(CF_3)_2CF$, 16.7; $CF_3(CF_2)_2$, 4.00; $CF_3(CF_2)_3$, 4.17; $CF_3(CF_2)_6$, 4.35; $CF_3(CF_2)_7$, 4.55

Then for a radical with the structure $^{\bullet}C(pfAk)_{n_0}F_{3-n_0}$,

$$\Sigma\sigma_{IZ} = n_0\sigma_{I,pfAk} + (3 - n_0)\sigma_{IF} \tag{58}$$

$$\Sigma\sigma_{DZ} = n_0\sigma_{D,pfAk} + (3 - n_0)\sigma_{DF} \tag{59}$$

or

$$\Sigma\sigma_{IZ} = n_0\sigma_{I,pfAk} - (n_0 - 3)\sigma_{IF} \tag{60}$$

$$\Sigma\sigma_{DZ} = n_0\sigma_{D,pfAk} - (n_0 - 3)\sigma_{DF} \tag{61}$$

Substituting equations (60) and (61) into equation (50) gives

$$\log k_1 = L_1 n_0(\sigma_{I,pfAk} - \sigma_{IF}) + D_1 n_0(\sigma_{D,pfAk} - DF) + S\upsilon_{CZ^1Z^2Z^3} + h \tag{62}$$

Then

$$\log k_1 = L_{11}n_0 + d_{11}n_0 + S_1\upsilon_{CZ^1Z^2Z^3} + h \tag{63}$$

$$= b_{10}n_0 + S_1\upsilon_{CZ^1Z^2Z^3} + h \tag{64}$$

Similarly for k_2,

$$\log k_2 = b_{20}n_0 + S_2\upsilon_{CZ^1Z^2Z^3} + h_2 \tag{65}$$

The branching equation (equation 33) is used to account for steric effects of alkyl groups. It can be extended to represent the steric effect of any type of group as follows[103]: (*i*) The replacement of a skeletal carbon atom by another type of atom is accounted for by the skeletal factor f_k. (*ii*) The replacement of a branching hydrogen atom with some other type of atom is accounted for by a branching factor f_B. Thus, the generalized branching equation is given by

$$Q = \sum_{i=1}^{m} a_i f_{ki}\left(\sum_{j=0}^{m} n_{ij} f_{Bj}\right) \tag{66}$$

For a group of the type C_pZ_{2p+1} as $f_{k,C} \equiv 1.00$, the steric effect is given by

$$Q = a_0[n_0 + (3 - n_0)f_{BZ}] + a_1[n_1 + (9 - n_1)f_{BZ}] + a_2[n_2 + (27 - n_2]f_{BZ} + \ldots \quad (67)$$

or

$$Q = \sum_{i=0}^{m} a_i[n_i + (3^{i+1} - n_i)f_{BZ}] \quad (68)$$

Then

$$Q = \sum_{i=0}^{m} a_i[n_i - (n_i + 3^{i+1})f_{BZ} \quad (69)$$

$$= \sum_{i=0}^{m} a_i[n_i(1 - f_{BZ}) + 3^{i+1}f_{BZ}] \quad (70)$$

$$= \sum_{i=0}^{m} a_i'n_i + \sum_{i=0}^{m} a_i 3^{i+1}f_{BZ} \quad (71)$$

For a given m the second term on the right-hand side of equation (71) is constant. Then,

$$Q = \sum_{i=0}^{m} a_i'n_i + \sum_{i=0}^{m} C_i \quad (72)$$

Thus, for $m = 2$,

$$Q = a_0'n_0 + a_1'n_1 + a_2'n_2 \quad (73)$$

From equations (64) and (65),

$$\log r_{21} = b_{21}n_0 + S_{21}\upsilon_{CZ^1Z^2Z^3} + h_{21} \quad (74)$$

The steric parameter of a perfluoroalkyl group should be given by equation (73) however. Thus,

$$\upsilon_{CZ^1Z^2Z^3} = a_0'n_0 + a_1'n_1 + a_2'n_2 \quad (75)$$

Combining equations (74) and (75) gives

$$\log r_{21} = a_{021}n_0 + a_{121}n_1 + a_{221}n_2 + h_{21} \quad (76)$$

As in the available data there was insufficient variation in n_1 and n_2 the correlation equation used was

$$\log r_{21} = a_{021}n_0 + h_{21} \quad (77)$$

Significant results were obtained, verifying the conclusion that orientation as a function of radical structure is dependent on electrical and/or steric effects.

We may now turn our attention to structural effects in the olefin. Data for the reaction of substituted ethylenes with methyl and trifluoromethyl radicals taken from the reviews of Tedder and Walton[99–102] are given in Table 10. Applying the same methodology as before we may obtain

$$\log r_{21} = L_{21}\sigma_{IX} + D_{21}\sigma_{DX} + S_{21}\upsilon_X + h_2 \quad (78)$$

The data available are rather limited, and necessitate the use of $\sigma_n^{\dagger}$ constants and the equation

$$\log r_{21} = \rho\sigma_{80}^{\dagger} + S\upsilon_X + h \quad (79)$$

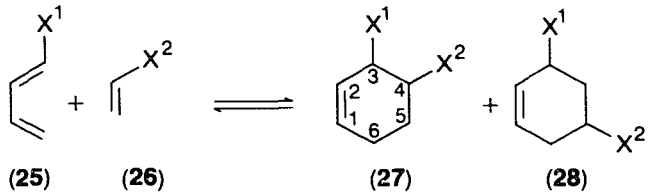
Significant results have been obtained. In view of the sparse data available the results can only be considered as suggestive. They do imply however a dependence of orientation on electrical and steric effects.

Although the results obtained are nowhere near as clear-cut as could be wished, due to the lack of sufficient data, they strongly suggest that orientation is dependent on electrical and/or steric effects of substituents on the radical or the substituted ethylene. When the coefficients of the appropriate equations have been accurately determined the directing effect of any substituent for which the appropriate substituent constants are available can easily be obtained.

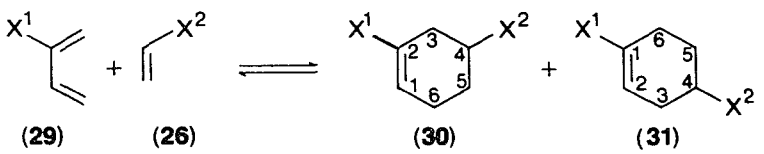
D. Cycloaddition Reactions

1. *The Diels–Alder reaction* ([2 + 4]*cycloaddition*)

The reaction of an unsymmetric diene with an unsymmetric dienophile can result in the formation of two different structural isomers. Consider for example the reaction of a 1-substituted butadiene, **25**, with a substituted ethylene, **26**. The products **27** and **28** may conveniently be referred to as the 3,4- and 3,5-adducts. If a 2-substituted butadiene, **29**, reacts with **26**, the products are **30** and **31**, or the 2,4- and 1,4-adducts.



(25) **(26)** **(27)** **(28)**



(29) **(26)** **(30)** **(31)**

Correlation analysis has been applied to the problem of orientation in the Diels–Alder reaction by Charton[104]. Using an approach similar to that described in IVB and IVC we may write for the case in which X^1 varies and X^2 is constant,

$$\log r = L_{1r}\sigma_{IX^1} + D_{1r}\sigma_{DX^1} + S_{1r}\upsilon_{X^1} + h_{1r} \qquad (80)$$

and for the case in which X^1 is constant and X^2 varies,

$$\log r = L_{2r}\sigma_{IX^2} + D_{2r}\sigma_{DX^2} + S_{2r}\upsilon_{X^2} + h_{2r} \qquad (81)$$

In equations (80) and (81), r is either $r_{34,35}$ or $r_{24,14}$. The available data are summarized in Table 11. Significant correlation has been obtained for the reaction of **29** with **26** ($X^2 = CO_2H$), using the LD equation. That steric effects can be important is shown however by the successful correlation of r from the reaction of **25** (X^1 = Ak) with ethyl acrylate (**26**, $X^2 = CO_2Et$) and of **29** (X^1 = Ak) with ethyl methacrylate, using the branching equation (equation 33) with $m = 1$. The data for the reaction of isoprene (**29**, X^1 = Me) with **26** have been correlated with equation (81). Unfortunately, not only is the set not well characterized but six of the seven substituents studied are of the planar π-bonded type. Both the steric and the delocalized electrical effects of this type of group are conformationally dependent. Thus, although the

TABLE 11. Orientation in cycloaddition reactions

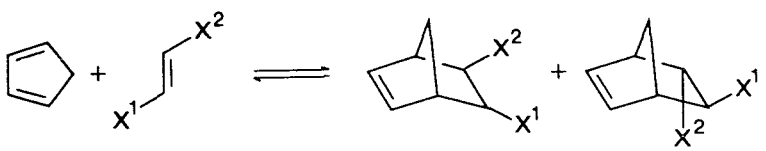
(1) $r_{34,35}$; 1-alkylbutadienes + ethyl acrylate[a]
Me, 6.8; Bu, 5.0; *i*-Pr, 5.1; *t*-Bu, 4.1
(2) $r_{14,24}$; 2-alkylbutadiene + ethyl acrylate[a]
Me, 2.0; *i*-Pr, 3.0; Pr, 2.4; *t*-Bu, 3.5
(3) $r_{14,24}$; 2-alkylbutadienes + ethyl methacrylate[a]
Me, 2.5; *i*-Pr, 7.3; Pr, 3.4; *t*-Bu, 10
(4) $r_{14,24}$; 2-substituted butadienes + acrylic acid[b,c]
Me, 1.9; OMe, 8; Cl, 9.3; Ph, 3; H, 1[d]
(5) $r_{14,24}$; 2-substituted butadienes + styrene[b,c]
Me, 3.5; OMe, 12; Cl, 14.3; H, 1[d]
(6) $r_{14,24}$; isoprene + substituted ethylenes[e]
CO_2Me, 2.0; CO_2Et, 1.9; Ac, 2.3; CHO, 1.8; NO_2, 3.7; Ph, 3.5; CN, 2.2
(7) $r_{X,n}$; cyclopentadiene + 4-ZPnCH=CHCOCl
NO_2, 1.78; Cl, 2.03; H, 2.03; MeO, 1.94
(8) $r_{X,n}$; cyclopentadiene + 4-ZPnCH=CHCO$_2$H[f]
NO_2, 0.429; Cl, 0.667; H, 0.754; MeO, 0.887
(9) $r_{X,n}$; cyclopentadiene + 4-O_2NPnCH=CHCOZ[f]
Cl, 1.78; OH, 0.429; OMe, 0.389; NH_2, 0.333
(10) $r_{X,n}$; cyclopentadiene + PhCH=CHCOZ[f]
Cl, 2.03; OH, 0.754; OMe, 0.786; NH_2, 0.515
(11) $r_{S,a}$; 2-substituted anthracene + maleic anhydride[g]
NO_2, 0.64; H, 1; NHAc, 1.08; NMe_2, 1.22
(12) $r_{3,4}$; substituted acetylene + diazomethane[h]
CMe_2OH, 1.84; CHMeOH, 2.56; CH_2OH, 2.99; CH_2OMe, 2.99; CHMeOPh, 2.71; CH_2OPh, 4.47; CH_2Br, 18.4; CMePhOH, 0.539; PhCHOH, 0.815

[a]Reference 105.
[b]Reference 106.
[c]Reference 107.
[d]By definition.
[e]Reference 108.
[f]Reference 109.
[g]Reference 110.
[h]Reference 111.

correlation provides some support for the validity of equation (81), the results can only be considered as suggestive.

In some Diels–Alder reactions two products of different stereochemistries may be obtained. Thus the reaction of cyclopentadiene with an unsymmetric disubstituted ethylene, **32**, can form either the *exo* product, **33**, or the *endo* product, **34**. In **32**, X^1 varies while X^2 is constant. *Exo* and *endo* refer to the geometry with respect to X^1, the variable group.

The available data are reported in Table 11; they can be correlated with the Hammett equation using the σ_n constants defined by equation (25). The data for

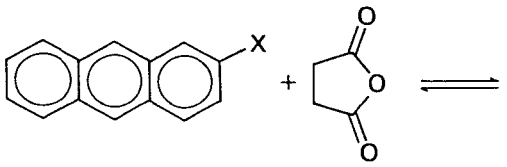


(32) **(34)** **(33)**

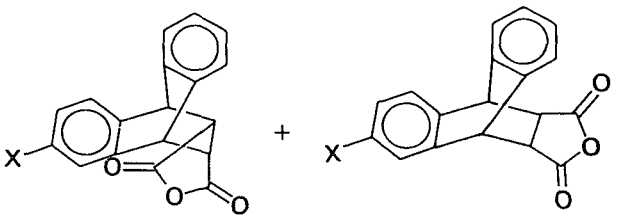
(a) X^1 = 4-ZPn, X^2 = CO_2H
(b) X^1 = ZCO, X^2 = Ph
(c) X^1 = ZCO, X^2 = Ph

32a, **b** and **c** are best correlated by the σ_{50}, σ_{20} and σ_{30} constants. As the data sets are not well characterized, the results can again only be considered as indicative. They do suggest that product composition is a function of electrical substituent effects.

The reaction of maleic anhydride with 2-substituted anthracenes, **35**, results in two stereoisomeric products, the *syn* adduct, **36**, and the *anti* adduct, **37**. The data are given in Table 11. The $r_{S,a}$ values are correlated by the Hammett equation using the σ_{30} constants.



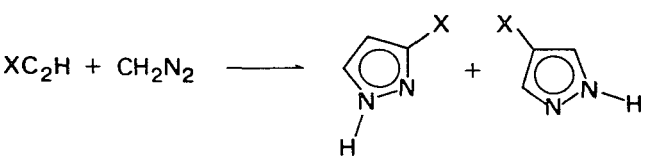
(35)



(36)(*syn*) **(37)**(*anti*)

2. 1,3-Dipolar [2 + 3]*cycloaddition*

Stephan, Vo-Quang and Vo-Quang[111] have reported rate constants for the formation of 3- and 4-substituted pyrazoles, **38** and **39** respectively, from the reaction of substituted acetylenes with diazomethane.



(38) **(39)**

As the X groups were all of the type $CZ^1Z^2Z^3$, the $\log kr$ values were correlated with the equation

$$\log kr = L\Sigma\sigma_{IZ} + Sv_X + h \tag{82}$$

Since

$$r_{3,4} = k_3/k_4 \tag{83}$$

the orientation must be given by

$$\log r_{3,4} = L'\sigma_{IZ} + S'v_X + h \tag{84}$$

Once again we observe that directing effects are a function of the electrical and steric effects of the substituents, and that if the correlation equation which relates substituent effects to orientation (r values) is known, the directing effect of any

substituent for which the appropriate substituent constants are also known may be calculated.

E. Other Reactions

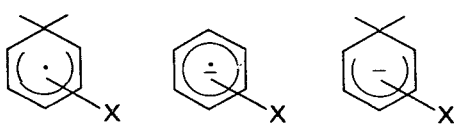
Many other reactions have been studied with regard to substituent effects on orientation. Some further examples are given below.

Kosugi, Takeuchi and Migita[112] have studied the homolytic chlorination of nitriles, including propionitrile and butyronitrile. Their results show predominant chlorination of propionitrile at the terminal methyl group and of butyronitrile at C^3. Under these reaction conditions, photoinitiation in CCl_4 at 40°C, the localized electrical effect of the cyano group is apparently predominant. Russell[113] has reviewed orientation in hydrogen-atom-transfer reactions. He cites data for chlorination of propionitrile under various conditions which shows the ratio $r_{3,2}$ to be greater than, or about, 1. By contrast, reaction of propionitrile with phenyl radicals at 60°C shows an $r_{3.2}$ value of 0.059. The ratios r_{ij} for this reaction are conveniently written

$$r_{ij} = \frac{n^i_H P_i}{n^i_H P_j} \tag{85}$$

where i and j refer to the ith and jth carbon atoms in the molecule, n^i_H and n^j_H are the number of hydrogen atoms bonded to the ith and jth carbon atoms, and P_i and P_j are the percents of the i-substituted and j-substituted products observed. Chlorination of butyronitrile with t-butyl hypochlorite at 40°C results in preferential attack at C^3 with $r_{4,3} = 0.61$, $r_{2,3} = 0.50$.

Birch, Hinde and Radom[114,115] have carried out *ab initio* calculations, generally with a restricted Hartree–Fock procedure and an STO-3G basis set, on the stabilization energies of substituted cyclohexadienyl radicals, **40**, relative proton affinities for radical anions of substituted benzenes, **41**, stabilization energies of substituted cyclohexadienyl anions, **42** (relative electron affinities of substituted cyclohexadienyl radicals), and relative hydride affinities of substituted benzenes. Groups which are π donors stabilize **42** in the order *ipso* > *meta* > *ortho* > *para*.



(40) **(41)** **(42)**

All the *ipso* and most of the *meta* isomers are stabilized, all of the *para* and most of the *ortho* isomers are destabilized. The π acceptor groups stabilize in the order *para* > *ortho* > *ipso* > *meta*. As a function of substituent the stabilization energies are in the order $NO_2 > CN > CO_2H > F > OH > NH_2\ CO_2^-$. The π acceptor groups induce *ipso* and/or *para* protonation of **41** under irreversible conditions, *ortho* and *para* under equilibrium conditions. The π donor groups prefer *ortho* and/or *meta* protonation under irreversible and *ortho* and *para* under equilibrium conditions. Except for the strong donors, OH, OMe and NH_2, and for Me, all groups prefer *para* to *ortho* under equilibrium conditions.

Biehl and coworkers[116] have reported that the cyano group influences orientation in the addition of amide ion to benzene in the 'usual way', by the localized electrical effect, contrary to earlier reports.

Values of $\log r_{2,1}$ for the reaction of diborane with substituted ethylenes have been correlated with the LD equation[117,118]. Similarly, $\log r_{2,1}$ values for unsymmetrically

substituted dialkylacetylenes with R^1R^2BH, R = Ak or H, are correlated by the modified Taft equation (equation 48). Also correlated are $r_{2,1}$ values for the addition of phenylselenyl chloride, PhSeCl, and phenylsulphenyl chloride, PhSCl, to unsymmetric disubstituted acetylenes in which the substituents are H or alkyl.

Values of $\log r_{2,1}$ for the addition of bis(2-methylallyl)zinc to 3′- or 4′-substituted styrenes have been correlated with the Hammett equation using the σ^+ constants[119].

There are many other examples which might have been presented to further demonstrate the importance of electrical and steric effects in determining orientation. The ring-opening of substituted oxiranes, homolytic aromatic substitution reactions of substituted benzenes, migratory aptitudes in carbenium ion rearrangements and nucleophilic substitutions of substituted perfluorobenzenes are some obvious examples. The conclusion to be derived from all of these examples is that orientation always depends upon the electrical and/or steric effects of the substituents present, and upon any statistical factors which may be present. If the correlation equation for the appropriate $\log r$ values is known, and if we also have available the substituent constants for any groups of interest, we can predict product composition.

It should be noted that there are many reactions for which substituents cause the formation of either one or the other of two possible products. This is true of many types of electrophilic additions to carbon–carbon double bonds. While obviously these results do not lend themselves to treatment by correlation analysis, the product can nevertheless be predicted from the electrical and steric effect substituent constants for the substituent(s) present.

F. Application to Triply Bonded Groups

We have remarked several times that if the correlation equation for r_{ij} as a function of electrical and steric effects is known we may calculate r for any group of interest. Table 12 gives values of r calculated for a number of triply bonded groups for some of the reactions described above, together with the correlation equations from which $\log r_{ij}$ was calculated.

In the electrophilic fluorination of substituted benzenes, $r_{2,4}$ is dependent almost entirely on σ_I and as all neutral triply bonded groups have σ_I values in the range 0.25 to 0.65 *para* substitution would be expected to predominate for all of them. An experimental value is available only for the cyano group for which $r_{2,4}$ is 1.0. The discrepancy may be due at least in part to experimental error in the determination of product composition. The $r_{3,4}$ values are dependent almost entirely on σ_R^+ and therefore show a preference for *meta* substitution when σ_R^+ is positive and *para* substitution when it is negative.

The $r_{2,1}$ values for addition of methyl radicals to substituted ethylenes are a function of the composite σ_{80}^+ constants which are a combination of σ_I and σ_R^+ that is 80% σ_R^+. It seems probable that all neutral triply bonded groups will have negative σ_R^+ values. We predict, then, that attack at the 2-position is preferred. In the reaction of substituted methyl radicals with trifluoroethylene the large negative σ_R^+ values of C≡P and C≡CH should result in predominant attack at the 2-position, whereas the small value for CN should result in attack at the 1-position.

In the Diels–Alder reaction of 2-substituted butadienes with acrylic acid the major factor is σ_{IX} and the 1,4-isomer should be preferred. In that of 2-substituted anthracenes with maleic anhydride the *anti* isomer should always be preferred, as σ_{30} should be in the range 0.15–0.70 for all neutral triply bonded groups.

Finally, in the addition of diborane to substituted ethylenes those triply bonded groups with positive σ_R values should prefer attack of boron at position 2 and those with negative σ_R values at position 1.

TABLE 12. Calculations of r_{ij} for triply bonded groups

(a) Correlation equations from which $\log r_{ij}$ was calculated

Reaction	Correlation equation	References
(1) PhX + F_2	$\log r_{2,4} = -0.76\sigma_{IX} - 0.04\sigma_{RX}^{+} + 0.020$ $\log r_{3,4} = 0.39\sigma_{IX} + 3.00\sigma_{RX}^{+} - 0.184$	87
(2) ViX + $Me^{\cdot}$	$\log r_{2,1} = -0.562\sigma_{80,X}^{\dagger} + 0.849\upsilon_X - 0.0726$	99, 100
(3) $F_2C{=}CFH + {}^{\cdot}CX_3$[a]	$\log r_{2,1} = -1.51\sigma_{IX} - 3.04\sigma_{RX}^{\dagger} - 0.591\upsilon_{CX_3} - 0.284$	99, 100
(4) $CH_2{=}CXVi + ViCO_2H$	$\log r_{14,24} = 1.52\sigma_{IX} - 0.426\sigma_{RX}^{\dagger} + 0.0721$	106, 107
(5) 2-*X*-anthracene + maleic anhydride	$\log r_{S,a} = -0.298\sigma_{30} + 0.0300$	110
(6) ViX + B_2H_6	$\log r_{2,1} = 1.84\sigma_{IX} + 3.11\sigma_{RX} - 0.518$	117, 118

[a]Values of υ_{CX_3} were calculated as described in Reference 85.

(b) Calculated values of r_{ij}

	X							
Reaction	—CN	—C≡CH	—C≡CMe	—C≡CPh	—C≡CCF$_3$	—C≡C—C≡CH	—C≡P	
(1)	0.383	0.637				0.538		
	1.90	0.376				0.287		
(2)	1.48	18.6					10.6	
(3)	0.00127	29.7					2.77	
(4)	9.57	5.07					6.10	
(5)	0.710	0.890	0.947	0.909	0.798			
(6)	6.02	0.778	0.15	0.273	2.23			

We have not attempted any predictions for ionic triply bonded groups due to the enormous importance of the medium on the effect of such groups. These results should provide examples of the use of correlation analysis in the prediction of the effect of triply bonded groups on orientation.

V. DIRECTING EFFECTS IN CHEMICAL EQUILIBRIA – TAUTOMERISM

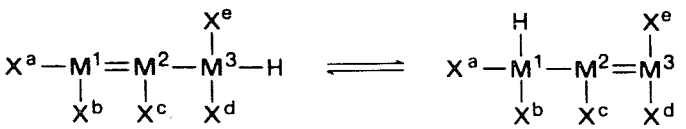
A. 1,3-Prototropy

1. Introduction

The name given to an equilibrium between structural isomers is tautomerism. When the isomers differ in the location of a proton the tautomeric equilibrium is termed prototropy. Many examples of prototropy are known, for example allyl–propenyl, allene–acetylene, keto–enol, imino–amino and thione–enthiol. These fall into a common category as is shown by the equilibrium **43**. This type of prototropy will be designated 1,3-prototropy. The X are either substituents or lone pairs. Some examples of 1,3-prototropy are summarized in Table 13.

TABLE 13. 1,3-Prototropy

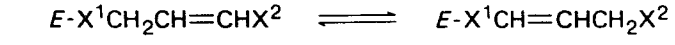
Type	M^1	M^2	M^3	Remarks
Allyl–propenyl	C	C	C	
Keto–enol	O	C	C	X^a, X^b are lone pairs
Thiono–enthiol	S	C	C	X^a, X^b are lone pairs
Imino–enamine	N	C	C	X^a is a lone pair
Nitroso–oximino	O	N	C	X^a, X^b, X^c are lone pairs
Azo–hydrazono	N	N	C	X^a, X^c are lone pairs
Imino–amido	N	C	O	X^a, X^d, X^e are lone pairs
Nitro–aci	O	N	C	X^a, X^b are lone pairs, X^c is O



(43)

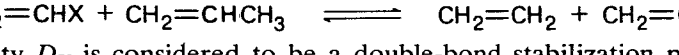
2. *Allyl–propenyl tautomerism*

Hine[120,121] has discussed allyl–propenyl prototropy in the system:



(44) (45)

It is assumed that steric effects in the *trans* olefins **44** and **45** are negligible. On the basis of the further assumption that the statistically corrected free energy change ΔG^{chem} can be written as a function of bond contributions and pairwise interactions, and that this assumption also applies to the free energy change D_X for the hypothetical reaction:



The quantity D_X is considered to be a double-bond stabilization parameter which measures the ability of the X group to stabilize the double bond. This leads to the relationship

$$\Delta G^{chem} = D_{X^2} - D_{X^1} \tag{86}$$

The fit of data to equation (86) is improved by taking into account the 'interactions across the double bond' of the substituents in **44** and **45**:

$$\Delta G_{\text{interaction:44}} = \tau_V \sigma_{X^1CH_2} \sigma_{X^2} \tag{87}$$

$$\Delta G_{\text{interaction:45}} = \tau_V \sigma_{X^1} \sigma_{X^2CH_2} \tag{88}$$

Then

$$\Delta G^{chem} = D_{X^2} - D_{X^1} + \tau_V(\sigma_{X^1}\sigma_{CH_2X^2} - \sigma_{X^2}\sigma_{CH_2X^1}) \tag{89}$$

Fitting the available data to equation (89) gives the set of D_X values reported in Table 14.

We have found that the D_X values can be correlated to the LDS equation using the σ_R constants.

TABLE 14. Values of D_X and K_T

(1) D_X (kcal mol^{-1}); double-bond stabilization parameters[a]
OMe, 5.2; Ph, 4.9; F, 3.3; *n*-Ak, 3.2; SMe, 3.2; CO_2Me, 3.2; NO_2, 2.9; CH_2OMe, 2.6; *i*-Pr, 2.5; CN, 2.3; CH_2CO_2Me, 2.1; Cl, 1.8; SOMe, 0.7; Br, 0.3; H, 0; SO_2Me, −0.4; NMe_2, 8.2; SO_2Bu, −0.1; Ac, 3.36
(2) $\log K_T$; $AcCHXCO_2Et$ (**46** ⇌ **49**)[b]
H, −1.060; Me, −1.279; F, −0.754; Cl, −0.754; Br, −1.279; CF_3, 0.908; CN, 1.124
(3) $\log K_T$; 4-$ZPnCH_2COCH_2CO_2Et$ (**46** ⇌ **49**)[c]
MeO, −1.130; Me, −1.097; H, −1.043; Cl, −1.073; CN, −1.158; NO_2, −1.104
(4) $\log K_T$; 4-$ZPnCOCH_2CO_2Et$ (**46** ⇌ **49**)[c]
MeO, −1.415; Me, −0.984; Cl, −0.845; CN, −0.378; NO_2, −0.300; H, −0.945
(5) $\log K_T$; 3-$ZPnCOCH_2CO_2Et$ (**46** ⇌ **49**)[c]
H, −0.945; MeO, −0.979; Me, −1.016; Cl, −0.670; CN, −0.550; NO_2, −0.515
(6) $\log K_T$; 4-$ZPnCOCH_2COMe$ (**46** ⇌ **49**), MeOH, 0°C[d]
H, 1.091; MeO, 1.097; Cl, 1.130; NO_2, 1.252
(7) $\log K_T$; 3- or 4-$ZPnCOCH_2COMe$ (**46** ⇌ **49**), H_2O, 25°C[e]
H, −0.292; 4-Me, −0.367; 4-*i*-Pr, −0.367; 4-*t*-Bu, −0.377; 4-F, −0.319; 4-Cl, −0.260; 4-Br, −0.161; 4-NO_2, 0.258; 3-MeO, −0.071; 3-NO_2, 0.155
(8) $\log K_T$; 2-, 3- or 4-substituted **54** (**54** ⇌ **55**)[f]
4-MeO, 0.14; 4-*t*-Bu, 0.09; 4-Me, 0.10; 3-Me, 0.04; H, 0.04; 3-MeO, −0.02; 4-Cl, −0.03; 4-Br, −0.02; 4-Ac, −0.07; 4-CO_2Et, −0.10; 4-CN, −0.14; 4-NO_2, −0.17; 2-Me, −0.23; 2-MeO, 0.52
(9) $\log K_T$ (**56** ⇌ **57**)[g]
H, −0.896; Et, −0.357; SH, 0.117; NH_2, 0.398; OH, 1.14

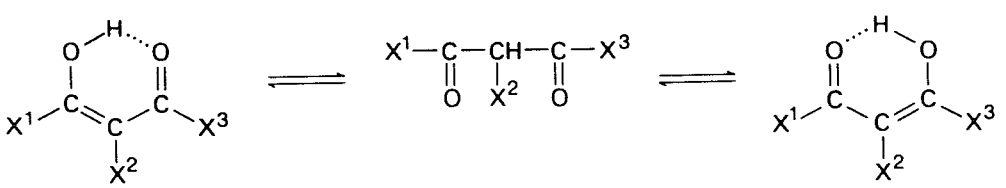
[a]References 120 and 121.
[b]Reference 122.
[c]Reference 123.
[d]Reference 124.
[e]References 125 and 126.
[f]Reference 133; $K_T = C_{55}/C_{54} = P_{55}/P_{54}$.
[g]Reference 134; $K_T = C_{57}/C_{56}$.

$$D_X = L\sigma_{IX} + D\sigma_{RX} + Sv_X + h \qquad (90)$$

All planar π-bonded groups were excluded from the correlation as both the delocalized electrical and the steric effects of these groups are strongly dependent on conformation. The cyano group was also excluded as its inclusion gave very poor results.

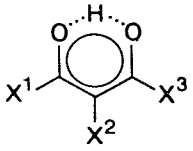
3. *Keto–enol tautomerism*

This subject has been investigated extensively and intensively for many years. Structural effects are most readily available for systems such as **46** which may be in equilibrium with the enols **47** and **48**. It is especially interesting to note that **47** and **48** are quasi-aromatic. If the p orbitals on the oxygen atoms can interact with each other then both of these species obey the Hückel rule with six π electrons and some degree



(47) **(46)** **(48)**

of aromaticity can be expected. If the degree of aromaticity is significant, then **47** and **48** are contributing structures and the enol can be described by **49**.



(49)

Burdett and Rogers[122] have reported the percent of enol(P_E) for the equilibrium between **46** and **49** with X^1 = Me, X^3 = OEt and X^2 variable. We may define the tautomeric equilibrium constant K_T by the expression

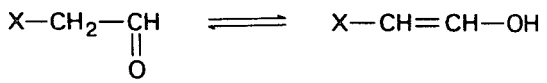
$$K_T = \frac{C_E}{C_K} = \frac{P_E}{P_K} = \frac{P_E}{(100 - P_E)} \tag{91}$$

where C is the concentration and P the percentage, the subscripts K and E indicating keto and enol. Values of K_T are given in Table 14. The LD equation

$$\log K_T = L\sigma_{IX} + D\sigma_{RX} + h \tag{92}$$

gave significant correlation. No dependence on the steric effect was observed. Bankowska and Kolaczkowska[123] have reported values of P_E for the enolization of **46** with X^1 = 4-ZPnCH$_2$, 4-ZPn or 3-ZPn, X^2 = H, X^3 = OEt. Values of K_T calculated from their data are also given in Table 14. The data were correlated with the Taft equation. Celiano, Cefola and Gentile[124] have determined P_E for the enolization of **46**, X^1 = 4-ZPn, X^2 = H, X^3 = Me in methanol. Bergon and Calmon[125,126] have reported K_T values for the same system in aqueous solution. The log K_T values were correlated by the simple Hammett equation.

Bouma and Radom[127–129] have carried out theoretical studies on the effect of substituents on keto–enol equilibria in substituted acetaldehydes, **50**. In a more recent paper Radom and his coworkers[130] have studied the effect of the diazonium substituent N_2^+ on the equilibrium between **50** and **51**. In accord with their previous work



(50) **(51)**

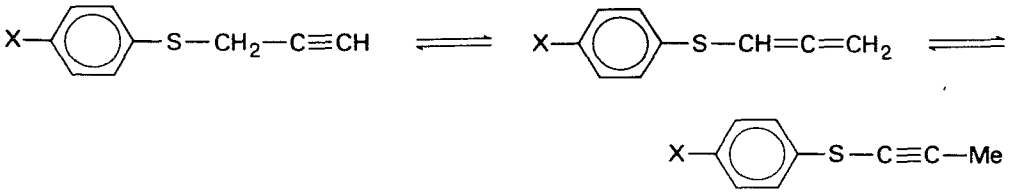
π-electron acceptor and σ-electron acceptor groups stabilize the enol **51** and destabilize the keto isomer, **50**. The effect of N_2^+, which is a very strong π acceptor and σ acceptor, is large enough to make the enol significantly more stable than the keto isomer; the calculated energy difference is 41.1 kJ mol^{-1}.

4. Acetylene–allene prototropy

It has long been known that acetylenes can undergo isomerization and that allenes are involved as intermediates. In the equilibrium between the acetylene **52** and the allene **53** is an example of 1,3-prototropy. The isomerization has been thoroughly

(52) **(53)**

reviewed[131,132]. Pourcelot and Georgoulis[132] have studied rates of base-catalysed isomerizations of 4-substituted phenyl propargyl sulphides:

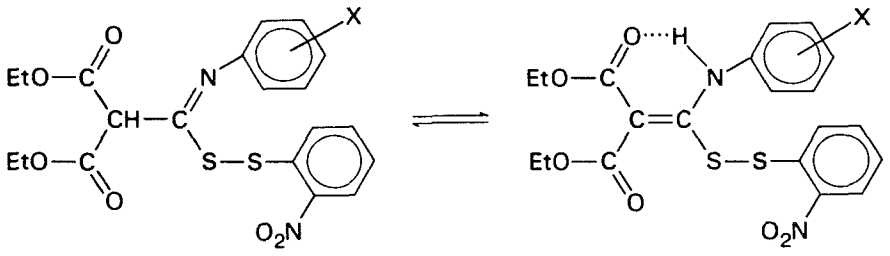


The rate constants have been correlated with the Hammett equation. The magnitude of ρ was thought to imply the formation of a carbanion intermediate.

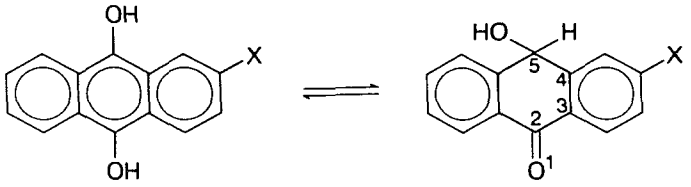
5. *Other 1,3-prototropic and related systems*

Walter and Meyer[133] have reported $\log K_T$ values for the imine–enamine equilibrium between **54** and **55**. These $\log K_T$ values have also been correlated with the Hammett equation. Enamine **55** is analogous to **49** in that it is quasi-aromatic.

There are many prototropic equilibria which are related to those of the 1,3-prototropic type. Consider for example the equilibrium **56** ⇌ **57**[134]. This is of course related



(54) **(55)**



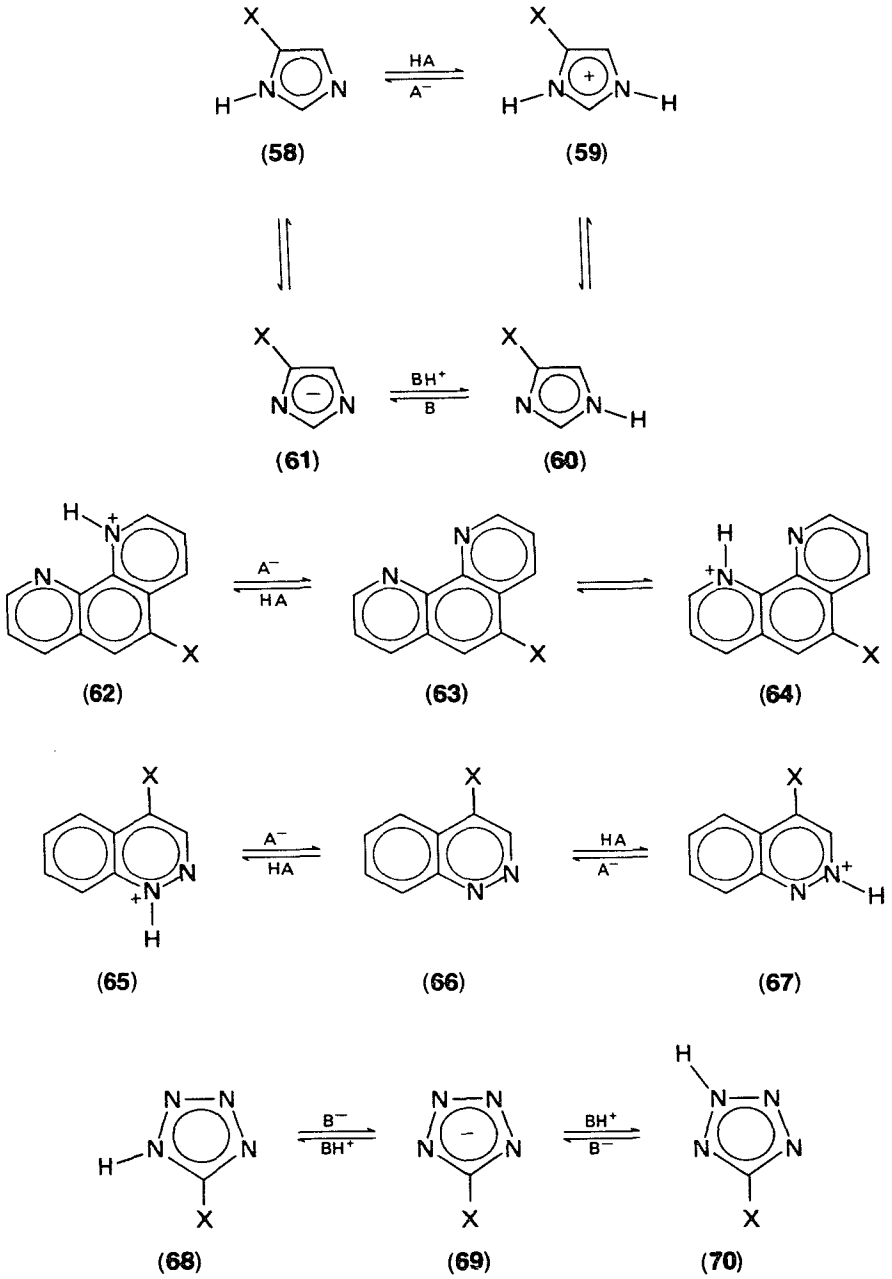
(56) **(57)**

to keto–enol tautomerism. As the proton is transferred from the first to the fifth atom it might be termed 1,5-prototropy. Values of K_T for this system are reported in Table 14.

B. Annular Tautomerism

Many heterocyclic systems are capable of exhibiting annular tautomerism[135], a form of prototropy in which a proton may be located at one or another of two or more nitrogen atoms in the heterocyclic ring. Some examples are shown in Scheme 2.

These systems fall into two categories, a simple one in which the unsubstituted



SCHEME 2

compound (X = H) is symmetric, and a more complicated one in which the unsubstituted compound is not symmetric. The imidazoles, **58** and **60**, and the 1,10-phenanthrolines, **62** and **64**, belong to the symmetric category. The cinnolines, **65** and **67**, and the tetrazoles, **68** and **70**, belong to the more complicated category. The macro-

constant K_M, given by the equation

$$K_M \simeq \frac{C_{H_3O^+} C_B}{C_{BH^+}} \tag{93}$$

for a basic heterocycle, or,

$$K_M \simeq \frac{C_{H_3O^+} C_{A^-}}{C_{HA}} \tag{94}$$

for an acidic heterocycle, is readily determined experimentally. The macroconstant is a composite equilibrium constant, which is related to the ionization constants of the individual tautomers, which are called microconstants. Unless one of the tautomers is predominant almost to the exclusion of the other, the microconstants are not directly measurable, at least by the usual methods. For the 1,10-phenanthrolines, for example, $C_{BH^+} = C_{62} + C_{64}$. Then following the treatment of Charton[136,137]

$$\frac{1}{K_M} = \frac{(C_{62} + C_{64})}{C_{H_3O} + C_B} = \frac{1}{K_{a,62}} + \frac{1}{K_{a,64}} \tag{95}$$

We may write the equilibrium constant K_T as

$$K_T = \frac{C_{62}}{C_{64}} = \frac{K_{a,64}}{K_{a,62}} \tag{96}$$

or

$$pK_T = pK_{64} - pK_{62} \tag{97}$$

But

$$pK_{64} = L_{64}\sigma_{IX} + D_{64}\sigma_{DX} + h_{64} \tag{98}$$

$$pK_{62} = L_{62}\sigma_{IX} + D_{62}\sigma_{DX} + h_{62} \tag{99}$$

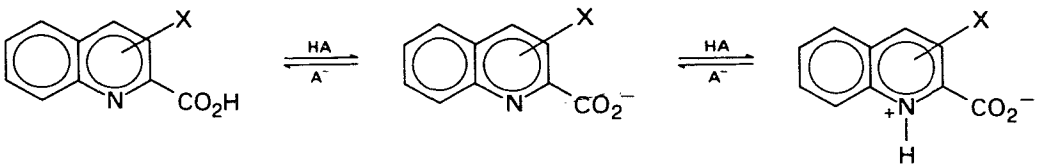
Then, as h is the calculated pK_a for the unsubstituted compound, and for X = H, **62** ≡ **64**,

$$pK_T = (L_{64} - L_{62})\sigma_{IX} + (D_{64} - D_{62})\sigma D_X \tag{100}$$

From suitable model systems, values of L_{62}, D_{62}, L_{64} and D_{64} can be estimated. A value of $h_{64} \equiv h_{62}$ can be determined experimentally. Then from equation (98) and (99), $pK_{a,62}$ and $pK_{a,64}$ can be calculated. From these the reciprocals of $K_{a,62}$ and $K_{a,64}$ are easily obtained and therefore K_M can be calculated. A comparison of calculated pK_M values with those found experimentally checks the validity of the L and D values obtained from the model. Values of pK_T can then be calculated from equation (100). The method has been applied using the simple Hammett equation to imidazoles[136] and using the LD equation to 1,10-phenanthrolines[137]. The problem of calculating K_T for members of the more complicated category such as the tetrazoles, **68** and **70**, or the cinnolines, **65** and **67**, is complicated by the fact that no method of estimating the pK_a values for the tautomers of the unsubstituted compound is available. The method chosen to circumvent this was to use values of $pK_{a,H}$ (equivalent to h) which ranged from essentially complete protonation at N^1 to essentially complete protonation at N^2 [138,139]. Values of pK_M were calculated using L and D values from appropriate model systems for each pair of h values. The h values which resulted in the smallest deviation between calculated and observed pK_M values were considered to be the best estimates. This model could then be used to calculate pK_T for 5-substituted tetrazoles. Annular tautomerism in 6-substituted 2,3-dimethylquinoxalines has also been treated by means of the Hammett equation[140,141].

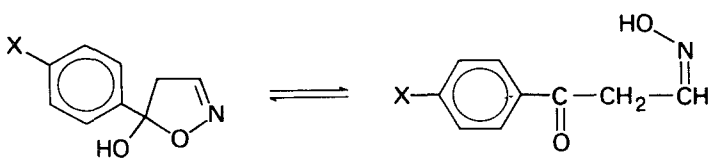
C. Other Tautomeric Equilibria

There are other types of tautomerism which are of interest. Consider for example the presence of two nonequivalent acidic and/or basic sites on a skeletal group. Prototropic tautomerism occurs in such systems. Jaffé and Jones[142] have discussed a Hammett-equation treatment of this problem in heterocyclic systems in some detail. In another treatment[143] ionization constants of 4-, 6- and 8-substituted quinoline-2-carboxylic acids (**72a**) have been correlated with substituent constants calculated by the Dewar–Grisdale[144] method (σ_{ij} constants). Two sets of σ_{ij} have been calculated, one assuming protonation of **71** at N (**72b**), the other assuming protonation at O (**72a**). As the constants calculated for *O*-protonation give the best correlation it has been suggested that the carboxylate ion is indeed the site of predominant protonation.



(**72a**) (**71**) (**72b**)

It has been argued that a comparison of the ρ values obtained with those for the ionization of the corresponding substituted quinolines supports this conclusion. Values of $\log K_T$ for ring–chain tautomerism of 5-(4′-substituted-phenyl)-5-hydroxy-1,2-isoxazolidines, **73** and **74**, have been determined and correlated with a form of the



(**73**) (**74**)

LD equation[145]. Finally, log K_T values for the equilibrium **75** ⇌ **76** have been determined and correlated with the Hammett equation[146]. Once again, if the correlation equation is known and the substituent constants are available, the composition of the tautomers can be calculated for any given group.

(**75**) (**76**)

D. Application to Triply Bonded Groups

Again we can show the actual use of the correlation equations in predicting the directing effects of triply bonded groups on product formation. In Table 15 we give calculated values of K_T for some of the reactions discussed above, together with the correlation equations from which they were calculated.

In the keto–enol tautomerism of the ethyl 4-substituted benzoylacetates (**46** ⇌ **49**); X^1 = 4-ZPn, X^3 = OEt), the keto form, **46**, should be preferred in all cases. With the ethyl 2-substituted 3-ketobutanoates, however (**46** ⇌ **49**; X^1 = Me, X^3 = OEt), when

TABLE 15. Calculations of K_T for triply bonded groups

(a) Correlation equations from which $\log K_T$ was calculated

Reaction	Correlation equation	References
(1) **46** ⇌ **49** (X^1 = 4-ZPn, X^3 = OEt)	$\log K_T = 0.668\sigma_{IX} + 1.24\sigma_{RX} - 0.867$	123
(2) **46** ⇌ **49** (X^1 = Me, X^3 = OEt)	$\log K_{T,49,46} = 2.66\sigma_{IX} + 2.82\sigma_{RX} - 0.997$	122
(3) 4-Substituted **54** ⇌ 4-substituted **55**	$\log K_{T,54,55} = -2.81\sigma_{IX} - 2.90\sigma_{RX} + 0.0432$	133
(4) **68** ⇌ **70**	$\log K_{T,2,3} = -5.3\sigma_{IX} - 0.6\sigma_{RX} - 0.6$	139
(5) **60** ⇌ **58**	$\log K_{T,3,1} = 3.2\sigma_{25,X}$	136
(6) **73** ⇌ **74**	$\log K_T = -1.36\sigma_{IX} - 2.03\sigma_{RX}^+ - 0.355$	145

(b) Calculated values of K_T

	X				
Reaction	—CN	—C≡CH	—C≡CMe	—C≡CPh	—C≡CCF$_3$
(1)	0.410	0.189	0.0997	0.124	0.282
(2)	5.56	0.459	0.110	0.194	1.60
(3)	0.0162	0.221	0.962	0.531	0.0597
(4)	0.00214	0.00771	0.00938	0.00598	0.00143
(5)	83.2	7.87	4.70	6.79	23.8
(6)	0.250	1.05	2.99	2.05	0.505

σ_R is positive the enol, **49**, should be preferred; when σ_R is negative, the keto form, **46**, should be preferred. The imine, **54**, seems to be preferred to the enamine, **55**, in all cases, although most strongly when σ_R is positive.

As regards annular tautomerism in tetrazoles, the correlation equation shows that σ_I is the predominant tautomer and therefore **68** is expected to be predominant for all neutral triply bonded groups. Similarly, the correlation equation for imidazoles is dependent on a composite substituent constant to which the predominant contribution is σ_I. As a result, **60** may be expected to be predominant for all neutral triply bonded groups.

Finally, we shall consider the ring–chain tautomerism involving **73** and **74**. When σ_R^+ is negative, **74** seems to be preferred, when it is positive, **73** is more likely.

The examples presented here simply illustrate the method. Obviously if the correlation equation is known and substituent constants for the triply bonded groups of interest are also known, we can predict the predominant tautomer. If due allowance is made for the medium, such predictions, although undoubtedly cruder, can also be made for ionic triply bonded groups.

VI. DIRECTING EFFECTS IN STEREOISOMERIC EQUILIBRIA

A. Geometric Isomerism

Cis and *trans* isomers of doubly bonded compounds such as olefins, oximes and hydrazones can exist in equilibrium. Thus, in the general case:

(77) **(78)**

Consider the simple example of the 1,2-disubstituted ethylenes:

(*E*-**79**) (*Z*-**79**)

Then

$$K_{EZ} = \frac{C_E}{C_Z} = \frac{P_E}{P_Z} \tag{101}$$

Hine has reviewed the problem and suggested that the predominance of the *cis* isomer observed in some compounds is due to London forces[147]. If we assume that the difference in stability is a function of intramolecular forces and steric interactions between *cis* groups, we can attempt a correlation of the data with an equation which includes terms which will account for dipole–dipole (dd), dipole–induced-dipole (di), and induced-dipole–induced-dipole (ii) intramolecular forces and for steric repulsions. The ratio of the van der Waals' equation of state constants (a/b), which are a measure of intermolecular forces, have been treated by the same approach[148]. The dipole–dipole term when both X^1 and X^2 vary will be given by

$$E_{dd} = a_{dd}\mu_{X^1}^2\mu_{X^2}^2 \tag{102}$$

where μ_X represents the X—C bond moment.

The di term when both X^1 and X^2 vary is

$$E_{di} = a_{di_1}\mu^2_{X^1}\alpha_{X^2} + a_{di_2}\mu^2_{X^2}\alpha_{X^1} \tag{103}$$

where α is the polarizability parameter. The ii term will be given by

$$E_{ii} = a_{ii}\alpha_{X^1}\alpha_{X^2} \tag{104}$$

Then ΔG^0_{EZ} should be given by the energy difference between the E and Z isomers.

For the E isomer:

$$E_E = E_{dd,X^1H} + E_{dd,X^2H} + E_{di,X^1H} + E_{di,X^2H} + E_{ii,X^1H} + E_{ii,X^2H} + S(\upsilon_{X^1} + \upsilon_H - d) + S(\upsilon_{X^2} + \upsilon_H - d) \tag{105}$$

For the Z isomer:

$$E_Z = E_{dd,X^1X^2} + E_{dd,HH} + E_{di,X^1X^2} + E_{di,HH} + E_{ii,X^1X^2} + E_{ii,HH} + S(\upsilon_{X^1} + \upsilon_{X^2} - d) + S(\upsilon_H + \upsilon_H - d) \tag{106}$$

where d is the distance between the centre of any group and the centre of the group which is *cis* to it.

As $\alpha_H = 0$, $\mu_H \simeq 0$ and d is generally larger than $\upsilon_X + \upsilon_H$,

$$E_E \simeq 0 \tag{107}$$

Then

$$\Delta G^0_{EZ} = E_Z - E_E \simeq E_Z \tag{108}$$

When X^2 is constant,

$$\Delta G^0_{EZ} = b'_1\mu^2_{X^1} + b'_2\alpha_{X^1} + b'_3\upsilon_{X^1} + b'_0 \tag{109}$$

and as

$$\Delta G^0_{EZ} = -RT \ln K_{EZ} \tag{110}$$

it follows that

$$\log K_{EZ} = b_1\mu^2_{X^1} + b_2\alpha_{X^1} + b_3\upsilon_{X^1} + b_0 \tag{111}$$

Since

$$\mu_X = \rho\sigma_{nX} + \mu^0 \tag{112}$$

$$\log K_{EZ} = C_1\sigma^2_{nX} + C_2\sigma_X + C_3\alpha_{X^1} + C_4\upsilon_1 + C_0 \tag{113}$$

Generally σ^2_{nX} is approximately linear in σ_{nX} and

$$\log K_{EZ} \simeq C'_2\sigma_{X^1} + C_3\alpha_{X^1} + C_4\upsilon_{X^1} + C_0 \tag{114}$$

Data taken from Hine[147] for X^1 = AkX^2 = Me were correlated successfully by the equation

$$\log K_{EZ} = a_1n_1 + a_Cn_C + a_0 \tag{115}$$

This equation can be applied because electrical effects of alkyl groups are approximately constant and therefore the term in σ is constant. Furthermore, υ_{AK} can of course be replaced by the branching equation. As only branching at C^1 is important for the limited data available, n_1 is the only parameter necessary. Finally, for alkyl groups

$$\alpha_{Ak} = d_1n_C + d_0 \tag{116}$$

where n_C is the number of carbon atoms in the alkyl group. The data used are reported in Table 16. Correlation with equation (114) was also successful; again, the data are

TABLE 16. Values of K_{EZ} and λ constants

(1) K_{EZ}; 2-MeVnX, 25°C[a]
Me[b], 3.0; Et[b], 4.6; Pr[b], 4.0; Bu[b], 4.0; *i*-Pr[b], 5.5; CH_2CN[c], 2.0; CO_2H[d], 12.0; CO_2Me[e], 11.0; CN[b], 0.62; NO_2[f], 30.0; OMe[g], 1.2; F[b], 0.28; Cl[b], 0.27; Br[b], 0.26; SO_2Me[h], ~40
(2) K_{EZ}; 2-X^1VnX^2, 25°C[a]
Et, Pr[b], 6.1; Ph, Ph[g], 480; Ph, mesityl[g], 13; Et, OMe[g], 1.8; $PhCH_2$, OMe[i], 0.56; Dc, SMe[i], 1.4; CO_2Me, OMe[g], 420; Vi, F[j], 0.54; F, F[b], 0.22; F, Cl[b], 0.30; F, I[d], 0.40; Cl, Cl[b], 0.39; Br, Br[d], 0.85; Br, I[d], 1.4; I, I[d], 3.1; PhS, PhS[k], 0.8
(3) λ^d constants[l]
1p[m], −0.6; H, 0.0; Me, 1; Et, 1.38; Pr, 1.41; Am, 1.41; *i*-Bu, 1.4; CH_2Bu-*t*, 1.41; $PhCH_2$, 1.25; *i*-Pr, 1.58; *s*-Bu, 1.55; cPr, 1.45; cHx, 1.45; $CHPh_2$, 1.5; *t*-Bu, ~3; CO_2R, ~2.5; $CHCl_2$, 1.6; NHR, 0.9; OR, 0.5; Cl, ~1.3; Br, ~1.6

[a]Reference 147.
[b]Gas.
[c]In *t*-BuOH.
[d]Liquid.
[e]In $(Me_2N)_3PO$.
[f]In heptane.
[g]In cyclohexane.
[h]In Et_3N.
[i]In Me_2SO.
[j]In benzene.
[k]In *p*-xylene.
[l]Reference 149.
[m]Lone pairs (full nonbonding orbital localized on a single atom)

given in Table 16. Correlation of log K_{EZ} for disubstituted olefins with both groups varying was also successful. The correlation equation used was

$$\log K_{EZ} = c_1\Pi\sigma_X + c_2\Pi\alpha_X + c_3\Sigma\upsilon_X + c_0 \qquad (117)$$

In the correlation with equation (114) only the σ term was significant; the σ_I values gave best results. In the correlation with equation (115) only the term in n_1 was significant. Thus, these results establish the importance of electrical and steric effects. In the correlation with equation (117) all of the terms were significant. The problem is complicated by the fact that υ and α are almost always linear in each other to some extent.

The values of c_1, c_2 and c_3 are −2.74, −10.6 and 0.980 for the data studied. Planar π-bonded groups were excluded from the correlation due to uncertainty regarding their conformation. The results show that an increase in σ_I or α favours the *cis* conformer, while an increase in υ favours the *trans* conformer. The proposed model does seem to fit the data.

Knorr has recently developed a set of empirical substituent parameters, λ^d, which can be used to calculate log K_{EZ} for olefins, enamines, hydrazones, imines, oximes, semicarbazones and nitrones[149]. The equation used is

$$\ln K_{EZ} = \rho_{M^1M^2}(\lambda^d_{X^1} - \lambda^d_{X^2})(\lambda^d_{X^3} - \lambda^d_{X^4}) \qquad (118)$$

where the equilibrium involved is **75** ⇌ **76**. Values of λ^d are reported in Table 16. The λ^d values are said to be related to the υ steric parameters

The results show that K_{EZ} is dependent upon the electrical, steric and polarizability effects of the substituents bonded to the carbon–carbon double bond. If the substituent constants are available for some group of interest, the K_{EZ} value can be predicted for that group.

B. Conformational Equilibria

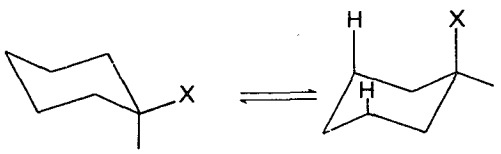
The importance of conformation as a factor in chemical reactivity, physical properties and biological activity is well known. Conformation is a function of substituent,

TABLE 17. Values of $-\Delta G_X$ and ΔE_X

(1) $-\Delta G^\circ_X$; cHxX[a]
Me, 1.71; Et, 1.80; *i*-Pr, 2,12; cHx, 2.15; HC_2, 0.41[b]; CN, 0.15; PhS, 0.8; MeS, 0.7; SH, 0.9; OEt, 0.98; OMe, 0.74; NH_2, 1.5; NMe_2, 2.1; F, 0.25; Cl, 0.415; Br, 0.48; I, 0.43; CF_3, 2.1; H, 0; OTs, 0.317; OAc, 0.463; NO_2, 1.02; CO_2H, 1.2; CO_2Me, 1.15; CO_2Et, 1.2; SO_2Ph, 2.5[c]; CO_2Pr-*i*, 0.96; Vi, 1.35[c]; Ph, 3.0[c]; COCl, 1.25[c]; —NC[b], 0.21; —SCN, 1.23[b]; ONO_2, 0.59; OH, 0.52
(2) ΔE_X; *gauche*, *trans* conformers of XCH_2CH_2Bu-*t*[d]
$SiMe_3$, 2.33; I, 1.61; PPh_3, 1.99; Ph, 1.70; CD_2OH, 1.57; MeS, 1.47; SCN, 1.50; SPh, 1.30; Br, 1.30; $CONH_2$, 1.28; Cl, 0.99; NH_2, 1.15; CO_2H, 0.99; Ac, 1.11; CO_2Me, 0.99; COCl, 1.03; NHCHO, 1.01; NMe_2, 1.12; CN, 0.75; OH, 0.73; H, 0

[a]From Reference 150 unless otherwise stated.
[b]From Reference 159.
[c]From Reference 160.
[d]From Reference 158.

electrical and steric effects and presumably polarizability as well. The system studied most frequently is substituted cyclohexanes:



(e-**80**) (a-**80**)

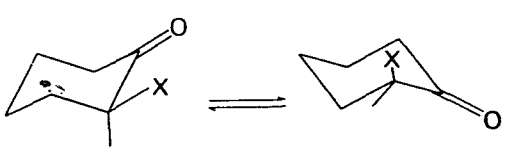
Values of $-\Delta G_X$ for substituted cyclohexanes are presented in Table 17. It has been reported[150] that the $-\Delta G_X$ values can be correlated with the L equation

$$-\Delta G_X = L\sigma_{IX} + h \qquad (119)$$

with H, Ak, OZ*, SH, CN and NH_2 lying on one line and planar π-bonded groups lying on another. This result suggests that the predominant effect of X is a dipole–dipole attraction between X and axial H present in a-**80** and not in e-**80**. If the $-\Delta G_X$ values for X = H or Ak, for which σ_I is constant and ~0, are correlated with the equation

$$-\Delta G_X = A\alpha_X + S\upsilon_X + h \qquad (120)$$

excellent results are obtained, showing that steric and/or polarizability effects are significant. One of the major difficulties in the application of correlation analysis to this problem is that many of the $-\Delta G_X$ values are unreliable. Values of $-\Delta G$ for **81** are correlated by the Hammett equation when Z is an electron acceptor[151].



(e-**81**) (a-**81**)

X = 4-ZPnO

When X is alkoxy the data fit the branching equation in the form

$$-\Delta G_X = a_1 n_1 + a_0 \qquad (121)$$

*Z = any atom or group.

again, suggesting that steric and/or polarizability effects can be significant. A number of other reports have appeared which support the importance of electrical effects upon confirmation in cyclic systems[152–155].

The $-\Delta G_X$ values obtained from equilibration of 3-β-substituted 5-α-cholestan-6-ones with the corresponding 5-β compounds[156] were also a function of σ_I[157].

Whitesides and his coworkers[158] have determined values of ΔE_X for the difference in energy between *gauche* and *trans* conformers of 1-substituted 3,3-dimethylbutanes and found them to be dependent on the van der Waals' radius of X. It has been reported that they are better correlated by the equation[157]

$$\Delta E_X = L\sigma_{IX} + S'r_{VX} + h \tag{122}$$

Overall, the electrical effect of a substituent seems to be a major factor in conformation in all the systems for which data are available. The steric effect seems to be usually significant. Polarizability may be a factor in some cases. It is difficult to separate it from the steric effect as they are frequently linearly related to a significant degree.

Again, the results show that conformational equilibria can be predicted from electrical, steric, and possibly polarizability, effects of the substituents.

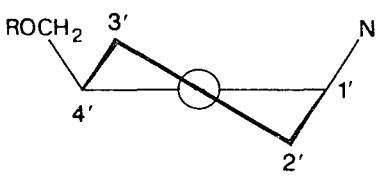
C. Application to Triply Bonded Groups

Here again we can demonstrate the use of correlation equations in the calculation of the values of directing effects of triply bonded groups (Table 18). Those groups which have small values of α and large values of σ_I seem to prefer the *trans* configuration, as in the case of the *trans*-1-substituted propenes, whereas those groups which have large α and small σ_I values seem to prefer the *cis* configuration. In the 1,2-disubstituted ethylenes those triply bonded groups with the smallest σ_I values seem to show a slight preference for the *cis* configuration, while the remaining groups apparently prefer the *trans* configuration.

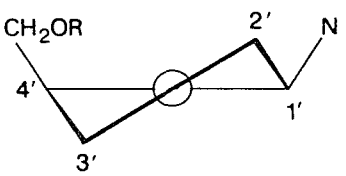
The correlation equation for ΔG_X for the conformational equilibrium in 2-(4′-substituted phenoxy)cyclohexanones shows that σ_I is the dominant factor; this is borne out by the results. The ΔG_X values for 4-substituted cyclohexanes are dependent on both electrical and steric effects. The —CN and —NC groups which have the largest σ_I and smallest υ values seem to show no strong preference for either the axial or the equatorial conformation. The other neutral triply bonded groups have ΔG_X values in the range 0.5–0.7 kcal mol^{-1}.

The conformation of the furanose ring in 2′-substituted 2′-deoxyadenosines is dependent on both σ_I and υ values. The larger the σ_I and smaller the υ, the greater the preference for the *N* conformer, ***N*-82**. Both the —CN and —NC groups apparently prefer the *N* conformation, the other neutral triply bonded groups seem to prefer the *S* conformation, ***S*-82**.

Lastly, ΔE_X values for the equilibrium between *gauche* and *trans* conformers for



(*N*-**82**)

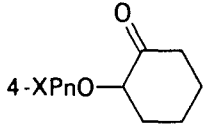
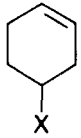


(*S*-**82**)

N = nucleotide

TABLE 18. Calculations of K_{EZ}, ΔG, K_{NS} and ΔE for triply bonded groups

(a) Correlation equations from which values were calculated

System	Correlation equation	References
(1) MeCH=CHX; $E \rightleftharpoons Z$	$\log K_{EZ,X} = -1.96\sigma_{IX} - 0.956\upsilon_X + 2.92\alpha_X + 0.850$	147
(2) XCH=CHX; $E \rightleftharpoons Z$	$\log K_{EZ,X} = -2.74\Pi\sigma_{IX} - 10.6\Pi\alpha_X + 0.980\Sigma\upsilon_X - 0.634$	147
(3)  ; e $\rightleftharpoons$ a	$\Delta G_X = 0.931\sigma_{IX} + 0.651\sigma_{RX}^- - 0.0294$	151
(4)  ; e $\rightleftharpoons$ a	$\Delta G_X = -1.38\sigma_{IX} + 1.37\upsilon_X + 0.295$	161
(5) 2′-Substituted 2′-deoxyadenosines	$\log K_{NS} = 2.24\sigma_{IX} - 1.88\upsilon_X - 0.399$	155
(6) XCH_2CH_2Bu-*t*; *gauche* $\rightleftharpoons$ *trans*	$\Delta E_X = -0.736\sigma_{IX} + 1.38\upsilon_X - 1.68\alpha_X + 0.817$	158

(b) Calculated values of K_{EZ}, ΔG, K_{NS} and ΔE

	X							
System	—CN	—NC	—C≡CH	—C≡CMe	—C≡CPh	—C≡CCF$_3$	—C≡CC≡CH	—C≡P
(1)	0.320	0.244	0.945	1.23	3.88	0.588	1.07	1.17
(2)	0.170	0.108	1.57	1.19	0.127	0.714	0.602	0.619
(3)	0.67		0.33				0.46	
(4)	0.06	−0.03	0.69	0.68	0.63	0.51	0.55	0.48
(5)	1.34	1.82	0.145	0.152	0.178	0.283	0.242	0.293
(6)	0.86	0.82	1.26	1.18	0.83	1.10	1.04	1.01

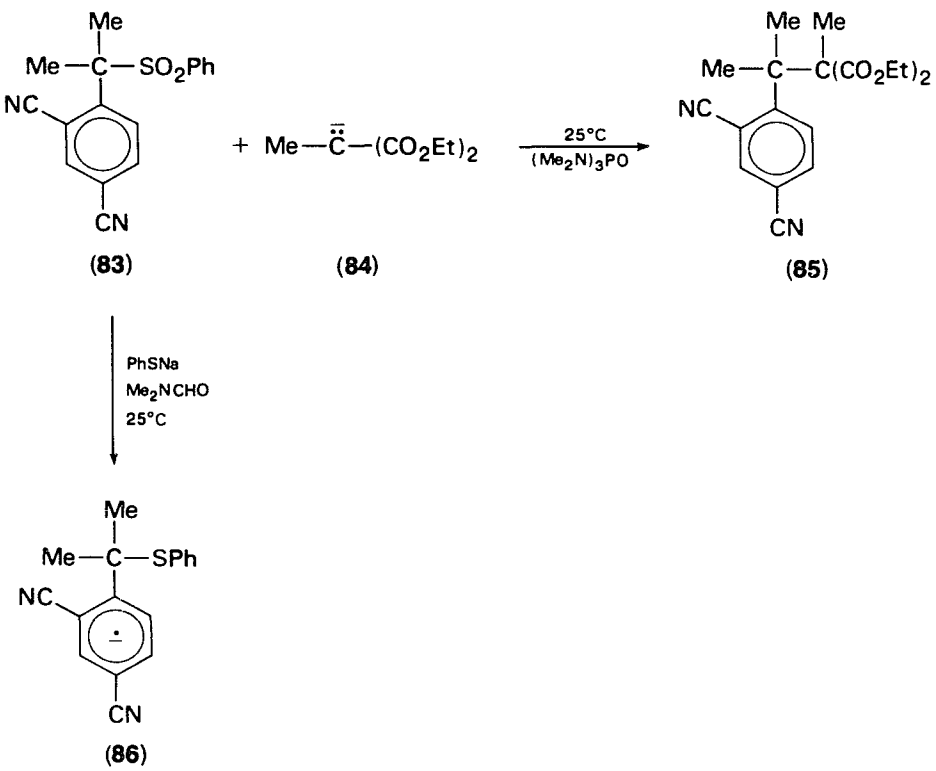
1-substituted 3,3-dimethylbutanes are predominantly dependent on υ and in general those groups with the largest υ and smallest σ_I values have ΔE values of 1.0–1.3 kcal mol^{-1}, whereas the —CN and —NC groups which have the largest σ_I and smallest υ values have ΔE_X between 0.8 and 0.9. The exception is the —C≡CPh group which makes up for its relatively small σ_I and large υ values by having an exceptionally large value of α.

Again, these results are simply intended to show that the directing effect of triply bonded groups can be estimated if the necessary correlation equations and substituent constants are known.

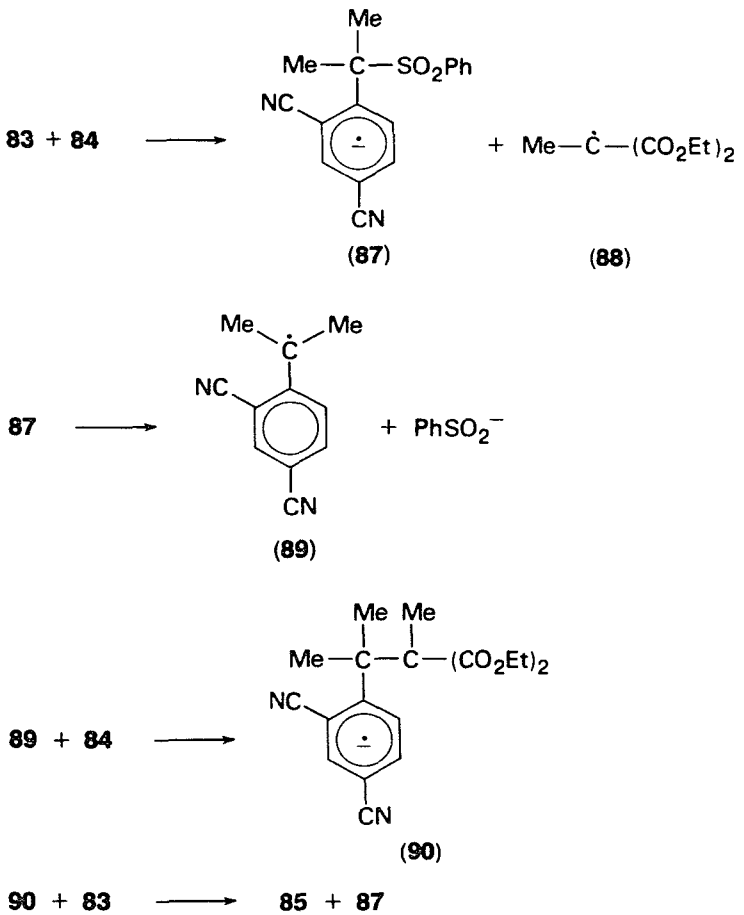
VII. ACTIVATION EFFECTS

A group is said to be activating if it either facilitates a reaction or if it makes possible a reaction which otherwise would not occur. Whether a group is activating or not depends on the electrical and steric effects of the group and the electrical requirements of the active site in the reaction. Thus, the alkyl ethynyl groups AkC≡C— will be activating in electrophilic aromatic substitution as they are effective delocalized effect donors, while the cyano, diazonium and acylium groups will be deactivating as they are localized and delocalized electrical effect acceptors. This situation will be reversed in nucleophilic situation by the S_N2Ar path, where a negative charge is to be stabilized in the Wheland intermediate. A recent example of a case in which the cyano group makes a reaction possible has been described by Kornblum and Fifolt[162] who

Reaction



Mechanism



SCHEME 3

have observed that electron-transfer chain nucleophilic substitution is facilitated by cyano groups (see Scheme 3).

From the substituent constants for triply bonded groups reported in Table 2 it should be possible to predict for any reaction for which the electrical demand of the active site in the rate-determining step is known, whether or not a particular triply bonded group will be activating.

VIII. CONCLUSION

The directing and activating effects of triply bonded groups, and their effects on physical properties and biological activity as well, are a function of the electrical and/or steric and/or polarizability (and in the case of biological activity and/or transport) effects of the groups. These properties can be characterized by appropriate substituent parameters. Then if the correlation equations are known a quantitative

prediction of the effect of a triply bonded group can be made for the chemical reactivity, physical property or biological activity of any group for which the substituent parameters are available. Methods of estimating the substituent parameters are also available in many cases. It is sometimes sufficient to know what electrical, steric or polarizability effects favour or disfavour a particular reaction or property in order to predict the effect of a group. Correlation analysis provides an excellent framework for the description and prediction of reactivity, properties and bioactivity of the triply bonded groups discussed here and, in the general case, for all types of substituents.

IX. REFERENCES

1. T. A. Cooper, H. W. Kroto, J. F. Nixon and O. Ohashi, *J. Chem. Soc., Chem. Commun.*, 333 (1980).
2. H. W. Kroto, J. F. Nixon, N. P. C. Simmons and N. P. C. Westwood, *J. Amer. Chem. Soc.*, **100**, 446 (1978).
3. H. W. Kroto, J. F. Nixon and N. P. C. Simmons, *J. Mol. Spectry.*, **77**, 270 (1979).
4. J. K. Tyler, *J. Chem. Phys.*, **40**, 1170 (1964).
5. S. P. Anderson, H. Goldwhite, D. Ko, A. Letson and F. Esparza, *J. Chem. Soc., Chem. Commun.*, 744 (1975).
6. H. W. Roesky in *Sulfur in Organic and Inorganic Chemistry*, Vol. 1 (Ed. A. Senning), Marcel Dekker, New York, 1971, pp. 13–38.
7. S. P. VonHalasz and O. Glemser in *Sulfur in Organic and Inorganic Chemistry*, Vol. 1 (Ed. A. Senning), Marcel Dekker, New York, 1971, pp. 209–238.
8. B. Buss, D. Altena, R. Hoefer and O. Glemser, *J. Chem. Soc., Chem. Commun.*, 266 (1978).
9. G. A. Olah, A. Germain and A. M. White, *Carbonium Ions*, Vol. 5 (Eds. G. A. Olah and P. v. R. Schleyer), John Wiley and Sons, New York, 1976, p. 2049.
10. J. Shorter, *Correlation Analysis in Organic Chemistry*, Clarendon Press, Oxford, 1973.
11. M. Charton, *Chem. Tech.*, 502 (1974); 245 (1975).
12. L. M. Stock, *J. Chem. Ed.*, **49**, 400 (1972).
13. T. W. Cole, Jr., C. J. Mayers and L. M. Stock, *J. Amer. Chem. Soc.*, **96**, 4555 (1974).
14. M. Charton, *Prog. Phys. Org. Chem.*, **13**, 119 (1981).
15. M. Charton in *Design of Biopharmaceutical Properties Through Prodrugs and Analogs* (Ed. E. B. Roche), American Pharmaceutical Society, Washington, D.C., 1977, p. 228.
16. M. Charton and B. I. Charton, *Abstracts Eurochemical Conference on Correlation Analysis in Organic Chemistry, Assisi, Italy*, 1979, p. O1.
17. B. F. Bistrov, A. V. Stelanyants, L. M. Yagupolskii and O. A. Fialkov, *Zh. Obshch. Khim.*, **34**, 3682 (1964).
18. O. Exner, *Collect. Czech. Chem. Commun.*, **31**, 65 (1966).
19. O. Exner and J. Lakony, *Collect. Czech. Chem. Commun.*, **35**, 1371 (1970).
20. J. J. Monagle, J. V. Mengenhauser and D. A. Jones, Jr., *J. Org. Chem.*, **32**, 2477 (1967).
21. S. Ehrenson, R. T. C. Brownlee and R. W. Taft, *Prog. Phys. Org. Chem.*, **10**, 1 (1973).
22. J. Hinze and H. H. Jaffé, *J. Amer. Chem. Soc.*, **84**, 540 (1962).
23. J. Hinze, M. A. Whitehead and H. H. Jaffé, *J. Amer. Chem. Soc.*, **85**, 148 (1963).
24. J. Hinze and H. H. Jaffé, *J. Phys. Chem.*, **67**, 1501 (1963).
25. M. Charton, *Prog. Phys. Org. Chem.*, **10**, 81 (1973).
26. M. Charton, unpublished results.
27. M. Charton in *Correlation Analysis in Chemistry: Recent Advances* (Eds. N. B. Chapman and J. Shorter), Plenum Press, New York, 1978, p. 175.
28. O. Exner in *Correlation Analysis in Chemistry: Recent Advances* (Eds. N. B. Chapman and J. Shorter), Plenum Press, New York, 1978, p. 439.
29. A. J. Hoefnagel, M. A. Hoefnagel and B. M. Wepster, *J. Org. Chem.*, **43**, 4720 (1978).
30. I. M. Koshkina, L. A. Remizova, E. V. Ermilova and I. A. Favorskaya, *Reakts. Spos. Org. Soedin.*, **7**, 944 (1970).
31. N. C. Cutress, T. B. Grindley, A. R. Katritzky, M. V. Sinnott and R. D. Topsom, *J. Chem. Soc., Perkin II*, 2255 (1972).

32. R. W. Taft and W. A. Sheppard, personal communication cited by R. T. C. Brownlee, R. E. J. Hutchinson, A. R. Katritzky, T. T. Tidwell and R. D. Topsom, *J. Amer. Chem. Soc.*, **90**, 1757 (1968).
33. J. A. Landgrebe and R. H. Rynbrandt, *J. Org. Chem.*, **31**, 2585 (1966).
34. S. C. J. Olivier, *Rec. Trav. Chim.*, **41**, 301, 406 (1922); **42**, 516 (1923).
35. R. W. Bott, C. Eaborn and T. W. Swaddle, *J. Chem. Soc.*, 2342 (1963).
36. J. E. Baines and C. Eaborn, *J. Chem. Soc.*, 1436 (1956).
37. C. Eaborn, *J. Chem. Soc.*, 3148 (1953).
38. C. Eaborn and J. A. Sperry, *J. Chem. Soc.*, 4921 (1961).
39. C. Eaborn and B. M. Rushton, *J. Organometal. Chem.*, **3**, 448 (1965).
40. C. Eaborn, A. R. Thompson and D. R. M. Walton, *J. Chem. Soc. (B)*, 859 (1969).
41. C. Eaborn, A. R. Thompson and D. R. M. Walton, *J. Chem. Soc. (B)*, 357 (1970).
42. C. Eaborn and S. H. Parker, *J. Chem. Soc.*, 126 (1955).
43. A. L. Allred and E. G. Rochow, *J. Inorg. Nucl. Chem.*, **5**, 264 (1958).
44. C. Hansch, A. Leo, S. H. Unger, K. H. Kim, D. Nikaitani and E. J. Lien, *J. Med. Chem.*, **16**, 1207 (1973).
45. P. G. Gassman and J. J. Talley, *J. Amer. Chem. Soc.*, **102**, 1214 (1980).
46. P. G. Gassman and J. J. Talley, *J. Amer. Chem. Soc.*, **102**, 4138 (1980).
47. D. A. Dixon, P. A. Charlier and P. G. Gassman, *J. Amer. Chem. Soc.*, **102**, 3957 (1980).
48. M. Dorado, O. Mo and M. Yanez, *J. Amer. Chem. Soc.*, **102**, 947 (1980).
49. G. A. Olah, G. K. Surya Prakash and M. Arvanaghi, *J. Amer. Chem. Soc.*, **102**, 6640 (1980).
50. K. M. Koshy and T. T. Tidwell, *J. Am. Chem. Soc.*, **102**, 1216 (1980).
51. X. Creary, *J. Org. Chem.*, **44**, 3938 (1979).
52. J. P. Bégué and M. Charpentier-Morize, *Acc. Chem. Res.*, **13**, 207 (1980).
53. M. N. Paddon-Row, C. Santiago and K. N. Houk, *J. Amer. Chem. Soc.*, **102**, 6561 (1980).
54. H. G. Richey, Jr. and J. M. Richey in *Carbonium Ions*, Vol. II, (Eds. G. A. Olah and P. v. R. Schleyer), John Wiley and Sons, New York, 1970, p. 944.
55. R. W. Taft, R. H. Martin and F. W. Lampe, *J. Amer. Chem. Soc.*, **87**, 2490 (1965).
56. K. W. Egger and T. A. Cocks, *Helv. Chim. Acta*, **56**, 1516, 1537 (1973).
57. J. A. Kerr, *Chem. Rev.*, **66**, 645 (1966).
58. F. G. Bordwell, *Faraday Symposia*, **10**, 100 (1975).
59. F. G. Bordwell, *Pure Appl. Chem.*, **49**, 963 (1977).
60. W. S. Matthews, J. E. Bares, J. E. Bartmess, F. G. Bordwell, F. J. Cornforth, G. E. Drucker, Z. Margolin, R. J. McCallun, G. J. McCollum and N. R. Vanier, *J. Amer. Chem. Soc.*, **97**, 7006 (1975).
61. F. G. Bordwell, M. Van der Puy and N. R. Vanier, *J. Org. Chem.*, **41**, 1883, 1885 (1976).
62. F. G. Bordwell, J. E. Bartmess and J. A. Hautala, *J. Org. Chem.*, **43**, 3095 (1978).
63. F. G. Bordwell and J. E. Bartmess, *J. Org. Chem.*, **43**, 3101 (1978).
64. F. G. Bordwell, J. C. Branca, D. L. Hughes and W. N. Olmstead, *J. Org. Chem.*, **45**, 3305 (1980).
65. A. I. Ivanov, V. I. Slovetskii, S. A. Shevelev, V. I. Erashko, A. A. Fainzelberg and S. S. Novikov, *Russ. J. Phys. Chem.*, **40**, 1234 (1966).
66. I. V. Tselenskii, A. S. Kosmynina, V. N. Dronov and I. N. Shokhor, *Org. React.*, **7**, 20 (1970).
67. E. K. Chess, B. S. Schatz and G. J. Gleicher, *J. Org. Chem.*, **42**, 752 (1977).
68. Y. Gonen, A. Horowitz and L. A. Rajbenbach, *J. Chem. Soc., Faraday Trans.*, **1**, 73, 866 (1977).
69. R. O. C. Norman and G. C. Gilbert, *Adv. Phys. Org. Chem.*, **5**, 53 (1967).
70. H. Fischer, *Z. Naturforsch.*, **19a**, 866 (1964).
71. H. Fischer, *Z. Naturforsch.*, **20a**, 428 (1965).
72. J. W. Timberlake, A. W. Garner and M. L. Hodges, *Tetrahedron Letters*, 309 (1973).
73. M. M. Martin and E. B. Sanders, *J. Amer. Chem. Soc.*, **89**, 3777 (1967).
74. P. D. Bartlett and R. R. Hiatt, *J. Amer. Chem. Soc.*, **80**, 1398 (1958).
75. S. F. Sarner, D. M. Gale, H. K. Hall, Jr. and A. B. Richmond, *J. Phys. Chem.*, **76**, 2817 (1972).
76. H. C. O'Neal and S. W. Benson, *Int. J. Chem. Kinet.*, **1**, 221 (1969).
77. D. A. Luckraft and P. J. Robinson, *Int. J. Chem. Kinet.*, **5**, 137 (1973).

78. F. G. Bordwell, J. C. Branca, C. R. Johnson and N. R. Vanier, *J. Org. Chem.*, **45**, 3884 (1980).
79. T. Bottin-Strzalko, J. Seyden-Penne, M. J. Pouet and M. P. Simonnin, *J. Org. Chem.*, **43**, 4346 (1978).
80. M. Charton, *J. Org. Chem.*, **43**, 3995 (1978).
81. M. Charton, *Proceedings of the 3rd Congress of the Hungarian Pharmaceutical Society*, Akademiai Kiado, Budapest, 1980, p. 210.
82. M. Charton, *Abstracts, 5th IUPAC Conference on Physical Organic Chemistry, Santa Cruz, California*, 1980, p. 63.
83. L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, **1**, 35 (1963).
84. M. Charton, *J. Org. Chem.*, **34**, 278 (1969).
85. M. Charton, *Prog. Phys. Org. Chem.*, **8**, 235 (1971).
86. J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, **6**, 506 (1938).
87. F. Cacace, P. Giacomello and A. P. Wolf, *J. Amer. Chem. Soc.*, **102**, 3511 (1980).
88. J. M. A. Baas and B. M. Wepster, *Rec. Trav. Chim.*, **90**, 1081 (1971).
89. J. M. A. Baas and B. M. Wepster, *Rec. Trav. Chim.*, **90**, 1089 (1971).
90. J. M. A. Baas and B. M. Wepster, *Rec. Trav. Chim.*, **91**, 285 (1972).
91. J. M. A. Baas and B. M. Wepster, *Rec. Trav. Chim.*, **91**, 517 (1972).
92. H. Cerfontain and Z. H. R. Schaasberg-Nienhuis, *J. Chem. Soc., Perkin Trans. II*, 536 (1974).
93. M. Charton, *J. Amer. Chem. Soc.*, **99**, 5687 (1977).
94. M. Charton, *J. Amer. Chem. Soc.*, **97**, 3691 (1975).
95. M. Charton, *J. Org. Chem.*, **44**, 2097 (1979).
96. F. G. Bordwell, G. E. Drucker and G. L. McCollum, *J. Org. Chem.*, **41**, 2786 (1976).
97. F. G. Bordwell and H. E. Fried, *Tetrahedron Letters*, 1121 (1977).
98. W. Adcock and T.-C. Khar, *J. Org. Chem.*, **43**, 1272 (1978).
99. J. M. Tedder and J. C. Walton, *Tetrahedron*, **36**, 701 (1980).
100. J. M. Tedder and J. C. Walton in *Fluorine-containing Free Radicals* (Ed. J. W. Root), ACS Symposium Series No. 66, American Chemical Society, Washington, D.C., 1978, p. 107.
101. J. M. Tedder and J. C. Walton, *Adv. Phys. Org. Chem.*, **16**, 86 (1978).
102. J. M. Tedder and J. C. Walton, *Acc. Chem. Res.*, **9**, 183 (1976).
103. M. Charton, *Abstracts, Eurochemical Conference on Correlation Analysis in Organic Chemistry, Assisi, Italy*, 1979, p. 4.
104. M. Charton, *J. Org. Chem.*, **31**, 3745 (1966).
105. I. N. Nazarov, Y. A. Titov and A. I. Kuznetsova, *Dokl. Akad. Nauk SSR*, 124, 586 (1959).
106. Y. A. Titov and A. I. Kuznetsova, *Izv. Akad. Nauk SSR, Otdl. Khim. Nauk*, 1810, 1815 (1960).
107. J. S. Meek, R. T. Merrow, D. E. Raney and S. J. Cristol, *J. Amer. Chem. Soc.*, **73**, 5563 (1951).
108. A. Titov and A. I. Kuznetsova, *Izv. Akad. Nauk SSR, Otdl. Khim. Nauk*, 1203 (1960).
109. C. S. Rondestvedt, Jr. and C. D. VerNooy, *J. Amer. Chem. Soc.*, **77**, 4878 (1955).
110. F. Caplan and H. Conroy, *J. Org. Chem.*, **28**, 1593 (1963).
111. E. Stephan, L. Vo-Quang and Y. Vo-Quang, *Bull. Soc. Chim. Fr.*, 1793 (1975).
112. M. Kosugi, K. Takeuchi and T. Migita, *Bull. Chem. Soc. Japan*, **42**, 3342 (1969).
113. G. A. Russell, *Free Radicals*, Vol. 1 (Ed. J. K. Kochi), John Wiley and Sons, New York, 1973, p. 275.
114. A. J. Birch, A. L. Hinde and L. Radom, *J. Amer. Chem. Soc.*, **102**, 4074 (1980).
115. A. J. Birch, A. L. Hinde and L. Radom, *J. Amer. Chem. Soc.*, **102**, 6430 (1980).
116. E. R. Biehl, W. Stewart, A. Marks and P. C. Reeves, *J. Org. Chem.*, **44**, 3674 (1979).
117. M. Charton, *Prog. Phys. Org. Chem.*, **10**, 81 (1973).
118. M. Charton and B. I. Charton, *J. Org. Chem.*, **37**, 3684 (1972).
119. H. Lehmkuhl and R. McLane, *Ann. Chim.*, 736 (1980).
120. J. Hine, *Structural Effects on Equilibria in Organic Chemistry*, John Wiley and Sons, New York, 1975, p. 270.
121. J. Hine, S.-M. Linden, A. Wang and V. Thingarajan, *J. Org. Chem.*, **45**, 2827 (1980).
122. J. L. Burdett and M. T. Rogers, *J. Amer. Chem. Soc.*, **86**, 2105 (1964).
123. Z. Bankowska and E. Kolaczkowska, *Rocz. Chem.*, **50**, 1827 (1976).

124. A. V. Celiano, M. Cefola and P. S. Gentile, *J. Phys. Chem.*, **66**, 1132 (1962).
125. M. Bergon and J. P. Calmon, *Bull. Soc. Chim. Fr.*, 1819 (1972).
126. M. Bergon and J. P. Calmon, *Compt. Rend. (C)*, 273, 181 (1971).
127. W. J. Bouma and L. Radom, *Australian J. Chem.*, **31**, 1167 (1978).
128. W. J. Bouma and L. Radom, *Australian J. Chem.*, **31**, 1649 (1978).
129. W. J. Bouma and L. Radom, *J. Amer. Chem. Soc.*, **101**, 3487 (1979).
130. M. J. Ballard, W. J. Bouma, L. Radom and M. V. Vincent, *Australian J. Chem.*, **32**, 1401 (1979).
131. H. Pines and W. M. Stalick, *Base-catalyzed Reactions of Hydrocarbons and Related Compounds*, Academic Press, New York, 1975, p. 124.
132. G. Pourcelot and G. Georgoulis, *J. Chim. Phys.*, 1393 (1974).
133. W. Walter and H. W. Meyer, *Ann. Chem.*, 776 (1974).
134. K. Bredereck and E. F. Sommermann, *Tetrahedron Letters*, 5009 (1966).
135. J. Elguero, C. Marzin, A. R. Katritzky and P. Linda, *The Tautomerism of Heterocycles*, Academic Press, New York, 1976.
136. M. Charton, *J. Org. Chem.*, **30**, 3346 (1965).
137. M. Charton, *J. Org. Chem.*, **31**, 3739 (1966).
138. M. Charton, *Abstract, 1st International Congress of Heterocyclic Chemistry, Albuquerque, New Mexico*, 1967, No. 77.
139. M. Charton, *J. Chem. Soc. (B)*, 1240 (1969).
140. P. Vetesnik, J. Karalek, V. Beranek and O. Exner, *Collect. Czech. Chem. Commun.*, **33**, 566 (1968).
141. P. Vetesnik, J. Karalek and V. Beranek, *Collect. Czech. Chem. Commun.*, **36**, 2486 (1971).
142. H. H. Jaffé and H. L. Jones, *Advan. Het. Chem.*, **3**, 209 (1964).
143. C. W. Donaldson and M. M. Jouille, *J. Org. Chem.*, **33**, 1504 (1968).
144. M. J. S. Dewar and P. J. Grisdale, *J. Amer. Chem. Soc.*, **84**, 3539, 3546, 3548 (1962).
145. R. Escale, R. Jacquier, B. Ly, F. Petrus and J. Verducci, *Tetrahedron*, **32**, 1369 (1976).
146. R. Faure, J. P. Galy, E. J. Vincent and J. Elguero, *J. Het. Chem.*, **14**, 1299 (1977).
147. J. Hine, *Structural Effects on Equilibria in Organic Chemistry*, John Wiley and Sons, New York, 1975, p. 122.
148. M. Charton and B. I. Charton, *J. Org. Chem.*, **44**, 2284 (1979).
149. R. Knörr, *Chem. Ber.*, **113**, 2441 (1980).
150. M. Charton and B. I. Charton, *J. Chem. Soc. (B)*, 43 (1967).
151. D. Cantacuzene and M. Tordeux, *Can. J. Chem.*, **54**, 2759 (1976).
152. H. F. van Woerden, H. Cerfontain, C. H. Green and R. J. Reijerkerk, *Tetrahedron Letters*, 6107 (1968).
153. L. J. Collins and D. N. Kirk, *Tetrahedron Letters*, 1547 (1970).
154. F. Borremans and M. J. O. Anteunis, *Bull. Soc. Chim. Belg.*, **85**, 681 (1976).
155. S. Uesugi, H. Miki, M. Ikehara, H. Iwahashi and Y. Kyogoku, *Tetrahedron Letters*, 4073 (1979).
156. D. N. Jones and D. E. Kime, *J. Chem. Soc. (C)*, 846 (1966).
157. M. Charton and B. I. Charton, *Abstracts, 3rd Middle Atlantic Regional Meeting*, American Chemical Society, 1968, p. 89.
158. G. M. Whitesides, J. P. Sevenair and R. W. Goetz, *J. Amer. Chem. Soc.*, **89**, 1135 (1967).
159. F. R. Jensen, C. H. Bushweller and B. H. Beck, *J. Amer. Chem. Soc.*, **91**, 344 (1969).
160. J. A. Hirsch, *Top. Stereochem.*, **1**, 199 (1967).
161. E. J. Corey and N. F. Feiner, *J. Org. Chem.*, **45**, 765 (1980).
162. N. Kornblum and M. J. Fifolt, *J. Org. Chem.*, **45**, 360 (1980).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 9

Biological formation and metabolic transformations of compounds containing the cyano group

J. P. FERRIS
Rensselaer Polytechnic Institute, Troy, N.Y., U.S.A.

I. INTRODUCTION

The developments in the biochemistry of the cyano compounds for the decade 1969–1979 will be reviewed in this chapter. The work of the preceding period was reviewed in an earlier volume of this series[1]. Progress in this period has generally proceeded along the lines noted in this previous chapter, with the exception of the controversy concerning the alleged utility of amygdalin (laetrile) in the treatment of cancer. The emphasis will be on the results published in 1969–1979 but a certain amount of earlier material will be given so that the present chapter can be read without reference to the previous one.

II. CYANOGENIC GLYCOSIDES IN PLANTS

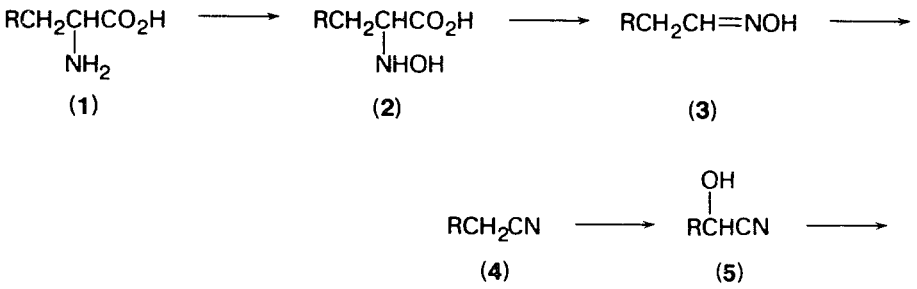
A. Occurrence and Toxicity

Approximately 2000 plants produce cyano compounds which release HCN when the plant is crushed[2,3]. About 10% of these plants have been shown to contain cyanogenic glycosides[4]. The toxicity of many of these plants, and of the cyanogenic glycosides, is due to this release of HCN when they are eaten by mammals. Ingestion of plants which contain large concentrations of the glycosides, such as peach and almond pits, bitter almonds and western choke berries has resulted in deaths due to cyanide poisoning[5,6].

It appears that the hydrolysis of the cyanogenic glycosides is affected by microflora present in the mammalian intestine[6]. The more extensively used foods which contain these cyanogens pose an even greater hazard[5,6]. Certain varieties of lima beans, cassava, apricot pits and bamboo have caused the death of both humans and livestock. Cassava meal which has been properly processed to cleave the cyanogenic glycoside is an important foodstuff in Africa. The processing results in the extensive hydrolysis of the cyanogenic glycosides with the release of most of the HCN. There is concern that the constant consumption of cassava results in the ingestion of low levels of cyanide which may be the cause of blindness and other neurological diseases. It is not clear if these symptoms are due only to cyanide or to other dietary imbalances as well.

B. Biosynthesis

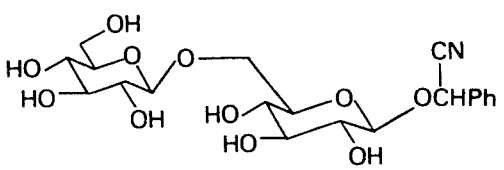
Amino acids (**1**) have been shown to be the biosynthetic precursors of the cyanogenic glycosides (**6**) and recent studies have centred on elucidating the intermediates in the reaction pathway. The formation of the *N*-hydroxyamino acid **2** as the first step in the conversion of amino acids to cyanogenic glucosides was established by trapping experiments where a ^{14}C-labelled amino acid was incubated with a plant microsomal fraction together with excess unlabelled *N*-hydroxyamino acid[7]. The recovered *N*-hydroxyamino acid was found to be ^{14}C-labelled after it was reisolated, indicating that the oxidation of the amino acid to *N*-hydroxyamino acid was catalysed by oxygenase enzymes present in the microsomal fraction. Oxime **3** has been shown to be



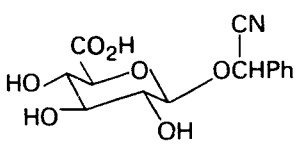
a reaction intermediate by trapping experiments and by feeding experiments in which the ^{14}C-oxime is efficiently converted to a ^{14}C-cyanogenic glucoside[8,9]. The conversion of the oxime **3** to the nitrile **4** as the next step in the biosynthetic process was established by trapping experiments using microsomal particles from plant homogenates[10]. The conversion of the nitrile **4** to the hydroxynitrile **5** is an oxidative process in which one of the oxygen atoms of molecular oxygen is incorporated into the cyanohydrin[11]. This process is catalysed by the enzymes present in a cell-free microsomal preparation of plant cells. The synthesis of the cyanogenic glycoside **6** proceeds via the reaction of the cyanohydrin **5** with the 5′-glucoside of uridine diphosphate. This reaction is catalysed by a soluble enzyme isolated from plant-cell homogenates[12,13].

C. Pharmacology

Recent pharmacological interest in the cyanogenic glycosides centres on the reputed efficacy of amygdalin as an antitumour agent. Although amygdalin **7** is called laetrile in the popular press, compound **7** is the drug that is being tested as an antitumour agent. Laetrile **8** is formed in low yield by the hydrolysis and oxidation of amygdalin[14].



(7)



(8)

The reputed antitumour activity of amygdalin has yet to be verified in controlled experiments. Retrospective analysis of instances where it had been used in cancer chemotherapy give no definitive conclusions[15]. Recent studies clearly show that amygdalin does not cause the remission of experimental tumours in rats[16]. The amygdalin does undergo hydrolysis *in vivo* as indicated by the detection of HCN in the serum of the amygdalin-treated rats. This hydrolysis is due to microflora present in the intestine of the rats[6].

D. Biological Function of Cyanogenic Glycosides

One study suggests that the cyanogenic glycosides serve as defensive agents for plants[17]. There is a high concentration of these cyano derivatives in the seeds of the wild lima beam (*Phaseolus Lunatus L.*) and they are rapidly transferred to the leaves and shoot-tips after the seed germinates. The experiments indicate that the glycosides are not synthesized during this early growth phase but rather are transported in the

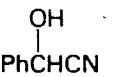
growing seedling. Thus the seed is protected from herbivores by the high concentration of the cyanogenic glycosides present. Once the seed germinates and no longer requires protection, the cyanogenic glycosides are transferred to the newly formed leaves to protect the seedling from attack. It should be emphasized that all cyanogenic plants do not utilize the cyanogenic glycosides as defensive agents in the same way. *Sorghum vulgare* seeds do not contain a cyanogenic glucoside but the seedlings synthesize large amounts of it[18].

Cyanogenic glycosides have a central role in a minor pathway for the environmental cycling of carbon and nitrogen. *Sorghum* plants, a fungus (*Gloeocercospora sorghi*) and a bacterium (*Pseudomonas SL-4*) carry out the steps in the cycle[19]. The cyanogenic glucoside produced by *Sorghum* is converted to formamide by the fungus when it attacks the plant[20]. *Pseudomonas SL-4* grows in the same plant lesion as the fungus and converts formamide to carbon dioxide and ammonia[19]. Nitrobacteria convert the ammonia to nitrate which, along with the carbon dioxide, is converted back to cyanogenic glucosides by *Sorghum* and other plants.

III. CYANOGENIC COMPOUNDS IN ARTHROPODS

The defensive secretions of millipedes contain HCN and cyano compounds[1]. In most cases the HCN is stored as the cyanohydrin of benzaldehyde (mandelonitrile) (**9**) or as the benzoic acid ester of mandelonitrile. When the insect is attacked, the cyanohydrin is secreted together with an enzyme which catalyses its dissociation to HCN and benzaldehyde[1,21].

Benzoyl cyanide (**10**) has recently been identified as another source of HCN in the defense secretion[22,23]. This is the first example of a biochemical synthesis of the reactive benzoyl cyanide. It is probably formed by the oxidation of the cyanohydrin of benzaldehyde (**9**). Although acyl cyanides are readily hydrolysed to give HCN it is likely that the insects also secrete an enzyme which accelerates the hydrolytic release of cyanide.



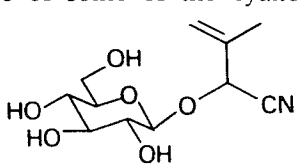
(**9**)

(**10**)

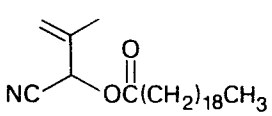
The cyano derivatives constitute only a portion of the active compounds present in the defensive secretions of millipedes. In one instance sticky (proteinaceous) material which hardens on exposure to air is emitted with the cyanogen. Predatory insects become immobilized or stick together when massively wetted with this secretion[22].

IV. CYANOGENIC LIPIDS

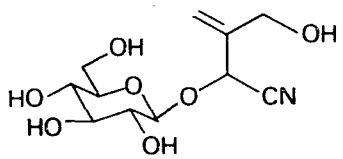
Cyanolipids are found in several genera of the soapberry family (*Sapindaceae*)[24–28]. In some instances the cyanolipids constitute 35% of the lipid fraction[26]. These are mainly allyl and vinyl cyanides, e.g. **12**, **14–16**, which readily release HCN on hydrolysis. The structures of some of the cyanolipids are similar to those of certain cyanogenic



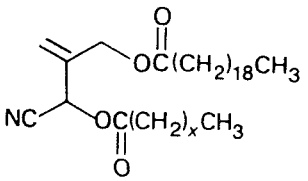
(**11**)



(**12**)

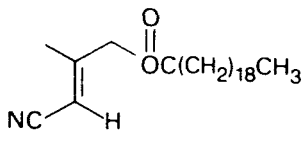


(13)

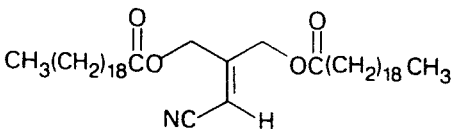


x = 14, 16, 18, 20

(14)



(15)



(16)

glucosides except that the glucose is replaced by a fatty acid (compare structure **11** with structure **12** and structure **13** with structure **14**). Presumably the biosynthesis of the cyanolipids parallels that of the cyanoglucosides. These compounds, like the cyanoglycosides, may also serve as defensive agents.

V. CYANIDE FORMATION BY MOULDS AND MICROORGANISMS

A. Occurrence

Cyanide production is widespread in fungi but only a few bacterial species are known to produce HCN[29]. The pathway for the production of HCN by the photosynthetic *Chlorella* species differs from that of the fungi and other microorganisms and will be considered separately.

1. *Fungi*

Many of the fungi which synthesize cyanide have cyanogenic plants as their hosts[29]. Although these fungi secrete cyanide its concentration is not sufficiently high to be toxic to the whole plant. The cyanide may damage the crown buds and shoots of the plant where the fungus can start to grow. The fungus then secretes an extracellular β-glucosidase which accelerates the release of cyanide present in the host. This massive release of cyanide is toxic to the plant and permits the growth of the fungus. Those plants with the highest concentrations of cyanogenic glycosides are the least resistant to fungal infection. It is ironic that the fungus is able to utilize the plant's own defenses (the cyanogenic glucosides) to kill it. These fungi are able to do this because they are able to grow in the presence of the large amounts of cyanide released from the plant.

2. Pseudomonas *and* Chromobacterium

Cyanide appears to be a secondary metabolite in *Pseudomonas* and *Chromobacterium* as indicated by the facts that its synthesis occurs late in the growth phase and it does not have a central role in the bacterial metabolic processes[30]. The formation of cyanide may serve to regulate the level of its biosynthetic precursor (glycine) in the cell[31, 32]. Cyanide production is stimulated when glycine and methionine are added to the

growth medium. In one instance it was shown that electron acceptors such as oxygen, methylene blue, dichloroindophenol and ferricyanide stimulate cyanide formation[33]. Presumably these compounds accelerate the oxidative conversion of glycine to hydrogen cyanide. A bacterial cell-free extract capable of producing cyanide from glycine has been discovered and it may facilitate the investigation of HCN biosynthesis[34a].

B. Biosynthesis of HCN

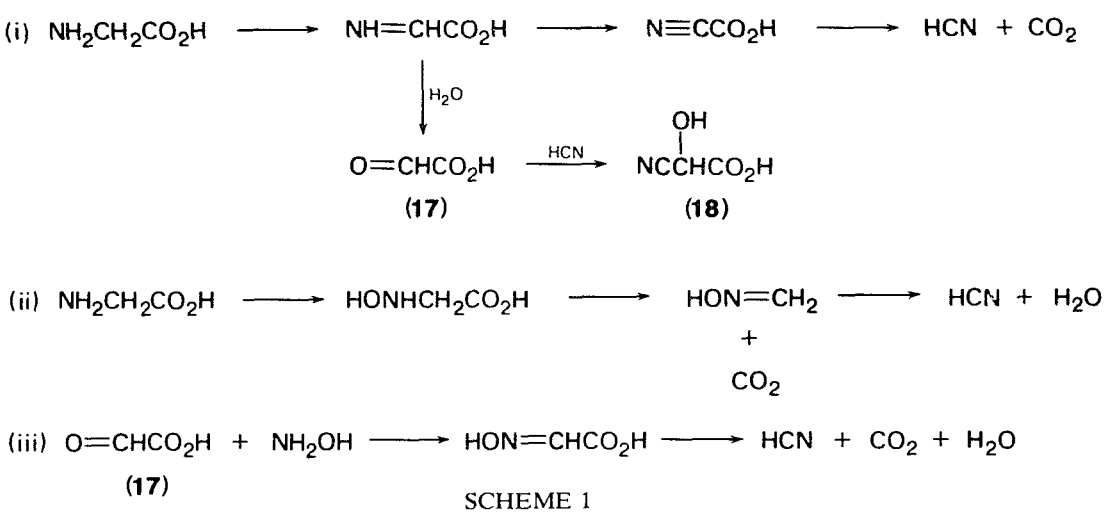
1. *Fungi,* Chromobacterium violaceum *and* Pseudomonas *species*

Glycine is the biochemical precursor of cyanide in these species[34b,c]. Threonine has also been shown to stimulate HCN production in *C. violaceum*[34d]. This is due to the efficient conversion of threonine to glycine by this organism. Methionine and its analogues also stimulate HCN formation, but the mechanism of this stimulation is not known[1,34d]. Studies with ^{14}C-labelled glycine have established that the cyanide carbon is derived from the glycine methylene group. The cyanohydrin of glyoxylic acid (**18**) has been isolated from cultures of the snow mould fungus indicating that it may be a biochemical intermediate between glycine and cyanide. No intermediates have been detected in the bacterial systems.

Two pathways (*i* and *ii*) have been proposed for the conversion of glycine to cyanide in these species (Scheme 1). Glyoxylic acid (**17**) is a side-product of the formation of HCN in fungi (*i*)[29]. Pathway (*ii*) was suggested as an alternative, because it is the route by which cyanide is formed in higher plants[3]. The present experimental data does not permit a choice between these two alternatives.

2. *Chlorella*

Nitrate arising from chemical fertilizers and industrial wastes is a major factor in the growth of photosynthetic microorganisms which leads to the eutrophication of lakes. Nitrate is reduced sequentially to NO_2^-, NH_2OH and then NH_4^+, which is incorporated into amino acids. The reduction of NO_3^- to NO_2^- is catalysed by NADH-nitrate reductase to an enzyme–coenzyme complex which is inhibited by very

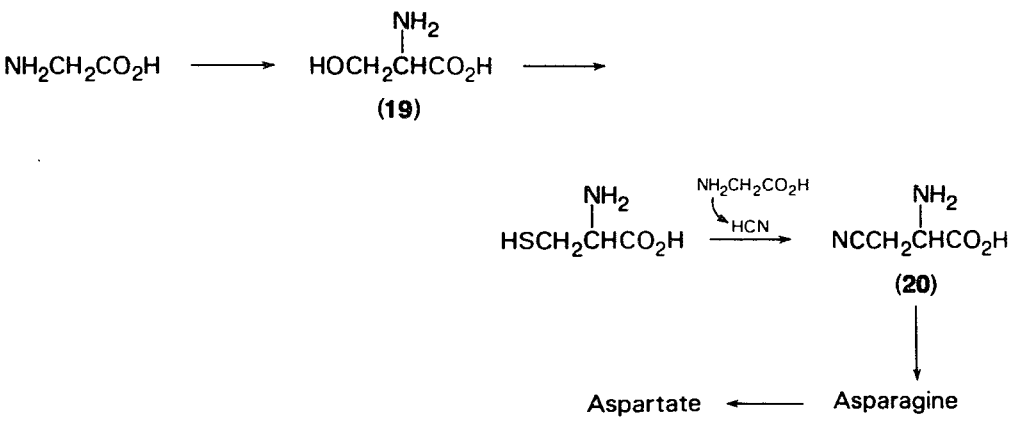


SCHEME 1

low concentrations of cyanide ($K_I \sim 10^{-10}$ M)[35]. It has been postulated that cyanide regulates the rate of nitrate reduction by its inhibitory effect on nitrate reductase[36,37]. The cyanide may be formed by the dehydrative decarboxylation of the oxime of glyoxylic acid (Scheme 1, pathway *iii*), the oxime being formed by the reaction of the hydroxylamine produced from nitrate with glyoxylic acid (**17**)[3]. This reaction pathway (*iii*) is very similar to pathways *i* and *ii* proposed for HCN biosynthesis in fungi and other microorganisms. The cyanide formed is consumed by its conversion to β-cyanoalanine[38] by a pathway outlined in Section V.B.3. The observation that *Chlorella vulgaris* extracts catalyse the formation of cyanide from the oxime of glyoxylic acid supports this postulate[39]. However, the formation of HCN by the action of *Chlorella vulgaris* extracts on D-histidine and other aromatic amino acids has also been reported[40] and this may also be an important pathway for cyanide formation.

3. *Amino acid synthesis from hydrogen cyanide*

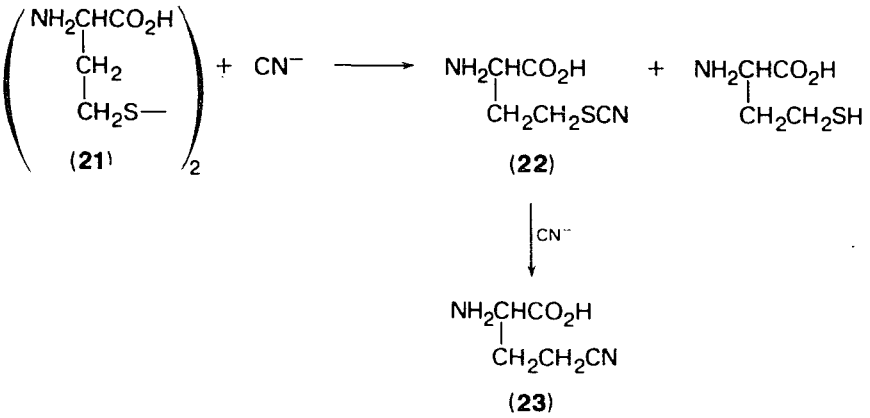
Some of the cyanide generated by microorganisms is metabolized by conversion to β-cyanoalanine (**20**). The metabolic pathway is similar to that observed for β-cyanoalanine synthesis in higher plants[1]. Glycine is the precursor to both cyanide and serine (**19**) in this biosynthetic pathway, as shown for cyanide by both single- and double-labelling studies[41a,b].



One strain of *C. violaceum* has the unique ability to synthesize γ-cyano-α-L-aminobutyric acid (**23**)[42]. An enzyme isolated from this strain catalyses the synthesis of **23** from homocystine (**21**) and cyanide. The first step is the nonenzymatic cleavage of the disulphide link with cyanide and the second is the enzymic displacement of the thiocyano group of γ-thiocyano-α-aminobutyric acid (**22**) with cyanide[43].

The formation of cyanide is stimulated by the addition of glycine to the growth media of *C. violaceum*[44] and *P. aeruginosa*[31,45,46]. The stimulation is reversed by chloramphenicol, an inhibitor of protein synthesis, if it is added before cyanogenesis begins[32,44]. Chloramphenicol also inhibits the formation of β-cyanoalanine and γ-cyano-α-L-aminobutyric acid in *C. violaceum*[44]. The enzymes which convert cyanide to the cyanoamino acids are apparently inhibited by cyanide. By inhibiting the synthesis of cyanide, chloramphenicol thereby inhibits the induction of the enzymes responsible for the synthesis of these cyanoamino acids.

Large amounts of cyanide (2–3 millimoles per litre)[34d,41] are produced by *C. violaceum*. Although some cyanide is utilized for amino acid synthesis, these metabolic



processes do not consume all the cyanide produced by microorganisms. The toxic properties of the cyanide is avoided in *C. violaceum*[44] and *P. aeruginosa*[40] by their switching to a cyanide-resistant respiratory system. This respiratory change has been shown to be in response to the presence of cyanide rather than some other environmental change. Postulates have been made concerning the nature of the cyanide-resistant system[29] but few experimental data have been obtained.

Some microorganisms which utilize cyanide have been isolated from environments with high cyanide concentrations. An actinomycete, probably of the genus *Nocardia*, has been isolated from a cyanide-acclimatized sludge[29]. *Bacillus pumilus* has been isolated from clay samples in which cyanogenic flax had been planted. This microorganism metabolized cyanide to carbon dioxide and ammonia. Other examples of the growth of microorganisms on cyanide and their utilization for the disposal of cyanide wastes are discussed in the review by Knowles[29].

VI. CYANIDE FROM THIOCYANATES

The cleavage of the thiocyano group of γ-thiocyanoaminobutyric acid (**22**) by rat liver extracts has been observed in the course of the investigation of the metabolism of **22** in *C. violaceum*[47]. The products of the cleavage are α-ketobutyric acid, ammonia and thiocyanate. The thiocyanate is efficiently cleaved to cyanide by a peroxidase, a reaction which is the reverse of the rhodanese-catalysed conversion of cyanide to thiocyanate[1]. The formation of cyanide is very efficient, as indicated by the observation that DL-**22** is more than half as lethal as cyanide in rats. In addition toxic cyanide levels have been observed in the blood of rats following administration of toxic amounts of **22**. Although the formation of cyanide from thiocyanate ion is a likely reaction pathway, the direct conversion of the thiocyano group in **22** to cyanide was not eliminated in these studies[48].

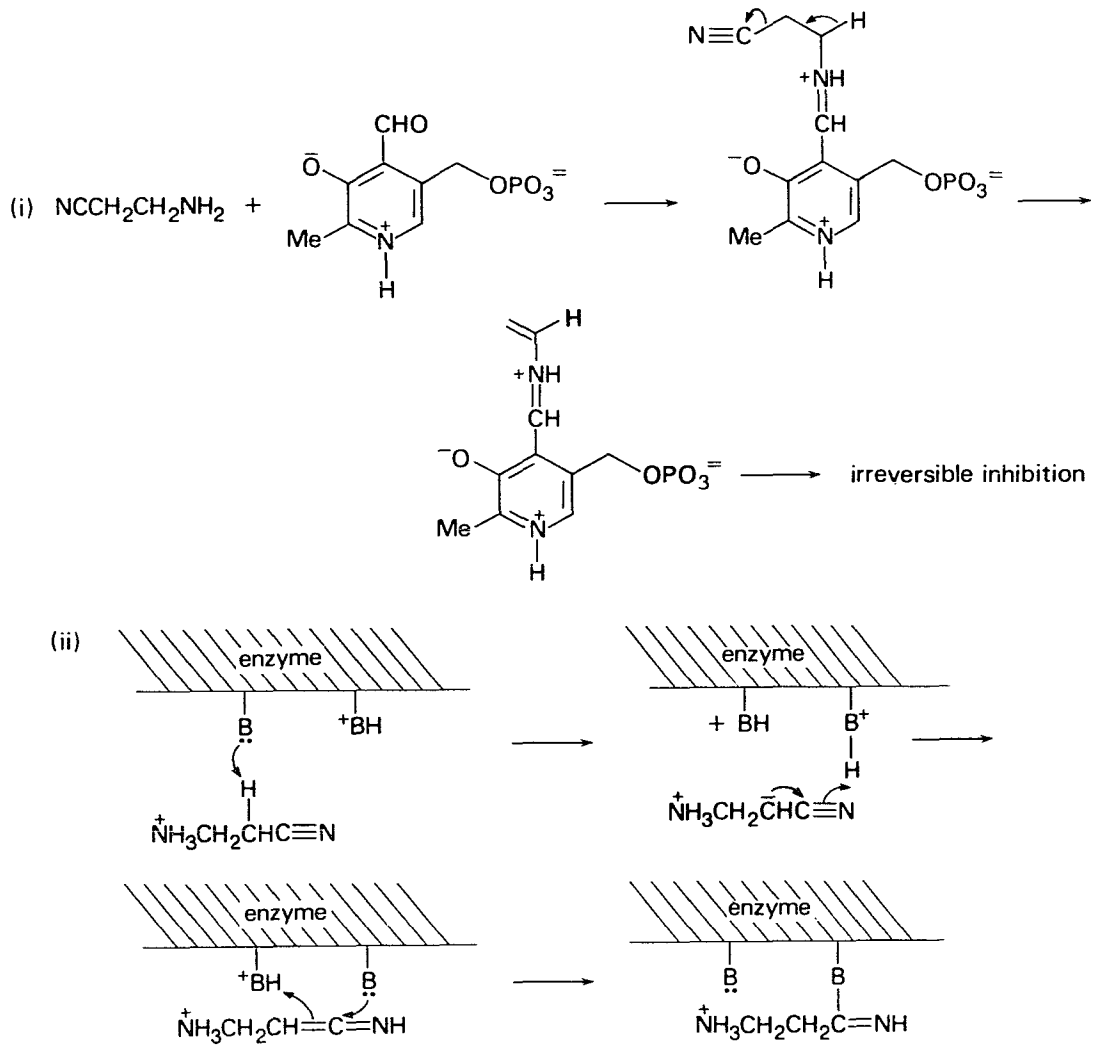
VII. LATHYROGENIC CYANO COMPOUNDS

Ingestion of certain species of the *Lathyrus* and *Vicia* plant family sometimes results in the nutritional disease, lathyrism. The symptoms of lathyrism include skeletal deformations and neurological disorders. The cyanoamino acids and other nitriles present in these plant families elicit some of these same biological effects in test animals[1]. Consequently analogues of these cyanoamino acids have been synthesized as part of an attempt to elucidate structure–activity relationships[49,50]. The biological properties of these compounds are outlined below.

A. β-Aminopropionitrile ($NH_2CH_2CH_2CN$)

The active principal constituent of *Lathrus odoratus* causes defective connective tissues in a variety of test animals. Collagen and elastin with decreased strength are formed, which results in abnormalities such as hernia, aortic aneurysms and displaced lenses[51]. The weakened collagen is due to diminished cross-links. A novel application of β-aminopropionitrile is as an anti-aging drug because it inhibits the maturation (cross-linking) of collagen[52].

The decreased aldehyde content of the lathyritic collagen indicates that β-aminopropionitrile inhibits lysine amino oxidase, the enzyme which catalyses the oxidation of the ε-amino group of lysine to the corresponding aldehyde[53]. Reaction of this aldehyde with other collagen residues results in the cross-linking which gives collagen its rigidity.



SCHEME 2

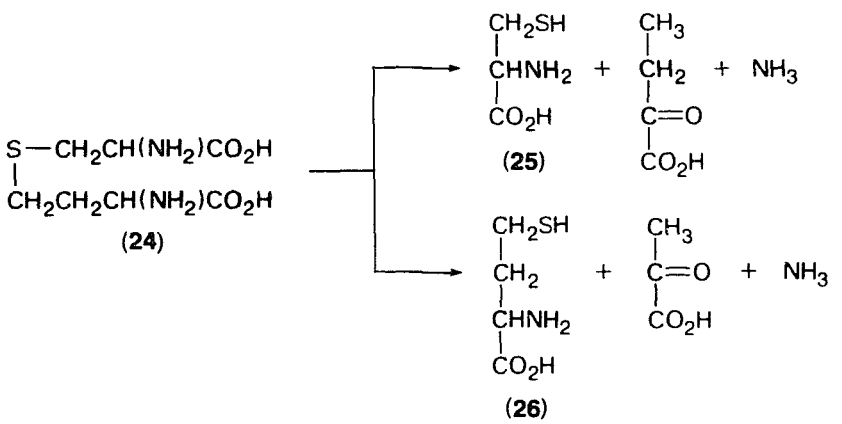
β-Aminopropionitrile is an irreversible inhibitor of lysine amino oxidase[54]. Two mechanisms have been proposed for this inhibition (Scheme 2, pathways *i* and *ii*). β-Elimination of hydrogen cyanide from the pyridoxal phosphate adduct of β-aminopropionitrile has been suggested as one mechanistic pathway (*i*)[55]. In an alternative proposal a covalent adduct is formed with the enzyme by reaction with the ketene imine form of the protonated amino-nitrile (pathway *ii*)[56].

α-Aminoacetonitrile, a potent lathrogenic agent, has been found to react with a plasma amine oxidase by pathway *ii* of Scheme 2[56]. It probably inactivates the lysine amino oxidase associated with collagen in the same way. Tryptophan synthetase, another enzyme which requires pyridoxal phosphate, is inhibited by α-cyanoglycine by the mechanism outlined by pathway *ii* in Scheme 2[57].

B. β-Cyanoalanine [$NCCH_2CH(NH_2)CO_2H$]

β-Cyanoalanine (and its γ-glutamyl derivative) occurs principally in *Vicia* plant species, but it is also produced by two strains of the microorganism *Chromobacterium*[51]. It is moderately toxic to rats (LD_{50} = 13.5 mg/kg) and chicks, while sublethal doses can cause convulsions[58]. Some of the β-cyanoalanine administered to rats is converted to γ-glutamyl-β-cyanoalanine and γ-glutamyl-β-cyanoalanylglycine, while the rest is excreted unchanged as the free amino acid[51].

β-Cyanoalanine inhibits several biochemical processes. It is a competitive inhibitor of rat and mammalian cystathionase, an enzyme which catalyses the conversion of **24** to cysteine **25**[47,59]. It also inhibits the formation of homocysteine **26** from **24**, a reaction catalysed by spinach β-cystathionase[60]. It is a competitive inhibitor of bacterial aspartate decarboxylase (k_I = 0.3 mM), an enzyme which catalyses the conversion of aspartic acid to alanine[61]. It is a much poorer inhibitor of glutamate decarboxylase[62a]. β-Cyanoalanine acts as though it were a suicide inactivator of alanine aminotransferase except that the covalent bonding to the enzyme is reversible[62b]. β-Cyanoalanine is hydrolysed to aspartic acid by asparaginase, an enzyme from *E. coli* and guinea pig serum, which catalyses the hydrolysis of asparagine, but is a competitive inhibitor of glutaminase[51,62c].



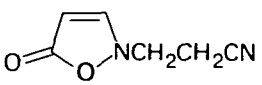
The known biological effects of γ-cyano-α-aminobutyric acid are comparable to those of β-cyanoalanine. It causes convulsions when administered to rats and inhibits glutaminase.

C. γ-Cyano-γ-aminobutyric Acid [$NCCH(NH_2)CH_2CH_2CO_2H$]

The reported formation of this compound as a product of cyanide assimilation in an unidentified psychrophylic basidiomycete[63] has been questioned[49]. The compound is an effective competitive inhibitor of glutamate decarboxylase (K_I = 0.014 mM), an enzyme found chiefly in nervous tissue. Presumably the aminonitrile competes with glutamate in binding with the pyridoxal–enzyme complex. When administered to chicks it causes convulsions and depression. Other nitriles including β-cyano-β-alanine, α-aminoacetonitrile and β-cyanopropionic acid are less effective inhibitors of glutamate decarboxylase[62a]. *n*-Butyronitrile is a noncompetitive inhibitor of glutamate decarboxylase and it causes long-acting sedation and prostation in chicks[62a].

D. 2(2-Cyanoethyl)-3-isoxazolin-5-one

A series of isoxazolin-5-ones were isolated from *L. odoratus* including the nitrile derivative 2(2-cyanoethyl)-3-isoxazolin-5-one (**27**)[64]. Since **27** is a derivative of β-aminopropionitrile, a known lathyrogenic compound, its biological properties were evaluated in weanling rats[65]. Growth retardation and skeletal abnormalities were somewhat less severe than those observed with β-aminopropionitrile. The biological effects observed are probably due to the metabolism of **27** to β-aminopropionitrile, since significant amounts of the latter were found in the urine. This conclusion is consistent with other observations which indicate that a free primary amino group or a similar basic function is a structural requirement for lathyrogenic activity[51]. Consequently, **27** would not be expected to be directly responsible for the lathyrogenic effects that were observed.



(27)

VIII. DETOXIFICATION OF CYANIDE AND THE METABOLISM OF NITRILES

A. Cyanide Toxicity

Cyanide inhibits many cellular processes but its mammalian toxicity is due principally to its inhibition of the cytochrome oxidase system. The cyanide binds to the iron of the cytochromes and inhibits the electron transfer processes[1]. This inhibitory effect can be reversed in man and other mammals by placing the subject in a pressure chamber containing 2–3 atmospheres of oxygen[66,67]. The increased oxygen concentration in the bloodstream due to the increased pressure may be sufficient to displace the cyanide from the cytochrome oxidase.

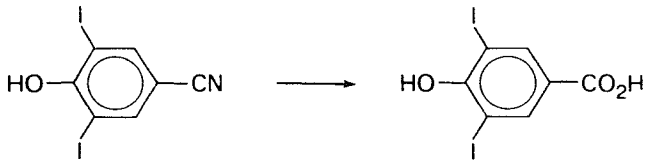
B. Nitrile Metabolism

1. Aliphatic nitriles

Aliphatic nitriles such as acetonitrile, propionitrile and succinonitrile can serve as the sole source of carbon and nitrogen for the bacterium *Norcardia rhodochrous*[68]. Other nitriles have been metabolized by this species but would only serve as a source of the nitrogen required for growth. Acetamide is the initial product formed in the degradation of acetonitrile by *Norcardia*[68] and *Pseudomonas*[69] species. The acetamide is then converted to acetic acid which is incorporated into the intermediates in the tricarboxylic acid pathway.

2. Aromatic nitriles

The observation that the nitrile group in herbicide ioxynil (**28**) is hydrolysed to the acid in soil samples prompted an investigation of the metabolism of aromatic nitriles[70,71]. It was found that eight bacterial species and two fungi in soil degrade **28** to the acid **29**[71]. A detailed investigation of one of these fungi, *Fusarium solani*, indicated



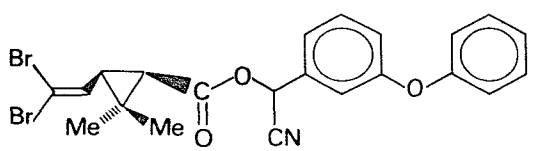
(**28**) (**29**)

that it would grow on benzonitrile as its sole carbon source. The nitrilase enzyme present in this fungus was isolated and it was found that it would catalyse the hydrolysis of a wide variety of aromatic nitriles to the corresponding acids[70]. Of particular interest was the failure to detect the corresponding amides as reaction intermediates. In fact benzamide is not a substrate for this enzyme suggesting that benzonitrile is converted to benzoic acid in one step.

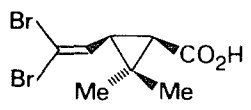
3. Multifunctional nitriles

a. Decamethrin. This compound (**30**), a potent synthetic pyrethroid insecticide, contains a cyano group. The metabolism and environmental degradation of this compound has been studied extensively to evaluate its toxicity to mammals and the environmental effects due to its use as an insecticide.

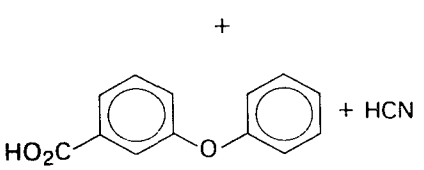
Decamethrin is cleaved oxidatively at the ester grouping in rats[72] and mice[73] and the cyano group is liberated as HCN in the process. After 24 hours 60% of the cyanide present in the insecticide can be detected as SCN^-. Small amounts of 2-iminothiazolidine-4-carboxylic acid (**32**) are also formed in the rats by reaction of cyanide with cystine[1]. Compound **32** is not formed in mice[73].



(**30**)

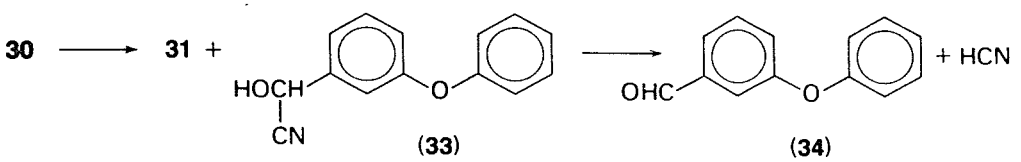


(**31**)



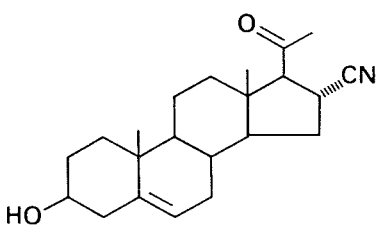
(**32**)

Decamethrin is hydrolysed on the leaves of cotton plants to **31** and the cyanohydrin **33**[74]. The cyanohydrin **33** may be stabilized by conversion to a glucoside acetal or else it spontaneously decomposes to HCN and the aldehyde **34**.



(33) (34)

b. Cyano steroids. Certain cyano steroids have been found to protect rats from the effects of toxic agents[75]. Those cyano steroids which exhibit the greatest protective effect have nitrile functions in the 16α or 2α positions. Little or no activity has been observed with the corresponding β isomer or with nitrile substituents at other positions on the steriod skeleton. The protective action of these compounds is not due to their rapid metabolism to their corresponding amides or acids because these derivatives are devoid of activity. Pregnenolone-16-α-carbonitrile (**35**) exhibits the most extensive protection against a variety of toxicants and it has been used extensively in more recent studies.



(35)

The protective effect of **35** is due to its induction of the cytochrome P-450 monooxygenase system which catalyses the oxidation of foreign substances[76]. The oxidized compounds have increased water solubility and are more readily excreted. Other chemical agents also induce these oxidase enzymes (e.g. phenobarbital and 3-methylcholanthrene) but the cytochrome P-450 induced by (**35**) is appreciably different from the P-450 induced by these other compounds[77–79].

IX. SPECULATIONS ON THE ORIGINS OF CYANIDE BIOCHEMISTRY

For many years the observation of nitriles in biochemical systems was limited to the cyanogenic glycosides. It was assumed that these cyano derivatives resulted from a quirk of plant biochemistry. However, numerous organisms which produce and degrade cyanide and cyano compounds have been found in the course of a direct search for such species. Cyanide and cyano compounds are found abundantly in the interstellar media[80] and are produced in large amounts in experiments which simulate conditions on the primitive earth[81]. Cyanide has also been shown to be a sole source of purines, pyrimidines and amino acids when it condenses under reaction conditions which may have existed on the primitive earth[81]. The conversion of cyanide to amino acids is just the reverse of the synthesis of cyanide from glycine, a common reaction in cyanogenic bacteria and fungi. If cyanide had a central role in the origins of life it is likely that it was also involved in the biochemistry of primitive life. If this is correct then the enzymes involved in the biological formation and degradation of nitriles may represent biochemical fossils of these primitive enzymes. The detection of similar

enzymes in the primitive *Archebacteria*[82] which utilize cyanide or simple nitriles as substrates would provide stronger support for the hypothesis that these are descendents of some of the first enzymes formed on the earth some 4.5 billion years ago.

X. ACKNOWLEDGEMENTS

I wish to thank Professors P. Castric, E. E. Conn and C. Ressler for commenting on a preliminary draft of this chapter. My research discussed in this review is supported by the National Aeronautics and Space Administration and the National Science Foundation.

XI. REFERENCES

1. J. P. Ferris, *The Chemistry of the Cyano Group* (Ed. Z. Rappoport), John Wiley and Sons, London, 1970, pp. 717–742.
2. E. E. Conn, *Naturwissenschaften*, **66**, 28 (1979).
3. E. E. Conn, *Biochem. Soc. Symp.*, **38**, 277 (1974); E. E. Conn. *Ann. Rev. Plant Physiol.*, **31**, 433 (1980); E. E. Conn, *Intern. Rev. Biochem.*, **27**, 21 (1979).
4. D. S. Seigler, *Phytochemistry*, **14**, 9 (1975).
5. E. E. Conn in *Toxicants Occurring Naturally in Foods*, National Academy of Science, U.S., Washington, D.C., 1973, pp. 299–308; R. D. Montgomery, *Toxic Constituents of Plant Foodstuffs* (Ed. I. E. Liener), Academic Press, New York, 1969, pp. 143–157.
6. J. H. Carter, M. A. McLafferty and P. Goldman, *Biochem. Pharmacol.*, **29**, 301 (1980).
7. B. L. Moller and E. E. Conn, *J. Biol. Chem.*, **245**, 8575 (1979).
8. B. A. Tapper and G. W. Butler, *Phytochemistry*, **11**, 1041 (1972).
9. K. J. F. Farnden, M. A. Rosen and D. R. Liljegren, *Phytochemistry* , **12**, 2673 (1973).
10. M. Shimada and E. E. Conn, *Arch. Biochem. Biophys.*, **180**, 199 (1977).
11. H. Zilg, B. A. Tapper and E. E. Conn, *J. Biol. Chem.*, **247**, 2384 (1972).
12. K. Hahlbrock and E. E. Conn, *J. Biol. Chem.*, **245**, 917 (1970).
13. P. F. Reay and E. E. Conn, *J. Biol. Chem.*, **249**, 5826 (1974).
14. T. Cairns, J. E. Froberg, S. Gonzales, W. S. Langham, J. J. Stamp, J. K. Howle and D. T. Sawyer, *Anal. Chem.*, **50**, 317 (1978).
15. G. M. Rosen and R. T. Shorr, *Ann. Intern. Med.*, **90**, 418 (1979).
16. J. D. Khandekar and H. Edelman, *J. Amer. Med. Assn.*, **242**, 169 (1979).
17. D. O. Clegg, E. E. Conn and D. H. Janzen, *Nature (London)*, **278**, 343 (1979).
18. H. A. Stafford, *Phytochemistry*, **8**, 743 (1969).
19. R. C. Thatcher and T. L. Weaver, *Science*, **192**, 1234 (1976).
20. W. Fry and D. Munch, *Proc. Ann. Phytopathol. Soc.*, **1**, 34 (1974).
21. H. E. Eisner, W. F. Wood and T. Eisner, *Psyche*, **82**, 20 (1975).
22. H. T. Jones, U. E. Conner, J. Meinwald, H. E. Eisner and T. Eisner, *J. Chem. Ecol.*, **2**, 421 (1976).
23. W. E. Conner, T. H. Jones, T. Eisner and J. Meinwald, *Experientia*, **33**, 206 (1977).
24. D. S. Seigler, *Phytochemistry*, **14**, 9 (1975).
25. D. S. Seigler, F. Seaman and T. J. Mabry, *Phytochemistry*, **10**, 485 (1971).
26. K. L. Mikolajczak, D. S. Seigler, C. R. Smith, Jr., F. A. Wolff and R. B. Bates, *Lipids*, **4**, 617 (1969).
27. M. K. Kundu, *Fette. Seifen. Anstrichm.*, **75**, 370 (1970).
28. D. S. Seigler, *Phytochemistry*, **13**, 841 (1974).
29. C. J. Knowles, *Bacteriological Rev.*, **40**, 652 (1976).
30. P. A. Castric, *Can. J. Microbiol.*, **21**, 613 (1975).
31. P. A. Castric, *J. Bacteriol.*, **130**, 826 (1977).
32. R. Meganathan and P. A. Castric, *Arch. Microbiol.*, **114**, 51 (1977).
33. F. Wissing, *J. Bacteriol.*, **117**, 1289 (1974).
34. (a) F. Wissing, *J. Bacteriol.*, **121**, 695 (1975).

(b) A. W. Bunch and C. J. Knowles, *J. Gen. Microbiol.*, **116**, 9 (1980).
(c) E. W. B. Ward, A. N. Starratt and J. R. Robinson, *Can. J. Bot.*, **55**, 2065 (1977).
(d) P. A. Collins, P. B. Rodgers and C. J. Knowles, *J. Gen. Microbiol.*, **117**, 73 (1980).
35. G. H. Lorimer, H.-S. Gewitz, W. Völker, L. P. Solomonson and B. Vennesland, *J. Biol. Chem.*, **249**, 6074 (1974).
36. L. P. Solomonson, *Biochim. Biophys. Acta*, **334**, 297 (1974).
37. L. P. Solomonson and A. M. Spehar, *Nature (London)*, **265**, 373 (1977).
38. L. Fowden and E. A. Bell, *Nature (London)*, **206**, 110 (1965).
39. L. P. Solomonson and A. M. Spehar, *J. Biol. Chem.*, **254**, 2176 (1979).
40. E. F. Pistorius, H.-S. Gewitz, H. Voss and B. Vennesland, *Biochim. Biophys. Acta*, **481**, 384 (1977).
41. (a) M. M. Brysk, W. A. Corpe and L. V. Hankes, *J. Bacteriol.*, **97**, 322 (1969).
(b) M. M. Brysk and C. Lauinger and C. Ressler, *Biochim. Biophys. Acta*, **184**, 583 (1969).
42. M. M. Brysk and C. Ressler, *J. Biol. Chem.*, **245**, 1156 (1970).
43. C. Ressler, O. Abe, Y. Kondo, B. Cottrell and K. Abe, *Biochemistry*, **12**, 5369 (1973).
44. P. B. Rodgers and C. J. Knowles, *J. Gen. Microbiol.*, **108**, 261 (1978).
45. P. A. Castric, R. F. Ebert and K. F. Castric, *Current Microbiol.*, **2**, 287 (1979).
46. C. A. Kralik and P. A. Castric, *Current Microbiol.*, **3**, 71 (1979).
47. K. Abe and C. Ressler, *Biochem. Pharmacol.*, **24**, 2167 (1975).
48. H. Ohkawa and J. E. Casida, *Biochem. Pharmacol.*, **20**, 1709 (1971).
49. C. Ressler, G. R. Nagarajan, M. Kirisawa and D. U. Kashelikar, *J. Org. Chem.*, **36**, 3960 (1971).
50. N. Banerjee and C. Ressler, *Int. J. Peptide Protein Res.*, **14**, 234 (1979).
51. C. Ressler, *Recent Advan. Phytochem.*, **9**, 151 (1975).
52. F. S. LaBella, *Gerontologist*, **8**, 13 (1968).
53. R. C. Page and E. P. Benditt, *Proc. Soc. Exper. Biol. Med.*, **124**, 459 (1967).
54. A. S. Narayanan, R. C. Siegel and G. R. Martin, *Biochim. Biophys. Res. Commun.*, **46**, 745 (1972).
55. R. C. Rando, *Acc. Chem. Res.*, **8**, 281 (1975).
56. A. L. Maycock, R. H. Suva and R. H. Abeles, *J. Amer. Chem. Soc.*, **97**, 5613 (1975).
57. E. W. Miles, *Biochem. Biophys. Res. Commun.*, **64**, 248 (1975).
58. C. Ressler, J. Nelson and M. Pfeffer, *Biochem. Pharmacol.*, **16**, 2309 (1967).
59. M. Pfeffer and C. Ressler, *Biochem. Pharmacol.*, **16**, 2299 (1967).
60. J. Giovanelli and S. H. Mudd, *Biochim. Biophys. Acta*, **227**, 654 (1971).
61. S. S. Tate and A. Meister, *Biochemistry*, **8**, 1660 (1969).
62. (a) C. Ressler and T. Koga, *Biochim. Biophys. Acta*, **242**, 473 (1971).
(b) T. A. Alston, D. J. T. Porter, L. Mela and H. J. Bright, *Biochem. Biophys. Res. Commun.*, **92**, 299 (1980).
(c) C. Lauinger and C. Ressler, *Biochim. Biophys. Acta*, **198**, 316 (1970).
63. G. A. Strobel, *J. Biol. Chem.*, **242**, 3265 (1967).
64. L. Van Rompuy, F. Lambein, R. DeGussen and R. Van Parijs, *Biochim. Biophys. Res. Commun.*, **56**, 199 (1974).
65. L. Van Rompuy, F. Lambein, R. Van Parijs and C. Ressler, *Experientia*, **30**, 1379 (1974).
66. W. G. Trapp, *Can. Med. Ass. J.*, **102**, 517 (1970).
67. W. G. Skene, J. N. Norman and G. S. Smith, *Proceedings of* 3rd *International Congress on hyperbaric Oxygen* (Eds. I. Brown and B. Cox), National Academy of Sciences, National Research Council, Washington, D.C., 1966, pp. 705–710.
68. M. J. DiGeronimo and A. D. Antoine, *Appl. Environ. Microbiol.*, **31**, 900 (1976).
69. J. L. Firmin and D. O. Gray, *Biochem. J.*, **158**, 223 (1976).
70. D. B. Harper, *Biochem. J.*, **167**, 685 (1977).
71. J. C. Hsu and D. Camper, *Can. J. Microbiol.*, **22**, 537 (1976).
72. L. O. Ruzo, T. Unai and J. E. Casida, *J. Agric. Food Chem.*, **26**, 918 (1978).
73. L. O. Ruzo, J. L. Engel and J. Casida, *J. Agric. Food Chem.*, **26**, 725 (1979).
74. L. O. Ruzo and J. E. Casida, *J. Agric. Food Chem.*, **27**, 572 (1979).
75. H. Selye, *J. Pharm. Sci.*, **60**, 1 (1971).
76. B. Solymoss, J. Werringloer and S. Toth, *Steroids*, **17**, 427 (1971).
77. A. Y. H. Lu, A. Somogyi, S. West, R. Kuntzman and A. H. Conney, *Arch. Biochem. Biophys.*, **152**, 457 (1972).

78. M. F. Angus, C. Hoch-Ligeti, J. C. Arcos and A. H. Conney, *J. Natl. Cancer Inst.*, **61**, 441 (1978).
79. N. A. Elshourbagy and P. S. Guzelian, *J. Biol. Chem.*, **255**, 1279 (1980).
80. A. P. C. Mann and D. A. Williams, *Nature (London)*, **233**, 721 (1980).
81. J. P. Ferris, P. C. Joshi, E. H. Edelson and J. G. Lawless, *J. Mol. Evol.*, **11**, 293 (1978).
82. C. R. Woese, L. J. Magrum and G. E. Fox, *J. Mol. Evol.*, **11**, 245 (1978).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 10

Free-radical reactions involving the C≡C group

Y. AMIEL
The Weizmann Institute of Science, Rehovot, Israel

I. INTRODUCTION

The chemistry of free-radical reactions involving carbon–carbon multiple bonds has been extensively treated in numerous textbooks[1–8]. Most attention has been given to reactions involving the double bond and comparatively much less to those involving the triple-bond function; nonetheless, several review articles on free-radical additions to carbon–carbon multiple bonds have presented extensive tabular surveys, which have included C≡C group compounds[3,9,10]. Some reviewers have written short separate sections for free-radical reactions involving acetylenes[11,12]. The only complete chapter in the literature on this subject was written by Julia in 1969[13].

The present chapter excludes some aspects of free-radical acetylene chemistry which have already been discussed in chapters in preceding parts of this series; these include fragmentations, reactions involving rearrangement, cycloadditions and cyclizations, photochemistry of the triple bond, electron-transfer processes carried out by electrochemical methods and organometallic free-radical reactions involving the C≡C group.

The specific free-radical reactions dealt with in this chapter have been arranged according to the atoms carrying the unpaired electron.

II. GENERAL BACKGROUND

A. Mechanism of Free-radical Addition

Free-radical reactions involving the C≡C group resemble very much those of the C=C group[14]. Such reactions are initiated (*a*) via irradiation or thermolysis, in the absence of free-radical initiators, (*b*) in the presence of thermally labile free-radical initiators (peroxides, azo compounds, etc.), or by one-electron transfer processes, either (*c*) electrochemically or (*d*) via a redox system involving metals or ions of various transition elements (M = Cu, Fe, Ti, etc.), which undergo oxidation to higher valence states.

Free-radical initiations:

(*a*) by irradiation or thermolysis: $RX \xrightarrow{h\nu \text{ or } \Delta} R\cdot + X\cdot$

(*b*) by a free-radical initiator: $In\cdot + RX \longrightarrow InX + R\cdot$

(*c*) by an electrode process, e.g.: $RCO_2^- \xrightarrow[-e]{\text{anode}} RCO_2\cdot \longrightarrow R\cdot + CO_2$

(*d*) by a redox-transfer process: $M^{I}X_n + RX \longrightarrow M^{II}X_{n+1} + R\cdot$

All free-radical reactions involving multiple bonds are addition reactions operating either inter- or intra-molecularly by changing one unsaturated π bond into a saturated σ bond and simultaneously forming a secondary free-radical intermediate.

Free-radical addition reaction mechanisms involve most frequently free-radical chains or redox-transfer cycles, as shown in the following two propagation steps:

Free-radical attack: $R\cdot + -C\equiv C- \longrightarrow -CR=\dot{C}-$

Product-forming step, via:

a regular chain transfer: $-CR=\dot{C}- + RX \longrightarrow -CR=CX- + R\cdot$

or a competitive chain transfer: $-CR=\dot{C}- + YX \longrightarrow -CR=CX- + Y\cdot$

or a redox process: $-CR=\dot{C}- + M^{II}X_{n+1} \longrightarrow -CR=CX- + M^{I}X_n$

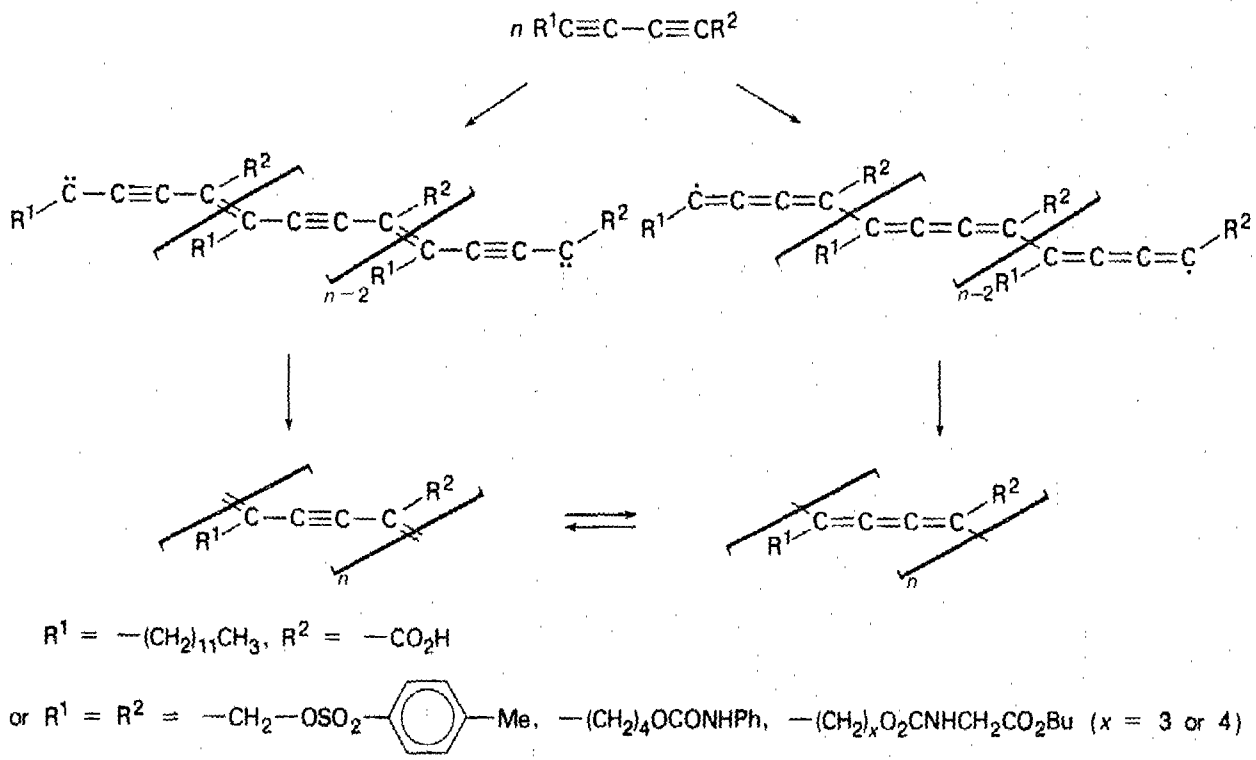
In the latter step, the reactive transition metal ion M^{II} is reduced by the free-radical intermediate to a lower valence state; $M^{I}X_n$ is thus capable of generating, in a conjugate process, a successive new free radical (*d*).

Addend molecules, which are considered to be good transfer agents, have usually low bond dissociation energies. The rate constants of such transfer steps are large and their reactions are fast, therefore one free radical arising from an initiation may lead to very long kinetic chains resulting in the formation of many adduct molecules. On the other hand, poor transfer agents enable radical intermediates to add competitively to successive unsaturated molecules, thus giving rise, by consecutive processes, to telomer formation (equation 1). Such highly conjugated polyene chains can readily

$$-CR=\dot{C}- + n(-C\equiv C-) \longrightarrow -CR=\underset{|}{C}+\underset{|}{C}=\underset{|}{C}+_{n-1}\underset{|}{C}=\dot{C}- \xrightarrow{RX} -CR=\underset{|}{C}+\underset{|}{C}=\underset{|}{C}+_{n}X + R\cdot \quad (1)$$

cross-link in a free-radical way to form generally undesirably intractable polymers. However, there are particular instances in which cross-linking of C≡C bonds is desired, as for example in the curing process, where subunits such as polyimides are linked to yield corresponding cross-linked resins. Acetylene-terminated monomers form in this way high-strength, high-temperature polymers, used for moulded parts, coatings, adhesive, composites and laminates[15].

The solid-state polymerization of crystalline disubstituted α-diacetylenes[16–19], initiated by heat, light or high-energy radiation, proceeds via a 1,4-*anti*-addition reaction. Wegner and his coworkers have shown[16] that carbenes are involved in the chain-propagation process. However, thermodynamic and kinetic arguments have suggested a free-radical mechanism involving the initial generation of butatriene biradicals[18,19]; ESR studies have indeed confirmed that the free-radical mechanism is operative under certain conditions, as for example, at low radiation dosage in the X-ray-initiated solid-state polymerization[20]. An acetylene–butatriene transformation has been invoked to explain the thermochromic phase changes observed for many polydiacetylenes[21,22] (Scheme 1).



$R^1 = -(CH_2)_{11}CH_3$, $R^2 = -CO_2H$

or $R^1 = R^2 =$ Me, $-(CH_2)_4OCONHPh$, $-(CH_2)_xO_2CNHCH_2CO_2Bu$ (x = 3 or 4)

SCHEME 1

B. Regioselectivity

Terminal acetylenes, like terminal olefins, undergoing Kharasch-type reactions are attacked by free radicals at their terminal carbon atom, which is least sterically hindered, thus generating the more stable tertiary radical intermediate (equation 2); subsequent chain-transfer atom abstraction leads to the formation of non-Markownikoff orientation products (equation 3). Very little is known about the

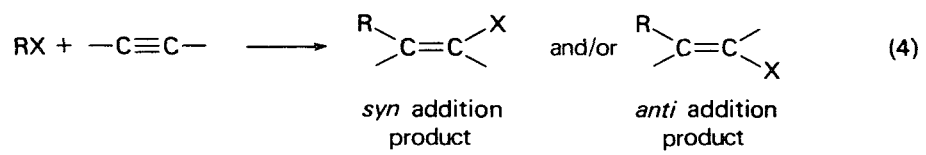
$$X\cdot + HC{\equiv}C- \longrightarrow XCH{=}\dot{C}- \quad (2)$$

$$XCH{=}\dot{C}- + HX \longrightarrow XCH{=}CH- + X\cdot \quad (3)$$

regioselectivity of free-radical additions to internal acetylenes; apparently, steric hindrance and relative stability of radical intermediates, and quite often inductive effects exhibited by neighbouring groups, are among the governing factors in directing the free-radical attack.

C. Stereochemical Course of Addition

The course of addition processes has been an intriguing subject ever since stereochemistry was recognized. Many ionic as well as free-radical additions across multiple bonds have been noted to proceed predominantly via an *anti* stereochemical course[23]. The reverse process, namely *anti* elimination, also generally occurs more easily than *syn* elimination[24]. Evidence on the stereochemical course of addition reactions is usually based on the possibility of obtaining distinguishable adducts having opposite configurations. The stereochemistry of free-radical additions to olefins, particularly cyclic olefinic systems, has been thoroughly studied[25]. In the acyclic series, only olefins yielding chiral products can furnish stereochemically significant information. Many free-radical additions to olefins are not stereospecific, being reversible, thus giving rise to *cis–trans* isomerization products. This complication does not occur with cyclic olefins, and this is the main reason why such substrates have been favoured for the study of the stereochemical course of the addition process. On the other hand, reactions of double bonds of rigid cyclic systems are often affected by steric factors. Such interfering interactions are not encountered in additions across acyclic, nonhindered, triple bonds. Moreover, the resulting vinyl radical intermediates are much more reactive species than the corresponding alkyl radicals. The formed double bonds of substituted vinylic radical intermediates do not invert readily, particularly at low temperatures; hence the stereochemical course of the addition process can easily be determined. Fragments of homolysed molecules, such as RX, may add by either a *syn* or *anti* process to form two geometrical isomers (equation 4).

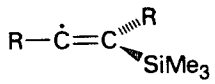


syn addition product — *anti* addition product (4)

Free-radical additions are stepwise reactions. In the first step of the propagation, as shown earlier, free radicals having unpaired electron centres attack the triply bonded carbon perpendicularly to the acetylenic cylindrically symmetric bond to form an electron-paired σ linkage by pulling the required electron out of the acetylenic π orbital system; it has been assumed, that synchronously to the addition process, the remaining odd-electron orbital, which is situated at the adjacent carbon, is being

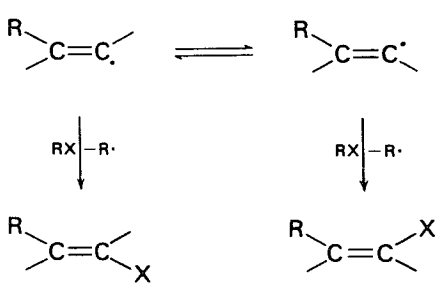
imposed to accomodate a position opposite to the direction of the attacking free radical due to stereoelectronic requirements. The resulting vinyl radical intermediate adopts in most cases the bent structure **1**. The only examples of vinyl radicals having a linear geometrical structure are the very severely crowded radicals with bulky substituents (*t*-Bu or $SiMe_3$) at the β carbon, e.g. **2**[26]. By absorbing the energy, vinyl

(1)

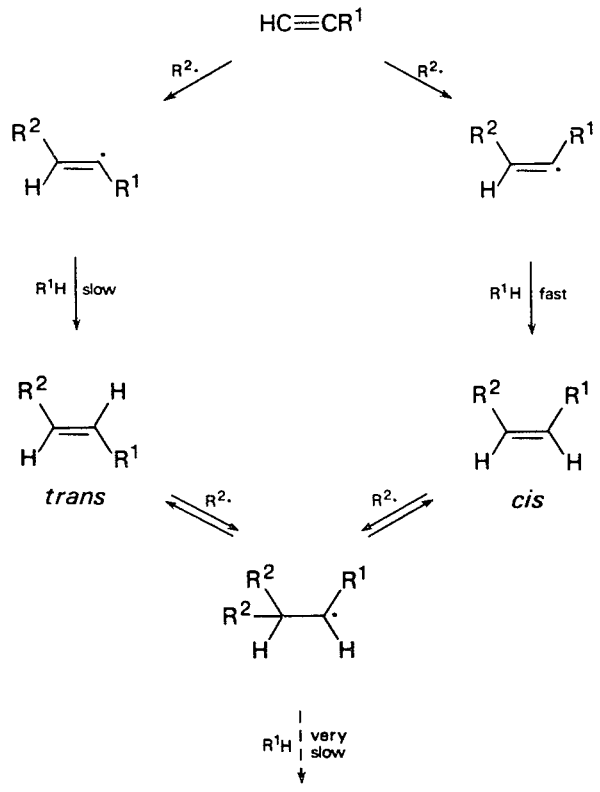


(2)

radical intermediates can undergo partial inversion of configuration to yield after the chain-transfer step mixtures of *syn* and *anti* addition products (Scheme 2). If the chain-transfer step is much faster than inversion, kinetically controlled *anti* addition products are formed; but if the chain transfer is not as rapid as inversion, equilibration can be reached provided that inversion is energetically feasible and there are no steric obstacles. In such cases the initial configuration of the vinyl radical intermediate has no relevance to the configuration of the formed adduct. Steric effects have a dominant role in determining which configuration would require less free energy in the transition state. Polar and solvent interactions operating in the environment may have a contributing effect on this process as well as on the subsequent chain-transfer product-forming step. Chain-transfer agents may interact stereoselectively with either *cis* or *trans* vinyl radical intermediates by different rates, thus preferring less hindered radical centres. The predominance of the *anti* addition process, which prevails also in many ionic-type reactions, had already been observed by Michael in the last century, and could perhaps also be explained by disregarding the presumably stereoelectronic factors mentioned above. In the absence of directing factors due to steric hindrance, or other stereoelectronic effects, both *cis* and *trans* radical intermediates can equally be formed as a result of a nonselective free-radical attack on the triple bond. The often encountered preferentially *anti* addition product, which is in many instances the thermodynamically less stable stereoisomer, could conceivably arise only as a result of *trans* vinyl radicals undergoing isomerization via an equilibration process to the configurationally more favourable *cis* isomers, provided



SCHEME 2



SCHEME 3

that postisomerization has been eliminated. The stereoselectivity has been found to be strongly dependent on the molar ratio of the reactants thus minimizing or even eliminating postisomerization. It has therefore been suggested that the predominant formation of *anti* addition products is a result of the preferable steric interactions taking place in the chain-transfer product-forming step, as shown by the mechanism in Scheme 3[27–35]. However, the fact that most free-radical additions result in the formation of predominantly *cis* adducts, particularly at low temperatures, as will be shown in the following sections, seems to support the validity of the *anti* rule.

The interconversion of the stereoisomeric vinyl radical intermediates is an energy-demanding process. Inductive effects of substituents, apart from their size giving rise to steric effects, may also influence the inversion ability. Electron-withdrawing substituents may enhance considerably the configurational stability of the initially formed vinyl radicals, thus enabling the preferential formation of 1:1 *anti* addition products, even at high reaction temperatures. Electron-withdrawing substituents also deactivate the resulting olefinic bond by lowering the electron density of that bond, thus preventing diadduct formation.

D. The Relative Reactivity of C≡C and C=C Groups Towards Free Radicals

In general, acetylenes are less reactive than olefins towards electrophiles and free radicals. On the other hand, acetylenes are generally more reactive than olefins towards nucleophiles[36].

The fact that acetylenic bonds are energetically weaker than olefinic bonds does not explain why reactions involving triple bonds often require higher activation energy than those involving double bonds, although reactions of acetylenic bonds have a higher entropy of activation, thus being capable of offsetting more exothermic heat of reaction than expected in analogous reactions involving olefinic double bonds.

Classifying the C≡C group as being more unsaturated than the C= C group is also misleading, as shown by comparison of the electron density of these bonds and their nature. While the two olefinic carbon atoms, $\diagdown C{=}C \diagup$, are surrounded by 12 bonding electrons, the acetylenic carbon atoms, —C≡C—, are surrounded by 10 bonding electrons, and are therefore comparatively more electron-deficient. Moreover, the sp-hybridized orbitals of the acetylenic bond exhibit a more pronounced s character than the sp^2-hybridized orbitals of the olefinic bond. Hence, the π electrons of the triple bond do not tend to polarize as easily as those of the double bond; they are more tightly bound in the shorter acetylenic carbon–carbon bond and consequently it is generally much easier for electrophiles, as well as for free radicals, to pull electrons out from an olefinic bond than from a comparable acetylenic bond which is more electrophilic in character. Due to their electrophilic character, acetylenes are more reactive than olefins towards nucleophiles, and the resulting vinyl carbanions are also more stable than saturated carbanionic intermediates, since the electron pair in the former occupies an orbital, with higher s-character compared with the latter. On the other hand, saturated carbon-centred radicals are considerably more stable than the corresponding vinyl radicals, as are the saturated carbonium intermediates which are formed by addition of electrophiles to C=C bonds.

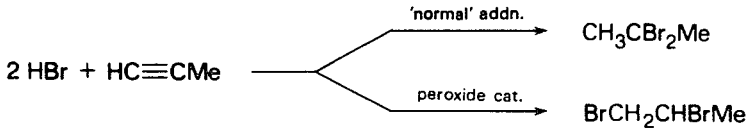
It seems that because of its electrophilic character, the C≡C bond undergoes catalytic hydrogenation much faster than the C=C bond by being adsorbed more strongly on the electron-rich catalyst surface.

The higher reactivity of the C=C compared to the C≡C bond toward free radicals has recently been examined in terms of *ab initio* molecular orbital calculations on the transition state and barrier height for the free-radical addition process, thus involving various types of intermolecular interactions and intramolecular deformation energies. In the conclusion of this publication it was stated: 'clearly, more extensive studies together with kinetic treatments are needed to understand reactivity differences between alkenes and alkynes toward nucleophiles, electrophiles, and free radicals from a unified point of view'[37].

III. ADDITION OF HALIDE-CENTRED FREE RADICALS

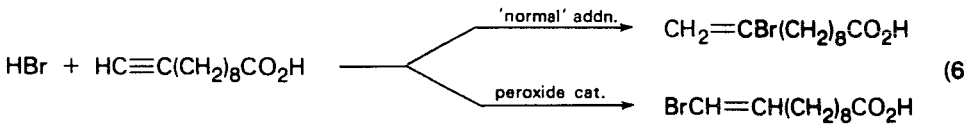
A. Hydrogen Halides

In October 1935, two reports[39,40] were independently submitted for publication on the directive peroxide effect on the addition of hydrogen bromide to terminal acetylenes as being opposite to that carried out under peroxide-free conditions. These results were analogous to those observed two years earlier by Kharasch and Mayo in the olefin series[38]. Kharasch and coworkers[39] described the two-fold addition of hydrogen bromide to methylacetylene, yielding 2,2-dibromopropane under 'normal' conditions and 1,2-dibromopropane at low temperatures in the presence of peroxides



(5)

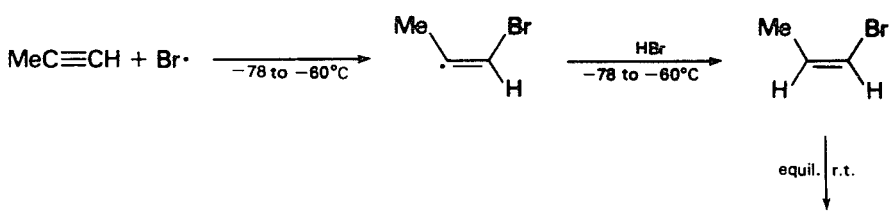
(ascaridole) (equation 5). Harris and Smith[40] succeeded in obtaining monoadducts by adding hydrogen bromide to an ice-cold solution of 10-undecynoic acid; in the presence of perbenzoic acid, addition of the bromine atom occurred at the terminal position of the triple bond, whereas the reverse orientation was observed in the noncatalytic reaction (equation 6). The peroxide-catalysed reactions turned out to



(6)

proceed much faster than the ionic reactions[41], as for example with 1-hexyne which gave 1:1 as well as 2:1 adducts. It was subsequently found that the non-Markownikoff addition of hydrogen or deuterium bromide to acetylene or deuteroacetylene could also be initiated by light to give the 1:1 adduct and the 2:1 abnormal adduct[42]. The UV-induced addition of hydrogen bromide to trifluoropropyne or to hexafluoro-2-butyne affords 1:1 adducts[43]. Phenylpropiolic acid adds hydrogen bromide without any catalyst to give a 1:1 *trans* adduct; this addition is assumed to proceed via a free-radical mechanism, since the formation of this adduct is inhibited by catechol[44].

The stereochemical course of the addition, as mentioned earlier, gained much interest. For example, the peroxide-initiated addition of two moles of hydrogen bromide to 2-butyne gave *d,l*-2,3-dibromobutane, a product that could arise from two successive either *anti* or *syn* additions[45]. It was realized only later that these two additions proceeded by an *anti* process. Skell and Allen have demonstrated that the photochemical radical-chain addition of hydrogen bromide to propyne, carried out either in the liquid or the gas phase, proceeds at −78 to −60°C exclusively by an *anti* process to give *cis*-1-bromo-1-propene[46] (equation 7). At room temperature *cis* and



cis and *trans* isomers (7)

trans isomers are produced in equilibrium or near-equilibrium mixtures in both gas- and liquid-phase reactions, probably due to postisomerization by addition–elimination of bromine radical; the inversion of the intermediate radical is an activated process which requires, according to these authors, at least 17 kcal mol^{-1} and a half-life of more than 3×10^{-7} s, or $k_{cis \rightarrow trans} \leqslant 2 \times 10^{6}\ s^{-1}$, thus indicating that there is a substantial barrier to *cis–trans* isomerization of this vinyl free radical. Addition of hydrogen bromide to propargyl bromide in the liquid phase also proceeds via an *anti* addition process[47] (equation 8). Apparently the only example in the literature of a free-radical reaction of hydrogen bromide with an acetylenic compound which is presumed to proceed via a *syn* mechanism has been reported by Bergel'son[48]. In this case, hydrogen bromide is

$$HBr + HC{\equiv}CCH_2Br \xrightarrow[-78°C]{h\nu} \begin{matrix} Br & CH_2Br \\ \diagdown & \diagup \\ C{=}C \\ \diagup & \diagdown \\ H & H \end{matrix} \qquad (8)$$

added photochemically to 1-bromopropyne or 1-bromo-3,3-dimethyl-1-butyne at −78°C to produce predominantly the corresponding *trans*-1,2-dibromo-1-alkene and also some 1,1-dibromo-1-alkene derivative (equation 9). An alternative possible

$$HBr + BrC{\equiv}CR \xrightarrow[-78°C]{h\nu} \underset{\text{major product}}{\begin{matrix} Br & R \\ \diagdown & \diagup \\ C{=}C \\ \diagup & \diagdown \\ H & Br \end{matrix}} + \underset{\text{minor by-product}}{\begin{matrix} Br & R \\ \diagdown & \diagup \\ C{=}C \\ \diagup & \diagdown \\ Br & H \end{matrix}} \qquad (9)$$

R = Me or *t*-Bu

mechanism has been suggested, where positive halogen compounds such as 1-bromo-1-alkynes would react with hydrogen bromide to yield bromine and the 1-alkyne, which would then react with one another in an *anti* electrophilic addition to yield *trans*-1,2-dibromo-1-alkene[46b].

The hydrogen–fluorine bond is remarkably strong; hydrogen chloride is also a poor hydrogen-transfer agent, and free-radical additions to multiple bonds occur only under special circumstances. Hydrogen iodide, on the other hand, donates hydrogen atoms to free radicals very easily and exothermically but the iodine atom does not add favourably by a free-radical mechanism. However, additions of these hydrogen halides to multiple-bond systems proceed nicely by ionic processes.

B. Halogenation

Halogenation of acetylenes in polar solvents is usually a facile ionic process, whereas addition in neat or in nonpolar solvents, particularly under illumination conditions, proceeds by a free-radical pathway which is often a more complicated reaction giving rise to substitution products. Reaction may occur sometimes spontaneously[49,50], as for instance by mixing *t*-butyl hypohalites and 2-butyne in the dark[49]; slower spontaneous initiations occur with 1-phenylalkynes. In these reactions *t*-butoxy radicals readily attack acetylenes to give good yields of propargylic halides with little tendency to add to the triple bond[49] (equation 10). Similar reactions afford almost the same mixture of

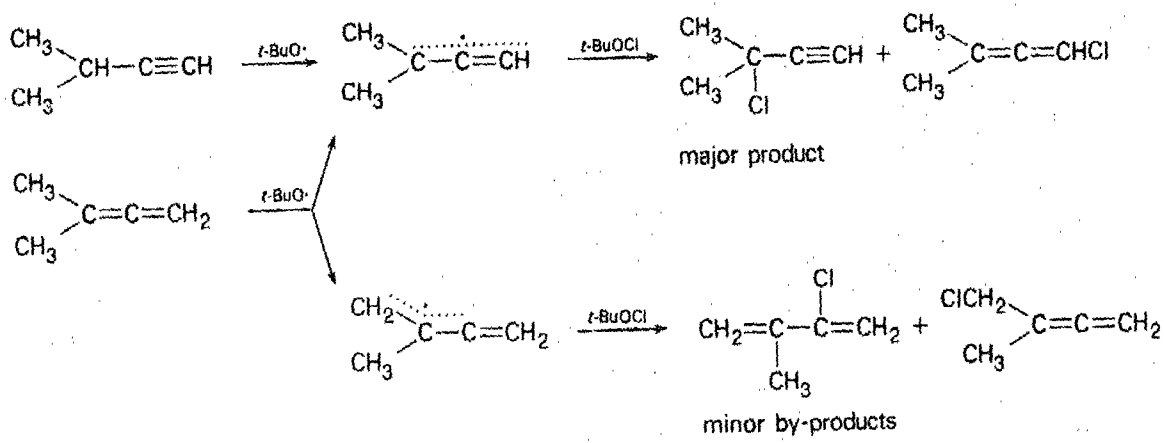
$$t\text{-BuOCl} \longrightarrow t\text{-BuO}\cdot + \text{Cl}\cdot \qquad (10a)$$

$$t\text{-BuO}\cdot + CH_3C{\equiv}CMe \longrightarrow t\text{-BuOH} + \cdot CH_2C{\equiv}CMe \qquad (10b)$$

$$\cdot CH_2C{\equiv}CMe + t\text{-BuOCl} \longrightarrow ClCH_2C{\equiv}CMe + t\text{-BuO}\cdot \qquad (10c)$$

products by reacting either 3-methyl-1-butyne[51] or 3-methyl-1,2-butadiene with *t*-butyl hypochlorite[52] (Scheme 4).

In this context it is perhaps worthwhile mentioning that propargylic hydrogens are evidently more reactive than allylic hydrogens towards bromination, as shown in equation (11)[53]. The free-radical addition of *t*-butyl hypochlorite to conjugated enynes occurs mainly across the double bond and to a much lesser extent across the triple bond; the latter adduct suffers a rapid secondary electrophilic chlorination, thus yielding 2,4-dichloro-2-butenal[54] (equation 12). However, bromination of the conjugated enyne systems shown in equations (13) and (14) occurs only at the triple bond[55].



SCHEME 4

$$HC{\equiv}CCH_2CH_2CH{=}CH_2 \xrightarrow{NBS} \underset{95\%}{HC{\equiv}CCHBrCH_2CH{=}CH_2} + \underset{5\%}{HC{\equiv}CCH_2CH{=}CHCH_2Br} \quad (11)$$

$$CH_2{=}CHC{\equiv}CH \xrightarrow[h\nu]{t\text{-BuOCl}} t\text{-BuOH} + t\text{-BuOCH}_2\text{CHClC}{\equiv}\text{CH} + t\text{-BuOCH}_2\text{CH}{=}\text{C}{=}\text{CHCl} +$$

$$[CH_2{=}CHCCl{=}CHOBu\text{-}t] \longrightarrow ClCH_2CH{=}CClCHO \quad (12)$$

$$R_3SiC{\equiv}CCH{=}CH_2 \xrightarrow{Br_2} R_3SiCBr{=}CBrCH{=}CH_2 \quad (13)$$

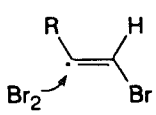
$$R_2Si(C{\equiv}CCH{=}CH_2)_2 \xrightarrow{Br_2} R_2Si(CBr{=}CBrCH{=}CH_2)_2 \quad (14)$$

Acetylene and chlorine can coexist in the vapour phase at ambient conditions, but on illumination, addition takes place and results in the formation of dichloroethylenes and tetrachloroethane; this reaction can be inhibited by oxygen[56]. Chlorination of several terminal and internal acetylenes, carried out in a mixed vapour–liquid-phase reactor in the presence of an 'infrared lamp', affords mainly *trans*-dichloroalkenes, as well as minor substitution by-products; there is no proof as to whether these reactions are of ionic or free-radical character[57,58]. Irradiation of 1-butyne with chlorine in the liquid phase at −9°C gives *trans*-1,2-dichloro-1-butene in 85–90% yield[59] (equation 15).

$$Cl_2 + HC{\equiv}CEt \xrightarrow{h\nu} \begin{array}{c} H \quad Cl \\ \diagdown \; / \\ C{=}C \\ / \; \diagdown \\ Cl \quad Et \end{array} \quad (15)$$

Chlorination (or bromination) of perfluorobutyne initiated by UV gives a quantitative yield of 1,4-hexafluoro-2,3-dichloro(or dibromo)-2-butene and a minor amount of 4-chloro(or bromo)-1-butyne[60].

Nazarov and Bergel'son have investigated the stereochemistry of ionic and free-radical bromination of terminal[61] and disubstituted acetylenes[62]. While addition of bromine across the triple bond of disubstituted acetylenes has shown an increased tendency to proceed by an *anti* process with the more bulky substituents, *syn* additions were preferred in the case of terminal acetylenes, as a result of steric hindrance between the bulky substituent and the added bromine atom, thus forcing the inversion of the intermediate radical to a sterically favoured configuration. The tendency for *syn* addition, as depicted below, increased with the size of the substituents, H < Me < CH_2OH < Me_2COH < 1-hydroxycyclohexyl < *t*-Bu:



Here again, as in the case of the presumably *syn* addition of hydrogen bromide to acetylenes which was reported at the same time by Bergel'son[48], the results are inconclusive because the possibility of ionic addition and postisomerization of products cannot be excluded[63].

IV. ADDITION OF CARBON-CENTRED FREE RADICALS

A. Polyhaloalkanes

1. Carbon tetrachloride

In 1945 Kharasch and coworkers reported for the first time that carbon tetrachloride as well as other polyhaloalkanes add to 1-octene and other olefins, under illumination or in the presence of acyl peroxides, thus resulting in the formation of a new carbon–carbon bond; 1-octene for instance, gave a 1:1 adduct in 85% yield[64]. The addition was ascribed as involving trichloromethyl free radicals as the chain-carrying species, functioning similarly to the bromine atoms in the free-radical addition of hydrogen bromide to carbon–carbon multiple bonds. Five years later, Kharasch and coworkers[65] reported that attempts to add carbon tetrachloride to 1-octyne resulted in the formation of extremely small yields of 1:1 adducts; however, this alkyne was successfully attacked by trichloromethyl radicals which were generated from bromotrichloromethane, and the resulting adduct, which was obtained in 80% yield, was 1,1,1-trichloro-3-bromo-2-nonene (equation 16). Any acetylenic compound

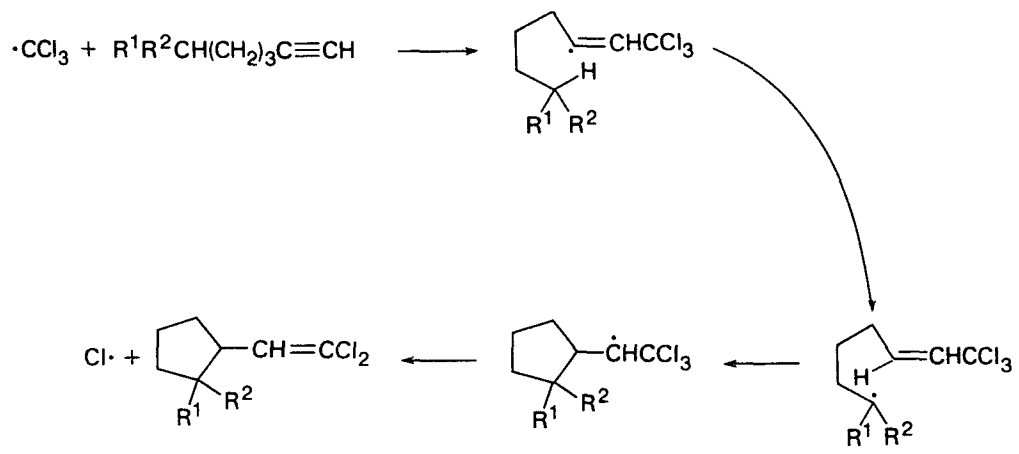
$$\cdot CCl_3 + HC{\equiv}CC_6H_{13} \longrightarrow CCl_3CH{=}\dot{C}C_6H_{13} \qquad (16a)$$

$$CCl_3CH{=}\dot{C}C_6H_{13} + BrCCl_3 \longrightarrow CCl_3CH{=}CBrC_6H_{13} + \cdot CCl_3 \qquad (16b)$$

was found to be less reactive than the corresponding olefinic compound, both in the ability to add trichloromethyl free radicals and in the ability of the free radical thus formed to react with bromotrichloromethane. Phenylacetylene, which was also found to be less reactive than styrene, gave with carbon tetrachloride a black, tarry residue. Kharasch observed that phenylacetylene completely inhibits the addition of carbon tetrachloride to 1-octene although the 1:1 phenylacetylene adduct is not formed either (however, styrene does form an adduct even in presence of phenylacetylene). This observation indicates that the primary attack of trichloromethyl radicals on phenylacetylene occurs preferably and quite efficiently; however, the resonance-stabilized intermediate radical does not apparently tend to participate in a chain-transfer process; the reason for disinclining to abstract a chlorine atom from either carbon tetrachloride, or another added chlorine-atom donor, such as cupric chloride[66], which is a much more efficient radical scavenger[67], is unclear; it is evidently not due to steric hindrance, since the same radical intermediate does abstract a bromine atom from bromotrichloromethane.

The benzoyl peroxide-catalysed addition of carbon tetrachloride to 1-heptyne which has been reported by Heiba and Dessau[34], affords a mixture of 1,2-dichloro-1-heptene in 6% yield, the expected 1:1 adduct in 40% yield and a 2,2-dichlorovinylcyclopentane derivative, which is formed in 20% yield. In a parallel reaction with 6-methyl-1-heptyne, the cyclic compound is obtained as a major product; on the other hand, 1-hexyne affords predominantly the expected 1:1 adduct and only a small yield of 2,2-dichlorovinylcyclopentane. These authors have proposed that the cyclic compound is formed as a result of a rearrangement of the vinyl radical intermediates which undergo a 1,5-internal hydrogen shift followed by an intramolecular cyclization and loss of a chlorine atom (Scheme 5). It is interesting that even the presence of thiyl radicals does not prevent cyclization.

Addition of trichloromethyl radicals to acetylene and rates of hydrogen abstraction from a variety of substrates by the vinyl intermediate radical have been reported by Russian workers; however, no description of adduct formation was given[68].

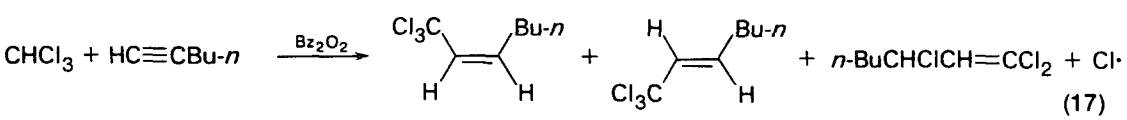


$R^1 = R^2 = H$, Me

SCHEME 5

2. Chloroform

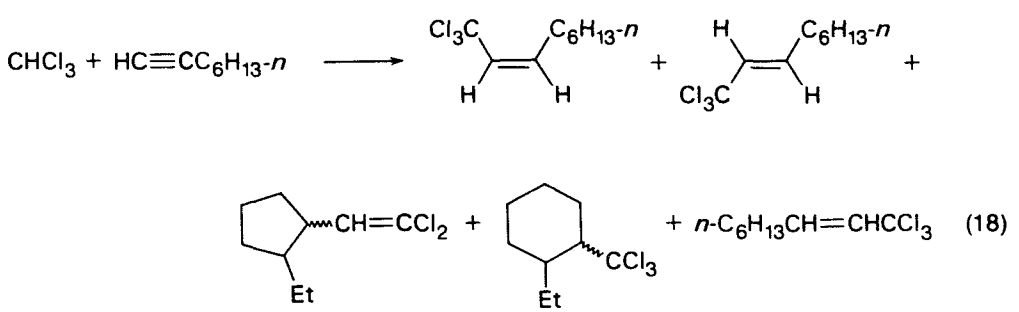
The benzoyl peroxide-catalysed addition of chloroform to 1-hexyne and 1-heptyne has been reported by Heiba and Dessau to proceed analogously to the carbon tetrachloride addition[34]. Kopchik and Kampmeier have reported that the benzoyl peroxide-catalysed addition of 1-hexyne gives a complex mixture consisting of *cis*- and *trans*-1,1,1-trichloro-2-heptenes and the allylic rearrangement product, 1,1,3-trichloro-1-heptene[31] (equation 17). They have also obtained similar results in the



(17)

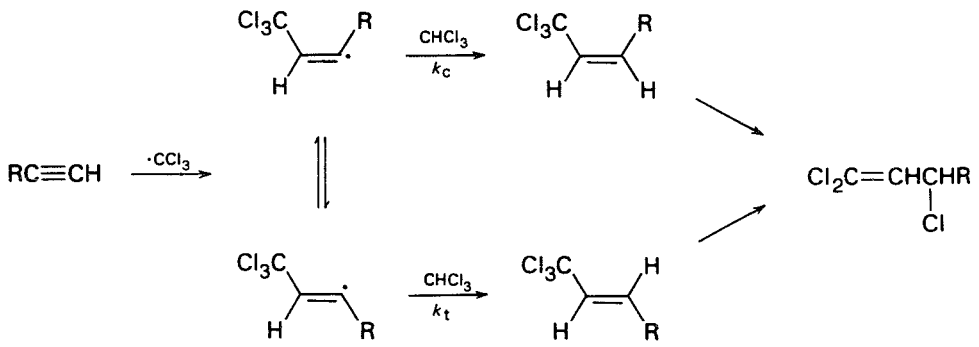
cis 82 : 18 *trans*

addition of chloroform to 1-octyne. Apart from the allylic rearrangement product, cyclization of the intermediate radicals, resembling those described by Heiba and Dessau[34], leads to the formation of cyclopentane and cyclohexane derivatives (equation 18). Appropriate control experiments have shown that the *cis/trans* adduct ratio is the same as in the previous 1-hexyne adduct formation, and also like those observed in the



(18)

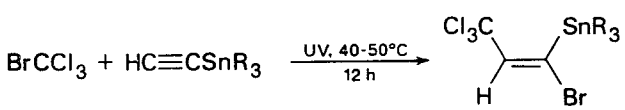
free-radical addition of thioacetic acid to 1-hexyne, as mentioned later, thus indicating that this 82:18 *cis*: *trans* isomer ratio is kinetically determined; neither cumene nor thioacetic acid can capture alkyl vinyl radicals and interfere in the rapid interconversion and equilibration of the vinyl radical intermediates and with respect to the subsequent reactions. These authors have proposed that the normal noncyclic adducts are formed according to the mechanism shown in Scheme 6.



SCHEME 6

3. *Bromo- and iodo-trichloromethane*

The peroxide-catalysed addition of bromo- and iodo-trichloromethane to carbon–carbon multiple bonds occurs easily, requiring only a very small amount of a free-radical initiator; the yields of 1:1 adduct are better than those with carbon tetrachloride. As mentioned earlier, Kharasch and coworkers have demonstrated[65] that bromotrichloromethane is much more reactive than carbon tetrachloride and is capable of forming an adduct with 1-octyne in a good yield. Kharasch and coworkers have also reported that this reagent adds to 2-octyne to give a 1:1 adduct in 33% yield as well as a 2:1 adduct in about 5% yield. Phenylacetylene is also capable of adding bromotrichlorometane to give an impure mixture, which contains mainly the 1:1 adduct and a small amount of the 2:1 adduct; however, here the yields are much lower[65]. Propargyl alcohol acetate reacts with this reagent in presence of AIBN to give a 1:1 adduct in 30% yield[69]. Dichloroacetylene adds to bromotrichloromethane, either photochemically or in the presence of *t*-butyl peroxide to give a 1:1 adduct in 46% yield[70]. The photochemical reaction of bromotrichloromethane with various trialkyltin substituted ethynes affords 1:1 *trans* addition products in 70–80% yield[71] (equation 19). Bromotrichloromethane reacts with dimethylethynyl carbinol and its methyl ether



(19)

R = Et, Pr, Bu

to give a 1:1 adduct[72] (equation 20). The photochemical reaction of iodotrichloromethane with 3,3,3-trifluoropropyne affords a 1:1 adduct in 74% yield[73] (equation 21).

$$BrCCl_3 + HC{\equiv}CCMe_2OR \xrightarrow{Bz_2O_2} CCl_3CH{=}CBrCMe_2OR \quad (20)$$

R = H or Me

$$CCl_3I + HC{\equiv}CCF_3 \longrightarrow CCl_3CH{=}CCF_3I \quad (21)$$

4. Trifluoromethane

Trifluoromethyl radicals, which are generated electrochemically by electrolysis of CF_3CO_2H in $MeCN–H_2O–NaOH$ solution, react with 1-hexyne to give a mixture of (*E*), (*Z*)-$CF_3CH{=}CHBu$-*n* and (*E*), (*Z*)-$CF_3CH{=}C(CF_3)Bu$-*n*[74].

5. Perfluoroiodoalkanes

This group of reagents is more reactive. Trifluoroiodomethane adds photochemically to acetylenes to give 1:1 adducts in good yields[75–77] (equation 22).

$$CF_3I + HC{\equiv}CR \xrightarrow{h\nu} CF_3CH{=}CRI \quad (22)$$

R = H, Me, Et, CF_3, CH_2OH, C_2F_5

Haszeldine and coworkers have reported that trifluoroiodomethane can be added to disubstituted acetylene to form a 1:1 polyfluorinated adduct in 73% yield[78] (equation 23). Pentafluoroiodoethane and heptafluoroiodopropane (C_2F_5I and C_3F_7I) react with acetylene under UV light to give 1:1 adducts[76, 77, 79, 80] (equation 24).

$$CF_3I + CF_3C{\equiv}CCF_3 \xrightarrow[350°C,\ 5\ days]{autoclave} \begin{matrix} F_3C & & CF_3 \\ & \diagdown\!\!=\!\!\diagup & \\ F_3C & & CF_3 \end{matrix} \quad (23)$$

$$C_2F_5I + HC{\equiv}CH \longrightarrow C_2F_5CH{=}CHI \quad (24)$$

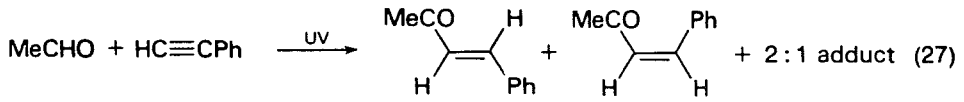
B Other Carbon-centred Free Radicals

1. Aldehydes and ketones

Acetaldehyde adds to acetylene in the presence of peroxides to give acetonyl acetone in 20% yield[81] (equation 25). Acetaldehyde adds to 1-pentyne to give a 1:1 adduct; excess acetaldehyde yields the corresponding diketone in 15% yield[82] (equation 26); such γ-diketones are in general difficult to prepare. Acetaldehyde adds to phenylacetylene to give a mixture of *cis* and *trans* 1:1 and 2:1 addition products[83] (equation 27). 2-Methylpropanal reacts with 1-hexyne differently; instead of the

$$MeCHO + HC{\equiv}CH \longrightarrow (MeCOCH{=}CH_2) \xrightarrow{MeCHO} MeCOCH_2CH_2COMe \quad (25)$$

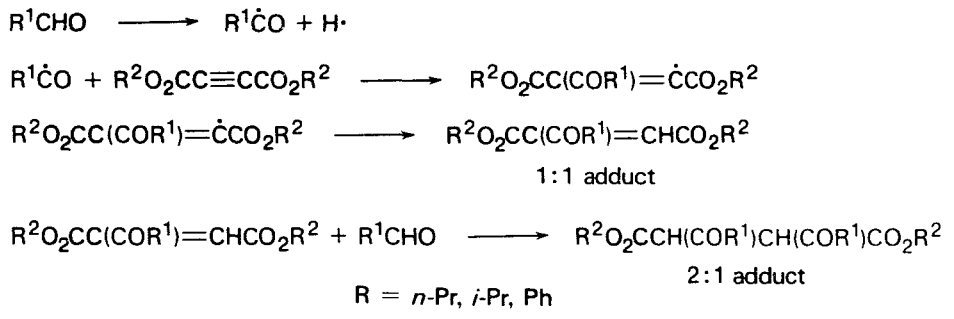
$$MeCHO + HC{\equiv}CPr\text{-}n \xrightarrow{UV} MeCOCH{=}CHPr\text{-}n \xrightarrow{MeCHO} MeCOCH_2CH(Pr\text{-}n)COMe \quad (26)$$



$$Me_2CHCHO + HC{\equiv}CBu\text{-}n \xrightarrow{UV} Me_2C(CHO)CH{=}CHBu\text{-}n \quad (28)$$

expected α,β-unsaturated ketone, e.g. $Me_2CHCOCH{=}CHBu\text{-}n$, the aldehyde shown in equation (28) is formed[84]. In the UV-initiated addition of benzaldehyde to 1-hexyne, the substituted hexenyl intermediate radical takes part in hydrogen abstraction and coupling reactions to yield a variety of products[85].

^{60}Co γ-irradiation initiates the addition of aldehyde to acetylenedicarboxylic acid to give 1:1 and 2:1 adducts in 9–31% yield[86] (Scheme 7). Aliphatic and alicyclic ketones add to 1-alkynes in the presence of $Mn^{III}(OAc)_3$[87,88]. Cyclohexanone adds to acetylene under 10 atm. pressure at 150°C in the presence of *t*-butyl peroxide to give 2-vinyl-1-cyclohexanone in 2.6% yield[89].



SCHEME 7

2. *Carboxylic acids, esters and cyano compounds*

Acetic acid adds to acetylene in the presence of *t*-butyl peroxide to yield vinylacetic acid; excess of acetic acid gives rise to the formation of adipic acid[90] (equation 29). The peroxide-initiated addition of triethyl methanetricarboxylate to 1-alkynes affords β,γ-unsaturated malonic acid derivatives in 26–38% yield[91] (equation 30). Ethyl

$$HC{\equiv}CH + CH_3CO_2H \xrightarrow{t\text{-}Bu_2O_2} CH_2{=}CHCH_2CO_2H \xrightarrow{CH_3CO_2H} HO_2C(CH_2)_4CO_2H \quad (29)$$

$$RC{\equiv}CH + HC(CO_2Et)_3 \xrightarrow{t\text{-}Bu_2O_2} RCH{=}CHC(CO_2Et)_3 \xrightarrow{HCl} RCH{=}CHCH(CO_2H)_2 \quad (30)$$

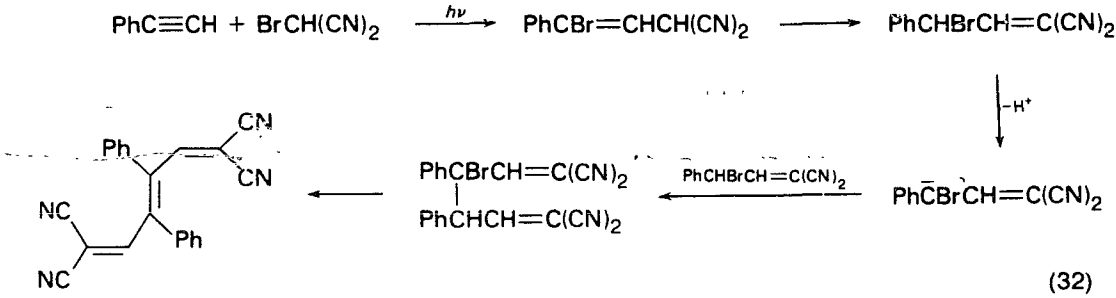
R = Pr, Bu, C_nH_{2n+1} (n = 6–8)

cyanoacetate adds to terminal alkynes in the presence of Bz_2O_2 to give the corresponding α,β-unsaturated ethyl cyanoacetates[92] (equation 31). Addition of

$$RC{\equiv}CH + \underset{\underset{CN}{|}}{CH_2CO_2Et} \xrightarrow{Bz_2O_2} RCH_2CH{=}\underset{\underset{CN}{|}}{CCO_2Et} \quad (31)$$

R = *n*-Bu, $Cl(CH_2)_3$

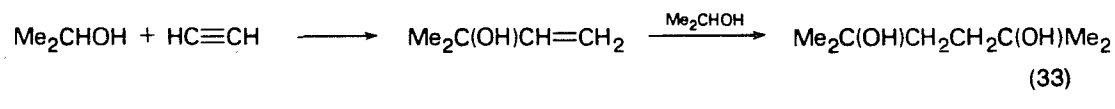
bromomalononitrile to phenylacetylene gives (*E*)-3,4-diphenyl-1,3,5-hexatriene-1,1,6,6-tetracarbonitrile according to the pathway shown in equation (32)[93].



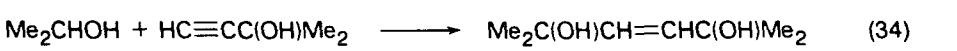
(32)

3. *Alcohols and ethers*

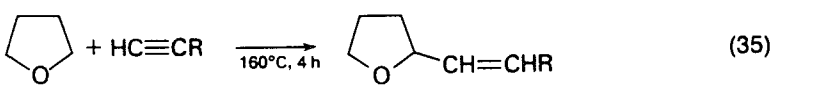
Isopropanol adds to acetylene either in the presence of peroxide catalysts[94] or photochemically[95] to yield dimethylvinyl carbinol and 2,5-dimethyl-2,5-hexanediol (equation 33). Isopropanol also adds to 3-methyl-1-butyn-3-ol to give 2,5-dimethyl-3-hexene-2,5-diol in high yield[94] (equation 34). Addition of various alcohols to propargyl alcohol yields ethylenic diols[96]. Addition of tetrahydrofuran or tetrahydropyran to terminal acetylenes in the presence of *t*-butyl peroxide gives the *cis* and *trans* addition products shown in equations (35) and (36)[97]. Addition of 2,2-dimethyl-1,3-dioxolane or 2,2-dimethyl-1,3-dioxane to 1-hexyne affords **3** or **4** respectively, which after hydrolysis yield 3-octene-1,2-diols or 4-nonene-1,3-diols[98].



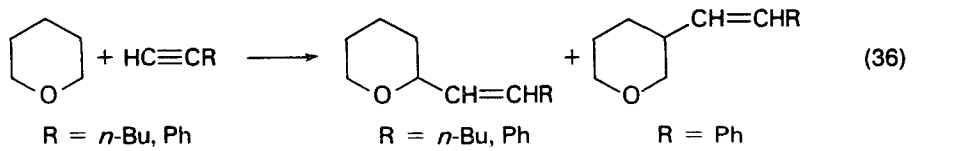
(33)



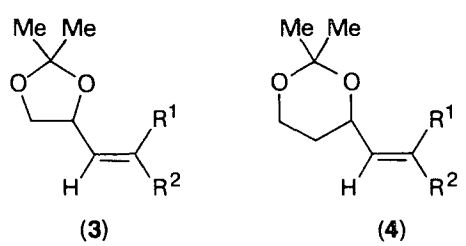
(34)



(35)



(36)



(3) (4)

R^1 = H, R^2 = *n*-Bu

or R^1 = *n*-Bu, R_2 = H

4. Alkanes and arylalkanes

Alkyl radicals have been generated by γ-irradiation with a ^{60}Co source; under such conditions propane, for instance, reacts with acetylene to give 3-methyl-1-butene[99]. Various alkyl or cycloalkyl radicals, generated in the presence of peroxides, react with acetylene under high pressure and elevated temperatures to give 1:1 adducts[100] (equation 37). The peroxide-initiated addition of isopropylbenzene to acetylene affords mainly a 1:1 adduct and a 2:1 adduct as a by-product[101] (equation 38).

$$RH + HC{\equiv}CH \xrightarrow[\text{autoclave at 140°C}]{t\text{-}Bu_2O_2} RCH{=}CH_2 \qquad (37)$$

$$R = i\text{-}PrCHMeCH_2,\ c\text{-}C_5H_9,\ c\text{-}C_6H_{11}$$

$$PhCHMe_2 + HC{\equiv}CH \xrightarrow[170°C]{t\text{-}Bu_2O_2} PhCMe_2CH{=}CH_2 + PhCMe_2CH_2CH_2CMe_2Ph \qquad (38)$$

V. ADDITION OF SULPHUR-CENTRED FREE RADICALS

A. Divalent Sulphur-centred Free Radicals

1. Thiols

The free-radical addition of thiols to carbon–carbon multiple-bond systems has been the subject of several comprehensive reviews[3,10,29,102,103]; some of them[3,10] include in their tabular surveys additions of various thiols to many types of acetylenic compounds.

The addition of thiols to acetylenes is a very convenient method for preparing β-vinyl sulphides (thioethers), vicinal disulphides and geminal disulphides (thioacetals), which are useful synthetic intermediates.

Acetylenes are apparently less reactive than olefins towards thiyl radicals as shown by some competitive reactions. For example, the addition of methanethiyl radicals to an equimolar mixture of propene and propyne proceeds about twice as fast to the olefin as to the acetylene[104]. However, in practice, addition of thiols to acetylenes occurs much more efficiently than to olefins, resulting in high yields of adducts. The main reason for the unsatisfactory addition of thiols to olefins is due to the fact that such reactions are reversible processes[105–107]. In many instances, the backward reaction is favoured over the hydrogen-abstraction adduct-forming step. The more efficient addition of thiols to acetylenes is attributed to the considerably greater reactivity of the vinyl radical intermediate, which undergoes much faster chain-transfer reactions than comparable secondary radical intermediates derived from olefins. The difference in the adduct formation ability between the two carbon–carbon multiple-bond systems is most marked in the aromatic series. Addition of one mole of benzenethiol to an equimolar mixture of phenylacetylene or phenylprop-1-yne and styrene yields only thiol–phenylacetylenic adducts[108].

Thiyl free radicals add much faster to multiple bonds than thiolate anions[109–111]. Thiyl free radicals attack a terminal triple bond more readily than internal bonds[109,112,113]. The addition of arylthiols to arylacetylene usually proceeds much more easily than does that of alkylthiols. Kohler and Potter reported in 1935 than *p*-toluenethiol reacted very exothermally and spontaneously with phenylacetylene without any catalyst to give a quantitative yield of adducts in approximately equal *cis/trans* ratio[112] (equation 39). It was confirmed, many years later, that this reaction does indeed operate via a free-radical chain mechanism[109].

$$p\text{-}MeC_6H_4SH + HC{\equiv}CPh \longrightarrow p\text{-}MeC_6H_4SCH{=}CHPh \quad (39)$$

The addition of thiols to acetylenes affords generally non-Markownikoff 1:1 adducts. Excess of thiol may result in a further addition of thiol molecules to the monoadducts to give 2:1 diadducts. Acetylenic bonds which are flanked by electron-donating substituents are particularly capable of doing so. Addition of a second mole of thiol to such vinyl sulphides may often take place more easily than the primary addition; thus, even equimolar amounts of both reactants may yield mixtures of 1:1 and 2:1 adducts. On the other hand, electron-withdrawing substituents have an opposite effect; hence production of monoaddition products is favoured[115-119]; for diaddition, more vigorous conditions need to be applied. It is worthwhile noting that in the two-fold addition of thiols to terminal alkylacetylenes, thiyl free radicals attack monoadducts in an orientation opposite to the primary addition process (non-Markownikoff) thus yielding vicinal disulphides[108,115,120-123] (equation 40). On the other hand, the two-fold addition of thiyl radicals to terminal arylacetylenes takes place via two consecutive non-Markownikoff orientations at the terminal carbon atom thus yielding geminal disulphides (thioacetals)[115] (equation 41). The addition of the second mole of ethanethiol to aromatic β-vinyl sulphides is a much slower process, being highly reversible, and it requires drastic conditions. The orientation of the attacking radical is assumed to be remarkably effected by resonance stabilization of the benzyl radical intermediates[115].

$$R^1SH + HC{\equiv}CR^2 \longrightarrow R^1SCH{=}CHR^2 \overset{R^1S\cdot}{\rightleftharpoons} R^1S\dot{C}H{-}CHR^2SR^1 \xrightarrow{R^1SH} R^1SCH_2{-}CHR^2SR^1 \quad (40)$$

R^1 = Me, Et, *n*-Bu, α-Tolyl, CF_3

R^2 = H, Me, Et, *n*-Bu, CH_2OH, CO_2H

$$EtSH + HC{\equiv}CPh \longrightarrow EtSCH{=}CHPh \overset{RS\cdot}{\rightleftharpoons} (EtS)_2CH{-}\dot{C}HPh \xrightarrow[slow]{RSH} (EtS)_2CHCH_2Ph \quad (41)$$

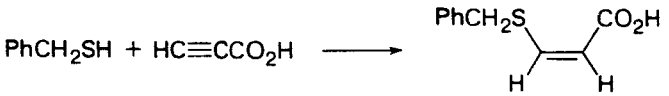
Two bonds of a C≡C group can also undergo reactions to give 1:1 saturated products. In this case, two functional groups are required to be present in the added molecules. Such reactions form cyclic products; for example, ethanedithiol adds to 2-butyne-1,4-diol diacetate to yield a 1,4-dithiane derivative[115] (equation 42). Addition of ethanethiol in excess to dimethyl acetylenedicarboxylate affords only a monoadduct[115].

$$HSCH_2CH_2SH + AcOCH_2C{\equiv}CCH_2OAc \longrightarrow \text{(1,4-dithiane-2,5-bis(CH}_2\text{OAc))} \quad (42)$$

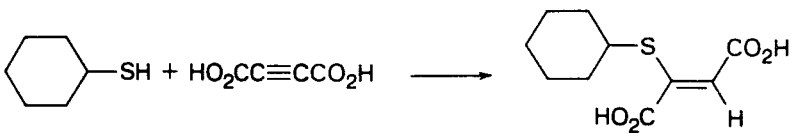
In general, thiols add across the triple bond of various types of mono- and di-substituted acetylenes, predominantly in a *anti* stereoselective manner[3,10,28,124]. For example, the addition of ethanethiol to propyne in the presence of azoisobutyronitrile (AIBN) gives mainly the *anti* addition product[125] (equation 43). Benzylthiol adds to

$$EtSH + HC{\equiv}CMe \longrightarrow \text{(EtS, Me, H, H)} \quad (43)$$

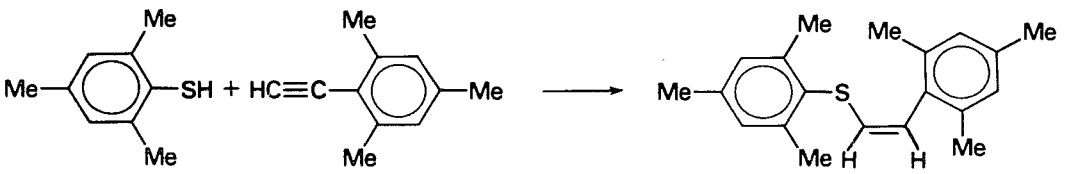
propiolic acid in a similar way[118] (equation 44). Likewise, cyclohexanethiol reacts with acetylenedicarboxylic acid to produce mainly the fumaric acid derivative[117] (equation 45). Mesitylthiol adds to mesitylacetylene to give an *anti* addition product[109] (equation 46). Apparently the steric requirements for the bulky groups in the transition state were not sufficiently large to change the stereochemical course of this addition.



(44)

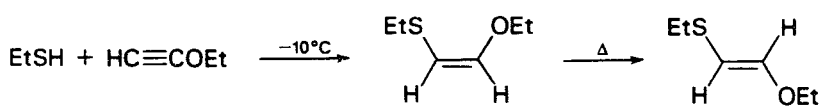


(45)



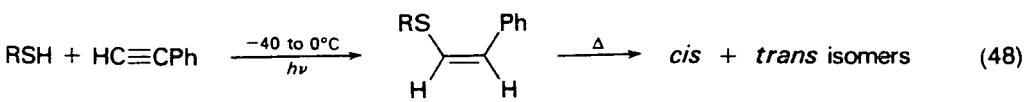
(46)

Higher stereoselectivity can be achieved by conducting such reactions at lower temperatures and with excess of the acetylenic reactant. Under controlled conditions, the addition of thiols to acetylenes gives rise to the formation of *anti* addition products; hence terminal acetylenes yield kinetically *cis* adducts; these partly isomerize at higher temperatures or in presence of excess free radicals to the thermodynamically more stable *trans* isomers, as for example in equation (47)[32,110].



(47)

Additions of several alkyl- and aryl-thiols to phenylacetylene have given similar results[27,108] (equation 48). The stereochemistry of these thiol additions has been



(48)

R = Me, *n*-Bu, Ph, *p*-MeC_6H_4

studied in more detail under a variety of conditions. It has been revealed that the stereoselectivity is strongly dependent on the molar ratio of the reactants, particularly in the additions to phenylacetylene. Apart from the energy-demanding equilibrium process operating in the transition state, *cis–trans* postisomerization takes place in the presence of excess thiyl radicals by addition to the primary *cis* addition products, and the subsequent elimination gives rise to higher ratios of the thermodynamically more stable *trans* isomers[27–30].

Thio acids add very readily to acetylenes[114–116,123,126–128] via a free-radical chain mechanism even at room temperature, often in the absence of free-radical initiators, to

$$R^1COSH + HC{\equiv}CR^2 \longrightarrow R^1COSCH{=}CHR^2 \xrightarrow{R^1COSH} R^1COSHCH_2CHR^2SCOR^1 \quad (49)$$

R^1 = Me, Et; R^2 = H, *n*-Bu, *t*-Bu, CH_2OH, Me_2COH, CH_2OR^3 (R^3 = Me, OAc), CH_2CH_2Cl, CO_2Me, *c*-C_6H_{11}, Ph, α-Tolyl

yield either monoadducts or, in excess of thio acids, 2:1 diadducts (equation 49). Many of these thio acid additions to olefins and acetylenes were first explored by Behringer[114] during World War II and by British researchers[126]. Terminal acetylenes bearing electron-withdrawing groups tend to give mainly 1:1 adducts[27,117,123,126]. Kampmeier and Chen[28] have reported that addition of thioacetic acid to 1-hexyne yields under kinetic control a 82:18 ratio of *cis* and *trans* addition products; a similar ratio has been obtained in the addition of chloroform to 1-hexyne, as mentioned earlier[31]. Equilibration gives equal amounts of both stereoisomers. Similar mechanistic pathways as those discussed in the introduction, account for the preferential formation of *anti* addition products.

While partial hydrolysis of 1:1 monothioacid–acetylene adducts yields thiols, full hydrolysis has turned out to be a very useful route of indirectly hydrating a terminal acetylene to the corresponding non-Markownikoff aldehydes or ketones[126] (equation 50).

$$R^1C{\equiv}CR^2 \xrightarrow{HSCOMe} R^1CH{=}CR^2SCOMe \xrightarrow[-MeCO_2H]{H_2O} R^1CH{=}CR^2SH \xrightarrow[-H_2S]{H_2O} R^1CH_2COR^2 \quad (50)$$

Numerous thiols and thio acids have been added via a free-radical mechanism to acetylenes bearing various functional groups including heteroatom substituents. Ethynyl ethers and thio ethers are very useful reactive synthons, since they undergo versatile transformations. The chemistry of these compounds has been reviewed by Arens[111] as well as by Shostakovskii and coworkers[102]. For example, ethanethiol reacts with ethynyl ethers or thio ethers to give 1:1 and 1:2 addition products[110,111,129,130] (equation 51). The predominantly formed *anti* addition products isomerize partly during distillation.

$$EtSH + RC{\equiv}CXEt \longrightarrow EtSCR{=}CHXEt \xrightarrow{EtSH} EtSCHR{-}CH\begin{matrix}XEt\\SEt\end{matrix} \quad (51)$$

cis and *trans*

R = H, Me

X = O, S

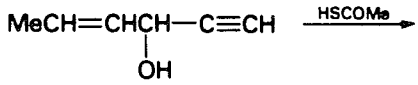
Addition of thiyl radicals to conjugated terminal ethynylvinyl analogues takes place preferentially at the apparently activated terminal acetylenic carbon atom[131,132] (equation 52).

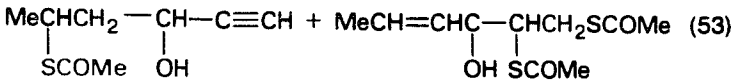
$$R^1SH + HC{\equiv}CCH{=}CHXR^2 \longrightarrow R^1SCH{=}CHCH{=}CHXR^2 \quad (52)$$

$R^1 = R^2$ = Et, *n*-Pr, *n*-Bu, Ac, Ph, etc.

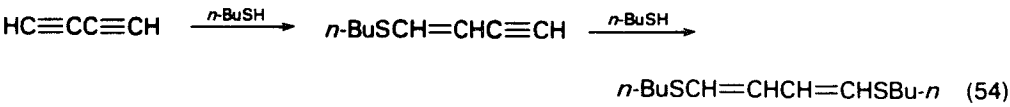
X = O, S

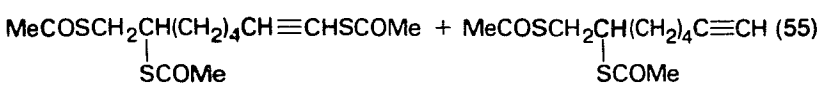
Addition of thiolacetic acid to 1-hexyn-4-en-3-ol results in either monoaddition to the double bond or diaddition to the triple bond[127] (equation 53).





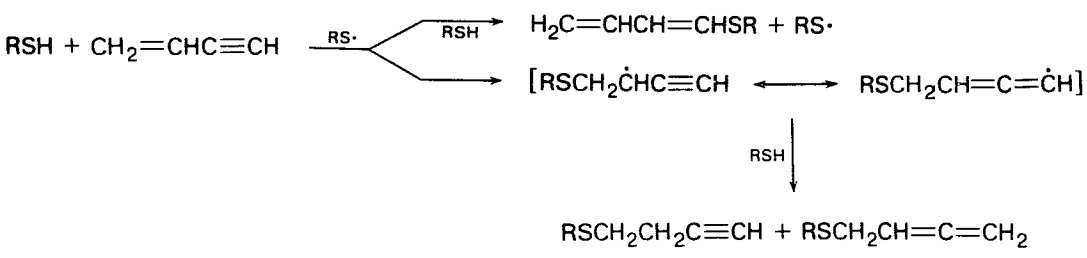
Addition of *n*-butanethiol in excess to diacetylene gives a small yield of *cis* and *trans* monoadducts and diadducts as well[124] (equation 54). Addition of thiolacetic acid to 1,7-octadiyne yields the mixture shown in equation (55).

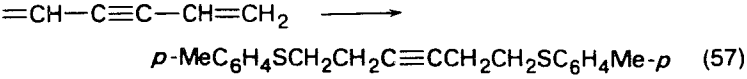




(3:2)

Thiols, in excess, react with vinylacetylene to give higher proportions of adduct resulting from addition to the double bond rather than to the triple bond, apparently due to propargylic resonance-stabilized radical intermediates; these isomerize partly into the corresponding allenes[133] (equation 56). Addition of two moles of *p*-toluenethiol to divinylacetylene takes place at the terminal double bonds to yield 80% of the diadduct[134] (equation 57).





Addition of thiols to acetylenes and carbon monoxide under drastic conditions affords mixtures of vicinal disulphides and the corresponding α,β-unsaturated carbonyl derivatives (equation 58); acetylene yields thioacrolein under these conditions[121,127].

$$R^1SH + HC{\equiv}CR^2 \xrightarrow{AIBN} R^1SCH{=}\dot{C}R^2$$

$$\xrightarrow[\text{trapping}]{CO} R^1SCH{=}C(R^2)(CO\cdot) \xrightarrow{R^1SH} R^1SCH{=}CR^2CHO + R^1S\cdot \quad (58)$$

$$\xrightarrow{R^1SH} R^1SCH{=}CHR^2 \xrightarrow{R^1SH} R^1SCH_2CHR^2SR^1$$

R^1 = *n*-Bu, $PhCH_2$, Ph

R^2 = H, Ph

2. *Hydrogen sulphide*

Free-radical additions of hydrogen sulphide to acetylenes had already been patented in 1946, but no example had been presented. It was demonstrated later than X-ray[135] or UV[136] radiation induced the addition of hydrogen sulphide to a variety of acetylenes; these reactions were carried out in closed vessels at −78°C or at room temperature (equation 59). Monoaddition to propyne yields an *anti* addition product.

$$R^1C{\equiv}CR^2 + H_2S \longrightarrow R^1CH{=}CR^2SH + R^1CH(SH)CHR^2SH \quad (59)$$

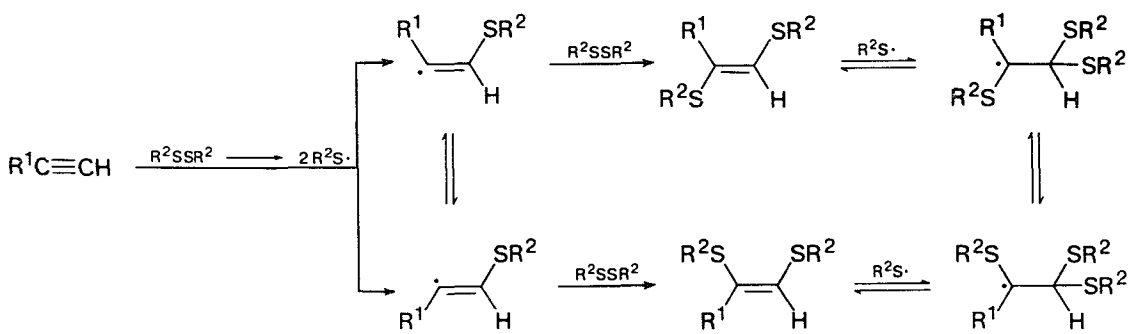
$R^1 = R^2$ = H, Me, CF_3, Ph

Likewise, hexafluoro-2-butyne affords only a 1:1 *trans* adduct. The major product which was obtained by the addition of hydrogen sulphide to phenylacetylene was the bis-β-phenylvinyl sulphide $(PhCH{=}CH)_2S$.

Hydrogen sulphide is much less reactive than thiols, since it is not a particularly good transfer agent; hence, telomerization occurs quite often.

3. *Disulphides*

The homolytic cleavage of the S—S bond of disulphides, being readily achieved either by UV irradiation[104,137] or in the presence of peroxides[104] has been utilized as a



SCHEME 8

convenient source for generating thiyl free radicals for addition to acetylenes. The mechanism shown in Scheme 8 has been proposed[104].

Dimethyl disulphide which was photolysed in the vapour phase in the presence of acetylene gave 1,2-bis(methylthio)ethene and oily oligomers of unknown structure[138].

4. Thiocyanogen

The S—S bond of thiocyanogen is similarly cleaved by irradiation with a mercury lamp; in presence of acetylene a symmetrical 1:1 adduct is formed[139] (equation 60).

$$HC{\equiv}CH + (SCN)_2 \xrightarrow{h\nu} NCSCH{=}CHSCN \qquad (60)$$

5. Sulphenyl halides

The free-radical character of additions of sulphenyl halides to acetylenes had not been firmly established. Sulphenyl halides prefer to react with acetylenes as electrophiles to form β-halovinyl sulphides. The electrophilic addition of sulphenyl halides to acetylenes has been reviewed by several authors[140–142].

6. Elemental sulphur

Elemental sulphur adds to activated triple bonds like bis-polyfluoroalkylacetylenes either on boiling and in atmosphere of nitrogen, or under pressure to yield 1,2-dithiene derivatives[143] (equation 61).

$$RCF_2C{\equiv}CCF_2R \xrightarrow{\cdot S{-}S\cdot} RCF_2\underset{|}{\overset{S-S}{C}}{=}\underset{|}{C}CF_2R \qquad (61)$$

$$R = F,\ ClCF_2,\ H(CF_2)_4$$

B. Higher Valent Sulphur-centred Free Radicals

1. Sulphur chloride pentafluoride

Photochemically induced additions of sulphur chloride pentafluoride to acetylene and propyne, carried out in autoclaves, have been reported to yield 1:1 adducts only[144,145] (equation 62).

$$F_5SCl + HC{\equiv}CR \longrightarrow F_5SCH{=}CClR \qquad (62)$$

$$R = H,\ Me$$

2. Sulphonyl halides

While the addition of benzenesulphonyl chloride to phenylacetylene, carried out in the presence of benzoyl peroxide, occurs sluggishly to give poor yields of telomeric sulphones, sulphonyl chlorides add smoothly to terminal and nonterminal acetylenes in the presence of a copper salt catalyst to give β-chlorovinyl sulphones[146] (equation 63).

Comparable copper-catalysed additions of benzenesulphonyl chloride to 1-hexyne and 1-hexene indicate that 1-alkenes react much more slowly than 1-alkynes, evidently due to the high reversibility of the sulphonyl free-radical addition to olefins. Chloromethanesulphonyl chloride adds to 1-octyne to give

$$R^1SO_2Cl + R^2C{\equiv}CR^3 \xrightarrow{Cu^I \text{ or } Cu^{II}} R^1SO_2CR^2{=}CClR^3 \quad (63)$$

cis and *trans*

R^1 = Me, CH_2Cl, Ph, *p*-MeC_6H_4

R^2 = H, Et

R^3 = Et, *n*-Bu, *n*-C_6H_{13}, Ph

1-chloromethanesulphonyl-2-chloro-1-octene, although in a very small yield (6%) (equation 64). 1-Octene, on the other hand, does not afford the corresponding adduct

$$ClCH_2SO_2Cl + HC{\equiv}CR \longrightarrow ClCH_2SO_2CH{=}CClR + ClCH_2CH{=}CClR + SO_2$$
$$R = n\text{-}C_6H_{13}, Ph \quad (64)$$

at all; in this case the reaction is much slower and the labile chloromethanesulphonyl chloride undergoes complete decomposition with elimination of sulphur dioxide, thus leading to the addition of chloromethyl radicals to the olefin[147]. However, addition of this reagent proceeds faster with aromatic analogues. Phenylacetylene in this case is less reactive towards chloromethylsulphonyl radicals than styrene; the latter furnished an adduct in 60% yield whereas phenylacetylene formed a corresponding adduct in 20% yield.

In the copper-catalysed addition of sulphonyl chlorides to carbon–carbon multiple bonds, for which a redox-transfer mechanism has been proposed[147], the copper catalyst participates in every single cycle of the chain propagation as a chlorine atom transfer agent (Scheme 9).

In its oxidized form the copper catalyst is a much more reactive chlorine atom donor[67] than the covalently bound chlorine of the sulphonyl chloride; hence the relatively slow transfer step of a conventional process (equation 65) is completely superseded in the presence of this catalyst by very fast reduction–oxidation steps.

$$R^1SO_2CR^2{=}\dot{C}R^3 + R^1SO_2Cl \longrightarrow R^1SO_2CR^2{=}CClR^3 \quad (65)$$

It is interesting to note that, in these redox-catalysed reactions conducted in the presence of copper(I) and (II) chlorides and alkylammonium chloride (added to help solubilize the copper salt in various polar and nonpolar solvents), no oxidative coupling products of terminal acetylenes are formed. Moreover, an attempted oxidative coupling of phenylacetylene itself under these conditions did not take

$$R^1SO_2Cl + CuCl \longrightarrow [R^1SO_2{-}ClCu^ICl \longleftrightarrow R^1SO_2{\cdot}ClCu^{II}Cl] \longrightarrow R^1SO_2{\cdot} + CuCl_2$$

$$R^1SO_2{\cdot} + R^2C{\equiv}CR^3 \longrightarrow R^1SO_2CR^2{=}\dot{C}R^3$$

$$R^1SO_2CR^2{=}\dot{C}R^3 + CuCl_2 \xrightarrow[\text{fast}]{\text{very}} \left[R^1SO_2CR^2{=}\dot{C}R^3 \;(ClCu^{II}Cl) \longrightarrow R^1SO_2CR^2{=}CR^3 \;(ClCu^ICl)\right]$$

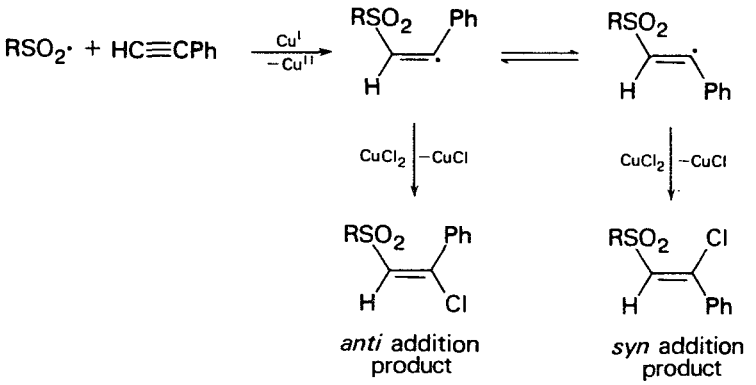
$$\downarrow$$

$$R^1SO_2CR^2{=}CClR^3 + Cu^ICl$$

SCHEME 9

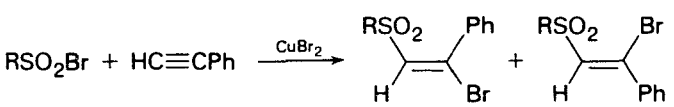
place[146]. It seems that such conditions favour a ligand-transfer process, whereas a one-electron transfer is unfavourable for an oxidative coupling reaction[148].

Since the copper-catalysed addition of sulphonyl chlorides to phenylacetylene gives rise to *anti* and *syn* addition products, the possibility of an equilibration process has been raised (Scheme 10). The addition is strongly dependent on polar factors and can be stereoselectively controlled to give preferentially either *anti* or *syn* addition products. For example, excess chloride ions or highly polar solvents promote formation of *anti* addition products, while *syn* addition predominates in low polarity solvent (e.g. carbon disulphide)[149].



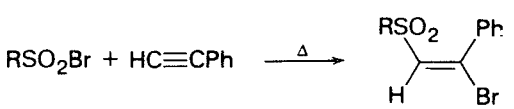
SCHEME 10

Isomerization of the kinetically controlled *anti* addition products into the thermodynamically more stable planar stereoisomers, via addition–elimination of sulphonyl free radicals, occurs only to a very small extent under drastic conditions; *syn* addition products do not isomerize at all under these conditions, and in both cases no diaddition product is found. This strongly suggests that sulphonyl free radicals, which are generated in the same way as in the original addition reaction, are very inefficient in attacking the double bond. This is probably due to the strong inductive effect of the electron-withdrawing sulphonyl group, which diminishes the reactivity of the olefinic bond towards free radicals of an electrophilic nature. The copper-catalysed addition of sulphonyl bromides to phenylacetylene furnishes similar results[150] (equation 66). In contrast to sulphonyl chlorides, the corresponding sulphonyl bromides interact thermally with acetylenes to give exclusively *anti* addition products (equation 67). The



(66)

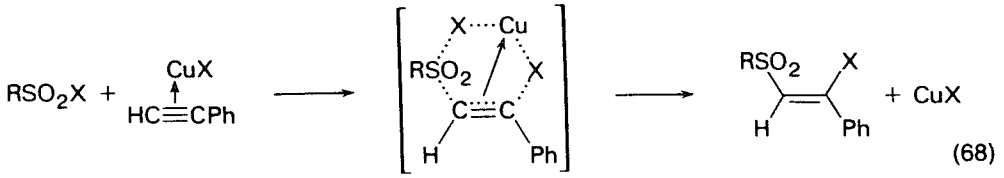
R = Me, Ph, *p*-MeC$_6$H$_4$



(67)

striking difference between the copper-catalysed reaction and the thermal process demonstrates the specific role of the copper catalyst enabling a *syn* addition process to take place. The fact that only *anti* addition products are produced under thermolytic conditions argues strongly against the possibility of an intervening equilibration

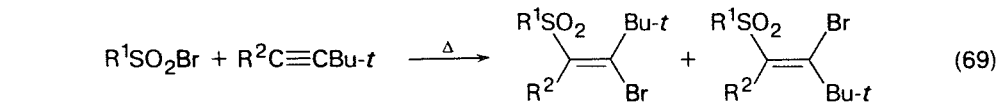
process. Evidently, the initially resonance-stabilized vinyl radical does not isomerize, but reacts with another sulphonyl halide molecule to give via a halogen chain transfer the *anti* addition product. Inversion of the initially formed vinyl radical becomes very improbable, suggesting that the energy barrier for such a process may be fairly high[151]. It has therefore been suggested that the two stereoisomers do not have a common intermediate, and in general, the formation of the *anti* addition product, either in the thermal or the copper-catalysed reaction is a result of a normal radical chain be it that, in the product-forming step, halogen is transferred from the sulphonyl halide or from the copper (II) halide. On the other hand, the *syn* addition product, which is also formed in the copper-catalysed reaction presumably arises from a concerted reaction as depicted in equation (68). Solubility of the copper catalyst is apparently a very important factor in this reaction.



(68)

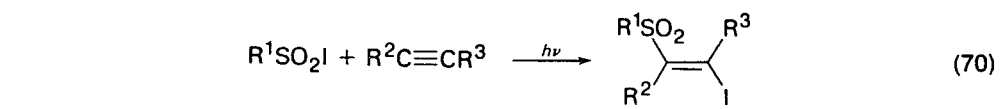
Excess halide ions give halocuprates with copper(II) ions, which are more soluble. In absence of such additives, or in solvents of low polarity the copper catalyst is only partly dissolved and reaction takes place on the surface of the undissolved copper catalyst leading to *syn* addition products.

The thermal addition of sulphonyl bromides to *t*-butylacetylene yields, in contrast to phenylacetylene, a mixture of *syn* and *anti* addition products, in absence of copper catalyst, presumably due to steric effects exerted by the bulky substituent[152] (equation 69).



(69)

Sulphonyl iodides add to acetylenes under irradiation conditions to give exclusively *trans*-β-iodovinyl sulphones[153] (equation 70).



(70)

R^1 = Me, Et, *i*-Pr, *n*-Bu, *t*-Bu, *p*-$R^4C_6H_4$ (R^4 = Me, NO_2)

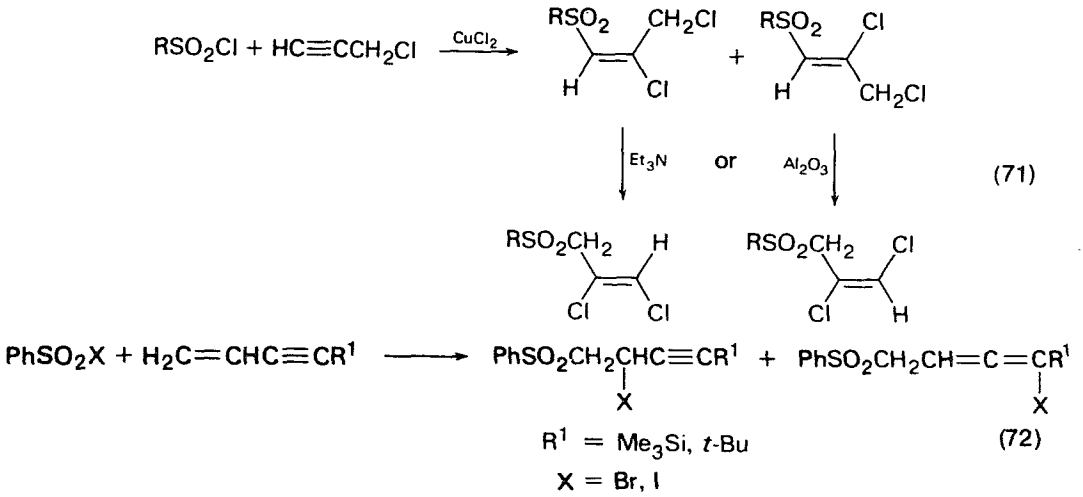
R^2 = H, Et, *i*-Pr, *n*-Bu, *t*-Bu, *n*-C_6H_{11}, Ph, PhCO, CN, EtO

R^3 = H, Et, *i*-Pr, *n*-Bu, *t*-Bu, Ph, Cl

Copper-catalysed addition of sulphonyl chlorides to propargyl chloride affords mixtures of *syn* and *anti* addition products, which under very mild basic conditions, like treatment with basic alumina or a tertiary base, undergo a prototropic rearrangement to give the corresponding allyl sulphones[154] (equation 71).

Both *syn* and *anti* vinyl and allyl sulphones, including those mentioned earlier, isomerize photochemically, by a mercury lamp in the presence of photosensitizers to yield the same photostationary-state *cis–trans* mixture[150,154].

In the copper-catalysed reaction shown in equation (72) sulphonyl halides add to conjugated enyne derivatives preferentially to the sterically less hindered terminal olefinic bond[155].

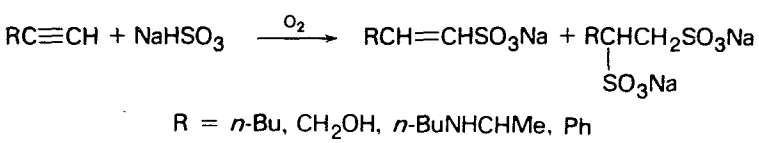


(71)

(72)

3. *Bisulphite*

The free-radical addition of bisulphite ions to acetylenes, carried out in aqueous buffered solutions, gives rise to 1:1 and 2:1 adducts. In contrast to thiol additions both alkylacetylenes and, surprisingly, phenylacetylene form vicinal disulphonate derivatives[156–158] (equation 73). 2-Butyn-1,4-diol reacts with sodium bisulphite without any catalyst to give a vicinal disubstituted adduct[156,158].



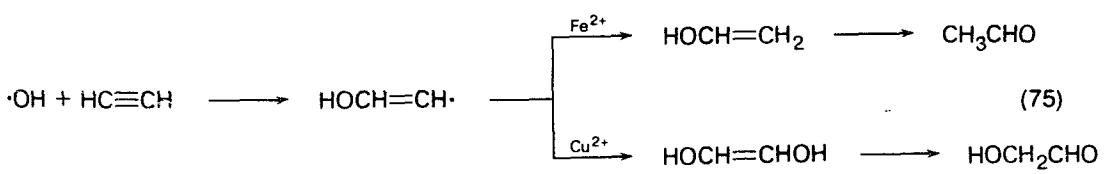
(73)

VI. ADDITION OF OXYGEN-CENTRED FREE RADICALS

A. Hydroxyl Free Radicals

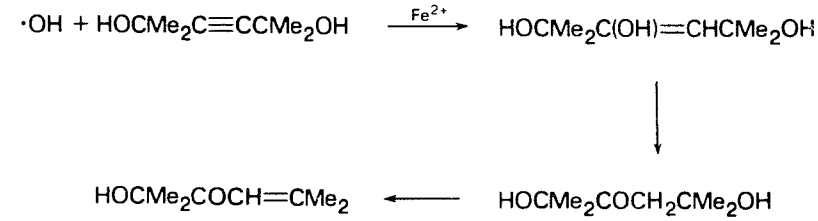
Hydroxyl radicals, generated by radiolysis of water, add to acetylene in presence of oxygen to give glyoxal[159] (equation 74). Hydroxyl radicals, generated from Fe^{2+}–H_2O_2 (Fentons reagent), add readily to acetylene[160] (equation 75); the intermediate β-hydroxyvinyl radicals are reduced by Fe^{2+} to give acetaldehyde as the major product. In the presence of Cu^{2+} the intermediate radical is oxidized to yield glycolaldehyde. Similarly, 3-hexyne yields in the presence of Fe^{2+} 3-hexanone. Propargyl alcohol gives in the presence of Cu^{2+} dihydroxyacetone; no product is detected by using Fe^{2+} alone. Again in the presence of Fe^{2+},

(74)



(75)

2,5-dihydroxy-2,5-dimethyl-3-hexyne yields 2,5-dimethyl-2-hydroxyhex-4-en-3-one[160] (equation 76).



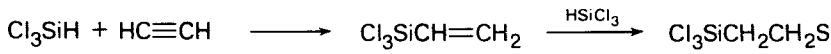
(76)

VII. ADDITION OF OTHER GROUP IVB-CENTRED FREE RADICALS

A. Silanes

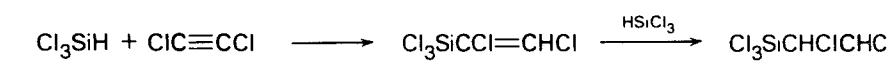
The homolysis of the silicon–hydrogen bond, which is much weaker than the silicon–chlorine bond, is more facile when electronegative groups are attached to the silicon[161]. Trichlorosilane reacts faster than dichlorsilanes, whereas trialkylsilanes and trialkyloxysilanes react very slowly.

The peroxide-initiated addition of trichlorosilane to acetylene was first reported in 1947 to yield a 2:1 bisadduct[162]. Acetylene adds either one or two trichlorosilane molecules[163] (equation 77). Trichlorosilane added to dichloroacetylene yields, in the



(77)

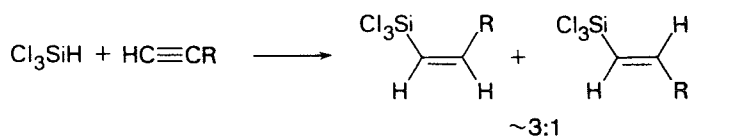
presence of benzoyl peroxide at 70–80°C, a 1:1 adduct; further addition of this reagent affords a 2:1 adduct[164] (equation 78). Trichlorosilyl radicals attack trimethylsilylpropyne at the silyl-substituted carbon atom[165] (equation 79).



(78)

(79)

Trichlorosilyl radicals generally attack monosubstituted acetylenes at the terminal carbon atom[163,166–169]. Benkeser and coworkers have shown that peroxide-initiated additions of trichlorosilanes to a variety of terminal alkynes give predominantly *anti* addition products[167–169] (equation 80).

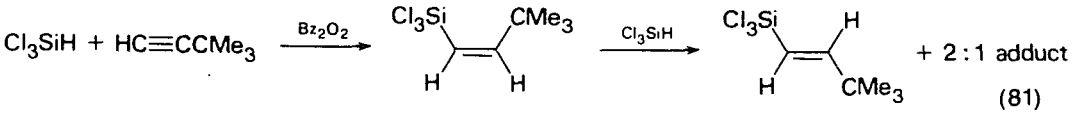


(80)

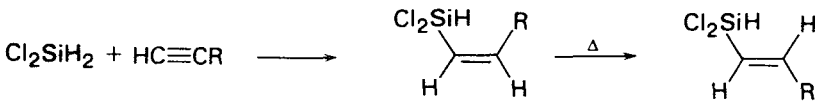
R = *n*-Pr, *i*-Pr, *n*-Bu, *t*-Bu, *n*-C_5H_{11}

The addition of trichlorosilanes to the highly hindered 3,3-dimethyl-1-butyne gives an *anti* addition product along with a considerable amount of the 2:1 adduct; the *cis* adduct partly isomerizes to the more stable *trans* isomer[168,169] (equation 81). However, chloroplatinic-acid-catalysed hydrosilylation of 1-hexyne proceeds via a *syn* addition process and gives the *trans* adduct[170].

The free-radical addition of dichlorosilanes to several acetylenes affords predominantly *anti* addition products; the hindered 3,3-dimethyl-1-butyne adduct isomerizes to the more stable form as in the trichlorosilane addition[171] (equation 82).



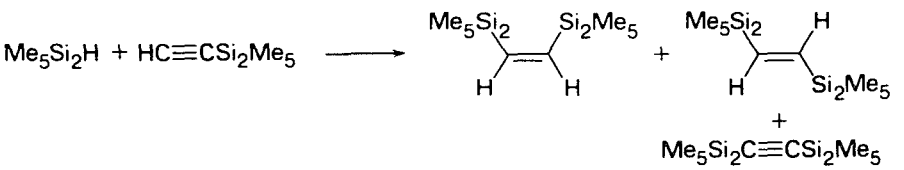
(81)



(82)

R = Et, *n*-Bu, *t*-Bu, *n*-C_6H_{11}

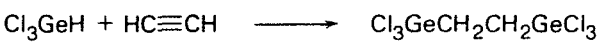
t-Butyl peroxide-catalysed reaction of pentamethyldisilane with pentamethyldisilyacetylene affords *cis* and *trans* 1:1 adducts, as well as an acetylenic substitution by-product, arising from the abstraction of an hydrogen atom from the vinyl radical intermediate by the peroxide radical[172] (equation 83).



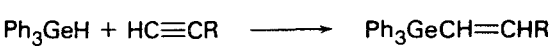
(83)

B. Germanes

Trichlorogermanes add much more readily than silanes to acetylene in the absence of any catalyst , to give exothermically a 2:1 adduct in 90% yield[173,174] (equation 84). Triphenylgermane adds to phenylacetylene at 110–135°C or to dimethylpropargylic alcohol at 50–70°C to give 1:1 adducts[175] (equation 85).



(84)

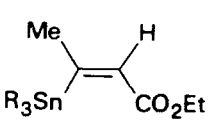


(85)

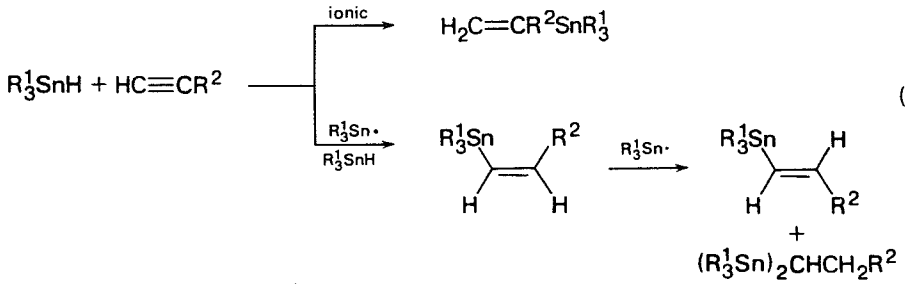
R = Ph or CMe_2OH

C. Organotin Hydrides (Stannanes)

Unlike the Sn—Cl bond, the Sn—H bond homolyses very easily[176–183]. Trialkylstannanes add to acetylenes either by a nucleophilic attack, thus yielding Markownikoff adducts, or by a free-radical chain mechanism to give non-Markownikoff *anti* addition products; these isomerize in the presence of triorganotin radicals to the more stable isomer[183] (equation 86). The presence of AIBN has been shown to improve the regiospecificity of the hydrostannation of terminal acetylenes and also furnish higher yields, e.g. equation (87)[178]. The trialkylstannane-ethyl 1-propynecarboxylate *anti* addition product (**5**) does not isomerize probably due to steric hindrance[183]. The nonregioselective addition of trimethylstannane to conjugated enynes affords, due to resonance effects, mixtures of 1,2-, 3,4- and 1,4-adducts, along with telomeric products (equation 88). The relative ratio of the products indicates that this addition is reversible[184].



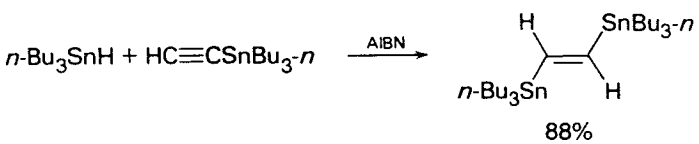
(**5**)



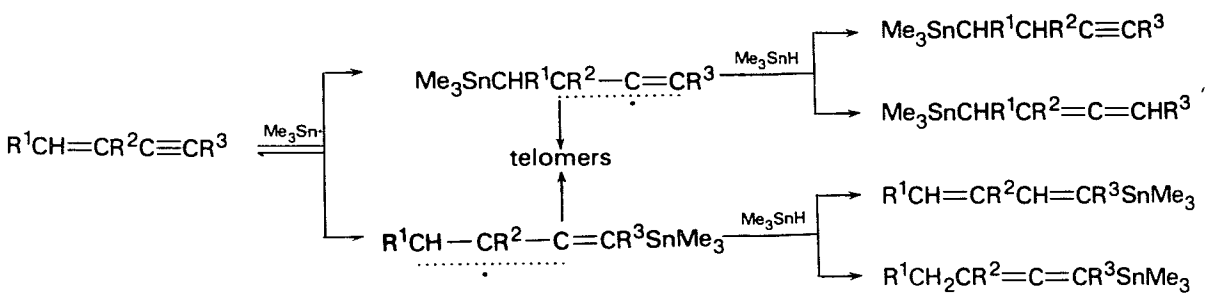
(86)

R^1 = Me, Et, *n*-Bu

R^2 = Me, *n*-Bu, Ph



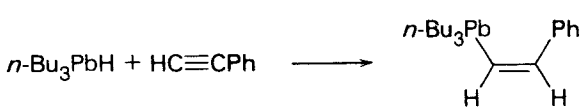
88% (87)



$R^1 = R^2 = R^3$ = H or Me (88)

D. Organolead Hydrides (Plumbanes)

Tri-*n*-butyllead hydride adds to ethylene at low temperatures under high pressure probably via a molecular process[185], whereas the addition of this hydride to conjugated olefins, as well as to phenylacetylene is probably a free-radical process[186] (equation 89).



(89)

VIII. ADDITION OF GROUP V-CENTRED FREE RADICALS

A. Nitrogen-centred Free Radicals

1. Dinitrogen tetroxide

Addition of dinitrogen tetroxide to terminal acetylenes gives rise to unstable reaction products[187–189]; for example, addition of N_2O_4 to propyne dissolved in ether

results in an explosion upon removal of solvent at a low temperature. Diacetylene also reacts violently[188]. N_2O_4 adds to phenylacetylene to give phenyldinitroethylene[190]. This reagent adds readily to nonterminal acetylenes to give mixtures of *cis*- and *trans*-dinitroalkenes in which the latter predominate[187–190] (equation 90). Unsymmetrical disubstituted acetylenes give similar results[189]. Diphenyldiacetylene and 2,4-hexadiyne react with N_2O_4 to give 1,4-dinitro-1,2,3-trienes[188] (equation 91). In the presence of chain-transfer agents like iodine (or other halogens) formation of dinitro adducts does not take place; the apparently formed vinyl free-radical intermediates abstract iodine atoms and form 1-nitro-2-iodoalkenes[190] (equation 92).

$$RC{\equiv}CR \xrightarrow{N_2O_4 \longrightarrow 2\,NO_2\cdot} NO_2CR{=}CRNO_2 \qquad (90)$$

R = Me, Et, *n*-Bu, Ph[187,191]

$$RC{\equiv}C{-}C{\equiv}CR \xrightarrow{N_2O_4 \longrightarrow 2\,NO_2\cdot} NO_2CR{=}C{=}C{=}CRNO_2 \qquad (91)$$

R = Me, Ph

$$PhC{\equiv}CR + \cdot NO_2 \longrightarrow \underset{\cdot}{Ph}\!\!>\!C{=}C\!<\!\begin{matrix}NO_2\\ R\end{matrix} \xrightarrow{I_2} \underset{I}{Ph}\!\!>\!C{=}C\!<\!\begin{matrix}NO_2\\ R\end{matrix} + I\cdot \qquad (92)$$

R = H or Ph

2. *Nitryl chlorides*

Nitryl chlorides add across the triple bond similarly; for example, dichloroacetylene yields 1,1,2-trichloro-2-nitroethylene[192]. Dibutylacetylene and 1-phenyl-2-butylacetylene afforded likewise 1:1 adducts[193]. Phenylacetylene yields 1-chloro-2-nitrostyrene and some by-products[191] (equation 93). This adduct can also be prepared by addition of nitrosyl chloride to phenylacetylene; the reaction affords 1-chloro-2-nitrosostyrene which is oxidized in the course of the reaction[194] (equation 94).

$$PhC{\equiv}CH + \cdot NO_2 \longrightarrow \underset{\cdot}{Ph}\!\!>\!C{=}C\!<\!\begin{matrix}NO_2\\ H\end{matrix} \xrightarrow{NO_2Cl} \underset{Cl}{Ph}\!\!>\!C{=}C\!<\!\begin{matrix}NO_2\\ H\end{matrix} + \cdot NO_2 \qquad (93)$$

$$PhC{\equiv}CH + NOCl \longrightarrow PhCCl{=}CHNO \xrightarrow{NOCl} PhCCl{=}CHNO_2 \qquad (94)$$

3. N-*Chloramines*

Addition of *N*-chloramines to acetylenes, which was first reported by Minisci and coworkers[195,196], proceeds via a redox process in the presence of iron, copper or titanium salt catalysts and concentrated sulphuric acid; the ligand-transfer mechanism shown in equation (95) has been proposed[195–199]. The *N*-chloramines are

$$R_2NCl + Fe^{II} \longrightarrow R_2N\cdot + Fe^{III}(Cl) \qquad (95a)$$

$$R_2N\cdot + {-}C{\equiv}C{-} \longrightarrow R_2N{-}\underset{|}{C}{=}\dot{C}{-} \qquad (95b)$$

$$R_2N{-}\underset{|}{C}{=}\dot{C}{-} + Fe^{III}(Cl) \longrightarrow R_2N{-}\underset{|}{C}{=}CCl{-} + Fe^{II} \qquad (95c)$$

actually protonated, and the acetylenic carbon is attacked by dialkylaminium ion-radicals, e.g. $R_2\dot{N}H^+$. The chloroamination of simple acetylenes, which has also been thoroughly studied by Neale[199], leads to the formation of β-chloroenamines, which hydrolyse on work-up to α-chloro aldehydes or ketones (equation 96).

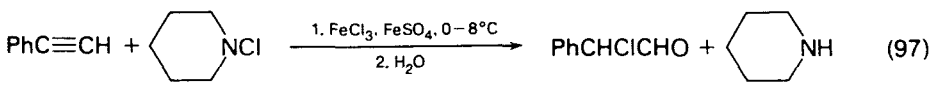
$$R^1C{\equiv}CR^2 + R^3R^4NCl \longrightarrow [R^1CCl{=}CR^2{-}NR^3R^4] \longrightarrow R^1CHClC(=O)R^2 \quad (96)$$

R^1 = $ClCH_2$, Et, *n*-Pr, *n*-Bu, *t*-Bu, Ph

R^2 = H, Me, Et

R^3 and R^4 = various dialkyls, cycloalkyl and piperidine[195,199]

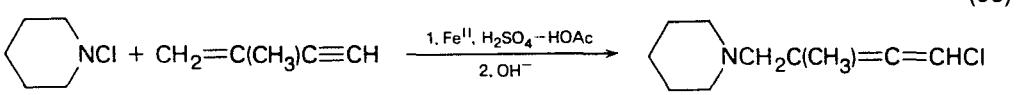
Addition of *N*-chloropiperidine to phenylacetylene results in the formation of α-chloro-α-phenylacetaldehyde[197] (equation 97). Addition of hydroxylamine-*O*-sulphonic acid to phenylacetylene in the presence of ferrous chloride affords



(97)

analogously the same product[195b] (equation 98). Poutsma and Ibarbia have obtained an allenic chloride by adding *N*-chloropiperidine to a conjugated enyne[200] (equation 99). A parallel reaction with $CH_2{=}CHC{\equiv}CH$ gives a complex mixture; the allenic analogue is obtained in a very poor yield[200].

$$PhC{\equiv}CH + H_2NOSO_3H \xrightarrow{FeCl_2} PhCCl{=}CHNH_2 \xrightarrow{H_2O} PhCHClCHO + NH_3 \quad (98)$$



70% (99)

4. Difluoramination

Tetrafluorohydrazine reacts with acetylene to produce α-fluoro-α-difluoraminofluorimines. These products are presumably formed by a rearrangement of the original α,β-bis(difluoramino) adduct. Diphenylacetylene also reacts thermally with tetrafluorohydrazine to yield a 1:1 rearrangement product[201] (equation 100). Dimethyl acetylenedicarboxylate reacts with this reagent in

$$PhC{\equiv}CPh + F_2NNF_2 \xrightarrow[\text{in } CH_2Cl_2]{80°C} [PhC(NF_2){=}C(NF_2)Ph] \longrightarrow PhCFC(=NF)Ph \quad (100)$$

52%

tetrachloroethane at 120°C under pressure to give $MeO_2CCF(NF_2)C(=NF)CO_2Me$. Isopropenylacetylene reacts smoothly with N_2F_4 to produce the mixture shown in equation (101)[201].

Irradiation of tetrafluorohydrazine [photodifluoramination (equation 102)] with methylacetylene yields, in addition to propargyldifluoramine [$CH_2(NF_2)C{\equiv}CH$], which is a substitution product, two regioisomeric adducts; these unstable vinyldifluoramines rearrange into the corresponding *N*-fluorimines; the latter products undergo dehydrofluorination and cleavage according to the pathways suggested in

$$CH_2{=}C(Me)C{\equiv}CH + F_2NNF_2 \longrightarrow CH_2NF_2C(Me)(NF_2)C{\equiv}CH + [CH_2(NF_2)C(Me){=}C{=}CHNF_2]$$

$$\downarrow$$

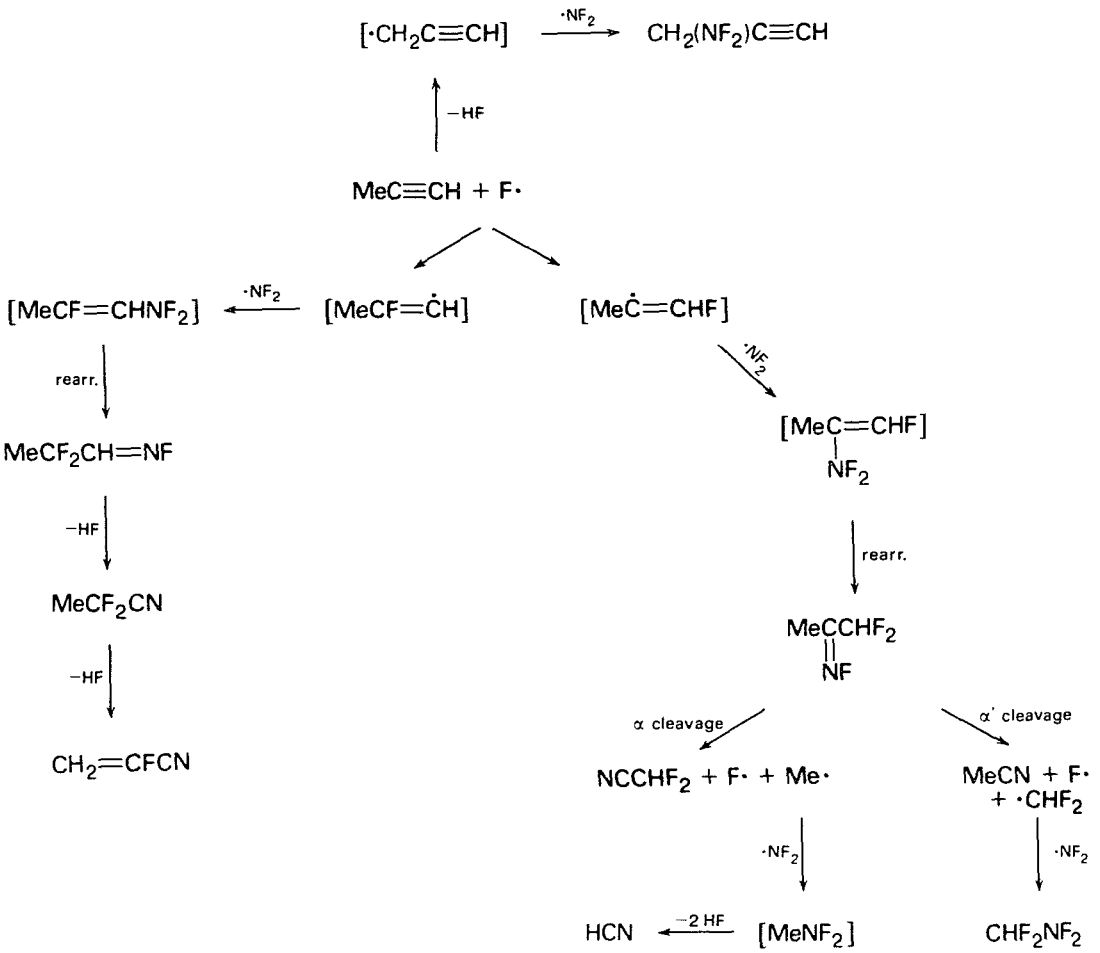
$$CH_2(NF_2)C(Me){=}CFCH{=}NF$$

major product

(101)

$$2\,N_2F_4 \xrightarrow{h\nu} 2\cdot NF_2 + N_2F_2 + 2\,F\cdot \qquad (102)$$

Scheme (11)[202]. Photodifluoramination of 2-butyne affords a rearranged addition product[205] (equation 103).



SCHEME 11

$$MeC{\equiv}CMe \xrightarrow[N_2F_4]{h\nu} [MeCF{=}C(NF_2)Me] \longrightarrow MeCF_2C(=NF)Me \quad (103)$$

B. Phosphorus-centred Free Radicals

The homolytic cleavage of the P—H bond occurs more readily than that of the P—Cl bond[204]. Only very few examples of free-radical addition of phosphorus compounds across the C≡C bond have been reported.

1. Phosphines

Addition of mono- or di-substituted phosphines to terminal acetylenes in the presence of azobis(isobutyronitrile) yields vinyl phosphorus derivatives[205] (equation 104).

$$R^1R^2PH + HC{\equiv}CR^3 \xrightarrow{AIBN} \underset{27-30\%}{R^1R^2PCH{=}CHR^3} \quad (104)$$

$R^1 = R^2 = H, NCCH_2CH_2$

$R^3 = n\text{-}C_5H_{11}, n\text{-}C_6H_{13}$

2. Phosphorus trichloride

Phosphorus trichloride adds to acetylenes in the presence of large amounts of oxygen to form β-chlorovinyl phosphonyl chlorides (equation 105). Acetylene itself yields the diphosphonyl chloride as well[206].

$$RC{\equiv}CH + PCl_3 + 1/2\,O_2 \longrightarrow RCCl{=}CHPOCl_2 \quad (105)$$

$R = H, n\text{-Bu}, Ph$

3. Other organophosphorus compounds

The peroxide-initiated addition of organophosphorus compounds having a reactive hydrogen atom, e.g. partial esters of phosphorous acid, thiophosphorous acid and phosphinic acids, to alkynes results in the formation of the corresponding 1,2-diphosphonoalkanes in good yields[207] (equation 106). Ethylenediphosphinates have been prepared under similar conditions[208] (equation 107).

$$R^1(R^2O)P(X)H + HC{\equiv}CR^3 \longrightarrow R^1(R^2O)P(X)CH{=}CHR^3$$

$$\downarrow R^1(R^2O)P(X)H \quad (106)$$

$$[R^1(R^2O)P(X)]_2CHCH_2R^3 + R^1(R^2O)P(X)CH_2CHR^3P(X)R^1(OR^2)$$

$X = O, S$

$R^1 = Et, OMe, OEt$

$R^2 = Me, Et$

$R^3 = n\text{-Bu}, C_5H_{11}, Ph$

$$R(Me_2CHCH_2O)POH + HC{\equiv}CH \xrightarrow[\text{or UV at } 120-90^\circ C]{t\text{-}Bu_2O_2} [R(Me_2CHCH_2O)P(O)CH_2]_2$$

$$R = Me \text{ or } Ph \qquad (107)$$

IX. REFERENCES

1. C. Walling, *Free Radicals in Solution*, John Wiley and Sons, New York, 1957.
2. W. A. Pryor, *Free Radicals*, McGraw-Hill, New York, 1966.
3. G. Sosnovksy, *Free Radical Reactions in Preparative Organic Chemistry*, Macmillan, New York, 1964.
4. E. S. Huyser, *Free Radical Chain Reactions*, Wiley–Interscience, New York, 1970.
5. J. K. Kochi (Ed.), *Free Radicals*, Vols. 1 and 2, Wiley–Interscience, New York, 1973.
6. W. A. Waters (Ed.), *Free Radical Reactions: MTP International Review of Science, Organic Chemistry Series One* (1973) and *Series Two* (1975), Vol. 10, Butterworths, London.
7. D. C. Nonhebel and J. C. Walton, *Free Radical Chemistry*, Cambridge University Press, Cambridge, 1974.
8. D. C. Nonhebel, J. M. Tedder and J. C. Walton, *Radicals*, Cambridge University Press, Cambridge, 1979.
9. C. Walling and E. S. Huyser in *Organic Reactions*, Vol. 13 (Ed. A. C. Cope), John Wiley and Sons, New York, 1963, Chap. 3.
10. F. W. Stacey and J. F. Harris, Jr. in *Organic Reactions*, Vol. 13 (Ed. A. C. Cope), John Wiley and Sons, New York, 1963, Chap. 4.
11. P. I. Abell in *Free Radicals*, Vol. 2 (Ed. J. K. Kochi), Wiley–Interscience, New York, 1973, p. 100.
12. D. I. Davis in *Free Radical Reactions: MTP International Review of Science, Organic Chemistry, Series One*, Vol. 10 (Ed. W. A. Waters), Butterworths, London, 1973, pp. 56–57.
13. M. Julia in *The Chemistry of Acetylenes* (Ed. H. G. Viehe), Marcel Dekker, New York, 1969, Chap. 5.
14. J. I. G. Cadogan and M. J. Perkins in *The Chemistry of Alkenes* (Ed. S. Patai), John Wiley and Sons, London, 1964, Chap. 9.
15. P. M. Hergenrother, *J. Macromol. Sci., Rev. Macromol. Chem.*, **C19**, 1 (1980).
16. G. Wegner, *Z. Naturforsch.*, **B24**, 824 (1969); *Makromol. Chem.*, **145**, 85 (1971); **154**, 35 (1972); *Chimia*, **28**, 475 (1974); *Pure Appl. Chem.*, **49**, 443 (1977); in *Molecular Metals* (Ed. W. E. Hatfield), Plenum, New York, 1979, pp. 209–242.
17. R. H. Baughman, *J. Appl. Phys.*, **43**, 4362 (1972); *J. Polym. Sci., Polym. Phys. Ed.*, **12**, 1511 (1974); *Contemporary Topics in Polymer Science*, Vol. 2 (Eds. E. M. Pearce and J. R. Schaefgen), Plenum, New York, 1977, pp. 205–233.
18. R. R. Chance and G. N. Patel, *J. Polym. Sci., Polym. Phys. Ed.*, **16**, 859 (1978).
19. G. N. Patel, R. R. Chance, E. A. Turi and Y. P. Khanna, *J. Amer. Chem. Soc.*, **100**, 6644 (1978).
20. Y. Hori and L. D. Kispert, *J. Amer. Chem. Soc.*, **101**, 3173 (1979).
21. R. R. Chance, R. H. Baughman, H. Müller and C. J. Eckhardt, *J. Chem. Phys.*, **67**, 3616 (1977).
22. R. R. Chance, *Macromolecules*, **13**, 396 (1980).
23. J. I. Dickstein and S. I. Miller in *The Chemistry of the Carbon—Carbon Triple Bond*, Part 2 (Ed. S. Patai), John Wiley and Sons, Chichester, 1978, pp. 819–826, and references therein.
24. D. V. Banthorpe, *Elimination Reactions*, Elsevier, Amsterdam, 1963, p. 142.
25. B. A. Bohm and P. I. Abell, *Chem. Rev.*, **62**, 599 (1962).
26. D. Griller and K. U. Ingold, *J. Amer. Chem. Soc.*, **96**, 6203 (1974); *Acc. Chem. Res.*, **9**, 13 (1976).
27. A. A. Oswald, K. Griesbaum, B. E. Hudson, Jr., and J. M. Bregman, *J. Amer. Chem. Soc.*, **86**, 2877 (1964).
28. J. A. Kampmeier and G. Chen, *J. Amer. Chem. Soc.*, **87**, 2608 (1965).

29. A. A. Oswald and K. Griesbaum in *The Chemistry of Organic Sulphur Compounds*, Vol. 2 (Eds. N. Kharasch and C. Y. Meyers), Pergamon Press, Oxford, 1966, p. 246.
30. K. Griesbaum, *Angew. Chem. (Intern. Ed.)*, **9**, 273 (1970).
31. R. M. Kopchik and J. A. Kampmeier, *J. Amer. Chem. Soc.*, **90**, 6733 (1968).
32. D. K. Wedegaertner, R. M. Kopchik, and J. A. Kampmeier, *J. Amer. Chem. Soc.*, **93**, 6890 (1971).
33. L. A. Singer and N. P. Kong, *Tetrahedron Letters*, 643 (1967); *J. Amer. Chem. Soc.*, **89**, 5251, 6805 (1967).
34. E. I. Heiba and R. M. Dessau, *J. Amer. Chem. Soc.*, **89**, 3772 (1967).
35. G. D. Sargent and M. W. Browne, *J. Amer. Chem. Soc.*, **89**, 2788 (1967).
36. J. I. Dickstein and S. I. Miller in *The Chemistry of the Carbon—Carbon Triple Bond*, Part 2 (Ed. S. Patai), John Wiley and Sons, Chichester, 1978, pp. 816–819, and references therein.
37. S. Nagase and C. W. Kern, *J. Amer. Chem. Soc.*, **102**, 4513 (1980).
38. M. S. Kharasch and F. R. Mayo, *J. Amer. Chem. Soc.*, **55**, 2468 (1933).
39. M. S. Kharasch, J. G. McNab and M. C. McNab, *J. Amer. Chem. Soc.*, **57**, 2463 (1935).
40. P. L. Harris and J. C. Smith, *J. Chem. Soc.*, 1572 (1935).
41. C. A. Young, R. R. Vogt and J. A. Nieuwland, *J. Amer. Chem. Soc.*, **58**, 1806 (1936).
42. J. Verhulst and J. C. Jungers, *Bull. Soc. Chim. Belg.*, **58**, 73 (1949).
43. R. N. Haszeldine, *J. Chem. Soc.*, 3490 (1952).
44. H. Kasiwagi, *Bull. Chem. Soc. Japan*, **25**, 81 (1952); **31**, 985 (1958).
45. C. Walling, M. S. Kharasch and F. R. Mayo, *J. Amer. Chem. Soc.*, **61**, 1711 (1939).
46. (a) P. S. Skell and R. G. Allen, *J. Amer. Chem. Soc.*, **80**, 5997 (1958).
(b) P. S. Skell and R. G. Allen, *J. Amer. Chem. Soc.*, **86**, 1559 (1964).
47. K. R. Kopecky and S. Grover, *Can. J. Chem.*, **47**, 3153 (1969).
48. L. D. Bergel'son, *Ivz. Akad. Nauk SSSR, Ser. Khim.*, 1499 (1958); *Bull. Acad. Sci. USSR, Chem. Sect. (Engl. Transl.)*, 1145 (1960).
49. C. Walling, L. D. Heaton and D. D. Tanner, *J. Amer. Chem. Soc.*, **87**, 1715 (1965).
50. M. L. Poutsma, *Science*, **157**, 997 (1967); in *Methods in Free Radical Chemistry*, Vol. 1 (Ed. E. S. Huyser), Marcel Dekker, New York, 1969, Chap. 3; in *Free Radicals*, Vol. 2 (Ed. J. K. Kochi), Wiley–Interscience, New York, 1973, pp. 204–209.
51. M. L. Poutsma, *Tetrahedron Letters*, 2925 (1969).
52. L. R. Byrd and M. C. Caserio, *J. Amer. Chem. Soc.*, **92**, 5422 (1970).
53. G. Peiffer, *Bull. Soc. Chim. Fr.*, 537, 540 (1963).
54. M. L. Poutsma and P. A. Ibarbia, *J. Org. Chem.*, **35**, 4038 (1970).
55. A. D. Petrov, S. I. Sadykhzade and Yu, P. Egorov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 722 (1954); *Bull. Acad. Sci. USSR, Chem. Sect. (Engl. Transl.)*, 621 (1954).
56. K. Peters and L. Neumann, *Angew. Chem.*, **45**, 261 (1932).
57. A. T. Morse and L. C. Leitch, *Can. J. Chem.*, **33**, 6 (1955).
58. M. L. Poutsma, *J. Amer. Chem. Soc.*, **87**, 2161, 2172, 4285 (1965); in *Methods in Free Radical Chemistry*, Vol. 1 (Ed. E. S. Huyser), Marcel Dekker, New York, 1969, p. 178.
59. M. L. Poutsma and J. L. Kartch, *Tetrahedron*, **22**, 2167 (1966).
60. R. N. Haszeldine, *J. Chem. Soc.*, 2504 (1952).
61. I. N. Nazarov and L. D. Bergel'son, *Zh. Obshch. Khim.*, **27**, 1540 (1957); *J. Gen. Chem. USSR (Engl. Transl.)*, **27**, 1614 (1957); *Izv. Akad. Nauk. SSSR, Ser. Khim.*, 887, 896 (1960); *Bull. Acad. Sci. USSR, Chem. Sect. (Engl. Transl.)*, 826, 834 (1960).
62. L. D. Bergel'son, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1066 (1960); *Bull. Acad. Sci. USSR, Chem. Sect. (Engl. Transl.)*, 1145 (1960).
63. W. A. Thaler in *Methods in Free Radical Chemistry*, Vol. 2 (Ed. E. S. Huyser), Marcel Dekker, New York, 1969, p. 198.
64. M. S. Kharasch, E. V. Jensen and W. H. Urry, *Science*, **102**, 128 (1945); *J. Amer. Chem. Soc.*, **69**, 1100 (1947).
65. M. S. Kharasch, J. J. Jerome and W. H. Urry, *J. Org. Chem.*, **15**, 966 (1950).
66. Y. Amiel, unpublished work: reaction was carried out by using acetonitrile as a cosolvent, under conditions similar to those described by M. Asscher and D. Vofsi [*J. Chem. Soc.*, 1887 (1963)] for the preparation of 1:1 carbon tetrachloride–styrene adduct (which gave 93% yield).
67. J. K. Kochi and D. M. Mog, *J. Amer. Chem. Soc.*, **87**, 522 (1965).

68. I. B. Afanas'ev, N. G. Baranova and G. I. Samokhvalov, *Zh. Org. Khim.*, **8**, 2449 (1972); *J. Org. Chem. USSR (Engl. Transl.)*, **8**, 2497 (1972).
69. E. C. Ladd, *U.S. Patent*, No. 2,554,533 (1951); *Chem. Abstr.*, **45**, 9556 (1951).
70. J. H. Wotiz, F. Huba and R. Vendley, *J. Org. Chem.*, **26**, 1626 (1961).
71. M. G. Voronkov, A. M. Sklyanova, E. O Tsetlina and R. G. Mirskov, *Zh. Obshch. Khim.*, **43**, 682 (1973); *J. Gen. Chem. USSR (Engl. Transl.)*, **43**, 679 (1973).
72. R. G. Sultangareev, Yu. G. Kryazev and M. A. Kuznetsova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2326 (1969); *Bull. Acad. Sci. USSR, Chem. Sect. (Engl. Transl.)*, 2182 (1969).
73. R. N. Haszeldine, *J. Chem. Soc.*, 922 (1953).
74. C. J. Brookes, P. L. Coe, A. E. Pedler and J. C. Tatlow, *J. Chem. Soc, Perkin I*, 202 (1978).
75. R. N. Haszeldine, *J. Chem. Soc.*, 3037 (1950); 588 (1951).
76. K. Leedham and R. N. Haszeldine, *J. Chem. Soc.*, 1261, 1634 (1954).
77. J. D. Park, F. E. Rogers and J. R. Lacher, *J. Org. Chem.*, **26**, 2089 (1961).
78. H. H. Evans, R. Fields, R. N. Haszeldine and M. Illingworth, *J. Chem. Soc., Perkin I*, 649 (1973).
79. R. N. Haszeldine and K. Leedham, *J. Chem. Soc.*, 3483 (1952).
80. G. V. D. Tiers, *J. Org. Chem.*, **27**, 2261 (1962).
81. H. H. Schlubach, V. Franzen and E. Dahl, *Ann. Chem.*, **587**, 124 (1954).
82. E. Montaudon, C., Gardrat and R. Lalande, *Compt. Rend.*, **C278**, 137 (1974).
83. C. Gardrat, E. Montaudon and R. Lalande, *Compt. Rend.*, **C278**, 1349 (1974).
84. E. Montaudon, C. Gardrat and R. Lalande, *Compt. Rend.*, **C278**, 367 (1974).
85. J. S. Bradshaw, R. D. Knudsen and W. W. Parish, *J. Org. Chem.*, **40**, 529 (1975).
86. R. H. Wiley and J. R. Harrell, *J. Org. Chem.*, **25**, 903 (1960).
87. M. G. Vinogradov, S. P. Verenchikov, T. M. Fedorova and G. I. Nikishin, *Zh. Org. Khim.*, **11**, 947 (1975); *J. Org. Chem. USSR (Engl. Transl.)*, **11**, 937 (1975).
88. M. G. Vinogradov, P. A. Direi and G. I. Nikishin, *Zh. Org. Khim.*, **13**, 2498 (1977); *J. Org. Chem. USSR (Engl. Transl.)*, **13**, 2323 (1977).
89. N. I. Shuikin, B. L. Lebedev and V. G. Nikol'skii, *Izv. Akad. Nauk SSSR, Ser Khim.*, 396 (1965); *Bull. Acad. Sci. USSR, Chem. Sect. (Engl. Transl.)*, 386 (1965).
90. J. DiPietro and W. J. Roberts, *Can. J. Chem.*, **44**, 2241 (1966).
91. B. Fell and H. H. Vogel, *Synthesis*, 76 (1969).
92. M. Julia and C. James, *Compt. Rend.*, **255**, 959 (1962).
93. H. Noerenberg, H. Kratzin, P. Boldt and W. S. Sheldrick, *Chem. Ber.*, **110**, 1284 (1977).
94. J. K. Hoffman, *U.S. Patent*, No. 3,304,247 (1967); *Chem. Abstr.*, **66**, 75,668 (1967).
95. I. B. Afanas'ev, M. B. Levinskii, and G. I. Samokhvalov, *Zh. Org. Khim.*, **10**, 1375 (1974); *J. Org. Chem. USSR (Engl. Transl.)*, **10**, 1388 (1974).
96. G. I. Nikishin and V. D. Vorob'ev, *Izv. Adad. Nauk SSSR, Ser. Khim.*, 892 (1962); *Bull. Acad. Sci. USSR (Engl. Transl.)*, 831 (1962).
97. E. Montaudon and R. Lalande, *Bull. Soc. Chim. Fr.*, 2635 (1974).
98. R. Lalande, B. Clin and B. Maillard, *Compt. Rend.*, **C278**, 963 (1974).
99. W. Bartok and P. J. Lucchesi, *J. Amer. Chem. Soc.*, **81**, 5918 (1959).
100. N. F. Cywinski and H. J. Hepp, *J. Org. Chem.*, **30**, 3814 (1965).
101. N. T. Sultanov, M. K. Mamedov, S. D. Mekhtiev and Sh. Ya. Khodzhaeva, *Azerb. Khim. Zh.*, 100 (1975); *Chem. Abstr.*, **83**, 78744 (1975).
102. M. F. Shostakovskii, A. V. Bogdanova and G. I. Plotnikova, *Usp. Khim.*, **33**, 129 (1964); *Russ. Chem. Rev. (Engl. Transl.)*, **33**, 66 (1964).
103. E. N. Prilezhaeva and M. F. Shostakovskii, *Usp. Khim.*, **32**, 897 (1963); *Russ. Chem. Rev. (Engl. Transl.)*, **32**, 399 (1963).
104. E. I. Heiba and R. M. Dessau, *J. Org. Chem.*, **32**, 3837 (1967).
105. C. Sivertz, W. Andrews, E. Elsdon and K. Graham, *J. Pol. Sci.*, **19**, 587 (1956).
106. C. Sivertz, *J. Phys. Chem.*, **63**, 34 (1959).
107. C. Walling and W. Helmreich, *J. Amer. Chem. Soc.*, **81**, 1144 (1959).
108. Y. C. Liu and T. I. Chang, *Hua Hsueh Hsueh Pao*, **30**, 197 (1964); *Chem. Abstr.*, **61**, 8217 (1964).
109. W. E. Truce, H. G. Klein, and R. B. Kruse, *J. Amer. Chem. Soc.*, **83**, 4636 (1961).
110. H. J. Alkema and J. F. Arens, *Rec. Trav. Chim.*, **79**, 1257 (1960).
111. J. F. Arens, *Advances in Organic Chemistry*, Vol. 2 (Eds. R. A. Raphael, E. C. Taylor and H. Wynberg), Interscience, New York, 1960, pp. 117–212.

112. E. P. Kohler and H. Potter, *J. Amer. Chem Soc.*, **57**, 1316 (1935).
113. L. I. Smith and H. R. Davis, Jr., *J. Org. Chem.*, **15**, 824 (1950).
114. H. Behringer, *Ann. Chem.*, **564**, 219 (1949).
115. A. T. Blomquist and J. Wolinsky, *J. Org. Chem.*, **23**, 551 (1958), and references therein.
116. H. Bader, *J. Chem. Soc.*, 116 (1956).
117. B. Weibull, *Arkiv Kemi*, **3**, 225 (1951); *Chem. Abstr.*, **46**, 3965 (1952).
118. L. N. Owen and M. U. S. Sultanbawa, *J. Chem. Soc.*, 3109 (1949).
119. Y. C. Liu and S. K. Wang, *K'o Hsüeh T'ung Pao*, 206 (1957); *Chem. Abstr.*, **53**, 9115 (1959).
120. K. Griesbaum, A. A. Oswald, E. R. Quiram and N. Naegele, *J. Org. Chem.*, **28**, 1952 (1963).
121. J. C. Sauer, *J. Amer. Chem. Soc.*, **79**, 5314 (1957).
122. K. Yamagishi, T. Tanaka and T. Hoshino, *Bull. Chem. Soc. Japan*, **29**, 447 (1956); **30**, 455 (1957).
123. L. W. C. Miles and L. N. Owen, *J. Chem. Soc.*, 817 (1952).
124. M. F. Shostakovskii, E. N. Prilezhaeva, L. V. Tsymbal and L. G. Stolyarova, *Zh. Obshch. Khim.*, **30**, 3143 (1960); *J. Gen. Chem. USSR (Engl. Transl.)*, **30**, 3116 (1960).
125. T. L. Jacobs and G. E. Illingworth, Jr., *J. Org. Chem.*, **28**, 2692 (1963).
126. H. Bader, L. C. Cross, I. Heilbron and E. R. H. Jones, *J. Chem. Soc.*, 619 (1949).
127. T. L. Cairns and J. C. Sauer, *U.S. Patent*, No. 2,776,995 (1957); *Chem. Abstr.*, **51**, 9679 (1957).
128. N. P. Petukhova and E. N. Prilzhaeva, *Zh. Org. Khim.*, **2**, 1947 (1966); *J. Org. Chem. USSR (Engl. Transl.)*, **2**, 1914 (1966).
129. J. F. Arens, H. C. Volger, T. Doornbos, J. Bonnema, J. W. Greidanus and J. H. V. D. Hende, *Rec. Trav. Chim.*, **75**, 1459 (1956).
130. H. C. Volger and J. F. Arens, *Rec. Trav. Chim.*, **77**, 1170 (1958).
131. M. F. Shostakovskii, A. V. Bogdanova, G. I. Plotnikova and N. S. Andre'ev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1279 (1960); *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)*, 1185 (1960).
132. E. N. Prilezhaeva, I. I. Guseinov, B. V. Lopatin and M. F. Shostakovskii, *Zh. Obshch. Khim.*, **29**, 3227 (1959); *J. Gen. Chem. USSR (Engl. Transl.)*, **29**, 3189 (1959).
133. I. G. Sulimov and A. A. Petrov, *Zh. Org. Khim.*, **2**, 767 (1966); *J. Org. Chem. USSR (Engl. Transl.)*, **2**, 770 (1966).
134. W. H. Carothers, *J. Amer. Chem. Soc.*, **55**, 2008 (1933).
135. F. W. Stacey and J. F. Harris, Jr., *J. Amer. Chem. Soc.*, **85**, 963 (1963).
136. O. P. Strausz, T. Hikida and H. E. Gunning, *Can. J. Chem.*, **43**, 717 (1965).
137. A. Lüttringhaus, U. Schmidt and H. Alpes, *Angew. Chem.*, **69**, 138 (1957).
138. Y. Takezaki and A. Kawakita, *Bull. Inst. Chem. Res. Kyoto Univ.*, **38**, 290 (1960); *Chem. Abstr.*, **55**, 19429 (1961).
139. J. L. Wood in *Organic Reactions*, Vol. 3 (Ed. R. Adams), John Wiley and Sons, New York, 1946, p. 246.
140. W. H. Meuller, *Angew. Chem. (Intern. Ed.)*, **8**, 482 (1969).
141. L. P. Rasteikiene, D. I. Greiciute, M. G. Lin'kova and I. L. Knunyants, *Usp. Khim.*, **46**, 1041 (1977); *Russ. Chem. Rev. (Engl. Transl.)*, **46**, 556 (1977).
142. R. C. Fahey, *Topics Stereochem.*, **3**, 304 (1968).
143. C. G. Krespan, *J. Amer. Chem. Soc.*, **83**, 3434 (1961).
144. J. R. Case, N. H. Ray and H. L. Roberts, *J. Chem. Soc.*, 2066, 2070 (1961).
145. H. L. Roberts, *Quart. Rev. (London)*, **15**, 40 (1961).
146. Y. Amiel, *Abstracts of Papers, Second International Symposium on Organic Sulphur Chemistry, Groningen, The Netherlands*, 1966; *Tetrahedron Letters*, 661 (1971); *J. Org. Chem.*, **36**, 3691 (1971).
147. M. Asscher and D. Vofsi, *J. Chem. Soc.*, 4962 (1964).
148. W. Eglinton and W. McCrea, *Advances in Organic Chemistry*, Vol. 4 (Eds. R. A. Raphael, E. C. Taylor and H. Wynberg), Interscience, New York, 1963, p. 225.
149. Y. Amiel, *J. Org. Chem.*, **36**, 3697 (1971).
150. Y. Amiel, *J. Org. Chem.*, **39**, 3867 (1974).
151. G. W. Koeppl., D. S. Sagatys, G. S. Krishnamurthy and S. I. Miller, *J. Amer. Chem. Soc.*, **89**, 3396 (1967).

152. Y. Amiel, unpublished results.
153. W. E. Truce and G. C. Wolf, *Chem. Commun.*, 150 (1969); *J. Org. Chem.*, **36**, 1727 (1971).
154. Y. Amiel, *Abstracts of Papers, Seventh International Symposium on Organic Sulphur Chemistry, Hamburg, Germany*, 1976, p. 118.
155. M. D. Stadnichuk, T. B. Kryukova and A. A. Petrov, *Zh. Obshch. Khim.*, **45**, 838 (1975); *J. Gen. Chem. USSR (Engl. Transl.)*, **45**, 823 (1975).
156. W. J. Wenisch, *Diss. Abstr.*, **18**, 808 (1958).
157. H. Helberger, *Angew. Chem.*, **73**, 69 (1961).
158. I. G. Farbenind, *French Patent*, No. 858,185 (1939).
159. P. G. Clay, G. R. A. Johnson and J. Weiss, *J. Phys. Chem.*, **63**, 862 (1959).
160. C. Walling and G. El-Taliawi, *J. Amer. Chem. Soc.*, **95**, 848 (1973).
161. E. W. Pietrusza, L. H. Sommer and F. C. Whitmore, *J. Amer. Chem. Soc.*, **70**, 484 (1948).
162. C. A. Burkhard and R. H. Krieble, *J. Amer. Chem. Soc.*, **69**, 2687 (1947).
163. G. H. Wagner, *U.S. Patent*, No. 2,637,738 (1953); *Chem. Abstr.*, **48**, 8254 (1954).
164. C. L. Agre, *J. Amer. Chem. Soc.*, **71**, 300 (1949).
165. L. L. Shchukovskaya, A. D. Petrov and Yu. P. Egorov, *Zh. Obsch. Khim.*, **26**, 3338 (1956); *J. Gen. Chem. USSR (Engl. Transl.)*, **26**, 3713 (1956).
166. C. A. Burkhard, *J. Amer. Chem. Soc.*, **72**, 1402 (1950).
167. R. A. Benkeser and R. A. Hickner, *J. Amer. Chem. Soc.*, **80**, 5298 (1958).
168. R. A. Benkeser, M. L. Burrous, L. E. Nelson and J. V. Swisher, *J. Amer. Chem. Soc.*, **83**, 4385 (1961).
169. R. A. Benkeser, *Pure Appl. Chem.*, **13**, 133 (1966).
170. R. A. Benkeser, R. F. Cunico, S. Dunny, P. R. Jones and P. G. Nerlekar, *J. Org. Chem.*, **32**, 2634 (1967).
171. R. A. Benkeser and D. F. Ehler, *J. Organometal. Chem.*, **69**, 193 (1974).
172. H. Sakurai and M. Yamagata, *Chem. Commun.*, 1144 (1970).
173. A. D. Petrov, V. F. Mironov and N. G. Dzhurinskaya, *Dokl. Akad. Nauk SSSR*, **128**, 302 (1959); *Proc. Acad. Sci. USSR, Chem. Sect. (Engl. Transl.)*, **128**, 739 (1959).
174. A. D. Petrov and V. F. Mironov, *Angew. Chem.*, **73**, 59 (1961).
175. M. C. Henry and M. F. Downey, *J. Org. Chem.*, **26**, 2299 (1961).
176. G. J. M. van der Kerk, L. G. A. Luijten and J. G. Noltes, *Chem. Ind. (London)*, 352 (1956).
177. W. P. Neumann and R. Sommer, *Ann. Chem.*, **675**, 10 (1964).
178. W. P. Neumann, *Angew Chem.*, **76**, 849 (1964); *The Organic Chemistry of Tin*, Vol. 1, John Wiley and Sons, London, 1970.
179. E. J. Corey and R. H. Wollenberg, *J. Amer. Chem. Soc.*, **96**, 5581 (1974).
180. J. Kupchik in *Organotin Compounds*, Vol. I (Ed. A. K. Sawyer), Marcel Dekker, New York, 1971, pp. 7–79.
181. H. G. Kuivila, *Adv. Organometal. Chem.*, **1**, 47 (1964).
182. R. F. Fulton, *Diss. Abstr.*, **22**, 3397 (1962).
183. A. J. Leusink, H. A. Budding and W. Drenth, *J. Organometal. Chem.*, **9**, 295 (1967); **11**, 533, 541 (1968).
184. M. L. Poutsma and P. A. Ibarbia, *J. Amer. Chem. Soc.*, **95**, 6000 (1973).
185. W. P. Neumann and K. Kühlein, *Angew. Chem. (Intern. Ed.)*, **4**, 784 (1965).
186. R. A. Jackson, *Essays on Free-Radical Chemistry*, Special Publication No. 24. The Chemical Society London, 1970, p. 312.
187. K. N. Campbell, J. Shavel, Jr. and B. K. Campbell, *J. Amer. Chem. Soc.*, **75**, 2400 (1953).
188. H. H. Schlubach and W. Rott, *Ann. Chem.*, **594**, 59 (1955).
189. J. P. Freeman and W. D. Emmons, *J. Amer. Chem. Soc.*, **79**, 1712 (1957).
190. T. E. Stevens and W. D. Emmons, *J. Amer. Chem. Soc.*, **80**, 338 (1958).
191. H. Wieland and E. Blümich, *Ann. Chem.*, **424**, 100 (1921).
192. H. Brintziger and K. Pfannstiel, *Z. Anorg. Chem.*, **255**, 325 (1945).
193. H. H. Schlubach and A. Braun, *Ann. Chem.*, **627**, 28 (1959).
194. R. Perrot and R. Berger, *Compt. Rend.*, **C235**, 185 (1952).
195. (a) F. Minisci and R. Galli, *Chim. Ind. (Milan)*, **46**, 546 (1964); *Tetrahedron Letters*, 167, 3197 (1964).
(b) F. Minisci and R. Galli, *Tetrahedron Letters*, 1679 (1965).
196. F. Minisci, R. Galli and G. Pollina, *Chim. Ind. (Milan)*, **47**, 736 (1965).

197. F. Minisci, R. Galli and M. Cecere, *Chim. Ind. (Milan)*, **48**, 132 (1966).
198. F. Minisci, *Synthesis*, 1 (1973); *Acc. Chem. Res.*, **8**, 165 (1975).
199. R. S. Neale, *J. Amer. Chem. Soc.*, **86**, 5340 (1964); *J. Org. Chem.*, **32**, 3263, 3273 (1967) and preceding papers.
200. M. L. Poutsma and P. A. Ibarbia, *J. Org. Chem.*, **36**, 2572 (1971).
201. R. C. Petry, C. O. Parker, F. A. Johnson, T. E. Stevens and J. P. Freeman, *J. Org. Chem.*, **32**, 1534 (1967).
202. C. L. Bumgardner and E. L. Lawton, *Acc. Chem. Res.*, **7**, 14 (1974).
203. C. L. Bumgardner, *Tetrahedron Letters*., 3683 (1964).
204. Reference 1, p. 341.
205. M. M. Rauhut, H. A. Currier, A. M. Semsel and V. P. Wystrach, *J. Org. Chem.*, **26**, 5138 (1961).
206. Yu. M. Zinov'ev, L. I. Muler and L. Z. Soborovskii, *Zh. Obshch. Khim.*, **24**, 380 (1954); *J. Gen. Chem. USSR, (Engl. Transl.)*, **24**, 391 (1954).
207. A. N. Pudovik and O. S. Shulyndina, *Zh. Obshch. Khim.*, **39**, 1014 (1969); *J. Gen. Chem. USSR, (Engl. Transl.)*, **39**, 986 (1969).
208. H. J. Kleiner and W. Rupp, *German Patent.*, N. 2,302,523 (1974); *Chem. Abstr.*, **81**, 136299 (1974).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 11

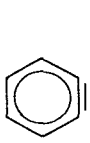
Arynes

THOMAS L. GILCHRIST
Department of Organic Chemistry, University of Liverpool, England

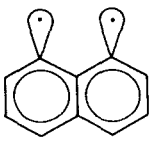
I. INTRODUCTION

Arynes are a group of reactive intermediates which are formally derived from carbocyclic aromatic compounds by the removal of two *ortho* substituents. Benzyne

(**1**) is the parent member of the group: its representation as (**1**) implies that the aromatic sextet is substantially preserved and that there is significant bonding interaction between the two *ortho* positions. This representation seems to be a valid one, as will be shown later. The result is that the molecule possesses a partial triple bond between the unsubstituted *ortho* carbon atoms: hence the 'yne' nomenclature which emphasizes the acetylenic character of these intermediates. An alternative way of naming this group of intermediates is to prefix the name of the aromatic system with 'dehydro-'; thus **1** is named 'dehydrobenzene' or, strictly, '1,2-dehydrobenzene' in order to specify which substituents are absent. Some intermediates have been postulated in which substituents are absent from nonadjacent carbon atoms, 1,8-dehydronaphthalene (**2**) being an example. Such species have been excluded from this review because of the lack of any relationship to acetylenes.



(**1**)



(**2**)

A great deal of fundamental research on the generation and properties of arynes was carried out in the 1950s and 1960s. Much of this work has been summarized by R. W. Hoffmann, in a comprehensive review published in 1967[1], and in a later review[2]. The purpose of the present article is to give a summary of the current picture of aryne chemistry. Most of the references are taken from the period 1970–1979, the literature having been covered up to the end of 1979. Little direct reference is made to earlier work since this is accessible from Hoffmann's reviews. Convincing evidence for the existence of arynes as intermediates in a variety of reactions was produced before 1970. In recent work the emphasis has shifted towards a more detailed investigation of the structures and bonding properties of arynes, and of the mechanisms of their reactions. Benzyne and other arynes have increasingly been regarded as routine synthetic intermediates, particularly for Diels–Alder and other cycloadditions and in reactions with nucleophiles, since there are now a number of convenient and well-established methods for their generation. The emphasis in this review will therefore be on these aspects of aryne chemistry rather than on the pioneering work which established the existence of arynes as intermediates.

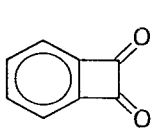
Several other short general reviews of aryne chemistry have been published since Hoffmann's book appeared[3].

II. THE STRUCTURE OF BENZYNE

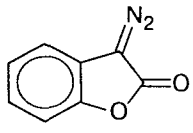
Benzyne can be generated in a nitrogen matrix at low temperatures and its lifetime is then sufficient for its infrared spectrum to be recorded. Chapman and his coworkers studied the matrix photolysis of benzocyclobutanedione (**3**) and were able to record a spectrum which they attributed to benzyne[4]. A later study, using the diazolactone (**4**) as the benzyne precursor, supported the earlier work, giving a spectrum with maxima at 1627, 1607, 1451, 1053, 1038, 849, 736 and 469 cm^{-1} and with an absorption at 2085 cm^{-1} which was attributed to a C≡C stretching vibration[5]. More recent independent work has confirmed all these absorptions, except that at 1627 cm^{-1}, as being assignable to benzyne[6]. The infrared spectrum was used as the basis for force-field calculations of the dimensions of benzyne, which were as shown in **5**[7]. Predictions were also made of the infrared spectrum of perdeuterobenzyne[7]. The matrix infrared spectrum was later recorded and the predicted values do not

completely correspond to those observed[6]; nevertheless, the structure **5** for benzyne is the most reliable one currently available, since it is experimentally based.

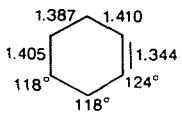
The structure **5** is interpreted as showing that benzyne is a true cyclic acetylene[7]. This is also indicated by a variety of molecular orbital calculations in which the geometry has been optimized[8–10]. The geometries **6** and **7** predicted by two such calculations (MINDO/3[8] and 4-31G[9], respectively) are shown. In both, the geometry is more distorted than that obtained by force-field calculations.



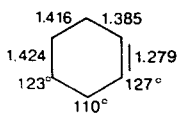
(3)



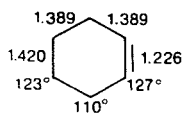
(4)



(5)



(6)



(7)

Estimates of the enthalpy of formation of benzyne by two independent experimental methods[11] gave the same value of 118 ± 5 kcal mol^{-1}, and some calculated values are close to this[8,10]. All recent calculations[8–10,12] predict a singlet ground state for benzyne and there is no evidence for triplet character in any of the reactions of arynes. Indeed, an attempt to generate triplet benzyne by the sensitized photolysis of phthaloyl peroxide gave products which were consistent only with the intermediacy of the singlet[13]. The lowest unoccupied molecular orbital of benzyne is, however, calculated to be significantly lower in energy than for a normal acetylene[14]. The 'arynic' bonding orbital, which is composed of almost pure p orbitals in the plane of the ring, is calculated to lie at −9.58 eV, which is little different from the energy of the corresponding orbital in an undistorted acetylene. The lowest unoccupied orbital is predicted to lie at 1.33 eV, which is much lower than for a linear acetylene. It is this low-lying empty orbital which can account for the marked electrophilic character of benzyne, because, according to frontier orbital theory, the smaller energy gap between this orbital and the occupied orbital of a nucleophile will make the reaction easier.

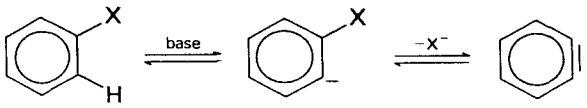
III. METHODS OF GENERATION

A. Generation of Benzyne

1. From 2-halogenophenyl anions

The two best established methods of generating benzyne from 2-halogenophenyl anions involve (*a*) the deprotonation of halogenobenzenes by strong bases and (*b*) halogen–metal exchange in *o*-dihalogenobenzenes.

The efficiency of benzyne formation from 2-halogenobenzenes depends on the nature of the halide leaving group, the base, and the solvent. The formation of benzyne involves two steps, both of which can be reversible (equation 1). The most commonly used procedures are those in which chlorobenzene or bromobenzene is reacted with a strong base such as sodamide or a lithium dialkylamide, at or below room temperature. With fluorobenzene, reprotonation of the anion prevents benzyne



(1)

formation except with very strong bases such as phenyllithium, and with iodobenzene the nucleophilic iodide ion can displace the second equilibrium to the left.

This potentially simple and attractive method of producing benzyne suffers from the disadvantage that if the bases used to generate the anions are also good nucleophiles, they can often compete very effectively with other external reagents for the benzyne. One solution to the problem is to use a sterically hindered base. Lithium 2,2,6,6-tetramethylpiperidide is an example of such a base: its use to generate benzyne from chlorobenzene allows the addition of carbanions and even of some dienes to the benzyne[15,16]. Caubère has also made important contributions by showing that sodamide can function as a base for the generation of benzyne in aprotic solvents such as tetrahydrofuran and 1,2-dimethoxyethane, if it is used in conjunction with a second anionic base such as sodium *t*-butoxide[17,18]. Even enolate anions are capable of acting as complexing agents in this way. It is known that hexamethylphosphoramide can activate sodamide in similar solvents, apparently bringing it into solution in complexed form. Sodamide is postulated to form aggregates with the anionic bases, these 'complex bases' then being more effective in the nonpolar solvent than either component alone. When such a base system is used to generate benzyne from bromobenzene, the benzyne can be intercepted by a wide range of other nucleophiles[17,18].

2-Halogenolithium compounds can be generated at low temperatures in ether solvents by the reaction of alkyl- or aryl-lithium derivatives with either halogenobenzenes or *o*-dihalogenobenzenes. They are stable in solution only at low temperatures, the stability being in the order F > Cl > Br and being somewhat greater in cyclic ethers: thus, 2-fluorolithiobenzene decomposes to benzyne in tetrahydrofuran above about −20°C, whereas 2-bromolithiobenzene is unstable in diethyl ether above about −85°C[1,19]. 2-Fluoromagnesium halides are considerably more stable[1] and benzyne is generated at a rapid rate only when the solutions are warmed. 2-Fluoromagnesium bromide prepared from 2-fluorobromobenzene and magnesium is therefore a useful and mild source of benzyne, which can be intercepted with dienes[20] and with other nucleophiles.

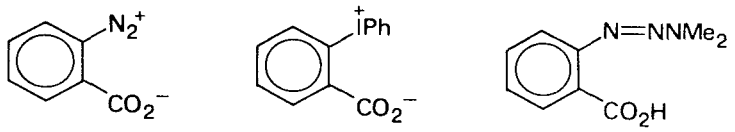
Several other sources of 2-halogenophenyl anions have been explored (for example, the thermal decomposition of salts of 2-halogenobenzoic acids[1]) but they offer no particular advantages as sources of benzyne. Leaving groups other than halides have also been investigated but these also appear to be no better than halide ions. For example, phenyl benzenesulphonate reacts with lithium 2,2,6,6-tetramethylpiperidide to give benzyne but the yields of adducts are not as good as in the corresponding reactions using bromobenzene as the precursor[21].

2. From benzenediazonium salts and related compounds

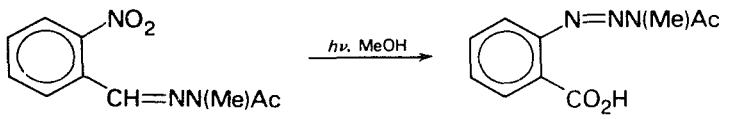
The aprotic diazotization of anthranilic acid, using organic nitrites such as isoamyl nitrite, leads to the formation of benzenediazonium-2-carboxylate (**8**)[1]. This internal salt is a very good source of benzyne as it decomposes in organic solvents at temperatures between 40°C and 80°C with the loss of nitrogen and carbon dioxide. 1,2-Dichloroethane is the solvent of choice for the reaction. The decomposition is a stepwise one, with nitrogen being lost first[22]. The solid benzenediazonium-2-carboxylate can be isolated, but it must be kept moist with solvent because it is violently explosive when dry. Procedures have been described for

preparing and handling the solvent-moist solid[23,24], but an alternative is to carry out the diazotization of anthranilic acid *in situ*, without attempting to isolate the diazonium carboxylate[25]. This is the method of generating benzyne which is probably the most widely used, because of its convenience, even though yields of benzyne adducts are sometimes moderate and side-reactions, involving the diazonium salt, can occur[26].

A number of related compounds have been used as sources of benzyne. Benzenediazonium-2-carboxylic acid hydrochloride can act as a benzyne precursor[27]. Two safe, isolable compounds which are useful sources of benzyne at 140–160°C are diphenyliodonium-2-carboxylate (**9**)[28] and 3,3-dimethyl-1-(2-carboxyphenyl)triazene (**10**)[29] (which is commercially available). Related triazenes are available from the light-induced rearrangement of hydrazones (e.g. **11**) of 2-nitrobenzaldehyde[30] (equation 2).



(**8**) (**9**) (**10**)



(**11**) (2)

Simple benzenediazonium salts can also act as benzyne precursors, by the loss of nitrogen and a proton. In the presence of a weak base such as potassium acetate and of the diene tetraphenylcyclopentadienone (tetracyclone), a good yield of the benzyne adduct can be obtained[31]. It has also been shown that *N*-nitrosoacetanilide will decompose in the presence of tetracyclone to give the benzyne adduct in good yield, even though this compound has also been used as a good source of phenyl radicals. Extensive work has established that there are two competing pathways for the decomposition of *N*-nitrosoacetanilide and related compounds, one leading to phenyl radicals by a chain process and the other to benzyne[32]. Tetracyclone suppresses the former and so acts in the dual role of radical acceptor and benzyne trap. Other radical-chain inhibitors, such as 1,1-diphenylethylene, can also be used to promote decomposition by the benzyne pathway[33]. The *N*-nitrosoamides can be prepared *in situ* from aniline or from acetanilide, and benzyne adducts can thus be obtained in reasonable yields under carefully controlled conditions[33,34]. Other precursors of benzenediazonium ions have been investigated as sources of benzyne but they are not as useful as the *N*-nitrosoamides[35].

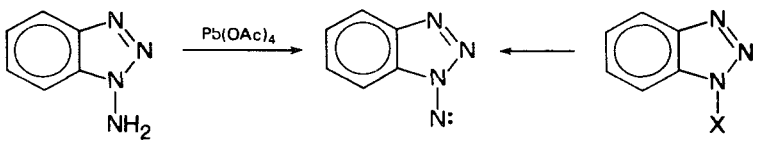
3. *By the fragmentation of benzo-fused cyclic systems*

Benzyne can be a product of the fragmentation of a large number of *ortho*-fused benzene derivatives. The most useful in practice are those in which the other fragments of decomposition are small stable molecules such as nitrogen and carbon dioxide. Several benzo-fused heterocyclic compounds incorporate the desired structural features.

The compound of this type which has found the most widespread use is 1-aminobenzotriazole (**12a**)[36]. This compound can be oxidized by lead tetraacetate to

give benzyne in a very rapid and clean reaction, even at −78°C. The other products of the reaction are nitrogen, lead diacetate and acetic acid, and these do not normally compete for the benzyne, which, in the absence of added reagents, dimerizes in high yield. The reaction by which benzyne is produced is postulated to involve the nitrene (**13**) as an intermediate (equation 3). 1-Aminobenzotriazole is prepared either by the amination of benzotriazole (when the 2-amino compound is also formed) or in several steps starting from 2-nitroaniline[36]. Despite the preparative work involved, the route has proved a valuable one when benzyne is required in high yields under mild reaction conditions.

Several variants of this method have been explored with the aim of avoiding the use of a strong oxidizing agent: these include the deoxygenation of the *N*-nitrosotriazole (**12b**)[37] and the photolysis of the iminophosphorane (**12c**)[38,39] and of the tosylhydrazone salt (**12d**)[38,39]. The best such derivative is the salt (**12e**), which gives benzyne when it is simply dissolved in a polar solvent at room temperature[40] (equation 3).



(3)

(**12a**) (**13**) (**12**)

(**b**) X = NO

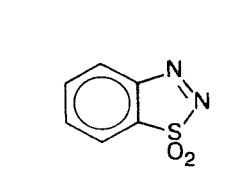
(**c**) X = $N{=}PPh_3$

(**d**) X = $\bar{N}Ts\ Li^+$

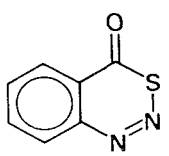
(**e**) X = $\bar{N}{-}N{=}N{-}NHTs\ Li^+$

(**13**) $\xrightarrow{-N_2}$ **1**

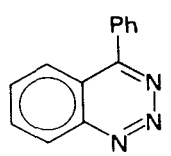
Benzothiadiazole-1,1-dioxide (**14**) is an isolable but unstable solid which can also decompose in organic solvents at room temperature without the addition of an external reagent[41]. At higher temperature (160°C) the thiadiazinone **15** has been shown to decompose to give benzyne in low yield[42]. Benzyne is a product of the flash thermolysis of a large number of benzo-fused heterocyclic compounds[43]: examples are compounds **16–21**.



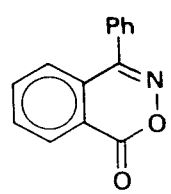
(**14**)



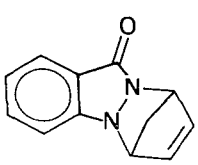
(**15**)



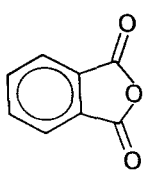
(**16**)[44]



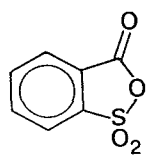
(**17**)[45]



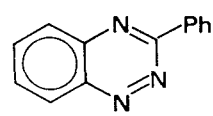
(**18**)[46]



(**19**)[47]

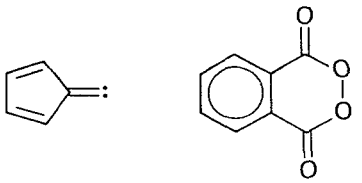


(**20**)[44]



(**21**)[44]

Benzyne is also proposed as an intermediate in the high-temperature decomposition of several simpler (monocyclic) benzene derivatives[3,48] and as a product of the rearrangement of the carbene **22** in the vapour phase[49]. Useful sources of benzyne under photochemical conditions include benzocyclobutanedione (**3**) (for matrix photolyses)[4,50] and phthaloyl peroxide (**23**).[51]

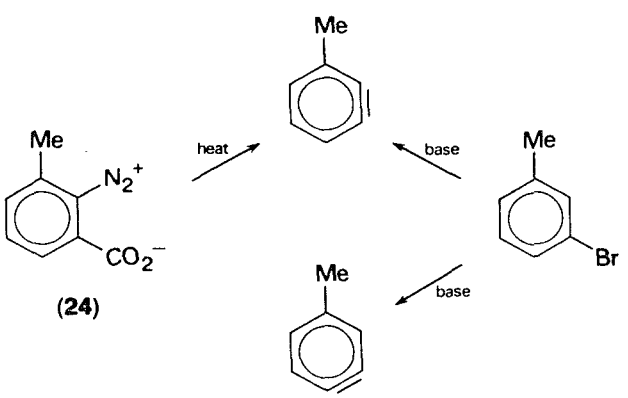


(22) (23)

B. Generation of Other Arynes

In applying the methods used for benzyne to the generation of other arynes, the problems most commonly encountered are (*a*) practical difficulties in synthesizing precursors with the correct substitution pattern and (*b*) the formation of more than one aryne from a given precursor.

The first problem is most severe with those methods which, for benzyne, start with an *ortho*-disubstituted benzene. For example, substituted anthranilic acids are generally less readily available than the parent compound. On the other hand, only one aryne can be formed from a precursor of this type. This is not true of methods which are based on the removal of a proton and an adjacent group. Thus decomposition of the diazonium carboxylate **24** gives exclusively 3-methylbenzyne whereas 3-bromotoluene can give both 3- and 4-methylbenzyne with strong base (equation 4).



(24) (4)

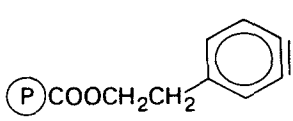
The factors which control the ratios of isomeric benzynes from precursors such as 3-bromotoluene have been analysed in detail[1]. In the majority of cases in which two arynes can, in principle, be formed from a single precursor, both are formed in practice, though not necessarily in a 1:1 ratio. The problem exists mainly with *meta*-substituted halogenobenzenes and similar aryne precursors. Polycyclic systems which have considerable bond fixation tend to undergo elimination mainly or exclusively in one direction: thus, 2-bromonaphthalene reacts with bases to give 1,2-napthalyne with little or none of the 2,3-isomer.

Many substituted benzynes have been generated from *o*-halogenoaryl anions, either by deprotonation of the halogenobenzene or by halogen–metal exchange[1]. As with

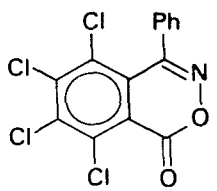
benzyne itself, the use of hindered[15,16] or complex[17,18] bases offers significant advantages in preparative work. Polyhalogenobenzenes have been widely used as sources of halogen-substituted benzynes, particularly via organolithium intermediates[19,52,53]. The stability of these intermediates varies considerably: for example, pentachlorophenyllithium is stable in ether solution up to about 20°C whereas pentafluorophenyllithium and mixed polychlorofluorophenyllithium derivatives are unstable at 0°C or below. The generation of benzynes from some of these can be complicated by the introduction of more than one lithium atom when alkyllithium bases are used, and also by S_N2 displacement reactions in the intermediate halogenolithium compounds[19]. Organomagnesium intermediates have also been used to generate substituted benzynes but these are generally more stable and may require elevated temperatures for their decomposition.

Diazonium carboxylates derived from substituted anthranilic acids have been used for the generation of several monosubstituted benzynes[25] and tetrahalogenobenzynes[52,54,55]. The limitation of the method is simply the availability of the substituted anthranilic acids. Diazonium salts derived from substituted anilines offer a more readily available source of arynes. The reaction appears to be particularly efficient when the arynic bond is flanked by one or more *t*-butyl groups[56], and moderate yields of benzynic products can be obtained from a range of other anilines, *meta*-substituted derivatives being generally the best[34].

Methods which require the decomposition of benzo-fused heterocyclic compounds suffer from the same preparative limitations as do those based on anthranilic acids. Some substituted benzynes have been generated by the 1-aminobenzotriazole route[36,38,57], as has the polymer-bound aryne **25**[58]. 5-Methylbenzothiadiazole-1,1-dioxide is a source of 4-methylbenzyne[1], and tetrachlorobenzyne can be generated from tetrachlorophthalic anhydride[59] and from the benzoxazinone **26**[45]. Tetradeuterobenzyne has also been prepared by the matrix photolysis of the phthalic anhydride[6].



(25)



(26)

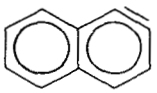
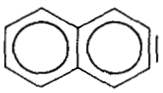
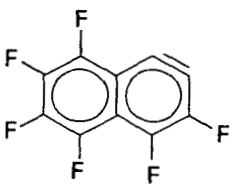
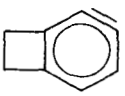
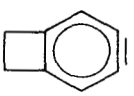
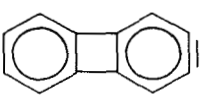
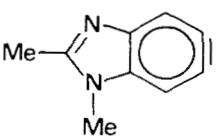
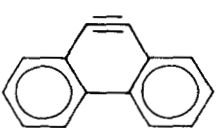
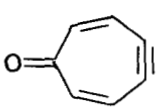
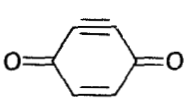
These routes can be adapted to the generation of naphthalynes, 9,10-phenanthryne and other types of arynes, although the problems involved in preparing some of the precursors preclude their large-scale use. Table 1 presents a selection of such arynes and of recent methods which have been used to generate them: reference should be made to Hoffmann's review[1] for details of the extensive earlier work on the generation of naphthalynes and of phenanthryne.

IV. THE CHEMISTRY OF ARYNES

A. General Features of Benzyne Reactivity

Benzyne shows many of the properties expected for a highly reactive electrophilic acetylene. As discussed in Section II, the effect of bending distortion on the triple bond is to lower the energy of the lowest occupied molecular orbital while leaving the energy of the occupied molecular orbital relatively unaffected[14]. This greatly facilitates

TABLE 1. The generation of polycyclic and other arynes

Aryne	Method of generation[a]	Reference
	A B C D	60, 62 61 63 64a
	D E	64a 25
	A	65
	B	66
	B	67
	E	68
	D	69
	D	64b
1,2-Dehydrotriptycene	A	70
	D	71
	D	57
	F	72

[a]Methods of generation: A, halogenoarene + base; B, *o*-dihalogenoarene + Mg or BuLi; C, 1-bromo-2-naphthol *p*-toluenesulphonate + BuLi; D, 1-aminotriazole + $Pb(OAc)_4$; E, *o*-diazonium carboxylate; F, *o*-diazocarboxylate.

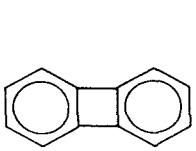
the reaction of benzyne with nucleophiles. Benzyne reacts most readily with 'soft', polarizable nucleophiles, as the formal triple bond is itself highly polarizable.

Substituted benzynes all seem to show less selectivity towards nucleophiles than benzyne itself[73]; this is explained by an inductive polarization of the arynes by the substituents, which results in an increase in reactivity. The effect of substituents is discussed further in Section IV.D. Tetrahalogenobenzynes appear to be significantly more reactive towards weak nucleophiles than is benzyne[52]: for example, all the tetrahalogenobenzynes will undergo Diels–Alder cycloaddition to benzene in moderate to good yields.

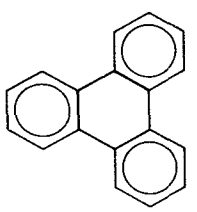
Since benzyne shows no tendency to undergo unimolecular decomposition at normal temperatures, its lifetime is determined by how well it is insulated from other potential reagents, including itself. Matrix-isolated benzyne has a lifetime which is sufficient for its infrared spectrum to be determined[5,6]. Polymer-bound benzyne appears to have a lifetime of several seconds under conditions which permit rapid dimerization of free benzyne[58].

B. Dimerization and Trimerization

Biphenylene (**27**) and triphenylene (**28**) are the dimer and trimer of benzyne. The dimerization of benzyne to biphenylene was first observed in gas-phase reactions[1]: benzyne generated by the flash pyrolysis or flash photolysis of a number of precursors gave biphenylene, sometimes together with a trace of triphenylene. The rate of dimerization of benzyne from the flash photolysis of phthalic anhydride vapour was determined as $(4.6 \pm 1.2) \times 10^9$ 1 mol^{-1} s^{-1}, and a biradical intermediate, which could rotate freely about the biphenyl bond, was proposed[74]



(27)

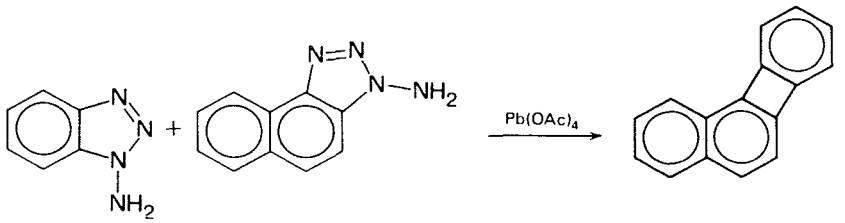


(28)

Useful small-scale preparations of biphenylene are now available from a number of precursors, such as **16**[44], **17**[45] and **18**[46]. A more important advance from a preparative point of view has been the development of methods for obtaining good yields of biphenylene in solution reactions. Benzenediazonium 2-carboxylate[23] and 1-aminobenzotriazole[36] are the best precursors for this purpose. Because the latter gives biphenylene rapidly and in high yield (80%), several other 1-aminotriazoles have been prepared with the aim of using them as sources of substituted and fused biphenylenes[38]. The yields of substituted biphenylenes produced in this way are not as good as for biphenylene itself: the efficiency of the dimerization falls off as the inductive effect of the aryne substituent increases. In general, yields are somewhat lower for 3- than for 4-substituted benzynes, possibly for steric reasons, although 3,6-dimethoxybenzyne dimerized (37%) while 4,5-dimethoxybenzyne did not[57]. A disadvantage of this route to substituted biphenylenes is that with unsymmetrically substituted arynes, a mixture of two biphenylenes is usually produced; little regioselectivity has been observed in the dimerization.

One useful application of the method has been to the preparation of unsymmetrical biphenylenes by the cooxidation of two different aminotriazoles[38,64]. For example, the

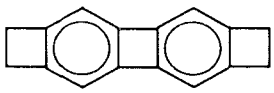
oxidation of a mixture of 1-aminobenzotriazole **12a** and the aminonaphthotriazole **29** gave the benzobiphenylene **30** as well as the two aryne dimers[64] (equation 5). The dimerization of naphthalynes provides a route to the dibenzobiphenylenes, but 9,10-phenanthryne failed to give any dimer.



(5)

(12a) **(29)** **(30)**

The aryne dimerization route has been used to prepare a number of other new biphenylene derivatives. The biphenylene **31** was prepared from the aryne, which was generated from the *o*-bromomagnesium iodide[67]. Tetrafluoro- and tetrachloro-benzynes, generated by a variety of routes, dimerized to the biphenylenes[45,52,59], and the copyrolysis of ninhydrin with tetrachlorophthalic anhydride gave tetrachlorobiphenylene[59].



(31)

Small amounts of triphenylene sometimes accompany the biphenylene formed from benzyne. This may be formed by a true trimerization of benzyne if its standing concentration is high enough. On the other hand triphenylenes formed from organometallic aryne precursors are produced by a stepwise route involving metallated biphenyls as intermediates[1,19]. Some of the benzyne precursors which normally give biphenylene in solution give triphenylene instead when they are decomposed in the presence of tetrakis(triphenylphosphine)platinum(0), and this has been taken as evidence for an organoplatinum intermediate[75].

C. Cycloaddition Reactions

1. Diels–Alder reactions

The Diels–Alder reaction is one of the most important reactions of arynes; it is used both as a means of detecting arynes and as a synthetic tool. Because of the highly electrophilic character of arynes the reaction is observed with a very wide range of dienes. These include aromatic compounds which are not normally regarded as viable partners in the Diels–Alder reaction, such as thiophens, styrenes and even simple benzene derivatives.

A concerted reaction between benzyne and a diene requires a transition state in which there is simultaneous overlap between the orbitals of the formal triple bond in the plane of the ring and the terminal lobes of the diene π-orbital system. The more important interaction will be between the low-lying lowest unoccupied molecular orbital of benzyne and the highest occupied π orbital of the diene; these will have the phases shown (using butadiene as an example) in Figure 1.

The consequences are (*a*) that the reaction will be stereoselective with respect to the

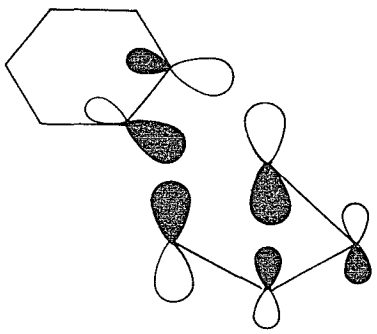
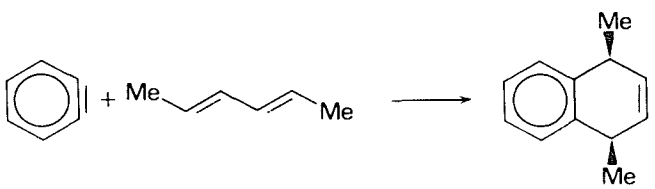


FIGURE 1. Dominant frontier orbital interactions in the cycloaddition of butadiene to benzyne.

diene, (*b*) that the reaction will be more favourable with more nucleophilic dienes (because the HOMO–LUMO energy gap will be smaller) and (c) the cycloaddition will compete favourably with other modes of reaction of benzyne only when the diene can readily achieve the correct conformation for interaction at both termini.

The stereoselectivity of the reaction between benzyne and *trans*, *trans*-hexa-2,4-diene was established by showing that only *cis*-1,4-dimethyl-1,4-dihydronaphthalene (**32**) was formed in the addition[76,77] (equation 6).



(6)

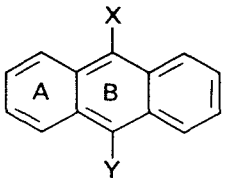
(**32**)

The greater reactivity of nucleophilic dienes was established specifically by experiments with substituted anthracenes, e.g. **33**, in which the ratio of addition to rings A and B is correlated with the nature of the substitution pattern[78] (Table 2). The range of relative reactivities is, however, quite small. Thus, although benzyne is regarded as an electrophilic partner in the Diels–Alder reaction, it can add quite successfully to electron-deficient diene systems, provided that they have the correct geometry for concerted addition. This is borne out by the addition reactions of the cyano- and nitro-anthracenes in Table 2, and of the dienes **34–37**.

The need for the diene to interact with the aryne simultaneously at both termini means that in general, five-membered cyclic dienes are the most efficient reagents. In these dienes the π system is planar and the termini are at the correct distance apart for effective overlap with the arynic orbital. Dienes of this type, particularly furan and tetracyclone, have been widely used to intercept arynes. Furan is particularly useful in organometallic reactions[20] because it can be used as a cosolvent. Tetracyclone is a good reagent for detecting arynes because it is highly coloured, and gives colourless tetraphenylnaphthalene derivatives as the products. Steric or polar effects seem to play little part in determining the regioselectivity of the addition of unsymmetrical reaction partners of this type: this is illustrated by the reaction between 3-methylbenzyne and some 2-substituted furans[83] (equation 7).

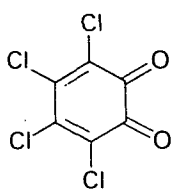
Adducts of arynes with furans are useful as intermediates in the synthesis of naphthalenes because the endoxide bridge is readily cleaved by acids. An example is

TABLE 2. Addition of benzyne to rings A and B of the substituted anthracenes **33**[78]

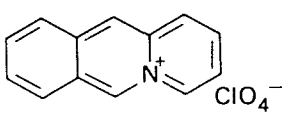


(33)

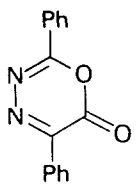
33			
X	Y	Ratio of adducts ring B/ring A	Relative reactivity
Me	Me	~200	19.2
Me	H	~70	4.0
H	H	30	1.0
CN	H	3.7	0.44
NO_2	H	4.3	0.29
CN	CN	1.0	0.15



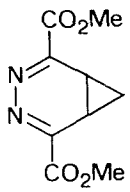
(34)[79]



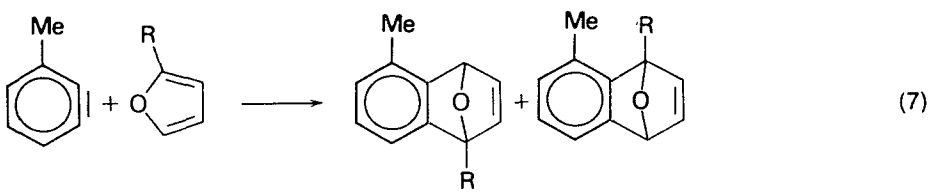
(35)[80]



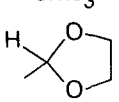
(36)[81]



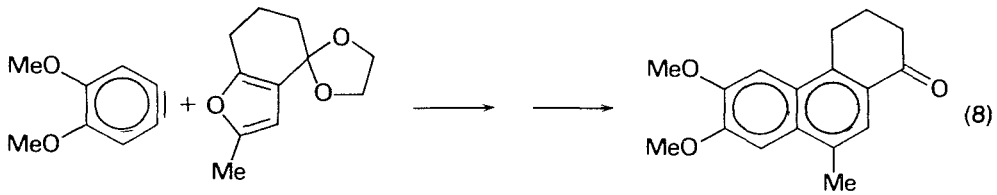
(37)[82]



(7)

R	Ratio of adducts
Me	58 : 42
CMe_3	64 : 36
	61 : 39
CO_2Me	57 : 43

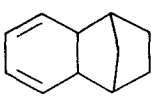
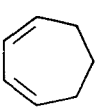
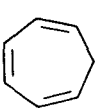
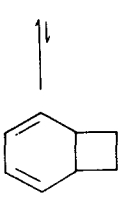
the synthesis of functionalized phenanthrenones such as **38** from 4,5-dimethoxybenzyne and the furan **39**[84] (equation 8).



(39) (38) (8)

Benzyne and tetrahalogenobenzynes also undergo Diels–Alder reactions with pyrroles[61,85,86] and isoindoles[61,87]. The bridging imino group in such adducts can be removed by oxidation, the fragment RNO being extruded[61]. Tetrafluorobenzyne also undergoes a Diels–Alder reaction with thiophen[86]. Many examples of other reactions

TABLE 3. The relationship between the twist angle in the π system of some cyclic dienes and the percentage of benzyne [2 + 4]cycloaddition products

Diene	Twist angle (deg.)	Percentage of [2 + 4]addition	Reference
	0	100	24
	17	50	24
	20–25	70	93
	40	0	93
	~60	–	24[a]
	0	100	

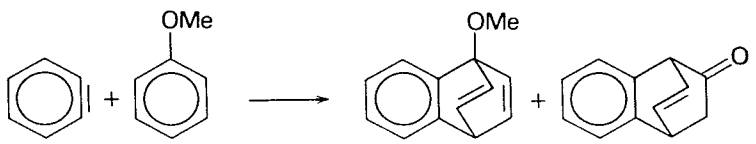
[a]Cyclooctatetraene is similar in that it adds through its bicyclic valence tautomer[94].

of arynes with five-membered ring dienes have been described[1]; more recent work includes additions to dienes containing an XMe_2 group in the ring (X = Si[88], Ge[89] and Sn[90]), the addition of tetrahalogenobenzynes to dimethylfulvene[91] and the addition of benzyne to substituted cyclopentadienes[92].

Six-membered cyclic dienes also add well to arynes if they are planar or nearly so. As the ring size increases the diene system tends to become twisted out of planarity and the termini become further apart. Both these factors make the Diels–Alder reaction less favourable and allow other reactions to compete. These may involve alternative modes of reaction of the aryne with the diene, particularly [2 + 2]cycloaddition (Section IV.C.3) and the ene reaction (Section IV.C.5). The relationship between the twist angle in the diene and the proportion of the adducts resulting from Diels–Alder reaction is clearly shown for the cyclic dienes in Table 3.

With acyclic dienes the yields of Diels–Alder adducts are again dependent upon the ease with which the diene can achieve a planar *cis* conformation. Butadiene adds to benzyne to give the Diels–Alder adduct in high yield[76]. Alkyl substitution can reduce the relative amount of the Diels–Alder product: for example, *trans*-penta-1,3-diene gives the [2 + 4] and [2 + 2]adducts in a 3:1 ratio, and *cis*-penta-1,3-diene gives only the [2 + 2]adduct[95,96].

Arynes are among the very few dienophiles which will undergo Diels–Alder reactions with simple benzene derivatives. When benzyne is generated in the presence of a large excess of benzene or of a substituted benzene, [4 + 2]adducts are formed, usually in rather low yields[97,98]. The substituents have a predictable effect, electron-releasing groups on the benzene promoting the reaction and favouring 1,4-addition over 2,5-addition. This is illustrated for the reaction with anisole, in which the 1,4-adduct (**40**) is formed in higher yield than compound **41**, which is derived from the 2,5-adduct[97] (equation 9).



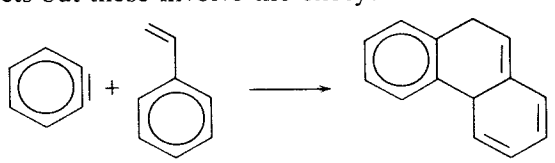
(9)

(**40**) (**41**)

32% 8%

The reaction is limited as a synthetic method by the low yields and by competing reactions (for example, toluene undergoes the ene reaction with benzyne[97]). With tetrahalogenobenzynes, yields of adducts are generally much higher. Benzene and alkylbenzenes give cycloadducts in good yields[52,86,99]. With methoxyarenes, adducts analogous to **40** and **41** are isolated, often in very good combined yields[100]. Even *N*,*N*-dimethylaniline, which reacts exclusively at nitrogen with benzyne, adds to tetrafluorobenzyne partly by cycloaddition, to give the adducts analogous to **40** and **41** in a combined yield of 25%[101].

Several other benzenoid aromatic compounds, including naphthalenes and biphenylene, give Diels–Alder adducts with arynes[52,102]. Styrene and its derivatives give [2 + 4]adducts but these involve the exocyclic double bond (equation 10).



(10)

(**42**)

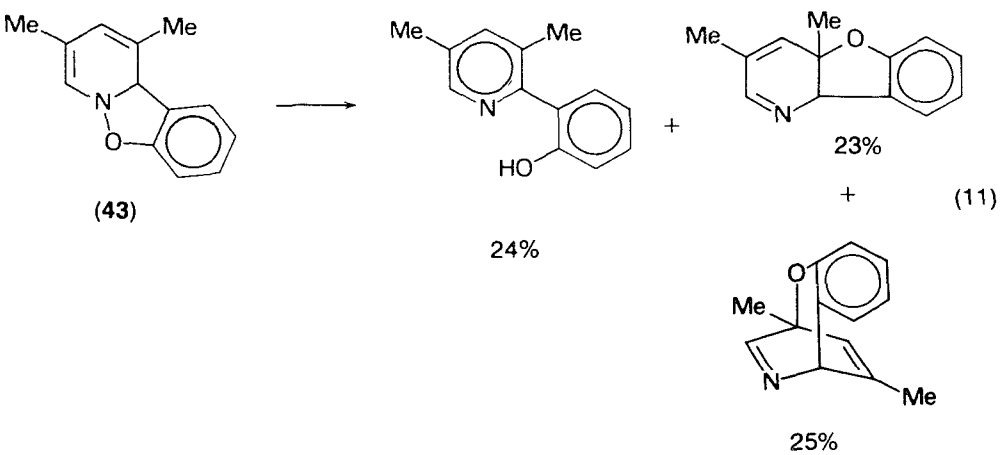
The primary adduct (**42**) is a dihydrophenanthrene, but this may react further, either to aromatize or to undergo the ene reaction with another molecule of the aryne[103]. As a result, the yields of individual products may be low: tetrahalogenobenzynes give the best yields[52].

Formal Diels–Alder adducts are formed in the reactions of arynes with a number of other 4π-electron systems, but it is doubtful whether a true concerted cycloaddition reaction is involved. Examples are dienolate anions[18,104,105] and dienamines[106], and several 'heterodienes' including thionylaniline (PhNSO)[107], phosphabenzenes[108], and benzaldehyde *N*-phenylimide[109].

The presence of traces of silver salts can greatly affect the yields of Diels–Alder adducts in aryne reactions: they are generally lowered[94,110], though exceptions have been noted[111]. It has been suggested that a benzyne–Ag^+ complex participates in such reactions.

2. *1,3-Dipolar cycloadditions*

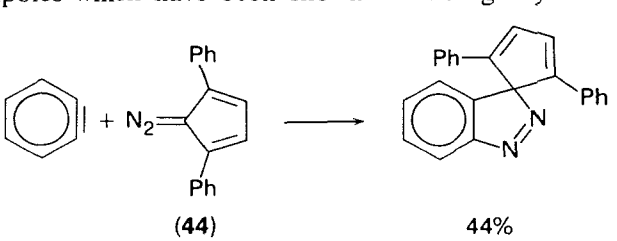
Benzyne is a suitable 2π-electron component for cycloaddition to 1,3-dipoles[112]. Several isolable 1,3-dipoles have been observed to add to benzyne[1]; these include nitrones[113] and heterocyclic *N*-oxides[114,115], which can be regarded as cyclic nitrones. The initially formed adducts often undergo further reactions, as for example, with the adduct (**43**) of benzyne and 3,5-dimethylpyridine-*N*-oxide[115] (equation 11).



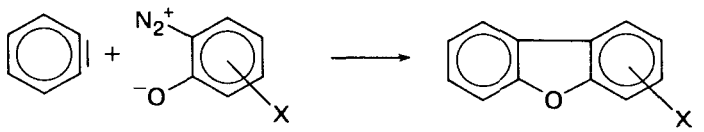
(11)

1,3-Dipolar addition of benzyne to azides and to diazo compounds is well established[1]. Further examples of the latter include the addition to diazocyclopentadienes (e.g. **44**)[116] (equation 12) and to diazoketones[117]. The reaction of arynes with benzenediazonium-2-oxides (**45**) provides a route to benzofurans[79] (equation 13).

Other 1,3-dipoles which have been shown to undergo cycloaddition to benzyne

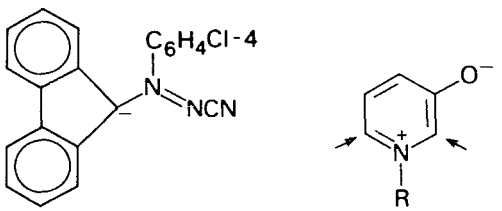


(12)



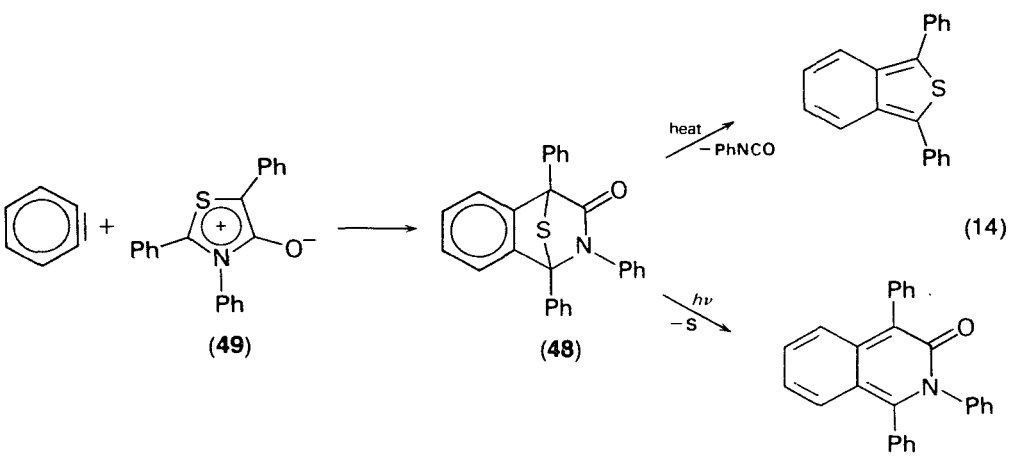
(45) (13)

include the azomethine imide (**46**)[118], pyridinium-3-oxides (**47**)[119], sydnones[120] and several other mesoionic ring-systems[120,121]. The initial cycloadduct (**48**) from triphenylthiazolium oxide (**49**) and benzyne can be isolated (78%)[120] (equation 14); different bridging groups are lost from it on heating and on irradiation.



(**46**) (**47**)

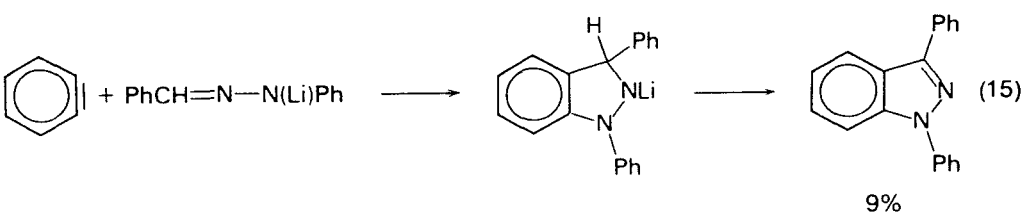
R = H, Me, Ph



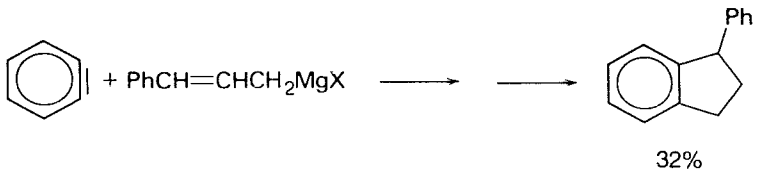
(**49**) (**48**) (14)

A few examples are known of cycloadditions to benzyne which appear to involve allyl anions, or their equivalent, acting as the 4π-electron component[121–123]; two of these are shown in equations (15) and (16).

Reactions which can formally be regarded as 1,3-dipolar cycloadditions take place between benzyne and carbon disulphide. These and related reactions are discussed in Section IV.D.7.



9% (15)



(16)

3. [2 + 2]*Cycloadditions*

Benzyne reacts with a wide range of olefins to give the [2 + 2]cycloadducts, benzocyclobutanes, in moderate to low yields. With alkenes the ene reaction often competes or predominates. The reaction is a forbidden one according to the Woodward–Hoffmann rules, and as such it would be expected to take place in a stepwise manner. Most of the studies of the reaction have been aimed primarily at investigating the mechanism, rather than at making use of it as a synthetic method. A major concern has been to establish the degree of retention or inversion of olefin stereochemistry in the cycloaddition. In general it is found that there is a predominance of the adduct in which olefin stereochemistry is retained, but that the other isomer is also formed as a minor product. The results of several such studies are summarized in Table 4.

These results have usually been interpreted as indicating a stepwise mechanism for the addition. The transition state for the cycloaddition, as determined by extended Hückel calculations, is an unsymmetrical one. The potential energy surface has a 'valley', which corresponds to the presence of an intermediate on the reaction pathway. The transition state is calculated to have an unsymmetrical charge distribution, with the benzyne acting as the electrophile towards the olefin. The transition state is mainly diradical in character, but with a slight charge imbalance which reflects the electrophilicity of the benzyne[129]. The reactions summarized in Table 4 can be envisaged as going through intermediates which preferentially, but not exclusively, collapse to the products before rotation and loss of stereochemistry can occur. Whether the intermediates are mainly dipolar or diradical in character probably depends on the nature of the olefins involved.

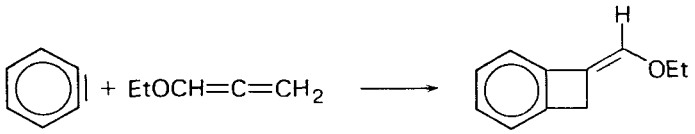
TABLE 4. Stereochemistry of the [2 + 2]cycloaddition of benzyne to olefins

Olefin	Product ratio of olefin stereochemistry retained/inverted	Reference
trans-Cyclooctene	4.6:1	13
	3.5:1	124
cis-Cyclooctene	40:1	125
cis,trans-Cycloocta-1,5-diene	13:1	125
cis,cis-Cycloocta-1,5-diene	6.4:1	125
cis-1,2-Dichloroethylene	2.2:1	51, 77
trans-1,2-Dichloroethylene	4.9:1	51, 77
trans-1-Deutero-3,3-dimethylbut-1-ene	3:1	126
cis-1-Ethoxypropene	16:1	127
trans-1-Ethoxypropene	3.8:1	127
cis-1-Methoxypropene	7.3:1	128
trans-1-Methoxypropene	1:1	128
cis-1-Acetoxypropene	4.6:1	128
trans-1-Acetoxypropene	1.6:1	128

If the electrophilic character of benzyne were the major factor in determining the ease of [2 + 2]cycloaddition, the reaction would be expected to go most readily with electron-rich olefins. A study of the relative reactivities of alkenes $CH_2{=}CR^1R^2$ towards benzyne showed that, although electron-rich olefins were generally the more reactive, overall differences were small and there was no strict correlation between nucleophilicity and reactivity. For example, the relative rates of reaction of ethyl vinyl ether and of acrylonitrile differed only by a factor of 2[14]. This could indicate a change in the character of the intermediates in the two reactions. In practical terms, the yields of cycloadducts in these reactions seem to depend more on the absence of possible competing reactions, particularly the ene reaction, and on the absence of unfavourable steric interactions, than on the nucleophilicity of the olefin.

Yields of adducts in the [2 + 2]cycloaddition reaction are rarely above about 40%, but even yields as low as 20% can be regarded as useful because of the direct entry which the reaction provides to benzocyclobutanes. Olefins which have been shown to add to arynes in yields of 20% or greater include acrylonitrile[1], α-chloroacrylonitrile[130], 1,1-dichloroethylene[130], norbornene[131], norbornadiene[131], and several simple enol ethers[1,127], enol acetates[1,127] and enamines[1,132]. Methyl vinyl ketone also adds in good yield[133] but with αβ-unsaturated aldehydes the primary interaction is through the carbonyl oxygen atom[52,133]. With simple alkenes and cycloalkenes, [2 + 2]addition occurs in very low yield unless the ene reaction is precluded for steric reasons. Thus, cyclohexene gives no cycloadduct but cyclohexadiene, cycloheptene, cycloheptadiene and cycloheptatriene all give the cycloadduct as well as other adducts[24,134].

Enolates derived from alicyclic ketones add to benzyne to give cyclobutanols[18]. This reaction will be described together with the other reactions of enolate anions in Section IV.D.4. Cycloadducts such as **50** have also been isolated from the reaction of benzyne with ethoxyallene (equation 17) and with chloroallene[135].

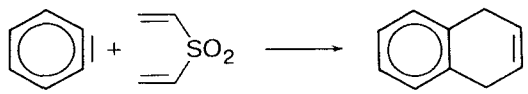


(17)

(50)
17%

4. Other modes of cycloaddition

The 'homo-Diels–Alder' reaction of benzyne with bis(ethenyl)sulphone (**51**) appears to be implicated in the formation of 1,4-dihydronaphthalene as the primary product[136] (equation 18). Norbornadiene can react similarly[131]. Tropones can undergo [2 + 6]- as well as [2 + 4]-addition to benzyne[137].



(18)

(51)

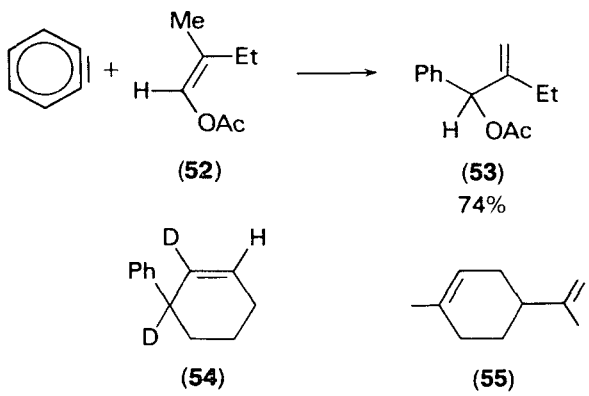
5. The ene reaction

The ene reaction[138] of benzyne with olefins bearing an allylic hydrogen atom is illustrated in equation (19). There is strong circumstantial evidence that the reaction is

(19)

a concerted process. It is found that with cyclic olefins the relative amounts of the products derived from the [2 + 2]- and ene reactions are very sensitive to the conformation of the olefin. If it is assumed that the optimum geometry for an olefin in the concerted ene process is one in which the allylic C—H bond is parallel to the π bond[138], and that the stepwise [2 + 2]addition is relatively insensitive to conformational effects, then the ratios of products arising from the two types of reaction can be related to the geometry of the olefin (Table 5)[24].

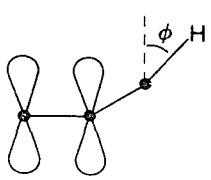
Steric effects are also very important in determining preferences in the ene reaction in enol ethers[127,128] and enol acetates[139]. In the reaction with *Z*-2-methylbut-1-en-1-yl acetate (**52**) benzyne reacts exclusively with the methyl group on the less hindered side of the olefin to give the allylic acetate (**53**) (equation 20). This is consistent with a concerted mechanism for the reaction. The concerted nature of the reaction is also supported by the observation that 1,2-dideuterocyclohexene reacts to give exclusively the 3-phenylcyclohexene (**54**)[140] and that optically active products are obtained from the ene reaction of benzyne with (+)-carvomenthene (**55**)[141].



(20)

(**52**) (**53**) 74% (**54**) (**55**)

TABLE 5. The ene reaction in cyclic olefins: the ratio of ene and [2 + 2] adducts as a function of the conformation of the allyl system[24]



Olefin	ϕ (approx.) (deg.)	Ratio of adducts, ene:[2 + 2]
Cyclohexene	4	(only ene)
Cyclohexa-1,3-diene	5	3:1
Cycloheptene	32	3:1
Cyclohepta-1,3-diene	33	0.8:1
Cycloheptatriene	37	0.07:1

The ene reactions is thus observed with those cyclic and acyclic olefins which can achieve the required geometry of the transition state. The ene reaction with methyl methacrylate has been used to detect benzyne[34]. Ene-type reactions have also been observed with a variety of other compounds including alkyl-acetylenes[51,142] and -allenes[135], toluene[97] and small strained ring-systems[51,143].

D. Reactions of Arynes with Nucleophiles

1. *The selectivities of arynes for different nucleophiles*

The relative reactivities of nucleophiles towards benzyne are determined, to a large extent, by the relative polarizability of the nucleophiles. Benzyne, as a 'soft' electrophile, reacts better with nucleophiles that are highly polarizable than with small basic anions. This is shown by the fact that strong bases such as sodamide or phenyllithium, when used to generate benzyne, do not always compete effectively with other nucleophiles in subsequent addition to the benzyne.

Estimates of the relative reactivities of various nucleophiles towards benzyne[1] place polarizable nucleophiles such as thiophenoxide and enolate ions above amide and alkoxide ions. In the case of base–solvent systems such as sodium methoxide–methanol, the anions are the more reactive but not overwhelmingly so, e.g. the ratio is about 100 for addition to 4-chlorobenzyne[144,145]. The importance of polarizability is also shown by the order of reactivity $I^- > Br^- > Cl^-$ for halide ions in alcohol. Steric factors are also important, as shown by the relative reactivities of 18:1 for diethylamine and diisopropylamine towards benzyne[146].

In general, substituted benzynes show less selectivity than does benzyne itself[73]. Benzyne and a series of 3- and 4-substituted benzynes were each allowed to compete for the cyanomethyl anion and for dimethylamine. The selectivity of the arynes decreased with increasing polarization of the triple bond; there was a linear relationship between the 'reactivity factors' of the arynes and the absolute values of the polar substituent constants, σ'.

In the case of 1,2-naphthalyne and of 9,10-phenanthryne, steric factors appear to play an important part in determining selectivity in nucleophilic addition. The selectivities of these arynes for two different pairs of nucleophiles are as shown in Figure 2, the values of benzyne being given as a comparison[147]. The polycyclic arynes show the most marked increase in selectivity at positions *peri* to a C—H bond: the *peri* hydrogen atom may cause the approach of bulky nucleophiles to be retarded.

2. *Nucleophilic addition to unsymmetrical arynes*

The substituents R in a 3-substituted benzyne influence the polarization of the formal triple bond mainly by an inductive effect. If it is assumed that the reactions of arynes with nucleophiles have early transition states, the position of attack will be influenced by the polarization of the arynic bond. Thus, the anion **56** will be formed if

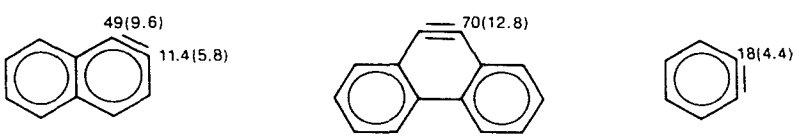
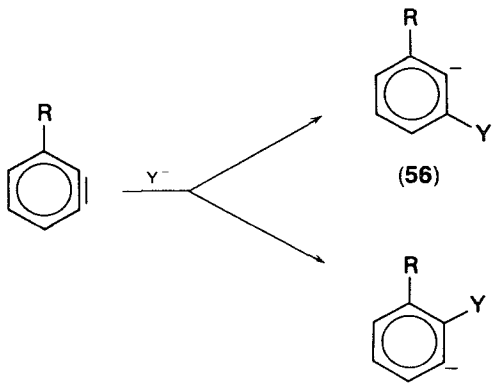


FIGURE 2. Selectivities of arynes for the pairs of nucleophiles diethylamine/diisopropylamine and (in parentheses) phenyllithium/lithium piperidide.

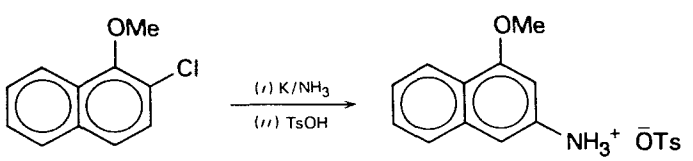
the substituent R is electron-withdrawing and anion **57** if R is electron-releasing (equation 21). Attack of the nucleophile to give the anion **56** will, of course, be preferred on steric grounds. Similar arguments can be applied to 4-substituted benzynes but the directive effects of the substituents should be less.



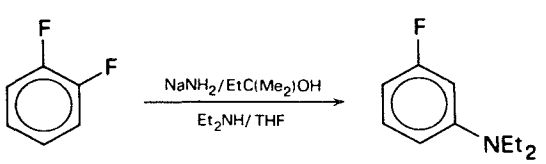
(21)

The results obtained from studies of nucleophilic attack on substituted benzynes are generally consistent with these predictions. For 3-substituted benzynes, *meta* substitution strongly predominates if the substituent R is inductively electron-withdrawing. Even when R is electron-releasing, the *ortho*/*meta* ratio is rarely greater than 1[1]. In such cases the ratio is, however, sensitive to factors such as the reactivity of the nucleophile (the stronger nucleophiles being less selective[145]) and even the nature of the associated cation. The latter point is illustrated by a study of the amination of 2-chlorotoluene by metal amides in which the *ortho*/*meta* product ratio decreases through the series $LiNH_2$, $NaNH_2$ and KNH_2[148]. This is ascribed to the different steric effects of the nucleophiles which result from different degrees of covalent bonding in the metal amides. For 4-substituted benzynes the isomer ratios are often close to unity, although there is some correlation between the inductive effect of the substituent and the predominance of *para* over *meta* substitution. Weak nucleophiles like ammonia also show some positional selectivity; e.g., the *para*/*meta* substitution ratio for 4-chlorobenzyne is 4.92 with ammonia as nucleophile, but unity for the amide anion[145].

The observation of *cine* substitution was of key importance in the early work on benzyne[1]. The predominant *meta* substitution by nucleophiles of arynes generated from *ortho*-substituted precursors continues to be used in a practical way, as a means of producing particular isomers. Two examples are shown in equations (22)[149] and (23)[150].



(22)

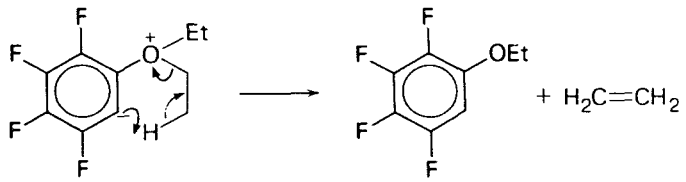


(23)

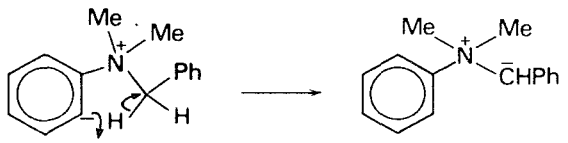
3. The fate of the aryl anion intermediate

It has been assumed in the preceding section that nucleophilic attack on benzyne leads to the formation of an aryl anion intermediate. This seems to be justified not only for anionic nucleophiles but also for their conjugate acids (a concerted four-centre mechanism for the addition of methanol and ammonia to benzyne has been rejected[145]). Other neutral nucleophiles, such as tertiary amines and sulphides, also add to give a zwitterionic intermediate as the primary product.

The most common subsequent reaction in protic solvents is intermolecular protonation of the aryl anion. Several intramolecular processes can, however, compete, particularly in an aprotic medium. The type of reaction depends very much on the nature of the nucleophile. Intramolecular transfer of a proton can occur in a number of ways, the two most common leading to fragmentation through a six-membered cyclic transition state (e.g. equation 24[52,54]) and to the formation of an ylide through a five-membered transition state (e.g. equation 25[151]). The aryl anion can also attack an electrophilic carbon centre within the molecule, leading either to cyclization or to the transfer of a group.



(24)



(25)

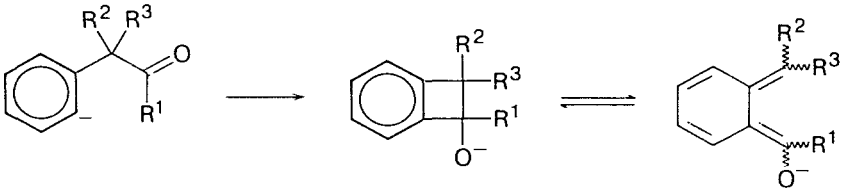
In the following sections these reactions are described; the classification is based on the nature of the nucleophilic centre, but there is a great deal in common in the mechanisms of these reactions. The attack of intramolecularly bonded nucleophiles on arynes, though not mechanistically distinct, is dealt with separately in Section IV.D.8, since the reaction has particular practical application as a method of preparing benzo-fused heterocyclic compounds.

4. Addition of carbon nucleophiles

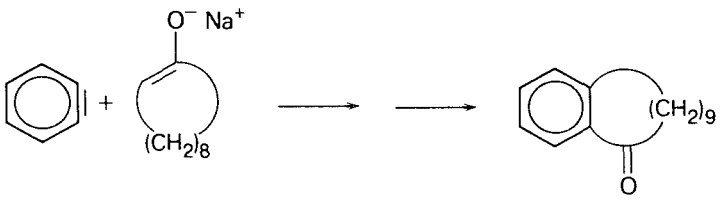
Benzyne is a useful intermediate for the phenylation of carbanions. The reaction of benzyne, generated from an aryl halide and sodamide or potassamide in liquid ammonia, with enolate anions leads to phenylation products in moderate yields[1]. By-products often arise from the introduction of more than one molecule of benzyne.

Phenylation results from proton transfer to the anion **58**. By carrying out the reaction in aprotic solvents such as tetrahydrofuran, Caubère was able to observe several other types of product[17,18]. Enolates derived from aliphatic ketones give, besides simple α-phenylation products, rearranged ketones derived from the collapse of the anion **58** to the benzocyclobutoxide **59** and its subsequent ring-opening (equation 26).

The reaction is particularly useful when it is carried out with alicyclic ketones, as it constitutes a means of benzo-annelation with ring-expansion. Thus, the sodium enolate of cyclodecanone reacts with bromobenzene and sodamide in dimethoxyethane to give the benzocyclododecanone **60** in 60% yield[152] (equation 27).



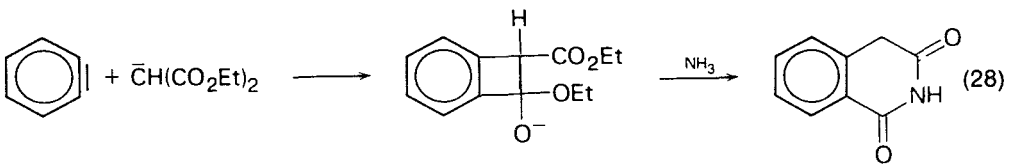
(58) (59) (26)



(60) (27)

Benzocyclobutanols, derived from anions of the type **59** by protonation, can also be isolated from reactions involving cycloalkanones[18]. The reactions can be directed either towards products of these types, or to the α-phenylated cycloalkanones, by a careful choice of the base and of the solvent[18].

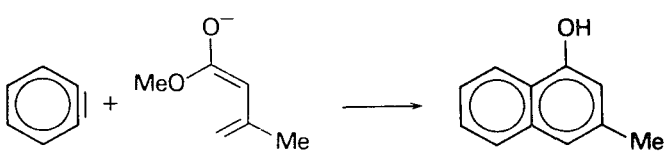
Hexamethylphosphoramide can also have a similar effect on the type of products that are obtained from benzyne and carbanions. An example is the reaction of benzyne (from bromobenzene and sodamide) with diethyl malonate, which, in the presence of hexamethylphosphoramide, gives homophthalimide (**61**) (50%) besides the usual product, diethyl phenylmalonate. This reaction, like those above, probably involves a cyclobutoxide anion (**62**) as an intermediate[153] (equation 28).



(62) (61) (28)

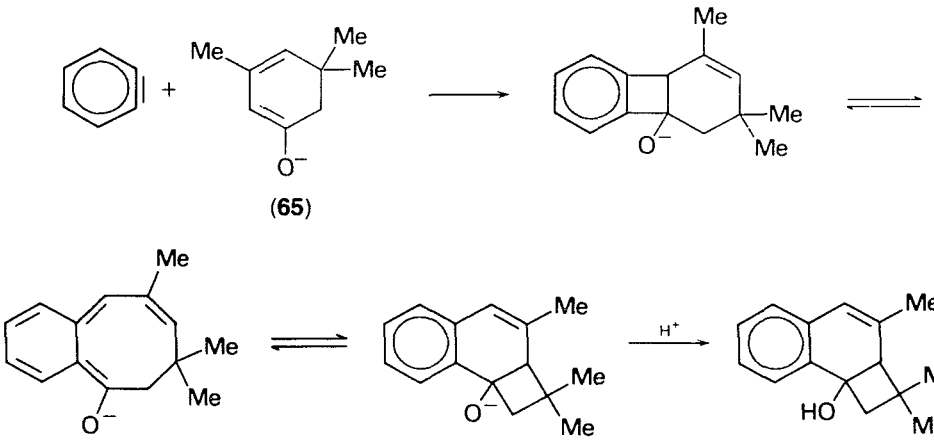
A variant of this type of cyclization occurs with enolates derived from α,β-unsaturated ketones[104,105,154]. With acyclic dienolate anions, benzyne can react at both the α- and γ- carbon atoms, though α-attack appears to predominate. Dienolate anions derived from esters also add to benzyne: thus, benzyne derived from bromobenzene and a 'complex base' adds to the dienolate anion **63** to give 3-methyl-1-naphthol in 37% yield (equation 29)[104].

With six-membered cyclic dienolate anions, α-attack is followed by a sequence of rearrangements which lead to the formation of cyclobutanols of rearranged structure.



(63) (29)

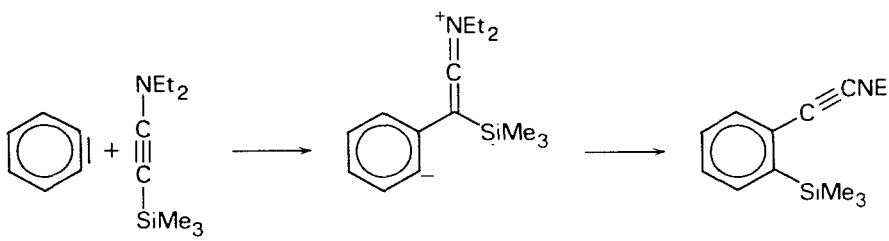
An example is the formation of the cyclobutanol **64** (30%) from the dienolate anion **65** and benzyne[154]. A possible route by which the product could be formed, which is a modified version of that suggested by the authors[154], is shown in equation (30) and involves opening of the first-formed cyclobutoxide anion enolate to a quinodimethane, followed by an alternative cyclization of the triene system so produced.



(65) (30)

(64)

Benzyne will also phenylate nucleophilic aromatic compounds. 2-Phenylanisole is the major product of the Ag^+-catalysed decomposition of benzenediazonium-2-carboxylate in anisole[110] and a small amount of *C*-phenylation also occurs in the reaction of benzyne and aniline[155]. Benzyne has also been shown to phenylate vinyllithium compounds[156] and the dianion of anthracene[157]. With silylated ynamines, e.g. **66**, benzyne reacts through carbon and the zwitterion is transformed into the final product (**67**) by a 1,3-shift of a trimethylsilyl group[158] (equation 31).



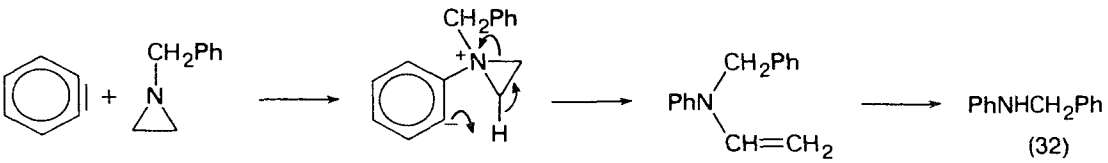
(66) (31)

(67)
21%

5. *Addition of nitrogen nucleophiles*

The reactions of benzynes with mono- and di-alkylamines have been used as a convenient method of synthesizing (alkylamino)benzenes[150,159]. With tertiary amines bearing a β-hydrogen atom the reaction with benzyne is known to go predominantly by an intramolecular proton transfer and elimination of an olefin from the intermediate zwitterion[1]. Examples of similar reactions include those with 2-(trimethylsilyl)ethylamine[160] and with 1-benzylaziridine (equation 32)[161].

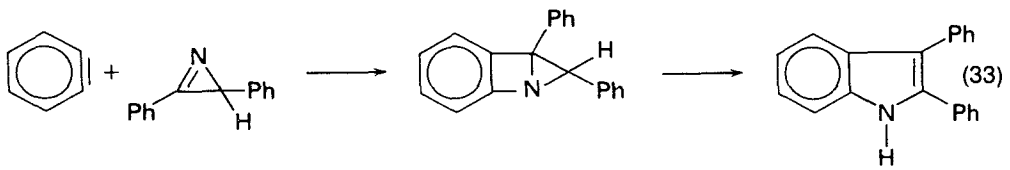
In the absence of a β-hydrogen atom in the tertiary amine, transfer of an α-proton commonly occurs to give an ylide as an intermediate. This can then undergo a



(32)

1,2-group migration (a Stevens rearrangement)[162]. An example is the reaction of *N*,*N*-dimethylbenzylamine with benzyne shown in equation (25)[151]. *N*,*N*-Dimethylaniline also reacts with benzyne in this way, but with tetrafluorobenzyne several additional products are formed, which come from cycloaddition to the benzene ring and from phenyl migration in the ylide[101]. Phenyl migration has also been observed in ylides derived from α-silylated amines[163].

Nitrosobenzene reacts with tetrachlorobenzyne through nitrogen; the zwitterion then cyclizes to give a *N*-hydroxycarbazole derivative[164]. Benzyne similarly gives *N*-hydroxycarbazole, but in very low yield. Several nitrogen heterocyclic compounds, including benzotriazoles and anthranil, react with benzyne at nitrogen[107,165]. 2,3-Diphenylazirine gives 2,3-diphenylindole as the major product; this is most simply rationalized as a stepwise [2 + 2]addition of benzyne to the C=N bond followed by rearrangement (equation 33)[166].

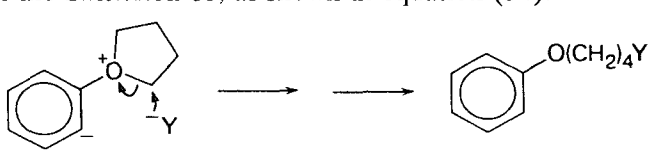


(33)

50%

6. *Addition of oxygen nucleophiles*

There are many examples of the interception of arynes by oxygen anions, such as alkoxides, phenoxides and carboxylate anions, and by their conjugate acids[1]. As was mentioned in Section IV.D.1, the competition of methoxide anions and neutral methanol for 4-chlorobenzyne has been studied in detail: the competition constant $MeO^-/MeOH$ is 170 for the *meta* position and 70 for the *para* position, and methanol adds stepwise through a zwitterionic intermediate[144,145]. Ethers can also add to arynes and give products derived from zwitterionic intermediates. As with tertiary amines, ethers bearing a β-hydrogen atom normally react by cycloelimination: this was shown in equation (24) for the reaction between tetrafluorobenzyne and diethyl ether. Similar reactions have been observed between benzyne and diethyl ether, and between benzyne and cyclohexene oxide[167]. In aryne reactions involving the use of tetrahydrofuran as a solvent, products have been isolated which incorporate a $(CH_2)_4O$ unit[168]. These products probably result from the attack of an external nucleophile on the zwitterion **68**, as shown in equation (34).

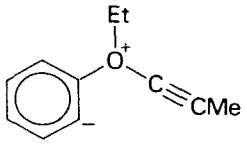


(34)

(68)

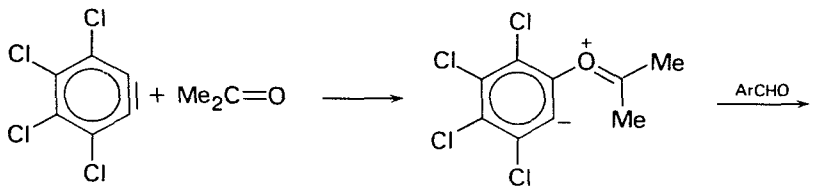
Y = OH, OCOR, OAr

Benzyne with the acetylenic ether 1-ethoxypropyne gives 3-methylbenzofuran (20%) among other products[169]. This may be formed by cyclization of an intermediate zwitterion **69**.



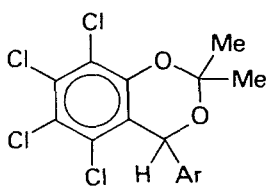
(69)

Aldehydes and ketones are not normally sufficiently nucleophilic to react with benzyne. With tetrachlorobenzyne, however, there is evidence that some carbonyl compounds (e.g. acetone, benzaldehyde and pentan-3-one) can react to form zwitterions such as **70**[52,170]. In the presence of a second carbonyl compound, 1,3-benzodioxan derivatives have been isolated (equation 35). The reaction of

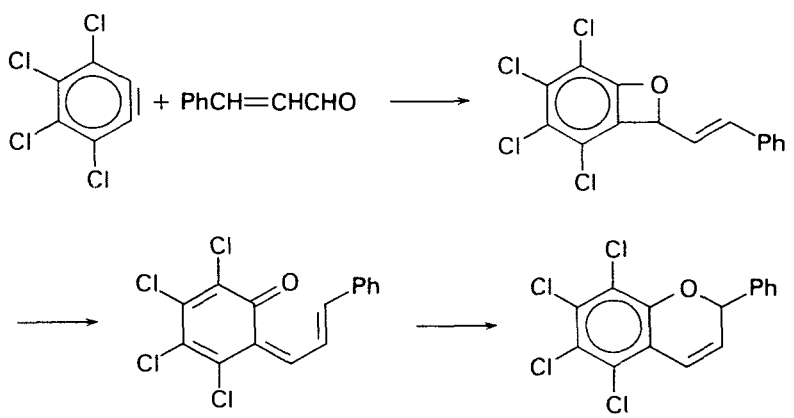


(70)

(35)



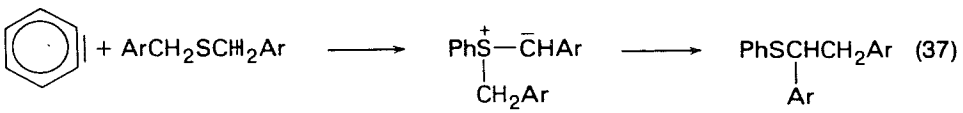
tetrachlorobenzyne with cinnamaldehyde has been shown to go through a benzoxetan intermediate (equation 36)[55]. It seems probable that this, too, involves an initial nucleophilic attack by the oxygen of the carbonyl group, although the absence of formal 1,4-cycloadducts was taken by the authors as evidence against such a mechanism[55].



(36)

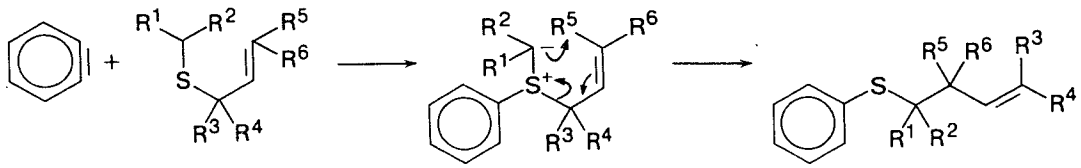
7. *Addition of other nucleophiles*

Thiols and their anions react readily with arynes[1]. Sulphides also add to benzynes to give zwitterions which can then undergo the same types of reaction (proton shifts followed by fragmentation or rearrangement) as have been described for tertiary amines and ethers[162,171,172]. The sequence of the reaction of a sulphide with benzyne, followed by Stevens rearrangement, is a useful method of carbon–carbon bond-formation (equation 37)[172]. The reaction has, for example, been employed in the



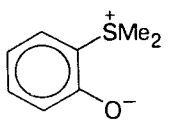
(37)

synthesis of cyclophanes[173]. With an allylic sulphide, addition to benzyne is followed by a [3,2]sigmatropic shift in the intermediate ylide (equation 38). This reaction was used as the key step in a synthesis of squalene[174].

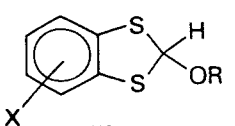


(38)

Benzyne reacts with a wide variety of other sulphur-containing nucleophiles. With dimethyl sulphoxide the betaine **71** is formed[175]: this appears to involve formal [2 + 2]addition to the S=O bond, followed by cleavage. Carbon disulphide undergoes an addition reaction with benzynes which leads to the formation of the cycloadducts **72** in the presence of alcohols[176]. The yields of the products are fairly good (30–50%) and the reaction therefore represents a useful way of introducing two *ortho* sulphur substituents. Related reactions have been observed with other compounds containing the structural unit S=C—S; these include dithio esters[177] and several heterocycles[178].



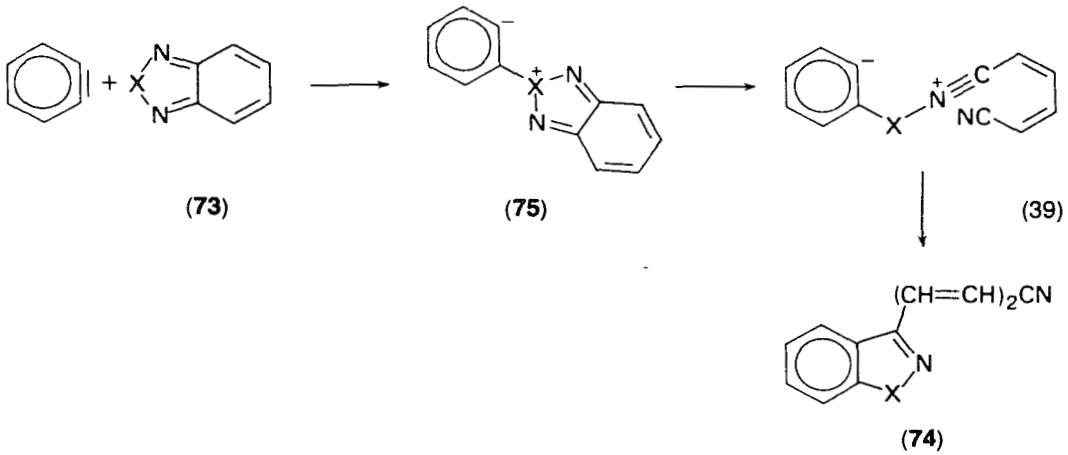
(71)



(72)

Other reactions of benzyne with sulphur-containing heterocycles which result in the fragmentation of the heterocycles have been observed[179,180]. 2,1,3-Benzothiadiazole (**73**, X = S) gives the unsaturated nitrile **74** in low yield. This reaction probably proceeds through the intermediate zwitterion **75**[180]. A similar reaction takes place with the corresponding selenadiazole (**73**, X = Se) and the nitrile is isolated in excellent yield (equation 39).

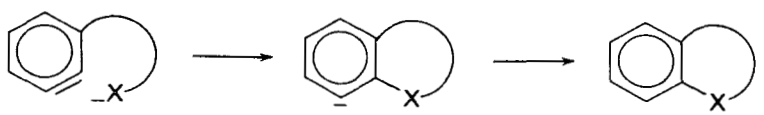
Diaryl diselenides and ditellurides will intercept benzyne to give the *ortho*-disubstituted adducts *o*-$C_6H_4(XAr)_2$[181]. Phosphines[1], halide anions[1,53] and the anion Ph_2P^-[182] also react with benzyne.



(73) (75) (39) (74)

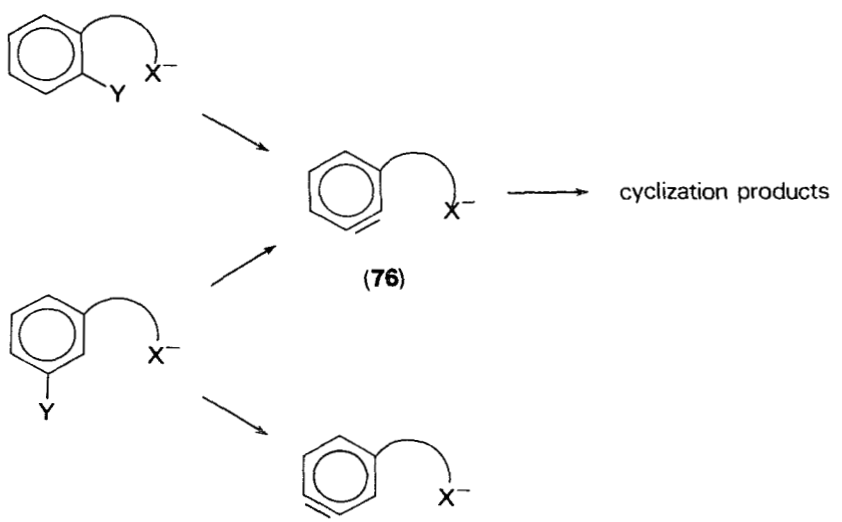
8. *Cyclization reactions involving arynes*

One of the most useful synthetic applications of aryne chemistry has been in the construction of benzo-fused carbocycles and heterocycles by the general route shown in equation (40).



(40)

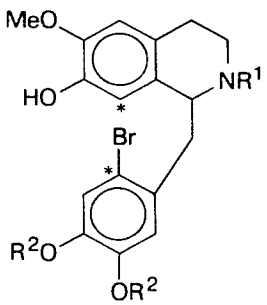
Several examples of such reactions were described during the 1960s and from these, some general features were recognized[1]. These are (*a*) that in common with other cyclizations, reactions leading to the formation of 5- or 6-membered rings tend to be most favourable; (*b*) in the formation of such rings, groups which are normally rather unreactive towards benzyne can participate as nucleophiles; and (*c*) that the aryne can be generated either from *ortho*- or from *meta*-substituted precursors (equation 41)



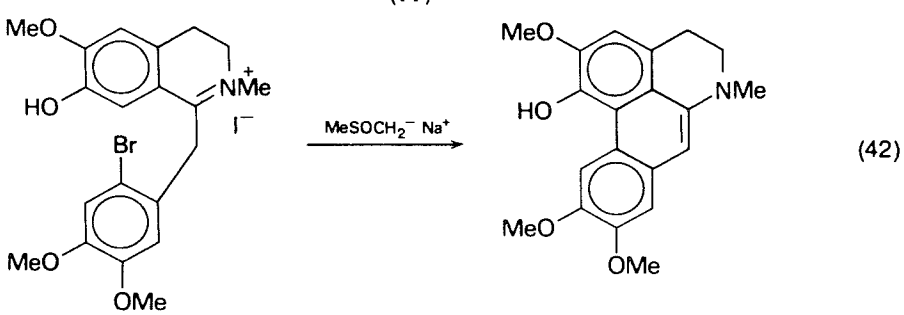
(76) (41)

although the former tend to give better yields because only the desired aryne (**76**) can be produced. In common with other cyclization reactions, it is also now recognized that the ease of ring-formation is related to the angle of approach of the attacking nucleophile[183].

During the last decade the most important applications of reactions of this type have been to the synthesis of isoquinoline alkaloids[184,185]. Much of this work has concerned the attempted arynic cyclization of compounds of the type **77**. The desired cyclization involves coupling across the starred positions. In general the reactions are not very efficient, partly because there is competitive intramolecular coupling via the *para* position of the phenol and via the nucleophilic nitrogen atom. The latter coupling can be prevented by quaternization of the nitrogen. Some intermolecular attack by the amide ion used to generate the aryne also occurs. An acceptable yield of the cyclization product **78** was, however, obtained in the reaction of the methiodide **79** with $MeSOCH_2^-Na^+$[185] (equation 42).



(**77**)

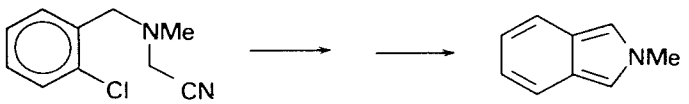


(42)

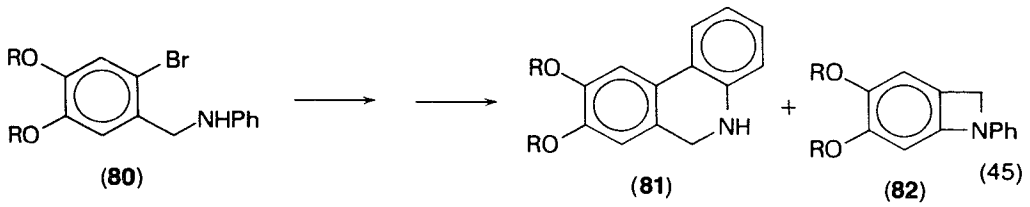
(**79**) (**78**)

Among other applications of the arynic cyclization reaction are the syntheses of indoles[186] (equation 43) and of isoindoles[187] (equation 44). The cyclization of anils derived from 2-chlorobenzaldehydes has been used as a route to phenanthridines[188]. Cyclization of substituted *N*-benzylanilines (e.g. **80**) gave, besides the dihydrophenanthridines (**81**), the *N*-phenylbenzazetines (**82**) in low yields[189] (equation 45). The enaminone (**83**) also undergoes competitive cyclization onto carbon and nitrogen[190].

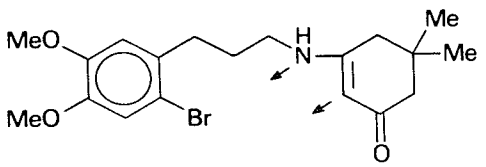
(43)



(44)



(80) (81) (82) (45)

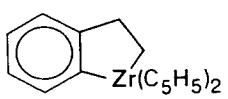


(83)

E. Aryne–Metal Complexes

Several examples have been given earlier of the influence of silver(I) cations on the course of aryne reactions. Complexation of the aryne to the metal is most often postulated to account for these results. The possibility of complexation of benzyne has also been discussed in the lead tetraacetate oxidation of 1-aminobenzotriazole[36].

An early claim that a benzyne–transition-metal complex had been isolated[191] was later shown to be erroneous[192]. An attempt to isolate a platinum(0) complex of benzyne was also unsuccessful, although it may have been formed as a transient intermediate[75]. The first benzyne complex to be characterized was an osmium cluster complex containing three osmium atoms formally bound to the benzyne[193]. Other complexes of this type are known[194]. The first complex containing a single transition-metal atom bonded to benzyne was the tantalum complex $Ta(\eta^5\text{-}C_5Me_5)(\eta^2\text{-}C_6H_4)Me_2$[195]. The X-ray crystal structure shows that the metal is directly bonded to the *ortho* carbon atoms. Another complex of this type is the titanium complex $Ti(\eta^2\text{-}C_6H_4)Ph_2$, which can be generated from Ph_2TiCl_2, *o*-fluorobromobenzene and magnesium[196]. Similar titanium[197] and zirconium[198,199] complexes have been shown to be reaction intermediates. These complexes will undergo addition reactions with small molecules such as olefins and acetylenes, and in the case of $Ti(C_6H_4)Ph_2$ with carbon dioxide and nitrogen. For example, the transient zirconium complex $(C_5H_5)_2Zr(C_6H_4)$ can be intercepted by ethylene to give **84**[199].



(84)

C_5H_5 = 

It seems unlikely that such complexes will prove to be capable of undergoing reactions typical of 'free' benzyne, and whether they are better regarded as σ-bonded *o*-phenylene complexes or as π-bonded benzyne complexes is a debatable point[195].

V. REFERENCES

1. R. W. Hoffmann, *Dehydrobenzene and Cycloalkynes*, Academic Press, New York, 1967.
2. R. W. Hoffmann in *Chemistry of Acetylenes* (Ed. H. G. Viehe), Dekker, New York, 1969, p. 1063.
3. W. Pritzkow, *Z. Chem.*, **10**, 330 (1970); E. K. Fields in *Organic Reactive Intermediates* (Ed. S. P. McManus), Academic Press, New York, 1973, pp. 449–508; W. J. le Noble, *Highlights of Organic Chemistry*, Dekker, New York, 1974, Chap. 19; J. T. Sharp in *Comprehensive Organic Chemistry*, Vol. 1 (Ed. J. F. Stoddard), Pergamon Press, Oxford, 1979, pp. 477–490.
4. O. L. Chapman, K. Mattes, C. L. McIntosh, J. Pacansky, G. V. Calder and G. Orr, *J. Amer. Chem. Soc.*, **95**, 6134 (1973).
5. O. L. Chapman, C.-C. Chang, J. Kolc, N. R. Rosenquist and H. Tomioka, *J. Amer. Chem. Soc.*, **97**, 6586 (1975).
6. I. R. Dunkin and J. G. MacDonald, *J. Chem. Soc., Chem. Commun.*, 772 (1979).
7. J. W. Laing and R. S. Berry, *J. Amer. Chem. Soc.*, **98**, 660 (1976).
8. M. J. S. Dewar and W.-K. Li, *J. Amer. Chem. Soc.*, **96**, 5569 (1974).
9. J. O. Noell and M. D. Newton, *J. Amer. Chem. Soc.*, **101**, 51 (1979).
10. E. Haselbach, *Helv. Chim. Acta*, **54**, 1987 (1971); H. A. Fraenkel and M. D. Newton, *Chem. Phys. Letters*, **18**, 244 (1973).
11. H.-F. Grützmacher and J. Lohmann, *Justus Liebigs Ann. Chem.*, **705**, 81 (1967); S. K. Pollack and W. J. Hehre, *Tetrahedron Letters*, 2483 (1980).
12. M. D. Gheorgiu and R. Hoffmann, *Rev. Roum. Chim.*, **14**, 947 (1969); R. Hoffmann, A. Imamura and W. J. Hehre, *J. Amer. Chem. Soc.*, **90**, 1499 (1968); R. W. Atkin and T. A. Claxton, *Trans. Faraday Soc.*, **66**, 257 (1970); D. L. Wilhite and J. L. Whitten, *J. Amer. Chem. Soc.*, **93**, 2858 (1971); P. Millie, L. Praud and J. Serre, *Intern. J. Quantum Chem.*, **4**, 187 (1971); F. M. Stoyanovich, Ya. L. Gol'dfarb, I. A. Abronin and G. M. Zhidomirov, *Tetrahedron Letters*, 1761 (1973).
13. R. T. Luibrand and R. W. Hoffmann, *J. Org. Chem.*, **39**, 3887 (1974).
14. N. G. Rondan, L. N. Domelsmith, K. N. Houk, A. T. Bowne and R. H. Levin, *Tetrahedron Letters*, 3237 (1979).
15. R. A. Olofson and C. M. Dougherty, *J. Amer. Chem. Soc.*, **95**, 582 (1973); K. L. Shepard, *Tetrahedron Letters*, 3371 (1975).
16. I. Fleming and T. Mah, *J. Chem. Soc., Perkin Trans. 1*, 964 (1975).
17. P. Caubère, *Acc. Chem. Res.*, **7**, 301 (1974).
18. P. Caubère, *Topics Current Chem.*, **73**, 49 (1978).
19. O. M. Nefedov, A. I. D'yachenko and A. K. Prokof'ev, *Russ. Chem. Rev.*, **46**, 941 (1977); O. M. Nefedov and A. I. D'yachenko, *Angew. Chem. (Intern. Ed.)*, **11**, 507 (1972); B. J. Wakefield, *The Chemistry of Organolithium Compounds*, Pergamon Press, Oxford, 1974, p. 172.
20. R. Harrison, H. Heaney and P. Lees, *Tetrahedron*, **24**, 4589 (1968).
21. I. Fleming and T. Mah, *J. Chem. Soc., Perkin Trans. 1*, 1577 (1976).
22. R. Gompper, G. Seybold and B. Schmolke, *Angew. Chem. (Intern. Ed.)*, **7**, 389 (1968).
23. F. M. Logullo, A. H. Seitz and L. Friedman, *Org. Synth., Collect. Vol. V*, 54 (1973).
24. P. Crews and J. Beard, *J. Org. Chem.*, **38**, 522 (1973).
25. L. Friedman and F. M. Logullo, *J. Org. Chem.*, **34**, 3089 (1969).
26. T. Miwa, M. Kato and T. Tamano, *Tetrahedron Letters*, 2743 (1968).
27. M. P. Cava and M. J. Mitchell, *Selected Experiments in Organic Chemistry*, Benjamin, New York, 1966, p. 93.
28. L. F. Fieser and M. J. Haddadin, *Org. Synth., Coll. Vol. V*, 1037 (1973).
29. J. Nakayama, O. Simamura and M. Yoshida, *Chem. Commun.*, 1222 (1970).
30. Y. Maki, T. Furuta and M. Suzuki, *J. Chem. Soc., Perkin Trans. 1*, 553 (1979).
31. C. Rüchardt and C. C. Tan, *Angew. Chem. (Intern. Ed.)*, **9**, 522 (1970).

32. J. I. G. Cadogan, *Acc. Chem. Res.*, **4**, 186 (1971); E. A. Bell, J. I. G. Cadogan, P. W. Milburn, C. D. Murray, R. M. Paton and J. T. Sharp, *J. Chem. Soc., Perkin Trans. 2*, 588 (1976); J. I. G. Cadogan, C. D. Murray and J. T. Sharp, *J. Chem. Soc., Perkin Trans. 2*, 583 (1976); B. H. Klanderman, D. P. Maier, G. W. Clark and J. A. Kampmeier, *Chem. Commun.*, 1003 (1971).
33. J. Brennan, J. I. G. Cadogan and J. T. Sharp, *J. Chem. Res. (S)*, 107 (1977).
34. B. Baigrie, J. I. G. Cadogan, J. R. Mitchell, A. K. Robertson and J. T. Sharp, *J. Chem. Soc., Perkin Trans. 1*, 2563 (1972).
35. J. I. G. Cadogan, A. G. Rowley, J. T. Sharp, B. Sledzinski and N. H. Wilson, *J. Chem. Soc., Perkin Trans. 1*, 1072 (1975).
36. C. D. Campbell and C. W. Rees, *J. Chem. Soc. (C)*, 742 (1969).
37. J. I. G. Cadogan and J. B. Thomson, *Chem. Commun.*, 770 (1969).
38. T. L. Gilchrist, C. W. Rees and R. C. Storr, *XXIIIrd International Congress Pure and Applied Chem.*, Vol. 4, Butterworths, London, 1971, pp. 105–127.
39. F. J. Graveling, *Ph. D. Thesis*, University of Leicester, 1969.
40. M. Keating, M. E. Peek, C. W. Rees and R. C. Storr, *J. Chem. Soc., Perkin Trans. 1*, 1315 (1972).
41. G. Wittig and R. W. Hoffmann, *Org. Synth., Coll. Vol. V*, 60 (1973).
42. A. T. Fanning and T. D. Roberts, *Tetrahedron Letters*, 805 (1971).
43. G. Seybold, *Angew. Chem. (Intern. Ed.)*, **16**, 365 (1977).
44. B. M. Adger, M. Keating, C. W. Rees and R. C. Storr, *J. Chem. Soc., Perkin Trans. 1*, 41 (1975).
45. M. P. David and J. F. W. McOmie, *Tetrahedron Letters*, 1361 (1973).
46. D. L. Forster, T. L. Gilchrist, C. W. Rees and E. Stanton, *Chem. Commun.*, 695 (1971).
47. R. F. C. Brown, D. V. Gardner, J. F. W. McOmie and R. K. Solly, *Australian J. Chem.*, **20**, 139 (1967).
48. E. K. Fields and S. Meyerson, *Acc. Chem. Res.*, **9**, 273 (1969); *J. Org. Chem.*, **37**, 3861 (1972); J. M. Patterson, C. Shiue and W. T. Smith, *J. Org. Chem.*, **38**, 387 (1973).
49. R. J. Armstrong, R. F. C. Brown, F. W. Eastwood and M. E. Romyn, *Australian J. Chem.*, **32**, 1767 (1979).
50. J. Kolc, *Tetrahedron Letters*, 5321 (1972).
51. M. Jones and M. R. DeCamp, *J. Org. Chem.*, **36**, 1536 (1971).
52. H. Heaney, *Fortsch. Chem. Forsch.*, **16**, 35 (1970).
53. D. J. Malcolme-Lawes, A. G. Massey and D. Wickens, *J. Chem. Soc., Chem. Commun.*, 933 (1977).
54. S. Hayashi and N. Ishikawa, *Bull. Chem. Soc. Japan*, **45**, 642 (1972).
55. H. Heaney, J. M. Jablonski and C. T. McCarty, *J. Chem. Soc., Perkin Trans. 1*, 2903 (1972).
56. R. W. Franck and K. Yanagi, *J. Amer. Chem. Soc.*, **90**, 5814 (1968); J. I. G. Cadogan, J. Cook, M. J. P. Harger, P. G. Hibbert and J. T. Sharp, *J. Chem. Soc. (B)*, 595 (1971).
57. C. W. Rees and D. E. West, *J. Chem. Soc. (C)*, 583 (1970).
58. S. Mazur and P. Jayalekshmy, *J. Amer. Chem. Soc.*, **101**, 677 (1979).
59. A. Martineau and D. C. DeJongh, *Can. J. Chem.*, **55**, 34 (1977).
60. R. H. Hales, J. S. Bradshaw and D. R. Pratt, *J. Org. Chem.*, **36**, 314 (1971); J. S. Bradshaw and R. H. Hales, *J. Org. Chem.*, **36**, 318 (1971).
61. G. W. Gribble, R. W. Allen, P. S. Anderson, M. E. Christy and C. D. Colton, *Tetrahedron Letters*, 3673 (1976).
62. P. Caubère and M. S. Mourad, *Bull. Soc. Chim. Fr.*, 1415 (1974).
63. W. Tochtermann, G. Stubenrauch, K. Reiff and U. Schumacher, *Chem. Ber.*, **107**, 3340 (1974).
64. (a) J. W. Barton and S. A. Jones, *J. Chem. Soc. (C)*, 1276 (1967).
(b) J. W. Barton and A. R. Grinham, *J. Chem. Soc., Perkin Trans. 1*, 634 (1972).
65. J. Burdon, H. S. Hill, I. W. Parsons and J. C. Tatlow, *J. Chem. Soc., Chem. Commun.*, 1147 (1979).
66. R. L. Hillard and K. P. C. Vollhardt, *Angew. Chem. (Intern. Ed.)*, **16**, 399 (1977).
67. R. L. Hillard and K. P. C. Vollhardt, *J. Amer. Chem. Soc.*, **98**, 3579 (1976); R. L. Funk and K. P. C. Vollhardt, *Angew. Chem. (Intern. Ed.)*, **15**, 53 (1976).
68. E. N. Losey and E. LeGoff, *J. Org. Chem.*, **38**, 3812 (1973).

69. R. C. Perera and R. K. Smalley, *Chem. Commun.*, 1458 (1970).
70. C. E. L. Peterson and A. Berg, *Acta Chem. Scand.*, **25**, 375 (1971).
71. T. Nakazawa and I. Murata, *Angew. Chem. (Intern. Ed.)*, **14**, 711 (1975).
72. J. C. Martin and D. R. Bloch, *J. Amer. Chem. Soc.*, **93**, 451 (1971).
73. E. R. Biehl, E. Nieh and K. C. Hsu, *J. Org. Chem.*, **34**, 3595 (1969).
74. G. Porter and J. I. Steinfeld, *J. Chem. Soc. (A)*, 877 (1968).
75. T. L. Gilchrist, F. J. Graveling and C. W. Rees, *J. Chem. Soc. (C)*, 977 (1971).
76. R. W. Atkin and C. W. Rees, *Chem. Commun.*, 152 (1969).
77. M. Jones and R. H. Levin, *J. Amer. Chem. Soc.*, **91**, 6411 (1969).
78. B. H. Klanderman and T. R. Criswell, *J. Org. Chem.*, **34**, 3426 (1969).
79. W. Ried and J. T. S. Eng, *Justus Liebigs Ann. Chem.*, **727**, 219 (1969).
80. D. L. Fields, T. H. Regan and R. E. Graves, *J. Org. Chem.*, **36**, 2995 (1971).
81. W. Steglich, E. Buschmann, G. Gansen and L. Wilschowitz, *Synthesis*, 252 (1977).
82. R. E. Moerck and M. A. Battiste, *J. Chem. Soc., Chem. Commun.*, 1171 (1972).
83. M. S. Newman and R. Kannan, *J. Org. Chem.*, **41**, 3356 (1976).
84. W. Tochtermann, G. Stubenrauch and H. Zimmerman, *Chem. Ber.*, **108**, 2510 (1975); W. Tochtermann, R. Strickler, H. A. Klein and E. Biegi, *Chem. Ber.*, **110**, 2456 (1977); W. Tochtermann and H. Maasland, *Justus Liebigs Ann. Chem.*, 297 (1979).
85. J. Bornstein, D. E. Remy and J. E. Shields, *Tetrahedron Letters*, 4247 (1974); P. S. Anderson, M. E. Christy, G. F. Lundell and G. S. Ponticello, *Tetrahedron Letters*, 2553 (1975); J. M. Vernon, M. Ahmed and J. M. Moran, *J. Chem. Soc., Perkin Trans. 1*, 1084 (1977); J. M. Vernon, M. Ahmed and L. J. Kricka, *J. Chem. Soc., Perkin Trans. 1*, 837 (1978); L. J. Kricka and J. M. Vernon, *Advan. Het. Chem.*, **16**, 87 (1974).
86. D. D. Callander, P. L. Coe, J. C. Tatlow and A. J. Uff, *Tetrahedron*, **25**, 25 (1969).
87. L. J. Kricka and J. M. Vernon, *J. Chem. Soc., Perkin Trans. 1*, 766 (1973).
88. R. Maruca, *J. Org. Chem.*, **36**, 1626 (1971).
89. W. P. Neumann and M. Schriewer, *Tetrahedron Letters*, 3273 (1980).
90. C. Grugel, W. P. Neumann and M. Schriewer, *Angew. Chem. (Intern. Ed.)*, **18**, 543 (1979).
91. B. Hankinson, H. Heaney, A. P. Price and R. P. Sharma, *J. Chem. Soc., Perkin Trans. 1*, 2569 (1973).
92. J. W. Wilt and E. Vasiliauskas, *J. Org. Chem.*, **35**, 2410 (1970); W. T. Ford, *J. Org. Chem.*, **36**, 3979 (1971).
93. L. Lombardo and D. Wege, *Tetrahedron*, **30**, 3945 (1974).
94. E. Vedejs and R. A. Shepherd, *Tetrahedron Letters*, 1863 (1970).
95. E. E. Waali, *J. Org. Chem.*, **40**, 1355 (1975).
96. M. R. DeCamp, R. H. Levin and M. Jones, *Tetrahedron Letters*, 3575 (1974).
97. I. Tabushi, H. Yamada, Z. Yoshida and R. Oda, *Bull. Chem. Soc. Japan*, **50**, 285 (1977).
98. M. Stiles, U. Burckhardt and G. Freund, *J. Org. Chem.*, **32**, 3718 (1967); L. Friedman and D. F. Lindow, *J. Amer. Chem. Soc.*, **90**, 2329 (1968); J. M. Brinkley and L. Friedman, *Tetrahedron Letters*, 4141 (1972).
99. J. P. N. Brewer, I. F. Eckhard, H. Heaney and B. A. Marples, *J. Chem. Soc. (C)*, 664 (1968); H. Heaney and J. M. Jablonski, *J. Chem. Soc. (C)*, 1895 (1968); D. J. Berry and B. J. Wakefield, *J. Chem. Soc. (C)*, 2342 (1969).
100. P. C. Buxton, N. J. Hales, B. Hankinson, H. Heaney, S. V. Ley and R. P. Sharma, *J. Chem. Soc., Perkin Trans. 1*, 2681 (1974).
101. J. P. N. Brewer, H. Heaney, S. V. Ley and T. J. Ward, *J. Chem. Soc., Perkin Trans. 1*, 2688 (1974).
102. F. Serratosa and P. Solá, *Tetrahedron Letters*, 821 (1973).
103. S. F. Dyke, A. J. Floyd and S. E. Ward, *Tetrahedron*, **26**, 4005 (1970); Y. Ittah, I. Shahak, J. Blum and J. Klein, *Synthesis*, 678 (1977); M. Zander and W. H. Franke, *Chem. Ber.*, **107**, 727 (1974).
104. P. G. Sammes and T. W. Wallace, *J. Chem. Soc., Perkin Trans. 1*, 1377 (1975).
105. P. G. Sammes and D. J. Dodsworth, *J. Chem. Soc., Chem. Commun.*, 33 (1979).
106. S. Tanimoto, *Tetrahedron Letters*, 2903 (1977).
107. C. D. Campbell and C. W. Rees, *J. Chem. Soc. (C)*, 748 (1969).
108. G. Märkl, F. Lieb and C. Martin, *Tetrahedron Letters*, 1249 (1971).
109. J. Nakayama, H. Midorikawa and M. Yoshida, *Bull. Chem. Soc. Japan*, **48**, 1063 (1975).
110. L. Friedman, *J. Amer. Chem. Soc.*, **89**, 3071 (1967); I. Tabushi, H. Yamada, Z. Yoshida and R. Oda, *Bull. Chem. Soc. Japan*, **50**, 291 (1977).

111. P. Crews and M. Loffgren, *Tetrahedron Letters*, 4697 (1971); P. Crews and J. Beard, *J. Org. Chem.*, **38**, 529 (1973).
112. G. Bianchi, C. De Micheli and R. Gandolfi in *The Chemistry of Double-bonded Functional Groups* (Ed. S. Patai), John Wiley and Sons, London, 1977, p. 369.
113. D. St. C. Black, R. F. Crozier and V. C. Davis, *Synthesis*, 205 (1975).
114. J. P. Freeman and R. C. Grabiak, *J. Org. Chem.*, **41**, 2531 (1976); D. W. S. Latham, O. Meth-Cohn, H. Suschitzky and J. A. L. Herbert, *J. Chem. Soc., Perkin Trans. 1*, 470 (1977).
115. R. A. Abramovitch and I. Shinkai, *J. Amer. Chem. Soc.*, **96**, 5265 (1974).
116. H. Dürr and A. Hackenberger, *Synthesis*, 594 (1978); see also P. Luger, C. Tuchscherer, M. Grosse and D. Rewicki, *Chem. Ber.*, **109**, 2596 (1976).
117. T. Yamazaki and H. Shechter, *Tetrahedron Letters*, 4533 (1972); 1417 (1973).
118. A. Eckell and R. Huisgen, *Chem. Ber.*, **110**, 559 (1977).
119. N. Dennis, A. R. Katritzky, T. Matsuo, S. K. Parton and Y. Takeuchi, *J. Chem. Soc., Perkin Trans. 1*, 746 (1974); N. Dennis, A. R. Katritzky and S. K. Parton, *J. Chem. Soc., Perkin Trans. 1*, 2285 (1976).
120. H. Kato, S. Nakazawa, T. Kiyosawa and K. Hirakawa, *J. Chem. Soc., Perkin Trans. 1*, 672 (1976).
121. G. V. Boyd, T. Norris, P. F. Lindley and M. M. Mahmoud, *J. Chem. Soc., Perkin Trans. 1*, 1612 (1977).
122. C. F. Huebner and E. M. Donoghue, *J. Org. Chem.*, **33**, 1678 (1968); W. T. Ford, R. Radue and J. A. Walker, *Chem. Commun.*, 966 (1970).
123. (a) T. Kauffmann, D. Berger, B. Scheerer and A. Woltermann, *Chem. Ber.*, **110**, 3034 (1977).
(b) J. G. Duboudin, B. Jousseaume and M. Pinet-Vallier, *J. Organomet. Chem.*, **172**, 1 (1979).
124. P. G. Gassman and H. P. Benecke, *Tetrahedron Letters*, 1089 (1969).
125. J. Leitich, *Tetrahedron Letters*, 3025 (1980).
126. A. T. Bowne, T. A. Christopher and R. H. Levin, *Tetrahedron Letters*, 4111 (1976).
127. H. H. Wasserman, A. J. Solodar and L. S. Keller, *Tetrahedron Letters*, 5597 (1968).
128. L. Friedman, R. J. Osiewicz and P. W. Rabideau, *Tetrahedron Letters*, 5735 (1968).
129. D. M. Hayes and R. Hoffmann, *J. Phys. Chem.*, **76**, 656 (1972); S. Inagaki and K. Fukui, *Bull. Chem. Soc. Japan*, **46**, 2240 (1973).
130. M. A. O'Leary, M. B. Stringer and D. Wege, *Australian J. Chem.*, **31**, 2003 (1978).
131. H. Heaney, J. M. Jablonski, K. G. Mason and J. M. Sketchley, *J. Chem. Soc. (C)*, 3129 (1971).
132. D. J. Keyton, G. W. Griffin, M. E. Kuehne and C. E. Bayha, *Tetrahedron Letters*, 4163 (1969); T. Kametani, K. Kigasawa, M. Hiiragi, T. Hayasaka and O. Kusama, *J. Chem. Soc. (C)*, 1051 (1971); H. Heaney and S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, 2693 (1974).
133. A. T. Bowne and R. H. Levin, *Tetrahedron Letters*, 2043 (1974).
134. L. Lombardo and D. Wege, *Tetrahedron Letters*, 3981 (1971).
135. H. H. Wasserman and L. S. Keller, *Chem. Commun.*, 1483 (1970).
136. E. E. Nunn, *Tetrahedron Letters*, 4199 (1976).
137. M. Kato, Y. Okamoto and T. Miwa, *Tetrahedron*, **27**, 4013 (1971).
138. H. M. R. Hoffmann, *Angew. Chem. (Intern. Ed.)*, **8**, 556 (1969).
139. H. H. Wasserman and L. S. Keller, *Tetrahedron Letters*, 4355 (1974).
140. G. Ahlgren and B. Åkermark, *Tetrahedron Letters*, 3047 (1970).
141. G. Mehta and B. P. Singh, *Tetrahedron*, **30**, 2409 (1974).
142. V. Usieli and S. Sarel, *Tetrahedron Letters*, 1349 (1973).
143. M. Pomerantz, G. W. Gruber and R. N. Wilker, *J. Amer. Chem. Soc.*, **90**, 5040 (1968); P. G. Gassman and G. D. Richmond, *J. Amer. Chem. Soc.*, **90**, 5637 (1968).
144. J. F. Bunnett and C. Pyun, *J. Org. Chem.*, **34**, 2035 (1969).
145. J. F. Bunnett and J. K. Kim, *J. Amer. Chem. Soc.*, **95**, 2254 (1973).
146. T. Kauffmann, H. Fischer, R. Nürnberg, M. Vestweber and R. Wirthwein, *Tetrahedron Letters*, 2911, 2917 (1967).
147. T. Kauffmann, H. Fischer, R. Nürnberg and R. Wirthwein, *Justus Liebigs Ann. Chem.*, **731**, 23 (1970).
148. R. Levine and E. R. Biehl, *J. Org. Chem.*, **40**, 1835 (1975).
149. E. L. Smithwick and R. T. Shuman, *Synthesis*, 582 (1974).

150. M. F. Moreau-Hochu and P. Caubère, *Tetrahedron*, **33**, 955 (1977).
151. A. R. Lepley, R. H. Becker and A. G. Giumanini, *J. Org. Chem.*, **36**, 1222 (1971).
152. P. Caubère, G. Guillaumet and M. S. Mourad, *Tetrahedron*, **29**, 1857 (1973); see also M. C. Carre, M. L. Viriot-Villaume and P. Caubère, *Synthesis*, 48 (1977).
153. M. Guyot and D. Molho, *Tetrahedron Letters*, 3433 (1973).
154. M. Essiz, G. Guillaumet, J.-J. Brunet and P. Caubère, *J. Org. Chem.*, **45**, 240 (1980); see also M. Essiz, G. Guillaumet and P. Caubère, *Tetrahedron*, **35**, 1167 (1979).
155. P. Haberfield and L. Sief, *J. Org. Chem.*, **34**, 1508 (1969).
156. D. Y. Curtin and R. P. Quirk, *Tetrahedron*, **24**, 5791 (1968).
157. R. A. Rossi, C. C. Camusso and O. D. Madoery, *J. Org. Chem.*, **39**, 3254 (1974).
158. Y. Sato, Y. Kobayashi, M. Sugiura and H. Shirai, *J. Org. Chem.*, **43**, 199 (1978).
159. F. Effenberger, E. Auer and P. Fischer, *Chem. Ber.*, **103**, 1440 (1970); F. Effenberger, G. Prossel, E. Auer and P. Fischer, *Chem. Ber.*, **103**, 1456 (1970); E. R. Biehl, S. M. Smith and P. C. Reeves, *J. Org. Chem.*, **36**, 1841 (1971).
160. Y. Sato, Y. Ban, T. Aoyama and H. Shirai, *J. Org. Chem.*, **41**, 1962 (1976).
161. A. G. Giumanini, *J. Org. Chem.*, **37**, 513 (1972).
162. A. R. Lepley and A. G. Giumanini in *Mechanisms of Molecular Migrations* (Ed. B. S. Thyagarajan), Vol. 3, John Wiley and Sons, New York, 1971, p. 394.
163. Y. Sato, T. Toyo'oka, T. Aoyama and H. Shirai, *J. Chem. Soc., Chem. Commun.*, 640 (1975); *J. Org. Chem.*, **41**, 3559 (1976).
164. P. C. Buxton, H. Heaney, K. G. Mason and J. M. Sketchley, *J. Chem. Soc., Perkin Trans. 1*, 2695 (1974).
165. C. D. Campbell and C. W. Rees, *J. Chem. Soc. (C)*, 752 (1969).
166. V. Nair and K. H. Kim, *J. Org. Chem.*, **40**, 3784 (1975).
167. G. D. Richmond and W. Spendel, *Tetrahedron Letters*, 4557 (1973); see also Reference 52.
168. E. Wolthuis, B. Bouma, J. Moddenran and L. Sytsma, *Tetrahedron Letters*, 407 (1970); S. Hayashi and N. Ishikawa, *Bull. Chem. Soc. Japan*, **48**, 1467 (1975); R. S. Pal and M. M. Bokadia, *Pol. J. Chem.*, **52**, 1473 (1978).
169. H. H. Wasserman and J. M. Fernandez, *J. Amer. Chem. Soc.*, **90**, 5322 (1968).
170. H. Heaney and C. T. McCarty, *Chem. Commun.*, 123 (1970).
171. J. P. N. Brewer, H. Heaney and T. J. Ward, *J. Chem. Soc. (C)*, 355 (1969); H. Iwamura, M. Iwamura, T. Nishida, M. Yoshida and J. Nakayama, *Tetrahedron Letters*, 63 (1971); L. Brandsma, S. Hoff and H. D. Verkruijsse, *Rec. Trav. Chim.* **92**, 272 (1973).
172. B. M. Trost and L. S. Melvin, *Sulfur Ylides*, Academic Press, New York, 1975, Chap. 7.
173. T. Otsubo and V. Boekelheide, *J. Org. Chem.*, **42**, 1085 (1977).
174. G. M. Blackburn, W. D. Ollis, C. Smith and I. O. Sutherland, *Chem. Commun.*, 99 (1969).
175. H. H. Szmant and S. Vázquez, *Chem. Ind. (London)*, 1000 (1967); M. Kise, T. Asari, N. Furukawa and S. Oae, *Chem. Ind. (London)*, 276 (1967); R. Gompper, E. Kutter and G. Seybold, *Chem. Ber.*, **101**, 2340 (1968).
176. J. Nakayama, *Synthesis*, 38 (1975); J. Nakayama, E. Seki and M. Hoshino, *J. Chem. Soc., Perkin Trans. 1*, 468 (1978).
177. D. Paquer, D. Reffet and C. G. Andrieu, *Rec. Trav. Chim.*, **97**, 88 (1978).
178. D. B. J. Easton, D. Leaver and T. J. Rawlings, *J. Chem. Soc., Perkin Trans. 1*, 41 (1972); D. Paquer and R. Pou, *Bull. Soc. Chim. Fr.*, 120 (1976).
179. K. Kobayashi and K. Mutai, *Tetrahedron Letters*, 905 (1978).
180. C. D. Campbell, C. W. Rees, M. R. Bryce, M. D. Cooke, P. Hanson and J. M. Vernon, *J. Chem. Soc., Perkin Trans. 1*, 1006 (1978).
181. N. Petragnani and V. G. Toscano, *Chem. Ber.*, **103**, 1652 (1970).
182. D. G. Gillespie, B. J. Walker, D. Stevens and C. A. McAuliffe, *Tetrahedron Letters*, 1905 (1976).
183. J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 734, 738 (1976).
184. M. S. Gibson, G. W. Prenton, and J. M. Walthew, *J. Chem. Soc. (C)*, 2234 (1970); S. V. Kessar, R. Randhawa and S. S. Ghandi, *Tetrahedron Letters*, 2923 (1973); S. Kano, T. Yokomatsu, N. Yamada, K. Matsumoto, S. Tokita and S. Shibuya, *Chem. Pharm. Bull.*, **22**, 1607 (1974); R. J. Spangler, D. C. Boop and J. H. Kim, *J. Org. Chem.*, **39**, 1368 (1974); T. Kametani, S. Shibuya, K. Kigasawa, M. Hiiragi and O. Kusama, *J. Chem. Soc. (C)*, 2712 (1971); T. Kametani, K. Fukumoto and T. Nakano, *J. Heterocycl. Chem.*, **9**, 1363 (1972); T. Kametani, A. Ujiie, K. Takahashi, T. Nakano, T. Susuki and K. Fukumoto, *Chem.*

Pharm. Bull., **21**, 766 (1973); T. Kametani in *The Total Synthesis of Natural Products*, Vol. 3 (Ed. J. ApSimon), Wiley–Interscience, New York, 1977. p. 215.
185. T. Kametani, S. Shibuya and S. Kano, *J. Chem. Soc., Perkin Trans. 1*, 1212 (1973).
186. I. Fleming and M. Woolias, *J. Chem. Soc., Perkin Trans. 1*, 827 (1979).
187. B. Jaques and R. G. Wallace, *Tetrahedron*, **33**, 581 (1977).
188. S. V. Kessar, R. Gopal and M. Singh, *Tetrahedron*, **29**, 167 (1973); S. V. Kessar, D. Pal and M. Singh., *Tetrahedron*, **29**, 177 (1973); S. V. Kessar and G. S. Joshi, *Tetrahedron*, **29**, 419 (1973).
189. K. Krohn, D. Carboo and U. Puttfarcken, *Justus Liebigs Ann. Chem.*, 608 (1978).
190. H. Iida, Y. Yuasa and C. Kibayashi, *J. Org. Chem.*, **44**, 3985 (1979).
191. E. W. Gowling, S. F. A. Kettle and G. M. Sharples, *Chem. Commun.*, 21 (1968).
192. N. A. Bailey, S. E. Hull, R. W. Jotham and S. F. A. Kettle, *Chem. Commun.*, 282 (1971).
193. C. W. Bradford, R. S. Nyholm, G. J. Gainsford, J. M. Guss, P. R. Ireland and R. Mason, *J. Chem. Soc., Chem. Commun.*, 87 (1972); K. A. Azam and A. J. Deeming, *J. Chem. Soc., Chem. Commun.*, 852 (1976).
194. R. D. Adams and N. M. Golembeski, *J. Organometal. Chem.*, **172**, 239 (1979); M. D. Rausch, R. G. Gastinger, S. A. Gardner, R. K. Brown and J. S. Wood, *J. Amer. Chem. Soc.*, **99**, 7870 (1977).
195. M. R. Churchill and W. J. Youngs, *Inorg. Chem.*, **18**, 1697 (1979); S. J. McLain, R. R. Schrock, P. R. Sharp, M. R. Churchill and W. J. Youngs, *J. Amer. Chem. Soc.*, **101**, 263 (1979).
196. E. G. Berkovich, V. B. Shur, M. E. Vol'pin, B. Lorenz, S. Rummel and M. Wahren, *Chem. Ber.*, **113**, 70 (1980).
197. M. D. Rausch and E. A. Mintz, *J. Organometal. Chem.*, **190**, 65 (1980).
198. G. Erker, *J. Organometal. Chem.*, **134**, 189 (1977).
199. G. Erker and K. Kropp, *J. Amer. Chem. Soc.*, **101**, 3659 (1979).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 12

Six-membered didehydroheteroarenes

H. C. VAN DER PLAS and F. ROETERDINK
Laboratory of Organic Chemistry, Landbouwhogeschool, Wageningen, The Netherlands

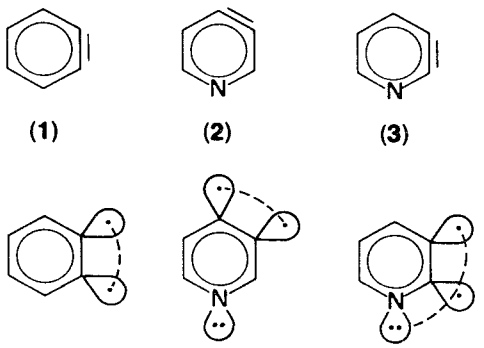
I. INTRODUCTION

In the last two decades many reactions have been described in which a didehydroheteroarene has been suggested as intermediate. These fascinating intermediates have attracted the attention of many chemists as is demonstrated by the many publications on this subject during the last twenty years and the several reviews, which have appeared[1-6].

After considerable knowledge of didehydroarene chemistry was collected in the mid-1950s, the development of the chemistry of didehydroheteroarenes could begin. In the decade of the 1960s special attention was paid to reactions which could lead to all kinds of didehydroheteroarenes; particularly, the reaction of heteroaryl halides with strong basic reagents was well studied. It cannot be denied that the results obtained in these studies were often uncritically evaluated. It became popular among organic chemists to explain nearly every substitution reaction, performed with strong basic nucleophiles and even weak nucleophiles(!), via the intermediacy of a didehydroheteroarene. Many chemists were infected in those days by the disease of 'heteroarynitis'. In the decade of the 1970s a more critical approach was taken. In several cases it could be unequivocally shown that reactions, first 'proven' to proceed via a didehydroheteroarene, follow a completely different pathway.

In this chapter we hope to show that one has to proceed with caution before reaching a conclusion about the occurrence or nonoccurrence of a didehydroheteroarene as intermediate. Furthermore, we confine ourselves in this chapter to the chemistry of the six-membered didehydroheteroarenes. Very recently a review on five-membered didehydroheteroarenes has been published, which makes it unnecessary to include in this chapter the generation and reactivity of these intermediates[6].

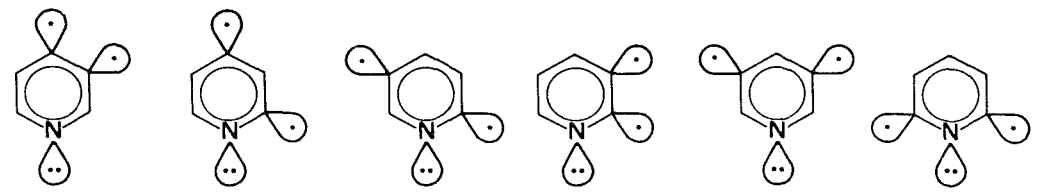
The replacement of a CH group in a 1,2-didehydroarene by a heteroatom leads to the occurrence of different isomeric species. For example, whereas only one *ortho* didehydrobenzene (**1**) can be discussed there are two isomeric *ortho* didehydropyridines, i.e. 3,4-didehydropyridine (**2**) and 2,3-didehydropyridine (**3**) (Scheme 1). In these isomeric didehydro species the different position of the nitrogen with respect to the 'triple' bond leads to a different reactivity of these isomers **2** and **3**.



SCHEME 1

Whereas **2** shows analogy in reactivity with *para*-substituted didehydrobenzene, species **3** behaves quite differently due to the fact the the sp^2 orbital of the nitrogen lone pair interacts with the electrons in the sp^2 radical lobes of the atoms 2 and 3. Thus in this group of didehydro compounds we do not meet structures with a real 'triple' bond between adjacent carbon atoms and it is for that reason that we prefer the term didehydroheteroarene to heteroaryne.

Besides the *ortho* didehydropyridines **2** and **3**, in principle we can also discuss three *meta* didehydro compounds: 2,4-didehydropyridine (**4**), 2,6-didehydropyridine (**7**) and 3,5-didehydropyridine (**6**) and the *para* didehydro compound 2,5-didehydropyridine (**5**). EHT calculations on these six possible didehydropyridines have been carried out and result in the stability sequence shown in Scheme 2[7]. Energy calculations in MNDO approximation suggest the same stability order, with the exception, however, that **7** is predicted to be more stable than **3** and **6**[8].



SCHEME 2

Thus, from these calculations **2** emerges as the most stable isomer and is 0.83 eV more stable than **3**. This result is in contrast to simple Hückel calculations[9] indicating that **2** should be less stable than **3** due to the fact that in **3** delocalization of the two electrons in the radical lobes and those of the nitrogen lone pair over the three atoms can take place leading to stabilization. However, the EHT calculations showed a

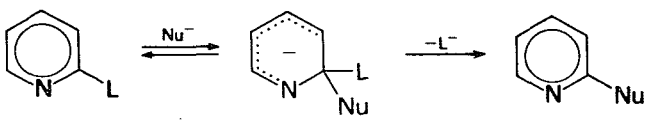
dominant effect of nitrogen lone-pair destabilization of both nearby radical lobes in **3**. Among the reactions in which didehydroheteroarenes are generated, those of heteroaryl halides with strong basic nucleophilic reagents are most extensively studied. The occurrence of *cine* substitution products has often been considered as a good indication for the intermediacy of a didehydro intermediate. Before describing these reactions in detail in the following sections, it seems useful to discuss shortly a few types of reaction which occur often with six-membered azaheterocycles and which are often competitive with didehydroheteroarene formation.

A. Direct Nucleophilic Substitution

One well-recognized reaction is the *direct* nucleophilic substitution, describing a reaction in which the nucleophile occupies the same position in the product as held by the leaving group in the starting material. These substitutions occur according to (1) the S_N(AE) mechanism or (2) the S_N(ANRORC) mechanism.

1. The S_N(AE) mechanism

The central feature of this reaction is the initial *A*ddition of the nucleophile Nu^- to the substrate to form a 1:1 σ adduct. Next follows *E*limination of the nucleofugic (leaving) group (L) in a step that often, but not always, is very fast. The *A*ddition–*E*limination route, abbreviated as S_N(AE), is exemplified in Scheme 3. Excellent reviews on these S_N(AE) reactions have appeared[10–13].



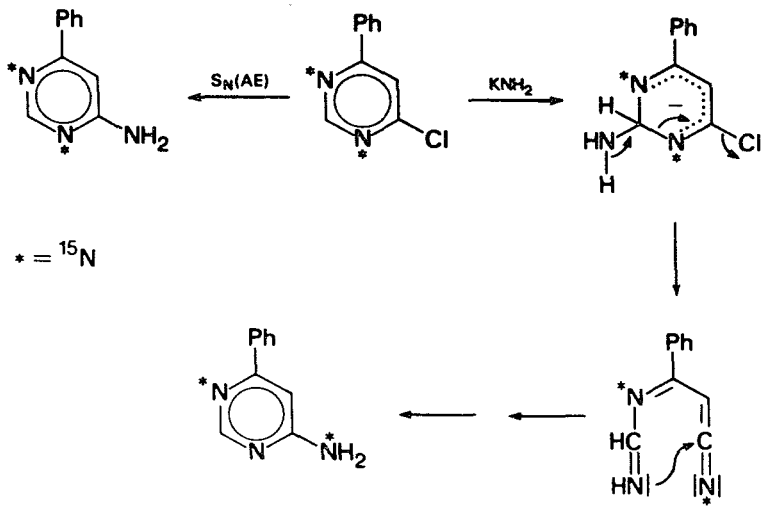
SCHEME 3

2. The S_N(ANRORC) mechanism

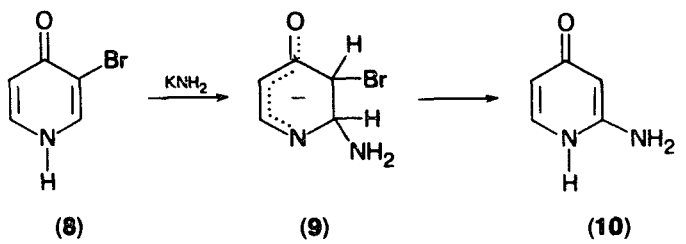
This mechanism for aromatic nucleophilic substitution, exemplified by the conversion of 6-chloro-4-phenylpyrimidine into 6-amino-4-phenylpyrimidine by potassium amide in liquid ammonia[14a,b], has recently been discovered and describes a process involving an initial *A*ddition of the *N*ucleophile, *R*ing-*O*pening and *R*ing-*C*losure. The proof that in this conversion the S_N(ANRORC), and not the S_N(AE), mechanism operates is provided by the results with ^{15}N-labelled 6-chloro-4-phenylpyrimidine, which in reaction with potassium amide, gave 6-amino-4-phenylpyrimidine, being ^{15}N-labelled on the *exo*cyclic nitrogen (Scheme 4). More details are given in Section IV.B. A review on this interesting mechanism has recently appeared[15].

B. *Cine* Substitutions

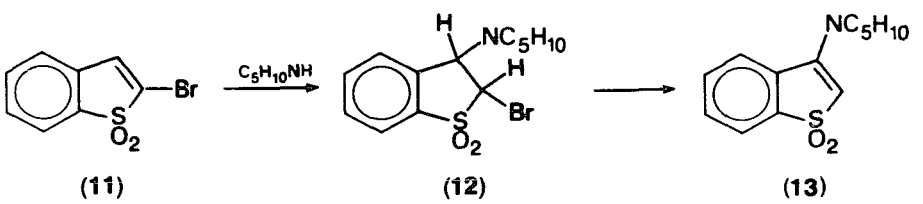
Cine substitutions refer to reactions in which the attacking nucleophile occupies a position *adjacent* to the one from which the leaving group has departed. One has to be aware that *cine* substitutions, besides occurring via the intermediacy of a didehydro compound (the subject of this chapter), can take place by the initial *A*ddition of the nucleophile to a carbon atom adjacent to the carbon, being attached to the leaving group, followed by *E*limination. We refer to this process as $S_N(AE)^{cine}$. An example of this reaction is the amination of 3-bromo-4-pyridone (**8**) with potassium amide in



SCHEME 4



SCHEME 5a

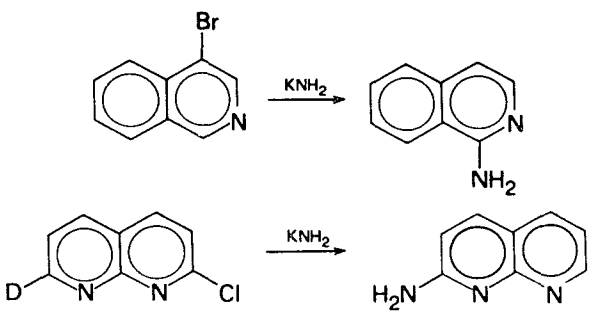


SCHEME 5b

liquid ammonia, yielding 2-amino-4-pyridone (**10**), via the nonisolated intermediate **9** (Scheme 5a)[16]. Another example of this type of *cine* substitution is the conversion of 2-bromobenzo[*b*]thiophene-1,1-dioxide (**11**) to 3-piperidinobenzo[*b*]thiophene-1,1-dioxide (**13**), involving as intermediate 2-bromo-3-piperidino-2,3-dihydrobenzo[*b*]thiophene-1,1-dioxide (**12**); this intermediate can be isolated (Scheme 5b)[17].

C. *Tele* Substitutions

Tele substitutions comprise those reactions in which the nucleophile enters into a position of the aromatic ring, being more than one position removed from the one which is left by the leaving group[18]. If the first step in the *tele* substitution is the *A*ddition of the nucleophile, which is followed by *E*limination we refer to this process as an $S_N(AE)^{tele}$. Examples of reactions which occur according to this $S_N(AE)^{tele}$ process are the amide-induced amination of 4-bromoisoquinoline into 1-aminoisoquinoline[19] and the conversion of 7-chloro-2-deutero-1,8-naphthyridine into 2-amino-1,8-naphthyridine[20,21] (Scheme 6).



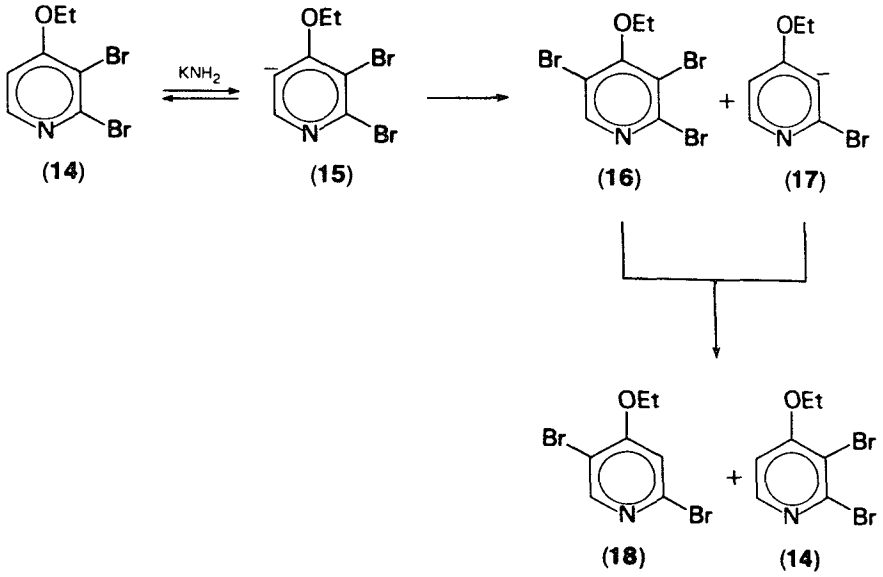
SCHEME 6

D. Halogen Migration

Another reaction which is often observed when halogeno(hetero)arenes are reacting with strong basic reagents, is the halogen migration. An example in the benzene series is the sodamide(or other base)-catalysed isomerization of 1,2,4-tribromobenzene into 1,3,5-tribromobenzene[22,23]. Examples in the five-membered heterocycle series are the sodamide-catalysed isomerization of 2-bromo(iodo)thiophene into 3-bromo(iodo)thiophene[24–26] and of 5-bromo-3-methylisothiazole into 4-bromo-3-methylisothiazole[27]. In the pyridine series potassium amide induces isomerization of 2,3,6-tribromopyridine into 2,4,6-tribromopyridine[28], of 2,3-dibromo-4-ethoxypyridine (**14**) into 2,5-dibromo-4-ethoxypyridine (**18**) (Scheme 7)[29] and of 2,3-dibromoquinoline into 2,4-dibromoquinoline[30]. A review on this interesting phenomenon of the halogen dance had appeared[31]. It is supposed that all these reactions start with the abstraction of the most acidic ring hydrogen, which in the case of the isomerization of **14** into its isomer **18** gives 2,3-dibromo-4-ethoxypyridyl 5-anion (**15**)[29]. Abstraction of bromine from a molecule of the starting material yields 2,3,5-tribromo-4-ethoxypyridine (**16**) and the 2-bromo-4-ethoxypyridyl 3-anion (**17**), from which, by a second bromine migration, **18** and **14** are obtained (Scheme 7).

E. Ring-transformation Reactions

In the reaction of heteroaryl halides with strong nucleophilic reagents ring-opening and recyclization reactions are often observed. Many halogeno derivatives of pyridine, pyrimidine, pyrazine, pyridazine, triazines, etc. are found to undergo these ring-fissions in basic medium. On ring-closure the open-chain compounds can yield heterocycles having a ring-system different from that of the starting material. Thus these ring-transformations also involve an ANRORC mechanism. It differs, however, from the S_N(ANRORC) mechanism, discussed in Section I.A.2, since this mechanism

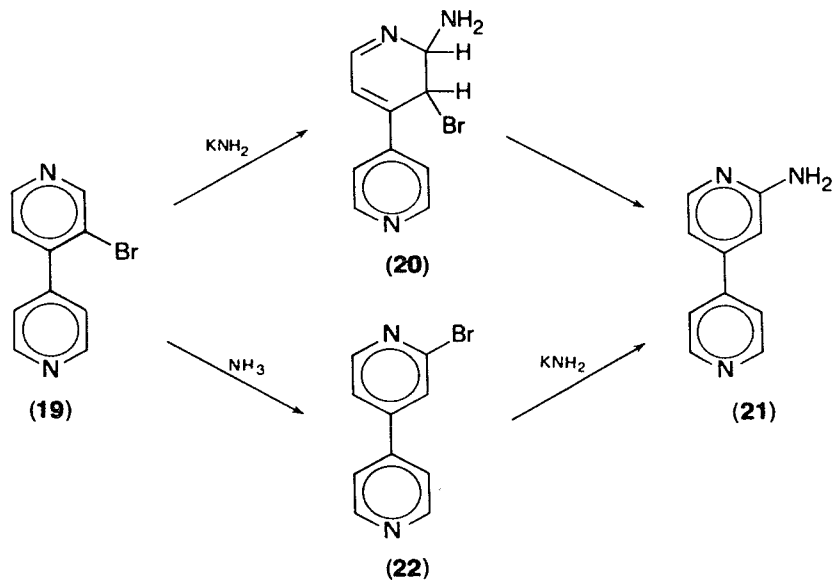


SCHEME 7

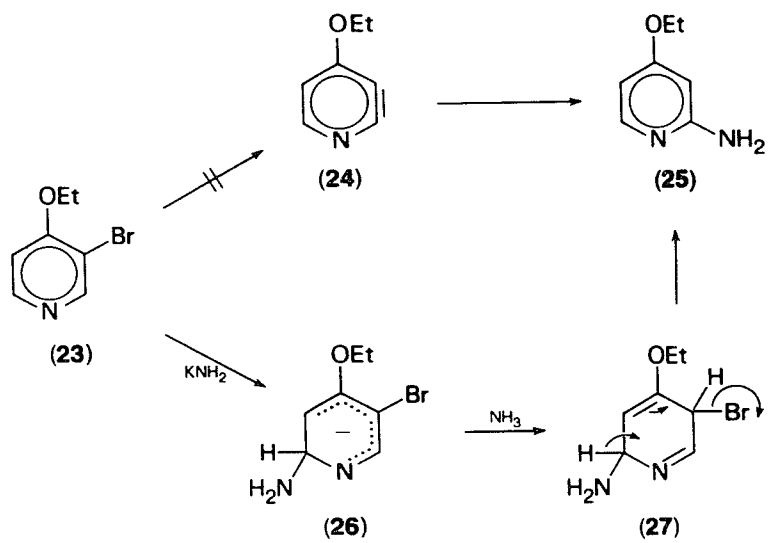
describes a nucleophilic substitution without changing the heterocyclic ring-system. It goes far beyond the scope of this review to discuss all these complicated ring-transformations, but in cases where it is necessary for a better understanding and evaluation of the scope of the didehydroheteroarene formation, we will discuss them. For more detailed information, the reader is referred to several reviews available on this subject[32–38].

Before passing on to detailed discussions on the generation and reactivity of the many didehydroheteroarenes in the following sections, one remark has to be made. The occurrence of *cine* substitutions in the reaction of heteroaryl halides with a strong base has often been considered as 'proof' for the intermediate formation of a didehydroheteroarene; this is, however, not always correct. One has always to be aware that an $S_N(AE)^{cine}$ process (see above) or a halogen migration followed by a nucleophilic substitution according to an $S_N(AE)$ mechanism can also explain the *cine* substitution. An interesting illustrative example is the conversion of 3-bromo-4-(4′-pyridyl)pyridine (**19**) with potassium amide in liquid ammonia into the 2-amino-4-(4′-pyridyl)pyridine (**21**)[29]. An $S_N(AE)^{cine}$ process via adduct **20** or an $S_N(EA)$ mechanism, combined with an exclusive addition to C-2 in the didehydro intermediate can explain the results. However, the fact that **19** has been found to isomerize easily into 2-bromo-4-(4′-pyridyl)pyridine (**22**), when dissolved in liquid ammonia and ether, points to the possibility that the 2-amino compound (**21**) is formed in an $S_N(AE)$ process from **22** (Scheme 8).

Another instructive example showing how careful one has to be with conclusions about the occurrence of intermediary didehydroheteroarenes is the amination of 3-bromo-4-ethoxypyridine (**23**) with potassium amide in liquid ammonia. The product 2-amino-4-ethoxypyridine (**25**) was obtained and its formation was proposed to take place by attack of the amide (or ammonia) on the intermediate 4-ethoxy-2,3-didehydropyridine (**24**) at C-2 only[39,40]. It was later found that this amination does not involve the didehydropyridine **24** at all, but occurs via an $S_N(AE)^{tele}$ mechanism, which starts by addition of the amide ion to position 6, to give **26**, followed by elimination of hydrogen bromide from the adduct **27** (Scheme 9)[29].



SCHEME 8



SCHEME 9

A relatively great part of this chapter is devoted to the generation and reactivity of 3,4-, 2,4-, 2,3- and 2,6-didehydropyridine and their derivatives. This is due to the fact that much research has been concentrated on these species, but moreover because discussions of the problems being encountered with these didehydropyridines are of fundamental importance for a better understanding of the chemistry of other didehydroheteroarenes.

II. MONOCYCLIC SIX-MEMBERED DIDEHYDROMONOAZAHETEROARENES

A. Didehydropyridines

1. 3,4-Didehydropyridine and 3,4-didehydropyridine-1-oxide and their derivatives

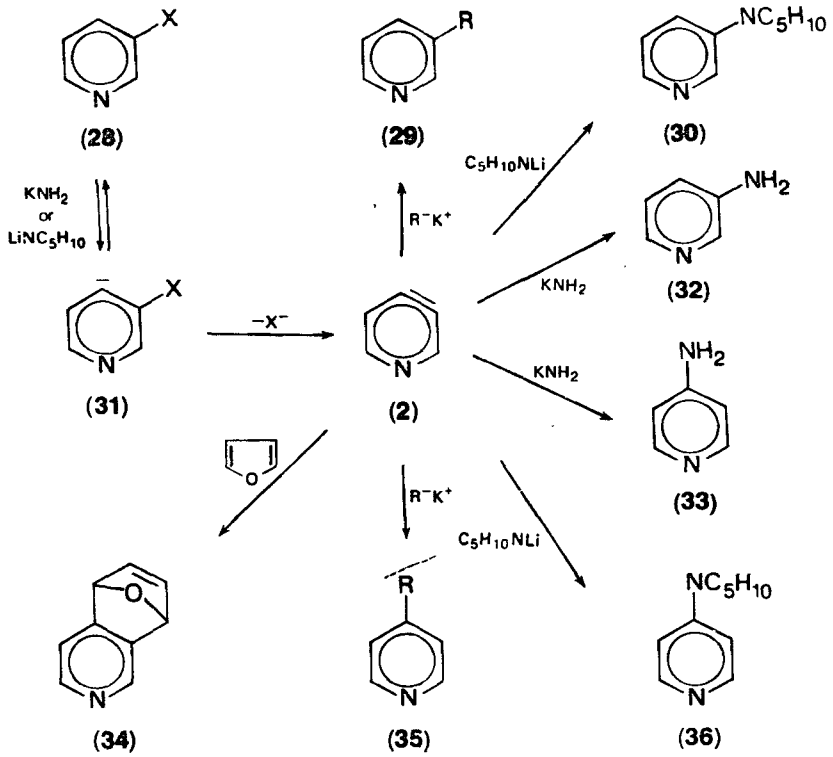
a. 3,4-Didehydropyridine. (i) 3,4-Didehydropyridine as intermediate in reactions of 3-halogenopyridines with strong bases. There is sound evidence for the generation of 3,4-didehydropyridine (**2**) in the reaction of 3-chloro-, 3-bromo- and 3-iodopyridine (**28**; X = Cl, Br, I) with potassium amide in liquid ammonia at −33°C[40,41]. This evidence is based on the fact that in all three reactions a mixture of 3- and 4-aminopyridine (**32** and **33**) is obtained in high yield, the composition of which is independent of the nature of the halogeno atom (ratio **32**:**33** = 35:65). In these reactions no 2-aminopyridine is formed. The reaction has been explained by an initial deprotonation at C-4, yielding 3-halogenopyridyl 4-anion (**31**), which by a subsequent loss of a halide ion forms **2**. Addition of the amide ion or ammonia to the 3,4-didehydro bond in **2** yields the mixture of 3- and 4-aminopyridine (Scheme 10). This process of *E*limination and subsequent *A*ddition is abbreviated as the S_N(EA) mechanism.

When the amination is carried out in the presence of furan, besides **32** and **33** the 5,8-dihydroisoquinoline-5,8-endoxide (**34**) is obtained, being formed by addition of furan to the 3,4-didehydro bond in **2**[42]. Another piece of evidence, affirming the intermediary existence of **2** has been taken from the fact that treatment of **28** (X = Br) with potassium amide in liquid ammonia in the presence of an additional nucleophile as didehydroheteroarene trapper, such as the potassium salt of acetophenone[43,44], of methyl mercaptan[45], of 3-pentanone[46] and of thiophenol[44] gives, besides **32** and **33**, 3- and 4-phenacylpyridine (**29** and **35**, R = CH_2COPh), 3- and 4-(thiomethyl)pyridine (**29** and **35**, R = SMe), 3- and 4-(3-oxo-2-pentyl)pyridine (**29** and **35**, R = $CH_3CHCOEt$) or 3- and 4-(phenylthio)pyridine (**29** and **35**, R = SPh) respectively (Scheme 10). The ratio in which the two isomers are formed, is not always representative of the ratio in which the addition takes place, since in several cases decomposition of one of the isomers by the strong base present has been observed.

The results of the amination of 3-chloro- and 3-bromopyridine (**28**; X = Cl, Br) with lithium piperidide (2.2 eq.) and piperidine (2.8 eq.) in boiling water, also strongly suggest the intermediacy of **2**[46,47].

In both reactions a mixture of 3- and 4-piperidinopyridine (**30** and **36**) is obtained (Scheme 10), which composition is *in*dependent of the nature of the halogen atom used (ratio **30**:**36** = 48:52). It has been found that by increasing the amounts of lithium piperidide and piperidine to 5 and 10 eq. the composition scarcely changes. It has been argued that this result supports the didehydropyridine mechanism:due to the greater amount of piperidine, the equilibrium between **28** (X = Cl, Br) and its 4-lithio derivative, the probable precursor of **2** would shift to the starting substance **28** (X = Cl, Br) making the formation of the 3-piperidino compound by the S_N(AE) mechanism at position 3 more competitive. Based on similar results, the occurrence of **2** as intermediate has also been proposed[5,48] in the reaction of **28** (X = Cl, Br) with the diethylamide ion.

It is of interest to note that in the amination of **28** (X = Cl, Br, I) by the aforementioned amides no competing S_N(AE) substitutions or other reactions seem to be involved. However, 3-fluoropyridine (**38**) forms an exception in the series of 3-halogenopyridines. Reaction of **38** with potassium amide gives *no* 4-aminopyridine, only a small amount of 3-aminopyridine **32** (formed via intermediate **37**) and as main products fluoro derivatives of bipyridine, e.g. **43a** (25%) (Scheme 11)[49]. The



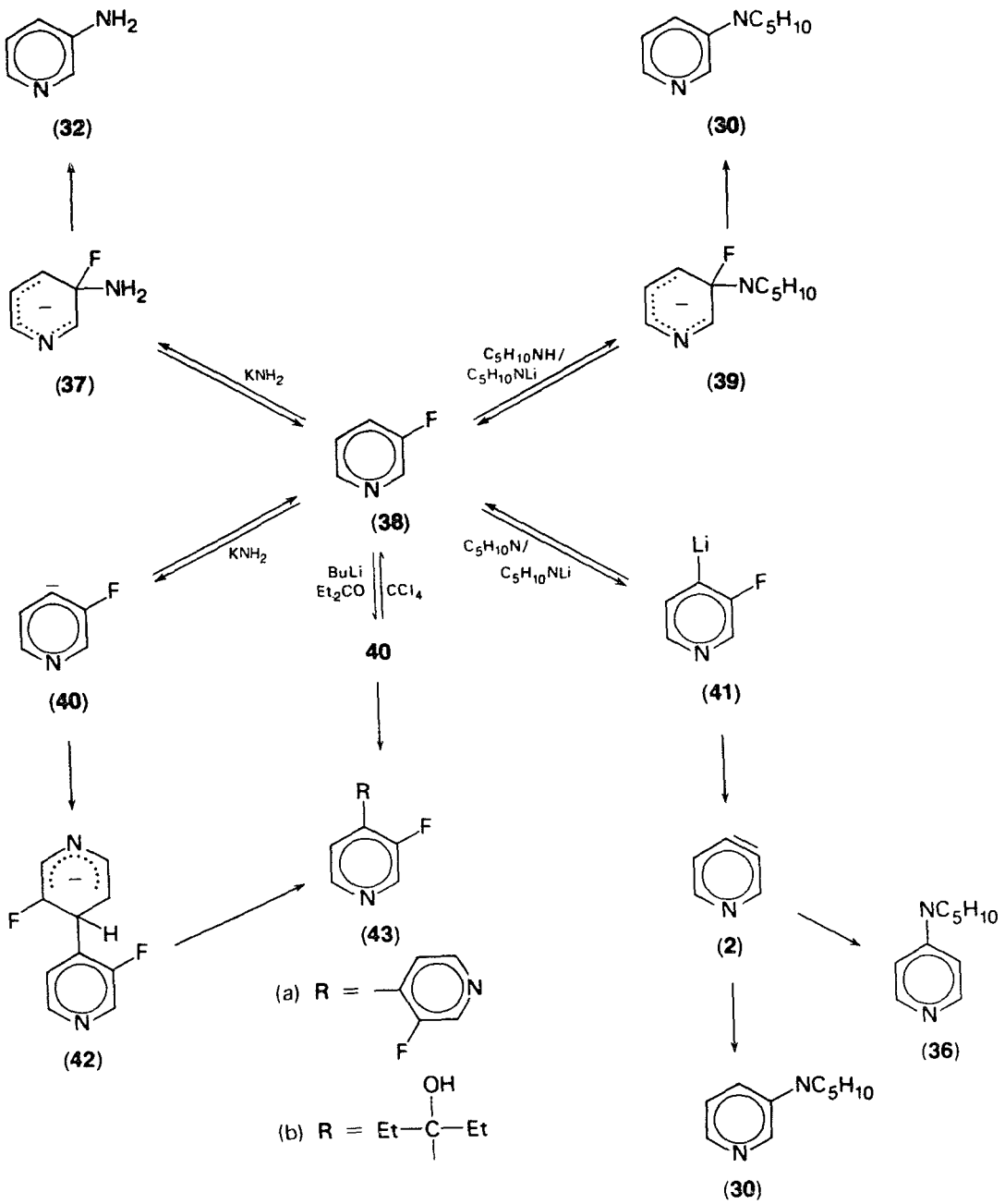
R = CH_2COPh, $CH_3CHCOEt$, SMe, SPh

SCHEME 10

formation of **43** can be understood as follows. The 3-fluoropyridyl 4-anion (**40**), being in this strong basic medium in equilibrium with its conjugate acid **38**, reacts with a second molecule of **38** giving the 4-pyridylpyridinide **42**, which aromatizes into **43**. Additional proof for the existence of the anionic species **40** was found when reacting the fluoro compound **38** with butyllithium in the presence of 3-pentanone, 3-(3-fluoro-4-pyridyl)pentanol-3 (**43b**) being obtained[50]. That from anionic species **40** no 2 is formed is in agreement with results found with fluorobenzene, which in liquid ammonia containing potassium amide, only undergoes deprotonation and not a subsequent loss of fluoride ion into didehydrobenzene[51].

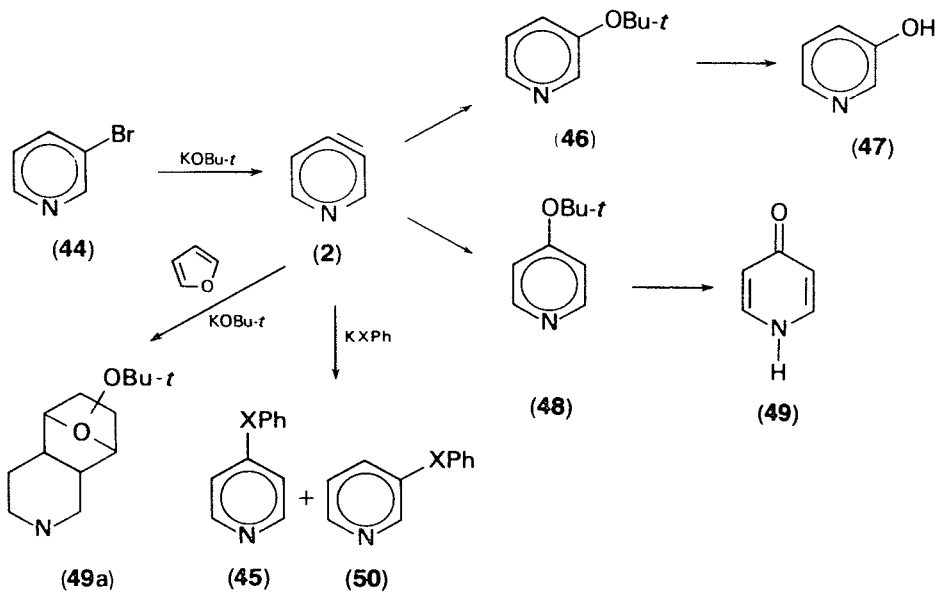
Reaction of 3-fluoropyridine (**38**) with lithium piperidide and piperidine has been found to give in a yield of more than 90% **30** and **36** (ratio 96:4)[46]. This means that in this reaction – taking into account the addition ratio found in the reaction of **28** (X = Cl, Br) with lithium piperidide – only 8% of **38** reacts via **2** and 92% of **38** via addition complex **39** into **30**. Apparently 3-fluoro-4-lithiopyridine (**41**), supposed to be the precursor of **2**, is so stable that the formation of **39** becomes highly competitive with the 3,4-didehydropyridine formation (Scheme 11).

The interesting results obtained with nitrogen-containing bases has stimulated strong interest in the reactivity of 3-halogenopyridines with oxygen-containing bases, mainly potassium *t*-butoxide[42] and potassium hydroxide[52]. Heating of 3-bromopyridine (**44**) with a fourfold excess of potassium *t*-butoxide in DMSO at 90°C gives a very complicated reaction mixture[42,53a], containing 3-*t*-butoxypyridine (**46**,


NH2
(32)
NC5H10
(30)
F
NH2
(37)
KNH2
C5H10NH/
C5H10NLi
F
NC5H10
(39)
F
(38)
KNH2
BuLi
Et2CO
CCl4
C5H10N/
C5H10NLi
Li
F
(40)
40
(41)
R
F
(43)
(a) R =
N
F
OH
(b) R = Et—C—Et
Et
N
F
H
F
(42)
(2)
NC5H10
(36)
NC5H10
(30)

SCHEME 11

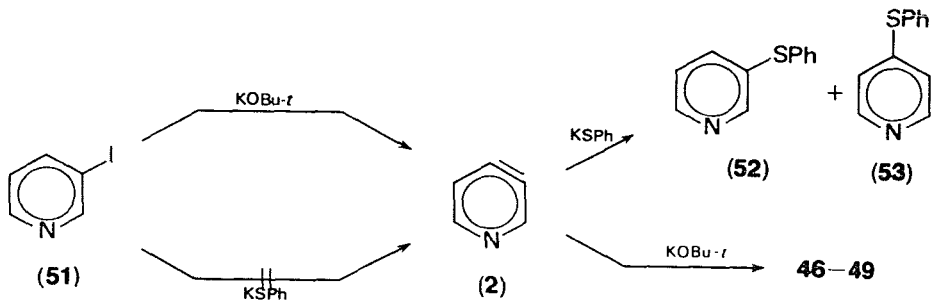
10–14%), 3-hydroxypyridine (**47**, 6–9%), 4-*t*-butoxypyridine (**48**, 4–7%) and 4-pyridone (**49**, 25–29%) as main products (Scheme 12). If one assumes that **47** is formed from **46**, and **49** from **48** and furthermore takes into account that the yields of the products can only be determined with limited accuracy due to the complexity of the mixture, a ratio of (**48** + **49**)/(**46** + **47**) of about 66:33 can be established. This ratio is reminiscent of the ratio in which 4- and 3-aminopyridine are formed by addition of the amide ion to **2**[40]. Additional evidence that in the reaction of **44** with potassium *t*-butoxide **2** is involved as intermediate is provided by the formation of the *t*-butoxy derivative of 5,6,7,8-tetrahydroisoquinoline-5,8-endoxide (**49a**) when the reaction was carried out in the presence of furan[42]. Compound **49a** is formed by addition of *t*-butyl alcohol to the 5,8-endoxide (**34**). Moreover, when **44** is heated with potassium *t*-butoxide in the presence of potassium thiophenoxide, a mixture of 3- and 4-(phenylthio)pyridine (**50** and **45**, X = S) (ratio 50:50) is obtained[42] in high yield (>90%). Similarly, 3- and 4-phenoxypyridine (**50** and **45**, X = O) are formed in the ratio of about 60:40 by treatment of **44** with potassium *t*-butoxide in the presence of potassium phenoxide (Scheme 12)[53a]. The ratio 60:40 does not reflect the addition to the 3,4-didehydro bond in **2**, since both phenoxy compounds decompose under the applied reaction conditions.



SCHEME 12

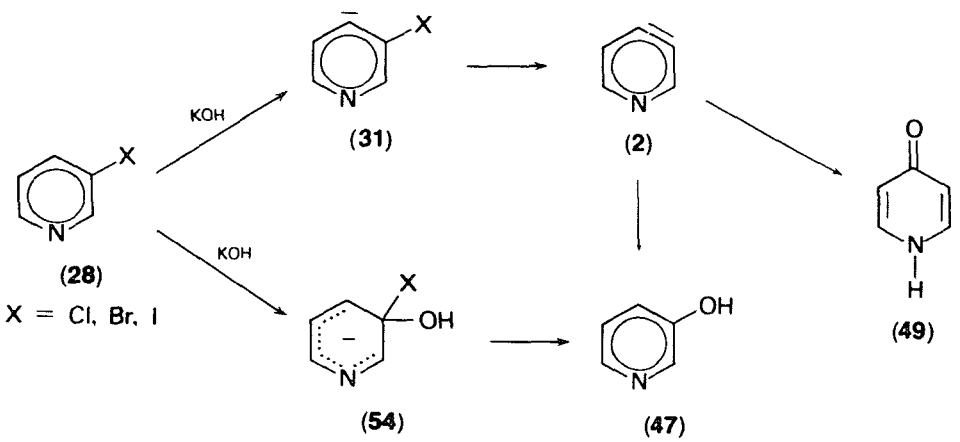
The reaction of 3-iodopyridine (**51**) with potassium *t*-butoxide gives results similar to those for the 3-bromo compound. The ratio in which the 3- and 4-(phenylthio)pyridines (**52** and **53**) are formed[42] in the reaction of **51** with potassium *t*-butoxide and potassium thiophenoxide, i.e. 60:40, indicates that besides the S_N(EA) mechanism (Scheme 13) a nucleophilic substitution takes place at C-3. The reaction of the 3-fluoro compound **38** with potassium *t*-butoxide, whether or not in the presence of potassium phenoxide or thiophenoxide, shows formation of products, which can only be explained by an addition–elimination substitution at C-3[42]. Thus in these reactions no indication for the occurrence of the didehydro intermediate **2** has been obtained.

Heating of 3-halogenopyridines (**28**) with a 4M aqueous solution of potassium



SCHEME 13

hydroxide has been found to give a mixture of 3-hydroxypyridine (**47**) and 4-pyridone (**49**)[52]. The ratio in which both compounds are formed appears to be strongly dependent on the nature of the halogen atom, as well as on the reaction temperature. The intermediate **2** is suggested, although a competitive direct substitution at C-3 via the σ adduct **54** may also take place (Scheme 14).



SCHEME 14

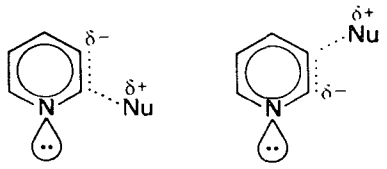
Butyllithium has also been applied for generation of **2** from 3-bromopyridine (**44**). In the presence of furan or substituted furans, the intermediate species **2** can be trapped, yielding isoquinoline derivatives[53b].

In conclusion, the results discussed in this section unambiguously show that in the reaction of the 3-halogenopyridines (**28**, X = Cl, Br, I) with potassium amide in liquid ammonia, lithium piperidide/piperidine, lithium diethylamide/diethylamine, potassium *t*-butoxide/DMSO and potassium hydroxide/water, the didehydro species **2** is an intermediate.

(ii) 3,4-Didehydro formation versus 2,3-didehydro formation in reactions of 3-halogenopyridines with strong bases. We have seen in the previous section (II.A.1.a.i) that in all the reactions of 3-*X*-pyridines (X = Cl, Br, I) with different strong bases, whether or not in the presence of various nucleophiles, the formation of a 2-substituted product has never been observed.

The correct conclusion was drawn that 2,3-didehydropyridine (**3**) cannot be an

intermediate in these reactions, since addition of the nucleophile to this intermediate must undoubtedly lead to preferential attack at C-2, leading to a 2-substituted product[1]. This preferential attack at C-2 has been explained by the fact that the transition state of the addition of the nucleophile at C-2 is favoured over that of the addition at C-3, since in that case the developing negative charge at C-2 undergoes a Coulomb repulsion by the nitrogen lone pair[54,55] (Scheme 15). These results are in accordance with EHT calculations which show that the pyridyl 3-anion is 0.25 eV more stable than the pyridyl 2-anion[7].

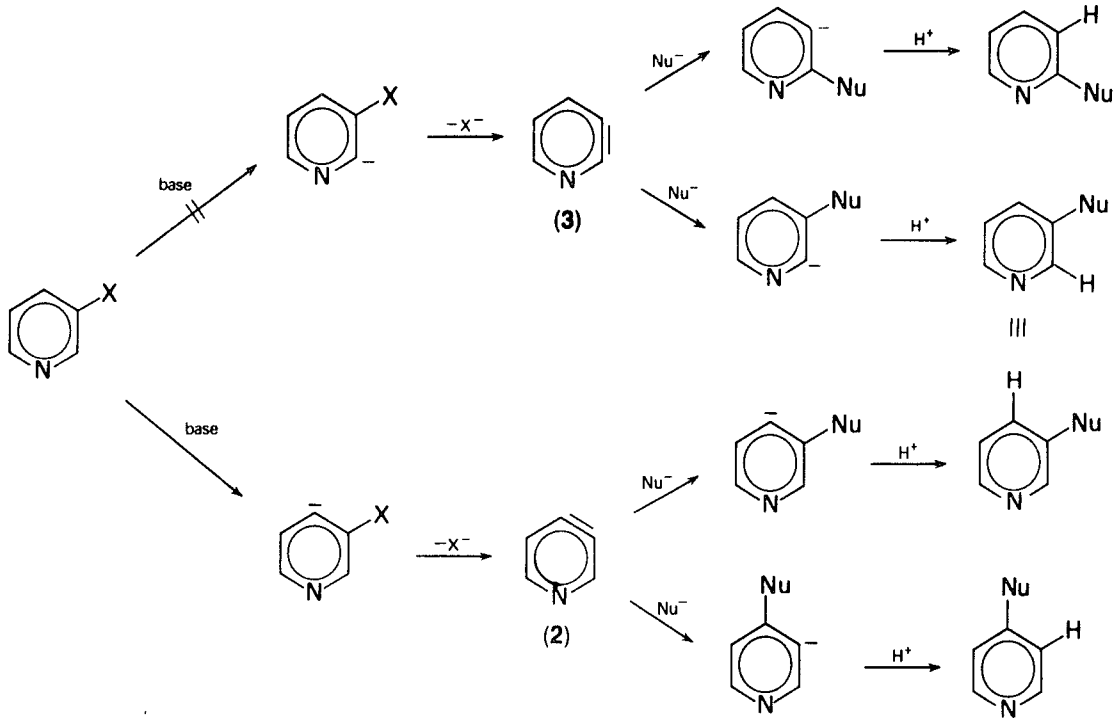


SCHEME 15

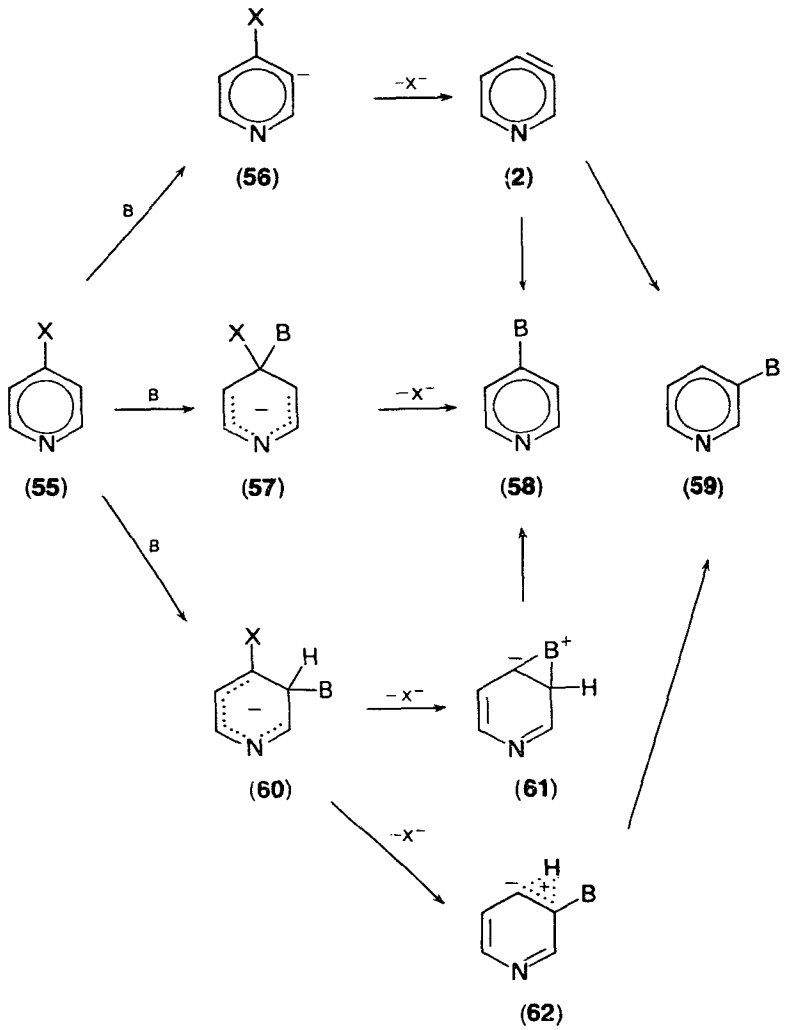
An important question is why the 3-*X*-pyridines (X = Cl, Br, I) are not inclined to the formation of 2,3-didehydropyridine (**3**), but favour formation of 3,4-didehydropyridine (**2**). The formation of the didehydro compound occurs in two steps (1) carbanion formation and (2) halide elimination (Scheme 16). Considering the energy requirements of each of the steps it has been calculated[7] that the pyridyl 4-anion is somewhat more stable than the pyridyl 2-anion. The loss of a proton from position 2 in 3-*X*-pyridines is thus less favoured than loss of the proton from position 4 (Scheme 16). This has been confirmed experimentally by the fact that 2-deutero-3-chloropyridine in potassium amide/liquid ammonia, does not show any H/D exchange at the C-2 position[56,57]. Also, D/H exchange studies of pyridine with $NaND_2$ in ND_3 at −25°C show that the 4-hydrogen atom has the relative highest rate of exchange (relative exchange of 2-, 3- and 4-hydrogen atoms of pyridine amounts to 1:100:1000)[58]. Moreover, as has been mentioned in the introduction, **2** is 0.83 eV more stable than **3**, indicating that the halide elimination leading to the didehydro compound **2** is more favoured than the halide elimination yielding **3**. Thus, experimental facts combined with the results of extended Hückel calculations show that 3-*X*-pyridines (X = Cl, Br, I) are more easily inclined to hydrogen halide elimination leading to **2** than to **3**.

(iii) 3,4-Didehydropyridine as intermediate in reactions of 4-halogenopyridines with strong bases. Since position 4 in pyridines is highly activated, 4-halogenopyridines (**55**) easily undergo a direct nucleophilic substitution according to the addition–elimination mechanism, $S_N(AE)$. When they are treated with base (B), direct nucleophilic attack at C-4 involving the σ adduct **57** can be, and often is, competitive with proton abstraction at C-3 to give **56**. It has been suggested[59] that the 4-halogenopyridines can also react via a β-addition–α-elimination onium rearrangement, involving the adducts **60**, **61** and **62**. Experimental material elaborating the validity of this route in heterocyclic chemistry has not been presented so far and therefore we shall refrain in this chapter from discussing their implications in the reactions treated in this section.

It has been found that **55** (X = Cl, Br, I) reacts with potassium amide in liquid ammonia at −35°C to give a mixture of 3- and 4-aminopyridine (**59**, B = NH_2 and **58**, B = NH_2) in a 35:65 ratio (Scheme 17)[40,41]. This ratio has been found to be *in*dependent of the nature of the halogeno atom, and moreover, to be the same as obtained in the amination of 3-*X*-pyridines (X = Cl, Br, I) (see Section II.A.1.a.i). Apparently proton abstraction at position 3 is highly favoured over addition of the nucleophile at C-4. 4-Fluoropyridine (**55**, X = F) behaves differently; only **58**



SCHEME 16



SCHEME 17

($B = NH_2$) is formed on treatment with potassium amide in liquid ammonia and no trace of **59** ($B = NH_2$) is detected[60]. Although the 4-fluoro compound will easily give the carbanion at C-3, the subsequent elimination does not occur; the direct $S_N(AE)$ substitution is then highly favoured (Scheme 17). On reacting **55** (X = Cl) with lithium piperidide/piperidine in ether, a mixture of 0.4% of 3- and 99.6% of 4-piperidinopyridine (**59**, $B = NC_5H_{10}$ and **58**, $B = NC_5H_{10}$) is formed[46] in a high yield (~95%). Thus, the didehydro intermediate **2** is formed only to a very limited extent (< 1%). This result can be explained by the fact that the system lithium piperidide/piperidine is more nucleophilic than potassium amide/liquid ammonia and therefore more effective in direct nucleophilic substitution, $S_N(AE)$. A more detailed study on the course of reactions of 4-halogenopyridines with amides of different size (lithium piperidide, lithium diethylamide and lithium diisopropylamide) has shown that **55** (X = Br) reacts with lithium piperidide/piperidine and with lithium

diisopropylamide/diisopropylamine almost exclusively according to the $S_N(EA)$ mechanism[61]. The steric bulk of the bromine and both amides prevent the formation of an adduct at C-4. Since the basicity of the amide system is high, deprotonation at C-3 can still occur, leading after bromide loss to **2**. Heating of 4-bromo- (**55**, X = Br) or 4-iodopyridine (**55**, X = I) with potassium *t*-butoxide in DMSO, containing an excess of potassium thiophenoxide at 90°C for 1.5 h gives a mixture of 3- and 4-(phenylthio)pyridine (**59**, B = SPh and **58**, B = SPh) in high yield. The yields of the two (phenylthio)pyridines from **55** (X = Br) are 36–40% and 51–55% respectively, and 24–28% and 56–60% respectively from **55** (X = I)[53]. No *t*-butoxy derivatives are formed. Since 3-bromo- and 3-iodopyridine give both phenylthiopyridines in a 50:50 ratio under equal conditions (see Section II.A.1.a.i) it seems justified to conclude that **55** (X = Br) and **55** (X = I) react partly via an $S_N(AE)$ route and partly via an $S_N(EA)$ mechanism. Based on the ratio of the products obtained, the contribution of the $S_N(EA)$ process is about 66% in **55** (X = Br). In a similar manner it can be calculated that **55** (X = I) reacts for about 50% according to the $S_N(EA)$ mechanism. 4-Fluoropyridine (**55**, X = F) has been found to react completely according to an addition–elimination reaction at C-4 when treated with potassium *t*-butoxide in the presence of potassium thiophenoxide in DMSO: only 4-substituted pyridines are formed.

(iv) Addition of nucleophiles to 3,4-didehydropyridine. Whereas only one final product is possible from 1,2-didehydrobenzene, nucleophilic addition to 3,4-didehydropyridine (**2**) gives two different isomeric products. The addition can be described as a two-step process: (1) addition of the nucleophile to C-4 and/or C-3 yielding the pyridyl 3-anion or the pyridyl 4-anion, respectively and (2) protonation of the 3- and/or 4-pyridyl anion (Scheme 16).

It is an interesting question as to whether the preference for addition of the nucleophile to C-4 or C-3 in **2** is determined by the stability of the adduct formed after addition of the nucleophile to C-3 and/or C-4 (thermodynamic control) or by the electron density at the two ends of the didehydro bond (kinetic control). EHT calculations[7] on total electron densities at C-3 and C-4 in **2** have shown that C-4 has a considerably lower total electron density (q) than C-3 ($q_4 = 3.97$ versus $q_3 = 4.35$). Moreover the pyridyl 3-anion has been calculated to be 0.17 eV more stable than the pyridyl 4-anion. Both thermodynamic and kinetic criteria lead to the conclusion that C-4 is the favourite site of attack for nucleophilic addition. On comparison, however, of the result of the calculations with the observed experimental addition ratios (C-3:C-4), obtained by reaction of 3-bromopyridine with strong bases in the presence of various nucleophiles we see interesting differences (Table 1).

As can be seen from Table 1, the addition ratios clearly fall into two groups: (1) the amide and *t*-butoxy anion give an addition ratio of about 35:65 and (2) the methyl mercaptide, thiophenoxide and lithium piperidide give a ratio of about 50:50. The

TABLE 1. Ratio of addition of various nucleophiles to C-3 and C-4 in 3,4-didehydropyridine

Nucleophile	Solvent	C-3 : C-4
KNH_2	liq. NH_3	35 : 65
KOBu-*t*	DMSO	~33 : 67
$NaSCH_3$	NH_3	50 : 50
KSPh	DMSO	~50 : 50
KSPh	NH_3	50 : 50
$LiNC_5H_{10}$	HNC_5H_{10}/ether	48 : 52

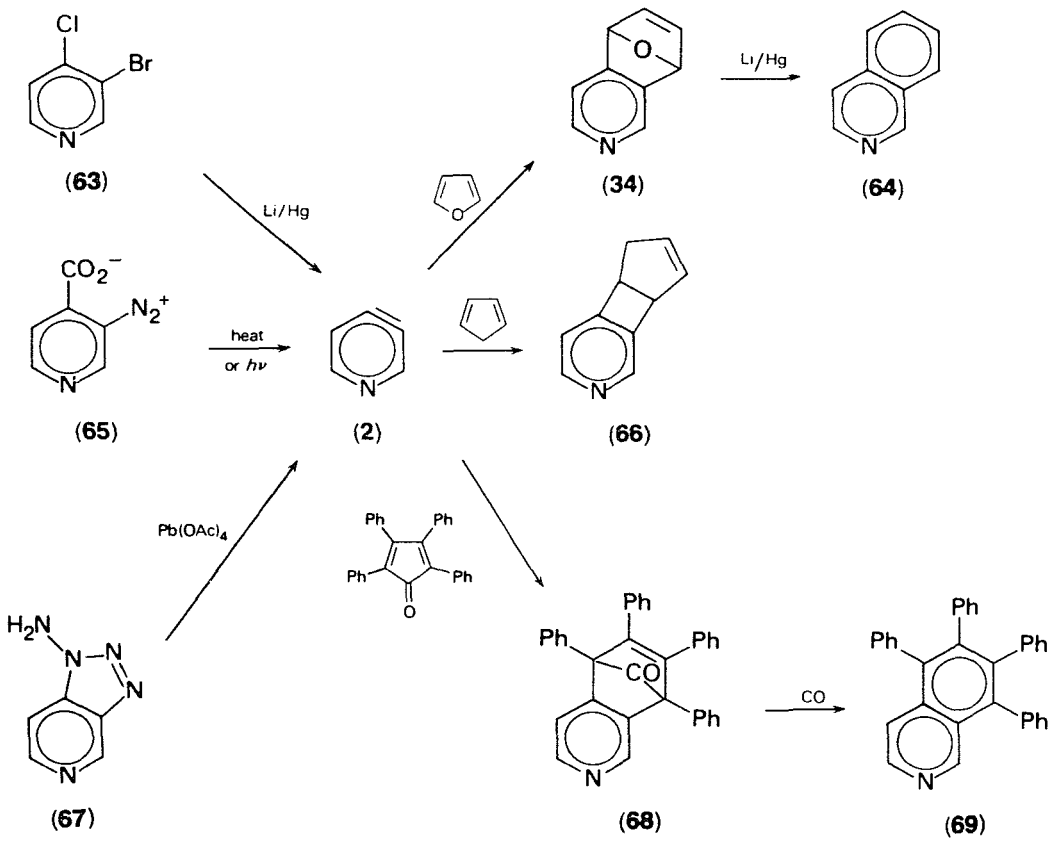
results show that – in contrast to the calculations mentioned above – for the second group of nucleophiles no pronounced preference for addition at C-4 is observed. This leads to the conclusion that the addition ratio is not only determined by thermodynamic and/or kinetic criteria but also – and this is not unexpected – by the nucleophilicity of the adding nucleophile. The second group of nucleophiles, especially the thiophenoxide anion, are much better nucleophiles than those of the first group. Accordingly, at the first encounter of these nucleophiles with **2** they will react and will thus show only a small, if any, selectivity of attack on the polarized didehydro bond of **2**. As a result, the isomer ratio has to be close to 1.0. With weaker nucleophiles, the selectivity of attack on the didehydro bond comes into full operation. Due to the inductive and mesomeric electron-withdrawing effect of the ring nitrogen, C-4 carries a partial positive charge. This charge influences the orthogonal radical orbital of the C-4 position inductively, facilitating the attack of the nucleophile at position 4.

An alternative way of explaining the significant difference in the isomer ratios between the two groups of nucleophiles is based on application of the HASB principle. The second group of nucleophiles (Table 1) can be considered as softer than the first group of nucleophiles. Consequently, the addition of the soft nucleophiles to the soft didehydro bond in **2** experiences less influence of the polarization in the bond. That in the reaction of 3-bromo- and 3-iodo-pyridine with potassium *t*-butoxide in the presence of potassium thiophenoxide only a mixture of 3- and 4-(phenylthio)- but none of the *t*-butoxy-pyridines is obtained (Scheme 13) can also be explained by the HASB principle: the soft thiophenoxide effectively surpasses the hard *t*-butoxy in the addition to the soft 3,4-didehydropyridine. That the competition of thiophenoxide and amide ions for addition to **2** leads, to mixtures of both 3- and 4-(phenylthio) pyridine and 3- and 4-aminopyridine, can be due to the fact that the difference in softness between thiophenoxide and amide ions is smaller than between thiophenoxide and *t*-butoxide ions.

Studies have been conducted on competitive addition of a mixture of nucleophiles to **1**[62] and **2**[48,63,64] in order to obtain information about the selectivity of these didehydroarenes. These studies are of interest since low selectivity of addition to a didehydro compound implies that this intermediate is more energy-rich than an intermediate with higher selectivity. Studies on the competitive addition of piperidine and diethylamine show[48] that **2** is more selective towards these nucleophiles than **1** [$k(C_5H_{10}NH)/k(Et_2NH) = 1.5$ for **2** and 1.0 for **1**]. However, when instead of the base pair piperidine/diethylamine the base pair diethylamine/diisopropylamine is used opposite results are obtained [$k(Et_2NH)/k(i\text{-}Pr_2NH) = 11.0$ for **2** and 18.0 for **1**]. It is evident that more work is necessary to evaluate more precisely the influence of the heteroatom on the selectivity.

(v) Generation of 3,4-didehydropyridine by other methods. 3,4-Didehydropyridine (**2**) has dienophilic properties as can be shown by the thermolysis of 3-pyridinediazonium-4-carboxylate (**65**) in furan[65], which gives the 5,8-dihydroisoquinoline-5,8-endoxide (**34**) in about 60% yield. This endoxide is assumed to be formed by a 1,4-addition of furan to **2**. Species **2** can also be obtained by photolysis of **65**[66,67]. Reaction of lithium amalgam with 3-bromo-4-chloropyridine (**63**) in the presence of furan as dienophile gives isoquinoline (**64**) by deoxygenation of the adduct **34**[47]. Oxidation of the *N*-aminotriazolopyridine **67** with lead tetraacetate also constitutes a very efficient method of generating **2**[68–70] as proved by its trapping with tetracyclone to form **68**, which, after loss of carbon monoxide gives 5,6,7,8-tetraphenylisoquinoline (**69**) (Scheme 18). It has been reported that the dienophilic properties of **2** differ from those of 1,2-didehydrobenzene[71], as appears from the fact that anthracene does not add to **2** and cyclopentadiene reacts in a 1,2-fashion, rather than in a Diels–Alder reaction, yielding **66** or its isomer[72]. The

structure of this 1,2-adduct has not been firmly established. Attempts to react **2** with norbornadiene in a 1,2-fashion have failed[2].



SCHEME 18

b. Derivatives of 3,4-didehydropyridine. (i) Generation of derivatives of 3,4-didehydropyridine. Extensive studies have been published on the influence of substituents on the generation of 3,4-didehydropyridine derivatives and on the polar addition of nucleophiles to the 3,4-didehydro bond. It can be expected, based on knowledge from didehydrobenzene chemistry, that the presence of a substituent, especially when it is adjacent to the didehydro bond, will lead to addition of the nucleophile at different rates to both ends of the didehydro bond. Table 2 gives a survey of the reactions described in the literature in which the base generating the 3,4-didehydropyridine derivative is also able to add to the didehydro bond. Table 2 also contains the results obtained in reactions where nucleophilic agents not able to generate a 3,4-didehydropyridine are present in the base system.

From these results it can be concluded that nearly all the 3-bromo- and 4-bromo-2-substituted pyridines (**70** and **71**) so far investigated give with strong bases a 2-substituted 3,4-didehydropyridine (**75**). From **71** no 2-substituted 4,5-didehydropyridine (**76**) is obtained (Scheme 19). The only exception is 4-bromo-2-methylpyridine (**71**, R = Me) which gives both a 3,4- and 4,5-didehydropyridine. The favoured formation of **75** is due to the higher acidity of the

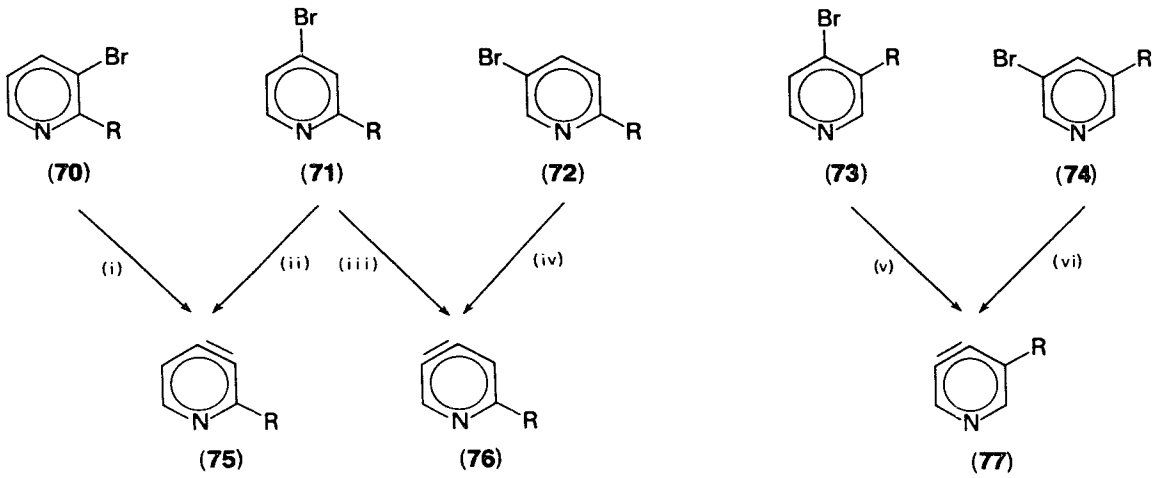
TABLE 2. Products formed by the action of strong bases on derivatives of 3-bromopyridine

Entry	Pyridine derivative	Base	Didehydropyridine	Pyridines formed	Yields (%)	References
1	3-Bromo-2-ethoxy-	KNH_2/NH_3	2-Ethoxy-3,4-didehydro-	3-Amino-2-ethoxy- 4-Amino-2-ethoxy-	3 90	73
2	3-Bromo-2-ethoxy-	KOBu-*t*/DMSO/KSPh	2-Ethoxy-3,4-didehydro-	2-Ethoxy-3(phenylthio)- 2-Ethoxy-4(phenylthio)-	6–10 60–64	53[a]
3	4-Bromo-2-ethoxy-	KNH_2/NH_3	2-Ethoxy-3,4-didehydro-	3-Amino-2-ethoxy- 4-Amino-2-ethoxy-	1 85	73
4	4-Bromo-2-ethoxy-	KOBu-*t*/DMSO/KSPh	2-Ethoxy-3,4-didehydro-	2-Ethoxy-3(phenylthio)- 2-Ethoxy-4(phenylthio)-	5–9 65–69	53[a]
5	5-Bromo-2-ethoxy-	KNH_2/NH_3	2-Ethoxy-4,5-didehydro-	4-Amino-2-ethoxy- 5-Amino-2-ethoxy-	65–70 10–15	40
6	4-Bromo-3-ethoxy-	KNH_2/NH_3	3-Ethoxy-4,5-didehydro-	5-Amino-3-ethoxy-	90	40
7	5-Bromo-3-ethoxy-	KNH_2/NH_3	3-Ethoxy-4,5-didehydro-	5-Amino-3-ethoxy-	90	40
8	5-Bromo-3-ethoxy-	KOBu-*t*/DMSO/KSPh	3-Ethoxy-4,5-didehydro-	3-Ethoxy-5(phenylthio)-	64–68	53[a]
9	3-Bromo-2-methyl-	KNH_2/NH_3	2-Methyl-3,4-didehydro-	3-Amino-2-methyl- 4-Amino-2-methyl-	25 10–15	74
10	4-Bromo-2-methyl-	KNH_2/NH_3	2-Methyl-3,4-didehydro- 2-Methyl-4,5-didehydro-	3-Amino-2-methyl- 4-Amino-2-methyl- 5-Amino-2-methyl-	15 40 10	74
11	5-Bromo-2-methyl-	KNH_2/NH_3	2-Methyl-4,5-didehydro-	4-Amino-2-methyl- 5-Amino-2-methyl-	50 15–20	74
11a	5-Bromo-2-*t*-butyl-	KNH_2/NH_3	2-*t*-Butyl-4,5-didehydro-	4-Amino-2-*t*-butyl- 5-Amino-2-*t*-butyl-	75–80 10–12	74
12	4-Bromo-3-methyl-	KNH_2/NH_3	3-Methyl-4,5-didehydro-	4-Amino-3-methyl- 5-Amino-3-methyl-	75 15	74
13	5-Bromo-3-methyl-	KNH_2/NH_3	3-Methyl-4,5-didehydro-	4-Amino-3-methyl- 5-Amino-3-methyl-	50 10	74
14	3-Bromo-2-amino-	KNH_2/NH_3	2-Amino-3,4-didehydro-	2,3-Diamino-	70	75
15	4-Bromo-2-amino-	KNH_2/NH_3	2-Amino-3,4-didehydro-	2,3-Diamino-	70	75
16	5-Bromo-2-amino-	KNH_2/NH_3	2-Amino-4,5-didehydro-	2,4-Diamino- 2,5-Diamino-	70 3	75
17	5-Bromo-3-amino-	KNH_2/NH_3	3-Amino-4,5-didehydro-	3,4-Diamino- 3,5-Diamino-	80 1	75

18	3-Bromo-2-hydroxy-	KNH_2/NH_3	2-Hydroxy-3,4-didehydro-	3-Amino-2-hydroxy- 4-Amino-2-hydroxy-	30 5	16
19	4-Bromo-2-hydroxy-	KNH_2/NH_3	2-Hydroxy-3,4-didehydro-	3-Amino-2-hydroxy- 4-Amino-2-hydroxy-	20 6–7	16
20	5-Bromo-2-hydroxy-	KNH_2/NH_3	2-Hydroxy-4,5-didehydro-	4-Amino-2-hydroxy- 5-Amino-2-hydroxy-	98 2	16
21	4-Bromo-2-piperidino-	Li piperidide/piperidine	2-Piperidino-3,4-didehydro-	2,4-Dipiperidino-	90	76
22	5-Bromo-2-piperidino-	Li piperidide/piperidine	2-Piperidino-4,5-didehydro-	2,4-Dipiperidino- 2,5-Dipiperidino-	65–70 20–25	76
23	5-Bromo-3-piperidino-	Li piperidide/piperidine	3-Piperidino-4,5-didehydro-	3,5-Dipiperidino-	90	76
24	2,3-Dibromo-	KNH_2/NH_3	2-Bromo-3,4-didehydro-	4-Amino-2-bromo-[a]	35–40	75, 77
25	2,4-Dibromo-	KNH_2/NH_3	2-Bromo-3,4-didehydro-	4-Amino-2-bromo-[a]	40–45	75, 77
26	2,5-Dibromo-	KNH_2/NH_3	2-Bromo-4,5-didehydro-	4-Amino-2-bromo-[a] 5-Amino-2-bromo-[b]	20–25 35–40	75, 77
27	3,4-Dibromo-	KNH_2/NH_3	3-Bromo-4,5-didehydro-	4-Amino-3-bromo- 5-Amino-3-bromo-[c]	5 —	77
28	3,4-Dibromo-	Li piperidide/piperidine	3-Bromo-4,5-didehydro-	3-Bromo-4-piperidino- 3-Bromo-5-piperidino-[d]	10 —	76
29	3,5-Dibromo-	KNH_2/NH_3	3-Bromo-4,5-didehydro-	4-Amino-3-bromo- 5-Amino-3-bromo-[c]	3–5 —	77
30	3,5-Dibromo-	Li piperidide/piperidine	3-Bromo-4,5-didehydro-	3-Bromo-4-piperidino- 3-Bromo-5-piperidino-[c]	6–7 —	76
31	3-Bromo-2,6-dimethyl-	KNH_2/NH_3	2,6-Dimethyl-3,4-didehydro-	3-Amino-2,6-dimethyl- 4-Amino-2,6-dimethyl-	27–30 20–25	74
32	4-Bromo-2,6-dimethyl-	KNH_2/NH_3	2,6-Dimethyl-3,4-didehydro-	3-Amino-2,6-dimethyl- 4-Amino-2,6-dimethyl-	27–30 20–25	74
33	3-Bromo-2,5-dimethyl-	KNH_2/NH_3	2,5-Dimethyl-3,4-didehydro-	3-Amino-2,5-dimethyl- 4-Amino-2,5-dimethyl-	20–25 30–35	60
34	4-Bromo-2,5-dimethyl-	KNH_2/NH_3	2,5-Dimethyl-3,4-didehydro-	3-Amino-2,5-dimethyl- 4-Amino-2,5-dimethyl-	15–20 30–35	60

[a]This compound is converted further into 2,4-diaminopyridine (70%).
[b]This compound is converted into 2,5-diaminopyridine.
[c]This compound is partly converted into a mixture of 3,5- and 3,4-diaminopyridine (see entry no. 17).
[d]This compound is converted via 3-piperidino-4,5-didehydropyridine into 3,5-dipiperidinopyridine (see entry no. 23).

hydrogen at C-3 than at C-5, although H-3 which is between the bromo atom at C-4 and the substituent at C-3 is more sterically hindered for abstraction by base. In the case of **71** (R = Me), the electron-donating effect of the methyl group 'deacidifies' the hydrogen at position 3 more than that at position 5, making the deprotonation at C-5 competitive with deprotonation at C-3. It is also evident from the results summarized



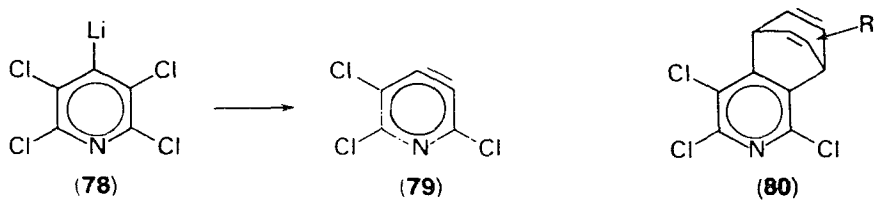
(i) R = Me, OEt, Br, NH_2, OH, NC_5H_{10}
(ii) R = Me, OEt, Br, NH_2, OH
(iii) R = Me
(iv) R = Me, Bu-*t*, OEt, Br, NH_2, OH, NC_5H_{10}
(v) R = Me, Bu-*t*, OEt, Br
(vi) R = Me, OEt, Br, NH_2, NC_5H_{10}

SCHEME 19

in Table 2 that all the 2- and 3-substituted 5-bromopyridines (**72** and **74**) and the 3-substituted 4-bromopyridines (**73**) react through the corresponding 4,5-didehydropyridines (**76** and **77**) as intermediates (Scheme 19). No indication for the occurrence of a 2- or 3-substituted 5,6-didehydropyridine from **72** and **74** has been obtained.

Investigation of the reaction of 2,3-, 2,4- and 2,5-dibromopyridine with lithium piperidide/piperidine in ether has revealed that in all these reactions an extensive tar formation takes place[76]. These decomposition reactions will be discussed later in Section II.A.4. The 2,5,6-trichloro derivative of 3,4-didehydropyridine, i.e. **79**, has been formed when heating 2,3,5,6-tetrachloro-4-lithiopyridine (**78**) in the presence of benzene, mesitylene or durene (Scheme 20)[78,79]. Tricyclic adducts such as **80** are formed in low yields. When using furan instead of these arenes, no reaction occurs.

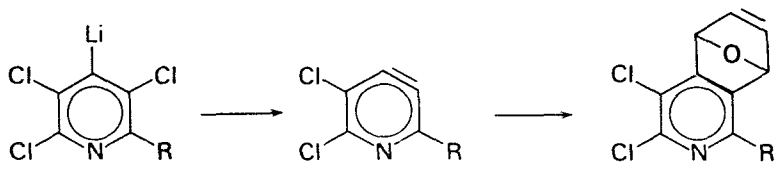
When 2-methoxy-, 2-dimethylamino-, 2-pyrrolidino- or 2-piperidino-4-lithio-3,5,6-trichloropyridine (**81**) is heated in furan, it gives the 2-substituted 5,6-dichloro-3,4-didehydropyridine (**82**) – and not a 2-substituted 3,6-dichloro-4,5-didehydropyridine – as proved by the formation of the 1-*R*-3,4-dichloro-5,8-dihydroisoquinoline-5,8-endoxide (**83**) (Scheme 21)[80]. 2,5,6-Trifluoro-3,4-didehydropyridine



(78) (79) (80)

R = H, Me

SCHEME 20



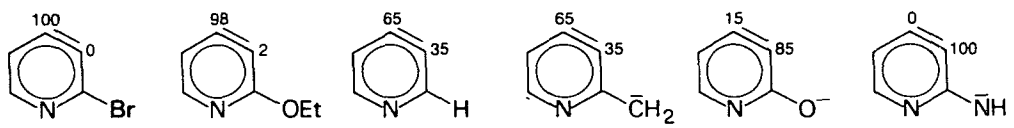
(81) (82) (83)

R = OMe, NMe_2, NC_4H_8, NC_5H_{10}

SCHEME 21

has been postulated as intermediate in the pyrolysis of the silver salt of 2,5,6-trifluoropyridine-3,4-dicarboxylic acid[81].

(ii) The isomer ratio as a function of the substituent present in 3,4(4,5)-didehydropyridine. The ratio of 2-substituted 3- and 4-aminopyridines formed on addition of the amide ion (or ammonia) to the 2-substituted 3,4-didehydropyridines (**84–88**) is shown in Scheme 22. As expected, there is a strong

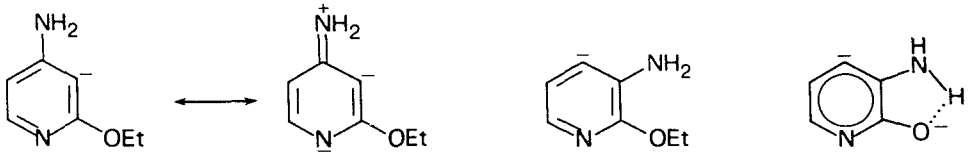


(84) (85) (2) (86) (87) (88)

SCHEME 22

substituent effect in this series, since the substituent is present in a position directly adjacent to the didehydro bond. The *meta*-directing orientation of the substituent is found to decrease in the order Br ~ OEt > H ~ CH_2^- > O^- > NH^-. In these series the bromo atom and the ethoxy group in **84** and **85**, respectively, are the most *meta*-directing substituents and clearly surpass the directing influence of the ring nitrogen. This can be understood on the basis of the stability of the 4-amino-2-ethoxypyridyl 3-anion (**89**) formed after addition of the amide ion to position 4 of **85**. Anion **89** is more stable than the isomeric pyridyl 4-anion (**90**) because of the strong 4-aminopyridine resonance stabilization (thermodynamic control) (Scheme 23). Moreover, it is known from D/H exchange studies in methoxybenzenes that the hydrogen *ortho* to the methoxy group is the most acidic[82], due to the inductive effect of the methoxy group. This argument is also valid in the case of the bromo atom. In the case of the anions of 2-hydroxy- and 2-amino-3,4-didehydropyridines **87** and **88** the very predominant addition at C-3 can

only be explained by their anionic character, since it has been found that 2,3-didehydrophenoxide gives mainly the *ortho* amino addition compounds[83]. Hydrogen bonding as indicated in **91** may also contribute to the addition at C-3 (Scheme 23).

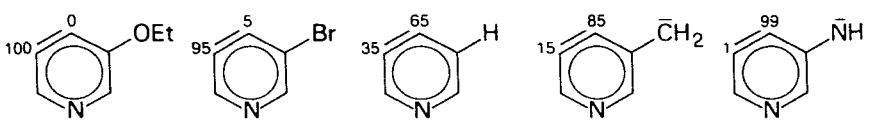


(89) **(90)** **(91)**

SCHEME 23

It is assumed that in the case of 2-methyl-3,4-didehydropyridine the selective intermediate is **86**. When comparing 1,2-didehydrobenzene with 2,3-didehydrotoluene with respect to amide addition the *meta*:*ortho* ratio shifts from 50:50 to 60:40[83,88]. In the case of 2-methyl-3,4-didehydropyridine one would expect that the 65:35 ratio found for the addition to C-4 and C-3 of 3,4-didehydropyridine would shift to a higher value. The fact that this has not been observed seems to indicate that the methyl substituent at position 2 is present as CH_2^- [84], which has a higher +I effect than the methyl group. Addition at C-3 is then more favoured and counterbalances the directing effect of the ring-nitrogen atom.

In the series of 3-substituted 4,5-didehydropyridines (**92–95**) a decreasing order of *meta* orientation towards amide addition shown in Scheme 24 has been found. It is evident from the discussions above that the directing power of the several substituents at position 3 is more or less the same as found for those at position 2. The methyl

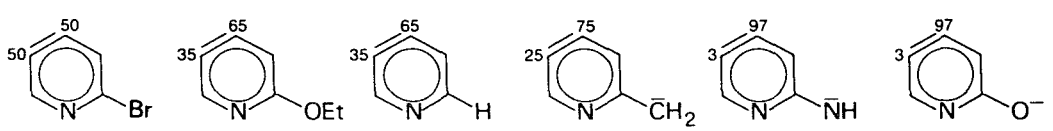


(92) **(93)** **(2)** **(94)** **(95)**

SCHEME 24

group at position 3 has also to be present as an anion in order to explain that the ratio of 4-amino- to 5-amino-3-methylpyridine (85:15) is higher than that for 3,4-didehydropyridine (65:35). In fact, its directing power approaches that of the NH^- group.

In the series of 2-substituted 4,5-didehydropyridines (**96–100**) the addition of the amide ion to the didehydro bond gives the orientation order shown in Scheme 25. These data show that the influence of the bromo atom and the ethoxy group is less



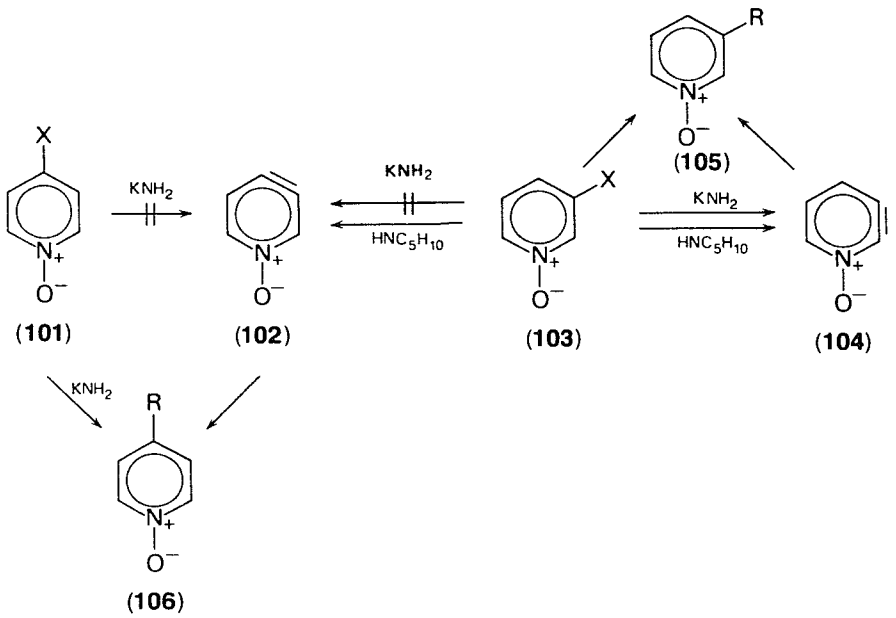
(96) **(97)** **(2)** **(98)** **(99)** **(100)**

SCHEME 25

pronounced than in the 2-substituted 3,4-didehydro- and the 3-substituted 4,5-didehydro-pyridines (R = OEt, Br). Furthermore, the results again indicate that the directing effect of the CH_2^- group approaches that of the NH^- and O^- substituents.

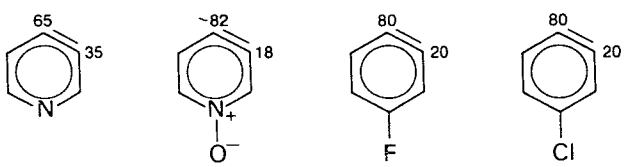
c. 3,4-Didehydropyridine-1-oxide and its derivatives. As discussed in Sections II.A.1.a.i and b.i, the 3-*X*-pyridines (X = Cl, Br, I) and their derivatives, containing substituents at the 2-, 5- and 6-positions, form in reaction with strong bases exclusively 3,4(4,5)-didehydropyridines. The formation of products requiring the intermediacy of 2,3-didehydropyridine or a derivative of this species has never been found. This phenomenon has been explained[7,54] by the destabilization effect of the lone pair of the nitrogen on the negative charge in the pyridyl 2-anion, the precursor of 2,3-didehydropyridine, and on the nearby radical lobes at C-2 and C-3 in the 2,3-didehydro compound (Scheme 16). Since in the 3-halogenopyridine-1-oxides (**103**, X = Hal) the nitrogen lone pair is not present, a destabilization effect of the nitrogen in the 2-pyridyl-1-oxide anion or in the 2,3-didehydropyridine-1-oxide (**104**) cannot be exerted. Therefore, it is expected that **103** (X = Hal) will react with bases in a different way to the 3-halogenopyridines. Experimental data, showing that the base-catalysed hydrogen–deuterium exchange in 3-chloropyridine-1-oxide (**103**, X = Cl) follows the reactivity order $2 > 6 > 4 \gg 5$[54], in sharp contrast to the order observed in 3-chloropyridine ($4 \gg 2,6$), support this expectation[56,57]. This reversed order has also been found with pyridine-1-oxide[54,85]. Thus, these studies clearly prove that the absence of the nitrogen lone pair promotes preferential exchange at the C-2 position over the C-4 position; it leads to the conclusion that **103** (X = Cl) will preferentially undergo formation of **104** instead of a 3,4-didehydropyridine-1-oxide (**102**). (For a discussion on the generation and reactivity of **104**, see Section II.A.3.c.) The 4-*X*-pyridine-1-oxides (**101**, X = Cl, Br) has been found to give only 4-aminopyridine-1-oxide (**106**, R = NH_2)[86a,b] on treatment with potassium amide in liquid ammonia. No indication for the formation of 3-aminopyridine-1-oxide (**105**, R = NH_2) has been obtained. Studies on the reactivity of appropriately substituted 3,4-didehydropyridine-1-oxides (see below) have revealed that **102** should undergo addition at both C-4 and C-3, with addition at C-4 as the main process. Since the reaction of **101** (X = Cl, Br) with potassium amide in liquid ammonia gives only **106** (R = NH_2), this reaction should be an addition–elimination process at C-4 [S_N(AE)] (Scheme 26). It is reported that by reacting 3-chloropyridine 1-oxide (**103**, X = Cl) with piperidine at an elevated temperature a mixture of 3- and 4-piperidinopyridine-1-oxide (**105**, R = NC_5H_{10} and **106**, R = NC_5H_{10}) is obtained in a 96:4 ratio[87]. The 4-piperidino compound **106** (R = NC_5H_{10}) is very probably formed via **102**, which undergoes addition of piperidine at C-4 as the main process. The main part of the 3-piperidino compound **105** (R = NC_5H_{10}) cannot be obtained by addition to **102**, but is formed either via an S_N(AE) process at position 3 and/or an addition only at C-3 in **104** (see Section II.A.3.c). The fact that in this reaction probably *two* didehydro compounds are formed is due to the elevated temperature, which makes the abstraction of the protons at C-4 and C-2 less selective (Scheme 26).

From the results mentioned above it is evident that for an exclusive generation of 3,4-didehydropyridine-1-oxides from 3-halogenopyridine-1-oxides, position 2 has to be occupied by a substituent. It has been found that 3-bromo-2,5-dimethylpyridine-1-oxide gives with potassium amide a 15:85 mixture of 3-amino- and 4-amino-2,5-dimethylpyridine-1-oxide in a good yield (70%)[85]. It seems justified to assume that this ratio is nearly the same as the addition ratio to the parent system 3,4-didehydropyridine-1-oxide (**102**). This assumption is based on the fact that the presence of the methyl groups at C-3 and C-5 does not influence considerably the amide addition ratio as shown by comparison of the addition ratio for 2,5-dimethyl-3,4-didehydropyridine (C-4:C-3 ~ 60:40) (see entry no. 33, Table 2)



SCHEME 26

with that found for 3,4-didehydropyridine (C-4:C-3 = 65:35). This preferential addition to position 4 of **102** has been supported by EHT calculations[7]. Comparison of the amide addition ratio of 3,4-didehydropyridine and its 1-oxide with that of 1-fluoro-[83,88] and 1-chloro-3,4-didehydrobenzene[89] has shown that the addition ratio of 3.4-didehydropyridine-1-oxide resembles more that for 4-substituted didehydrobenzenes, with strong −I substituents than that for 3,4-didehydropyridine (Scheme 27). The absence of the lone pair on nitrogen in the 1-oxide fundamentally changes its directing power when compared with the nitrogen in 3,4-didehydropyridine.

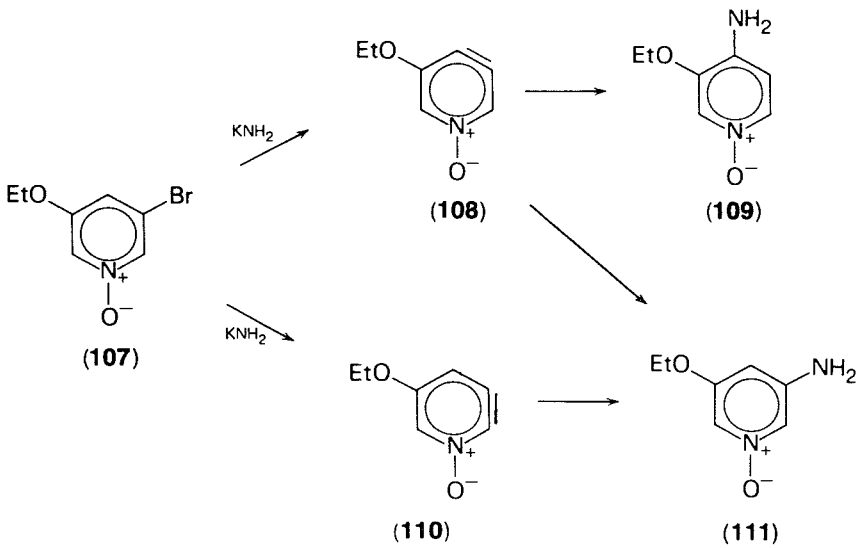


SCHEME 27

Amination of 3-chloro-2,6-dimethylpyridine 1-oxide with potassium amide also gives a mixture of the corresponding 3- and 4-amino compounds in a 21:79 ratio[90]. The intermediacy of 2,6-dimethyl-3,4-didehydropyridine-1-oxide has been proposed. 4-Bromo-2,6-dimethylpyridine-1-oxide gives only the 4-amino product, indicating that the bromo compound reacts according to an $S_N(AE)$ process[90]. 4-Bromo-3-ethoxypyridine-1-oxide gives with potassium amide mainly the 4-amino-3-ethoxypyridine-1-oxide (55–60%) and only traces of the 3-amino compound[86a]. The 4-amino compound can either be formed via the intermediacy of 3-ethoxy-4,5-didehydropyridine-1-oxide which undergoes a nearly exclusive addition at C-4, despite the

presence of the *meta*-directing effect of the ethoxy group, or by an $S_N(AE)$ process at C-4.

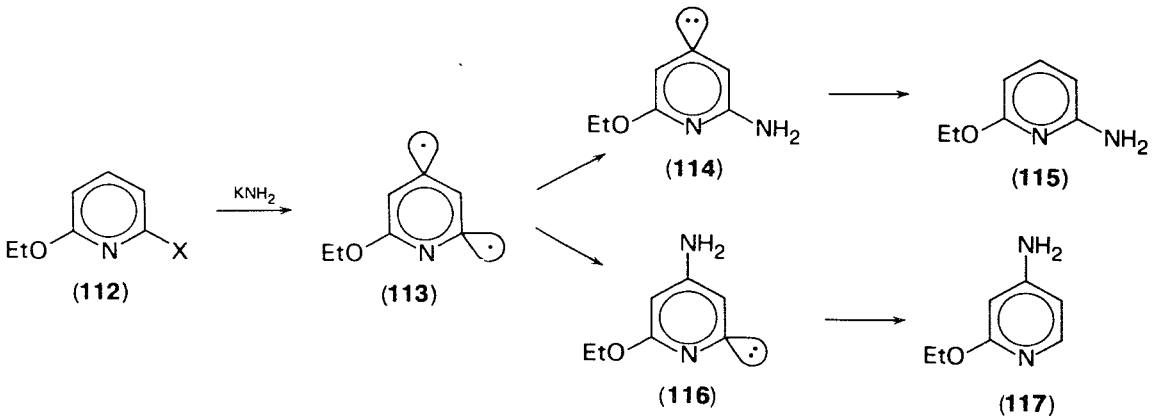
3-Bromo-5-ethoxypyridine-1-oxide (**107**) is reported to give with potassium amide a mixture of 3- and 4-amino-5-ethoxypyridine-1-oxides (**111** and **109**) in a 92:8 ratio[86a] (Scheme 28). The intermediacy of the two didehydropyridine-1-oxides **108** and **110** has been proposed. It has been suggested that the 5-ethoxy-3,4-didehydro compound **108** gives a mixture of the 4-amino compound **109** (despite the *meta*-directing effect of the ethoxy group) and some of the 3-amino compound **111**, whereas 5-ethoxy-2,3-didehydropyridine-1-oxide (**110**) yields only the 3-amino compound **111**.



SCHEME 28

2. 2,4-Didehydropyridine and its derivatives

As already mentioned in the introduction, 2,4-didehydropyridine (**4**) is calculated to be 0.5 eV less stable than 3,4-didehydropyridine (**2**)[7]. Till now no evidence has been presented for the intermediary existence of the parent species **4**. However, in a study of the reactivity of some derivatives of 2-halogenopyridine towards potassium amide in liquid ammonia, results have been found which suggest the intermediacy of a 2,4-didehydropyridine *derivative*. When 2-bromo-6-ethoxypyridine (**112**, X = Br) is reacted with a concentrated solution of potassium amide in liquid ammonia ($[KNH_2]$ = 0.25M) at −33°C, 2-amino-6-ethoxypyridine (**115**, 67–70%) and 4-amino-6-ethoxypyridine (**117**, 14–16%) were obtained in a fast reaction (Scheme 29)[44,91]. It is interesting that the same products are obtained from 2-iodo-6-ethoxypyridine (**112**, X = I) in about the same yields[44]. 2-Chloro-6-ethoxypyridine (**112**, X = Cl) reacts differently: a low-yield conversion into the 2-amino compound **115** takes place in a very slow reaction and only a trace, if any, of the 4-amino compound **117** is obtained [44]. Besides these pyridine derivatives, a ring-transformation product, i.e. 4-ethoxy-2-methylpyrimidine, is formed[92]. The fact that in the amination of **112** (X = Br) and **112** (X = I) the ratio of the aminopyridines **115** and **117** is independent of the nature of the halogen, has led to the interesting proposal of the intermediacy of 6-ethoxy-2,4-didehydropyridine (**113**). The addition of the nucleophile to this inter-

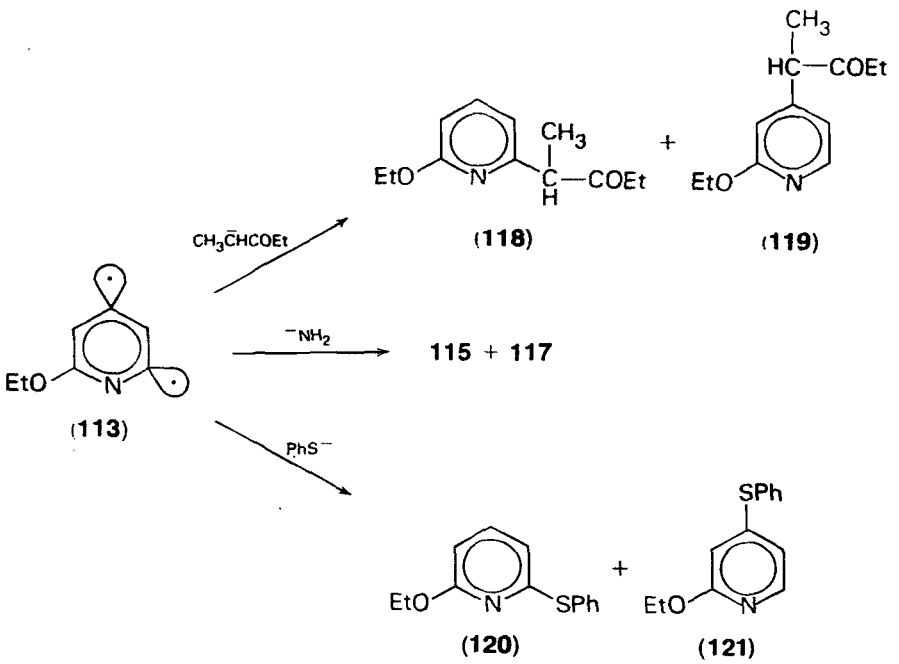


SCHEME 29

mediate will preferentially occur at C-2 since the 2-amino-6-ethoxypyridyl 4-anion (**114**) is more stable than the 4-amino-6-ethoxypyridyl 2-anion (**116**) due to a considerable destabilization effect of the nitrogen lone pair in **116** on the adjacent carbon orbital containing the two electrons (thermodynamic control). Moreover, calculations on total electron density in 2,4-didehydropyridine show that the 2-position has a lower electron density than position 4 (kinetic control)[7]. Thus, thermodynamic as well as kinetic control of the addition show preference for addition of the nucleophile at C-2.

The intermediacy of **113** is supported by the following experiments: (*a*) The reaction of **112** (X = Br) with liquid ammonia containing potassium amide was conducted in the presence of additional nucleophiles that are not capable of generating a didehydropyridine but are known to add easily to the didehydro bond in a didehydropyridine. For example, in the presence of the potassium salt of pentan-3-one 2- and 4-(3-oxo-2-pentyl)-6-ethoxypyridine (**118** and **119**) were obtained in a (80:20 ratio) in addition to the two amino compounds **115** and **117** (Scheme 30)[91]. When potassium thiophenoxide was used as an additional nucleophile to trap the didehydro compound 2- and 4-(phenylthio)-6-ethoxypyridine (**120** and **121**) could be isolated in a 92:8 ratio (Scheme 30)[44]. (*b*) Investigations on the influence of the potassium amide concentration on the ratio (Ra) of the isomeric 2-aminopyridine **115** to the 4-aminopyridine **117** showed an impressive effect[44]: $[KNH_2]$ = 0.30 M, Ra = 4.6; $[KNH_2]$ = 0.04 M, Ra = 6.7; $[KNH_2]$ = 0.02 M, Ra = 10.5. These results showed a relative increase of the 2-amino compound with a decreasing potassium amide concentration. This has been ascribed to the fact that in solutions with a low potassium amide concentration the addition of liquid ammonia solvent to the 2,4-didehydro bond becomes competitive with the addition of the amide ion. Since ammonia is a weaker nucleophile than the amide ion it is more sensitive to differences in the electron densities and therefore it can be expected to have higher preference than the amide ion for addition at C-2[93]. It was observed that when the $[KNH_2]$ was increased from 0.3 to 1.0 M, Ra also increased. This anomalous effect may be ascribed to a saturation effect of the amide ions to the addition at **113** and an increasing contribution of the $S_N(AE)$ reaction at higher amide concentration.

Although the results obtained in the amination of 2-*X*-6-ethoxypyridine (**112**; X = Br, I) convincingly support the hypothesis of the intermediacy of **113**, they do not exclude the possibility that in the formation of **115** the $S_N(AE)$ mechanism is partly operative.

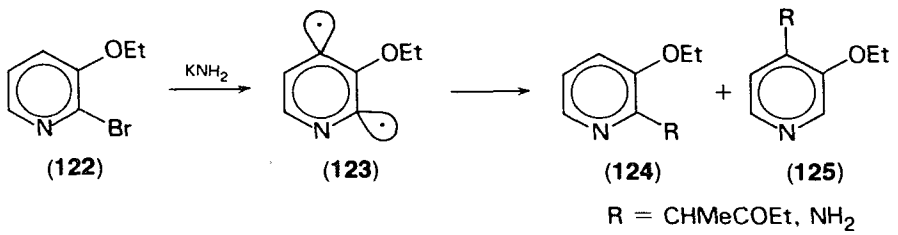


SCHEME 30

To our knowledge this reaction is the first example of the occurrence of a *tele* substitution product taking place according to an elimination–addition mechanism. As mentioned in the introduction *tele* substitution usually occurs in an addition–elimination process. To differentiate between the two types of *tele* substitutions we refer to them as $S_N(AE)^{tele}$ and $S_N(EA)^{tele}$. Investigations on the amination of 6-*R*-2-bromopyridines (R = OC_6H_5, *p*-$EtOC_6H_4O$, *m*-$EtOC_6H_4O$, *p*-FC_6H_4O) with potassium amide in liquid ammonia have revealed that the corresponding 4-amino-6(2)-*R*-pyridines are obtained from these compounds. Since no experiments have been carried out in the presence of a didehydro trapper, e.g., potassium thiophenoxide, it cannot be decided whether the formation of the 4-amino compound involves an $S_N(AE)^{tele}$ or an $S_N(EA)^{tele}$ process.

The possible intermediacy of **113**, in the reaction of **112** (X = Br) with potassium amide in liquid ammonia, have induced extensive research on the behaviour of 2-bromo-3-ethoxypyridine (**122**), 5-amino-2-*X*-pyridine (**126**) and 2-bromo-3-*R*-6-ethoxypyridines (**133**; R = F, OEt, NMe_2) towards various bases, in order to establish whether in these reactions also a 2,4-didehydropyridine derivative would be an intermediate.

Reaction of **122** with 0.17 M potassium amide in liquid ammonia gives 2- and 4-amino-3-ethoxypyridine (**124**, R = NH_2 and **125**, R = NH_2) in a ratio of ~99:1[44]. Carrying out the same reaction in the presence of the potassium salt of pentan-3-one gives 2- and 4-(3-oxo-2-pentyl)-3-ethoxypyridine (**124**, R = CHMeCOEt and **125**, R = CHMeCOEt) (*Scheme* 31)[44]. These results clearly pinpoint 3-ethoxy-2,4-didehydropyridine (**123**) as an active intermediate in these reactions, although they do not exclude the $S_N(AE)$ mechanisms for the formation of a large amount of **124** (R = NH_2). The possible elimination of hydrogen bromide at C-2 and C-6, leading to a 2,6-didehydropyridine derivative as an intermediate is discussed in

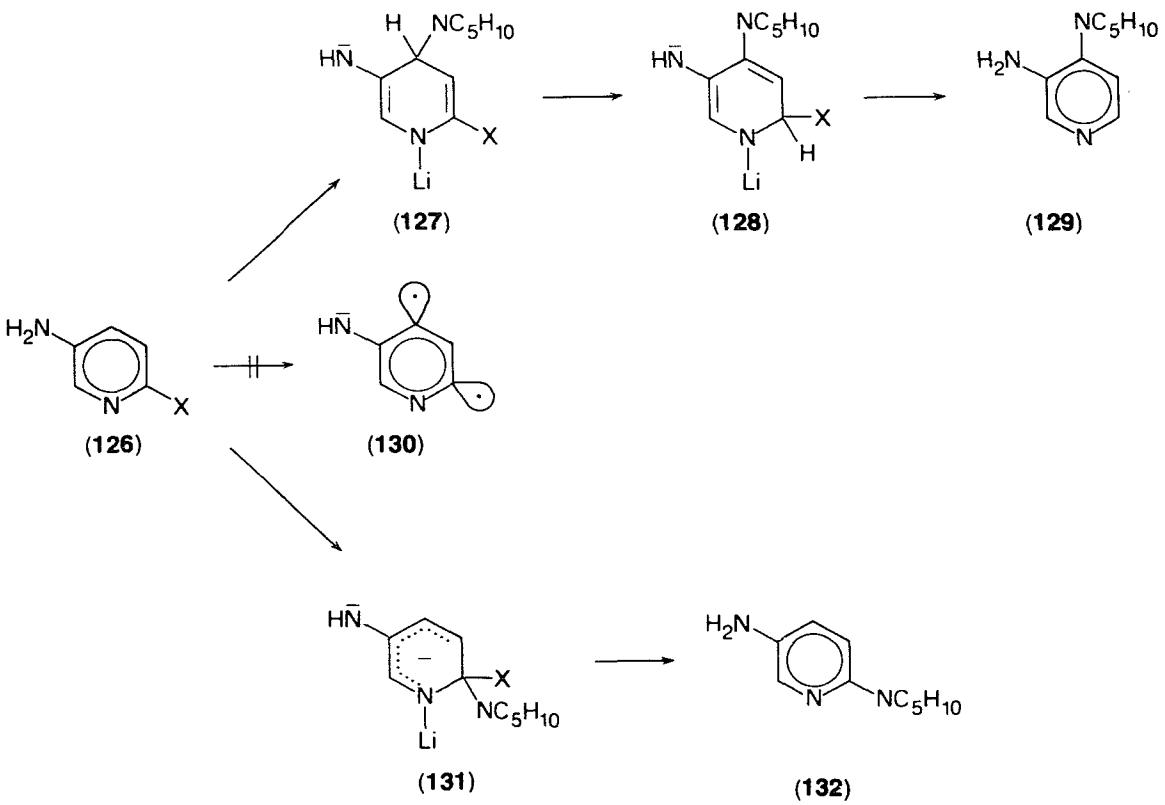


SCHEME 31

Section II.A.4. However, since no convincing experimental data have been presented so far for the occurrence of such an intermediate, its intermediacy in the reaction of **122** can be neglected.

Attempts to generate **123** from **122** by action of potassium *t*-butoxide/DMSO[53] or lithium piperidide/piperidine[95] have failed; only the 2-substituted 3-ethoxy derivatives have been found (see entries 13 and 15, Table 3).

Amination of 5-amino-2-bromopyridine (**126**, X = Br) with lithium piperidide/piperidine (see entry 36, Table 3) gives 2- and 4-piperidino-5-aminopyridine (**132** and **129**) among several products (Scheme 32)[95]. The ratio of **132** to **129** as determined by GLC is about 12:88. When carrying out the same reaction with 5-amino-



SCHEME 32

2-chloropyridine (**126**, X = Cl) the same compounds are formed, but the ratio of **132** to **129** amounts to 34:66[95]. This difference in the **132**:**129** ratio obtained from **126** (X = Br) and **126** (X = Cl) shows that 5-amino-2,4-didehydropyridine (**130**) cannot be an intermediate. The reaction can better be described by the simultaneous occurrence of an $S_N(AE)$ process at C-2 involving **131** and *tele* substitution $S_N(AE)^{tele}$, involving the intermediates **127** and **128** (Scheme 32).

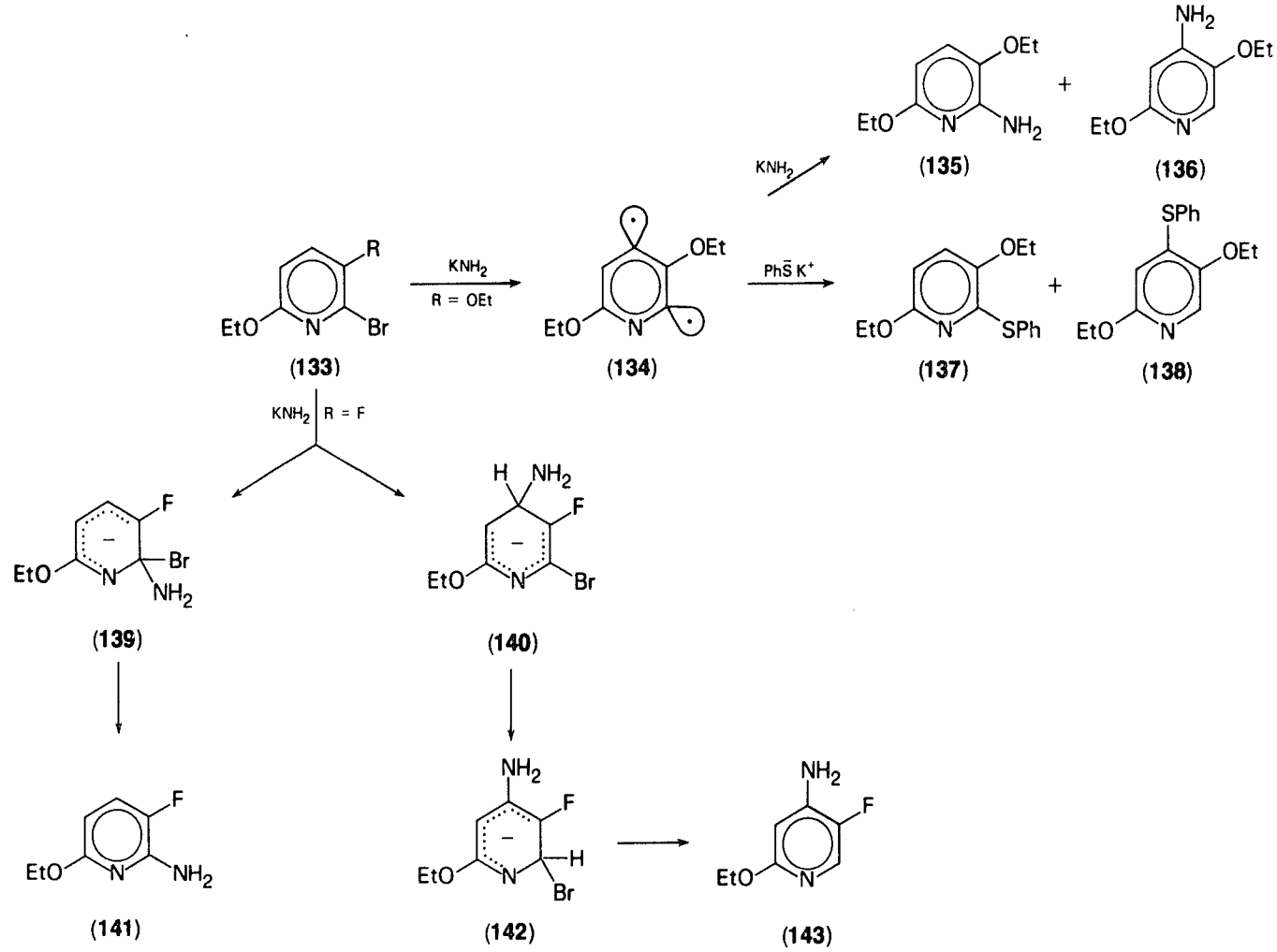
The simultaneous occurrence of the $S_N(AE)$ process at C-2 and the $S_N(AE)^{tele}$ process at C-4 is also proposed for the formation of 5-methylamino-2-piperidinopyridine and 3-methylamino-4-piperidinopyridine from 2-bromo-5-methylaminopyridine and lithium piperidide/piperidine (see entry 41, Table 3)[95]. In this reaction also no indication for the involvement of a 2,4-didehydropyridine derivative has been obtained.

Investigations on the course of the amination of 2-bromo-3-*R*-6-ethoxypyridines (**133**, R = OEt, F) with 0.25 M potassium amide have shown the formation of the 2-amino-6-ethoxypyridines **135** and **141**, together with the 4-amino-6-ethoxypyridines **136** and **143** (Scheme 33)[44]. The ratio (Ra) in which the 2- and 4-amino compounds is formed, is dependent of the nature of the substituent being ~7 for the 3-fluoro compound, and ~3 for the 3-ethoxy compound. Although it is tempting to postulate the occurrence of a 6-ethoxy-2,4-didehydropyridine derivative as intermediate in both reactions, competition experiments with potassium thiophenoxide have shown that in the reaction of the 3-fluoro compound **133** (R = F) with liquid ammonia, containing potassium amide *and* potassium thiophenoxide, *no* (phenylthio)pyridines were formed, but that in the corresponding reaction of 2-bromo-3,6-diethoxypyridine (**133**, R = OEt) the 2- and 4-(phenylthio)pyridines (**137** and **138**) are formed. Therefore, it has been correctly concluded that in the reaction of **133** (R = OEt) 3,6-diethoxy-2,4-didehydropyridine (**134**) is intermediate, but that in the reaction of 2-bromo-6-ethoxy-3-fluoropyridine (**133**, R = F), a 2,4-didehydropyridine derivative is not formed. The formation of 2- and 4-amino-6-ethoxy-3-fluoropyridines **141** and **143** has to be explained by an $S_N(AE)$ process at C-2, involving the σ adduct **139** and an $S_N(AE)^{tele}$ process at C-4, involving the σ adducts **140** and **142**. The results of a study of the reaction of the 3-*N*,*N*′-dimethylamino compound (**133**, R = NMe_2) with liquid ammonia containing potassium amide and the potassium salt of pentan-3-one have also led to the conclusion that in this reaction the intermediate 3-dimethylamino-6-ethoxy-2,4-didehydropyridine is involved.

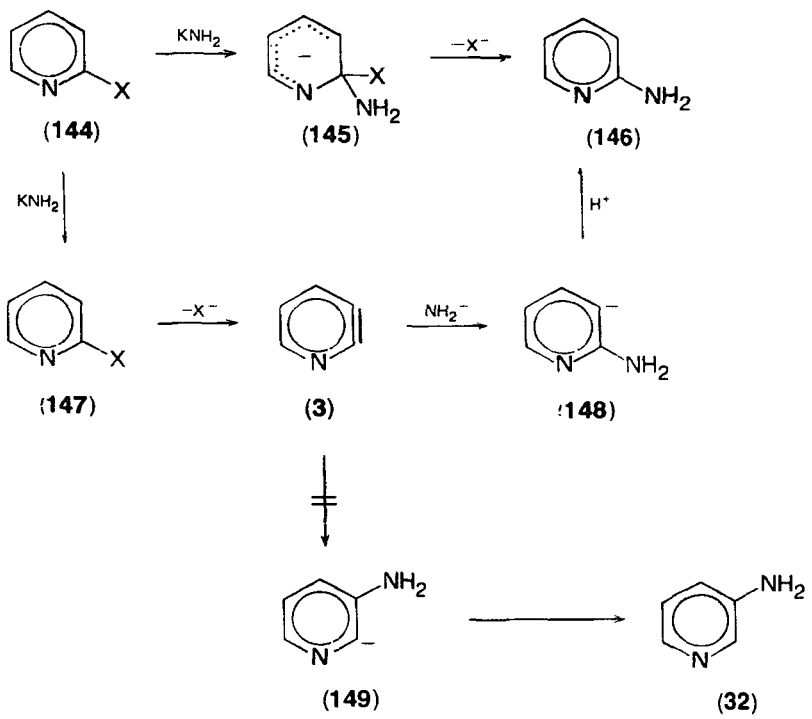
3. *2,3-Didehydropyridine, 2,3-didehydropyridine-1-oxide and their derivatives*

a. 2,3-Didehydropyridine. (i) Is 2,3-Didehydropyridine an intermediate in the reactions of 2- and 3-halogenopyridines with strong bases? As discussed in Section II.A.1.a.ii the species 2,3-didehydropyridine (**3**) is not generated from the 3-halogenopyridines on treatment with strong bases (Scheme 15). Also, from the study of the reaction of the 2-*X*-pyridines (**144**; X = F, Cl, Br, I) with strong bases no conclusive information on the intermediacy of **3** can be obtained. The reaction of the 2-halogenopyridines (**144**) with potassium amide gives only 2-aminopyridine (**146**), the formation of which can be explained either via the $S_N(AE)$ process, involving the σ adduct **145** or via **3**, which then undergoes an exclusive addition of the amide (or ammonia) to C-2 (Scheme 34)[94,96].

That the addition to C-2 of **3** should be favoured over addition to C-3 is derived from the fact that the intermediate 2-aminopyridyl 3-anion (**148**) is more stabilized than the 3-aminopyridyl 2-anion (**149**)[54]; moreover the total electron density at C-2 in **3** is calculated to be lower than at C-3[7]. Attempts have been made to distinguish between the $S_N(AE)$ and the $S_N(EA)$ mechanism by using 2-bromo-3-deuteropyridine as a substrate. If the $S_N(EA)$ mechanism is fully operative the 2-amino compound


KNH2
(135)
(136)
R
KNH2
R = OEt
OEt
PhS̄ K+
(133)
(134)
(137)
(138)
SPh
KNH2 R = F
(139)
(140)
(141)
(142)
(143)

SCHEME 33

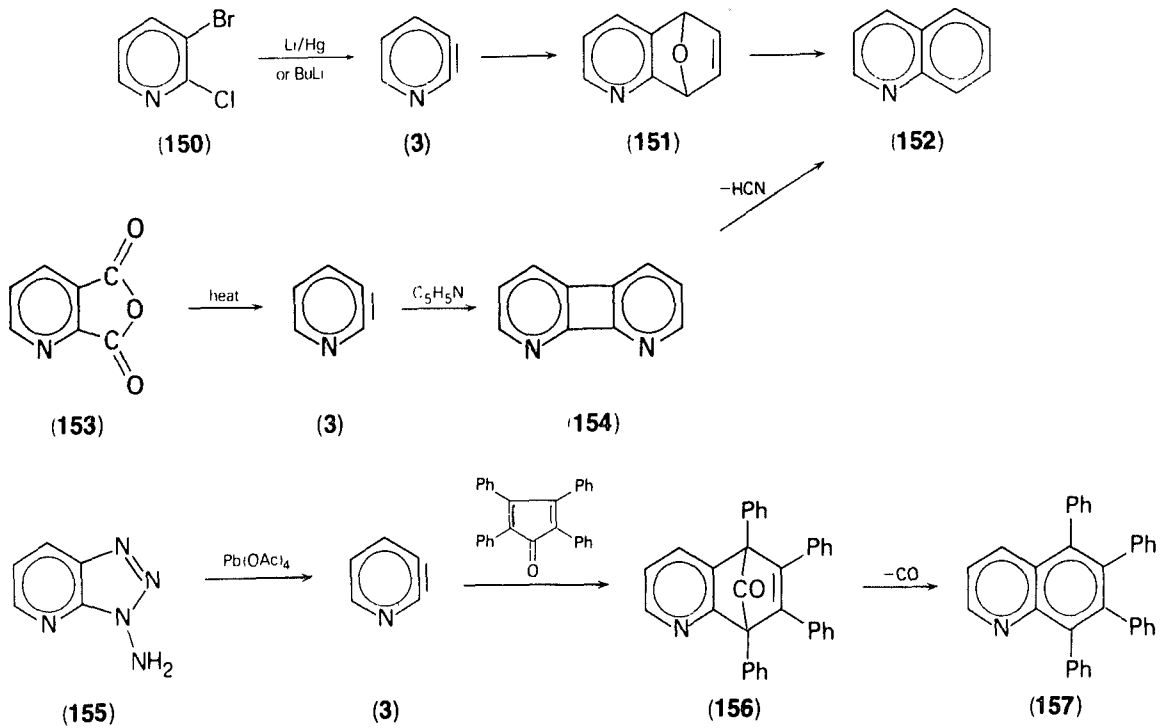


SCHEME 34

should contain no deuterium. However, these attempts have failed due to rapid D/H exchange in the 2-bromo compound, involving **147**[96]. Performing the amination of **144** (X = Br) in the presence of furan does not give even a trace of adduct[96]. Likewise the amination of **144** (X = Cl) with lithium piperidide[46], lithium diethylamide or lithium cyclohexylamide[97] gives no information on the occurrence of **3**; only a resinous mass, containing a small amount of a 2-substituted product, is obtained.

Reaction of **144** with potassium *t*-butoxide in DMSO gives 2-*t*-butoxypyridine as the main product[53]. When the reaction is carried out in the presence of furan no trace of an adduct can be found. Likewise, in the presence of potassium thiophenoxide or potassium phenoxide, only 2-substituted products are obtained. Thus, in all these reactions no indication for the formation of some 3-substituted pyridine has been obtained and the conclusion seems justified that there is a complete lack of evidence for the intermediacy of **3** in the reaction of **144** with strong bases. Until further evidence is available, it can be assumed that all these compounds undergo preferentially an $S_N(AE)$ process.

(ii) Generation of 2,3-didehydropyridine by other methods. There is evidence that in the reaction of 3-bromo-2-chloropyridine (**150**) with lithium amalgam[98] or butyllithium[99] in furan, 2,3-didehydropyridine (**3**) is formed. Quinoline (**152**) is the sole product and its formation can be rationalized by addition of furan to **3**, yielding the endoxide **151** which then undergoes a subsequent deoxidation (Scheme 35). The formation of **3** is also reported in the reaction of 3-bromo-2-fluoropyridine with butyl lithium[100]. Pyrolysis of the anhydride of pyridine-2,3-dicarboxylic acid (**153**) in the presence of pyridine gives **152** as one of the products[101]. Its formation is proposed to occur by a 1,2-addition of pyridine to **3** yielding the tricyclic intermediate **154** which loses HCN (Scheme 35).

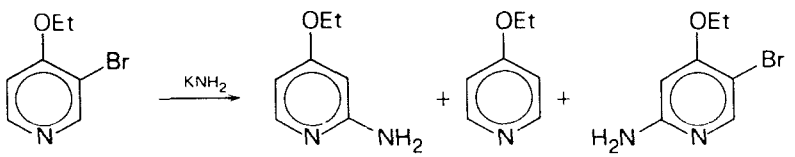

Br
Cl
N
Li/Hg
or BuLi
O
(150)
(3)
(151)
(152)
−HCN
O
C
O
C
O
heat
C_5H_5N
(153)
(3)
(154)
N
NH2
Pb(OAc)4
Ph
CO
−CO
(155)
(3)
(156)
(157)

SCHEME 35

The formation of 5,6,7,8-tetraphenylquinoline (**157**) on oxidation of the *N*-aminotriazolopyridine (**155**) with lead tetraacetate in the presence of tetracyclone presents good evidence for the intermediacy of **3**[69]. The adduct of **3** with tetracyclone, i.e., **156**, loses CO and gives **157** (Scheme 35). In all the reactions mentioned in this section the yields of **3** are much lower than in the corresponding reactions for generating 3,4-didehydropyridine (**2**). These lower yields probably reflect the greater instability of **3**.

b. Derivatives of 2,3-didehydropyridine. (i) Are derivatives of 2,3-didehydropyridine intermediates in the reaction of 2- and 3-halogenopyridine derivatives with strong bases? Since 3-halogenopyridines in reaction with strong bases undergo an $S_N(EA)$ process (see Section II.A.1.a.i) and 2-halogenopyridines undergo an $S_N(AE)$ reaction (see Sections II.A.1.a.ii and II.A.3.a.i) several attempts have been made to generate 2,3-didehydropyridine derivatives from 3-halogenopyridines, in which position 4 has been occupied by a substituent.

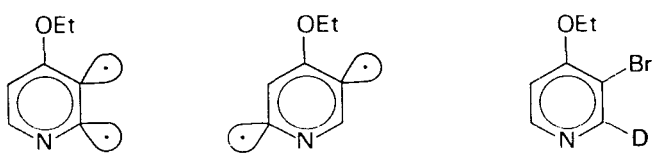
On reaction of 3-bromo-4-ethoxypyridine (**23**) with potassium amide in liquid ammonia at −33°C 2-amino-4-ethoxypyridine (**25**) is obtained in high yield together with some 4-ethoxypyridine (**158**) and some 2-amino-4-ethoxy-5-bromopyridine (**159**) (Scheme 36)[39]. The formation of **25** has been suggested as occurring by the



(**23**) (**25**) (**158**) (**159**)

SCHEME 36

intermediacy of 2,3-didehydro-4-ethoxypyridine (**24**) in which the directing effect of both the ethoxy group and the nitrogen atom operate in the same direction, resulting in the observed attack at C-2. The intermediacy of 2,5-didehydro-4-ethoxypyridine (**160**) could also have been suggested since 2,5-didehydropyridine is more stable than 2,3-didehydropyridine (see Introduction) (Scheme 37).



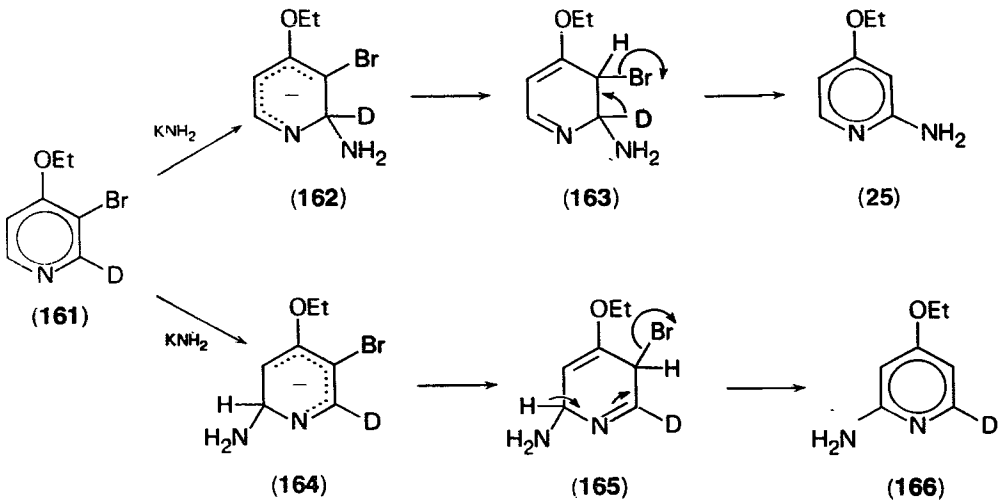
(**24**) (**160**) (**161**)

SCHEME 37

Amination of 4-methyl- and 4-amino-3-bromopyridine shows a somewhat analogous result, although they react much slower than **23**. 3-Bromo-4-methylpyridine gives some 2-amino-4-methylpyridine; more than 90% of the starting material is recovered unchanged[60]. The rate of the reaction of 4-amino-3-bromopyridine is even lower.

A renewed investigation of the course of the amination of **23**, using 3-bromo-2-deutero-4-ethoxypyridine (**161**, % D = 89.3) as substrate, has shown that 6-amino-2-deutero-4-ethoxypyridine **166** (78.7% D) is obtained[29]. Since D/H exchange takes place to only a small extent in the starting material, the conclusion is

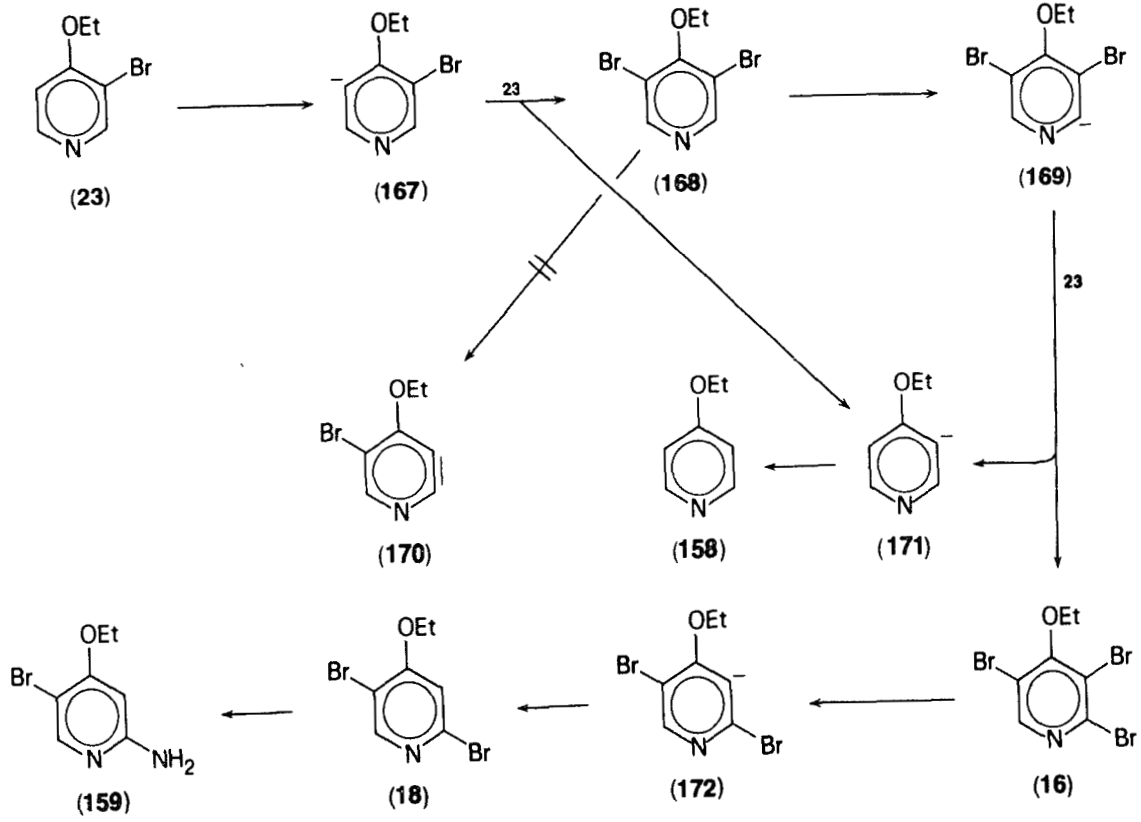
that **25** cannot be formed via a 2,3- or 2,5-didehydro compound but according to a process which involves the formation of a σ adduct (**164**) at position 6, followed by a 1,4-*tele* elimination of hydrogen bromide as in **165**. The small decrease of the D content in the 6-amino compound in comparison with the 3-bromo compound **161** indicates that a smaller part of **161** undergoes addition at position 2 to give a σ adduct **162**, followed by a 1,2-elimination of hydrogen bromide in **163** (Scheme 38). That the



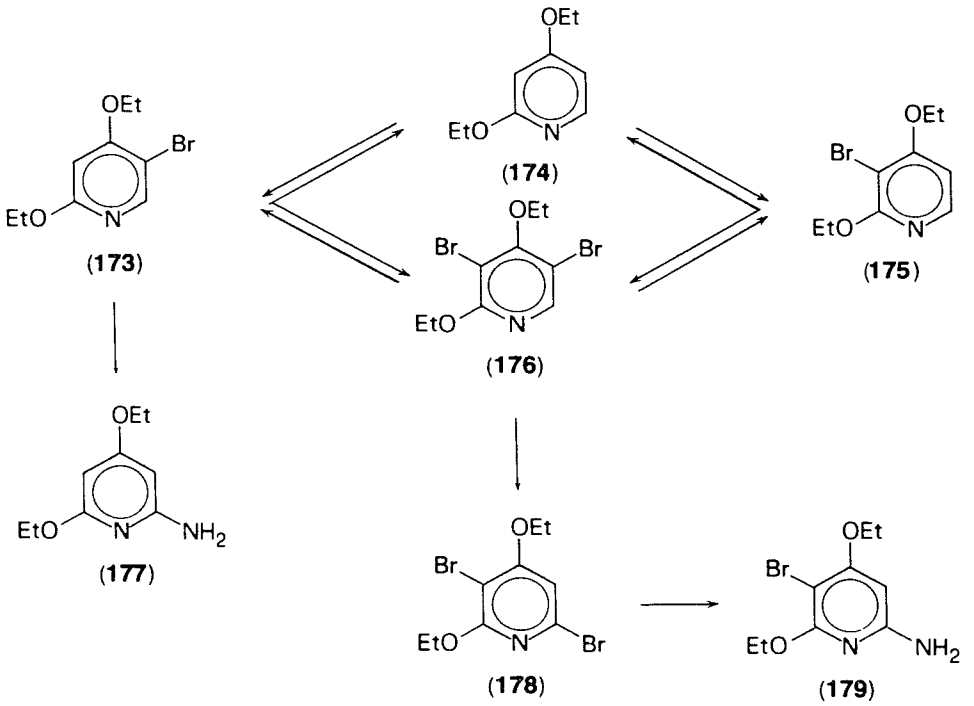
SCHEME 38

2,3-didehydropyridine derivative **24** is not an intermediate species in the amination of **23** has been further proven by the result that when the amination is carried out in the presence of potassium methylmercaptide, a very effective didehydroarene trapper, no trace of 2- of 3-(methylthio)-4-ethoxypyridine can be detected in the reaction mixture [29]. With regard to the formation of **158** and 2-amino-5-bromo-4-ethoxypyridine (**159**) is has been found[29] that when the reaction of **23** with potassium amide in liquid ammonia is carried out at −75°C (instead of the usual temperature of about −35°C) 2,5-dibromo-4-ethoxypyridine (**18**) was formed in about 15–20% yield in addition to **158** and **25**. Since it is known that 3,5-dibromo-4-ethoxypyridine (**168**) isomerizes in liquid ammonia into 2,5-dibromo-4-ethoxypyridine (**18**) the formation of **159** might proceed via the complex route of Scheme 39, involving in the various stages of the rearrangement the pyridyl 3-anions **167**, **171** and **172** and the pyridyl 2-anion **169**.

The suggestion made previously[39] that **168** would react via 5-bromo-4-ethoxy-2,3-didehydropyridine (**170**) to give **159** is not supported by the more recent results similar to those discussed above, and thus can be rejected. The reaction of 5-bromo-2,4-diethoxypyridine (**173**) with potassium amide gives similar results: the formation of 6-amino-2,4-diethoxypyridine (**177**) and 6-amino-3-bromo-2,4-diethoxypyridine (**179**) (Scheme 40)[29]. The formation of **179** can be explained by the route given in Scheme 40. The reaction course involves essentially the intermediate formation of 3,5-dibromo-2,4-diethoxypyridine (**176**), which rearranges into 3,6-dibromo-2,4-diethoxypyridine (**178**). Subsequent amination of **178** gives **179**. Both amino compounds **177** and **179** are also obtained[29] on treatment of 3-bromo-2,4-diethoxypyridine (**175**) with potassium amide in liquid ammonia, proving the reality of intermediate **176** in these aminations (Scheme 40). It is of interest



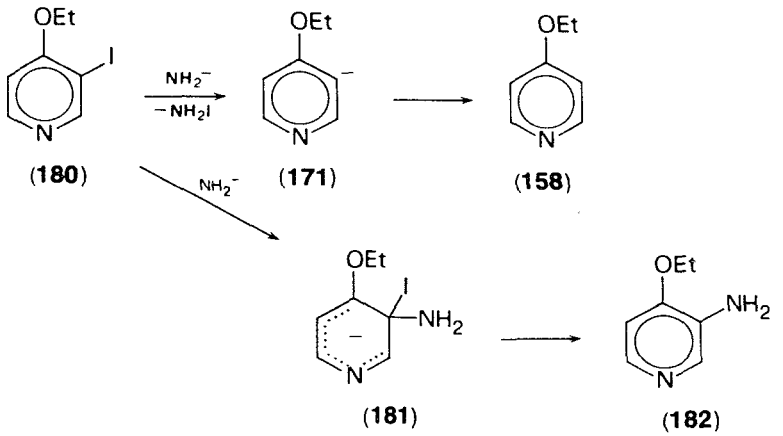
SCHEME 39



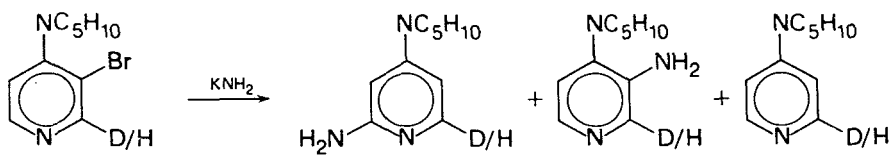
SCHEME 40

to mention[29] that 3-iodo-4-ethoxypyridine (**180**) reacts completely differently from **23**. Only a small amount of 3-amino-4-ethoxypyridine (**182**) (5–10%) is obtained, no trace of the 2-amino compound is found, and the main product is **158**. For the deiodination of **180** into **158**, either a radical anion mechanism – as postulated in the deiodination of 5- and 6-iodopseudocumene with potassium amide in liquid ammonia[102] – or a nucleophilic attack of the amide ion at the iodo substituent leading to a stable 4-ethoxypyridyl 3-anion (**171**) can be advanced. Since addition of the radical scavenger tetraphenylhydrazine has been found to have no influence on the yield of **158** and **182**, the reaction sequence in Scheme 41 has been proposed.

The reaction of 3-bromo-4-piperidinopyridine with potassium amide gives different results from those obtained in the reaction with 3-bromo-4-ethoxypyridine[60]. As a *main* product 3-amino-4-piperidinopyridine, is now obtained besides 2-amino-4-piperidinopyridine and 4-piperidinopyridine. The fact that in this reaction a mixture of 2- and 3-amino-4-piperidinopyridine is formed, strongly suggests the possibility of the intermediacy of 2,3-didehydro-4-piperidinopyridine. In order to probe the intermediacy of this didehydro compound, an amination has been carried out with 3-bromo-2-deutero-4-piperidinopyridine (% D = 34.1)[29]. The content of deuterium in the several products isolated, is shown in Scheme 42. The fact that the deuterium content in the 3-amino and the 2-amino-4-piperidinopyridines is considerably different, proves that 2,3-didehydro-4-piperidinopyridine cannot be the intermediate in the reaction. Since the deuterium content present in the 2-amino-4-piperidinopyridine is about 25% of that of the starting material, the 2-amino- and 6-amino-4-piperidinopyridine are formed in a ratio of about 3:1. The simultaneous occurrence of an $S_N(AE)^{cine}$ and an $S_N(AE)^{tele}$ process – with a

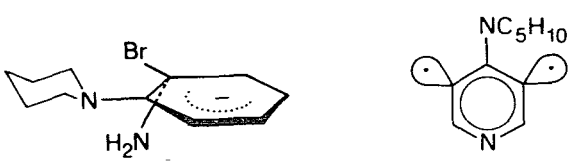


SCHEME 41



SCHEME 42

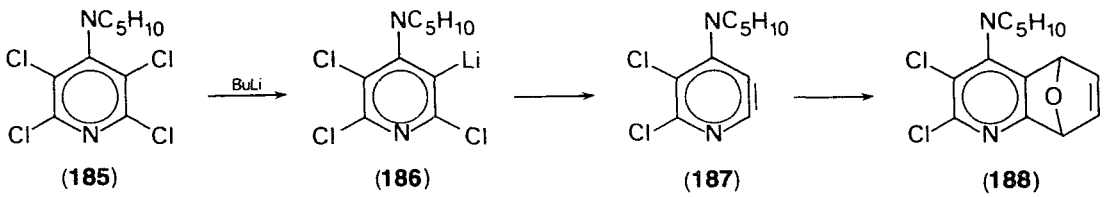
preference for the $S_N(AE)^{cine}$ mechanism – seems to explain these results. The somewhat unusual formation of the 3-amino-4-piperidinopyridine is of interest since the electron-donating character of the 4-piperidino group makes the 3-position even less accessible for nucleophilic attack according to an $S_N(AE)$ process. It can be suggested that the steric interference between the voluminous piperidino group and the adjacent bromo atom leads to relief of strain on addition of the nucleophile, yielding adduct **183** (Scheme 43). Some support for this hypothesis can be taken from the increasing amounts of the 3-amino compound formed on amination of 4-methyl-, 4-isopropyl- and 4-piperidino-3-bromopyridine (traces, 8–10%, 30–35%, respectively)[60]. It must be emphasized that this effect has not been found in the benzene series; *o*-bromopiperidinobenzene gives, on amination with potassium amide, only *m*-piperidinoaniline[103]. The intermediacy of 3,5-didehydro-4-piperidinopyridine (**184**) in the formation of 3-amino-4-piperidinopyridine (Scheme 43) cannot be excluded, although it is evident that more work has to be done in order to establish the existence of this interesting intermediate.



(183) (184)

SCHEME 43

(ii) Generation of 2,3-didehydropyridine derivatives by other methods. When the three isomeric ethoxy derivatives of 2,3-dibromopyridine are reacted with lithium amalgam in the presence of furan the 5,8-endoxide of the three isomeric ethoxy derivatives of 5,8-dihydroquinoline are obtained[104,105]. The yields are higher than those in the corresponding reaction of the parent species 2,3-didehydropyridine. It has also been reported that reaction of 2,3,5,6-tetrachloro-4-piperidinopyridine (**185**) with butyllithium in furan gives the 3-lithio compound **186** from which the 5,8-endoxide of 2,3-dichloro-4-piperidino-5,8-dihydroquinoline (**188**) is obtained via 5,6-dichloro-4-piperidino-2,3-didehydropyridine (**187**)[80,106] (Scheme 44). In a similar way 5,6-dichloro-4-phenyl-2,3-didehydropyridine has been formed[107]. A report is available[108] mentioning that in the reaction of 4-(trimethylsilyl)tetrachloropyridine with *n*-butyllithium, the existence of a short-lived 2,3-didehydropyridine derivative seems probable. 3-Lithio-4-methoxy-2,5,6-tribromopyridine gives on heating in furan the endoxide of 2,3-dibromo-4-methoxy-5,8-dihydroquinoline[80].



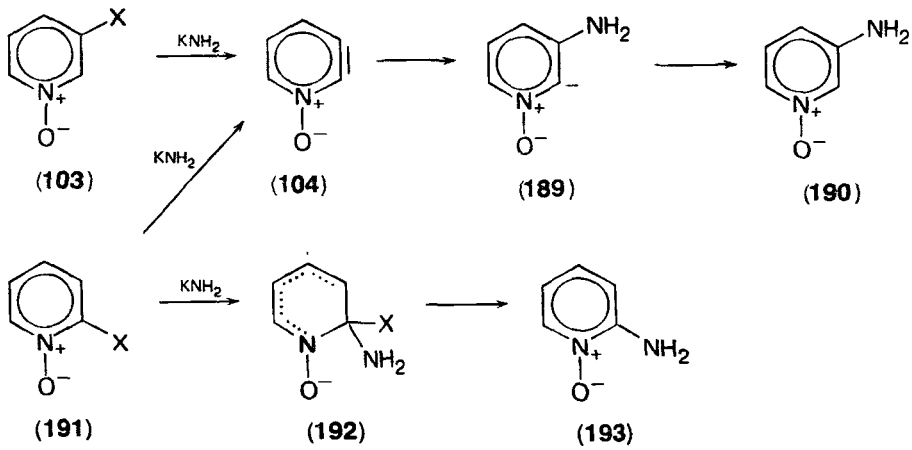
(185) (186) (187) (188)

SCHEME 44

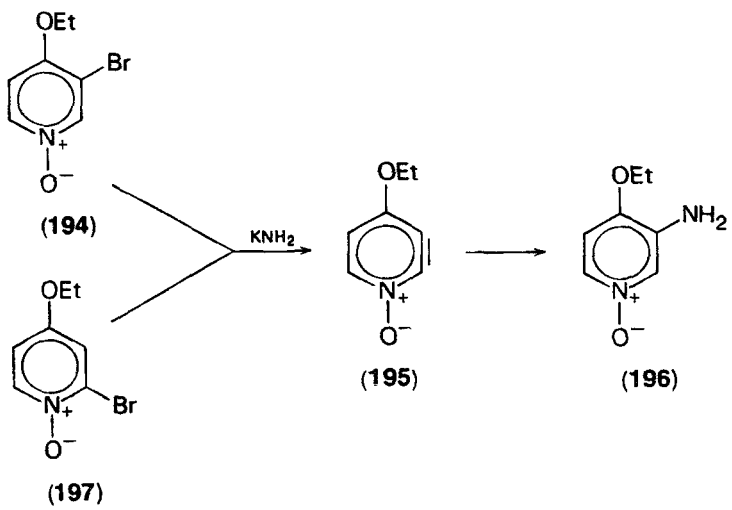
c. 2,3-Didehydropyridine-1-oxide and its derivatives. As already discussed in Section II.A.1.c, 3-halogenopyridine-1-oxides seem to react with amide ions preferentially via the 2,3-didehydro compound[86a]. Reaction of 3-*X*-pyridine-1-oxides (**103**; X = Cl, Br) with potassium amide in liquid ammonia gives 3-aminopyridine-1-oxide (**190**, 75–80%), the formation of which is proposed to be via 2,3-didehydropyridine-1-oxide (**104**) as the intermediary species (Scheme 45). Due to the strong −I effect of the *N*-oxide group there is strong preference for addition of the amide ion (or ammonia) at C-3. An $S_N(AE)$ process at C-3 can be excluded since 3-fluoropyridine-1-oxide – the compound which preeminently undergoes an addition–elimination reaction [$S_N(AE)$] – was found to be unreactive[86a]. As mentioned in Section II.A.1.c it has been found[87] that heating of 3-chloropyridine-1-oxide (**103**, X = Cl) with piperidine gives a mixture of 3- and 4-piperidinopyridine-1-oxides (**105**, R = NC_5H_{10} and **106**, R = NC_5C_{10}). The intermediacy of 3,4-didehydropyridine-1-oxide (**102**) has been suggested (Scheme 26). These results show that whether a 3,4- and/or 2,3-didehydro compound is(are) formed from **103** (X = Cl, Br) with a strong base, also depends on the nature of the base used.

2-*X*-Pyridine-1-oxides (**191**; X = Cl, Br) react[86a] with potassium amide in liquid ammonia to give a mixture of 2- and 3-aminopyridine-1-oxide (**193** and **190**). The yield is rather low. It has been assumed that the 3-amino compound **190** is exclusively formed via **189** by addition of the amide ion to C-3 of the intermediate **104**; the main part of **193** is formed by an $S_N(AE)$ process at C-2, involving the σ adduct **192** (Scheme 45).

The same conclusions can be drawn from the results obtained in the reaction of 4-ethoxy-3-bromo- (**194**)[86a] and 4-ethoxy-2-bromo-pyridine-1-oxide (**197**)[60] with potassium amide/liquid ammonia. The formation of 3-amino-4-ethoxypyridine-1-oxide (**196**), as the main product, in these reactions, has been explained by the intermediate formation of the 4-ethoxy-2,3-didehydropyridine-1-oxide (**195**), to which



SCHEME 45



SCHEME 46

the amide ion adds at C-3. Apparently the *meta*-directing effect of the *N*-oxide group is far superior to that of the ethoxy group (Scheme 46).

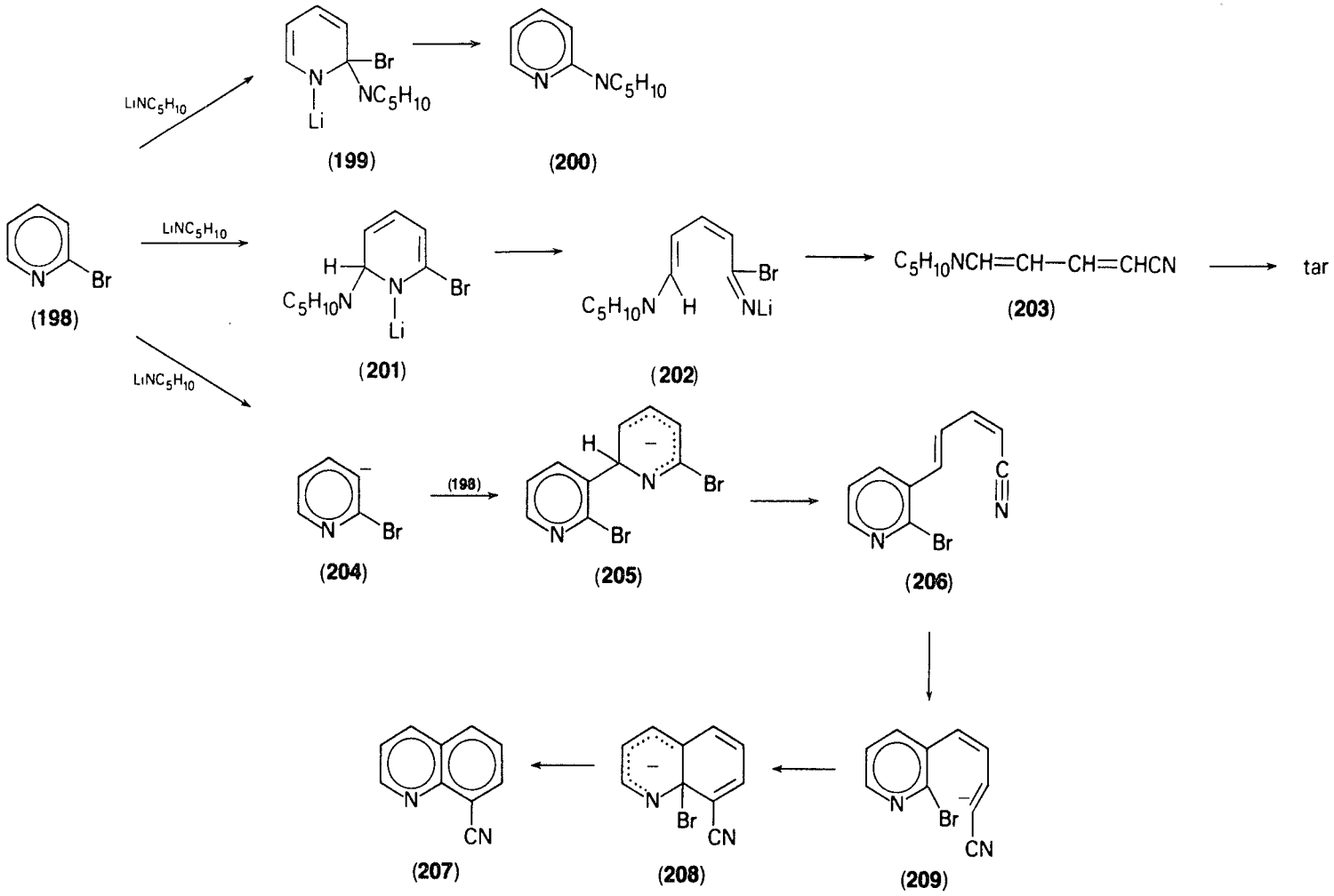
4. *Are 2,6-didehydropyridines involved in reactions of 2-halogenopyridines with strong bases?*

The occurrence of 2,6-didehydropyridine (**7**) as intermediate was first suggested by Kauffmann and Boettcher when they observed that reaction of 2-*X*-pyridines (X = Cl, Br) with lithium piperidide[46], lithium diethylamide[97] or lithium dicyclohexylamide[97] gave a resinous mass, but that 2-chloro-6-methylpyridine with lithium piperidide afforded 6-methyl-2-piperidinopyridine in a good yield. The suggestion was made that 2-chloropyridine does not undergo an initial addition of the amide at C-3, but a deprotonation at C-6, followed by chloride expulsion to give the very unstable **7** which

reacts further and gives tar. When a methyl group is present at C-6, no 2,6-didehydro compound can be formed and only piperidino-dechlorination according to the $S_N(AE)$ process can take place[2]. It has been suggested[9] that among the didehydropyridines, **7** should be a rather 'stable' intermediate due to overlap of the sp^2 carbon orbitals at C-2 and C-6 with the nitrogen sp^2 orbital, containing the lone pair. This is not supported by EHT and MNDO calculations[7,8], which show that this overlap leads in fact to destabilization. Therefore, it seems very questionable as to whether such an energy-rich intermediate would be formed under such mild conditions from 2-chloropyridine. Moreover, the hydrogen at C-6 is the least acidic hydrogen of all the five hydrogens present in the ring of 2-chloropyridine, due to the fact that the pyridyl 6-anion is strongly destabilized because of strong repulsion between the carbon pair of electrons and the nitrogen lone pair. Reinvestigation of the reaction of 2-bromopyridine (**198**) with lithium piperidide/piperidine has shown that, besides much tar and some 2-piperidinopyridine (**200**), a stereoisomeric mixture of the open-chain product 1-cyano-4-piperidino-1,3-butadiene (**203**) (0.5–1%) and 8-cyanoquinoline (**207**) (2–3%) is formed in low yield (see entry 1, Table 3). Whereas **200** is formed by a piperidino-debromination via the C_2-adduct **199**, the formation of tar and the open-chain compound can be explained if the lithium piperidide is also able to add to C-6[95,109]. The formed σ adduct (**201**) undergoes an opening of the pyridine ring to **202** by fission of the C(6)—N bond, whereupon 1-cyano-4-piperidino-1,3-butadiene (**203**) is formed. Because of its high reactivity **203** reacts further, forming a resinous mass (Scheme 47). An interesting and unexpected reaction product is 8-cyanoquinoline (**207**). Its formation shows that **198**, on reaction with lithium piperidide/piperidine, besides addition at C-2 and C-6, also undergoes a partial deprotonation at C-3. That the hydrogen at C-3 is indeed highly acidic has been proved by the fact that 2-bromo-3-deuteropyridine undergoes a very rapid D/H exchange at position 3 in strong basic medium (KNH_2/NH_3, −70°C, 15 s)[96]. This is probably the reason why the addition at C-6 in 2-bromopyridine is so highly favoured compared with addition at C-2, due to the strong electron-donating inductive effect of the negative charge at C-3, making the C-2 position less vulnerable for nucleophilic attack. As indicated in Scheme 47 the 2-bromopyridyl 3-anion (**204**) attacks another molecule of **198** at C-6 giving **205**. Ring-opening in the same way as described for the formation of the 1,3-butadiene derivative **203** yields **206** which deprotonates to the open-chain anionic species 4-(2-bromopyrid-3-yl)-1-cyano-1,3-butadiene (**209**)[110]. After ring-closure of **209** to **208** and aromatization, **207** is obtained (Scheme 47).

A great number of 2-bromopyridines containing substituents in different positions have been systematically investigated in their reactions with strong bases. The products obtained in these reactions, together with the yields (if determined) are summarized in Table 3.

From the results summarized in Table 3 it becomes evident that the formation of the tar, of the small amounts of derivatives of 8-cyanoquinoline and of 1,3-butadiene derivatives is characteristic of nearly all the reactions of 2-bromopyridines containing a substituent in positions 4 and 5 with lithium piperidide/piperidine (see entries 7, 9, 16, 18, 25, 28 and 34). The yields of the piperidino compounds are usually not high and in some cases extremely low. The 2-bromopyridines containing a substituent at position 6 usually give very little tar formation and the corresponding 2-piperidino compounds in reasonable to high yields (see entries 11, 20, 30, 38 and 45). In any case, from the results presented in Table 3 it is clear that the suggestion that 2-*X*-pyridines react by a hydrogen halide removal from positions 2 and 6, followed by addition, must be rejected[2]. On the contrary, the favoured reaction seems to be an *addition* of lithium piperidide at C-6. That addition to C-6 is indeed a favoured reaction is supported by the high yields of 3-amino-2-piperidinopyridine (**213**),


LiNC5H10
Br
N
Li
NC5H10
(199)
(200)
(198)
H
C5H10N
(201)
(202)
C5H10NCH=CH—CH=CHCN
(203)
tar
(204)
(205)
(206)
(207)
(208)
(209)
CN

SCHEME 47

TABLE 3. Products and yields obtained in the reaction of 2-bromopyridine and its derivatives with strong bases

Entry	Pyridine derivative	Base	Products	Yields (%)	Refs.
1	2-Bromo-	$LiNC_5H_{10}/HNC_5H_{10}$	Tar	—	95
			2-Piperidinopyridine	11	
			8-Cyanoquinoline	2–3[a]	
			1-Cyano-4-piperidino-1,3-butadiene	0.5–1	
2	2-Bromo-	KNH_2/NH_3	2-Aminopyridine	85–90	41
3	2-Bromo-	KOBu-*t*/*t*-BuOH	2-*t*-Butoxypyridine	50–54	41
			2-Pyridone	13–17	
4	2-Bromo-	KOBu-*t*/KSPh/DMSO	2-(Phenylthio)pyridine	30–34	53a
			2-*t*-Butoxypyridine	19–23	
			2-Pyridone	12–16	
5	2,3-Dibromo-	$LiNC_5H_{10}/HNC_5H_{10}$	Tar	—	76
6	2,3-Dibromo-	KNH_2/NH_3	2,4-Diaminopyridine	70	77
			4-Amino-2-methylpyrimidine	3	
7	2,4-Dibromo-	$LiNC_5H_{10}/HNC_5H_{10}$	Tar	—	76
			2,4-Dipiperidinopyridine	5–10	
8	2,4-Dibromo-	KNH_2/NH_3	2,4-Diaminopyridine	70	77
			4-Amino-2-methylpyrimidine	3	
9	2,5-Dibromo-	$LiNC_5H_{10}/HNC_5H_{10}$	Tar	—	76
			2,4- and 2,5-Dipiperidinopyridine	traces	
10	2,5-Dibromo-	KNH_2/NH_3	2,4-Diaminopyridine	40	77
			2,5-Diaminopyridine	20	
			2-Amino-5-bromopyridine	20	
			4-Amino-2-methylpyrimidine	3	
11	2,6-Dibromo-	$LiNC_5H_{10}/HNC_5H_{10}$	2,6-Dipiperidinopyridine	80	76
12	2,6-Dibromo-	KNH_2/NH_3	Tar	—	75
			4-Amino-2-methylpyrimidine	20–25	
13	2-Bromo-3-ethoxy-	$LiNC_5H_{10}/HNC_5H_{10}$	3-Ethoxy-2-piperidinopyridine	90–95	95
14	2-Bromo-3-ethoxy-	3M KNH_2/NH_3	2-Amino-3-ethoxypyridine	50–55	73
			4-Amino-3-ethoxypyridine	7–10	
15	2-Bromo-3-ethoxy-	KOBu-*t*/KSPh/DMSO	3-Ethoxy-2-(phenylthio)pyridine	18–22	53a
			3-Ethoxy-2-pyridone	4–7	

			2-Bromo-3-hydroxypyridine	2–5	
16	2-Bromo-4-ethoxy-	$LiNC_5H_{10}/HNC_5H_{10}$	4-Ethoxy-2-piperidinopyridine	10–15	95
			1-Cyano-3-ethoxy-4-cyano-1,3-butadiene	1–3	
			8-Cyano-4(7)-ethoxy-7(4)-piperidinoquinoline	traces	
17	2-Bromo-4-ethoxy-	KNH_2/NH_3	2-Amino-4-ethoxypyridine	95	73
18	2-Bromo-5-ethoxy-	$LiNC_5H_{10}/HNC_5H_{10}$	5-Ethoxy-2-piperidinopyridine	traces	95
			8-Cyano-3,6-diethoxyquinoline	traces	
			3-Ethoxy-2-piperidinopyridine	traces	
19	2-Bromo-5-ethoxy-	KNH_2/NH_3	2-amino-5-ethoxypyridine	90	73
20	2-Bromo-6-ethoxy	$LiNC_5H_{10}/HNC_5H_{10}$	6-Ethoxy-2-piperidinopyridine	—	111a
			6-Ethoxy-4-piperidinopyridine	—	
			2-Bromo-6-piperidinopyridine	—	
			2,6-Dipiperidinopyridine	—	
			2,4-Dipiperidinopyridine	—	
21	2-Bromo-6-ethoxy-	KNH_2/NH_3	2-Amino-6-ethoxypyridine	67–70	40
			4-Amino-6-ethoxypyridine	14–16	
22	2-Bromo-6-ethoxy-	KOBu-*t*/KSPh/DMSO	6-Ethoxy-2-(phenylthio)pyridine	19–23	53a
			2-Bromo-6-pyridone	<2%	
			2-Ethoxy-6-pyridone		
23	2-Bromo-3-methyl-	$LiNC_5H_{10}/HNC_5H_{10}$	3-Methyl-2-piperidinopyridine	25–30	95
			2-Cyano-5-piperidino-2,4-pentadiene	5–10	
24	2-Bromo-3-methyl-	KNH_2/NH_3	2-Amino-3-methylpyridine	20–25	60
25	2-Bromo-4-methyl-	$LiNC_5H_{10}/HNC_5H_{10}$	4-Methyl-2-piperidinopyridine	—	95
			1-Cyano-2-methyl-4-piperidino-1,3-butadiene	—	
26	2-Bromo-4-methyl-	KNH_2/NH_3	2-Amino-4-methylpyridine	10	60
27	2-Bromo-4-isopropyl-	KNH_2/NH_3	2-Amino-4-isopropylpyridine	55–60	60
28	2-Bromo-5-methyl-	$LiNC_5H_{10}/HNC_5H_{10}$	5-Methyl-2-piperidinopyridine	50	95
			1-Cyano-3,7-dimethylquinoline	traces	
29	2-Bromo-5-methyl-	KNH_2/NH_3	2-Amino-5-methylpyridine	35	112
30	2-Bromo-6-methyl-	$LiNC_5H_{10}/HNC_5H_{10}$	6-Methyl-2-piperidinopyridine	—	95
			2-(6-Bromopyridyl)-2′-(6′-methylpyridyl)methane	—	
31	2-Bromo-6-methyl-	KNH_2/NH_3	2-Amino-6-methylpyridine	25	94
			4-Amino-6-methylpyridine	<1	

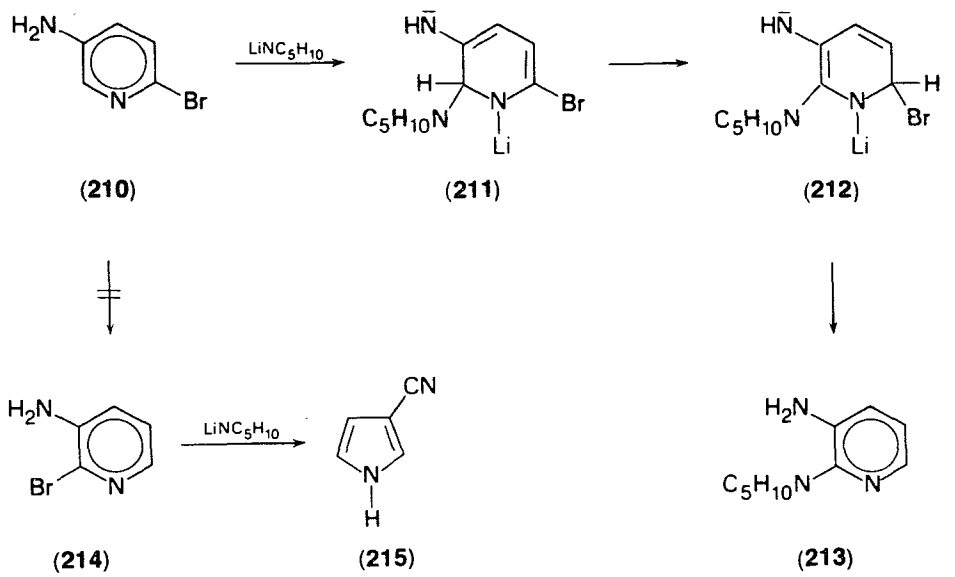
TABLE 3 (*continued*)

Entry	Pyridine derivative	Base	Products	Yields (%)	Refs.
32	3-Amino-2-bromo-	$LiNC_5H_{10}/HNC_5H_{10}$	3-Cyanopyrrole	70–75	95
			3-Amino-2-piperidinopyridine	traces	
33	3-Amino-2-bromo-	KNH_2/NH_3	3-Cyanopyrrole	80	60, 111b
34	4-Amino-2-bromo-	$LiNC_5H_{10}/HNC_5H_{10}$	1-Cyano-4-piperidino-3-aza-1,3-pentadiene	20	95
			4-Amino-2-piperidinopyridine	5–10	
			2-Methyl-4-piperidinopyrimidine	1–3	
35	4-Amino-2-bromo-	KNH_2/NH_3	2,4-Diaminopyridine	70	75
			4-Amino-2-methylpyrimidine	2	
36	5-Amino-2-bromo-	$LiNC_5H_{10}/HNC_5H_{10}$	5(3)-Amino-6(2)-piperidinopyridine	40–50	95
			5(3)-Amino-4-piperidinopyridine	10–15	
			5-Amino-2-piperidinopyridine	1	
37	5-Amino-2-bromo-	KNH_2/NH_3	2,5-Diaminopyridine	15	75
38	6-Amino-2-bromo-	$LiNC_5H_{10}/HNC_5H_{10}$	6-Amino-2-piperidinopyridine	80–85	95
39	6-Amino-2-bromo-	KNH_2/NH_3	1,3-Dicyanopropene	—	94
40	2-Bromo-3-methylamino-	$LiNC_5H_{10}/HNC_5H_{10}$	3-Methylamino-2-piperidinopyridine	75–80	95
			3-Methylaminopyridine	5–10	
41	2-Bromo-5-methylamino-	$LiNC_5H_{10}/HNC_5H_{10}$	5(3)-Methylamino-6(2)-piperidinopyridine	20	95
			5-Methylamino-3-piperidinopyridine	5	
			5(3)-Methylamino-4-piperidinopyridine	2	
			5-Methylamino-2-piperidinopyridine	1	
42	2-Bromo-5-dimethylamino-	$LiNC_5H_{10}/HNC_5H_{10}$	5-Dimethylamino-2-piperidinopyridine	—	95
43	2-Bromo-4-piperidino-	KNH_2/NH_3	2-Amino-4-piperidinopyridine	90	60
44	2-Bromo-4-piperidino-	$LiNC_5H_{10}/HNC_5H_{10}$	2,4-Dipiperidinopyridine	10–15	76
45	2-Bromo-6-piperidino-	$LiNC_5H_{10}/HNC_5H_{10}$	2,6-Dipiperidinopyridine	—	76
46	2-Bromo-3-hydroxy-	$LiNC_5H_{10}/HNC_5H_{10}$	Pyrrole-3-carboxpiperidide	35	16
			3-Hydroxy-2-piperidinopyridine	35–40	
47	2-Bromo-3-hydroxy-	KNH_2/NH_3	Pyrrole-2-carboxamide	85	16

[a]This yield was considerably improved (20%) when the reaction was carried out with a large excess of piperidine.

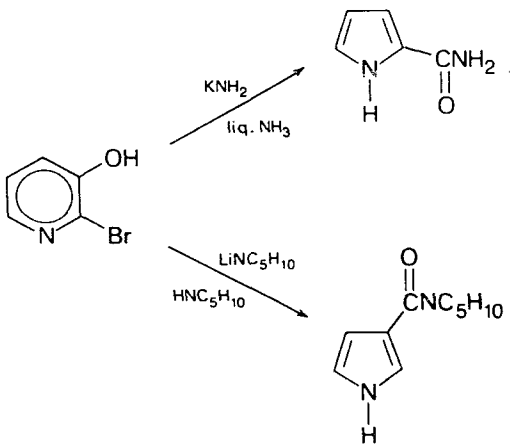
obtained in the reaction of 5-amino-2-bromopyridine (**210**) with lithium piperidide/piperidine (see entry 36, Table 3). This interesting *tele* substitution must be described as an initial addition of the lithium piperidide at C-6, yielding adduct **211**, which after prototropic rearrangement to **212** and loss of lithium bromide gives **213** (Scheme 48). An alternative way of explaining the *tele* substitution, i.e. by the occurrence of a bromine migration in this strong basic medium, leading to 3-amino-2-bromopyridine (**214**) followed by a piperidino-debromination at C-2, can be excluded, since **214** has been found to give only a very small amount of **213** whereas the main product is 3-cyanopyrrole (**215**)[60,111b] (see entry 32, Table 3).

In the reactions of 2-bromopyridine and its derivatives with potassium amide overwhelming evidence is now available that the attack of the amide ion usually takes place at C-2, the carbon being attached to the bromine atom. Only in the case of 2-bromo-3-ethoxy- and 2-bromo-6-ethoxy-pyridine (see entries 14 and 21) has evidence been presented that deprotonation at C-4 followed by bromide expulsion (2,4-didehydropyridine formation) takes place (see Section II.A.2). That in the reaction of the 3-amino compound **214** with the amide ion a ring-contraction into **215** was observed instead of an amino-debromination, is surprising. For a more detailed discussion on this ring-contraction the reader is referred to Reference111b. The same ring-contraction can also be performed with lithium piperidide/piperidine.



SCHEME 48

Comparison of the reactivity of **214** with that of 3-hydroxy-2-bromopyridine, (both the amino and the hydroxy groups are expected to be present in the anionic form in strong basic medium) shows that pyrrole-3-carboxpiperidide is formed with lithium piperidide, and pyrrole-2-carboxamide is formed with potassium amide (see entries 46 and 47, Table 3) (Scheme 49). It is beyond the scope of this review to discuss this interesting difference in behaviour between the 3-hydroxy- and 3-amino-2-bromo-pyridines towards the base systems potassium amide in liquid ammonia and lithium piperidide in piperidine. The reader is referred to Reference 16.



SCHEME 49

5. *Ring-closure via polar addition to didehydropyridine intermediates*

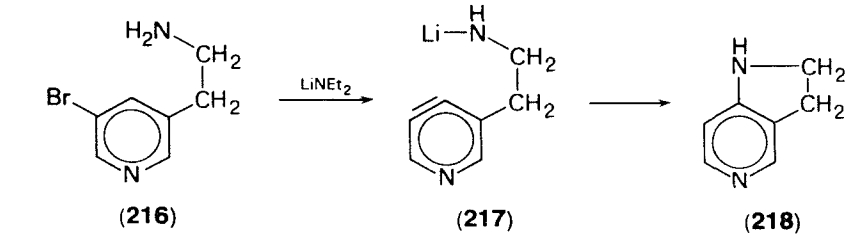
The polar addition of nucleophiles to didehydropyridines and their derivatives has been extensively described in previous sections. When the nucleophile is part of a side-chain, attached to the didehydropyridine, intramolecular addition can occur, resulting in annellation. This principle has been successfully exploited in didehydroarene chemistry and since the first reports on ring-closure reactions via polar addition to these intermediates, many examples have been accumulated. However, this method appears not to be generally applicable in the field of didehydropyridines; therefore only a few examples are mentioned in the literature. Treatment of the 3-alkylamino-5-bromopyridines **216**[113] and **219**[114] with strong base have been found to give the pyrrolo[3,2-*c*]pyridine derivative **218** and the pyrrolo[3,4-*c*]pyridine derivative **221**, respectively. In both reactions a 3,4(4,5)-didehydro compound, i.e. **217** and **220**, is postulated as intermediate; the results do not fully exclude the occurrence of an $S_N(AE)^{cine}$ mechanism (Scheme 50).

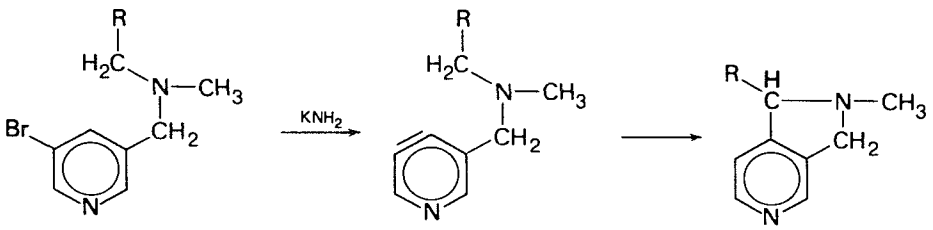
With compound **219** (R = 4-pyridyl) no ring-closure is observed, probably since the carbanion is not sufficiently nucleophilic, due to delocalization of the negative charge over the pyridine ring. Annellation involving the 3,4-didehydropyridine derivative **223** as intermediate has also been achieved: when 3-benzoylamino-5-bromopyridine (**222**) is reacted with lithium amides, 2-phenyloxazolo[4,5-*c*]pyridine (**224**) is obtained (8%) (Scheme 51)[113].

The compounds shown in Scheme 52 have been subjected to treatment with strong bases but found to withstand annellation[113]. From these results the conclusion seems justified that the ring-closure via polar addition of side-chain nucleophiles to a 3,4-didehydropyridine derivative is sensitive to small structural changes.

A preparation of 2,9-diazaphenanthrene (**227**) from reaction of the 5-bromo compound **225** with potassium amide has been reported. The cyclization involves an intramolecular ring-closure in 3-(*N*-phenylaminomethyl)-4,5-didehydropyridine (**226**) and subsequent oxidation with manganese dioxide (Scheme 53)[115].

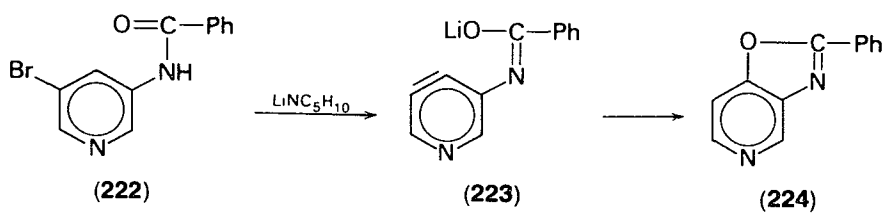
In a very similar way the alkaloid perlolidine (**228**)[115] and 2,11-diazachrysene[116] can be prepared. It has been reported that treatment of 3-bromo-4-*N*-(phenyl)amino-methylpyridine (**229**) with potassium amide in liquid ammonia and subsequent treatment with manganese dioxide in chloroform yields 9-azaphenanthridine (**230**)[116]



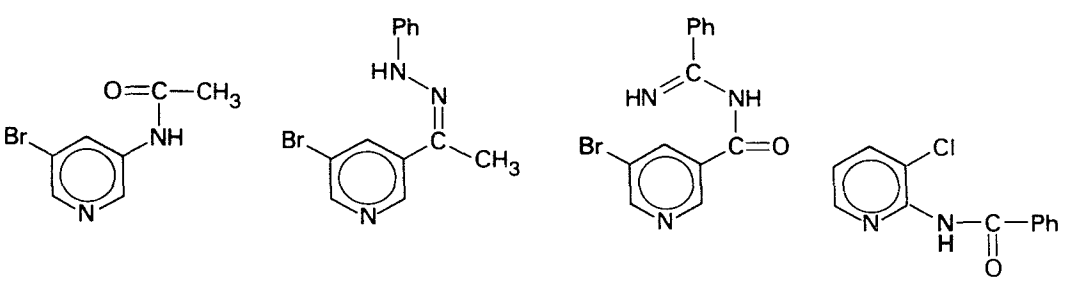


R = CN, CO_2Et, COPh

SCHEME 50

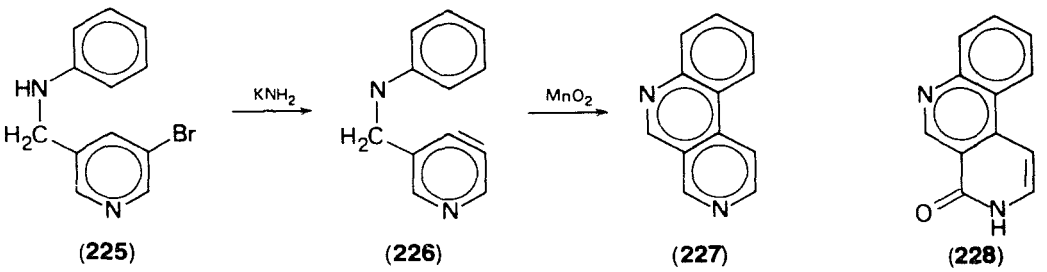


SCHEME 51



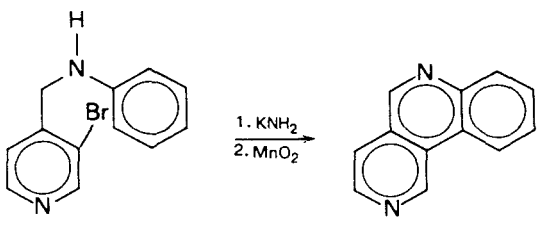
SCHEME 52

(Scheme 54). The authors claim the intermediacy of a 2,3-didehydropyridine derivative, but more evidence is certainly necessary to substantiate the occurrence of this intermediate in this ring-closure reaction. An $S_N(AE)^{cine}$ process seems a reasonable alternative pathway.



(225) (226) (227) (228)

SCHEME 53



(229) (230)

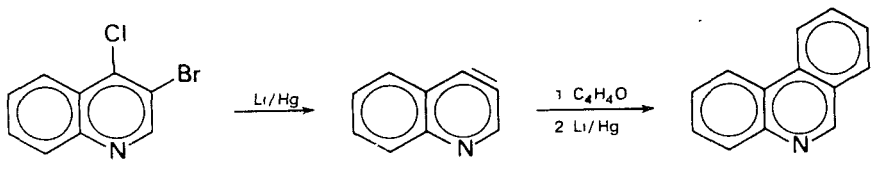
SCHEME 54

III. BICYCLIC SIX-MEMBERED DIDEHYDROHETEROARENES

A. Bicyclic Six-membered Didehydromonoazaheteroarenes

1. *3,4-Didehydroquinolines, 3,4-didehydroquinoline-*N*-oxides and didehydroisoquinolines*

a. 3,4-Didehydroquinolines and 3,4-didehydroquinoline-1-oxides. There is evidence for the intermediary existence of both 3,4- and 2,3- didehydroquinoline in reactions of *o*-dihalogenoquinolines with lithium amalgam. 3,4-Didehydroquinoline (**232**) is generated by the action of lithium amalgam on 3-bromo-4-chloroquinoline (**231**), since phenanthridine (**233**) is formed (9%) in the presence of furan, (Scheme 55)[117,118].

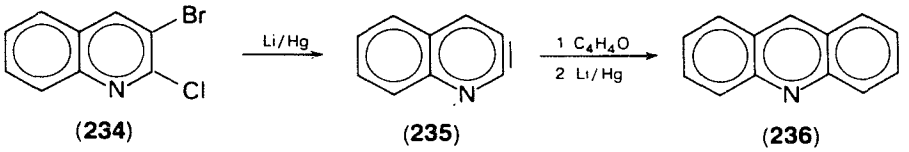


(231) (232) (233)

SCHEME 55

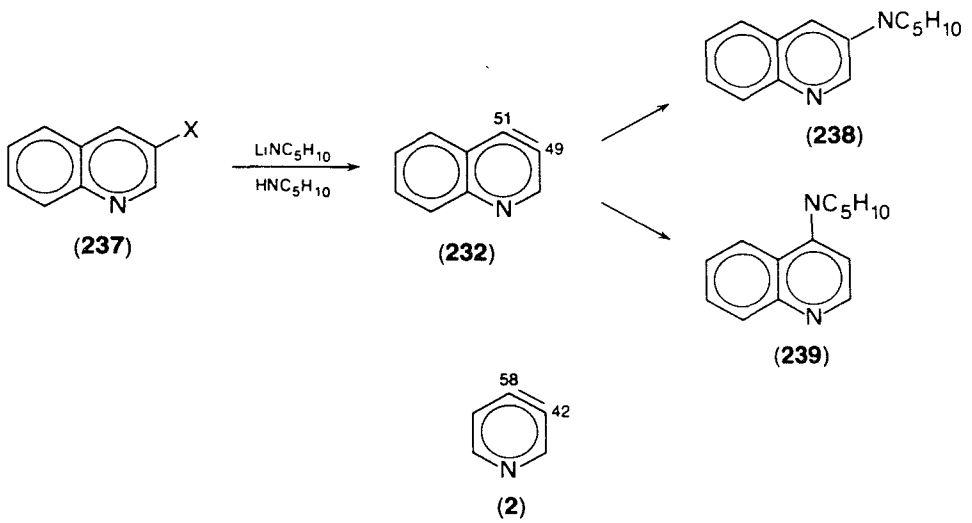
Reaction of 3-bromo-2-chloroquinoline (**234**) with lithium amalgam and furan gives acridine (**236**, 4%), suggesting the intermediacy of 2,3-didehydroquinoline (**235**) (Scheme 56)[119].

Convincing evidence for the intermediacy of **232** has been found in the reaction of



SCHEME 56

3-*X*-quinolines (**237**; X = Cl, Br, I) with lithium piperidide and piperidine in boiling ether[118]. From these three compounds identical mixtures of 3- and 4-piperidinoquinoline (**238** and **239**) have been obtained in a 49:51 ratio in 50–60% yield (Scheme 57). 3-Fluoroquinoline (**237**, X = F) reacts without rearrangement, **238** being formed, probably according to the $S_N(AE)$ mechanism[118]. Reaction of 4-chloroquinoline with lithium piperidide in piperidine/ether gives only **239** and no **238**[120].

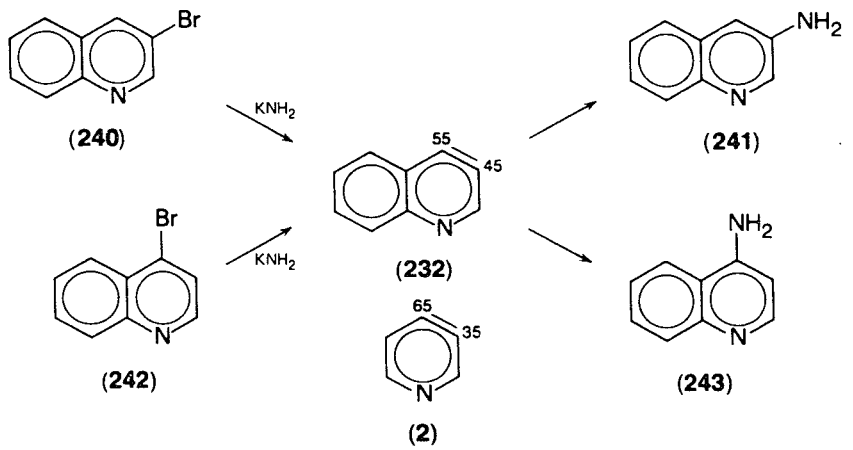


SCHEME 57

Comparison of the ratio of addition to C-3 and C-4 of the piperidino group in 3,4-didehydropyridine (**2**) and in **232** shows that annellation of the pyridine ring of **2** leads to a less pronounced addition at C-4. In fact positions 3 and 4 of **232** show an about equal reactivity for addition of the lithium piperidide. In studies on the competitive addition of the base pair diethylamine/piperidine to **2** and **232** it has been found[48,63,64,121] that the competition constants for both species are in the range of 1, showing that annellation has little influence on the selectivity of addition of these bases and that both didehydro compounds differ little in energy (see also discussions in Section II.A.1.a.iv).

The intermediacy of **232** has also been proposed in the reaction of 3- and 4-bromoquinoline (**240** and **242**) with potassium amide in liquid ammonia since a mixture of 4- and 3-aminoquinoline (**243** and **241**) of the same ratio (55:45) is obtained from both compounds (Scheme 58). Comparison of this addition ratio with that found for 3,4-didehydropyridine (65:35) shows that – just as found for the addition of secondary amides – annellation of the pyridine ring of 3,4-didehydropyridine (**2**) leads to a less favoured addition at C-4. When **240** is reacted

with sodium amide in liquid ammonia, containing alkyl cyanides, 4-(cyanoalkyl)quinolines are obtained. The 3,4-didehydro compound **232** is reported to be an intermediate[123]. It is remarkable that in these reactions the 3-(cyanoalkyl)quinolines are not formed. The argument put forward, that these compounds are not obtained due to – we quote – 'the electron-attracting power of the ring nitrogen in the hetaryne' does not seem convincing.

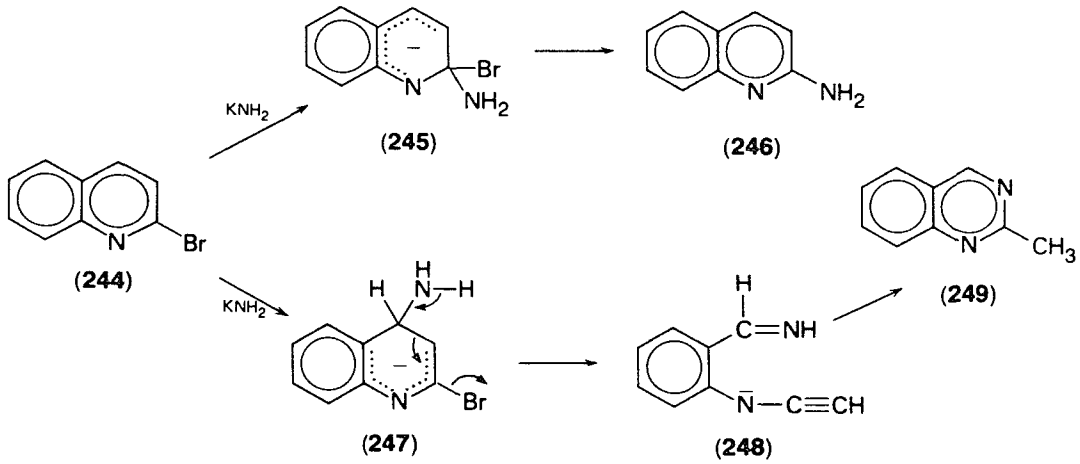


SCHEME 58

In all the reactions of the 3-halogenoquinolines with potassium amide in liquid ammonia, as well as with lithium piperidide in piperidine, no trace of a 2-substituted quinoline has been obtained, indicating that 2,3-didehydroquinoline (**235**) cannot be involved in these reactions. The reaction of 2-chloroquinoline with lithium piperidide[120], yielding 2-piperidinoquinoline and the reaction of 2-bromoquinoline (**244**) with potassium amide, yielding 2-aminoquinoline (**246**) and surprisingly 2-methylquinazoline (**249**)[122], also does not give any indication for the intermediacy of **235** (Scheme 59). The formation of the 2-aminoquinoline has been explained by the $S_N(AE)$ mechanism involving the σ adduct **245**. The interesting ring-transformation of **244** into **249** involves an initial addition of the amide ion to C-4, to form **247**, followed by ring-opening to the open-chain compound **248** and subsequent ring-closure to **249** (Scheme 59). Thus, in contrast to 2-bromopyridine which with potassium amide only undergoes addition at position 2[97], 2-bromoquinoline gives amide addition at position 2 as well as at position 4.

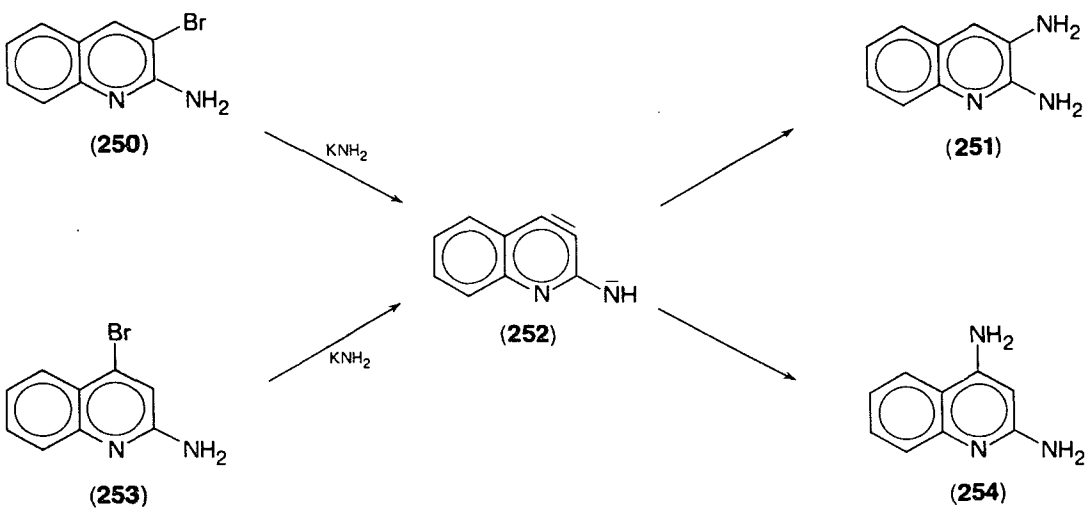
A systematic investigation of the reaction of 3- and 4-halogenoquinoline derivatives with potassium amide in liquid ammonia shows that there is a close analogy in the course of the reaction with that of the corresponding pyridine derivative (see Section II.A.1.b.i). Reaction of 3-bromo-2-ethoxyquinoline with potassium amide in liquid ammonia gives, via 2-ethoxy-3,4-didehydroquinoline, 4-amino-2-ethoxyquinoline (95%) and 3-amino-2-ethoxyquinoline (1–2%)[124]. In accordance with previous results, the *meta*-directing effect of the ethoxy group at position 2 surpasses that of the nitrogen and almost exclusively determines the addition.

The behaviour of all six isomeric aminobromoquinolines containing the amino as well as the bromo substituent in the pyridine ring, with potassium amide in liquid ammonia, has been investigated[125]. Reaction of 2-amino-3-bromo- (**250**) and 2-amino-4-bromo-quinoline (**253**) with potassium amide in liquid ammonia gives the same reaction product, i.e. 2,3-diaminoquinoline (**251**), in high yield (80–90%)



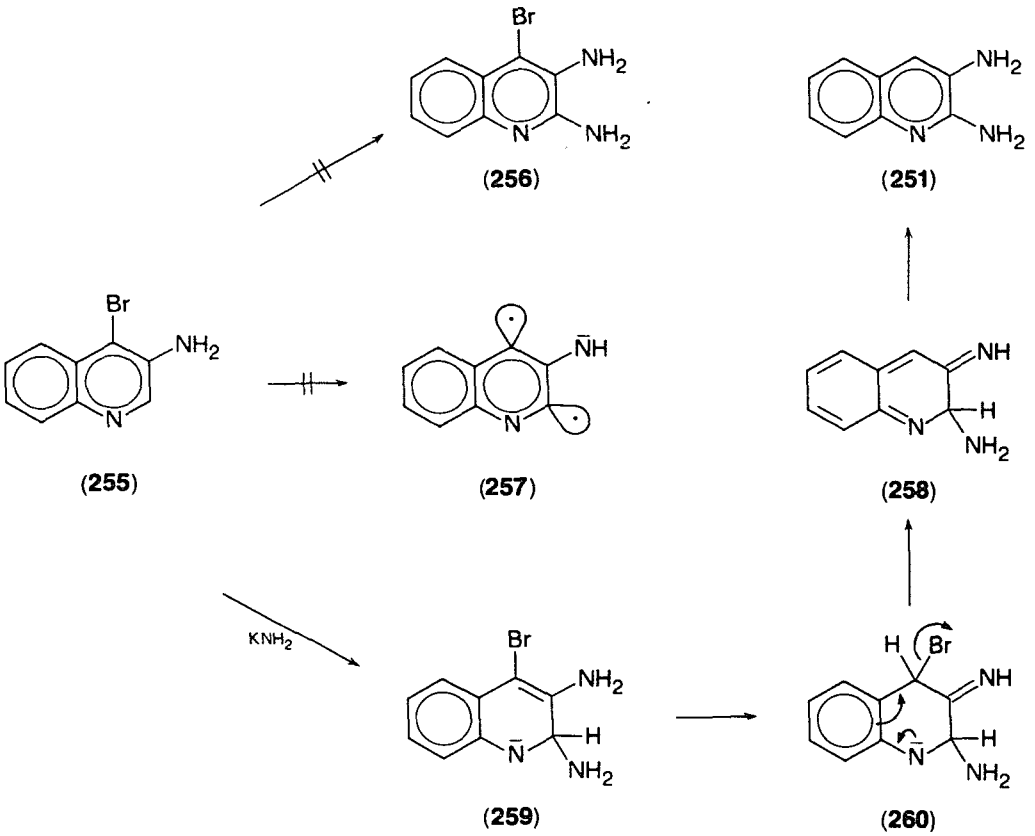
SCHEME 59

together with some 2,4-diaminoquinoline (**254**, 3%)[125]. This result strongly indicates the intermediacy of the anion of 2-amino-3,4-didehydroquinoline (**252**) in these aminations (Scheme 60). From the results of the aminations of the four remaining isomeric aminobromoquinolines, no evidence for the intermediacy of a substituted



SCHEME 60

3,4- or 2,3-didehydroquinoline can be obtained[125]. 4-Amino-3-bromoquinoline is, just like 4-amino-3-bromopyridine, unreactive towards potassium amide. 3-Amino-4-bromoquinoline (**255**) gives surprisingly as the main reaction product 2,3-diaminoquinoline (**251**). The reaction course for the formation of **251** is outlined in Scheme 61. The essential step is the formation of the 2,3-diamino-4-bromo-1,2-dihydroquinolinide (**259**), which via the intermediates **260** and **258** gives **251**. The possibility of the initial formation of 4-bromo-2,3-diaminoquinoline (**256**) by a Chichibabin-type amination followed by an amide-induced debromination reaction

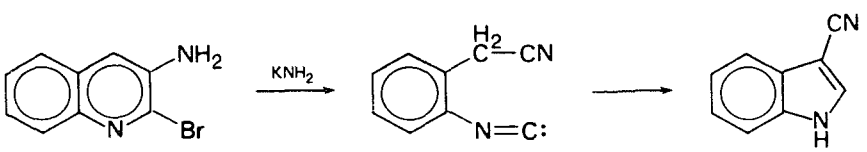


SCHEME 61

can be excluded since **256** is stable in potassium amide in liquid ammonia[125]. No indication for the occurrence of the 2,4-didehydroquinoline (**257**) has been obtained.

Attempts to prepare **251** from 3-amino-2-bromoquinoline (**261**) by treatment with potassium amide have failed. 3-Cyanoindole (**263**) together with *o*-cyanomethylphenylisocyanide (**262**) have been found as sole products[125]. The isocyanide **262** has been proved to be the precursor of **263** (Scheme 62).

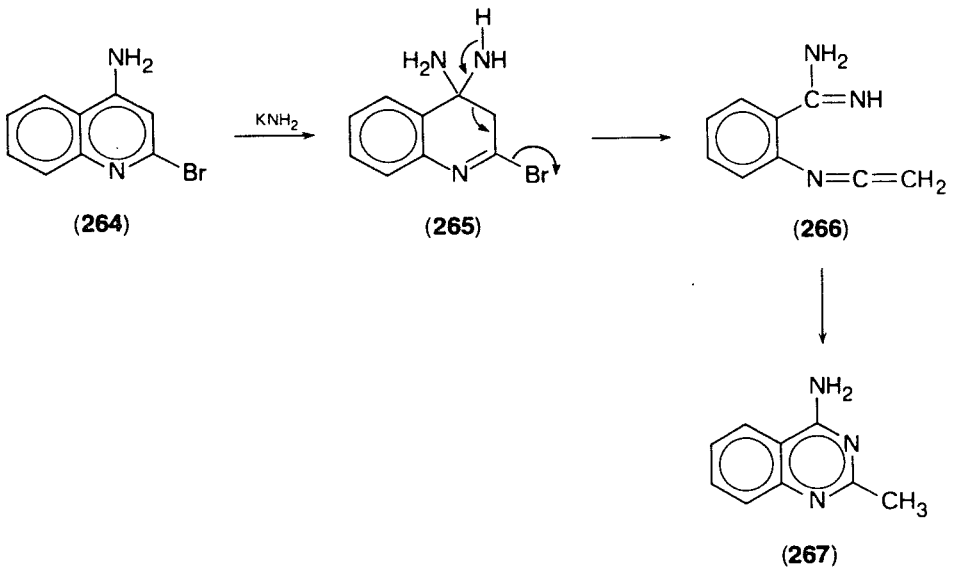
The same type of ring-contraction has also been found with 3-amino-2-bromopyridine (see entry 33, Table 3); for the mechanism of the reaction see Reference 111b. Another interesting ring-transformation has been found with 4-amino-2-bromoquinoline (**264**). Reaction with potassium amide gives instead of the expected 2,4-diaminoquinoline, 4-amino-2-methylquinazoline (**267**) as the main



(**261**) (**262**) (**263**)

SCHEME 62

product (Scheme 63)[125]. This result is in contrast to that obtained with 4-amino-2-bromopyridine which gives nearly exclusively 2,4-diaminopyridine[75]. The ring-transformation of **264** to **267** can be described by an initial addition of the amide ion at C-4, yielding **265**, followed by a bond fission between C-3 and C-4 giving the amidinophenylketenimine (**266**) which easily undergoes a ring-closure[125]. The same ring-transformation also takes place when lithium piperidide instead of potassium

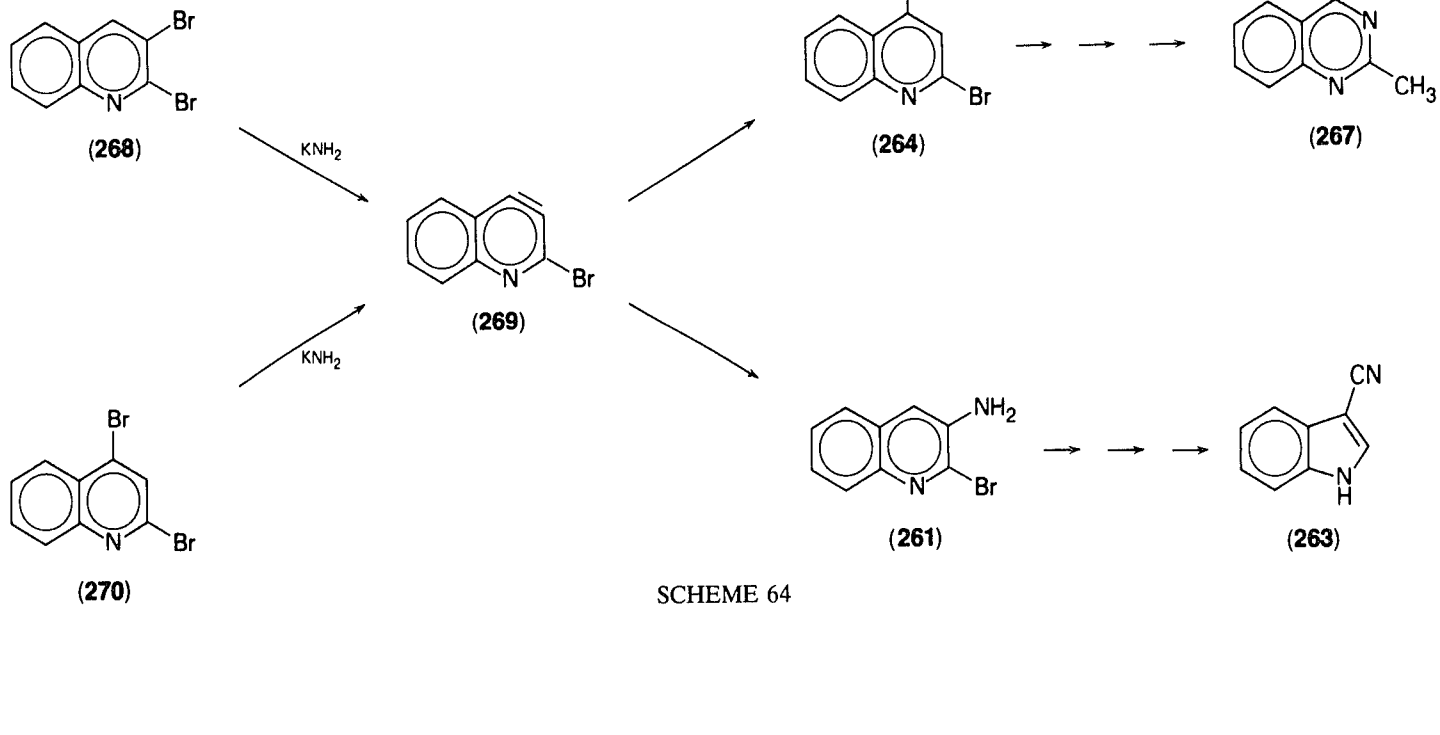


(**264**) (**265**) (**266**) (**267**)

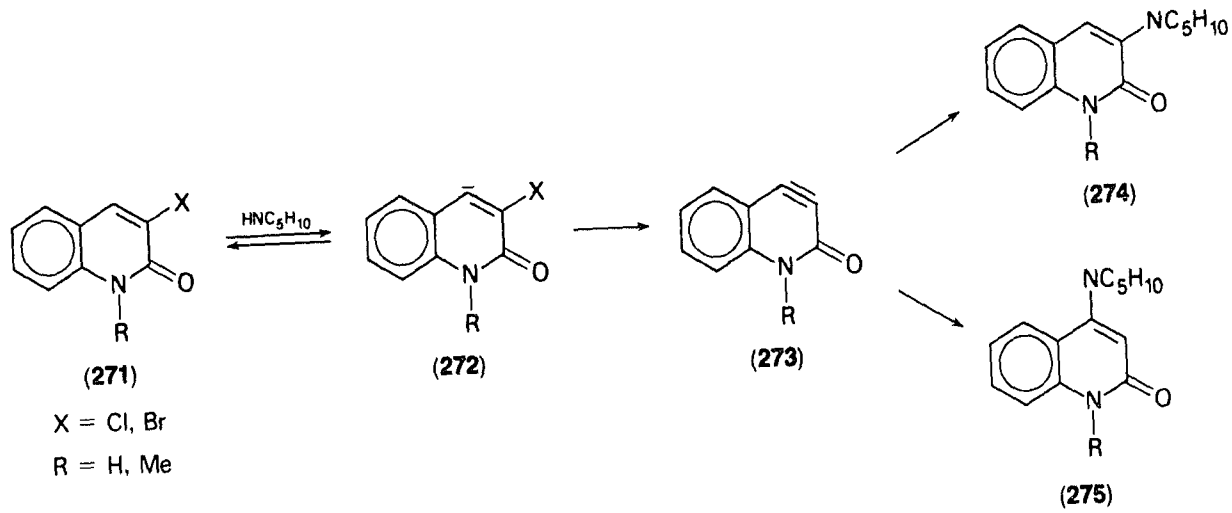
SCHEME 63

amide is used, 4-piperidino-2-methylquinazoline being formed[95]. Amination of 2,3-, 2,4- and 3,4-dibromoquinoline with potassium amide has also been extensively studied[30]. Complicated reaction patterns have been found. Without going into details, it can be mentioned that it has convincingly been shown that in the amination of both 2,3- and 2,4-dibromoquinoline (**268** and **270**) 2-bromo-3,4-didehydroquinoline (**269**) is the intermediate species (Scheme 64)[30]. From both compounds, **264** and **267** are the main products, together with a trace of **263**. As discussed above **267** is formed from **264** and **263** from **261**.

Reaction of 3-chloro- and 3-bromo-carbostyril (**271**; X = Cl, R = H and **271**; X = Br, R = H) with piperidine at 180°C gives identical 53:47 mixtures of 3- and 4-piperidinocarbostyril (**274**, R = H and **275**, R = H) in high yield (Scheme 65)[126]. Nearly the same ratio (56:44) of 3- and 4-piperidino-*N*-methylcarbostyril (**274**, R = Me and **275**, R = Me) is obtained when the *N*-methyl derivatives of 3-chloro- and 3-bromocarbostyril are used as substrates. These results seem to indicate that in all four reactions 3,4-didehydrocarbostyril (**273**, R = H, Me) is an intermediate. Further support for the intermediacy of the 3,4-didehydro compound **273** comes from the fact that when piperidine was used as a reagent in the presence of an excess of ethanol, no reaction is observed with **271** (X = Cl; R = H, Me) and **271** (X = Br, R = Me). Ethanol, being a better proton donor than piperidine reprotonates the anion **272** at C-4, preventing the formation of the 3,4-didehydro compound **273**. When **271** (X = Br, R = H) is subjected to treatment with piperidine/ethanol a mixture of the two piperidino compounds **274** (R = H) and **275** (R = H) is still obtained, although


Br
Br
N
(268)
KNH2
KNH2
Br
Br
N
(270)
N
Br
(269)
NH2
N
Br
(264)
NH2
N
N
CH3
(267)
NH2
N
Br
(261)
CN
N
H
(263)

SCHEME 64



SCHEME 65

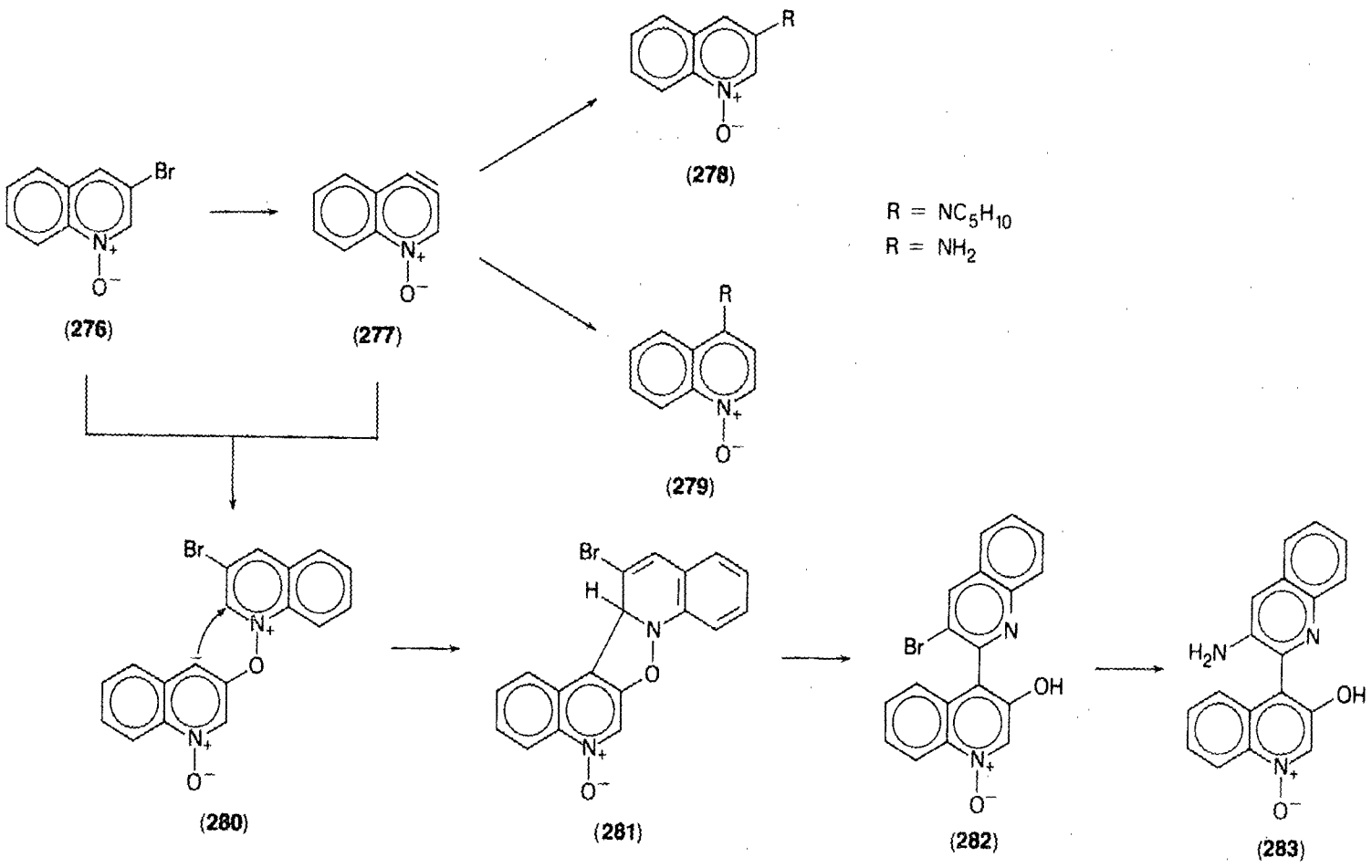
the amount of the 'unrearranged' product **274** (R = H) is increased, indicating that an S_N(AE) process at C-3 is now becoming competitive with the S_N(EA) reaction[126].

Reaction of 3-bromoquinoline 1-oxide (**276**) with piperidine at 100°C gives a mixture of 3- and 4-piperidinoquinoline 1-oxide (**278**, R = NC_5H_{10}, 20% and **279**, R = NC_5H_{10}, 22%)[87] whereas with potassium amide in liquid ammonia at −35°C a mixture of 3-amino- and 4-amino-quinoline-1-oxide (**278**, R = NH_2 and **279**, R = NH_2) is obtained[127]. This has been interpreted as an indication that in both reactions the 3,4-didehydroquinoline-1-oxide (**277**) plays an important role (Scheme 66). In the last-mentioned reaction, besides **278** (R = NH_2) and **279** (R = NH_2) a product has been isolated and assigned the structure of 3-hydroxy-4-(3-amino-2-quinolyl)quinoline-1-oxide (**283**)[127]. It is likely to be formed by an initial coupling between the 3,4-didehydro compound (**277**) and **276**, followed by the rearrangements indicated (**280** → **281** → **282**). An analogy to this reaction is the formation of 4-(2-hydroxyphenyl)acridine from the reaction of acridine-1-oxide with didehydrobenzene[128]. The results of the reaction of **276** with potassium amide, indicating the intermediate formation of the 3,4-didehydro compound **277** are in interesting contrast to those obtained in the amination of 3-bromopyridine-1-oxide (**103**, X = Br) in which the 2,3-didehydropyridine-1-oxide (**104**) seems to be the intermediate (Scheme 45). Semiquantitative measurements of the H/D exchange rate constants in **276** in the presence of 0.04N CH_3ONa in CH_3OD have shown that the ratio of k(H-4)/k(H-2) in **276** is considerably higher than in **103** (X = Br)[127].

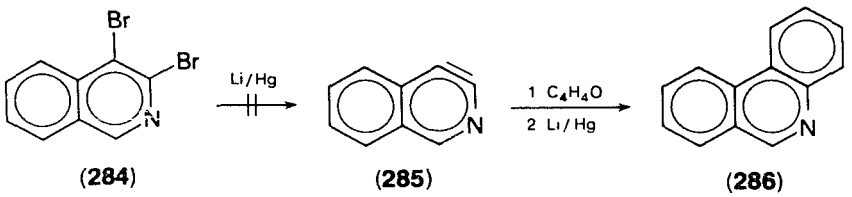
b. Didehydroisoquinolines. So far no convincing evidence has been produced for the intermediacy of didehydroisoquinolines in reactions of halogenoisoquinolines with strong bases. Attempts to generate 3,4-didehydroisoquinoline (**285**) by the reaction of 3,4-dibromoisoquinoline (**284**) with lithium amalgam in the presence of furan have failed[129]; no trace of phenanthridine (**286**) could be detected (Scheme 67). Also the reaction of 1-bromo- and 3-bromo-isoquinoline with potassium amide gives no indication for the occurrence of a didehydroisoquinoline[129]. 1-Aminoisoquinoline is obtained from 1-bromoisoquinoline in an S_N(AE) process. The formation of 3-aminoisoquinoline from 3-bromoisoquinoline (**287**) has been found to occur for 55% according to an S_N(ANRORC) mechanism (for an extensive discussion on this subject, see Section IV.B) and for 45% according to an S_N(AE) process. In the aminations of 4-*X*-isoquinolines (**287**; X = F, Cl, Br, I) with potassium amide also no indication for the occurrence of **285** is found. 1-amino-4-*X*-isoquinoline (**289**; X = F, Cl, Br, I), 1-aminoisoquinoline (**291**) and 4,4′-biisoquinolines being the main products[19]; only traces of 4-aminoisoquinoline are obtained. The formation of **289** and **291** starts by addition of the amide ion at C-1, as has been proved by ^{1}H-NMR spectroscopy. Aromatization gives **289**, whereas the formation of **291** must occur by a 1,4-*tele* elimination of HX from the 1,4-dihydro adduct **290** (Scheme 68).

The formation of the transient intermediate **285** has been suggested for the reaction of **287** (X = Br) with piperidine at 180°C. The formation of a mixture of 3-piperidino- (4%) and 4-piperidino-isoquinoline (35%) has been explained by addition of piperidine to **285**[130]. Reinvestigation of the reaction of **287** (X = Br) with piperidine has shown, however, the formation of 4-piperidino- and 1-piperidino-isoquinoline[19]; only a trace, if any, of 3-piperidinoisoquinoline (< 0.5%) could be detected by GLC analysis. The 4-*X*-isoquinolines (**287**; X = F, Cl, I) show the same behaviour. Based on these results and on those obtained in the pyridine and quinoline series, it seems doubtful whether **285** is an intermediate in the reaction of **287** with piperidine. Awaiting further results, it is more reasonable to explain the formation of the trace of 3-piperidinoisoquinoline from **287** (X = Br) by an S_N(AE)^{cine} substitution.

Studies of the amination of the six isomeric ethoxybromoisoquinolines, containing both the bromo atom and the ethoxy group in the pyridine nucleus, with potassium

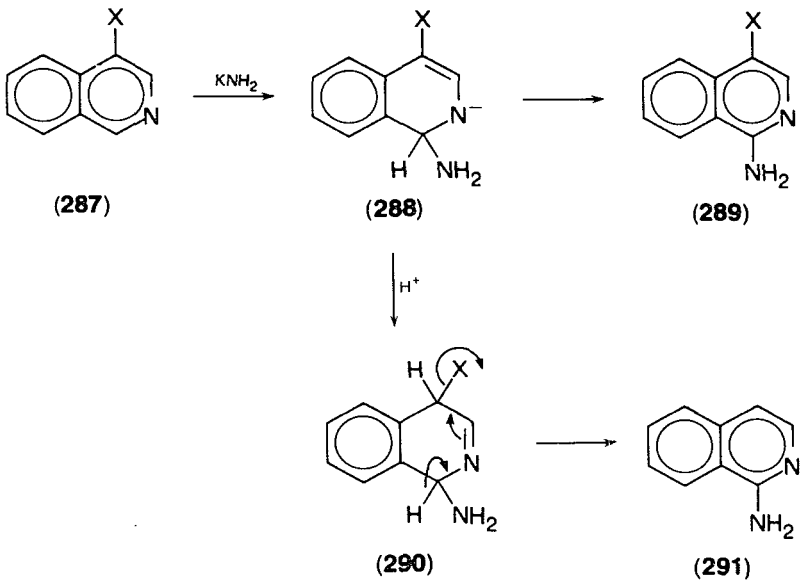

Br
(276)
(277)
R
(278)
R
(279)
R = NC5H10
R = NH2
(280)
(281)
Br
H
Br
OH
(282)
H2N
OH
(283)

SCHEME 66



(284) (285) (286)

SCHEME 67



(287) (288) (289)

(290) (291)

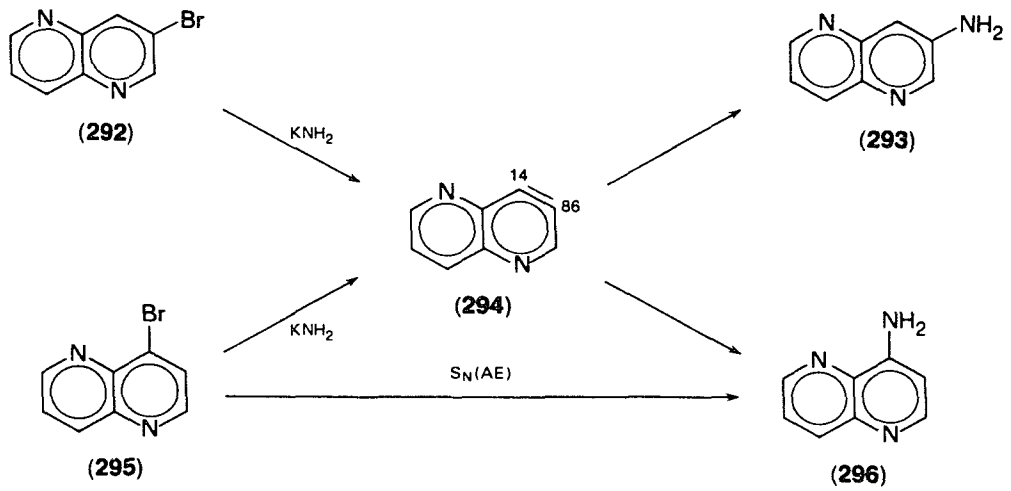
SCHEME 68

amide, showed that all, except the 4-bromo-3-ethoxyisoquinoline, react via a 'simple' aminodebromination according to an $S_N(AE)$ process[131].

4-Bromo-3-ethoxyisoquinoline gives a very complicated reaction mixture, containing besides substitution products, dehalogenated compounds and differently substituted biisoquinolines.

c. Didehydronaphthyridines. In recent years extensive investigations have been carried out in order to establish the intermediary occurrence of didehydro-1,5-, 1,6-, 1,7- and 1,8-naphthyridines in aminations of halonaphthyridines with potassium amide in liquid ammonia. As a result of these studies it has been established definitively that 3,4-didehydro-1,5-, 1,6-, 1,7- and 1,8-naphthyridines are intermediary species in many of these aminations.

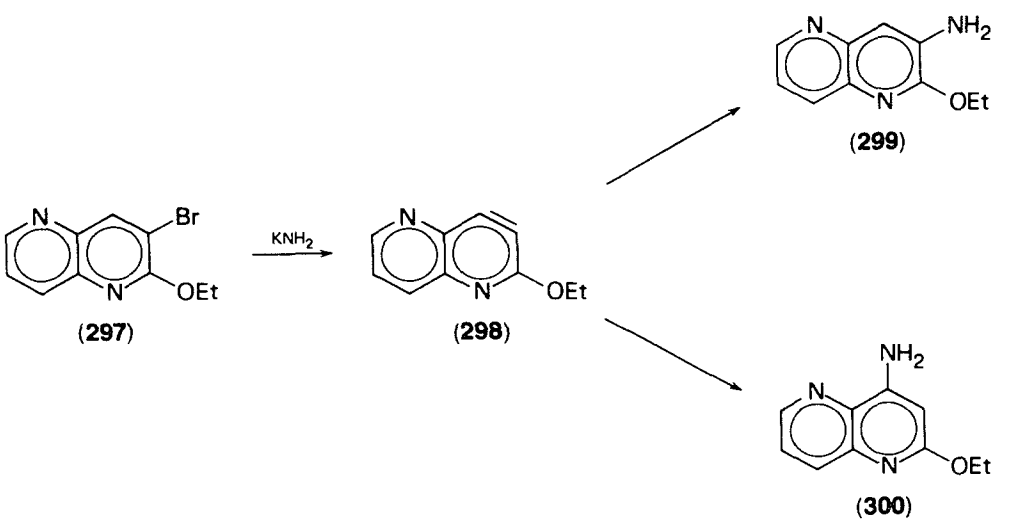
(i) Didehydro-1,5-naphthyridines. Reaction of 3-bromo-1,5-naphthyridine (**292**) with potassium amide in liquid ammonia gives a 86:14 mixture of 3-amino-(**293**) and 4-amino-1,5-naphthyridine (**296**) in high yield (Scheme 69)[132]. No 2-amino-1,5-naphthyridine can be detected in the reaction mixture. These results combined with those obtained in the aminations of the 3-halogenopyridines (see Section II.A.1.a.ii) and 3-halogenoquinolines (see Section III.A.1) indicate the occurrence of the intermediate 3,4-didehydro-1,5-naphthyridine (**294**) and exclude the occurrence of 2,3-didehydro-1,5-naphthyridine. 4-Bromo-1,5-naphthyridine (**295**) also gives a mixture of **293** and **296** in a 77:23 ratio, indicating that **295** also undergoes



SCHEME 69

a dehydrobromination to **294** (Scheme 69)[132]. Since the ratio of **293** to **296** obtained from **295** is smaller than the one obtained from **292**, it can be concluded that **295** undergoes besides an $S_N(EA)$ process an aminodebromination at C-4 [$S_N(AE)$]. The addition ratio to **294** (86:14) is very different from the 45:55 ratio obtained in the addition of the amide ion to C-3 and C-4 of 3,4-didehydroquinoline (**232**) (Scheme 58). The less favoured addition to C-4 of **294** is probably due to a hindered attack of the amide ion at C-4, due to the Coulomb electronic repulsion between the negatively charged, incoming amide ion and the sp^2 electron pair of the nitrogen at position 5.

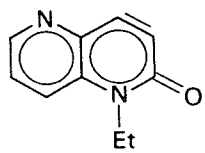
It has been reported[132] that 3-bromo-2-ethoxy-1,5-naphthyridine (**297**) gives with potassium amide as sole product the unrearranged 3-amino-2-ethoxy-1,5-naphthyridine (**299**) and not, as would be expected, 4-amino-2-ethoxy-1,5-naphthyridine (**300**)



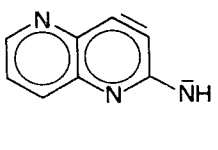
SCHEME 70

as the main product. This result is surprising if one bears in mind that both 3-bromo-2-ethoxypyridine and 3-bromo-2-ethoxyquinoline give the respective 4-amino-2-ethoxy compounds as the main products (see Sections II.A.1.b.i and II.A.1.a). Recent investigations have shown[133], however that the compound originally assigned as 3-bromo-2-ethoxy-1,5-naphthyridine was in fact the isomeric 3-bromo-1-ethyl-1,5-naphthyridin-2(1*H*)-one (**304**). Furthermore, 3-bromo-2-ethoxy-1,5-naphthyridine (**297**), prepared by an unambiguous method, gives with potassium amide a 18:82 mixture of 3- and 4-amino-2-ethoxy-1,5-naphthyridine (**299** and **300**) (Scheme 70). The formation of both aminoethoxy compounds pinpoints 3,4-didehydro-2-ethoxy-1,5-naphthyridine (**298**) as an intermediate. The ethoxy group is strongly *meta*-directing but somewhat less pronounced than in 3,4-didehydro-2-ethoxyquinoline (Section III.A.1.a).

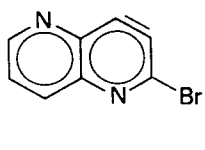
Convincing evidence has also been presented for the formation of 3,4-didehydro-1-ethyl-1,5-naphthyridin-2(1*H*)-one (**301**)[133], the anion of 2-amino-3,4-didehydro-1,5-naphthyridine (**302**)[124] and 2-bromo-3,4-didehydro-1,5-naphthyridine (**303**)[124] (Scheme 71).



(**301**)

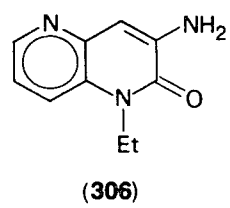


(**302**)

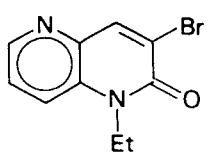


(**303**)

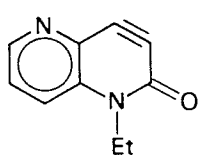
SCHEME 71



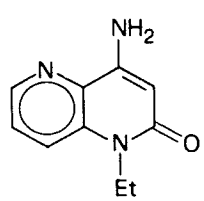
(**306**)



(**304**)



(**305**)



(**307**)

SCHEME 72

When 3-bromo-1-ethyl-1,5-naphthyridin-2(1*H*)-one (**304**) is subjected to treatment with potassium amide, a mixture of 3- and 4-amino-1-ethyl-1,5-naphthyridin-2(1*H*)-one (**306**, 13% and **307**, 58%) is obtained[133]. As intermediate species **305** has been proposed; the position of addition of the amide ion to **305** is governed by the electron-

attracting inductive effect (-I) of the carboxamido group, favouring attack of the amide ion at C-4 (Scheme 72).

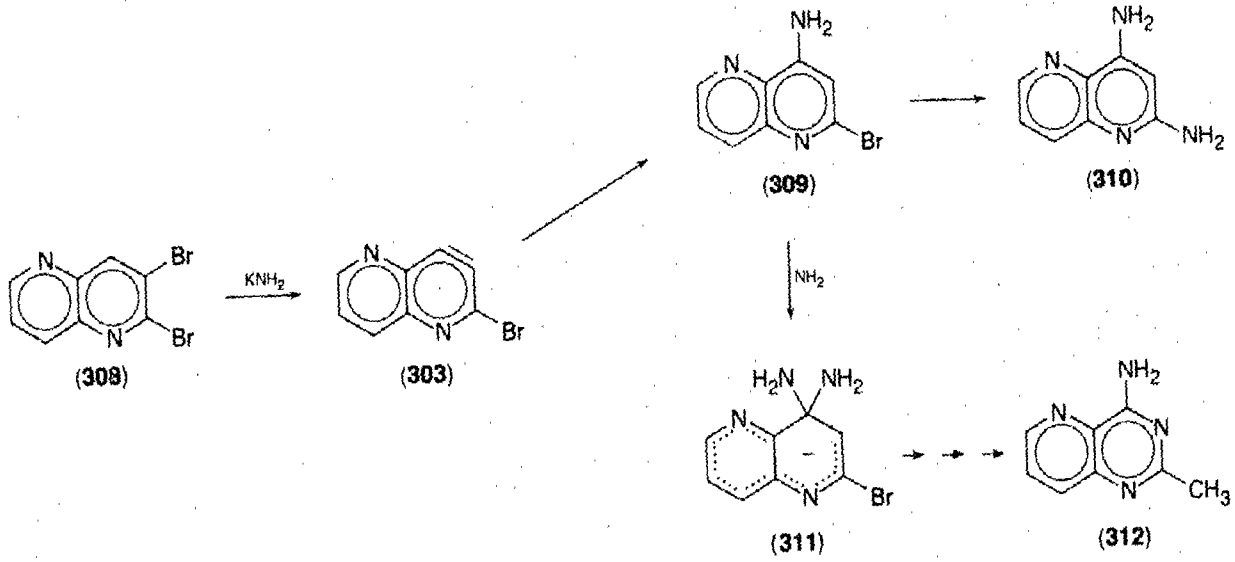
Reaction of 2-amino-3-bromo-1,5-naphthyridine with potassium amide gives 2,3-diamino-1,5-naphthyridine, the formation of which can be explained by an exclusive addition of the amide ion to C-3 of the anionic species **302**[124]. This addition pattern is very similar to the one observed for 2-amino-3,4-didehydroquinoline (**252**) (see Section III.A.1.a) and 2-amino-3,4-didehydropyridine (**88**) (see Section II.A.1.b.ii).

2-Bromo-3,4-didehydro-1,5-naphthyridine (**303**) has been proposed[124] as the intermediary species in the formation of 2,4-diamino-1,5-naphthyridine (**310**, 80%) and 4-amino-2-methyl-1,3,5-triazanaphthalene (**312**, 5–10%) from 2,3-dibromo-1,5-naphthyridine (**308**) and potassium amide (Scheme 73).

The 2,4-diamino compound **310**, as well as the triazanaphthalene **312**, have as a precursor 4-amino-2-bromo-1,5-naphthyridine (**309**) which is formed by addition of the amide ion to the 3,4-didehydro compound **303**[124]. Compound **309** reacts further to give **310** in an $S_N(AE)$ process and **312** in a process initiated by an addition of the amide ion to C-4, leading to the σ adduct **311** (for a similar ring-transformation reaction, see Scheme 63 in Section III.A.1).

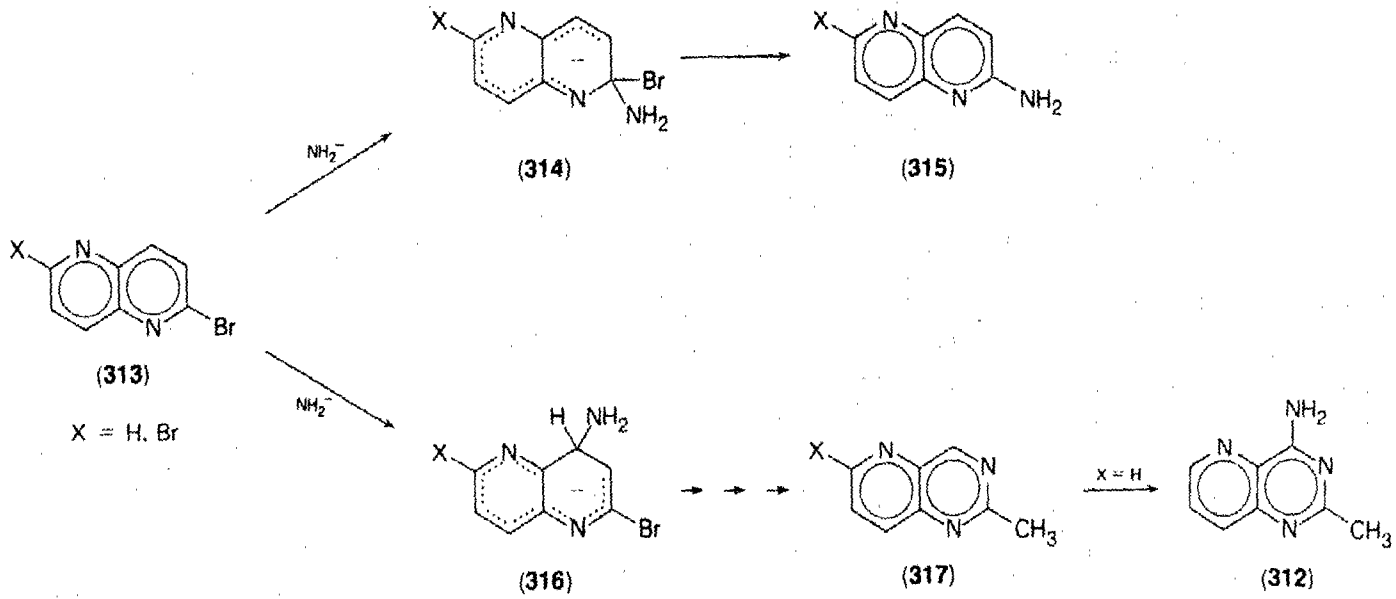
It is of interest to note that **312** has also been obtained, although in low yield, from 2-bromo-1,5-naphthyridine (**313**, X = H) (Scheme 74).[132,134]. The main product in this reaction is 2-amino-1,5-naphthyridine (**315**, X = H), formed in an $S_N(AE)$ process involving as intermediate adduct **314** (X = H). The formation of **312** is reminiscent of the conversion of 2-bromoquinoline (**244**) to 2-methylquinazoline (**249**) (Scheme 59) and it involves the formation of the C-4 adduct **316**. However, since 2-methyl-1,3,5-triazanaphthalene (**317**, X = H) is more susceptible to a nucleophilic attack than 2-methylquinazoline, it undergoes a subsequent Chichibabin amination at C-4. The amide-induced transformation of a 1,5-naphthyridine system into a 1,3,5-triazanaphthalene system has also been observed with 2,6-dibromo-1,5-naphthyridine (**313**, X = Br), 6-bromo-2-methyl-1,3,5-triazanaphthalene (**317**, X = Br) being formed[135].

(ii) Didehydro-1,6-naphthyridines. In the reaction of 3-bromo-1,6-naphthyridine (**318**) with potassium amide in liquid ammonia a mixture of 3- and 4-amino-1,6-naphthyridine (**320** and **321**) has been obtained[136] (Scheme 75). No trace of 2-amino-1,6-naphthyridine could be detected. These results indicate that in this reaction 3,4-didehydro-1,6-naphthyridine (**319**) is an intermediate. Based on the yields of the 3- and 4-amino compound, isolated by TLC, an addition ratio of NH_2^- to C-3 vs. C-4 of 73:27 was established. However, reinvestigation of the amination and direct measurement on the crude reaction mixture by ^{1}H-NMR spectroscopy has given a more accurate C-3/C-4 ratio of 44:56[21]. This addition ratio is nearly equal to the one found for amide addition to 3,4-didehydroquinoline (**232**). The similarity of the addition ratios seems to support the idea that **318** only undergoes an $S_N(EA)$ process and that an amino-debromination at C-3 [$S_N(AE)$] is not operative in the formation of the 3-amino compound **320**. The reactions of 3-chloro-, 4-chloro- and 4-bromo-1,6-naphthyridine with potassium amide also give a mixture of **320** and **321**[136]. Thus, in all three reactions **319** plays a role as an intermediate. The ratios of amino products, determined by weighing each of the amino compounds, after isolation by TLC, differ strongly. The **320**:**321** ratio is 43:57 for 4-Br, 77:23 for 3-Cl and 61:49 for 4-Cl. A more direct method for determining the ratio of the amino products, such as ^{1}H-NMR spectroscopy of the crude reaction mixture (see above), should provide us with more accurate values. Therefore it seems of interest to reinvestigate these reactions in order to establish whether this addition ratio is really independent of the nature of the halogen atom at C-3 and also to find out what is the contribution of the $S_N(AE)$ process in the amination of the 4-halogeno-1,6-naphthyridines.

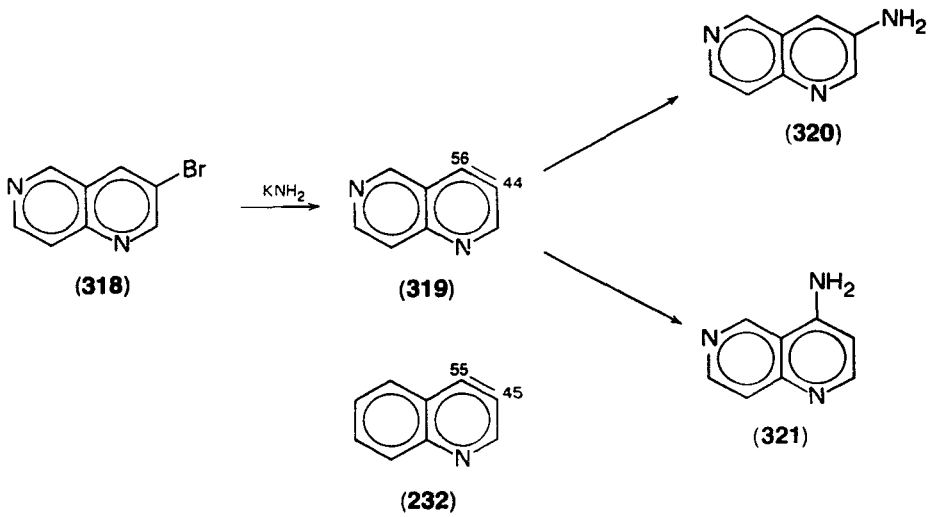


(308) (303) (309) (310) (311) (312)

SCHEME 73



SCHEME 74

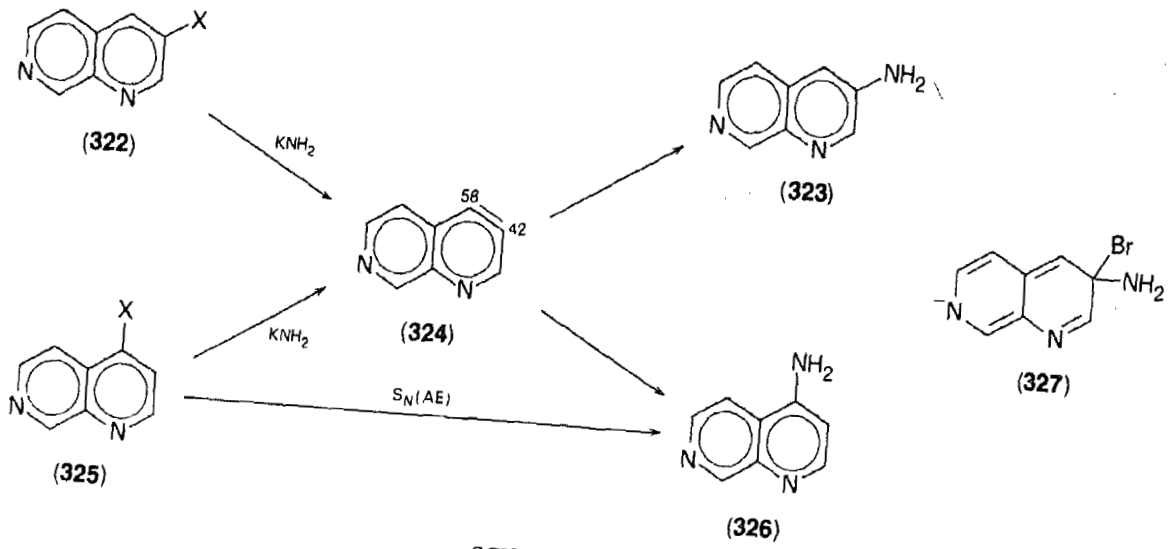


SCHEME 75

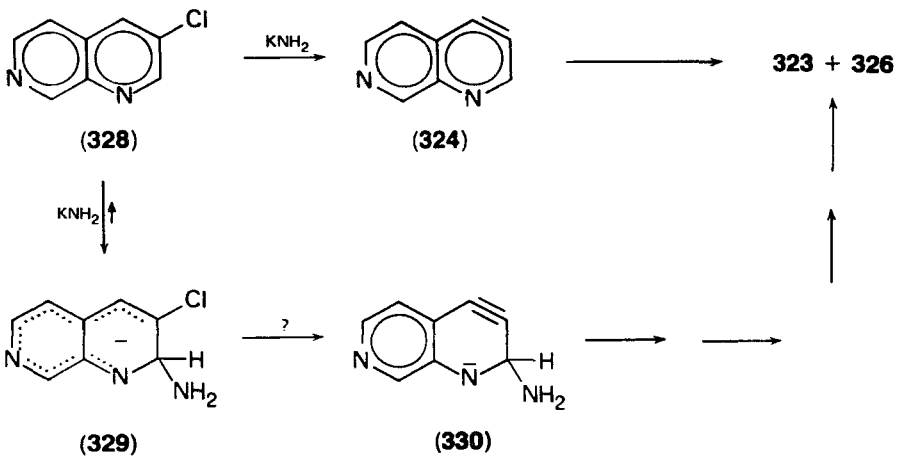
(iii) Didehydro-1,7-naphthyridines. 3- and 4-Amino-1,7-naphthyridine (**323** and **326**) are obtained from both 3-bromo- (**322**, X = Br) and 3-chloro-1,7-naphthyridine (**322**, X = Cl) on amination with potassium amide in liquid ammonia at −33°C for 4 h[137]. The rate of the amination for the bromo compound is higher than for the chloro compound, but the ratio in which the two amino compounds are formed (**323**:**326** = 42:58) is completely independent of the nature of the halogen atom. This result presents good evidence for the intermediacy of 3,4-didehydro-1,7-naphthyridine (**324**) (Scheme 76). The ratio of addition of the amide ion to C-3 and C-4 is nearly the same as the addition ratio to C-3 and C-4 in 3,4-didehydroquinoline (**232**, 45:55) and in 3,4-didehydro-1,6-naphthyridine (**319**, 44:56). Apparently, the presence of the nitrogen atom at position 7 has no influence on the addition pattern, and it seems to exclude the contribution of an addition–elimination reaction, involving the σ adduct **327** as a pathway, which was suggested for the amination at C-3[137].

On dissolving 3-chloro-1,7-naphthyridine (**328**) in liquid ammonia containing potassium amide, unambiguous ^{1}H-NMR evidence for the formation of the σ adduct 2-amino-3-chloro-1,2-dihydro-1,7-naphthyridinide (**329**) has been obtained (Scheme 77). The formation of a σ adduct at C-2 is in agreement with π-electron density calculations of 1,7-naphthyridine which show that position 2 has the lowest electron density (C-6 > C-4 > C-3 > C-2) and is the most reactive position towards nucleophiles[138]. Apparently, the σ adduct formation at C-2 precedes the formation of the 3,4-didehydro compound **324**. This interesting ^{1}H-NMR result raises the question as to whether the amino compounds **323** and **326** are formed by dehydrochlorination of the σ adduct **329** to 2-amino-1,2-dihydro-3,4-didehydro-1,7-naphthyridinide (**330**), which is followed by an amide addition to C-3 and C-4, or directly from **324** (Scheme 77).

When reacting 4-*X*-1,7-naphthyridine (**325**; X = Cl, Br) with potassium amide in liquid ammonia at −33°C for 4 h, a mixture of **323** and **326** has also been obtained[139]. This result justifies the conclusion that **325** (X = Cl, Br) is aminated according to an S_N(EA) process, involving **324** as an intermediate (Scheme 76). However, the ratio in which both amino compounds are formed is strongly dependent on the nature of the halogen atom at position 4: for X = 4-Cl, the **323**:**326** ratio is 22:78 and for X = 4-Br,


X
N
N
(322)
KNH2
58
42
N
N
(324)
NH2
N
N
(323)
Br
NH2
N
N
(327)
X
N
N
(325)
KNH2
SN(AE)
NH2
N
N
(326)

SCHEME 76



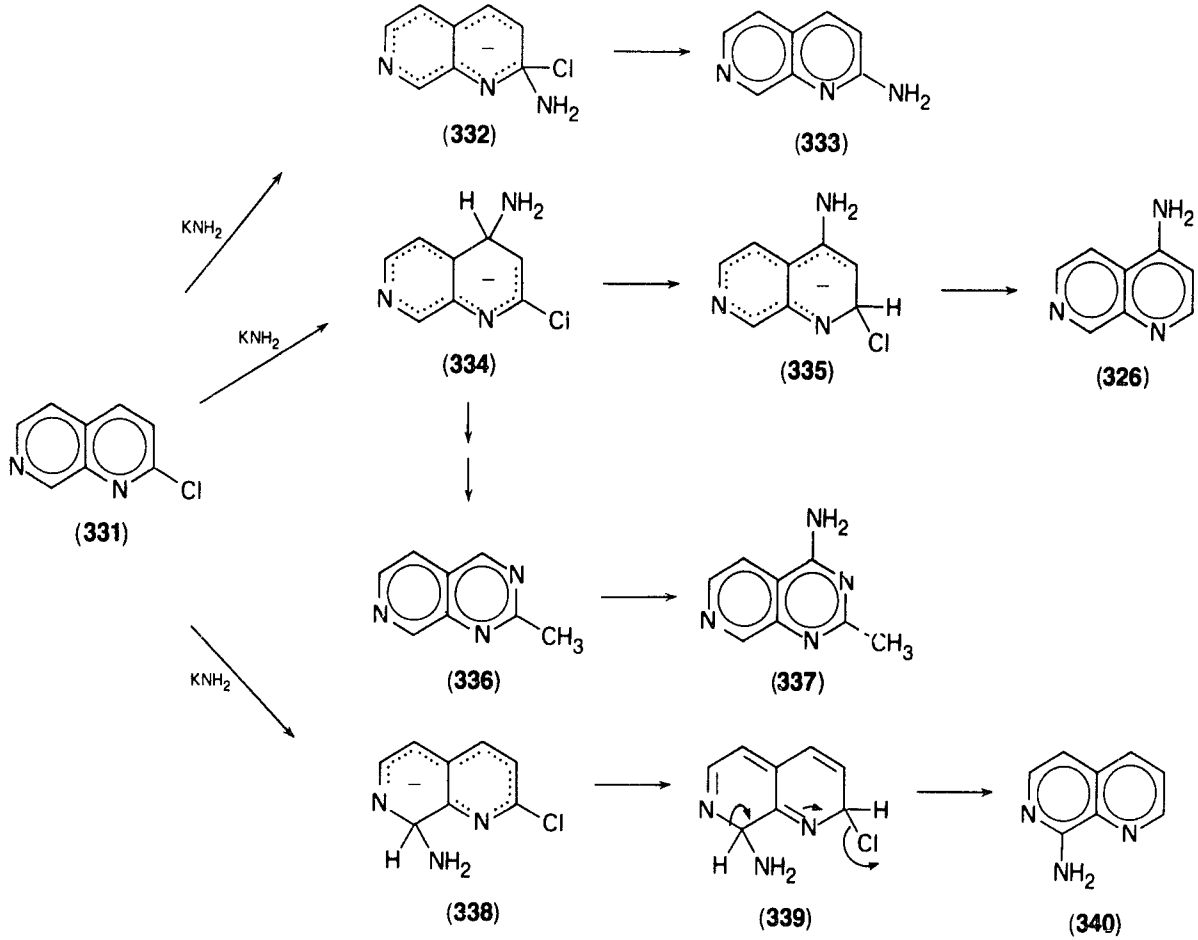
SCHEME 77

the ratio is 35:65. Since these addition ratios are different from the 42:58 ratio observed in the reaction of **322** (X = Br), it is evident that the addition–elimination process [S_N(AE)] is also operative in the amination of **325** (X = Cl, Br). Based on the data obtained it has been calculated that 20–30% of **325** (X = Br) reacts according to this S_N(AE) process.

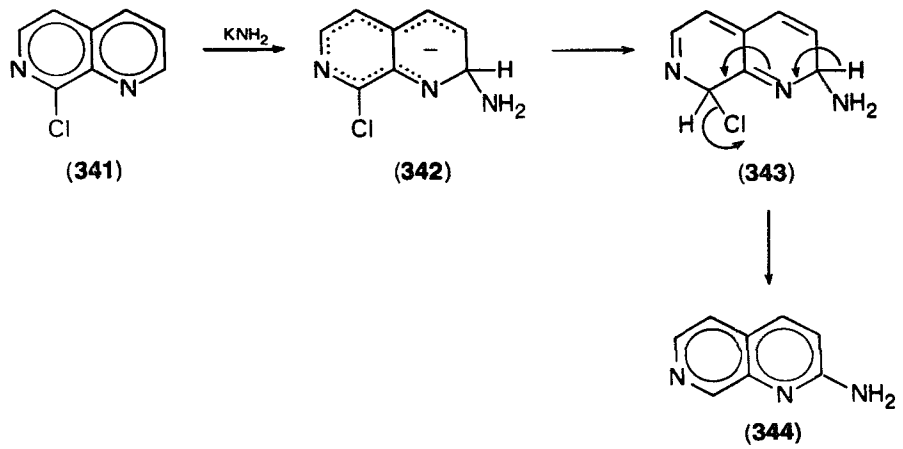
Reaction of 2-chloro-1,7-naphthyridine (**331**) with potassium amide gives 2-amino-1,7-naphthyridine (**333**) [S_N(AE)], two *tele* substitution products 4- and 8-amino-1,7-naphthyridine (**326** and **340**) [S_N(AE)^{tele}] and a ring-transformation product 2-methyl-4-amino-1,3,7-triazanaphthalene (**337**)[140]. The ring-transformation takes place by the same mechanisms as proposed for the corresponding conversion of 2-bromoquinoline to 2-methylquinazoline (Section III.A.1a) and of 2-bromo-1,5-naphthyridine to 4-amino-2-methyl-1,3,5-triazanaphthalene (Section III.A.1.c.i), and involves the C-4 adduct **334** and 2-methyl-1,3,7-triazanaphthalene (**336**). The mechanisms for the different conversions are summarized in Scheme 78. It shows that **331** does not undergo a dehydrochlorination to a didehydro compound but is more inclined to addition of the amide ion at C-2, C-4 and C-8, yielding the σ adducts **332**, **334** and **338**, respectively. ^{1}H-NMR spectroscopy of a solution of **331** and its 8-deutero and 6,8-dideutero derivatives in potassium amide in liquid ammonia supports unequivocally the formation of both adducts **334** and **338**. The formation of both *tele* amination products **326** and **340** can easily be explained by a prototropic rearrangement of **334** into **335** and of **338** into **339**.

Treatment of 8-chloro-1,7-naphthyridine (**341**) with potassium amide gives, besides the unrearranged 8-amino-1,7-naphthyridine [S_N(AE)], the *tele* amination product 2-amino-1,7-naphthyridine **344**)[20]. The compound is formed via the anionic σ adduct **342**, whose existence has been proven by ^{1}H-NMR spectroscopy. This adduct undergoes a protonation at C-8 yielding the 2-amino-8-chloro-2,8-dihydro-1,7-naphthyridine (**343**) from which the 2-amino compound **344** is obtained by a base-catalysed 1,4-*tele* dehydrochlorination (Scheme 79).

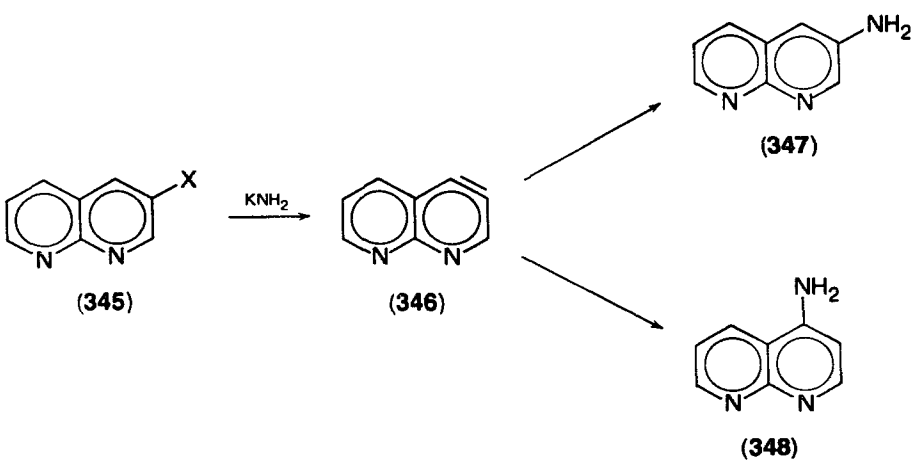
(iv) Didehydro-1,8-naphthyridines. Evidence has been presented for the occurrence of 3,4-didehydro-1,8-naphthyridine (**346**) in the reaction of 3-bromo- (**345**, X = Br) and 3-chloro-1,8-naphthyridine (**345**, X = Cl) with potassium amide in liquid ammonia[21]. In both reactions a mixture of 3- and 4-amino-1,8-naphthyridine (**347** and **348**) has been obtained (Scheme 80). The ratio of **347** and **348**, determined by



SCHEME 78



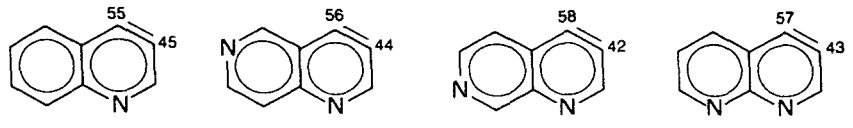
SCHEME 79



SCHEME 80

quantitative ^{1}H-NMR spectroscopy, is 43:57 when **345** (X = Br) is used as a starting material and 33:66 starting from **345** (X = Cl). Since in the reaction with **345** (X = Br) much higher yields of the amino compounds are obtained than with **345** (X = Cl) and the amination of **345** (X = Cl) yields many highly coloured and tarry substances, the ratio of **347** to **348** obtained from **345** (X = Br) is considered as a more reliable one. It is of interest to note that this ratio is nearly the same as the addition ratio to C-3 and C-4 in 3,4-didehydroquinoline (**232**)[122], 3,4-didehydro-1,6-naphthyridine (**319**)[21] and 3,4-didehydro-1,7-naphthyridine (**324**)[137]. It proves that the presence of nitrogen at positions 6, 7 and 8 of the 1,*X*-naphthyridines, i.e. in those positions of the ring being annellated to the didehydropyridine ring, hardly influences the addition ratio (Scheme 81).

Amination of 4-bromo- and 4-chloro-1,8-naphthyridine also affords a ca. 30:70

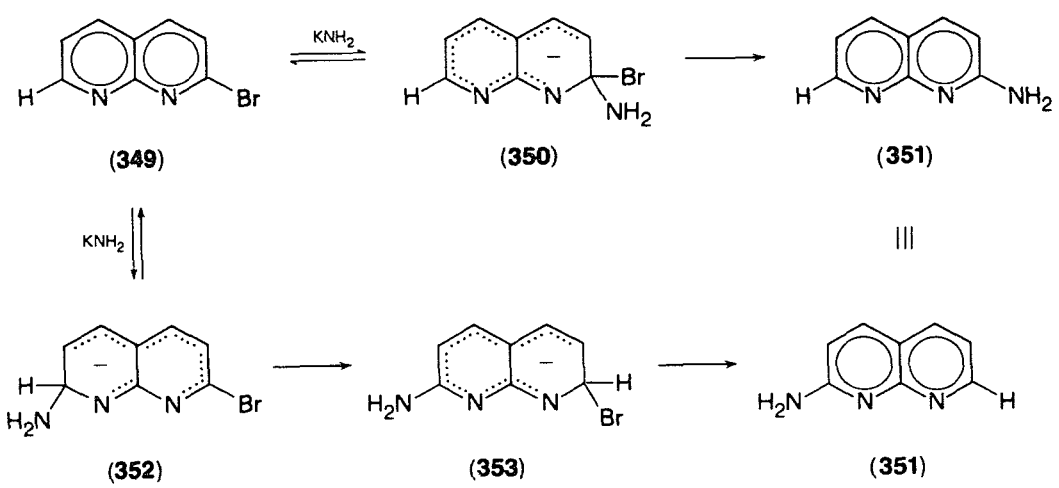


(232) (319) (324) (346)

SCHEME 81

mixture of **347** and **348** as determined by ^{1}H-NMR spectroscopy[21]. This ratio is different from that found in the amination of **345** (X = Br) (43:57) and indicates that besides **346** an aminodebromination has taken place at C-4 [S_N(AE)]. It has been calculated that about 40% of 4-bromo-1,8-naphthyridine reacts according to this process and 60% according to the S_N(EA) mechanism.

Amination of 2-bromo-1,8-naphthyridine (**349**) with potassium amide gives exclusively 2-amino-1,8-naphthyridine (**351**), although in low yield[21]. A ^{1}H-NMR spectrum of the 2-bromo compound **349** in liquid ammonia, containing potassium amide, unequivocally showed the presence of the 1:1 σ adduct **352**, raising the interesting question as to whether **351** is formed by an S_N(AE) process starting by formation of adduct **350** or by an S_N(AE)^{tele} reaction involving the initial adduct **352** which forms **353**, by a prototropic rearrangement (Scheme 82). By use of 2-bromo-7-deutero-1,8-naphthyridine it can be established[21] that the formation of 2-amino-1,8-naphthyridine involves *both* adducts **350** and **352**. By measuring the deuterium content in the starting substance, and in the unreacted 2-bromo-1,8-naphthyridine recovered after the amination, as well as in the 2-amino-1,8-naphthyridine, a decrease of deuterium content in the 2-amino compound is found. It can be calculated that about 27% of the 2-bromo-1,8-naphthyridine reacts according to the *tele* substitution [S_N(AE)^{tele}]. Using a similar method, the amination of 2-chloro-8-deutero-1,8-naphthyridine is found to proceed for only 8% according to the S_N(AE)^{tele} process[20,21].



(349) (350) (351)

(352) (353) (351)

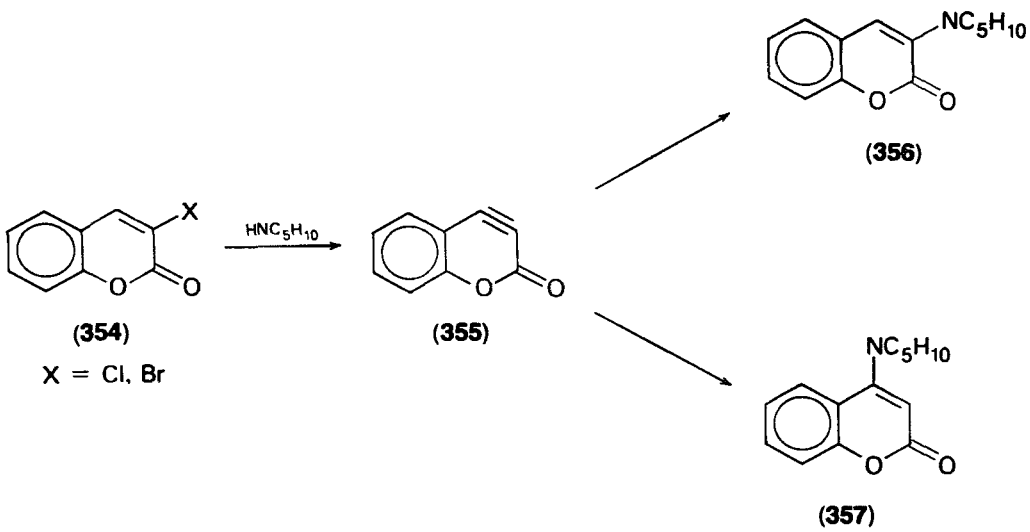
SCHEME 82

B. Bicyclic Six-membered Didehydroheteroarenes Containing One Oxygen Atom

1. *Didehydrocoumarins*

There is only one six-membered didehydroheteroarene containing an oxygen atom in the ring, reported in the literature, i.e. 3,4-didehydrocoumarin (**355**).

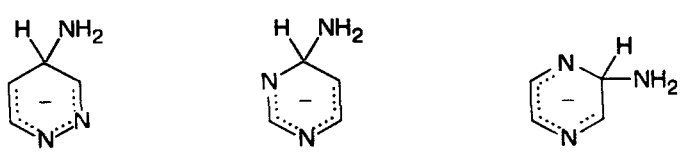
Reactions of 3-chloro- (**354**, X = Cl) and 3-bromo-coumarin (**354**, X = Br) with piperidine give mixtures of 3- and 4-piperidinocoumarins (**356** and **357**) in ratios of 39:61 and 30:70, respectively (Scheme 83). 4-Chloro- and 4-bromo-coumarins only yield the corresponding 4-piperidino compounds. In the presence of proton donors such as methanol and aniline **354** (X = Cl, Br) gives a higher yield of **356**, together with 4-methoxy- or 4-anilino-coumarin[141–143]. From these results it has been concluded that compounds **354** react according to an $S_N(EA)$ process and the 4-halogenocoumarins probably react according to the $S_N(AE)$ mechanism.



SCHEME 83

IV. MONOCYCLIC SIX-MEMBERED DIDEHYDRODIAZAHETEROARENES

It has been established that in contrast to pyridine the parent diazines easily undergo addition with potassium amide. In liquid ammonia containing potassium amide, pyridazine, pyrimidine and pyrazine give 1:1 σ adducts, i.e. the 4-amino-1,4-dihydropyridazinide (**358**), the 4-amino-1(3),4-dihydropyrimidinide (**359**) and the 2-amino-1,2-dihydropyrazinide (**360**) respectively (Scheme 84)[144,145].



SCHEME 84

The easy accessibility of the parent diazines for addition by the amide ion has also been found with halogenodiazines[146–152]. This means that one has to reckon with the fact that halogenodiazines, when treated with potassium amide, can undergo besides dehydrohalogenation to a didehydrodiazine, reactions which are initiated by an addition step. In many cases these reactions were found to be the sole reaction pathways.

A. Didehydropyridazines

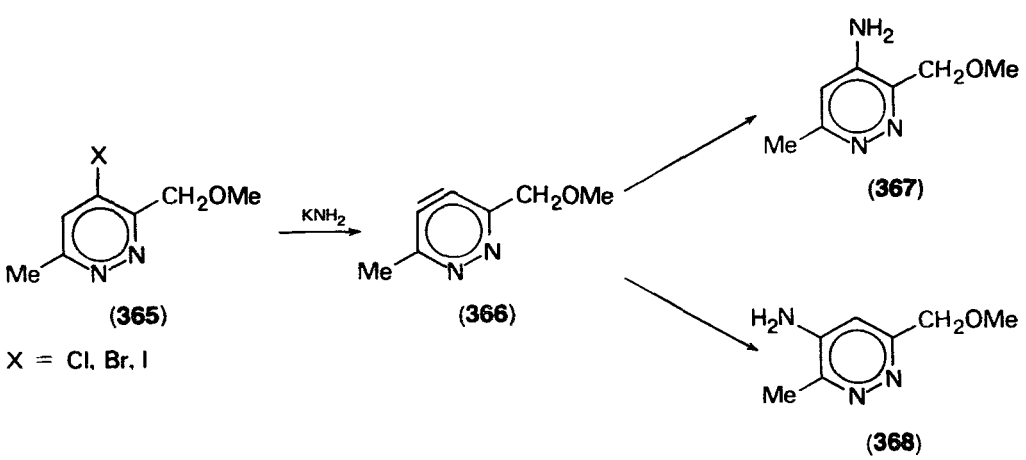
Extended Hückel calculations on the stability of the four possible didehydropyridazines result in the following stability order **361** > **362** > **363** > **364** (Scheme 85). This order shows that of the two possible *o*-didehydropyridazines

(361) **(362)** **(363)** **(364)**

−507.55 eV −506.83 eV −506.74 eV −506.63 eV

SCHEME 85

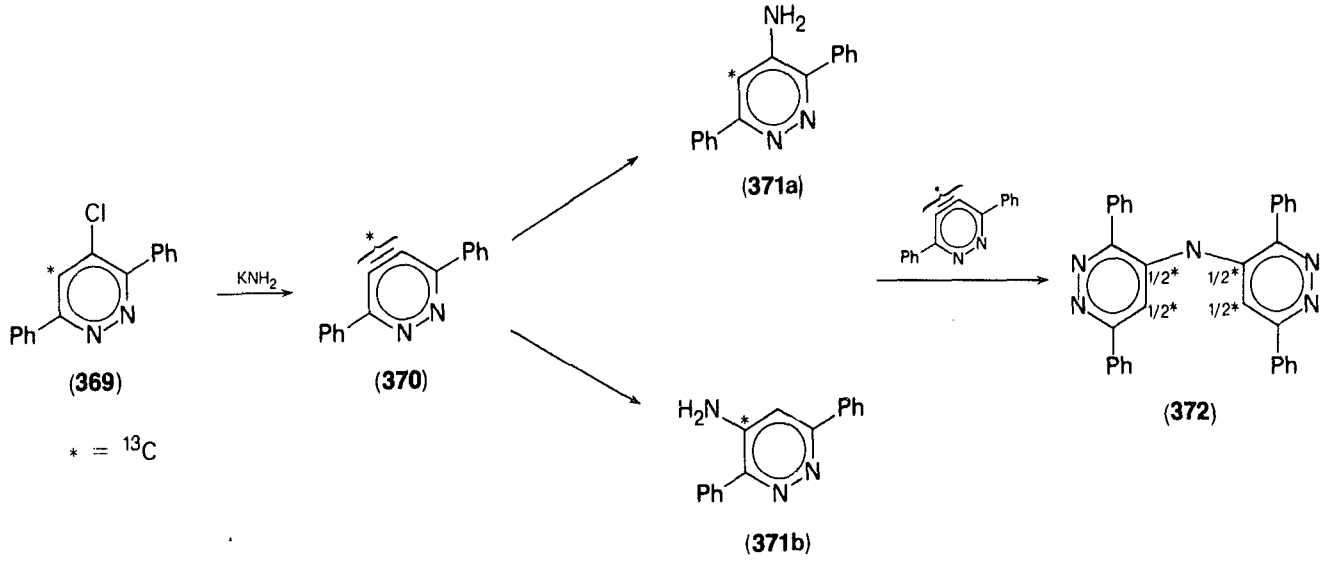
3,4-didehydropyridazine (**363**) is 0.81 eV less stable than 4,5-didehydropyridazine (**361**); this is due to the dominant effect of the nitrogen lone-pair destabilization (see Introduction). Even the *m*-didehydropyridazine, i.e. 3,5-didehydropyridazine (**362**) is more stable than **363**. So far there is no evidence for any of these parent didehydropyridazines. There is, however, good evidence for the occurrence of 4,5-didehydropyridazine *derivatives* as intermediate species in the reactions of 4-halogenopyridazines with potassium amide. Reaction of 4-*X*-3-(methoxymethyl)-6-methylpyridazine (**365**; X = Cl, Br, I) with potassium amide in liquid ammonia gives a mixture of 4- and 5-amino-3-(methoxymethyl)-6-methylpyridazine (**367** and **368**) in



(365) **(366)** **(367)** **(368)**

X = Cl, Br, I

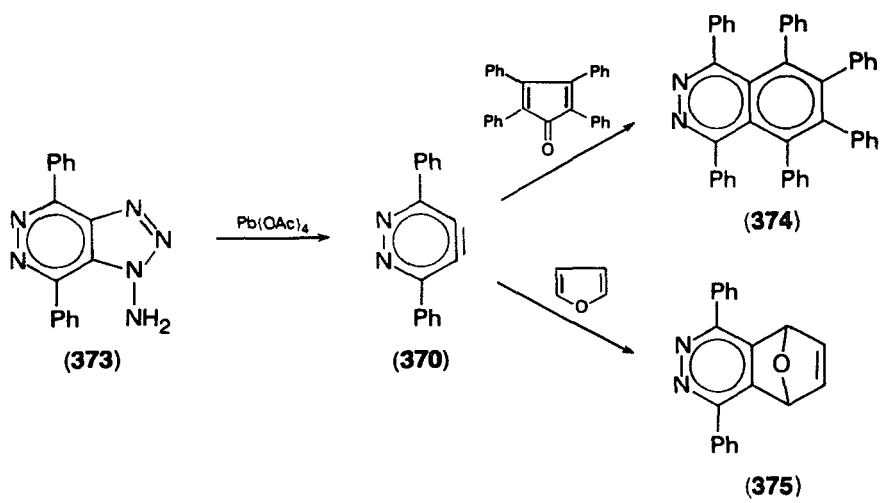
SCHEME 86



SCHEME 87

a 16:84 ratio[153]. This ratio is found to be fully *independent* of the nature of the halogen atom. These results provide good evidence for the occurrence of 3-(methoxymethyl)-6-methyl-4,5-didehydropyridazine (**366**) as intermediate (Scheme 86). The higher electron-attracting character of the methoxymethyl group compared with that of the methyl group explains the favoured addition of the amide ion at position 5. An interesting piece of research, proving unambiguously the intermediary existence of 3,6-diphenyl-4,5-didehydropyridazine (**370**), is the study of the amination of 4-chloro-3,6-diphenylpyridazine [5-^{13}C] (**369**) with potassium amide[154]. It gives 4-amino-3,6-diphenylpyridazine [(4,5)-^{13}C] (**371a**) and (**371b**) and imino-4,4′-bis(3,6-diphenylpyridazine) [(4,4′), (5,5′)-^{13}C] (**372**) (Scheme 87). By quantitative ^{13}C-NMR spectroscopy it has been established that the distribution of the ^{13}C-label over positions 4 and 5 in the 4-amino compound (**371**) and over positions 4,4′ and 5,5′ in the product **372** is exactly 1:1. The simultaneous occurrence of an $S_N(AE)$ and $S_N(AE)^{cine}$ process, both of which should then contribute exactly 50% to the overall reaction, can be excluded; therefore it seems fully justified to propose **370** as an intermediate in this amination.

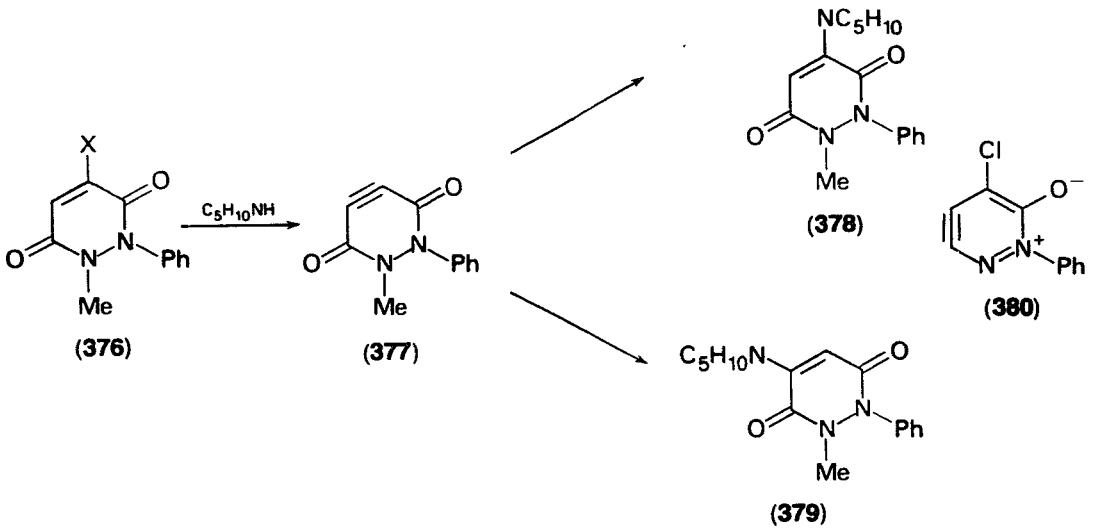
The reactive intermediate **370** has also been obtained on oxidation of 1-amino-4,7-diphenyltriazolo[4,5-*d*]pyridazine (**373**) with lead tetraacetate[155]. The occurrence of **370** has been proven by interception with tetracyclone, which yields after CO evolution 1,4,5,6,7,8-hexaphenylphthalazine (**374**), or with furan, which gives 5,8-epoxy-5,8-dihydro-1,4-diphenylphthalazine (**375**) (Scheme 88).



SCHEME 88

1-Methyl-2-phenyl-4,5-didehydropyridazine-3,6-dione (**377**) has been proposed as intermediate in the reaction of 1-methyl-2-phenyl-4-*X*-pyridazine-3,6-dione (**376**; X = Cl, Br) with piperidine. An isomeric mixture of the 4- and 5-piperidino-1-methyl-2-phenylpyridazine-3,6-dione (**378** and **379**) of about the same 15:85 composition is obtained (Scheme 89)[156]. Addition of ethanol surpresses the reaction and the amount of the 4-piperidino compound **378** is found to increase.

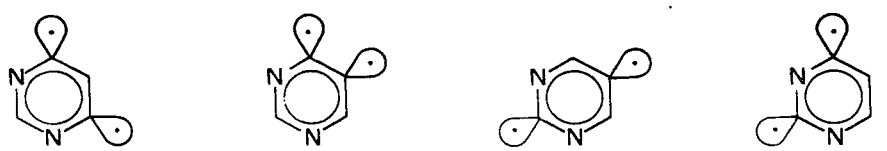
The suggestion has also been made[157] that the zwitterionic 3,4-didehydropyridazine derivative **380** is one of the intermediates in the base-catalysed ring-contraction of 4,5-dichloro-2-phenyl-3(2*H*)-pyridazinone to 3-hydroxy-1-phenylpyrazole-5-carboxylic acid. Evidence for the intermediary existence of **380** is poor and its occurrence seems highly speculative.



SCHEME 89

B. Didehydropyrimidines

EHT calculations on the electronic structures of the four possible didehydropyrimidines, show[7] the following order of decreasing stability: **381** > **382** > **383** > **384**. It appears that the *meta* didehydro species 4,6-didehydropyrimidine (**381**) is the most stable in this series (Scheme 90).

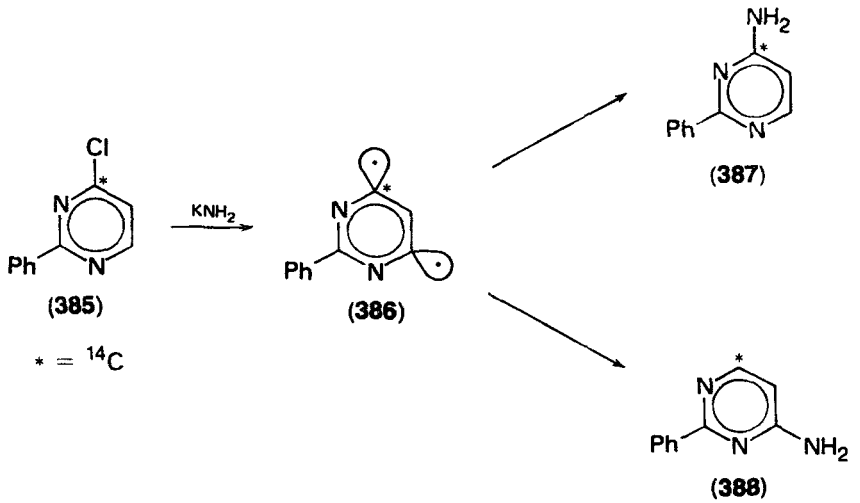


(**381**) −508.10 eV (**382**) −507.87 eV (**383**) −507.39 eV (**384**) −507.05 eV

SCHEME 90

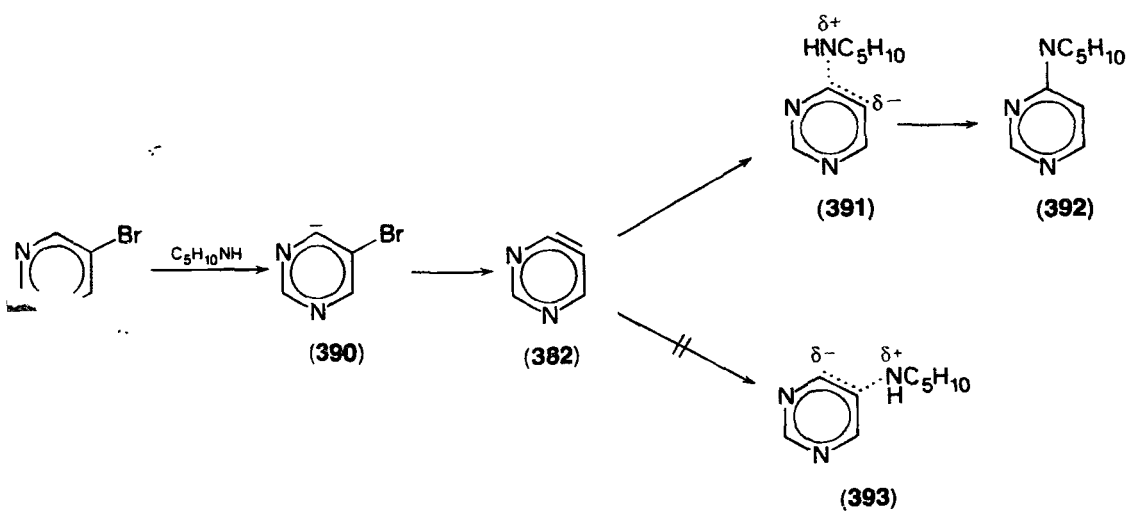
So far there is no evidence available for the occurrence of **381** as intermediate in the reactions of 4- and 5-halogenopyrimidine with bases. An attempt to prove the intermediary existence of 2-phenyl-4,6-didehydropyrimidine (**386**) was made by studying the amination of 4-chloro-2-phenylpyrimidine-[4-^{14}C](**385**) with potassium amide[158]. If **386** were an intermediate, it would lead to a 1:1 mixture of 4-amino-2-phenylpyrimidine-[4-^{14}C] (**387**) and 6-amino-2-phenylpyrimidine-[4-^{14}C] (**388**). It was found that only **387** is formed, excluding the intermediacy of **386** (Scheme 91).

The intermediacy of 4,5-didehydropyrimidine (**382**) has been suggested in the reaction of 5-bromopyrimidine (**389**) with piperidine at about 100°C[159]. 4-Piperidinopyrimidine (**392**) is formed, and its formation has been explained by an exclusive nucleophilic attack at position 4 of **382**, since transition state **391** is more favoured than **393**. The orientational effect is in agreement with (*i*) calculations on total electron densities[7] (q) in positions 4 and 5 of **382** which predict that $q(4)$ is lower than



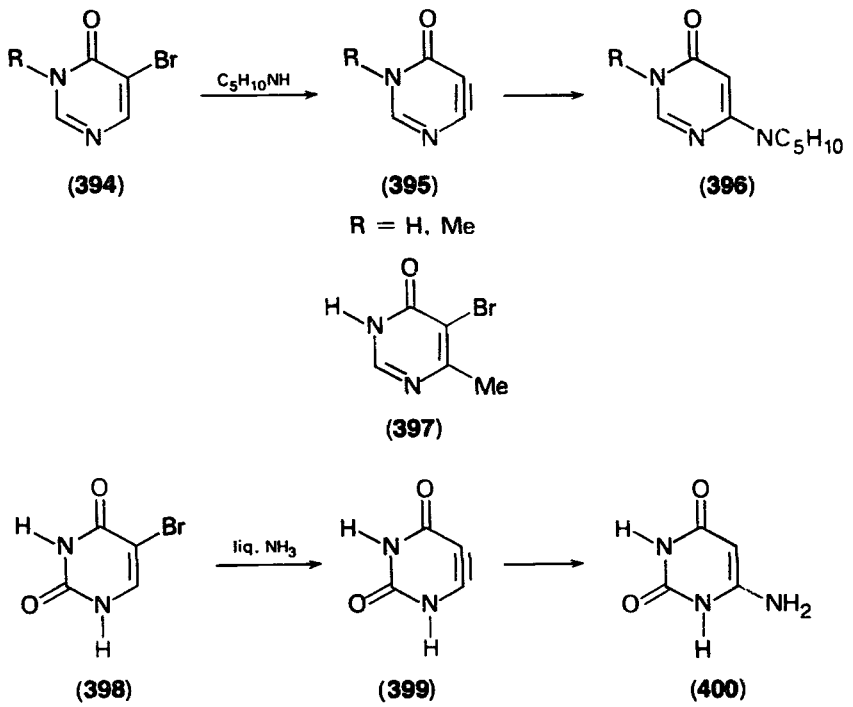
SCHEME 91

$q(5)$ and (*ii*) calculations on total energies[7] which predict that the pyrimidinyl 4-anion is less stable than the pyrimidinyl 5-anion (Scheme 92). Support for the formation of **382** as intermediate in this reaction comes from the fact that when **389** is reacted with piperidine in the presence of proton donors such as aniline or ethanol the amination is surpressed[159]. The carbanion **390**, which is the precursor of **382**, is then reprotonated, preventing or retarding the didehydro derivative formation (Scheme 92). The stronger base system lithium piperidide/piperidine is not able to convert **389** to the 4-piperidino compound **392**. It has been assumed[159] that the precursor of **382**, i.e. 4-lithio-5-bromopyrimidine, is very stable under the applied conditions and does not decompose into **382**. However, when 5-bromo-4(6)-deutero-pyrimidine is treated with lithium piperidide/piperidine it does not undergo a D/H



SCHEME 92

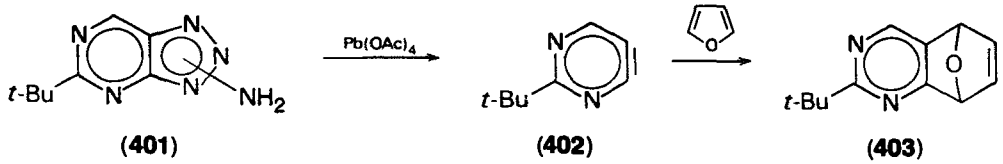
exchange, suggesting that 4-lithio-5-bromopyrimidine cannot be formed under these conditions[160]. Similar results are obtained in the reaction of **389** with diethylamine[159]. More experimental data are necessary to establish more firmly the intermediacy of **382** in these reactions. Reaction of 5-bromopyrimid-4-one (**394**, R = H) with piperidine gives the 6-piperidinopyrimid-4-one (**396**, R = H)[161]. The isomeric 5-piperidino compound is not detected in the reaction mixture. The same results are obtained with the 3-methyl derivative (**394**, R = Me). The 5-bromo-6-methylpyrimid-4-one (**397**) is found to be completely inert under the same experimental conditions. These results have been presented as good evidence that the conversion of **394** to **396** proceeds via 5,6-didehydropyrimid-4-one (**395**) (Scheme 93)[161]. Similarly, reaction of 5-bromouracil (**398**) with liquid ammonia at 180°C gives partially 6-aminouracil (**400**); the intermediacy of the didehydrouracil **399** is proposed (Scheme 93)[162]. Some support for this proposal comes from the fact that addition of ethanol to the reaction mixture promotes the formation of the unrearranged 5-aminouracil.



SCHEME 93

Convincing evidence for the existence of 2-*t*-butyl-4,5-didehydropyrimidine (**402**) has been reported in the oxidation of the *N*-aminotriazolopyrimidine (**401**) with lead tetraacetate: in the presence of furan the 5,8-endoxide-5,8-dihydro-2-*t*-butylquinazoline (**403**) can be isolated (Scheme 94)[163]. Attempts to generate 2-phenyl-4,5-didehydropyrimidine by heating 5-amino-2-phenylpyrimidinecarboxylic acid with *n*-amyl nitrite failed, since in the presence of a large excess of furan 5-(2-furyl)-2-phenylpyrimidine and not the 5,8-endoxide of 5,8-dihydro-2-phenylquinazoline was isolated[161].

The study of the amination of 5- and 6-bromopyrimidines with potassium amide will

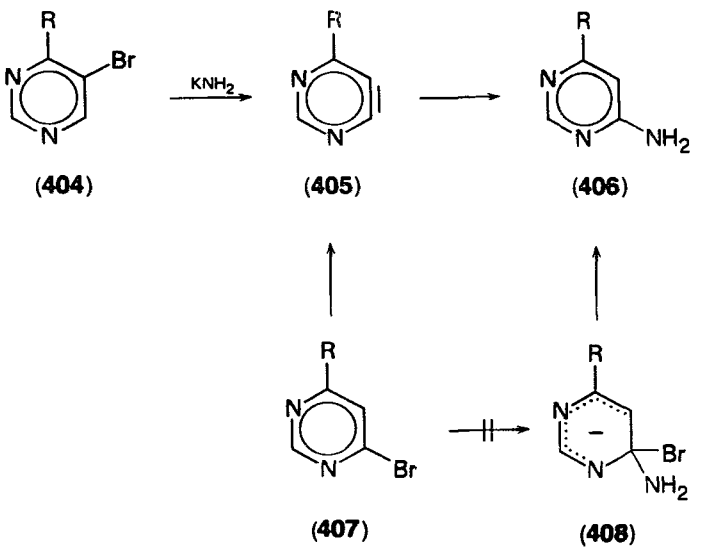


(401) (402) (403)

SCHEME 94

be described in somewhat more detail, since these studies show how the original mechanistic concept of a 4,5-didehydropyrimidine as intermediary species in these reactions has had to be abandoned and replaced by a new mechanism, the S_N(ANRORC) mechanism.

Reaction of the 5-bromo-4-*R*-pyrimidines (**404**, R = *t*-Bu, Ph, Me, OMe, OH or NH_2) with potassium amide in liquid ammonia at −33°C gives the 6-amino-4-*R*-pyrimidine (**406**) in reasonable yields[164,165]. Only in the reaction of 5-bromo-4-*t*-butylpyrimidine (**404**, R = *t*-Bu) can a very small amount of 5-amino-4-*t*-butylpyrimidine be detected by GLC. 5,6-Didehydro-4-*R*-pyrimidines (**405**) which undergo addition of the nucleophile only to the carbon atom adjacent to



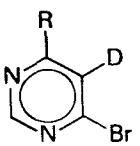
(404) (405) (406)

(407) (408)

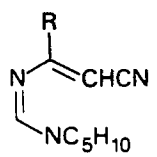
SCHEME 95

the nitrogen, i.e. to C-6, were proposed as intermediates in these *cine* substitutions (Scheme 95). The amination of the 6-bromo-4-*R*-pyrimidines (**407**; R = *t*-Bu, Ph) was found to give exclusively the 6-amino compounds (**406**) in fast reactions at −75°C[14a,b,166]. Although an S_N(AE) process via the σ intermediate **408** seemed to be a reasonable pathway, an alternative S_N(EA) process via **405** could not be definitely excluded. The hydrogen at C-5 in **407** is more acidic than the hydrogen at C-6 in **404** as shown by H/D exchange studies in pyrimidine (relative rate of exchange H(1):H(4,6):H(5) = 1:3.2:48)[167]. Reactions of 5-deuteropyrimidine (**409**, R = *t*-Bu) with potassium amide in liquid ammonia, gave the 6-amino product, which did *not* contain deuterium. Since under these reaction conditions **409** only gave little D/H exchange and 6-amino-5-deutero-4-*t*-butylpyrimidine no D/H exchange at all (Scheme

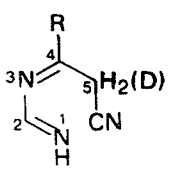
96) the conclusion seemed justified that the 5,6-didehydropyrimidine **405** is an intermediate in the conversion of **407**. This was a surprising result, inasmuch as a halogen atom at position 6 of the pyrimidine ring is usually reactive in an $S_N(AE)$ process. In an extension of the study of the amination of 6-bromopyrimidines with other strong bases, the reaction of **407** (R = *t*-Bu, Ph) with lithium piperidide in piperidine/ether was investigated[168]. It gave a mixture from which surprisingly no trace of a 6-piperidino-4-*R*-pyrimidine could be isolated but instead a 2-aza-4-cyano-1-piperidino-3-*R*-1,3-butadiene (**410**), which, in the case of R = Ph, was proved to be a *Z*/*E* mixture. Thus, no replacement of the bromine atom had taken place in the usual manner. Instead, the lithium piperidide had attacked position 2 of



(409)



(410)



(411)

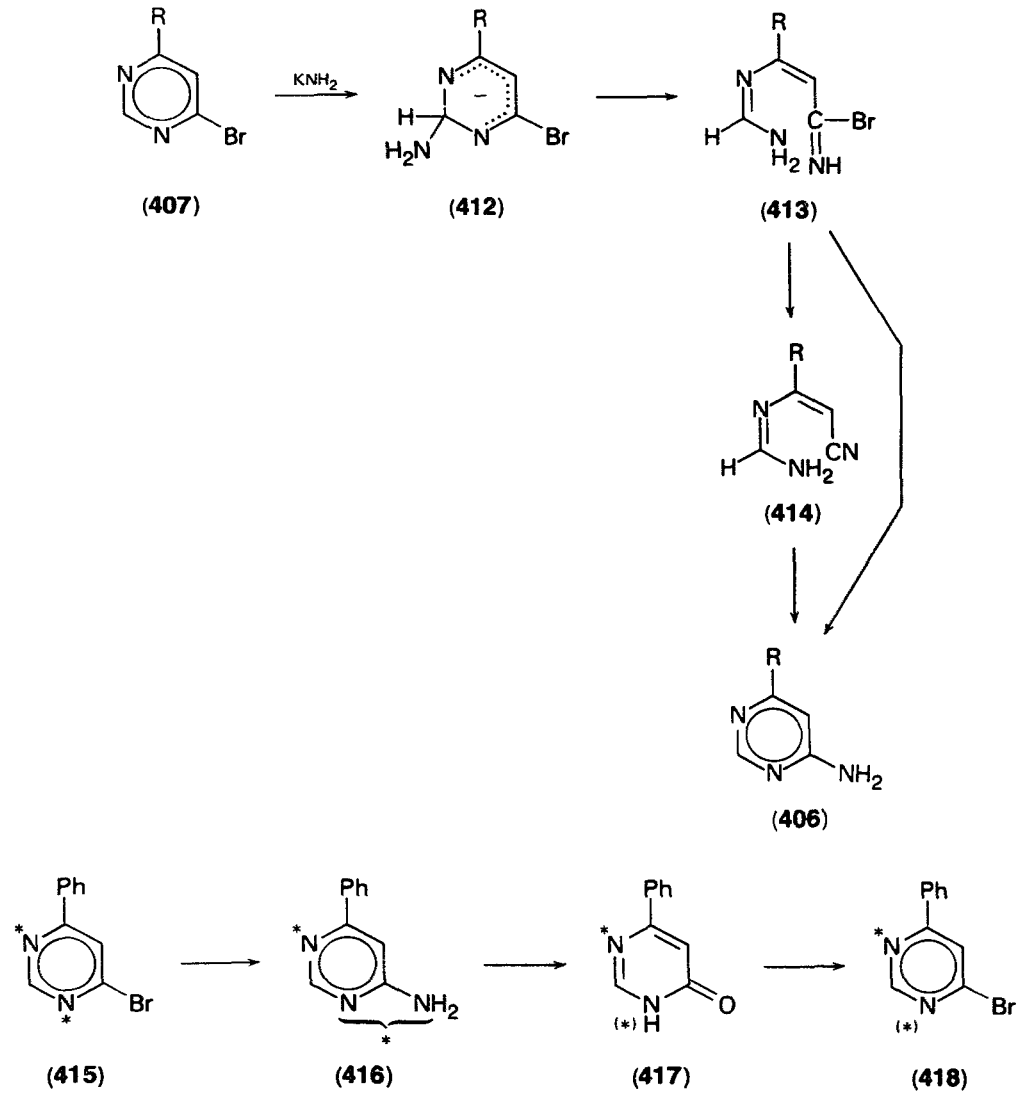
SCHEME 96

the pyrimidine ring, followed by ring-opening with loss of bromide ion. Since it seemed inconsistent that potassium amide should react with **407** by an initial deprotonation at C-5 followed by elimination of a bromide ion, and lithium piperidide by addition at C-2, the question was asked as to whether in the reaction with potassium amide an initial attack at C-2 would also occur. This would form σ complex **412** from which, after ring-opening by fission of the N-1 and C-2 bond, the highly reactive imidoyl bromide **413** would be formed. This imidoyl bromide might easily cyclize to the 6-amino compound **406** or lose hydrogen bromide in an exceedingly rapid step yielding the aminocyano compound **414** which might also undergo ring-closure to **406** (Scheme 97).

In order to prove whether this hypothesis was correct the reaction was conducted with monolabelled 6-bromo-4-phenyl[1(3)-^{15}N]pyrimidine (**415**) containing 6.0% of ^{15}N excess scrambled over both nitrogen atoms[14a,b]. It was found that in the 6-amino compound **416** also 6.0% of ^{15}N excess was present. Treatment of **416** with acid gave 4-phenylpyrimidin-6-one (**417**), which was converted to **418** by treatment with phosphoryl bromide. In **418** 3.5% of ^{15}N excess was found to be present, indicating that in **416** the exocyclic nitrogen contained 2.5% excess of ^{15}N. Since under these conditions no ring-nitrogen–exocyclic-nitrogen exchange occurred in the 6-amino compound, it means that in the 'simple' amino debromination of **407** (R = Ph) 2.5/3.0 = 83% of the 6-bromo compound reacted via a series of steps, involving an *A*ddition of the *N*ucleophile, *R*ing *O*pening and *R*ing *C*losure [S_N(ANRORC) mechanism].

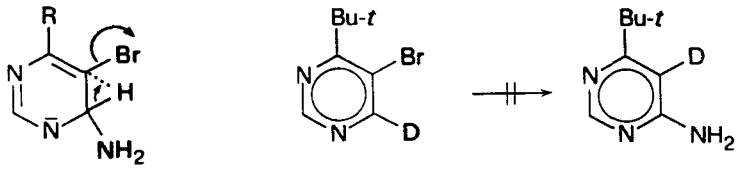
The loss of deuterium in the amination of **407** can be also explained by this mechanism. No D/H exchange has been found to take place in the starting material or product, therefore the fast D/H exchange can only take place in a reaction intermediate. The open-chain compound **414** – which is in tautomeric equilibrium with **411** – is the appropriate intermediate for exchange at C-5 under these basic conditions.

The discovery of the S_N(ANRORC) mechanism as an important pathway for the aminodebromination of 6-bromopyrimidines induced a reinvestigation of the *cine* amination of the 4-*R*-5-bromopyrimidines (**404**). It was found that measurements of ^{1}H-NMR spectra of solutions of **404** in liquid ammonia containing potassium amide, as well as the use of ^{15}N-labelled pyrimidines, gave new insights into the course of the



SCHEME 97

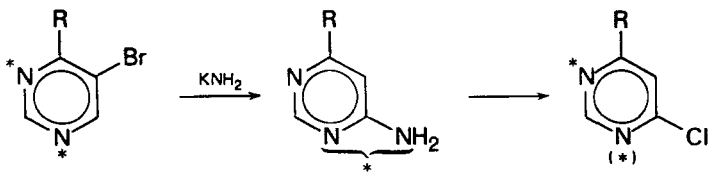
cine amination. It was observed that ^{1}H-NMR spectra of solutions of **404** (R = *t*-Bu, Ph, C_6H_5(Me)N, OMe, Me) in ammonia containing 2 equivalents of potassium amide which were measured after 5–10 min gave no signals of unreacted **404** but only those of the 1:1 σ adduct **419**[147]. The formation of **419** raised doubts as to the validity of the didehydropyrimidine mechanism. A possible alternative pathway for the formation of the 6-amino compounds, i.e. the stereoelectronically unfavourable internal hydride shift in the σ adduct **419**, could be rejected[169]; from 5-bromo-4-*t*-butyl-6-deutero-pyrimidine (**420**) no 6-amino-4-*t*-butyl-5-deutero-pyrimidine (**421**) was obtained (Scheme 98).



(419) (420) (421)

SCHEME 98

Reaction of monolabelled 5-bromo-4-*R*-[1(3)-^{15}N]pyrimidine (**422**, R = *t*-Bu, Ph, OMe, NH_2) (^{15}N-scrambled over both positions) with potassium amide gives, besides recovered starting material, the 6-amino-4-*R*-pyrimidine compound (**423**) which can be converted to the 6-chloro-4-*R*-pyrimidine (**424**) by diazotization in hydrochloric acid[170,171]. By measuring the excess of ^{15}N in **422**, **423** and **424** when R = *t*-Bu, Ph or OMe a decrease of ^{15}N excess was found, irresistibly leading to the conclusion that a part of the molecules react according to an S_N(ANRORC) mechanism (Scheme 99). For R = *t*-Bu and Ph about 50% of the 5-bromo-4-*R*-pyrimidines react according to this process, whereas for R = OMe the percentage is 26%. The results obtained by



(422) (423) (424)

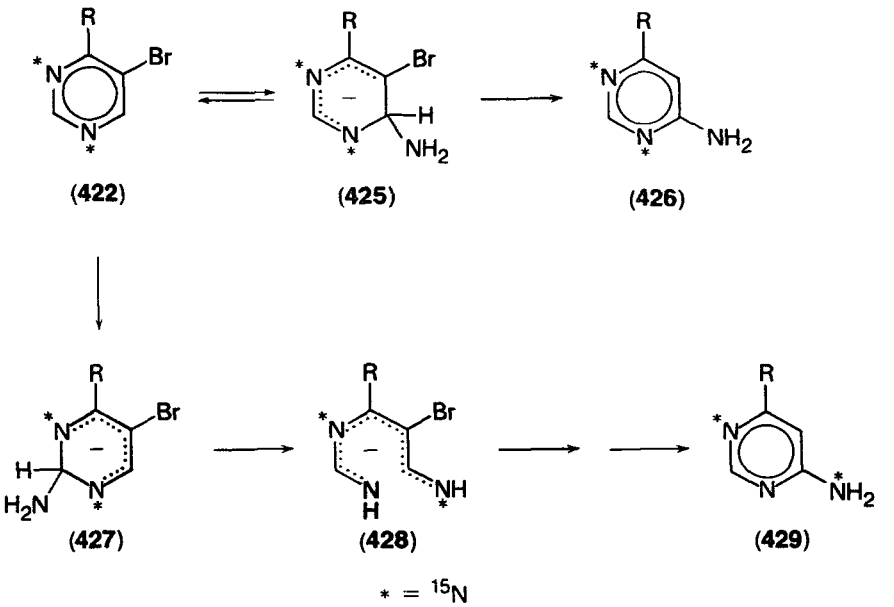
* = ^{15}N

SCHEME 99

^{1}H-NMR spectroscopy and by ^{15}N labelling seem to be in conflict, since a reaction via the σ adduct **425** could never lead to the distribution of ^{15}N over the ring nitrogen atom and the exocyclic amino function (see **426**). One has to conclude that not **425** but the 1:1 σ adduct at C-2, i.e. **427**, plays the key role in the mechanism, although by ^{1}H-NMR spectroscopy no indication for its existence can be found (Scheme 100). It seems that the favoured σ adduct **425** is rather unreactive while the isomeric σ adduct **427** quickly reacts as formed via the resonance-stabilized open-chain intermediate **428** giving **429**. It is probable that for the part of the 4-*R*-5-bromopyrimidines which do not react according to the S_N(ANRORC) mechanism the S_N(AE)*cine* process takes place for about 50% when R = *t*-Bu or Ph and for about 74% when R = OMe.

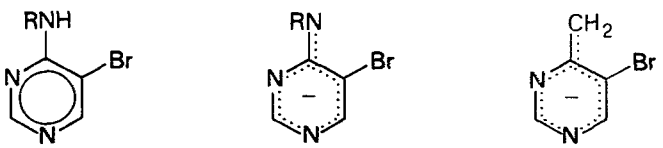
The above mentioned results make it questionable whether the proposal that the amide-induced conversion of 5-chloro-2-methylpyrimidine into 6-amino-2-methylpyrimidine involves 2-methyl-4,5-didehydropyrimidine – the first reported didehydropyrimidine – is still valid[172]. A more detailed study seems necessary to prove the existence of this intermediate.

4-Amino-5-bromopyrimidine (**430**, R = H) reacts without ring-opening to give 4,6-diaminopyrimidine[171]. 4-Amino-5,6-didehydropyrimidine is not the intermediate since the strong *ortho*-directing influence of the NH^- group (see Section II.A.1.b.ii) would certainly lead to the formation of some 4,5-diaminopyrimidine; this has not been found. A *cine* amination, involving an addition of the amide ion at C-6 – as has



SCHEME 100

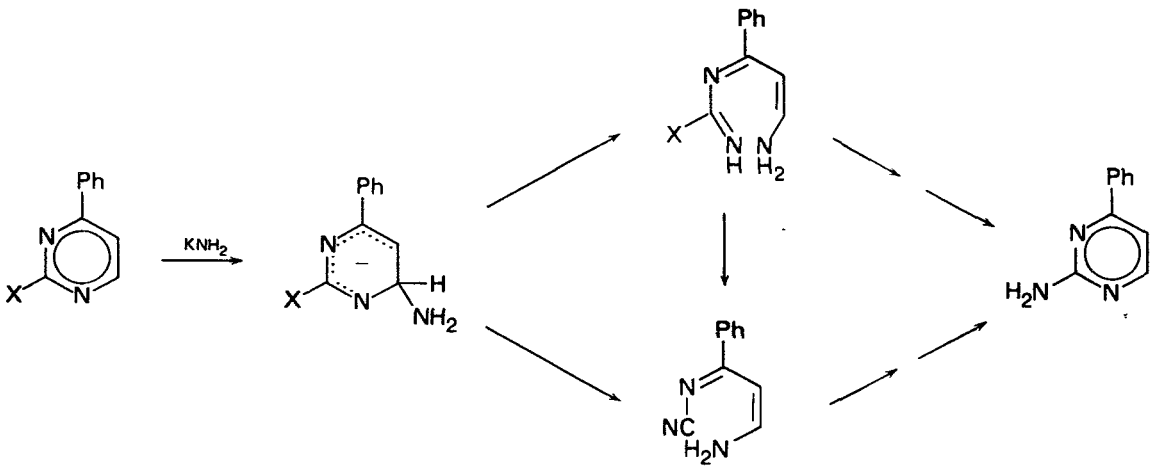
been proven by NMR spectroscopy – followed by dehydrobromination seems the most plausible pathway [S_N(AE)^{cine}]. The reason that 4-amino-5-bromopyrimidine does not react according to an S_N(ANRORC) mechanism lies in the fact that in the strong basic medium the amino group is deprotonated and the negative charge in the anion **431** formed is delocalized over the pyrimidine ring, mainly over both nitrogen atoms, making position C-2 less susceptible for the nucleophilic addition than position C-6 (Scheme 101). Also in the *cine* amination of 4-*R*-5-bromopyrimidines (R = Me, NHMe, NHPh) no S_N(ANRORC) process is involved, since these substituents too are easily deprotonated (see **431** and **432**). The deprotonation of some of these substituents has been proven by NMR spectroscopy.



SCHEME 101

Investigations on the amination of 2-*X*-4-phenylpyrimidine (X = F, Cl, Ph, I, Me, SO_2Me, SCN) by potassium amide/liquid ammonia show that all these compounds react for 80–100% according to the S_N(ANRORC) mechanism (Scheme 102)[173–176].

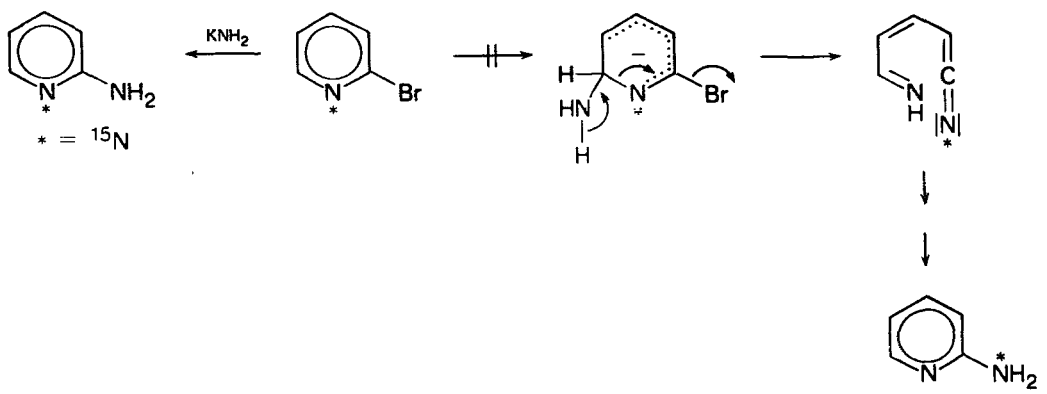
From all the results mentioned above it is clear that there is no indication for the occurrence of a 4,5-didehydropyrimidine intermediate. It must be concluded that in the *cine* aminations of the 5-bromopyrimidines and in the amination of the 2- and



SCHEME 102

6-halogenopyrimidines only the $S_N(AE)^{cine}$ and $S_N(ANRORC)$ mechanisms are operative. For an extensive review on this subject see Reference 15.

The phenomenon of the $S_N(ANRORC)$ process as a new mechanism for nucleophilic substitution also induced a reinvestigation of the amino-debromination of 2-bromopyridine[97]. As mentioned in Section II.A.3.a.i, 2-bromopyridine gives exclusively 2-aminopyridine on amination with potassium amide and an $S_N(AE)$ process was supposed to be the most reasonable mechanism. However, it was questioned whether in the amination of 2-bromopyridine an $S_N(ANRORC)$ mechanism would also operate as indicated in Scheme 103. Reaction of



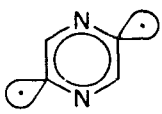
SCHEME 103

2-bromopyridine[^{15}N]with potassium amide revealed that in the 2-aminopyridine obtained all the ^{15}N is present in the ring[97]. Consequently, the $S_N(ANRORC)$ is not operative in the amination. Investigation of the mechanism of the formation of 3-aminoisoquinoline from 3-bromoisoquinoline with potassium amide, and using 3-bromoisoquinoline[^{15}N] showed that about 55% of the 3-amino compound is formed according to this process. The initial addition of the amide ion must take place at C-1[129].

It has been reported that 2,6-bis(methylthio)-4,5-didehydropyrimidine is intermediate in the formation of 6,6'- and 5,5'-di[2,4-bis(methylthio) pyrimidyl] from 2,4-bis(methylthio)-5-bromopyrimidine and butyllithium[177].

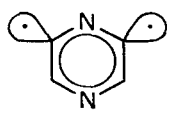
C. Didehydropyrazines

EHT calculations using idealized geometries show that the three possible didehydropyrazines (**433–435**) (Scheme 104) have the stability sequence **433** > **434** > **435**[7]. Although 2,3-didehydropyrazine (**435**) has the lowest stability of these three didehydropyrazines, so far the only reactions described are those in which



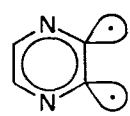
(433)

−507.57 eV



(434)

−506.68 eV

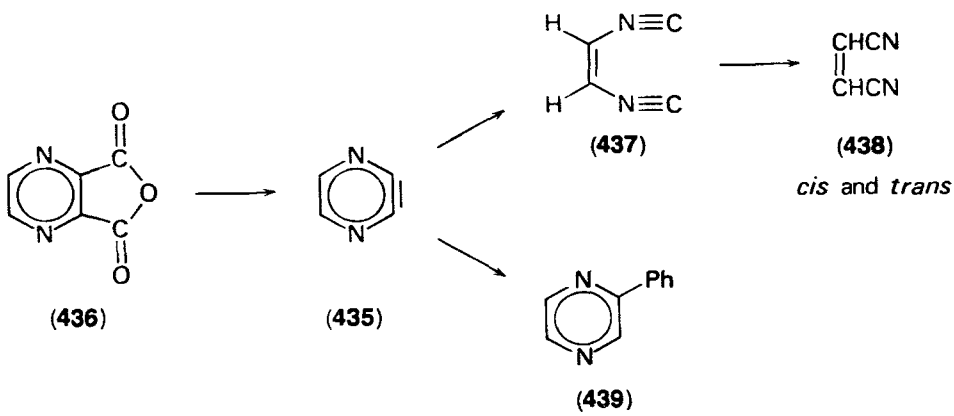


(435)

−506.43 eV

SCHEME 104

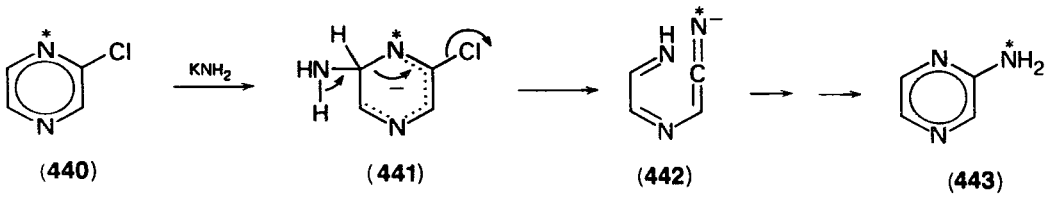
the intermediacy of **435** has been proposed. Indications for 2,5- or 3,5-didehydropyrazine (**433** and **434**) have never been found. Thermolysis of pyrazine-2,3-dicarboxylic anhydride (**436**) in a silica tube at 830°C/0.05 mm gives, possibly via **435** and **437** a mixture of *cis*- and *trans*-dicyanoethene (**438**)[178]. Pyrolysis of **436** in the presence of benzene gives phenylpyrazine (**439**), suggested as being formed by addition of benzene to **435** (Scheme 105)[102].



(436) **(435)** **(437)** **(438)** *cis* and *trans* **(439)**

SCHEME 105

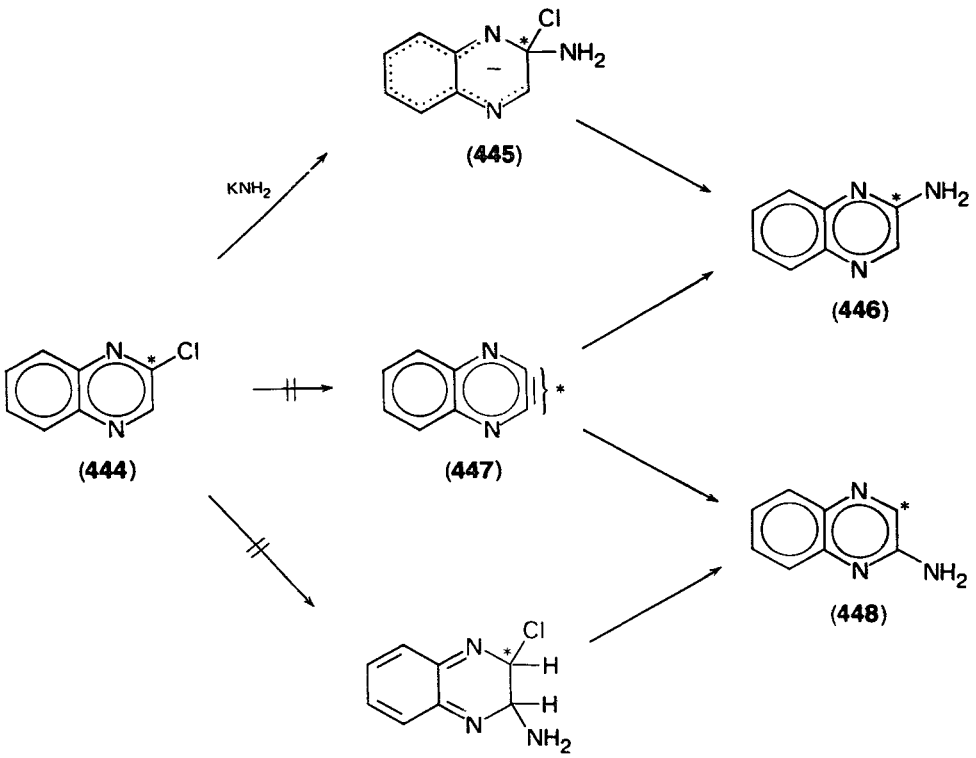
Reaction of chloropyrazine with potassium amide gives, besides ring-contraction products (imidazole and 2-cyanoimidazole), aminopyrazine[179–182]. It has unequivocally been established – using 2-chloropyrazine[1-^{15}N] (**440**) – that the amino-dechlorination gives 2-aminopyrazine (**443**) containing the excess of ^{15}N exclusively on the exocyclic nitrogen of the amino group[180]. This result leads to the conclusion that the amination of chloropyrazine occurs 100% via an S_N(ANRORC) process (see Section IV.B), initiated by addition of the amide ion at position 6, to give adduct **441** which after ring-opening to **442** and subsequent ring-closure yields **443**



SCHEME 106

(Scheme 106). Thus an $S_N(AE)$, an $S_N(EA)$ or an $S_N(AE)^{cine}$ process can be excluded since in all these processes the ^{15}N will be maintained in the pyrazine ring.

Further support for the occurrence of the $S_N(ANRORC)$ mechanism in amino-dechlorination has been obtained by the finding that the 2-chloro-6-phenylpyrazine does not give with potassium amide the corresponding 2-amino-6-phenylpyrazine but only ring-contraction products[183]. Position 6, being occupied by the phenyl group, is blocked for addition of the amide ion and the $S_N(ANRORC)$ process is prevented.



SCHEME 107

Amination of 2-chloroquinoxaline has also been investigated in detail[180,184] 2-Aminoquinoxaline is formed in high yield and it has been proved that this compound is not formed by the S_N(ANRORC) process. Investigation of the aminodechlorination of 2-chloroquinoxaline[2-^{14}C] (**444**) has shown that 2-aminoquinoxaline[2-^{14}C] (**446**) and not 3-aminoquinoxaline[2-^{14}C] (**448**) is obtained. This excludes the intermediacy of 2,3-didehydroquinoxaline (**447**) or an S_N(AE)^{cine} process involving **449**. Thus, the amination takes place exclusively via adduct **445** (Scheme 107).

V. REFERENCES

1. H. J. den Hertog and H. C. van der Plas, *Advan. Het. Chem.*, **4**, 121 (1965).
2. Th. Kauffmann, *Angew. Chem. (Intern. Ed. Engl.)*, **4**, 543 (1965).
3. R. W. Hoffmann, *Dehydrobenzene and Cycloalkenes*, Academic Press, New York, 1967, pp. 275–309.
4. H. J. den Hertog and H. C. van der Plas in *Chemistry of Acetylenes* (ed. H. G. Viehe), Dekker, New York, 1969, pp. 1149–1197.
5. Th. Kauffmann and R. Wirthwein, *Angew. Chem. (Intern. Ed. Engl.)*, **10**, 20 (1971).
6. M. G. Reinecke in *Reactive Intermediates*, Vol. 2 (Ed. R. A. Abramovitch), Plenum Press, New York, 1981.
7. W. Adam, A. Grimison and R. Hoffmann, *J. Amer. Chem. Soc.*, **91**, 2590 (1969).
8. M. J. S. Dewar and G. P. Ford, *J. Chem. Soc., Chem. Commun.*, 539 (1977).
9. H. L. Jones and D. L. Beveridge, *Tetrahedron Letters*, 1577 (1964).
10. J. Miller, *Aromatic Nucleophilic Substitution*, Elsevier, Amsterdam, 1968.
11. R. G. Shepherd and J. L. Fedrick, *Advan. Het. Chem.*, **4**, 145 (1965).
12. G. Illuminati, *Advan. Het. Chem.*, **3**, 285 (1964).
13. J. A. Zoltewicz, *Topics Current Chemistry*, **59**, 33 (1975).
14. (a) J. de Valk and H. C. van der Plas, *Rec. Trav. Chim.*, **90**, 1239 (1971).
    (b) J. de Valk and H. C. van der Plas, *Rec. Trav. Chim.*, **91**, 1414 (1972).
15. H. C. van der Plas, *Acc. Chem. Res.*, **11**, 462 (1978).
16. W. A. Roelfsema, *Ph.D. Thesis*, Wageningen, 1972; *Mededelingen Landbouwhogeschool Wageningen*, 72–5 (1972).
17. F. G. Bordwell, B. B. Lampert and W. H. McKellin, *J. Amer. Chem. Soc.*, **71**, 1702 (1949).
18. In this respect we follow closely the definition given for the *tele* substitution, see G. Guanti, S. Thea, M. Novi and C. Dell'Erba, *Tetrahedron Letters*, 1429 (1977).
19. G. M. Sanders, M. van Dijk and H. J. den Hertog, *Rec. Trav. Chim.*, **93**, 273 (1974).
20. H. C. van der Plas, M. Wozniak and A. van Veldhuizen, *Tetrahedron Letters*, 2087 (1976).
21. H. C. van der Plas, M. Wozniak and A. van Veldhuizen, *Rec. Trav. Chim.*, **97**, 130 (1978).
22. J. H. Wotiz and F. Huba, *J. Org. Chem.*, **24**, 595 (1959).
23. J. F. Bunnett and J. N. Feit, *J. Amer. Chem. Soc.*, **93**, 1202 (1971).
24. M. G. Reinecke and H. W. Adickes, *J. Amer. Chem. Soc.*, **90**, 511 (1968).
25. M. G. Reinecke, H. W. Adickes and C. Pyan, *J. Org. Chem.*, **36**, 2690 (1971).
26. H. C. van der Plas, D. A. de Bie, G. Geurtsen. M. G. Reinecke and H. W. Adickes, *Rec. Trav. Chim.*, **93**, 33 (1974).
27. D. A. de Bie and H. C. van der Plas, *Tetrahedron Letters*, 3905 (1968).
28. H. J. den Hertog and D. J. Buurman, unpublished results.
29. P. Vrijhof, *Ph.D. Thesis*, Wageningen, 1974; *Mededelingen Landbouwhogeschool Wageningen*, 74–3 (1974).
30. H. J. den Hertog and D. J. Buurman, *Rec. Trav. Chim.*, **92**, 304 (1973).
31. J. F. Bunnett, *Acc. Chem. Res.*, **5**, 139 (1972).
32. H. C. van der Plas, *Ring Transformations of Heterocycles*, Vols. 1 and 2, Academic Press, New York, 1973.
33. H. C. van der Plas, *Lectures in Heterocyclic Chemistry*, Vol. 2 (Eds. R. N. Castle and L. B. Townsend), Hetero Corporation, Utah, 1974.
34. H. C. van der Plas and J. W. Streef, *Aromatic and Heteroaromatic Chemistry*, Vol. 4, The Chemical Society, London, 1976.
35. H. C. van der Plas and J. W. Streef, *Aromatic and Heteroaromatic Chemistry*, Vol. 5, The Chemical Society, London, 1977.

36. H. C. van der Plas, *Heterocycles*, **9**, 33 (1978).
37. H. Paradowska and W. Czuba, *Wiad. Chem.*, **29**, 255 (1975).
38. H. Paradowska and W. Czuba, *Wiad. Chem.*, **29**, 173 (1975).
39. M. J. Pieterse and H. J. den Hertog, *Rec. Trav. Chim.*, **81**, 855 (1962).
40. M. J. Pieterse and H. J. den Hertog, *Rec. Trav. Chim.*, **80**, 1376 (1961).
41. M. J. Pieterse and H. J. den Hertog, *J. S. Afr. Inst.*, 41 (1964).
42. W. J. van Zoest and H. J. den Hertog, *Rec. Trav. Chim.*, **93**, 166 (1974).
43. R. Levine and W. W. Leake, *Science*, **121**, 780 (1955).
44. H. Boer, *Ph.D. Thesis*, Wageningen, 1973; *Mededelingen Landbouwhogeschool Wageningen*, 73–14 (1973).
45. J. A. Zoltewicz and C. Nisi, *J. Org. Chem.*, **34**, 765 (1969).
46. Th. Kauffmann and F. P. Boettcher, *Chem. Ber.*, **95**, 1528 (1962).
47. Th. Kauffmann and F. P. Boettcher, *Angew. Chem.*, **73**, 65 (1961).
48. Th. Kauffmann, H. Fischer, R. Nürnberg, M. Vestweber and R. Wirthwein, *Tetrahedron Letters*, 2911 (1967).
49. R. J. Martens, H. J. den Hertog and M. van Ammers, *Tetrahedron Letters*, 3207 (1964).
50. F. Marsais, M. Mallet, G. Quequiner and P. Pastour, *Compt. Rend., Ser. C*, **275**, 1535 (1972).
51. J. D. Roberts, D. A. Semenow, H. E. Simmons and L. A. Carlsmith, *J. Amer. Chem. Soc.*, **78**, 601 (1956).
52. J. A. Zoltewicz and A. A. Sale, *J. Org. Chem.*, **36**, 1455 (1971).
53. (a) W. J. van Zoest, *Ph.D Thesis*, 1975; *Mededelingen Landbouwhogeschool*, Wageningen, 75–1 (1975).
(b) M. Mallet, F. Marsais, G. Quequiner and P. Pastour, *Compt. Rend., Ser. C*, **275**, 1439 (1972).
54. R. A. Abramovitch, G. M. Singer and A. R. Vinutha, *J. Chem. Soc., Chem. Commun.*, 55 (1967).
55. For an interesting discussion on the addition of nucleophiles to 3,4- and 2,3-didehydropyridine see I. Fleming, *Frontier Orbitals and Organic Chemical Reactions* John Wiley and Sons, New York–London, 1976, p. 73–74.
56. J. A. Zoltewicz and C. L. Smith, *J. Amer. Chem. Soc.*, **88**, 4766 (1968).
57. J. A. Zoltewicz and C. L. Smith, *Tetrahedron*, **25**, 4331 (1969).
58. I. F. Tupitsyn and N. K. Semonova, *Tr. Gos. Inst. Prikl. Khim.*, **49**, 120 (1962); *Chem. Abstr.*, **60**, 6721b (1965).
59. H. G. Viehe and S. G. Delavarenne, quoted in H. G. Viehe, *Angew. Chem.*, **79**, 744 (1967).
60. R. J. Martens, *Ph.D. Thesis*, Leiden, 1966.
61. Th. Kauffmann and R. Nürnberg, *Chem. Ber.*, **100**, 3427 (1967).
62. R. Huisgen, W. Mack and L. Möbius, *Tetrahedron*, **9**, 29 (1960).
63. Th. Kauffmann, M. Fischer, R. Nürnberg and R. Wirthwein, *Justus Liebigs Ann. Chem.*, **731**, 23 (1970).
64. Th. Kauffmann, R. Nürnberg and R. Wirthwein, *Chem. Ber.*, **102**, 1161 (1969).
65. Th. Kauffmann and F. P. Boettcher, *Chem. Ber.*, **95**, 949 (1962).
66. J. M. Kramer and R. S. Berry, *J. Amer. Chem. Soc.*, **93**, 1303 (1971).
67. J. M. Kramer and R. S. Berry, *J. Amer. Chem. Soc.*, **94**, 8336 (1972).
68. G. W. J. Fleet and I. Fleming, *J. Chem. Soc. (C)*, 1758 (1969).
69. G. W. J. Fleet, I. Fleming and D. Philippides, *J. Chem. Soc. (C)*, 3948 (1971).
70. T. Sasaski, K. Kanematsu and M. Uchide, *Bull. Chem. Soc. Japan*, **44**, 858 (1971).
71. G. Wittig and E. Knaus, *Chem. Ber.*, **91**, 895 (1958).
72. K. Udluft and R. Wirthwein, *Angew. Chem. (Intern. Ed. Engl.)*, **3**, 650 (1964).
73. H. J. Den Hertog, M. J. Pieterse and D. J. Buurman, *Rec. Trav. Chim.*, **82**, 1173 (1963).
74. L. van der Does and H. J. den Hertog, *Rec. Trav. Chim.*, **91**, 1403 (1973).
75. J. W. Streef, *Ph.D. Thesis*, Utrecht, 1970.
76. L. B. Bos and H. J. den Hertog, *Rec. Trav. Chim.*, **88**, 881 (1969).
77. J. W. Streef and H. J. den Hertog, *Rec. Trav. Chim.*, **85**, 803 (1966).
78. J. D. Cook and B. J. Wakefield, *Tetrahedron Letters*, 2535 (1967).
79. J. D. Cook, B. J. Wakefield, H. Heany and J. M. Jaklonski, *J. Chem. Soc. (C)*, 2727 (1968).
80. B. J. Wakefield, D. J. Berry and J. D. Cook, *J. Chem. Soc. (C)*, 1227 (1971).
81. E. G. Bartsch, A. Gollock and R. Sartori, *Chem. Ber.*, **105**, 3463 (1972).

82. A. J. Shatenshtein in V. Gold, *Advan. Phys. Org. Chem.*, **1**, 155 (1963).
83. G. B. R. de Graaff, H. J. den Hertog and W. Ch. Melger, *Tetrahedron Letters*, 963 (1965).
84. H. Smith, *Chemistry in Anhydrous Liquid Ammonia*, Part 2: *Organic Reactions in Liquid Ammonia*, Interscience, New York, 1963.
85. Y. Kawazoe, M. Ohnishi and Y. Yoshioka, *Chem. Pharm. Bull.*, **12**, 1384 (1964).
86. (a) R. J. Martens and H. J. den Hertog, *Rec. Trav. Chim.*, **86**, 655 (1967).
(b) T. Kato, T. Niitsuma and N. Kusaka, *J. Pharm. Soc. Japan*, **84**, 432 (1964).
87. Th. Kauffmann and R. Wirthwein, *Angew. Chem.*, **76**, 993 (1964).
88. J. D. Roberts, C. W. Vaughan, L. A. Carlsmith and D. A. Semenov, *J. Amer. Chem. Soc.*, **78**, 611 (1956).
89. J. A. Zoltewicz and J. F. Bunnett, *J. Amer. Chem. Soc.*, **87**, 2640 (1965).
90. T. Kato and T. Niitsuma, *Chem. Pharm. Bull. Japan*, **13**, 967 (1965).
91. H. Boer and H. J. den Hertog, *Tetrahedron Letters*, 1943 (1969).
92. The formation of this product will not be discussed in detail since ring-transformations are beyond the scope of this chapter. For leading references see References 32–36.
93. J. F. Bunnett and J. M. Kim, *J. Amer. Chem. Soc.*, **95**, 2254 (1973).
94. J. W. Streef and H. J. den Hertog, *Rec. Trav. Chim.*, **88**, 1391 (1969).
95. H. N. M. van der Lans, *Ph.D. Thesis*, Leiden, 1973.
96. H. J. den Hertog, H. Boer, J. W. Streef, F. C. A. Vekemans and W. J. van Zoest, *Rec. Trav. Chim.*, **93**, 195 (1974).
97. Th. Kauffmann, survey cited in Reference 2, pp. 545, 557
98. R. J. Martens and H. J. den Hertog, *Tetrahedron Letters*, 643 (1962).
99. J. D. Cook and B. J. Wakefield, *J. Chem. Soc. (C)*., 1973 (1969).
100. M. Mallet and G. Quequiner, *Compt. Rend, Ser. C*, **274**, 719 (1972).
101. E. K. Fields and S. Meyerson, *J. Org. Chem.*, 31, 3307 (1966).
102. J. K. Kim and J. F. Bunnett, *J. Amer. Chem. Soc.*, **92**, 7463 (1970).
103. G. B. R. de Graaff, H. J. den Hertog, W. Ch. Melger and W. A. Houwing, unpublished results.
104. H. N. M. van der Lans and H. J. den Hertog, *Rec. Trav. Chim.*, **87**, 549 (1968).
105. R. J. Martens and H. J. den Hertog, *Rec. Trav. Chim.*, **83**, 621 (1964).
106. J. D. Cook and B. J. Wakefield, *Chem. Commun.*, 297 (1968).
107. J. D. Cook and B. J. Wakefield, *J. Chem. Soc. (C)*, 2376 (1969).
108. S. S. Dua and H. Gilman, *J. Organomet. Chem.*, **12**, 299 (1969).
109. H. N. M. van der Lans, H. J. den Hertog and A. van Veldhuizen, *Tetrahedron Letters*, 1875 (1971).
110. Recent work on deprotonation of *trans*-cinnamoylnitrile has indicated that deprotonation of **206** in the position α to the cyano group is possible: R. R. Schmidt and H. Speer, *Synthesis*, 797 (1979).
111. (a) H. C. van der Plas, T. Hijwegen and H. J. den Hertog, *Rec. Trav. Chim.* **84**, 53 (1965).
(b) H. J. den Hertog, R. J. Martens, H. C. van der Plas and J. Bon, *Tetrahedron Letters*, 4325 (1966).
112. L. van der Does and H. J. den Hertog, unpublished results.
113. Th. Kauffmann and H. Fischer, *Chem. Ber.*, **106**, 220 (1973).
114. I. Ahmed, G. W. H. Cheeseman and B. Jaques, *Tetrahedron*, 1145 (1979).
115. S. V. Kessar, Y. P. Gupta, P. S. Pahwa and Paramjit Sing, *Tetrahedron Letters*, 3207 (1976); S. V. Kessar, *Acc. Chem. Res.*, **11**, 283 (1978).
116. S. V. Kessar, Y. P. Gupta, Paramjit Singh, S. K. Gupta and P. S. Pahwa, *Proc. Indian Acad. Sci.*, **88A**, 191 (1979).
117. Th. Kauffmann, F. P. Boettcher and J. Hansen, *Angew. Chem.*, **73**, 341 (1961).
118. Th. Kauffmann, F. P. Boettcher and J. Hansen, *Ann. Chem.*, **659**, 102 (1962).
119. Th. Kauffmann and K. Udluft, *Angew. Chem.*, **75**, 89 (1963).
120. Th. Kauffmann, survey cited in Reference 2, p. 554.
121. Th. Kauffmann, H. Fischer, R. Nürnberg, M. Vestweber and R. Wirthwein, *Tetrahedron Letters*, 2917 (1967).
122. H. J. den Hertog and D. J. Buurman, *Rec. Trav. Chim.*, **86**, 187 (1967).
123. T. Kametani, K. Kigasawa, M. Miiragi and O. S. Kusama, *J. Het. Chem.*, **6**, 933, (1969).
124. J. Pomorski, H. J. den Hertog, N. H. Bakker and D. J. Buurman, *Rec. Trav. Chim.*, **92**, 970 (1973).

125. H. J. den Hertog and D. J. Buurman, *Rec. Trav. Chim.*, **91**, 841 (1972).
126. Th. Kauffmann and J. Schulz, *Chem. Ber.*, **99**, 1837 (1966).
127. R. Peereboom and H. J. den Hertog, *Rec. Trav. Chim.*, **93**, 281 (1974).
128. G. Wittig and G. Steinhoff, *Ann. Chem.*, **676**, 21 (1964).
129. G. M. Sanders, M. van Dijk and H. J. den Hertog, *Rec. Trav. Chim.*, **93**, 198 (1974).
130. Th. Kauffmann, survey cited in Reference 2, p. 548.
131. G. M. Sanders, M. van Dijk and H. J. den Hertog, *Rec. Trav. Chim.*, **95**, 31 (1976).
132. W. Czuba, *Rec. Trav. Chim.*, **82**, 997 (1963).
133. H. J. W. van den Haak and H. C. van der Plas, *Rec. Trav. Chim.*, **99**, 83 (1980).
134. W. Czuba and T. Kowalska, *Rocz. Chem.*, **49**, 193 (1975).
135. J. Pomorski and H. J. den Hertog, *Rocz. Chem.*, **47**, 549 (1973).
136. W. Czuba and M. Wozniak, *Rec. Trav. Chim.*, **93**, 143 (1974).
137. H. C. van der Plas, M. Wozniak and A. van Veldhuizen, *Rec. Trav. Chim.*, **95**, 233 (1976).
138. W. W. Paudler and T. J. Kress, *J. Org. Chem.*, **33**, 1384 (1968).
139. M. Wozniak, W. Czuba and H. C. van der Plas, *Rocz. Chem.*, **50**, 451 (1976).
140. H. C. van der Plas, M. Wozniak and A. van Veldhuizen, *Rec. Trav. Chim.*, **96**, 151 (1977).
141. Th. Kauffmann, J. Hansen, K. Udluft and R. Wirthwein, *Angew. Chem. (Intern. Ed. Engl.)*, **3**, 650 (1964).
142. Th. Kauffmann, A. Risberg, J. Schulz and R. Weber, *Tetrahedron Letters*, 3563 (1964).
143. V. A. Zagorevskii, V. L. Savel'ev and S. L. Portnova, *Zh. Org. Khim.*, **1**, 1899 (1965).
144. J. A. Zoltewicz and L. S. Helmick, *J. Amer. Chem. Soc.*, **94**, 682 (1972).
145. J. P. Geerts, H. C. van der Plas and A. van Veldhuizen, *Org. Magn. Reson.*, **7**, 86 (1975).
146. J. P. Geerts, H. C. van der Plas and A. van Veldhuizen, *Rec. Trav. Chim.*, **92**, 1232 (1973).
147. J. P. Geerts, C. A. H. Rasmussen, H. C. van der Plas and A. van Veldhuizen, *Rec. Trav. Chem.*, **93**, 231 (1974).
148. P. J. Lont, H. C. van der Plas and A. van Veldhuizen, *Rec. Trav. Chim.*, **92**, 708 (1973).
149. E. A. Oostveen, H. C. van der Plas and H. Jongejan, *Rec. Trav. Chim.*, **93**, 114 (1974).
150. A. Nagel, H. C. van der Plas and A. van Veldhuizen, *Rec. Trav. Chim.*, **94**, 45 (1975).
151. N. J. Kos, H. C. van der Plas and A. van Veldhuizen, *J. Org. Chem.*, **44**, 3140 (1979).
152. N. J. Kos and H. C. van der Plas, *J. Org. Chem.*, **45**, 2942 (1980).
153. D. E. Klinge, H. C. van der Plas and A. Koudijs, *Rec. Trav. Chim.*, **93**, 201 (1974).
154. D. E. Klinge and H. C. van der Plas, *Rec. Trav. Chim.*, **95**, 34 (1976).
155. T. L. Gilchrist, G. E. Gymer and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1747 (1975).
156. Th. Kauffmann and A. Risberg, *Tetrahedron Letters*, 1459 (1963).
157. Y. Maki and M. Takaya, *Chem. Pharm. Bull. Japan*, **20**, 747 (1972).
158. H. W. van Meeteren and H. C. van der Plas, *Rec. Trav. Chim.*, **86**, 15 (1967).
159. Th. Kauffmann, R. Nürnberg and K. Udluft, *Chem. Ber.*, **102**, 1177 (1969).
160. H. C. van der Plas and A. Koudijs, unpublished results.
161. R. Promel, A. Cardon, M. Daniel, G. Jacques and A. Vandersmissen, *Tetrahedron Letters*, 3067 (1968).
162. Th. Kauffmann, survey cited in Reference 2, p. 552.
163. D. Christophe, R. Promel and M. Maeck, *Tetrahedron Letters*, 4435 (1978).
164. H. C. van der Plas and G. Geurtsen, *Tetrahedron Letters*, 2093 (1964).
165. H. C. van der Plas, *Tetrahedron Letters*, 555 (1965).
166. H. C. van der Plas, P. Smit and A. Koudijs, *Tetrahedron Letters*, 9 (1968).
167. J. A. Zoltewicz, G. Grahe and C. L. Smith, *J. Amer. Chem. Soc.*, **91**, 5501 (1969).
168. H. C. van der Plas and A. Koudijs, *Rec. Trav. Chim.*, **89**, 129 (1970).
169. A similar mechanism was suggested by Benkeser and Schroll to explain the exclusive formation of *m*-aminomethoxybenzene from *o*-bromomethoxybenzene by KNH_2 in ammonia: C. R. A. Benkeser and G. Schroll, *J. Amer. Chem. Soc.*, **75**, 3196 (1953). However, this proposal was superseded by the benzyne mechanism.
170. C. A. H. Rasmussen and H. C. van der Plas, *Rec. Trav. Chim.*, **96**, 101 (1977).
171. C. A. H. Rasmussen, H. C. van der Plas, P. Grotenhuis and A. Koudijs, *J. Het. Chem.*, **15**, 121 (1978).
172. T. J. Schwan and H. Tieckelmann, *J. Org. Chem.*, **29**, 941 (1964).
173. A. P. Kroon and H. C. van der Plas, *Rec. Trav. Chim.*, **92**, 1020 (1973).
174. A. P. Kroon and H. C. van der Plas, *Rec. Trav. Chim.*, **93**, 111 (1974).
175. A. P. Kroon and H. C. van der Plas, *Rec. Trav. Chim.*, **93**, 227 (1974).

176. A. P. Kroon, H. C. van der Plas and G. van Garderen, *Rec. Trav. Chim.*, **93**, 325 (1974).
177. L. Strekowski, *Rocz. Chem.*, **49**, 1693 (1975).
178. R. F. C. Brown, W. D. Crow and R. K. Solly, *Chem. Ind. (London)*, 343 (1966).
179. P. J. Lont, H. C. van der Plas and A. Koudijs, *Rec. Trav. Chim.*, **90**, 207 (1971).
180. P. J. Lont, H. C. van der Plas and A. J. Verbeek, *Rec. Trav. Chim.*, **91**, 949 (1972).
181. P. J. Lont, H. C. van der Plas and E. Bosma, *Rec. Trav. Chim.*, **91**, 1352 (1972).
182. P. J. Lont and H. C. van der Plas, *Rec. Trav. Chim.*, **92**, 331 (1973).
183. P. J. Lont and H. C. van der Plas, *Rec. Trav. Chim.*, **92**, 449 (1973).
184. P. J. Lont and H. C. van der Plas, *Rec. Trav. Chim.*, **91**, 850 (1972).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 13

Oxidation of triple-bonded groups

LÁSZLÓ I. SIMÁNDI
Central Research Institute for Chemistry, Budapest, Hungary

I. INTRODUCTION

Alkyne derivatives are susceptible to oxidation and the carbon–carbon triple bond may or may not remain intact upon interaction with oxidants. Although there is much information in the literature, with the exception of a brief review[178], there has been no attempt to cover the subject systematically. Previous volumes in this series[125] carry information on oxidation scattered in different chapters. The same is true of the oxidation of the triple-bonded groups in cyano, isocyano, and diazo compounds, though the pertinent literature is more limited in these cases.

There are various operational definitions of oxidation and reduction, perhaps the most widely used being the concept of electron loss (oxidation) and electron gain (reduction). Although this approach is perfectly unambiguous and general for most inorganic redox phenomena, it is not immediately clear how organic reactions can be classified on these grounds. The formal oxidation state of carbon in organic compounds seems to be the most helpful version[77] of the electron loss and gain concept in electron book-keeping. In terms of this concept, oxidation is a net increase in the formal oxidation state of the atom(s) involved in the reaction, due to bond formation with more electronegative atom(s). Each one of such bonds contributes +1 unit to the oxidation state of the carbon (or other) atom concerned while each bond between carbon and a less electronegative atom contributes −1 unit. Examples of the introduction of some common heteroatoms are shown in equations (1–5) (oxidation states shown under the carbon atoms).

$$\underset{-3}{R{-}CH_3} \longrightarrow \underset{+1}{R{-}CHO} \qquad (1)$$

$$\underset{0\ \ 0}{R{-}C{\equiv}C{-}R} \longrightarrow \underset{+2\ \ +2}{R{-}CO{-}CO{-}R} \qquad (2)$$

$$\underset{-3}{R{-}CH_3} \longrightarrow \underset{-1}{R{-}CH_2NO_2} \quad (3)$$

$$\underset{-3}{R{-}CH_3} \longrightarrow \underset{-1}{R{-}CH_2Cl} \quad (4)$$

$$\underset{0\ -1}{R{-}C{\equiv}CH} \longrightarrow \underset{+1\quad 0}{R{-}CCl{=}CHCl} \quad (5)$$

It should, however, be noted that the last example is usually termed chlorine addition, which disregards the fact that oxidation of the molecule has taken place. In contrast, addition of HCl to an unsaturated compound does not involve a net oxidation (equation 6).

$$\underset{0\ -1}{R{-}C{\equiv}CH} \xrightarrow{HCl} \underset{+1\quad -2}{R{-}CCl{=}CH_2} \quad (6)$$

The material in this chapter has been selected along these guidelines. Some exceptions have had to be made when less electronegative analogues of oxygen (viz. sulphur and selenium) are the heteroatoms introduced. Although unjustified by the oxidation state conventions, a few examples of this type have been included on grounds of analogy.

II. OXIDATION OF ALKYNES

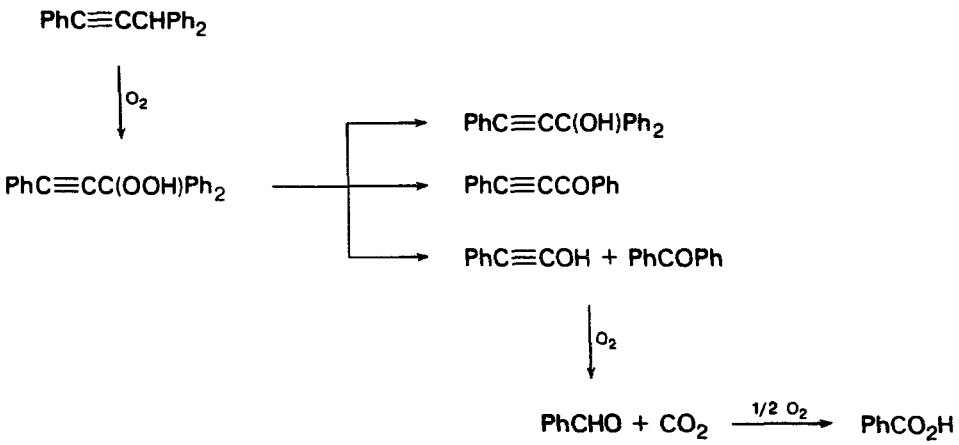
A. Oxidation by Oxygen Species

1. *Autoxidation*

The oxidation of acetylene by O_2 around 300°C has been extensively studied[75,118,159a,160,163]. The reaction has a typical free-radical chain character, leading to a variety of products. The main stable products are carbon monoxide, carbon dioxide, water, hydrogen and formic acid. Detectable but reactive intermediates include glyoxal, formaldehyde, hydrogen peroxide, acetaldehyde and acrolein. Considerable effort has been expended to gain more insight into the details of this complex process. The oxidation of acetylene, propyne and 2-butyne under conditions of slow combustion has been investigated at 330°C, utilizing mass spectrometry and isotopic labelling for following the concentration and fate of a variety of intermediates[72–74]. Kinetic orders have been determined for many intermediates and products with respect to acetylene. Chain initiation and termination have been shown to occur in the gas phase, with some contribution from surface termination. Without direct information on the initiation step, it has been assumed to involve an unspecified excited state of acetylene resulting from the reaction of two acetylene molecules. Chain termination presumably occurs via the interaction of two hydroperoxyl radicals. The main chain carriers are hydroxyl and hydroperoxyl radicals. The ·OH radicals enter into both abstraction and addition reactions with acetylene, while the hydroperoxyvinyl radicals undergo mainly intramolecular hydrogen transfer. The product distribution and kinetic behaviour have been interpreted in terms of a complex, multistep mechanism. After an initial phase, the complexity of the reaction

increases. The slow combustion of propyne and 2-butyne is similar to that of acetylene. The products detected are the methyl- and dimethyl-substituted analogues of the corresponding acetylene combustion products and the proposed reaction mechanism is also similar. A point of difference between the oxidation of acetylene and its two higher homologues is degenerate branching of the radical chain process in the latter case. Chain branching in propyne oxidation is due to a peracid formed from an aldehyde, and to an acyl radical in 2-butyne combustion[74].

The autoxidation of higher alkyne derivatives in the liquid phase has been studied using a number of model compounds. Generally, the primary product of interaction with dioxygen is an α-hydroperoxide[23,24,26,28,30] and the triple bond remains intact up until the later stages of the reaction. A typical autoxidation scheme exemplifying the characteristic behaviour of a substituted alkyne is shown in Scheme 1.



SCHEME 1

In the case of alkenynes, e.g. 2,3,6-trimethyl-2-hepten-4-yne and 5-cyclohexyl-2,3-dimethyl-2-penten-4-yne, epoxidation of the double bond is a detectable side-reaction, occurring apparently via interaction with the peroxyl radical or the hydroperoxide, the latter being a well-known epoxidizing agent[27].

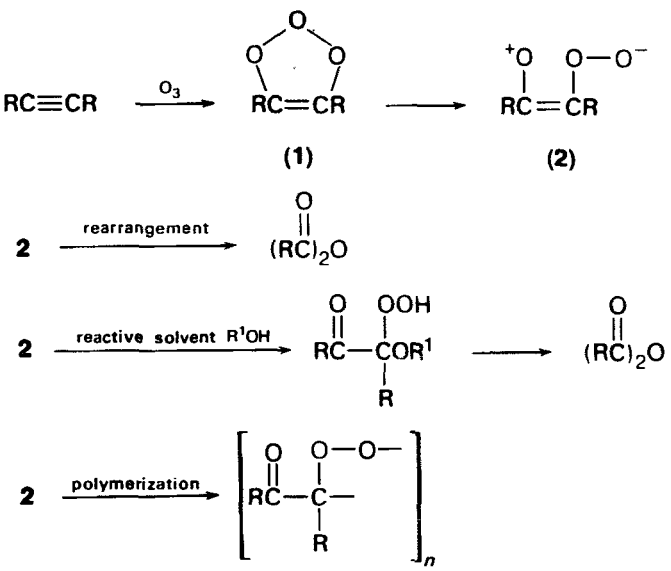
In line with its radical-chain character, the autoxidation of substituted acetylenes can be accelerated by known initiators (e.g. azobisisobutyronitrile), and by cobalt acetate, butyrate, caprylate and lactate; cobalt formate acts as an inhibitor[25].

2. *Catalytic oxidation with dioxygen*

The unselective, complete oxidation (to CO_2 and H_2O) of 1-alkynes (C_2–C_8) at 200–300°C on cuprous oxide has been studied with reference to the surface intermediates involved[4,5]. The key intermediate is a formate–carboxylate surface species, which decomposes to CO_2 and H_2O more rapidly than do similar intermediates formed from analogous olefins: the relative reactivity observed increases in the order aromatics < olefins < acetylenes. An associative mechanism is suggested for the lower temperatures studied, where the rate-determining step is the decomposition of the surface complex with O_2. At higher temperatures, a stepwise mechanism becomes operative.

3. Ozonation

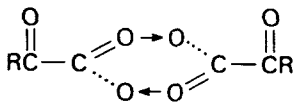
The reaction of alkynes with ozone has received considerably less attention than the corresponding transformations of alkenes[9]. Early work on alkyne ozonolysis[80] led to the isolation of less than 50% carboxylic acids derived from cleavage of the triple bond. It was soon recognized that the extent of chain rupture depends on the reaction conditions and that dicarbonyl compounds are isolable intermediates[83]. Reductive trapping in the case of 1,4-dibenzoxy-2-butyne gave 97% of the corresponding dioxo derivative[38]. A detailed study of this model alkyne[39] has led to a mechanism for the ozonolysis of acetylenic compounds which is similar to the analogous scheme for olefins (Scheme 2). The essential features of this mechanism remain valid to date, though there is considerable controversy as to the nature of the proposed intermediate(s). The primary addition product **1** was assigned the structure shown, but a π-complex structure was regarded as a conceivable alternative. The zwitterion intermediate **2** can react in three ways but reduction produces the diketone RCOCOR directly from **2**. It is formed upon reductive treatment of the hydroperoxide species too.



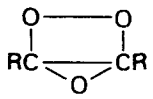
SCHEME 2

Attempts at obtaining a more detailed insight into the nature of reactive intermediates were made by utilizing low temperatures.

The ozonation of acetylene, propyne, 1-butyne and 2-butyne has been studied at −45°C[42b] in liquid carbon dioxide. With the exception of acetylene, a transient strong carbonyl band was observed near 1740 cm^{-1}. The corresponding intermediates were found to be the unstable precursors of the product acid anhydrides. These precursors were formulated as dimeric acylcarbonyl oxides (**3**), originally proposed to be the first intermediates in alkyne ozonation[39]. The observation of the 1740 cm^{-1} band prompted DeMore and Lin[42b] to rule out the ozonide structures **1** and **4** for the alkynes studied. The formation of α-dicarbonyl compounds (e.g. biacetyl from dimethylacetylene, or methylglyoxal from methylacetylene) presumably takes place via the acylcarbonyl oxide intermediate.

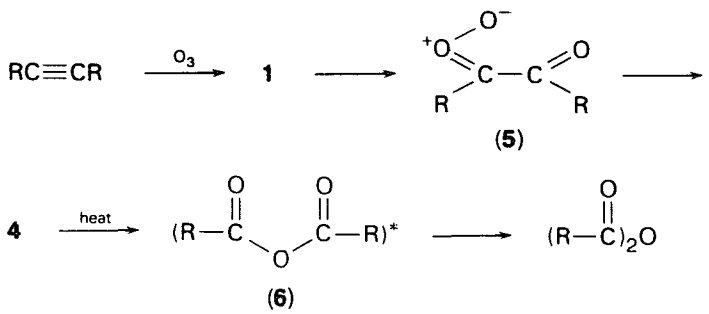


(3)



(4)

The ozonation of diphenylacetylene yields benzil, benzoic anhydride and benzoic acid[41a]. Approximately the same product mixtures were obtained at room temperature and at low temperatures (−93 and −42°C)[82]. Reductive trapping was extensively used and the observed behaviour was rationalized in terms of the reaction mechanism shown in Scheme 3 (R = Ph). This scheme involves the 1,2,3-trioxolene

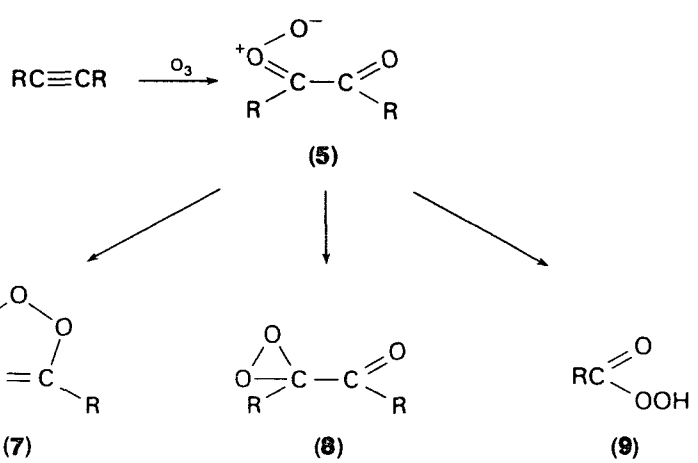


(5)

(6)

SCHEME 3

intermediate **1**, which is a 1,3-dipolar cycloaddition product analogous to the 1,2,3-trioxolane species formed in alkene ozonation. This view contradicts earlier conclusions against the ozonide structure **1** for aliphatic acetylenes. Direct evidence is apparently needed to set the argument over the 1,2,3-trioxolene intermediate. In the above ozonation scheme, species **5** is the zwitterion intermediate **2**, formulated as an acylcarbonyl oxide. Both **5** and **4** may be the precursors of benzoic anhydride, a question still open to debate. The stability of dioxetanes and the observation of



(5)

(7)

(8)

(9)

SCHEME 4

chemiluminescence during decomposition of the precursors directly indicate the presence of **4**.

Interesting mechanistic conclusions have been drawn from cyclohexene epoxidation studies with the ozonation products of simple alkynes[91]. Dichloromethane solutions of acetylene, 2-butyne, di-*t*-butylacetylene, methylphenylacetylene and diphenylacetylene, treated with O_3 at $-70°C$, gave 5–30% of cyclohexene oxide at room temperature when reacted with cyclohexene. The results were interpreted by assuming that the α-carbonyl carbonyl oxide (acylcarbonyl oxide) (**5**) is a first common intermediate. This species, sometimes referred to as 'vinylogous ozone', was shown to transform to three distinct epoxidizing agents (**7**, **8** and **9**), active at low ($-70°C$), intermediate ($-25°C$) and room temperature, respectively (Scheme 4). Also, an inactive polymeric peroxide was formed from the vinylogous ozone. Structure **7** is supported by trapping experiments with diethyl sulphide.

Similar epoxidation experiments[90] have led to conclusions showing that the epoxidant is probably **5** or **7**, the latter being slightly favoured on thermodynamic grounds.

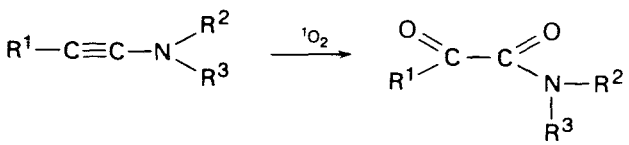
4. *Atomic oxygen*

Oxygen atoms react with alkynes such as acetylene and propyne, leading to fragmentation of initially formed excited products[8,16,78,89]. 1,3-Biradicals, ketocarbenes and excited ketenes are possible intermediates. The reaction of 2-butyne with $O(^3P)$ atoms also yields some of the unfragmented product, 3-buten-2-one[54]. Unfragmented carbonyl compounds constitute the major portion of isolated products from the reaction of $O(^3P)$ with C_4, C_5 and C_6 acetylenes[70], whereas fragmented products such as carbon monoxide, olefins and cyclopropanes are presumably formed via the decomposition of excited ketenes to carbenes. The presence of ketenes was proved by trapping them as their methanol adducts. It was concluded that the $O(^3P)$–alkyne adduct rearranges to the ketene without detachment of the migrating group, i.e. the process is intramolecular.

5. *Singlet oxygen*

Recently there has been increasing interest in the reactions of singlet oxygen with organic substrates. Compounds with acetylenic triple bonds react with $^1O_2$ if activating substituents are present or when the alkyne molecule is strained.

In the dye-sensitized photooxygenation of the ynamines **10**[57], one mole of oxygen is taken up to produce the dioxo derivative **11** (equation 7). Zwitterionic and dioxetene intermediates have been considered.



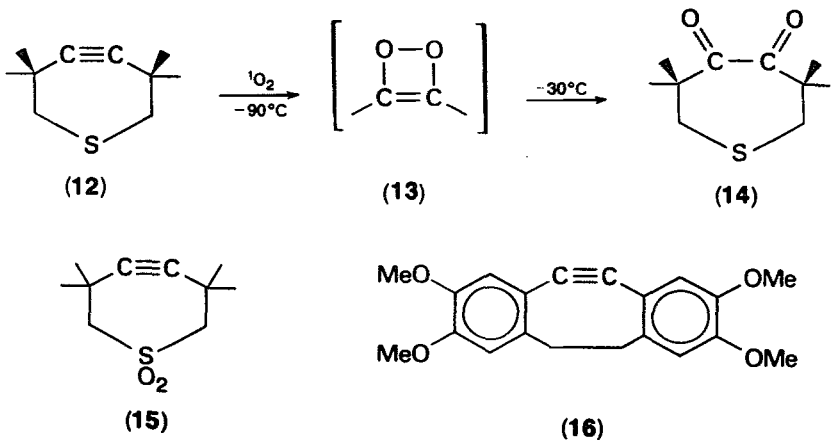
(7)

(10) **(11)**

(a) R^1 = Me, R^2 = R^3 = Et

(b) R^1 = Ph, R^2 = R^3 = $(CH_2)_5$

The strained acetylene **12** reacts with photochemically generated $^1O_2$ at $-90°C$[166] to produce an intermediate which yields the dioxo derivative **14** at $-30°C$. The reaction is accompanied by chemiluminescence, which indicates that the intermediate is the precursor of the excited state of the product **14**. It has been suggested that the intermediate has a dioxetene structure (**13**). Similar reactions have been observed with acetylenes **15** and **16** (Scheme 5).



SCHEME 5

B. Oxidation by Peroxy Acids and Peroxides

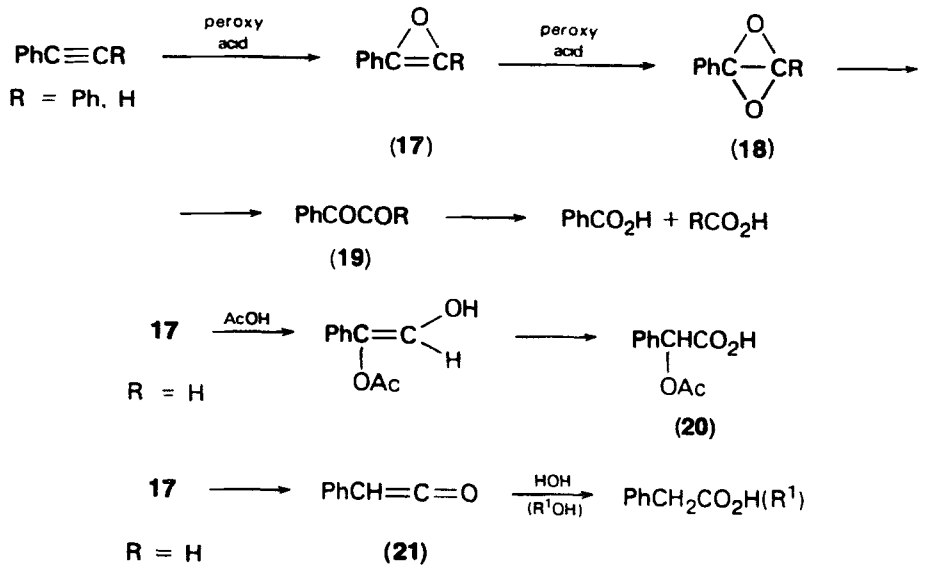
The reactions of peroxy acids and other peroxo compounds with olefins have been extensively studied and are widely applied in synthetic practice especially for the epoxidation of double bonds. A recent review of the subject is available[130].

The peroxidation of acetylenes has received considerably less attention, but interest in the nature of the possible oxirene intermediate has given impetus to clarifying the products and the main mechanistic features of these reactions.

1. Peroxy acids

The oxidation of diphenylacetylene by trifluoroperoxyacetic acid gives benzil and benzoic acid, whereas the same peroxy acid oxidizes phenylacetylene to phenylacetic and benzoic acids[108]. Peroxybenzoic acid oxidizes phenylacetylene to methyl and ethyl phenylacetates (MeOH and EtOH are impurities in the $CHCl_3$ solvent), methyl benzoate, benzaldehyde and benzoic acid. When treated with peroxyacetic acid, phenylacetylene is converted to benzyl acetate, acetylmadelic acid, phenylacetic acid and benzoic acid[108]. The overwhelming majority of these products (except perhaps acetylmandelic acid) can be rationalized in terms of an oxirene intermediate (**17**) (Scheme 6). Its further oxidation leads first through a 2,4-dioxabicyclobutane (**18**) to a diketone (**19**), then to an acid anhydride and finally to the cleavage products. Attack of the oxirene by the solvent acetic acid accounts for the formation of acetylmandelic acid (**20**). Rearrangement to a ketene (**21**), with subsequent addition of an alcohol or water, which are present as impurities, yields methyl and ethyl phenylacetates or phenylacetic acid.

Direct isolation of the oxirene intermediate was not successful but the sodium-tungstate-catalysed peroxidation of acetylenedicarboxylic acid monopotassium salt with hydrogen peroxide afforded a product that analysed well for



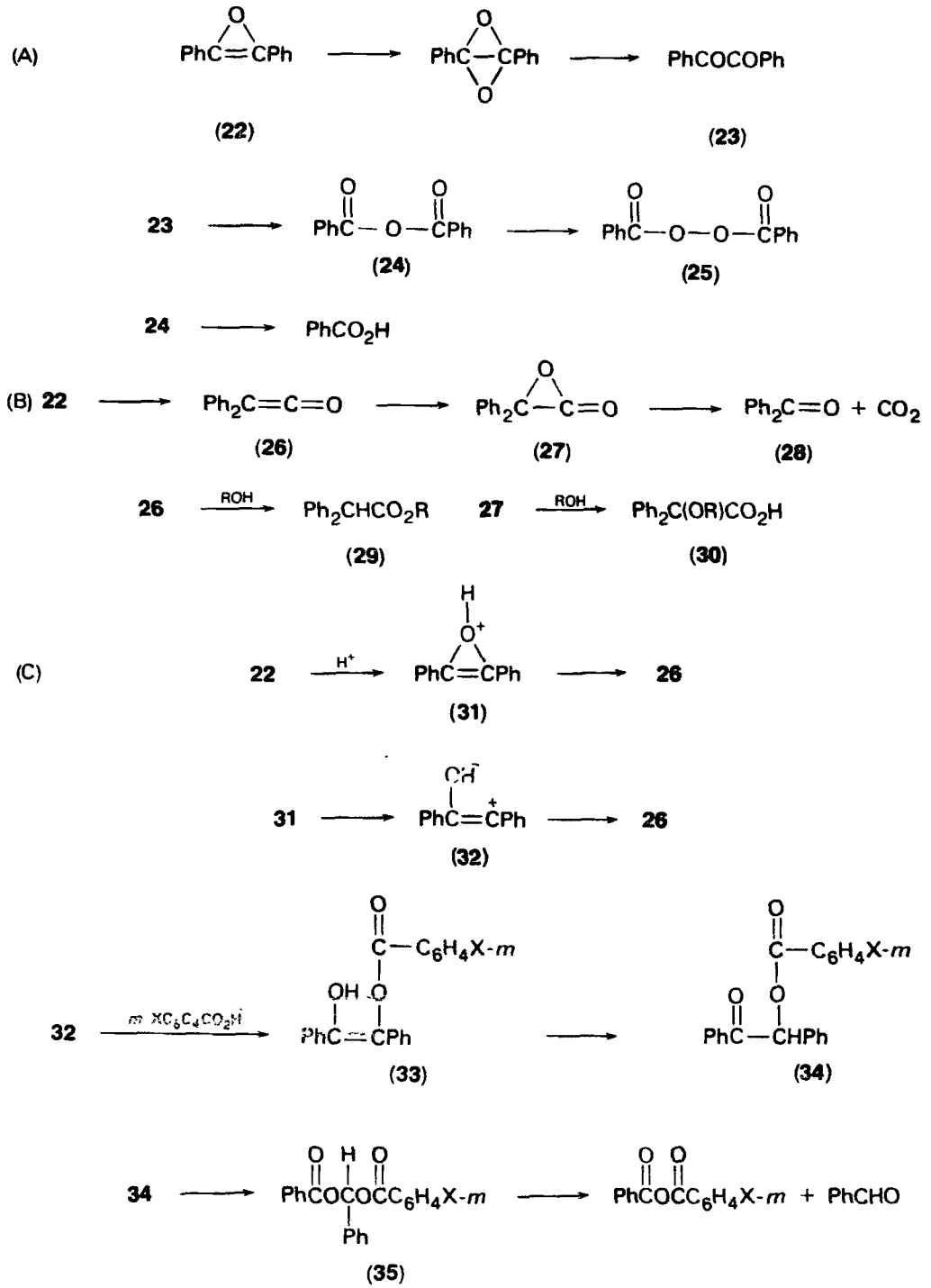
SCHEME 6

dipotassium oxirene-2,3-dicarboxylate, and whose NMR and IR spectra did not contradict such a structure. The oxirene was assumed to be formed via electrophilic addition of 'singlet' oxygen (oxgen atom) to the triple bond[108] (equation 8). Alternative dipolar and ketocarbene structures were considered and discarded.

(8)

Simultaneously with the above paper, another study of the peroxidation of diphenylacetylene in which slightly different results were reported appeared[161]. Diphenylacetylene was oxidized with peroxybenzoic, *m*-chloroperoxybenzoic and *p*-nitroperoxybenzoic acids in different solvents. 2,3-Diphenyloxirene (**22**) was regarded as the common intermediate leading to all the products observed. Its mechanistic fate was found to be sensitive to the polarity and acidity of the solvent. In acetic acid, *m*-chloroperoxybenzoic acid gave mainly benzoic acid and smaller amounts of benzil and *O*-acetylbenzoin. In benzene, with solid Na_2CO_3 present, the major products were benzophenone and *O*-benzoyl-*O'*-(*m*-chlorobenzoyl)dihydroxyphenylmethane (**35**). In ethanol as solvent, the main oxidation products were benzoic acid and ethyl diphenylacetate.

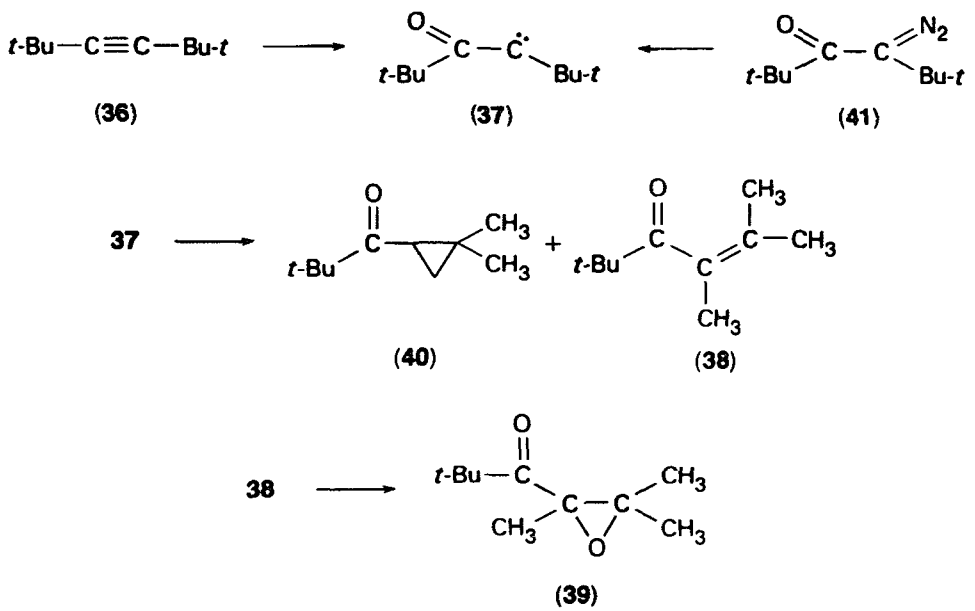
Identification of a total of eight intermediates and products (**23**, **25**, benzoic acid, **28**, **29**, **30**, **34**, **35**) led to the proposal of a detailed scheme of the possible transformations of the 2,3-diphenyloxirene intermediate. The products are of three distinct types, viz. those formed via cleavage (A) and rearrangement (B) of the intermediates or via addition to them (C). For oxidation with *m*-chloroperoxybenzoic (X = Cl) and peroxybenzoic (X = H) acids Scheme 7 is applicable. In Scheme 7(A) the common oxirene intermediate is oxidized further to give 2,4-diphenyl-1,3-dioxabicyclo[1.1.0]butane, which isomerizes to benzil (**23**), although the latter may also be produced by the oxidation of benzoin formed from **31** or **32** with


(A)
PhC=CPh
(22)
PhCOCOPh
(23)
23
(24)
(25)
24
PhCO2H
(B) 22
Ph2C=C=O
(26)
Ph2C—C=O
(27)
Ph2C=O + CO2
(28)
26
ROH
Ph2CHCO2R
(29)
27
ROH
Ph2C(OR)CO2H
(30)
(C)
22
H+
PhC=CPh
(31)
26
31
PhC=CPh
(32)
26
32
m-XC6H4CO3H
C—C6H4X-m
OH O
PhC=CPh
(33)
C—C6H4X-m
O O
PhC—CHPh
(34)
34
PhCOCOCOCC6H4X-m
Ph
(35)
PhCOCOCC6H4X-m + PhCHO

SCHEME 7

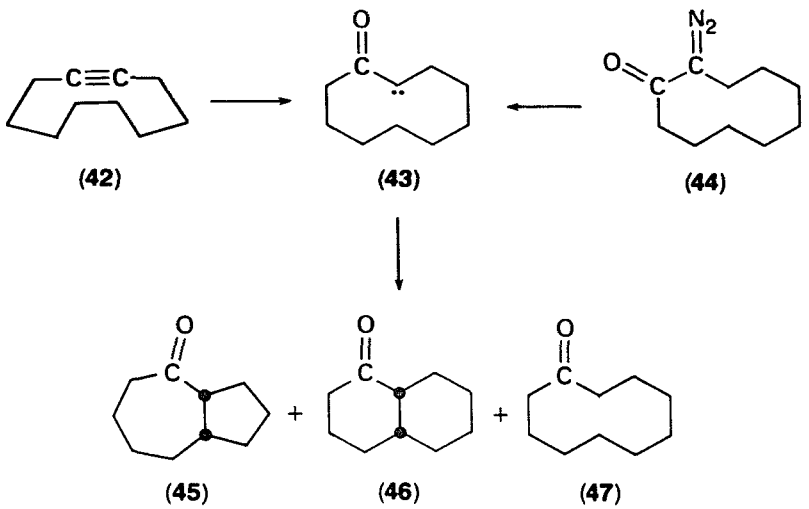
water. Oxidation of benzil followed by cleavage accounts for products **24** and **25**, as well as for benzoic acid. Rearrangement of the oxirene to the ketene **26**, followed by oxidation to the α-lactone **27** explains the formation of benzophenone (**28**). Diphenylacetic acid derivatives **29** and **30** are produced from the ketene intermediate via alcohol addition. The α-keto ester **34** and the product of its base-catalysed Baeyer–Villiger oxidation (**35**) are derived from **32**, which in turn is an isomer of the protonated oxirene **31**. Although this work provides no direct evidence for the oxirene intermediate, its formation receives strong support from the nature of the products identified. A conceivable alternative to oxirene would be an α-ketocarbene. However, this is not the case as α-ketocarbenes are known to produce α-keto ethers when generated in alcohol, and the peroxidation of diphenylacetylene gives no such products.

The oxidations of di-*t*-butylacetylene (**36**) and cyclodecyne (**42**) with *m*-chloroperoxybenzoic acid yield the first examples of product formation involving 1,2-methyl migration, cyclopropane formation and stereoselective 1,5- and 1,6-transannular insertion[32]. Thus the peroxidation of **36** gives the unsaturated ketone **38**, the epoxyketone **39** and the cyclopropyl ketone (**40**) (Scheme 8). The true ratio of **38** to **40**, corrected for the secondary oxidation product **39**, is exactly the same as in the thermal decomposition of the α-diazoketone **41**. The identical product distributions



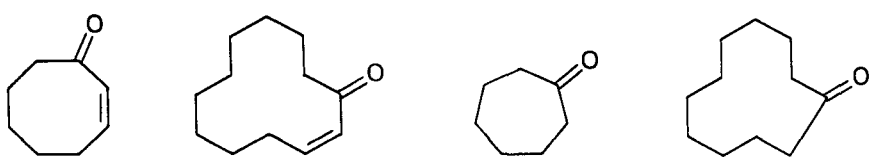
SCHEME 8

seem to favour an α-ketocarbene intermediate (**37**) over the oxirene structure discussed earlier, e.g. **22**. However, when the oxidation of cyclodecyne (**42**) was compared with the thermal decomposition of 2-diazocyclodecanone (**44**) (Scheme 9), the major products **45**, **46** and **47** were identical but their ratios were remarkably different. In terms of a ketocarbene intermediate (**43**), **42** affords mainly 1,5- and 1,6-transannular insertion products **45** and **46**, respectively, whereas the thermal decomposition of **44** yields primarily the 1,2-insertion product **47**. This behaviour was interpreted by assuming an equilibrium between the ketocarbene and the oxirene intermediates, as well as by different activation entropies for the insertion processes.



SCHEME 9

The possibilities offered by comparative studies on diazoketone decomposition and acetylene peroxidation have been explored further[36]. Cyclooctyne, cyclononyne, cyclodecyne and cyclododecyne were oxidized with *m*-chloroperoxybenzoic acid in methylene chloride, as well as with tetralin hydroperoxide—cyclohexyl metaborate or peroxybenzimidic acid. Cyclononyne and cyclodecyne gave mainly *cis*-bicyclic ketones (e.g. **45** and **46** for the latter), whereas cyclooctyne and cyclododecyne afforded primarily the α,β-unsaturated ketones **48** and **49**, in addition to ring-contracted ketones **50** and **51**, respectively. The thermal decomposition of the corresponding



2-diazocycloalkanones yielded an α,β-unsaturated ketone and a ring-contracted polymethyleneketene as main products. The results in the peroxy acid oxidation of acetylenes and the thermal aprotic decomposition of α-diazoketones were found to be consistent with α-ketocarbene intermediates or α-ketocarbenoid transition states. Several possible explanations were put forward to explain why these two reactions lead to identical products but in different relative amounts. For example, the α-ketocarbene intermediates from the two reactions may differ in conformation and energy. Alternatively, the α-diazoketone decomposition may involve concerted nitrogen departure and product formation without the intervention of free ketocarbene. Another possibility is the intramolecular trapping of the oxirene intermediate from cycloalkyne oxidation as opposed to α-diazoketone decomposition, which may not involve oxirenes. These mechanistic paths may also operate simultaneously.

The rate of oxidation of substituted phenylacetylenes (PA) by peroxybenzoic acid (PBA) has been measured in benzene as solvent, at 25°C[119]. The rate law was found to be:

$$\text{rate} = k[\text{PA}][\text{PBA}]$$

k varying in the range of 1×10^{-4}–1×10^{-6} $\text{M}^{-1}\text{s}^{-1}$ at 25°C as a function of the ring substituent.

The two reactants are consumed in a 1:1 molar ratio. The addition of the more polar ethanol was found to decrease the rate, presumably due to breakdown of intramolecular hydrogen bonding in the peroxy acid. However, the rate in ethanol–water is higher than in benzene–ethanol, indicating that more polar solvents hydrogen-bonded to PBA increase the rate, as does decreased solvent basicity. The relative rates for ring-substituted phenylacetylenes give a reasonably good Hammett plot with a ρ value of -1.40, indicating electrophilic attack of the peroxy oxygen on the triple bond to form an oxirene intermediate. The ratio of the ρ values for the PBA oxidation of phenylacetylenes and styrenes is 1.08, and that for the proton-catalysed hydration of these two compounds is 1.12. The similarity of the relative ρ values was interpreted as indicating similar polar effects in peroxidation and protonation. Phenylacetylenes are about 60 times less reactive toward PBA than the corresponding styrenes.

New evidence for the involvement of oxirene (rather than α-ketocarbene) intermediates in the peroxy acid oxidation of acetylenes has been obtained from the close linear correlation between the logarithms of the rate constants of 4-octyne and cyclohexene peroxidation in different solvents[81]. Olefin oxidation with peroxy compounds leads to an oxirane (epoxide), a fact which is the original source of the assumption that oxirenes are intermediates in acetylene peroxidation. The linear free-energy relationship found has a slope of 1.0, indicating identical roles of the solvent in the two oxidations. The only important solute–solvent interactions are those involving the peroxy acid in the initial and transition state. As the solvation energies of the neutral 4-octyne and cyclohexene are presumably small and essentially equal to each other, the transition state for acetylene peroxidation must closely resemble that of olefin epoxidation. In other words, the outer, electrophilic peroxy oxygen is captured by the π electrons of the acetylene or the olefin in a completely analogous fashion, which requires an oxirene-type transition state for the triple bond. The unstable oxirene intermediate is rapidly converted to isolable products and these transformations may involve α-ketocarbenes as subsequent intermediates. It seems that the formation of oxirene intermediates in the peroxy acid oxidation of acetylene derivatives is firmly established.

2. t-Butyl hydroperoxide

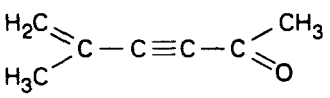
Similarly to the well-known metal-complex-catalysed oxidation of olefins, acetylenes can be expected to react with organic hydroperoxides. In connection with the oxirene versus ketocarbene problem of alkyne peroxidation, the $Mo(CO)_6$-catalysed oxidation of diphenylacetylene by *t*-butyl hydroperoxide has been investigated[107]. This work was prompted by the known effect of metal salts on the rate of decomposition of diazoketones[55,183], which suggests the possible involvement of metal–carbene complexes. It has been found[107] that upon this type of oxidation, diphenylacetylene yields mainly benzil and benzoic acid derivatives but the Wolff-rearranged diphenylacetic acid structure is conspicuously absent, in contrast to peroxy acid oxidations[108,161]. Likewise, 1-(4-methoxyphenyl)-2-phenylacetylene has shown no aryl migration upon the same treatment. Since a Wolff rearrangement would

be expected if oxirene intermediates were involved, these results favour the intermediacy of molybdenum–oxocarbene complexes.

In contrast to $Mo(CO)_6$-catalysed oxidations by *t*-butyl hydroperoxide, the triple bond remains intact if SeO_2 is used as a catalyst[21]. In a detailed study of a series of internal acetylenes, α,α′-dioxygenation has been shown to be a general phenomenon. Depending on the type of α- and α′-carbons, the reactivity sequence is $CH_2 \approx CH > CH_3$. The reaction presumably occurs via an α-hydroxy intermediate, which may be converted to α,α′-dihydroxy, α-oxo-α′-hydroxy and α-oxo derivatives in various proportions, as illustrated by the transformations of 2-decyne in dichloromethane at room temperature (equation 9). Exclusive formation of the

$$\begin{aligned} CH_3(CH_2)_6C{\equiv}CCH_3 \longrightarrow\ & CH_3(CH_2)_5CH(OH)C{\equiv}CCH_3\ (70\%) + \\ + & \ CH_3(CH_2)_5COC{\equiv}CCH_3\ (9\%) + \\ + & \ CH_3(CH_2)_5CH(OH)C{\equiv}CCH_2OH\ (20\%) + \\ + & \ CH_3(CH_2)_5COC{\equiv}CCH_2OH\ (1\%) \end{aligned} \qquad (9)$$

α,α′-diol is observed with cyclododecyne, whereas 2-methyl-3-hexyne affords a mixture of the α- and α′-monohydroxy derivatives, together with enynone **52** which is formed in considerable yield. Products similar to **52** are generally observed with acetylenes bearing an α-methylene and an α-methyne substituent. The enynone is presumably due to dehydration at the diol and/or the ketol stage.



(52)

3. *Hydrogen peroxide*

This oxidant has been applied in fewer instances than peroxy acids and less information is available on the corresponding oxidation mechanism.

A series of alkynes of the general formula R—C≡C—X (X = CO_2H, CO_2Et, COPr, COPh, COC_6H_4Cl-*p*, SO_2Ph, Ph; R = H, Ph) was oxidized with alkaline H_2O_2[99]. Cleavage of both the triple bond and the C—X bond was observed, producing the corresponding carboxylic acid and CO_2. Benzenesulphonic acid was formed with X = SO_2Ph. When the oxidation was carried out with *t*-butyl hydroperoxide or cumene-7-hydroperoxide, essentially the same products were formed.

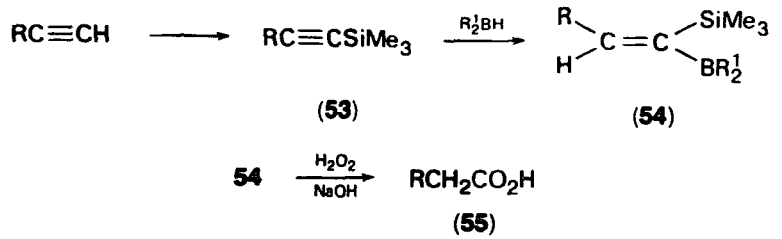
The cleavage of the C—X bond for R = H, X = CO_2H and CO_2Et involves attack of the HO_2^- group on the carboxylate of the ethoxycarbonyl group with displacement of an acetylide ion.

In the case of ketoalkynes and the sulphoalkyne studied, a nucleophilic attack of the HO_2^- ion on the triple bond is assumed. The vinyl carbanion formed is stabilized by elimination of OH^- to the corresponding oxirene (equation 10). Formation of the observed products can be explained by rearrangement and cleavage of the oxirene intermediate.

A method which involves oxidation by alkaline H_2O_2 has been utilized to transform 1-alkynes, alk-3-en-1-ynes and 3-hydroxy-1-alkynes to substituted acetic acids, β,γ- and α,β-unsaturated acids[184], respectively. No cleavage of the carbon chain occurs and

$$RC{\equiv}CX + HO_2^- \longrightarrow RC(O){=}CX + OH^- \quad (10)$$

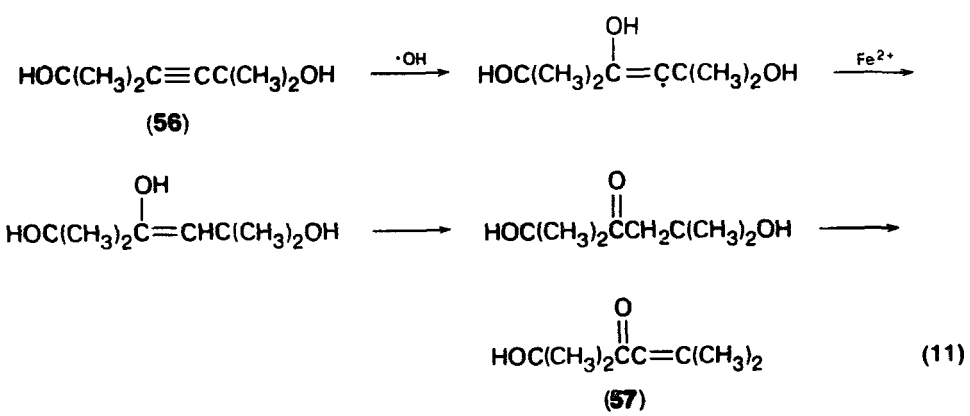
the resulting acids contain the same number of carbon atoms as do the starting alkyne derivatives. The essence of this novel method (Scheme 10) is silylation of the alkyne to produce 1-alkynyl(trimethyl)silane (**53**), which is then reacted with dicyclohexylborane to yield 1-boryl-1-silylalkenes (**54**). These can be readily oxidized to the corresponding carboxylic acids (**55**) with alkaline H_2O_2.



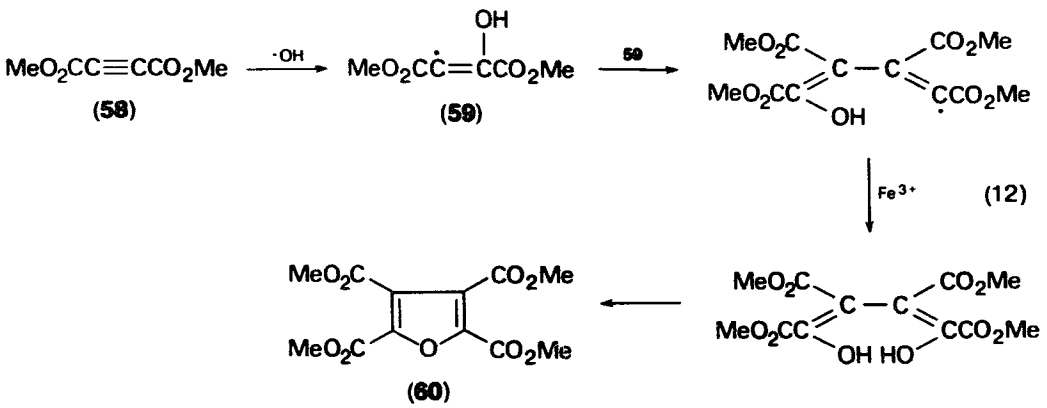
SCHEME 10

4. Fenton's reagent

As indicated by the pulse radiolysis of aqueous acetylene solutions[33], hydroxyl radicals add readily to the triple bond. The transformations of various acetylenes, occurring in the presence of Fenton's reagent ($Fe^{2+} + H_2O_2$), has revealed that β-hydroxyvinyl radicals are the first intermediates of the attack of •OH radicals on alkynes[174]. These intermediates are susceptible to both reduction and oxidation, leading to the final products observed. Upon treating acetylene with Fenton's reagent acetaldehyde is the main product, due to reduction of β-hydroxyvinyl radicals by Fe^{2+}. In the presence of added Cu^{2+}, the major product is glycolaldehyde, which is formed via oxidation of the intermediate radical by Cu^{2+}. Fe^{3+} is not capable of this type of oxidation. Propargyl alcohol gives dihydroxyacetone in the presence of Cu^{2+}. 2,5-Dihydroxy-2,5-dimethyl-3-hexyne (**56**) is converted to 2,5-dimethyl-2-hydroxyhex-4-en-3-one (**57**) presumably via reduction of the vinyl radical intermediate, followed by dehydration (equation 11). Cu^{2+} ions show but a small effect on this reaction. Dimethyl acetylenedicarboxylate (**58**) gives a small amount of tetramethyl furantetracarboxylate (**60**), whose yield is increased in the



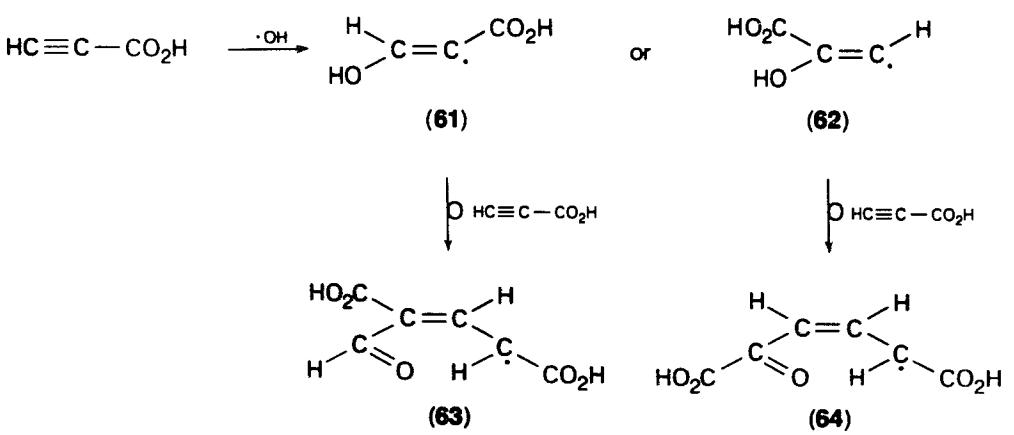
presence of added Fe^{3+}. This is ascribed to oxidation of an intermediate radical by Fe^{3+} (equation 12).



(12)

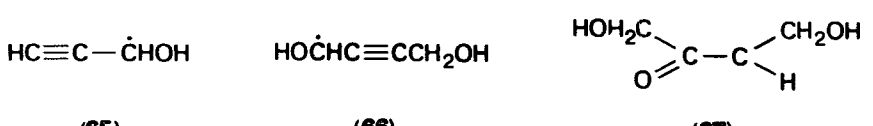
5. *Titanium(III) + H_2O_2*

The attack of •OH radicals on alkyne derivatives has been studied by the ESR technique in a flow system[43]. Hydroxyl radicals are generated by the Ti(III)–H_2O_2 system in aqueous solution. Attack of hydroxyl on propynoic acid gives two isomeric radicals **61** and **62**, which after reacting with a second alkyne molecule and subsequent 1,5-hydrogen shift afforded the allylic radicals **63** and **64** (Scheme 11).



SCHEME 11

Under the same conditions, propargyl alcohol gives the radical **65** via hydrogen-atom abstraction, but butyne-1,4-diol yields radicals formed by both hydrogen-atom abstraction (**66**) and •OH addition (followed by 1,3-hydrogen shift) (**67**). Two radicals have been identified from butynedioic acid too, a pH effect also being observed.



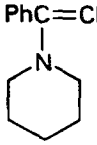
6. *Nickel peroxide*

A convenient route to α-ketoalkynes is the oxidation of acetylenic alcohols and glycols by nickel peroxide[61]. The active reagent is prepared by treatment of nickel hydroxide with sodium hypochlorite and subsequent removal of water from the raw black solid by azeotropic distillation with benzene. For example, 1,3-diphenyl-2-propyn-1-ol gives 1,3-diphenyl-2-propyn-1-one in 90.8% yield. The acetylenic diol **68** affords the corresponding dione (**69**) (equation 13). If the oxidation

$$\underset{\textbf{(68)}}{\text{PhCH(OH)C}\equiv\text{CCH(OH)Ph}} \longrightarrow \underset{\textbf{(69)}}{\text{PhCOC}\equiv\text{CCOPh}} \qquad (13)$$

is carried out in the presence of secondary amines (e.g. piperidine), addition of the latter across the triple bond leads to the β-aminovinyl ketone **70** (equation 14). Primary α-acetylenic alcohols (**71**) are converted to the corresponding substituted propiolic acids (**72**) (equation 15). The triple bond is remarkably resistant to oxidation by this reagent.

$$\text{PhC}\equiv\text{CCH(OH)Ph} \xrightarrow[NiO_2]{\text{piperidine}} \text{PhC}=\text{CHCOPh} \qquad (14)$$



(70)

$$\underset{\textbf{(71)}}{\text{PhC}\equiv\text{CCH}_2\text{OH}} \longrightarrow \underset{\textbf{(72)}}{\text{PhC}\equiv\text{CCO}_2\text{H}} \qquad (15)$$

C. Oxidative Coupling of Acetylenes

Interest in the chemistry of polyacetylenes has led to the development of synthetic methods consisting of the oxidative coupling of terminal acetylenes and some of their derivatives. This type of reaction is an intermolecular dehydrogenation, discovered more than a hundred years ago by Glaser[63,64] with phenylacetylene (equation 16). The

$$2\ \text{PhC}\equiv\text{CH} \xrightarrow[\text{air}]{Cu^{+}/NH_4OH} \text{PhC}\equiv\text{C}-\text{C}\equiv\text{CPh} \qquad (16)$$

reaction was carried out in two stages. The cuprous derivative formed in the first stage was oxidized to the diyne in the second phase. The Glaser coupling has found wide synthetic applications, mostly in preparing symmetrical polyacetylenes.

The oxidation of acetylenes by copper(II) salts in pyridine[44] is also useful for the synthesis of symmetrical polyacetylenes (equation 17). Unsymmetrical coupling can

$$2\ \text{RC}\equiv\text{CH} \xrightarrow{Cu^{2+}/\text{pyridine}} \text{RC}\equiv\text{C}-\text{C}\equiv\text{CR} \qquad (17)$$

be achieved by reacting haloacetylenes with terminal acetylenes[31] (equation 18), which, however, is not an oxidative process.

Excellent reviews are available on various oxidative couplings of acetylene derivatives, to which the reader is referred for experimental details and actual syntheses[18,116].

There are many versions of Glaser coupling, differing primarily in the oxidants

$$RC{\equiv}CH + BrC{\equiv}CR^1 \xrightarrow{Cu^+/amine} RC{\equiv}C{-}C{\equiv}CR^1 \quad (18)$$

employed. In addition to air and O_2, $CuCl_2$ and $K_3Fe(CN)_6$ are the most widely used oxidants. The copper(II) salt in the Eglinton coupling of terminal acetylenes is invariably $Cu(OCOMe)_2$ in pyridine; the copper(I) derivative of the alkyne seems to be the reaction intermediate.

Symmetrical oxidative coupling of acetylene sodium or Grignard derivatives (equation 19) can be performed in the presence of oxidants such as iodine[7,11],

$$2\,RC{\equiv}CM \xrightarrow{oxidation} RC{\equiv}C{-}C{\equiv}CR \quad (19)$$

$$M = Na \text{ (in liq. } NH_3), MgBr$$

copper(II) salts[6], cobalt(III) salts[11], potassium permanganate[46] and potassium manganate[143].

Catalytic amounts of copper(I) amine complexes have been found to be very efficient catalysts for oxidative coupling of acetylenes at room temperature under air or dioxygen[71]. Pyridine can serve as both ligand and solvent. The reaction has been demonstrated with phenylacetylene. *m*-Diethynylbenzene is oxidized to a pale yellow polymer; a similar reaction occurs with *p*-diethynylbenzene.

The first attempt to give a mechanism for the oxidative coupling[95] implicated alkynyl radicals according to Scheme 12, where R = Me_2COH.

$$RC{\equiv}CH \rightleftharpoons RC{\equiv}C^- + H^+$$

$$RC{\equiv}C^- + Cu^{2+} \longrightarrow RC{\equiv}C\cdot + Cu^+$$

$$2\,RC{\equiv}C\cdot \longrightarrow RC{\equiv}C{-}C{\equiv}CR$$

SCHEME 12

Using a homogeneous solution of propargyl alcohol and a buffer to control the pH, kinetic studies[34] of the copper(II) acetate oxidation in the absence of air in pyridine reveals the autocatalytic character of the reaction. Eventually, a zero-order reaction with respect to copper(II) is observed. The rate of oxidation depends in a complex manner on the copper(I) and propargyl alcohol concentration, which suggests π-complex formation between Cu^+ and the acetylene derivative[34] (equation 20). This

$$RC{\equiv}CH + CuOAc \rightleftharpoons \underset{\underset{CuOAc}{\downarrow}}{H{-}C{\equiv}C{-}R} \quad CuOAc \quad (20)$$

simultaneous equilibrium is assumed to decrease the actual reactant concentrations available for the reaction shown in Scheme 13. Additional coordination of pyridine occurs in an unspecified fashion to all the copper species shown. The copper acetylide $R{-}C{\equiv}C{-}Cu$ does not accumulate (and is not precipitated), thus supporting its reversible formation. Assuming a steady-state concentration of this key intermediate, a rate equation in accord with the experimental findings can be derived. Coupled

$$RC{\equiv}CH + B \rightleftharpoons RC{\equiv}C^- + BH^+ \quad \text{(slow)}$$

$$RC{\equiv}C^- + CuOAc \rightleftharpoons RC{\equiv}C{-}Cu + OAc^- \quad \text{(slow)}$$

$$RC{\equiv}C{-}Cu + CuOAc \longrightarrow RC{\equiv}C\cdot + 2\,CuOAc \quad \text{(fast)}$$

$$2\,RC{\equiv}C\cdot \longrightarrow RC{\equiv}C{-}C{\equiv}CR \quad \text{(fast)}$$

SCHEME 13

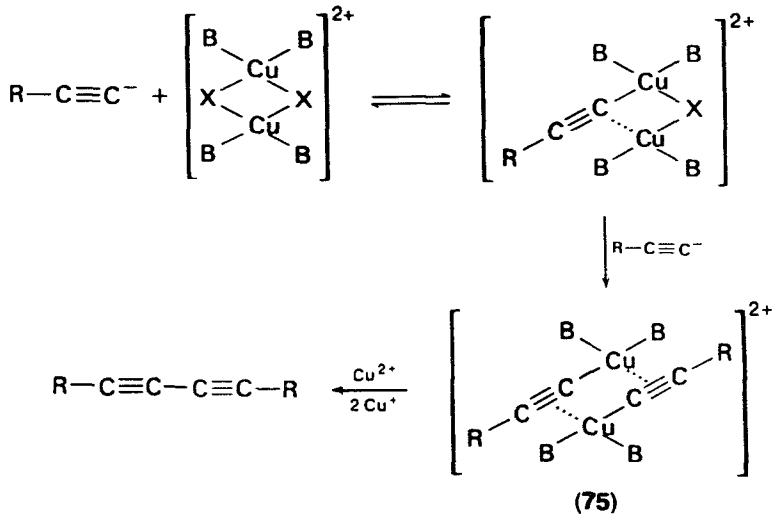
π-complex formation eliminates simple first-order dependence on the alkyne concentration. The actual oxidation step seems to be an electron transfer from copper(I) acetylide to copper(II) acetate, which apparently occurs via an acetato bridge. No evidence other than consistency with the kinetic results was provided for the assumed slowness of R—C≡CH deprotonation and the nucleophilic attack of R—C≡C⁻ on CuOAc.

The early mechanism proposed by Klebanskii and coworkers.[95] (Scheme 12) has also been criticized on the basis of results emerging from a study of the effect of acetylene structure on the mechanism of oxidative dimerization[12]. The authors of this study were apparently unaware of the paper by Clifford and Waters[34], which is closely related to the problems discussed by them. (The half-lives of the dimerization of a number of substituted mono- and di-acetylenes have been measured[12] in 80% methanol, using the chloroethanolaminecopper(I) complex and copper(II) chloride in various proportions but always in excess.) At pH 3, spectrophotometric measurements indicated that dimerization is second-order in the acetylene. The half-life was found to increase strongly on increasing the number of conjugated triple bonds. Surprisingly, under Eglinton's conditions, i.e. in pyridine as solvent, the half-life varied in the opposite direction: dimerization was much faster for compounds having a greater number of conjugated triple bonds. It was concluded that different mechanisms are operative in acidic and alkaline media. Copper(I) was assumed to form π complexes with the alkynes (an idea proposed earlier by Clifford and Waters[34]), in which the mobile hydrogen atom is more acidic than in the corresponding acetylene (equation 21). If the formation of the anion is favoured, oxidative dimerization, occurring via

$$\underset{\substack{\downarrow \\ Cu^+}}{RC{\equiv}CH} \rightleftharpoons \underset{\substack{\downarrow \\ Cu^+}}{R{-}C{\equiv}C^-} + H^+ \qquad (21)$$

(73) (74)

this species, becomes faster. The π-complexed anion is responsible for the reaction in acidic medium, where proton dissociation of the acetylenes is suppressed. In alkaline media, dimerization is due to both the free and Cu^+-complexed anion, as indicated by the accelerating effect of added Cu^+. The second-order kinetics in the alkyne, persisting at large Cu^{2+} excess too, must be due to the formation of a dinuclear copper(II) complex with the alkyne (**75**) (Scheme 14) which affords the dimer. In acidic solutions, the reactant R—C≡C⁻ is replaced by the π complex **73** or **74**. The formation of **75** is supported by the observation of ring-closure with terminal diacetylenes having a sufficiently long chain to permit the facile approach of the terminal C≡C groups. When mixtures of two acetylenes are reacted, symmetrical products predominate if the reactivities are largely different. Similar reactivities lead to considerable amounts of asymmetric coupling products.



(75)

B = ethanolamine, pyridine

SCHEME 14

The kinetics of the oxidative coupling of phenylacetylene in the presence of copper(II) in N_2 atmosphere have been studied with the aim of establishing the mechanism in the absence of dioxygen[48]. The measurements were carried out spectrophotometrically in pyridine solvent, controlling the acidity with added Et_3N–CH_3CO_2H buffer. The rate of disappearance of copper(II) was found to be independent of the copper(I) concentration, and the following rate expression was established:

$$\frac{d[Cu^{2+}]}{dt} = kK^2[Cu^{2+}]^2[PhC{\equiv}CH]^2/[H^+]^2$$

where k is a rate constant and K is a composite equilibrium constant (cf. mechanism). The mechanism proposed on the basis of the kinetic law is shown in Scheme 15. In this scheme displacement of a coordinated pyridine (py) by phenylacetylene leads to a complex (**76**) that by dissociation of a proton produces **77**, which can be oxidized via electron transfer to copper(II). The two equilibria ($K = K_1K_2$) control the concentration of **77**, whose oxidation is rate-determining. This mechanism discards

$$Cupy^{2+} + PhC{\equiv}CH \overset{K_1}{\rightleftharpoons} Cu^{2+}(PhC{\equiv}CH) + py$$

(76)

$$\mathbf{76} \overset{K_2}{\rightleftharpoons} Cu^{2+}(PhC{\equiv}C^-) + H^+$$

(77)

$$2\,\mathbf{77} \xrightarrow{k} 2\,Cu^+ + PhC{\equiv}C{-}C{\equiv}CPh$$

SCHEME 15

Ph—C≡C· radicals as intermediates. It is argued that hydrogen-atom abstraction from phenylacetylene is highly endothermic and thus would apparently require prohibitively large activation energies, which seems in contrast with the observed value of 21 kcal/mol. The above mechanism is quite similar to that suggested by Bohlmann and coworkers.[12]

The kinetic studies of the oxidative coupling have been extended by Fedenok, Berdnikov and Shvartsberg to a number of various acetylenes[48]. In the absence of O_2, the kinetic behaviour found for phenylacetylene is also valid for its *para*-substituted derivatives such as *p*-methoxy-, *p*-methyl-, *p*-fluoro-, *p*-phenyl-, *p*-bromo- and *p*-carbomethoxy-phenylacetylene. The apparent first-order rate constant increases in the above order from 2.43 min^{-1} to 66.5 min^{-1}. This sequence also represents the order of increasing acidity of the acetylenic hydrogen, in support of the mechanism proposed for phenylacetylene. In addition to the *para*-substituted phenylacetylene derivatives, the validity of the mechanism involving deprotonation and complex formation has also been demonstrated for 1-heptyne, 1,1-diethoxy-4-butyne, 1,3,5-trimethyl-4-ethynylpyrazole and 3-phenyl-1-butyn-3-ol.

In an atmosphere of dioxygen, oxidative coupling is a catalytic reaction. The role of O_2 may be restricted to the reoxidation of copper(I), i.e. regeneration of the catalyst[49]. In the case of phenylacetylene, the catalytic coupling was found to be zero order with respect to O_2 above a critical dioxygen pressure. Under zero-order conditions, the same kinetic law found earlier for the copper(II) oxidation of phenylacetylene is valid[48]. Although, under otherwise identical conditions (Et_3N–CH_3CO_2H buffer in pyridine), the reaction in O_2 is somewhat slower than is the copper(II) oxidation, the essential identity of the two mechanisms has been concluded. ESR measurements have shown that a limiting copper(II) concentration is already reached at rather low dioxygen pressures. Consequently, some copper must be in the +1 oxidation state, suggesting some involvement of Cu^+ in the reaction mechanism.

Subsequent studies by the same authors[50] provide further support for the importance of copper(I) in the oxidative coupling of phenylacetylene, and suggest modification of the mechanism proposed originally[48]. In pyridine, in the absence of buffer, the initial rate has a maximum at a dioxygen pressure which depends on the temperature and the phenylacetylene concentration. The order with respect to phenylacetylene varies from about 1.5 at low concentrations to zero at higher ones. The order with respect to the catalyst (CuCl) also changes from second at low concentrations, to a fractional order (less than unity) at higher concentrations. This kinetic behaviour is quite different from that reported for phenylacetylene oxidation under N_2 by copper(II) in the presence of buffer and also contrasts the kinetics observed for the catalytic coupling in the presence of dioxygen and a buffer[48]. The mechanism shown in Scheme 16, which apparently reflects the present views of these authors, implicates copper (I) acetylide as an important intermediate. Here Cu(II)* is an oxygen-containing copper(II) complex, which, together with a chlorocopper(II) complex, is the product of copper(I) oxidation. This scheme receives support from the observed rapid oxidation of copper(I) acetylide by copper(II).

A kinetic study of the oxidative coupling of propargyl alcohol in the presence of copper(II) acetate in buffered pyridine solutions[51] indicates two reaction paths, one involving and the other not involving copper(I). The addition of water controlled the relative contribution of the two paths.

Similarly to the oxidative coupling (dimerization) of terminal monoalkynes, α,ω-diacetylenes can be converted to a wide variety of large-ring unsaturated compounds using copper(I) chloride and ammonium chloride or copper(II) acetate in pyridine[44,45,157].

For example, treatment of 1,5-hexadiyne (**80**) with copper(II) acetate in pyridine at

$$CuCl_n^{1-n} + O_2 \longrightarrow CuCl_n^{2-n} + Cu(II)^*$$

$$2\ PhC{\equiv}CH + 2\ CuCl_n^{1-n} + Cu(II)^* \rightleftharpoons 2\ PhC{\equiv}CCu(I) + CuCl_n^{2-n} + H_2O$$

$$2\ PhC{\equiv}CCu(I) \rightleftharpoons [PhC{\equiv}CCu(I)]_2$$

(78)

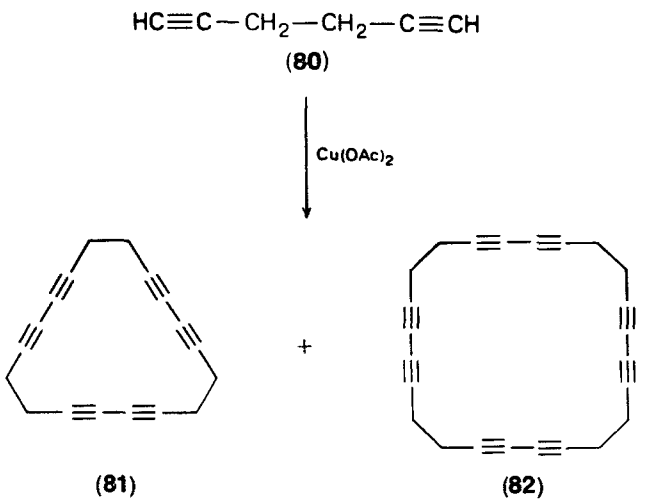
$$78 + 2\ CuCl_n^{2-n} \longrightarrow [PhC{\equiv}CCu(I)]_2 + CuCl_n^{1-n}$$

(79)

$$79 \longrightarrow PhC{\equiv}C{-}C{\equiv}CPh + 2\ Cu(I)$$

SCHEME 16

55°C affords, among other products, the cyclic trimer (**81**), tetramer (**82**), pentamer and hexamer in a total of 21%[157,158] (equation 22).



(22)

Oxidative cyclization must be similar in mechanism to oxidative dimerization. The occurrence of cyclization has been used to demonstrate the necessity of formation of a dinuclear copper(II) complex involving two bridging acetylenide ligands[12]. The chemistry of cyclic acetylenes has been reviewed[98].

D. Oxidations with Nonmetallic Compounds

1. *Nitric acid*

In the presence of palladium nitrate as catalyst, acetylene can be oxidized to oxalic acid by 48% nitric acid[100]. The optimum temperature for the reaction is 24°C, above which oxidation to CO_2 becomes predominant. No mechanistic information is available on this reaction.

2. N-*Chlorosuccinimide*

Acetylenes have been found to react with *N*-chlorosuccinimide (NCS) in methanol to give α,α-dichlorodimethylketals (**83**) in good yield[138] (equation 23). The reaction leads to one major product except with unsymmetrically disubstituted acetylenes. For example, 2-pentyne gives both 2,2-dichloro-3,3-dimethoxypentane and 2,2-dimethoxy-3,3-dichloropentane. The reaction is feasible with propyne, 1-butyne,

$$R^1C{\equiv}CR^2 \xrightarrow[NCS]{MeOH} R^1{-}\underset{\displaystyle MeO}{\overset{\displaystyle MeO}{\overset{|}{\underset{|}{C}}}}{-}\underset{\displaystyle Cl}{\overset{\displaystyle Cl}{\overset{|}{\underset{|}{C}}}}{-}R^2 \qquad (23)$$

(83)

R^1 = alkyl, aryl

R^2 = alkyl, H

2-butyne, 1-pentyne, 1-hexyne, 3-hexyne and phenylacetylene and it occurs readily at room temperature. Small amounts of the dichloroketone are also detected. The dichloroketals **83** can be hydrolysed with dilute hydrochloric acid to produce α,α-dichloroketones (**84**) (equation 24).

$$\mathbf{83} \xrightarrow{HCl} R^1COCCl_2R^2 \qquad (24)$$

(84)

Similar products were obtained when *t*-butyl hypochlorite was added to a methanolic solution of 1-butyne, 2-butyne, 1-pentyne, 1-hexyne and phenylacetylene[138]. By analogy to the reaction of *t*-butyl hypochlorite with olefins[3], the mechanism of oxidation by both NCS and *t*-butyl hypochlorite is interpreted as involving an electrophilic attack of a positively charged chlorine species (Cl^+) on the triple bond to produce a β-chlorovinyl ether (**86**) (equation 25). This species is, however, rarely isolable but not unknown[171] under chlorination conditions. The

$$RC{\equiv}CH \xrightarrow{Cl^+} [\overset{+}{R}C{=}CHCl] \xrightarrow[\text{or } MeO^-]{MeOH} \underset{\displaystyle OMe}{\overset{\displaystyle OMe}{\overset{|}{\underset{|}{RC}}}}{=}CHCl \qquad (25)$$

(85) **(86)**

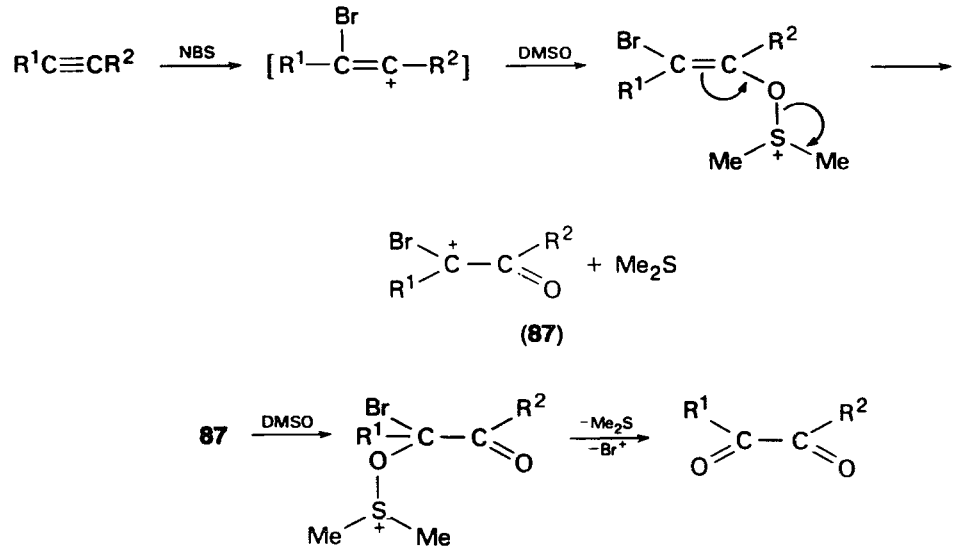
$$\mathbf{86} \xrightarrow{Cl^+} \underset{\displaystyle OMe}{\overset{\displaystyle +}{\overset{|}{\underset{|}{RC}}}}CHCl_2 \xrightarrow[\text{or } MeO^-]{MeO} RC(OMe)_2CHCl_2 \qquad (26)$$

reaction is completed by two similar steps starting from **86** (equation 26). The analogous bromo products are formed when acetylenes are reacted with hypobromous acid or with *N*-bromosuccinimide[128,182].

3. N-*Bromosuccinimide-induced oxidation by DMSO*

The idea of the intermediate formation of a halovinyl cation of the type **85** has been supported by subsequent work aimed at trapping **85** with DMSO[181] in the reaction of

acetylenes with *N*-bromosuccinimide (NBS). These experiments have led to the discovery of NBS-induced oxidation by DMSO. For example, diphenylacetylene is converted to benzil in 98% yield at room temperature in DMSO. Only traces of this product are detected with stoichiometric DMSO in other solvents such as methylene chloride, benzene, CCl_4 or dioxane. The proposed reaction sequence is as shown in



SCHEME 17

Scheme 17. This reaction takes place also with 2-butyne, phenylacetylene and diphenylbutadiyne (**88**), the latter affording diphenyltetraketone (**89**) (equation 27).

$$\underset{\textbf{(88)}}{Ph{\equiv}C{-}C{\equiv}CPh} \xrightarrow[DMSO]{NBS} \underset{\textbf{(89)}}{PhCOCOCOCOPh} \qquad (27)$$

4. *Halogens*

Traditionally, the reaction of olefins and acetylenes with molecular halogens is regarded as addition and is treated accordingly in textbooks and reviews. The situation is similar concerning halogen substitution with Br_2 and Cl_2. The oxidative nature of these reactions is however clear if the conventions for establishing the formal oxidation states of elements in organic compounds are given due consideration[77]. As the electronegativities of F, Cl and Br are greater than that of C, the introduction of any of these atoms involves oxidation of the carbon atom to which they are attached. Consequently, the compounds concerned undergo oxidation. The addition of HX across multiple carbon–carbon bonds is *not* oxidation as the overall oxidation state does not change. In view of these considerations, the halogenation of acetylenes has been included into this chapter. Several reviews have appeared on electrophilic additions to acetylenic compounds[42a,144,180].

The halogenation of acetylenes usually proceeds readily at or below room temperature, resulting in the formation of various halogeno-alkenes and -alkanes. By varying the experimental conditions (solvent, temperature, additives, light) the

isomeric composition of the products can be influenced. Mechanistic information is available from kinetic studies and investigation of the isomer distribution.

The rates of halogen additon (Cl_2 and Br_2) have been measured for several olefins and acetylenes having closely related structures[139]. In acetic acid medium, the olefins were found to be more reactive by factors varying between 23 (1-benzoyl-2-*o*-chlorophenylethylene vs. 1-benzoyl-2-*o*-chlorophenylacetylene) and 5×10^4 (oleic acid vs. stearolic acid). It was concluded from these data that acetylenic compounds may add bromine by either a nucleophilic or an electrophilic mechanism, depending on the substituents on the alkyne. Strongly electron-withdrawing groups favour nucleophilic attack, whereas electron-releasing substituents favour electrophilic attack. Catalysis by lithium chloride and bromide, and the superiority of the latter also support this conclusion.

The mechanistic conclusions emerging from studies on the halogenation of higher conjugated polyynes also indicate a strictly nucleophilic addition[13]. The rate of halogen addition was found to increase with increasing number of triple bonds in the chain, which parallels the trend observed for the nucleophilic addition of alcohols to these compounds. The possibility of radical reactions was excluded.

At this stage it should be pointed out that the addition of bromine to triple bonds had been regarded as an electrophilic reaction, mainly on the basis of an assumed analogy to olefin bromination. Practically no experimental evidence was available to support this view, which had been a 'textbook statement' until it was challenged by Bohlmann and coworkers[13] and Sinn and coworkers[155].

Elaborate work on bromine addition to symmetrically substituted stilbene and tolane (diphenylacetylene) derivatives[155] lends further support to the nucleophilic nature of these reactions. These symmetrical compounds were chosen in order to ensure that both carbons of the triple bond assumed the same degree of cationic character under the influence of electron-attracting substituents in the *p* and *p'* positions. A difference in the substituent effects would have led to ambiguities in assigning the nature of the reaction centre. The probe for elucidating the mechanism involved was the comparison of the activation energies for identically substituted members of the stilbene and tolane series. In bromobenzene as solvent, the kinetic equation for the bromination was found to be

$$-\mathrm{d}[Br_2]/\mathrm{d}t = k[\text{alkyne}][Br_2]^2$$

for all of the alkynes studied, and activation energies were derived from this equation. It was assumed that the activation energy can be represented in the two series of reactions as

$$E_{d,S} = abE_d$$

and

$$E_{t,S} = a'bE_t$$

where E_d and E_t are the activation energies for a selected pair of identically substituted stilbenes and tolanes (taken as reference pair), $E_{d,S}$ and $E_{t,S}$ are the activation energies for a given substituted stilbene and tolane, respectively, b is a factor accounting for the effect of polarizability, which is supposed to be identical in the two series, and a and a' are proportionality factors apparently characterizing the inherent sensitivity toward substitution in the two series. The ratio of the relative activation energies is:

$$\frac{E_{d,S}}{E_d} \Big/ \frac{E_{t,S}}{E_t} = a/a'$$

Sinn and coworkers[155] maintain that if the bromination mechanism in the two series is identical (i.e. either electrophilic or nucleophilic), then a/a' should be constant. Conversely, different mechanisms would supposedly result in a variable a/a'. The experimental results for six pairs of substituted stilbenes and tolanes (with the attempted use of three different reference pairs) demonstrate that a/a' varies strongly (by a factor of 3–4), leading to the conclusion that different mechanisms operate in the two series of brominations. As olefin bromination is known to be an electrophilic process, the bromination of the substituted alkynes must be a nucleophilic reaction.

This rather complicated approach seems to be justified by ambiguities encountered earlier and mainly by the possible presence of both electrophilic and nucleophilic centres in both substrate and reactant. Such a situation may render mechanistic conclusions meaningless. This interesting approach should probably be explored further.

It has been shown that under conditions favouring an ionic reaction (in acetic acid and in the dark) *trans*-bromination is an exclusive process for 3-hydroxy-3-methyl-1-butyne and ethynylcyclohexanol[113]. Similarly, acetylene, methylacetylene and *t*-butylacetylene afford *trans*-dibromo derivatives under such conditions[114].

The halogenation of diynes and vinylacetylenes has been extensively studied by Petrov and coworkers. in diynes where mono- and di-substituted triple bonds are simultaneously present, the latter are halogenated preferentially, e.g. equation (28). If

$$H_3CC{\equiv}CCH_2C{\equiv}CH \xrightarrow{Br_2} H_3CC(Br)=C(Br)CH_2C{\equiv}CH \qquad (28)$$

both triple bonds are disubstituted, bromination occurs at the least branched triple bond, e.g. equation (29)[126,133]. The same rule seems to hold for the dibromide formed from conjugated diynes in addition to the tetrabromides[127,131,132].

$$H_3CC{\equiv}C-CH_2-C{\equiv}C-Bu\text{-}t \xrightarrow{Br_2} H_3CC(Br)=C(Br)-CH_2-C{\equiv}C-Bu\text{-}t \qquad (29)$$

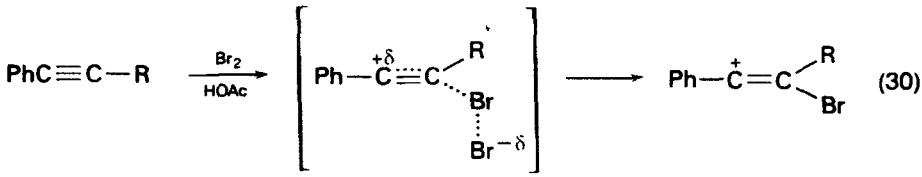
Bromination of phenylacetylene with Br_2 in chloroform or acetic acid has been found to yield predominantly *trans*-dibromostyrene[96]. Added LiBr enhances the stereoselectivity.

The kinetics and product composition for the bromination of several phenyl- and alkyl-acetylenes in acetic acid have been studied with and without added bromide salts[129]. In the absence of bromide salts the following rate equation was found:

$$-d[Br_2]/dt = [\text{alkene}](k_2[Br_2] + k_3[Br_2]^2)$$

Rate constant k_2 varied in the interval from 0.174 $M^{-1}\,s^{-1}$ (1-hexyne) to 247 $M^{-1}\,s^{-1}$ (4-methylphenylacetylene) at 25°C. The value of k_3 was determined for 4-methylphenylacetylene only (2.6 $M^{-2}\,s^{-1}$, 25°C). A Hammett plot of k_2 vs. σ^+ gave $\rho = -5.17$, which indicates an electrophilic bromination of phenylacetylenes in acetic acid. This contradicts the proposal of Sinn and coworkers[155], of a nucleophilic mechanism for substituted diphenylacetylenes in bromobenzene. The differences are probably due to the different solvents employed, which even change the kinetics of bromination, since the $[Br_2]^2$ term is predominant in bromobenzene.

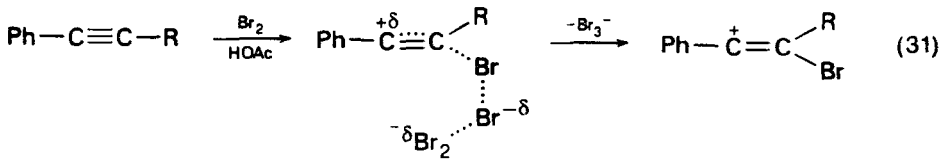
The ρ value of -5.17 is similar to the value of -4.5 found for hydration of phenylacetylenes[14], which was interpreted to indicate a rate-determining formation of a vinyl cation through a transition state similar to **90** (equation 30). The large negative



(30)

(90)

entropies of activation, $-(30-40)$ cal mol^{-1} deg^{-1}, are consistent with the extensive ordering of the reactants required by transition state **90**. The second-order term in Br_2 was assumed to imply bromine-assisted heterolysis of the Br—Br bond (equation 31).



(31)

Typical ratios of rate constants k_2 for olefins and acetylenes are 2×10^3 (styrene: phenylacetylene) and 1.4×10^5 (3-hexene:3-hexyne).

The bromination products of acetylenes are the corresponding bromoacetylenes (from terminal alkynes only), *cis*- and *trans*-dibromoalkenes, *cis*- and *trans*-bromoacetates (solvent-incorporated products), as well as dibromoketones (secondary products). The nonstereospecific nature of the reaction and the formation of solvent-incorporated products point to the intermediate formation of vinyl cations. Excessive ion-pairing is assumed and attempts have been made to interpret the intricacies of the bromination process in terms of 'intimate' ion pairs. No simple explanation has been found for the dibromide ratios from the phenylacetylenes studies.

Alkylacetylenes, e.g. 3-hexyne and 1-hexyne, produce only *trans*-dibromides and no solvent-incorporated products are observed. For these compounds a cyclic bromonium ion is assumed to be an intermediate in an Ad_E2 mechanism.

The presence of added bromide salts yields the kinetic equation of the bromination:

$$-d[Br_2]_T/dt = [\text{alkyne}](k_2[Br_2]_{free} + k_{Br^-}[Br_3^-])$$

or alternatively the kinetically indistinguishable equation:

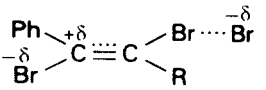
$$-d[Br_2]_T/dt = [\text{alkyne}](k_2[Br_2]_{free} + k_{Br^-}[Br_2]_{free}[Br^-])$$

With $k_{Br^-} = K\,k_{Br_3^-}$, one obtains the observed second-order rate constant K_{obs} as

$$k_0 = \frac{k_2 + k_{Br^-}[Br^-]}{1 + K[Br^-]}$$

Both k_2 and k_{Br^-} have been determined for phenylacetylenes: k_{Br^-} varies between 0.25 for 3-chlorophenylacetylene and 12.8 M^{-2} s^{-1} for 4-methylphenylacetylene, whereas the range of k_2 is between 6.5 for 4-bromophenylacetylene and 830 M^{-1} s^{-1} for 4-methylphenylacetylene. This implies that in the presence of bromide salt, a

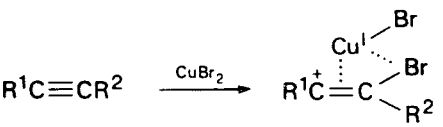
completely different kinetic law prevails as the k_{Br^-} term predominates over the k_2 path. This also changes the product ratios. The proposed transition state (**91**) implies a



(**91**)

bromide-ion-catalysed process. This assumption gives good agreement between calculated and observed *trans* : *cis* dibromide ratios for 4-methylphenylacetylene, where k_2 and k_{Br^-} are competitive. The bromide-ion-catalysed path is clearly preferred over direct electrophilic attack by tribromide ion.

The bromination of alkyl- and phenyl-acetylenes with Br_2 in chloroform gives a mixture of *cis*- and *trans*-dibromoalkenes in high yield[167]. The *trans* isomer usually predominates under kinetic control, except for PhC≡CBu-*t* which affords the *cis* isomer as the sole product. The thermodynamic equilibrium compositions have been determined under UV irradiation in the presence of excess Br_2. Bromination with copper(II) bromide in acetonitrile affords the same products but the reaction is much slower and the stereospecificity much higher than for bromination with molecular bromine. Product ratios have also been determined for the reaction with iodine, iodine monochloride and chlorine. A cyclic iodonium ion intermediate was postulated for I_2 and ICl and an open vinyl cation for Cl_2. The intermediate in bromination with copper(II) bromide was assumed to be a Cu(I)-coordinated open vinyl cation (equation 32). This type of intermediate implies electrophilic attack, though this was not expressly stated.

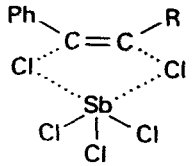


(32)

Similar conclusions have been reached in a study of the chlorination and chloroiodination of alkyl- and phenyl-acetylenes with copper(II) chloride[168]. In acetonitrile as solvent, $CuCl_2$–LiCl gives *trans*-dichloroalkenes in good yield and with high stereoselectivity. Again an exception is PhC≡CBu-*t*, from which the *cis*-dichloro derivative is predominantly formed. With $CuCl_2 + I_2$ or $CuCl_2$ + KI, the acetylenes studied are regiospecifically converted to the corresponding *trans*-chloroiodoalkenes. Iodine chloride affords the same chloroiodoalkenes but the yields and stereoselectivity are poorer. An open vinyl cation coordinated to copper(I) is assumed as an intermediate.

When the chlorination of alkylphenylacetylenes was carried out with antimony pentachloride in chloroform[169], the *cis*-dichloro derivatives were predominantly formed. If the reaction is conducted in the presence of iodine or lead(II) thiocyanate, interhalogenation occurs to produce chloroiodo or chlorothiocyanato derivatives, respectively. The predominant formation of *cis* isomers has been interpreted by molecular *cis* addition of $SbCl_5$ via the transition state **92**. Iodine monochloride and chlorothiocyanogen have been invoked as the species involved in the interhalogenation.

The chlorination of acetylenes with acidic copper(II) chloride solutions has been utilized to obtain other products than dichloroalkenes. For example, the chlorination of acetylene with concentrated aqueous $CuCl_2$ solutions, containing practically no copper(I), is found to afford also monochloroacetylene[17]. With fresh $CuCl_2$ solution,



(92)

the rate of formation of monochloroacetylene passes through a maximum, and other products predominate at later stages. The formation of ClC≡CH can be explained by the sequence shown in Scheme 18.

In moderately acidic solutions and at high Cu(II) to Cu(I) ratios, tri- and tetra-chloroethylene can be synthesized directly from acetylene in very high yields[120].

$$CuCl_2 + HC{\equiv}CH + H_2O \rightleftharpoons ClCuC{\equiv}CH + H_3O^+ + Cl^-$$

$$ClCuC{\equiv}CH + CuCl_2 \longrightarrow ClC{\equiv}CH + 2\,CuCl$$

SCHEME 18

E. Metal Ions and Salts

1. *Lead tetraacetate*

Lead tetraacetate reacts with alkynes in acetic acid slowly and only above 80°C. Complex product mixtures are usually observed. Under such conditions 5-decyne is converted in 20% yield to α-acetoxy-substituted derivatives[58]. Phenylbenzylacetylene gives allylic substitution products in 61% yield[84], but excess $Pb(OAc)_4$ affords phenylbenzoylacetylene. Propargyl alcohol gives a diacetoxy compound which, upon hydrolysis with $NaHCO_3$, yields 78% dihydroxyacetone (**93**) (equation 33).

$$HOCH_2C{\equiv}CH \xrightarrow{Pb(OAc)_4} HOCH_2C(OAc){=}CHOAc \xrightarrow{NaHCO_3} HOCH_2COCH_2OH \quad (33)$$

(**93**)

2. *Thallium(III) nitrate*

Thallium(III) nitrate has been found to effect oxidation, rather than hydration, of the triple bond[109]. Hydration might have been expected on the basis of the classic reaction of acetylene hydration catalysed by the isoelectronic mercury(II) salts.

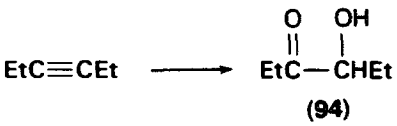
The nature of the oxidation product in water-glyme–perchloric acid media at room temperature is strongly dependent on the structure of the acetylene. Monoalkylacetylenes react exothermically to afford carboxylic acids containing one carbon atom less than the starting material in 70–90% yields. For example, 1-octyne gives an 80% yield of heptanoic acid (equation 34). Dialkylacetylenes are converted to

$$C_6H_{13}C{\equiv}CH \longrightarrow C_6H_{13}COOH \quad (34)$$

acyloins in 60–85% yield on treatment with 1 equivalent of thallium(III) nitrate. Thus, 3-hexyne affords 4-hydroxy-3-hexanone (**94**) (equation 35).

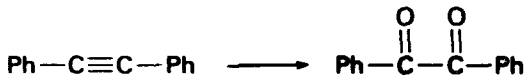
The oxidation of diarylacetylenes with two equivalents of thallium(III) nitrate gives the corresponding benzil, e.g. diphenylacetylene yields 85% benzil (**95**) (equation 36).

Mixtures of products are obtained in the thallium(III) nitrate oxidation of



(35)

(94)



(36)

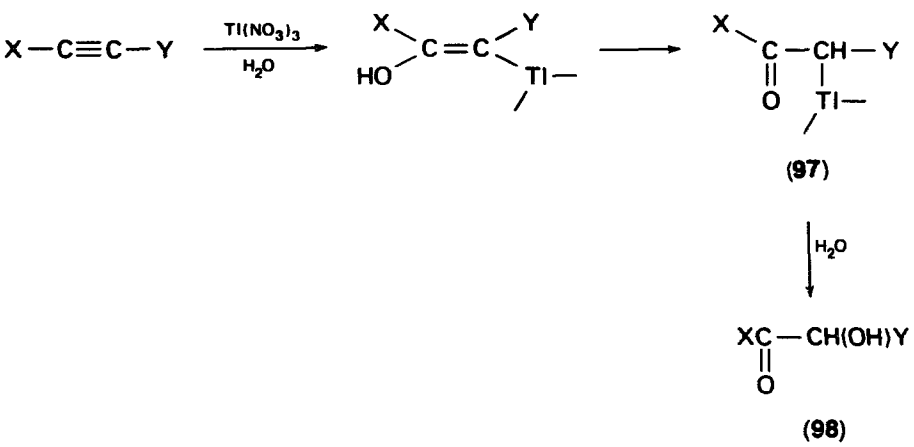
(95)

alkylarylacetylenes. For example, the oxidation of methylphenylacetylene in aqueous acidic glyme gives a mixture of unreacted starting material, methyl phenyl diketone, methyl benzyl ketone, and ethyl phenyl ketone. Upon oxidation in methanol, oxidative rearrangement occurs to give methyl arylacetates. Thus, methylphenylacetylene is converted into methyl α-phenylpropionate (**96**) in 85% yield (equation 37).

(37)

(96)

The oxidation of all types of acetylenes is proposed to occur via the α-hydroxyketone **98**, which is the solvolysis product of the initially formed organothallium(III) derivative **97** (equation 38).



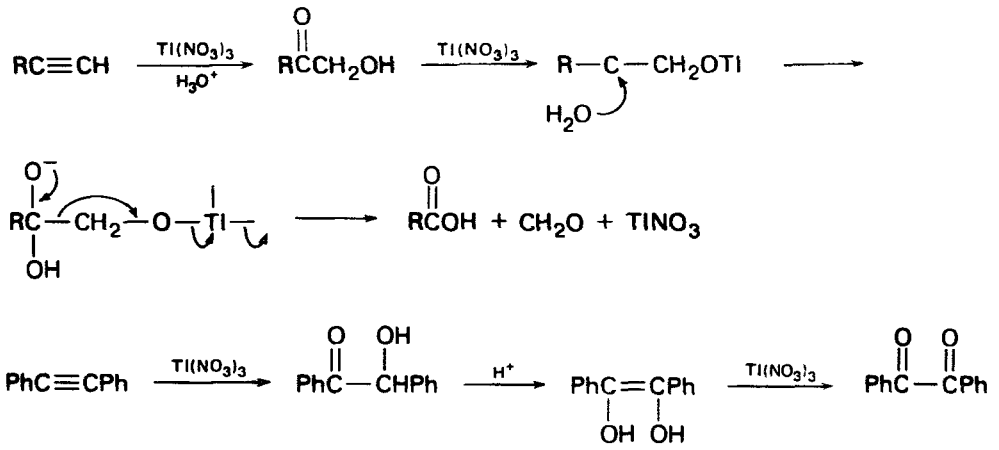
(38)

(97)

(98)

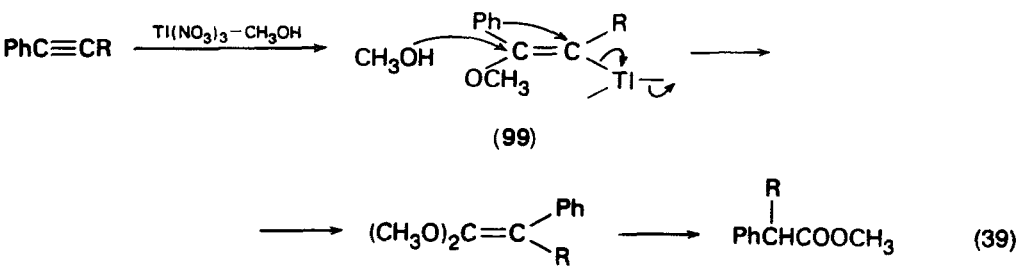
This reaction sequence explains the formation of acyloins from dialkylacetylenes. Acyloins have been shown to be oxidized only slowly by thallium(III) nitrate. However, monoalkylacetylenes and diarylacetylenes undergo a second oxidation step (Scheme 19).

No product requiring the oxidative rearrangement of the initial oxythallation intermediate has been isolated, the preferred pathway in aqueous solution being an S_N2-type solvolysis of the thallium substituent. The oxidative rearrangement of



SCHEME 19

alkylarylacetylenes observed in methanol solution probably occurs via the route shown in equation (39), where the initial methoxythallation product **99** is ideally disposed for aryl migration.

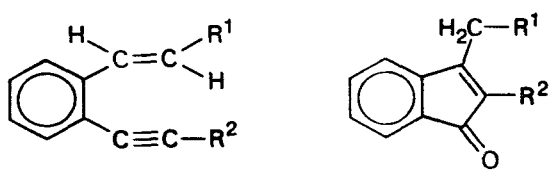


(99)

(39)

3. *Palladium(II)*

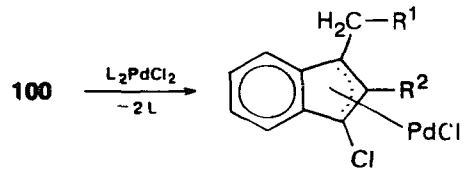
Enynes of structure **100** (R^1 = Ph, *i*-Bu, Me, Me; R^2 = Ph, Ph, Ph, Me, respectively) can be oxidized to substituted indenones (**101**) in benzene solution in the presence of bis(benzonitrile)dichloropalladium(II)[112]. The benzonitrile ligand is first rapidly



(100) (101)

displaced from the complex by the enyne ligand. Upon addition of NaOH, metallic Pd precipitates and the indenones **101** are formed in 15–54% yield. NMR evidence shows that the double bond is retained in the products but the triple bond undergoes oxidation. Oxidants other than palladium(II), e.g. dioxygen, lead to other products. The proposed mechanism is analogous to that of the palladium-catalysed synthesis of

dienes from diphenylacetylene and a terminal alkene[111b] (equation 40) where L = PhCN. The intermediate is a nonisolable palladium π-allyl complex.

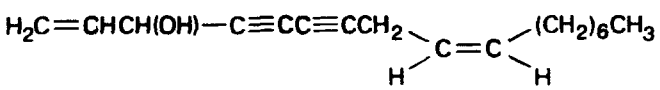


(40)

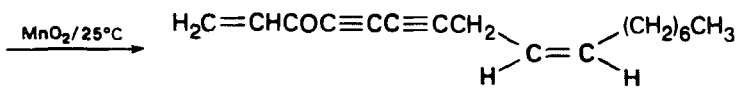
F. Metal Oxides

1. *Active MnO_2*

Acetylenic alcohols behave like α,β-unsaturated olefinic alcohols towards MnO_2 oxidation. The presence of one or more triple bonds facilitates rapid oxidation of the conjugated hydroxy group[47] but the triple bond itself remains intact. For example, *cis*-heptadeca-1,9-diene-4,6-diyn-3-ol (**102**) affords the *cis*-3-ketone **103** without isomerization[10b] (equation 41). Unsymmetrical acetylenic diols such as **104**



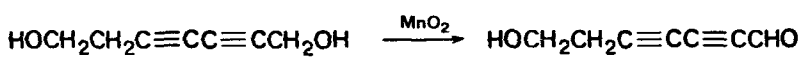
(**102**)



(41)

(**103**)

produce aldols (or ketols) instead of dicarbonyl compounds[142] (equation 42). However, more extensive multiple conjugation can activate more than one hydroxy group.



(42)

(**104**)

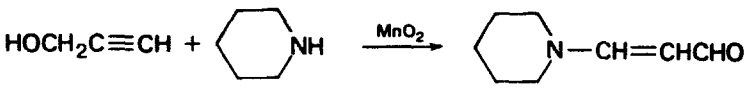
Secondary acetylenic alcohols **105** give the corresponding ketones (**106**) (equation 43). The scope of this reaction has been reviewed[47].

(43)

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

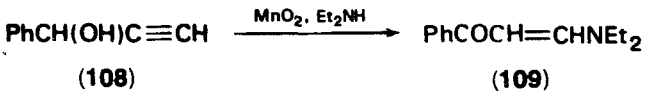
The oxidation of propargyl alcohol by MnO_2 in the presence of piperidine affords β-piperidinoacrylaldehyde (**107**) in 86% yield[104] (equation 44). The reaction can be extended to other aminoacroleins using the appropriate secondary amine.

If the oxidation of secondary acetylenic alcohols and glycols with active MnO_2 is carried out in the presence of secondary amines, alcohols and phenols, addition of the latter across the triple bond of the primary α-ketoalkyne product is observed[172]. For example, 1-phenyl-2-propyn-1-ol (**108**) and 1-phenyl-2-heptyn-1-ol (**110**) give, in the

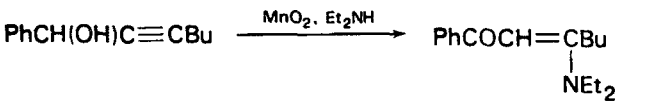


(107) (44)

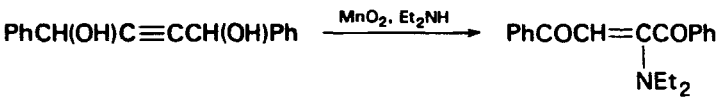
presence of diethylamine, the corresponding unsaturated aminoketones **109** and **111**. The acetylenic glycol **112** undergoes simultaneous oxidation at both hydroxy groups and addition of diethylamine, affording the unsaturated aminodione **113**. The



(108) (109) (45)

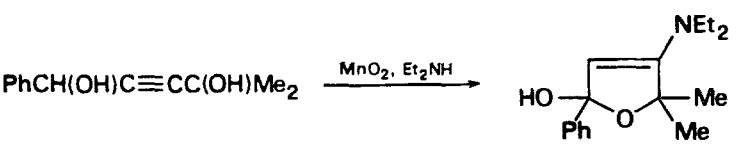


(110) (111) (46)



(112) (113) (47)

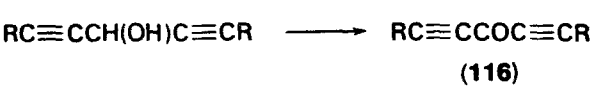
secondary–tertiary glycol **114** yields the substituted dihydrofuran derivative **115** via subsequent cyclization (equation 48).



(114) (115) (48)

2. *MnO_2 on carbon*

Manganese dioxide formed in the presence of active carbon[20] is reported to be an efficient oxidant for the conversion of alcohols to ketones. It has been found to produce the conjugated dialkynones **116** from the corresponding dialkynols[69] (equation 49). Apparently, this reagent is unreactive towards the carbon–carbon triple bond.



(116) (49)

R = Me, *t*-Bu, Ph, Me_3Si

3. *Ruthenium tetraoxide*

In the presence of catalytic amounts of ruthenium tetraoxide, alkynes are oxidized to α-diketones or cleaved to the corresponding carboxylic acids[65]. RuO_4 is generated *in situ* from a small amount of RuO_2 using sodium metaperiodate or sodium hypochlorite. These oxidants do not attack the alkynes studied and serve only for

regenerating the active species RuO_4. Internal acetylenes such as diphenylacetylene, dibutylacetylene and dipropylacetylene afford the corresponding α-diketones and some carboxylic acids as cleavage products. Terminal acetylenes such as phenylacetylene or *t*-butylacetylene gave only benzoic and propionic acids.

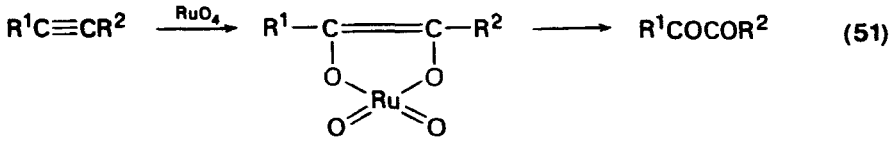
Alkyne **117** is converted to the diketone **118** with RuO_4[124] (equation 50).

(50)

(117) **(118)**

Apparently, the key intermediate in these oxidations is **119**, which is formed by oxidative cycloaddition of RuO_4 to the alkyne (equation 51).

Cleavage of terminal acetylenes may be due to the reaction of **119** with a second RuO_4 molecule, which might be sterically more feasible than with internal alkynes.

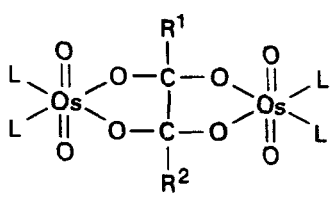


(51)

(119)

4. Osmium tetraoxide

Acetylene is known to reduce osmium tetraoxide[105], a reaction utilized in analytical chemistry. In the presence of excess tertiary amine (pyridine or isoquinoline) OsO_4 reacts with acetylene to produce adducts of the composition $2\ OsO_4 \cdot 4L \cdot C_2H_2$[35,40]. These compounds have been proposed to have the structure **120**[145], in which the



(120)

acetylene moiety is present as a tetrolato ligand. Upon hydrolysis, **120** gives oxidation products derived from the acetylene derivative used in preparing the osmium complex. Thus diphenylacetylene affords benzil and benzoic acid, phenylacetylene produces benzoic acid and some phenylglyoxal and methylphenylacetylene gives 1-phenylpropane-1,2-dione in 54% yield. It has been found that adduct formation and hydrolysis can be combined into a catalytic cycle for alkyne oxidation if a suitable oxidant is added to the system. Thus, potassium chlorate has been successfully applied in a *t*-butanol–acetone–water mixture to effect the oxidation of diphenylacetylene to benzil in 79% yield, using only a catalytic amount of OsO_4.

α-Oxo esters of the type $R^1COCO_2R^2$ (where R^1 and R^2 are identical or different alkyl, aryl, aralkyl or cycloalkyl groups) have been prepared by oxidizing acetylenic

ethers $R^1C{\equiv}COR^2$ by OsO_4 and $KClO_4$. For example, $Me_2CH{-}C{\equiv}COMe$ was oxidized to $Me_2CH{-}CO{-}CO_2Me$ in 79.9% yield[136].

G. Chromium(VI)

Chromic acid in acetone has been reported to oxidize secondary acetylenic alcohols and glycols to the corresponding ketones. This reaction has also been extended to primary acetylenic alcohols and glycols, which afford the corresponding acids[76]. The triple bond and eventual double bonds present in the molecules remain intact under the effect of this oxidant.

Pyridinium dichromate has been employed for similar purposes, **121** and **122** being examples of relatively sensitive conjugated carbonyl compounds prepared with this reagent[37].

$C_5H_{11}C{\equiv}CCHO$ **(121)**

$C_5H_{11}COC{\equiv}CC_5H_{11}$ **(122)**

The chromium trioxide–pyridine complex, $CrO_3(py)_2$, and anhydrous sodium chromate have been reported to effect the α-oxidation of alkynes, affording conjugated acetylenic ketones[147] (equation 52). These reagents are also used for the allylic oxidation of olefins[41b].

$$RC{\equiv}CCH_2R \xrightarrow[\text{or } Na_2CrO_4]{CrO_3(py)_2} RC{\equiv}CCOR \qquad (52)$$

Typically, 4-octyne in CH_2Cl_2 at room temperature, under stirring for 24 h with a slight excess of isolated $CrO_3(py)_2$, affords a 42% yield of 4-octyn-3-one as the only product. The same product has been obtained in 19% yield with anhydrous Na_2CrO_4 in acetic acid/acetic anhydride at 40–45°C. 5-Decyne, 1-phenyl-1-butyne and 2-decyne also give the corresponding ketones, but the terminal 1-decyne and 5-phenyl-1-pentyne do not react. 2-Decyne gives exclusively 2-decyn-4-one, indicating that a methyl group on a triple bond is not readily oxidized. The ketone yield does not increase with increasing the excess of the chromium(VI) reagent. Some cleavage at the triple bond was suspected but the product acids are apparently lost in the basic work-up[147].

In a search for the most efficient reagent for the α-oxidation of alkynes, chromic acid, chromyl acetate, chromyl chloride, *t*-butyl chromate, $CrO_3(py)_2$ and pyridinium chlorochromate have been tested with regard to their ability to oxidize diphenylacetylene, phenylacetylene, 2-decyne, 5-decyne, 4-octyne, and 7-tetradecyne[148]. The oxidation products included α-dicarbonyl compounds, acids formed via cleavage of the triple bond and α-carbonyl compounds. The $CrO_3(py)_2$ complex and pyridinium chlorochromate were found to be the most efficient reagents for preparing the conjugated ynones.

H. Permanganate

Acidic permanganate is known to react rapidly with acetylenic compounds. This reaction is utilized in analytical chemistry for the detection of carbon–carbon unsaturation. There is some controversy concerning the nature of these reactions. The intermediate formation of diketones is often assumed but until recently few well-documented examples of this transformation were known. Frequently the

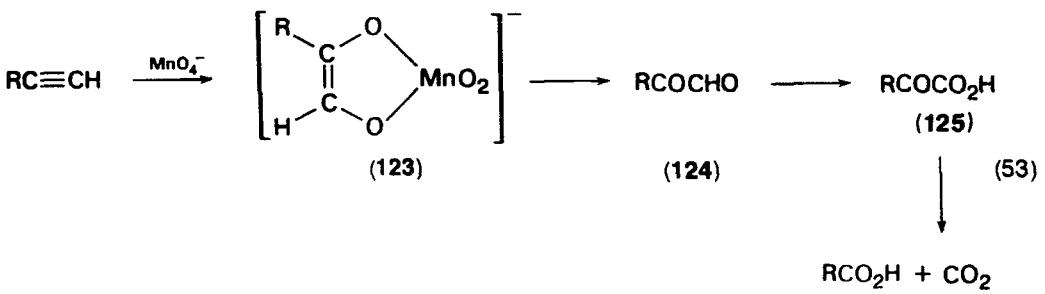
oxidation products are simply stated to be the carboxylic acids derived from cleavage at the triple bond.

In an early report, the oxidation of 3-dodecyne with aqueous permanganate was found to yield propionic and pelargonic acids[87]. The formation of a diketo compound was first demonstrated in the oxidation of stearolic acid to 9,10-diketostearic acid[92].

The direction of alkyne oxidation by permanganate appears to be strongly dependent on the pH of the medium and on the solubility of the diketo intermediate.

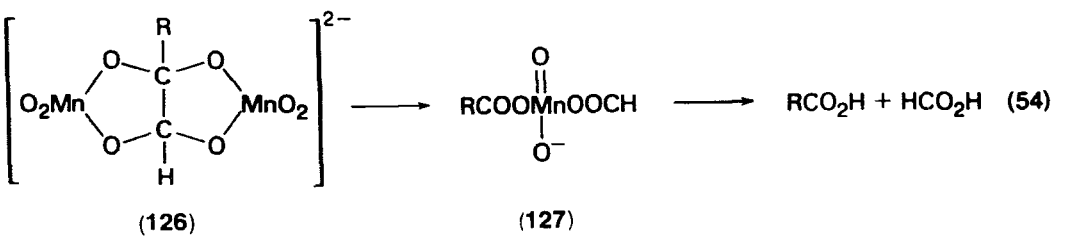
The permanganate oxidation of several terminal alkynes has been studied in order to find optimum conditions for their conversion to carboxylic acids of one less carbon atom[97]. 1-Hexyne was found to give valeric acid in 94–99% yield under a variety of conditions. Two-phase systems including water and pentane were used with various additives such as acetic acid, KOH and benzylhexadecyldimethylammonium chloride or Aliquat 336 (phase-transfer agents). In the case of 1-octyne, the amount of overoxidation to hexanoic acid was found to increase on increasing the KOH concentration and a maximum of 50% was achieved with 0.5 M KOH. Added acetic acid completely suppressed the overoxidation. Additives had little effect on the extent of overoxidation in the case of 1-hexyne and 1-decyne, which never exceeded 6%.

Two mechanistic pathways were regarded as possible sources of the corresponding carboxylic acids. The formation of a cyclic manganese(V) ester **123** could lead to the α-keto aldehyde **124** which would be oxidized to the α-keto acid **125** which by decarboxylation would give RCO_2H (equation 53). Alternatively, a bicyclic intermediate



(53)

(**126**) which could lead to the same products, possibly via **127**, could be involved (equation 54). It is not clear why the basicity of the aqueous phase increased the extent of overoxidation in the case of 1-octyne.



(54)

Terminal acetylenes have also been found to be oxidized by $KMnO_4$ to carboxylic acids of one less carbon in boiling dichloromethane using Adogen-464 [methyltrialkyl(C_8–C_{10})ammonium chloride] as a phase-transfer agent[102]. However, non-terminal alkynes do not undergo cleavage as readily and good yields (71–93%) of α-diones can be achieved (equation 55).

$$R^1C{\equiv}CR^2 \xrightarrow{KMnO_4} R^1COCOR^2 \quad (55)$$

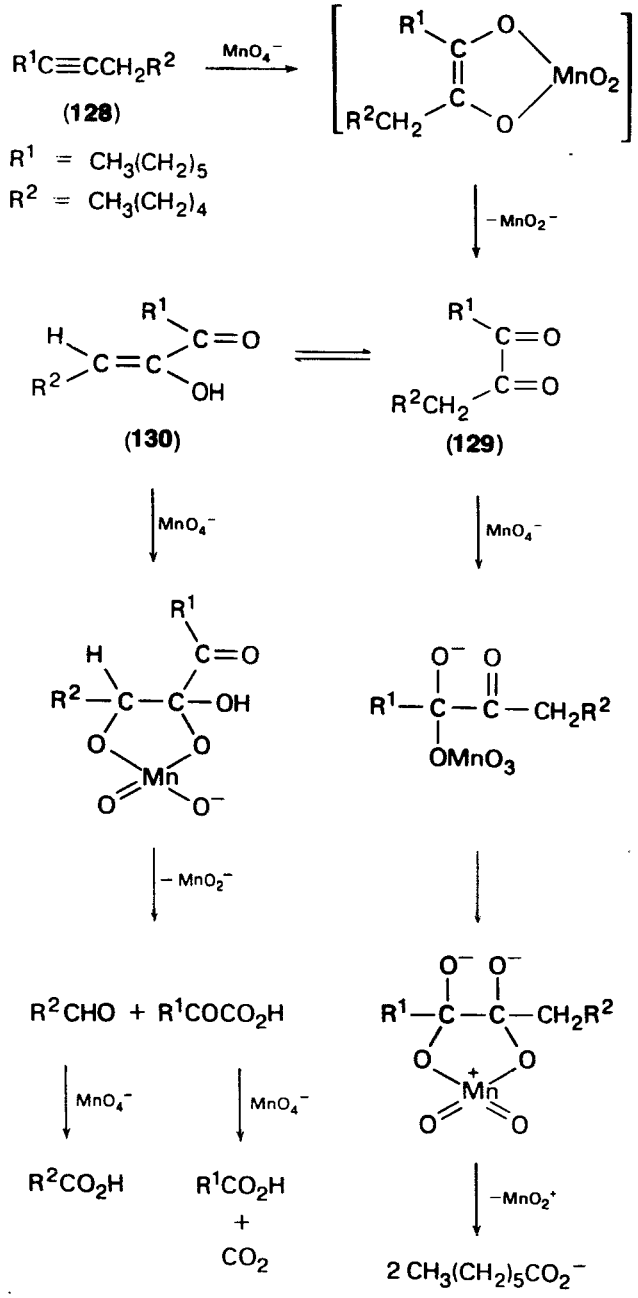
R^1 = Ph, *n*-C_6H_{13}, *n*-C_7H_{15},

R^2 = Ph, *n*-C_3H_7, *n*-C_4H_9, *n*-C_6H_{13}, *n*-C_7H_{15}

According to a recent report[159b] the oxidation of alkynes to α-diones is a general reaction, provided that the reactant solution is maintained approximately neutral. This is achieved by adding solid acids such as $NaHCO_3$ and $MgSO_4$ to neutralize the OH^- ions formed upon the reduction of the permanganate. 5-Decyne, 7-tetradecyne, 8-hexadecyne, 1-phenyl-1-pentyne, and diphenylacetylene are oxidized in aqueous acetone solution at room temperature to the corresponding α-diones in 40–88% yield.

A more detailed investigation of the possible pathways of the permanganate oxidation of nonterminal alkynes has revealed[103] that the reaction can be directed along any of three different routes by the appropriate choice of experimental conditions. In *aqueous solutions* cleavage at the triple bond to carboxylic acids is the predominant process. For example, 1-phenyl-1-pentyne gives benzoic acid and 5-pentyne affords valeric acid, whereas 4-octyne is converted mainly to butyric acid, together with some propionic acid at longer reaction times. 8-Hexadecyne and 7-tetradecyne are not oxidized under these conditions. In *'wet' methylene chloride*, i.e. in two-phase systems consisting of an aqueous permanganate solution in contact with the organic phase containing a phase-transfer agent, α-diketones and cleavage products are formed. For example, diphenylacetylene gives benzil (93%) and benzoic acid (2%), 1-phenyl-1-pentyne produces 1-phenyl-1,2-pentanedione (56%), benzoic acid (24%) and propionic acid (16%), and 7-tetradecyne affords 7,8-tetradecanedione (54%), heptanoic acid (25%) and hexanoic acid (17%). When the oxidation is carried out in *anhydrous methylene chloride* using solid $KMnO_4$ and a phase-transfer agent [Adogen-464, a methyltrialkyl(C_8–C_{10})ammonium chloride], the α-diketones are formed almost exclusively. The results have been interpreted in terms of a common α-diketo intermediate (**129**), which may or may not undergo further oxidative cleavage. The possible conversions are illustrated by the example of 7-tetradecyne (**128**) (Scheme 20). The formation of substantial amounts of both heptanoic and hexanoic acid implies a significant contribution from cleavage of **129** via its enol form (**130**), which is an activated alkene, known to be susceptible to attack by MnO_4^-. In order to throw further light on the mechanism of these reactions, the oxidation of 7,8-tetradecanedione and 8,9-hexadecanedione by $KMnO_4$ has also been studied. The oxidative cleavage of these diones in water occurred in an almost entirely symmetrical fashion. However, in wet organic solvents both diketones were cleaved with the loss of a carbon atom. This is in full accord with the results observed for the oxidative cleavage of the corresponding alkynes, and strongly supports the assumption of a common dione intermediate. It is interesting that wet organic solvents facilitate cleavage with the loss of a carbon atom, but this is not the case in aqueous solutions. It was suggested that enol formation could be suppressed in water as compared with organic solvents, or that symmetrical cleavage could occur via a more polar transition state which would be stabilized by solvation in aqueous solvents.

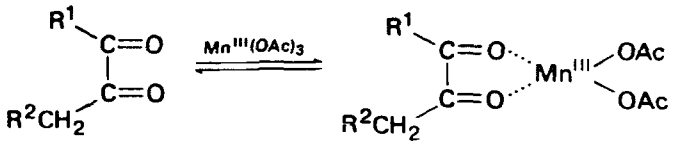
It seems that this feature of the cleavage process might be due to the intervention of short-lived manganese(III) species, which are known to react preferentially with bidentate oxygen donor ligands such as the α-dioxo intermediate or its enol isomer[151]. If the dioxo compound is first formed and subsequently enolized, then highly reactive manganese(III) may attack it before it has a chance to enolize. It is likely that manganese(III) would be more abundant in aqueous solution than in wet organic solvents. The



SCHEME 20

formation of transient manganese(III) is especially favoured in acidic aqueous solutions: 3–12% acetic acid was added in most experiments in aqueous solutions. A possible scheme involving manganese(III) acetate complexes is shown in equation

(56). Cleavage reactions of this type are well known in the chemistry of manganese(III) oxidations[175].



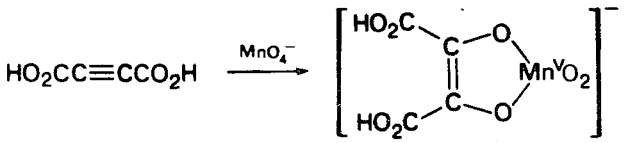
$$\xrightarrow{Mn^{III}(OAc)_3} R^1CO_2H + R^2CH_2CO_2H \qquad (56)$$

In acidic aqueous solutions, acetylenedicarboxylic acid (H_2A) is oxidized by permanganate ion according to equation (57) if the reactants are present in a ratio of 1:2.

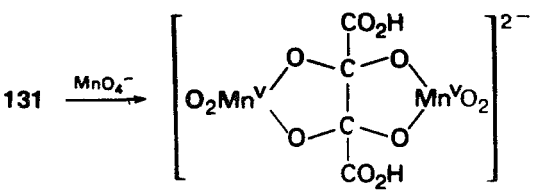
$$HO_2C-C\equiv C-CO_2H + 2\,MnO_4^- + 6\,H^+ \longrightarrow 4\,CO_2 + 2\,Mn^{2+} + 4\,H_2O \qquad (57)$$

The reaction is very fast and special techniques are required for studying its kinetics and short-lived intermediates[85]. It has been shown by the stopped-flow method that the first detectable inorganic intermediate in aqueous perchloric and sulphuric acid is manganese(III). If H_2A is present in excess of the stoichiometric ratio of 1:2, a maximum of 0.5 mole oxalic acid per mole MnO_4^- is formed as a product. If the reacting solution is quenched by the rapid addition of sulphite or iron(II) to remove unreacted manganese(III), the amount of oxalic acid increases to 0.6–0.7 mole per mole MnO_4^-. Consequently, the oxalic acid concentration passes through a maximum during the reaction. Complete removal of unreacted manganese(III) is possible by carrying out the oxidation in the presence of pyrophosphate, an efficient scavenger suppressing oxidations by this ion. Under such conditions, 1.0 mole oxalic acid per mole MnO_4^- is found in the scavenged solutions. Clearly, any reaction sequence proposed for describing the oxidation of H_2A should be consistent with these variations of oxalic acid yield. Additional mechanistic information has been obtained from tracer experiments in oxygen-18-enriched water, which indicated complete oxygen-atom transfer from MnO_4^- to H_2A. The possible mechanism of the overall reaction was approached by comparing the quantitative results for five types of experiments [oxalic acid yield under three sets of conditions, amount of oxygen transfer and the intermediate formation of Mn(III)] with values predicted for various combinations of conceivable reaction sequences. Only a single combination of reactions did correctly predict the results of all experiments. The reaction sequence thus deduced requires the formation of a very short-lived manganese(IV) species from **132** (only so is it possible to explain both complete oxygen transfer and the presence of 1.0 oxalic acid per mole MnO_4^- in scavenged solutions) (Scheme 21). (Only the species important for the redox changes are shown.) By analogy with olefin oxidation[179], a cyclic hypomanganate ester (**131**) is assumed to be the first (undetectable) intermediate. A subsequent attack by a second MnO_4^- ion on **131** results in the transient formation of a bicyclic manganese(V) intermediate (**132**). Significantly, only this sequence of steps is consistent with the amount of oxalic acid detected under various conditions and with the amount of oxygen-atom transfer found by tracer studies. Consequently, it serves as an indirect proof for the existence of these hypomanganate esters. For example, intramolecular oxidation of **131** with manganese(III) formation, an apparently reasonable sequence, is incompatible with the amount of oxalic acid formed and the oxygen-atom transfer.

The oxidation of acetylenedicarboxylic acid by MnO_4^- has also been studied



(131)



(132)

$$\mathbf{132} \longrightarrow \mathbf{2\ Mn(IV) + 2\ HO_2C{-}CO_2H}$$

$$\mathbf{131} + \mathbf{4\ Mn(IV)} \longrightarrow \mathbf{5\ Mn(III) + HO_2CCO_2H + 2\ CO_2}$$

$$\mathbf{HO_2CCO_2H + 2\ Mn(III)} \longrightarrow \mathbf{2\ Mn(II) + 2\ CO_2}$$

SCHEME 21

kinetically in the pH range of 0.25–5.3[150], by means of the stopped-flow technique. The reaction is first order with respect to both MnO_4^- and acetylendedicarboxylic acid. The pH dependence of the apparent second-order rate constant k is given by the equation:

$$k = 5(k_1 a_H^2 + k_2 K_1 a_H + k_3 K_1 K_2)/3F$$

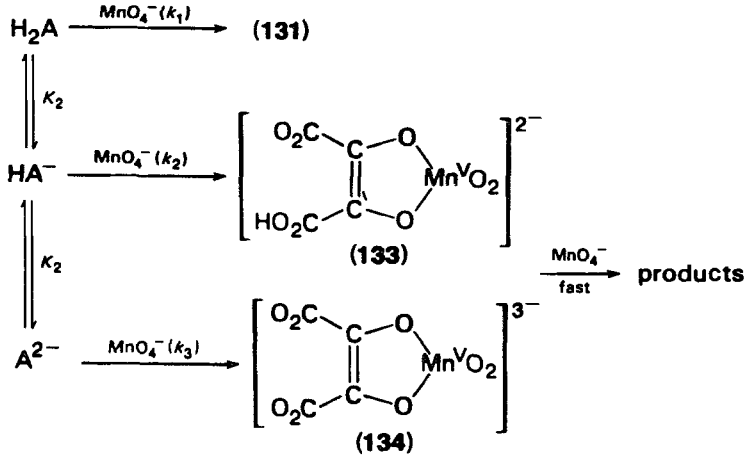
where

$$F = K_1 K_2 + K_1 a_H + a_H^2$$

a_H is the hydrogen-ion activity, K_1 and K_2 are the acid dissociation constants of acetylenedicarboxylic acid and k_1, k_2 and k_3 are the second-order rate constants for the permanganate oxidation of the undissociated acid, and its mono- and di-anion, respectively.

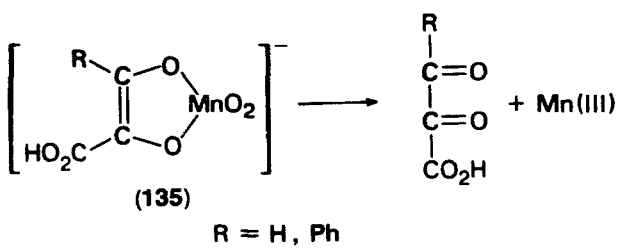
The validity of this equation implies that the variation of k with the pH is due solely to shifts in the acid dissociation equilibria and no specific acid catalysis is involved. The acid–base equilbiria are considered to be much faster than the oxidation of any of the species involved in the equilibria. The observed kinetic behaviour is consistent with a rate-determining formation of the intermediate **131** and a fast attack of a second MnO_4^- to produce **132**. The acid–base equilibria and the rate-determining steps are illustrated by Scheme 22, where H_2A stands for acetylenedicarboxylic acid.

A similar kinetic analysis of the permanganate oxidation of propiolic and phenylpropiolic acids[153] has shown that essentially the same mechanism applies to these alkynoic acids as has been found for acetylenedicarboxylic acid. However, the rate-determining formation of the five-membered cyclic manganese(V) intermediate of type **131** is *not* followed by attack of a second MnO_4^-. Instead, intramolecular oxidation occurs, affording dioxo compounds and manganese(III) as intermediates



SCHEME 22

(equation 58). Again the acids and the monoanions react at different rates but they are in fast acid–base equilibrium with each other. If the reacting solutions are



(58)

R = H, Ph

quenched with sulphite anion the dioxo compounds can be isolated as their 2,4-dinitrophenylhydrazones. Without quenching, manganese(III) will oxidize one half of the intermediates to the corresponding acids. Apparently, the intermediate **135** is not reactive enough to be attacked by a second MnO_4^- ion.

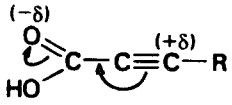
Intermediates of type **135** have been detected in the oxidations of propargyl alcohol and 2-butyne-1,4-diol. They are subsequently transformed to the corresponding dioxo compounds[151]. Propargyl chloride and bromide follow the same reaction pattern.

The rate constants for the oxidation of various alkyne derivatives by acidic permanganate are listed in Table 1.

TABLE 1. Rate constants ($M^{-1}\,s^{-1}$) for the permanganate oxidation of alkynes at 25°C

Alkyne	k_1	k_2	k_3
Acetylenedicarboxylic acid	1420	632	40
Propiolic acid	183	43	—
Phenylpropiolic acid	39	12.3	—
Propargyl alcohol	10	—	—
Propargyl chloride	11.5.	—	—
Propargyl bromide	11.5	—	—
2-Butyne-1,4-diol	12.5	—	—

It is apparent that the undissociated acids are more reactive than the corresponding mono- and di-anions. Remarkably, this points to a rate-determining nucleophilic attack by MnO_4^-. This feature does not contradict the fact that in the overall process MnO_4^- is a strong electrophile, making oxidation thermodynamically favourable. Also, the presence of carboxyl groups which are conjugated with the triple bond strongly enhances the reactivity, again emphasizing nucleophilic attack at the electrophilic β-carbon (cf. **136**). A point related to the intimate mechanism of the



(136)

rate-determining step is the invariably small activation energy (5–7 kcal mol^{-1}) and the large negative activation entropy (−30–36 cal mol^{-1} deg^{-1}). This is consistent with extensive bond-making and very little bond-breaking in the rate-determining step. In combination with the considerable ordering of the reactants which is apparent from the activation entropies, this indicates a near-concerted process in which two oxygens of the MnO_4^- attack the triple bond almost simultaneously. Similar reactivity trends have been observed for olefinic acids[86,152,154].

III. OXIDATION OF NITRILES

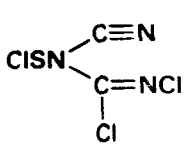
Little information is available on the oxidation of the cyano group in organic compounds. In most cases oxidation of nitriles leads to removal of the cyano group from the molecule. Under milder conditions, oxidation takes place at sites other than the cyano group, which remains intact. A notable exception is chlorination.

The chemistry of nitriles has been reviewed in a previous volume of this series.[134]

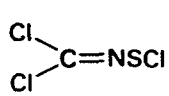
A. Chlorine

The addition of chlorine to the C≡N bond involves oxidation at the nitrogen atom since chlorine is more electronegative than carbon.

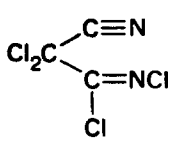
In the chlorination of malononitrile[123] a by-product was isolated which was later identified as *N*,2,2-trichlorocyanoacetimidoyl chloride (**137**)[19]. The chlorination of



(137)

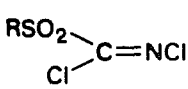


(138)



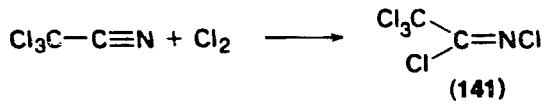
(139)

thiocyanogen[52] gives *N*-(chlorothio)chloroformimidoyl chloride (**138**). The reaction of thionyl chloride with dicyanamide salts affords *N*-chloro-(*N'*-chlorothio-*N'*-cyanamino)formimidoyl chloride (**139**)[66]. The chlorination of sulphonyl cyanides yields the corresponding *N*-chloroformimidoyl chlorides (**140**)[173].



(140)

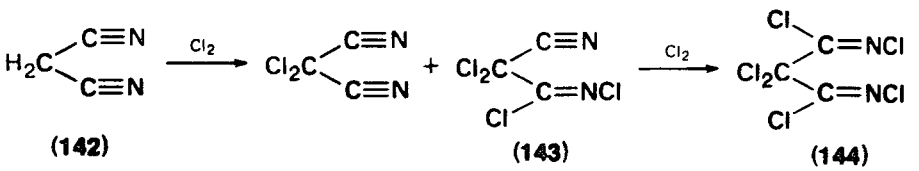
The chlorination of acetonitrile affords trichloroacetonitrile without chlorination of the CN bond. However, treatment of trichloroacetonitrile with NCl_3 in the presence of catalytic amounts of tetramethylammonium chloride[165] affords some *N*-chlorotrichloroacetimidoyl chloride (**141**) (equation 59).



(59)

(**141**)

Chlorination of malononitrile (**142**) with free chlorine at atmospheric pressure leads to **143** in 45–60% yield, whereas under pressure **144** is obtained in 60% yield (equation 60).

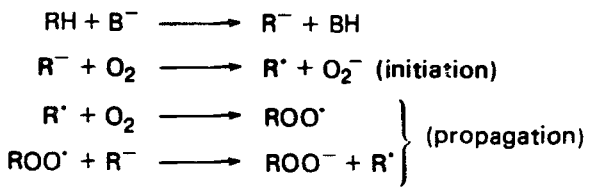


(60)

(**142**) (**143**) (**144**)

B. Autoxidation

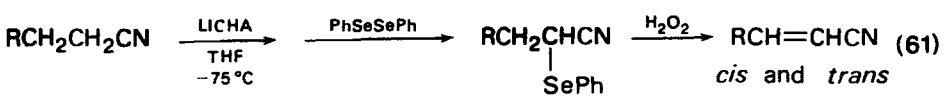
Isobutyronitrile, diphenylacetonitrile and cyclopentyl cyanide can be oxidized by O_2 in the presence of *t*-butoxide in dimethoxyethane at −40 to −75°C to α-hydroperoxides, in yields of 50–65%[62]. This type of oxidation is due to ionization of the weakly acidic α-hydrogen by the strong base employed. The carbanion formed initiates a chain-reaction with O_2, affording the hydroperoxides (Scheme 23). Termination occurs by radical–radical combinations.



SCHEME 23

C. Hydrogen Peroxide

Selenylated nitriles **145**, accessible via the reaction of α-lithiated nitriles with diphenyl diselenide, afford α,β-unsaturated nitriles upon oxidation with H_2O_2[15]. α-Lithiation is carried out with lithium isopropylcyclohexylamide (LICHA) (equation 61). The same transformation can be effected with phenylselenyl bromide or dimethyl disulphide.

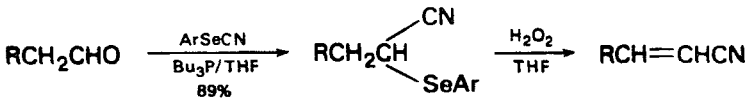


(61)

R = *n*-pentyl (**145**)

The cyanoselenides **146** obtained from the reaction of aldehydes with aryl selenocyanates can be oxidized with H_2O_2 to β-unsaturated nitriles **147** in high yield[67]

(equation 62). This is a useful one-carbon homologation process. For example, dodecanal, heptanal, cyclopentylmethanal and cyclohexenylmethanal were converted with better than 90% yield, to the corresponding derivatives[147].

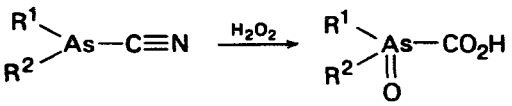


(62)

(146) (147)

Ar = Ph, *o*-$NO_2C_6H_4$

Cyanoarsines **148** can be oxidized with hydrogen peroxide to the corresponding arsinocarboxylic acid oxides **149**[60] (equation 63). If the oxidation is carried out with aqueous $KMnO_4$, the *p*-Me substituent is converted to a CO_2H group.



(63)

(148) (149)

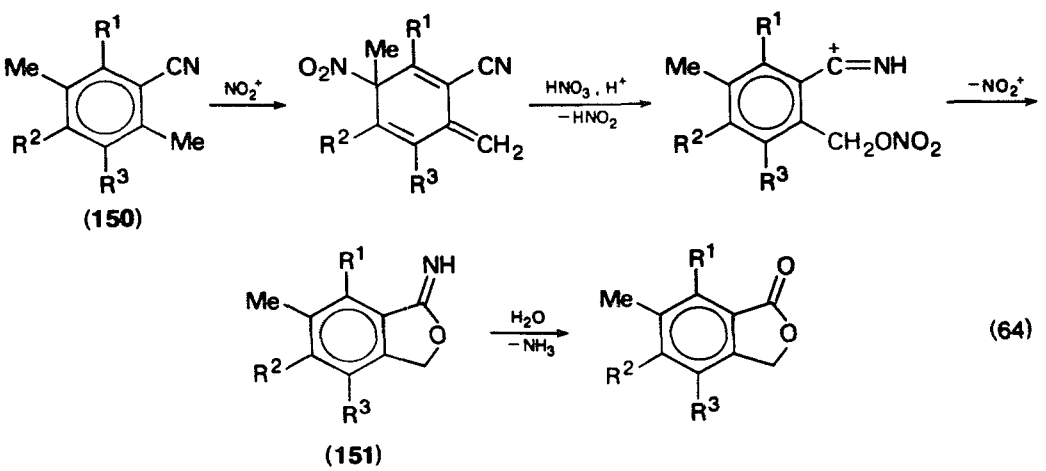
R^1 = Me, Et, *n*-Pr
R^2 = Ph, *p*-MeC_6H_4

D. Sodium Hypochlorite

Using a 20-fold excess of sodium hypochlorite, *o*-toluonitrile can be converted to phthalic acid (21%). *p*-Toluonitrile affords *p*-cyanobenzoic acid (92%) and *m*-toluonitrile gives *m*-cyanobenzoic acid (72%)[21].

E. Nitric Acid

The nitration of aryl cyanides usually leaves the cyano group intact[134]. Some *p*-xylonitriles (**150**), however, upon treatment with concentrated nitric acid, undergo oxidative cyclization to 1-imino-1,3-dihydroisobenzofurans (**151**)[162] (equation 64).



(64)

(150) (151)

The formation of iminophthalans (**151**) is limited to nitriles having at least one pair of methyl groups *para* to each other.

F. Peroxydisulphate

In the presence of $AgNO_3$, α-cyanoalkanols are oxidized by $Na_2S_2O_8$ to α-ketonitriles[117] (equation 65). The reaction is apparently initiated by hydrogen-atom abstraction, which is followed by a regioselective rearrangement of the intermediate α-cyanoalkoxyl radical.

$$R^1(CH_2)_3C(OH)R^2 \longrightarrow R^1CHCH_2CH_2COR^2 \quad (65)$$
$$\text{CN} \qquad\qquad\qquad \text{CN}$$

R^1 = H, Me, *n*-Pr
R^2 = Me, *n*-Pr

G. Dehydrocyanation of Nitriles

The removal of HCN from organic cyanides may be regarded as oxidation because the formal oxidation states shown under the carbon atoms concerned change as shown in equation (66). The oxidative nature of HCN elimination is particularly apparent if it

$$\begin{array}{l} \text{H R} \\ \text{RC—CCN} \\ \text{R R} \\ -1 \quad 0{+}3 \end{array} \longrightarrow \text{HCN} + \begin{array}{l} \text{RC=CR} \\ \text{R R} \\ 0 \quad 0 \end{array} \qquad (66)$$
$$+2$$

occurs with oxygen incorporation (equation 67), since the carbon atom substituted by the CN group undergoes a three-unit change in its oxidation state.

$$\begin{array}{l} \text{H} \\ \text{RCCN} + \text{O} \\ \text{R} \\ -1 \; {+}3 \quad 0 \end{array} \longrightarrow \begin{array}{l} \text{RC=O} + \text{HCN} \\ \text{R} \\ +2 \; -2 \quad +2 \end{array} \qquad (67)$$

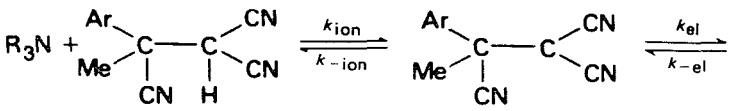
Dehydrocyanation is reductive in nature if the C—CN bond is cleaved via hydrogenolysis to afford CH + HCN.

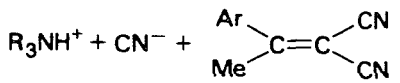
These considerations justify a brief treatment of dehydrocyanation in the present chapter.

The tributylamine-promoted dehydrocyanation of 2-aryl-1,1,2-tricyanopropanes has been investigated in chloroform and acetonitrile[2].

The general two-step reaction scheme (equation 68), which corresponds to base-catalysed carbanionic elimination (ElcB) has been analysed in detail on the basis of kinetic measurements. Evidence is provided for carbanion formation and its ion pairing with R_3NH^+. Abstraction of CN^- within the ion pair is the rate-determining step. 2,6-Dimethyl-4-(1,1,2,2-tetracyanoethyl) aniline eliminates HCN by a similar route except that carbanion formation is more extensive[135].

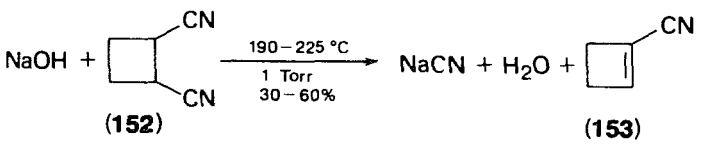
The dehydrocyanation of 1,2-cyclobutanedicarbonitrile (**152**) in the gas phase affords 1-cyclobutene carbonitrile (**153**) in high purity and good yield[59] (equation 69).





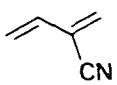
(68)

Ar = *p*-$MeOC_6H_4$, *p*-MeC_6H_4, Ph



(69)

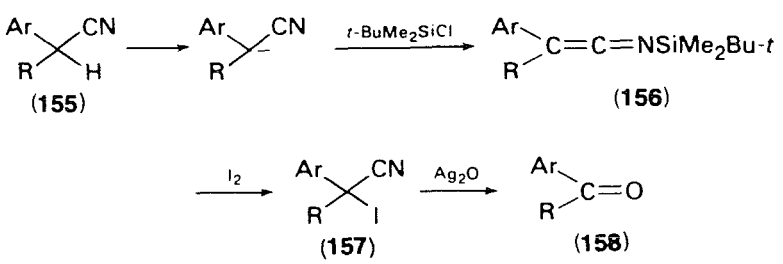
(152) (153)



(154)

This simple and direct procedure has been recommended as a synthetic method. The dehydrocyanation of **152** has also been realized over various basic catalysts such as ZnO–MgO mixtures. Upon heating, **153** is converted to **154**. The loss of CN^- from **152** is assumed to be the rate-determining step in the reaction leading to **153**.

Substituted arylacetonitriles **155** can be converted to alkyl aryl ketones and diaryl ketones[176]. The anions derived from the reaction of **155** with lithium diisopropylamide undergo regioselective *N*-silylation with *t*-$BuMe_2SiCl$ to produce *N*-*t*-butyldimethylsilylketenimines (**156**), which, on bromination or iodination afford α-halonitriles. The treatment of the α-iodonitrile (**157**), (but not of the inert bromonitriles), with silver oxide in THF gives alkyl aryl ketones or diaryl ketones (**158**) in 63–82% yield (Scheme 24).



(155) (156)

(157) (158)

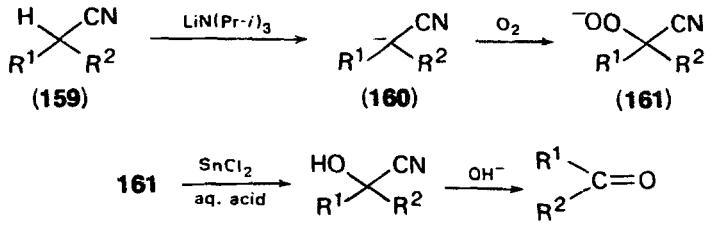
Ar = Ph, *p*-FC_6H_4, *p*-ClC_6H_4, α-naphthyl

R = Me, Et, *i*-Pr, *n*-octyl, Ph

SCHEME 24

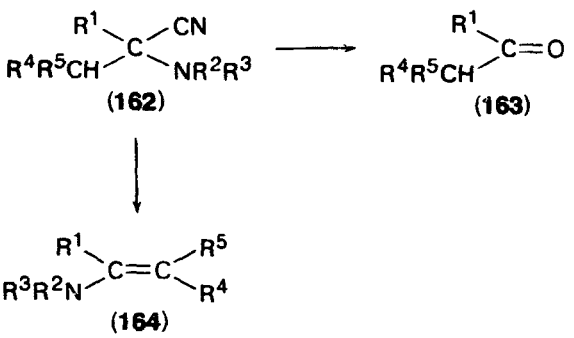
The oxidative dehydrocyanation of secondary nitriles (**159**, where R^1 and R^2 may be various alkyl, aralkyl or aryl groups) has been effected by generating nitrile anions (**160**) and trapping them with molecular oxygen, reducing the resulting

α-hydroperoxynitriles (**161**) to cyanohydrins with $SnCl_2$, and converting the cyanohydrins to ketones with NaOH in 64–92% isolated yield[177] (Scheme 25).



SCHEME 25

α-Aminonitriles with a hydrogen atom in the β-position (**162**) can be readily dehydrocyanated in boiling toluene or benzene with excess powdered KOH or *t*-BuOK to the ketones (**163**) or to the enamines (**164**)[1] (Scheme 26).



SCHEME 26

IV. OXIDATION OF ISOCYANIDES

The oxidations of isocyanides reported thus far lead to the formation of isocyanates or isothiocyanates. The subject has been briefly reviewed[170].

A. Ozone

Ethyl, *i*-propyl, *n*-butyl, *n*-hexyl and *n*-octyl isocyanides can be oxidized by ozone to the corresponding isocyanates[53]. Extensive losses occur due to tar formation.

B. Dioxygen

The introduction of O_2 into an ethereal solution of the complex bis(cycloocta-1,5-diene)nickel(0), containing *t*-butyl isocyanide, leads to the formation of *t*-butyl isocyanate in 60–70% yield[122]. The nickel complex is first converted to $(t\text{-BuNC})_4Ni$, and then to the peroxonickel complex (**165**), which is believed to be responsible for the isocyanide oxidation (equation 70).

$Co(Hdmg)_2py_2$ and $Co(Hdmg)_2(PPh_3)_2$, ($Hdmg^-$ = the monoanion of dimethylglyoxime; py = pyridine), were found to be catalytically active in the oxidation of butyl and octyl isocyanide by dioxygen to the corresponding isocyanates[115]. When the reactions were conducted for 24 h at room temperature in acetone the only products detected were the isocyanates which were formed in 30–35% yield.

$$(1,5\text{-}C_8H_{12})_2Ni \xrightarrow{t\text{-BuNC}} (t\text{-BuNC})_4Ni \xrightarrow{O_2}$$

$$\longrightarrow \underset{t\text{-BuNC}}{\overset{t\text{-BuNC}}{\text{Ni}}}\!\!<\!\!\begin{matrix}O\\|\\O\end{matrix} \xrightarrow[t\text{-BuNC}]{\text{excess}} t\text{-BuNCO} + (t\text{-BuNC})_4Ni \qquad (70)$$

(165)

C. Nitrogen Oxides

Nitrogen oxide has been found to oxidize cyclohexyl, *t*-butyl and *n*-hexyl isocyanides to the corresponding isocyanates in 50–80% yield, in benzene, ether or EtOH at 80–120°C in a pressure tube[141] (equation 71). The oxidation of cyclohexyl isocyanide

$$RNC + NO \longrightarrow RNCO + 1/2\ N_2 \qquad (71)$$

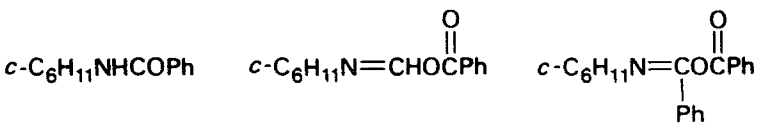
proceeds even at room temperature in toluene in a 56% yield.

Dinitrogen oxide (N_2O) is also active in this reaction, though cyclohexyl isocyanate could only be obtained in 22% yield at 120–130°C. As N_2O is more sluggish to react, a stepwise reduction of NO is not indicated.

D. Peroxybenzoic Acid and Benzoyl Peroxide

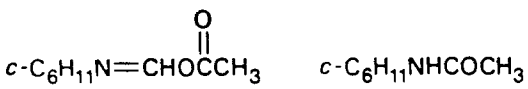
The treatment of cyclohexyl isocyanide with peroxybenzoic acid affords 61% cyclohexyl isocyanate and *N*-cyclohexylbenzamide[149].

The reaction of cyclohexyl isocyanide with benzoyl peroxide gives **166**, **167** and **168** as products[149].



(166) (167) (168)

N-Nitrosoacetanilide gives the products expected (**169** and **170**) for a reaction of acetoxy radicals with the isocyanide.



(169) (170)

E. Dimethyl Sulphoxide, Pyridine *N*-Oxide and Nitrile Oxides

In the presence of catalytic amounts of Br_2 (5%), isopropyl isocyanide is oxidized by DMSO in $CHCl_3$ to isopropyl isocyanate[88]. Iodine is less effective as catalyst but chlorine is equally useful. Phenyl isocyanide reacts similarly. The dihaloimine **171** is believed to be a reactive intermediate, in a process which is an ionic chain reaction (equation 72). Transfer of X_2 may occur without actual formation of a free X_2.

$$RNC \xrightarrow{X_2} \underset{(171)}{R\text{—}N{=}CX_2} \xrightarrow{DMSO} RNCO + (CH_3)_2S + X_2 \qquad (72)$$

Anhydrous acids such as *p*-toluenesulphonic acid and HCl, or trityl perchlorate catalyse the oxidation of isocyanides by DMSO[160]. At 50–80°C a rapid exothermic reaction takes place, affording dimethyl sulphide and isocyanate. *n*-Butyl, cyclohexyl, benzyl and *p*-methylphenyl isocyanides are converted to the corresponding isocyanates in 50–90% yield.

Pyridine *N*-oxide was reported to react with isocyanides but no details were supplied[88].

Isocyanides react readily with benzonitrile oxide to form isocyanates and benzonitrile[56] (equation 73). For example, on heating an ethereal solution of

$$\text{Ph—CNO} + \text{R—NC} \longrightarrow \text{Ph—CN} + \text{R—NCO} \qquad (73)$$

benzonitrile oxide with an equimolar amount of cyclohexyl isocyanide cyclohexyl isocyanate is formed together with some diphenylfuroxan, which is the dimerization product of benzonitrile oxide. Benzonitrile oxide also reacts with phenyl, *p*-chlorophenyl, *p*-bromophenyl and *t*-butyl isocyanides.

F. Thallium(III) Nitrate

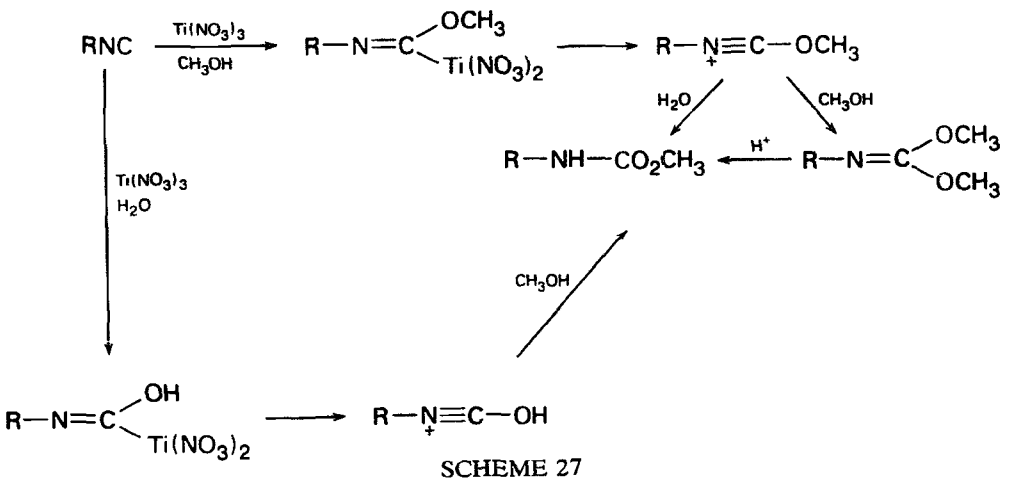
Thallium(III) nitrate trihydrate reacts rapidly with isocyanides to give carbamates in 35–97% yield[93] (equation 74). Mercury(II) nitrate is also effective, though the yields are lower (23–40%).

$$\text{RNC} + \text{Tl(NO}_3\text{)}_3 \xrightarrow[\text{H}_2\text{O}]{\text{CH}_3\text{OH}} \text{R—NH—CO}_2\text{CH}_3 + \text{TlNO}_3 + 2\,\text{HNO}_3 \qquad (74)$$

R = cyclohexyl, *t*-Bu, *p*-MeC_6H_4, Ph, 2-naphthyl, $EtOCOCH_2$

Carbamate formation in this reaction has been explained by invoking the ability of isocyanides to undergo α-addition (Scheme 27).

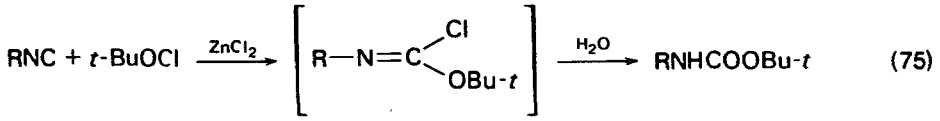
This method of isocyanide oxidation seems to be free of apparent complicating factors.



SCHEME 27

G. *t*-Butyl Hypochlorite and Br^+

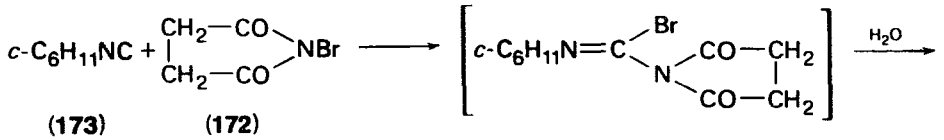
Cyclohexyl isocyanide reacts with *t*-butyl hypochlorite in the presence of $ZnCl_2$ to form *t*-butyl *N*-cyclohexylcarbamate (20%) in addition to cyclohexyl isocyanate (16%)[121]. In the absence of $ZnCl_2$, the isocyanate is the sole product (40%). Phenyl isocyanide gives *t*-butyl *N*-phenylcarbamate (69%). The reactions presumably involve an imidoyl chloride intermediate (equation 75).



$$RNC + t\text{-}BuOCl \xrightarrow{ZnCl_2} \left[R{-}N{=}C(Cl)(OBu\text{-}t) \right] \xrightarrow{H_2O} RNHCOOBu\text{-}t \qquad (75)$$

$$R = c\text{-}C_6H_{11},\ Ph$$

Wet *N*-bromosuccinimide (**172**) reacts with cyclohexyl isocyanide (**173**) at room temperature, yielding 21% of *N*-(cyclohexylcarbamoyl)succinamic acid (**174**) after hydrolysis (equation 76).



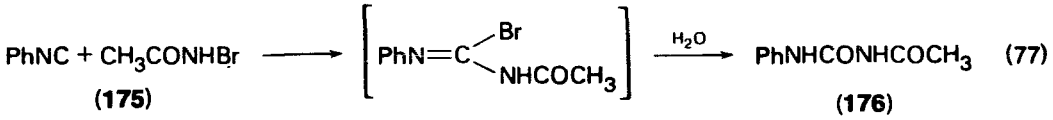
$$c\text{-}C_6H_{11}NC + \text{succinimide-NBr} \longrightarrow \left[c\text{-}C_6H_{11}N{=}C(Br)(\text{succinimide}) \right] \xrightarrow{H_2O}$$

(**173**) (**172**)

$$c\text{-}C_6H_{11}NHCONHCOCH_2CH_2CO_2H \qquad (76)$$

(**174**)

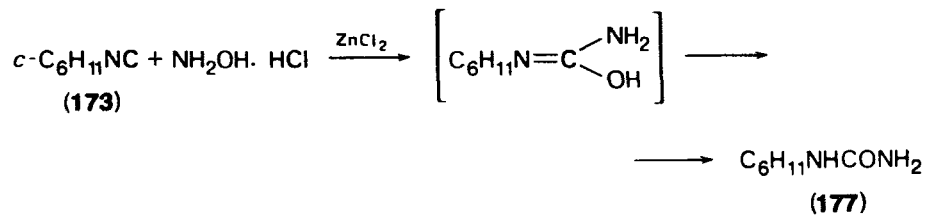
The analogous reaction of phenyl isocyanide with *N*-bromoacetamide (**175**) affords *N*-acetyl *N'*-phenylurea (**176**) in 38% yield (equation 77).



$$PhNC + CH_3CONHBr \longrightarrow \left[PhN{=}C(Br)(NHCOCH_3) \right] \xrightarrow{H_2O} PhNHCONHCOCH_3 \qquad (77)$$

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

Treatment of a mixture of **173** and hydroxylamine with $ZnCl_2$ gives *N*-cyclohexylurea (**177**) in 42% yield (equation 78). Phenyl isocyanide gives no similar reaction.



$$c\text{-}C_6H_{11}NC + NH_2OH \cdot HCl \xrightarrow{ZnCl_2} \left[C_6H_{11}N{=}C(NH_2)(OH) \right] \longrightarrow$$

(**173**)

$$\longrightarrow C_6H_{11}NHCONH_2 \qquad (78)$$

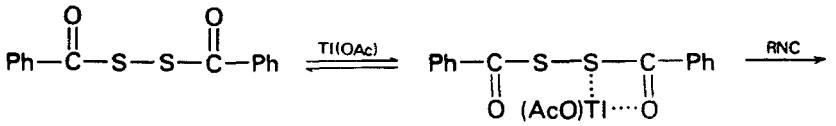
(**177**)

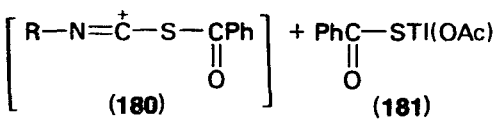
H. Oxidation to Isothiocyanate

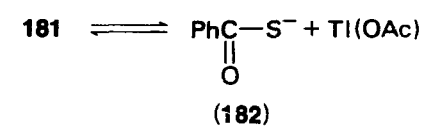
The treatment of cyclohexyl isocyanide (**173**) with dibenzoyl disulphide (**178**) in the presence of thallium(I) thiobenzoate in refluxing chloroform affords cyclohexyl isothiocyanate (**179**) in 77% yield[164] (equation 79).

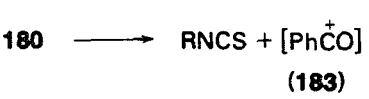
$$\underset{\textbf{(173)}}{c\text{-}C_6H_{11}NC} + \underset{\textbf{(178)}}{PhCOSSCOPh} \xrightarrow{Tl(SCOPh)} \underset{\textbf{(179)}}{c\text{-}C_6H_{11}NCS} \qquad (79)$$

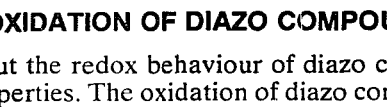
The reaction has been extended to phenyl, *t*-butyl, *n*-butyl and ethoxybutyl isocyanides with dibenzoyl disulphide, tetraethylthiuram disulphide [$(Et_2NC(S)S)_2$] and diacetyl disulphide, using thallium(I) acetate and thiobenzoate as catalysts. The yields are very good, being nearly quantitative in some cases. Dialkyl and diaryl disulphides are inactive. The best catalyst is Tl(OAc). Other metal ions also catalyse the reaction; their activity decreases in the order $Tl^+ \geqslant Pb^{2+} \geqslant Cd^{2+} \geqslant Ag^+ \geqslant Cu^+ \geqslant Hg^+$. The reaction mechanism is assumed to involve nucleophilic attack of the isocyanide on one of the sulphur atoms in a metal-complexed disulphide (Scheme 28).











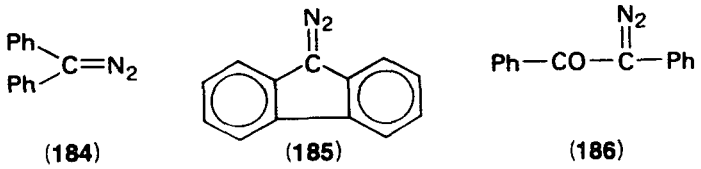
SCHEME 28

V. OXIDATION OF DIAZO COMPOUNDS

From what is known about the redox behaviour of diazo compounds, it appears that they exhibit oxidative properties. The oxidation of diazo compounds, therefore, can be effected only with strong oxidants, e.g., ozone and peroxy acids.

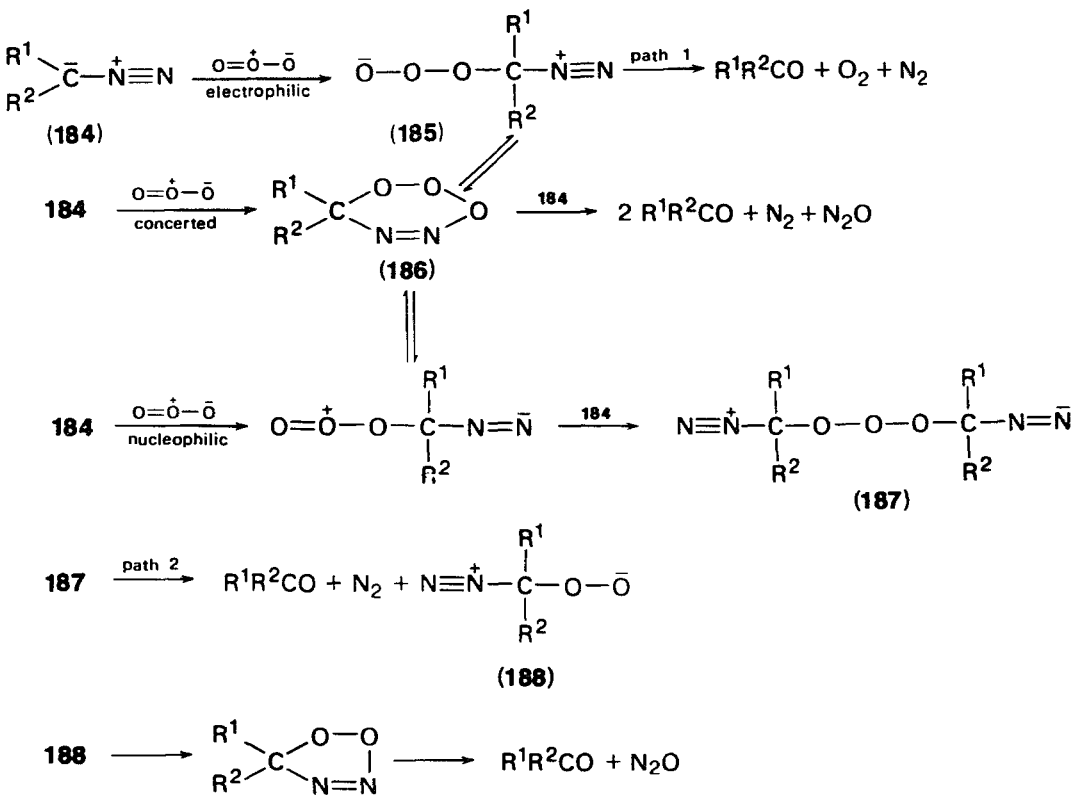
A. Ozone

Ozonation of diphenyldiazomethane (**184**), diazofluorene (**185**) and azobenzyl (**186**) leads to cleavage of the carbon–nitrogen bond, resulting in the formation of ketones in high yield[137]. Depending on the solvent (CCl_4, CH_2Cl_2, MeOH), temperature (−78 to 30°C) and concentration, the stoichiometry of ozonation varies from 1:1 to nearly 2:1 mole diazo compound/mole O_3. With ozone–nitrogen mixtures, oxygen is detected as



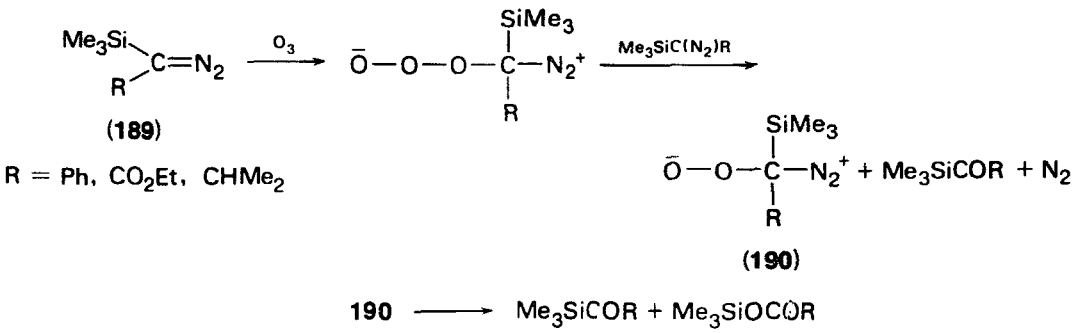
(**184**) (**185**) (**186**)

a product. Nitrous oxide is formed when the substrate is in large excess. In methanol as solvent, some carbon dioxide is detected as a product. The observed behaviour has been rationalized in terms of two reaction paths (Scheme 29).



SCHEME 29

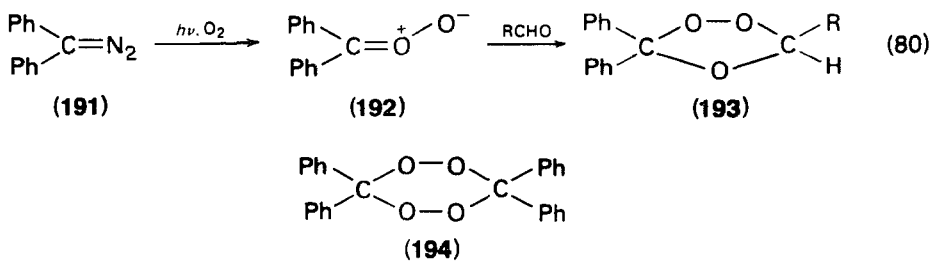
The ozonolysis of silyl diazo compounds (**189**) has been found to give silyl ketones which react further to form silyl esters[146] (Scheme 30).



SCHEME 30

B. Photooxidation

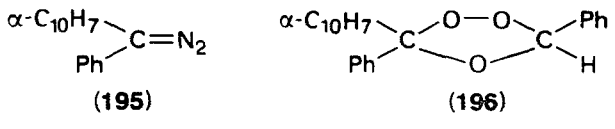
The photooxidation of diphenyldiazomethane (**191**) was suggested to proceed via a carbonyl oxide intermediate[94]. This was later supported by the isolation of benzophenone diperoxide in such photooxidations[10a]. Additional evidence for the carbonyl oxide intermediate was provided by the fact that the hydrocarbon solvent underwent oxidation during the photooxidation of dimethyldiazomethane[68]. In an aldehyde solvent, the photooxidation of **191** leads to the formation of an ozonide (**193**) which is the cycloadduct of the aldehyde and the zwitterion (carbonyl oxide) intermediate **192**[110] (equation 80). In the absence of aldehyde the photooxidation of **191** leads to benzophenone diperoxide (**194**), apparently via dimerization of **192**.



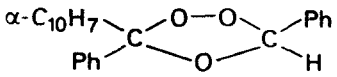
(80)

Ozonide formation via the photooxidation of diaryl diazo compounds in the presence of aldehydes was further explored with special reference to stereochemistry[111a]. The photooxidation of α-naphthylphenyldiazomethane (**195**) in benzene gave α-naphthyl phenyl ketone diperoxide. Photooxidation of the same diazo compound in acetaldehyde or benzaldehyde afforded 1-(α-naphthyl)-1-phenyl-1-propene ozonide (**196**) or 1-(α-naphthyl)stilbene ozonide (**197**). The *cis* to *trans* ratio was found to be the same as formed in the ozonolysis of *trans*-1-(α-naphthyl)-1-phenylpropene and *trans*-1-(α-naphthyl)stilbene.

Diazo compounds can also be converted to ozonides via reaction with singlet oxygen[79].



(*cis* and *trans*)

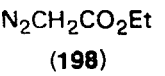


(197)

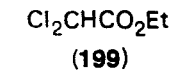
(*cis* and *trans*)

C. Copper(II) Chloride

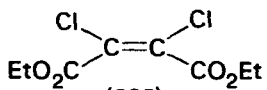
Ethyl diazoacetate (**198**) reacts with $CuCl_2$ to give ethyl dichloroacetate (**199**), diethyl dichloromaleate (**200**) and diethyl dichlorofumarate (**201**)[140]. **198** also reacts with copper(I) chloride, but the products (diethyl maleate and fumarate) represent no formal oxidation.



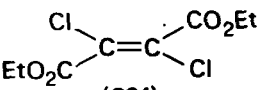
(198)



(199)



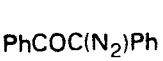
(200)



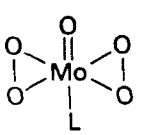
(201)

D. Metal-catalysed Oxidation

2-Diazo-2-phenylacetophenone (**202**) is oxidized with *t*-butyl hydroperoxide in the presence of $Mo(CO)_6$ as catalyst[107]. The products are benzil (37%) and benzoic acid (19%), together with some *t*-butyl benzoate (3%) and peroxybenzoate (9%). The oxidation of **202** with the diperoxomolybdenum complex **203** affords 79% benzil with no other products detected. The reaction of 3-diazoheptan-4-one with **203** gives



(202)



(203)

L = $PO(NMe_2)_3$

mainly heptan-3,4-dione and a 55:45 mixture of *cis*- and *trans*-hept-2-en-4-ones. It has been concluded from these results that the catalysed oxidations proceed via the initial formation of molybdenum oxocarbene complexes.

VI. REFERENCES

1. H. Ahlbrecht, W. Raab and C. Vonderheid, *Synthesis*, 127 (1979).
2. M. Albeck, S. Hoz and Z. Rappoport, *J. Chem. Soc., Perkin Trans. 2*, 124 (1972).
3. M. Anbar and D. Ginsburg, *Chem. Rev.*, **54**, 925 (1954).
4. A. G. Anshitz, V. D. Sokolovskii and G. K. Boreskov, *Kinet. Katal.*, **19**, 372 (1978).
5. A. G. Anshitz, V. D. Sokolovskii, G. K. Boreskov and A. A. Davydov, *Kinet. Katal.*, **19**, 366 (1978).
6. J. B. Armitage, E. Entwistle, E. R. H. Jones and M. C. Whiting, *J. Chem. Soc.*, 147 (1954).
7. J. B. Armitage, E. R. H. Jones and M. C. Whiting, *J. Chem. Soc.*, 2014 (1952).
8. C. A. Arrington, W. Brennen, G. P. Glass and J. V. Michael, *J. Chem. Phys.*, **43**, 525 (1965).

9. P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958).
10. (a) P. D. Bartlett and T. G. Traylor, *J. Amer. Chem. Soc.*, **84**, 3408 (1962).
    (b) R. K. Bentley, D. Bhattacharjee, E. R. H. Jones and V. Thaller, *J. Chem. Soc. (C)*, 685 (1969).
11. H. K. Black, D. H. S. Horn and B. C. L. Weedon, *J. Chem. Soc.*, 1704 (1954).
12. F. Bohlmann, H. Schönowsky, E. Inhoffen and G. Grau, *Chem. Ber.*, **97**, 794 (1964).
13. F. Bohlmann, H. J. Sinn, J. Politt and E. Inhoffen, *Chem. Ber.*, **89**, 1281 (1956).
14. R. W. Bott, C. Eaborn and D. R. M. Walton, *J. Chem. Soc.*, 384 (1965).
15. D. N. Brattesani and C. H. Heathcock, *Tetrahedron Letters*, 2279 (1974).
16. J. M. Brown and B. A. Thrush, *Trans. Faraday Soc.*, **63**, 630 (1967).
17. L. G. Bruk, S. M. Brailovskii, O. N. Temkin, R. M. Flid and A. S. Kostyushin, *Zh. Org. Khim.*, **10**, 2262 (1974).
18. P. Cadiot and W. Chodkiewicz in *Chemistry of Acetylenes* (Ed. H. G. Viehe), Marcel Dekker, New York, 1969.
19. W. R. Carpenter and B. Armstrong, *J. Org. Chem.*, **29**, 2772 (1964).
20. L. A. Carpino, *J. Org. Chem.*, **35**, 3971 (1970).
21. B. Chabaud and K. B. Sharpless, *J. Org. Chem.*, **44**, 4202 (1979).
22. S. K. Chakrabartty and H. O. Kretschmer, *J. Chem. Soc., Perkin Trans. 1*, 222 (1974).
23. A. I. Chirko, K. I. Ivanov, I. G. Tishchenko and T. I. Girko, *Zh. Org. Khim.*, **10**, 2040 (1974).
24. A. I. Chirko, K. I. Ivanov and I. G. Tishchenko, *Vestsi Akad. Navuk BSSR, Ser. Khim. Navuk*, 64 (1975).
25. A. I. Chirko, I. G. Tishchenko and M. V. Kudrevatkykh, *Vestsi Akad. Navuk BSSR, Ser. Khim. Navuk*, 78 (1977).
26. A. I. Chirko, I. G. Tishchenko and G. M. Sosnovskii, *Zh. Org. Khim.*, **14**, 930 (1978).
27. A. I. Chirko, I. G. Tishchenko, G. M. Sosnovskii and T. Derevtsova, *Zh. Org. Khim.*, **13**, 1579 (1977).
28. A. I. Chirko, I. G. Tischchenko, S. G. Stepin and A. F. Abremov, *Zh. Org. Khim.*, **9**, 2497 (1973).
29. A. I. Chirko, I. G. Tishchenko, S. G. Stepin and K. I. Ivanov, *Zh. Org. Khim.*, **9**, 1687 (1973).
30. A. I. Chirko, I. G. Tishchenko and G. V. Vashchuk, *Zh. Org. Khim.*, **9**, 2493 (1973).
31. W. Chodkiewicz and P. Cadiot, *Compt. Rend.*, **241**, 1055 (1955).
32. J. Ciabattoni, R. A. Campbell, C. A. Renner and P. W. Concannon, *J. Amer. Chem. Soc.*, **92**, 3826 (1970).
33. P. G. Clay, G. R. A. Johnson and J. Weiss, *J. Phys. Chem.*, **63**, 862 (1969).
34. A. A. Clifford and W. A. Waters, *J. Chem. Soc.*, 3056 (1963).
35. R. J. Collin, J. Jones and W. P. Griffith, *J. Chem. Soc., Dalton*, 1074 (1974).
36. P. W. Concannon and J. Ciabattoni, *J. Amer. Chem. Soc.*, **95**, 3284 (1973).
37. E. J. Corey and G. Schmidt, *Tetrahedron Letters*, 399 (1979).
38. R. Criegee, *Ann. Chem.*, **583**, 1 (1953).
39. R. Criegee and M. Lederer, *Ann. Chem.*, **583**, 29 (1953).
40. R. Criegee, B. Marchand and H. Wannowius, *Ann. Chem.*, **550**, 99 (1942).
41. (a) E. Dallwigh, H. Paillard and E. Briner, *Helv. Chim. Acta*, **35**, 1377 (1952).
    (b) W. G. Dauben, M. Lorber and D. S. Fullerton, *J. Org. Chem.*, **34**, 3587 (1969).
42. (a) P. B. D. de la Mare and R. Bolton, *Electrophilic Additions to Unsaturated Systems*, Elsevier, Amsterdam–London–New York, 1966.
    (b) W. B. DeMore and Ch.-L. Lin, *J. Org. Chem.*, **38**, 985 (1973).
43. W. T. Dixon, J. Foxall, G. H. Williams, D. J. Edge, B. C. Gilbert, H. Kazarians-Moghaddam and R. O. C. Norman, *J. Chem. Soc., Perkin Trans. 2*, 827 (1977).
44. G. Eglinton and A. R. Galbraith, *Chem. Ind. (London)*, 737 (1956).
45. G. Eglinton and A. R. Galbraith, *J. Chem. Soc.*, 889 (1959).
46. G. Eglinton and W. McCrae, *Advan. Org. Chem.*, **4**, 225 (1963).
47. A. J. Fatiadi, *Synthesis*, 65 (1976).
48. L. G. Fedenok, V. M. Berdnikov and M. S. Shvartsberg, *Zh. Org. Khim.*, **9**, 1781 (1973); **10**, 922 (1974).
49. L. G. Fedenok, V. M. Berdnikov and M. S. Shvartsberg, *Zh. Org. Khim.*, **12**, 1395 (1976).

50. L. G. Fedenok, V. M. Berdnikov and M. S. Shvartsberg, *Zh. Org. Khim.*, **14**, 1423 (1978).
51. L. G. Fedenok, V. M. Berdnikov and M. S. Shvartsberg, *Zh. Org. Khim.*, **14**, 1429 (1978).
52. F. Fehér and H. Weber, *Chem. Ber.*, **91**, 2523 (1958).
53. H. Feuer, H. Rubinstein and A. T. Nielsen, *J. Org. Chem.*, **23**, 1107 (1958).
54. J. Fenwick, G. Frater, K. Ogi and O. P. Strausz, *J. Amer. Chem. Soc.*, **95**, 124 (1973).
55. J. Ficini and G. Stork, *J. Amer. Chem. Soc.*, **83**, 4678 (1961).
56. P. V. Finzi and M. Arbasino, *Tetrahedron Letters*, 4645 (1965).
57. C. S. Foote and J. Wei-Ping Lin, *Tetrahedron Letters*, 3267 (1968).
58. V. Franzen, *Chem. Ber*, **87**, 1478 (1954).
59. D. M. Gale and S. C. Cherkofsky, *J. Org. Chem.*, **38**, 475 (1973).
60. Yu. F. Gatilov, L. B. Ionov, A. P. Korovyakov and L. G. Kokorina, *Zh. Obshch. Khim.*, **43**, 2677 (1973).
61. L. D. Gavrilov, M. I. Klopotova and L. I. Vereshchagin, *Zh. Org. Khim.*, **10**, 2064 (1974).
62. H. R. Gersmann and A. F. Bickel, *J. Chem. Soc. (B)*, 2230 (1971).
63. C. Glaser, *Chem. Ber.*, **2**, 422 (1869).
64. C. Glaser, *Ann. Chem.*, **137**, 154 (1870).
65. H. Gopal and A. J. Gordon, *Tetrahedron Letters*, 2941 (1971).
66. J. Greevers, J. Th. Hackmann and W. P. Trompen, *J. Chem. Soc.*, 875 (1970).
67. P. A. Grieco and Y. Yokoyama, *J. Amer. Chem. Soc.*, **99**, 5210 (1977).
68. G. A. Hamilton and J. R. Giacin, *J. Amer. Chem. Soc.*, **88**, 2584 (1966).
69. H. Hauptmann, *Tetrahedron*, **32**, 1293 (1976).
70. J. J. Havel and K. H. Chan, *J. Org. Chem.*, **42**, 569 (1977).
71. A. S. Hay, *J. Org. Chem.*, **25**, 1275 (1960).
72. J. M. Hay and D. Lyon, *Proc. Roy. Soc. (London)*, **A317**, 1 (1970).
73. J. M. Hay and D. Lyon, *Proc. Roy. Soc. (London)*, **A317**, 21 (1970).
74. J. M. Hay and D. Lyon, *Proc. Roy. Soc. (London)*, **A317**, 41 (1970).
75. J. M. Hay and R. G. W. Norrish, *Proc. Roy. Soc. (London)*, **A288**, 17 (1965).
76. I. Heilbron, E. R. H. Jones and F. Sondheimer, *J. Chem. Soc.*, 604 (1949).
77. J. B. Hendrickson, D. J. Cram and G. S. Hammond, *Organic Chemistry*, 3rd ed., McGraw-Hill, New York, 1970.
78. P. Herbrechtsmeier and H. G. Wagner, *Z. Phys. Chem. Neue Folge*, **93**, 143 (1974).
79. D. P. Higley and R. W. Murray, *J. Amer. Chem. Soc.*, **96**, 3330 (1974).
80. C. D. Hurd and R. E. Christ, *J. Org. Chem.*, **1**, 141 (1936).
81. K. M. Ibne-Rasa, R. H. Pater, J. Ciabattoni and J. O. Edwards, *J. Amer. Chem. Soc.*, **95**, 7894 (1973).
82. S. Jackson and L. A. Hull, *J. Org. Chem.*, **41**, 3340 (1976).
83. T. L. Jacobs, *J. Amer. Chem. Soc.*, **58**, 2272 (1936).
84. J. Jadot and M. Neuray, *Bul. Soc. Roy. Sci. Liege*, **31**, 247 (1962).
85. M. Jáky and L. I. Samándi, *J. Chem. Soc., Perkin Trans. 2*, 1481 (1972).
86. M. Jáky and L. I. Simándi, *J. Chem. Soc., Perkin Trans. 2*, 939 (1976).
87. J. R. Johnson, A. M. Schwartz and T. L. Jacobs, *J. Amer. Chem. Soc.*, **60**, 1882 (1938).
88. H. W. Johnson, Jr and P. M. Daughhetee, Jr., *J. Org. Chem.*, **29**, 246 (1964).
89. J. R. Kanofsky, D. Lucas, F. Pruss and D. Gutman, *J. Phys. Chem.*, **78**, 311 (1974).
90. R. E. Keay and G. A. Hamilton, *J. Amer. Chem. Soc.*, **97**, 6876 (1975).
91. R. E. Keay and G. A. Hamilton, *J. Amer. Chem. Soc.*, **98**, 6578 (1976).
92. N. A. Khan, and M. S. Newman, *J. Org. Chem.*, **17**, 1063 (1952).
93. F. Kienzle, *Tetrahedron Letters*, 1771 (1972).
94. W. Kirmse, L. Horner and H. Hoffmann, *Ann. Chem.*, **614**, 22 (1958).
95. A. L. Klebanskii, I. V. Grachev and O. M. Kuznetsova, *Zh. Obshch. Khim.*, **27**, 2977 (1957).
96. J. König and V. Wolf, *Tetrahedron Letters*, 1629 (1970).
97. A. P. Krapcho, J. R. Larson and J. M. Eldridge, *J. Org. Chem.*, **42**, 3749 (1977).
98. A. Krebs in *Chemistry of Acetylenes* (Ed. H. G. Viehe), Marcel Dekker, New York, 1969.
99. H. Kropf and R. Schröder, *Ann. Chem.*, 2325 (1976).
100. Yu. N. Kukushkin, V. V. Kobzev and L. P. Morozova, *Zh. Prikl. Khim.*, **43**, 2759 (1970).
101. E. Kühle, B. Anders and G. Zumach, *Chem. Ber.*, **79**, 663 (1967).
102. D. G. Lee and V. S. Chang, *Synthesis*, 462 (1978).
103. D. G. Lee and V. S. Chang, *J. Org. Chem.*, **44**, 2726 (1979).

104. S. M. Makin, A. A. Ismail, V. V. Yastrebov and K. I. Petrov, *Zh. Org. Khim.*, **7**, 2120 (1971).
105. O. Makowka, *Chem. Ber.* **41**, 943 (1908).
106. D. Martin and A. Weise, *Angew. Chem.*, **79**, 145 (1967).
107. S. A. Matlin and P. G. Sammes, *J. Chem. Soc. Perkin Trans. 1*, 2851 (1973).
108. R. N. McDonald and P. A. Schwab, *J. Amer. Chem. Soc.*, **86**, 4866 (1964).
109. A. McKillop, O. M. Oldenziel, B. P. Swann, E. C. Taylor and R. L. Robley, *J. Amer. Chem. Soc.*, **93**, 7331 (1971).
110. R. W. Murray and A. Suzui, *J. Amer. Chem. Soc.*, **93**, 4963 (1971).
111. (a) R. W. Murray and A. Suzui, *J. Amer. Chem. Soc.*, **95**, 3343 (1973).
(b) P. Mushak and M. A. Battiste, *Chem. Commun.*, 1146 (1969).
112. W. Münzenmaier and H. Straub, *Synthesis*, 49 (1976).
113. I. N. Nazarov and L. D. Bergelson, *Izv. Akad. Nauk SSSR, Ser. Khim. Nauk*, 896 (1960).
114. I. N. Nazarov and L. D. Bergelson, *Izv. Akad. Nauk SSSR, Ser. Khim. Nauk*, 887 (1960).
115. S. Németh, Z. Szeverényi, A. Fülep and L. I. Simándi, *Proceedings XXI International Conference on Coordination Chemistry, Toulouse, France*, 1980, p. 167.
116. W. G. Nigh in *Oxidation in Organic Chemistry*, Part B (Ed. W. S. Trahanovsky). Academic Press, New York and London, 1973, p. 1.
117. G. I. Nikishin, E. I. Troyanskii, D. S. Velibekova and Yu. P. Ogibin, *Izv. Akad. Nauk SSSR*, 2430 (1978).
118. R. G. W. Norrish and J. D. Reagh, *Proc. Roy. Soc. (London)*, **A176**, 479 (1940).
119. Y. Ogata, Y. Sawaki and H. Inoue, *J. Org. Chem.*, **38**, 1044 (1973).
120. R. Ohlson, *Acta Chem. Scand.*, **20**, 585 (1966).
121. M. Okano, Y. Ito, T. Shono and R. Oda, *Bull. Chem. Soc. Japan*, **36**, 1314 (1963).
122. S. Otsuka, A. Nakamura and Y. Tatsuno, *Chem. Commun.*, 836 (1967).
123. E. Ott and B. Löpmann, *Chem. Ber.*, **55B**, 1255 (1922).
124. R. Pappo and A. Becker, *Bull. Res. Counc. Israel.*, Sect. A, **5**, 300 (1956).
125. S. Patai (Ed), *The Chemistry of the Carbon–Carbon Triple Bond*, Wiley–Interscience, Chichester–New York, 1978.
126. A. A. Petrov and M. P. Forost, *Zh. Obshch. Khim.*, **34**, 3292 (1964).
127. A. A. Petrov, Yu. I. Porfireva and L. B. Sokolov, *Dokl. Akad. Nauk SSSR*, **151**, 1343 (1964).
128. W. R. Pilgrim, *Ph.D. Thesis*, Queen's University, Kingston, Ontario, 1969.
129. J. A. Pincock and K. Yates, *Can. J. Chem.*, **48**, 3332 (1970).
130. B. Plesnicar, *Oxidation in Organic Chemistry* in *Organic Chemistry: A Series of Monographs*, Vol. 5C (Ed. W. S. Trahanovsky). Academic Press, New York–San Francisco–London, 1978, pp. 211–294.
131. Yu. I. Porfireva, A. A. Petrov and L. B. Sokolov, *Zh. Obshch. Khim.*, **34**, 1873 (1964).
132. Yu. I. Porfireva, E. S. Turbanova and A. A. Petrov, *Zh. Obshch. Khim.*, **34**, 3966 (1965).
133. Yu. I. Porfireva, E. S. Turbanova and A. A. Petrov, *Zh. Org. Khim.*, **2**, 777 (1966).
134. Z. Rappoport (Ed.), *Chemistry of the Cyano Group*, Interscience, London, 1970.
135. Z. Rappoport and E. Shohamy, *J. Chem. Soc. (B)*, 2060 (1971).
136. L. Re, A. Brandt and L. Bassignani, *German Patent* 2,744,828 (1978).
137. A. M. Reader, P. S. Bailey and H. M. White, *J. Org. Chem.*, **30**, 784 (1965).
138. S. F. Reed, Jr., *J. Org. Chem.*, **30**, 2195 (1965).
139. P. W. Robertson, W. E. Dasent, R. M. Milburn and W. H. Oliver, *J. Chem. Soc.*, 1628 (1950).
140. T. Saegusa, Y. Ito, T. Shimizu and S. Kobayashi, *Bull. Chem. Soc. Japan*, **42**, 3535 (1969).
141. T. Saegusa, S. Kobayashi and Y. Ito, *Bull. Chem. Soc. Japan*, **43**, 275 (1970).
142. K. Schlögl and A. Mohar, *Monatsh. Chem.*, **93**, 1309 (1962).
143. H. H. Schlubach and V. Wolf, *Ann. Chem.*, **568**, 14 (1950).
144. G. H. Schmid in *The Chemistry of the Carbon–Carbon Triple Bond* (Ed. S. Patai), Wiley–Interscience, Chichester–New York, 1978.
145. M. Schröder and W. P. Griffith, *J. Chem. Soc.*, Dalton, 1599 (1978).
146. A. Sekiguchi and W. Ando, *J. Chem. Soc., Chem. Commun.*, 575 (1979).
147. J. E. Shaw and J. J. Sherry, *Tetrahedron Letters*, 4379 (1971).
148. W. B. Sheats, L. K. Olli, R. Stout, J. T. Londeen, R. Justus and W. G. Nigh, *J. Org. Chem.*, **44**, 4075 (1979).

149. T. Shono, A. Kimura, Y. Ito, K. Nishida and R. Oda, *Bull. Chem. Soc. Japan*, **37**, 635 (1964).
150. L. I. Simándi and M. Jáky, *J. Chem. Soc., Perkin Trans. 2*, 2326 (1972).
151. L. I. Simándi and M. Jáky, *J. Chem. Soc., Perkin Trans. 2*, 1861 (1973).
152. L. I. Simándi and M. Jáky, *J. Chem. Soc., Perkin Trans. 2*, 1856 (1973).
153. L. I. Simándi and M. Jáky, *J. Chem. Soc., Perkin Trans. 2*, 630 (1977).
154. L. I. Simándi, M. Jáky, N. T. Son and J. Hegedüs-Vajda, *J. Chem. Soc., Perkin Trans. 2*, 1794 (1977).
155. H. Sinn, S. Hopperdietzel and D. Sauermann, *Monatsh. Chem.*, **96**, 1036 (1965).
156. F. Sondheimer, Y. Amiel and R. Wolovsky, *J. Amer. Chem. Soc.*, **79**, 4247 (1957).
157. F. Sondheimer, Y. Amiel and R. Wolovsky, *J. Amer. Chem. Soc.*, **81**, 4600 (1959).
158. F. Sondheimer and R. Wolovsky, *J. Amer. Chem. Soc.*, **84**, 260 (1962).
159. (a) R. Spence and G. B. Kistiakowsky, *J. Amer. Chem. Soc.*, **52**, 483 (1930).
(b) N. S. Srinivasan and D. G. Lee, *J. Org. Chem.*, **44**, 1574 (1979).
160. E. W. R. Steacie and R. D. McDonald, *J. Chem. Phys.*, **4**, 75 (1936).
161. J. K. Stille and D. D. Whitehurst, *J. Amer. Chem. Soc.*, **86**, 4871 (1964).
162. H. Suzuki, M. Koge and T. Hanafusa, *J. Chem. Soc., Chem. Commun.*, 341 (1977).
163. Z. G. Szabó and D. Gál, *Acta Chim. Acad. Sci. Hung.*, **11**, 263 (1957).
164. S. Tanaka, S. Uemura and M. Okano, *Bull. Chem. Soc. Japan*, **50**, 2785 (1977).
165. W. P. Trompen, J. Greevers and J. Th. Hackmann, *Recueil*, **90**, 458 (1971).
166. N. J. Turro, V. Ramamurthy, K.-Ch. Lin, A. Krebs and R. Kemper, *J. Amer. Chem. Soc.*, **98**, 6758 (1976).
167. S. Uemura, H. Okazaki and M. Okano, *J. Chem. Soc., Perkin Trans. 1*, 1278 (1978).
168. S. Uemura, H. Okazaki, A. Onoe and M. Okano, *J. Chem. Soc., Perkin Trans. 1*, 676 (1977).
169. S. Uemura, H. Okazaki, A. Onoe and M. Okano, *J. Chem. Soc., Perkin Trans. 1*, 548 (1979).
170. I. Ugi (Ed.), *Isonitrile Chemistry* in *Organic Chemistry: A Series of Monographs*, Vol. 20, Academic Press, New York–London, 1971, p. 79.
171. J. J. Verbanc and G. F. Hennion, *J. Amer. Chem. Soc.*, **60**, 1711 (1938).
172. L. I. Vereschchagin, L. G. Tikhonova, E. I. Titova, V. P. Latyshev and L. D. Gavrilov, *Zh. Org. Khim.*, **9**, 1355 (1973).
173. M. S. A. Vrijland and J. Th. Hackmann, *Tetrahedron Letters*, 3763 (1970).
174. C. Walling and G. El-Taliawi, *J. Amer. Chem. Soc.*, **95**, 848 (1973).
175. W. A. Waters and J. S. Littler in *Oxidation in Organic Chemistry* (Ed. K. B. Wiberg), Academic Press, New York–London, 1965.
176. D. S. Watt, *J. Org. Chem.*, **39**, 2799 (1974).
177. D. S. Watt and S. J. Selikson, *J. Org. Chem.*, **40**, 267 (1975).
178. G. H. Whitam in *Comprehensive Organic Chemistry*, Vol. 1 (Eds. D. Barton and W. D. Ollis), Pergamon Press, 1979, p. 164.
179. K. B. Wiberg and K. A. Saegebarth, *J. Amer. Chem. Soc.*, **79**, 2822 (1957).
180. E. Winterfeldt in *Chemistry of Acetylenes* (Ed. H. C. Viehe), Marcel Dekker, New York, 1969.
181. S. Wolfe, W. R. Pilgrim, T. F. Garrard and P. Chamberlain, *Can. J. Chem.*, **49**, 1099 (1971).
182. S. Wolfe and W. R. Pilgrim, *49th Canadian Chemical Conference, Saskatoon, Saskatchewan*, 1966, p. 78.
183. P. Yates, *J. Amer. Chem. Soc.*, **74**, 5376 (1952).
184. G. Zweifel and S. J. Backlund, *J. Amer. Chem. Soc.*, **99**, 3184 (1977).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 14

Reduction of triple-bonded groups

ROBERT O. HUTCHINS
Drexel University, Philadelphia, Pennsylvania, U.S.A.

MARY GAIL K. HUTCHINS
Temple University, Philadelphia, Pennsylvania, U.S.A.

I. INTRODUCTION

The partial or complete reduction of carbon–carbon or carbon–nitrogen triple-bonded functionalities occupys an important niche in synthetic methodology. Conversions involving alkynes are particularly useful since hydrogen addition to one of the two π bonds allows the selective preparation of either the corresponding *E* or *Z* alkene stereoisomers, depending on the choice of reductive conditions. The classical method (and still one of the most general) for alkyne reduction involves catalytic hydrogenation and several reviews have appeared[1–6]. Other techniques, particularly those involving organoboron and organoaluminium intermediates and hydride-transfer reagents in combination with metal salts have also assumed importance in recent years. The sheer volume of applications reported precludes complete coverage here and this chapter will present only an overview of the topic with emphasis given to those studies which have focused on uncovering general methods and reagents. Specific applications are scattered throughout the literature and will be presented only as illustrative examples where appropriate. Total reduction of alkynes to alkanes, while often synthetically useful, is very similar to alkene hydrogenations and therefore will not be included here.

The conversions of nitriles to either imines (which may be hydrolysed to aldehydes) or amines constitute other synthetically useful reductions which have been used. Again, treatment will be selective and focus on general investigations. Since nitrile reductions were covered in 1970[7], this discussion emphasizes the literature from that point although some overlap is unavoidable for completeness and cohesiveness. The less useful decyanation processes were adequately described in the earlier work[7] and will not be repeated.

The reduction of other triple-bonded groups such as isocyanides and diazonium ions has not been extensively explored and coverage will accordingly be brief.

II. PARTIAL REDUCTION OF ALKYNES TO ALKENES

A. Catalytic Hydrogenation

1. Palladium catalysts

As mentioned, the metal-catalysed addition of 1 mole of hydrogen across an alkyne π bond has been utilized extensively and the area has been reviewed several times[1–6]. The usefulness of this general method relies on the ability to control both the stereoselectivity of the addition and functional group selectivity. This latter requirement particularly demands that reduction be halted at the alkene stage. A great many catalytic systems, especially those involving palladium have been investigated over the years[1–6], but by far the most successful and general, at least until recently, has been the

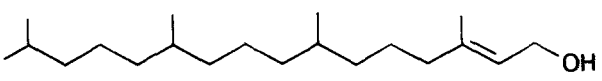
lead-poisoned Pd on $CaCO_3$ catalyst introduced in 1952 by Lindlar[8a] and subsequently improved by the addition of quinoline[8b]. A detailed experimental procedure for the preparation of the catalyst is available[8b].

Since its introduction, the Lindlar catalyst has enjoyed great popularity in synthesis primarily because, with isolated triple bonds, nearly totally complete stereoselective *cis* addition of hydrogen is obtained to afford *cis* alkenes and over-reduction to alkanes is minimized. In addition, unlike many similar palladium systems, the Lindlar catalyst does not appreciably isomerize alkenes[9] so that the *cis* isomers produced retain their stereochemical integrity. Thus, Raphael and coworkers[9] demonstrated that most palladium-based catalysts ($Pd/CaCO_3$, $Pd/BaSO_4$, Pd/C) initially afford the *cis* alkene from 4-octyne but, in the presence of hydrogen, extensive isomerization occurs to the more stable *trans* isomers (32–68%). However, the Lindlar system gave only ca. 4% of the *trans* isomer and generally the amount of isomerization is below 10%[10]. However, isomerization does not always appear to be a major problem with other palladium catalysts[11–16] and, in fact, the isomerization was beneficial in one case[17].

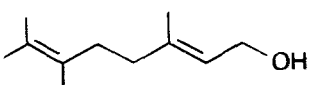
The stereoselectivity available with palladium catalysts has been exploited extensively in synthetic schemes including the preparation of *cis* medium-size ring alkenes[15,16], various annulenes[17,18], oleic (**1**)[19] and linoleic (2) acids[11], phytol (**3**)[20], ε-methylgeraniol (**4**)[21], geranyllinalool (**5**)[22], *Z*(−)-14-methyl-8-hexadecen-1-ol (**6**)[23] (a sex pheromone component of dermestid beetles), β-carotene (**7**)[24–27], lycopene (**8**)[28–30], vitamin A (**9**)[31,32] and similar polyene molecules. Thus, Karrer and Eugster[28] used Lindlar

Z-$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$ (**1**)

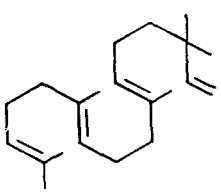
Z,*Z*-$CH_3(CH_2)_5(CH{=}CH)_2(CH_2)_7COOH$ (**2**)



(**3**)

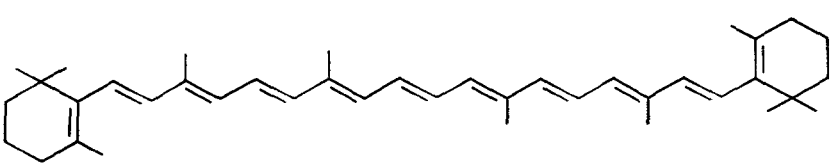


(**4**)

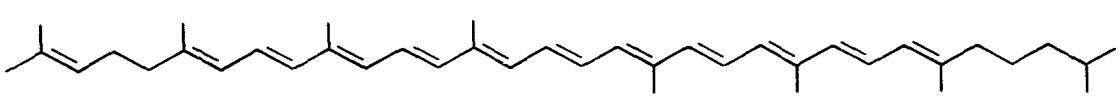


(**5**)

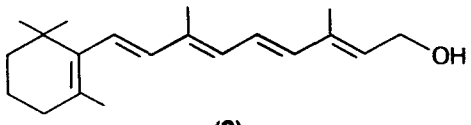
Z-$CH_3CH_2CH(CH_3)(CH_2)_4CH{=}CH(CH_2)_7OH$ (**6**)



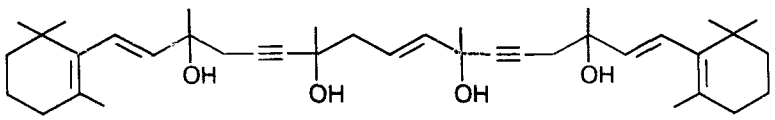
(**7**)



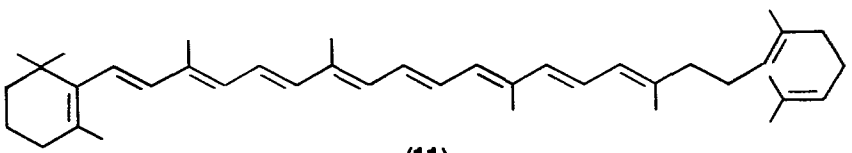
(**8**)



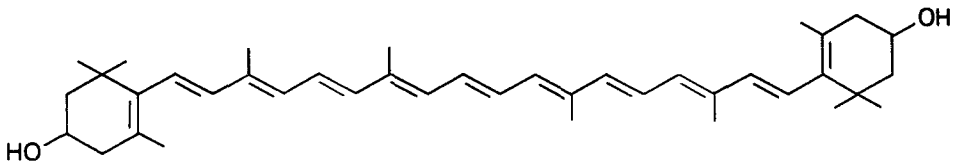
(9)



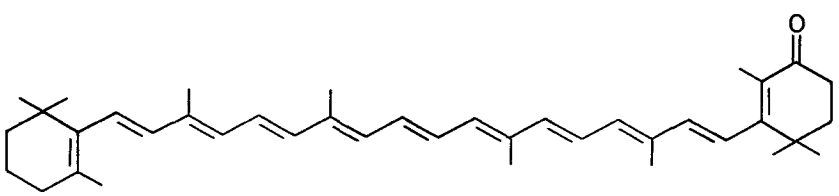
(10)



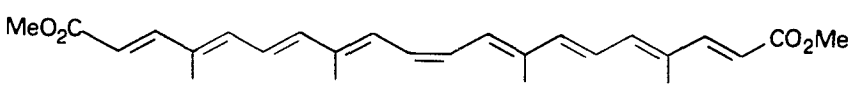
(11)



(12)



(13)

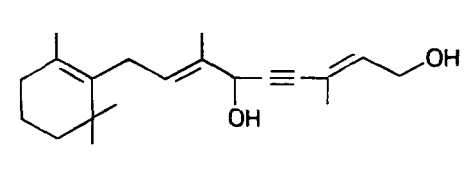


(14)

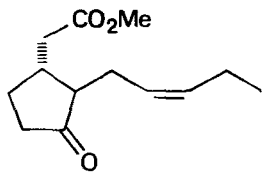
catalyst for the conversion of the triple bonds in **10** to the corresponding *cis* alkenes and for hydrogenation of a similar diyne to the *cis* diene en route to lycopene[29]. A second approach to lycopene also employed Lindlar catalyst for alkyne reduction[30]. Other palladium catalysts (i.e. $Pd/CaCO_3$[24,25], Pd/C-quinoline[26,27]) have been utilized to reduce alkyne intermediates in schemes leading to β-carotene. Furthermore, Lindlar catalyst has been used for partial hydrogenation of alkyne intermediates in the synthesis of β-zeacarotene (**11**)[34], zeaxanthin (**12**)[35], echinenone (**13**)[36], *cis*-10,10-bixin dimethyl ester (**14**)[37] and the termite communication pheromone *cis*-3-*cis*-6-*trans*-8-dodecatriene-1-ol[38]. Palladium on barium sulphate has been successfully used for the partial reduction of **15** in one total synthesis of vitamin A[31] while Lindlar catalyst has been employed for partial triple-bond reduction by two groups[32,33] en route to the same target molecule.

It is noteworthy that in the β-carotene and vitamin A syntheses[24–27,29,30] mentioned above, the choice of palladium catalysts was made to exploit the selectivity toward triple bonds in the presence of alkenes and not the *cis* stereoselectivity available since β-carotene and vitamin A are *all-trans* polyenes; isomerization of the *cis*-produced double bonds was necessary.

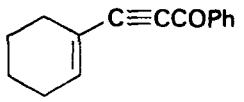
The *cis* stereoselectivity available via reduction with Lindlar catalyst was exploited by two groups[39,40] in the total synthesis of methyl jasmonate (**16**) and this demonstrates the inertness of esters and ketones toward the catalyst system. Likewise, hydrogenolysis of carbon–halogen bonds does not occur since hydrogenation of 1-chloro-7-tetradecyne with Pd/C, $Pd/CaCO_3$ or Lindlar catalyst gave the corresponding chloroalkene although the latter system gave superior *cis* stereoselectivity[41]. Also, amide linkages are not affected[42]. However, problems have been encountered in reductions of certain alkynes conjugated to aldehydes or ketones. With simple α,β-ynones, reduction to the corresponding *cis* enones can be accomplished most successfully using $Pd/CaCO_3$[43,44] which, in this case, is superior to Lindlar catalyst. The products are acid-sensitive and readily rearrange to the more stable *trans* enones. Further conjugation with alkenes often leads to complications. Thus, with palladium catalysts, the enynone **17** afforded a mixture composed of the saturated derivative **18** along the dihydropyran **19** and pyran **20**[45]. Likewise, a mixture of dienones and a pyran was obtained upon reduction of **21**[46]. However, successful reductions to dienones have



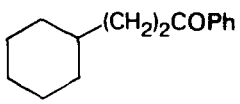
(15)



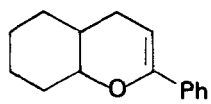
(16)



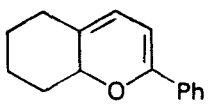
(17)



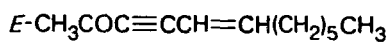
(18)



(19)

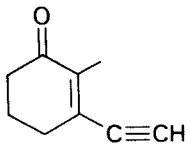


(20)

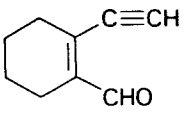


(21)

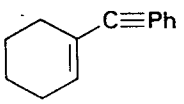
been reported although yields are often low and the isolated products are the *trans* alkenes resulting from double-bond isomerization[47–49]. Enynones in which the triple bond is not directly conjugated to the carbonyl are much less prone toward over-reduction or cyclization. Thus, compounds **22**, **23**, **24**, **25** and **26** all gave respectable yields of products resulting from partial *cis* reduction of the alkyne linkages[50–54]. Thus, the selective partial reductions of triple bonds conjugated to other π systems apparently depends on the positioning of the alkyne. Thus, the terminal alkyne in ethynyl cyclohexene is selectively attacked using $Pd/SrCO_3$[55] or Lindlar catalyst[56] and several examples are known in which an internal triple bond is selectively reduced in the presence of internal alkenes[18,57–62]. However, discrimination is not so clean when



(22)



(23)



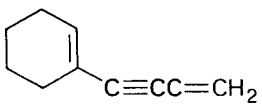
(24)

OHCC(Me)=CHC≡CC=C(Me)CHO

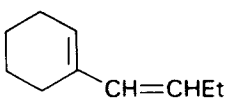
(25)

OHCC(Me)=CHC≡CCH=C(Me)CH=CHCO$_2$Me

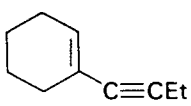
(26)



(27)



(28)



(29)

an enyne contains a terminal alkene and an internal triple bond, such as **27**, which gave a mixture composed of the triene (54%), diene **28** (21%), enyne **29** (8%) and 1-butylcyclohexane (4%)[63].

The selective reduction of alkyne ethers has been utilized by Arens' group as a synthetic procedure for the preparation of α,β-unsaturated aldehydes[64]. Thus, an alkyne intermediate **30** is prepared via a Grignard addition to a ketone followed by partial catalytic hydrogenation (Pd/$BaSO_4$) and hydrolysis of the resulting enol ether **31** (equation 1). The process has been successfully employed in the synthesis of β-ionone[65], citral[65], ε-methylcitral[66] and vitamin A[67].

$$\underset{\textbf{(30)}}{R^1R^2C(OH)C{\equiv}COEt} \xrightarrow{H_2} \underset{\textbf{(31)}}{R^1R^2C(OH)CH{=}CHOEt} \xrightarrow[H^+]{H_2O} R^1R^2C{=}CHCHO \qquad (1)$$

In summary, catalytic hydrogenation using palladium especially Lindlar's catalyst and Pd/$BaSO_4$, provides a usually reliable, mild method for converting alkynes to *cis* alkenes, often with high stereoselectivity and without damage to most other functional groups.

2. *Nickel catalysts*

Partial catalytic hydrogenation of alkynes using Raney nickel has seen sporadic usage over the years with conflicting results[68–76].

With this catalyst some reports have suggested reasonably clean conversions to *cis* alkenes[68,69,72,74], but other studies have indicated mixtures containing considerable quantities of *trans* isomers and/or alkanes[70,71,73,75]. With conjugated systems, Raney nickel poisoned with piperidine and zinc acetate reportedly selectively reduces alkyne linkages[60,76]. Nickel-catalysed hydrogenations have been utilized in syntheses directed toward α-irone[77], civetone[78], cis-6-undecenoic acid[79] and vitamin A ether[60].

More recently, nickel catalysts produced by reduction of nickel (II) acetate with borohydride (P-2 nickel)[80] reportedly convert alkynes cleanly to *cis* alkenes. Thus, 3-hexyne affords a quantitative yield of 3-hexene with a *cis*:*trans* ratio of >30:1. Terminal alkynes, however, give ca. 20% alkane[80]. The selectivity is considerably enhanced by using amine additives. For example, with ethylene diamine internal alkynes are converted to *cis* alkenes in 80–95% yields with *cis*:*trans* ratios from 97:1 to 200:1[81]. Nickel catalysts generated by reaction of nickel (II) acetate with sodium hydride were also effective for clean conversion of alkynes to *cis* alkenes with high stereoselectivity[82].

3. Other metal catalysts

Several other metal catalysts have been used for alkyne reductions including rhodium/C[83], Raney iron[84,85], platinum[83,86], $[(C_6H_5)_3P]_3RuCl_2$[87] and $(\pi\text{-}C_5H_5)_2ZrH_2$[88], but these have not been extensively explored.

B. Hydrometalation and Other Transition Metal Reductions

1. Introduction

The hydrometalation[89,90] of alkynes followed by hydrolysis (equation 2) represents an important method for partial reduction of triple bonds, especially since the reactions can often be controlled to yield net *cis* or *trans* addition of hydrogen,

$$RC{\equiv}CR + MH \longrightarrow RCH{=}CMR \longrightarrow RCH{=}CHR \qquad (2)$$

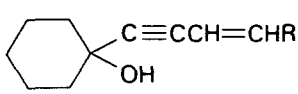
depending on the metal and reaction conditions. The most extensively studied and utilized systems involve aluminium and boron hydrides and these will be considered separately below. In addition, many reducing systems involving the combination of a metal salt and a metal hydride are known and are considered here since several probably involve hydrometalation although some may proceed via catalytic hydrogenation.

2. Hydroalumination

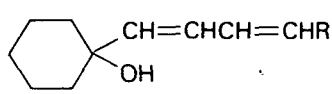
a. Lithium aluminium hydride. The partial reduction of acetylenic alcohols[91,92], acids[92] and esters[93] to allylic alcohols was noted by several workers soon after the introduction of the reagent[91–93]. Thus, propiolic acid and acetylenedicarboxylic acid were converted to allyl alcohol (85%) and 1,4-butanediol (84%), respectively[92]. Application to conjugated diacetylene glycols (**32**) and vinyl acetylenic alcohols (**33**) gave the corresponding diene diols (**34**) and dieneols (**35**)[93]. However, similar alcohols with terminal alkyne links (**36**) afforded allenic alcohols (**37**), providing a convenient

$$HOCR^1R^2(C{\equiv}C)_2CR^1R^2OH \longrightarrow HOCR^1R^2(HC{=}CH)_2CR^1R^2OH \qquad (3)$$

(**32**) (**34**)



(**33**)



(**35**) (4)

$$HOCR^1R^2CH{=}CHC{\equiv}CH \longrightarrow HOCR^1R^2CH_2CH{=}C{=}CH_2 \qquad (5)$$

(**36**) (**37**)

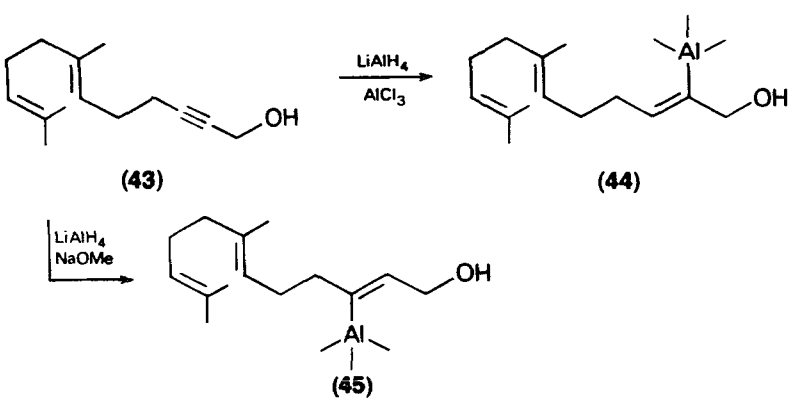
synthetic method for terminal allenes[93]. The diyne **38** gave first the alkyne–en alcohol **39** selectively; subsequent treatment with additional lithium aluminium hydride gave the diene alcohol **40** indicating the initial intermediate to be an aluminate incapable of being further reduced[93]. Polyacetylene alcohols with excess lithium aluminium hydride gave selective conversion of the acetylenic bonds adjacent to the alcohols (i.e. **41** to **42**) indicating the importance of the nearby hydroxyl group. This was probably due to initial reaction of the OH with $LiAlH_4$ and subsequent intramolecular deliverance of hydride.

$$\underset{\textbf{(38)}}{HOCMe_2C{\equiv}CC{\equiv}CH} \longrightarrow \underset{\textbf{(39)}}{HOCMe_2CH{=}CHC{\equiv}CH} \longrightarrow \underset{\textbf{(40)}}{HOCMe_2CH_2CH{=}C{=}CH_2} \quad (6)$$

$$\underset{\textbf{(41)}}{HOCMe_2(C{\equiv}C)_4CMe_2OH} \longrightarrow \underset{\textbf{(42)}}{HOCMe_2CH{=}CH(C{\equiv}C)_2CH{=}CHCMe_2OH} \quad (7)$$

The mechanism of the conversions involves specific *trans* hydroalumination to afford a vinyl aluminate followed by protonolysis with retention upon treatment with water to give net *trans* addition of H_2 across the π bond[89,90,92,94]. Treatment of the intermediate organoaluminium with D_2O results in deuterium incorporation[94].

Corey and coworkers[95] observed that while the addition occurs stereospecifically *trans*, the regioselectivity is poor, giving variable amounts of both β and γ aluminium-substituted isomer intermediates. This is not important if the intermediate is protonated since both regioisomers afford the same alkene, but is a major problem if the aluminium is replaced with deuterium or other atoms such as iodine. However, the regioselectivity could be controlled and directed by choice of the reaction conditions. Thus, treatment of **43** with a mixture of $LiAlH_4$ and $AlCl_3$ (ratio 60:1) afforded isomer **44** exclusively in which the aluminium entered the position β to the OH as evidenced by conversion to the corresponding vinyl iodide. On the other hand, a combination of $LiAlH_4$ and NaOMe (ratio 1:2) gave isomer **45** in which the aluminium entered the γ position (Scheme 1). Although the reasons for this reversal are unclear, the procedures provide techniques for regiospecific preparation of deuterated alkenes and other vinyl derivatives[95].



SCHEME 1

The reduction of acetylenic alcohols of type **46** containing an additional adjacent leaving group (X = Cl[96,97], R_2N[98], THPoxy[98], alkoxy[100],)[188] gives good yields of β-allenic alcohols (**47**) via concomitant hydride addition and X^- elimination (equation 8). In refluxing THF, allenes such as **47** undergo reductive elimination with $LiAlH_4$ to give conjugated dienes[188].

$$\underset{\textbf{(46)}}{R_2CXC{\equiv}CCOHR_2} \longrightarrow \underset{\textbf{(47)}}{R_2C{=}C{=}CHCOHR_2} \quad (8)$$

Alkynes not activated by an adjacent hydroxyl group react much slower with $LiAlH_4$. Thus, 1-ethynylcyclohexene does not react in refluxing ether but does give a mixture of unsaturated hydrocarbons in refluxing dioxane[92]. Magoon and Slaugh[94] have demonstrated that isolated alkynes are fairly cleanly converted to *trans* alkenes by sequential treatment with $LiAlH_4$ in refluxing THF (66°C) or THF/diglyme (117–150°C) followed by protonolysis with water. Usually very little *cis* isomer is obtained and the higher boiling solvent system is favoured for internal alkynes. For instance, 3-hexyne affords a 96% yield of 3-hexene consisting of 96% *trans* and 4% *cis* in THF/diglyme[94]. Extended reaction times may be detrimental. Reaction of diphenylethyne with $LiAlH_4$ for <2 h followed by hydrolysis gives a 97:3 ratio of *trans*:*cis* stilbene (100% yield) but a 74:26 *trans*:*cis* isomer ratio after 14 h. Apparently, the initially produced *trans* adduct is slowly isomerized. The use of toluene as solvent also is not beneficial, giving principally saturated hydrocarbons[94].

Trans alkenes are also produced from alkynes by reduction with lithium diisobutylmethylaluminium hydride (produced from methyllithium and diisobutylaluminium hydride) followed by protonation[101].

The reduction of alkynes with $LiAlH_4$ has been exploited synthetically for the preparation of cosmine (**48**)[102] and for the introduction of a *trans* double bond in a total synthesis of vitamin A[103].

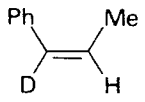
$$H_2C{=}C(CH_3)CH{=}CHCH{=}C(CH_3)CH{=}CH_2$$

(48)

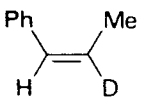
In addition, Corey has utilized the regiospecific $LiAlH_4$ addition methods developed in his laboratories in the syntheses of farnesol[95], the cecropia juvenile hormone[104], and α-santalol[105]. In these cases, the initially generated alkenyl aluminium intermediates were converted to trisubstituted alkenes.

The major limitation to the use of $LiAlH_4$ for reduction of alkynes to alkenes resides in the powerful reducing capabilities of the reagent toward most other functional groups including aldehyde, ketone, carboxylic acid, ester, amide, nitrile, nitro, expoxide and halide[106]. Therefore, the alkyne must be devoid of these functionalities or they must be amenable to protection for the conversion to be successful. A further limitation stems from the fact that terminal alkynes do not hydroaluminate but rather afford alkynylaluminates via removal of the acidic acetylenic hydrogen by $LiAlH_4$.

b. Diisobutylaluminium hydride. Contrary to the situation with $LiAlH_4$, the hydroalumination of alkynes with dialkylaluminium hydrides occurs in a stereospecific, probably concerted[107–110] *cis* fashion to give vinylaluminium derivatives which may be hydrolysed with retention of configuration to afford *cis* alkenes[89,90,109–113]. However, extended reaction times, high temperatures (>100°C), and excess aluminium reagent affords the *trans* adduct probably via a diaddition–elimination mechanism[112]. Furthermore, at higher temperatures significant quantities of saturated and dimerized products are observed after hydrolysis[113]. Thus, 1-phenylpropyne gave almost exclusively *cis*-1-phenylpropene upon reduction with diisobutylaluminium hydride at 50°C for 8–26 h, but at 75–100°C a mixture was obtained composed of *cis*-1-phenylpropene, *trans*-1-phenylpropene, propylbenzene and *cis*,*cis*-2,3-dimethyl-1,4-diphenyl-1,3-butadiene (ratios 3.8:2.9:4.0:1.0, respectively). Likewise diphenylacetylene gave a 15.5:1 *cis*:*trans* ratio of stilbene at 50°C but a 1.0:4.4 *cis*:*trans* ratio at 90°C[113]. The regioselectivity of addition relies more on electronic effects than the steric environment with the aluminium entering the most electropositive site. For instance, 1-phenylpropyne afforded a 4.4:1 ratio of the regioisomers **49** and **50** when the intermediate aluminium adduct was treated with D_2O[113]. Substitution of trimethyl-

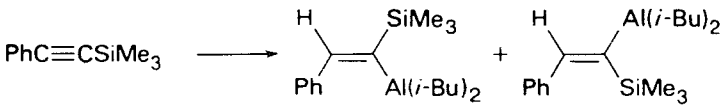


(49)



(50)

silyl or trimethylgermanyl groups for carbon attached to the triple bond changes both the stereo- and regio-selectivity of the reaction giving predominately the *trans* adduct and selective aluminium attack adjacent to the silyl or germanyl group (i.e. **51** to **52** and **53**; ratio 96:4 respectively)[114,115]. The reason for the change in stereochemistry



(9)

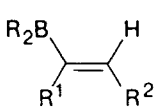
(51) (52) (53)

apparently arises from stereomutation of initially produced *cis* adducts caused by low carbon–carbon bond barriers induced by adjacent Si, Ge and Al atoms[115,116]. Use of a tertiary amine in combination with diisobutylaluminium hydride reverses this stereoselectivity giving a 4:96 ratio of **52**:**53**, respectively, presumably by complexing the aluminium adduct which raises the double-bond rotational barrier[114,115]. The ease of obtaining either *cis* or *trans* vinylsilanes via hydroalumination is important since these derivatives have considerable utility in synthesis[117].

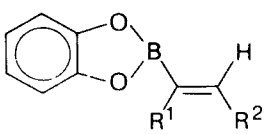
As with $LiAlH_4$, the major limitation of hydroalumination with dialkylaluminium hydrides is its potent reducing power[118]. Thus, diisobutylaluminium hydride readily attacks most common functional groups including ketones, acids, esters, amides, cyanides or epoxides and synthetic usage of hydroalumination must be designed accordingly[118].

3. Hydroboration

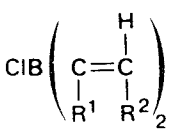
The hydroboration of alkynes occurs in a stereospecific *cis* fashion with boron attachment at the less substituted site[119,120]. Although borane may be used[121], monoaddition is difficult to control especially with terminal alkynes[119] and most successful applications have utilized dialkylboranes[121,122], diaryloxyboranes (catecholborane)[123,124] monochloroborane[125] or dibromoborane[126] to obtain excellent yields of the corresponding alkenyldialkylboranes (**54**), alkenylcatecholboranes (**55**), dialkenylchloroboranes (**56**) or alkenyldibromoboranes (**57**), respectively. The synthetic utility of



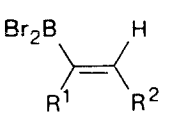
(54)



(55)



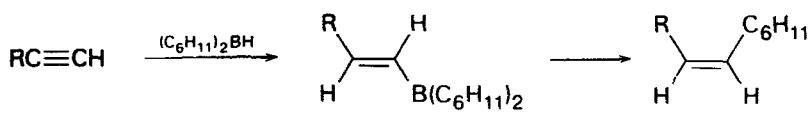
(56)



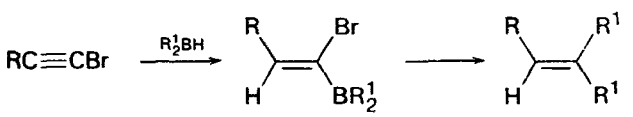
(57)

these intermediates for partial reduction of alkynes stems from the ease of replacement of the boron by hydrogen with complete retention of stereochemistry to give *cis* alkenes. The usual reagent for protonation is a carboxylic acid[119–121,124], but the transformation of diakylboron derivatives (**54**) may also be effected by sequential treatment with lithium reagents followed by base[127], Pd(II) acetate or lead(IV) acetate (internal derivatives of **54** only)[128]. Thus, hydroboration with diisoamylborane-(bis-3-methyl-2-butylborane)[121], catecholborane[123,124] or chloroborane[125] followed by treatment with acetic acid affords good to excellent yields (60–90%) of *cis* alkenes uncontaminated with *trans* isomers[121,123–125]. Use of deuterated acetic acid affords the corresponding monodeuterated alkene[123–125]. In these cases the regioselectivity is important, but the hindered dialkylborane derivatives show high discrimination in placing the boron at the less sterically crowded site[119–121,129]. For acid-sensitive molecules, protonolysis using the alkyllithium–aqueous base[127] or $Pb(OAc)_4$[128] procedures are excellent alternatives. Hydroboration of 5-decyne with dicyclohexylborane followed by sequential treatment with butyllithium and aqueous NaOH affords a 92% yield of *cis*-5-decene[127]. With tosylhydrazones of conjugated acetylenic ketones, catecholborane affords allenes resulting from migration of one of the alkyne π bonds[193].

Diorganoboranes, formed by dihydroboration of internal alkynes with borane[119,130], react with alkaline silver nitrate to give 72–89% yields of *trans* alkenes[131]. With dialkylalkynes, the stereoselectivity is excellent (ca. 98%) while aryl and large-ring cyclic systems afford more of the *cis* isomers[131]. The conversion of phenylorganoboranes to *trans* alkenes is also accomplished with CrO_3 in pyridine[167]. Dialkylalkenylboranes are also useful intermediates for producing *cis* or *trans* alkenes from alkynes via migration of an alkyl group from boron to carbon stereospecifically with retention at both the migrating alkyl group and migrating terminus[129,132]. Thus, treatment of the dicyclohexylalkenylborane **58** with NaOH and iodine results in transfer of one cyclohexyl group to carbon followed by deboronoiodination to give the pure *cis* alkene **59**[122,123] (equation 10). Similar treatment of 1-bromo-1-alkenyldialkylboranes **60**, produced from 1-bromoalkynes, gives trialkylalkenes resulting from migration of



(58) (59) (10)



(60) (11)

two groups on boron (equation 11)[133]. On the other hand, treatment of dialkylalkenylboranes with BrCN results in >90% formation of the corresponding *trans* alkene isomers[134]. Likewise, *trans* alkenes also result from treatment of the dialkylalkenylboranes derived from terminal alkynes with $PdCl_2$[128,135], lead acetate[16] or diacetoxyiodobenzene[136].

The alkyl groups transfered in the above procedures are limited to those produced from alkenes which give dialkylboranes on hydroboration. This limitation is overcome by utilizing a thexylalkylborane for addition to 1-bromoalkynes followed by sequential treatment with methoxide and protonolysis with isobutyric acid to afford *trans*

alkenes. The method relies on the reluctance of the thexyl group to migrate and expands the scope of the procedure since a variety of thexylalkylboranes are available from thexylborane and alkenes[137].

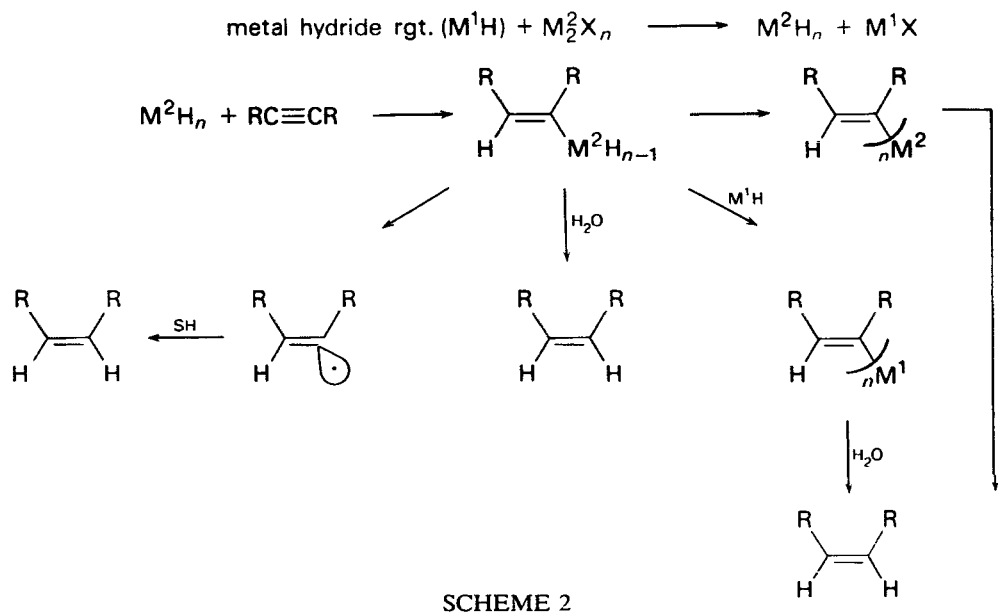
4. *Other hydrometalations*

A number of other transition metal hydrides have been observed to hydrometalate alkynes including $HIrCl_2(Me_2SO)_3$[138], $HRh(CO)(Ph_3P)_3$[139], $(Ph_3P)_3Pt/CF_3CO_2H$[140,141], $HMn(CO)_5$[142,143], Cp_2ZrH_2[144,145] and Cp_2TiCl_2/isopropylmagnesium bromide[145]. However, none have been explored thoroughly or found significant application in partial reduction of alkynes.

5. *Metal hydride and transition metal derivative combinations*

In recent years considerable interest has developed in the use of combinations of transition metal derivatives and various hydride-transfer agents to reduce a number of functional groups including alkynes[146–167]. Although the exact nature of the actual reducing agent is unclear in many cases, the majority appear to involve the intermediacy of transition metal hydride species which hydrometalate alkynes in a similar fashion to organoaluminium and organoboron reagents. Therefore for convenience, these are grouped together and considered in this section even though some, particularly those involving borohydride may not involve hydrometalation but rather internal catalytic hydrogenations.

Mechanistically, the hydrometalation reactions probably involve initial reaction of the hydride reagent with the transition metal derivative to generate the transition metal hydride, followed by addition to the alkyne to generate the hydrometalated alkenes. This in turn may undergo transmetalation with the hydride transfer agent, cleave homolytically to radical species which abstract hydrogen from solvent and/or react with water upon work-up to replace the metal with hydrogen as depicted in Scheme 2.



SCHEME 2

TABLE 1. Reduction of alkynes with hydride reagents in combination with metal derivatives

Reducing system[a]	Conditions		Reduction	Stereochemistry		Other groups reduced	Refs.
	Time(h)	Temp(°C)		% *cis*:% *trans*	% yield		
$LiAlH_4$–$TiCl_4$		0	$RC{\equiv}CH \rightarrow RCH_2CH_3$		81	Alkene	146
$LiAlH_4$–$TiCl_4$		−40	$RC{\equiv}CR \rightarrow RCH{=}CHR$	73:<7	81	Alkene	146
			RCH_2CH_3R		11		
$LiAlH_4$–$NiCl_2$ (10:1)	1	−40	$RC{\equiv}CH \rightarrow RCH{=}CH_2$		94–96	Halides	147, 148
			RCH_2CH_3		0–1		147, 148
	24	25	$RC{\equiv}CH \rightarrow RCH_2CH_3$		99	Halide, alkenes	148
	24	25	$RC{\equiv}CR \rightarrow RCH{=}CHR$	75–91:0	75–91	Halide	
			RCH_2CH_2R		4–15		
$LiAlH_4$–$FeCl_2$	48	25	$RC{\equiv}CH \rightarrow RCH_2CH_3$		98	Alkene	148
$NaBH_4$–$CoCl_2$ (10:1)	3	25	$RC{\equiv}CH \rightarrow RCH_2CH_3$		98	Alkene	154
$NaBH_4$–$CoCl_2$ (5:1)	3	25	$RC{\equiv}CH \rightarrow RCH{=}CH_2$		95		154
$NaBH_4$–$[Fe_4S_4(SPh)_4]^{2-}$ (100:1)	1	20	$RC{\equiv}CR \rightarrow RCH{=}CHR$	70:2	70		155
$LiAlH_4$–Et_2Mg cat. Cp_2TiCl_2	1	25	$RC{\equiv}CR \rightarrow RCH{=}CHR$	100:0	100		149
$LiAlH_4$–Et_2Mg–CuI	24–28	25	$RC{\equiv}CH \rightarrow RCH{=}CH_2$		80–98		150
			$RC{\equiv}CR \rightarrow RCH{=}CHR$	100:0	80–95		
$NaAlH_2(OCH_2CH_2OCH_2)_2$–CuBr	0.25	−20	$RC{\equiv}CCO_2Me \rightarrow RCH{=}CHCO_2Me$	61:14	75	Halide, aldehyde, ketone	152
			$RCH_2CH_2CO_2Me$		4		
KBH(s-Bu)$_3$–CuI	3	0	$RC{\equiv}CR \rightarrow RCH{=}CHR$	88:12	94	Halide, ketone, ester	156
n,s-RMgX–CuI (2:1)	0.75–6	25	$RC{\equiv}CR \rightarrow RCH{=}CHR$	100:0	65–100		158
NaH–RONa–$Ni(OAc)_2$ (4:2:1)	15–40	55–65	$RC{\equiv}CH \rightarrow RCH_2CH_3$		80–100	Ketone, halide	160
	40–45	20–25	$RC{\equiv}CH \rightarrow RCH{=}CH_2$		100		
			$RC{\equiv}CR \rightarrow RCH{=}CHR$	100:0, alk. 63–67:37–33, aryl	73–100		
NaH–BuONa–$FeCl_3$ (4:2:1)	6–9	35–45	$RC{\equiv}CH \rightarrow RCH_2CH_3$		95–98	Alkene, ketone	161
			$RC{\equiv}CR \rightarrow RCH_2CH_2R$		95		
NaH–$FeCl_2$ (2:1)	15–48	0–5	$RC{\equiv}CR \rightarrow RCH_2CH_2R$		65–90	Ketone, aldehyde	162
R_3NHO_2CH–Pd/C (110:1)	1.3–2	100	$RC{\equiv}CR \rightarrow RCH{=}CHR$	100:0	70–93	Conj. diene	163
			RCH_2CH_2R		2–18		
R_3NHO_2CH–$Pd(OAc)_2$–Ar_3P (110:2:1)	30	25	$RC{\equiv}CR \rightarrow RCH{=}CHR$	100:0	85		163
			RCH_2CH_2R				
i-PrMgBr–Cp_2TiCl_2			$RC{\equiv}CR \rightarrow RCH{=}CHR$		70		145
			RCH_2CH_2R		30		

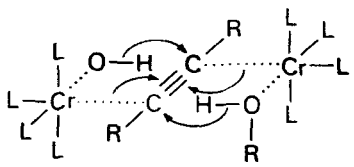
[a]Ratio hydride:M.

Lithium aluminium hydride[146–150] and related derivatives[151,152] react with a number of transition metal compounds including $TiCl_4$[146], Cp_2TiCl_2 [146], $NiCl_2$[147,148], $CoCl_2$[147,148], $FeCl_2$[147,148], $FeCl_3$[148], VCl_3[148], Et_2Mg[149,150] and CuBr[151,152] to give transition metal hydrides which are capable, to varying degrees, of reducing alkynes to alkenes and/or alkanes. Similarly, sodium borohydride[153,155] and derivatives[156] afford alkyne-reducing systems with $CoCl_2{\cdot}6H_2O$[154], $CoBr_2$[154], Co(III)-porphyrin[153], $Fe_4S_4(SR)_4^{-2}$[155], CuI[156] or dichlorobis (*N*-phenyl-*S*-methyl-2-aminoethanethiol)-iron(II)[157] as does sodium hydride in combination with alkoxide–$Ni(OAc)_2$[160], alkoxide–$FeCl_3$[161], $FeCl_2$[162] and $FeCl_3$[162]. Other successful hydride systems include RMgBr–CuI[158], *i*-PrMgBr–Cp_2TiCl_2[145], $V(OH)_2$–$Mg(OH)_2$[164], $[C_5H_4MoSC_2H_4S]_2$[165], Pd/C or $Pd(OAc)_2$–triarylphosphine with R_3NH^+ formate[163] and MoO_4^{2-}–thiol with $NaBH_4$ or $Na_2S_2O_4$[166,169].

The products and stereochemistry (where investigated) of many of the above systems are dependent on temperature and reaction conditions. In general, lower temperatures (<25°C) often favour enhanced *cis* stereoselectivity[146,148] and/or allow the reduction to be halted at the alkene stage[147,148,151,152,160]. Space limitations preclude discussion of each system especially since many have not been completely investigated and, as mentioned, the actual reducing species have not been studied in detail. Table 1 outlines those which, at this stage, appear to offer synthetic possibilities for producing either *cis* alkenes or alkanes. The choice for a particular synthetic conversion depends on several variables particularly the presence of other functional groups which must remain intact. Table 1 lists other functional groups in which the authors indicated reduction; however, with many systems, changes in conditions (i.e. temperature, ratio of reactants, etc.) give concomitant changes in selectivity so that with particular conditions a group may or may not be affected. Therefore, the original investigations should be consulted for specific details and discussions. It should be noted that several of the combinations are expected to reduce other functionalities not listed. This is especially true when a metal salt is utilized in catalytic amounts with strong reducing agents such as lithium aluminium hydride. Such systems would probably attack all the functionalities normally reduced by the reagent (i.e. carbonyl, amide, nitrile, nitro, etc.). In addition, combinations such as $NaBH_4$–$CoCl_2$[154] are known to reduce several functional groups including nitriles, amides and nitro compounds[168].

6. *Chromium(II) reductions*

Chromium(II) sulphate in aqueous dimethylformamide reduces alkynes cleanly to *trans* alkenes (84–94%)[189]. The mechanism apparently involves an initial Cr(II)-triple-bond complex which is attacked by a second Cr(II) species from the side opposite the complexed metal with concomitant transfer of hydrogen ions to the alkyne π bond giving the *trans* adduct. The transition state is pictured as **61**. The reactivity of alkynes follows the order $HOCH_2C{\equiv}CCH_2OH \sim HC{\equiv}CCH_2OH > CH_3C{\equiv}CCH_2OH$, $HC{\equiv}CBu \gg CH_3C{\equiv}CCH_2CH_3$, $(CH_3)_2COHC{\equiv}CCOH(CH_3)_2$ with the latter two inert. Thus, association with a hydroxyl group is important as well as accessibility of coordination sites on acetylene[189].

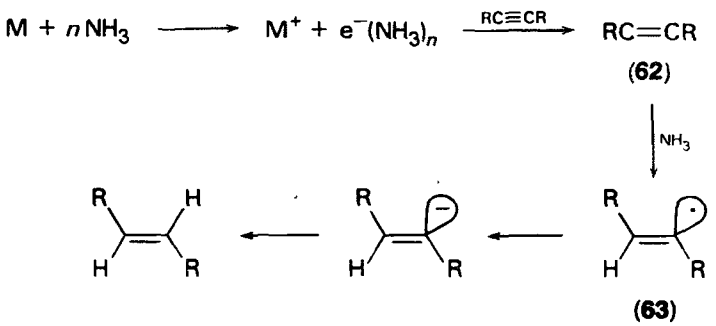


(61)

In the presence of amines, chromium(II) reduces phenylalkyl- and diphenylacetylenes to *cis* alkenes with no *trans* isomers detected[190]. The best results are obtained with ethylenediamine and triethylamine with which yields range from ca. 58–100%. Terminal alkynes give 1-alkenes in excellent yields but dialkylacetylenes are completely inert. Interestingly, propargyl alcohols afford a predominance of either *trans* or *cis* alkenes depending on the amine used. For instance, 2-butyn-1-ol gives a 97:3 *trans*:*cis* ratio with Cr(II) ethylenediamine (97% yield) while use of triethylamine affords a 19:81 *trans*:*cis* mixture (79% conversion)[190]. Apparently, reduction of propargyl alcohols by Cr(II) amine reagents proceeds through two competing processes, a *cis* reduction of unknown mechanism and a *trans* reduction pathway which is the same as that observed without amines[189].

C. Dissolving Metal Reductions

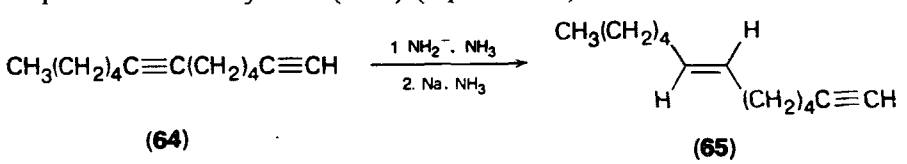
Solutions of sodium or lithium metals in liquid ammonia[170–175] or aliphatic amines[172–176] effectively reduce alkynes to *trans* alkenes via two successive electron transfers and protonations[171,174,175,177] as shown in equation (12). The reductions are



(12)

also accomplished with ytterbium in liquid ammonia[178] and electrochemically[179–181]. The reason for the high *trans* stereoselectivity is not completely understood but appears to be related to protonation of the linear anion radical **62** specifically to give the *trans* radical **63** which is further reduced and protonated faster than inversion[182].

With internal alkynes, sodium in ammonia gives excellent yields of the *trans* isomers. For instance, 4-octyne is coverted to *trans*-4-octene in 80–90% yield[171]. With 1-alkynes, the reductions are conducted in combination with ammonium sulphate which protonates any sodioacetylides formed and allows reduction to proceed cleanly to 1-alkenes[177]. Internal acetylenes may be selectively reduced in the presence of terminal alkynes by prior conversion of the latter to an acetylide anion with sodium amide in NH_3 followed by the addition of sodium[183]. Thus the diyne **64** is converted by this process to the enyne **65** (75%) (equation 13).



(64) (65) (13)

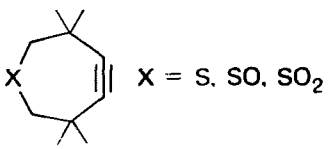
The ratio of reagents and reaction conditions must be carefully controlled in lithium/amine procedures since the systems are capable of reducing alkenes[173,176]. In general, for partial reduction of alkynes, an excess of lithium should be avoided and the reactions should be conducted at low temperatures. For example, reduction of

5-decyne with lithium/ethylamine at −78°C gives *trans*-5-decene. However, with excess lithium and a reaction temperature of 17°C, the product is mostly decane[176]. Alkynes are also converted to alkanes with sodium in hexamethylphosphorus triamide using *t*-butanol as a proton source[184].

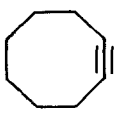
Reduction of alkynes to *trans* alkenes has been exploited in numerous synthetic schemes including routes to fichtelite[185] and *d,l*-progesterone[186]. As with other reduction methods, the user of dissolving metal reductions must bear in mind the effect on other functional groups present. This is particularly true if a proton source (i.e. alcohol, NH_4^+ salt) is used in combination with the metal since such systems reduce a variety of functional groups including ketones, esters, α,β-unsaturated carbonyls, allylic alcohols, amides and certain aromatic systems (Birch and Benkeser reductions)[173,175].

D. Miscellaneous Reductions

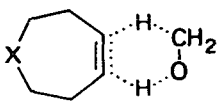
Certain strained seven-[191] and eight-[192] membered ring alkynes (i.e. **66** and **67**) are reduced by alcohols alone to the corresponding *cis* alkenes. The mechanism suggested[191] involves a concerted transfer of two hydrogens from the alcohol to give net hydrogenation of the triple bond (i.e. via **68**).



(66)



(67)



(68)

III. REDUCTION OF NITRILES

A. Introduction

Reductions of nitriles to aldehydes or amines are extremely important functional-group transformations and consequently considerable effort has been expended devising methods for these conversions. The literature on this topic has been reviewed[7,194] and includes such classic reductive procedures as catalytic hydrogenation and chemical reductions using metals. This discussion will minimize repeat coverage although some overlap is essential for completeness, comparison of methods, and in those cases where the procedures have been updated or improved.

B. Reduction to Aldehydes

1. Introduction

The conversion of nitriles to aldehydes relies on the selective reduction of one π bond to give imine derivatives which are subsequently hydrolysed to the carbonyl (equation 14). Many procedures have been devised to accomplish this transformation,

$$RC{\equiv}N \xrightarrow{\text{reduction}} RCH{=}N{-} \xrightarrow{H_2O} RCHO \qquad (14)$$

the most important of which are: (*a*) chemical reductions including the Stephens and related methods, (*b*) partial catalytic hydrogenation and (*c*) partial reductions via hydride-transfer reagents.

2. Metal and metal salt reductions

Although a number of metals (Zn, Fe, Cr, Al) in acidic (or with Al, basic) media partially reduce nitriles to aldehydes, the reactions are not general and proper reaction conditions must be carefully maintained. A far better procedure is the classical Stephens method[7,195] which involves addition of HCl to the nitrile followed by reduction with $SnCl_2$ and hydrolysis (equation 15). The procedure is generally quite

$$RC{\equiv}N + HCl \longrightarrow RCCl{=}NH \xrightarrow{SnCl_2} \xrightarrow{H_2O} RCHO \qquad (15)$$

effective for the preparation of aromatic and heterocyclic aldehydes but is less successful with aliphatic nitriles, often leading to amides[7].

3. Catalytic hydrogenation

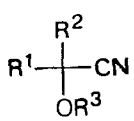
Catalytic hydrogenation of nitriles to give aldehydes via imine intermediates suffers from the difficulty in stopping the reduction after one mole of hydrogen has been added. For aromatic examples the problem is overcome by using Raney nickel with sodium hypophosphite[196] or, better, aqueous formic acid[197,198] as the hydrogen source. Over-reduction may also be suppressed by use of trapping reagents such as hydrazine[199,200], phenylhydrazine[201,202], semicarbazide[203,204] or *N,N'*-diphenylethylenediamine[202,203]. These methods rely upon interception of the intermediate imines by the trapping agent to generate Schiff bases which are resistant to further reduction (equation 16). In most cases the procedure is good for aromatic nitriles but

$$RC{\equiv}N \xrightarrow{H_2} RCH{=}NH \xrightarrow{H_2NNHR^1} RCH{=}NNHR^1 \qquad (16)$$

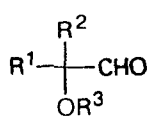
fails with aliphatic cases. An exception to this involves the use of Raney nickel catalyst with phenylhydrazine which gives good yields of aromatic, heterocyclic and aliphatic aldehydes.

4. Reduction with metal hydrides

Various hydride-donating species, especially those derived from aluminium and boron have been utilized successfully for the conversion of nitriles to aldehydes[7]. As with other methods, reduction must be halted at the imine stage. With powerful reducing agents such as lithium aluminium hydride, this is sometimes possible by inverse addition so that an excess of hydride reagent is avoided[205] or by conducting the reduction at low temperatures (−70°C)[206,207]. However, much better results have been obtained by using hydride reagents in which the reducing capacity is lowered by replacement of three of the four hydrogens with alkoxy groups. Thus, lithium triethoxyaluminium hydride effectively converts aromatic and aliphatic nitriles to aldehydes at 0°C in yields of 68–96%. This represents one of the most general methods available and apparently fails only when relatively acidic hydrogens are present adjacent to the nitrile (i.e. as in phenylacetonitrile)[208]. Aldehydes are also obtained by the inverse addition of sodium bis(2-methoxyethoxy)aluminium hydride to nitriles. Thus, the protected cyanohydrins **69** have been converted to the aldehydes **70** in yields of 53–97%[209].



(69)



(70)

Diisobutylaluminium hydride (DIBAH) is also an effective reagent for the reduction of nitriles to aldehydes[210–214] via intermediacy of aldimine precursors (equation 17).

$$RC{\equiv}N + HAl(i\text{-}Bu)_2 \longrightarrow RCH{=}NAl(i\text{-}Bu)_2 \longrightarrow RCHO \qquad (17)$$

The reactions are usually conducted using a 1:1 to 1:1.5 ratio of substrate to DIBAH and at temperatures ranging from −75°C to reflux; the usual solvents are benzene, toluene, hexane or ether. The procedure is successful with aromatic, heterocyclic[215,216], and aliphatic nitriles[217–231,244,245] and reliably affords good to excellent yields, usually 50–90%. Consequently, DIBAH has enjoyed considerable usage in synthetic endeavours and, at present, is probably the method of choice for the preparation of aldehydes from nitriles. The versatility is illustrated in Table 2 in which a number of conversions are listed covering a variety of structural types. It should be noted that electrophilic DIBAH, unlike many nucleophilic hydride reagents, does not reduce double bonds conjugated to the nitrile (i.e. entry 1)[217,237,240]. In some cases (i.e. entry 5), the intermediate imines may be isolated.

TABLE 2. Reduction of nitriles to aldehydes with DIBAH

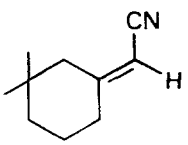
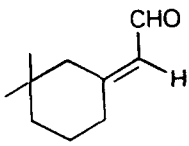
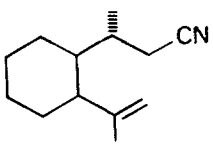
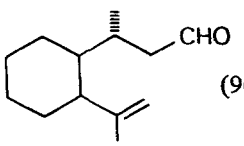
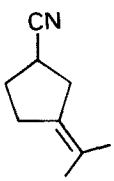
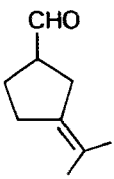
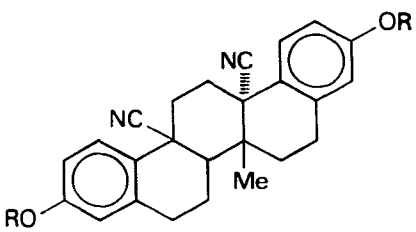
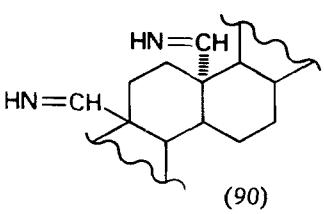
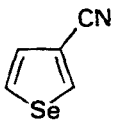
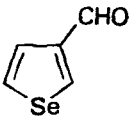
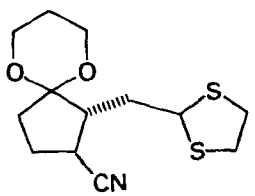
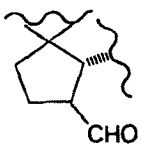
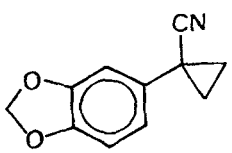
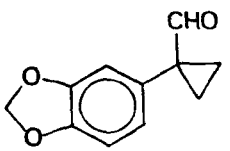
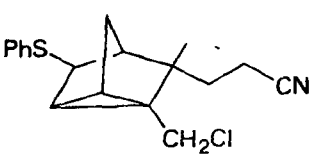
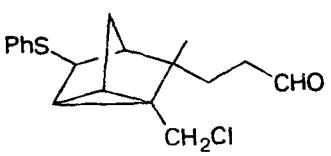
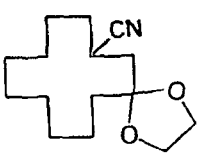
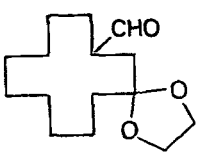
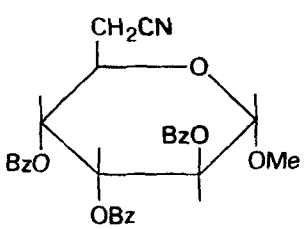
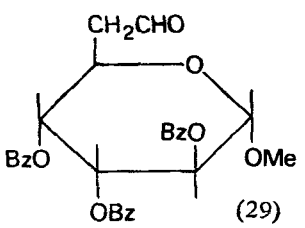
Entry	Nitrile	Product (% yield)	Ref.
1		 (80–90)	217
2		 (96)	219
3		 (86)	220
4	$R^1R^2C{=}CR^3CH_2CH(Ph)CN$	$R^1R^2C{=}CR^3CH_2CH(Ph)CHO$ (30–60)	241
5		 (90)	243
6	$H_2C{=}CH(CH_2)_9CN$	$H_2C{=}CH(CH_2)_9CHO$ (75)	242

TABLE 2. *continued*

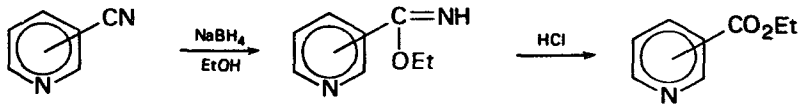
Entry	Nitrile	Product (% yield)	Ref.
7		 (80)	216
8	$Pr_2C{=}CH(CH_2)_2CN$	$Pr_2C{=}CH(CH_2)_2CHO$ (62)	234
9			232
10		 (75–85)	220
11			239
12		 (86)	235, 236
13		 (29)	238

Certain borane derivatives are also capable of partial reduction of nitriles to aldehydes although the reactions are slow. Thus, thexylborane affords 60% capraldehyde in 12 hours and 40% benzaldehyde in 3 days from the nitriles[246].

Another approach to partial reduction involves initial activation of nitriles toward nucleophilic attack by conversion to *N*-alkylnitrilium ions followed by reduction with a hydride reagent (equation 18). Although $NaBH_4$ completely reduces such ions to

$$RC{\equiv}N \longrightarrow RC{\equiv}\overset{+}{N}R^1 \xrightarrow{Et_3SiH} RCH{=}NHR^1 \xrightarrow{hyd.} RCHO \qquad (18)$$

amines[247], triethylsilane gives *N*-alkylaldimines which can be hydrolyzed to aldehydes[248]. Thus, *n*-butyl, *i*-propyl, *t*-butyl, 1-adamantyl, benzyl and phenyl nitriles afford the corresponding aldehydes in % yields of 71, 85, 61, 83, 41 and 90, respectively[248]. A related procedure involves treatment of heteroaromatic nitriles with a catalytic amount of $NaBH_4$ in ethanol to give imidates which are inert toward further reduction. Hydrolysis affords esters in good yields (equation 19)[249].



(19)

C. Reduction to Amines

1. Introduction

The conversion of nitriles to amines involves hydrogen addition to both π bonds and represents a principal method for the preparation of primary amines. Consequently, a great deal of effort has been directed toward developing efficient reductive procedures for such conversions and a number of reviews concerning synthetic aspects have appeared covering the literature to 1969[7,250] and, to a lesser extent, into the seventies[251,252]. Recent investigations have, for the most part, concentrated on methods involving various hydride systems and this section will focus on such reagents. Other techniques such as catalytic hydrogenation and metal reducing systems are more thoroughly covered in previous articles[7,250–252].

2. Catalytic hydrogenation

The conversion of nitriles using hydrogen and a metal catalyst has been known for many years[7,250–252]. Several catalyst systems have been employed but the most efficient, general system is probably Raney nickel employed in acetic anhydride in the presence of a base (NaOAc or NaOH)[253]. Using this method, yields of aromatic and aliphatic amines are moderate to excellent (40–100%) and low hydrogen pressures (3–4 atm) are adequate. The procedure relies on trapping the amine as the amide to prevent further reactions. Another effective procedure employs Pd/C or PtO_2 catalyst in ethanol containing chloroform[254]. Hydrogenation (3 atm) affords 90% yields of aromatic or aliphatic amines as the hydrochlorides.

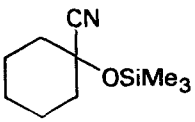
3. Metal–hydrogen reductions

Nitriles are reduced by a number of metals under a variety of conditions but mixtures of amines and hydrocarbons (resulting from reductive decyanation) are usually obtained[255–263]. For instance, with lithium–ethylamine, dodecyl cyanide affords 65% tridecylamine and 35% dodecane[261]. In general, the amount of decyanation decreases in the order tertiary > secondary > primary nitriles[261–263]. Calcium in ammonia suppresses decyanation in most instances (except with diphenylacetonitrile) but the yields of amines are only moderate (31–63%)[263].

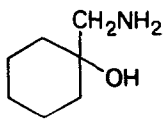
4. Metal hydride reductions

a. Aluminium reagents. Lithium aluminium hydride[7,264,265] or, less commonly, the sodium derivative[266], in ether solution has long been known to reduce nitriles to

amines. The overall reduction requires two hydrides per nitrile group, but investigations have shown that at least a mole equivalent of $LiAlH_4$ is necessary for effective conversion[267]. The reduction is complicated with nitriles bearing α hydrogens in that the strongly basic AlH_4^- anion reacts with evolution of hydrogen to form the nitrile anion[267–270]. This is detrimental in that hydride reagent is destroyed and, more importantly, the nitrile anion resists reduction and may undergo side-reactions to give dimeric products[267]. Sodium bis(2-methoxyethoxy)aluminium hydride is likewise reported to abstract α hydrogens of aliphatic nitriles although aromatic derivatives give good yields of amines[271–273]. In the absence of offending α hydrogens, reductions generally proceed smoothly (i.e. **71** to **72**)[274]. The reduction of nitriles at the expense



(71)

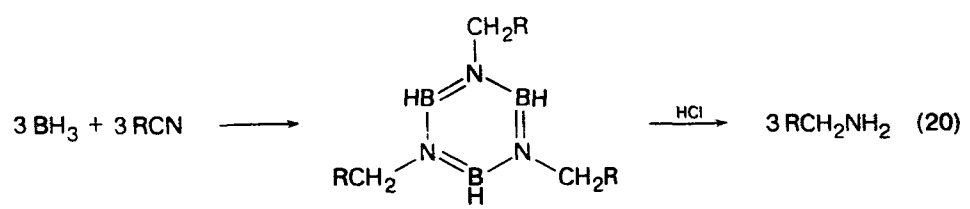


(72)

of α-proton removal is enhanced using a 1:1 ratio of $LiAlH_4$:$AlCl_3$[269]. Thus, the yield of 2,2-diphenylethylamine (from diphenylacetonitrile) is increased from 46% with $LiAlH_4$ to 91% with $LiAlH_4$–$AlCl_3$[269].

The nonbasic, electrophilic reagent aluminium hydride[275,276] avoids the problem of proton abstraction and affords good to excellent yields of amines from aromatic and aliphatic nitriles (50–98%)[276]. Table 3 lists several successful conversions and compares yields with those obtained with $LiAlH_4$[276]. Diisobutylaluminium hydride also reportedly gives good yields of amines (60–90%) when utilized in a 2:1 DIBAH: nitrile ratio[277], but this reagent appears to be more useful for the previously discussed conversion of nitriles to aldehydes.

b. Boron reagents. (i) Borane and alkylboranes. Both aromatic and aliphatic nitriles are reduced cleanly and rapidly by borane–THF[278] or borane–dimethyl sulphide[279,280] at room temperature. The reactions proceed via trialkylborazoles which must be hydrolysed with acid to obtain the amines (equation 20)[281]. Several examples



are presented in Table 4 and some illustrate that other functional groups are tolerated. Dialkylboranes, on the other hand, apparently react too slowly with nitriles to be synthetically useful[286].

TABLE 3. Reduction of nitriles with aluminium hydride and lithium aluminium hydride[276]

Compound	Product	AlH_3 (% yield)	$LiAlH_4$ (% yield)
3-Butenonitrile	3-Butenylamine	83	0
Capronitrile	*n*-Hexylamine	91	63
Phenylacetonitrile	2-Phenylethylamine	94	46
Diphenylacetonitrile	2,2-Diphenylethylamine	98	61
Benzonitrile	Benzylamine	97	72

TABLE 4. Reduction of nitriles with borane

Compound	Reagent	Product	% yield	Ref.
Benzonitrile	BH_3THF	Benzylamine	84	282
m-Nitrobenzonitrile	BH_3THF	*m*-Nitrobenzylamine	79	282
t-Butylmalononitrile	BH_3THF	2-*t*-Butyl-1,3-diaminopropane	36–48	283
PhCOCN	BH_3THF	$PhCOCH_2NH_2$	60	284
2,6-Dichlorophenyl-acetonitrile	$BH_3(CH_3)_2S$	2-(2,6-Dichlorophenyl)ethylamine	64	285

(ii) Sodium borohydride and derivatives. Although sodium borohydride does not usually reduce nitriles[287], 2- and 4-cyanopyridines have been converted in moderate yields (43–53%) to the amines under conditions (ethanol, reflux) in which benzonitrile is inert[288]. Apparently, the pyridine ring renders the nitrile carbon electrophilic enough for attack by this mild reagent[288]. Increasing the electrophilicity of the nitrile carbon may also be accomplished by formation of the nitrilium ion[247] or by coordination with cobalt salts[289]. Reduction with borohydride then proceeds smoothly to the amines. In the former case, secondary amines are produced in yields of 66–89% (equation 21)[247].

$$RC{\equiv}N \xrightarrow[BF_3]{(R^1O)_3CH} RC{\equiv}\overset{+}{N}R^1 \xrightarrow{BH_4^-} RCH_2NHR^1 \qquad (21)$$

Successful reductions are also accomplished using borohydride in combination with metals or metal salts. Thus 3:1[290] or 4:1[291] ratios of $NaBH_4$:$AlCl_3$ in diglyme rapidly reduce aromatic and aliphatic nitriles at 25°C[290]. The reducing species is probably a mixture of sodium diboroheptahydride and AlH_3[292].

Sodium borohydride and cobalt(II) chloride also provide an effective combination for reducing nitriles to amines in good to excellent yields[293–295] (Table 5). The reducing species is not known but hydrogen is evolved and a black precipitate of cobalt or cobalt boride is formed[293]. Borohydride and Raney nickel in basic aqueous methanol also reduce nitriles to amines in moderate to good yields (34–80%)[296] and the method has been successfully used in synthetic schemes[297,298].

TABLE 5. Reduction of nitriles with $NaBH_4$–$CoCl_2$

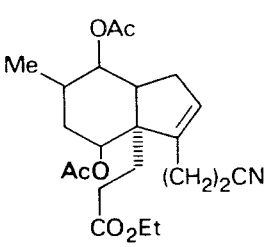
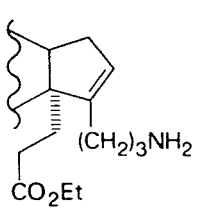
Compound	Product	% yield	Reference
PhCN	$PhCH_2NH_2$	72	293
p-$NO_2C_6H_4CH_2CN$	*p*-$NO_2C_6H_4(CH_2)_2NH_2$	60	293
n-$C_7H_{15}CN$	*n*-$C_8H_{17}NH_2$	80	293
α-Cyanofuran	α-Aminomethylfuran	75	293
$CH_2{=}CHCN$	$H_2C{=}CHCH_2NH_2$	70	293
		—	294

TABLE 6. Reduction of nitriles with sodium trifluoroacetoxyborohydride[300]

Compound	Product	% yield
PhCN	$PhCH_2NH_2$	82
Ph_2CHCN	$Ph_2CHCH_2NH_2$	70
$4\text{-}O_2NC_6H_4CH_2CN$	$4\text{-}O_2NC_6H_4(CH_2)_2NH_2$	71
$4\text{-}MeO_2CC_6H_4CN$	$4\text{-}MeO_2CC_6H_4CH_2NH_2$	89

The reducing ability of borohydride may also be augmented by replacement of one or more hydrogens with sulphur (to give $NaBH_2S_2$)[299] or acyloxy groups (to give $NaBH_3O_2CCF_3$)[300] and these derivatives readily reduce nitriles to amines although the former reagent usually gives thioamides as side-products[299]. Sodium trifluoroacetoxyborohydride in THF is particularly effective and affords good yields with a variety of nitriles (Table 6). It should be noted that neither $NaBH_3O_2CCH_3$ nor $NaBH(O_2CCF_3)_3$ reduces nitriles[300].

IV. REDUCTION OF OTHER TRIPLE-BONDED GROUPS

A. Introduction

The reduction of other triple bonds such as isocyanides and aromatic diazonium ions has not received the interest accorded alkynes and nitriles. Nevertheless, reductions of these functional groups do provide limited, but useful, synthetic transformations primarily as methods for deamination of amines to hydrocarbons. Future studies, especially with the gamut of available hydride transfer reagents may provide additional synthetically useful methods for preparation of hydrazines and methylamines.

B. Reduction of Aromatic Diazonium Ions

The reduction of aromatic diazonium ions provides an efficient method for the displacement of amines by hydrogen since these intermediates are generated by treatment of amines with nitrous acid or an alkyl nitrite[301,302]. A number of reagents accomplish this displacement including the classical methods using alkaline formaldehyde, hypophosphorous acid, sodium stannite or alcohols[301]. More recent synthetically useful methods include THF, 1,4-dioxane, 1,3-dioxolane or 1,2-dimethoxyethane in aqueous sodium acetate[303], tetramethylurea[304], rhodium complexes[305], hypophosphorous acid–Cu_2O in $CHCl_3$[306], hexamethylphosphoramide[307], benzeneselenol[308], sodium borohydride in CH_3OH or DMF[309], triphenylphosphine[312], trialkyltin hydrides and trialkylsilyl hydrides[313]. The mechanism for the reductive eliminations appears to involve either a radical process[301,306-308,311,313] (equation 22) or, at least with hydride-transfer reagents, a diazine intermediate which decomposes to the product arene[310,313] (equation 23).

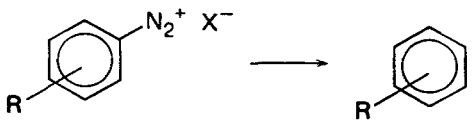
$$ArN_2^+ + X \longrightarrow ArN_2^{\cdot} + X^{\cdot} + N_2$$

$$ArN_2^{\cdot} \longrightarrow Ar^{\cdot} + N_2 \qquad (22)$$

$$Ar^{\cdot} + H \longrightarrow ArH$$

$$ArN_2^+ + H^- \longrightarrow Ar{-}N{=}NH \longrightarrow ArH + N_2 \qquad (23)$$

TABLE 7. Reduction of aromatic diazonium salts

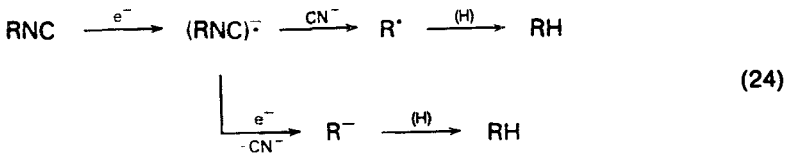


R	X	Reagent (solvent)	% yield	Reference
H	Cl^-	$THF–H_2O$	70	303
H	BF_4^-	*n*-Bu_3SnH	100	313
H	BF_4^-	PhSeH (THF)	80	308
p-EtO_2C	Cl^-	$THF–H_2O$	83	303
p-EtO_2C	BF_4^-	$NaBH_4(CH_3OH)$	54	309
o-HO_2C	Cl^-	Bu_3SnH(THF)	98	313
o-HO_2C	BF_4^-	$NaBH_4(CH_3OH)$	77	309
p-O_2N	BF_4^-	HMPA	82	307
p-O_2N	BF_4^-	Bu_3SnH	52	313
p-O_2N	BF_4^-	H_3PO_2, $Cu_2O(CHCl_3)$	99	306
p-O_2N	Cl^-	$THF–H_2O$	84	303
2,4-Dinitro	BF_4^-	$NaBH_4(CH_3OH)$	48	309
4-MeO	BF_4^-	Bu_3SnH(THF)	94	313
4-MeO	BF_4^-	H_3PO_2, $Cu_2O(CHCl_3)$, 18-crown-6	88	306
4-MeO	BF_4^-	HMPA	90	307

Table 7 presents representative examples of successful reductions using several of the above reagents, chosen, when possible, to illustrate comparisons between different systems. As evident, a number of choices are available which permit the efficient conversion of aromatic amines to hydrocarbons via diazonium intermediates.

C. Reduction of Isocyanides

Treatment of isocyanides with reducing systems results in either removal of the NC group and replacement with hydrogen[314,318,321] (equation 24) or addition to one π bond to give imine derivatives[319,320] (equation 25). Less common pathways include reductive cleavage to afford primary amines[321], or, complete reduction to alkylamines[322].



(24)

(25)

X = R^1Si, RS, RO, R^1NH

The process depicted in equation (24) is accomplished with a variety of reducing systems including alkali metals in liquid ammonia[314] or tetrahydrofuran[315], trialkyltin hydrides[316,317] or sodium naphthalene in dimethoxyethane (DME)[318]. The mechanism involves either radical[314,316,317,318] and/or carbanion[315,318] formation as illustrated. Synthetically, the procedures are useful for deamination reactions since both aromatic

and aliphatic amines can be readily converted to isocyanides in high yields[323]. The sodium naphthalene/DME system[318] is particularly attractive since yields are high and side-reactions are few.

A number of reagent systems effect addition across a π bond of isocyanides (equation 25) to give imine derivatives. These include thiols (with $Fe_4S_4L_4$ clusters)[320] and amines, alcohols or trialkylsilanes [with Co(II) catalysts][319].

The reduction of isocyanides to alkylamines has not been extensively explored[322].

V. REFERENCES

1. K. N. Campbell and B. K. Campbell, *Chem. Rev.*, **31**, 77 (1942).
2. L. Crombie, *Quart. Rev.*, **6**, 101 (1952).
3. R. L. Burwell, *Chem. Rev.*, **57**, 895 (1957).
4. R. L. Augustine, *Catalytic Hydrogenation*, Marcel Dekker, New York, 1965 p. 69.
5. P. N. Rylander, *Catalytic Hydrogenation over Platinum Metals*, Academic Press, New York, 1967; M. Friefelder, *Practical Catalytic Hydrogenation*, Wiley–Interscience, London–New York, 1971.
6. E. N. Marvell and T. Li, *Synthesis*, 457 (1973).
7. M. Rabinowitz in *Chemistry of the Cyano Group* (Ed. Z. Rappoport), John Wiley and Sons, London, 1970.
8. (a) H. Lindlar, *Helv. Chim. Acta*, **35**, 446 (1952).
   (b) H. Lindlar and R. Dubuis, *Org. Synth., Collect. Vol. V*, 880 (1973).
9. N. A. Dobson, G. Eglinton, M. Krishnamurti, R. A. Raphael and R. G. Willis, *Tetrahedron*, **16**, 16 (1961).
10. E. K. Raunio and W. A. Bonner, *J. Org. Chem.*, **31**, 396 (1966).
11. R. A. Raphael and F. Sondheimer, *J. Chem. Soc.*, 2100 (1950).
12. O. Isler, W. Huber, A. Ronco and M. Kofler, *Helv. Chim. Acta*, **30**, 1911 (1947).
13. D. J. Cram and N. L. Allinger, *J. Amer. Chem. Soc.*, **78**, 2518 (1956).
14. D. J. Cram and M. Cordon, *J. Amer. Chem. Soc.*, **77**, 4090 (1955).
15. A. T. Blomquist, R. E. Burge and A. C. Sucsy, *J. Amer. Chem, Soc.*, 74, 3636 (1952).
16. A. T. Blomquist, L. H. Lim and J. C. Bohrer, *J. Amer. Chem. Soc.*, **74**, 3643 (1952).
17. F. Sondheimer, R. Wolovsky and Y. Amiel, *J. Amer. Chem. Soc.*, **84**, 274 (1962).
18. F. Sondheimer and Y. Amiel, *J. Amer. Chem. Soc.*, **82**, 5765 (1960).
19. B. W. Baker, R. P. Linstead and B. C. L. Weedon, *J. Chem. Soc.*, 2218 (1955).
20. F. G. Fischer and K. Lowenberg, *Ann. Chem.*, **475**, 183 (1923).
21. H. Schinz, L. Ruzicka, C. F. Seidel and C. Tavel, *Helv. Chim. Acta*, **30**, 1810 (1947).
22. L. Ruzicka and G. Firmenick, *Helv. Chim. Acta*, **22**, 292 (1939).
23. R. Rossi and A. Carpita, *Tetrahedron*, **33**, 2447 (1977).
24. N. A. Milas, P. Davis, I. Belie and D. A. Fles, *J. Amer. Chem. Soc.*, **72**, 4844 (1950).
25. H. H. Inhoffen, F. Bohlman, K. Bartram, G. Rummert and H. Pommer, *Ann. Chem.*, **570**, 54 (1950).
26. H. H. Inhoffen, F. Bohlman and G. Rummert, *Ann. Chem.*, **569**, 226 (1950).
27. H. H. Inhoffen, H. Pommer and F. Bohlman, *Ann. Chem.*, **569**, 237 (1950).
28. P. Karrer and C. H. Eugster, *Helv. Chim. Acta*, **33**, 1172 (1950).
29. P. Karrer, C. H. Eugster and E. Tobler, *Helv. Chim. Acta*, **33**, 1349 (1950).
30. O. Isler, H. Gutmann, H. Lindlar, M. Montavon, R. Ruegg and P. Zeller, *Helv. Chim. Acta*, **39**, 449 (1956).
31. O. Isler, A. Ronco, W. Guex, N. C. Hindley, W. Huber, K. Diale and M. Kofler, *Helv. Chim. Acta*, **32**, 489 (1949).
32. W. J. Humphlett and D. M. Burness, *U.S. Patent*, No. 2,676,990 (1954); *Chem. Abstr.*, **50**, 408a (1956).
33. H. Pommer and W. Sarnecki, *German Patent*, No. 1,059,900 (1959); *Chem. Abstr.*, **55**, 14511a (1961).
34. R. Ruegg, U. Schwieter, G. Ryser, P. Schudel and O. Isler, *Helv. Chim. Acta*, **44**, 994 (1961).

35. O. Isler, H. Lindlar, M. Monatvon, R. Ruegg, G. Saucy and P. Zeller, *Helv. Chim. Acta.*, **39**, 2041 (1956).
36. M. Akhtar and B. C. L. Weedon, *J. Chem. Soc.*, 4058 (1959).
37. H. H. Inhoffen and G. Raspe, *Ann. Chem.*, **592**, 214 (1955).
38. A. Tai, F. Matsumura and H. C. Coppel, *J. Org. Chem.*, **34**, 2180 (1969).
39. G. Buchi and B. Egger, *J. Org. Chem.*, **36**, 2021 (1971).
40. K. Sisido, S. Kurozumi and K. Utimoto, *J. Org. Chem.*, **34**, 2661 (1969).
41. B. Loev and C. R. Dawson, *J. Org. Chem.*, **24**, 980 (1959).
42. R. B. Woodward, M. P. Cava, W. D. Ollis, A. Hunger, H. U. Daeniker and K. Schenker, *Tetrahedron*, **19**, 247 (1963).
43. V. Theus, W. Surber, L. Colombi and H. Schinz, *Helv. Chim. Acta*, **38**, 239 (1955).
44. V. Theus and H. Schinz, *Helv. Chim. Acta.*, **39**, 1290 (1956).
45. T. A. Gosink, *Ph.D. Thesis*, Oregon State University, June 1966.
46. W. Surber, V. Theus, L. Colombi and H. Schinz, *Helv. Chim. Acta*, **41**, 1299 (1958).
47. I. Heilbron, E. R. H. Jones, R. W. Richards and F. Sondheimer, *J. Chem. Soc.*, 737 (1949).
48. I. Heilbron, E. R. H. Jones, J. B. Toogood and B. C. L. Weedon, *J. Chem. Soc.*, 1827 (1949).
49. I. Heilbron, E. R. H. Jones, J. B. Toogood and B. C. L. Weedon, *J. Chem. Soc.*, 2028 (1949).
50. A. Eschenmoser, J. Schreiber and S. A. Julia, *Helv. Chim. Acta*, **36**, 483 (1953).
51. P. Schiess and H. L. Chia, *Helv. Chim. Acta*, **53**, 485 (1970).
52. P. Schiess, R. Seegar and C. Suter, *Helv. Chim. Acta*, **53**, 1713 (1970).
53. H. H. Inhoffen and G. von der Bey, *Ann. Chem.*, **583**, 100 (1953).
54. P. Mildner and B. C. L. Weedon, *J. Chem. Soc.*, 3282 (1953).
55. P. A. Robins and J. Walker, *J. Chem. Soc.*, 642 (1952).
56. H. H. Inhoffen and G. von der Bey, *Ann. Chem.*, **583**, 100 (1953).
57. P. Mildner and B. C. L. Weedon, *J. Chem. Soc.*, 3294 (1953).
58. H. H. Inhoffen, H. Pommer and F. Bohlman, *Ann. Chem.*, **569**, 237 (1950).
59. H. H. Inhoffen, H. Pommer, K. Winkelmann and H.-J. Aldag, *Chem. Ber.*, **84**, 87 (1951).
60. W. Oroshnik and A. O. Mebane, *J. Amer. Chem. Soc.*, **76**, 5719 (1954).
61. O. Isler, H. Lindlar, M. Montavon, P. Ruegg and P. Zeller, *Helv. Chim. Acta*, **39**, 249 (1956).
62. F. Sondheimer, R. Wolovsky and Y. Amiel, *J. Amer. Chem. Soc.*, **84**, 274 (1962).
63. E. N. Marvel and J. Tashiro, *J. Org. Chem.*, **30**, 3991 (1965).
64. J. F. Arens and D. A. van Dorp, *Rec. Trav. Chim.*, **67**, 973 (1948).
65. J. F. Arens, D. A. van Dorp, G. van Dijk, B. J. Brant, P. J. Hubers and H. Peters, *Rec. Trav. Chim.*, **67**, 973 (1948).
66. A. Rouve and M. Stoll, *Helv. Chim. Acta*, **33**, 2019 (1950).
67. J. F. Arens and D. A. van Dorp, *Rec. Trav. Chim.*, **68**, 604 (1949).
68. G. Dupont, *Bull. Soc. Chim. Fr.*, **3**, 1030 (1936).
69. K. N. Campbell and M. J. O'Connar, *J. Amer. Chem. Soc.*, **61**, 2897 (1939).
70. N. A. Khan, *J. Amer. Oil Chem. Soc.*, **30**, 40 (1953).
71. L. Crombie, *J. Chem. Soc.*, 3510 (1955).
72. K. N. Campbell and L. T. Eby, *J. Amer. Chem. Soc.*, **63**, 216 (1941).
73. A. L. Herne and K. W. Greenlee, *J. Amer. Chem. Soc.*, **65**, 2020 (1943).
74. M. C. Hoff, K. W. Greenlee and C. E. Boord, *J. Amer. Chem. Soc.*, **73**, 3229 (1951).
75. N. A. Khan, *J. Amer. Chem. Soc.*, **74**, 3018 (1952).
76. W. Oroshnik, G. Karmas and A. D. Mebane, *J. Amer. Chem. Soc.*, **74**, 3807 (1952).
77. H. Grutter, R. Helg and H. Schinz, *Helv. Chim. Acta*, **35**, 771 (1952).
78. M. Stoll, J. Hulstkamp and A. Rouve, *Helv. Chim. Acta*, **31**, 543 (1948).
79. K. Ahmad and F. M. Strong, *J. Amer. Chem. Soc.*, **70**, 1699 (1948); F. M. Bumpus, W. R. Taylor and F. M. Strong, *J. Amer. Chem. Soc.*, **72**, 2166 (1950).
80. C. A. Brown and V. K. Ahuja, *J. Org. Chem.*, **38**, 2226 (1973).
81. C. A. Brown and V. K. Ahuja, *Chem. Commun.*, 553 (1973).
82. J. J. Brunet, P. Gallois and P. Caubere, *J. Org. Chem.*, **45**, 1937 (1980); P. Gallois, J. J. Brunet and P. Caubere, *J. Org. Chem.*, **45**, 1946 (1980).
83. R. Tedeschi and G. Clark, Jr., *J. Org. Chem.*, **27**, 4323 (1962).
84. R. Paul and G. Hilly, *Bull. Chim. Soc. Fr.*, **6**, 218 (1939).

85. A. F. Thompson, Jr. and S. B. Wyatt, *J. Amer. Chem. Soc.*, **62**, 2555 (1940).
86. L. Crombie, *J. Chem. Soc.*, 3510 (1955).
87. I. Jardine and F. J. McQuillin, *Tetrahedron Letters*, 4871 (1966).
88. P. C. Wailes, H. Weigold and A. P. Bell, *J. Organometal. Chem.*, **43**, C32 (1972).
89. E. Negishi, *Organometallics in Organic Synthesis*, Vol. 1, Wiley–Interscience, London–New York, 1980.
90. R. F. Heck, *Organotransition Metal Chemistry*, Academic Press, New York, 1974.
91. J. D. Chanley and H. Sobotka, *J. Amer. Chem. Soc.*, **71**, 4140 (1949).
92. G. E. Benedict and R. R. Russell, *J. Amer. Chem. Soc.*, 73, 5444 (1951).
93. E. B. Bates, E. R. H. Jones and M. C. Whiting, *J. Chem. Soc.*, 1854 (1954).
94. E. F. Magoon and L. H. Slaugh, *Tetrahedron*, **23**, 4509 (1967).
95. E. J. Corey, J. A. Katzenellenbogen and G. H. Posner, *J. Amer. Chem. Soc.*, **89**, 4245 (1967).
96. W. J. Bailey and C. R. Pfeifer, *J. Org. Chem.*, **20**, 1337 (1955).
97. P. D. Landor, S. R. Landor and E. S. Pepper, *J. Chem. Soc.*, 185 (1967).
98. E. Galantay and D. Habeck, Belgian Patent, No. 742,137 (1969); *Chem. Abstr.*, **73**, P35625s (1969).
99. J. S. Cowie, P. D. Landor and S. R. Landor, *Chem. Commun.*, 541 (1969).
100. L. Olsson, A. Claesson and C. Bogentoff, *Acta Chim. Scand.*, **B28**, 765 (1974).
101. G. Zweifel and R. B. Steele, *J. Amer. Chem. Soc.*, **89**, 5085 (1967).
102. P. Nayler and M. C. Whiting, *J. Chem. Soc.*, 4006 (1954).
103. J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen and T. Walker, *J. Chem. Soc.*, 1094 (1952).
104. E. J. Corey, J. A. Katzenellenbogen, N. W. Gilman, S. A. Roman and B. W. Erickson, *J. Amer. Chem. Soc.*, **90**, 5618 (1968).
105. E. J. Corey, H. A. Kirst and J. A. Katzenellenbogen, *J. Amer. Chem. Soc.*, **92**, 6314 (1970).
106. A. Hajos, *Complex Hydrides*, Elsevier, New York, 1979.
107. G. Wilke and H. Muller, *Chem. Ber.*, **89**, 444 (1956).
108. G. Wilke and H. Muller, *Ann. Chem.*, **618**, 267 (1958).
109. G. Wilke and H. Muller, *Ann. Chem.*, **629**, 222 (1960).
110. J. J. Eisch and W. C. Kaska, *J. Amer. Chem. Soc.*, **88**, 2213 (1966).
111. T. Mole and E. A. Jeffery, *Organoaluminum Compounds*, Elsevier, Amsterdam, 1972, Chap. 11.
112. J. J. Eisch and M. W. Foxton, *J. Organometal. Chem.*, **11**, P8 (1968).
113. J. J. Eisch and W. C. Kaska, *J. Amer. Chem. Soc.*, **88**, 2213 (1966).
114. J. J. Eisch and M. W. Foxton, *J. Organometal. Chem.*, **11**, P24 (1968).
115. J. J. Eisch and M. W. Foxton, *J. Org. Chem.*, **36**, 3520 (1971).
116. J. J. Eisch and J. T. Trainor, *J. Org. Chem.*, **28**, 487 (1963).
117. P. Magnus, *Aldrichimica Acta*, **13**, 43 (1980).
118. Reference 89, p. 377.
119. H. C. Brown, *Boranes in Organic Chemistry*, Cornell University Press, 1972, pp. 277, 287–290.
120. H. C. Brown, *Organic Synthesis via Boranes*, Wiley–Interscience, London–New York, 1975.
121. H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, **83**, 3834 (1961).
122. G. Zweifel, H. Arzoumanian and C. C. Whitney, *J. Amer. Chem. Soc.*, **89**, 3652 (1967).
123. H. C. Brown and S. K. Gupta, *J. Amer. Chem. Soc.*, **94**, 4370 (1972).
124. H. C. Brown and S. K. Gupta, *J. Amer. Chem. Soc.*, **97**, 5249 (1975).
125. H. C. Brown and N. Ravindran, *J. Org. Chem.*, **38**, 1617 (1973).
126. H. C. Brown and J. B. Campbell, Jr., *J. Org. Chem.*, **45**, 389 (1980).
127. E. Negishi and K. W. Chiu, *J. Org. Chem.*, **41**, 3484 (1976).
128. H. Yatagai, *Bull. Chem. Soc. Japan*, **53**, 1670 (1980).
129. G. Zweifel, G. M. Clark and N. L. Polston, *J. Amer. Chem. Soc.*, **93**, 3395 (1971).
130. D. J. Pasto, *J. Amer. Chem. Soc.*, **86**, 3039 (1964).
131. K. Avasthi, S. S. Ghosh and D. Devaprabhakara, *Tetrahedron Letters*, 4871 (1976).
132. G. Zweifel, R. P. Fisher, J. T. Snow and C. C. Whitney, *J. Amer. Chem. Soc.*, **93**, 6309 (1971).
133. G. Zweifel and R. P. Fisher, *Synthesis*, 557 (1972).

134. G. Zweifel, R. P. Fisher, J. T. Snow and C. C. Whitney, *J. Amer. Chem. Soc.*, **94**, 6560 (1972).
135. H. Yatagai, Y. Yamamoto and K. Muruyama, *J. Chem. Soc., Chem. Commun.*, 852 (1977).
136. Y. Masuda, A. Arase and A. Suzuki, *Bull. Chem. Soc. Japan*, **53**, 1652 (1980).
137. E. Negishi, J. J. Katz and H. C. Brown, *Synthesis*, 555 (1972).
138. J. Trocha-Grimshaw and H. B. Henbest, *Chem. Commun.*, 757 (1968).
139. B. L. Booth and A. D. Lloyd, *J. Organometal. Chem.*, **35**, 195 (1972).
140. D. M. Barlex, R. D. W. Kemmitt and G. W. Littlecott, *Chem. Commun.*, 613 (1969).
141. M. Michman and M. Balog, *J. Organometal. Chem.*, **31**, 395 (1971).
142. B. L. Booth and R. G. Hargreaves, *J. Organometal. Chem.*, **33**, 365 (1971).
143. B. L. Booth and R. G. Hargreaves, *J. Chem. Soc. (A)*, 308 (1970).
144. D. W. Hart, T. F. Blackburn and J. Schwartz, *J. Amer. Chem. Soc.*, **97**, 679 (1975).
145. E. Colomer and R. Carriu, *J. Organometal. Chem.*, **82**, 367 (1974).
146. P. W. Chum and S. E. Wilson, *Tetrahedron Letters*, 15 (1976).
147. E. C. Ashby and J. J. Lim, *Tetrahedron Letters*, 4481 (1977).
148. E. C. Ashby and J. J. Lim, *J. Org. Chem.*, **43**, 2567 (1978).
149. E. C. Ashby and T. Smith, *J. Chem. Soc., Chem. Commun.*, 30 (1978).
150. E. C. Ashby, J. J. Lim and A. B. Goel, *J. Org. Chem.*, **43**, 757 (1978).
151. M. F. Semmelhack and R. D. Stauffer, *J. Org. Chem.*, **40**, 3619 (1975).
152. M. F. Semmelhack, R. D. Stauffer and A. Yamashita, *J. Org. Chem.*, **42**, 3180 (1977).
153. E. B. Fleischer and M. Krishnamurthy, *J. Amer. Chem. Soc.*, **94**, 1382 (1972).
154. S. K. Chung, *J. Org. Chem.*, **44**, 1014 (1979).
155. T. Itoh, T. Nagano and M. Hirobe, *Tetrahedron Letters*, 1343 (1980).
156. T. Yoshida and E. Negishi, *J. Chem. Soc., Chem. Commun.*, 762 (1974).
157. W. E. Newton, J. C. Corbin, P. W. Schneider and W. A. Bulen, *J. Amer. Chem. Soc.*, **93**, 268 (1971).
158. J. K. Crandall and F. Collonges, *J. Org. Chem.*, **41**, 4089 (1976).
159. P. Vermeer, J. Meijer, C. Eylander and L. Brandsma, *Rec. Trav. Chim.*, **95**, 25 (1975).
160. J. J. Brunet, L. Mordenti, B. Loubinoux and P. Caubere, *Tetrahedron Letters*, 1069 (1977).
161. J. J. Brunet and P. Caubere, *Tetrahedron Letters*, 3947 (1977).
162. T. Fujisawa, K. Sugimoto and H. Ohta, *Chem. Letters*, 581 (1976).
163. N. A. Cortese and R. F. Heck, *J. Org. Chem.*, **43**, 3985 (1978).
164. S. I. Jones, M. R. Palmer, J. G. Palmer, J. M. Doemeny and G. N. Schrauzer, *J. Amer. Chem. Soc.*, **100**, 2113 (1978).
165. M. R. Dubois, R. C. Haltiwanger, D. J. Miller and G. Glatzmaier, *J. Amer. Chem. Soc.*, **101**, 5245 (1979).
166. G. N. Schrauzer and P. A. Doemeny, *J. Amer. Chem. Soc.*, **93**, 1608 (1971).
167. M. M. Bhagwat, I. Mehrotra and D. Devaprabhakara, *Tetrahedron Letters*, 167 (1975).
168. T. Satoh, S. Suzuki, Y. Suzuki, Y. Miyaji and Z. Imai, *Tetrahedron Letters*, 4555 (1969).
169. T. A. Vorontsova, A. P. Khrushch and A. E. Shilov, *Kinet. Katal.*, **16**, 1618 (1975).
170. K. N. Campbell and L. T. Eby, *J. Amer. Chem. Soc.*, **63**, 216 (1941).
171. K. N. Campbell and L. T. Eby, *J. Amer. Chem. Soc.*, **63**, 2683 (1941).
172. M. Smith in *Reduction* (Ed. R. L. Augustine), Marcel Dekker, New York, 1968, p. 95.
173. E. M. Kaiser, *Synthesis*, 391 (1972).
174. H. O. House, *Modern Synthetic Reactions*, Benjamin, Menlo Park, California, 1972, Chap. 3.
175. A. J. Birch and G. Subba Rao in *Advances in Organic Chemistry, Methods and Results* (Ed. E. C. Taylor), Wiley–Interscience, London–New York, 1972, p. 1.
176. R. A. Benkeser, G. Schroll and D. M. Sauve, *J. Amer. Chem. Soc.*, **77**, 3378 (1955).
177. A. L. Henne and K. W. Greenlee, *J. Amer. Chem. Soc.*, **65**, 2020 (1943).
178. J. D. White and G. L. Larson, *J. Org. Chem.*, **43**, 4555 (1978).
179. R. A. Benkeser and C. A. Tincher, *J. Org. Chem.*, **33**, 2727 (1968).
180. L. Horner and R. Roder, *Ann. Chem.*, **723**, 11 (1969).
181. A. P. Tomilov, *Russ. Chem. Rev.*, **31**, 569 (1962).
182. G. D. Sargent and M. W. Browne, *J. Amer. Chem. Soc.*, **89**, 2788 (1967).
183. N. A. Dobson and R. A. Raphael, *J. Chem. Soc.*, 3558 (1955).
184. G. M. Whitesides and W. J. Ehmann, *J. Org. Chem.*, **35**, 3665 (1970).
185. W. S. Johnson, N. P. Jensen and J. Hooz, *J. Amer. Chem. Soc.*, **88**, 3859 (1966).

186. W. S. Johnson, M. F. Semmelhack, M. U. S. Sultanbawa and L. A. Dolak, *J. Amer. Chem. Soc.*, **90**, 2994 (1968).
187. H. Yatagai, Y. Yamamoto and K. Maruyama, *J. Chem. Soc., Chem. Commun.*, 702 (1978).
188. A. Claesson, *Acta Chem. Scand.*, **B29**, 609 (1975).
189. C. E. Castro and R. D. Stephens, *J. Amer. Chem. Soc.*, **86**, 4358 (1964).
190. J. K. Crandall and W. R. Heitman, *J. Org. Chem.*, **44**, 3471 (1979).
191. A. Krebs and H. Colberg, *Chem. Ber.*, **113**, 2007 (1980).
192. W. Spang and M. Hanack, *Chem. Ber.*, **113**, 2025 (1980).
193. G. W. Kabalka, R. J. Newton, Jr. and J. H. Chandler, *J. Chem. Soc., Chem. Commun.*, 726 (1978).
194. J. Carnduff, *Quart. Rev.*, **20**, 169 (1966).
195. H. Stephen, *J. Chem. Soc.*, 1874 (1925).
196. O. G. Backeberg and B. Staskun, *J. Chem. Soc.*, 3961 (1962).
197. B. Statkun and O. G. Backeberg, *J. Chem. Soc.*, 5880 (1964).
198. T. van Es and B. Staskun, *J. Chem. Soc.*, 5774 (1965).
199. S. Pietra and C. Trinchera, *Gazz. Chim. Ital.*, **85**, 1705 (1955).
200. W. W. Zajac, Jr., J. F. Siuda, M. J. Nolan and T. M. Santosusso, *J. Org. Chem.*, **36**, 3539 (1971).
201. H. Rupe and E. Hodel, *Helv. Chim. Acta*, **6**, 865 (1923).
202. A. Gaiffe, *Chim. Ind. (Milan)*, **93**, 259 (1965).
203. H. Plieninger and G. Werst, *Chem. Ber.*, **88**, 1956 (1955).
204. H. Plieninger and B. Kiefer, *Chem. Ber.*, **90**, 617 (1957).
205. T. D. Perrine and E. L. May, *J. Org. Chem.*, **19**, 773 (1954).
206. L. T. Smith and E. R. Rogier, *J. Amer. Chem. Soc.*, **73**, 4047 (1951).
207. A. L. Henne, R. L. Pelly and R. M. Alm, *J. Amer. Chem. Soc.*, **72**, 3370 (1950).
208. H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, **86**, 1085 (1964).
209. M. Schlosser and Z. Brich, *Helv. Chim. Acta*, **61**, 1903 (1978).
210. L. I. Zajharkin and I. M. Khorlina, *Dokl. Akad. Nauk SSSR*, **116**, 422 (1957).
211. A. E. G. Miller, J. W. Biss and L. H. Schwartzman, *J. Org. Chem.*, **24**, 627 (1959).
212. G. Winterfeldt, *Synthesis*, 617 (1975).
213. J. A. Marshall, N. H. Anderson and P. C. Johnson, *J. Amer. Chem. Soc.*, **89**, 2748 (1967).
214. S. Trofimenko, *J. Org. Chem.*, **29**, 3046 (1964).
215. M. C. Zaluski, N. Robba and M. Bonhomme, *Bull. Soc. Chim. Fr.*, 1445 (1970).
216. C. Paulmier, J. Morel, P. Pastour and D. Semmard, *Bull. Soc. Chim. Fr.*, 2511 (1969).
217. J. H. Babler and T. R. Mortell, *Tetrahedron Letters*, 669 (1972).
218. J. A. Marshall, N. H. Anderson and C. P. Johnson, *J. Org. Chem.*, **35**, 186 (1970).
219. J. A. Marshall, N. H. Anderson and J. W. Schlicher, *J. Org. Chem.*, **35**, 858 (1970).
220. R. V. Stevens, L. E. DuPree, Jr. and P. L. Loewenstein, *J. Org. Chem.*, **37**, 977 (1972).
221. P. M. McCrury, Jr. and R. K. Singh, *Tetrahedron Letters*, 3325 (1973).
222. R. E. Ireland, S. W. Baldwin, D. J. Dawson, M. I. Dawson, J. E. Dolfini and J. Newbould, *J. Amer. Chem. Soc.*, **92**, 5743 (1970).
223. R. E. Ireland and S. C. Welch, *J. Amer. Chem. Soc.*, **92**, 7232 (1970).
224. W. Nagata and H. Itazaki, *Chem. Ind. (London)*, 1194 (1964).
225. W. Nagata, *Nippon Kagaku Zasshi*, **90**, 837 (1969).
226. L. Botta and J. Kalvoda, *Experentia*, **28**, 628 (1972).
227. R. Van Moorselaar and S. J. Holkes, *Rec. Trav. Chim.*, **88**, 737 (1969).
228. W. Nagata, T. Okumura and M. Yoshioka, *J. Chem. Soc. (C)*, 2347 (1970).
229. W. Nagata, T. Wakabayashi, M. Narisada, M. Yamaguchi and Y. Hayase, *Chem. Pharm. Bull.*, **19**, 1582 (1971).
230. W. Nagata, T. Wakabayashi, Y. Hayase, M. Narisada and S. Kamata, *J. Amer. Chem. Soc.*, **93**, 3202 (1971).
231. W. Nagata, T. Wakabayashi, Y. Hayase, M. Narisada and S. Kamata, *J. Amer. Chem. Soc.*, **93**, 5740 (1971).
232. W. Bartmann, G. Beck and U. Lerch, *Tetrahedron Letters*, 2441 (1974).
233. H. Plieninger, E. Meyer, F. S. Nassirian and E. Weidman, *Tetrahedron Letters*, 97 (1976).
234. K. Utimoto, N. Sakai, M. Obayashi and H. Nozaki, *Tetrahedron*, **32**, 769 (1976).
235. H. H. Wasserman, E. Gosselink, D. D. Keith, J. Nadelson and R. J. Sykes, *Tetrahedron*, **32**, 1863 (1976).

236. H. H. Wasserman, D. D. Keith and J. Nadelson, *Tetrahedron*, **32**, 1867 (1976).
237. G. L. Grunewald, J. M. Grindel, P. N. Patil and K. N. Salman, *J. Med. Chem.*, **19**, 10 (1976).
238. P. J. Garegg, J. Hoffman, B. Lindberg and B. Samuelsson, *Carbohyd. Res.*, **67**, 263 (1978).
239. D. Heissler and J. J. Riehl, *Tetrahedron Letters*, 3957 (1979).
240. H. Plieninger, E. Meyer, F. S. Nassirian and E. Weidman, *Ann. Chem.*, 1475 (1976).
241. P. Vittorelli, J. P. Katalinic, G. M. Muller, H. J. Hansen and H. Schmid, *Helv. Chim. Acta*, **58**, 1379 (1975).
242. R. A. Amos and J. A. Katzenellenbogen, *J. Org. Chem.*, **43**, 560 (1978).
243. T. Kametani, Y. Hirai, Y. Shiratori, K. Fukomoto and F. Satoh, *J. Amer. Chem. Soc.*, **100**, 554 (1978).
244. F. Jung and J. J. Riehl, *Tetrahedron Letters*, 509 (1972).
245. Y. Kojima and N. Kato, *Tetrahedron Letters*, 5033 (1980).
246. H. C. Brown, P. Heim and N. M. Yoon, *J. Org. Chem.*, **37**, 2942 (1972).
247. R. F. Borch, *Chem. Commun.*, 442 (1968); *J. Org. Chem.*, **34**, 627 (1969).
248. J. L. Fry, *J. Chem. Soc., Chem. Commun.*, 45 (1974).
249. H. Watanabe, Y. Kikugawa and S. I. Yamada, *Chem. Pharm. Bull.*, **21**, 465 (1973).
250. R. B. Wagner and H. D. Zook, *Synthetic Organic Chemistry*, Wiley–Interscience, London–New York, 1953.
251. Reference 174, Chap. 2.
252. F. A. Carey and R. J. Sundberg, *Advanced Organic Chemistry*, Part B, Plenum/Rosetta, New York, 1977.
253. F. E. Gould, G. S. Johnson and A. F. Ferris, *J. Org. Chem.*, **25**, 1658 (1960).
254. J. A. Secrist, III and M. W. Logue, *J. Org. Chem.*, **37**, 335 (1972).
255. M. M. Rising and E. W. Lowe, *J. Amer. Chem. Soc.*, **52**, 2524 (1930).
256. L. A. Watter and S. M. McElvain, *J. Amer. Chem. Soc.*, **56**, 1614 (1934).
257. G. W. Watt, *Chem. Rev.*, **46**, 317 (1950).
258. R. A. Benkeser, C. Arnold, Jr., R. F. Lambert and O. H. Thomas. *J. Amer. Chem. Soc.*, **77**, 6042 (1955).
259. M. Tomita and T. Sato, *Yakugaku Zasshi*, **77**, 1024 (1957).
260. P. G. Arapakos, *J. Amer. Chem. Soc.*, **89**, 6794 (1967).
261. P. G. Arapakos, M. K. Scott and F. E. Huber, Jr., *J. Amer. Chem. Soc.*, **91**, 2059 (1969).
262. M. Smith in *Reduction, Techniques and Applications in Organic Synthesis* (Ed. R. L. Augustine), Marcel Dekker, New York, 1968.
263. A. R. Doumaux, Jr., *J. Org. Chem.*, **37**, 508 (1972).
264. R. F. Nystrom and W. G. Brown, *J. Amer. Chem. Soc.*, **70**, 3738 (1948).
265. N. C. Gaylord, *Reduction with Complex Metal Hydrides*, Interscience, New York, 1956.
266. A. E. Finholt, E. C. Jacobson, A. E. Ogard and P. Thompson, *J. Amer. Chem. Soc.*, **77**, 4163 (1955).
267. L. M. Soffer and M. Katz, *J. Amer. Chem. Soc.*, **78**, 1705 (1956).
268. H. C. Brown, P. M. Weissman and N. M. Yoon, *J. Amer. Chem. Soc.*, **88**, 1458 (1966); H. C. Brown and N. M. Yoon, *J. Amer. Chem. Soc.*, **88**, 1464 (1966).
269. R. F. Nystrom, *J. Amer. Chem. Soc.*, **77**, 2544 (1955).
270. G. F. Morris and C. R. Hauser, *J. Org. Chem.*, **27**, 465 (1962).
271. V. Bazant, M. Capka, M. Cerny, V. Chvalousky, K. Kochloefl, M. Kraus and J. Malek, *Tetrahedron Letters*, 3303 (1968).
272. M. Cerny, J. Malek, M. Capka and V. Chvalousky, *Collect. Czech. Chem. Commun.*, 1033 (1969).
273. See however, *J. Vit. Technical Information Bulletin*, Hexcel Speciality Chemicals, 1978, in which acetonitrile and propionitrile were reduced to the corresponding amines in 97% and 94% yield, respectively.
274. W. E. Parham and C. S. Roosevelt, *Tetrahedron Letters*, 923 (1971).
275. H. C. Brown and N. M. Yoon, *J. Amer. Chem. Soc.*, **88**, 1464 (1966).
276. N. M. Yoon and H. C. Brown, *J. Amer. Chem. Soc.*, **90**, 2927 (1968).
277. K. Ziegler, K. Schneider and J. Schneider, *Ann. Chem.*, **623**, 9 (1959).
278. C. F. Lane, *Chem. Rev.*, **76**, 773 (1976).
279. L. M. Braun, R. A. Braun, H. R. Chrissman, M. Opperman and R. M. Adams, *J. Org. Chem.*, **36**, 2388 (1971).
280. R. O. Hutchins and F. Cistone, *Org. Prep. Proced. Int.*, **13**, 225 (1981).

281. H. C. Brown, P. Heim and N. M. Yoon. *J. Amer. Chem. Soc.*, **92**, 1637 (1970).
282. H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, **82**, 681 (1960).
283. R. O. Hutchins and B. E. Maryanoff, *Org. Synth.*, **53**, 21 (1973).
284. B. C. Subba Rao and G. P. Thakar, *Curr. Sci.*, 404 (1963).
285. C. F. Lane, *Aldrichimia Acta*, **8**, 20 (1975).
286. H. C. Brown, D. B. Bigley, S. K. Arora and N. M. Yoon, *J. Amer. Chem. Soc.*, **92**, 7161 (1970).
287. J. A. Meschino and C. J. Bond, *J. Org. Chem.*, **28**, 3129 (1963); J. A. Marshall and R. D. Carroll, *J. Org. Chem.*, **30**, 2748 (1965); S. B. Kadin, *J. Org. Chem.*, **31**, 620 (1966).
288. Y. Kikugawa, M. Kuramoto, I. Saito and S. I. Yamada, *Chem. Phar. Bull.*, **9**, 1927 (1973).
289. I. I. Creaser and A. M. Sargeson, *J. Chem. Soc., Chem. Commun.*, 974 (1975).
290. H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, **78**, 2582 (1956).
291. G. W. Stacy, A. J. Papa, F. W. Villaescusa and S. C. Ray. *J. Org. Chem.*, **29**, 607 (1964).
292. H. Noth, *Nachr. Chem. Techn.*, **23**, 107 (1975).
293. T. Satoh, S. Suzuki, Y. Suzuki, Y. Miyaji and Z. Imai, *Tetrahedron Letters*, 4555 (1969).
294. T. Harayama, M. Ohtani, M. Oki and Y. Inubushi, *Chem. Commun.*, 827 (1974).
295. A. R. Battersby, J. E. Kelsey and J. Staunton, *Chem. Commun.*, 183 (1971).
296. R. A. Egli, *Helv. Chim. Acta*, **53**, 47 (1970).
297. T. Wieland, C. Birr and P. Fleckenstein, *Ann. Chem.*, **756**, 14 (1972).
298. J. Hine and W. S. Li, *J. Org. Chem.*, **43**, 289 (1978).
299. J. M. Lalancette and J. R. Brindle, *Can. J. Chem.*, **49**, 2990 (1971).
300. N. Umino, T. Iwakuma and N. Itoh, *Tetrahedron Letters*, 2875 (1976); T. Iwakuma, N. Umino and N. Itoh, *Yuki Gosei Kagaku Kyokaishi*, **35**, 300 (1977). For an review of the use of sodium borohydride in carboxylic acid media, see G. W. Gribble, *Eastman Org. Chem. Bull.*, **51**, 1 (1979).
301. N. Kornblum, *Organic Reactions*, Vol. 2, Wiley–Interscience, London–New York, 1944.
302. R. Putter in *Methoden der Organischen Chemie (Houben–Weyl)*, Vol. X/3, 4th ed., Georg Thieme Verlag, Stuttgart, 1965.
303. H. Meerwein, H. Allendorfer, P. Beekmann, Fr. Kunert, H. Morschel, F. Pawellek and Kl. Wunderlich, *Angew. Chem.*, **70**, 211 (1958).
304. K. G. Rutherford and W. A. Redmond, *J. Org. Chem.*, **28**, 568 (1963).
305. G. S. Marx, *J. Org. Chem.*, **36**, 1725 (1971).
306. S. H. Korzeniowski, L. Blum and G. W. Gokel, *J. Org. Chem.*, **42**, 1469 (1977).
307. F. Trondlin and C. Ruchardt, *Chem. Ber.*, **110**, 2494 (1977).
308. F. G. James, M. J. Perkins, O. Porta and B. V. Smith, *J. Chem. Soc., Chem. Commun.*, 131 (1977).
309. J. B. Hendrickson, *J. Amer. Chem. Soc.*, **83**, 1251 (1961).
310. C. E. McKenna and T. G. Traylor, *J. Amer. Chem. Soc.*, **93**, 2313 (1971); M. Bloch, H. Musso and U. I. Zahorszky, *Angew. Chem. (Intern. Ed. Engl.)*, **8**, 370 (1969); T. Severin, R. Schmitz, J. Loske and J. Hufnagel, *Chem. Ber.*, **102**, 4152 (1969).
311. A. Rieker, P. Niederer and D. Leibfritz, *Tetrahedron Letters*, 4287 (1969); L. A. Rykova, L. A. Kiprianova, A. F. Levit and I. P. Gragerov, *Teor. Eksp. Khim.*, **14**, 256 (1978).
312. L. Horner and H. Stohl, *Chem. Ber.*, **86**, 1073 (1953); L. Horner and H. Hoffman, *Chem. Ber.*, **91**, 45 (1958).
313. J. Nakayama, M. Yoshida and O. Simamura, *Tetrahedron*, **26**, 4609 (1970).
314. I. Ugi and F. Bodesheim, *Chem. Ber.*, **94**, 1157 (1961).
315. W. Buchner and R. Dufax, *Helv. Chim. Acta*, **49**, 1145 (1966).
316. T. Saegusa, S. Kobayashi, Y. Ito and N. Yasuda, *J. Amer. Chem. Soc.*, **90**, 4182 (1968).
317. D. H. R. Barton, G. Bringmann, G. Lamotte, R. S. H. Motherwell and W. B. Motherwell, *Tetrahedron Letters*, 2291 (1979).
318. G. E. Niznik and H. M. Walborsky, *J. Org. Chem.*, **43**, 2396 (1978).
319. T. Saegusa, Y. Ito, S. Kobayashi and K. Kirota, *J. Amer. Chem. Soc.*, **89**, 2240 (1967).
320. A. Schwartz and E. E. van Tamelen, *J. Amer. Chem. Soc.*, **99**, 3189 (1977).
321. E. L. Moorehead, B. J. Weathers, E. A. Ufkes, P. R. Robinson and G. N. Schrauzer, *J. Amer. Chem. Soc.*, **99**, 6089 (1977).
322. E. Larsson, *Chalmers Tekn. Hogskolas Handl.*, **94**, 15 (1950); *Chem. Abstr.*, **45**, 1494 (1951).
323. H. M. Walborsky and G. E. Niznik, *J. Org. Chem.*, **37**, 187 (1972).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER **15**

Dediazoniations of arenediazonium ions and related compounds

HEINRICH ZOLLINGER

Technisch-Chemisches Laboratorium, Eidgenössische Technische Hochschule (ETH), Zürich, Switzerland

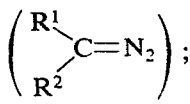
I. INTRODUCTION

The term dediazoniation was introduced by Bunnett[1] as early as 1954, but has only become widely known since the seventies. This terminology will form the basis of a system of naming chemical reactions which is in the process of development by the IUPAC Commission on Physical Organic Chemistry[2].

Dediazoniation refers to all reactions in which a N_2 molecule is one of the products. The designation of the entering group precedes the term dediazoniation, i.e. hydro-dediazoniation for the substitution of the diazonio group by hydrogen, or aryl-dediazoniation for a Gomberg–Bachmann reaction.

As far as our present knowledge is concerned there are five groups of reagents which undergo such reactions, namely:

(*a*) aromatic and heteroaromatic diazonium ions ($Ar—N_2^+$) and their derivatives;
(*b*) aliphatic and alicyclic diazonium ions ($R—N_2^+$);

(*c*) diazoalkanes  ;

(*d*) azides ($R—N_3$ and $Ar—N_3$);
(*e*) open-chain and cyclic compounds containing azo groups (—N=N—) such as azoalkanes, azoarenes, pyrazoles, pyrazolines, triazolines etc.

As this volume treats reactions of triple-bonded compounds, only dediazoniations of groups (*a*) and (*b*) belong properly to this subject. Yet, dediazoniations of diazoalkanes (group *c*) involve alkanediazonium ions in many cases; the dediazoniation of azides (group *d*) yields nitrenes. Although it is usually assumed that the diazoalkane-like mesomeric structural formula of azides ($R—\overset{+}{N}=N=\bar{N}$) represents the properties of these compounds better, a β,γ-triple-bonded mesomeric structure ($R—\bar{N}—\overset{+}{N}\equiv N$) must also be considered. The dediazoniations of these two groups will be discussed in this chapter only briefly, as most readers will not expect them in a book which treats triple-bonded functional groups.

Dediazoniations of alkenediazonium ions are not discussed as reactions of alkenediazonium ions are the subject of another Chapter of this volume.

Groups (*a*) and (*c*) have already been treated by Hegarty[3] in the volume on *The Chemistry of Diazonium and Diazo Groups* of this series. Hegarty's chapter includes literature up until 1975. Some significant clarifications of major problems related to dediazoniations in group (*a*) took place soon after that time. They will be discussed in the following Sections in a broader context; in Section III they will be briefly compared with dediazoniations of group (*b*).

II. DEDIAZONIATIONS OF ARENEDIAZONIUM IONS

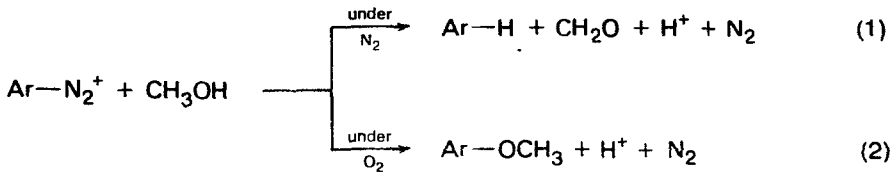
A. Multiplicity of Pathways and Products

A variety of mechanisms has been found in the dediazoniations of aromatic diazonium ions.

Three characteristic examples should suffice to show that seemingly slight modifications in the reaction system can lead to entirely different reaction products; these suggest fundamentally different dediazoniations mechanisms:

(1) As already observed by Horner and Stöhr[4] and by DeTar and Kosuge[5], and thoroughly investigated by Bunnett and coworkers[6–8], numerous arenediazonium ions

in methanol decompose in a nitrogen atmosphere with formation of the corresponding hydrocarbon, i.e. a hydro-dediazoniation occurs (equation 1); in the presence of oxygen, however, methoxy-dediazoniation (equation 2) takes place.



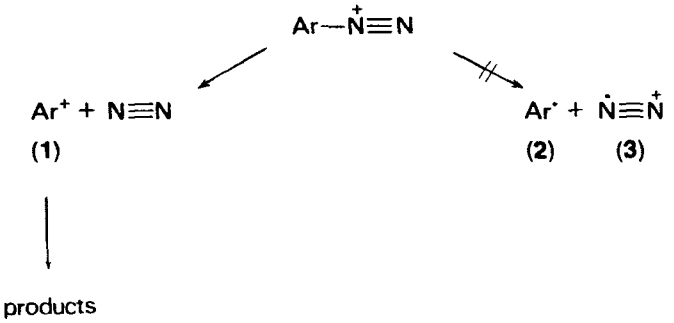
(2) In DMSO as solvent, aryl-dediazoniation of the unsubstituted benzenediazonium ion with nitrobenzene leads mainly via *meta* substitution to 3-nitrobiphenyl, whereas in the case of the *p*-nitrobenzenediazonium ion the formation of *ortho*- and *para*-substituted products (2.4′- and 4,4′-dinitrobiphenyl) prevails[9].

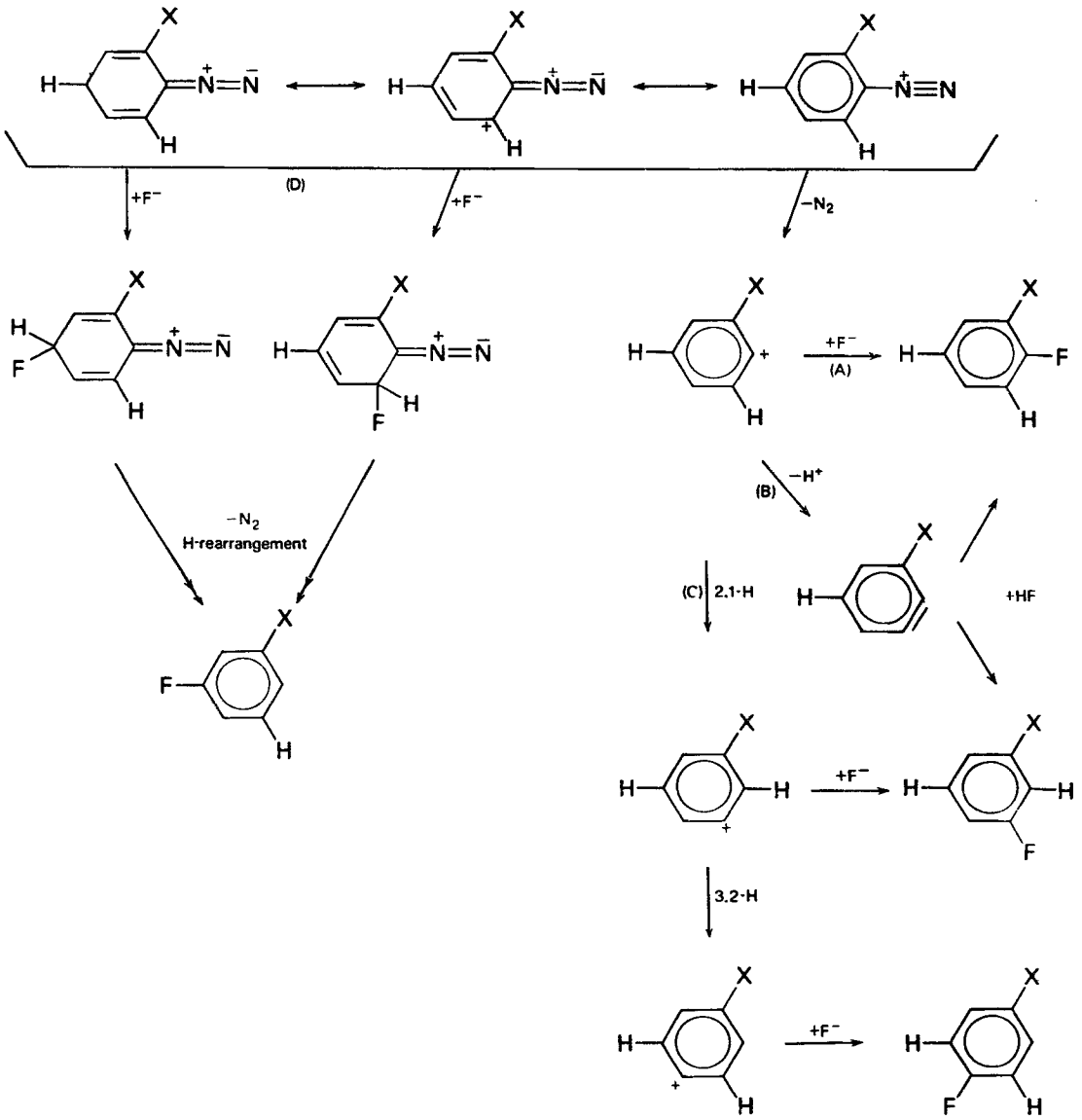
(3) Dediazoniations of three *ortho*-substituted benzenediazonium salts in pyridinium poly(hydrogen fluoride) yield different products, depending on the substituent, as Olah and Welch[10] have found: The *o*-methyl derivative gives *o*-fluorotoluene. With *o*-nitrobenzenediazonium ion, the main product is *m*-nitrofluorobenzene, the *ortho* isomer being formed only in small quantities. Finally, the *o*-trifluoromethyl derivative yields all three isomeric trifluoromethylfluorobenzenes.

The first two examples indicate clearly that slight modifications (O_2 to N_2 atmosphere, unsubstituted to *p*-nitrobenzenediazonium ion) change a heterolytic reaction into a homolytic process. The changeover from heterolytic to homolytic dediazoniations will be discussed in more detail in Section II.D.1 of this chapter. The product ratio of the third example suggests, as formulated in Scheme 1, that S_N1 substitutions (A), reactions via arynes (B), σ substitutions of the type described by Kovacic and Gormisk[11] (D) and S_N1 substitutions with 2,1- and 3,2-hydrogen shifts (C) may occur.

Dediazoniations of aromatic diazonium salts have been reviewed by Hegarty[3], Chlebowski[12], Richey and Richey[13], and more recently by Ambroz and Kemp[14] and Zollinger[15,16]. These articles concentrate exclusively[3,12–14] or mainly[15,16] on heterolytic dediazoniations where the literature is much more extensive.

This is understandable because simple mechanistic considerations 'explain' easily why a heterolytic dissociation of the C—N bond in a diazonium ion is likely to occur, as a nitrogen molecule is already 'preformed' in a diazonium ion. On the other hand, a homolytic dissociation of the C—N bond is very unlikely from an energetic point of view. Whereas in heterolysis N_2, a very stable product, is formed in addition to the aryl cation (**1**), which is a metastable intermediate, in homolysis *two* metastable primary





SCHEME 1

products, the aryl radical (**2**) and the dinitrogen radical cation (**3**) would be formed. This is unlikely, and indeed, as discussed in Section II.D.4, homolytic dediazoniations do not proceed by simple homolysis of a diazonium ion.

B. The S_N1 Mechanism of Dediazoniation

In a classic study in 1940, Crossley and coworkers[17] demonstrated that the rates of nucleophilic substitutions of the diazonio group of the arenediazonium ion in acidic aqueous solution were independent of the concentrations of nucleophiles and that

these rates were identical with the rate of hydrolysis. Since that time it has therefore been accepted without question that these reactions proceed by an S_N1 mechanism, i.e. that they consist of a rate-determining irreversible dissociation of the diazonium ion into an aryl cation and nitrogen and fast subsequent reactions of the cation with water or other nucleophiles present in solution (equations 3–5).

$$Ar{-}N_2^+ \xrightarrow{\text{slow}} Ar^+ + N_2 \tag{3}$$

$$Ar^+ + H_2O \xrightarrow{\text{fast}} Ar{-}\overset{+}{O}H_2 \xrightleftharpoons{\text{fast}} Ar{-}OH + H^+ \tag{4}$$

$$Ar^+ + Nu^{n-} \xrightarrow{\text{fast}} Ar{-}Nu^{(n-1)-} \tag{5}$$

Nu = nucleophile, n = 0, 1, 2, etc.

Scant attention has been given to a paper published in 1952 by Lewis and Hinds[18] who demonstrated that the dediazoniation rate of *p*-nitrobenzenediazonium ions in water is linearly proportional to added bromide ion. Later, Lewis and coworkers[19] made a careful investigation of salt effects on the rate of dediazoniation of several arenediazonium ions in water; linear dependences of the rates on the concentration of the anion were found; this suggested participation of the nucleophile in the rate-determining steps.

A kinetic demonstration of nucleophilic participation was found in arylations of toluene, benzene, trifluoromethylbenzene, and anisole with benzenediazonium tetrafluoroborate in trifluoroethanol[20,21] In this solvent, fluorobenzene and phenyl 2,2,2-trifluoroethyl ether are formed in addition to biphenyl derivatives from the arylation reactions. The biphenyl isomer proportions show clearly that the reaction is not homolytic. The reaction rates with the four aromatic substrates are linearly dependent on the concentration of the substrates and the calculated second-order rate constants increase in the sequence $C_6H_5CF_3 < C_6H_5OCH_3 < C_6H_6 \sim C_6H_5CH_3$. The apparent decrease in the reactivity of anisole may be due to complex formation with BF_3 which is produced in the competitive Schiemann fluorination.

The results are consistent with an S_N2-like mechanism, i.e. a concerted attack of the nucleophile with the release of N_2 or with a two-step S_NAr mechanism. On the other hand, substituent effects, as found by Crossley and coworkers[17] and later verified by Schulte-Frohlinde and Blume[22] are not understandable on the basis of such bimolecular mechanisms. Instead of an acceleration by −M substituents (*p*-NO_2 etc.) expected on the basis of such mechanisms, a decrease in rate was found for almost all types of substituents in the *meta* and *para* positions.

Substituent effects supported, however, the aryl cation as a key intermediate in dediazoniations, provided they were evaluated in an appropriate way. As discussed already in Hegarty's review[23] on the basis of Swain's work[24], no meaningful correlation of the logarithms of rate constants is obtainable with the various types of Hammett substituent constants. Swain and coworkers[24] analysed the kinetic results by use of the dual parameter substituent constants $\mathcal{F}$(= field effect) and $\mathcal{R}$(= resonance effect) of equations (6) and (7) which had been developed by Swain and Lupton[25] some years previously.

$$\log \frac{k_m}{k_H} = f_m \mathcal{F} + r_m \mathcal{R} + i_m \tag{6}$$

$$\log \frac{k_p}{k_H} = f_p \mathcal{F} + r_p \mathcal{R} + i_p \tag{7}$$

k_m, k_p and k_H are rate constants of the *meta*-, *para*- and un-substituted benzene derivatives respectively; the f_m and f_p reaction constants represent the sensitivities of these reactions to the field substituent constants $\mathcal{F}$ of substituents; r_m and r_p are the respective reaction constants related to the resonance substituent constants $\mathcal{R}$; i_m and i_p are residual factors without any intelligible meaning. Compared to the extensive experience with the Hammett equation (as a two-parameter relationship for rates and equilibria of benzene derivatives), the Swain–Lupton equations as a *pair* of four-parameter (six if i_m and i_p are also considered) relationships have clearly demonstrated their usefulness for dediazoniations. The field reaction constants are the same within experimental error for *meta*- and *para*- substituted diazonium ions ($f_m = -2.74 \pm 0.20$, $f_p = -2.60 \pm 0.16$); the resonance reaction constants, however, are even different in sign! ($r_m = -3.18 \pm 0.36$, $r_p = +5.08 \pm 0.37$). The correlation coefficients are very good: 0.984 for ten *meta* substituents and 0.992 for seven *para* substituents.

This is the first satisfactory quantitative correlation of substituent effects for dediazoniations of arenediazonium ions; it is in line with the S_N1 mechanism, i.e. the formation of an aryl cation. It implies that the stabilization of the aryl cation is most important for *meta* substituents while for *para*-substituted derivatives the most important factor is the stabilization of the arenediazonium ion. Swain's f values are, however, not explainable on the basis of either an S_N2-like or an S_NAr mechanism.

A good relationship with the Swain–Lupton parameters was found recently by Kuokkanen and Virtanen[26] for the rates of dediazoniation of ten substituted benzenediazonium tetrafluoroborates in 1,2-dichloroethane at three temperatures.

Additional evidence for aryl cations as intermediates comes from primary nitrogen and secondary deuterium isotope effects, also investigated by Swain's group[27,28]. The kinetic isotope effect measured in the dediazoniation of Ph—^{15}N≡N in 1% aqueous H_2SO_4 at 25°C is $k_{14}/k_{15} = 1.038$, close to the calculated value (1.040–1.045) expected for complete C—N bond cleavage in the transition state. It might be mentioned, however, that a partial or almost complete cleavage of the C—N bond and therefore a nitrogen isotope effect is also to be expected for an S_N2-like mechanism; but not, however, for an S_NAr mechanism.

Swain's group[27] was actually not the first to measure kinetic nitrogen isotope effects in dediazoniations. Loudon, Maccoll and Smith[29] determined k_{14}/k_{15} for the unsubstituted, *m*-chloro-, *p*-nitro- and *p*-methoxy-benzenediazonium ion in the presence and absence of salts (SCN^-, Br^-, HSO_4^-). In their discussion these authors favour slightly an S_N1 mechanism, keeping open the possibility of an S_N2-like mechanism for the *p*-methoxy derivative.

The deuterium isotope effect for each hydrogen *ortho* to the diazonio group ($k_H/k_D = 1.22$)[27] is the largest secondary aromatic hydrogen isotope effect yet observed. It is comparable to those observed for α-deuterium in reactions involving carbenium ion formation from secondary aliphatic esters. Obviously this is evidence for hyperconjugative stabilization of the aryl cation by the *ortho* hydrogens.

Finally, Swain and coworkers[24] presented evidence supporting that of Crossley and coworkers[17] to show that in hydroxy-dediazoniation water as a nucleophile does not enter the kinetic equation. There is a less than 2% change in rate when the system is changed gradually from 80% H_2SO_4 to a mixture of 100% H_2SO_4 and 5% SO_3 in spite of the fact that this change corresponds to a 10^3-fold decrease in the activity of H_2O molecules (Swain's results on the solvent effect in general will be treated in Section II.D.1).

In summary, there was, therefore, in 1975 overwhelming evidence for the S_N1 mechanism (equations 3–5). We have reviewed it here, in spite of the fact that Hegarty[30] has already done so, for one specific reason. The kinetic results[18–21]

mentioned before, which clearly suggest that there are indeed heterolytic dediazoniations whose rate increases with increasing concentration of nucleophiles, can positively not be explained by the S_N1 mechanism as written in equations 3–5. Hegarty has considered these cases, suspecting that there might be a different ('bimolecular') mechanism which operates. He stresses, however, that '... clearly these data warrant reinvestigation'.

Today, we know that the solution to this dilemma had already been visualized in a paper published in 1973[15], but was not evaluated experimentally and in detail until the period 1976–1979[31–34]. As it is an interesting example of the influence of logical and psychological factors in the development of scientific discoveries, it was also discussed briefly in a short essay on such factors in the philosophy of science[35].

In 1973, the hypothesis was put forward that a rate dependence on the concentration(s) of the nucleophile(s) is compatible with the aryl cation pathway if the back-reaction of the first step (equation 8) is faster than the attack of the nucleophile on the aryl cation (**1**) (equation 9), i.e. $k_{-1}[N_2] \gg k_2[Nu^{n-}]$ in equation (10).

$$Ar{-}N_2^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ar^+ + N_2 \tag{8}$$

$$Ar^+ + Nu^{n-} \xrightarrow{k_2} Ar{-}Nu^{(n-1)-} \tag{9}$$

$$\frac{d[Ar{-}N_2^+]}{dt} = [Ar{-}N_2^+]\frac{k_1k_2[Nu^{n-}]}{k_{-1}[N_2]+k_2[Nu^{n-}]} \tag{10}$$

This hypothesis is rather unconventional as it obviates a long-standing dogma of organic chemists, namely 'simple organic compounds do not react with molecular nitrogen'. Such a reaction is, however, postulated for the reverse process of equation (8), and furthermore the claim is made that molecular nitrogen is a reasonably good nucleophile!

How can the hypothesis be tested? There are, at least, two possibilities, a qualitative and a quantitative approach.

For the qualitative test one has to run dediazoniations with a diazonium ion, labelled with ^{15}N in either the α or β position or in both positions, in a solution of as high as possible concentration of unlabelled molecular nitrogen ($^{14}N_2$). If the reaction is stopped before completion, the ^{15}N content of the residual diazonium ion should be smaller due to the back-reaction of equation (8). The result of this test was indeed positive[31,36]!

This result explains without difficulty the astonishing discovery of Lewis and coworkers[37–39] made ten years previously which was thought[40] to be an artifact: They found that in aqueous solution the hydrolysis is accompanied by a very slow rearrangement of the two nitrogen atoms, (equation 11) at a rate 1.6% of that of hydrolysis. On the basis of equation 8, this result is understandable. The aryl cation may react with the other nitrogen atom of the N_2 molecule released in the forward reaction. Lewis' result in water was later supported by the work of other groups[28,31]. In less nucleophilic solvents such as 2,2,2-trifluoroethanol (TFE)[31] and 1,1,1,3,3,3-hexafluoroisopropanol (HFIP)[32] and with a suitably substituted diazonium salt (2,4,6-trimethylbenzenediazonium tetrafluoroborate)[33] the extent of the N_α,N_β rearrangement reaches 20.9% and 37.0% respectively, after 70% completion of the overall dediazoniation[31–33].

$$Ar{-}{}^{15}\overset{+}{N}{\equiv}N \rightleftharpoons Ar^+ + {}^{15}N{\equiv}N \rightleftharpoons Ar{-}\overset{+}{N}{\equiv}{}^{15}N \tag{11}$$

(**1**)

The second test for mechanism of equations (8) and (9) is an evaluation of equation 10 with kinetic results for dediazoniations with varying concentrations of molecular nitrogen [N_2]. As the solubility of N_2 is relatively low in most solvents, kinetic runs have to be made under pressure of N_2. Dediazoniations have a positive volume of activation (9.0–11.4 cm^3 mol^{-1})[33,41]; therefore kinetics have to be measured at constant pressure of argon/N_2 mixtures. The results[33] did *not* fit equation 10 well, but suggested a mechanism involving the 'free' (solvated) aryl cation (**1**) only as a second intermediate following a first-formed complex which has the structure of a tight ion-molecule pair (**4**) (Scheme 2).

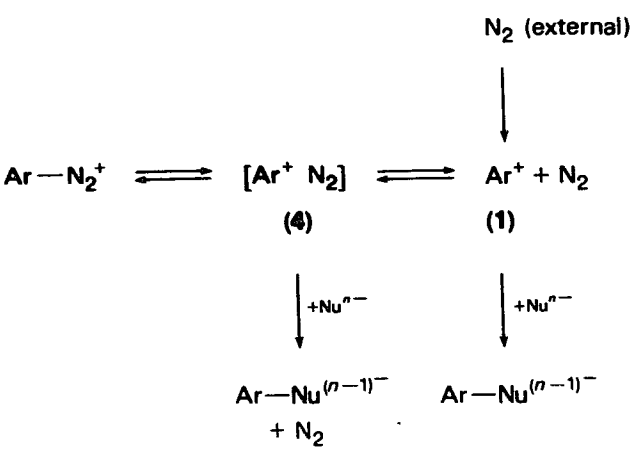
By a statistical treatment of the kinetic data, Scheme 2 can be shown to fit the experimental results better than all the other mechanisms considered[34]. The hypothesis of an intermediate similar to **4** was put forward briefly, but without direct evidence, also by Hong and coworkers[42].

In Scheme 2 **4** and **1** are steady-state intermediates. It is therefore impossible to determine their structure directly, i.e. by spectroscopy and other methods for which a certain measurable concentration is necessary.

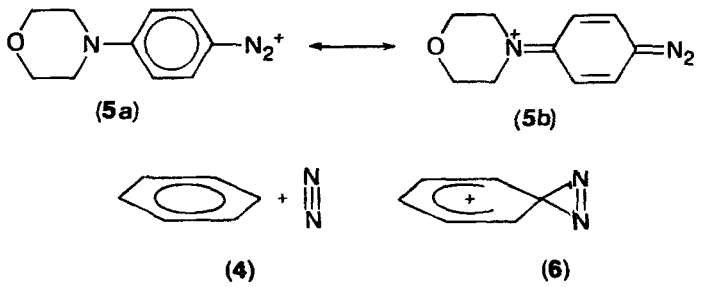
With respect to the aryl cation **1**, biradical and triplet structures have been proposed by various authors[43–45] because, as mentioned above, the substituent effects are not explainable with conventional (Hammett) parameters. After the evaluation with the Swain–Lupton parameters there is now no reason to consider a triplet structure for **1**.

A series of semiempirical MO treatments of the benzenediazonium ion and the phenyl cation were made in the sixties and seventies. They have been surpassed by recent *ab initio* MO calculations with minimal (STO-3G) and split-valence (4-31G) basis sets carried out by Vincent and Radom[46]. They are consistent with Scheme 2 including the tight ion-molecule pair (**4**). In spite of the fact that the author has also cooperated in MO evaluations of reactions of diazonium salts[47], a warning must be expressed concerning their reliability. As shown recently by Kemp and coworkers[48], SCF calculations by several methods predict a shortening of the C-2 to C-3 bond in 4-morpholinobenzenediazonium ion (**5**), a result which is, however, not observed by X-ray crystallography. The contribution of a quinoidal form (**5b**) is therefore less than expected on the basis of MO calculations.

Concerning the first intermediate in Scheme 2, differentiation between a tight ion-molecule pair (**4**, the N—N bond perpendicular to the six-membered ring) and a spirodiazine cation (**6**) was originally left open.



SCHEME 2



(5a) (5b)

(4) (6)

Recently two sets of arguments have been developed which, in addition to the *ab initio* calculations mentioned above (which refer only to the gas phase) both favour **4**.

(*a*) For an intermediate of type **4** one expects a secondary deuterium isotope effect in the N_α,N_β rearrangement (r) with 2,4,6-d_3-benzenediazonium ions of $k_H/k_{D_3} > 1$ and this is expected to have about the same magnitude as the isotope effect of the solvolysis (s); for (**6**), however, the isotope effect for the N_α,N_β rearrangement is expected to be slightly smaller than 1. The result is $(k_H/k_{D_3})_r = 1.45$, $(k_H/k_{D_3})_s = 1.46$[49].

(*b*) CNDO/2 calculations including six water molecules demonstrate that there are even three minima on the dediazoniation pathway and that structure **4** is energetically more favourable than **6** or structures in which the two nitrogen atoms are in the same axis as in the diazonium ion, but with a greater C—N distance, or perpendicular to that axis, and in the same plane as the phenyl residue (not perpendicular to it as in **4**). Geometries and net charges (in electrons) for the three calculated intermediates and the six water molecules are given in Figure 1.

A homolytic alternative to the N_α,N_β rearrangement was postulated by Bargon and Seifert[50]. Rüchardt and coworkers[51] have been able to show that under conditions which favour homolytic dediazoniations practically no rearrangement takes place; this mechanism can therefore be excluded.

We now return to the question of whether, in addition to the S_N1 mechanism in Scheme 2, a bimolecular dediazoniation mechanism exists. There are no data available which are not explainable by Scheme 2 or even by its simplified form as in equations 8–9. Dediazoniations with strong nucleophiles (SCN^-) do not show a linear but an asymptotic increase in rate with increase in thiocyanate concentration[33,49]; the ^{15}N isotope effects with the *p*-methoxy derivative measured by Maccoll and coworkers[31] are understandable by the S_N1 mechanism if the arguments are based on the Swain–Lupton and not on a Hammett treatment. We emphasize, however, that all these observations do not definitely exclude the possibility of a bimolecular mechanism.

The heterolytic dediazoniation of arenediazonium salts is still the only feasible route to aryl cations. The only other successful reaction to obtain these metastable intermediates has been described recently by Hanack and Michel[52]; due to the difficult accessibility of the necessary starting materials, Hanack's method has, however, no practical importance. Other potential synthetic routes, analogous to those used for vinyl cations, have been investigated by five groups, but without success[53,54].

As discussed in Sections II.A and II.D, arenediazonium ions have a latent tendency to form aryl radicals and not aryl cations. Radical formation is minimized in polar solvents of low nucleophilicity. Water at pH values below about 1 fits these conditions well except for diazonium ions of high electrophilicity, i.e. those substituted with strong −M substituents (—NO_2, etc.). Better than water is trifluoroacetic acid[55] and fluorinated alcohols such as 2,2,2-trifluoroethanol (TFE)[20,21,31–33] and 1,1,1,3,3,3-hexafluoroisopropanol (HFIP)[32].

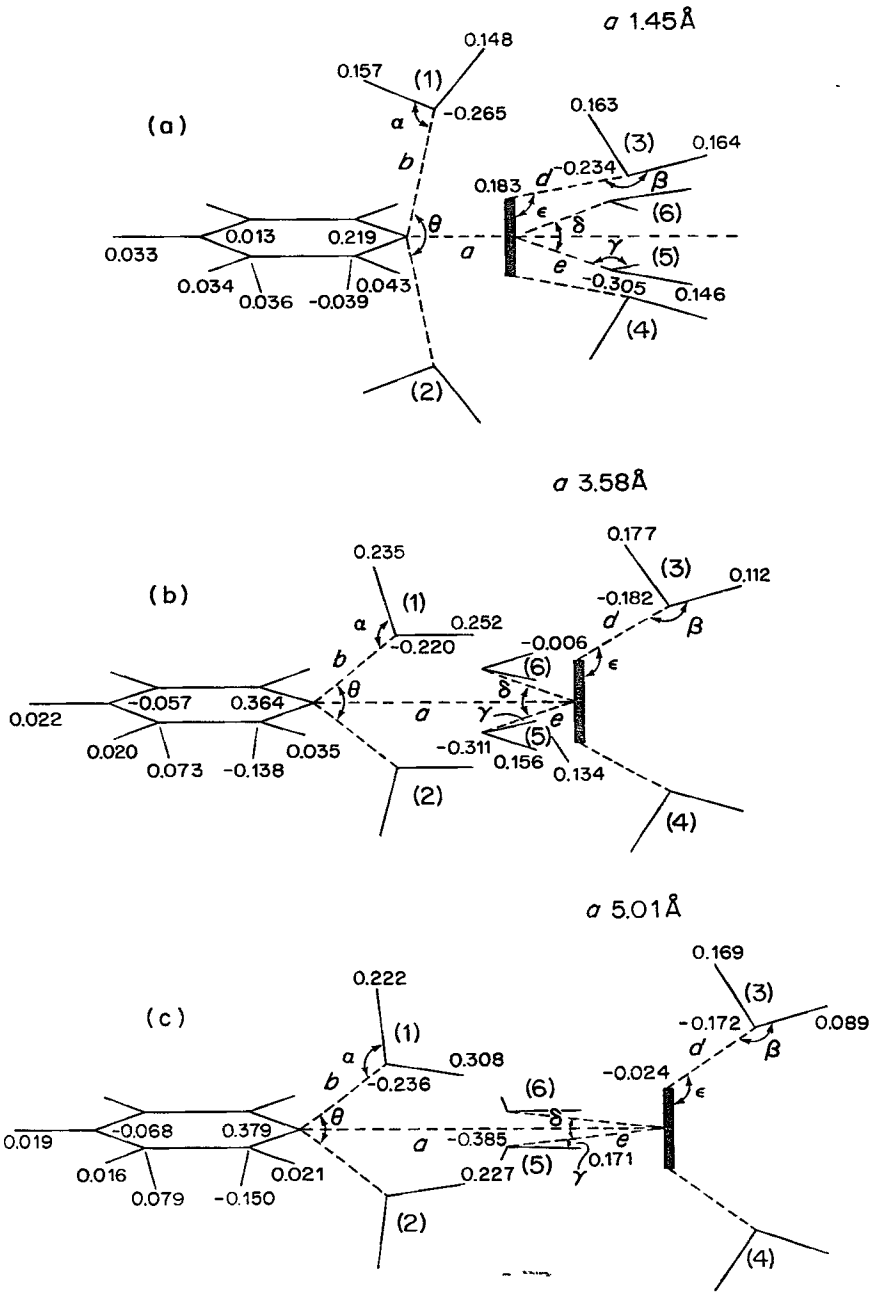


FIGURE 1. Geometries and net charges (in electrons) for the three intermediates calculated by CNDO/2 for the dediazoniation of the benzenediazonium ion in the presence of six water molecules. Reproduced by permission of the Chemical Society from A. Gamba, M. Simonetta, G. Suffritti, I. Szele and H. Zollinger, *J. Chem. Soc., Perkin Trans. 2*, 493 (1980).

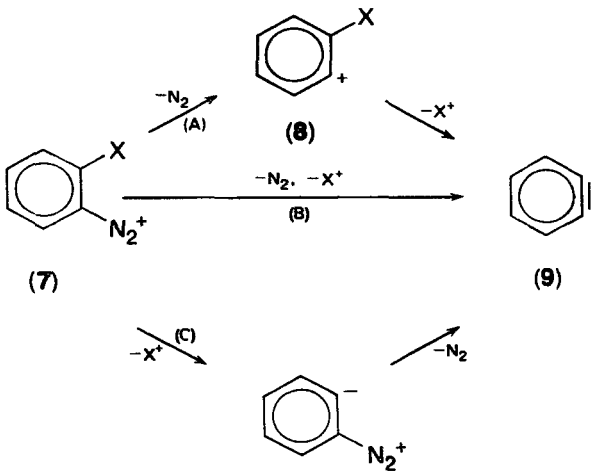
Solvent effects on heterolytic dediazoniations are small. They will be discussed in Section II.D.1 in the context of the influence of solvents on the changeover from the heterolytic to homolytic mechanisms.

C. Dediazoniations via Aryne Intermediates

Arynes as metastable intermediates in heterolytic aromatic substitutions were detected in the fifties in reactions of halobenzenes with $NaNH_2$. Arynes are also formed in dediazoniations of *o*-carboxybenzenediazonium ions[56] and of unsubstituted benzenediazonium ions[57], as found in 1960 and 1964, respectively.

Arynes in general are the subject of a monograph[58] and of chapters in Viehe's book[59] as well as in the present volume. The formation of arynes from diazonium salts is treated in two chapters in a previous volume of this series[60,61].

The major mechanistic problem of aryne formation is the question as to whether dediazoniation takes place before or after the release of the electrofugic group (H^+ and CO_2 respectively) or if N_2 and the other group are eliminated in a concerted process. As it exists this problem may be answered differently, depending on the nature of the electrofugic leaving group (X) and on the reaction conditions. The alternatives are given in Scheme 3. Corresponding pathways have to be discussed for the formation of 1,3- and 1,4 -dehydroaromatics.



X = H, COO^-, etc.

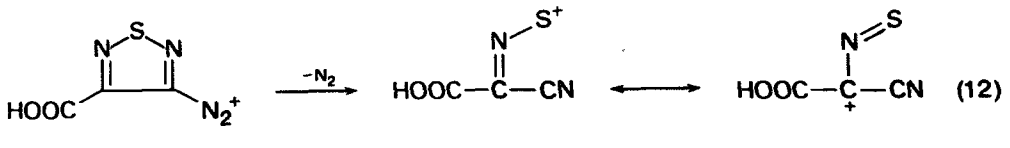
SCHEME 3

Hegarty[61] has already reviewed the experimental data which are compatible with the stepwise mechanism (A) (Scheme 3), of X = COO^-, and with the concerted mechanism (B), if X = H. There is no necessity to summarize these data in the present review.

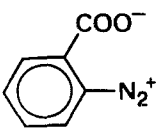
Until recently, benzyne formation from arenediazonium ions containing hydrogen in one or both *ortho* positions to the diazonio group (7, X = H) had been observed only in aprotic solvents containing bases, especially carboxylate ions[57,62–68], but not in alcohols[21]. More recently, however, Broxton and Bunnett[69] have found that *m*-nitroanisole is formed in the dediazoniation of *o*-nitrobenzenediazonium ions in methanol in the presence of methoxide ions. This has to be interpreted as a product arising from 3-nitro-1,2-benzyne as an intermediate. Simultaneously reductive

dediazoniation (formation of nitrobenzene) takes place; this reaction is discussed in Section II.D.2. The occurrence of the aryne mechanism in poly(hydrogen fluoride)-pyridine mixture, as discovered by Olah and Welch[10] is mentioned in Section II.A.

Heteroaromatic diazonium salts yield hetarynes in analogy to Scheme 3[70]. An interesting case is 3-diazo-1,2,5-thiadiazole-4-carboxylic acid (**10**). In an attempt[71] to generate the dehydroheterocycle, ring-opening took place (equation 12) and the sulphur of the electrophilic intermediate (**11**) reacted with anthracene which was present as an aryne-trapping reagent.

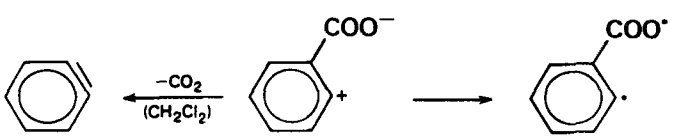


(10) (11)



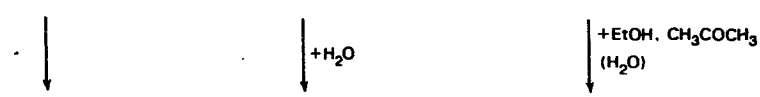
(7)

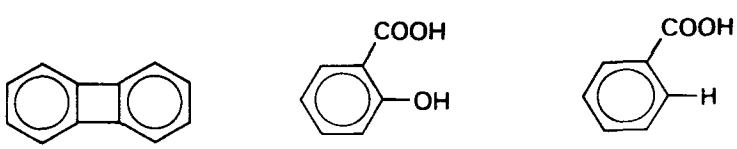
X = COO⁻



(9) (8) (12)

X = COO⁻





(13) (14) (15)

SCHEME 4

Benzenediazonium-*o*-carboxylate (**7**, X = COO^-) was, as mentioned, the first diazonium ion shown to form benzyne (**9**) in a thermal reaction. More recently this dediazoniation was also studied photochemically[72]. The reaction was investigated in water, ethanol, acetone and methylene chloride, using a high-pressure mercury lamp. In every case, the primary step was a dediazoniation, i.e. the zwitterion **8** (X = COO^-) was formed. The consecutive reactions were however different from the thermal reaction of Scheme 3. The product varied, depending on the solvent; and in the case of methylene chloride a small yield (10%) of biphenylene (**13**) was formed. This is most probably the dimerization product of two molecules of benzyne. In addition, 20% benzoic acid (**15**) was found in this solvent, whereas in ethanol and in acetone benzoic acid was formed in higher yields (92% and 45%, respectively). In water 24% of salicylic (**14**) and 9% of benzoic acid were obtained. As a hydrogen atom is more efficiently abstracted from ethanol or acetone than from water, it appears likely that not only **8**, but also the biradical **12** is formed (Scheme 4). Without irradiation, the thermal dediazoniation gave much smaller yields of benzoic acid in ethanol and in acetone (18% and 15%, respectively).

D. Homolytic Dediazoniations

1. Solvent effects in competitive heterolytic and homolytic dediazoniations

As already mentioned in Section II.A of this chapter, a variety of complex mechanisms operate in thermal dediazoniations of arenediazonium salts, giving a wide range of products. For the following discussion in this section and in Sections D.2,3 and 4 it is useful to summarize some representative results relating to solvolysis products from the extensive literature on this subject (Table 1). One recognizes from these data:

(*a*) The influence of the solvent on the mechanism, e.g. examples 1 and 3 versus 4.
(*b*) The influence of acidity, e.g. examples 1 versus 2 or 9 versus 11.
(*c*) The influence of the atmosphere (N_2 or O_2) in examples 8 versus 9.
(*d*) The influence of substituents, e.g. examples 3 versus 6 and 7, or 18 versus 19.

In the following paragraphs we present a critical discussion of the factors which govern the competition between heterolytic and homolytic dediazoniation before proceeding to review specific homolytic dediazoniations in Sections II.D.2–5.

Szele and Zollinger[79] have shown that in 19 solvents the rates of heterolytic dediazoniation of benzenediazonium tetrafluoroborate vary by a factor of only 9 and that it seems to be impossible to recognize *one* of the known solvent parameters to be correlated with the ratios of rates in these solvents. Rates of dediazoniations which follow a homolytic mechanism are however always (as far as they are known today) *faster*. A good example is afforded by the rates in methanol: In a careful study, Bunnett and Yijima[7] have shown that the homolytic rate is 4–32 times higher than the heterolytic rate, the latter being essentially independent of additives and the atmosphere (N_2, O_2 or argon). In water the rate of heterolytic dediazoniations, measured at pH < 3, are lower than those of homolytic reactions which take place in the range pH 8 to 11[80–82].

Szele and Zollinger[79] have found that homolytic dediazoniations are favoured by an increase in the nucleophilicity of the solvent and by an increase in electrophilicity of the β nitrogen atom of the arenediazonium ions resulting from substituents. In Table 2 we list some solvents in which the products of dediazoniation have been investigated in detail. Products obtained from heterolytic and homolytic intermediates are designated

TABLE 1. Products of thermal dediazoniations (representative examples)

$X-C_6H_4-N_2^+ \rightarrow$ products

Example	X	Solvent	Products	Yield	Mechanism[a]	Ref.
1	H and others	H_2O/dilute H_2SO_4	XC_6H_4OH	>90%	C	24
2	*p*-Cl	H_2O(pH 9–11)	Polymers containing —O—, —NH—, —N=N—; Ar–Ar, ArNHAr etc.	–	R	73
3	H, *p*-Cl	CF_3CH_2OH	$XC_6H_4OCH_2CF_3$ $+XC_6H_4F$[b]	ca.65% ca.35%	C C	21
4	H	CF_3CH_2OH/pyridine	C_6H_6, C_6H_5–C_6H_5, polymers etc.	–	R	74
5	2,4,6-$(CH_3)_3$	$(CF_3)_2CHOH$	$(CH_3)_3C_6H_2OCH(CF_3)_2$ $(CH_3)_3C_6H_2F$	ca.95% ca. 5%	C C	32
6	2,4,6-Cl_3	CF_3CH_2OH	$Cl_3C_6H_3$	ca.35%	R	32
7	2,4,6-Br_3	CF_3CH_2OH	$Br_3C_6H_3$	ca.59%	R	32
8	H, *p*-Br	CH_3OH/0.1M TsOH/O_2	$XC_6H_4OCH_3$	92% (H) 72% (*p*-Br)	C	8
9	H	CH_3OH/0.1M TsOH/N_2	$C_6H_5OCH_3$	88%	C	8
10	*p*-Br	CH_3OH/0.1M TsOH/N_2	$BrC_6H_4OCH_3$ $+BrC_6H_5$	73% 19%	C R	8
11	H	CH_3OH/1.1M CH_3ONa/N_2	C_6H_6	64%	R	8
12	*p*-Br	CH_3OH/0.01M CH_3ONa/N_2	BrC_6H_5	66%	R	8
13	*o*-CH_3	$(HF)_n$/pyridine	*o*-$CH_3C_6H_4F$	100%	C	10
14	*o*-NO_2	$(HF)_n$/pyridine	*m*-$NO_2C_6H_4F$	100%	Aryne	10
15	*o*-CF_3	$(HF)_n$/pyridine	*o/m/p*-$CF_3C_6H_4F$	8/91/1	Various	10
16	*p*-NO_2	DMSO[c]	$NO_2C_6H_4OH$	89%	R	75
17	H	DMSO	$C_6H_4(OH)CH_2SCH_3$ $+C_6H_5OH$ etc.	65%	C	76
18	*p*-NO_2	DMSO/nitrobenzene	$NO_2C_6H_4C_6H_4NO_2$ (*o* > *p* > *m*)	63/27/10	R	9
19	H	DMSO/nitrobenzene	$C_6H_5C_6H_4NO_2$ (*m* > *o* > *p*)	55/29/16	C	9
20	H and others	HMPT[d]	XC_6H_5	82–93%	R	77

[a]C = Cationic (heterolytic), R = Radical (homolytic). [b]Production of reaction with tetrafluoroborate, see also Swain and Rogers.[78]
[c]DMSO = dimethyl sulphoxide. [d]HMPT = hexamethyl phosphoric acid triamide.

TABLE 2. Main products of dediazoniation of substituted benzenediazonium salts in solvents of different nucleophilicity

Solvent	Products[a]				Solvent parameters[b]	
	p-NO_2	*p*-Cl	H	*p*-OCH_3	*B*	N_{BS}
HFIP	—	—	C	—	—	−3.93
TFE	C	C	C	C	—	−2.78
CH_3COOH	C	C	C	C	131	−2.05
H_2O(pH <1)	C	C	C	C	156[c]	−0.26[c]
CH_3OH/O_2/0.1M TsOH	C/R	C	C	C	218[c]	+0.01[c]
CH_3OH/N_2/0.1M TsOH	R	C	C	C	218[c]	+0.01[c]
DMSO	R	—	C	—	362	—
HMPT	—	—	R	—	471	—
Pyridine	R	R	R	R	472	—

[a]C = heterolytic (cationic intermediates); R = homolytic (radical intermediates).
[b]*B*: Koppel and Paju[83]; N_{BS}: Schleyer and coworkers[84].
[c]Parameters for pure H_2O or CH_3OH, respectively.

by C (cationic) and R (radical), respectively for four characteristically substituted benzenediazonium salts. The last two columns contain the parameters which give the most reliable information on the nucleophilic character of the solvent for a wide range of solvents, namely Koppel and Paju's *B* values[83] and Schleyer's N_{BS} values[84].

The columns showing the type of product demonstrate clearly that increasing nucleophilicity favours the formation of products of homolytic intermediates. A comparison of the products of the four substituted benzenediazonium salts also makes it clear that an increase in the electrophilicity of the diazonium ion favours homolytic dediazoniations in border line solvents. On the other hand, as has been shown previously[16], there is no observable correlation between the electrophilicity of solvents and the ease of homolytic dediazoniations. The same is true for 'classical' solvent parameters such as polarity or polarisability.

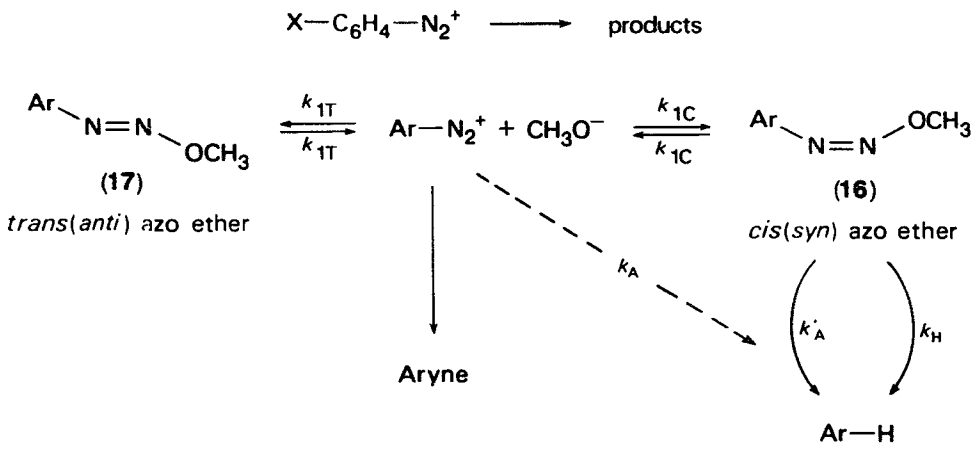
In conclusion, it is very likely that the influence of solvents on the change from the heterolytic mechanism of dissociation of the C—N bond in aromatic diazonium ions to homolytic dissociation can be accounted for by a mechanism in which a solvent molecule acts as a nucleophile or an electron donor to the β nitrogen atom. This process is followed by a one- or a two-step homolytic dissociation to an aryl radical, a solvent radical and a nitrogen molecule. In such a way the unfavourable formation of a dinitrogen radical cation (**3**), as mentioned in Section II.A is eliminated.

The mechanisms of interaction of nucleophiles and electron-transfer reagents will be discussed in Sections II.D.2–4 and II.D.5.

In conclusion it can be said therefore that homolytic products in dediazoniations of unsubstituted benzenediazonium salts are expected in solvents which have a value of *B*[83] higher than ca. 400. This borderline value depends on the electrophilicity of the diazonium salt, e.g. it is shifted to ca. 190 for *p*-nitrobenzenediazonium salts.

2. *Dediazoniations in methanol and ethanol*

The present knowledge of products and mechanisms of dediazoniations in methanol is essentially due to the work of Bunnett and coworkers[6–8,69,85–90], Broxton and coworkers[91–93] and Ritchie and Virtanen[94] during the last 15 years.



SCHEME 5

We start with the discussion of these reactions under alkaline conditions, i.e. in the presence of methoxide ions. Dediazoniations in acidic methanol will follow.

Scheme 5 summarizes the reactions in methanol containing methoxide ion as far as they refer to dediazoniations. As shown by Broxton and Bunnett[69], nucleophilic aromatic substitutions of appropriate substituents, e.g. nitro groups by methoxide ions, occur as well, but these do not belong to the present subject.

Scheme 5 shows that the primary products are the isomeric addition products at the β nitrogen, the *cis* and *trans* arylazo ethers **16** and **17**. In the classical literature these are referred to as *syn* and *anti* aryldiazo ethers; but we prefer the more systematic nomenclature. Full arrows (→) refer to thoroughly investigated reactions; in the case of reactions with dashed arrows (- - - →) good evidence is available for products, but not with respect to mechanisms.

Firstly it has to be emphasized that under alkaline conditions no methoxy-dediazoniation products are detectable. Products which arise from aryne intermediates have been discussed already in Section II.C of this chapter.

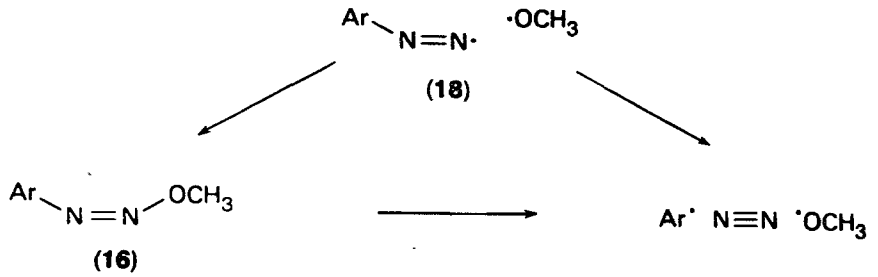
There are two, possibly three ways (k_H, referring to *h*omolytic mechanism, and k_A and k'_A, referring to aryl *a*nion mechanism) of hydro-dediazoniations.

The elucidation of the *homolytic mechanism* consists of two major problems, namely (*a*) from which isomeric azo ether or any other potential starting species the radicals are formed, and (*b*) how hydro-dediazoniation products are formed from the radicals.

The first question was solved through investigations of rates and equilibria in the system *trans* azo ether ⇄ $ArN_2^+ + CH_3O^-$ ⇄ *cis* azo ether made by Broxton and coworkers[91–93] based on former preliminary work of Bunnett and coworkers[88,89] and Ritchie and Virtanen[94]. The first interaction of a diazonium ion on dissolution in alkaline methanol is the very fast formation of the *cis* arylazo ether ($k_{1C} = 3 \times 10^8$ mol^{-1} s^{-1} for Ar = *p*-$NO_2C_6H_4$ at 23°C[94]). The equilibrium lies far to the side of the ether ($K = k_{1C}/k_{-1C} = 5.6 \times 10^7$ 1 mol^{-1}). This phase of reaction is essentially complete as soon as the diazonium salt is dissolved. It is followed by a partition which is complete in 60 s at 30°C[89]. Part of the *cis* ether is decomposed to the dediazoniation product (ArH) and the remainder comes into equilibrium, through the diazonium ion, with the more stable *trans* ether. In a subsequent phase a slow dediazoniation takes place ($t_{1/2}$ ca. 2 h at 30°C). The evaluation of the measured rate of this phase with equilibrium and rate data of the *cis* ether/diazonium ion/*trans* ether system is compatible with a mechanism in which the rate of hydro-dediazoniation of the *cis*

ether is much faster than the respective *direct* reaction of the *trans* ether or where the *cis* dediazoniation is the only way at all[91–93].

It is likely that in this reaction radicals are formed by a one-or a two-step homolytic dissociation of the *cis* arylazo ether (**16**) i.e. with or without an aryldiazenyl radical (**18**) as intermediate (equation 13).



(13)

The aryldiazenyl radical was demonstrated to exist as an intermediate by Closs and coworkers[95]. The rate constant of its decomposition into an aryl radical and N_2 was estimated to be 10^7–10^9 s^{-1}.

For the consequent steps Bunnett and coworkers favour a mechanism involving a chain-propagating cycle of steps (equation 14–17).

$$Ar\cdot + CH_3OH \longrightarrow Ar{-}H + \cdot CH_2OH \quad (14)$$

$$\cdot CH_2OH + CH_3O^- \rightleftharpoons \cdot CH_2O^- + CH_3OH \quad (15)$$

$$\cdot CH_2O^- + Ar{-}N_2^+ \longrightarrow Ar{-}N_2\cdot + CH_2O \quad (16)$$

$$Ar{-}N_2\cdot \longrightarrow Ar\cdot + N_2 \quad (17)$$

The source of the hydrogen atom in the product Ar—H is therefore the methyl group of methanol and not its OH group. This was demonstrated by experiments in CH_3OD. Under conditions where the aryl anion mechanism (see below) does not take place, practically no deuterium was incorporated in the aromatic hydrocarbon formed[88]. It had already been shown that aryl radicals from sources other than arenediazonium ions do react with hydrogen from the methyl group and not with the hydrogen from the OH group of methanol[96].

Bunnett and coworkers[85,86,88] found however that deuterium is incorporated at higher concentrations of methoxide ion in CH_3OD. For example, when one equivalent of $NaOCH_3$ is provided per mole of *o*-chlorobenzenediazonium ions, the chlorobenzene formed is nearly deuterium-free; but when 2 M $NaOCH_3$ is used, it is mainly *o*-deuteriochlorobenzene. This observation indicates the occurrence of a mechanism involving *aryl anions*.

Although additional data on the degree of deuteration of products have been published recently by Broxton and Bunnett[69], the mechanism of the formation of aryl anions is not yet known. Two possibilities which are shown in equations 18 and 19 involve the formation of an aryldiimide (**19**) or its anion (**20**). These could undergo further decomposition as outlined in equation (20)[88]. The configuration of the azo compounds in equations 18–20, i.e. *cis* or *trans*, is unknown.

We started this section with the discussion of dediazoniations in methanol containing methoxide ion because the reactions in the alkaline system are better understood and

$$Ar{-}N_2^+ + CH_3O^- \longrightarrow \underset{(19)}{Ar{-}N{=}N{-}H} + CH_2O \quad (18)$$

$$Ar{-}N{=}N{-}OCH_3 + CH_3O^- \longrightarrow \underset{(20)}{Ar{-}N{=}N^-}.+ CH_2O + CH_3OH \quad (19)$$

$$Ar{-}N{=}N{-}H \underset{}{\overset{CH_3OD}{\rightleftharpoons}} Ar{-}N{=}N{-}D \overset{CH_3O^-}{\rightleftharpoons} Ar{-}N{=}N^- \xrightarrow{-N_2}$$

$$Ar^- \xrightarrow{CH_3OD} Ar{-}D \quad (20)$$

less sensitive to atmosphere, traces of additives etc. This is a remarkable contrast to the dediazoniations in aqueous alkaline solutions, which are the subject of Section II.D.3.

Our knowledge of dediazoniations in acidic methanol is due essentially to the work of Bunnett's group[6,8]. Based on product analyses and kinetics one can summarize that under acidic conditions the complexity of products is greater relative to that in alkaline solutions. In general hydro-dediazoniation is still dominant, although the heterolytic mechanism, i.e. methoxy-dediazoniation, can be favoured, e.g. by working in the presence of oxygen or of other radical scavengers like aryl iodides, which are known to react readily with aryl radicals[97,98], or in the presence of scavengers like iodine, 2-methyl-2-nitrosopropane, nitrous acid or ferrous sulphate. On the other hand phenylazotriphenylmethane and galvinoxyl have the opposite effect, namely that of promoting the formation of products typical for homolysis.

For the *m*-Br-, *p*-Br-, *m*-Cl-, *p*-Cl- and *p*-OCH_3-substituted benzenediazonium salts the radical mechanism predominates under a N_2 atmosphere and the ionic mechanism predominates under O_2. For the H, *p*-CH_3, *m*-CH_3 and *m*-OCH_3 compounds the ionic mechanism predominates under both atmospheres while for the *p*-NO_2 compound the radical mechanism predominates under both. In other words the dependence of the competition between radical and cationic mechanisms on the electrophilicity of the diazonium ion, discussed in Section II.D.I (Table 2) is very well substantiated by these results. In contrast to heterolytic dediazoniation, it has not been possible until now to rationalize substituent effects in the homolysis of diazonium ions with any known linear free-energy relationship.

It is likely that the homolytic dediazoniation in acidic methanol is also a chain-reaction, but with slightly different chain-propagation steps than in the presence of methoxide (equations 21–23).

$$Ar\cdot + CH_3OH \longrightarrow Ar{-}H + \cdot CH_2OH \quad (21)$$

$$\cdot CH_2OH + Ar{-}N_2^+ \longrightarrow Ar{-}N{=}N\cdot + CH_2\overset{+}{O}H \quad (22)$$

$$Ar{-}N{=}N\cdot \longrightarrow Ar\cdot + N_2 \quad (23)$$

This chain-reaction appears reasonable since it would give $CH_2\dot{O}H$ from which two thermodynamically high stable compounds, i.e. formaldehyde (equation 24) and methoxymethanol (**21**) (equation 25) can be formed by proton transfer to the solvent.

$$CH_2\overset{+}{O}H + CH_3OH \longrightarrow CH_2O + CH_3\overset{+}{O}H_2 \quad (24)$$

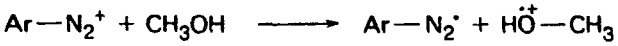
$$CH_2O + CH_3OH \longrightarrow \underset{(21)}{CH_3OCH_2OH} \quad (25)$$

A question remaining unanswered by Bunnett's investigation is that of the chain-initiating reaction. It could be homolysis of the addition product (22) of the diazonium ion and the solvent (equations 26 and 27) or electron transfer from methanol to the diazonium ion (equation 28).

(26)

(22)

(27)



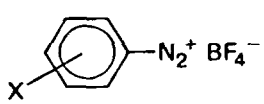
(28)

Bunnett and coworkers[6,8] consider equation (28) to be more likely. We shall return to the fundamental problem of distinguishing between these two possibilities of generating the aryldiazo radicals in Section II.D.4.

The reactions of arenediazonium ions in *ethanol* are not as well investigated and understood with respect to mechanistic aspects as those in methanol. This is astonishing, as the reaction of diazonium ions in boiling ethanol was advocated for many decades since its discovery by Griess[99] in 1864 as a synthetic method for the replacement of aromatic amino groups by hydrogen (hydro-dediazoniation). The justified criticism against the general applicability of this method has been discussed in the volume on diazonium ions of this series by Wulfman[100]; moreover some new synthetically useful ways to substitute diazonio groups by hydrogen will be reviewed in Section II.E.5 of this chapter.

In a comparative study Broxton and Bunnett[69] analysed the products of dediazoniation of three substituted arenediazonium ions in alkaline methanol and ethanol, respectively (Table 3).

TABLE 3. Effect of solvent on the yields of products from the reaction of arenediazonium salts (23) with alkoxide ions in methanol and ethanol[69]



(23)

X	Yield. Ar—OR (via S_N1)(%)		Yield Ar—H(%)		Yield Ar—OR (via Aryne)(%)	
	MeOH	EtOH	MeOH	EtOH	MeOH	EtOH
2-NO_2	11.1	0.0	56.6	100	2.75	0.0
3-NO_2, 4-Cl	4.1	0.81	34.9	82.9	46.0	12.8
2-NO_2, 4-OCH_3	37.4	3.9	37.0	72.6	*a*	*a*

[a]Not determined.

Changing the solvent from methanol to ethanol causes an increase in the yield of the hydro-dediazoniation product and a consequent reduction in the yields of alkoxy-dediazoniation and arynic products. This is attributed to an increase in the rate of formation of *cis* azo ether (k_{1C} in Scheme 5) as a result of the nucleophile (ethoxide ion) being more basic and the solvent less polar and less nucleophilic (Koppel and Paju's *B* parameter[83] of ethanol is however 235, whereas that of methanol is 218, see Section II.D.1). Furthermore, reversion of the *cis* azo ether to free diazonium ion and alkoxide ions is less probable again because of the higher basicity of the ethoxide ion and the lower polarity of ethanol.

As discussed already (Section II.B), dediazoniations in fluorinated alcohols follow in practically all cases the heterolytic pathway (for exceptions for steric reasons see Table 1, examples 6 and 7), although the alcohols used for these investigations[20,21,31–33] have one or two hydrogen atoms at the α carbon atom. This dominance of heterolysis is due to the low nucleophilicity of the fluorinated alcohols (Section II.D.1, Table 2).

3. *Dediazoniations in alkaline aqueous solutions*

Water is by far the most important solvent for diazonium salts. In the presence of ca. 10^{-2} mol l^{-1} or more mineral acid, dediazoniation proceeds almost exclusively via an S_N1-type mechanism involving the aryl cation (cf. Sections II.B and II.D.1). Strongly alkaline (pH > 12) solutions of diazonium salts are very stable because – as shown by Hantzsch in classical physical organic studies (for a review see Zollinger[101], – they rearrange via *cis* (*'syn'*) diazotates to the *trans* (*'anti'*) diazotates. It has long been known that diazonium salts decompose with comparative ease in the weakly alkaline range[102]. In spite of the considerable importance of such solutions for preparative work, surprisingly little has been published about these dediazoniations.

The reason is soon discovered on making a serious attempt to investigate such a system: on the one hand, numerous polymeric products (diazo tars) that are difficult to identify are formed at pH values between 6 and 11, and on the other hand these preparative and kinetic experiments are not readily reproducible. The material of the reaction vessel, light and the atmosphere influence the product formation and the rate and order of the reaction to an extent rarely encountered in organic chemistry.

The dediazoniation of *p*-chlorobenzenediazonium tetrafluoroborate in HCO_3^-/CO_3^{2-} buffers can be cited as an example[81,82]; in the presence of less than 5 ppb of O_2 it obeys first-order kinetics in glass vessels, but zero-order kinetics in Teflon vessels; between 60 and 100 ppb of O_2 a fast initial reaction slackens off after about 15% conversion; autocatalysis is observed on exposure to air, but a first-order reaction once again in 100% O_2.

On the basis of the nucleophilicity parameters *B* and N_{BS} (see Table 2, Section II.D.1) one expects less homolytic products in water than in methanol. This is however not the case. It has been known for many decades[102] that a very complex mixture of products is formed in the decomposition of diazonium ions, including polymeric products, the so-called diazo tars. In alcohols this is not the case. The number of products exceeds three or four only in exceptional cases, diazo tars are hardly formed. For dediazoniations in weakly alkaline aqueous solutions, there is, to our knowledge, only one detailed study[73] on the products of decomposition of *p*-chlorobenzenediazonium fluoroborate in aqueous HCO_3^-/CO_3^{2-} buffers at pH values between 9.00 and 10.30. Depending on reaction conditions up to ten low-molecular -weight compounds were identified besides the diazo tar.

Very little is known about the chemical structure of such tars. It may be characteristic that in the volumes on diazonium ions and diazo compounds in this

series, published in 1978, no reference to the key word 'diazo tar' can be found in the subject index! In the investigation mentioned before[73], the tar formed from *p*-chlorobenzenediazonium ions was analysed by elementary analysis: per six carbon atoms (i.e. per aromatic nucleus) it contained 4.18 hydrogen atoms, 0.56 nitrogens, 0.52 oxygens and 0.78 chlorines. There are indications that the nitrogens are partly present as azo groups and partly as —NH— groups. Oxygen originates from hetero- and homolytic hydroxy-dediazoniation as well as from hydroxy-dechlorination.

There is also a difference in the kinetics of dediazoniations in aqueous alkaline solutions relative to those in alkaline methanol. In methanol the rate increases with increasing methoxide ion concentrations without going through a maximum (at least as it is known today – no detailed study has been made at high concentrations of methoxide ion). In water, there is a maximum rate at a pH value which corresponds numerically to the negative logarithm of the diazonium ion – *cis* diazotate equilibrium constant pK_m[16,81,103]. Sterba and coworkers[104,105] also observed maxima at pK_m of reactions of 4,2- and 4,3-chloronitrobenzenediazonium salts in water. That of the 4,2-isomer is however not due to dediazoniation reactions as these authors assume, but to a hydroxy-denitration, i.e. to nucleophilic aromatic substitution of the nitro group by hydroxyl ions, as shown very recently[106].

The acid–base equilibria of diazonium ions are fundamentally different in water and in alcohols, as in alcohols there is only one conjugate base (the *cis* azo ether), whereas the respective conjugate in the aqueous system, the *cis* diazohydroxide is a Brønsted acid which can form a second-step conjugate base, the *cis* diazotate. This two-step equilibrium (equation 29) is recognized[107] as unusual in that K_1 is smaller than K_2;

$$\mathrm{Ar{-}N_2^+} \underset{-OH^-}{\overset{+OH^-}{\rightleftharpoons}} \textit{cis}\text{-Ar{-}N}_2\text{{-}OH} \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} \textit{cis}\text{-Ar{-}N}_2\text{{-}O}^- \qquad (29)$$

K_1 $\qquad$ K_2

hence there is no pH region in which the middle equilibrium species, the *cis* diazohydroxide, accumulates to any significant extent. The experimental value pK_m corresponds to $1/2\ (pK_1 + pK_2)$. At $pH = pK_m$, the *cis* diazohydroxide is actually present in very low concentration (normally < 0.1% of the analytical concentration of diazo compound); at this pH, however, a maximum of the possible concentration of diazohydroxide (Figure 2) occurs. This provides substance for the supposition that dediazoniation proceeds via the diazohydroxide since the rate maximum of this reaction lies at $pH = pK_m$.

Moreover the equilibrium of equation (30) at the same pH value shows a concentration maximum for the diazoanhydride (Figure 2). The diazoanhydrides (there are three feasible conformations, namely *cis–cis, cis–trans* and *trans–trans*) are also, like the diazotates, compounds which can be formed in water, but not in alcohols.

$$\mathrm{Ar{-}N_2^+ + Ar{-}N_2{-}O^- \rightleftharpoons Ar{-}N_2{-}O{-}N_2{-}Ar} \qquad (30)$$

The maximum rate of the dediazoniation at $pH = pK_m$ can therefore be explained just as well in terms of a mechanism involving the diazoanhydride. Such an interpretation would correspond to the results obtained by Rüchardt and coworkers[108–110] for the Gomberg–Bachmann reaction in water/arene mixtures.

A logarithmic plot of the percentages of diazoanhydride (equation 30) and diazohydroxide present at equilibrium (equation 29) versus the pH value has slopes of 2.0 and 1.0 respectively on the left side of the maxima and corresponding negative slopes on the right side of the maximum in Figure 2. This should provide an opportunity of distinguishing between diazoanhydride and diazohydroxide as

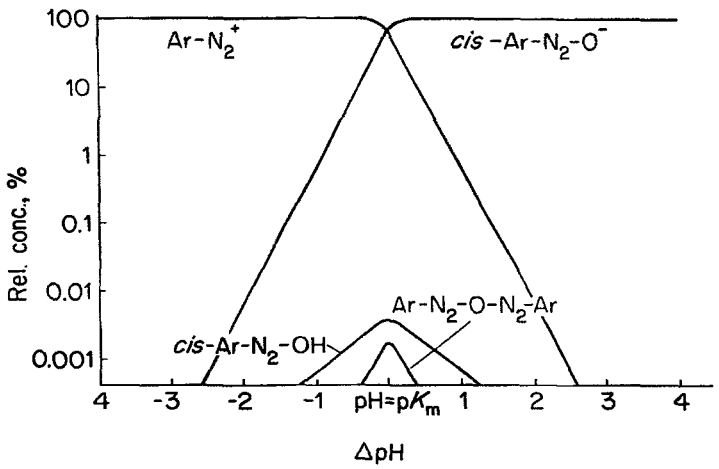


FIGURE 2. Dependence of the relative concentration of the diazo equilibrium forms on the pH values (schematic). Reproduced by permission of Angewandte Chemie from H. Zollinger, *Angew. Chem. (Intern. Ed. Engl.)*, **17**, 147 (1978).

dediazoniation intermediates on the basis of the slopes of the logarithmic reaction rates as plotted against the pH value. However, the slopes which were found experimentally were 1.0 and −1.0 only for the case of the 4,3-chloronitrobenzenediazonium ion[105], indicating the diazohydroxide as key intermediate. For the 4,2-isomer[104,106] and for the 2,4-compound[106] however, fractional slope values were found. This indicates either that more than one parallel reaction with different dependence(ies) on pH occurs and/or that radical chain reactions are involved.

These reactions in weakly alkaline solutions are faster than the heterolytic S_N1-like hydroxy-dediazoniation which, for most diazonium ions, (depending on their electrophilicity). is dominant below pH 2 to 4. As shown by Ishino and coworkers[111], an increase in rate, corresponding to the occurrence of other mechanisms in addition to the heterolytic hydroxy-dediazoniation, is observable at pH values which are dependent on the type of substitution of the arenediazonium ions investigated (Table 4).

The results of Table 4 show clearly that very different slopes, i.e. different reaction-rate orders with respect to hydroxyl ion concentrations, are obtained for reasonably large ranges of pH.

The mechanisms of thermal dediazoniations in aqueous or partly aqueous systems at pH > 6 have been investigated in recent years with kinetic methods and with the help of CIDNP measurements by Rieker and coworkers[112–115], Kiprianova, Levit, Gragerov and coworkers[116–119], Zollinger and coworkers[81,82,115] and other groups[95,120–124]. Although the present situation is still far removed from a more or less consistent understanding of the mechanisms involved, it can be stated that in this area, in which around about 1970 very little was known, significant progress has been made in recent years. CIDNP and kinetics supplement one another to a certain degree. One may say that kinetics give information on the particles which enter the rate-limiting part of the mechanism and CIDNP tells us what comes out of that part. However, this simplified statement has to be combined with a warning. Kinetics inform us about the *sum* of all competitive reactions, CIDNP only on certain types of radical-pair

TABLE 4. Dependence of the rate of dediazoniation of substituted benzenediazonium salts in water on pH[111]

Substituent	Temp (°C)	pH		Slope [d(log k)/d(pH)]
		Region of constant rate	Region of Increasing rate	
p-CH_3	50.4	3.6–6.1	6.2–7.0	0.58
p-CN	50.4	0.7–3.8	3.9–5.6	0.22
p-Cl	50.4	2.5–3.9	4.0–6.2	0.38
m-OCH_3	40.0	0.7–3.9	—	—
H	40.0	0.7–5.1	—	0.03[a]
m-Cl	40.0	0.7–1.5	2.0–5.0	0.08
m-CN	40.0	1.1–3.6	3.7–5.0	1.09

[a]Refers to pH 0.7 to 5.1.

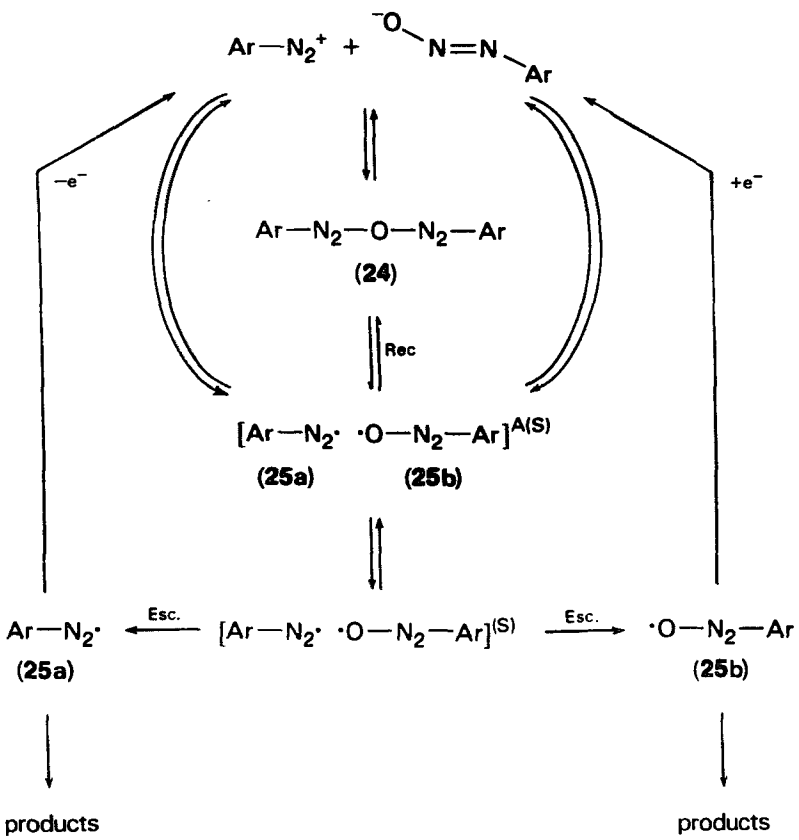
reactions, e.g. in general not on radical-chain reactions[125–127]. As it is difficult to draw conclusions from CIDNP signals about the concentrations of the species involved, it is dangerous to conclude from the occurrence of CIDNP signals that no chain-reaction is involved. It may well be that, besides the radical reaction giving rise to CIDNP, a parallel chain-reaction takes place also. The multiplicity of products found in dediazoniations of this type[73] is a strong indication of multiple pathways.

On the other hand CIDNP results obtained with diazonium salts in water-free systems (References 128–136 and others) have only a limited value for the interpretation of mechanisms in aqueous systems because of the reasons mentioned at the beginning of this section.

^{1}H- and ^{13}C-CIDNP results[112,113] demonstrate that dediazoniations under alkaline conditions may follow a homolytic pathway in which the diazonium ion can be regenerated. Detailed information is available from ^{15}N-CIDNP investigations with p-chlorobenzenediazonium ions in which either the α or the β or both nitrogen atoms are labelled with ^{15}N[115]. In aqueous alkaline solutions (D_2O or H_2O) at 60°C under argon, signals of enhanced absorption and emission are obtainable. They can be attributed to the diazonium ion, the diazotate ion and the N_2 molecule. The interpretation with the help of the Kaptein rules[137] and correlations with other CIDNP data show that the diazonium ion is regenerated from a radical precursor which still contains both nitrogen atoms. The *cis* diazotate is not present in detectable concentrations, but the *trans* isomer is. The results are consistent with the formation of diazoanhydride(s) **24** (probably the *cis–trans* or less likely, the *trans–trans* isomer) from which a primary radical cage A(S) consisting of a diazenyl (**25a**) and a *trans* diazotate radical (**25b**) (Scheme 6) is formed.

The diazenyl radical **25a** as well as the *trans* diazotate radical **25b** can form the diazonium ion and the *trans* diazotate ion respectively by three mechanisms: Firstly, by recombination, (Rec.) i.e. disproportionation in the primary cage A(S) and formation of the diazoanhydride **24**, which dissociates further. Secondly, the formation of the two ions may take place from the escaped (Esc.) radicals, potentially through an intermediate solvent-separated cage (S). This is, however, less likely. The formation and dissociation of the radical pair by 'direct' electron transfer as a third alternative is consistent with the experimental data. Until now it could not be differentiated from the mechanism with **24** as intermediate.

It is therefore likely that the key intermediate in the homolytic dediazoniation in alkaline aqueous systems is one or several of the isomeric diazoanhydrides, and not the



SCHEME 6

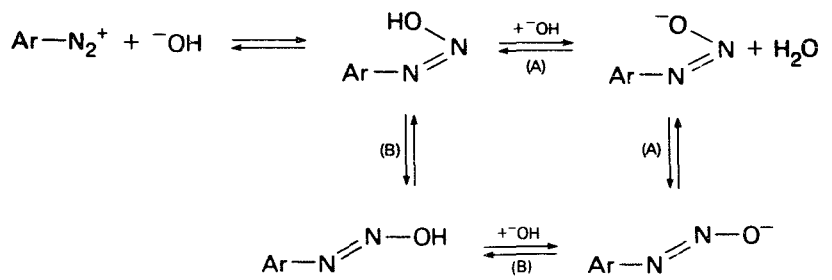
diazohydroxide. Besides Rieker, Zollinger and coworkers[115], Gragerov and coworkers[116,118,119] and others[123,124] have come to the same conclusion. Gragerov has also investigated[116] the question as to whether the diazoacetate ($Ar—N_2—OCOCH_3$) might be an intermediate in the homolysis in the presence of acetate ions at pH 5 to 8. There is no evidence for this however. In the presence of tertiary amines R_3N (R = Me, Et, Bu) Gragerov and coworkers[117] showed, however, that the rate-determining step of the reaction is the dissociation of the primary addition product, the diazoammonium ion ($Ar—N_2—\dot{N}R_3$) into diazenyl radicals ($Ar—N_2^{\cdot}$) and tertiary amine radical cations ($R_3\dot{N}$).

The kinetics of the decomposition of the *p*-chlorobenzenediazonium ion under strict exclusion of oxygen (<5 ppb O_2)[81] are compatible with the CIDNP results – with the reservation mentioned already, namely that CIDNP as a probe does not necessarily give results for *all* pathways, whereas kinetic measurements are normally related to the sum of all competitive mechanisms. The first reaction to be observable with conventional kinetic methods is the formation of *trans* diazotate ($\tau_{1/2}$ ca. 30 min. at 50°C and pH = 9.70). The dediazoniation proper is significantly slower ($\tau_{1/2}$ ca. 200 min), but it is also first-order with respect to the diazonium ion concentration.

The dependence of the rate of *trans* diazotate formation on buffer concentration and on pH is complex. If however the relatively rapid diazonium ion $\rightleftarrows$ *cis* diazotate equilibrium is taken into account, a linear relation between rate and the *first* power of

hydroxide ion concentration results. This is a remarkable contrast to investigations of the pH dependence of the rate of formation of the *trans* diazotate of the *p*-nitro- and other benzenediazonium salts with electron-withdrawing substituents in the *meta* or *para* position which have been investigated by Lewis[138], Yoshito[139], Littler[140], Ritchie[141], Štěrba[142], Virtanen[143] and their coworkers. In these cases the rates are proportional to the *second* power of the hydroxide ion concentration.

Mechanistically this leads to the conclusion that the *cis–trans* rearrangement in the *p*-chloro-substituted diazo compound does not take place via the diazotate, as with the *p*-nitro and other derivatives mentioned, but via the diazohydroxide. The situation is summarized in Scheme 7, where the two pathways (A) for *p*-nitro and related diazo compounds) and (B) (for the *p*-chloro derivative) are shown.



SCHEME 7

The remarkable change in mechanism of the *cis–trans* rearrangement can be rationalized on the basis of the investigations of Haberfield and coworkers[144] regarding the *cis–trans* isomerization of azobenzene derivatives. They have found that azobenzene itself and monosubstituted derivatives rearrange by inversion at one of the nitrogen atoms, whereas azobenzene derivatives with an electron donor in one benzene ring and an acceptor in the other ring rearrange by rotation about the central N=N bond, since this bond now has less double-bond character.

p-Nitrobenzenediazotate can be considered as an azo compound of the second type. The acceptor–donor relationship is more dominant in the *cis–trans* diazotate pair than in the diazohydroxide pair; the N=N rotation is therefore favoured. On the other hand, *p*-Cl is not a −M substituent, therefore inversion at the β-N becomes dominant.

The fact that there are obviously two pathways for the formation of *trans* diazotates from diazonium ions makes an evaluation of the mechanism or mechanisms of homolytic dediazoniations extremely difficult. In the case of the *p*-chloro derivative[81] analysis of the decrease of the sum of concentrations of the diazonium ion and the *trans* diazotate as a function of time leads to the detection of two reactions; one is observable only at the beginning and at relatively low temperatures (20°C), and it is first order with respect to the sum of concentrations mentioned and to the hydroxide ion concentration. The second and main reaction is also first order with respect to the diazo concentration, but it is a complex function of the hydroxide ion concentration, which did not allow a mechanistic interpretation.

In the presence of oxygen (from 60 ppb O_2 to 99% O_2) the results are even more complex[82]. Under a nitrogen atmosphere containing 60 to 100 ppb O_2 the dediazoniation is zero order in a polytetrafluoroethylene vessel, and somewhat higher in order ($n \sim 0.5$), but slower, in glass. In air the material of the vessel no longer has any influence; the reaction is autocatalysed. It can be shown that the corresponding phenol is the source of the autocatalysis. The phenol is formed mainly through a reaction involving molecular oxygen; the heterolytic S_NAr hydroxy-dediazoniation as

a source of the phenol has only a negligible influence. Radical scavengers influence the rate[82] and also the products[73] significantly.

The kinetics can be explained on the basis of various chain mechanisms[82], but these mechanisms have to be regarded as rather speculative at the present time!

Much work is obviously needed in order to obtain concrete knowledge on these processes. This raises the question as to whether such work is worthwhile. It is difficult to answer this question, as such investigations will probably be fruitful only through a combination of experience in analytical chemistry, physical organic chemistry and, hopefully, macromolecular chemistry (diazo tars!). The result would be, optimistically viewed, increased knowledge of reactions which are not particularly pleasing—reactions which lead to unwanted by-products. However at least 10 per cent of syntheses of diazonium salts made today do not yield the required products, either on a laboratory scale or industrially, but give these unwanted dediazoniation products. There may at least be a chance that a thorough knowledge of the mechanism of formation of dediazoniation products could lead to effective methods for blocking their formation.

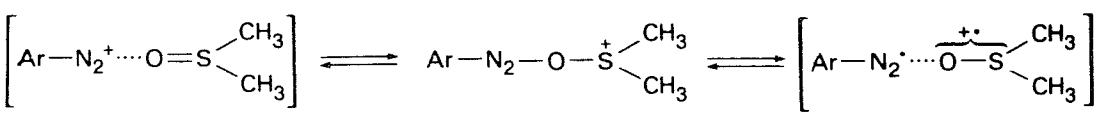
4. *Dediazoniations in highly nucleophilic solvents and in the presence of good nucleophiles*

We have mentioned in Section II.D.1 that there is a good correlation between the nucleophilicity of the solvent and the rate of homolytic dediazoniations. In this section such reactions are discussed in more detail and general mechanistic conclusions drawn.

In dimethyl sulphoxide (DMSO) isomer ratios of aryl-dediazoniations with *p*-nitrobenzenediazonium ions demonstrate that the *p*-nitrophenyl radical is the arylating reagent[9] (Section II.A).

In the absence of a substrate capable of undergoing arylation, *p*-nitrobenzenediazonium tetrafluoroborate forms *p*-nitrophenol in high yield. If the reaction is performed in ^{18}O-DMSO, the oxygen of the phenolic OH group is found to arise exclusively from DMSO. In the presence of iodobenzene the yield of *p*-nitrophenol falls off sharply; nitrobenzene (from hydro-dediazoniation) is accompanied by 1-iodo-4-nitrobenzene and also by a large amount of unidentified polymeric material. All these products, and especially ArI which is formed by iodine transfer according to Bunnett and Wamser[97] and Brydon and Cadogan[98], are unmistakable indications of a radical decomposition. Up to 90% conversion, the reaction strictly obeys first-order kinetics. The reaction rate is constant within the limits of experimental error whether the reaction is performed under nitrogen, air, in glass or Teflon vessels, or even in a mixture of DMSO and benzene (2:1) in the absence and presence of an equivalent of iodobenzene, although different products are formed under the two last-mentioned sets of conditions. The reaction proceeds about ten times faster than in acidic aqueous solution where it follows a heterolytic course.

It is also remarkable that the electronic spectrum of this diazonium salt in DMSO differs significantly from that recorded in water or trifluoroethanol, and that admixture of benzene up to a ratio DMSO:benzene of 1:2 hardly alters the spectrum from that in pure DMSO.



(26) **(27)** **(28)**

The UV spectra suggest that equilibrium between the diazonium ion and the solvent, on the one hand, and an electron donor–acceptor complex (**26**) on the other, lies on the side of the complex. The latter may possibly exist also as a radical pair (**28**) or covalent compound (**27**). Dissociation of this complex in a cage to form an aryl radical, a nitrogen molecule, and the radical cation corresponding to DMSO is slow and rate-determining. Fast subsequent steps lead to the products obtained.

The observation that addition of pyridine enhances the rate of decomposition, shifts the order of reaction from unity to zero, and considerably diminishes formation of *p*-nitrophenol also warrants attention. This is compatible with the superior electron-donor properties of pyridine as compared to DMSO[83,145,146]: generation of the corresponding diazopyridinium cation in one or several of the forms corresponding to **27** and **28** competes with formation of **26**.

In another investigation[147] dediazoniation was studied in TFE and in acetonitrile in the presence of pyridine. There is UV and NMR evidence for the formation of a diazopyridinium cation; in addition, ^{1}H-CIDNP absorption and emission signals were observed. Systems containing diazonium salts and pyridine are important in industrial chemistry as in a considerable number of syntheses of azo dyes pyridine is used as a proton acceptor in the diazo coupling reaction[148–150]. At the same time pyridine has an unfavourable effect on the yield because of the competing homolytic dediazoniation.

An interesting reaction of diazonium salts was discovered by Newman and Hung[151] in hexamethylphosphoric acid triamide (HMPA). The diazonio group is substituted by hydrogen originating from one of the methyl groups of the solvent. Yields are in general good; the reaction might have some significance for synthetic purposes.

This dediazoniation has been investigated mechanistically by Tröndlin and Rüchardt[77]. It is significantly faster than the reaction in DMSO. Determination and evaluation of the order of reaction according to time and concentration (n_t and n_c, respectively) with respect to diazonium salt and HMPA in HMPA/acetonitrile mixtures, and the effects of inhibitors and initiators are compatible with a chain mechanism. The IR spectrum strongly suggests occurrence of the immonium salt **29** (Scheme 8).

$$Ar^{\bullet} + H_3C{-}\underset{\displaystyle CH_3}{\overset{\displaystyle |}{N}}{-}PO[N(CH_3)_2]_2 \longrightarrow Ar{-}H + H_2\dot{C}{-}\underset{\displaystyle CH_3}{\overset{\displaystyle |}{N}}{-}PO[N(CH_3)_2]_2$$

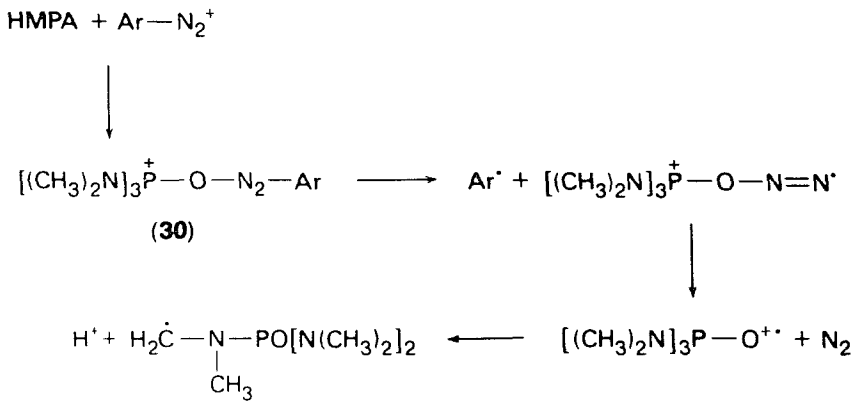
$$Ar{-}N_2^{+} + H_2\dot{C}{-}\underset{\displaystyle CH_3}{\overset{\displaystyle |}{N}}{-}PO[N(CH_3)_2]_2 \longrightarrow Ar{-}N_2^{\bullet} + H_2C{=}\overset{+}{\underset{\displaystyle CH_3}{\overset{\displaystyle |}{N}}}{-}PO[N(CH_3)_2]_2$$

(29)

$$Ar{-}N_2^{\bullet} \longrightarrow Ar^{\bullet} + N_2$$

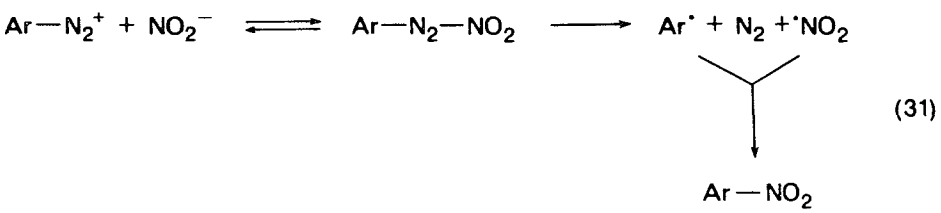
SCHEME 8

Measurements of redox potentials disfavour electron transfer from HMPA to the diazonium ion; a diazoanhydride intermediate ($Ar{-}N_2{-}O{-}N_2{-}Ar$) analogous to the Gomberg–Bachmann reaction in water/arene mixtures[108–110] can be ruled out for kinetic reasons. The authors therefore suspect an initiation reaction via formation of an adduct (**30**) by reaction of the nucleophilic centre, i.e. the oxygen of HMPA, with the diazonium ion (Scheme 9).



SCHEME 9

These examples demonstrate that solvation, and probably covalent adduct formation with a solvent molecule, is essential for the actual electron transfer to the diazonium ion; however, it is not the only condition. The donor particle must also have a favourable redox potential, i.e. it must be capable of forming a relatively stable species on release of an electron. The nitrite ion, which is transformed into nitrogen dioxide when dissolved in an aqueous solution of diazonium salts, is an excellent example. This reaction has also been investigated by Opgenorth and Rüchardt[152], and by Gragerov and coworkers[153]. Kinetics, trapping effects and products are consistent with equation (**31**).

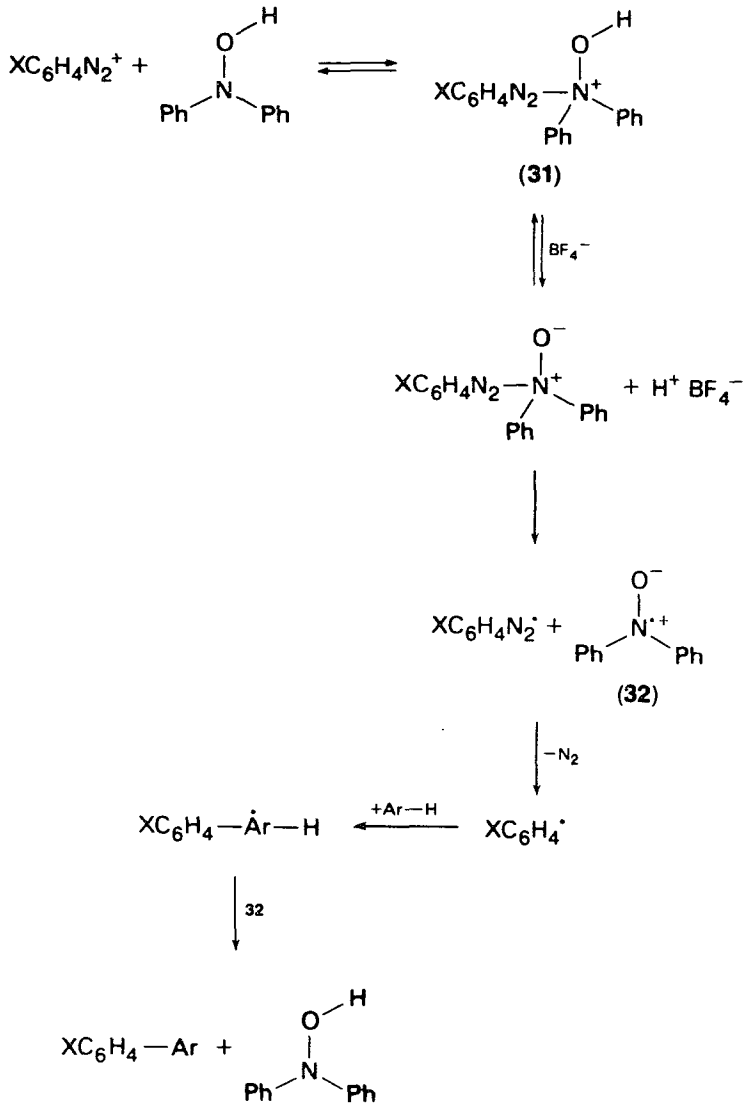


(31)

A similar case is the catalysis of Gomberg–Bachmann arylations by *N,N*-diphenylhydroxylamine which was discovered by Cooper and Perkins[154]. As Scheme 10 shows, the covalent adduct cation **31** loses first a proton. This facilitates the homolytic dissociation as a *stable* radical, *N,N*-diphenylnitroxide (**32**), is formed. This radical is an acceptor for the subsequent reaction of the aryl radical with the aromatic hydrocarbon.

Becker and coworkers[155,156] have compiled interesting correlations between the oxidation potential of the donor and the reduction potential of the diazonium ion. They were able to demonstrate that, of two fundamentally possible dediazoniation reactions, that reaction in which the electron required for elimination of N_2 can be supplied with the lowest expenditure of energy is favoured. For the heterolytic reaction mode this will be 'intramolecular' electron transfer from the aryl group to form an aryl cation with or without participation of an external acceptor solvent; in homolytic dediazoniation it is electron transfer from an external donor.

We have chosen the term 'nucleofugic homolytic leaving group' to describe a group possessing both nucleophilic character and the ability to release an electron[15,16]. In principle, it should be possible to predict quantitatively the reactivity of such particles towards diazonium ions with the aid of a dual-parameter equation. One parameter



SCHEME 10

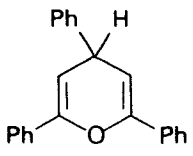
serves as a measure of the donor property of the particle; the other parameter is the redox potential. The complex nature of the kinetics of homolytic dediazoniations will most likely be a great obstacle to efforts to obtain comparable rate constants referring only to the radical-generation step.

It has to be emphasized, however, that these results, and conclusions concerning formation of *covalent* adducts of diazonium ions with nucleophiles as precursors of radical dissociation, cannot be generalized for all cases.

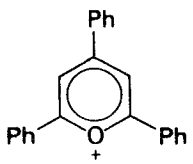
Besides reactions involving transition metal ions, as in the Sandmeyer and the Meerwein reaction, there is, at least in one case, convincing evidence that 'free' electrons can also be transferred from an organic donor to a diazonium ion. Becker

and coworkers[157,158] observed that diazonium salts quench the fluorescence of pyrene (and other arenes) at a rate $k_1 = 2.5 \times 10^{10}$ l mol^{-1} s^{-1}. The pyrene radical cation and the arenediazo radical would appear to be the likely products of electron transfer. However, pyrene is a weak nucleophile; the concentration of its covalent product with the diazonium ion is estimated to lie below 0.01% at equilibrium. If electron transfer were to proceed via this potential intermediate present in such a low concentration then the measured rate constant could not be so large. However, dynamic fluorescence quenching in the excited state of the electron donor–acceptor complex preferred at equilibrium would fit the facts. Evidence supporting a diffusion-controlled electron transfer ($k = 1.8 \times 10^{10}$ to 2.5×10^{10} s^{-1}) was provided by pulse radiolysis.

An interesting example of electron donation to diazonium ions has been reported recently by Gragerov's group[159]. The reaction of substituted benzenediazonium ions with 2,4,6-triphenyl-4*H*-pyran (**33**) is zero order in diazonium ions and second order in **33**; pyrylium ions (**34**) are formed, probably via a chain-reaction. The pyran acts as an electron donor in the formation of aryl radicals.

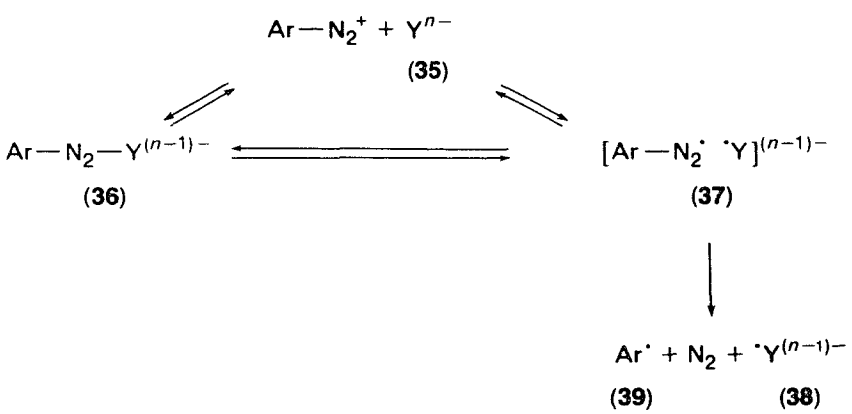


(33)



(34)

In summary, thermal homolytic dediazoniations (Scheme 11) proceed by interaction with an electron donor (**35**), either through a covalent adduct (**36**) or by 'direct' electron transfer, forming in both cases primarily the radical pair (**37**) consisting of the diazenyl radical and the electron deficient radical of the donor (**38**). The arenediazenyl radical dissociates very rapidly[160] to an aryl radical (**39**) and a nitrogen molecule. **38** and **39** can react further depending on the specific reaction system.



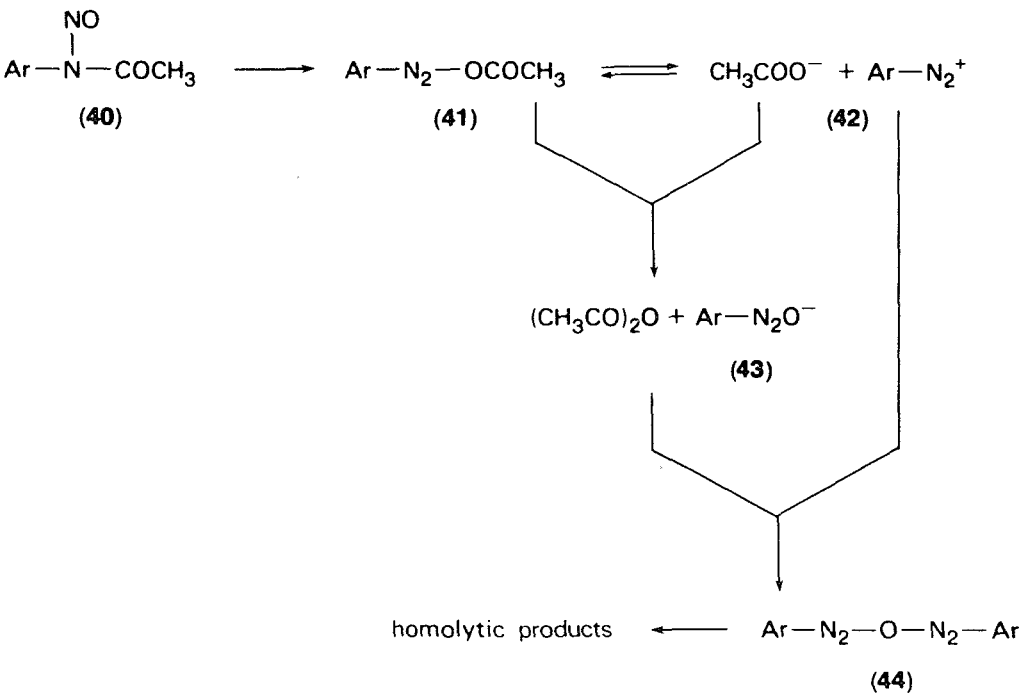
SCHEME 11

5. Dediazoniations in aprotic, relatively apolar solvents

Owing to low solubility, the dediazoniation of diazonium salts in relatively apolar solvents has not been extensively investigated. In a paper published in the late sixties[161] the thermal decomposition of benzenediazonium tetrafluoroborate and

chloride in deuterated solvents (C_6D_6, C_6D_{12}, $C_6D_5CH_3$, C_6D_5Br and $CDCl_3$) was investigated, but the results leave many questions unanswered.

In such solvents arenediazonium salts can, however, be formed *in situ* in the so-called Grieve–Hey–Heilbron syntheses by rearrangement of *N*-nitrosoacetanilides (**40**) (for earlier literature see Zollinger[162], Hegarty[163] and Wulfman[164]) into covalent arenediazoacetates (**41**) and diazonium acetates (**42**) (Scheme 12). In the subsequent reaction **41** and the acetate ion are probably in equilibrium with diazotate **43** and acetic anhydride. The diazotate ion and the diazonium ion react to form the diazoanhydride (**44**). The usual Gomberg–Bachmann[108–110] reaction then takes place in the presence of aromatic hydrocarbons.



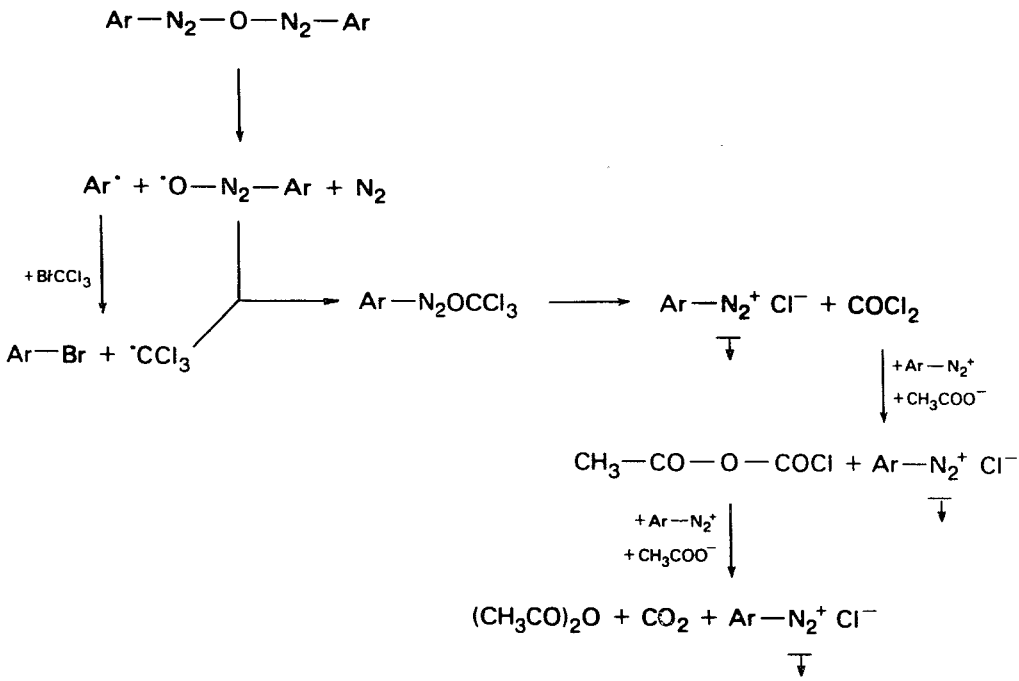
SCHEME 12

Some relatively old observations do not, however, fit this scheme. Grieve and Hey[165] observed in 1934 that benzenediazonium chloride was formed in the presence of carbon tetrachloride. Also unexplained are the observations that the nitrosoacetanilide rearrangement yielded significant amounts of chlorobenzene and benzene, but no hexachloroethane in chloroform[166]. Similar anomalies occur in bromoform[166,167] and in bromotrichloromethane[165].

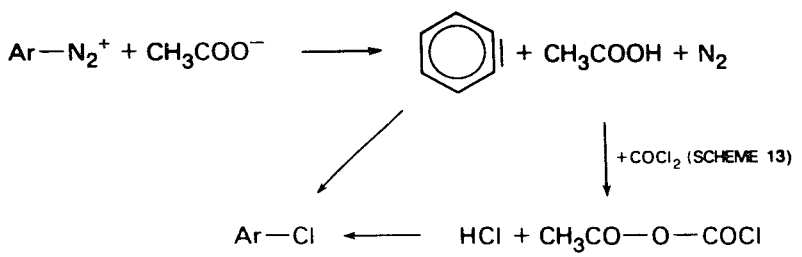
Product analyses made recently by Cadogan and coworkers[168] explain the formation of these products (Schemes 13–15). The diazonium chloride can precipitate as a salt or decompose in a Schieman-type reaction into chloroarene and molecular nitrogen.

An interesting and novel type of dediazoniation was observed[169] when 2-acetoxybenzenediazonium acetate (**45**), formed *in situ*, was boiled in xylene. 22% of the oxocarbene-derived benzofulvalene **46** was obtained.

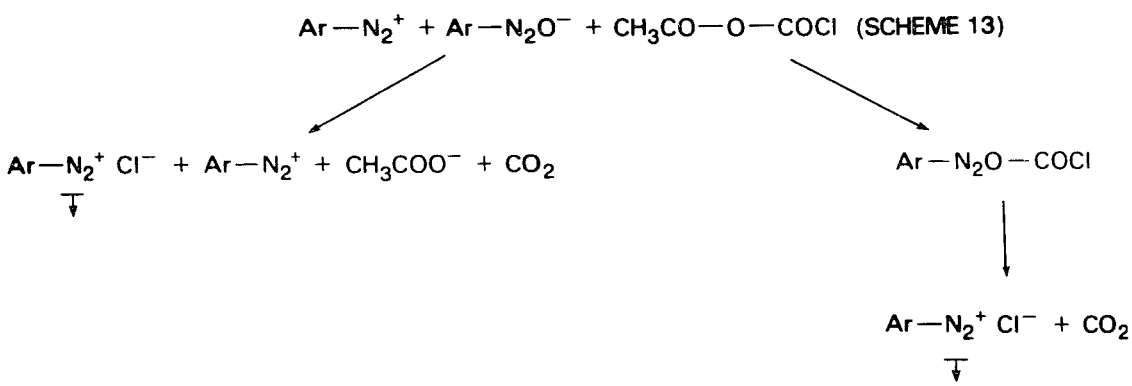
Barclay and coworkers[170] have investigated the dediazoniation of a sterically hindered diazo compound, namely the 2,4,6-tri-*t*-butylbenzenediazonium salt with



SCHEME 13



SCHEME 14



SCHEME 15

(45) (46)

ESR and product studies. The corresponding aryl radical was spin-trapped by butyl nitrite and the phenoxy radical was also detected. In the presence of pivalic acid the *o-t*-butyl group underwent rearrangement to a *s*-butyl group and other products.

6. *Dediazoniations catalysed by metals and metal ions*

In spite of the fact that dediazoniations catalysed by metals and metal ions are important in organic synthesis (Sandmeyer, Meerwein, Pschorr and other reactions) our knowledge concerning the interactions between diazonium ions and metals and metal ions as well as the mechanism of these catalysed reactions is still meagre. The elucidation of these problems is definitely an area for fruitful collaboration between physical organic and inorganic (coordination) chemists in the future.

The available literature has been competently reviewed in recent years by various authors[171–174]. The present chapter concentrates therefore on some basic principles and on recent literature not previously reviewed.

Sutton[171] has suggested that in metal complexes in which an arenediazonium ion enters as a ligand, the ligand group should be called an aryldiazenate group (as with diazonium ions, it is an open question whether or not 'arenediazenate' is better!).

According to the classification of Carroll and Lalor[175], aryldiazenate complexes have two types of structure. In structure **47** bonding takes place by σ donation from an sp orbital on the β nitrogen with π back-donation from the d orbitals of the metal into a p orbital on the β nitrogen; the oxidation state is not changed by this type of complex formation. In structure **48** the aryldiazenate group is in a *trans* configuration. The

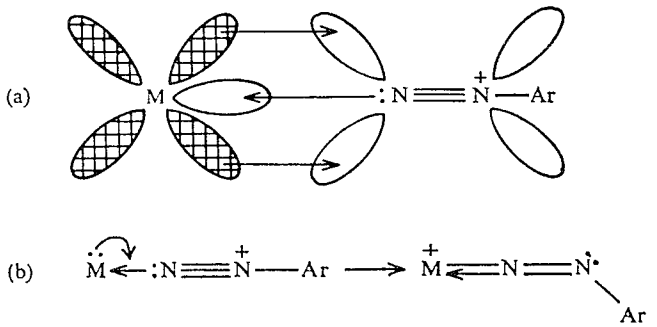
(47) (48)

respective *cis* isomer might exist, but has not yet been found. There is a single bond formed by overlap between an sp^2 orbital on the β nitrogen with a hybrid orbital on the metal. This leads to a two-electron oxidation of the metal; formally at least the ligand is an aryldiazo *anion* ($Ar—N_2^-$).

Complexes of type **47** can be described with their electronic structure by notation (a) or (b) in Scheme 16[171]. The population of the π^* orbitals on N_2Ar leaves the N—N—Ar angle close to 180° (a), whereas the simple VB picture (b) predicts this angle to be about 120°. Dimensions of Mo-, Re-, Fe-, Ru- and Mn- carbonyldiazenate complexes from X-ray diffraction studies, summarized by Sutton[171], yield N—N—Ar angles between 118° and 137°, and M—N—N angles between 170° and 179°.

The X-ray analysis of a diazenate–rhenium complex which belongs to type **48** gives an N—N—Ar angle of 119°, and an M—N—N angle of 125°[171]. The N—N distance is longer (1.17 Å) compared to type **47** complexes as expected from the simple VB description.

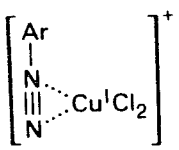
From the point of view of applications in organic synthesis, interactions of arenediazonium ions with copper in various states of oxidation are by far the most



SCHEME 16. Reproduced by permission of the Chemical Society from D. Sutton, *Chem. Soc. Rev.*, **4**, 443 (1975).

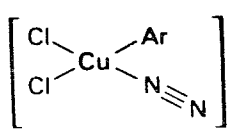
important examples of the catalysis of dediazoniations by metals. Formation of diazenate complexes have been postulated for the Sandmeyer[176–179], Meerwein[173] and related reactions, but no structural investigations appear to have been made until 1980.

On the basis of work carried out in coordination chemistry since the sixties, it is apparent that the diazonium ion is not the electron acceptor for a lone pair of one of the two chloride ions in the complex $Cu^{I}Cl_2^-$ as was proposed in 1961[177]. It is likely that there is coordination between the cuprous ion and the β nitrogen of the diazonium ion yielding either a structure of type **47** or **48**. In the case of **48**, one has to assume that copper enters into complex formation as Cu^0 (becoming Cu^{II}). This only seems strange from a superficial point of view; it could be argued in favour of **48** that in Sandmeyer reactions cuprous ions are used, but that cuprous ions disproportionate easily into $Cu^0 + Cu^{II}$. If, however, Cu^I is the oxidation stage entering complex formation, one might consider in addition to **47** a 'side-on' complex of type **49**. It fulfills the tendency of Cu^I to have coordination number four.



(49)

Vol'pin and coworkers[180,181] suggested a mechanism for diazenate–copper reactions involving the complex **50** in analogy to the complexes with ruthenium (II). **50** looks less reasonable for Cu^I complexes than for Ru^{II} complexes where back-donation between Ru^{II} and N_2 is known.

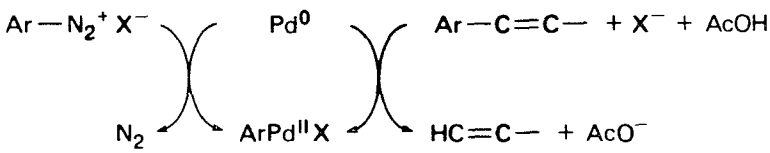


(50)

Infrared and ^{19}F-NMR spectroscopy have provided information on a large number of metal complexes containing diazenate ligands. ^{19}F-NMR was used to investigate the *o*-, *m*- and *p*-fluorobenzenediazonium salts. The results are consistent with the

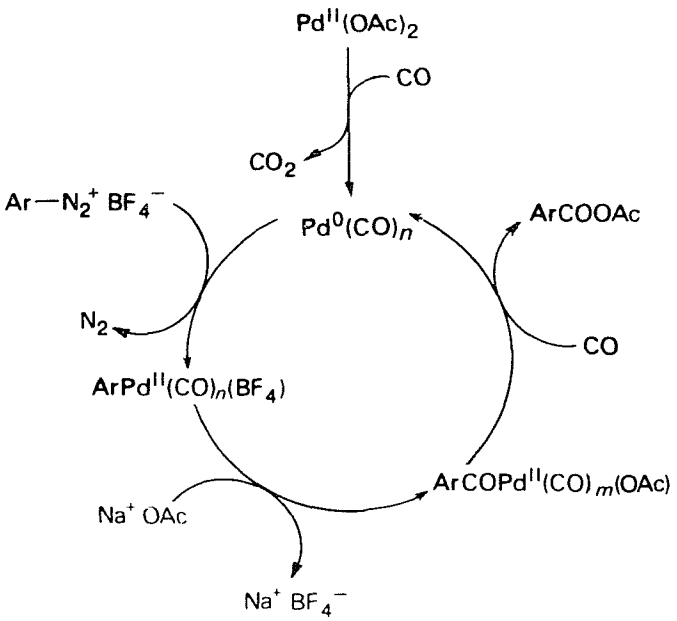
decrease of the triple-bond character of the NN group in the complexes with various metal ions and with additional substituents in the aromatic nucleus. The subject has been reviewed by Niemeyer[182]. To our knowledge no new information has been published since 1978.

An interesting extension of the Meerwein reaction was found by Kikukawa, Matsuda and coworkers[183–185]. In the presence of palladium(0) catalysts and sodium acetate, arenediazonium salts can be conveniently utilized for the arylation of various olefins. In contrast to the classical Meerwein reaction, where copper catalysts are used, the new reaction does not require activated olefins with electron-withdrawing groups. The palladium-catalysed arylation can be applied to olefins having both electron-releasing and -withdrawing substituents. The mechanism of this reaction appears to be related to the analogous reaction of palladium-catalysed arylation by aryl halides[186–188] (Scheme 17).



SCHEME 17

The same authors[189] recently found that arenediazonium salts give arenecarboxylic acids in good yields with carbon monoxide in the presence of Pd^0 and Pd^{II} catalysts. They suggest the mechanism shown in Scheme 18 for reaction with palladium(II) acetate. The reactions are run in methylene chloride, acetone, acetonitrile and mixtures of these solvents.



SCHEME 18

Structures **47** and **48**, as systematized by Sutton[171], and also **49** and **50**, are *intermediates* which are, at least in principle, analogous to the adducts with nucleophiles discussed in Section II.D.4. They are precursors of the electron transfer leading to the arenediazenyl radical and finally to the aryl radical. As we have already mentioned, for these dediazoniations one has also to consider a 'free' electron transfer in addition to the radical formation via an adduct.

Cases of free electron transfer have been investigated by Becker, Bagal and their coworkers[156,190,191]. Particularly convincing are dediazoniations catalysed by the ferro-ferri-hexacyanide redox system $[Fe^{II}(CN)_6]^{4-}/[Fe^{III}(CN)_6]^{3-}$ studied with *p*-methoxy- and *p*-dimethylamino-benzenediazonium tetrafluoroborate in water[191]. As in both iron complexes all six coordination sites are saturated, it is hardly feasible that a diazenate complex is formed as an intermediate.

Becker and Schukat[190] measured the initial rates of dediazoniations of substituted benzenediazonium ions in aqueous solution in the presence of the four redox systems $[Fe^{II}(CN)_6]^{4-}/[Fe^{III}(CN)_6]^{3-}$, Fe^{2+}/Fe^{3+}, I^-/I_2 and hydroquinone/benzoquinone. By variation of the pH values various redox potentials were obtainable for each of these systems, whereas it is known that the redox potentials of diazonium salts are essentially independent of pH[192] (at least at pH values below pH = pK_m, see Section II.D.3, Figure 2).

The kinetic data were evaluated on the basis of equation (32) in which ED refers to the electron donor. Under the condition that the back-transfer of the electron (k_{-1}) is much faster than the forward reaction, i.e. the formation of the aryl radical from the diazenyl radical, the measured rate constant k_{obs} is a linear function of the electron transfer equilibrium constant K (equation 33a).

$$\mathrm{Ar{-}N_2^+ + {:}ED \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ar{-}N_2^{\bullet}\ {}^{\bullet}ED^+ \xrightarrow{k_2} Ar^{\bullet} + N_2 + {}^{\bullet}ED^+} \qquad (32)$$

$$\downarrow$$

products

$$k_{obs} = \frac{k_1}{k_{-1}} k_2 = K k_2 \qquad (33a)$$

$$\log k_{obs} = \frac{-\Delta G}{2.3\,RT} + \log k_2 \qquad (33b)$$

Free reaction energies ($-\Delta G$ in equation 33b) and logarithms of initial rate constants (k_{obs}) correlate fairly well. The slope of the regression is $-2.7\ kJ^{-1}$. This value is close to the theoretical value[193] which one expects for a complete electron transfer.

Some new applications of metal catalysis in dediazoniation, in addition to the work of Kikukawa and Matsuda's group[183–185,189] reported above, will be discussed in the following section on applications in organic synthesis.

E. Applications in Organic Synthesis

Applications of dediazoniation reactions of arenediazonium salts in organic synthesis have been treated extensively in the volume on diazonium and diazo groups of this series[3,194] and in a recent review on the Meerwein reaction[173]. Therefore we shall only discuss here some new applications which have not already been treated in former sections of this chapter.

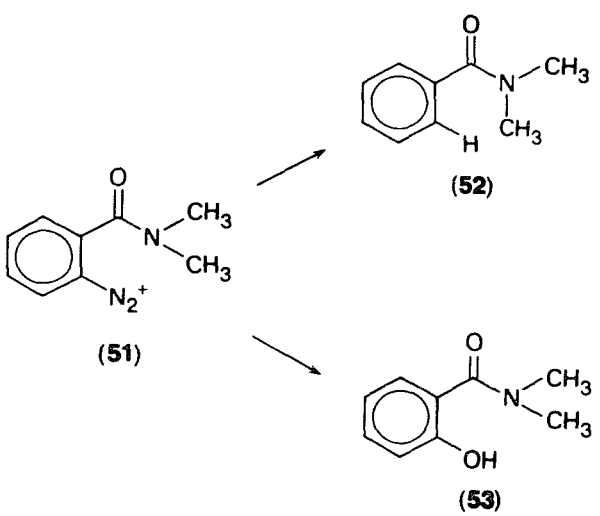
1. Hydroxy-dediazoniations

The standard method for the substitution of a dizonio group by a hydroxyl function is the thermal heterolytic dediazoniation in acidic aqueous solution. An aqueous solution of the diazonium salt, normally the solution in which the diazotization of the aromatic amine is carried out, is added slowly to hot (boiling) dilute sulphuric acid (5–15% H_2SO_4). The mechanism of this reaction is discussed in detail in Section II.B of this chapter. The solution has to have a fairly high acidity in order to avoid diazo coupling of the phenol formed with the unreacted diazonium salt. Diazo coupling forming hydroxyazo compounds involves the phenoxide ion, not the undissociated phenol[195]; at high acidities the concentration of phenoxide ions is negligibly small.

There are, however, a series of reports on dediazoniations which surprisingly did not yield the expected hydroxy compounds. Cohen and coworkers[196] mention not less than 24 references! In the opinion of the present author one should not conclude that the straightforward hydrolytic dediazoniation should be abandoned, as most of these examples are rather special cases, except for those where a highly nucleophilic (compared to the diazonio group or an aryl cation) group is present in the position *ortho* to the diazonio group. Examples of such groups are *o*-carboxamido groups (yielding a benzo-1,2,3-triazene)[197], *o*-hydroxy groups (yielding a diazooxazole)[198], *o*-thiol groups (yielding a benzothiadiazole)[199] and *o*-benzoyl groups (yielding benzofluorenone in a thermal heterolytic Pschorr reaction)[200–202].

Cohen and coworkers[196] recommend a new method for hydroxy-dediazoniations. It is based upon an earlier observation[202] that aryl radicals, produced by cuprous-oxide-induced dediazoniations of arenediazonium salts, could be oxidized to phenols by hydrated cupric ions. To a cold (0°C) acidic solution of the arenediazonium salt, obtained from the diazotization in dilute aqueous sulphuric acid, is added a solution of cupric nitrate followed by solid cuprous oxide under vigorous stirring. Nitrogen is evolved; the reaction is over after a few minutes. In the case of the *N,N*-dimethylbenzamide-*o*-diazonium ion **51**, the presence of silver nitrate changes the proportion of the products **52** and **53** in favour of the *o*-hydroxy-*N,N*-dimethylbenzamide **53** (Scheme 19).

The disadvantage of Cohen's method is that large amounts of cupric nitrate are



SCHEME 19

necessary. Normally the molar ratios of diazonium salt:$Cu(NO_3)_2$:Cu_2O are 1:15-100:1.

It is likely that Cohen's method is a Sandmeyer-type reaction. The catalysis can be represented by equations 34–36.

$$Ar{-}N_2^+ + Cu_{aq}^+ \longrightarrow Ar{-}N_2^{\bullet} + Cu_{aq}^{2+} \quad (34)$$

$$Ar{-}N_2^{\bullet} \longrightarrow Ar^{\bullet} + N_2 \quad (35)$$

$$Ar^{\bullet} + Cu_{aq}^{2+} + H_2O \longrightarrow Ar{-}OH + H^+ + Cu_{aq}^+ \quad (36)$$

Another method for hydroxy-dediazoniations has been described by Horning and coworkers[55]. Diazonium tetrafluoroborates decompose in refluxing trifluoroacetic acid containing potassium trifluoroacetate to give the respective phenols in good yield. Consideration of solvent effects in dediazoniations[79] (see Section II.D.1) suggests that this method involves aryl cations and not radicals as intermediates.

2. *Fluoro-dediazoniations*

The classical method for substituting a diazonio group by fluorine is the Balz–Schiemann reaction[203] in which the arenediazonium tetrafluoroborate is heated without a solvent. Although it has been known since 1927 and gives fairly good yields in the majority of cases, it can lead to difficulties. These were discussed by Wulfman[204] in the volume on diazonium and diazo groups in this series.

There is a report[205] which indicates that the fluoro-dediazoniation gives better yields if the hexafluoroantimonates are used instead of diazonium salts with any other complex fluoro acid. A comparison of the yields of the fluorination products of the *p-t*-butylbenzenediazonium ion with tetrafluoroborate and hexafluorophosphate as counterions in 1,2-dichloroethane as solvent shows that the yields with BF_4^- (39%) are higher than with PF_6^- (29%)[209].

Two recent investigations[207,208] describe fluoro-dediazoniations of *p-t*-butylbenzenediazonium tetrafluoroborate in solution; one of them[208] also includes information concerning the reaction of the *p*-methyl derivative. Yields of the fluoroarene up to 85% (*p-t*-butyl derivative in $CHCl_3$) are obtainable. With the *p*-methyl diazonium salt the yield is, however, small (up to 26%).

In both investigations it is emphasized that the reaction is heterolytic (involving the aryl cation) and takes place in the ion pair with the tetrafluoroborate, and not, as one might imagine, with a fluoride anion originating from the dissociation of the tetrafluoroborate into boron trifluoride and fluoride ions. This is demonstrated[207] by the insensitivity of the ratio of products ArF/ArCl in methylene chloride solution at 25°C to excess BF_3 concentration.

Becker and Israel[208] have studied the influence of the solvent in more detail. They determined the constant K_D of the equilibrium between free ions and ion pairs (equations 37 and 38) conductometrically in five solvents (H_2O, MeCN, MeOH, EtOH and Me_2CO).

$$[Ar{-}N_2^+\ BF_4^-] \overset{K_D}{\rightleftharpoons} Ar{-}N_2^+ + BF_4^- \quad (37)$$

$$K_D = \frac{[Ar{-}N_2^+][BF_4^-]}{[Ar{-}N_2^+\ BF_4^-]} \quad (38)$$

An inverse linear relationship was found between the ratio of products [ArOS]/[ArF] (where ArOS is the product of heterolytic solvolysis) and K_D/ε (ε = dielectric constant). This result indicates that solvolysis products are formed mainly from free diazonium ions, whereas fluoro-dediazoniation takes place in the ion pair. Of the solvents used, K_D is lowest in acetone, thus the yield of the fluorinated product is highest in this solvent.

An interesting observation[208] is that the photochemical dediazoniation gives the same product ratio as the thermal reaction in the same solvent. Both types of reaction probably proceed therefore via the same intermediate, i.e. the aryl cation.

In a recent report, Stepitis[209] claims that the decomposition of arenediazonium tetrafluoroborates in hexamethylphosphoric acid triamide (HMPA) results in a fluoro-dediazoniation (70% with *o*-nitrobenzenediazonium salt). This is certainly in contradiction to the work of Rüchardt[77] who found good yields of hydro-dediazoniation in HMPA (see Section II.D.4). It is not possible to offer comment on Stepitis' paper since we could obtain it in abstract form only.

3. *Other halogeno-dediazoniations*

Chloro- and bromo-dediazoniations are carried out in most cases via the Sandmeyer reaction. This can also be applied to substitutions by cyano, nitro and other groups. Iodo- and astatino-dediazoniations proceed in general without a cuprous salt as catalyst. These reactions have been reviewed by Wulfman[210].

Based on a suggestion by Hodgson[211], it is often assumed that the relatively smooth and catalyst-free iodo-dediazoniation is caused by reaction with triiodide ions (I_3^-). This question has been critically investigated recently by Rössler and coworkers[212] by tracer experiments with radiohalides ($^{131}I^-$ and $^{211}At^-$) in the picomole region using the benzenediazonium ion and *ortho*-, *meta*- and *para*-substituted derivatives (F, Cl, Br I, CH_3). The dediazoniations took place in 6M HCl at 80°C. Generally the yields were significantly higher with $^{211}At^-$ than with $^{131}I^-$. Considering the extremely low concentration of At^- and I^- in the experiments ($\leq 10^{-12}$ and 10^{-9} mol l^{-1}, respectively) it is surprising to find 10–20% astato- and 6–10% iodo-dediazoniation, since hydrolysis of the diazonium ion is a competing process. Even higher yields have been obtained in the syntheses of a 5-astatouracil[213] and *p*-astatobenzoic acid[214]. Hodgson's mechanism[211] cannot explain these results since the formation of trihalide ions must be negligible at these low halide concentrations, nor can any mechanism involving chain-type reaction steps provide a convincing explanation.

Owing to the smaller electronegativities of I^- and particularly At^-, relative to the lower halides, an electron-transfer mechanism is feasible, particularly as the higher halides have greater tendencies to form ion pairs with diazonium ions. As shown in equation (39), electron transfer in the ion pair is proposed to explain the results.

$$\mathrm{Ar{-}N_2^+ + At^-} \longrightarrow [\mathrm{Ar{-}N_2^+\,At^-}] \longrightarrow [\mathrm{Ar{-}N_2^{\bullet}\,At^{\bullet}}] \longrightarrow \mathrm{Ar{-}At + N_2} \qquad (39)$$

4. *Carboxyanhydro-dediazoniations*

A synthetically interesting extension of their work on interactions of diazonium salts with palladium catalysts[183–185] (see Section II.D.6) has been published recently by

Kikukawa, Matsuda and coworkers[215]. It leads from diazonium ions to mixed and symmetric acid anhydrides. An arenediazonium tetrafluoroborate was treated at room temperature for half an hour with 1.5 equivalents of sodium benzoate or acetate and palladium(II) acetate under a pressure of 9 kg/cm^2 of carbon monoxide. From the reaction mixture the mixed anhydride was obtained (equation 40). It could be easily disproportionated into a mixture of the two symmetric anhydrides in 81–98% yield (equation 41). The carboxyanhydro-dediazoniation of the benzenediazonium salt and its *p*-methyl, *p*-bromo, *p*-iodo and *p*-nitro derivatives as well as that of naphthalene-1-diazonium salt gave yields of 42–83%.

$$Ar{-}N_2^+ + CO + RCOO^- Na^+ + Pd(OAc)_2 \longrightarrow Ar{-}CO{-}O{-}COR + N_2 + Na^+ \quad (40)$$

$$Ar{-}CO{-}O{-}COR \xrightarrow[dry]{100-120°C} (Ar{-}CO{-})_2O + (R{-}CO{-})_2O \quad (41)$$

5. *Hydro-dediazoniations*

The classic method for replacing a diazonio group by hydrogen involves treatment in boiling ethanol under acidic conditions. As already discussed in Section II.D.2, in most cases mixtures of the desired compound with the ethoxy derivative, i.e. the product of solvolysis, are obtained.

Kornblum[216–218] suggested therefore, 30 years ago, that this 'textbook method' should be abandoned and be replaced by a treatment with hypophosphorous acid. The procedures described by Kornblum[217] have not changed in recent years; they give, in general, yields of 70–80%. The reaction has been investigated mechanistically by Gragerov and coworkers[219,220].

Arenediazonium salts dissolved in hexamethylphosphoric acid triamide (HMPA) are also substituted by hydrogen[77] (see Section II.D.4). Shono and coworkers[221] have reported recently that hydro- and deutero-dediazoniations take place with good yields using thiophenol and thiophenol-d (PhSD), respectively, as a reducing reagent. In the case of the deuterated reagent 100% isotopic purity is obtained.

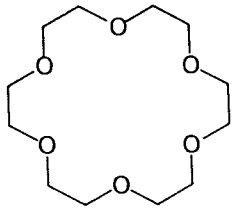
F. Stabilization of Arenediazonium Salts

1. *Solid diazonium salts*

Since their discovery by Griess in 1858, diazonium salts are known to explode in the dry state. The main chemical reaction causing the explosion is a dediazoniation. Since diazonium salts are manufactured on a fairly large industrial scale (batches up to 4000 moles), their thermal characteristics have an important technical aspect.

In recent years stabilization of diazonium ions has also aroused interest from a purely academic point of view, namely after Gokel and Cram[222] found that crown ethers, in particular 18-crown-6 (**54**), yield complexes with diazonium ions in solution. These complexes will be discussed in Section II.F.2.

If possible diazonium salts should not be isolated from the solution in which they were synthesized, but used in the dissolved state. In their investigations on diazonium carboxylates.Rüchardt and Tan[223] observed that the solid salts exploded and the ease with which this occurred increased with the nucleophilicity of the carboxylate used. This is consistent with the general experience that, for safety reasons, tetrafluoroborates should be made if it is necessary to isolate a diazonium salt.



(54)

If solid diazonium salts are required on an industrial scale, two types are available:

(1) Zinc tetrachloride double salts of the structure $(ArN_2^+)_2(ZnCl_4^{2-})$. They can be isolated with relatively little danger of explosion[224]. Their stability may be due to the formation of an inner complex (but without electron transfer, as Zn^{2+} cannot be oxidized) or simply because $ZnCl_4^{2-}$ complexes are less nucleophilic than free chloride ions. The X-ray structure of the tetrachlorozincate complex of the *p-N,N*-dimethylaminophenyldiazonium ion was determined by Nesterova and Porai-Koshits[225]. In aqueous solution, tetrachlorozincate complexes of arenediazonium ions show an ultraviolet band which is shifted bathochromically[226].

(2) The stability of diazonium salts containing chloride or hydrogen sulphate as anions is significantly increased in the presence of arenesulphonic acids, particularly naphthalenesulphonic acids and derivatives of benzenesulphonic acid which contain methyl groups[227]. It should be noted that present evidence points to the formation of molecular complexes[228] and not diazosulphonates ($Ar^1N_2OSO_2Ar^2$) as previously thought. The complex equilibrium constants of a diazonium ion in solutions of naphthalene derivatives increase in the sequence naphthalene < 1-methylnaphthalene < naphthalene-1-sulphonic acid < 1-naphthylmethanesulphonic acid. The sequence reflects a combination of the electron donor characteristics of these compounds, superimposed on the Coulomb attraction between the diazonium cation and the sulphonate anions.

As mentioned above, the stability of diazonium salts is important from the industrial safety point of view. In 1969 the unexpected decomposition of 1200 moles of 2-chloro-4,6-dinitrobenzenediazonium bisulphate in concentrated sulphuric acid caused the death of three workmen. It is through the joint efforts of analytical, physical and physical organic chemists that the causes of such explosions can be elucidated and precautions taken to prevent industrial accidents.

A report is available on the determination of the causes of the above explosion[229]. For several years some hundred batches of the diazotization of 1000 (later 1200) moles of 2-chloro-4,6-dinitroaniline in concentrated sulphuric acid using nitrosylsulphuric acid as nitrosating reagent were prepared without serious difficulties at a reaction temperature of 50°C. In 1969, nitrosylsulphuric acid dissolved in sulphuric acid at three times higher concentration became available. The third batch with this product exploded. Thermograms of laboratory batches demonstrated later that, at the lower concentration used previously, an exothermic decomposition with 2.1 J g^{-1} of 2-chloro-4,6-dinitroaniline begins at about 145°C, i.e. 95° above the usual reaction temperature. A batch with a 2.4 times higher concentration shows, however, an exothermic reaction producing 1500 J g^{-1} reagent beginning already at 75°C. The temperature safety margin of 25°C in the latter case is, of course, not sufficient!

The products of thermal decomposition of five benzenediazonium chlorides containing a carboxy group in a position *meta* or *para* to the diazonio group were investigated by Rossi and coworkers[230,231]. The formation of the different products is

in agreement with the intermediacy of 1,3- and 1,4-dehydro aromatic compounds, i.e. with aryne-type intermediates. An asynchronic mechanism is proposed with elimination of nitrogen prior to elimination of carbon dioxide.

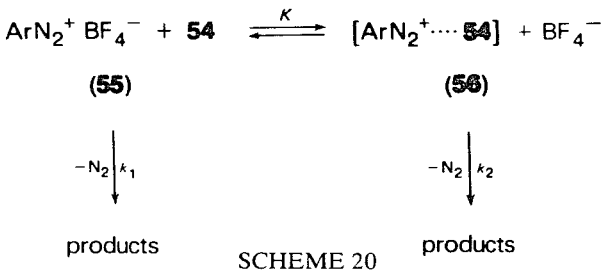
2. *Complexes of diazonium ions with crown ethers*

Gokel and Cram[222] first observed the interaction of arenediazonium ions with crown ethers of type **54**. They reported increased solubility of diazonium salts in nonpolar solvents and the nonreactivity of the complexed diazonium salts in diazo coupling reactions. Bartsch and coworkers[232] observed the markedly enhanced thermal stability of the complex of *p-t*-butylbenzenediazonium tetrafluoroborate with **54** relative to the uncomplexed diazonium ion.

The relative reactivity of such complexes has been studied in recent years with respect to several typical reactions of diazonium ions, e.g. diazo coupling and nucleophilic aromatic substitutions of substituents on the benzene ring which are activated by the diazonio group.

These reactions will not be reviewed in this chapter but in that by Bartsch[233]. Here we discuss only the influence of complexation by crown ethers on dediazoniation.

In their original investigation[232], Bartsch and coworkers measured the rate of dediazoniation of *p-t*-butylbenzenediazonium tetrafluoroborate in 1,2-dichloroethane in the presence of varying 18-crown-6 (**54**) concentrations. If Scheme 20 applies with different rates of dediazoniation for the diazonium ion pair **55** and the crown-ether-complexed diazonium ion (**56**), the kinetic evaluation leads to the result that $k_2 = 0$, or at least $k_1 > 100\, k_2$. Thus the crown-ether-complexed diazonium ion does not detectably decompose under conditions where uncomplexed diazonium ions – or more correctly in this case diazonium salts in the form of ion pairs – are converted into dediazoniation products.



SCHEME 20

Subsequently, Bartsch and coworkers[234] demonstrated that complexation with 18-crown-6 results also in photochemical stabilization. Further Gokel and coworkers[235] found that the shock sensitivity of diazonium salts complexed by crown ethers is decreased.

18-Crown-6 is not the only ionophore capable of stabilizing diazonium salts in solution. Bartsch and Juri[236] have determined the rate of dediazoniation of *p-t*-butylbenzenediazonium tetrafluoroborate in 1,2-dichloroethane in the presence of 40 macrocyclic multidentate compounds. Some examples of rate constants are given in Table 5. Their numerical value is proportional to the complex dissociation constant, assuming that as in the former investigation with 18-crown-6 (Scheme 20), $k_1 > 100\, k_2 \cong 0$ and maximum complexation is achieved with 21-crown-7. This compound has an estimated cavity diameter of 3.4–4.2 Å.

It is therefore astonishing that in spite of the fairly large amount of semiquantitative

TABLE 5. Rate constants of dediazoniations of *p-t*-butylbenzenediazonium tetrafluoroborate in 1,2-dichloroethane in the presence of 1 equivalent of a macrocyclic multidentate compound at 50.0°C[236]

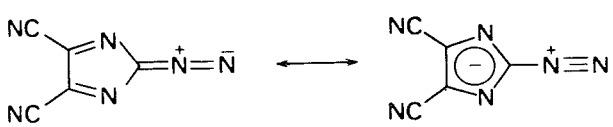
Complexing reagent	10^4k (s^{-1})
None	2.51
12-Crown-4	2.48
15-Crown-5	1.22
18-Crown-6	1.35
21-Crown-7	0.13
1,9-Dicyclohexano-18-crown-6	1.34
1,9-Dicyclohexano-21-crown-7	0.76
1,12-Dicyclohexano-24-crown-8	1.33
1,9-Dibenzo-18-crown-6	1.94

work with crown-ether-complexed diazonium salts, constants K were first determined systematically only in 1979. Kuokkanen and Virtanen[26] measured this constant for nine substituted benzenediazonium tetrafluoroborates with 18-crown-6 in 1,2-dichloroethane at 50°C. The data obey the Hammett equation satisfactorily with a ρ value of 1.19, indicating a moderate influence of substituent effects. The complex formation constant for the unsubstituted benzenediazonium tetrafluoroborate is 2.77×10^4 l mol^{-1}, that of the *p-t*-butyl derivative 1.92×10^4 l mol^{-1}. The calculation of k_1 and k_2 demonstrated that only with *p*-chlorobenzenediazonium ion had k_2 a value significantly different from zero.

Shortly afterwards the complex formation constant K was determined by Hashida and Matsui[237a] for various substituted benzenediazonium salts in methanol, dioxane, tetrahydrofuran, acetone and chlorinated hydrocarbons.

Complex formation equilibrium constants K together with respective dediazoniation rate constants k_1 and k_2 for the free and for the benzenediazonium and *p*-chlorobenzenediazonium tetrafluoroborate complexed with 18-crown-6, 21-crown-7 and dicyclohexano-24-crown-8 were determined recently by Nakazumi, Szele and Zollinger[237b]. The data demonstrate that the rate constant for the dediazoniation within the complex is smallest for the complex with 21-crown-7, but that there is not a linear relationship of K to k_2 for the complexes with the three crown ethers mentioned.

Ortho-substituted benzenediazonium salts probably do not form the same type of complexes[222,26]. If diazonio groups are present in only one of two or more mesomeric structures, such as in diazodicyanoimidazole (**57**), significant complex formation cannot be observed[235].

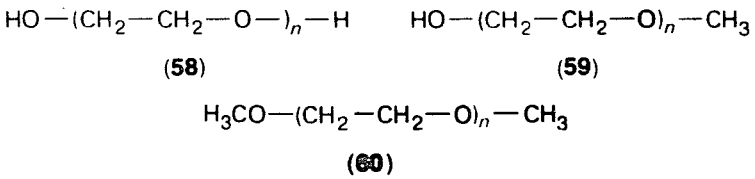


(**57a**) (**57b**)

The anion of the diazonium salt has a certain effect on the complex formation in Scheme 20. A hexafluorophosphate anion gives a slightly larger decrease in the rate of dediazoniation than the tetrafluoroborate with 18-crown-6[206]. This result is consistent

with the observation, mentioned in Section II.E.2, that tetrafluoroborate forms more stable ion pairs with diazonium ions than hexafluorophosphate.

The rate of dediazoniation of arenediazonium ions is also decreased by open-chain analogues of the crown ethers, i.e. by polyethylene glycol and polyethylene glycol mono- and di-methyl ether (**58–60**) of molecular weights 1000 to 1500[238]. The complexation constants are only about 12–18% of that for 18-crown-6. Polyethylene glycol has, however, an interesting application in organic synthesis as it catalyses the (probably homolytic) iodo- and phenyl-dediazoniations of arenediazonium salts in chloroform[239].



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

(**60**)

From an electron spectroscopic (ESCA) study[240] it was concluded that, as expected, the complex of *p*-*t*-butylbenzenediazonium ion with 18-crown-6 has a structure in which the positive end of the diazonium ion is inserted into the ring of the ionophore.

G. Photolytic Dediazoniations

It is not widely known that the photolysis of arenediazonium salts was one of the first large-scale applications of light-induced reactions in organic technology. In 1924 the German company Kalle & Co. in Wiesbaden-Biebrich began production of diazoreprographic paper (Ozalid M) in which an image-wise exposed sheet coated with a diazonium compound was developed by diazo coupling with a mono- or di-hydroxynaphthalene derivative at high pH under wet (later also dry) conditions. In the exposure step previous to development the diazonium compound was destroyed by photolytic dediazoniation; therefore the azo dye was formed only on those parts of the sheet which were not irradiated with visible light. The technology of the diazoreprographic processes has been described by Dinaberg[241] and by Pinot de Moira[242].

Although the relative importance of the diazoreprographic method decreased after the development of electrographic processes based on the photoconductive properties of selenium, zinc oxide etc., it is astonishing that, until recently, the photolysis of arenediazonium salts had not been extensively studied. The investigations carried out up to the mid-seventies have been reviewed comprehensively by Ando in a previous volume of this series[243]. The present section concentrates therefore mainly on work carried out in the late seventies.

Under comparable conditions, there are striking similarities between the photolytic dediazoniation and the thermal reaction with respect to the products formed. At the same time, there are dissimilarities in the kinetics; photolytic dediazoniations may be up to 10^7 times faster[158].

The similarity of the products formed in photolytic and thermal dediazoniations was investigated in aqueous systems by Lewis and coworkers[244,245]. In the presence of chloride ions the product ratios of hydroxy- and chloro-dediazoniations were not significantly different for photolyses and thermolyses[244], except in the cases of the *p*-methyl- and the *p*-chloro-benzenediazonium chloride where the percentage of chloro-dediazoniation was higher in photolysis[245]. It was also found that under photolytic conditions the two nitrogen atoms of the diazonio group rearrange to a

TABLE 6. Products of photolysis and thermolysis of *p*-methylbenzenediazonium tetrafluoroborate ($ArN_2^+ BF_4^-$) in methanol[205]

	Products (% yield)			
	Ar—F	Ar—OCH_3	Ar—H	Total
Photolysis (λ = 313 nm)	5.4	83.5	6.3	95
Thermolysis (50°C)	3.3	83	7.2	94

slightly greater extent than in thermolysis. The rearrangement is discussed in Section II.B. On the basis of investigations of the groups of Swain[24,27,28] and Zollinger[31–34,36,47,49] the original explanation, also accepted by Ando[246], has to be revised. It is unlikely that a bimolecular heterolytic hydroxy- or chloro-dediazoniation exists (see Section II.B).

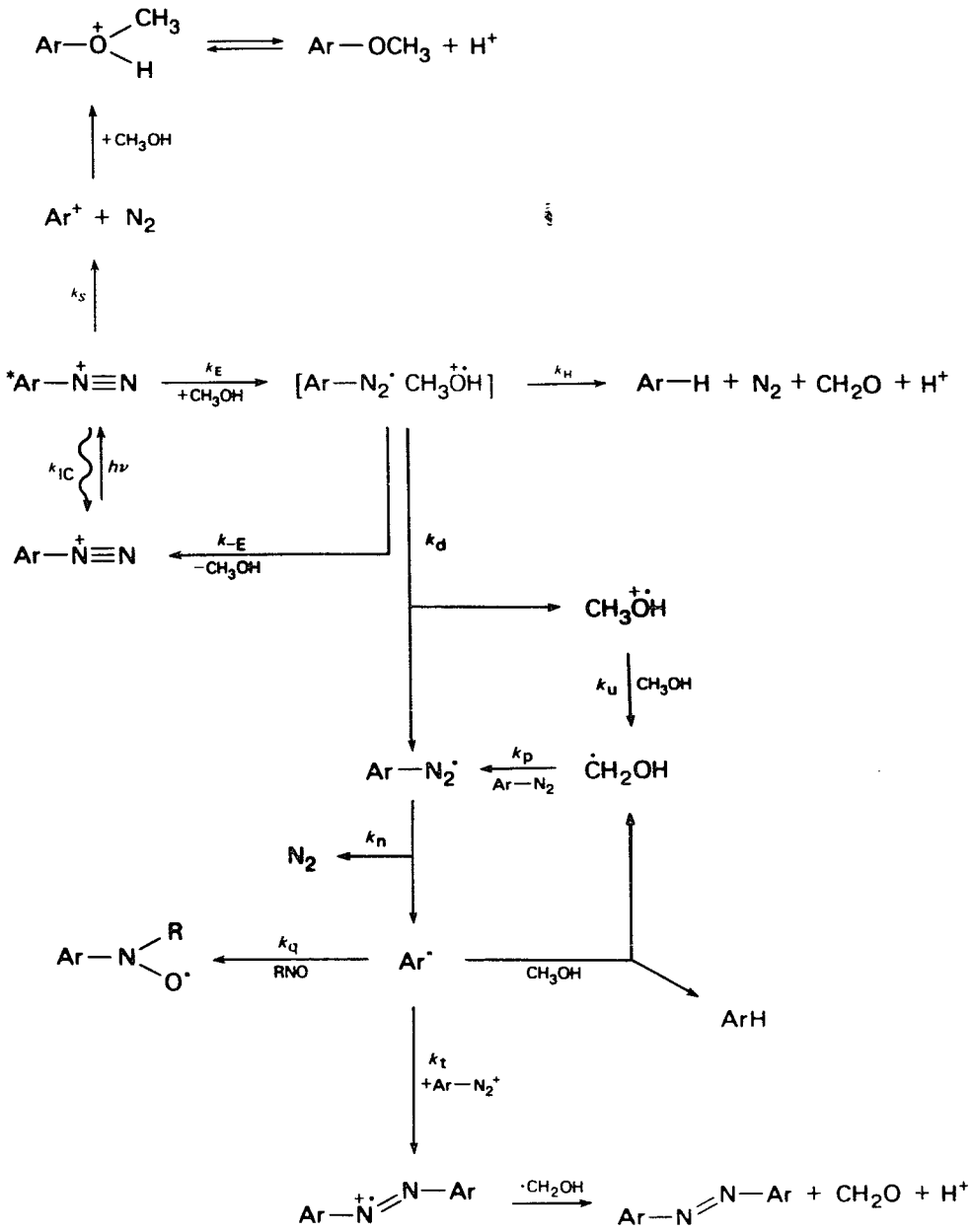
Comparisons of thermal and photolytic dediazoniations in alcohols have been made by Lee and coworkers in EtOH[247] and by Becker and coworkers in MeOH[158,208]. An example is given in Table 6.

The investigations of Bunnett and others[85–93] on thermal dediazoniations in methanol (see Section II.D.2) have demonstrated clearly that, in the absence of strong bases (CH_3O^-) dediazoniation takes place through two key intermediates, the aryl cation and the aryl radical. Obviously these two intermediates are also involved in the corresponding photolytic system. Here, the kinetics and mechanisms have been elucidated carefully by Becker and coworkers[156,158]. Today, the reactions in methanol are, thanks to the work of this research group, by far the best investigated photolytic dediazoniations.

The same group also determined quantum yields for the photolyses (313 nm) in the presence of varying concentrations of 2-methyl-2-nitrosopropane as a quencher for the thermal chain-reaction. The evaluation of the kinetic results was based on a system of 14 reactions assuming that all intermediates are in steady-state concentration. This resulted in the mechanism shown in Scheme 21[158].

The numerical values of the rate constants are interesting. Photosolvolysis through the aryl cation is astonishingly fast with $k_2 \geqslant 10^{11}\ s^{-1}$, assuming that the electron transfer is diffusion-controlled ($k_E \approx 2 \times 10^{10}\ 1\ mol^{-1}\ s^{-1}$). The heterolytic dediazoniation probably takes place from a hot ground state formed by deactivation of the singlet state $^*AR—\dot{N}{=}N$. The rate constant for the hydro-dediazoniation from the cage radical pair is also very large: $k_H \approx 10^{11}\ s^{-1}$. This value is significantly larger than that of the dissociation of the aryldiazenyl radical ($Ar—N_2^{\bullet}$) into an aryl radical and N_2 for which CIDNP data[95] indicate a value of 10^7–$10^8\ s^{-1}$. Becker and coworkers interpreted their large value for k_H with a one-step disproportionation reaction within the radical cage. The rate constant k_t for the formation of the azobenzene radical cation was known from previous work[248] and allowed the determination of the quenching rate with 2-methyl-2-nitrosopropane: $k_q \approx 2 \times 10^7\ 1\ mol^{-1}\ s^{-1}$.

The electron transfer from a methanol molecule to the activated diazonium ion is obviously a diffusion-controlled reaction. The rate constant is of the same order of magnitude as the electron transfer in acetonitrile solution in the presence of pyrene or benzanthracene as donors, which was measured by quenching the donor fluorescence[157,208]. Again, the same rate of electron transfer is obtained with solvated electrons generated by pulse radiolysis in *t*-butanol–water mixtures[208]. As expected for diffusion-controlled reactions, the rate constants are independent of substituents on the benzene ring of the diazonium ion whereas the rate constants of thermal dediazoniations in the presence of the donors mentioned show a substituent effect.



SCHEME 21

In addition to the investigations of photolytic dediazoniations sensitized by pyrene and benzanthracene, sensitization by derivatives of benzophenone and anthraquinone has been investigated recently by Fomin and coworkers[249–251].

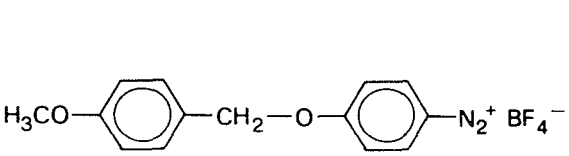
In Becker's opinion[156,252] there is no convincing evidence for triplet processes in photolytic dediazoniations. Kemp and coworkers[253] conclude, however, from, ESR

spectra recorded at 77 K on the photolysis of arenediazonium salts bearing electron-donor substituents in the *para* position that a triplet aryl cation in the ground state is involved. As this investigation was published before Swain's analysis of substituent effects (Section II.D.1), Kemp's interpretation is questionable. Koser[254] has interpreted the influence of diluent on the stereospecificity of addition of *cis*-2-butene to 2,6-di-*t*-butyl-4-diazo-2,5-cyclohexadienone also with a triplet intermediate.

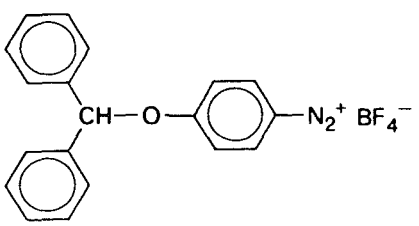
The solvent effects on photolytic dediazoniations are very similar to those of the thermal reactions. Becker and Israel[208] conclude from this observation that ion pairs are also involved in photolyses.

The similarity between photolytic and thermal dediazoniations is, however, limited, as the product ratio in photolysis is also dependent on the spectrum of the light used for photodecompositions. A series of substituted benzenediazonium salts underwent predominant heterolytic decomposition in methanol or ethanol/acetonitrile if irradiated at 313 nm, i.e. the wavelength which corresponds approximately to the main absorption maximum of the diazonium ion. When light of wavelengths longer than 330 nm was used, mainly homolytic products were formed[255].

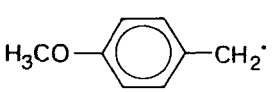
Benzenediazonium salts with certain benzyloxy groups in the *para* position (**61** and **62**) do not only give the products of heterolytic and homolytic dediazoniation with ultraviolet light, but also products which originate from the benzyl radicals **63** and **64**, respectively[256]. It is interesting to note that the analogue of compound **61** without the methoxy group does not dissociate homolytically at the C—O bond of the benzyloxy residue.



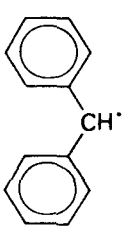
(61)



(62)



(63)



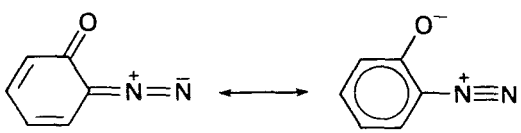
(64)

It is also appropriate to discuss in this section work concerning γ-radiation-induced radical-chain reduction of arenediazonium salts. This is advantageous for mechanistic investigations because it allows a more direct elucidation of the chain-propagation steps which follow the radical-forming initiation. Packer and coworkers[248] investigated the reaction of *p*-methylbenzenediazonium ions and methanol in aqueous solution initiated by γ-radiation from a ^{60}Co source. They found the number of diazonium ions destroyed per 100 eV of radiation energy absorbed to be proportional to the

concentration ratio $[CH_3OH]:[Ar—N_2^+]$ and independent of dose rate. This result confirms the propagation steps of equations (14)–(17) of the Bunnett–Broxton mechanism (Section II.D.2). In subsequent experiments[257] the rate of hydrogen abstraction by the *p*-methylphenyl radical from various hydrogen donors was measured under comparable conditions. This was in the order hypophosphite ($H_2PO_2^-$) and phosphite ($H_2PO_3^-$) > formate ($HCOO^-$) > CH_3OH > formic acid (HCOOH). The kinetic orders are, however, not the same with all these hydrogen donors.

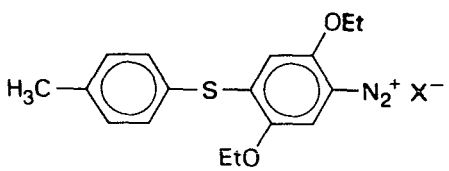
As discussed in Section II.C, benzenediazonium-*o*-carboxylate zwitterions yield in photolytic dediazoniation in methylene chloride 10% biphenylene[72]. This demonstrates that aryne intermediates can also be formed photochemically and not only thermally.

At the beginning of this section we mentioned the use of photolytic dediazoniations for a technical application, the diazoreprographic process. Industrially useful benzenediazonium compounds for this application contain electron donors in positions *ortho* and/or *para* to the diazonio group. Of historical importance are 6-diazo-2,4-cyclohexadiene-1-one (**65a**) and its 1,4-isomer 4-diazo-2,5-cyclohexadiene-1-one. They are, of course, identical with their mesomeric structures, the 1,2-diazoniophenoxide zwitterions, e.g. **65b**.



(**65a**) (**65b**)

Today, more sophisticated compounds are used, e.g. 2,5-diethoxy-4-*p*'-tolylthio- (**66**) as well as *p*-amino-substituted benzenediazonium salts.



(**66**)

Obviously a major factor of the usefulness of diazonium salts for these reprographic processes is the quantum yield in the dediazoniation. For the heterolytic photochemical dediazoniation of Scheme 21 via the aryl cation the quantum yield cannot be higher than 1; but for the homolytic processes of the scheme, quantum yields are higher, as they may lead to chain-reactions.

Heterolytic photochemical dediazoniation found an application in the photopolymerization of epoxides[257b,c]: Epoxides can be polymerized by Lewis acids like BF_3, SbF_5, $FeCl_3$ and others. Arenediazonium salts with the respective anions of these compounds (BF_4^- etc.) yield in a photochemical Schiemann type reaction aryl fluorides (or chlorides) and the Lewis acids which catalyse the epoxide polymerization. With appropriate substituents of the diazonium salt as additive, epoxides can be polymerized using ultraviolet light of specific wavelengths in the range 250–400 nm.

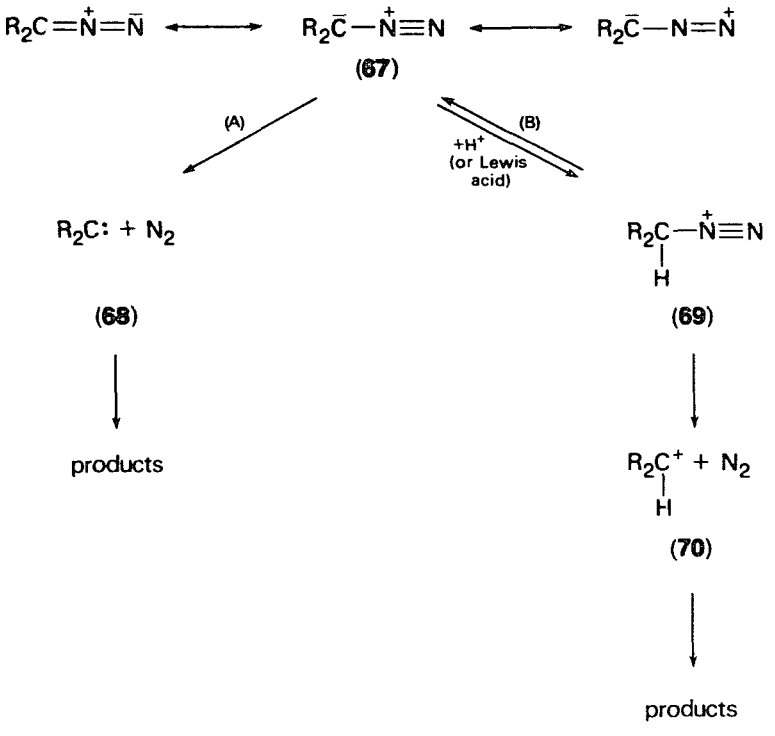
A comprehensive investigation on the influence of substituents on the quantum yield of the photolysis of 19 monosubstituted benzenediazonium salts was made by

Tsunoda and Yamaoka[258]. *Para*-substituted electron-releasing groups (OCH_3, NR_2) increased quantum yields while the *ortho-* and *para-* substituted electron-withdrawing groups (NO_2, Br) decreased them. The results are consistent with a similar investigation on *p*-amino-substituted benzenediazonium salts[259] and with MO calculations[260] on 4-diazo-2,5-cyclohexadiene-1-one.

III. COMPARATIVE DISCUSSION CONCERNING THE DEDIAZONIATIONS OF DIAZOALKANES AND RELATED COMPOUNDS

A. Dediazoniations of Alkanediazonium Ions

As mentioned in the introductory section of this chapter, it is generally assumed that diazoalkanes (**67**) undergo dediazoniations by two basic pathways, either directly, forming carbenes (**68**) as primary, highly reactive intermediates, or, after reaction with a Brønsted or Lewis acid, via alkanediazonium ions (**69**) and carbocations (**70**) (Pathways A and B respectively in Scheme 22). Pathway (B) belongs mechanistically to the subject of this volume; diazo groups of diazoalkanes will, however, not normally be considered as triple-bond functional groups in spite of the fact that they can be described in terms of three mesomeric structures (**67**), one of which contains a diazonio triple bond. The formation of nitrenes from azides corresponds to pathway (A). Alkanediazonium ions (**69**) are not only intermediates in pathway (B), but also in the so-called deamination of aliphatic amines; this is one of the classical routes to carbocations (**70**).



R = alkyl, acyl, etc.

SCHEME 22

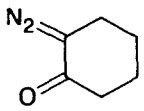
It has been shown conclusively in the chapter of Hegarty[3], and also in those of McGarrity[261], Wulfman[262], Ando[243], Fry[263] and Wulfman, Linstrumelle and Cooper[264] in the volume on diazonium and diazo groups of this series that a comprehensive discussion of the dediazoniation proper in the reactions in Scheme 22 is of significance only if a thorough treatment of the structures, reactions and products of carbenes in pathway (A) and of the protonation step in pathway (B) is considered. For the latter pathway, a discussion of the reactions of the carbocations formed in other reactions (deaminations, dehalogenations, dearylsulphations etc.) must be included. The situation is similar in the case of dediazoniations of azides, i.e. for the formation of nitrenes.

Since such a comprehensive treatment of dediazoniations of diazoalkanes and azides is far beyond the scope of this chapter, we shall restrict ourselves to remarks concerning a comparison of dediazoniation mechanisms of arenediazonium ions with those of diazoalkanes.

The assumption that aromatic and aliphatic dediazoniations are mechanistically very similar is probably wrong. It is historically correct, however, for Hegarty[265] to write for *aliphatic* dediazoniations 'whether or not the nucleophile ... reacts with the carbonium ion ... or with the diazonium ion ... has been a matter of controversy reminiscent of the corresponding dediazoniation of arenediazonium ions ...'. As discussed in Section II.B of this chapter this controversy has been solved for aromatic diazonium ions in favour of an S_N1-like mechanism.

The extrapolation of this result to acid-catalysed dediazoniations of diazoalkanes and related compounds is, however, not justified. Orbital overlap in alkanediazonium ions is very different from that in the aryl analogues, as the diazonio group is bound to an sp^3 and not to an sp^2 carbon atom.

The difference in orbital overlap is often assumed to be the only cause for the much higher thermal stability of arenediazonium ions. For decades this argument has been quoted in many textbooks; experimentally it is, however, supported only in solution. Berner and McGarrity[266] discovered the methanediazonium ion recently; it is reasonably stable only at $-120°C$ in a fluorosulphuric acid–sulphuryl chlorofluoride solution (together with the isomeric N_β-protonated conjugate acid of diazomethane). The relative stability of the few alkanediazonium ions known is due either to strongly electron-withdrawing substituents ($CF_3CH_2N_2^+$ [267], $(CF_3)_2CHN_2^+$ [268] and the cyclic diazoketone **71**[269]) or to a bridgehead position of the diazonio group[270].



(71)

In the gas phase, however, the methanediazonium ion is very stable, as Foster and Beauchamp[271] have shown using the ion cyclotron resonance technique. As Kirmse[272] has mentioned, the benzenediazonium ion is expected to occupy a position intermediate between the methane- and the ethane-diazonium ion, if the ionization potentials of the corresponding radicals[273,274] are adopted as a measure of the stability of the respective cations and it is assumed that the dediazoniation proper is energetically the same for all three compounds.

Such considerations demonstrate that the dediazoniation proper, i.e. the heterolytic dissociation of the (formal) single bond C—N in diazonium ions, is probably more complex than thought today. First of all, a true monomolecular reaction, even for the aromatic diazonium ion, does not appear to occur. The detection of an intermediate

ion-molecule pair, as described in Scheme 2 (Section II.B), and also the significantly increased stabilization of arenediazonium ions by complexation with crown ethers (Section II.F.2) indicate that interactions with solvent molecules may play a decisive role. The crown ether molecule forms a collar-like ring around the diazonio group and in this way protects the latter against collisions with solvent molecules. Such collisions may initiate the heterolytic dissociation of the sp^2-C—N_α bond. The CNDO calculations of Simonetta and collaborators[47] discussed in Section II.B are consistent with such a hypothesis.

It is not yet known whether this type of 'pseudo-monomolecular' dissociation is also possible for sp^3-C—N_α bonds of alkanediazonium ions. This problem has, to the author's knowledge, not been discussed or investigated experimentally for *any* S_N1 reaction.

Recently, however, Simonetta and coworkers[275] calculated the dynamics of the dediazoniation of the methanediazonium ion in the gas phase and in the presence of nine water molecule using the same CNDO/2 programme with which the same authors[47] verified the experimental results of Zollinger and coworkers[31–34] for the dediazoniation of benzenediazonium ions. The CNDO calculation indicates *no* intermediate in the dissociation of the C—N_α bond in CH_3—$\dot{N}_\alpha{\equiv}N_\beta$ in the presence of water, whereas for benzenediazonium ions two energy minima resulted between the diazonium ion and the phenyl cation + N_2, corroborating the formation of the ion-molecule pair indicated from kinetic data.

It should be emphasized—on the basis of the following discussion of S_N2 dediazoniations of alkanediazonium ions—that it is astonishing that there is no clear evidence for bimolecular aromatic dediazoniations. Bimolecular nucleophilic aromatic substitutions (S_NAr) are well known for aromatic compounds with electron-withdrawing substituents (NO_2 etc.), but only with leaving groups (halogens, etc.) other than the diazonio group.

Dediazoniations of alkanediazonium ions, however, probably take place following either an S_N1 or an S_N2 mechanism. Their investigation is complicated by the fact that, in practically all cases, the alkanediazonium ion is not the starting material, but is formed by protonation of a diazoalkane or by other processes; the alkanediazonium ion is therefore a steady-state intermediate.

It is well known[265] that in aliphatic dediazoniations protonation of the diazoalkane is either a fast preequilibrium (A2 mechanism) or rate-determining (A-S_E2 mechanism). There is ample evidence that in dediazoniations of primary diazo ketones[2,76–278], primary diazo esters[279,280], diazosulphones[281–283] and 2,2,2-trifluorodiazoethane[284] the reaction follows the A2 mechanism. This can be demonstrated by the inverse kinetic solvent isotope effect ($k_{H_2O}/k_{D_2O} > 1$), by H–D exchange, by the importance of specific acid catalysis and by the strong acceleration by added nucleophiles.

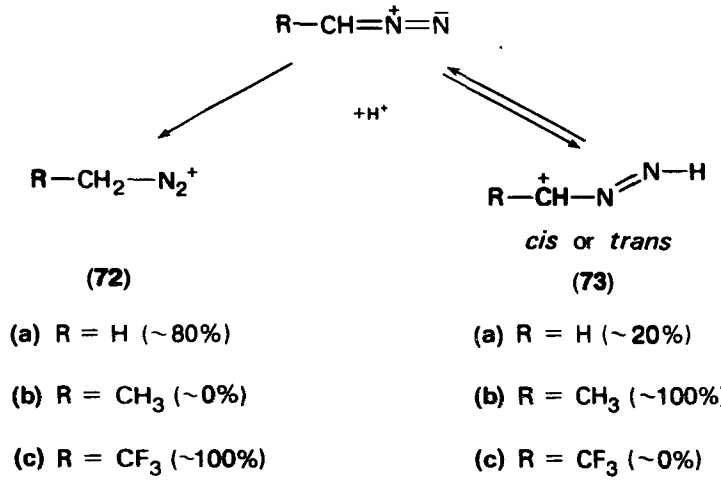
On the other hand, the dediazoniations of secondary diazo ketones[279,285–291], secondary diazo esters[292], mono- and di-phenyldiazomethane[293–295] and 1,1,1-trifluoro-2-diazopropane[284] are examples of reactions following the A-S_E2 mechanism, the major evidence for which is the observation of Brønsted general acid catalysis. The detailed analysis of general-acid-catalysed dediazoniations of diazo compounds, e.g. the sharp curvature of Brønsted plots found by Albery and coworkers[292] demonstrates, however, the complexity of the apparently 'simple' protonation of diazoalkanes. A discussion of these effects is not within the scope of this chapter.

Diazomethane[295–297] is also hydrolysed by this mechanism. This is explicable by the fact that the C—N bond is not stabilized. The solvent isotope effect criterion used to differentiate these mechanisms has been discussed recently by Bui-Nguyen, Dahn and McGarrity[298,299]. An instructive example of an analysis of experimental (total) isotope

effects in H_2O/D_2O mixtures into product, solvent, primary and secondary isotope effects on the basis of the general isotope effect theory[300,301] was given by Diderich and Dahn[302] for the dediazoniation of *p*-nitrophenyldiazomethane some years ago.

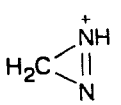
The investigation of the mechanism of the dediazoniation proper (**69** → **70**) in pathway (B) (Scheme 22) is more difficult than for aromatic diazonium ions owing to the prior acid–base equilibrium. It becomes even more complex because under certain conditions the α carbon atom in diazoalkanes is not the only position capable of being protonated.

Protonation of diazoalkanes at the β nitrogen has already been mentioned briefly above. Berner and McGarrity[266] have observed and identified by NMR the methylenediazonium ion **73a** besides the methanediazonium ion **72a** when diazomethane is protonated in superacids (Scheme 23).



SCHEME 23

^{15}N-labelling confirms that a proton in **73a** is located on the β nitrogen[303]; the formation of detectable amounts of protonated diazirene (**74**) can be excluded. It is likely that dediazoniation takes place with methanediazonium ion (**72a**) only and that methylenediazonium ions (**73a**) are formed in a side-equilibrium. It is also interesting to note that, under the conditions used by McGarrity, the back-reaction of the methanediazonium ion (**72a**) to diazomethane was not detectable. In water–tetrahydrofuran (40/60 v/v), however, *C*-protonation of diazomethane is an equilibrium process ($pK_a \sim 10$); yet the dediazoniation of the methanediazonium ion is faster than the deprotonation by water molecules[304]. On the other hand, hydroxide ion reacts more rapidly as a base (i.e. as a deprotonating reagent) than as a nucleophile reacting at the β nitrogen.



(**74**)

The tautomeric equilibrium of the two protonated species **72** and **73** is strongly influenced by substituents R: the ethanediazonium ion (**72b**) was not detectable, only the *N*-protonated compound **73b** was found. 2,2,2-Trifluorodiazoethane, on the other

hand, yields only the *C*-protonated conjugate acid in fluorosulphuric acid/sulphuryl chlorofluoride mixtures at $-120°C$[303]. The results are consistent with MNDO molecular orbital calculations.

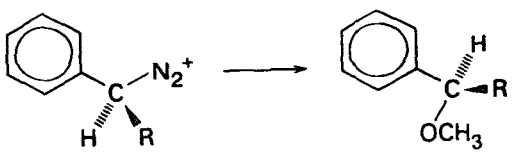
Diazo ketones are protonated predominantly at the carbonyl oxygen if treated in superacids ($HF/SbF_5/SO_2$ and $FSO_3H/SbF_5/SO_2$ at $-60°C$)[305]. This is obviously also a side-equilibrium relative to *C*-protonation which leads to dediazoniation. Reaction of α-diazo ketones and esters with nitrous acid yields α-carbonyl nitrile oxides ($R—CO—C\equiv\overset{+}{N}—\overline{O}$)[306]; this demonstrates that a Lewis acid attacks the α carbon atom. This does not of course, exclude the possibility of *N*- or *O*-attack by Lewis acids; yet if such reactions take place, they are only side-equilibrium processes. A recent observation by a Japanese group[307] also demonstrates the possibility of activation of diazoalkanes by Lewis acids. The reaction of diphenyldiazomethane, diazophenyl ketone and diazoacetic ester with 1,3-cyclohexanedione is catalysed by BF_3.

With these complications, it is obvious that the elucidation of the dediazoniation proper (**69** → **70**) is a complex problem.

The problem is, of course, related to the classical differentiation between S_N1 and S_N2 mechanisms in nucleophilic aliphatic substitution.

There is experimental evidence that, depending on the structure of reagents and on the reaction conditions, dediazoniations of aliphatic diazonium ions can take place by the S_N1 or the S_N2 pathway.

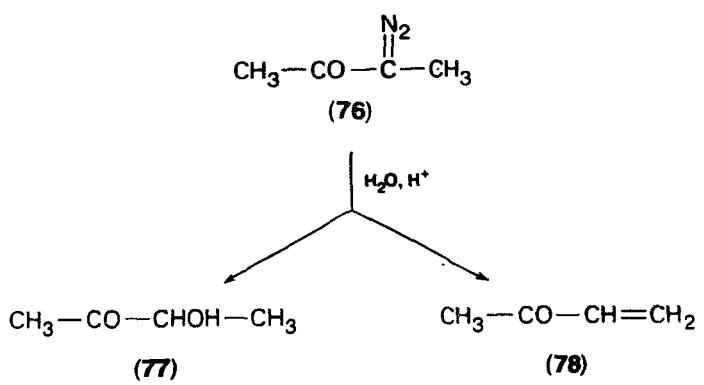
A good example of an S_N1 reaction is the methanolysis of 1-phenylethanediazonium ions (**75**, R = CH_3) (equation 42). The extent of inversion is independent of base concentration[308]. A change in substituent (**75**, R = D) leads, however, to an increase in the percentage of inverted product[309]; this demonstrates the sensitivity of dediazoniations to the mechanism of substitution.



(42)

(**75**)

Another good example is given by the product ratio in the dediazoniation of 3-diazo-2-butanone (**76**). The dediazoniation yields not only the product of hydrolytic substitution, acetoin (**77**), but also the product of elimination, methyl vinyl ketone (**78**) in a ratio which is independent of acid and buffer concentration[290] (Scheme 24).

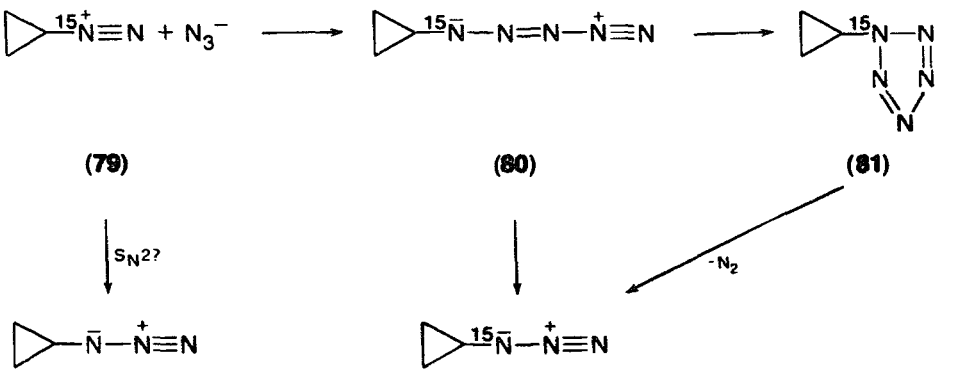


SCHEME 24

As molecular nitrogen is a very good leaving group, dediazoniations require less assistance from neighbouring groups or external nucleophiles than the nucleophilic substitution of halides or sulphonic acid esters. Yet there are clear cases of second-order kinetics which indicate an S_N2 mechanism (see, however, the remark at the end of this section). 1,1,1,3,3,3-Hexafluoro-2-diazopropane solvolyses in fluorosulphuric acid in a reaction first-order in the fluorosulphate ion[268]. This is very probably due to the energy barrier to formation, in an S_N1 reaction, of the extremely unstable carbocation.

Many cases are known where substitution by added nucleophiles occurs in a competition to solvolyses of diazo ketones and diazo esters. A plot of the logarithms of the product ratios in this reaction gives linear relationship with the nucleophilicity parameter *n* of Swain and Scott[310]. Examples are given in the reviews of Hegarty[265], Kirmse[272], Dahn and collaborators[311] and others.

An interesting case is the reaction of alkanediazonium ions with azide ions. In analogy to the respective reaction of aromatic diazonium salts[312–316] cyclopropanediazonium ions (**79**) are substituted almost exclusively by azo coupling and subsequent decomposition of the pentazene (**80**) and/or the pentazole (**81**), as Kirmse and coworkers[317] have shown using ^{15}N labelling. Small amounts of unlabelled azide were detected; they may be the product of an S_N2-type azido-dediazoniation (see Scheme 25).



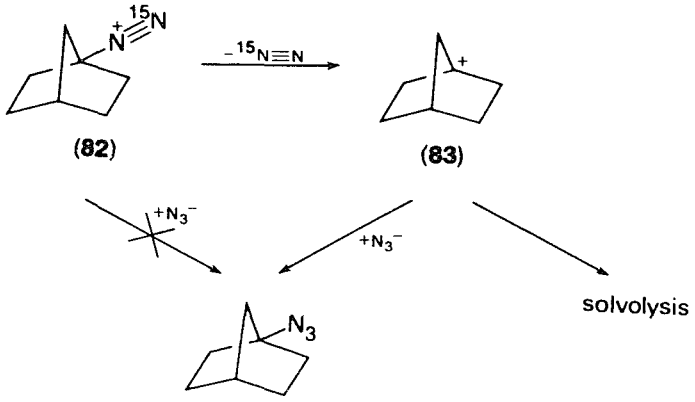
SCHEME 25

With the bridgehead diazonium ion **82** (bicyclo[2.2.1]heptane-1-diazonium ion), however, the $^{15}N_\beta$ labelling of the diazonia group was completely lost in the azide, indicating intermediate formation of the carbocation **83**[318] or an S_N2 substitution (Scheme 26).

Neighbouring-group effects have been investigated for the case of the deamination of α-aminoacetic acid since 1948 (see Kirmse's review)[272] and more recently for an α-amino acid with an alkyl group in the α position (isoleucine) by Kirmse and Rauleder[319]. The work demonstrates the operation of a neighbouring-group effect and the influence of micelle formation. The latter impedes, as already shown by Moss and coworkers[320,321], back-side attack by the solvent or nucleophile. Inversion decreases with increasing concentration until retention is finally observed. The influence of ion-pair formation has also been observed[273].

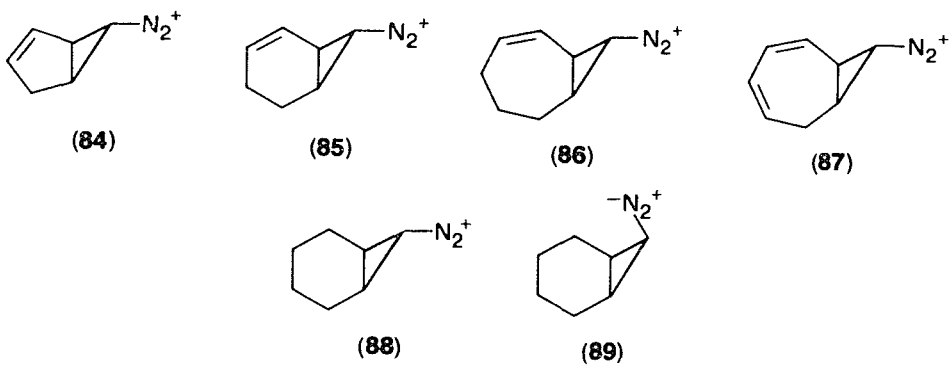
The neighbouring-group influence of the carboxylate group is, as expected, much greater than that of a (undissociated) hydroxy group[322].

Participation of neighbouring double bonds was first observed by Mander and coworkers[323] and later investigated in more detail with bicyclic compounds by the

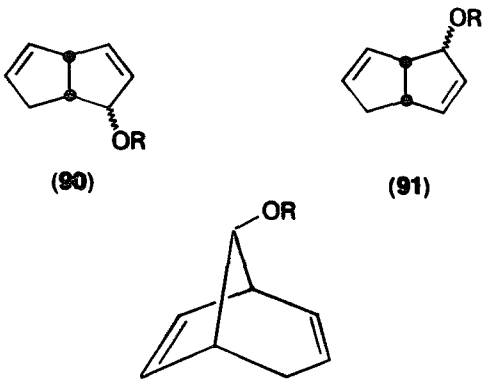


SCHEME 26

groups of Dahn[324] and Kirmse[325–329]. Particularly interesting are the studies on the series of bicyclic cyclopropanediazonium ions **84–87** which contain one or two double bonds in the annellated ring. The products of the saturated compounds **88** and **89** were investigated too. Here we discuss only the influence of the neighbouring double bonds on the products, i.e. those of compounds **84–87**.



The *exo*-bicyclo[3.1.0]hex-2-en-6-diazonium ion (**84**) reacts in slightly alkaline solution with participation of the double bond[325]. Ring-opening is only possible after isomerization to the *endo* isomer. In the case of the *exo*-bicyclo[4.1.0]hept-2-en-7-diazonium ion (**85**) direct substitution with retention double-bond participation and ring-opening is observed[327]. The *exo*-bicyclo[5.1.0]oct-2-en-8-diazonium ion (**86**) yields no products indicative of double-bond participation. Besides little direct substitution (2.3%) ring-opening compounds [3-methoxy-1(*Z*),4(*E*)-cyclooctadiene and 5-methoxy-1(*Z*),3(*E*)-cyclooctadiene] are the main products. For the compound with two double bonds (**87**) the respective eight-membered ring with three double bonds [5-methoxy-1(*Z*),3(*Z*),6(*E*)-cyclooctatriene] is formed in 19–58% yield depending on conditions, but completely different bicyclic compounds, namely methoxy derivatives of bicyclo[3.3.0]octa-2,7-diene (**90**) and bicyclo[3.3.0]octa-2,6-diene (**91**) are also found. In the presence of sodium methoxide the main product is *syn*-8-methoxybicyclo[3.2.1]octa-2,6-diene (**92**), probably formed by way of a carbene intermediate[329].



(90) (91)

(92)

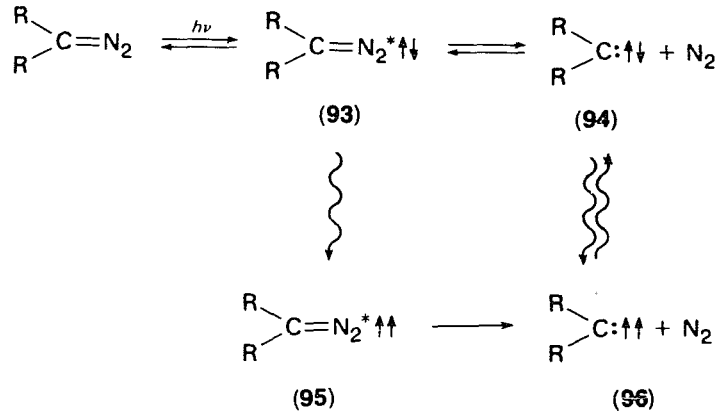
In concluding this section we refer to the title, i.e. the comparison of aliphatic and aromatic dediazoniations. There is evidence for an S_N1 mechanism in the aliphatic series comparable to the 'classic' mechanism of arenediazonium ions. There are, however, also good examples of S_N2 reactions, a type not (or not yet) positively known for aromatic dediazoniations. On the other hand, there are aliphatic dediazoniations for which participation of nucleophiles in the rate-determining step has been found, for which, however, no or only partial stereochemical evidence for an S_N2 mechanism is available. These may follow an S_N1-type mechanism similar to that of some aromatic compounds, namely that of Scheme 2 (Section II.B) in which the back-reaction of the dediazoniation proper is faster than the reaction of the carbocation with a nucleophile. Although not very likely, such a mechanism has as yet not been disproven for acid-catalysed reactions of diazoalkanes.

B. Dediazoniations via Carbenes, Nitrenes and Other Intermediates

The discussion of acid-catalysed reactions of diazoalkanes in Section III.A leads to the conclusion that the formation of a carbocation from an alkanediazonium ion has a higher first-order rate constant than the (unassisted) formation of a carbene from a diazoalkane (Scheme 22). The question now arises whether or not the process of carbene formation is really as simple as the monomolecular dissociation of the (formal) double bond in the diazoalkane.

The structure of the most simple carbene, methylene, as well as that of its derivatives, has been investigated very intensively. The compilation of data given by Wentrup[330] corroborates this statement clearly. On the other hand, relatively little is known about the process of dediazoniation proper. In 1975, Dürr[331] emphasized in a comprehensive review on triplet carbenes that more work is needed to clarify the fine structure of the absorption of diazoalkanes between 400 and 500 nm in order to understand their photoexcitation.

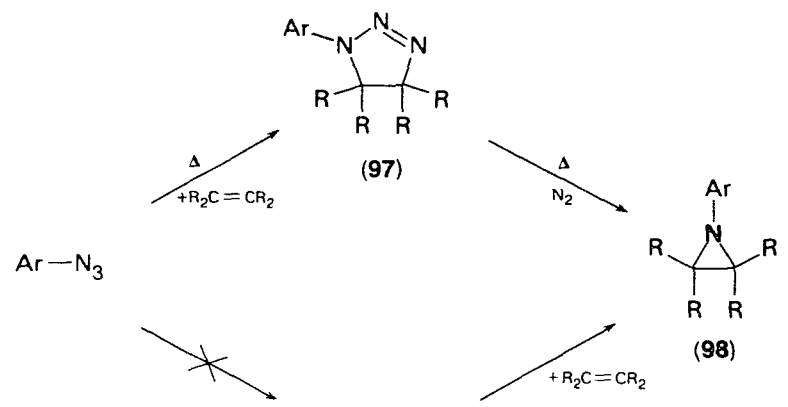
Scheme 27 summarizes the processes in photochemical dediazoniations of diazoalkanes. The excited singlet-state diazo compound **93** may undergo intersystem crossing to the triplet diazoalkane (**95**), or return to starting material in a radiationless decay. It can also dediazonize to the singlet carbene (**94**) which, in turn, may form a triplet (**96**). In the context of this chapter, it is interesting to see that the singlet carbene can also react with molecular nitrogen and regenerate the diazoalkane. This was demonstrated by the exchange of nitrogen in diazomethane with solid and gaseous $^{15}N_2$ [332,333].



SCHEME 27

The mechanism of dediazoniation of azides is also rather complex. There is some evidence from solvent interaction effects[334,335] that in the photolysis of azides the formation of nitrenes is not as simple as was thought ten years ago when the loss of N_2 was assumed to be an unassisted reaction step.

In solvents with reactive double bonds, azides decompose thermally much faster than in saturated hydrocarbons (Scheme 28). This is due to 1,3-dipolar addition of the azide to the olefin to form a triazoline (**97**) which decomposes to the aziridine **98**[336].

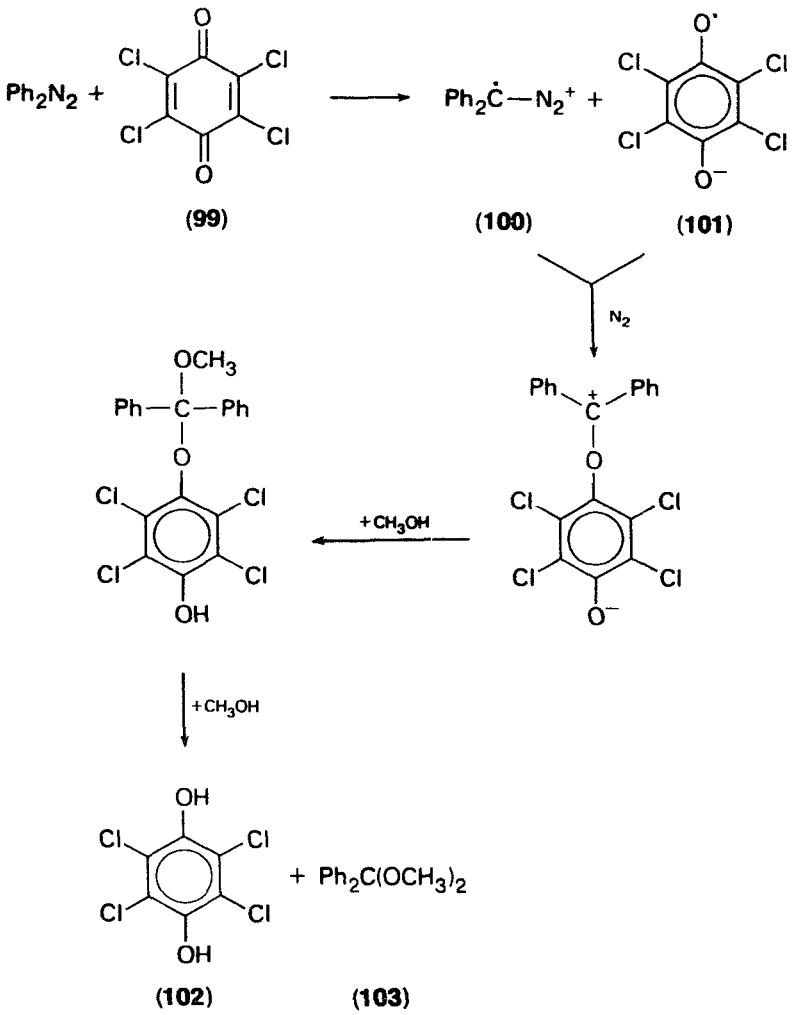


SCHEME 28

Furthermore, it is well known that photolytic dediazoniations of diazoalkanes do not proceed 'directly' in the presence of olefins but through 1,3-dipolar addition products (pyrazolines) which lose N_2 thermally to form a cyclopropane derivative[337].

Assisted dediazoniations of diazoalkanes are also possible with the help of electron acceptors and by electron transfer.

Nagai and coworkers[338,339] have reported that mono- and di-aryldiazomethanes and 9-diazofluorene undergo dediazoniation in acetonitrile through the corresponding radical-ion intermediates (**100**) under the influence of chloranil (**99**), tetracyanoethylene and other electron acceptors (Scheme 29). With



SCHEME 29

diphenyldiazomethane, tetrachlorohydroquinone (**102**) and benzophenone dimethylacetal (**103**) are formed in the presence of excess methanol. In dry acetonitrile the radical anion **101** can be identified by ESR[338].

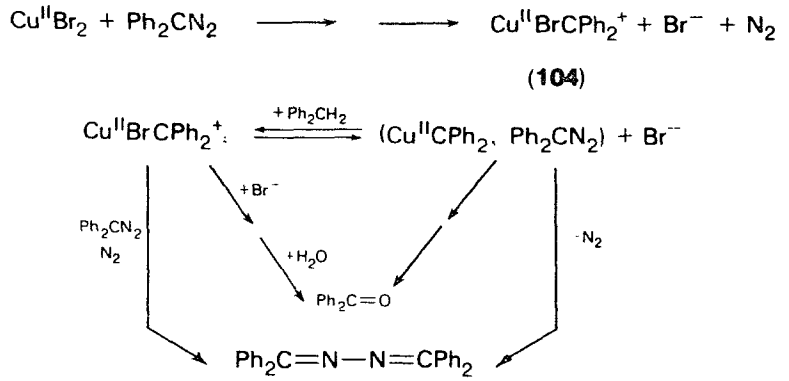
In the reaction of 9-diazofluorene and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone visible spectra allow the differentiation of two intermediates, namely a charge-transfer complex followed by a radical pair[339].

From the point of view of the general subject of this volume it is important to recognize that dediazoniation of the radical cation **100** is much faster than that of the respective diazoalkane, because it contains a 'true' diazonio triple bond.

The extensive work of Bethell and coworkers on catalysed decompositions of diazoalkanes can be rationalized on the same basis.

It has long been known that metallic copper and copper compounds facilitate dediazoniations of diazoalkanes[340]. Bethell and Eeles[341] were the first to investigate the kinetics of such reactions in the presence of $CuBr_2$. They showed that in acetonitrile $CuBr_2$ reacts with diphenyldiazomethane in a two-step process, yielding

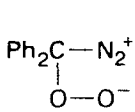
first in a rapid step a nitrogen-free copper complex which may have diphenylmethylene as a ligand (**104**). The copper complex then reacts with the excess diazoalkane in a much slower step (Scheme 30).



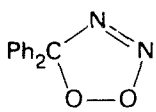
SCHEME 30

In later investigations[342,343] Bethell and coworkers, using ESR, demonstrated for the decomposition induced by copper(II) perchlorate that two radical cations are involved, one of which corresponds to the radical **100** discussed above in the context of Nagai's work. Cuprous salts are also good catalysts; the influence of anions is, however, much more dominant; the mechanism is therefore only understood in part[344]. The same can be said for catalysis by Zn salts[345].

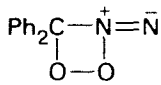
Dediazoniation of diazoalkanes is also catalysed by singlet molecular oxygen. Bethell and McKeiver[346] have found good evidence for the two intermediates **105** and **106** whereas **107** can be excluded.



(**105**)



(**106**)



(**107**)

These two intermediates fit well into the basic concept of our discussion, namely the intermediacy of either a diazonio group (**105**) or a 1,3-dipolar addition compound (**106**).

On the other hand, it should be mentioned that dediazoniations can be facilitated not only by electron removal from the diazoalkane as the various examples in this and the preceding section (III.A) demonstrate, but also by electron transfer from a carbanion to a diazoalkane. This was shown by Beringer and coworkers[347] for the reaction of 9-fluorenyllithium with 9-diazofluorene. Bethell and coworkers[348] have demonstrated that this electron transfer initiates an anion-radical chain-reaction. As no triple-bond intermediates are involved, this reaction is not within the scope of our discussion.

IV. ACKNOWLEDGEMENTS

I thank my coworkers Dr. John Penton, for help in correcting my English manuscript and for comments, and Dr. Ivanka Szele for help in providing literature data. Our work on dediazoniations has been supported by the Swiss National Science Foundation (projects 2.722.72, 2.406-0.75 and 2.120-0.78).

V. REFERENCES

1. J. F. Bunnett, *J. Chem. Soc.*, 4717 (1954).
2. *IUPAC, Nomenclature of Organic Reactions*: Part I. *Straightforward Transformations (Substitutions, Additions, Eliminations)* edited by J. F. Bunnett, *Pure Appl. Chem.*, **53**, 305 (1981).
3. A. F. Hegarty in *The Chemistry of Diazonium and Diazo Groups* (Ed. S. Patai), John Wiley and Sons, London, 1978, p. 511.
4. L. Horner and H. Stöhr, *Chem. Ber.*, **85**, 993 (1952).
5. D. F. DeTar and T. Kosuge, *J. Amer. Chem. Soc.*, **80**, 6072 (1958).
6. T. J. Broxton, J. F. Bunnett and C. H. Paik, *Chem. Commun.*, 1303 (1970).
7. J. F. Bunnett and C. Yijima, *J. Org. Chem.*, **42**, 639 (1977).
8. T. J. Broxton, J. F. Bunnett and C. H. Paik, *J. Org. Chem.*, **42**, 643 (1977).
9. B. Gloor, B. L. Kaul and H. Zollinger, *Helv. Chim. Acta*, **55**, 1596 (1972).
10. G. A. Olah, and J. Welch, *J. Amer. Chem. Soc.*, **97**, 208 (1975).
11. P. Kovacic and J. F. Gormisk, *J. Amer. Chem. Soc.*, **88**, 3819 (1966).
12. J. F. Chlebowski in *Carbonium Ions* (Eds. G. A. Olah and P. von R. Schleyer), Vol. 2, John Wiley and Sons, New York, 1970, p. 700.
13. H. G. Richey, Jr. and J. M. Richey in *Carbonium Ions* (Eds. G. A. Olah and P. von R. Schleyer), Vol. 2, John Wiley and Sons, New York, 1970, p. 923.
14. H. B. Ambroz and T. J. Kemp, *Chem. Soc. Rev.*, **8**, 353 (1979).
15. H. Zollinger, *Accounts Chem. Res.*, **6**, 335 (1973).
16. H. Zollinger, *Angew. Chem. (Intern. Ed. Engl.)*, **17**, 141 (1978).
17. M. L. Crossley, R. H. Kienle and C. H. Benbrook, *J. Amer. Chem. Soc.*, **62**, 1400 (1940).
18. E. S. Lewis and W. H. Hinds, *J. Amer. Chem. Soc.*, **74**, 304 (1952).
19. E. S. Lewis, L. D. Hartung and B. M. McKay, *J. Amer. Chem. Soc.*, **91**, 419 (1969).
20. P. Burri and H. Zollinger, *Helv. Chim. Acta*, **56**, 2204 (1973).
21. P. Burri, G. H. Wahl, Jr. and H. Zollinger, *Helv. Chim. Acta*, **57**, 2099 (1974).
22. D. Schulte-Frohlinde and H. Blume, *Z. Physik. Chem. (Frankfurt)* **59**, 299 (1968).
23. Reference 3, p 523.
24. C. G. Swain, J. E. Sheats and K. G. Harbison, *J. Amer. Chem. Soc.*, **97**, 783 (1975).
25. C. G. Swain and E. C. Lupton, *J. Amer. Chem. Soc.*, **90**, 4328 (1968).
26. T. Kuokkanen and P. O. I. Virtanen, *Acta Chem. Scand.*, **B 33**, 725 (1979).
27. C. G. Swain, J. E. Sheats, D. G. Gorenstein and K. G. Harbison, *J. Amer. Chem. Soc.*, **97**, 791 (1975).
28. C. G. Swain, J. E. Sheats and K. G. Harbison, *J. Amer. Chem. Soc.*, **97**, 796 (1975).
29. A. G. Loudon, A. Maccoll and D. Smith, *J. Chem. Soc., Faraday Trans.*, 899 (1973).
30. Reference 3, p 520–526.
31. R. G. Bergstrom, R. G. M. Landells, G. H. Wahl, Jr. and H. Zollinger, *J. Amer. Chem. Soc.*, **98**, 3301 (1976)
32. I. Szele and H. Zollinger, *J. Amer. Chem. Soc.*, **100**, 2811 (1978).
33. Y. Hashida, R. G. M. Landells, G. E. Lewis, I. Szele and H. Zollinger, *J. Amer. Chem,. Soc.*, **100**, 2816 (1978).
34. J. Maurer, I. Szele and H. Zollinger, *Helv. Chim. Acta*, **62**, 1079 (1979).
35. H. Zollinger, *Chem. Brit.*, **16**, 258 (1980).
36. R. G. Bergstrom, G. H. Wahl, Jr. and H. Zollinger, *Tetrahedron Letters*, 2975 (1974).
37. E. S. Lewis and J. M. Insole, *J. Amer. Chem. Soc.*, **86**, 32, 34 (1964).
38. E. S. Lewis and R. E. Holliday, *J. Amer. Chem. Soc.*, **88**, 5043 (1966).
39. E. S. Lewis and P. G. Kotcher, *Tetrahedron*, **25**, 4873 (1969).
40. A. K. Rose and I. Kugayevsky, *J. Amer. Chem. Soc.*, **88**, 2335 (1966).
41. K. R. Brower, *J. Amer. Chem. Soc.*, **82**, 4535 (1960).
42. S.-Y. Hong, Y.-T. Park and Y.-W. Kwak, *Daehan Hwahae Hwoejel*, **19**, 471 (1975) (Korean J. Chem., in English).
43. R. W. Taft, *J. Amer. Chem. Soc.*, **83**, 3350 (1961).
44. R. A. Abramovitch and F. F. Gadallah, *J. Chem. Soc. (B)*, 497 (1968).
45. R. J. Cox, P. Bushnell and E. M. Evleth, *Tetrahedron Letters*, 209 (1970).
46. M. A. Vincent and L. Radom, *J. Amer. Chem. Soc.*, **100**, 3306 (1978).

47. A. Gamba, M. Simonetta, G. Suffritti, I. Szele and H. Zollinger, *J. Chem. Soc., Perkin Trans. 2*, 493 (1980).
48. N. W. Alcock, T. J. Greenhough, D. M. Hirst, T. J. Kemp and D. R. Payne, *J. Chem. Soc., Perkin Trans. 2*, 8 (1980).
49. I. Szele and H. Zollinger, *Helv. Chim. Acta*, **64**, 2721, 2728 (1981).
50. J. Bargon and K.-G. Seifert, *Tetrahedron Letters*, 2265 (1974).
51. F. Tröndlin, R. Medina and C. Rüchardt, *Chem. Ber.*, **112**, 1835 (1979).
52. M. Hanack and U. Michel, *Angew. Chem.*, **91**, 928 (1979).
53. L. R. Subramanian, M. Hanack, L. W. K. Chang, M. A. Imhoff, P. von R. Schleyer, F. Effenberger, W. Kurtz, P. J. Stang and Th. E. Dueber, *J. Org. Chem.*, **41**, 4099 (1976).
54. A. Streitwieser, Jr. and A. Dafforn, *Tetrahedron Letters*, 1435 (1976).
55. D. E. Horning, D. A. Ross and J. M. Muchowski, *Can. J. Chem.*, **51**, 2347 (1973).
56. M. Stiles and R. G. Miller, *J. Amer. Chem. Soc.*, **82**, 3802 (1960).
57. J. I. G. Cadogan and P. G. Hibbert, *Proc. Chem. Soc.*, 338 (1964).
58. R. W. Hoffman, *Dehydrobenzene and Cycloalkynes*, Academic Press, New York, 1967.
59. R. W. Hoffman in *The Chemistry of Acetylenes* (Ed. H. G. Viehe), Marcel Dekker, New York, 1969.
60. D. S. Wulfman in *The Chemistry of Diazonium and Diazo Groups* (Ed. S. Patai), John Wiley and Sons, London, 1978, p. 305.
61. Reference 3, p. 528.
62. R. W. Franck and K. Yanagi, *J. Amer. Chem. Soc.*, **90**, 5814 (1968).
63. C. Rüchardt and C. C. Tan, *Angew. Chem.*, **90**, 547 (1970).
64. J. I. G. Cadogan, J. R. Mitchell and J. T. Sharp, *Chem. Commun.*, 1 (1971).
65. J. I. G. Cadogan, *Accounts Chem. Res.*, **4**, 186 (1971).
66. D. L. Brydon, J. I. G. Cadogan, J. Cook, M. J. P. Harger and J. T. Sharp, *J. Chem. Soc.(B)*, 1996 (1971).
67. J. I. G. Cadogan, Ch. D. Murray and J. T. Sharp, *J. Chem. Soc., Chem. Commun.*, 133 (1974).
68. J. I. G. Cadogan, Ch. D. Murray and J. T. Sharp, *J. Chem. Soc., Chem. Commun.*, 901 (1974).
69. T. J. Broxton and J. F. Bunnett, *Nouv. J. Chim.*, **3**, 133 (1979).
70. Reference 58, p. 275.
71. C. W. Bird and C. K. Wong, *Tetrahedron Letters*, 2143 (1971).
72. M. Kato, T. Tamano and T. Miwa, *Bull. Chem. Soc. Japan*, **48**, 291 (1975).
73. J. Besse, W. Schwarz and H. Zollinger, *Helv. Chim. Acta*, **64**, 504 (1981).
74. P. Burri, H. Loewenschuss, H. Zollinger and G. K. Zwolinski, *Helv. Chim. Acta*, **57**, 395 (1974).
75. Y. Hirose, G. H. Wahl, Jr. and H. Zollinger, *Helv. Chim. Acta*, **59**, 1427 (1976).
76. K. Ishida, N. Kobori, M. Kobayashi and H. Minato, *Bull. Chem. Soc. Japan*, **43**, 285 (1970).
77. F. Tröndlin and C. Rüchardt, *Chem. Ber.*, **110**, 2494 (1977).
78. C. G. Swain and R. J. Rogers, *J. Amer. Chem. Soc.*, **97**, 799 (1975).
79. I. Szele and H. Zollinger, *Helv. Chim. Acta*, **61**, 1721 (1978).
80. M. Matrka, Z. Ságner, V. Chmátal, V. Štěrba and M. Vesely, *Collect. Czech. Chem. Commun.*, **32**, 1462 (1967).
81. W. Schwarz and H. Zollinger, *Helv. Chim. Acta*, **64**, 513 (1981).
82. J. Besse and H. Zollinger, *Helv. Chim. Acta*, **64**, 529 (1981).
83. I. A. Koppel and A. I. Paju, *Organic Reactivity* (English translation of *Reakts. Sposobnost org. Soedin, Tartu State University*), **11**, 121 (1974).
84. F. L. Schadt, T. W. Bentley and P. von R. Schleyer, *J. Amer. Chem. Soc.*, **98**, 7667 (1976).
85. J. F. Bunnett, D. A. R. Happer and H. Takayama, *Chem. Commun.*, 367 (1966).
86. J. F. Bunnett and D. A. R. Happer, *J. Org. Chem.*, **32**, 2701 (1967).
87. J. F. Bunnett and H. Takayama, *J. Org. Chem.*, **33**, 1924 (1968).
88. J. F. Bunnett and H. Takayama, *J. Amer. Chem. Soc.*, **90**, 5173 (1968).
89. W. J. Boyle, Jr., T. J. Broxton and J. F. Bunnett, *Chem. Commun.*, 1469 (1971).
90. W. J. Boyle, Jr. and J. F. Bunnett, *J. Amer. Chem. Soc.*, **96**, 1418 (1974).
91. T. J. Broxton and D. L. Roper, *J. Org. Chem.*, **41**, 2157 (1976).
92. C. S. Anderson and T. J. Broxton, *J. Org. Chem.*, **42**, 2454 (1977).

93. T. J. Broxton and A. C. Stray, *J. Org. Chem.*, **45**, 2409 (1980).
94. C. D. Ritchie and P. O. I. Virtanen, *J. Amer. Chem. Soc.*, **94**, 1589. (1972).
95. N. A. Porter, L. J. Marnett, C. H. Lochmüller, G. L. Closs and M. Shobataki, *J. Amer. Chem. Soc.*, **94**, 3664 (1972).
96. R. O. C. Norman and B. C. Gilbert, *Advan. Phys. Org. Chem.*, **5**, 74 (1967) and literature cited therein.
97. J. F. Bunnett and C. C. Wamser, *J. Amer. Chem. Soc.*, **88**, 5534 (1966).
98. D. L. Brydon and J. I. G. Cadogan, *J. Chem. Soc. (C)*, 819 (1968).
99. J. P. Griess, *Phil. Trans.*, **164**, 683 (1864).
100. Reference 60, p. 286.
101. H. Zollinger, *Diazo and Azo Chemistry*, Interscience, New York, 1961, p. 57.
102. K. H. Saunders, *The Aromatic Diazo Compounds*, 2nd ed., Arnold, London, 1949, p. 99.
103. W. Schwarz, *Ph.D. Thesis*, ETH Zürich, 1979.
104. M. Matrka, Z. Ságner, V. Chmátal, V. Štěrba and M. Vesely, *Collect. Czech. Chem. Commun.*, **32**, 1462 (1967).
105. C. Macháčková and V. Štěrba, *Collect. Czech. Chem. Commun.*, **36**, 3197 (1971).
106. I. Pikulik, R. U. Weber and H. Zollinger, *Helv. Chim. Acta*, **64**, 1777 (1981).
107. C. Wittwer and H. Zollinger, *Helv. Chim. Acta*, **37**, 1954 (1954).
108. C. Rüchardt and E. Merz, *Tetrahedron Letters*, 2431 (1964).
109. C. Rüchardt and B. Freudenberg, *Tetrahedron Letters*, 3623 (1964).
110. C. Rüchardt, B. Freudenberg and E. Merz, *Chem. Soc., Spec. Publ.*, **19**, 154 (1965).
111. Y. Ishino, T. Hirashima and D. Manabe, *Nippon Kaguku Kaishi*, 968 (1976).
112. A. Rieker, P. Niederer and D. Leibfritz, *Tetrahedron Letters*, 4287 (1969).
113. A. Rieker, P. Niederer and H. B. Stegmann, *Tetrahedron Letters*, 387 (1971).
114. S. Berger, S. Hauff, P. Niederer and A. Rieker, *Tetrahedron Letters*, 2581 (1972).
115. E.-L. Dreher, P. Niederer, A. Rieker, W. Schwarz and H. Zollinger, *Helv. Chim. Acta*, **64**, 488 (1981).
116. T. G. Sterleva, L. A. Kiprianova, A. F. Levit and I. P. Gragerov, *Dokl. Akad. Nauk SSSR*, **219**, 1140 (1974).
117. A. F. Levit, T. G. Sterleva, L. A. Kiprianova and I. P. Gragerov, *Teor. Eksp. Khim.*, **10**, 487 (1974); *Chem. Abstr.*, **81**, 135261d (1974).
118. T. G. Sterleva, L. A. Kiprianova, A. F. Levit and I. P. Gragerov, *Teor. Eksp. Khim.*, **11**, 485 (1975); *Chem. Abstr.*, **83**, 177941x (1975).
119. I. P. Gragerov, A. F. Levit and L. A. Kiprianova, *Tezisy Dokl.-Vses. Konf. 'Polyariz. Yader Elektronov Eff. Magn. Polya Khim. Reakts.'*, 12 (1975); *Chem. Abstr.*, **89**, 196530c (1978).
120. N. A. Porter, J. G. Brenn and G. R. Dubay, *Tetrahedron Letters*, 3363 (1975).
121. K. A. Bilevitch, N. N. Bubnov, B. Ya. Medvedev, O. Yu. Okhlobystin and L. V. Ermanson, *Dokl. Akad. Nauk SSSR*, **193**, 583 (1970).
122. J. Brokken-Zlip and H. van der Bogaert, *Tetrahedron Letters*, 249 (1974).
123. T. V. Leshina, R. Z. Sagdeev, S. M. Shein and Yu. N. Molin, *Kratk. Tezisy-Vses. Soveschch. Probl. Mekk. Geterolititcheskikh Reakts.*, 31, (1974); *Chem. Abstr.*, **85**, 108171a (1975).
124. A. V. Dushkin, Yu. A. Grishin, T. V. Leshina and R. Z. Sagdeev, *Tetrahedron Letters*, 1309 (1977).
125. R. Kaptein and L. Oosterhoff, *Chem. Phys. Letters*, **4**, 195 (1969).
126. G. Closs and A. Trifunac, *J. Amer. Chem. Soc.*, **92**, 2183 (1970).
127. A. F. Levit, L. A. Kiprianova and I. P. Gragerov, *Dokl. Akad. Nauk SSSR*, **213**, 634 (1973).
128. E. Lippmaa, T. Pehk and T. Saluvere, *Ind. Chim. Belg.*, **36**, 1070 (1971).
129. E. Lippmaa, T. Pehk and T. Saluvere, *Org. Mag. Res.*, **5**, 441 (1973).
130. I. P. Gragerov, A. F. Levit, L. A. Kiprianova and A. Buchachenko, *Org. Mag. Res.*, **5**. 445 (1973).
131. N. N. Bubnov, B. Ya Medvedev, L. A. Poljakova, K. A. Bilevitch and O. Y. Okhlobystin, *Org. Mag. Res.*, **5**. 437 (1973).
132. A. F. Levit, A. L. Buchachenko, L. A. Kiprianova and I. P. Gragerov, *Dokl. Akad. Nauk SSSR*, **203**, 628 (1972).
133. K. A. Bilevitch, N. N. Bubnov, N. T. Ioffe, M. A. Kalinkin, O. Y. Okhlobystin and P. V. Petrooskii, *Izv. Akad Nauk SSSR Ser. Khim.*, **8**, 1814 (1971).

134. N. N. Bubnov, K. A. Bilevitch, L. A. Poljakova and O. Y. Okhlobystin, *J. Chem. Soc., Chem. Commun.*, 1058 (1972).
135. H. Sterk and G. Lechner, *Org. Mag. Res.*, **11**, 453 (1978).
136. R. O. Duthaler, H. G. Förster and J. D. Roberts, *J. Amer. Chem. Soc.*, **100**, 4974 (1978).
137. R. Kaptein in *Advan. Free Radical Chemistry*, 5, 319 (1975).
138. E. S. Lewis and H. Suhr, *J. Amer. Chem. Soc.*, **80**, 1367 (1958).
139. M. Yoshito, K. Hamamoto and T. Kubota, *Bull. Chem. Soc. Japan*, **35**, 1723 (1962).
140. J. S. Littler, *Trans. Faraday Soc.*, **59**, 2296 (1963).
141. C. D. Ritchie and D. J. Wright, *J. Amer. Chem. Soc.*, **93**, 2425 (1971).
142. J. Jabelka, O. Macháčková, V. Štěrba and K. Valter, *Collect. Czech. Chem. Commun.*, **38**, 3290 (1973).
143. P. O. I. Virtanen and T. Kuokkanen, *Acta Univ. Ouluensis*, **A53**, Chem. 4, 3 (1977).
144. P. Haberfield, P. M. Block and M. S. Lux, *J. Amer. Chem. Soc.*, **97**, 5804 (1975).
145. V. Gutmann, *Electrochim. Acta*, **21**, 661 (1976).
146. V. Gutmann, *Chimia*, **31**, 1 (1977).
147. H. Loewenschuss, G. H. Wahl, Jr. and H. Zollinger, *Helv. Chim. Acta*, 59, 1438 (1976).
148. R. Pütter, *Angew. Chem.*, **63**, 188 (1951).
149. Reference 101, p. 250.
150. P. Rys and H. Zollinger, *Fundamentals of the Chemistry and Application of Dyes*, John Wiley and Sons, Chichester–New York, 1972, p. 46.
151. M. S. Newman and W. H. Hung, *J. Org. Chem.*, **39**, 1317 (1974).
152. H.-J. Opgenorth and C. Rüchardt, *Justus Liebigs Ann. Chem.*, 1333 (1974).
153. L. A. Kiprianova, A. F. Levit and I. P. Gragerov, *Teor. Eksp. Khim.*, **12**, 219 (1976); *Chem. Abstr.*, **85**, 624lly (1976).
154. R. M. Cooper and M. J. Perkins, *Tetrahedron Letters*, 2477 (1969).
155. H. G. O. Becker, E. Fanghänel and K. Schiller, *Wiss. Z. Tech. Hochsch. Leuna-Merseburg*, **16**, 322 (1974); *Chem. Abstr.*, **82**, 97185t (1975).
156. H. G. O. Becker, *Wiss. Z. Tech. Hochsch. Leuna-Merseburg*, **20**, 253 (1978); *Chem. Abstr.*, **90**, 71379z (1979).
157. H. G. O. Becker, G. Schukat and M. G. Kuzmin, *J. Prakt. Chem.*, **317**, 229 (1975).
158. H. G. O. Becker, R. Ebisch, G. Israel, G. Kroha, W. Kroha, O. Brede and R., Mehnert, *J. Prakt. Chem.*, **319**, 98 (1977).
159. A. F. Levit, L. A. Kiprianova, V. I. Bogillo, M. V. Nekhoroshev, V. B. Panov, I. P. Gragerov and O. Y. Okhlobystin, *Zh. Org. Khim.*, **15**, 1344 (1979).
160. O. Brede, R. Mehnert, W. Naumann and H. G. O. Becker, *Radiochem. Radioanal. Letters*, **39**, 247 (1979); *Chem. Abstr.*, **91**, 132017z (1979).
161. M. Ya. Turkina, A. F. Levit, B. V. Chizhov and I. P. Gragerov, *Zh. Org. Khim.*, **5**, 1238 (1969).
162. Reference 101, p 153.
163. Reference 3, p. 529.
164. Reference 60, p. 293.
165. W. S. M. Grieve and D. H. Hey, *J. Chem. Soc.*, 1797 (1934).
166. D. H. Hey and J. Peters, *J. Chem. Soc.*, 79 (1960).
167. J. I. G. Cadogan, D. A. Roy and D. M. Smith, *J. Chem. Soc. (C)*, 1249 (1966).
168. J. I. G. Cadogan, R. G. M. Landells and J. T. Sharp, *J. Chem. Soc., Chem. Commun.*, 851 (1976).
169. J. Brennan, J. I. G. Cadogan and J. T. Sharp, *J. Chem. Soc., Chem. Commun.*, 851 (1976).
170. L. R. C. Barclay, A. G. Briggs, W. E. Briggs, J. M. Dust and J. A. Gray, *Can. J. Chem.*, **57**, 2172 (1979).
171. D. Sutton, *Chem. Soc. Rev.*, **4**, 443 (1975).
172. F. Minisci, *Accounts Chem. Res.*, **8**, 165 (1975).
173. C. S. Rondestvedt, Jr., *Org. React.*, **24**, 225 (1977).
174. H. N. Niemeyer in *The Chemistry of Diazonium and Diazo Groups* (Ed. S. Patai), John Wiley and Sons, London, 1978, p. 238.
175. W. E. Carroll and F. J. Lalor, *J. Chem. Soc., Dalton*, 1754 (1973).
176. J. K. Kochi, *J. Amer. Chem. Soc.*, **79**, 2942 (1957).
177. Reference 101, p 167.

178. Y. Nakatani, *Tetrahedron Letters*, 4455 (1970).
179. N. Ganushchak, V. D. Golik and I. V. Migaichuk, *Zh. Org. Khim.*, **8**, 2356 (1972); *Chem. Abstr.*, **78**, 123556d (1972).
180. V. B. Shur, E. G. Berkovich and M. E. Vol'pin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2358 (1971).
181. M. E. Vol'pin, *Pure Appl. Chem.*, **30**, 607 (1972).
182. Reference 174, p. 240, 242.
183. K. Kikukawa and T. Matsuda, *Chem. Letters*, 159 (1977).
184. K. Kikukawa, K. Nagira, N. Terao, F. Wada and T. Matsuda, *Bull. Chem. Soc. Japan*, **52**, 2609 (1979).
185. K. Kikukawa, K. Nagira, F. Wada and T. Matsuda, unpublished results.
186. A. Scheonberg, I. Bartoletti and R. F. Heck, *J. Org. Chem.*, **39**, 3318 (1974).
187. R. F. Heck, *Pure Appl. Chem.*, **50**, 691 (1978).
188. R. F. Heck, *Accounts Chem. Res.*, **12**, 146 (1979).
189. K. Nagira, K. Kikukawa, F. Wada and T. Matsuda, *J. Org. Chem.*, **45**, 2365 (1980).
190. H. G. O. Becker and G. Schukat, quoted in Reference 156.
191. L. L. Bagal, N. O. Stepanov, T. D. Belik and A. V. El'Zoo, *Zh. Org. Khim.*, **1**, 1744 (1974).
192. J. A. Kochi, *J. Amer. Chem. Soc.*, **77**, 2208 (1955).
193. D. Rehm and A. Weller, *Ber. Bunsen-Ges. Phys. Chem.*, **73**, 229 (1975).
194. Reference 60, p 247.
195. Reference 101, p. 221.
196. T. Cohen, A. G. Dietz, Jr. and J. R. Miser, *J. Org. Chem.*, **42**, 2053 (1977).
197. J. G. Erickson, P. F. Wiley and V. P. Wystrach in *The 1,2,3- and 1,2,4-Triazines, Tetrazines and Pentazines: The Chemistry of Heterocyclic Compounds*, Vol. 10 (Ed. A. Weissberger), Interscience, New York, 1956, Chap. 1.
198. G. T. Morgan and E. D. Evans, *J. Chem. Soc.*, **116**, 1126 (1919).
199. L. Benati and P. C. Montevecchi, *J. Org. Chem.*, **42**, 2025 (1977).
200. P. H. Leake, *Chem. Rev.*, **56**, 27 (1956).
201. D. F. DeTar, *Org. React.*, **9**, 409 (1957).
202. A. H. Lewin and T. Cohen, *J. Org. Chem.*, **32**, 3844 (1967).
203. G. Balz and G. Schiemann, *Chem. Ber.*, **60**, 1186 (1927).
204. Reference 60, p. 288.
205. C. Sellers and H. Suschitzky, *J. Chem. Soc. (C)*, 2317 (1968).
206. P. N. Juri and R. A. Bartsch, *J. Org. Chem.*, **45**, 2028 (1980).
207. C. G. Swain and R. J. Rogers, *J. Amer. Chem. Soc.*, **97**, 799 (1975).
208. H. G. O. Becker and G. Israel, *J. Prakt. Chem.*, **321**, 579 (1979).
209. I. Stepitis, *Zh. Vses. Khim. O-va.*, **24**, 200 (1979); *Chem. Abstr.*, **91**, 19177p (1979).
210. Reference 60, p 289.
211. H. H. Hodgson, *Chem. Rev.*, **40**, 251 (1947).
212. G.-J. Meyer, K. Rössler and G. Stöcklin, *J. Amer. Chem. Soc.*, **101**, 3121 (1979).
213. G.-J. Meyer, K. Rössler and G. Stöcklin, *J. Labelled Comp. Radiopharm.*, **22**, 449.
214. A. M. Friedman, M. R. Zalutsky, W. Wung, F. Buckingham, P. V. Harper, G. H. Scherr, B. Wainer, R. L. Hunter, E. H. Appelman, R. M. Rothberg, F. W. Fitch, F. P. Stuart and S. J. Simonian, *Intern. J. Nucl. Med. Biol.*, **4**, 219 (1977).
215. K. Kikukawa, K. Kono, K. Nagira, F. Wada and T. Matsuda, *Tetrahedron Letters*, 2877 (1980).
216. R. Adams and N. Kornblum, *J. Amer. Chem. Soc.*, **63**, 144 (1941).
217. N. Kornblum, *Organic Reactions*, Vol. 2, John Wiley and Sons, New York, 1944, p. 262.
218. N. Kornblum and A. E. Kelley, *Science*, **117**, 379 (1953).
219. A. F. Levit, L. A. Kiprianova and I. P. Gragerov, *Dokl. Akad. Nauk SSSR*, **213**, 634 (1973).
220. A. F. Levit, L. A. Kiprianova and I. P. Gragerov, *Zh. Org. Khim.*, **11**, 2351 (1975).
221. T. Shono, Y. Matsumura and K. Tsubata, *Chem. Letters*, 1051 (1979).
222. G. W. Gokel and D. J. Cram, *J. Chem. Soc., Chem. Commun.*, 481 (1973).
223. C. Rüchardt and C. C. Tan, *Chem. Ber.*, **103**, 1774 (1970).
224. Reference 101, p. 53.
225. Y. M.. Nesterova and M. A. Porai-Koshits, *Zh. Strukt. Khim.*, **12**, 108 (1971); *Chem. Abstr.*, **75**, 11677a (1971).

226. R. Barraclough, F. Jones, D. Patterson and A. Tetlow, *J. Soc. Dyers Colourists*, **88**, 22 (1972).
227. Reference 101, p. 175.
228. S. Koller and H. Zollinger, *Helv. Chim. Acta*, **53**, 78 (1970).
229. P. Bersier, L. Valpiana and H. Zubler, *Chemie-Ingenieur-Technik*, **43**, 1311 (1971).
230. R. H. de Rossi, H. E. Bertorello and R. A. Rossi, *J. Org. Chem.*, **35**, 3328 (1970).
231. H. E. Bertorello, R. A. Rossi and R. H. de Rossi, *J. Org. Chem.*, **35**, 3332 (1970).
232. R. A. Bartsch, H. Chen, N. F. Haddock and P. N. Juri, *J. Amer. Chem. Soc.*, **98**, 6753 (1976).
233. R. A. Bartsch, this volume, Chap. 21.
234. R. A. Bartsch, N. F. Haddock and D. W. McCann, *Tetrahedron Letters*, 3779 (1977).
235. W. A. Sheppard, G. W. Gokel, O. W. Webster, K. Betterton and J. W. Timberlake, *J. Org. Chem.*, **44**, 1717 (1979).
236. R. A. Bartsch and P. N. Juri, *J. Org. Chem.*, **45**, 1011 (1980).
237. (a) Y. Hashida and K. Matsui, *Bull. Chem. Soc. Japan*, **53**, 551 (1980).
(b) H. Nakazumi, I. Szele and H. Zollinger, *Tetrahedron Letters*, 3053 (1981).
238. R. A. Bartsch, P. N. Juri and M. A. Mills, *Tetrahedron Letters*, 2499 (1979).
239. R. A. Bartsch and I. W. Yang, *Tetrahedron Letters*, 2503 (1979).
240. O. Bohman, P. Ahlberg, R. Nyholm, N. Martensson, K. Siegbahn and R. A. Bartsch, *J. Chem. Res. (S)*, 292 (1979).
241. M. S. Dinaberg, *Photosensitive Diazo Chemistry*, Focal Press, London, 1964, Chap. 5.
242. P. Pinot de Moira, *J. Photographic Sci.*, **22**, 187 (1974).
243. W. Ando in *The Chemistry of Diazonium and Diazo Groups* (Ed. S. Patai), John Wiley and Sons, London, 1978, p. 341.
244. E. S. Lewis, R. E. Holliday and L. D. Hartung, *J. Amer. Chem. Soc.*, **91**, 430 (1969).
245. E. S. Lewis and L. D. Hartung, *J. Amer. Chem. Soc.*, **91**, 426 (1969).
246. Reference 243, p. 359.
247. W. E. Lee, J. G. Calvert and E. W. Malmberg, *J. Amer. Chem. Soc.*, **83**, 1928 (1961).
248. J. E. Packer, D. B. House and E. J. Rasburn, *J. Chem. Soc. (B)*, 1574 (1971).
249. G. V. Fomin, P. I. Mordvintsev, R. A. Mkhitarov and T. A. Gordina, *Zh. Fiz. Khim.*, **54**, 238 (1980); *Chem. Abstr.*, **92**, 197571r (1980).
250. G. V. Fomin, P. I. Mordvintsev, R. A. Mkhitarov and T. A. Gordina, *Zh. Fiz. Khim.*, **54**, 240 (1980); *Chem. Abstr.*, **92**, 180328u (1980).
251. G. V. Fomin, P. I. Mordvintsev, R. A. Mkhitarov and T. A. Gordina, *Zh. Fiz. Khim.*, **54**, 242 (1980); *Chem. Abstr.*, **92**, 180329v (1980).
252. H. G. O. Becker, D. Pfeifer and R. Radeglia, *Z. Chem.*, **17**, 439 (1977).
253. A. Cox, T. J. Kemp, D. R. Payne, M. C. R. Symons, D. M. Allen and P. Pinot de Moira, *J. Chem. Soc., Chem. Commun.*, 693 (1976).
254. G. F. Koser, *J. Org. Chem.*, **42**, 1474 (1977).
255. H. G. O. Becker, G. Hoffmann and G. Israel, *J. Prakt. Chem.*, **319**, 1021 (1977).
256. H. Baumann, H. G. O. Becker and S. Thiele, *J. Prakt. Chem.*, **319**, 140 (1977).
257. (a) J. E. Packer, R. K. Richardson, P. J. Soole and D. R. Webster, *J. Chem. Soc., Perkin Trans. 2*, 1472 (1974).
(b) S. I. Schlesinger, *Photographic Sci. Eng.*, **18**, 387 (1974).
(c) G. E. Green and P. B. Stark, *Chem. Brit.*, **17**, 228 (1981).
258. T. Tsunoda and T. Yamaoka, *Chiba Daigaku Kogakubu Kenkyn Hokoku*, **19**, 129 (1968) (Chemical Research Proceedings of the Chiba University, in English).
259. M. F. Mizianty, E. A. Fitzgerald and G. H. Kimber, *Photographic Sci. Eng.*, **15**, 331 (1971).
260. M. Tsuda and S. Oikawa, *Photographic Sci. Eng.*, **23**, 177 (1979).
261. J. F. McGarrity in *The Chemistry of Diazonium and Diazo Groups* (Ed. S. Patai), John Wiley and Sons, London, 1978, p. 179.
262. Reference 60, p. 297.
263. A. J. Fry in *The Chemistry of Diazonium and Diazo Groups* (Ed. S. Patai), John Wiley and Sons, London, 1978, p. 489.
264. D. S. Wulfman, G. Linstrumelle and C. F. Cooper in *The Chemistry of Diazonium and Diazo Groups* (Ed. S. Patai), John Wiley and Sons, London, 1978, p. 821.
265. Reference 3, p. 572.
266. D. Berner and J. F. McGarrity, *J. Amer. Chem. Soc.*, **101**, 3135 (1979).

267. J. R. Mohrig and K. Keegstra, *J. Amer. Chem. Soc.*, **89**, 5492 (1967).
268. J. R. Mohrig, K. Keegstra, A. Maverick, R. Roberts and S. Wells, *J. Chem. Soc., Chem. Commun.*, 780 (1974).
269. M. Avaro, J. Levisalles and J. M. Sommer, *J. Chem. Soc., Chem. Commun.*, 410 (1968).
270. D. Y. Curtin, B. H. Klanderman and D. F. Tavares, *J. Org. Chem.*, **27**, 2709 (1962).
271. M. S. Foster and J. L. Beauchamp, *J. Amer. Chem. Soc.*, **94**, 2425 (1972).
272. W. Kirmse, *Angew. Chem. (Intern. Ed. Engl.)*, **15**, 251 (1976).
273. I. P. Fisher, T. F. Palmer and F. P. Lossing, *J. Amer. Chem. Soc.*, **86**, 2741 (1964).
274. B. Brehm, *Z. Naturforsch.*, **21a**, 196 (1966).
275. P. Demontis, R. Ercoli, A. Gamba, G. B. Suffritti and M. Simonetta, *J. Chem. Soc., Perkin Trans. 2*, 488 (1981).
276. C. E. McCauley and C. V. King, *J. Amer. Chem. Soc.*, **74**, 6221 (1952).
277. H. Dahn and H. Gold, *Helv. Chim. Acta*, **46**, 983 (1963).
278. R. Malherbe and H. Dahn, *Helv. Chim. Acta*, **57**, 2492 (1974).
279. W. J. Albery and R. P. Bell, *Trans. Faraday Soc.*, **57**, 1942 (1961).
280. W. J. Albery, J. E. C. Hutchins, R. M. Hyde and R. H. Johnson, *J. Chem. Soc. (B)*, 219 (1968).
281. B. Zwanenburg and J. B. F. N. Engberts, *Rec. Trav. Chim.*, **84**, 165 (1965).
282. J. B. F. N. Engberts and B. Zwanenburg, *Tetrahedron*, **24**, 1737 (1968).
283. J. B. F. N. Engberts, G. Zuidema, B. Zwanenburg and J. Strating, *Rev. Trav. Chim.*, **88**, 641 (1969).
284. H. Dahn and J. H. Lenoir, *Helv. Chim. Acta*, **62**, 2218 (1979).
285. J. B. F. N. Engberts, N. F. Bosch and B. Zwanenburg, *Rec. Trav. Chim.*, **85**, 1068 (1966).
286. W. Jugelt and L. Berseck, *Z. Chem.*, **6**, 420 (1966).
287. W. Jugelt and D. Schmidt, *Tetrahedron Letters*, 985 (1967).
288. W. Jugelt and L. Berseck, *Tetrahedron Letters*, 2659 (1968).
289. W. Jugelt and L. Berseck, *Tetrahedron Letters*, 2665 (1968).
290. H. Dahn, H. Gold, M. Ballenegger, J. H. Lenoir, G. Diderich and R. Malherbe, *Helv. Chim. Acta*, **51**, 2065 (1968).
291. H. Dahn and M. Ballenegger, *Helv. Chim. Acta*, **52**, 2417 (1969).
292. W. J. Albery, A. N. Campbell-Crawford and K. S. Hobbs, *J. Chem. Soc., Perkin Trans. 2*, 2180 (1972).
293. J. D. Roberts and C. M. Regan, *J. Amer. Chem. Soc.*, **74**, 3695 (1952).
294. R. A. More O'Ferrall, W. K. Kwok and S. I. Miller, *J. Amer. Chem. Soc.*, **86**, 5553 (1964).
295. H. Dahn and G. Diderich, *Helv. Chim. Acta*, **54**, 1950 (1971).
296. J. F. McGarrity and T. Smyth, *J. Chem. Soc., Chem. Commun.*, 347 (1977).
297. M. M. Kreevoy and S. J. Thomas, *J. Org. Chem.*, **42**, 3979 (1977).
298. M.-H. Bui-Nguyen, H. Dahn and J. F. McGarrity, *Helv. Chim. Acta*, **63**, 63 (1980).
299. J. F. McGarrity, *Helv. Chim. Acta*, **63**, 1767 (1980).
300. W. J. Albery, *Progr. React. Kinetics*, **4**, 355 (1967).
301. V. Gold, *Advan. Phys. Org. Chem.*, **7**, 259 (1969).
302. G. Diderich and H. Dahn, *Helv. Chim. Acta*, **55**, 1 (1972).
303. J. F. McGarrity, D. P. Cox and J. Prodolliet, *IUPAC Conference on Physical Organic Chemistry, Santa Cruz*, 1980.
304. J. F. McGarrity and T. Smyth, *J. Amer. Chem. Soc.*, **102**, 7303 (1980).
305. C. Wentrup and H. Dahn, *Helv. Chim. Acta*, **53**, 1637 (1970).
306. H. Dahn, B. Favre and J.-P. Leresche, *Helv. Chim. Acta*, **56**, 457 (1973).
307. T. Ibata, K. Miyauchi and S. Nakata, *Bull. Chem. Soc. Japan*, **52**, 3467 (1979).
308. W. Kirmse and H. Arnold, *Chem. Ber.*, **103**, 3722 (1970).
309. W. J. Baron and W. Kirmse, quoted in Reference 272.
310. C. G. Swain and C. B. Scott, *J. Amer. Chem. Soc.*, **75**, 141 (1953).
311. G. Fierz, J. F. McGarrity and H. Dahn, *Helv. Chim. Acta*, **58**, 1058 (1975).
312. K. Clusius and H. Hürzeler, *Helv. Chim. Acta*, **37**, 798 (1954).
313. K. Clusius and M. Vecchi, *Helv. Chim. Acta*, **39**, 1469 (1956).
314. R. Huisgen and I. Ugi, *Angew. Chem.*, **68**, 705 (1956).
315. I. Ugi, R. Huisgen, K. Clusius and M. Vecchi, *Angew. Chem.*, **68**, 753 (1956).
316. R. Huisgen and I. Ugi, *Chem. Ber.*, **90**, 2914 (1957).
317. W. Kirmse, W. J. Baron and U. Seipp, *Angew. Chem. (Intern. Ed. Engl.)*, **12**, 924 (1973).

318. W. Kirmse, O. Schnurr and H. Jendralla, *Chem. Ber.*, **112**, 2120 (1979).
319. W. Kirmse and G. Rauleder, *Justus Liebigs Ann. Chem.*, 1333 (1976).
320. R. A. Moss and C. J. Talkowski, *Tetrahedron Letters*, 703 (1971).
321. R. A. Moss, C. J. Talkowski, D. W. Reger and C. E. Powell, *J. Amer. Chem. Soc.*, **95**, 5215 (1973).
322. B.-R. Günther and W. Kirmse, *Justus Liebigs Ann. Chem.*, 518 (1980).
323. D. J. Beames, T. R. Klose and L. N. Mander, *J. Chem. Soc., Chem. Commun.*, 773 (1971).
324. R. Malherbe, N. T. T. Tam and H. Dahn, *Helv. Chim. Acta*, **55**, 245 (1972).
325. W. Kirmse and F. Scheidt, *Angew. Chem. (Intern. Ed. Engl.)*, **10**, 263 (1971).
326. W. Kirmse and H. Jendralla, *Chem. Ber.*, **111**, 1857 (1978).
327. W. Kirmse and H. Jendralla, *Chem. Ber.*, **111**, 1873 (1978).
328. W. Kirmse and U. Richarz, *Chem. ber.*, **111**, 1883 (1978).
329. W. Kirmse and U. Richarz, *Chem. Ber.*, **111**, 1895 (1978).
330. C. Wentrup, *Reaktive Zwischenstufen*, Georg Thieme Verlag, Stuttgart, 1979, p. 140.
331. H. Dürr, *Topics Curr. Chem.*, **55**, 87 (1975).
332. C. B. Moore and G. C. Pimentel, *J. Chem. Phys.*, **41**, 3504 (1964).
333. Y. G. Borodko, A. E. Shilov and A. A. Shteinmann, *Dokl. Akad. Nauk SSSR*, **168**, 581 (1966).
334. Reference 330, p. 157.
335. V. P. Semenov, A. N. Sutdenikov, A. D. Bespalov and K. A. Oglbin, *Zh. Org. Khim.*, **13**, 2202 (1977); *Chem. Abstr.*, **88**, 49962a (1978).
336. H. Takeuchi, T. Igura, M. Mitani, T. Tsuchida and K. Koyama, *J. Chem. Soc., Perkin Trans.2*, 783 (1978).
337. N. Filipescu and J. R. DeMember, *Tetrahedron*, **24**, 5181 (1968).
338. T. Oshima, A. Yoshioka and T. Nagi, *Tetrahedron Letters*, 1789 (1977).
339. T. Oshima and T. Nagai, *Tetrahedron Letters*, 3715 (1977).
340. D. J. Cardin, B. Cetinkaya, M. J. Doyle and M. F. Lappert, *Chem. Soc. Rev.*, **2**, 99 (1973).
341. D. Bethell and M. F. Eeles, *J. Chem. Soc., Perkin Trans. 2*, 704 (1974).
342. D. Bethell, K. L. Handoo, S. A. Fairhurst and L. H. Sutcliffe, *J. Chem. Soc., Chem. Commun.*, 326 (1977).
343. D. Bethell, K. L. Handoo, S. A. Fairhurst and L. H. Sutcliffe, *J. Chem. Soc., Perkin Trans. 2*, 707 (1979).
344. D. Bethell, M. F. Eeles and K. L. Handoo, *J. Chem. Soc., Perkin Trans. 2*, 714 (1979).
345. D. Bethell and K. C. Brown, *J. Chem. Soc., Perkin Trans. 2*, 895 (1972).
346. D. Bethell and R. McKeivor, *J. Chem. Soc., Perkin Trans. 2*, 327 (1977).
347. F. M. Beringer, J. A. Farr and S. Sands, *J. Amer. Chem. Soc.*, **75**, 3984 (1953).
348. J. M. Bakke, D. Bethell, P. J. Galsworthy, K. L. Handoo and D. Jackson, *J. Chem. Soc., Chem. Commun.*, 890 (1979).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 16

Alkenediazonium compounds

KASPAR BOTT
Hauptlaboratorium der BASF Aktiengesellschaft, D-6700 Ludwigshafen, Federal Republic of Germany

I. INTRODUCTION

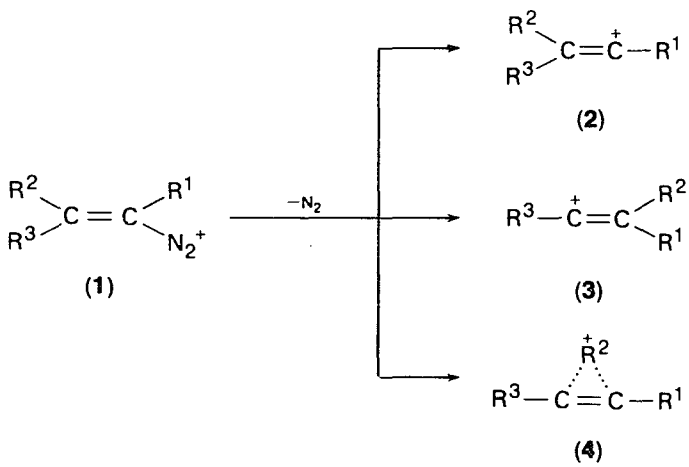
Since their discovery by Griess in 1858[1], aromatic diazonium compounds have acquired considerable importance in theoretical, synthetic and industrial chemistry[2,3]. Until a few years ago, their aliphatic analogues, the alkenediazonium salts, were considered to exist only as short-lived intermediates which could not be isolated because of their great instability, although in numerous reactions their occurrence has

been established by the products which were expected to arise from the loss of nitrogen (see Section III.B). During the last decade, a series of stable alkenediazonium salts has been synthesized, with the result that compounds of this kind are available for extensive research of their physical and chemical properties.

Among several reasons why previous approaches to the preparation of olefindiazonium salts have failed, two stand out: (*a*) alkenediazonium compounds exhibit a remarkably strong dependence of thermal stability on structure, and (*b*) they display an especially high reactivity toward nucleophilic agents.

A. Thermal Stability

As compared to the arenediazonium ions, alkenediazonium ions (**1**) can more easily eliminate nitrogen to form linear vinyl cations (**2**) the carbon skeleton of which is free from bent σ bonds. In such a process, the generation of **2** is considerably enhanced by substituents that are able to stabilize a carbocation. This includes both the concerted migration of β substituents to afford the energetically favoured species **3** and the formation of bridged ions **4** (e.g. thiirenium ions) according to Scheme 1.



SCHEME 1

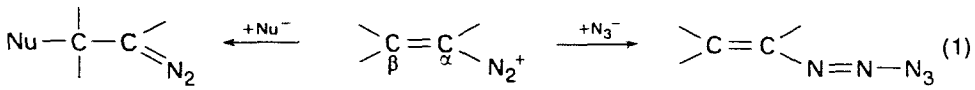
On the other hand, the incorporation of the carbon–carbon double bond in a five- or six-membered ring can lead to alkenediazonium ions in which the tendency to lose nitrogen is strongly suppressed. In these ions (**5**), similarly to the arenediazonium ions,

(**5**) (**6**)

the elimination of nitrogen can no longer produce a vinyl cation with colinear σ bonds. In addition, the alkenediazonium ions (**1**) become essentially more stable, when electron-donating substituents at the β carbon are capable of displaying a resonance with the diazonium group (e.g. in **6**).

B. Reactivity toward Nucleophilic Agents

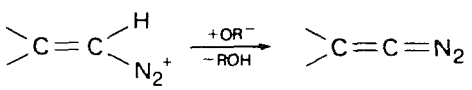
Arenediazonium ions are known to undergo nucleophilic displacement reactions in the *ortho* or *para* position which proceed under relatively mild conditions[4]. Therefore, the corresponding addition of nucleophilic agents to the carbon–carbon double bond of alkenediazonium ions is expected to have a very low activation energy. In full agreement with this expectation, the alkenediazonium ions having lifetimes long enough to permit isolation can exist only with the anions of very strong acids (see Section III.A). In the reaction of alkenediazonium ions (**7**) with nucleophilic agents, the latter ones prefer to attack the β carbon of **7** instead of azo coupling (equation 1).



(1)

(**7**) (**8**)

Among several investigated anions, only the azide anion has been found to couple with the terminal nitrogen of **7** (see Section III.B) forming a short-lived diazoazide (**8**). When primary olefindiazonium ions (**9**) are opposed to the action of basic agents such as alkoxide ions, the generation of the unstable α-diazoalkenes (**10**) will become a



(**9**) (**10**)

predominant process. However, the presence of electron-releasing substituents in the β position of alkenediazonium ions causes a striking rate deceleration in all reactions shown above.

II. SYNTHESIS OF ALKENEDIAZONIUM SALTS

A. Diazonium Salts from α-Diazocarbonyl Compounds

At the turn of century, Wolff[5] and Staudinger[6] were able to show that α-diazo-β-dicarbonyl compounds could be dissolved in cold sulphuric acid without decomposition. However, subsequent attempts[7] to isolate the protonation products assumed to be present in such solutions were unsuccessful.

A kinetic study of the decomposition of diazomalonic ester with chlorosulphonic acid or methylsulphuric acid suggested the formation of a diazonium salt similar to **12**, which decomposes according to a first-order rate law with the elimination of nitrogen[8]. As demonstrated by Figure 1, the rate of nitrogen evolution is largely independent both of the concentration and the strength of acid used in excess. Analogous measurements with α-diazo-β-disulphones have shown that, at the same temperature and concentration, chlorosulphonic acid reacts about 3000 times more rapidly than methylsulphuric acid[9].

Dissolution of hydrogen chloride, antimony pentachloride and methyl benzoyldiazoacetate, or benzoyldiazoacetone, or benzoyldiazoacetophenone in dichloromethane affords crystalline salts **12** of hexachloroantimonic acid with diazo compounds **11**[10] (equation 2). The colourless salts **12** contain diazonium ions derived from the enolic form of a β-oxo ester or a β-diketone. Because of the low vapour pressure of HCl, it can be assumed that these hydroxyalkenediazonium ions have the *cis* configuration, with a strong intramolecular hydrogen bond[11]. The thermal stability

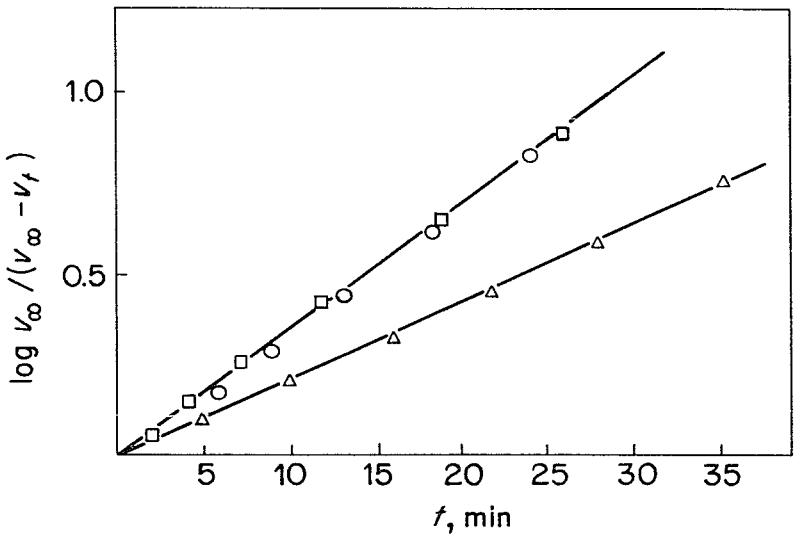
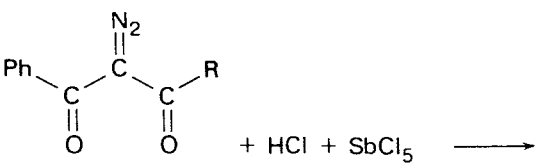
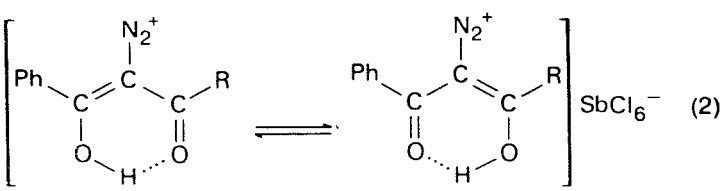


FIGURE 1. Decomposition of diazomalonic ester at 16°C in 1,2-dichloroethane (0.020 mol l^{-1})) with chlorosulphonic acid (△, 0.242 mol l^{-1}) or methylsulphuric acid (○, 0.238 mol l^{-1}; □, 0.443 mol l^{-1}).



(11)

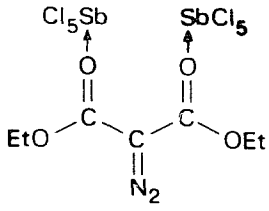


(2)

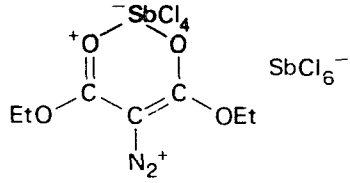
(12)

R	Yield (%)	Decomposition temperature (°C)
OCH_3	81	114
CH_3	92	97
C_6H_5	96	116

of the salts **12** is remarkable; their chemical behaviour is determined largely by the acidic character. Thus, the action of triethylamine leads to complete deprotonation and regenerates the α-diazo-β-dicarbonyl compounds **11**. In the presence of hydrogen chloride and antimony pentachloride, diazomalonic ester does not add a proton, but reacts with two molecules of the Lewis acid. Regarding the two structural possibilities, namely an addition complex (**13**) or a diazonium chelate (**14**) with salt character,

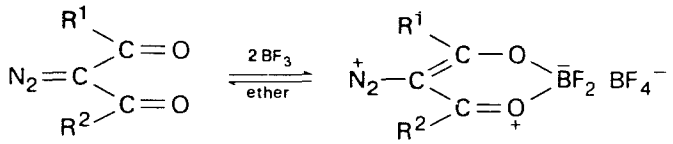


(13)



(14)

measurement of the electrical conductivity in liquid sulphur dioxide provides convincing evidence in favour of **14**. Furthermore, boron trifluoride also combines with dicarbonyl diazo compounds to form 2:1 addition products for which Fahr and Hörmann proposed a structure analogous to the complex **13**[7]. However, recent investigations of the ^{1}H- and ^{19}F-NMR spectra have established that the products resulting from the reaction of open-chain α-diazo-β-dicarbonyl compounds (**15**) and boron trifluoride must be considered as BF_2-chelate diazonium tetrafluoroborates (**16**)[12]. The salts **16** are decomposed by the interaction with nucleophiles such as ether yielding the starting materials **15**.



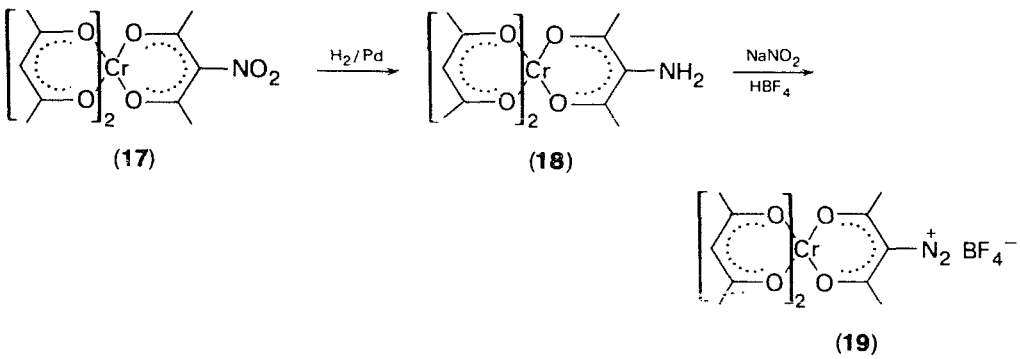
(15) **(16)**

R^1	R^2
Me	Me
Me	Ph
Ph	Ph

The preparation of the chromium chelate diazonium salt (**19**) with a remarkably great complex stability has been accomplished by Collman[13] according to Scheme 2. Herein, the readily accessible mononitrochromium acetylacetonate (**17**) was reduced to the chelate amine (**18**) which could be transformed into the stable chelate diazonium fluoroborate (**19**). The complex **19** resembles the arenediazonium salts with respect to some replacement reactions of the diazonium group.

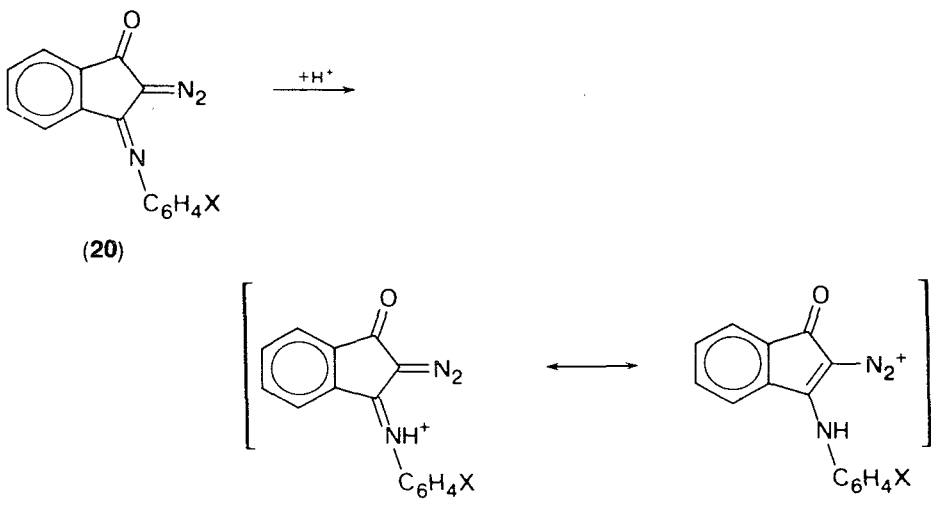
The more strongly basic imines (**20**) of 2-diazo-1,3-indanediones are protonated in ethanol/water by mineral acids yielding salts of type **21**, whose properties are in agreement with the two resonance structures, viz. diazoimonium ion and aminoalkenediazonium ion[14].

The conversion of α-diazomonoketones (**23**) into stable enoldiazonium ions (**22**) can only be achieved in superstrong acids such as $HF/SbF_5/SO_2$ or $FSO_3H/SbF_5/SO_2$



(17) (18) (19)

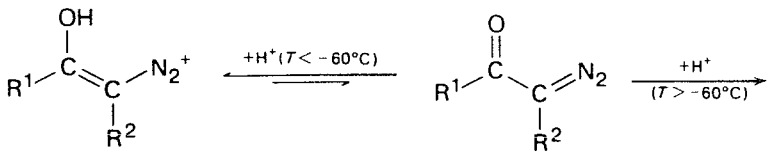
SCHEME 2



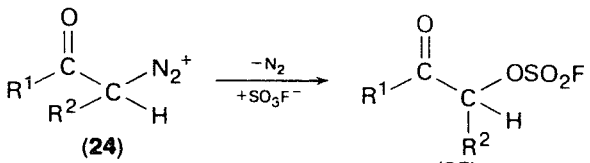
(20) (21)

X = H, *p*-Cl, NO_2, Me, I, OMe

mixtures, provided that the temperature does not exceed −60°C[15,16]. At higher temperatures the deprotonation of **22** becomes a more important process. Formation of a *C*-protonated alkanediazonium ion (**24**) gives rise to the elimination of nitrogen. The products resulting from the decomposition of **23** with fluorosulphonic acid were shown to have the fluorosulphonate structure **25**[16]. In Scheme 3, the reaction step **23** → **24** has been confirmed to be irreversible. This behaviour contrasts with the acidolysis of **23** in aqueous solutions[17,18]. Unlike α-diazo ketones (**23**), α-diazo esters are unable to undergo *O*-protonation in strong acidic media without being decomposed[16], even at very low temperatures. Nevertheless, the alkylation of both diazoacetic ester (**26**) and *p*-nitrophenyldiazoacetic acid piperidide (**28**) with triethyloxonium hexachloroantimonate affords the isolable diazonium salts **27** and **29**, which can also be regarded as oxonium or as imonium compounds[10]. In **27** and **29**, fixation of the ethyl cation seems to be very strong, because the interaction of tertiary phosphine or alkyl sulphide fails to regenerate the diazo compounds **26** and **28**, respectively. As compared to their precursors **26** and **28**, the ions **27** and **29** are less sensitive to acids but more reactive toward base agents.



(22) (23)

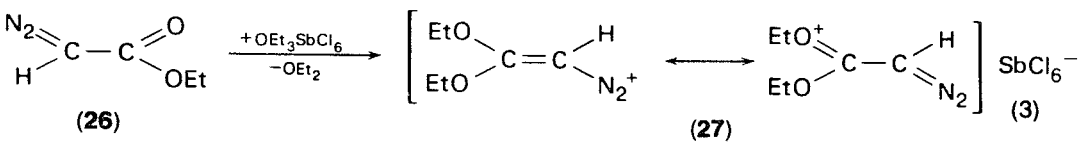


(24) (25)

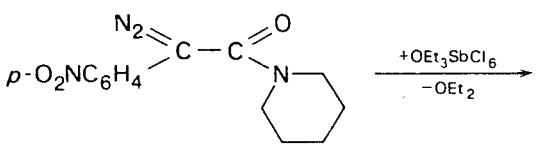
R^1 = Me, Ph, *p*-$MeOC_6H_4$

R^2 = H, Me

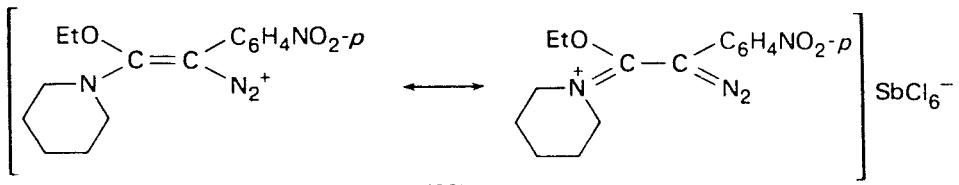
SCHEME 3



(26) (27) (3)



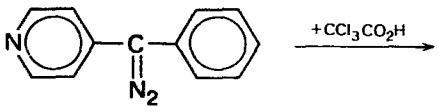
(28)



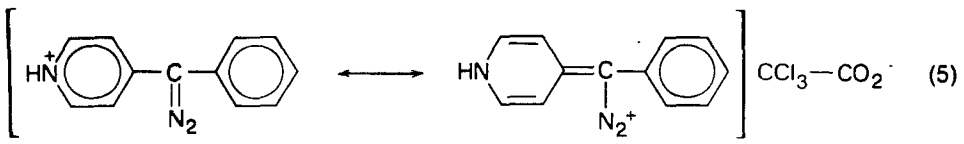
(29) (4)

Another example of the protonation of an aliphatic diazoalkane to yield the stable diazonium salt **31** is shown by reaction (5)[19]. However, the IR spectrum of **31** obviously reveals that in the ground state the resonance form **B** does only contribute to a small extent.

The diazonium ions described in this section originate from the addition of cations to aliphatic diazo compounds. Although claimed as olefindiazonium salts, all these substances display ability to adopt another resonance form with a positively charged oxygen or nitrogen (from amino groups). In addition, when carbonyl diazo compounds are transformed into ions, the frequencies of the respective N—N stretching vibrations



(30)



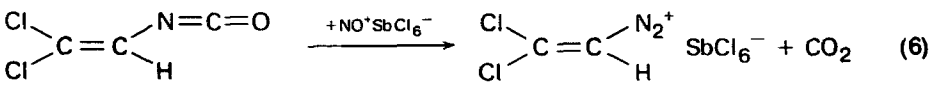
(31) (5)

are shifted to shorter wavelengths. The magnitude of this frequency shift and the position of the diazo absorption band provide a simple means of estimating the approach to a real nitrogen–nitrogen triple bond (see Section IV).

B. Diazonium Salts from Isocyanates and Sulphinylamines

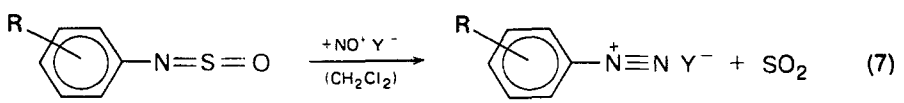
The crucial point in developing the syntheses of ethylenediazonium salts without noticeable resonance stabilization was the observation that **27** is resistant to acetic acid at room temperature but loses nitrogen spontaneously with methanol. Consequently, olefindiazonium ions bearing no substituents such as alkoxy or amino groups at C_β are expected to react rapidly with nucleophiles more weakly basic than alcohols and water.

On the basis of such conclusions, the synthesis of the 2,2-dichloroethylene diazonium hexachloroantimonate (**33**) was achieved by the action of nitrosyl hexachloroantimonate on **32**[20] (equation 6). It still remains to be established whether



(32) (33) (6)

other vinyl isocyanates are also suitable for this reaction. The analogous conversion of aryl sulphinylamines (**34**) into arenediazonium salts (**35**) and sulphur dioxide according to equation (7)[21] should provide another pattern for the preparation of alkenediazonium ions. But in this case, the appropriate starting materials, i.e. the vinylsulphinylamines are still unknown.

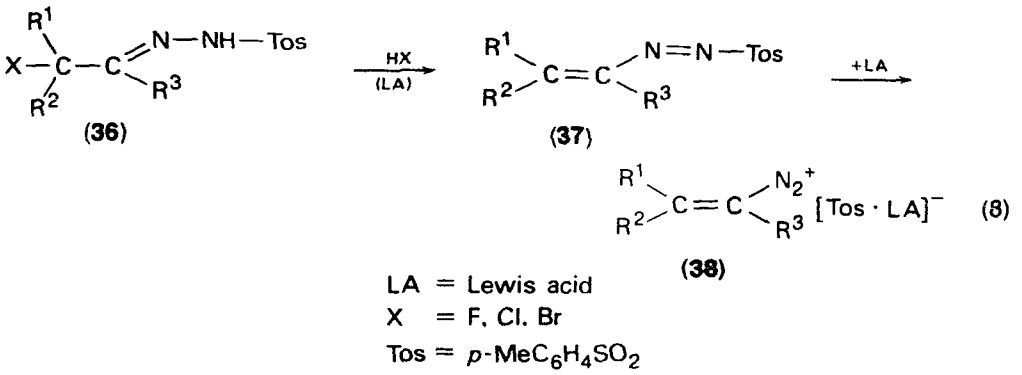


(34) (35) (7)

R = *p*-Cl, *p*-O_2N, *m*-O_2N
Y = $SbCl_6$, ClO_4

C. Alkenediazonium Salts from Sulphonylhydrazones

The action of Lewis acids on the *p*-toluenesulphonylhydrazones (**36**) of α-halo aldehydes or ketones gives a simple and efficient synthesis of alkenediazonium salts



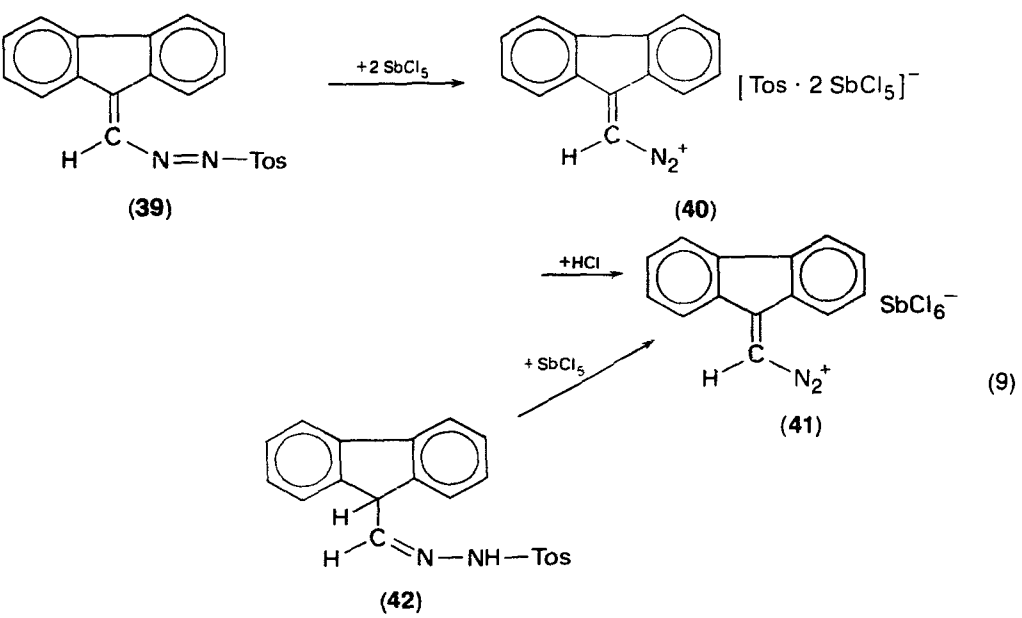
(36) (37) (38)

LA = Lewis acid
X = F, Cl, Br
Tos = *p*-$MeC_6H_4SO_2$

(8)

(38)[8,22,23]. Suitable Lewis acids are antimony pentachloride, stannic chloride and aluminium trichloride. According to reaction sequence (8), the Lewis acids catalyse the elimination of hydrogen halide from the sulphonylhydrazones (**36**). Furthermore, they remove the *p*-toluenesulphinate anion from the azosulphone intermediate (**37**), and finally, they are necessary for the formation of the complex anion in **38**. In the hydrazones (**36**), the α-halogen can be replaced by an alkoxy or acyloxy group, provided that their removal is favoured by geminal substituents R^1 and R^2. The rates of the formation of **38** parallel the well-known order of Lewis-acid strengths in Friedel–Crafts reactions[24], i.e. $AlCl_3 > SbCl_5 > SnCl_4$. As the first step of sequence (8), the hydrogen halide elimination can sometimes become rate-determining for the overall reaction, when relatively weak Lewis acids such as $SnCl_4$ are employed. In such cases it is advantageous to generate the sulphonylazoalkene (**37**) separately, using a suitable base[25] (see Section II.C.1).

Antimony pentachloride is preferably applied as the Lewis acid, since the diazonium hexachloroantimonates then resulting are found to be crystalline compounds. In agreement with this observation, the salt **40**, which arises from the azofulvene **39** and



(39) (40) (41) (42)

(9)

two molecules of $SbCl_5$, is transformed almost quantitatively into **41** by the action of hydrogen chloride (equation 9). Furthermore, **41** can be directly produced on treatment of 9-fluorenecarbaldehyde tosylhydrazone with antimony pentachloride, the latter also functioning as oxidizing agent. On the other hand, the synthesis of 2-chloro-3,3-dimethylbutenediazonium tetrachloro-(*p*-toluenesulphinato)stannate (**44**) from **43** and stannic chloride (equation 10) demonstrates that the anion of **44** is resistant to hydrogen chloride[23].

$$\underset{\textbf{(43)}}{(CH_3)_3C-CCl_2-CH=N-NH-Tos} \xrightarrow{+SnCl_4} \underset{\textbf{(44)}}{(CH_3)_3C-CCl=CH-N_2^+[SnCl_4 \cdot Tos]^-} + HCl \quad (10)$$

1. *Preparation of the toluenesulphonylazoalkene intermediate*

The occurrence of the azoalkenes **37** in the synthesis of **38** can be considered as a new variant of the Chattaway reaction[26]. Moreover, several compounds of this species have become available during recent years[22,23,25,27–33], and they have been utilized for the synthesis of alkynes[30,34,35] or alkylidenecyclopropanes[33].

Table 1 comprises a selection of tosylazoalkenes (**45–51**) which have been isolated in the pure state[22,23,25,29] in order to investigate their behaviour toward Lewis acids. According to the first three examples, the reactions of *p*-toluenesulphonyl hydrazide with α-halogenated aldehydes and ketones that also contain an aryl or trichlorovinyl group attached to the α carbon lead directly to the sulphonylazoalkenes **45–47**. The azo olefins **45** and **46** can also be prepared by oxidation of the halogen-free sulphonylhydrazones with iodine/pyridine or bromine/pyridine, a method which has been suggested by Schantl[36]. Toluenesulphonylhydrazones of aldehydes and ketones bearing only halogen or halogen and *t*-alkyl groups at the α carbon require the assistance of a base for the elimination of hydrogen halide. Among the azoalkenes **48–51** synthesized by this route, **50** and **51** are stable at room temperature for only a few hours.

2. *Diazonium salts from aldehyde sulphonylhydrazones*[8,23]

In Table 2 there is listed a series of β-substituted ethylenediazonium salts which have been prepared by means of the appropriate toluenesulphonylhydrazones, in the order of decreasing decomposition temperatures. The stabilizing effect of chlorine at β carbon appears to be very significant. Consequently, the β,β-dichloroethylenediazonium hexachloroantimonate was found to have the highest decomposition point. The stepwise replacement of chlorine by hydrogen or by *t*-alkyl groups and bromine always gives rise to a decrease in thermal stability of the resulting diazonium compounds. The analogous introduction of a trichlorovinyl or 2,2′-biphenylyl group diminishes the stability to a smaller extent. All attempts to obtain the unsubstituted ethylenediazonium ion have been unsuccessful so far.

A plausible explanation for the different thermal stabilities of β-substituted ethylenediazonium salts is provided by the assumption that, in general, the elimination of nitrogen does not yield the particularly unfavourable primary vinyl cations, but rather bridged ions such as **57–59**, which can already profit from the lower energy level of a completely rearranged intermediate[37–41]. In accord with this suggestion, the alkenediazonium ions **55** and **56**, generated from the toluenesulphonylhydrazones of

TABLE 1. Synthesis of *p*-toluenesulphonylazoalkenes (**45–51**), $R^1R^2C{=}CR^3{-}N{=}N{-}SO_2C_6H_4Me\text{-}p$ from α-halogenated carbonyl compounds (**52**), $R^1R^2CX{-}C(O)R^3$, and *p*-toluenesulphonyl hydrazide or from *p*-toluenesulphonylhydrazones (**53**), $R^1R^2CX{-}CR^3{=}N{-}NHSO_2C_6H_4Me\text{-}p$[23]

Starting materials	Products	R^1	R^2	R^3	Yield (%)	Dec. pt.[a] (°C)
52 (X = Br) + tosyl hydrazide **53** (X = H) + Br_2/pyridine	**45** (=**39**)	2,2′-Biphenylylene		H	84 87	125–126
52 (X = Br) + tosyl hydrazide **53** (X = H) + I_2/pyridine	**46**	2,2′-Biphenylylene		Me	77 89	140–141
52 (X = Cl) + tosyl hydrazide	**47**	$Cl_2C{=}CCl$	Cl	H	—	88
53 (X = Br) + NaOH	**48**	Br	Br	H	83	*90–91*
53 (X = Cl) + NEt_3	**49**	Cl	Cl	Me	69	108–109
53 (X = Cl) + NEt_3	**50**	*t*-Bu	Cl	H	69	70
53 (X = Br) + NEt_3	**51**	*t*-Bu	Br	H	67	72–74

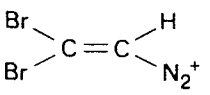
[a]Decomposition point.

TABLE 2. β-Substituted ethylenediazonium hexachloroantimonates and tetrachloro(toluenesulphinato)stannates $R^1R^2C{=}CH{-}N_2^+Y^-$

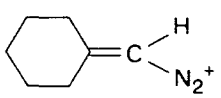
R^1	R^2	Y	Dec. pt.[a] (°C)	Colour
Cl	Cl	$SbCl_6$	131–132	Colourless
$Cl_2C{=}CCl$	Cl	$[Tos{\cdot}SnCl_4]$	112[b]	Yellow
Cl	H	$SbCl_6$	97–98	Colourless
2,2'-Biphenylylene		$SbCl_6$	95	Green–brown
t-Bu	Cl	$SbCl_6$	86–87	Colourless
t-Bu	Cl	$[Tos{\cdot}SnCl_4]$	78–80	Colourless
Br	Br	$SbCl_6$	58	Pale yellow
t-Bu	Br	$[Tos{\cdot}SnCl_4]$	58	Colourless
1-Adamantyl	Br	$SbCl_6$	50–52	Pale Yellow
Et	Cl	$SbCl_6$	[c]	—

[a]Decomposition point.
[b]$CCl_2{=}CCl{-}CCl{=}CH{-}N_2^+[2\ SbCl_5{\cdot}Tos]^-$ decomposes at 90°C.
[c]The compound can only be obtained as a solution in CH_2Cl_2, stable at room temperature.

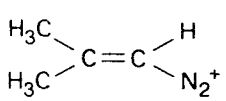
1-chlorocyclohexanecarbaldehyde and α-chloroisobutyraldehyde, respectively, spontaneously eliminate nitrogen at temperatures as low as 5–10°C. The pronounced tendency of the cyclohexylidenemethanediazonium ion (**55**) to undergo decomposition corresponds to the accelerated solvolysis of cyclohexylidenemethyl trifluoromethanesulphonate, which undergoes ring-expansion to give cycloheptanone, probably via **58**[42].



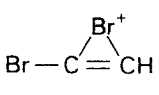
(**54**)



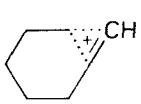
(**55**)



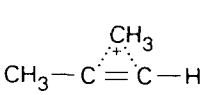
(**56**)



(**57**)



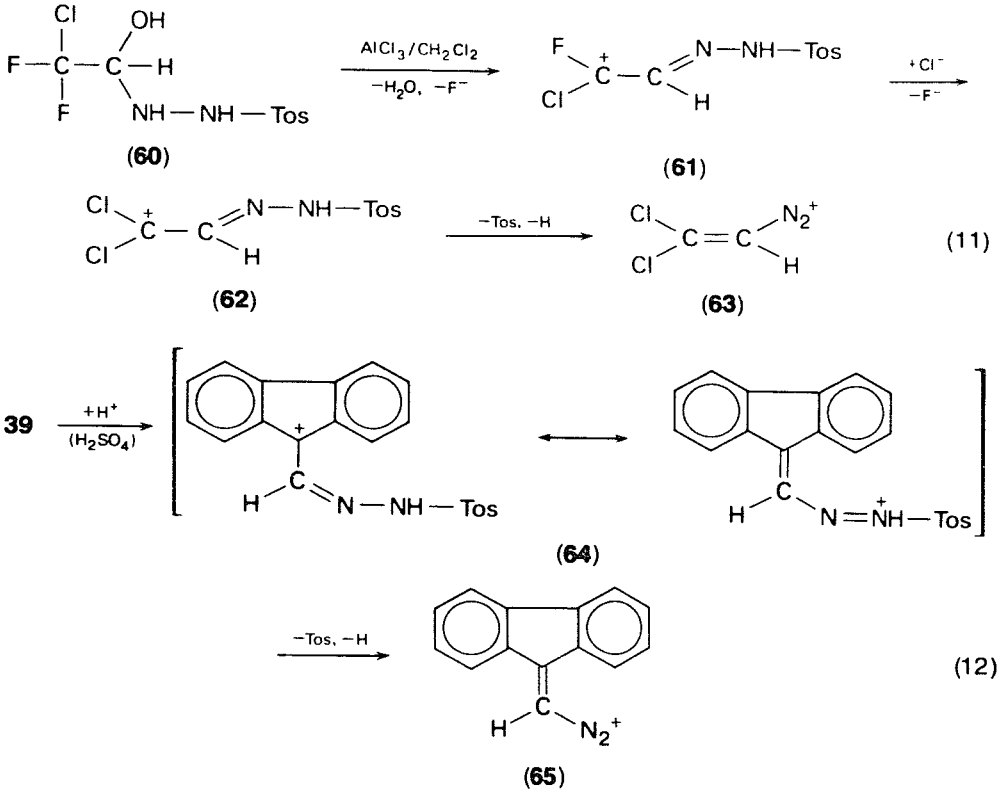
(**58**)



(**59**)

In order to study the influence of fluorine in the β position upon the stability of ethylenediazonium salts, the chlorodifluoroacetaldehyde tosylhydrazone **60** (as hydrate) has been treated with aluminium trichloride. However, the product formed in this reaction was not the expected 2,2-difluoroethylenediazonium ion, but the chloro analogue (**63**) which could be isolated as the hexachloroantimonate **33**[23]. The exchange of fluorine for chlorine, necessary for the formation of **63**, probably takes place in the resonance-stabilized cationic intermediate (**61**) (equation 11).

The product **64** resulting from the protonation of azofulvene **39** corresponds to the short-lived species **61** and **62**. In sulphuric acid, the dark-red **64** can be directly observed, since its transformation into the olive-green diazonium ion **65** goes to completion only after one or two minutes even at room temperature (equation 12).



3. *Diazonium salts from ketone sulphonylhydrazones*[8,23]

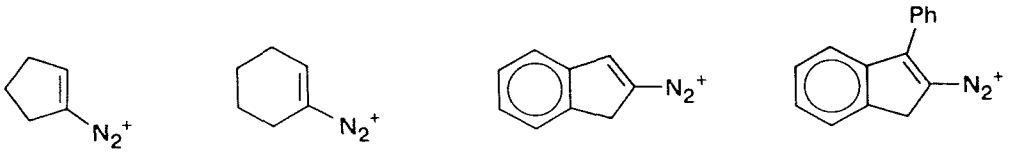
The diazonium group plays an important role[43] in the generation of carbenium ions by heterolytic bond fission because of the great ease with which a nitrogen molecule can be eliminated. This is why alkenediazonium ions with an alkyl or aryl substituent at the diazo carbon can exist under normal conditions only if special effects arising from reactant stabilization or product destabilization (see Section I.A) become important.

For example, the methyl analogues of the diazonium ions **63** and **65**, i.e. **66** and **67**, are quite unstable. The salts of the 1,1-dichloropropene-2-diazonium ion (**66**) can only

(**66**) (**67**)

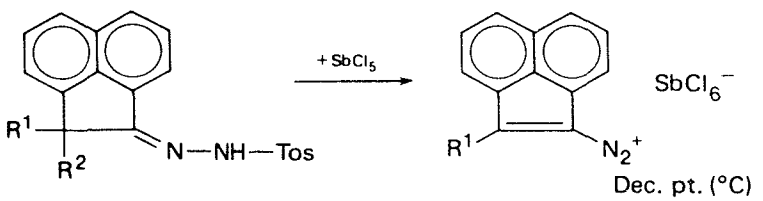
be isolated and characterized at temperatures below −20°C, since they decompose with evolution of nitrogen even at −10 to 0°C, both as solids and in solution. Even at −20°C, the reaction of the azo compound **46** with antimony pentachloride shows that **67** is unable to exist for more than a few minutes under these conditions.

As shown by the solvolyses of cyclic vinyl trifluoromethanesulphonates[44], vinyl cations with nonlinear σ bonds are less stable than those with linear bonds. However, the higher energy level of the 1-cyclopentenyl and 1-cyclohexenyl cations still does not permit the isolation of **68**[45] and **69** at 0°C. Only in the indene-2-diazonium ion (**70**), and in its 3-phenyl derivative **71**, does the five-membered ring become so rigid by the incorporation of four sp^2 centres that **70** and **71** fail to eliminate nitrogen at room temperature[23].



(68) **(69)** **(70)** **(71)**

The reaction of the hydrazones **72** and **73** with antimony pentachloride yields the even more strained acenaphthylene-1-diazonium hexachloroantimonates **74** and **75** with an aryl substituent at the diazonium carbon (equation 13). The remarkable stability of **74**, which is even greater in its fluoro derivative **75**, arises from geometric reasons: in the diazonium ion **74** the aryl substituent can only stabilize the vinyl cation



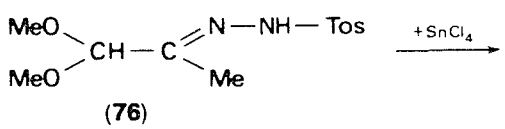
(13)

(72) R^1 = H, R^2 = OMe
(73) R^1 = R^2 = F

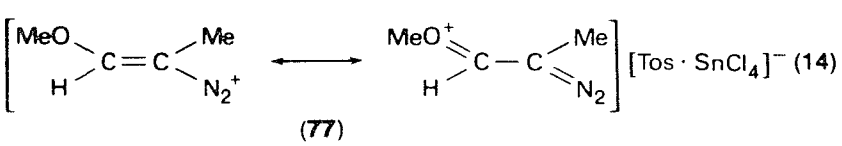
		Dec. pt. (°C)
(74)	R^1 = H	140–141
(75)	R^1 = F	187–188

resulting from the loss of nitrogen when it is oriented perpendicularly to the σ-bond skeleton of the olefinic carbons. Such an orientation is completely ruled out because of the fusion of the five-membered ring with the naphthalene system. Likewise, the 3-phenyl-2-indenyl cation which corresponds to **71** is unable to lower its energy level by migration of the phenyl group to C(2). It is noticeable that 'aromatic' diazonium ions derived from acenaphthylene are still unknown.

In addition, the stability of α-alkyl- or α-aryl-ethylenediazonium compounds can be increased by substituents capable of displaying a resonance with the diazonium group. Thus, the 1-methoxypropene-2-diazonium salt (**77**) obtained from 1,1-dimethoxyacetone tosylhydrazone (**76**) and stannic chloride (equation 14) does not decompose below 95°C.



(76)



(14)

(77)

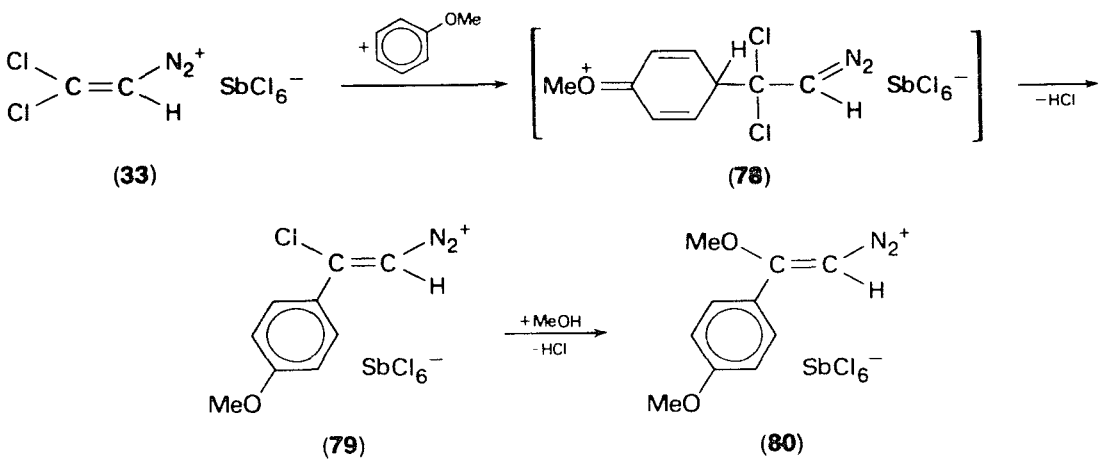
In this context, there must also be mentioned the surprisingly high stability of the α-(*p*-nitrophenyl)ethylenediazonium hexachloroantimonate (**29**) and the Reimlinger salt (**31**) which have been synthesized from aliphatic diazo compounds (see Section II.A). In **29** and in **31** the aryl group can no longer facilitate the elimination of nitrogen, due to an extensive delocalization of the positive charge.

III. REACTIONS OF ALKENEDIAZONIUM SALTS

The chemistry of alkenediazonium ions can be classified into the two major types of processes: (*a*) the unimolecular liberation of nitrogen which results in the formation of vinyl cations and (*b*) the reactions with a variety of nucleophilic agents leading to a broad spectrum of products. The reaction rates in pathway (*a*) generally correlate to the stability of the vinyl cations arising from the loss of nitrogen, provided that charge delocalization in the diazonium species does not become an important factor. Owing to their strongly electrophilic character, many of the substituted ethylenediazonium ions are capable of reacting with basic agents before nitrogen is eliminated. This behaviour is not restricted to diazonium ions with lifetimes long enough to permit observation of their physical properties.

A. Isolable Alkenediazonium Salts[23]

Isolable alkenediazonium salts have been shown to react spontaneously with water, alcohols, carboxylic acids and other carbonyl compounds, even below room temperature. The products resulting from these decomposition reactions have not been elucidated as yet. However, the two substitution reactions of β-chloroethylenediazonium ions given in Scheme 4 demonstrate the characteristic differences which exist between alkenediazonium compounds and their aromatic

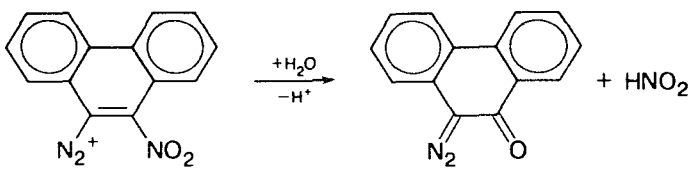


SCHEME 4

counterparts. The particularly electrophilic salt **33** can attack the *para* position of anisole at 0–20°C. Subsequent elimination of hydrogen chloride forms the 2-chloro-2-(*p*-methoxyphenyl)ethylenediazonium salt (**79**). While an excess of anisole does not react with **79**, the more strongly basic methanol can also substitute the second chlorine atom. The yields of the hexachloroantimonates **79** and **80**, isolated in an

analytically pure state and free from isomers, are 61 and 56%, respectively. The postulated intermediate (**78**) comprises a strong protonic acid and an acid-sensitive diazoalkane group united in a single molecule, but the usual displacement of nitrogen does not occur. The reaction **79** → **80** is expected to proceed through the corresponding addition compound. This process requires two or three moles of methanol per mole of **79**, because some of the alcohol is intercepted by the hydrogen chloride which is produced. Compound **80** ultimately decomposes on addition of yet more methanol.

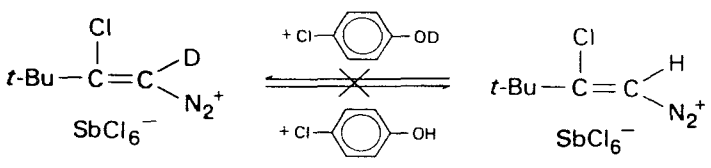
The NO_2 group of the 10-nitrophenanthrene-9-diazonium ion **81**, whose C(9)—C(10) bond has a partly alkene-like character, is displaced by water in dilute mineral acids, forming diazophenanthrone (**82**)[46] (equation 15).



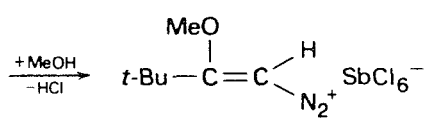
(15)

(**81**) (**82**)

In the 2-chloro-3,3-dimethyl-1-butenediazonium salt (**83**), the addition of a nucleophilic agent at C(2) is considerably hindered by the bulky *t*-butyl group. Thus, under conditions mentioned above, neither anisole nor phenol are able to accomplish the halogen exchange. However, the rapid transformation of **83** into the corresponding 2-methoxybutenediazonium salt **84** by methanol (equation 16) can be confirmed spectroscopically, since this reaction is accompanied by a characteristic shift of the diazo stretching band toward longer wavelengths (Section IV). The strong deshielding effect of the *t*-butyl group on the β carbon in **83** offers a method of checking whether the acidity of α hydrogen is sufficiently high to establish an acid–base equilibrium in the presence of *p*-chlorophenol. When **83** is exposed to an excess of *O*-deuterated *p*-chlorophenol at room temperature, no exchange of α-H for deuterium can be observed[23].



(**83**)



(16)

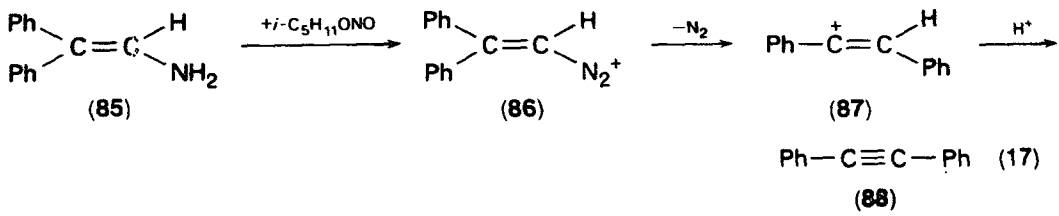
(**84**)

B. Alkenediazonium Ions as Short-lived Intermediates

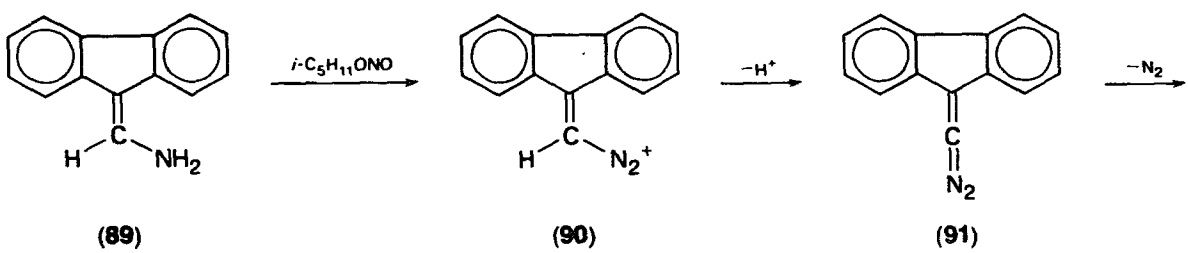
Besides the preparation of stable alkenediazonium salts, there have been developed several synthetic routes generating alkenediazonium ions as short-lived intermediates only. These methods provide a useful tool for studying diazonium compounds which exhibit a very low thermal stability.

1. *Nitrosation reactions of primary vinylamines*

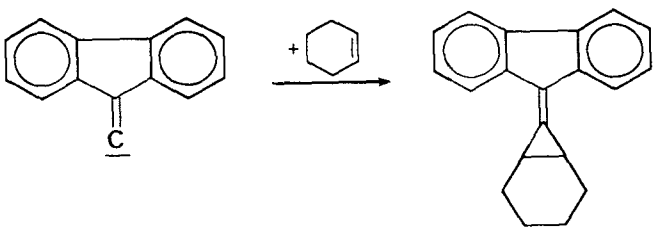
The diazotization of primary vinylamines by NO^+-donating agents is an appropriate process for the generation of alkenediazonium ions[47,48]. When diphenylvinylamine (**85**) is treated with *i*-amyl nitrite in boiling benzene, diphenylacetylene (**88**) is formed in 85% yield[47] (equation 17). The course of this reaction can reasonably be interpreted in terms of the diphenylethylenediazonium ion (**86**) which rapidly loses nitrogen to form the rearranged vinyl cation **87**. Attempts to intercept the diazonium ion **86** by carrying out the diazotization reaction with nitrosyl chloride at low temperatures and adding β-naphthol or its sodium salt have thus far proved unsuccessful.



(**85**) (**86**) (**87**) (**88**)

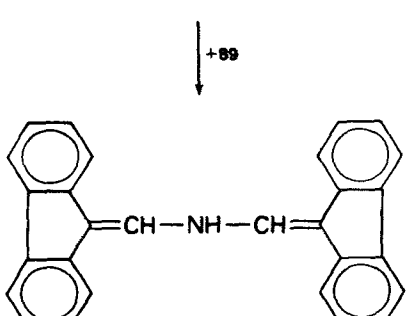


(**89**) (**90**) (**91**)



(**92**) (**93**)

(**92**)

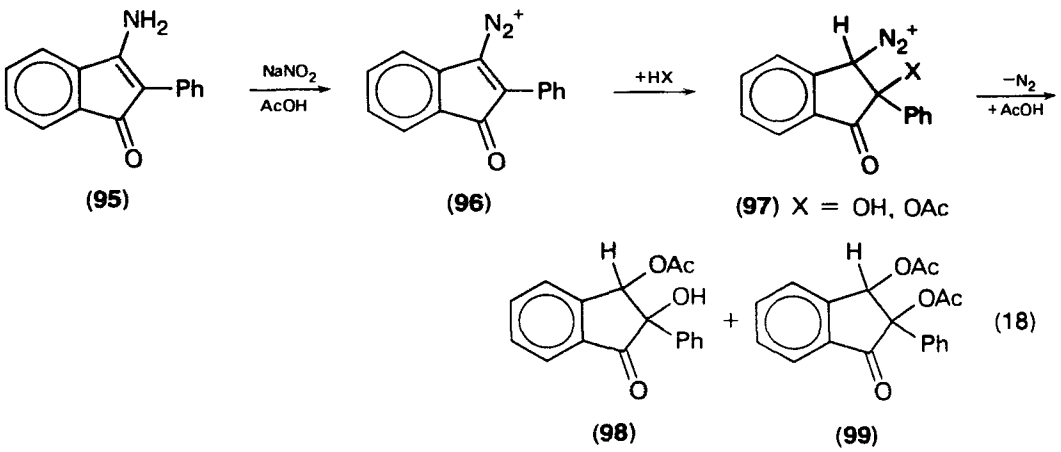


(**94**)

SCHEME 5

In this context, it is of interest to examine the reaction of *i*-amyl nitrite with the vinylamine **89**, since the analogous rearrangement of the resulting diazonium ion **90** is strongly suppressed for geometrical reasons. The product isolated from the nitrosation of **89** in benzene is shown to be the divinylamine **94** (Scheme 5). When the reaction of **89** with *i*-amyl nitrite is carried out in cyclohexene, the bicycloheptylidenefluorene **93** is obtained in yields of about 80%. In both processes the divalent carbon species **92** must be regarded as the key intermediate which can either undergo insertion into the N—H bond of **89** or suffer a cycloaddition to cyclohexene. The unsaturated carbene **92** is probably formed via an unstable α-diazoalkene **91**. Thus, the generation of the unfavourable primary vinyl cation from **90** can be avoided.

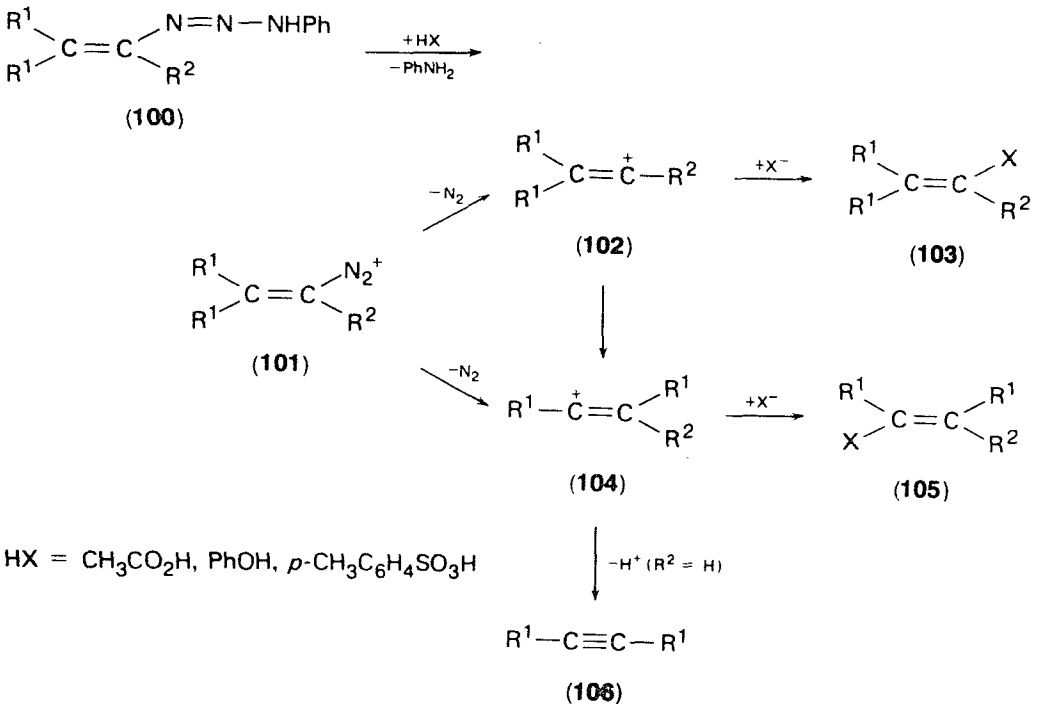
Another diazonium ion **96** which does not tend to eliminate nitrogen has been generated from 3-amino-2-phenylindenone (**95**)[48]. The action of sodium nitrite on **95** in acetic acid below room temperature affords the monoacetate **98** and the diacetate **99** of *cis*-2,3-dihydroxy-2-phenyl-1-indanone (equation 18). It is interesting to note that the ratio of **98**:**99** is not altered seriously by addition of acetic anhydride or water to the acetic acid. Apparently, the acetates **98** and **99** arise from the addition of water or acetic acid to **96** and subsequent decomposition of the alkyldiazonium ion **97**.



(95) (96) (97) X = OH, OAc (98) (99) (18)

2. *Acidolysis of vinyltriazenes*

The classical reaction of diaryltriazenes with acid to give aryldiazonium salts can be extended to the production of alkenediazonium ions (**101**) from the analogous vinyltriazenes (**100**)[49]. In all cases studied, the products **103**, **105** and **106** are those that would be expected to arise from a vinyl cation formation followed by reaction with the nucleophile either before or after rearrangement (Scheme 6). For example, treatment of **100a** with acetic acid gives triphenylvinyl acetate (**103**, X = OCOMe) in 100% yield. The reactions are accompanied by the migration of aryl groups which can occur either via the concerted route **101** → **104** or via a separate pathway **102** → **104**. The analogous generation of the less stable vinyl cation **102c** from **100c** leads almost completely to the rearranged acetate **105c** (X = OCOMe). As predicted on the basis of a vinyl cation mechanism, the conversion **102** → **104** is suppressed by the addition of potassium acetate. Nevertheless, the decomposition of **100d** with acetic acid results exclusively in the formation of rearranged products **105** and **106**, even in the presence of added alkali acetate. This statement is compatible with the assumption that the elimination of nitrogen from **101d** takes place synchronously with phenyl migration



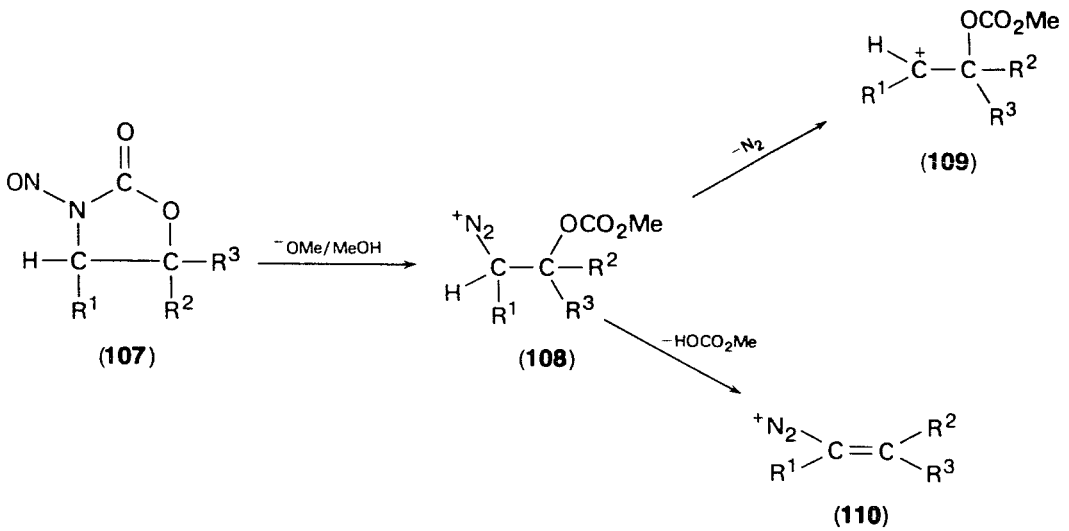
R^1	R^2
(a) Ph	Ph
(b) *p*-$CH_3C_6H_4$	Ph
(c) Ph	Me
(d) Ph	H

SCHEME 6

(see Section III.B.1). The acidolysis of vinyltriazenes presents a useful method for the synthesis of vinyl esters. The potential generality of this reaction is emphasized by the fact that even the conjugate bases of strong acids, e.g. the *p*-toluenesulphonate anion, are able to intercept the appropriate vinyl cation intermediate.

3. *Base-promoted decomposition of* N-*nitrosooxazolidones*

The base-promoted decomposition of *N*-nitrosooxazolidones is a well-known source of alkenediazonium ions that has been widely explored with respect to its scope, synthetic utility and mechanistic aspects[50–60]. Scheme 7 presents the mechanism of the reaction that has been elaborated by Hassner and coworkers[59]. Using sodium methoxide as the base, the initiating process consists in the generation of the alkanediazonium ion **108**. Subsequently, **108** can either lose nitrogen to form the alkyl cation **109** or suffer an elimination of monomethyl carbonate to afford the alkenediazonium species **110**. In agreement with Scheme 7, the yields of products originating from the alkenediazonium intermediate **110** mainly depend on the substitution pattern of *N*-nitrosooxazolidone **107**. If in **107** C(4) is primary (R^1 = H),



SCHEME 7

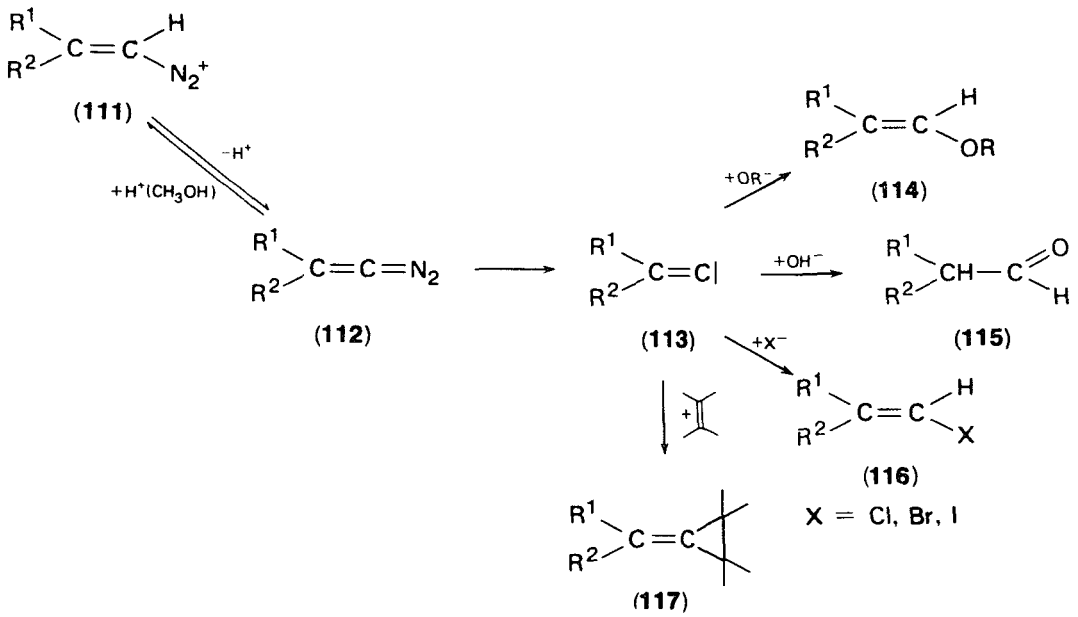
C(5) must be tertiary or benzylic in order to furnish a good yield of products derived from **110**. If C(4) is secondary, then C(5) must be benzhydrylic for the decomposition via **110** to be the predominant pathway (see Table 3).

Treatment of the *N*-nitroso-5,5-dialkyloxazolidones with an appropriate base leads preferably to 2,2-dialkylethylenediazonium ions (**111**). Deprotonation of **111** results in the generation of α-diazoalkenes (**112**) which subsequently decompose to form the unsaturated carbene intermediate **113** (Scheme 8). In protic solvents such as methanol the reacton **111** → **112** becomes a reversible process. The fate of the divalent species **113** is determined by the nucleophilic agents present in the reaction medium. Many of the products **114**[52,57], **115**[50–52], **116**[54] and **117**[52,53] arising from **113** can be obtained in good to excellent yields.

An exception to the reaction sequence of Scheme 8 is given by the decomposition of **111** with lithium azide. In this case, more or less large amounts of the resulting vinyl azides are produced via an azo coupling of **111**. According to equation (19), the azo coupling route has been established by utilizing ^{15}N-labelled *N*-nitrosooxazolidones (**118**) as starting materials[60].

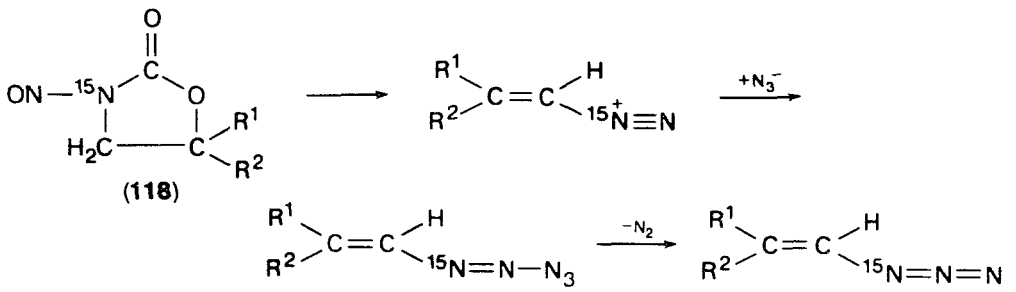
TABLE 3. Yields of alkenediazonium ion (**110**) derived products from base decomposition of 3-nitroso-2-oxazolidones (**107**) in protic solvents[59]

R^1	R^2	R^3	Yield (%)
H	Alkyl	Alkyl	70–85
H	H	Ph	65–90
H	Alkyl	Ph	90
H	Ph	Ph	100
Et	H	H	0
Ph	H	H	14
Ph	Ph	Ph	60
Me	*o,o'*-Biphenylylene		85



R^1 = Me, R^2 = *t*-Bu
R^1 = R^2 = Me, Et
R^1, R^2 = $(CH_2)_4$, $(CH_2)_5$, $(CH_2)_6$

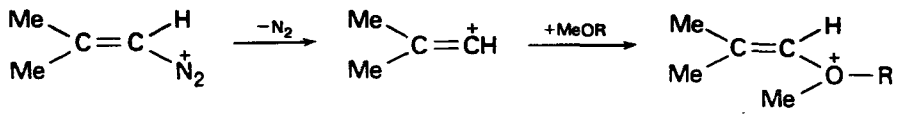
SCHEME 8



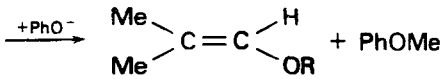
R^1 = R^2 = Me, R^1, R^2 = $(CH_2)_5$ (19)

The action of sodium phenoxide on 5,5-dimethyl-*N*-nitrosooxazolidone (**107**, R^1 = H, R^2 = R^3 = Me) and phenol in 1,2-dimethoxyethane as solvent gives rise to the formation of 2-methoxyethyl 2-methylpropenyl ether (**122**) and anisole. A mechanism involving the generation of an unsaturated oxonium ion **121** from solvent and the vinyl cation **120** is proposed to account for the results[55]. However, recent investigations have revealed that carbenes of type **113** are also capable of effecting the cleavage of ethers analogously to equation (20)[61].

In contrast to **111**, the 2,2-diphenylethylenediazonium ion resulting from decomposition of the corresponding nitrosooxazolidone is almost quantitatively converted into diphenylacetylene[50] (compare with equation 17). This result is in



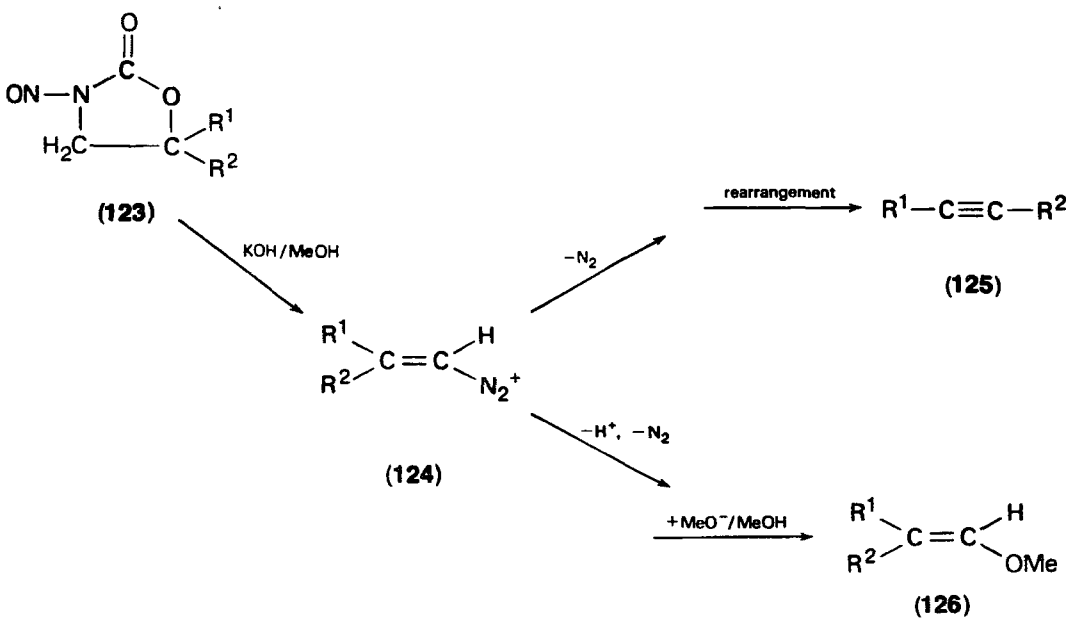
(119) (120) (121)



(122)

$$R = CH_2CH_2OMe$$

accordance with the well-known ability of aryl groups both to stabilize a carbocation and to undergo a facile migration in reactions involving cationic intermediates. Furthermore, *N*-nitrosooxazolidones **123** bearing cyclopropyl groups at C(5) react with potassium hydroxide in methanolic solution to yield the rearranged acetylenes **125** and methyl vinyl ethers **126**[58]. However, when starting from the 5-cyclopropyl-5-phenyl derivative (**123**, R^1 = Ph, R^2 = *c*-Pr), the cyclopropyl phenyl acetylene is obtained as the only product. The yields of **125** and **126** given in Scheme 9 clearly demonstrate that rearrangement of a phenyl group in intermediates of type **124** (or in the vinyl cation



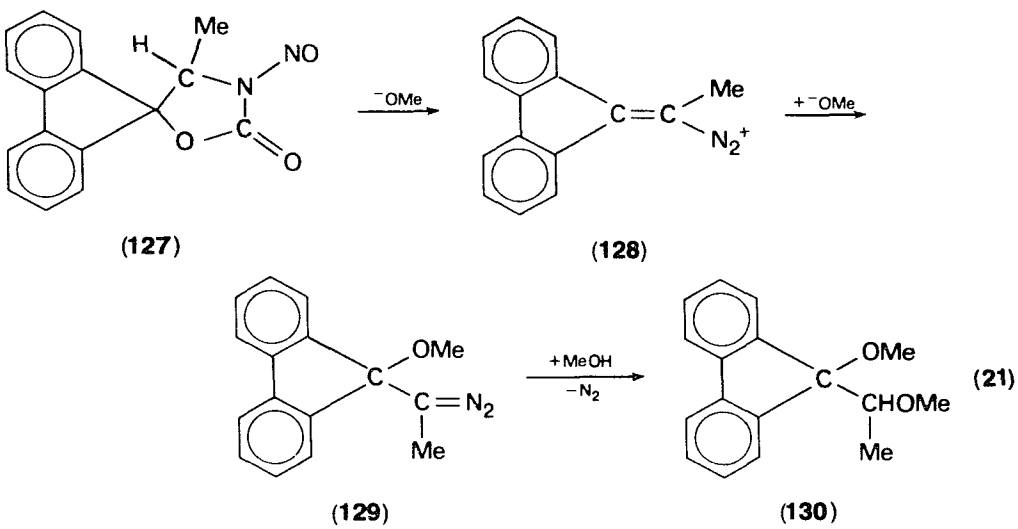
(123) (124) (125) (126)

		Yield %	
R^1	R^2	(125)	(126)
(a) Ph	*c*-Pr	90	—
(b) *c*-Pr	*c*-Pr	52	21
(c) *c*-Pr	Me	16	64

SCHEME 9

corresponding to **124**) occurs more readily than that of a cyclopropyl group and that methyl has little, if any, tendency to migrate.

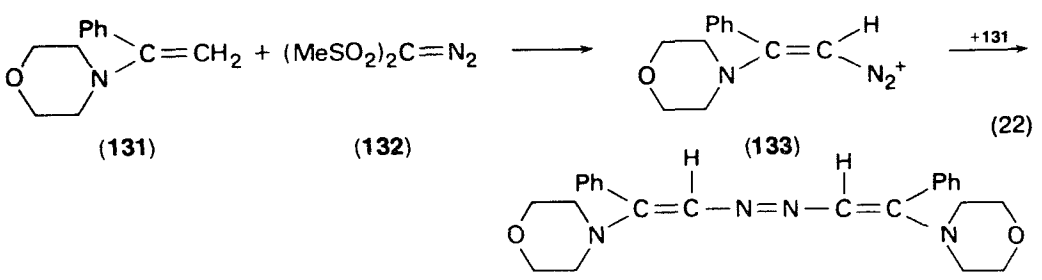
The reluctance of the biphenylyleneethylenediazonium ion (**90**) to undergo rearrangement reactions has been already rationalized in Section III.B.1. Accordingly, the behaviour of **90** toward nucleophiles resembles that of 2,2-dialkylethylenediazonium ions (**111**) (see Scheme 8)[52]. Treatment of the spiro-nitrosooxazolidone **127** with sodium methoxide in methanol affords the alkenediazonium compound **128** as an intermediate which carries a methyl group attached to diazo carbon. Since **128** cannot form an unsaturated carbene, it is assumed to react stepwise with methoxide and methanol leading to the 9-methoxy-9-methoxyethylfluorene **130** in high yield[52] (equation 21).



(**127**) (**128**) (**129**) (**130**) (21)

4. *Transfer of diazo groups*

Reaction of bismethanesulphonyl diazomethane (**132**) with α-morpholinostyrene (**131**) in trichloromethane yields the azostyrene **134**. The generation of **134** has been explained in terms of the reaction sequence given in equation (22)[62]. Presumably the initiating step consists of a transfer of the diazo group from **132** to **131**. The stabilized β-morpholinoethylenediazonium ion **133** thus formed can undergo an azo coupling reaction with **131** to produce the azo compound **134**.



(**131**) (**132**) (**133**) (22)

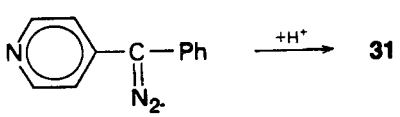
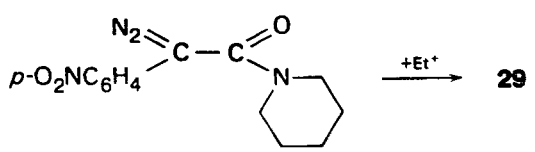
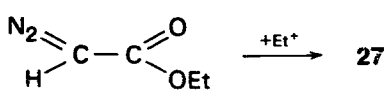
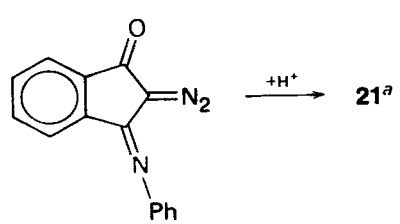
(**134**)

TABLE 4. NN stretching frequencies of alkenediazonium salts $R^1R^2C{=}CR^3N_2^+\,Y^-$

R^1	R^2	R^3	Y	$\tilde{\nu}(cm^{-1})$
Cl	H	H	$SbCl_6$	2260[a]
Cl	Cl	H	$SbCl_6$	2240[b]
t-Bu	Cl	H	$SbCl_6$	2240[a]
Br	Br	H	$SbCl_6$	2240[b]
1-Adamantyl	Br	H	$SbCl_6$	2240[a]
t-Bu	Br	H	$[Tos{\cdot}SnCl_4]$	2240[a]
$Cl_2C{=}CCl$	Cl	H	$[Tos{\cdot}SnCl_4]$	2220[a]
2,2′-Biphenylylene		H	$SbCl_6$	2210[c]
t-Bu	MeO	H	$SbCl_6$	2205[a]
MeO	H	Me	$[Tos{\cdot}SnCl_4]$	2200[a]
p-$MeOC_6H_4$	Cl	H	$SbCl_6$	2200[c]
p-$MeOC_6H_4$	MeO	H	$SbCl_6$	2190[c]
EtO	EtO	H	$SbCl_6$	2180[d]
Piperidino	EtO	*p*-$O_2NC_6H_4$	$SbCl_6$	2110[d]
—CH=CH—NH—CH=CH—		Ph	CCl_3CO_2	2062[d]

[a]Solid in Nujol.
[b]In 1,2-dichloroethane.
[c]In nitrobenzene.
[d]KBr disc.

TABLE 5. NN frequency shifts $\Delta\tilde{\nu}$ originating from alkylation and protonation of aliphatic diazo compounds

Salt formation reaction	$\Delta\tilde{\nu}(cm^{-1})$	Ref.
	21	19
	30	10
	80	10
	64	14

[a]As perchlorate.

IV. DIAZO STRETCHING VIBRATIONAL SPECTRA

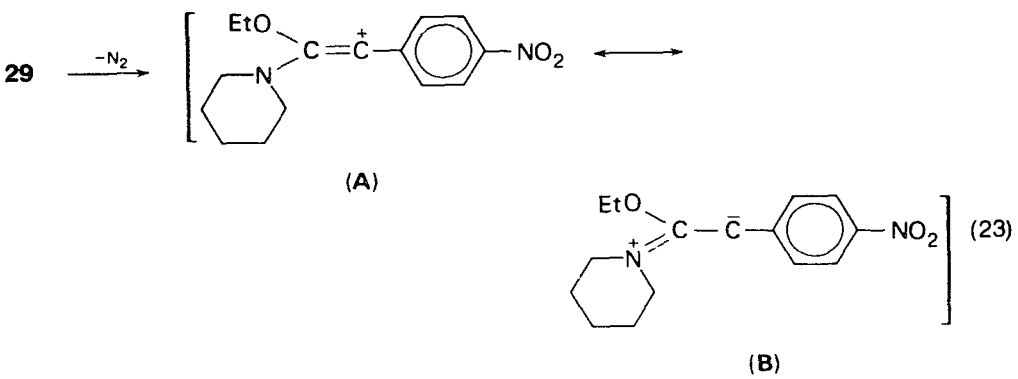
In context with the syntheses of diazonium salts from α-diazocarbonyl compounds (see Section II.A), it has been mentioned that electron-donating substituents at C(2) of ethylenediazonium ions are able to accept the positive charge and can thus reduce the bond order of the NN triple bond. Therefore, with increasing proportion of this resonance structure the frequency of the relevant diazo stretching vibration is expected to decrease. Examples of this are shown in Table 4. 2-Chloroethylenediazonium hexachloroantimonate and the next five compounds with halogen and *t*-alkyl groups at C(β) exhibit diazo absorption bands with the shortest wavelengths. In the two subsequent salts a trichlorovinyl or biphenylylene group is involved in the resonance with the diazonium nitrogen. In the succeeding diazonium compounds the presence of *p*-methoxyphenyl and alkoxy groups leads to an even more marked shift of the NN vibrational frequencies. Owing to its long wave absorption maximum, the 1-nitrophenyl-2-ethoxy-2-piperidinoethylenediazonium hexachloroantimonate can already be compared with diazoacetic ester ($\tilde{\nu}$ = 2105 cm^{-1}), while the last example (Reimlinger salt) must be regarded as *N*-protonated phenyl-(4-pyridyl)-diazomethane according to its IR spectrum.

These conclusions are underlined by comparison of the frequency shifts observed when converting the aliphatic diazo compounds into their conjugate cations. According to the data given in Table 5, only the formation of **21** and **27** occurs with a significant change of the position of the corresponding diazo absorption bands.

V. FINAL REMARKS AND OUTLOOK

From the various syntheses of alkenediazonium salts considered, we can conclude that these compounds are in general stable enough to be isolated if they form highly unstable vinyl cations on elimination of nitrogen. The only exceptions to this rule are the β-alkoxy- and β-dialkyl-aminoethylenediazonium salts in which resonance stabilization plays an important role. These species, products of the *O*-alkylation of α-diazocarboxylic acid amides or esters, α-diazo ketones and α-diazo aldehydes, are the links between real alkenediazonium ions and the uncharged aliphatic diazo compounds.

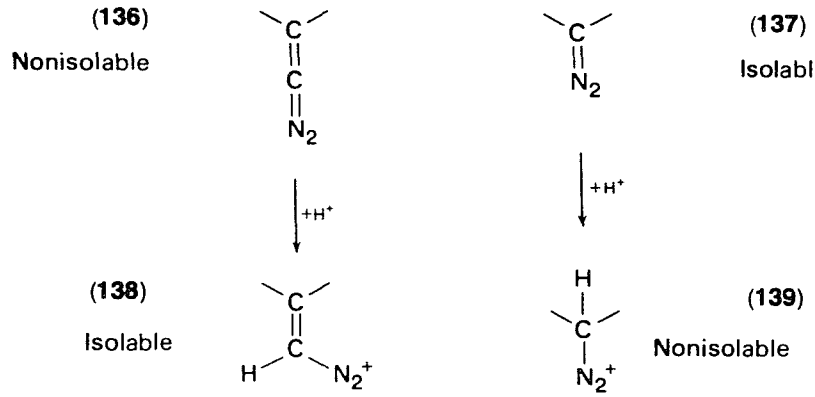
Furthermore, the vinyl cation **135** resulting from the decomposition of the highly stabilized alkenediazonium salt **29** (equation 23) assumes a similar transition state since, in the resonance form **B**, it can also be regarded as an imonium derivative of a carbalkoxycarbene. However, the gain in energy due to charge delocalization in **135**



(135)

must be considerably smaller than the loss in resonance energy which arises from the decay of **29**. Otherwise, in **29** and in a variety of alkenediazonium compounds, analogously stabilized by resonance, the nitrogen would not fail to function as the best leaving group.

Alkenediazonium ions **138** with hydrogen attached to the α carbon represent the protonation products of the unstable α-diazoalkenes (**136**). A comparison of **136** with the diazoalkanes **137** reveals that in the first case only the protonated species **138** can be isolated, whereas the alkyldiazonium ions **139** derived from the isolable **137** occur merely as short-lived intermediates (see Scheme 10).



SCHEME 10

The introduction of the diazonium group into alkenes gives rise to the generation of agents surpassing even tetracyanoethylene in their electrophilic properties. For this reason the reactions of ethylenediazonium salts with other alkenes, '1,3-dipoles', and dienes most likely possess considerable synthetic potential. An indication of cycloadditions of alkenediazonium ions to the nitro group is provided by the observation that the particularly reactive compounds **33** and **74** eliminate nitrogen in nitrobenzene solution even at room temperature.

Furthermore, alkenediazonium ions provide a means of investigating the stability of vinyl cations in a range that is inaccessible by the heterolysis of vinyl perfluoroalkanesulphonates. In this field, interest is centred mainly on the generation of primary vinyl cations which have so far only been unequivocally detected on the addition of 1-adamantyl cations to acetylene[63] or on the photolysis of iodo olefins[64].

VI. REFERENCES

1. P. Griess, *Justus Liebigs Ann. Chem.*, **106**, 123 (1858).
2. K. H. Saunders, *The Aromatic Diazo Compounds and their Technical Application*, Edward Arnold, London, 1949.
3. H. Zollinger, *Azo and Diazo Chemistry*, Wiley–Interscience, New York, 1961.
4. J. Sauer and R. Huisgen, *Angew. Chem.*, **72**, 294 (1960).
5. L. Wolff, P. Bock, G. Lorentz and P. Trappe, *Justus Liebigs Ann. Chem.*, **325**, 129 (1902).
6. H. Staudinger, J. Becker and H. Hirzel, *Ber. Dtsch. Chem. Ges.*, **49**, 1978 (1916).
7. E. Fahr and W. D. Hörmann, *Justus Liebigs Ann. Chem.*, **682**, 48 (1965).
8. K. Bott, *Angew. Chem. (Intern. Ed.)*, **18**, 259 (1979).
9. F. Klages, H. A. Jung and P. Hegenberg, *Chem. Ber.*, **99**, 1704 (1966).
10. K. Bott, *Angew. Chem. (Intern. Ed.)*, **3**, 804 (1964); *Tetrahedron*, **22**, 1251 (1966).
11. F. Klages and E. Zange, *Chem. Ber.*, **92**, 1828 (1959).

12. K. Schank and W. Gombler, unpublished results; K. Schank in *The Chemistry of Diazonium and Diazo Groups*, Part 2 (Ed. S. Patai), John Wiley and Sons, New York, 1978, p. 646.
13. J. P. Collman and M. Yamada, *J. Org. Chem.*, **28**, 3017 (1963).
14. M. Regitz and H. Schwall, *Justus Liebigs Ann. Chem.*, **728**, 99 (1969).
15. M. Allard, J. Levisalles and J. M. Sommer, *Chem. Commun.*, 1515 (1969).
16. C. Wentrup and H. Dahn, *Helv. Chim. Acta*, **53**, 1637 (1970).
17. H. Dahn, H. Gold, M. Ballenegger, J. Lenoir, G. Diderich and R. Malherbe, *Helv. Chim. Acta*, **51**, 2065 (1968).
18. H. Dahn and M. Ballenegger, *Helv. Chim. Acta*, **52**, 2417 (1969).
19. H. Reimlinger, *Angew. Chem. (Intern. Ed.)*, **2**, 482 (1963).
20. K. Bott, *Tetrahedron Letters*, 2227 (1971).
21. K. Bott, *Angew. Chem. (Intern. Ed.)*, **4**, 148 (1965).
22. K. Bott, *Angew. Chem. (Intern. Ed.)*, **9**, 954 (1970).
23. K. Bott, *Chem. Ber.*, **108**, 402 (1975).
24. K. Bodendorf and H. Böhme, *Justus Liebigs Ann. Chem.*, **516**, 1 (1935).
25. K. Bott, *Synthesis*, 161 (1973).
26. F. D. Chattaway and R. Bennett, *J. Chem. Soc.*, 2850 (1927).
27. A. Dondoni, G. Rosini, G. Mossa and L. Caglioti, *J. Chem. Soc. (B)*, 1401 (1968).
28. G. Rosini and R. Ranza, *J. Org. Chem.*, **36**, 1915 (1971).
29. K. Bott, *Angew. Chem. (Intern. Ed.)*, **10**, 821 (1971).
30. G. Rosini and S. Cacchi, *J. Org. Chem.*, **37**, 1856 (1972).
31. L. Caglioti, F. Gasparini, G. Paolucci, G. Rosini and P. Masi, *J. Org. Chem.*, **38**, 920 (1973).
32. G. Rosini and G. Baccolini, *J. Org. Chem.*, **39**, 826 (1974).
33. P. J. Stang and D. P. Fox, *J. Org. Chem.*, **42**, 1667 (1977).
34. A. Eschenmoser, D. Felix and G. Ohloff, *Helv. Chim. Acta*, **50**, 708 (1967).
35. P. Wieland, *Helv. Chim. Acta*, **53**, 171 (1970).
36. J. Schantl, *Monatsh. Chem.*, **103**, 1705 (1972).
37. G. Modena and U. Tonellato, *Advan. Phys. Org. Chem.*, **9**, 185 (1971).
38. P. Bassi and U. Tonellato, *Gazz. Chim. Ital.*, **102**, 387 (1972).
39. M. Hanack, *Acc. Chem. Res.*, **9**, 364 (1976).
40. M. Hanack, *Angew. Chem. (Intern. Ed.)*, **17**, 333 (1978).
41. P. J. Stang, *Acc. Chem. Res.*, **11**, 107 (1978).
42. P. J. Stang and T. E. Dueber, *Tetrahedron Letters*, 563 (1977).
43. W. Kirmse, *Angew. Chem. (Intern. Ed.)*, **15**, 251 (1976).
44. W. D. Pfeifer, C. A. Bahn, P. v. R. Schleyer, S. Bocher, C. E. Harding, K. Hummel, M. Hanack and P. J. Stang, *J. Amer. Chem. Soc.*, **93**, 1513 (1971).
45. H. Klingelhöfer, *Ingenieurarbeit*, Fachhochschule Münster, 1972.
46. J. W. Barton, A. R. Grinham and E. K. Whitaker, *J. Chem. Soc. (C)*, 1384 (1971).
47. D. Y. Curtin, J. A. Kampmeier and B. R. O'Connor, *J. Amer. Chem. Soc.*, **87**, 863 (1965).
48. D. Y. Curtin, J. A. Kampmeier and M. L. Farmer, *J. Amer. Chem. Soc.*, **87**, 874 (1965).
49. W. M. Jones and F. W. Miller, *J. Amer. Chem. Soc.*, **89**, 1960 (1967).
50. M. S. Newman and A. Kutner, *J. Amer. Chem. Soc.*, **73**, 4199 (1951).
51. M. S. Newman and W. M. Edwards, *J. Amer. Chem. Soc.*, **76**, 1840 (1954).
52. M. S. Newman and A. O. M. Okorodudu, *J. Org. Chem.*, **34**, 1220 (1969).
53. M. S. Newman and T. B. Patrick, *J. Amer. Chem. Soc.*, **91**, 6461 (1969); *J. Amer. Chem. Soc.*, **92**, 4312 (1970).
54. M. S. Newman and C. D. Beard, *J. Amer. Chem. Soc.*, **92**, 4309 (1970); *J. Org. Chem.*, **35**, 2412 (1970).
55. M. S. Newman and C. D. Beard, *J. Amer. Chem. Soc.*, **92**, 7564 (1970).
56. M. S. Newman and V. Lee, *J. Org. Chem.*, **38**, 2435 (1973).
57. M. S. Newman and W. C. Liang, *J. Org. Chem.*, **38**, 2438 (1973).
58. M. S. Newman and S. J. Gromelski, *J. Org. Chem.*, **37**, 3220 (1972).
59. A. Hassner and R. H. Reuss, *J. Org. Chem.*, **39**, 553 (1974).
60. W. Kirmse, O. Schnurr and H. Jendralla, *Chem. Ber.*, **112**, 2120 (1979).
61. J. C. Gilbert and U. Weerasooriya, *J. Org. Chem.*, **44**, 4997 (1979).
62. U. Schöllkopf, E. Wiskott and K. Riedel, *Angew. Chem. (Intern. Ed.)*, **7**, 138 (1968).
63. K. Bott, *Justus Liebigs Ann. Chem.*, **766**, 51 (1972).
64. S. A. McNeely and P. J. Kropp, *J. Amer. Chem. Soc.*, **98**, 4319 (1976).

The Chemistry of Functional Groups, Supplement C
Edited by S. Patai and Z. Rappoport

CHAPTER 17

Acidity and proton transfer of cyanocarbon acids

FRANK HIBBERT
Department of Chemistry, King's College, Strand, London WC2R 2LS, England

I. INTRODUCTION

In this chapter various aspects of the dissociation of protons from carbon acids containing a C≡N group will be covered. The ionization of carbon acids containing a C≡C group has been treated previously in this series[1].

Studies of the ionization of carbon acids are important because the carbanions produced are common reaction intermediates in organic chemistry. These may occur as short-lived species in a reaction mechanism[2] or may be purposely generated[3] as reagents in a synthetic scheme. The carbanions may be formed directly by the ionization of a carbon acid or they may be produced indirectly from some other reagent[3]. Often, unsubstituted hydrocarbons are too weakly acidic for the purpose of generating a carbanion for organic synthesis and even if the carbanion is produced indirectly it will undergo rapid and irreversible protonation to give the hydrocarbon. Hence, substituents are frequently used to stabilize the carbanion and increase the acidity of the carbon acid. Cyano groups are used in this way. Cyanocarbanions are frequently observed as reactive intermediates in organic reaction mechanisms[2,4,5] and have been used as reagents in synthesis[6–8]. The ionization of cyanocarbon acids has been studied widely to provide information about cyanocarbanions. This latter topic forms the basis of this review.

Cyanocarbon acids have been prepared with acidities covering a wide range and some examples are given in Table 1. Acetonitrile will ionize in solution to a significant extent only under extremely basic conditions and special techniques are needed to estimate the pK value of this carbon acid[14]. The ionizations of hydrogen cyanide and malononitrile occur in the normal pH range and can be studied by standard techniques. Tricyanomethane is fully ionized in aqueous solution except in the presence of concentrated mineral acids and an acidity function method is needed to estimate its pK value[22].

The first section of this review, Section II.A.1, deals with the acidity of weak cyanocarbon acids like malononitrile which ionize in aqueous solution. The stronger acids like tricyanomethane are dealt with in Section II.A.2. Very weak acids such as acetonitrile, for which the acidity can only be estimated by using kinetic methods or by using solutions of strong bases in nonaqueous solvents to bring about dissociation are covered in Section II.B. Carbanions derived from these very weak acids are of importance because these are the species which occur most often as intermediates in organic reaction mechanisms. After a brief survey of gas-phase acidity studies (Section II.C), the pK values for the cyanocarbon acids presented in Section II are used to discuss the factors which affect the stability of cyanocarbanions (Section III). The kinetics of proton-transfer reactions involving cyanocarbon acids are considered in Section IV which deals with the rates at which the cyanocarbanions are generated from the corresponding carbon acids (equation 1), as well as with the rates at which cyanocarbanions are protonated to regenerate the parent acid (equation 2).

$$R^1R^2R^3CH + B \longrightarrow R^1R^2R^3C^- + BH^+ \quad (1)$$

$$R^1R^2R^3C^- + BH^+ \longrightarrow R^1R^2R^3CH + B \quad (2)$$

Limited aspects of the ionization of cyanocarbon acids have been reviewed previously. Cyanocarbanions are discussed in Cram's book on carbanion chemistry[10]

TABLE 1. Acidities of cyanocarbon acids

Acid	pK	Reference
CH_4	40–50	9
CH_3CN	25–31	14
$CH_2(CN)_2$	11.20	16
HCN	9.21	21
$CH(CN)_3$	−5.13	22

and the acidity of cyanocarbon acids has been included in other reviews[23,24]. Kinetic aspects of the ionization of cyanocarbon acids have been covered in wider reviews[11,25–28] dealing with proton transfer from carbon acids.

II. ACIDITY OF CYANOCARBON ACIDS

A. Acidity in Aqueous Solution

1. Weak cyanocarbon acids

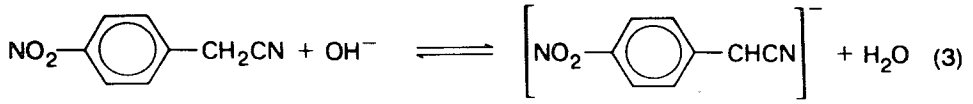
A large number of cyanocarbon acids with pK values in the range 0–14 have been prepared and some examples are given in Table 2. Apart from hydrogen cyanide and malononitrile the acids in Table 2 possess other acid-strengthening groups as well as cyano. The compilations by Kortum, Vogel and Andrussow[29] and by Serjeant and Dempsey[30] of dissociation constants of organic acids in aqueous solution contain references to several cyano-substituted carbon acids.

The cyanocarbon acids in Table 2 ionize in aqueous solution in the pH range 0–14 to produce stable carbanions. In a number of cases, solid salts consisting of the cyanocarbanion and an alkali metal ion are quite stable and have been isolated[41]. Measurements of the ionization of the acids shown in Table 2 were mostly made spectrophotometrically. The carbanions produced on ionization usually have a more intense absorption in the uv or the visible spectrum than the undissociated acid. This is particularly true when the charge on the carbanion is delocalized by conjugation with other groups in the molecule[42]. A spectrophotometric method was used for acids **1**, **2**, **4**, **6**, **7**, **8**, **10**, **12**, **14**, **15**, **16**, **17** and **18** and the dissociation of acids **5** and **9** was determined by potentiometric titration.

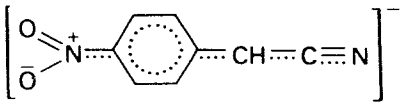
The carbanion derived from *p*-nitrobenzyl cyanide (**1**) shows some interesting properties. The conclusions drawn from the original spectrophotometric measurements[32] of the dissociation have been questioned[33,34] and as a result of further experiments it was suggested that the changes in the visible absorption spectrum which

TABLE 2. Weak cyanocarbon acids

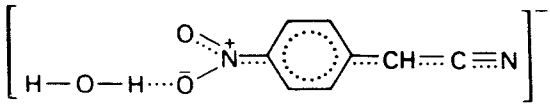
Acid	pK	Reference
(**1**) *p*-$NO_2C_6H_4CH_2CN$	13.4	31–34
(**2**) *t*-$BuCH(CN)_2$	13.1	36
(**3**) $CH_2(CN)CO_2Et$	11.7	17
(**4**) $CH_2(CN)_2$	11.20	16
(**5**) HCN	9.21	21
(**6**) $CH_2(CN)COSEt$	9.2	17
(**7**) $CH_2(CN)COSCH_2CH_2NHCOMe$	8.85	17
(**8**) $BrCH(CN)_2$	7.81	37
(**9**) $BrCH(CN)CO_2Et$	6	13
(**10**) $PhCH(CN)_2$	5.80	38
(**11**) $HC(CN)_2CH(CN)_2$	3.6	39
(**12**) $MeCOCH(CN)CO_2Et$	3.0	17
(**13**) $HC(CN)_2C(CN)_2SO_3^-$	2.62	39
(**14**) *p*-$NO_2C_6H_4CH(CN)_2$	1.89	38
(**15**) $MeCOCH(CN)COSCH_2CH_2NHCOMe$	1.8	17
(**16**) $MeCOCH(CN)_2$	1.0	17
(**17**) *p*-$(CN)_2C{=}C(CN)C_6H_4CH(CN)_2$	0.60	22
(**18**) $PhCH(CN)NO_2$	0.29	40



occur when solutions of *p*-nitrobenzyl cyanide are made basic may not correspond to a simple ionization to give the carbanion (equation 3). It was considered possible that addition to the aromatic ring to give a Meisenheimer complex was occurring but later work showed that no such complex was formed[43]. The situation appears to have been made clearer by Walters[35] who has studied the ionization of *p*-nitrobenzyl cyanide in Me_2SO–H_2O mixtures containing hydroxide ion. In this work it was deduced that the spectral changes were consistent with the presence of two carbanions, **19** and **20**.



(19)



(20)

Carbanion **19** is a nonspecifically solvated species whereas **20** involves hydrogen bonding between the nitro group and a water molecule. It was considered that there would be a difference in the visible spectrum of **19** and **20**. The spectral changes in the presence of base were therefore accounted for in terms of the equilibrium shown in equation (3) together with a further equilibrium involving **20**. Carbanion **19** is the predominant species in aprotic solvents and in Me_2SO–H_2O mixtures at high mole fractions of Me_2SO, whereas **20** predominates in aqueous solution.

In all of the examples given in Table 2 a cyano substituent enhances the acidity of the carbon acids although the magnitude of the effect varies considerably. The results in Table 1 indicate that the effect of a cyano group is to increase the acidity of a carbon acid by ca. 16 pK units. Comparison of the pK values of *p*-nitrobenzyl cyanide (**1**) and *p*-nitrophenyldicyanomethane (**14**) in Table 2 shows that introduction of the second cyano substituent increases the acidity by 11.5 units. The effect in the case of ethyl acetoacetate ($CH_3COCH_2CO_2Et$, pK = 10.7[44]) and ethyl acetocyanoacetate (compound **12**, pK = 3.0) is smaller (7.7 pK units). For phenylnitromethane ($PhCH_2NO_2$, pK = 6.88[45]) and phenylcyanonitromethane (compound **18**, pK = 0.29) the effect is smaller still.

In the acids in Table 2 the cyano substituent is attached to the carbon atom bearing the acidic proton. If the cyano group is more remote, the activating effect decreases and this is illustrated by the pK values of the dinitro-substituted carbon acids in Table 3a. The results in Table 3b provide a comparison between the effects of cyano and halogen substituents on the acidity of dinitroalkanes and it is clear that the cyano group exerts a much greater acid-strengthening effect. The acidities of the halogen-substituted dinitroalkanes decrease in the order I > Br > Cl > F and replacement of hydrogen by a fluorine atom in dinitromethane actually weakens the carbon acid by four pK units. The same order of acidity of halogen-substituted carbon acids has been deduced from the rates of proton exchange of haloforms[50]. This latter method of estimating acidity will be discussed in Section II.B.1.

In Table 4 the effect of cyano groups on hydrocarbon acidity is compared with the effects of nitro, sulphone, keto and ester groups. From the data in Table 3b and Table 4 the following order of increasing acid-strengthening effects is apparent:

$$F < Cl < Br < I < CO_2Et \sim SO_2Me < CN < COCH_3 < NO_2$$

TABLE 3. Acidity of dinitroalkanes

$$RCH(NO_2)_2 + H_2O \rightleftharpoons R\bar{C}(NO_2)_2 + H_3O^+$$

(a) Effect of remote cyano substituents[46]

R	pK	R	pK
H	3.63	CN	−6.22
CH_3	5.30	$NCCH_2$	2.34
CH_3CH_2	5.61	$NCCH_2CH_2$	3.50
—	—	$NCCH_2CH_2CH_2$	4.34
$CH_3CH_2CH_2CH_2$	5.45	$NCCH_2CH_2CH_2CH_2$	5.00

(b) Comparison of cyano and halogen substituents

R	pK	Reference
H	3.63	46
CN	−6.22	46
F	7.52	47
Cl	3.80	48
Br	3.47	46, 49
I	3.19	46

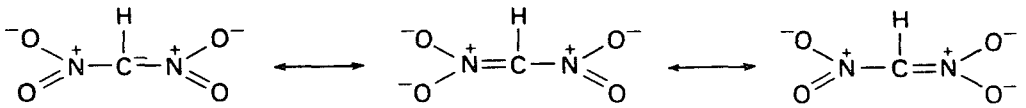
A different order is obtained when effects on the acidity of acids HOX are considered[13]. In this case the acid-strengthening effects increase in the order X = Halogen < CO < CN < NO_2 < SO_2Me. It is argued[61] that this arises because resonance effects are more important than inductive effects in the stabilisation of carbanions than in the stabilisation of oxygen anions. For oxygen anions the charge is localized on oxygen whereas in carbanions the charge is distributed over the molecule. Hence substituents for which resonance effects are larger than inductive effects (for example nitro and keto) are more effective in increasing the strength of carbon acids.

One further point emerges from the results given in Table 4. The acid-strengthening effect of a nitro or keto group is very much larger for introduction of the first group than for introduction of the second and third groups. Successive substitution of two or three cyano or methylsulphonyl groups has about the same effect on the acidity of the carbon acid as substitution of the first cyano or methylsulphonyl group. An explanation[42,62] for the decreasing effect of successive nitro substituents assumes that nitrocarbanions (**21**) are stabilized by conjugation which places most of the negative charge on oxygen and that this is most effective when the carbanion is planar. It is then

TABLE 4. Comparison of the activating effects of substituents on the strength of carbon acids

	pK values			
X	CH_4	CH_3X	CH_2X_2	CHX_3
CN	40–50[9]	25–31[14]	11.20[16]	−5.13[22]
NO_2	40–50	10.2[51]	3.57[52]	0.14[40,53]
SO_2CH_3	40–50	31.1[15,54]	12.55[55–57]	ca.0[13]
$COCH_3$	40–50	19–20[58]	8.9[44,59]	5.8[13,60]
CO_2Et	40–50	25[13]	13.3[13]	—

(21)



(22)

argued that the carbanions derived from dinitromethane (22) and trinitromethane are not fully planar because of repulsive interactions between oxygen atoms on adjacent nitro groups and hence conjugative stabilization by the second and third nitro substituents is less effective. Perhaps a similar explanation can be used to account for the reduced acid-strengthening effects of two and three keto groups as in methane (pK = 40–50), acetone (pK = 19–20), acetylacetone (pK = 8.9) and 1,1-diacetylacetone (pK = 5.8). However the third cyano substituent in tricyanomethane has about the same acid-strengthening effect as the first cyano substituent and similar results are found for methylsulphonyl groups. This may mean that inductive effects are more important than conjugative effects in the stabilization of cyano- and methylsulphonyl-carbanions or alternatively that steric hindrance to resonance in these carbanions is smaller than for nitrocarbanions.

2. *Strong cyanocarbon acids*

Cyanocarbon acids with pK values around zero and below will be considered in this section. When these acids are introduced in low concentration into aqueous solution they dissociate fully into the carbanion and ionization is only suppressed by the presence of mineral acids in high concentration.

Dissociation of the cyanocarbon acids given in Table 5 was investigated[22] in concentrated solutions of perchloric acid or sulphuric acid (0–12 M) by making spectrophotometric measurements at wavelengths at which the carbanions absorb strongly. The ionization of *p*-tricyanovinylphenyldicyanomethane (equation 4) was studied in the presence of up to 0.1 M mineral acid and the pK value (0.60) therefore refers to conditions

$$p\text{-}(CN)_2C{=}C(CN)C_6H_4CH(CN)_2 + H_2O \rightleftharpoons p\text{-}(CN)_2C{=}C(CN)C_6H_4C(CN)_2^- + H_3O^+ \quad (4)$$

TABLE 5. Strong cyanocarbon acids[22]

	pK
(23) $C\underline{H}(CN)_2CO_2CH_3$	−2.78[a]
(24) $(CN)_2C{=}C(CN)CH{=}C(CN)C\underline{H}(CN)_2$	−3.55[a]
(25) $CH(CN)_3$	−5.13
(26) $(CN)_2C{=}C(CN)N{=}C(CN)CH(CN)_2$	−6.07
(27) $(CN)_2C{=}CHC\underline{H}(CN)_2$	−8[a]
(28) $(CN)_2C{=}C(C(CN)_2\underline{H})_2$	$pK_1 = -8.5$[a], $pK_2 = -2.5$[a]

[a]The proton which dissociates is underlined.

for which activity coefficients are approximately given by Debye–Hückel theory. The ionization of *p*-tricyanovinylphenyldicyanomethane was then investigated in more concentrated mineral acid solution and an acidity function (H_-) was measured for the mineral acid solution (equation 5).

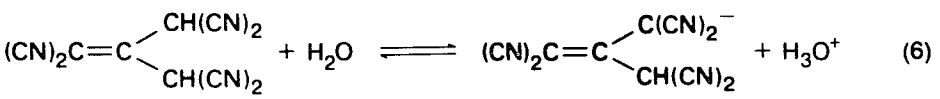
$$H_- = pK + \log (C_{A^-}/C_{HA}) \tag{5}$$

In equation (5) pK refers to the acidity of *p*-tricyanovinylphenyldicyanomethane in dilute aqueous solution and C_{A^-}/C_{HA} is the measured ionization ratio of the cyanocarbon acid at a particular concentration of mineral acid. For a solution containing a certain concentration of mineral acid the acidity function at this concentration measures the tendency of an acid HA with acidity pK to dissociate in this solution and should apply to all acids HA of the same charge type[63]. The ionization of the stronger cyanocarbon acid methyl dicyanoacetate (compound **23** in Table 5) was studied in mineral acid solutions for which H_- had been established by the studies with *p*-tricyanovinylphenyldicyanomethane and in this way a pK value (−2.78) was determined for methyl dicyanoacetate. The acidity function was then extended to solutions containing higher concentrations of mineral acid by further studies with methyl dicyanoacetate. The acidity function was determined for solutions with up to 12M H_2SO_4 or 11M $HClO_4$ using the cyanocarbon acids in Table 5 and the pK values of the acids were obtained.

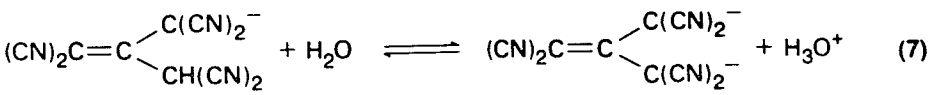
The acids in Table 5 are derivatives of malononitrile, $CH_2(CN)_2$ (pK = 11.20). Some of the acids are stronger than mineral acids and Boyd[22] explains this strength in terms of stabilization of the carbanions by conjugation with the group R, as shown in **29**.

(29)

For acid **28** in Table 5 two separate equilibria are observed. These correspond to the ionization of both protons as shown in equations (6) and (7).



(6)

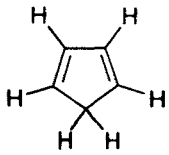
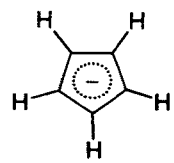
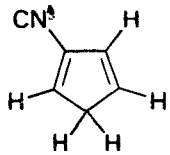
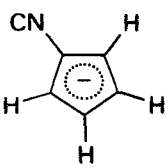
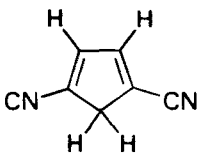
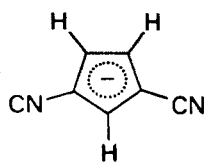
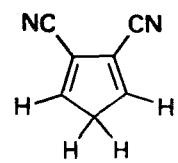
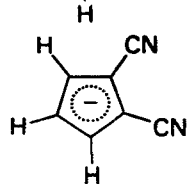
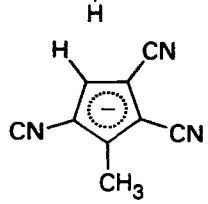
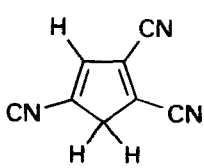
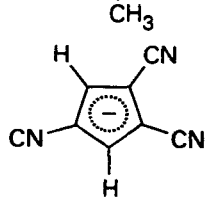
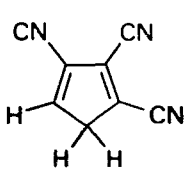
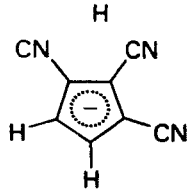
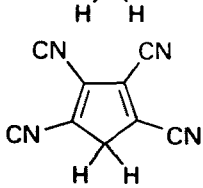
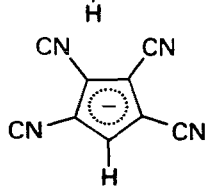
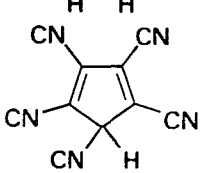
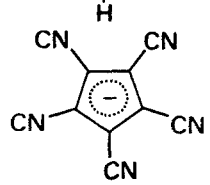


(7)

By investigating the temperature dependence of the dissociation constants of these strong cyanocarbon acids, values for the enthalpy (ΔH^0) and entropy (ΔS^0) of ionization were obtained[18]. The variation in pK with structure of the cyanocarbon acids was found to be due mainly to a variation in ΔH^0. It was found that the value of ΔS^0 varied only slightly in going from acid **23** to acid **28**, becoming less negative as the acidity increases. This slight trend in ΔS^0 is compatible with decreased solvent orientation around the anion as charge delocalization in the anion increases and the cyanocarbon acid becomes stronger. The variation of ΔH^0 with structure was explained as being the result of an increase in conjugative stabilization of the carbanion which brings about an increase in the strength of the cyanocarbon acid.

The cyano-substituted cyclopentadienes in Table 6 also show remarkably high acidity[64]. The ionizations were observed spectrophotometrically by making use of the

TABLE 6. Acidity of cyanocyclopentadienes[64]

	Conjugate acid		Conjugate base + H^+	p*K*
(30)		⇌	 + H^+	15
(31)		⇌	 + H^+	9.78
(32)		⇌	 + H^+	2.52
(33)	 or 	⇌	 + H^+	1.1
(34)		⇌	 + H^+	−5.7
(35)		⇌	 + H^+	−6.1
(36)		⇌	 + H^+	−7.5
(37)		⇌	 + H^+	−9.0
(38)		⇌	 + H^+ < −11.0	

difference in absorbance of the carbanion and undissociated acid in the UV region. Compounds **30–33** were studied in aqueous solution and **33** together with **34–38** were studied in acetonitrile. Since **33** was studied in both solvents, the pK values of compounds **34–38** determined in acetonitrile were corrected to refer to aqueous solution by using a correction term equal to the difference in pK for **33** between water and acetonitrile. These corrected values are given in the table.

B. Very Weak Cyanocarbon Acids

There are two ways of investigating the acidity of acids which are too weakly acidic to dissociate significantly in the normal pH range. The ionization can be studied in a nonaqueous or in a mixed aqueous solvent containing base. For a carbon acid which will not dissociate to a measurable extent even under the most strongly basic conditions or which dissociates to give an unstable carbanion, a kinetic method of measuring acidity may be applicable. A reaction involving the intermediate formation of a carbanion from the carbon acid may be studied and information about the acidity of the carbon acid may be obtained from the rate of reaction. The rate measurements can often be made in aqueous solution. These two procedures which have been used to investigate the acidity of weak cyanocarbon acids will be described in this section.

1. Kinetic measurements of acidity

A limited number of cyanocarbon acids have been studied using this technique but the method has been applied widely to many other carbon acids[27,65]. For example, the rate of tritium exchange of phenylacetylene which occurs in mildly basic aqueous solution has been widely investigated[66,67] and has been used to estimate the pK value of this carbon acid. The experiment may be carried out with the isotope label initially in phenylacetylene or in the solvent and the mechanism of exchange[66,67] is shown in equations (8) and (9). According to the rate expression (equation 10) the rate of

$$\mathrm{PhC{\equiv}CT + B} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{PhC{\equiv}C^- + BT^+} \tag{8}$$

$$\mathrm{PhC{\equiv}C^- + BH^+} \xrightarrow{k_2} \mathrm{PhC{\equiv}CH + B} \tag{9}$$

$$-\mathrm{d[PhC{\equiv}CT]}/dt = k_1[\mathrm{B}][\mathrm{PhC{\equiv}CT}] \tag{10}$$

exchange measures the rate coefficient (k_1) for the base catalysed dissociation of the tritiated carbon acid. Under the conditions of the isotope exchange experiment less than one part in 10^{12} of phenylacetylene is dissociated into the carbanion. The value of the rate coefficient k_1 can be used in two different ways to provide an approximate value for the acid dissociation constant of phenylacetylene pK = ca. 21[66,67]. If the value of the rate coefficient for the reverse reaction between the carbanion and acid BH^+ can be estimated, the equilibrium constant (K) can be obtained from the relation $K = k_1/k_{-1}$, after some allowance is made for the isotope effect. There is good evidence that for several carbon acids reaction between the carbanions and hydronium ion or other acidic species is diffusion-controlled with a second-order rate coefficient ca. 1.0×10^{10} l mol^{-1} s^{-1}. This topic is discussed more fully in Section IV but some examples which will be referred to again in Section IV are given in Table 7. The values of k_{-1} given in Table 7 were not obtained from direct measurements but the results were deduced from other evidence. In these cases for which k_{-1} = ca.

TABLE 7. Examples of rapid protonation of carbanions[a]

			Ref.
$Me_3CC(CN)_2^- + H_3O^+$	$\xrightarrow{4.0 \times 10^9}$	$Me_3CCH(CN)_2 + H_2O$	36
$Me_3CC(CN)_2^- + CH_3COOH$	$\xrightarrow{1.0 \times 10^8}$	$Me_3CCH(CN)_2 + CH_3CO_2^-$	36
$CCl_3^- + H_2O$	$\xrightarrow{\text{ca. } 1 \times 10^{10}}$	$CHCl_3 + OH^-$	68
$CCl_3^- + \dot{N}H_3(CH_2)_3\dot{N}Me_3$	$\xrightarrow{\text{ca. } 1 \times 10^{10}}$	$CHCl_3 + NH_2(CH_2)_3\dot{N}Me_3$	69
$PhC{\equiv}C^- + H_2O$	$\xrightarrow{\text{ca. } 1 \times 10^{10}}$	$PhC{\equiv}CH + OH^-$	67
$PhC{\equiv}C^- + PhCH_2NH_3^+$	$\xrightarrow{\text{ca. } 1 \times 10^{10}}$	$PhC{\equiv}CH + PhCH_2NH_2$	67
$(MeSO_2)_2CH^- + H_3O^+$	$\xrightarrow{2.3 \times 10^{10}}$	$(MeSO_2)_2CH_2 + H_2O$	70
$(MeSO_2)_2CH^- + ClCH_2CH_2CO_2H$	$\xrightarrow{9.4 \times 10^7}$	$(MeSO_2)_2CH_2 + ClCH_2CH_2CO_2^-$	57
$CH_3COCH_2^- + H_3O^+$	$\xrightarrow{5 \times 10^9 - 5 \times 10^{10}}$	$CH_3COCH_3 + H_2O$	71

[a]Rate coefficients (over the arrows) in l mol^{-1} s^{-1} refer to aqueous solution at 25°C.

1×10^{10} l mol^{-1} s^{-1} a rough value for the dissociation constant of the carbon acid can be calculated from the rate coefficient for isotope exchange. However, for many carbon acids the rate of recombination of the carbanions with acid is well below the diffusion limit and this procedure is not valid. For example, the rate coefficient for recombination of the anion of nitroethane with hydronium ion (equation 11), is quite slow[72].

$$CH_3CHNO_2^- + H_3O^+ \xrightarrow{k_{-1} = 15 \text{ l mol}^{-1}\text{s}^{-1}} CH_3CH_2NO_2 + H_2O \qquad (11)$$

Using this isotope exchange procedure a value of $pK = 25$ has been estimated[13] for acetonitrile from the rate of exchange[73] between acetonitrile and deuterium oxide containing deuteroxide ion. Similarly, $pK = 30$ was estimated for the acid dissociation of 2-methyl-3-phenylpropionitrile from the rate of methoxide-ion-catalysed dedeuteration in methanol[74] (equation 12).

$$PhCH_2{-}\underset{\displaystyle CH_3}{\overset{\displaystyle CN}{\overset{|}{\underset{|}{C}}}}{-}D + MeO^- \xrightarrow{MeOH} PhCH_2{-}\underset{\displaystyle CH_3}{\overset{\displaystyle CN}{\overset{|}{\underset{|}{C}}}}{-}H + MeOD \qquad (12)$$

The second procedure for estimating the acidity of a carbon acid from the rate coefficient for isotope exchange is illustrated by Streitwieser's experiments with polyarylmethanes[75]. Earlier applications of a similar method include Shatenstein's studies of isotope exchange in olefins and acetylenes[76]. Although this procedure has not been used for measuring absolute acidities of cyanocarbon acids, relative acidities of cyanocarbon acids have been obtained in this way. In Streitwieser's work the equilibrium dissociation of several hydrocarbons with acidities in the pK range 30–40 was studied by spectrophotometric measurements in cyclohexylamine containing lithium cyclohexylamide or caesium cyclohexylamide. The rate of isotope exchange of the hydrocarbons was investigated under similar conditions and it was found that the

rate of exchange (k_e) varied with the pK of the acid according to equation (13) with an α value of 0.31. Equation (13) is a form of the Brønsted

$$\log k_e = -\alpha \,.\, (pK) + \text{constant} \qquad (13)$$

relation in which the rate of dissociation of a carbon acid is related to the acidity of the carbon acid. The equation expresses the result that the rate of proton transfer increases as the acidity of the carbon acid increases[25,27]. It was found that toluene was too weakly acidic to detect equilibrium dissociation in cyclohexylamine containing cyclohexylamide anion but the rate of isotope exchange was observable. The exchange occurs through a low steady-state concentration of the carbanion which would be too low to observe by spectrophotometric measurements. Hence the pK value of toluene was estimated as 40.9 from the rate of isotope exchange by extrapolation of the Brønsted plot (equation 13). The acidities and rates of exchange of halogen-substituted hydrocarbons (for example chloroform, pK = 24.4) have been measured using the same procedure[77].

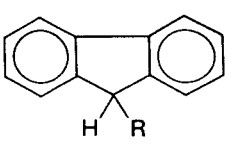
2. *Equilibrium acidity measurements in nonaqueous solvents*

Methods have been developed over the last few years for measuring the equilibrium acidity of very weak carbon acids with pK values up to ca. 40. One technique which has been used by Bordwell is to study dissociation of the carbon acid in dimethyl sulphoxide containing the potassium or caesium salt of dimethyl sulphoxide (dimsyl potassium or caesium). Since the pK of dimethyl sulphoxide in the pure solvent has been estimated[15] as 35.1, carbon acids which are more strongly acidic than this will dissociate into the carbanion when placed in dimethyl sulphoxide containing dimsyl potassium or caesium. Other solvents used for studying the ionization of weak acids include mixtures of dimethyl sulphoxide with water containing hydroxide ion[78,79] which can be used up to pK of ca. 25. Streitwieser has used cyclohexylamine containing lithium or caesium cyclohexylamide as solvent for studying[75] the dissociation of weak carbon acids with pK values up to ca. 40. The results using these different techniques are not always the same, possibly because of different ion-pairing effects in the different solvents[80]. Since most of the studies with cyanocarbon acids have been made by Bordwell using dimethyl sulphoxide as solvent, this procedure will be discussed in detail here.

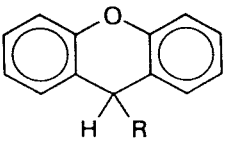
Two methods can be used for measuring the equilibrium position between the carbon acid and its carbanion in dimethyl sulphoxide containing dimsyl potassium. The equilibrium position can be measured potentiometrically using a glass electrode[81] although for weaker acids a spectrophotometric technique has been found to be more useful[15]. In this latter method a solution of the carbon acid (R^1CH) and its carbanion is prepared by adding a known concentration of the carbon acid to a known concentration of dimsyl potassium in dimethyl sulphoxide. This solution is titrated with a solution of a second carbon acid (R^2CH). One of the carbon acids is chosen to produce a carbanion which absorbs in the UV or visible region. The position of the acid–base equilibrium between the two acids (equation 14) is then measured

$$R^1CH + R^2C^- \longrightarrow R^1C^- + R^2CH \qquad (14)$$

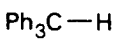
spectrophotometrically and the relative acidity of the two carbon acids in dimethyl sulphoxide is therefore determined. The procedure is most accurate if the pK values of the two acids differ by less than two units. In order to measure an absolute pK one of the acids is chosen with a known pK and Bordwell has set up a series of indicator acids for this purpose. The indicators, which are mostly derivatives of fluorene (**39**) and



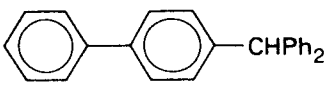
(39)



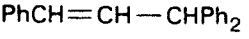
(40)



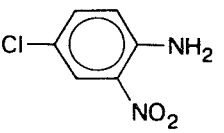
(41)



(42)



(43)



(44)

TABLE 8. Indicators for pK measurement in dimethyl sulphoxide[15]

Indicator acids	pK
Triphenylmethane	30.6
Biphenylyldiphenylmethane	29.4
9-Phenylxanthene	27.9
9-(3-Chlorophenyl)xanthene	26.6
1,3,3-Triphenylpropene	25.6
9-*t*-Butylfluorene	24.3
Fluorene	22.6
4-Chloro-2-nitroaniline	18.9
9-Phenylfluorene	17.9
9-Phenylthiofluorene	15.4
9-Phenylsulphonylfluorene	11.5
9-Carbomethoxyfluorene	10.3
9-Cyanofluorene	8.3

xanthene (**40**) as well as triphenylmethane (**41**), *p*-biphenylyldiphenylmethane (**42**), 1,3,3-triphenylpropene (**43**) and 4-chloro-2-nitroaniline (**44**) are given in Table 8 with their pK values. The pK values of the indicators were determined by successive measurements of relative acidities progressing to stronger acids whose absolute pKs could be measured potentiometrically. It is interesting to note that for fluorene the pK value determined in dimethyl sulphoxide (22.6) compares well with the value obtained[84] in Me_2SO–H_2O mixtures (22.1) and in cyclohexylamine (22.7)[85]. The precise procedure for making pK measurements in dimethyl sulphoxide, including details of solvent purification and handling, has been described[15].

Some examples of very weak cyanocarbon acids which have been studied using the potentiometric or indicator method in Me_2SO are given in Table 9. Although it is the relative acidities of the acids in Table 9 which are perhaps more important, it is useful to compare the pK values determined in Me_2SO with results which have been obtained in aqueous solution. A rough pK value of ca. 25 for acetonitrile has been determined by an approximate calculation using the rate of isotope exchange in water (see Section II. B.1) and gives poor agreement with the pK of 31.3 obtained in Me_2SO. The pK value of phenylacetylene (28.7)[87,91] determined in Me_2SO is not compatible with the value in aqueous solution (20–21) deduced from the rate of

TABLE 9. Acidities of weak cyanocarbon acids and other carbon acids determined in dimethyl sulphoxide

Carbon acid	pK	Reference
CH_3CN	31.3	86
$CH_3SO_2CH_3$	31.1	86
$PhC{\equiv}CH$	28.7	87
CH_3COCH_3	26.5	86
$PhCH_2CN$	21.9	88
$NCCH_2CH{=}CHCH_2CN$	20–21[a]	89
$PhSCH_2CN$	20.8	90
$Me_3\overset{+}{N}CH_2CN$	20.6	90
m-$FC_6H_4CH_2CN$	20.0	87
Ph_2CHCN	17.5	87
CH_3NO_2	17.2	86
$PhSO_2CH_2CN$	12.0	90
$CH_2(CN)_2$	11.1	90
$PhCOCH_2CN$	10.2	90

[a]Determined in Me_2SO–H_2O mixtures.

amine-catalysed istotope exchange[67]. The rate coefficient for isotope exchange is identified as the rate coefficient k_1 in equation (15) and there is good evidence[67] that

$$PhC{\equiv}CH + RNH_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} PhC{\equiv}C^- + RNH_3^+ \qquad (15)$$

the rate coefficient for the reverse reaction of the carbanion with acids has the diffusion-limited value, k_{-1} = ca. 1×10^{10} l mol^{-1} s^{-1}. From these results a value pK = 20–21 is obtained for phenylacetylene in aqueous solution. If a value for k_{-1} is chosen which is lower than the diffusion limit a pK lower than 20–21 is obtained. Therefore the pK value of 28.7 as determined in dimethyl sulphoxide cannot be applicable to aqueous solution because it would mean that k_{-1} would be higher than the diffusion-limited rate coefficient. The acidity of acetone determined in Me_2SO, pK = 26.5, is different from the pK of 20–21 estimated from rate measurements in aqueous solution[58]. Similarly the acidity of nitromethane determined in Me_2SO, pK = 17.2, is not compatible with the result pK = 10.2 obtained[51] in water. However, similar results are obtained for the acidity of malononitrile in water (pK = 11.20) and Me_2SO (pK = 11.1). It is found that phenols and carboxylic acids are about 6–7 pK units more acidic in water than in Me_2SO[93]. All this means that the pK values listed in Table 9 referring to dimethyl sulphoxide solutions are not the same as the values which are found in aqueous solution. It is generally agreed that dimethyl sulphoxide is less able to stabilize anions than water and is a much weaker hydrogen-bond donor[94]. However, dimethyl sulphoxide is thought to be a better hydrogen bond acceptor[94].

We now turn to a discussion of the relative pK values of the acids given in Table 9. The series CH_3CN (pK 31.3), $CH_3SO_2CH_3$ (31.0), CH_3COCH_3 (26.5) and CH_3NO_2 (15.1) suggests that the order of substituents in increasing the acidity of carbon acids is $CN \sim SO_2CH_3 < COCH_3 < NO_2$. The following p$K$ values of acids of the type XCH_2CN are given in Table 9: for X = H (pK 31.3), X = $PhSO_2$ (12.0), X = CN (11.1) and X = PhCO (10.2). This suggests that a cyano group is slightly more effective than a sulphonyl group and this was the conclusion reached in Section II.A.1. The pK values for toluene (pK 40.9)[75], benzyl cyanide (21.9) and phenylmalononitrile (5.80)[38] illustrate the effects of one and two cyano groups.

C. Acidity in the Gas Phase

In theory, the acidities of carbon acids in the gas phase should be more easy to interpret than acidities in solution because the effects of solvent are absent. A comparison of gas-phase and solution acidities for similar compounds should give information about the effects of solvation on acidities. In this section the gas-phase acidities of cyanocarbon acids will be compared with the acidities of other carbon acids in the gas phase and with acidities in solution.

The first studies of carbon acids in the gas phase were made by Brauman and Blair using ion cyclotron resonance spectroscopy[95]. It was concluded that in the gas phase acidity increased in the order $HCN < CH_3COCN < CH_3COCH_2COCH_3$. Using the same technique the relative acidities of amines[96] and alcohols[97] have since been measured.

Using the flowing afterglow technique, rates and equilibrium constants for several proton-transfer reactions involving carbon acids have been measured in the gas phase[98]. Some examples with values of the equilibrium constants are given in equations (16), (17) and (18). From these and similar results the following order of

$$CH_2CN^- + CHCl_3 \rightleftharpoons CH_3CN + CCl_3^- \quad K>20 \tag{16}$$

$$CH_2CN^- + CH_3COCH_3 \rightleftharpoons CH_3CN + CH_3COCH_2^- \quad K>3 \tag{17}$$

$$CH_3CN + CH_3SOCH_2^- \rightleftharpoons CH_2CN^- + CH_3SOCH_3 \quad K>20 \tag{18}$$

increasing acidity in the gas phase was deduced: $CH_3SOCH_3 \sim CH_2Cl_2 < CH_3CN < CH_3COCH_3 < CHCl_3 < CH_3NO_2$. By comparison with the order obtained for acidities in solution it is clear that specific solvation of some of the anions in these reactions is playing an important role in determining solution acidities. For example the difference in acidity between water and acetonitrile in aqueous solution $pK^{H_2O}(H_2O) - pK^{H_2O}(CH_3CN) = -9$ is very different from the acidity difference measured in the gas phase $pK^{gas}(H_2O) - pK^{gas}(CH_3CN) > 2.7$. This means that the equilibrium constant for reaction (19) increases by a factor of ca. 10^{12} in going from

TABLE 10. Comparison of carbon acid strengths in the gas phase and in dimethyl sulphoxide

Carbon acid	ΔG^0 (Me_2SO)[a]	ΔG^0 (gas)[a]
CH_3SOCH_3	46	368
CH_3CN	43	366
CH_3COCH_3	36	363
$CH_3SO_2CH_3$	42	359
Ph_2CH_2	42	356
$PhCOCH_3$	32	356
$PhSO_2CH_3$	40	355
CH_3NO_2	22	350
$PhCH_2COCH_3$	27	346
$PhCH_2CN$	30	345
$(CH_3CO)_2CH_2$	38	338
$CH_2(CN)_2$	15	329

[a]Values of ΔG^0 (the free energy of dissociation into ions) are given in kcal mol^{-1} and rounded up to the nearest whole number.

aqueous solution to the gas phase. For reaction (20) the equilibrium constant is 10^7-fold higher in the gas phase than in aqueous solution.

$$CH_3CN + OH^- \rightleftharpoons CH_2CN^- + H_2O \quad (19)$$

$$CH_3COCH_3 + OH^- \rightleftharpoons CH_3COCH_2^- + H_2O \quad (20)$$

On the basis of acidity measurements by mass spectrometry McMahon and Kebarle[99] have commented on the difference in acidities of malononitrile and chloroacetic acid in the gas phase and in aqueous solution. In the gas phase malononitrile is slightly more acidic than monochloroacetic acid but in aqueous solution malononitrile is weaker by 8 pK units. This is thought to arise because in

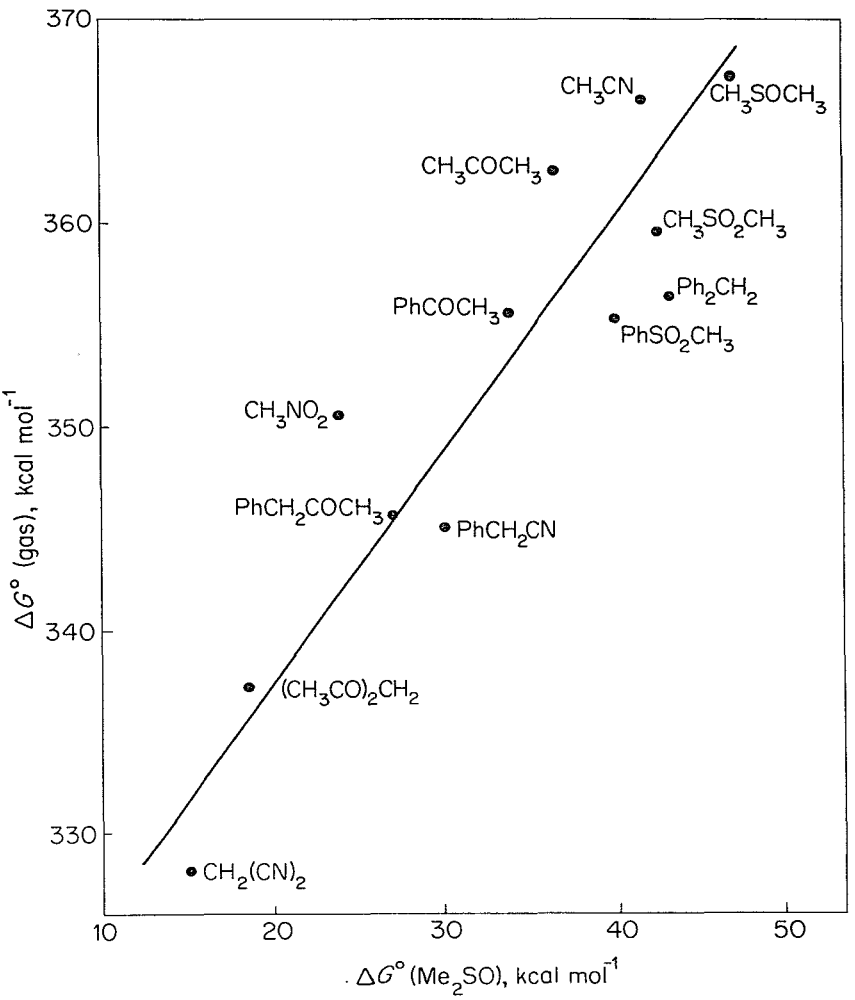


FIGURE 1. Comparison of acidities of carbon acids in the gas phase and in dimethyl sulphoxide solution. The values of ΔG^0 (gas) and ΔG^0 (Me_2SO) refer to the free energy change (kcal mol^{-1}) for the reaction $R^1R^2R^3CH \rightarrow R^1R^2R^3C^- + H^+$. Drawn from data given in Reference 103.

aqueous solution the carboxylate ion is more strongly solvated than the carbanion owing to the greater charge dispersal in the carbanion and the presence of only one hydrogen-bonding site. A similar conclusion is drawn from the relative acidities of methanol and acetonitrile in the gas phase and in aqueous solution[100]. In solution acetonitrile is weaker by 9 pK units but in the gas phase acetonitrile is a much stronger acid than methanol.

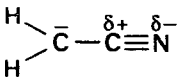
Interesting comparisons between gas-phase acidities and acidities in dimethyl sulphoxide have been made by Bordwell[101] and by Kebarle[102,103]. A selection of these data is given in Table 10. The values of ΔG^0 (kcal mol^{-1}) refer to the free-energy change for reaction (21) in Me_2SO and in the gas phase. An earlier measurement[99] for acetonitrile which

$$R^1R^2R^3CH \rightarrow R^1R^2R^3C^- + H^+ \qquad (21)$$

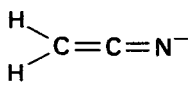
indicated that the latter is more acidic than acetone in the gas phase has been corrected[102] and acetone is now considered to be more acidic by ca. 3 kcal mol^{-1}. For a given carbon acid the free energy of dissociation is much larger in the gas phase than in solution because of the large and negative enthalpies of solvation of the ions. The correlation between acidities in the gas phase and in Me_2SO is illustrated in Figure 1. Deviations from this correlation are explained in terms of the effects of the differences in electron delocalization in the anions on their solvation. The deviations are quite small, however, and the relative effects of different groups on the acidity of carbon acids in the gas phase and in dimethyl sulphoxide are very similar. In the gas phase the size of the acid-strengthening effect of substituents increases in the order $SOCH_3 < CN < COCH_3 < SO_2CH_3 < NO_2$ whereas in dimethyl sulphoxide the order is $SOCH_3 < CN \sim SO_2CH_3 < COCH_3 < NO_2$. The gas-phase acidities of a wide range of acids including some cyanocarbon acids have been tabulated in a recent paper[104].

III. ELECTRONIC EFFECTS IN THE STABILIZATION OF CYANOCARBANIONS

It is a long standing problem in organic chemistry to assess the relative importance of polar and resonance (conjugative) effects of substituents on the equilibrium position or rate of a chemical reaction[105–107]. The effect of a cyano group on the acidity of carbon acids is explained in terms of stabilization of the carbanion but there is uncertainty as to whether the important effect is polar or conjugative, as shown in **45** and **46** respectively. A cyano group can stabilize a negative charge in both ways[106]. Some of the evidence will be reviewed here.



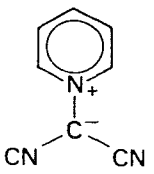
(45)



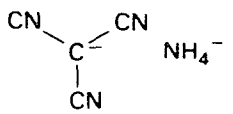
(46)

Crystal structures[108] of pyridinium dicyanomethylide (**47**) and of the ammonium salt of tricyanomethane (**48**) indicate that the carbanions are planar and trigonal. The extremely high acidity of tricyanomethane is explained[22] by conjugative stabilization in the carbanion by cyano groups and this is confirmed by simple MO calculations[109].

Bell[110] comments on the observation that one keto, cyano or sulphonyl group increases the acidity of a carbon acid by ca. 10–15 pK units (see Table 4). He proposes that most of the stabilization in the case of cyano and sulphonyl groups arises from a polar effect rather than by conjugation because these groups also have large effects on



(47)



(48)

the acidity of carboxylic acids for which conjugative stabilization of the carboxylate ion by the substituent is not possible. This point is illustrated by the results for substituted acetic acids: CH_3COOH (pK 4.75), CH_3COCH_2COOH (pK 3.58), $NCCH_2COOH$ (pK 2.47) and CH_3SO_2COOH (pK 2.36). We have already discussed in Section II.A.1 the observation that keto groups are more effective in stabilizing carbanions than cyano or sulphone groups but less effective in stabilising oxygen anions. Because conjugative effects are thought to be less important for oxygen anions where the negative charge can remain on oxygen, it has been argued[61] that keto and nitro groups are more effective in conjugative stabilization than cyano or sulphonyl substituents.

A similar conclusion to this is reached in two papers which deal with substituent effects on the acidity of carbon acids in the gas phase[111] and in dimethyl sulphoxide[90]. In the gas-phase study[111] the effect of a substituent (X) on the acidity of methane as measured by the difference between the free energy of dissociation of methane ($\Delta G^0_{CH_4}$) into CH_3^- and H^+ and the free energy of dissociation of the substituted acid ($\Delta G^0_{CH_3X}$), $\delta\Delta G^0 = \Delta G^0_{CH_4} - \Delta G^0_{CH_3X}$, was plotted against the value of σ_I for the substituent where σ_I is the Taft parameter for polar effects[105,107]. This plot is illustrated in Figure 2. A straight line is drawn through the data in Figure 2 and it is clear that the data fall into two groups. The general trend in $\delta\Delta G^0$ for various substituents with the value of σ_I for that substituent shows that polar effects are important in the stabilization of the carbanions. However in some cases conjugative effects are also important. Those substituents such as CO_2Me and COMe for which $\sigma_{R^-} > \sigma_I$, where σ_{R^-} is the Taft parameter for conjugative electron withdrawal[105,107], fall above the linear correlation in Figure 2 and are more effective in increasing the acidity of carbon acids than expected from the value of σ_I. Groups like SO_2Me and CN, for which $\sigma_{R^-} < \sigma_I$, fall below the linear correlation and this suggests that conjugative effects are less important for CN and SO_2Me than for COMe in the stabilization of carbanions.

A similar analysis of substituent effects has been made on the basis of acidities of carbon acids in Me_2SO[90]. The data which were analysed are shown in Table 11 and these results were used to assess the relative importance of polar and conjugative effects for the groups CH_3CO, PhCO, $PhSO_2$, CN and NO_2 on the stabilization of carbanions. Since the trimethylammonium substituent cannot act as a π acceptor the effect of Me_3N^+ on the acidity of carbon acids must be due solely to a polar effect and this group was therefore used as a standard for assessing the size of the polar effects of the other substituents. The procedure was carried out as follows. For each series of acids, A, B and C, the size of the polar effect of Me_3N^+ on the acidity was calculated as the difference in pK (ΔpK) of the acids with X = Me and X = Me_3N^+. The effect is quite large in each series, amounting to 9–12 pK units. Using the Taft parameter as a measure of the polar effect of Me_3N^+, $\sigma_I = 0.82$, the value of ρ_I for each series of acids A, B and C was calculated from the Taft relation (equation 22). Then the polar effect

$$\Delta pK = \rho_I \sigma_I \tag{22}$$

for each substituent was calculated (ΔpK_{calc}) by using the calculated value of ρ_I for each series and the value of σ_I for that substituent. This was carried out for each series

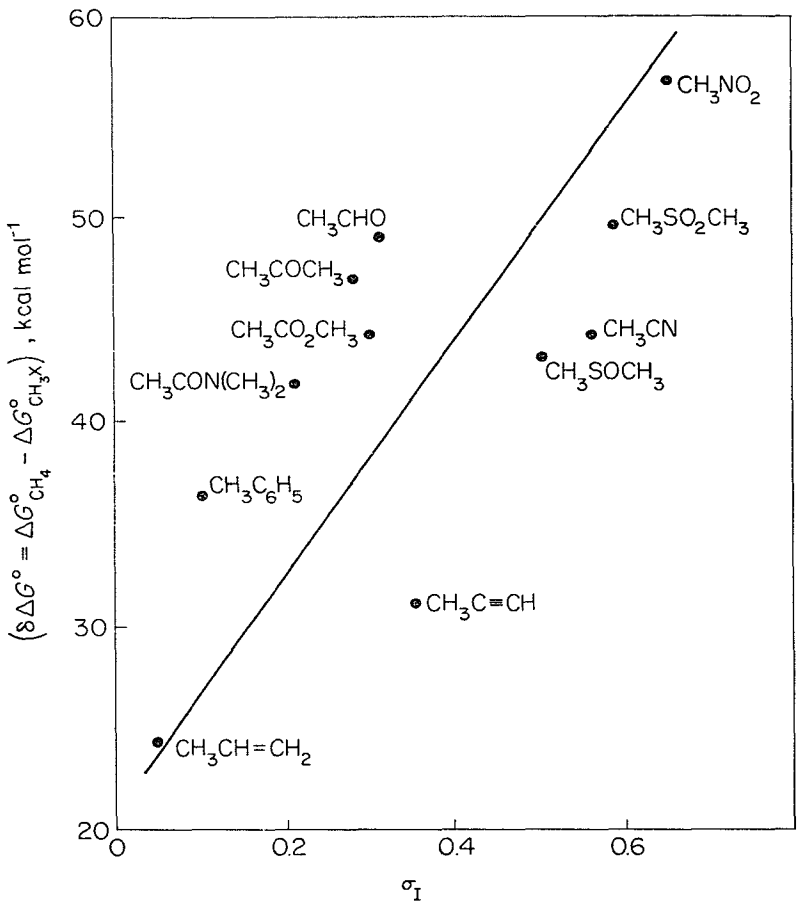


FIGURE 2. Substituent effects on the acidity of carbon acids (CH_3X) in the gas phase. The ordinate is the difference in free energy of dissociation (kcal mol^{-1}) of the acids CH_4 and CH_3X and the abscissa is the value of the Taft parameter (σ_I) of the substituent (X). Drawn from data given in Reference 111.

TABLE 11. Acidities (pK) of carbon acids in dimethyl sulphoxide[90]

X	Series A XCH_2CN	Series B XCH_2SO_2Ph	Series C XCH_2COPh
Me_3C	—	31.2	25.3
Me	32.5	31.0	24.4
H	31.3	29.0	24.6
Me_3N^+	20.6	19.4	14.6
CH_3CO	—	12.5	12.7
$PhSO_2$	12.0	12.2	11.4
CN	11.1	12.0	10.2
PhCO	10.2	11.4	13.1
NO_2	—	7.1	7.7

TABLE 12. Separation of polar and conjugative effects of substituents in the stabilization of carbanions

X	σ_I	ΔpK_{calc} Polar	ΔpK_{obs} Polar and conjugative	$\Delta\Delta pK = \Delta pK_{obs} - \Delta pK_{calc}$ Conjugative
		Series A: XCH_2CN, $\rho_I = 14.5$		
Me	−0.04	—	0.0	—
Me_3N^+	0.82	(11.9)	11.9	0.0
PhCO	0.30	4.3	22.3	18.0
CN	0.56	8.1	21.4	13.3
$PhSO_2$	0.57	8.3	20.5	12.2
		Series B: XCH_2SO_2Ph, $\rho_I = 14.1$		
Me	−0.04	—	0.0	—
Me_3N^+	0.82	(11.6)	11.6	0.0
CH_3CO	0.28	4.0	18.5	14.5
PhCO	0.30	4.2	19.6	15.4
CN	0.56	7.9	19.0	11.1
$PhSO_2$	0.57	8.1	18.8	10.7
NO_2	0.65	9.2	23.9	14.7
		Series C: XCH_2COPh, $\rho_I = 11.9$		
Me	−0.04	—	0.0	—
Me_3N^+	0.82	(9.8)	9.8	0.0
CH_3CO	0.28	3.3	11.7	8.4
PhCO	0.30	3.6	11.3	7.7
CN	0.56	6.7	14.2	7.5
$PhSO_2$	0.57	6.8	13.0	6.2
NO_2	0.65	7.8	16.7	8.9

of acids A, B and C and the results are given in Table 12. The value of the calculated polar contribution of each substituent (ΔpK_{calc}) was then compared with the actual activating effect of that substituent (ΔpK_{obs}) as measured by the difference in pK between the acid with X = Me and the substituted acid. The difference between ΔpK_{obs} and ΔpK_{calc}, $\Delta\Delta pK = \Delta pK_{obs} - \Delta pK_{calc}$ was taken as a measure of the conjugative effect of that substituent. It follows from these results which are given in the final column of Table 12 that the substituents CH_3CO, PhCO, $PhSO_2$, CN, and NO_2 are exerting a large conjugative effect. For CH_3CO, PhCO and NO_2 the conjugative effect is much more important than the polar effect. In the cases of $PhSO_2$ and CN, polar effects are important and polar and conjugate effects make roughly equal contributions to the stability of the carbanions.

IV. KINETICS OF PROTON TRANSFER FROM CYANOCARBON ACIDS

A. Rates of Proton Transfer in Aqueous Solution

Before discussing in detail the rates of ionization of cyanocarbon acids and the rates of protonation of cyanocarbanions, a description of the proton-transfer kinetics of other carbon acids and of oxygen and nitrogen acids will be given.

The development of relaxation techniques[112,113] for measuring the rates of fast chemical reactions in solution enabled Eigen[114] to observe and completely describe the ionization behaviour of nitrogen and oxygen acids. For an equilibrium such as that

$$HA + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} BH^+ + A^- \quad (23)$$

shown in equation (23) involving oxygen or nitrogen acids and bases, values of the rate coefficients k_1 and k_{-1} vary in a predictable way with the acid dissociation constants of HA and BH^+, K_{HA} and K_{BH^+}, respectively. The relationship between the equilibrium constants and the rate coefficients is given by equations (24) and (25). It was found[114]

$$K = [BH^+][A^-]/[HA][B] = K_{HA}/K_{BH^+};\ -\log_{10}K = pK_{HA} - pK_{BH^+} = \Delta pK \quad (24)$$

$$K = k_1/k_{-1};\ -\log_{10}k_1 + \log_{10}k_{-1} = \Delta pK \quad (25)$$

that for a wide variety of oxygen and nitrogen acids and bases, for example carboxylic acids, phenols and amines, the values of k_1 and k_{-1} vary with the acidity of HA and BH^+ as shown in Figure 3 which is usually referred to as an Eigen plot. Acids which involve an intramolecular hydrogen bond behave differently[115]. The acids and bases which give results like those in Figure 3 are called normal acids and bases and one feature of their behaviour is that proton transfer in the thermodynamically favourable direction is diffusion-controlled with a second-order rate coefficient ca. 1×10^{10} l mol^{-1} s^{-1}. Consider the case where results are obtained for proton transfer from an acid HA to a series of bases B of different strength. For bases for which $pK_{HA} < pK_{BH^+}$ ($\Delta pK < 0$), reaction in the forward direction of equilibrium (23) is thermodynamically favourable and k_1 has the diffusion-limited value which remains unchanged as the base B is varied from weaker to stronger bases, providing it still remains true that $pK_{HA} < pK_{BH^+}$. It is seen from equation (25) that in this case the rate coefficient k_{-1} must vary directly with the strength of the base B, as measured by the acid dissociation constant of BH^+, such that a plot of $\log_{10}k_{-1}$ against ΔpK is of unit slope as in Figure 3. For

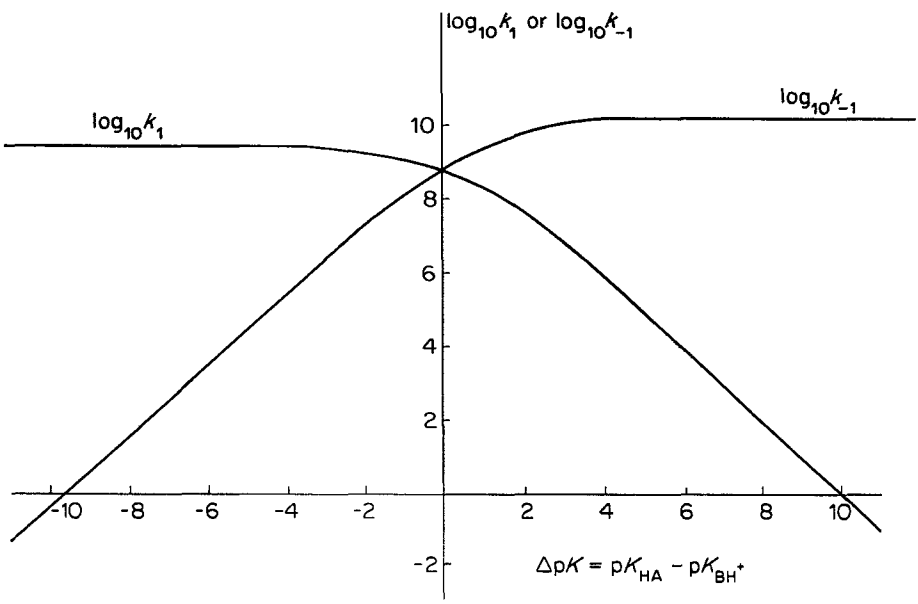
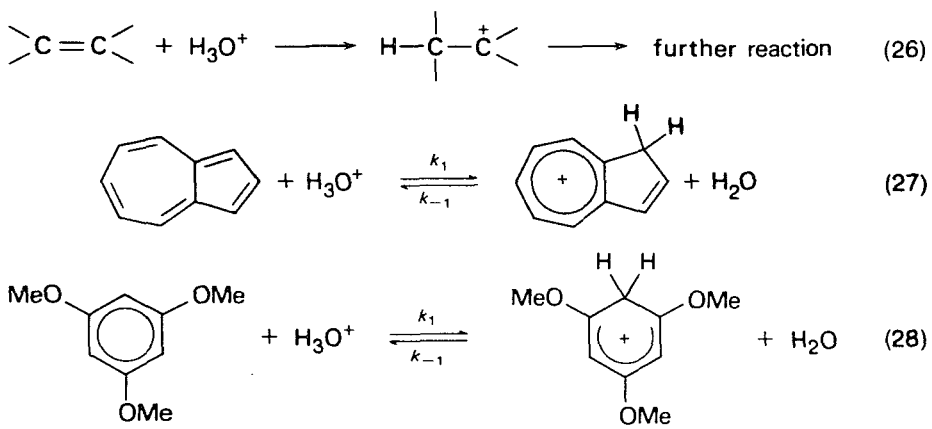


FIGURE 3. Eigen plot illustrating the variation of the forward (k_1) and reverse (k_{-1}) rate coefficients for a normal proton-transfer reaction $HA + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} A^- + BH^+$ with the difference in pK of the proton donor (HA) and acceptor (B).

bases where $pK_{HA} > pK_{BH^+}(\Delta pK > 0)$ reaction in the reverse direction of equilibrium (23) is now thermodynamically favourable and therefore k_{-1} has the diffusion-controlled value. Hence $\log_{10}k_{-1}$ is now constant and independent of the basicity of B and therefore $\log_{10}k_1$ varies directly with ΔpK. The diffusion-limited rate for the reverse reaction of equilibrium (23) will have a slightly higher value than for the forward reaction as seen in Figure 3 because convergent diffusion is more rapid for species of opposite charge. Curvature in the plots of log k_1 and log k_{-1} against ΔpK is restricted to the range $-3 < \Delta pK < +3$ and outside this range log k_1 and log k_{-1} are linear functions of ΔpK with zero or unit slope. Outside the range $-3 < \Delta pK < +3$ diffusion of the reactant or product species is rate-limiting and it is only around $\Delta pK = 0$ that the actual proton-transfer step contributes to the rate of reaction[116]. Since these results are quite general for oxygen and nitrogen acids, it is possible to predict rates of proton transfer for a particular reaction if the pK values of the acid and base are known.

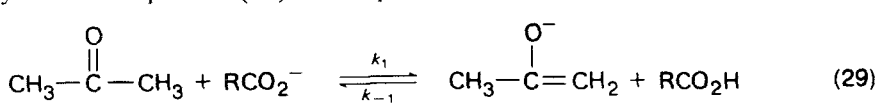
The situation for proton transfer from carbon acids is much more complicated than that described for oxygen and nitrogen acids. Unsubstituted saturated hydrocarbons are too weakly acidic to permit investigation of their ionization in aqueous solution and it is necessary to introduce acid-strengthening groups. The proton-transfer behaviour observed depends upon the nature of the activating group which is introduced.

Up until 1970 the carbon acids which had been most studied were ketones, esters and nitro paraffins. Reactions involving unsaturated hydrocarbons such as olefins (equation 26) and aromatic substrates like azulene (equation 27) and 1,3,5-trimethoxybenzene (equation 28) had also been studied. In all these cases, striking



contrasts with the behaviour of oxygen and nitrogen acids were observed. Proton transfer to or from carbon was found to be slow and even in the thermodynamically favourable direction it was found that reaction occurred with rate coefficients which were well below the diffusion-limited values. In cases where Eigen plots have been constructed the results are very different from that shown in Figure 3 for normal acids. Some examples will be chosen to illustrate this and to provide a background for our discussion of the behaviour of cyanocarbon acids.

Most of the available information of the ionization of ketones and esters has been obtained by Bell[117]. Equation (29) shows proton transfer from acetone to a carboxy-



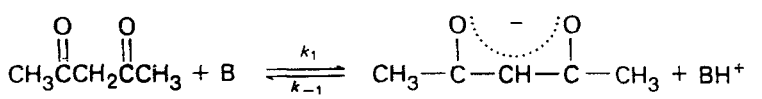
late ion to give an enolate ion with the charge located on oxygen. Before Eigen's review[114] it was usual to express the observed values of k_1 and k_{-1} for different carboxylate ions in the form of a Brønsted plot of log k_1 against log K_{RCOOH}, especially for carbon acids for which the pK values were unknown and ΔpK could therefore not be calculated. This procedure was first suggested by Brønsted and Pedersen[25,118,119] from the observation that the rate coefficients (k_1) for proton transfer from nitramide to bases (B) varied with base strength as shown in equations (30) and (31). In equations (30) and (31) K_{BH^+} is the acid dissociation constant and G_B and

$$k_1 = G_B\,(1/K_{BH^+})^{\beta} \tag{30}$$

$$\log k_1 = \log G_B - \beta \log K_{BH^+} \tag{31}$$

β are roughly constant for a particular reaction over a limited range of base strengths. The Eigen plot in Figure 3 is an alternative way of plotting equation (31) and for proton transfer from oxygen and nitrogen acids the result $\beta = 0$ is observed in the range $\Delta pK < -3$ and $\beta = 1.0$ is observed for $\Delta pK > +3$. In between, in the range $-3 < \Delta pK < +3$, the value of β varies very sharply from zero to unity as ΔpK changes.

The value observed for the Brønsted exponent β for ketones depends upon ΔpK, the difference in pK between the ketone and carboxylic acid, although over small ranges of ΔpK β is constant. For a weakly acidic ketone such as acetone (pK = 19–20[58]) the Brønsted exponent for proton transfer to carboxylate ions is quite large (β = 0.88) and therefore approaches the value found for a normal acid. The reverse rate coefficients for recombination of the carbanion with carboxylic acids to regenerate the ketone have values ca. 10^7–10^8 l mol^{-1} s^{-1}. When the ΔpK value is very large, for example for the reaction with hydronium ion, a recombination rate coefficient of $5 \times 10^9 - 5 \times 10^{10}$ l mol^{-1} s^{-1} has been estimated (Table 7). For more strongly acidic ketones for which ΔpK between the ketone and carboxylate ion catalyst is smaller, Brønsted exponents as low as $\beta = 0.42$ have been found[117]. This implies that if proton transfer from a ketone to a variety of catalysts could be studied over a wide range of ΔpK, the Eigen or Brønsted plot would be curved with a varying value of β. This has in fact been observed for proton transfer from acetylacetone (pK = 8.9) (equation 32) which has been studied[120] over the range $-5 < \Delta pK < 10$. The plots of



(32)

log k_1 and log k_{-1} against ΔpK are curved and the slope of log k_1 against ΔpK varies from β ca. 0.8 to ca. 0.3 as ΔpK goes from +10 to −5. These slopes are well away from the values of zero and unity shown in Figure 3 and at $\Delta pK = 0$, where $k_1 = k_{-1}$ = ca. 10^9–10^{10} l mol^{-1} s^{-1} for a normal proton-transfer reaction, the value $k_1 = k_{-1}$ = ca. 10^4 l mol^{-1} s^{-1} is observed for proton transfer involving acetylacetone.

For proton transfer to and from aromatic substrates such as substituted azulenes and benzenes (equations 27 and 28) the picture is similar[121]. Rate coefficients (k_1) for proton transfer from hydronium ion to a series of these aromatic substrates have been measured covering a ΔpK range of −5 to +20. At $\Delta pK = 0$ the rate coefficients in the forward and reverse direction have values ca. 1.0 l mol^{-1} s^{-1}, well below the values for normal proton transfer. The slope of the plot of log k_1 against ΔpK varies from $\beta = 0.87$ at $\Delta pK = 20$ to $\beta = 0.43$ for $\Delta pK = -5$. In the protonation of azulene by hydronium ion (equation 27) the values of the forward and reverse rate coefficients are k_1 = ca. k_{-1} = 1 l mol^{-1} s^{-1} and for 1,3,5-trimethoxybenzene (equation 28) the

values are k_1 = ca. 0.1 l mol^{-1} s^{-1} and k_{-1} = ca. 10^4 l mol^{-1} s^{-1}. These results are again well below diffusion-limited values.

Proton transfer from ethyl nitroacetate[122] to bases (equation 33) is characterized by a linear plot of log k_1 against ΔpK over the range $-5 < \Delta pK < 5$ with a slope $\beta = 0.65$.

$$O_2NCH_2CO_2Et + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} {}^{-}O_2N{=}CHCO_2Et + BH^+ \qquad (33)$$

These results are quite typical for a nitro paraffin but for a normal acid over this range the slope of the Brønsted plot would have varied from $\beta = 0.0$ to $\beta = 1.0$. For ethyl nitroacetate at $\Delta pK = 0$ the value $k_1 = k_{-1}$ = ca. 1×10^2 l mol^{-1} s^{-1} was observed.

The reason which is usually put forward to account for the slow proton-transfer behaviour of carbon acids is that for many carbon acids the carbanions are stabilized by groups which conjugate strongly and the charge on the carbanion is delocalized by electronic and nuclear reorganization. The difference in structure between the carbanion and carbon acid is illustrated for acetone and nitromethane in equations (34) and (35). This structural difference introduces a considerable activation energy into proton

$$CH_3{-}\overset{\overset{O}{\|}}{C}{-}CH_3 \rightleftharpoons CH_2{=}\overset{\overset{O^-}{|}}{C}{-}CH_3 + H^+ \qquad (34)$$

$$CH_3{-}\overset{+}{N}\begin{matrix}\diagup O^- \\ \diagdown O\end{matrix} \rightleftharpoons CH_2{=}\overset{+}{N}\begin{matrix}\diagup O^- \\ \diagdown O^-\end{matrix} + H^+ \qquad (35)$$

transfer to and from carbon but the effect is absent from the ionization of an oxygen or nitrogen acid. The magnitude of the effect will vary depending upon the particular substituent in the carbon acid and the extent of nuclear reorganization accompanying the ionization of the carbon acid to its carbanion[25,26,27,123,124]. The inability of carbon acids to form strong hydrogen bonds with the solvent in the formation of a reaction intermediate prior to proton transfer may also contribute to the slowness of proton transfer[125]. These factors and the behaviour of carbon acids are dealt with more fully elsewhere[24–28,123]. The brief review we have given here provides sufficient background for our discussion of the proton-transfer behaviour of cyanocarbon acids to which we now turn.

The first detailed kinetic study of base-catalysed proton transfer from a cyanocarbon acid was made by Long and coworkers[89]. The rate coefficients for proton transfer from 1,4-dicyano-2-butene to phenolate ions (equation 36) and to amines were obtained

$$NCCH_2CH{=}CHCH_2CN + XC_6H_4O^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} NCCH_2CH{=}\bar{C}HCHCN + XC_6H_4OH \qquad (36)$$

by measuring the rate of isotope exchange from the tritiated carbon acid by the technique described in Section II. B.1. For reaction (36) the reverse protonation of the cyanocarbanion is thermodynamically favourable. It was found that the rate coefficient k_1 was almost directly proportional to the base strength of the catalysing base and Brønsted plots of log k_1 against log $K_{XC_6H_4OH}$ and log $K_{RNH_3^+}$ were linear with slopes of $\beta = 0.94 \pm 0.02$ for catalysis by five phenolate ions and $\beta = 0.98 \pm 0.08$ for catalysis by six secondary amines. The values of the Brønsted exponents are very close to the value $\beta = 1.0$ which would be observed for proton transfer from an oxygen or nitrogen acid. This carbon acid is therefore behaving in contrast to the results obtained for other carbon acids which had been studied at that time (ketones, nitro paraffins and esters) but very similarly to normal proton-transfer behaviour. In the reverse

direction of equation (36) the rate coefficient k_{-1} was almost independent of the strength of the protonating acid as expected for a diffusion-controlled process. However, the actual values of the reverse rate coefficients could not be calculated with certainty because the pK value of 1,4-dicyano-2-butene was not known. However the results k_{-1} = ca. 1×10^9 l mol^{-1} s^{-1} for protonation of the cyanocarbanion by phenols and k_{-1} = ca. 7×10^9 l mol^{-1} s^{-1} for protonation by secondary ammonium ions were calculated using an approximate value pK = ca. 21 for 1,4-dicyano-2-butene obtained from preliminary measurements in dimethyl sulphoxide–water mixtures. Since these results are close to those expected for a diffusion-controlled process it was important to study a stronger cyanocarbon acid for which an accurate pK value could be obtained which would then permit values for the reverse rate coefficients to be calculated accurately.

Hence, base-catalysed proton transfers from malononitrile (pK = 11.20) and *t*-butylmalononitrile (pK = 13.10) were studied[36] using the isotope exchange procedure. For *t*-butylmalononitrile (equation 37) proton transfer to three carboxylate

$$t\text{-BuCH(CN)}_2 + \text{RCO}_2^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} t\text{-BuC(CN)}_2^- + \text{RCO}_2\text{H} \qquad (37)$$

ions was studied and a β value of 0.98 ± 0.02 was obtained from the Brønsted plot. Values of the rate coefficients k_{-1} for protonation of the carbanions by carboxylic acids were calculated from the acid dissociation constant of *t*-butylmalononitrile and these results together with the rate coefficient for protonation of malononitrile anion by formic acid are given in Table 13. Rate coefficients for protonation of the carbanions by hydronium ion are also given in Table 13. Previously, a value for the rate coefficient for protonation of malononitrile anion by hydronium ion of $k_{-1} = 2.3 \times 10^9$ l mol^{-1} s^{-1} had been calculated[13] from the rate of bromination[126] of the carbon acid. The rate coefficients for protonation of the carbanions by carboxylic acids are almost constant at 1×10^8 l mol^{-1} s^{-1} and the magnitude of this value is close to the diffusion-limited value. However, for a diffusion-controlled protonation of an oxygen or a nitrogen base the rate coefficient would be at least ten-fold higher. The reverse rate coefficients for protonation of the carbanions by hydronium ion are ca. 3×10^9 l mol^{-1} s^{-1}, about thirty-fold larger than for carboxylic acids, but about ten-fold lower than would be found for protonation of an oxygen anion by hydronium ion. The thirty-fold difference in the rates of protonation of the carbanions by

TABLE 13. Rate coefficients for protonation of cyanocarbanions

$$\text{RCH(CN)}_2 + \text{B} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{RC(CN)}_2^- + \text{BH}^+$$

B	BH^+	k_1(l mol^{-1} s^{-1})	$10^{-8}k_{-1}$(l mol^{-1} s^{-1})
Malononitrile, R = H			
H_2O	H_3O^+	5.16×10^{-4}	26
HCO_2^-	HCOOH	4.20	1.2
t-Butylmalononitrile, R = t-Bu			
H_2O	H_3O^+	9.66×10^{-6}	40
$ClCH_2CO_2^-$	$ClCH_2CO_2H$	5.66×10^{-3}	1.01
HCO_2^-	HCO_2H	4.38×10^{-2}	0.98
$CH_3CO_2^-$	CH_3CO_2H	0.403	0.88

hydronium ion and by carboxylic acids is about the difference normally observed in diffusion-controlled proton transfers and the higher rate for hydronium ion is usually attributed to the abnormally high mobility of the proton in aqueous solution. Therefore, from these results, it appears that the kinetics of ionization of cyanocarbon acids are quite close to the behaviour of normal acids.

To test this point further, kinetic measurements were made for a cyanocarbon acid in the region of $\Delta pK = 0$, because, as we have seen, it is in this region that quite marked differences in the results for carbon acids and normal acids are observed. To study this region, proton transfer from bromomalononitrile ($pK = 7.81$) was investigated[38] (equation 38). This reaction occurs more rapidly than the reactions of

$$BrCH(CN)_2 + HPO_4^{2-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} BrC(CN)_2^- + H_2PO_4^- \qquad (38)$$

1,4-dicyano-2-butene, malononitrile and *t*-butylmalononitrile and it was necessary to use the temperature-jump method to follow the kinetics. For proton transfer from bromomalononitrile to orthophosphate dianion, $k_1 = 8.2 \pm 0.6 \times 10^6$ l mol^{-1} s^{-1} and $k_{-1} = 4.3 \pm 0.3 \times 10^7$ l mol^{-1} s^{-1} were obtained, and similar values were observed for proton transfer from bromomalononitrile to morpholine. These values are about 20-fold below the values which are observed for a normal proton-transfer reaction around $\Delta pK = 0$.

The data for 1,4-dicyano-2-butene and for the malononitriles are given on the same Eigen plot in Figure 4. In order to fit the data for 1,4-dicyano-2-butene on the same line as the other data it was necessary to assume that $pK = 20$ for this acid rather than the approximate value (pK = ca. 21) measured in dimethyl sulphoxide–water mixtures. The Eigen plot for cyanocarbon acids is quite similar to the plot given in Figure 3 for a normal proton transfer, but there are some differences. The slopes of the lines are quite close to the values of $\beta = 1.0$ and 0.0, but the rate coefficients in the thermodynamically favourable direction are about ten-fold below the diffusion-limited values. Thus, the behaviour of this class of carbon acids is different from that of ketones and nitro paraffins but the behaviour is not fully normal.

Further measurements have been made with *t*-butylmalononitrile by Pratt and Bruice[127] who obtained rate coefficients (k_1) for proton removal by five amines, by trifluoroethoxide ion and by peroxide anion. When taken together with the results for proton transfer to carboxylate ions, a plot of log k_1 against the pK values of the catalysts gave a straight line with slope β = ca. 0.8. However, it is very unlikely that the Brønsted exponent has a value as low as this. First, amines and oxygen anions may well not lie on the same Brønsted line. Second, the straight line with the slope of ca. 0.8 was drawn through all the points including the stronger bases (HO_2^-, $pK = 11.6$ and $CF_3CH_2O^-$, $pK = 12.4$) which are in the region of $\Delta pK = 0$. Even for a normal proton-transfer reaction, curvature in the Eigen plot sets in around $\Delta pK = +3$ and since for HO_2^- and $CF_3CH_2O^-$ $\Delta pK = 1.5$ and 0.7, respectively, the points for these bases will fall below the line which gives the true value of the Brønsted exponent. The value of $\beta = 0.98$ based on catalysis by three carboxylate ions may provide a better comparison with the behaviour of ketones for which Brønsted exponents between 0.42 and 0.88 were obtained for catalysis by carboxylate ions[117]. However, not too much weight can be given to the value $\beta = 0.98$ since only three carboxylate ions were used.

The evidence shows that the results with cyanocarbon acids are closer to those obtained for normal acids than has previously been found for proton transfer from carbon. The explanation for this may be that cyanocarbanions are stabilized mainly by polar effects and that the extensive charge delocalization by conjugation which is important in the stabilization of carbanions derived from ketones and nitro paraffins and which introduces a considerable activation energy into the proton transfer, may be

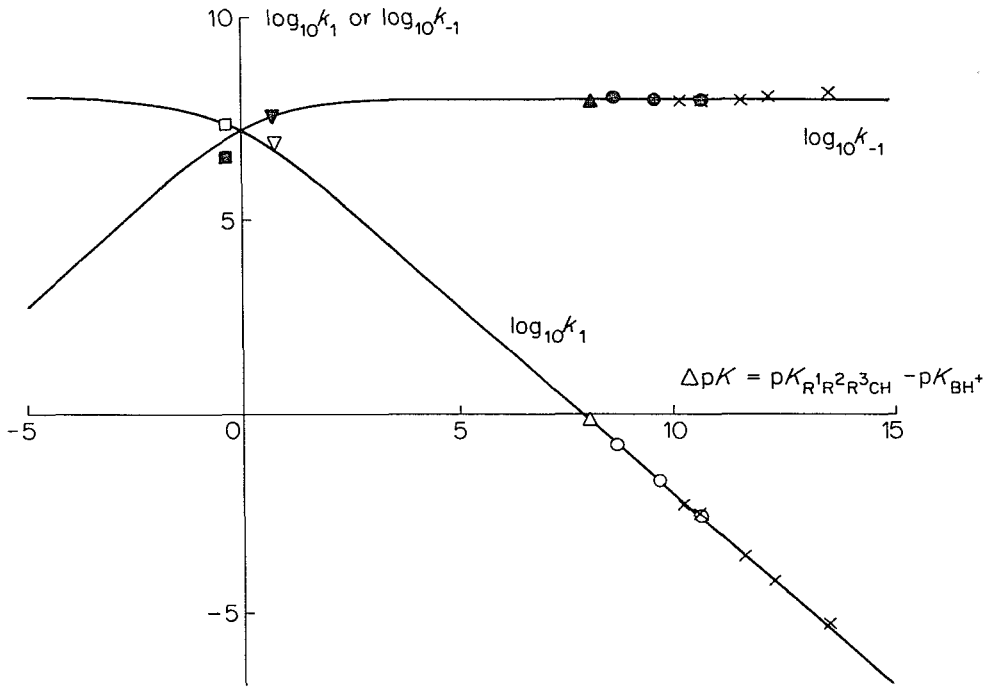


FIGURE 4. Eigen plot for proton transfer from cyanocarbon acids ($R^1R^2R^3CH$) to various bases (B), $R^1R^2R^3CH + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^1R^2R^3C^- + BH^+$. The points refer to the following reactions: □, bromomalononitrile and morpholine; ▽, bromomalononitrile and orthophosphate dianion; ×, 1,4-dicyano-2-butene and phenolate ions; △ malononitrile and formate ion; ○, *t*-butylmalononitrile and carboxylate ions. Drawn from data given in Reference 37.

less important in the case of cyanocarbanions. Following the experiments with cyanocarbon acids, more recent measurements with sulphones[70], chloroform[68,69] and phenylacetylene[67] have shown that these carbon acids also approach normal proton-transfer behaviour. In the carbanions formed from these carbon acids polar effects may again be more important (c.f. Figure 2) than conjugative effects.

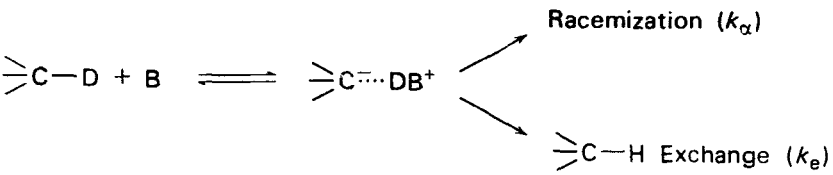
In predicting the kinetic behaviour of other cyanocarbon acids such as those given in Table 2 which contain a variety of activating groups in addition to cyano the following observations can be made. For those cyanocarbon acids with halogen or sulphone substituents, ionization will be rapid and close to that described in Figure 4. Proton-transfer rates for these acids are therefore predictable from the acidities of the acids and bases involved. For cyanocarbon acids which additionally possess nitro, ester and keto groups it is likely that proton transfer will be slow. This was confirmed[37] in a study of proton transfer from *p*-nitrobenzyl cyanide (equation 39). It was found that the catalytic coefficients (k_1) for proton transfer to amines gave a Brønsted exponent

$$p\text{-}NO_2C_6H_4CH_2CN + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} p\text{-}NO_2C_6H_4CHCN^- + BH^+ \qquad (39)$$

$\beta = 0.61$. The Brønsted plot extrapolated to $\Delta pK = 0$ indicated that in this region the rate coefficients for the forward and reverse proton transfer have the values $k_1 = k_{-1} =$ ca. 10^2 l mol^{-1} s^{-1}.

B. Proton Transfer in Nonaqueous Solvents

Proton transfers involving cyanocarbon acids have been widely studied in nonaqueous solvents. One type of experiment which has been carried out involves measuring the rate coefficient for racemization of an optically active cyanocarbon acid (k_α) and comparing it with the rate coefficient for isotope exchange (k_e) of a proton attached to the asymmetric carbon atom. Both processes (equation 40) involve

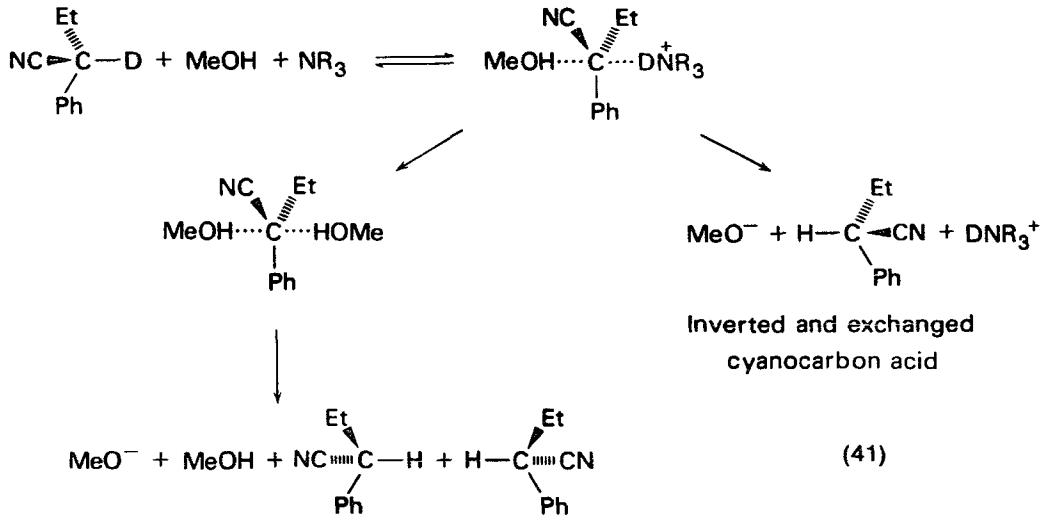


(40)

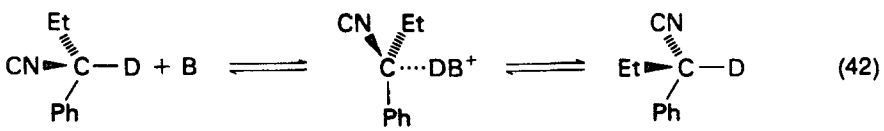
ionization of the C—H bond in the presence of base to give a carbanion or a carbanion ion pair, but often the rates and the detailed mechanisms are not the same. The procedure which has been used for a variety of carbon acids by Cram and his research group provides information about the stereochemistry of the carbanion and about the mechanisms of isotope exchange and racemization. A range of k_e/k_α values may be obtained depending upon the particular carbon acid which is involved and the conditions under which it is studied, such as the solvent and the base. If a mechanism for exchange with retention of configuration is occurring, in which the incoming hydrogen isotope attacks the same face of the carbanion from which the outgoing isotope is lost, a $k_e/k_\alpha > 1$ will be observed. If $k_e = k_\alpha$ is observed, this means that the carbanion intermediate is attacked by the incoming isotopic hydrogen equally at both faces. A k_e/k_α value of 0.5 will be observed if exchange occurs with complete inversion so that the incoming isotope attacks the opposite face of the carbanion from which the outgoing isotope leaves. The factor of two in the rates arises because the final optical rotation is of equal magnitude but of opposite sign compared with the initial value. A k_e/k_α value < 0.5 indicates that there is a mechanism for racemization without exchange which will arise if the carbanion ion pair can undergo racemization and then revert to unexchanged carbon acid.

Several cyanocarbon acids have been subjected to this technique and the results have usually been explained by assuming that the cyanocarbanions are practically planar and symmetrical[128]. In methanol containing tripropylamine and in ethylene glycol in the presence of potassium bicarbonate, ratios of $k_e/k_\alpha = 0.84$ and 0.87, respectively, have been observed in studies with 2-D-2-phenylbutyronitrile[129]. The mechanism whereby these values arise is shown in equation (41). When the same experiments were carried out with 2-D-2-phenylbutyronitrile in tetrahydrofuran containing 1.5 M *t*-butyl alcohol and in the presence of tripropylamine a k_e/k_α value of 0.05 was observed[129], showing that the ion-pair intermediates can racemize and collapse back to starting material of inverted configuration without undergoing proton exchange (equation 42).

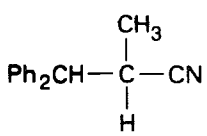
Comparison of the rates of exchange and racemization of **49** and **50** in methanol-D containing sodium methoxide has led to the conclusion[130] that the carbanion derived from **49** is planar and can be protonated almost equally on each face, whereas for **50** the carbanion is pyramidal and is protonated more rapidly on one face than it can undergo inversion. These experiments have been extended to vinyl carbanions[131] and



(41)

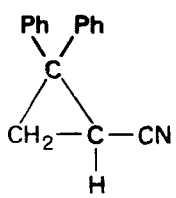


(42)



(49)

$k_e/k_\alpha = 1.87$

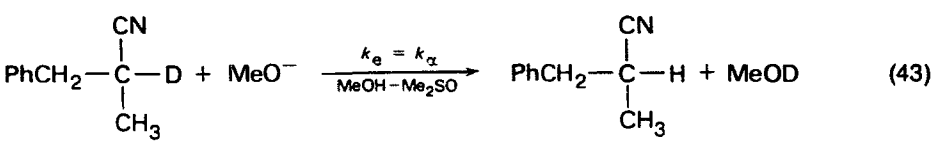


(50)

$k_e/k_\alpha = 9 \times 10^3$

it was found useful to introduce a cyano group into the molecule to acidify the C—H bond in order that exchange and racemization should occur sufficiently rapidly to be conveniently observable.

A study of a different sort[74] was carried out with the weak cyanocarbon acid 2-methyl-3-phenylpropionitrile in methanol–dimethyl sulphoxide mixtures containing methoxide ion (equation 43). It was found that the rate coefficients for racemi-

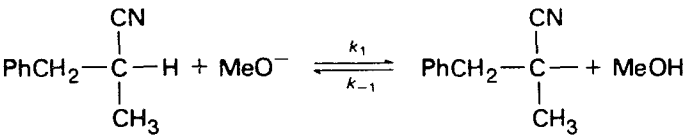


(43)

zation (k_α) and isotope exchange (k_e) for this cyanocarbon acid were identical, confirming the conclusions of previous experiments with this system[132]. In going from pure methanol to 90.2 wt. % Me_2SO–9.8 wt. % MeOH the rate coefficient for racemization and exchange was found to increase steadily and overall by a factor of 5×10^3. This is a result of the desolvation of the methoxide ion which becomes a stronger base as the solvent becomes richer in Me_2SO[132,133]. The same is found for hydroxide ion in Me_2SO–H_2O mixtures[63,78]. For 2-methyl-3-phenylpropionitrile, the measured change in the rate of racemization with solvent composition[132] was used[74,133] to calculate a Brønsted exponent for this reaction by means of the following procedure. An acidity function (H_-) has been measured[134] for MeOH–Me_2SO mixtures containing methoxide ion. The measurements involved spectrophotometric observations of the dissociation of a series of aniline and diphenylamine indicators with pK values in the range 12–18. The acidity function is defined by equation (44) in

$$H_- = pK_{SH} - \log_{10}[SH]/[S^-] \tag{44}$$

which $[SH]/[S^-]$ is the measured indicator ratio and pK_{SH} is known for the indicator. Once the H_- function has been determined using indicators of known pK_{SH}, the acidity function can be used to determine pK_{XH} for an acid (XH) by measuring the degree of dissociation ($[XH]/[X^-]$) of the acid in a solvent mixture of known H_- value. In the work under discussion it was assumed that the acidity function applied to the dissociation of 2-methyl-3-phenylpropionitrile. Therefore, equation (50) was obtained for the ΔpK value of the equilibrium of equation (45) using equations (47)–(49). Thus



(45)

$$XH + MeO^- \rightleftharpoons X^- + MeOH \tag{46}$$

$$K_{XH} = [X^-][H_3O^+]/[XH]; \quad K_{MeOH} = [MeO^-][H_3O^+]/[MeOH] \tag{47}$$

$$\Delta pK = pK_{XH} - pK_{MeOH} = -\log_{10}([X^-][MeOH]/[XH][MeO^-]) \tag{48}$$

$$H_- = pK_{XH} - \log_{10}[XH]/[X^-] \tag{49}$$

$$\Delta pK = pK_{XH} - H_- - \log_{10}([MeOH]/[MeO^-]) \tag{50}$$

the variation of ΔpK with the solvent composition could be calculated from the value of H_-. It was also assumed[74] that the rate of racemization measured the rate coefficient for proton transfer (k_1). Hence, the simultaneous changes of the rate coefficient k_1 and the value of ΔpK for the proton-transfer equilibrium with the solvent composition were calculated. These data are shown as a Brønsted plot in Figure 5. Actually the absolute value for ΔpK in Figure 5 is not known because the value of pK_{XH} is not known accurately, but the change in ΔpK with the solvent composition can be calculated and is directly proportional to the change in H_-. It was found that $\log k_1$ was a linear function of H_- with slope $\beta = 1.1$. This plot is analogous to the Brønsted and Eigen plots presented in Section IV.A except that in these cases data were obtained by varying the base catalyst and the dependence of the rate on the base strength was thereby explored. In the present case the composition of the solvent was changed in

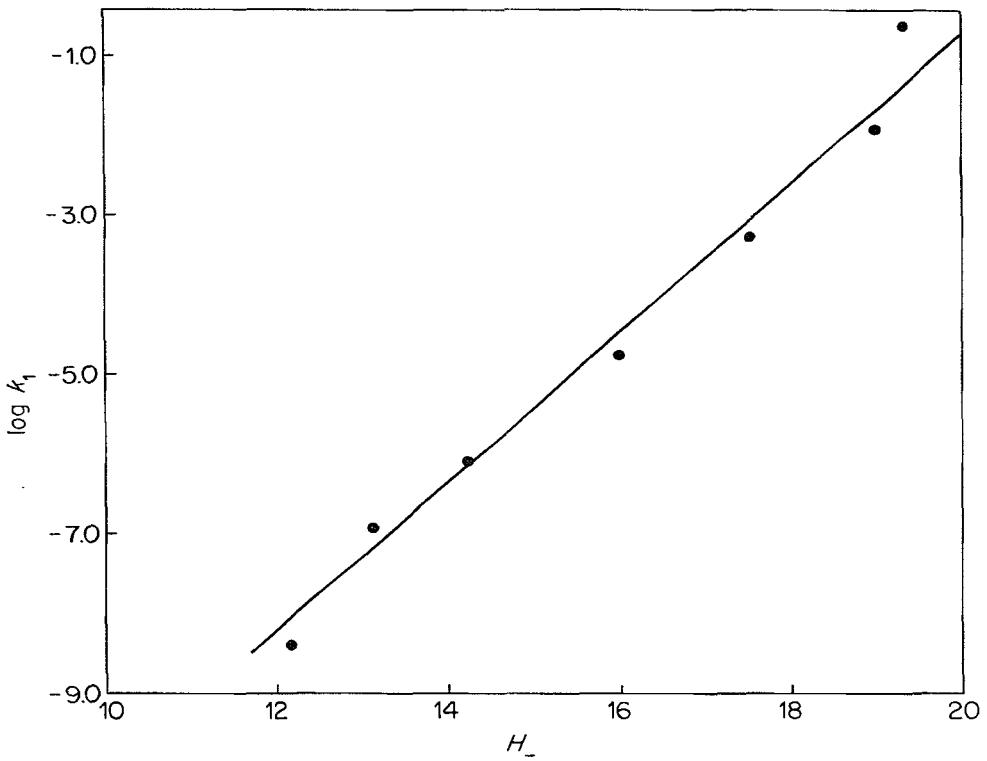
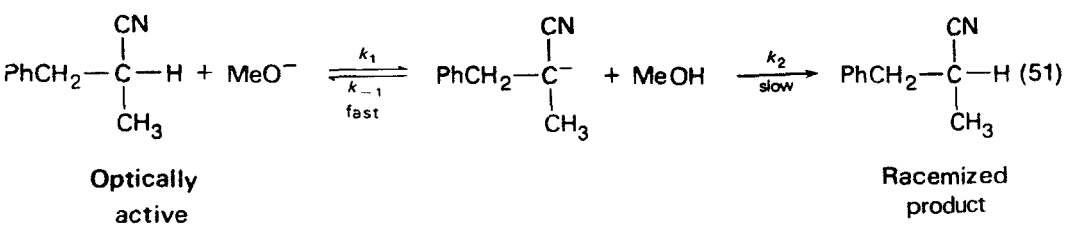


FIGURE 5. Variation of rate coefficient (k_1) for the methoxide-ion-catalysed racemization of 2-methyl-3-phenylpropionitrile in methanol–dimethyl sulphoxide mixtures with H_- for the solvent mixture. Drawn from data given in References 132 and 134.

order to bring about a change in the strength of the base (MeO^-) and the effect of this on the rate of proton transfer was investigated. In view of the assumptions involved, the value obtained for the Brønsted exponent ($\beta = 1.1$) for proton transfer from 2-methyl-3-phenylpropionitrile is in very good agreement with the value obtained for the Brønsted exponent for proton transfer from cyanocarbon acids in aqueous solution (Section IV.A). Actually, there is some disagreement as to whether the rate of racemization of 2-methyl-3-phenylpropionitrile can be identified with the rate coefficient k_1. The view held by Melander[74,135] is that the rate coefficient for racemization and exchange is a measure of k_1 in equation (45). However, in the opinion of Cram[133] the mechanism for racemization should be written as shown in equation (51). According to this mechanism the rate coefficient for racemization is



given by a product of rate coefficients (k_1k_2/k_{-1}). The choice between these two possibilities depends upon the interpretation of the kinetic isotope effect for the reaction and this will be discussed in the following section.

C. Isotope Effects on Proton Transfer from Cyanocarbon Acids

In the studies of base-catalysed proton transfer from malononitriles[36] described in Section IV.A it was concluded that proton transfer to water and carboxylate ions has many of the characteristics of a normal proton transfer. The Brønsted exponent for the reaction has a value of almost unity and the rates of the thermodynamically favourable reverse reactions between the carbanions and acids are close to the diffusion-controlled limit with rate coefficients of ca. 1×10^8 and 3×10^9 l mol^{-1} s^{-1} for reaction with carboxylic acids and hydronium ion, respectively. Thus, proton transfer from cyanocarbon acids to bases is visualized as occurring through a transition state in which the proton is almost fully transferred to base and therefore approaches the structure of an encounter complex between the carbanion and the protonated base. To test this finding which at the time of the experiments was considered unusual for a carbon acid, primary and solvent isotope effects for the reaction were measured[36,136].

The kinetic data for malononitriles were obtained[36,136] by observing the rate of exchange of tritium-substituted malononitrile or *t*-butylmalononitrile [$RC(CN)_2T$]. Catalytic coefficients were obtained for proton transfer to water and to carboxylate ions by making measurements in dilute hydrochloric acid solution or in carboxylic-acid–carboxylate buffers, respectively. The mechanism of exchange is given in equation (52) and the rate of exchange therefore gives a value for the rate

$$\begin{aligned} RC(CN)_2T + B &\xrightarrow[\text{slow}]{k^T} RC(CN)_2^- + BT^+ \\ RC(CN)_2^- + \text{acid} &\xrightarrow[\text{fast}]{} RC(CN)_2H \end{aligned} \qquad (52)$$

coefficient for ionization of the C—T bond (k^T). To measure primary kinetic isotope effects for the reaction, the rates of bromination of the malononitriles were measured. The reaction is zero order in bromine concentration and the mechanism of bromination is shown in equation (53). Therefore, the rate of bromination measures

$$\begin{aligned} RC(CN)_2H \text{ or } RC(CN)_2D + B &\xrightarrow[\text{slow}]{k^H \text{ or } k^D} RC(CN)_2^- + BH^+(BD^+) \\ RC(CN)_2^- + Br_2 &\xrightarrow[\text{fast}]{} RC(CN)_2Br + Br^- \end{aligned} \qquad (53)$$

the rate coefficient for ionization of the C—H bond. The rates of bromination of the deuterium-substituted acids were also studied to give a value of the rate coefficient for ionization of the C—D bond. Hence, in the water-catalysed ionization of malononitrile and *t*-butylmalononitrile, values of the isotope effects k^H/k^D and k^H/k^T were obtained. The experimental k^H/k^D value was in good agreement with the k^H/k^D value calculated from the experimental k^H/k^T value using the Swain relationship[137] (equation 54) and this is consistent with the assumption that bromination and isotope exchange occur through similar mechanisms.

$$k^H/k^T = (k^H/k^D)^{1.442} \qquad (54)$$

TABLE 14. Primary kinetic isotope effects in the ionization of malononitriles

$$RC(CN)_2L + B \xrightarrow{k^L} RC(CN)_2^- + BL^+$$

L = H, D or T

		Experimental values		Calculated value[a]
$RC(CN)_2L$	B	k^H/k^T	k^H/k^D	k^H/k^D
$LCH(CN)_2$	H_2O	1.71 ± 0.10	1.51	1.45
$Me_3CCL(CN)_2$	H_2O	1.64 ± 0.05	1.46	1.41
$Me_3CCL(CN)_2$	$CH_3CO_2^-$	1.74 ± 0.05	—	1.47

[a]Calculated from the measured value of k^H/k^T using the Swain relationship[137].

The kinetic isotope effects given in Table 14 are about the lowest that have been observed for proton transfer from carbon. Before these measurements[138] low isotope effects had been found in the hydroxide-ion-catalysed exchange of dichlorofluoromethane for which Hine[140] observed $k^H/k^D = 1.52$. Bell[141] measured a k^H/k^D of 1.97 for water-catalysed proton transfer from ethyl malonate. In other proton transfers from carbon the primary isotope effect has been shown to reach a maximum value around ca. 10, when the proton in the transition state is held roughly equally by the two atoms between which the transfer is occurring[142]. Low isotope effects are observed when the proton in the transition state is either almost fully or only slightly transferred. The kinetic isotope effects for proton transfer from malononitrile and *t*-butylmalononitrile to water are almost identical with the equilibrium isotope effect for this reaction, indicating that the transition state very closely resembles the products of the proton-transfer step. The equilibrium isotope effect is given by equation (57) (cf. equations 55 and 56). Since K_1 (equation 58) has an estimated value ca. 1.0 and l (equation 59) is known (0.69), the calculated result is $K^H/K^D = 1.45$, which is very

$$RC(CN)_2H + H_2O \rightleftharpoons RC(CN)_2^- + H_3O^+ \quad K^H/3 \tag{55}$$

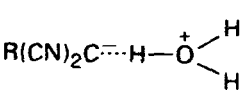
$$RC(CN)_2D + H_2O \rightleftharpoons RC(CN)_2^- + DH_2O^+ \quad K^D \tag{56}$$

$$K^H/K^D = K_1/l \tag{57}$$

$$RC(CN)_2H + \tfrac{1}{2}D_2O \rightleftharpoons RC(CN)_2D + \tfrac{1}{2}H_2O \quad K_1 \tag{58}$$

$$\tfrac{1}{3}H_3O^+ + \tfrac{1}{2}D_2O \rightleftharpoons \tfrac{1}{3}D_3O^+ + \tfrac{1}{2}H_2O \quad l \tag{59}$$

close to the experimental value of the kinetic isotope effect for proton transfer to water from malononitrile ($k^H/k^D = 1.51$) and from *t*-butylmalononitrile ($k^H/k^D = 1.46$). This agreement implies that the transition state for the reaction closely resembles the products of reaction as shown in **51**. If in the transition state the

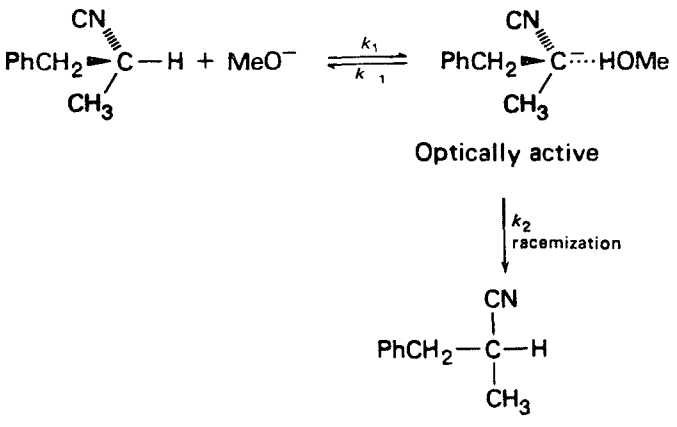


(51)

$R(CN)_2C^- \ldots H$ bond remained more intact, a much higher isotope effect would have been expected, as was found for most proton transfers from carbon. In the case of proton transfer to acetate ion, the situation is slightly different. The equilibrium isotope effect in this case has a value K^H/K^D = ca. 1.0 but the observed kinetic isotope effect is much higher ($k^H/k^D = 1.47$). This implies that for this reaction in the transition state the proton may not be fully transferred to the base catalyst[143]. The overall conclusion which emerges from these studies is that proton transfer from cyanocarbon acids in the thermodynamically unfavourable direction occurs through a transition state in which the proton is almost fully transferred to the base catalyst and thus the reaction gives kinetic results which are quite close to those observed for normal proton-transfer reactions.

In reaching conclusions about the mechanism of a reaction from the size of the kinetic hydrogen isotope effect (k^H/k^D) it has usually been assumed that an isotope effect $k^H/k^D <$ ca. 2.0 implies that the mechanism for the reaction does not involve a rate-determining proton-transfer step. However, the results described here show that proton transfer from a cyanocarbon acid is associated with an extremely low isotope effect. The same is probably true for the ionization of a number of other carbon acids (for example polyarylmethanes, halocarbons, sulphones, acetylenes) provided that the proton-transfer step is highly unsymmetrical, namely that ΔpK for the acid–base pair is large and positive or large and negative. Hence, the observation of a small kinetic hydrogen isotope effect for a reaction does not necessarily rule out a rate-determining proton-transfer step in the mechanism of reaction. Melander[135] has emphasized the importance of the low isotope effects observed for cyanocarbon acids in this respect and has drawn conclusions about the mechanism of racemization and exchange of 2-methyl-3-phenylpropionitrile on this basis.

For the racemization and isotope exchange of 2-methyl-3-phenylpropionitrile in MeOH–Me_2SO mixtures containing methoxide ion two possible mechanisms have been suggested[133,135]. The rate coefficients for racemization and isotope exchange are equal. The overall scheme for the racemization is given in equation (60) for which the rate expression of equation (61) applies, assuming that the carbanions are present in



(60)

$$-d\alpha/dt = \{k_1k_2/(k_{-1} + k_2)\}[PhCH_2CH(CN)CH_3][MeO^-]$$
$$= k_{obs}[PhCH_2CH(CN)CH_3][,MeO^-] \quad (61)$$

low concentration. The first mechanism arises if $k_{-1} \gg k_2$ which corresponds to a rate-determining racemization step and the measured rate coefficient for racemization

is given by $k_{obs} = k_1k_2/k_{-1}$. In the case when $k_{-1} \ll k_2$, $k_{obs} = k_1$ and the proton-transfer step is then rate-determining. The kinetic isotope effect is the ratio of rates of racemization of the two substrates $PhCH_2CH(CN)CH_3$ and $PhCH_2CD(CN)CH_3$. The observed value[74] is $k^H/k^D = 1.15$ in pure methanol and $k^H/k^D = 1.49$ in 9.8 wt. % MeOH–90.2 wt. % Me_2SO. These values are not incompatible with the mechanism of equation (60) having a rate-determining proton-transfer step; Melander argues that for the acid–base pair involved in the proton transfer ΔpK = ca. 9–15 and for this reaction the transition state will be extremely unsymmetrical. By comparison with the results obtained for malononitriles in aqueous solution, a low isotope effect would therefore be expected. It should be noted that the low isotope effect is also compatible with a rate-determining racemization step giving an observed rate coefficient for racemization $k_{obs} = k_1k_2/k_{-1}$. In this case the isotope effect is likely to be small because the rate-determining step does not involve the making or breaking of a covalent bond to hydrogen. However, the observation of a low isotope effect is no reason for ruling out a rate-limiting proton-transfer step in the racemization. This has been the tendency in the past[144]. The converse of this still holds though, namely that if a large isotope effect, i.e. $k^H/k^D >$ ca. 2.0 is observed the mechanism probably does involve formation or breakage of a bond to the isotopically substituted hydrogen atom in the rate-determining step of the reaction.

V. SUMMARY

Using the results given in Tables 1, 2 and 4 it should be possible to make rough estimates of the acidity of a weak or moderately weak cyanocarbon acid of unknown pK. Likewise, for the situation where a cyanocarbanion is generated in solution from a cyanocarbon acid in one step of a reaction mechanism, the discussion in Section IV.A makes it possible to roughly estimate the magnitude of rate coefficients for the generation and protonation of the cyanocarbanions. Often it can be assumed that for cyanocarbon acids in equilibrium with cyanocarbanions the rate in the thermodynamically favourable direction will be close to the diffusion limit. Therefore, the rate coefficients for generation and protonation of the cyanocarbanions can be estimated from the acidities of the species involved in the proton transfer. Care must be taken when additional activating groups such as keto, nitro or ester are present in the carbon acid since then the situation is more complicated. However, the discussion in Section IV.A provides some indication of what to expect in these cases.

VI. REFERENCES

1. A. C. Hopkinson in *The Chemistry of Carbon–Carbon Triple Bond*, Part I (Ed. S. Patai), John Wiley and Sons, London–New York, 1978, Chap. 4, pp. 75–136.
2. N. S. Isaacs, *Reactive Intermediates in Organic Chemistry*, John Wiley and Sons, London–New York, 1974, Chap. 4, pp. 234–285.
3. J. C. Stowell, *Carbanions in Organic Synthesis*, John Wiley and Sons, London–New York, 1980.
4. A. J. Bellamy, G. Howat and I. S. MacKirdy, *J. Chem. Soc., Perkin Trans. 2*, 786 (1978).
5. S. Hoz and D. Aurbach, *J. Amer. Chem. Soc.*, **102**, 2340 (1980).
6. A. J. Fatiadi, *Synthesis*, **10**, 165 (1978).
7. M. El Bouz, M.-C. Roux-Schmitt and L. Wartski, *J. Chem. Soc., Chem. Commun.*, 779 (1979).
8. F. Freeman, *Chem. Rev.*, **69**, 591 (1969).
9. Several estimates have been made of the acidity of methane. Cram[10] gives values of 48 and 40. Bell[11] has estimated pK =46 as a revision of an earlier[12] value of pK = 58. Pearson and Dillon[13] quote pK = 40.
10. D. J. Cram, *Fundamentals of Carbanion Chemistry*, Academic Press, New York, 1965, pp. 15 and 20.

11. R. P. Bell, *The Proton in Chemistry*, 2nd ed., Chapman and Hall, London, 1973, p. 86.
12. R. P. Bell, *The Proton in Chemistry*, 1st ed., Methuen, London, 1959, p. 87.
13. R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **75**, 2439 (1953).
14. A value of pK = 25 has been estimated[13] from kinetic results whereas pK = 31.3 has been obtained[15] from spectrophotometric measurements in dimethyl sulphoxide.
15. W. S. Matthews, J. E. Bares, J. E. Bartmess, F. G. Bordwell, F. J. Cornforth, G. E. Drucker, Z. Margolin, R. J. McCallum, G. J. McCollum and N. R. Vanier, *J. Amer. Chem. Soc.*, **97**, 7006 (1975).
16. This is an average of published values[13,17,18,19,20].
17. G. E. Lienhard and W. P. Jencks, *J. Amer. Chem. Soc.*, **87**, 3863 (1965).
18. R. H. Boyd and C.-H. Wang, *J. Amer. Chem. Soc.*., **87**, 430 (1965).
19. F. Hashimoto, J. Tanaka and S. Nagakura, *J. Mol. Spectry*, **10**, 401 (1963).
20. K. Bowden and R. Stewart, *Tetrahedron*, **21**, 261 (1965).
21. R. M. Izatt, J. J. Christensen, J. D. Hale, R. T. Park and R. Bench, *Inorg. Chem.*, **1**, 828 (1962).
22. R. H. Boyd, *J. Amer. Chem. Soc.*, **83**, 4288 (1961); R. H. Boyd, *J. Phys. Chem.*, **67**, 737 (1963).
23. E. Ciganek, W. J. Linn and O. W. Webster in *The Chemistry of the Cyano Group* (Ed. Z. Rappoport), John Wiley and Sons, London–New York, 1970, Chap. 9, pp. 423–638.
24. J. R. Jones, *The Ionisation of Carbon Acids*, Academic Press, London, 1973.
25. A. J. Kresge, *Chem. Soc. Rev.*, **2**, 475 (1973).
26. A. J. Kresge, *Acc. Chem. Res.*, **8**, 354 (1975).
27. F. Hibbert in *Comprehensive Chemical Kinetics*, Vol. 8 (Eds. C. H. Bamford and C. F. H. Tipper), Elsevier, Amsterdam, 1977, Chap. 2, pp. 97–196.
28. J. E. Crooks in *Proton Transfer Reactions* (Eds. E. F. Caldin and V. Gold), Chapman and Hall, London, 1975, Chap. 6, pp. 153–177.
29. G. Kortum, W. Vogel and K. Andrussow, *Dissociation Constants of Organic Acids in Aqueous Solution*, Butterworths, London, 1961.
30. E. P. Serjeant and B. Dempsey, *Ionisation Constants of Organic Acids in Aqueous Solution*, Pergamon Press, Oxford, 1979.
31. Some doubt has been expressed as to whether pK = 13.4[32] corresponds to a simple ionization to give the carbanion[33,34], but recently the situation has been clarified[35].
32. R. S. Stearns and G. W. Wheland, *J. Amer. Chem. Soc.*, **69**, 2025 (1947).
33. R. A. More O'Ferrall and J. H. Ridd, *J. Chem. Soc.*, 5030 (1963).
34. R. Stewart, J. P. O'Donnell and K. Bowden, *Can. J. Chem.*, **43**, 1225 (1965).
35. E. A. Walters, *J. Phys. Chem.*, **81**, 1995 (1977).
36. F. Hibbert, F. A. Long and E. A. Walters, *J. Amer. Chem. Soc.*, **93**, 2829 (1971).
37. F. Hibbert and F. A. Long, *J. Amer. Chem. Soc.*, **94**, 2647 (1972).
38. H. D. Hartzler, *J. Amer. Chem. Soc.*, **86**, 2174 (1964).
39. W. J. Middleton, R. E. Heckert, E. L. Little and C. G. Krespan, *J. Amer. Chem. Soc.*, **80**, 2783 (1958).
40. I. V. Tselenskii, G. I. Koletskaya, A. S. Kesmynina, *Organic Reactivity (USSR)*, **6**, 100 (1969).
41. Reference 23, p. 590.
42. M. J. Kamlet and D. J. Glover, *J. Org. Chem.*, **27**, 537 (1962).
43. M. R. Crampton, *J. Chem. Soc. (B)*, 85 (1967); M. J. Minch, M. Giaccio and R. Wolff, *J. Amer. Chem. Soc.*, **97**, 3766 (1975).
44. M. L. Eidenoff, *J. Amer. Chem. Soc.*, **67**, 2072 (1945).
45. F. G. Bordwell and W. J. Boyle Jr., *J. Amer. Chem. Soc.*, **94**, 3907 (1972).
46. I. V. Tselenskii, A. S. Kosmynina, V. N. Dronov and I. N. Shokhor, *Organic Reactivity (USSR)*, **7**, 20 (1970).
47. V. I. Slovetskii, L. V. Okhlokystina, A. A. Fainzilberg, A. I. Ivanov, L. I. Biryukova and S. S. Novikov, *Bull. Acad. Sci. USSR (Engl. Transl.)* 2032 (1965).
48. H. G. Adolf and M. J. Kamlet, *J. Amer. Chem. Soc.*, **88**, 4761 (1966).
49. T. N. Hall, *J. Org. Chem.*, **29**, 3587 (1964).
50. J. Hine, N. W. Burske, M. Hine and P. B. Langford, *J. Amer. Chem. Soc.*, **79**, 1406 (1957).
51. O. Reitz, *Z. Phys. Chem.*, **176A**, 363 (1936); G. W. Wheland and J. Farr, *J. Amer. Chem. Soc.*, **65**, 1433 (1943).

52. M. E. Sitzmann, H. G. Adolph and M. J. Kamlet, *J. Amer. Chem. Soc.*, **90**, 2815 (1968).
53. S. S. Novikov, V. I. Slovetskii, S. A. Shevelev and A. A. Fainzilberg, *Bull. Acad. Sci. USSR (Eng. Transl.)*, 552 (1962).
54. F. G. Bordwell, R. H. Imes and E. C. Steiner, *J. Amer. Chem. Soc.*, **89**, 3905 (1967).
55. E. J. Corey, H. König and T. H. Lowry, *Tetrahedron Letters*, 515 (1962).
56. J. Hine, J. C. Philips and J. I. Maxwell, *J. Org. Chem.*, **35**, 3943 (1970).
57. R. P. Bell and B. G. Cox, *J. Chem. Soc. (B)*, 652 (1971).
58. R. P. Bell and P. W. Smith, *J. Chem. Soc. (B)*, 241 (1966).
59. G. Schwarzenbach and E. Felder, *Helv. Chim. Acta*, **27**, 1701 (1944).
60. L. Birkenbach, K. Kellerman and W. Stein, *Chem. Ber.*, **65**, 1072 (1932).
61. J. Hine, *Structural Effects on Equilibria in Organic Chemistry*, John Wiley and Sons, London–New York, 1975, p. 185.
62. Reference 24, p. 70.
63. C. H. Rochester, *Acidity Functions*, Academic Press, London, 1970.
64. O. W. Webster, *J. Amer. Chem. Soc.*, **88**, 3046 (1966).
65. Reference 24, p. 57; Reference 10, p. 20.
66. E. A. Halevi and F. A. Long, *J. Amer. Chem. Soc.*, **83**, 2809 (1961).
67. A. J. Kresge and A. C. Lin, *J. Chem. Soc., Chem. Commun.*, 761 (1973).
68. Z. Margolin and F. A. Long, *J. Amer. Chem. Soc.*, **94**, 5108 (1972); Z. Margolin and F. A. Long, *J. Amer. Chem. Soc.*, **95**, 2757 (1973).
69. D. B. Dahlberg, A. J. Kresge and A. C. Lin, *J. Chem. Soc., Chem. Commun.*, 35 (1976).
70. F. Hibbert, *J. Chem. Soc., Perkin Trans. 2*, 1289 (1973).
71. R. P. Bell and O. M. Lidwell, *Proc. Roy. Soc. London*, **176A**, 88 (1940); R. P. Bell, *Trans. Faraday Soc.*, **39**, 253 (1943).
72. R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **72**, 3574 (1950).
73. K. F. Bonhoeffer, K. H. Geib and O. Reitz, *J. Chem. Phys.*, **7**, 664 (1939).
74. L. Melander and N.-Å. Bergman, *Acta Chem. Scand.*, **25**, 2264 (1971).
75. A. Streitwieser Jr., M. P. Granger, F. Mares and R. A. Wolff, *J. Amer. Chem. Soc.*, **95**, 4257 (1973).
76. A. I. Shatenstein in *Advances in Physical Organic Chemistry*, Vol. 1 (Ed. V. Gold), Academic Press, London, 1963, pp. 155–201.
77. A. Streitwieser, D. Holtz, G. R. Ziegler, J. O. Stoffer, M. L. Brokaw and F. Guibe, *J. Amer. Chem. Soc.*, **98**, 5229 (1976).
78. D. Dolman and R. Stewart, *Can. J. Chem.*, **45**, 911 (1967).
79. E. C. Steiner and J. D. Starkey, *J. Amer. Chem. Soc.*, **89**, 2751 (1967).
80. M. Szwarc, A. Streitwieser and P. C. Mowery in *Ions and Ion Pairs in Organic Reactions*, Vol. 2 (Ed. M. Szwarc), John Wiley and Sons, London–New York, 1974, Chap. 2, pp. 151–245.
81. The potentiometric method was first used by Kolthoff and Reddy[82] and by Ritchie and Uschold[83].
82. I. M. Kolthoff and T. B. Reddy, *Inorg. Chem.*, **1**, 189 (1962).
83. C. D. Ritchie and R. E. Uschold, *J. Amer. Chem. Soc.*, **89**, 1721 (1967); C. D. Ritchie and R. E. Uschold, *J. Amer. Chem. Soc.*, **89**, 2752 (1967).
84. K. Bowden and A. F. Cockerill, *J. Chem. Soc. (B)*, 173 (1970).
85. A. Streitwieser Jr., E. Ciuffarin and J. H. Hammons, *J. Amer. Chem. Soc.*, **89**, 63 (1967).
86. F. G. Bordwell and W. S. Matthews, *J. Amer. Chem. Soc.*, **96**, 1216 (1974). The pK values given in this paper have since been corrected by 2.1 units[15], but the relative values still hold.
87. F. G. Bordwell, D. Algrim and H. E. Fried, *J. Chem. Soc., Perkin Trans. 2*, 726 (1979).
88. F. G. Bordwell, J. E. Bares, J. E. Bartmess, G. E. Drucker, J. Gerhold, G. J. McCollum, M. Van der Puy, N. R. Vanier and W. S. Matthews, *J. Org. Chem.*, **42**, 326 (1977).
89. E. A. Walters and F. A. Long, *J. Amer. Chem. Soc.*, **91**, 3733 (1969).
90. F. G. Bordwell, M. Van der Puy and N. R. Vanier, *J. Org. Chem.*, **41**, 1883 (1976).
91. A much lower value (pK = 22.6) has been measured in Me_2SO by Delpuech[92], but see Reference 87 for a discussion of this.
92. J. Chrisment and J.-J. Delpuech, *J. Chem. Soc., Perkin Trans. 2*, 407 (1977).
93. C. D. Ritchie in *Solute–Solvent Interactions* (Eds. J. F. Coetzee and C. D. Ritchie), Dekker, New York, 1969, Chap. 4, pp. 219–300.
94. M. J. Kamlet, J. L. Abboud and R. W. Taft, *J. Amer. Chem. Soc.*, **99**, 6027 (1977).

95. J. I. Brauman and L. K. Blair, *J. Amer. Chem. Soc.*, **90**, 5636 (1968).
96. J. I. Brauman and L. K. Blair, *J. Amer. Chem. Soc.*, **93**, 3911 (1971).
97. J. I. Brauman and L. K. Blair, *J. Amer. Chem. Soc.*, **90**, 6561 (1968); J. I. Brauman and L. K. Blair, *J. Amer. Chem. Soc.*, **92**, 5986 (1970).
98. D. K. Bohme, E. Lee-Ruff and L. B. Young, *J. Amer. Chem. Soc.*, **94**, 5153 (1972).
99. T. B. McMahon and P. Kebarle, *J. Amer. Chem. Soc.*, **96**, 5940 (1974).
100. T. B. McMahon and P. Kebarle, *J. Amer. Chem. Soc.*, **98**, 3399 (1976).
101. F. G. Bordwell, J. E. Bartmess, G. E. Drucker, Z. Margolin and W. S. Matthews, *J. Amer. Chem. Soc.*, **97**, 3226 (1975).
102. T. B. McMahon and P. Kebarle, *J. Amer. Chem. Soc.*, **98**, 3399 (1976).
103. J. B. Cumming and P. Kebarle, *J. Amer. Chem. Soc.*, **100**, 1835 (1978).
104. J. E. Bartmess, J. A. Scott and R. T. McIver Jr., *J. Amer. Chem. Soc.*, **101**, 6046 (1979).
105. Reference 61, Chap. 3, pp. 55–102.
106. R. D. Topsom in *Progress in Physical Organic Chemistry*, Vol. 12 (Ed. R. W. Taft), John Wiley and Sons, London–New York, 1976, pp. 1–20.
107. S. Ehrenson, R. T. C. Brownlee and R. W. Taft in *Progress in Physical Organic Chemistry*, Vol. 10 (Ed. A. Streitwieser Jr. and R. W. Taft), John Wiley and Sons, London–New York, 1973, pp. 1–80.
108. C. Bugg, R. Desiderato and R. L. Sass, *J. Amer. Chem. Soc.*, **86**, 3157 (1964).
109. R. H. Boyd, *J. Phys. Chem.*, **65**, 1834 (1961).
110. Reference 11, p. 109.
111. J. E. Bartmess, J. A. Scott and R. T. McIver Jr., *J. Amer. Chem. Soc.*, **101**, 6056 (1979).
112. M. Eigen and L. de Maeyer in *Techniques of Organic Chemistry*, Vol. VIII, Part 2 (Eds. S. L. Friess, E. S. Lewis and A. Weissberger), Interscience, London–New York, 1963, pp. 895–1054; see also G. G. Hammes (Ed.) *Investigation of Rates and Mechanisms of Reactions*, Vol. VI, 3rd ed., Part II, John Wiley and Sons, London–New York, 1974.
113. C. F. Bernasconi, *Relaxation Kinetics*, Academic Press, New York, 1976.
114. M. Eigen, *Angew. Chem. (Intern. Ed.)*, **3**, 1 (1964).
115. F. Hibbert and A. Awwal, *J. Chem. Soc., Perkin Trans. 2*, 939 (1978).
116. N.-Å. Bergman, Y. Chiang and A. J. Kresge, *J. Amer. Chem. Soc.*, **100**, 5954 (1978).
117. For a summary see Reference 12, p. 161.
118. J. N. Brønsted and K. Pedersen, *Z. Phys. Chem.*, **108**, 185 (1924).
119. A. J. Kresge and Y. C. Tang, *J. Chem. Soc., Chem. Commun.*, 309 (1980).
120. M.-L. Ahrens, M. Eigen, W. Kruse and G. Maass, *Ber. Bunsenges Phys. Chem.*, **74**, 380 (1970).
121. A. J. Kresge, S. G. Mylonakis, Y. Sato and V. P. Vitullo, *J. Amer. Chem. Soc.*, **93**, 6181 (1971).
122. D. J. Barnes and R. P. Bell, *Proc. Roy. Soc., London*, **318A**, 421 (1970).
123. Reference 11, Chap. 10, pp. 194–225.
124. T. Okuyama, Y. Ikenouchi and T. Fueno, *J. Amer. Chem. Soc.*, **100**, 6162 (1978).
125. J. R. Keefe, J. Morey, C. A. Palmer and J. C. Lee, *J. Amer. Chem. Soc.*, **101**, 1295 (1979).
126. Details of this technique are given in Section IV.C.
127. R. F. Pratt and T. C. Bruice, *J. Org. Chem.*, **37**, 3563 (1972).
128. Reference 10, p. 86.
129. D. J. Cram and L. Gossar, *J. Amer. Chem. Soc.*, **86**, 5457 (1964).
130. H. M. Walborsky and J. M. Motes, *J. Amer. Chem. Soc.*, **92**, 2445 (1970).
131. H. M. Walborsky and L. M. Turner, *J. Amer. Chem. Soc.*, **94**, 2273 (1972).
132. D. J. Cram, B. Rickborn, C. A. Kingsbury and P. Haberfield, *J. Amer. Chem. Soc.*, **83**, 3678 (1961).
133. Reference 10, p. 38.
134. R. Stewart, J. P. O'Donnell, D. J. Cram and B. Rickborn, *Tetrahedron*, **18**, 917 (1962).
135. L. Melander, *Acta Chem. Scand.*, **25**, 3821 (1971).
136. F. Hibbert and F. A. Long, *J. Amer. Chem. Soc.*, **93**, 2836 (1971).
137. C. G. Swain, E. C. Stivers, J. F. Reuwer Jr. and J. L. Schaad, *J. Amer. Chem. Soc.*, **80**, 5885 (1958).
138. Since the publication of the work with malononitriles, low isotope effects have also been reported on proton transfer from chloroform[68,77,139], phenylacetylene[67] and from sulphones[70]. These reactions also show some of the features of normal proton transfers,

(Section IV.A) and occur through transition states in which the proton is almost fully transferred.
139. A. J. Kresge and A. C. Lin, *J. Amer. Chem. Soc.*, **97**, 6257 (1975).
140. J. Hine and N. W. Burske, *J. Amer. Chem. Soc.*, **78**, 3337 (1956).
141. R. P. Bell and J. E. Crooks, *Proc. Roy. Soc., London*, **286A**, 285 (1965).
142. R. A. More O'Ferrall in *Proton Transfer Reactions* (Eds. E. F. Caldin and V. Gold), Chapman and Hall, London, 1975, Chap. 8, pp. 201–261.
143. W. J. Albery in *Proton Transfer Reactions* (Eds. E. F. Caldin and V. Gold), Chapman and Hall, London, 1975, Chap. 9, pp. 263–315.
144. Reference 10, p. 28.