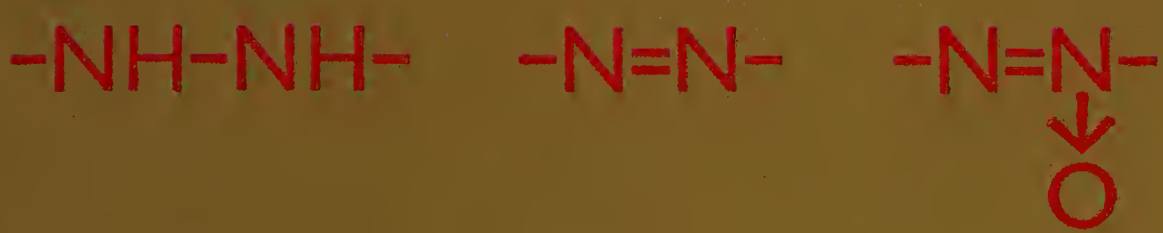
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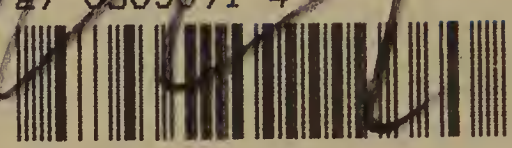

The chemistry of
the hydrazo, azo and azoxy groups

Part 2

THE CHEMISTRY OF FUNCTIONAL GROUPS

A series of advanced treatises under the general editorship of Professor Saul Patai

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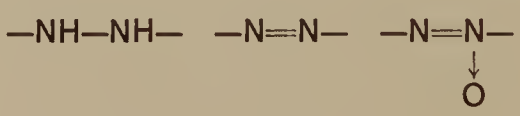

The chemistry of **the hydrazo, azo and azoxy groups**

Part 2

Edited by

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The Hebrew University, Jerusalem

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Foreword

The present volume, 'The Chemistry of the Hydrazo, Azo and Azoxy Groups' is organized and presented on the same general lines as the other volumes of the series and which are described in the 'Preface to the series' printed on the following pages.

The subject matter of this volume does not include either diazonium salts or diazo-alkanes. These groups will be treated in a separate forthcoming volume of the series. In addition it was decided not to treat azo dyes as such extensively since this would have enlarged the volume to unreasonable proportions while recent and satisfactory treatises exist on this subject.

The plan of the present volume included also a chapter on 'Detection and Determination of Hydrazo, Azo and Azoxy Groups' which however owing to the illness of the author, did not materialize.

Some additional material on the Azo and Azoxy Groups will also be available soon in the first supplementary volume of the series now in the press which will include material on double-bonded groups. While this supplementary volume will treat mainly the C═C, C═O and C═N groups it will also treat some aspects of the N═N groups in several of its chapters.

Jerusalem, January 1975 SAUL PATAI

The Chemistry of Functional Groups
Preface to the series

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

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

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

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

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

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

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

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

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

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

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

The Chemistry of Alkenes (*published in two volumes*)
The Chemistry of the Carbonyl Group (*published in two volumes*)
The Chemistry of the Ether Linkage (*published*)
The Chemistry of the Amino Group (*published*)
The Chemistry of the Nitro and the Nitroso Group (*published in two parts*)
The Chemistry of Carboxylic Acids and Esters (*published*)
The Chemistry of the Carbon–Nitrogen Double Bond (*published*)
The Chemistry of the Cyano Group (*published*)
The Chemistry of Amides (*published*)
The Chemistry of the Hydroxyl Group (*published in two parts*)
The Chemistry of the Azido Group (*published*)
The Chemistry of Acyl Halides (*published*)
The Chemistry of the Carbon–Halogen Bond (*published in two parts*)
The Chemistry of the Quinonoid Compounds (*published in two parts*)
The Chemistry of the Thiol Group (*published in two parts*)
The Chemistry of the Carbon–Carbon Triple Bond
The Chemistry of Amidines and Imidates (*in press*)
The Chemistry of the Hydrazo, Azo and Azoxy Groups (*published*)
The Chemistry of the Cyanates and their Thio-derivatives (*in preparation*)
The Chemistry of the Diazonium and Diazo Groups (*in preparation*)
Supplementary Volume on the Chemistry of Double-bonded Groups (*in press*)

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

CHAPTER 15

Reduction and synthetic uses of hydrazo, azo and azoxy compounds

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Moncton, New Brunswick, Canada

I. INTRODUCTION

This chapter is concerned with fairly recent developments relating to the reduction of aliphatic and aromatic azo, azoxy and hydrazo compounds, and the use of these reactions in syntheses. Much of the earlier literature touching on various aspects of this topic has been covered elsewhere, a number of pertinent reference works being available[1–10]. Reduction of the azo group in azo dyes has not been included since it has been reviewed by Zollinger[1, 11].

Since the conditions under which reductions are carried out are often important and in some cases even determine the success or failure of a reaction, they are frequently mentioned in this chapter and since we are also concerned here with synthesis, yields of products are given in many instances. Mention is also made wherever possible of mechanisms proposed for reduction reactions, but unfortunately mechanistic studies on reductions in general have received much less attention than those on other reactions, and consequently information in this regard is often lacking. This also applies to systematic investigations of the influence of substituents on the course of reduction of azo and related compounds, which have been few and far between.

Many of the research papers dealing with azo and azoxy compounds do not indicate the geometric configurations of these substances[9], however, in most cases one would suspect that the compounds referred to have the more stable *trans*-configuration, and especially when one considers the methods of synthesis employed[1]. In this review the geometric configurations of the azo and azoxy compounds mentioned are given by name or shown by structural formulae whenever the original reference cited provides such information. This also applies to the position isomers of unsymmetrically substituted azoxy compounds. In general, the nomenclature used is that reported in the original literature, but in some cases names have been changed in an effort to conform to the IUPAC system of nomenclature. The various naming systems in use for azo and azoxy compounds have been conveniently summarized recently by Sandler and Karo[9].

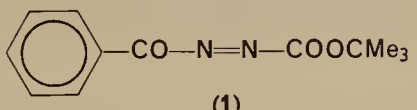
II. REDUCTION OF ALIPHATIC AZO AND AZOXY COMPOUNDS

Little attention appears to have been paid to the reduction of aliphatic azo compounds over the last few years. Some work has been done on the reduction of aliphatic azoxy derivatives, including a number of cyclic

systems, to azo and hydrazo products. Reduction of azoxy compounds with appropriate reagents is a useful preparative route to azo derivatives; and may also be used for confirmation of structure.

A. Aliphatic Azo to Hydrazo Derivatives

Few studies have apparently been carried out recently on the reduction of aliphatic azo compounds to the corresponding hydrazines, for which carefully controlled reaction conditions and mild reagents are usually essential. Examples of reductions of acylazo derivatives are the transformation of t-butyl benzoylazoformate (**1**) to the hydrazo derivative with hydrazine hydrate[12], (equation 1); and the conversion of di(3,3,3-triphenylpropionyl)-di-imide (**2**) in benzene to *N,N'*-di(3,3,3-triphenylpropionyl)-hydrazine (**3**) in 70% yield, by hydrogenation at 25°C and 1 atm over platinum oxide[13], (equation 2). Some phenylazoacyl compounds, such as Ph—N=N—$CONMe_2$ and Ph—N=N—COOK have also been reduced to give excellent yields of the appropriate hydrazines[14].

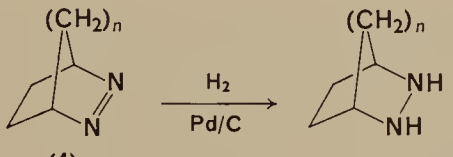


(1) (1)

$Ph_3CCH_2CO—N=N—OCCH_2CPh_3$ $\xrightarrow{H_2/PtO}$ $Ph_3CCH_2CO—NH—NH—OCCH_2CPh_3$ (2)

(2) (3)

Very recently[15], bicyclic hydrazines have been smoothly and efficiently synthesized by catalytic hydrogenation of bicycloazoalkanes. Compounds of general formula (**4**) e.g. 2,3-diazabicycloheptane ($n = 1$) were quantitatively converted to the bicyclo hydrazines by hydrogenation over 5% palladium on charcoal in methanol at a pressure of 40 lb/in^2, (equation 3).

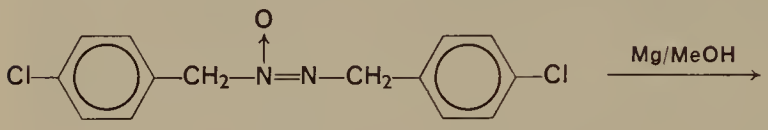


(4) (3)

$n = 1$–3

B. Aliphatic Azoxy to Azo Compounds

A number of open chain aliphatic and also alicyclic azoxy derivatives have been successfully reduced to the azo compounds with different reagents. For instance, ω-azoxy-*p*-chlorotoluene (**5**) was reduced with magnesium turnings in dry methanol to ω-azo-*p*-chlorotoluene (**6**) (equation 4), some di-*p*-chlorobenzylhydrazine also being formed[16].



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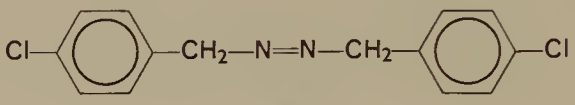
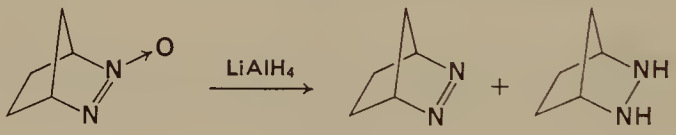


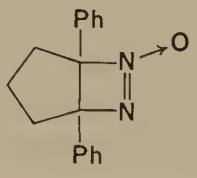
(6) (4)

In recent years, interest seems to have turned more to reduction of alicyclic azoxy systems rather than open chain compounds. Thus, the *cis*-bicycloazoxy compound (**7**) has been reduced with lithium aluminium hydride to give both the azo and hydrazo derivatives[17], (equation 5). On the



(7) (5)

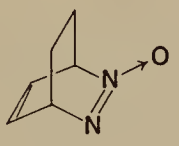
other hand, after similar reduction of **8** in ether at 26°C, the unstable cyclic azo derivative was not detected, the corresponding hydrocarbon(1,2-diphenylcyclopentene) being isolated in quantitative yield[18].



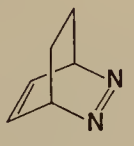
(8)

Although *trans*-azoxyalkanes have been known for quite some time, until recently relatively few *cis*-azoxyalkanes had been made[19, 20]. In 1972, Snyder and co-workers[21] synthesized some interesting cyclic *cis*-azoxyalkanes, for example, 2,3-diazabicyclo-[2.2.2.]-octadiene *N*-oxide (**9**), and treated them with excess hexachlorodisilane in an n.m.r. tube at 25°C in attempts to

detect the appropriate azoalkanes. This readily available reducing agent, which can be used under mild conditions and had been successfully employed for the deoxygenation of acyclic phosphine oxides[22], caused a mildly exothermic reaction accompanied by immediate disappearance of the azoxy spectrum. However, the only product was the corresponding hydrocarbon as shown by the nuclear magnetic resonance spectrum. Thus, (**9**) was converted to cyclohexadiene without detection of **10** under the



(**9**)

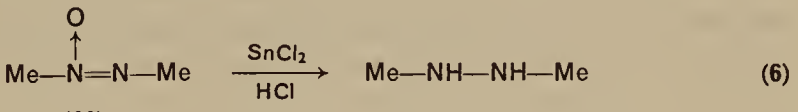


(**10**)

conditions used. This study also showed that azoxyalkanes of the type mentioned have remarkable thermal stability, resisting change below 175° C either alone or in solution, in complete contrast to the corresponding *cis*-azoalkanes which proved to be unstable. The latter may in fact be conveniently stored in the form of their *cis*-azoxy derivatives[22].

C. Aliphatic Azoxy to Hydrazo Compounds

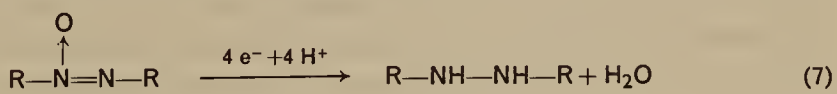
Several cases of direct conversion of aliphatic azoxy compounds to their hydrazo derivatives have been reported in the literature. Azoxymethane (**11**) and other azoxyalkanes have been smoothly reduced to the corresponding hydrazines by treatment with stannous chloride in cold 12N-hydrochloric



(**11**) (6)

acid[16], (equation 6). Catalytic hydrogenation of azoxyalkanes in methanol at room temperature and pressure over platinum oxide also leads to efficient conversion to *N,N'*-dialkylhydrazines in good yield. For instance, 1- and 2-azoxypropane and azoxycyclohexane have been reduced in this manner[16].

Aliphatic azoxy compounds may be converted to symmetrical hydrazines in good yield by electrochemical reduction (equation 7). For example, **11** is



(7)

reduced to 1,2-dimethylhydrazine in this way. This type of reduction takes place readily and has made it possible to convert nitroalkanes, such as nitromethane, directly to *N*,*N*′-dialkylhydrazines without isolating the various intermediates (e.g. *N*-methylhydroxylamine, nitrosomethane, and **11**) by simply twice reversing the current[23].

III. REDUCTION OF AROMATIC AZO AND AZOXY COMPOUNDS

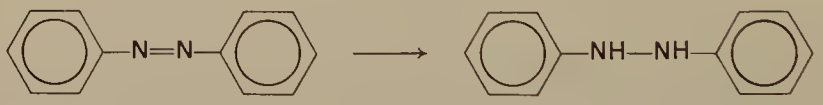
The reduction of aromatic azo and azoxy compounds, and especially azo and azoxybenzenes (including the parent substances), has received a good deal of attention lately; with many reducing agents and various reaction conditions being used. The early literature on the reduction of azoxybenzenes was briefly reviewed by Bigelow[24], and more extensively later on by Zollinger[1], who also reviewed the reduction of azobenzenes and other azoarenes. Recently, Sandler and Karo[9] have surveyed the methods available for the preparation of aromatic azo compounds from azoxy derivatives.

A. Aromatic Azo to Hydrazo Compounds

The reduction of azobenzenes to hydrazobenzenes is an important reaction since it constitutes a convenient route to the latter, which are needed as starting materials for studies on the benzidine rearrangement.

1. Azobenzene

A wide variety of reagents has been used to reduce the parent substance, azobenzene (**12**) to hydrazobenzene (**13**), and because of the importance of this reaction (equation 8) research on it continues.



(12) (13) (8)

Corey and co-workers[25] have shown that this conversion may be readily brought about by the use of hydrazine as reducing agent under certain conditions. Reduction in methanol took place completely (isolated yield of hydrazobenzene, 95%) with either hydrazine and oxygen (air) or hydrazine and hydrogen peroxide, in the presence of copper ion. However, only very slow reduction occurred in the absence of copper ion (a powerful catalyst

for oxidation of hydrazine), and little or no reaction took place without an oxidizing agent being present, even over a prolonged period of time. It was concluded that oxidation of hydrazine to nitrogen, via di-imide (NH=NH), played a role in this conversion. These workers also found that addition of an excess of potassium azodiformate to azobenzene in aqueous methanol effected rapid reduction to hydrazobenzene.

It is well known that hydrazobenzene easily rearranges to benzidine in acidic media and hence it has often been found that attempts to reduce azobenzene under acidic conditions lead to the preferential formation of benzidine. This was the case for instance when using stannous chloride in acid solution[26]. The reduction of *trans*-azobenzene with titanous chloride in aqueous-alcoholic solution has been studied[27], and found to give hydrazobenzene, some 84% of which was very rapidly transformed into benzidine (or its isomers); the rest undergoing reduction or disproportionation to aniline. The kinetics of the reaction showed it to be first-order with respect to both substrate and reducing agent, the rate-determining step being the transfer of an electron from the titanous entity to diprotonated azobenzene. This study also revealed that *cis*-azobenzene was very rapidly reduced by the agent employed.

Lithium aluminium hydride and other metal hydrides have been used for the conversion of azobenzene to hydrazobenzene. Originally azobenzene proved to be difficult to reduce using lithium aluminium hydride alone, drastic conditions such as large excess of hydride, prolonged reaction time, and high temperature being necessary to bring about successful reaction. However, in later work[28] it was reported that the addition of small amounts of certain metal halides (e.g. $MoCl_5$, $TiCl_4$, VCl_3, $FeCl_3$, $PbCl_2$) had a marked catalytic effect on the reaction, such that very fast reduction giving a high yield of hydrazobenzene occurred in ether solution at room temperature. Brown and co-workers[29–31] have extensively investigated the reactions of azobenzene with lithium aluminium hydride and a number of its derivatives. In contrast to lithium aluminium hydride, which under appropriate conditions (excess hydride in tetrahydrofuran at 0°C) caused smooth reduction to hydrazobenzene, lithium trimethoxyaluminohydride (a weaker reducing agent) produced only very sluggish reduction to hydrazobenzene, the reaction being incomplete even after 48 h at 25°C; and lithium tri-t-butoxyaluminohydride (a much milder reagent) did not react with azobenzene. In addition, azobenzene reacted only very slowly with aluminium hydride under the same conditions.

Diborane, a Lewis acid which attacks sites of high electron density such as the azo linkage, when used in excess rapidly reduces azobenzene in diglyme to hydrazobenzene at room temperature[32]. Treatment of azo-

benzene with sodium borohydride–boron trifluoride etherate under like conditions gives similar results[32]. Neilson and colleagues[33] have shown that sodium borohydride catalysed by palladised charcoal reduces azobenzene in alkaline solution or aqueous methanol to hydrazobenzene (isolated as benzidine, 61 %), and not to aniline.

Catalytic hydrogenation has also proved to be a useful means for reduction of azobenzene to the hydrazo compound without further reaction to aniline, and several groups of workers have used different catalysts for this hydrogenation. A recent example was the rapid conversion of azobenzene to hydrazobenzene in almost quantitative yield using the homogeneous catalyst bis(dimethylglyoximato) cobalt(II)[34].

The electrochemical reduction of azobenzene has been studied extensively in protic media. This substrate is easily reduced to hydrazobenzene using various cathodes, e.g. platinum, but may also be cleaved to aniline in either acidic or basic catholytes. Mixtures of hydrazobenzene, benzidine, and aniline have been obtained when using this method. The azobenzene–hydrazobenzene system has been investigated using the dropping mercury electrode and shown to be a virtually reversible redox couple[35]. In more recent years, interest in the electrochemical reduction of azobenzene in aprotic media, such as dimethylformamide (DMF) has grown and a number of studies have led to revealing conclusions regarding the mechanisms involved. Aylward and co-workers[36] carried out both a.c. and d.c. polarographic reductions of azobenzene in DMF and considered that reduction to the anion radical by a fast one-electron transfer reaction took place, followed by a second slow electron transfer process leading to a stable dianion.

Sadler and Bard[37] have used a variety of electrochemical techniques (polarography, cyclic voltammetry, and controlled-potential coulometry) to study the reduction of azobenzene in DMF in both the absence and presence of proton donors, and confirmed the mechanism proposed by Aylward and co-workers. They reported that the second electron transfer to yield the dianion was followed by a reaction giving rise to a protonated species which was oxidizable to azobenzene, but also afforded hydrazobenzene in a subsequent reaction. It has also been shown[38] that electrolytic reduction of a solution containing azobenzene, benzaldehyde(depolarizator), benzyltriphenylphosphonium bromide and lithium chloride in DMF affords an isolated yield of benzidine of 68 % after consumption of 2·1 F/mol, thus indicating quantitative production of hydrazobenzene.

In a very recent investigation[39] the polarograms of azobenzene and hydrazobenzene in three media having different pH were examined and information regarding the nature of the mechanism of the azobenzene–

hydrazobenzene electrode process on mercury was obtained. After considering three plausible mechanisms—(1) simultaneous uptake of two electrons by azobenzene or vice versa, simultaneous release of two electrons by hydrazobenzene; (2) gradual transfer of two consecutive electrons from Hg to azobenzene to give an unstable intermediate, or vice versa; and (3) transfer of one electron from Hg to azobenzene to produce an intermediate which undergoes chemical reaction to another species that is subsequently electroreduced to hydrazobenzene—it was concluded that the third mechanism was in operation. When going towards reduction it was considered that the rate-determining step was the first one-electron transfer; whereas that in the direction of oxidation was thought to be the intermediate chemical reaction.

2. *Substituted Azobenzenes*

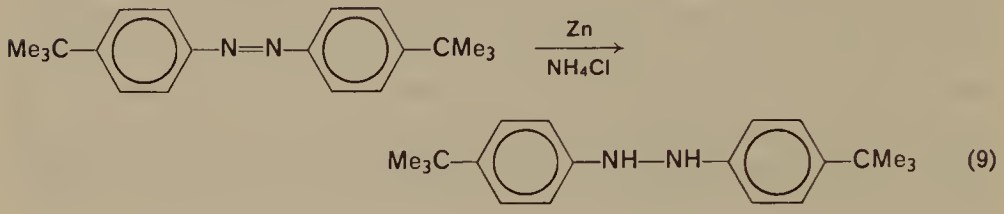
a. Symmetrical azobenzenes. In recent years, a variety of symmetrically disubstituted azobenzenes has been reduced to the corresponding hydrazo derivatives using a number of reagents. For example, 4,4′-difluoro- and dichloroazobenzene were reduced by lithium aluminium hydride catalysed with various metal halides to give the hydrazo compounds in yields of at least 90%[28]. Similar conversions of these substrates were also achieved using other metal salts (e.g. nitrates, carbonates, and acetates) and metal oxides (e.g. CuO, NiO, and V_2O_5) as catalysts, but the latter were less active and led to slower reaction. 4,4′-Diethoxyazobenzene has been reduced to 4,4′-diethoxyhydrazobenzene by heating with 30% alcoholic potassium hydroxide and zinc dust[40].

Treatment of azobenzenes, including symmetrically disubstituted compounds, with 40% sodium hydroxide and an excess of zinc dust in a minimum of ethanol under reflux conditions has proved to be an effective means for preparing hydrazobenzenes. For instance, 2,2′- and 4,4′-diethylhydrazobenzene have been synthesized in this way[41]. This technique has been successfully applied to a wide range of substituted azobenzenes possessing stable groups, although in some cases precautions must be taken to prevent air oxidation of the hydrazobenzene during isolation[42]. The method is not suitable however for the preparation of 2,2′- and 4,4′-di-iodohydrazobenzene, because with 2,2′- and 4,4′-di-iodoazobenezene deiodination rather than reduction takes place, the product always being unsubstituted azobenzene[43].

However, careful reduction of 2,2′-di-iodoazobenzene with zinc dust and a little acetic acid in ethanol affords the desired 2,2′-di-iodohydrazobenzene[44]. 4,4′-Diacetoxyazobenzene has been reduced to the hydrazo

derivative by zinc dust and acetic acid, but is not affected by alcoholic ammonium sulphide[45].

Shine and Chamness[46] have synthesized 4,4′-di-t-butylhydrazobenzene (**14**) for benzidine rearrangement studies, by reduction of the azo compound with zinc and ammonium chloride (equation 9).

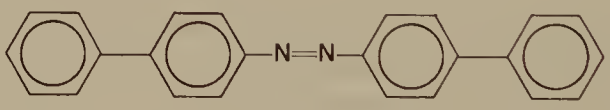


(9)

(**14**)

Symmetrical hydrazophenols have been obtained in excellent yield via reduction of the acetyl derivatives of 2,2′- and 4,4′-dihydroxyazobenzene[47]. Symmetrically dihalogenated azobenzenes have also been converted to the hydrazobenzenes by reduction[48]. Nesmeyanov and co-workers[49] have used tetralin in the presence of boron trifluoride for the reduction of substituted azobenzenes to their hydrazo derivatives. Thus, by heating at 100–110°C with this reagent in anisole for 3 h, 2,2′-dimethylazobenzene gives 2,2′-dimethylhydrazobenzene in 42% yield, together with traces of *o*-toluidine. Similar treatment of the 3,3′-isomer gave rise to 3,3′-dimethylhydrazobenzene in lower yield, and again traces of the amine.

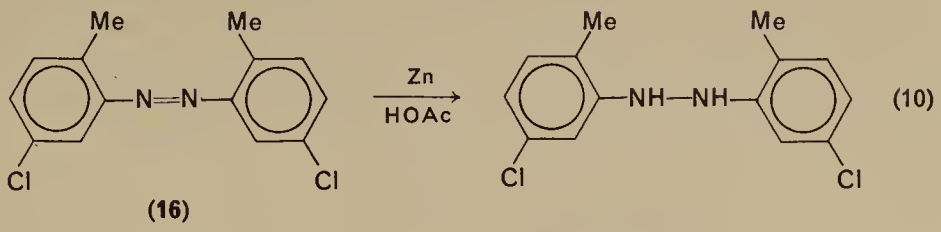
Electrochemical methods may be used to prepare hydrazo compounds from azobenzenes, which are more easily reduced than azoxybenzenes by this means. The electrochemical reduction of a number of disubstituted azobenzenes to the hydrazo compounds in DMF solution has been studied and a general mechanism consistent with the experimental results was proposed[37]. 3,3′-Dimethylazobenzene, 4,4′-azobiphenyl (**15**), and 4,4′-azopyridine were reduced in this manner.



(**15**)

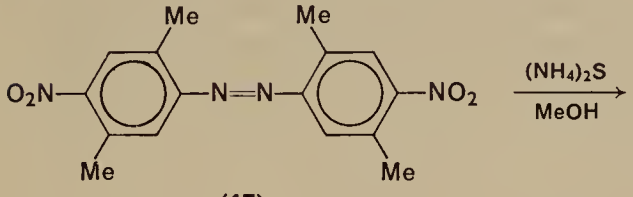
In contrast to the disubstituted derivatives, there has been little recent work concerned with the reduction of symmetrically tetrasubstituted azobenzenes to hydrazobenzenes. One of the rare examples is the conversion of 5,5′-dichloro-2,2′-dimethylazobenzene (**16**) to the corresponding

hydrazobenzene in 60% yield by treatment with zinc and glacial acetic acid at 80°C for 1 h[50], (equation 10).



(16) (10)

Singh and co-workers[50] also carried out some interesting studies on reductions of two symmetrically polysubstituted azobenzenes. They found that exposure of 5,5′-dichloro-2,2′-dimethyl-4,4′-dinitroazobenzene to sodium sulphide in methanol at 50°C caused reduction of both nitro groups but not the azo linkage, the product being the 4,4′-diaminoazo derivative in 75% yield. This result was explained on the basis of the electromeric effects of the chlorine atoms and the electron-donating nature of the azo group, both of which augment electron density at the nitro group which favours reduction there. Furthermore, reduction of 2,2′,5,5′-tetramethyl-4,4′-dinitroazobenzene (**17**) with the same reagent under similar conditions also gave the 4,4′-diaminoazo compound. However, reaction of **17** with ammonium sulphide in methanol at 50°C rather surprisingly afforded 2,2′,5,5′-tetramethyl-4,4′-dinitrohydrazobenzene (**18**), (equation 11). In



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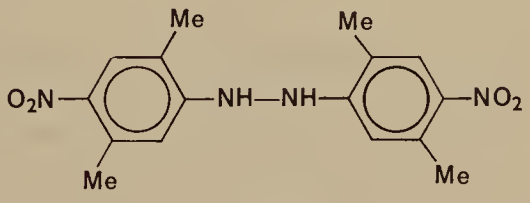
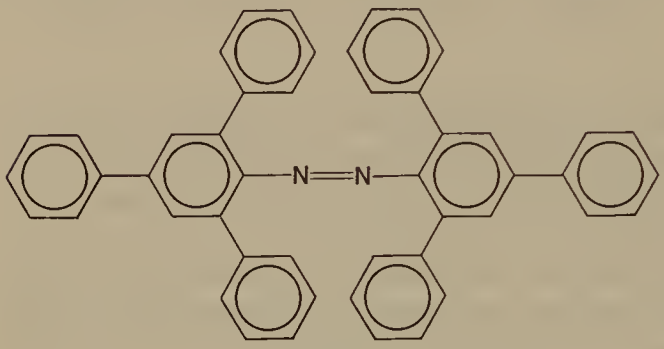


(18) (11)

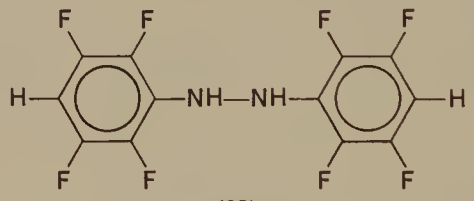
explanation of this attack on the azo linkage rather than the nitro groups, it was suggested that the 2 and 2′ methyl substituents, because of their positive inductive effects, might prevent the electromeric shift of electrons from the azo group to the nitro substituents, thus favouring attack at the electron-rich azo linkage.

Attempts have been made to reduce 2,2′,4,4′,6,6′-hexaphenylazobenzene (**19**) to the hexaphenylhydrazobenzene, but these have all failed[51]. Thus, **19** was not affected by reducing agents such as iron or zinc in acidic medium, sodium and ethanol, or sodium hydrosulphite in alkaline medium. This lack of reactivity can be accounted for by steric hindrance around the azo group due to the four adjacent bulky phenyl substituents in this molecule.



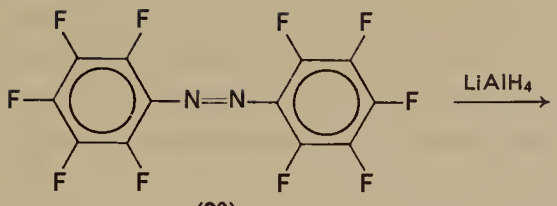
(19)

More recent work on the reduction of polysubstituted azobenzenes has concerned highly fluorinated substrates. Burdon and co-workers[52] have reported that catalytic hydrogenation of polyfluoroazobenzenes gives the corresponding pure hydrazo compounds. Thus, hydrogenation of decafluoroazobenzene (**20**) and 4*H*,4′*H*-octafluoroazobenzene (**21**) over 5% palladium on asbestos at atmospheric pressure and room temperature produces decafluorohydrazobenzene (**22**) and 4*H*,4′*H*-octafluorohydrazobenzene (**23**), respectively. Reduction of **20** with lithium aluminium hydride



(23)

in ether also gave **22** as the major product, but some evidence for the presence of **23** and **21** was also obtained, showing that nucleophilic replacement had occurred. Furthermore, since it was found that **22** did not react with lithium aluminium hydride under the conditions employed, it was concluded that the reaction sequence shown in equation 12 had taken place to some extent.



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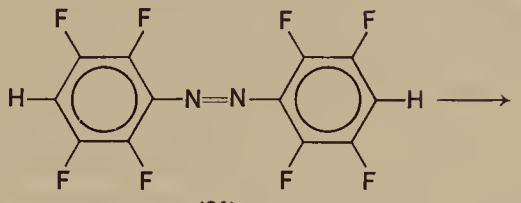


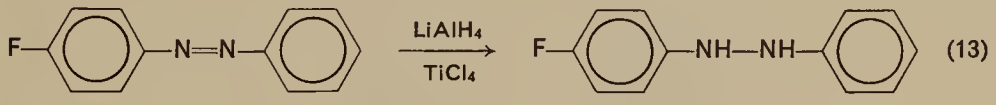
(21)

(23) (12)

Alternative routes to **20**, **21** and **22** in improved yield have been established by Birchall and co-workers[53]. Reduction of **20** with zinc dust and ammonium chloride in aqueous ethanol at room temperature proceeds rapidly to give **22** in 80% yield. In addition, **22** was obtained in even higher yield (85%) by treating **20** with aqueous sodium dithionate in refluxing methanol.

b. Unsymmetrical azobenzenes. Several reagents have been tried out on monosubstituted azobenzenes to effect reduction to the hydrazo stage, and in one of the studies involved interesting conclusions regarding substituent effects were reached.

Lithium aluminium hydride activated by metal halides or oxides reduces 4-fluoro-(**24**) and 3-trifluoromethylazobenzene to the hydrazobenzenes in yields of better than 90%[28], (equation 13). Azobenzene-2-carboxylic acid



(24) (13)

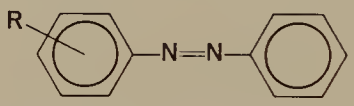
when subjected to the action of tetralin and boron trifluoride in anisole at 90°C gives the benzidine; whereas when using excess boron trifluoride the product is unsubstituted hydrazobenzene, both reduction and decarboxylation having taken place without subsequent rearrangement[49].

Khalifa[45] has investigated the effect of the substituent on the reduction of some monosubstituted azobenzenes with alcoholic ammonium sulphide and also zinc dust and acetic acid. He found that the course of reaction could be correlated with the electronic effect of the substituent and its influence on the electron density of the azo group. When using zinc and acetic acid with an azobenzene having an electron-attracting group (—CO_2H or —CO_2Me) in the 4 position, which lowers the electron density

of the azo group, reduction to the hydrazo derivative occurred. Furthermore, with alcoholic ammonium sulphide the work was extended to include substrates having nitro and sulphonate groups, and in general similar results were observed. On the other hand, with compounds possessing electron-releasing substituents reduction to the anilines took place with both reagents.

Kira and colleagues[54] have reported that monosubstituted azobenzenes are smoothly converted to the corresponding hydrazo derivatives, without any side-reactions, when the gases evolving from a boiling ethanolic hydrazine hydrate–flowers of sulphur mixture are passed into ethanolic solutions of the substrates. The yields obtained were in general higher than those given by reduction with ammonium sulphide or by other methods. Some of the yields achieved are listed in Table 1. In addition, *p*-methoxyazo-

Table 1. Reductions of monosubstituted azobenzenes with di-imide[54]



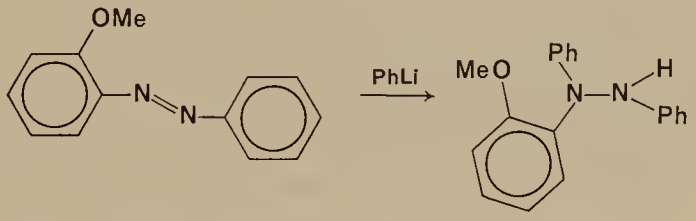
R	Substituted hydrazobenzene (%)
p-Methyl-	89
o-Methyl-	72
m-Methyl-	80
p-Chloro-	90
p-Bromo-	75
p-CO_2Na	100

benzene, which was not reduced by gaseous ammonium sulphide, underwent reaction to *p*-methoxyhydrazobenzene (83%) when the above method was applied. These reductions are presumably brought about by di-imide (HN=NH), which is thought to be present in the gases evolved from the reagent used[54].

Hinshelwood and co-workers[27, 55] have carried out detailed studies on the kinetics and mechanism of the reduction of a number of monosubstituted azobenzenes, e.g. *trans*-4-amino- and 4-hydroxyazobenzene, using titanous

chloride in dilute hydrochloric acid, which gave rise to amines via the hydrazobenzenes. The reactions were found to be first-order with respect to azo compound and to titanous chloride, but the rates of reaction varied in a complex way with the concentration of hydrochloric acid. The effect of substituents was also complex, apparently due to opposing influences on the process of electron transfer from the reducing agent, and the equilibrium between protonated and unprotonated azo species. In addition, it was shown that when an excess of azo compound was used, the latter competed successfully with the hydrazo intermediate (which could accumulate to a considerable extent) for the available reducing agent.

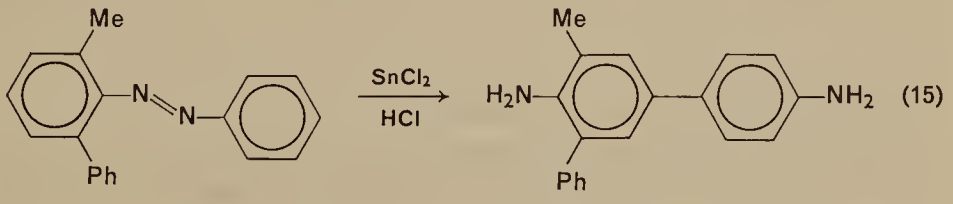
In another investigation[56] it has been found that whereas phenyllithium behaves simply as a reducing agent with 2-methylazobenzene, with 2-methoxyazobenzene (**25**) it causes conversion to 1,2-diphenyl-1-*o*-methoxyphenylhydrazine (**26**), addition across the azo group having taken place (equation 14).



(14)

(25) (26)

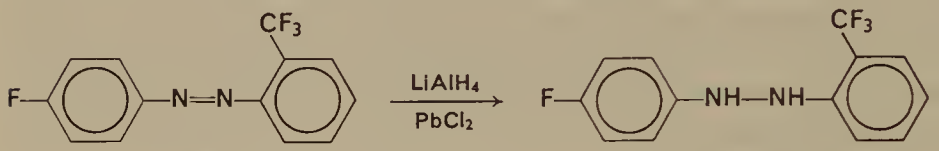
There have been relatively few recent reports of successful conversions of unsymmetrically disubstituted azobenzenes to hydrazo compounds. Reductions of this type of substrate, having both substituents on the same ring, with stannous chloride and hydrochloric acid have been reported, but rearrangement of the hydrazo products to the benzidines resulted. Thus, treatment of 3,5-dibromoazobenzene with this reagent gives 2,6-dibromobenzidine in 50% yield[48]. Similar treatment of 2-methyl-6-phenylazobenzene (**27**) causes reduction to the hydrazobenzene, which undergoes immediate rearrangement to 3-methyl-5-phenylbenzidine (**28**) (equation 15). Hydrogenation of **27** over 5% palladium on charcoal at room temperature, followed by addition of hydrochloric acid also led to **28**.



(15)

(27) (28)

In contrast, reaction of 2,4-dichloroazobenzene with di-imide affords an 85% yield of 2,4-dichlorohydrazobenzene[54]. On the other hand, 2,4-diamino-(and also 2,4,4′-triamino) azobenzene are reduced to the anilines via the intermediate hydrazo derivatives when subjected to the action of titanous chloride[55]. An example of a successful reduction of an unsymmetrically disubstituted azobenzene having one substituent on each benzene ring, is the conversion of 4-fluoro-3′-trifluoromethylazobenzene (**29**) to the hydrazo compound in excellent yield by the action of lithium aluminium hydride catalysed by metal hydrides or oxides[28] (equation 16).

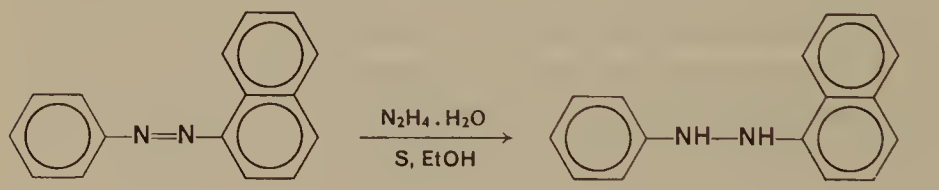


(29) (16)

There are even fewer recent reports of reductions of unsymmetrically polysubstituted azobenzenes. Attempts to reduce 2,2′,5,5′-tetrachloro-4-nitroazobenzene with sodium sulphide in methanol at 50°C, and also by prolonged treatment with ammonium sulphide in the same solvent at 25°C failed, the substrate being recovered almost quantitatively in each case[50].

3. Other azoarenes

Electrochemical reduction of 1,1′- and 2,2′-azonaphthalene in DMF solution leads to the corresponding hydrazonaphthalenes[37]. 1-Phenylazonaphthalene (**30**) has been converted to the hydrazo compound (equation 17) in good yield (80%)[54]. As far as the author is aware, reductions of other azoarenes to hydrazo systems have not been reported.



(30) (17)

B. Aromatic Azoxy to Azo Compounds

In general, aromatic azo compounds may be quite conveniently synthesized from the azoxy precursors by means of reduction with readily available reagents.

I. Azoxybenzene

A number of reducing agents have been applied to the parent compound, azoxybenzene (**31**) to achieve conversion to azobenzene (**12**) (equation 18).

(31) (12) (18)

Badger and colleagues[59] have used lithium aluminium hydride to reduce the *cis* and *trans* isomers of azoxybenzene, and found that *trans*-azoxybenzene gave *trans*-azobenzene; and that *cis*-azoxybenzene also afforded the *trans*-azo product. The reduction of *cis*-azoxybenzene to *trans*-azobenzene was carried out at room temperature, and a mechanism was suggested for this transformation that involved an intermediate having an —N—N— linkage with free rotation around the single bond. However, it was recently pointed out[9] that this reaction gave only a low yield of *trans*-azobenzene, the rest of the product fraction not being accounted for, and it was suggested that the 'product loss' here may be caused by complexing with inorganic products formed during decomposition of the lithium aluminium hydride reaction mixture with water. This loss of product has been noted with other reductions carried out with this reagent, and would appear to constitute a disadvantage regarding its use. However, the situation is not clear since lithium aluminium hydride has been reported on a number of occasions to give very good yields of azobenzenes. For instance, the use of an excess of lithium aluminium hydride has been claimed to produce azobenzene in 99% yield[60].

Sodium and ethylene glycol (sodium 2-hydroxyethoxide) reduces azoxybenzene in petroleum ether to azobenzene as reported by Tadros and co-workers[61]. The importance of reaction conditions for reduction of azoxybenzene is shown by the fact that although the deoxygenating agent triethyl phosphite does not react with this substrate in benzene under nitrogen and at 0°C even after 18 h[62], it was found that successful conversion to azobenzene can be achieved using this reagent at 160°C for 9 h[63]. Triphenyl phosphine, which is easily oxidized, is also capable of deoxygenating azoxybenzene. Carbon monoxide has been tried as a reducing agent for azoxybenzene. For example, heating azoxybenzene in benzene with carbon monoxide (pressure ca. 2900 psi) at 204–216°C in the presence of iron pentacarbonyl produces azobenzene in good yield (78·5%)[64].

Some work has also been done on the hydrogenation of azoxybenzene using cobalt coordination compounds as catalysts. It has been reported[65]

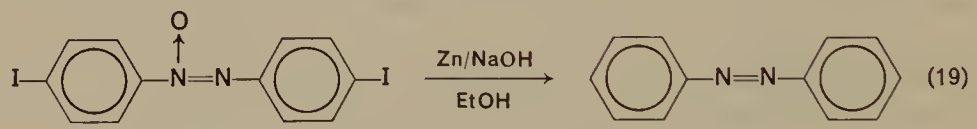
that hydrogenation of azoxybenzene in aqueous solution at room temperature with a hydrogen pressure of 1 atm and in the presence of pentacyanocobaltate(II) gives azobenzene; and more recently[34] rapid hydrogenation to give azobenzene in 76% yield was achieved by using bis(dimethylglyoximato)cobalt(II) as catalyst.

Electrochemical reduction of azoxybenzene occurs readily in acidic solution giving rise to azobenzene and hydrazobenzene, as well as benzidine and aniline[66], as might be expected in protic medium.

2. Substituted azoxybenzenes

Considerable attention has been paid recently to studies on the reduction of substituted azoxybenzenes to azo derivatives, most of which have been concerned with symmetrically substituted compounds. Various reducing agents have been tried in this regard and often with good results.

a. Symmetrical azoxybenzenes. Over the past few years some symmetrically disubstituted azoxybenzenes have been reduced to the azo derivatives. Thus, 2,2′-dimethoxyazoxybenzene was reduced to the azo compound with lithium aluminium hydride at 0°C[67]; and both 2,2′-dimethyl- and 4,4′-dichloroazoxybenzene were converted to the corresponding azo derivatives by heating for a short time with sodium 2-hydroxyethoxide and ethylene glycol in a suitable inert solvent[61]. The latter substrate was similarly reduced with zinc dust and alkali[68]. However, zinc and sodium hydroxide is not suitable for reduction of azoxybenzenes having iodine atoms in the *ortho* or *para* positions since deiodination as well as reduction takes place. For instance, attempts to convert 2,2′- and 4,4′-di-iodoazoxybenzene (**32**) to the di-iodoazo derivatives with zinc dust and 40% aqueous sodium hydroxide in ethanol have resulted in the formation of unsubstituted azobenzene[43,44] (equation 19). It will be recalled that



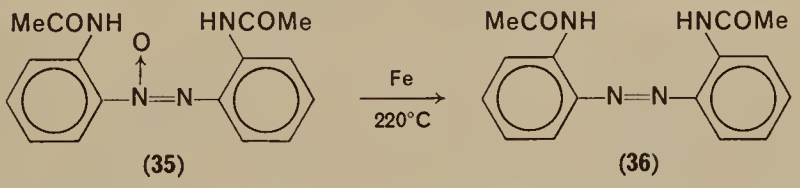
(32) (12) (19)

deiodination also occurs with the corresponding di-iodoazobenzenes (see Section III, A, 2a) when using this method. Analogous deiodinations have also been observed with other azoxy and azobenzenes when using the above reagent[69].

It has been claimed by Gore and Wheeler[67] that lithium aluminium hydride reduces 2,2′-di-iodoazoxybenzene (**33**) to the corresponding azo

compound (**34**), but the properties of their product did not match with those of the 2,2′-di-iodoazobenzene (**34**) prepared previously by Leffler and Wilson[70] via perbenzoic acid oxidation of *o*-iodobenzoyl azide. However, **34** was later synthesized in high yield by Newbold[44] by treatment of **33** with concentrated sulphuric acid, and also by Wheeler and Gonzalez[71] by means of oxidation of *o*-iodoaniline with active manganese dioxide; and the products from the latter syntheses were found to have similar properties to those reported by Leffler and Wilson for **34**. Furthermore, attempts to repeat the results claimed for the lithium aluminium hydride reduction of **33** have failed[72]. It would indeed be surprising if such a powerful reducing agent as lithium aluminium hydride did not remove the labile iodine atoms in **33** since it is known that nucleophilic replacement occurs when this reagent is applied to decafluoroazobenzene[52].

2,2′-Diacetylaminoazoxybenzene (**35**) when heated with purified iron powder under somewhat drastic conditions, i.e. at 220°C for 2 h, gives the diacetylaminoazo compound (**36**) in 65% yield (equation 20); the diaminoazo derivative being obtained by subsequent hydrolysis[73]. Very recently[74] 4,4′-diacetylazobenzene (**37**) was synthesized by catalytic hydrogenation of the azoxy precursor (**38**) using 10% palladium on charcoal (equation 21).



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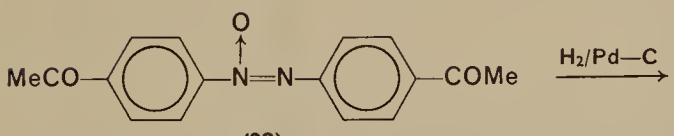

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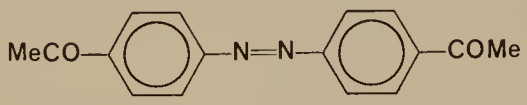
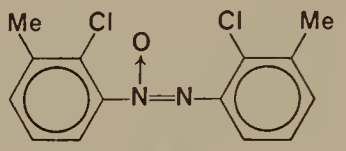


(37) (21)

Recent research on the reduction of symmetrically tetrasubstituted azoxybenzenes to azo compounds has mainly concerned the use of three reducing agents, namely zinc dust and ethanolic sodium hydroxide, zinc dust and glacial acetic acid, and lithium aluminium hydride. The reductions reported were usually performed for the determination of the structure of azoxy compounds, but in a number of cases reduction of the azoxybenzene provided a useful alternate route to the azobenzene when it was discovered

that attempted reductions of the appropriate substituted nitrobenzene did not lead to the desired azo compound.

Tetrachloroazoxybenzenes, for example the 2,2′,3,3′-, 2,2′,4,4′-, and 2,2′,5,5′-isomers, have been converted quite successfully to the corresponding azobenzenes by refluxing with zinc dust and 40% aqueous sodium hydroxide in a minimum of ethanol[68,75]. This reagent has been used to reduce similarly dihalodialkylazoxybenzenes, such as 2,2′-dichloro-3,3′-dimethylazoxybenzene (**39**) and 3,3′-dichloro-2,2′-dimethylazoxybenzene, good yields of the azo derivatives being obtained[68,76]. The same reagent has also been applied to series of dihalodialkoxy and dialkoxydialkylazoxybenzenes under reflux conditions and excellent conversions to the pure azo derivatives resulted[77]. Some of the results obtained in this study are summarized in Table 2.



(39)

TABLE 2. Reductions of tetrasubstituted azoxybenzenes with ethanolic sodium hydroxide and zinc dust[a,77]

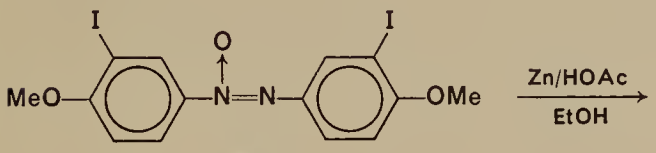
Azoxybenzene Substituents	Amount (g)	NaOH (g)	EtOH (ml)	Azo derivative (%)
5,5′-Dichloro-2,2′-dimethoxy-	1·0	1·3	50	90
2,2′-Dichloro-5,5′-dimethoxy-	1·0	1·4	50	95
4,4′-Dichloro-2,2′-dimethoxy-	1·1	1·3	50	97
3,3′-Dichloro-4,4′-dimethoxy-	1·1	1·3	50	96
4,4′-Dichloro-3,3′-dimethoxy-	1·1	1·2	50	97
3,3′-Dibromo-4,4′-dimethoxy-	1·0	2·2	20	90
4,4′-Dibromo-3,3′-dimethoxy-	1·0	2·1	22	92
3,3′-Dimethoxy-4,4′-dimethyl-	0·2	1·8	15	86
3,3′-Dimethoxy-2,2′-dimethyl-	0·2	2·0	15	89

[a] All reductions were carried out under reflux using 5 ml of water and 2·0 g of zinc dust, with the reaction time ranging from 20 to 60 min.

However, attempts to reduce 4,4′-di-iodo-3,3′-dimethoxy- and 3,3′-di-iodo-4,4′-dimethoxyazoxybenzene (**40**) with ethanolic sodium hydroxide and zinc gave rise to mixtures of orange products which could not be separated by chromatography. On the other hand, reduction of 2,2′-

dimethoxy-6,6′-dimethylazoxybenzene with this reagent produced only 2-methoxy-6-methylaniline and tars. This method was also found to be unsuitable for the reduction of a number of tetra-alkoxyazoxybenzenes, tars and recovered starting materials being obtained[77].

Treatment of some tetrasubstituted azoxybenzenes in ethanol with zinc dust and a few drops of glacial acetic acid, followed by boiling of the filtered reaction mixture (to oxidize the hydrazo derivative), is a useful method for conversion to the corresponding azo derivatives, even for substrates having sensitive substituents such as iodine atoms. For example, when **40** was so treated smooth reaction affording 3,3′-di-iodo-4,4′-dimethoxyazobenzene (**41**) in 85% yield took place[77], (equation 22). It is



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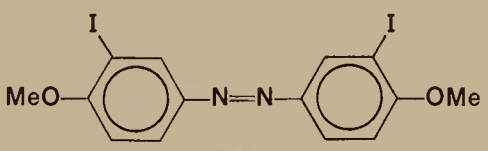


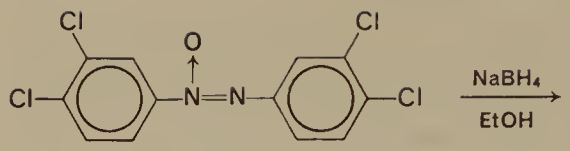
(41) (22)

worth noting here that **41** could not be obtained by direct reduction of 2-iodo-4-nitroanisole, hence the above reaction became an important route to **41**[77]. Recently[78] 3,3′-di-iodo-4,4′-dimethylazobenzene was similarly prepared in 90% yield.

Lithium aluminium hydride has also been used to advantage for the reduction of tetrasubstituted azoxybenzenes to azo derivatives. An example is the conversion of 2,2′,5,5′-tetraethoxyazoxybenzene to the tetraethoxyazo compound in 82% yield by reaction with this hydride in ether at room temperature[77].

Recently the first case of reduction of an azoxybenzene with sodium borohydride was reported[78]. Thus, 3,3′,4,4′-tetrachloroazoxybenzene (**42**) was reduced to the azo derivative (**43**) in over 80% yield by refluxing in ethanol with this hydride for 24 h, (equation 23). This method, which would appear to offer interesting possibilities since ethanol may be used as solvent, could be usefully exploited for similar conversions of azoxy compounds.

Some reductions of polysubstituted azoxybenzenes have been reported. Singh and colleagues[50] have studied the reduction of 3,3′-dichloro-2,2′-dimethyl-4,4′-dinitroazoxybenzene (**44**), which is an interesting compound



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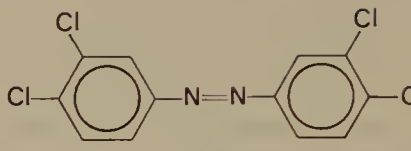
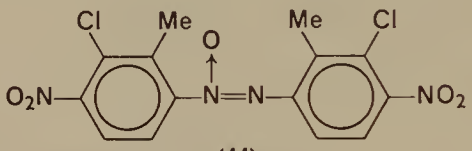


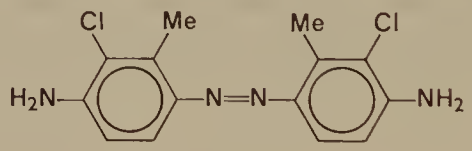
(43) (23)

in that it contains two types of reducible groups. They discovered that reaction of **44** with excess hydrazine hydrate in ethanol at 100°C effected reduction of both nitro groups but not the azoxy linkage, the product being 3,3′-dichloro-2,2′-dimethyl-4,4′-diaminoazoxybenzene (88%). This result



(44)

was attributed to the presence of two electron-releasing chlorine substituents adjacent to each of the electron-attracting nitro groups. These workers did however manage to bring about reduction of the azoxy group in **44** by a change of reducing agent to sodium sulphide, the nitro substituents again undergoing attack. Use of the latter reagent in excess in aqueous methanol at 60°C brought about conversion to 3,3′-dichloro-2,2′-dimethyl-4,4′-diaminoazobenzene (**45**) in yields of the order of 90%.

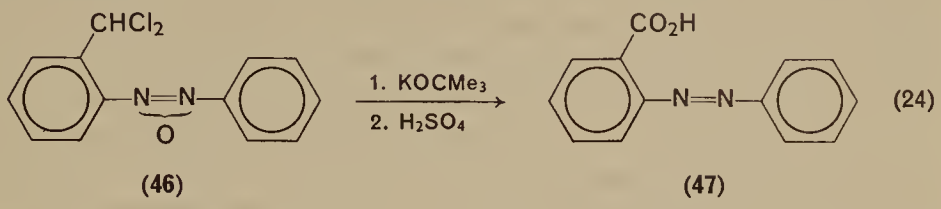


(45)

Attempts have been made to convert decachloroazoxybenzene to the azo compound by means of catalytic hydrogenation over 5% palladium on charcoal, but these were not successful, the product always being the corresponding amine, pentachloroaniline, after exhaustive treatment[79].

b. Unsymmetrical azoxybenzenes. Little research has apparently been performed in recent years on reactions of unsymmetrically substituted azoxybenzenes leading to azobenzenes. In one case[80], potassium t-butoxide

was used to reduce 2-dichloromethylazoxybenzene (**46**) with subsequent hydrolysis and oxidation of the reaction mixture giving rise to a 94% yield of azobenzene-2-carboxylic acid (**47**) (equation 24).

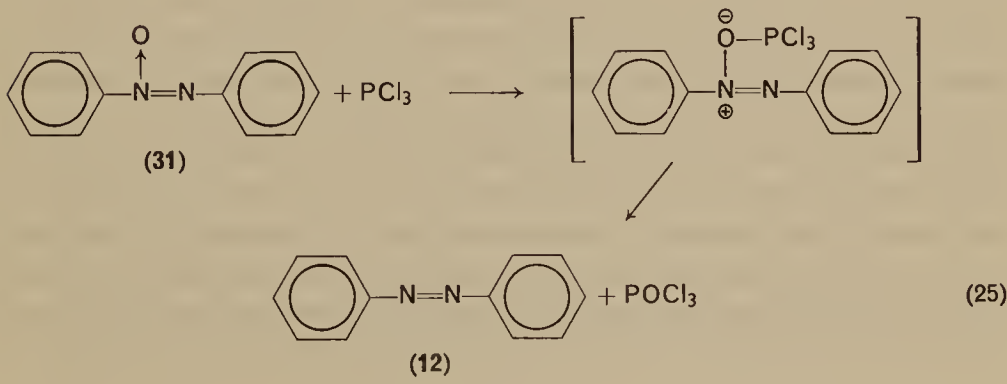


(46) (47) (24)

3. Azoxy to azobenzenes via Wallach rearrangement and allied studies

Since the discovery of the rearrangement of azoxybenzene to *p*-hydroxyazobenzene on treatment with concentrated sulphuric acid by Wallach and Belli in 1880, it has been known that azobenzene is also formed in this reaction as well as several other products. Later studies on the Wallach rearrangement by Lachman, and Gore and Hughes confirmed that azobenzene was a by-product, and showed that its yield varied with the reaction conditions. However, the routes proposed by these workers for the formation of azobenzene differed. Buncel[81] has recently reviewed these studies and subsequent work by other groups of researchers relating to the mechanism of formation of azo by-products from the Wallach rearrangement of azoxybenzenes, and concluded that 'A deeper understanding of the processes in azoarene formation is clearly desirable'.

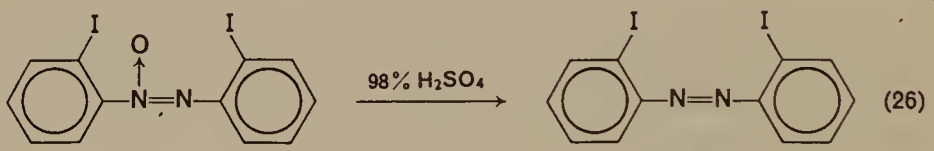
In an interesting recent study, Vozza[82] has shown that azoxybenzene (**31**) is almost quantitatively reduced to azobenzene (**12**) by the action of phosphorous trichloride; and proposed a mechanism for this transformation (equation 25). Deoxygenation to azobenzene was also found to take place on refluxing **31** with liquid acidic halides (capable of oxidation), e.g. S_2Cl_2,



(31) (12) (25)

$SOCl_2$ or on treatment with acetyl bromide or iodide (at less than 20°C); and on refluxing **31** with certain solid acidic halides (e.g. $ZnBr_2$, ZnI_2, SbF_3) in solution in acetyl chloride. These reactions in some cases gave quite high yields of azobenzene, for instance 72% with S_2Cl_2 and 92% with ZnI_2. In addition, this investigation revealed that an unusual deoxygenation and chlorination took place when azoxybenzene was refluxed in carbon disulphide with aluminium chloride, 4-chloroazobenzene being formed in 83% yield. Moreover, it was observed that $AlBr_3$ and AlI_3 even reduced azoxybenzene at 0°C, and that reaction of azoxybenzene with $AlCl_3$ and SO_2Cl_2 gave rise to a mixture of 4,4′-dichloroazobenzene (70%) and 4-chloroazobenzene (13%). Furthermore, reaction of azoxybenzene with $AlCl_3$ in benzene afforded 4-phenylazobenzene in 84% yield. In view of the simple procedure used and the yields obtained, these types of reactions would appear to be worthwhile extending to substituted azoxybenzenes and other azoxyarenes.

Azobenzenes have been frequently reported to be obtained from Wallach rearrangement studies on substituted azoxybenzenes using concentrated sulphuric acid, and in some cases constitute the major product[75,83]. For instance, heating of 2,2′-di-iodoazoxybenzene (**33**) with 98% sulphuric acid affords 2,2′-di-iodoazobenzene (**34**) in 82% yield[44] (equation 26).

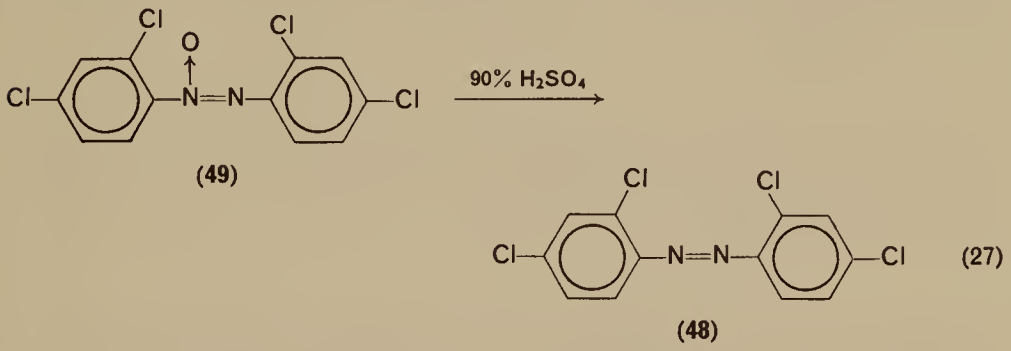


(33) (34) (26)

An extensive and systematic study of the products of reaction of a series of symmetrically disubstituted azoxybenzenes, including dihalo- and dimethylazoxybenzenes, with sulphuric acid, has been carried out by Akhtar[75], in which it was observed that the azobenzenes were usually formed, along with the hydroxyazobenzenes and other products, and in several cases in quite good yield. The effects of the substituents and the reaction conditions on the production of azobenzenes were also assessed. For 2,2′- and 4,4′-dihalogenated azoxybenzenes, the yield of the azo derivative increased with the diminishing inductive effect of the halogen atom. With azoxybenzenes having both 4 and 4′-positions occupied, there was always considerable conversion to the corresponding azobenzene, presumably because rearrangement is difficult in these instances. In the case of 3,3′-dihalogenated azoxybenzenes, the increasing size of the halo substituents favoured the formation of the azobenzene as expected because

this would impede rearrangement due to steric hindrance around the 2 and 2′ and 4 and 4′-positions. Increasing the concentration of sulphuric acid (73·5 to 90%) decreased the yields of dimethylazobenzenes. This study also showed that azobenzenes may arise from two sources, the azoxybenzenes and the hydroxyazobenzenes, with the former predominating under the conditions employed. Data concerning the reaction conditions used and some of the yields of disubstituted azobenzenes from this investigation have been summarized elsewhere[81].

Some tetrasubstituted azobenzenes have also been obtained via studies on the Wallach rearrangement. For example, 2,2′,4,4′-tetrachloroazobenzene (**48**), in 69% yield, is one of the products resulting from reaction of the azoxy precursor (**49**) with 90% sulphuric acid[75] (equation 27). Some similar



(49) (48) (27)

conversions to tetrahalo-, dichlorodimethyl- and tetramethylazobenzenes are listed in Table 3. A more recent investigation[84] has indicated that symmetrical dihalodimethoxy- and tetra-alkoxyazobenzenes, including those having substituents in the 2 and 2′-positions, are formed by the action of 60–90% sulphuric acid on the azoxybenzenes at 100°C, quite good yields (50–80%) often being encountered. The conversions involving the tetra-alkoxy compounds are of some interest since, as mentioned earlier (Section III, B, 2, a), this type of substance has proved to be difficult to reduce to the azo stage with certain reagents.

Instances of deoxygenation of hexasubstituted azoxybenzenes under Wallach rearrangement conditions are also known. Thus, it was reported that 2,2′,4,4′,6,6′-hexabromoazobenzene was obtained from the Wallach rearrangement of the hexabromoazoxy compound in sulphuric acid medium[67]. Very recently, Buncel and Cox[85,86] have reported the formation of 2,2′,4,4′,6,6′-hexamethylazobenzene from the azoxybenzene by treatment with 84% sulphuric acid, but unlike the earlier reported reduction of hexabromoazoxybenzene in strong acid[67], here reduction was shown to be a negligible process under kinetic conditions.

TABLE 3. Azobenzenes from Wallach rearrangements of tetrasubstituted azoxybenzenes[a,75]

Azoxybenzene Substituents	Amount (g)	H_2SO_4 (%)	H_2SO_4 (ml)	Tetrasubstituted azobenzene,[b] (%)
2,2′,3,3′-Tetrachloro-	1·0	90	20	19
3,3′,4,4′-Tetrachloro-	2·0	90	40	75
3,3′,5,5′-Tetrachloro-	1·0	98	30	10
2,2′-Dichloro-3,3′-dimethyl-	0·9	83	18	21
2,2′-Dichloro-5,5′-dimethyl-	1·0	83	20	16
3,3′-Dichloro-2,2′-dimethyl-	1·0	90	20	11
4,4′-Dichloro-3,3′-dimethyl-	1·0	90	20	53
5,5′-Dichloro-2,2′-dimethyl-	1·0	90	20	52
2,2′,3,3′-Tetramethyl-	1·0	74	20	13
2,2′,5,5′-Tetramethyl-	0·8	69	15	24

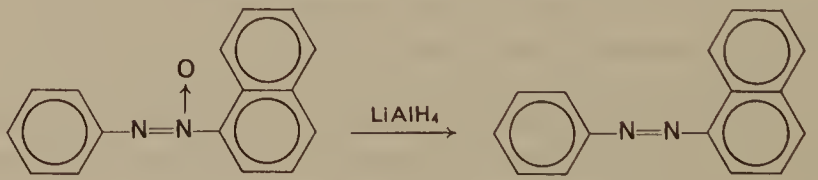
[a] All reactions carried out at 100°C for 30 min, except for 3,3′,5,5′-tetrachloroazoxybenzene where the reaction time was 90 min.

[b] Hydroxyazobenzenes, tars and polymers, sulphonic acids, and traces of amine were also formed in most cases.

The deoxygenations occurring via the Wallach rearrangement and associated reactions are a useful alternate source of azobenzenes, particularly when azoxy compounds having the 4 and 4′-positions occupied are used, since in the latter cases the azoarene is often the main product.

4. Other azoxyarenes

Reductions of other types of azoxyarenes appear to have received little attention lately. Badger and Lewis[87] reduced both 2-phenyl-NNO-(**50**) and 2-phenyl-ONN-azoxynaphthalene with lithium aluminium hydride and obtained in each case 2-phenylazonaphthalene (**51**), as part of studies carried out to confirm the structures of the two isomeric azoxy compounds (equation 28).



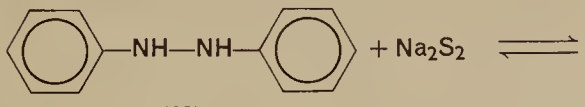
(50) (51) (28)

C. Azoxybenzenes to Hydrazobenzenes

There are a number of reducing agents that are capable of converting azoxybenzenes to the hydrazo derivatives, via the azobenzenes which are not usually isolated. However, these reactions are greatly dependent upon conditions and in some instances an excess of reagent is required.

1. Azoxybenzene

It has been reported[88] that azoxybenzene is reduced to hydrazobenzene (**13**) by sodium disulphide, and that kinetic studies with this reagent under various conditions have shown that reduction to the azo stage is quite rapid, the rate of reaction depending upon the solubility of azoxybenzene in the medium. It was also found that **13**, the final product of reaction, entered into equilibrium with azobenzene (**12**) (equation 29).



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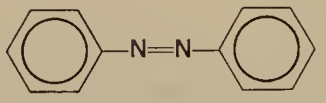


(12) (29)

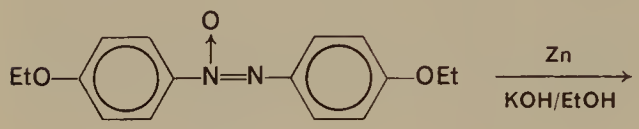
Azoxybenzene may also be reduced electrochemically to hydrazobenzene, but reoxidation to azobenzene can occur, and as previously mentioned (Section III, A, 1) if the reduction is perfomed in acidic medium rearrangement to benzidine may also take place[89].

Reduction of azoxybenzene (**31**) to hydrazobenzene has been achieved by treatment with an excess of the powerful reagent lithium aluminium hydride in tetrahydrofuran at 0°C, rapid reaction taking place with uptake of four equivalents of hydride[30]. In contrast, **31** reacts very sluggishly with the milder lithium trimethoxyaluminohydride under the same conditions[29]. However, with the latter reagent at 25°C reduction occurs to the hydrazo stage after 48 h. On the other hand, neither lithium tri-t-butoxyaluminohydride nor aluminium hydride reduce **31** at any significant rate in tetrahydrofuran at 0°C[31].

2. Substituted azoxybenzenes

a. Symmetrical azoxybenzenes. Symmetrically disubstituted azoxybenzenes have been reduced to the corresponding hydrazobenzenes by the action of sodium disulphide in aqueous solution and in aqueous

alcoholic (methanol, ethylene glycol monoethyl ether) medium[90]. Some dialkylated azoxybenzenes have been converted to the hydrazo derivatives using zinc dust and sodium hydroxide. For instance, 2,2′-diethyl-[41,62] and 4,4′-diethylhydrazobenzene[41] were synthesized in this way. A number of dihalogenated hydrazobenzenes were also made using this method[68]. Khalifa and Abou-Ouf[40] have reduced 4,4′-diethoxyazoxybenzene (**52**) to 4,4′-diethoxyhydrazobenzene (**53**) by means of zinc and ethanolic potassium hydroxide (equation 30); and found that the reaction was twice as fast as that of the azo compound when using the same conditions.



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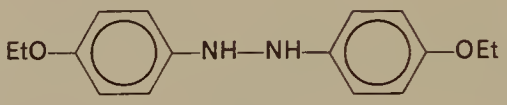
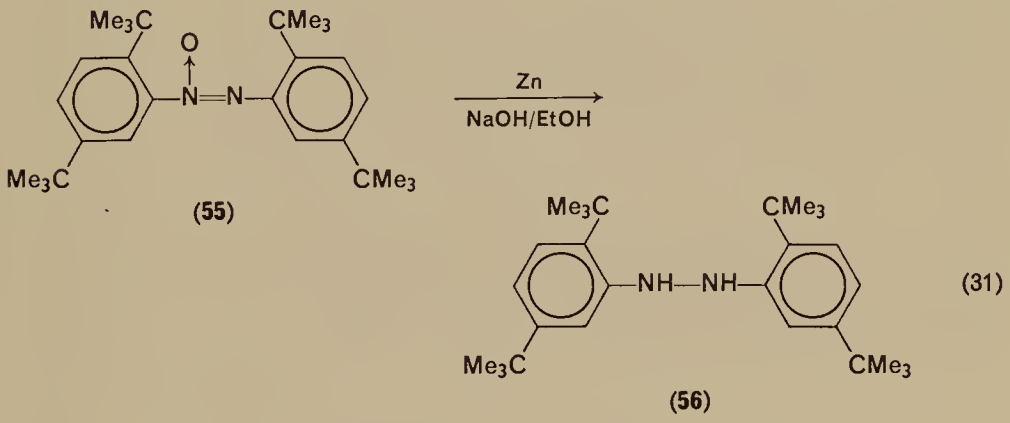


(53) (30)

Electrochemical reduction may be used to convert substituted azoxybenzenes to the hydrazobenzenes by a process involving four electrons. Hazard and Tallec[91] recently carried out a detailed study of the electrochemical behaviour of a series of substituted azoxybenzenes, including some symmetrically disubstituted substrates such as 3,3′-dinitro- and 4,4′-dimethoxyazoxybenzene, on a mercury cathode in essentially neutral medium, by employing polarographic and coulometric techniques. They reached a number of interesting conclusions, and also proposed mechanisms to explain the results obtained. With a controlled potential and aqueous alcoholic medium, azoxybenzenes having substituents other than nitro were always reduced to the corresponding hydrazobenzenes, without further reduction occurring under the conditions employed. Furthermore, most of the hydrazobenzenes prepared were stable and could be electrochemically oxidized to the azo compounds thus providing an indirect route to the latter. However, the presence of electron-donating groups in the *ortho* or *para* positions of the hydrazo products caused them to be unstable, subsequent disproportionation giving rise to the azobenzenes and anilines. On the other hand, the hydrazobenzenes having a nitro group in the *ortho* or *para* position underwent a dehydration reaction. For 2,2′- and 4,4′-dinitroazoxybenzene the azoxy linkage was more readily reduced than the nitro groups, whereas the opposite was the case with 3,3′-dinitroazoxybenzene.

Some direct conversions of tetrasubstituted azoxybenzenes to hydrazo derivatives have been recently reported. For example, 5,5′-dichloro-2,2′-dimethylazoxybenzene (**54**) when treated with zinc dust and acetic acid is reduced to the appropriate hydrazobenzene in good yield. On the other hand, reduction of **54** with zinc dust and sodium hydroxide gives only a low yield of the hydrazo derivative, the latter reportedly undergoing decomposition readily in alkaline medium[50]. In contrast, 2,2′,5,5′-tetra-t-



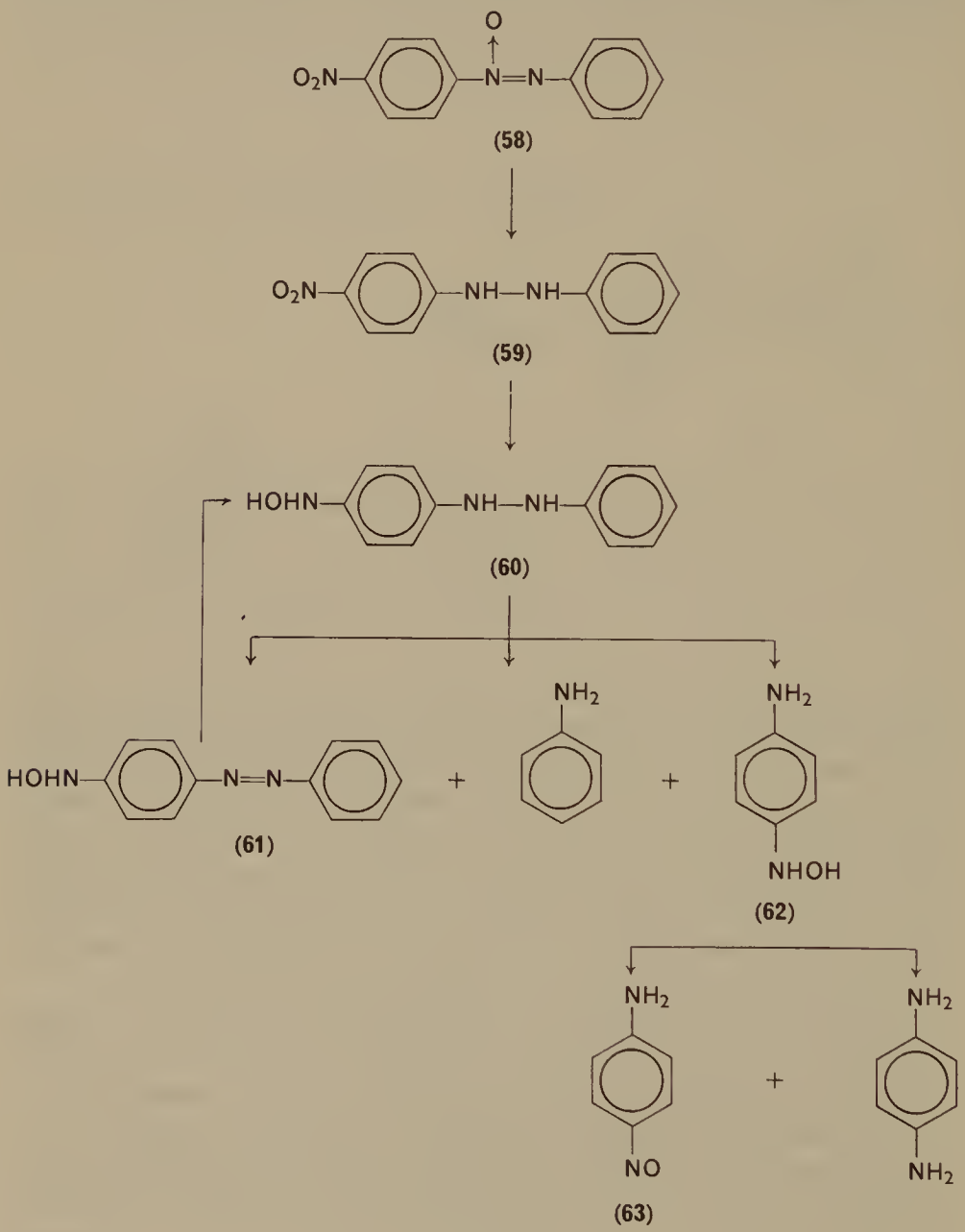
(55) (56) (31)

An example of the conversion of a polyfluorinated azoxybenzene to the hydrazo derivative is the hydrogenation of decafluoroazoxybenzene (**57**) over palladium to give a good yield of decafluorohydrazobenzene (**22**). It was claimed earlier by Wall and co-workers[93] that the above reaction afforded decafluoroazobenzene (**20**), but Burdon and colleagues[52] showed that the product formed was indeed **22**. It should be pointed out here that **22** decomposes quite quickly in solution to a red material and decomposes slowly in the solid state as well[52]. Compound **57** has also been reduced to **22** by means of zinc and ammonium chloride in aqueous ethanol[53].

b. Unsymmetrical azoxybenzenes. As compared to symmetrical analogues relatively little appears to have been reported on the transformation of unsymmetrically substituted azoxybenzenes into hydrazo derivatives.

An interesting investigation on the electrochemical reduction of 4-nitroazoxybenzene (**58**) at controlled potential on a mercury cathode was carried out recently[91]. By the use of polarographic and coulometric techniques, it was found that the azoxy linkage in **58** suffered reduction

before the nitro group. Reduction at very negative potential afforded the aniline and *p*-phenylenediamine as final products, with transitory appearance of substituted hydrazobenzenes, which underwent disproportionation to several products. It was suggested, as shown in Scheme 1, that most probably reduction to 4-nitrohydrazobenzene (**59**) had occurred, followed by reduction of **59** to 4-hydroxylaminohydrazobenzene (**60**), with dispro-



SCHEME 1.

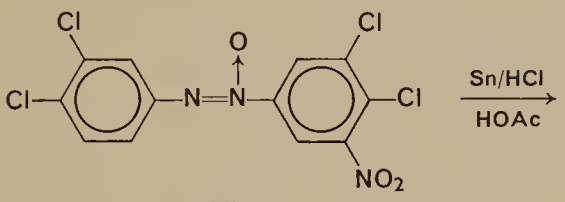
portionation of the latter to 4-hydroxylaminoazobenzene (**61**), aniline, and 4-hydroxylaminoaniline (**62**). Derivative **62** then disproportionates giving rise to 4-nitrosoaniline (**63**) and *p*-phenylenediamine. Compounds **61** and **63** being more easily reducible than **58** regenerate **60** and **62**, respectively. Repetition of disproportionation reactions would lead eventually to total reduction to amines.

The results obtained from reduction with slightly negative potential on the other hand were interpreted in terms of the formation of 4-nitrosoazobenzene (**64**) (oxidant in a first reversible system), and **59** (reductant in a second reversible system), thus rendering possible the following oxidoreduction system:

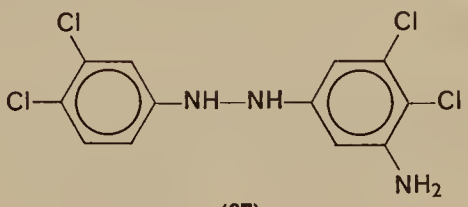
(59) + **(64)** ⟶ 4-nitroazobenzene **(65)** + **(61)**

Reduction of **65** gives **59** and the reaction process restarts, while **61** is reducible to **60**, from which the disproportionation sequence (Scheme 1) leads finally to the aniline and *p*-phenylenediamine. Similar studies were also made on 2-nitroazoxybenzene and analogous mechanisms were proposed to explain the results obtained[91].

It has been reported[58] that with 3,3′,4,4′-tetrachloro-5-nitro-NNO-azoxybenzene (**66**) both reduction of the azoxy linkage and the nitro substituent arises on treatment with tin and hydrochloric acid in glacial acetic acid, to give 3,3′,4,4′-tetrachloro-5-aminohydrazobenzene (**67**) in 30% yield (equation 32).



(66)



(67) (32)

IV. REDUCTIVE CLEAVAGE OF HYDRAZO, AZO AND AZOXY COMPOUNDS

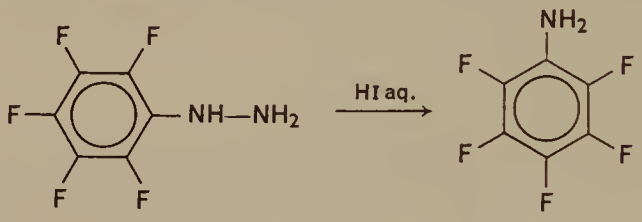
Over the past ten years or so, most of the literature references relating to reductive cleavages of azo and azoxy compounds have concerned aromatic

derivatives. This type of reduction, which leads to the formation of the corresponding amine(s), is usually used in connection with structural determination studies; but some cleavages have come about during attempted syntheses. In addition, some rather unusual cleavage reactions have been observed.

A. Cleavage of Hydrazo Compounds

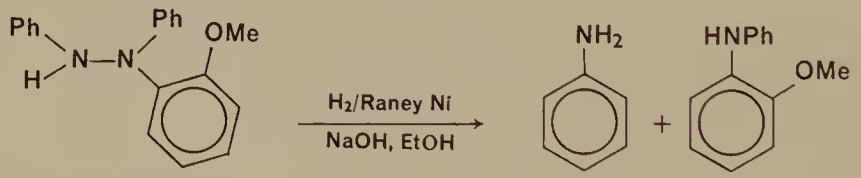
There are few instances of reductive cleavages of the hydrazo group in the recent literature, presumably because these reactions are of little preparative interest, there being many more direct methods available for the synthesis of amines.

Aqueous hydriodic acid, a rather unusual cleavage agent for hydrazines, has been used to convert pentafluorophenylhydrazine (**68**) to pentafluoroaniline[94] (equation 33).



(**68**) (33)

Reductive cleavage of hydrazines, brought about by catalytic hydrogenation, has been used to determine the structures of these substrates[56]. For example, 1,2-diphenyl-1-*o*-anisylhydrazine (**69**) is cleaved to the corresponding anilines by hydrogenation over Raney nickel at room temperature in the presence of ethanol and 20% sodium hydroxide (equation 34). 1,1-Diphenyl-2-*o*-tolylhydrazine undergoes similar cleavage[56].

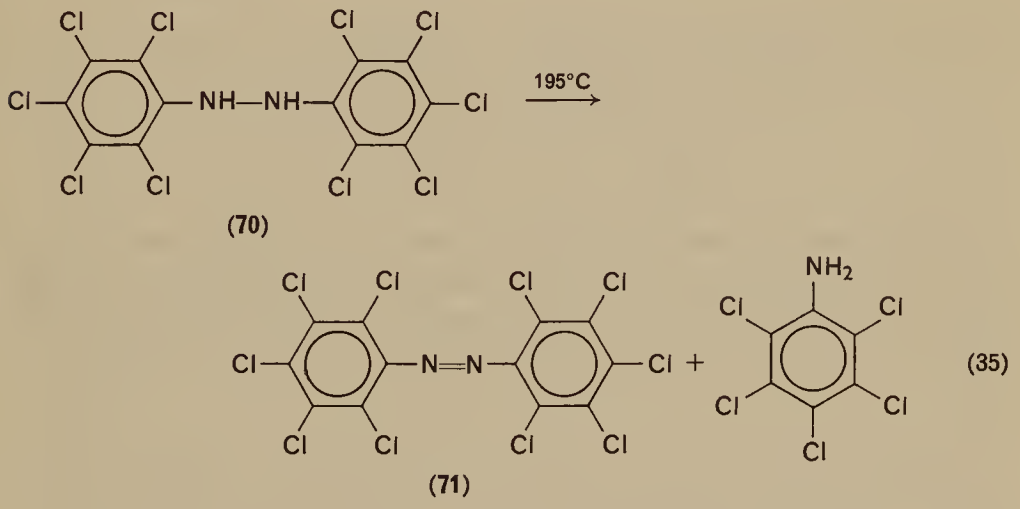


(**69**) (34)

Polarographic reductions of azo- and azoxybenzene have been carried out in acid solution and at pH less than 4 a second reduction corresponding to fission to aniline has been detected, which has been explained on the basis

of reduction of diprotonated hydrazobenzene[95]. However, unfortunately studies on the possible reduction of hydrazobenzene in acidic media are complicated by facile rearrangement to benzidine. On the other hand, hydrazobenzene cannot be reduced polarographically in media having a pH above 4.

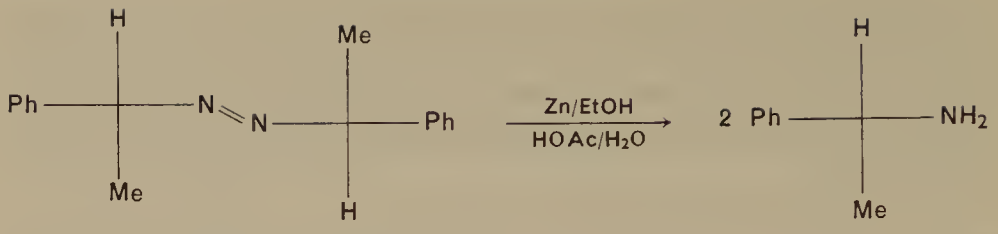
Quite severe reaction conditions together with a suitable reagent are generally required to cleave polyfluoro- and chlorohydrazobenzenes. Thus, decafluorohydrazobenzene (**22**) is not cleaved to the aniline by the action of excess lithium aluminium hydride at 0°C[52]. However, when refluxed with aqueous 55% hydriodic acid for 3 h, **22** is reduced to pentafluoroaniline, which is obtained in 63% yield[53]. Decachlorohydrazobenzene (**70**) undergoes a disproportionation reaction when heated to 195°C (a higher temperature than that needed to effect similar reaction of hydrazobenzene), the products being the azo derivative (**71**) and pentachloroaniline[79] (equation 35). Investigations of the benzidine rearrangement have shown



that in many cases hydrazobenzenes also undergo disproportionation reactions to the corresponding azo compounds and amines under acidic conditions[96].

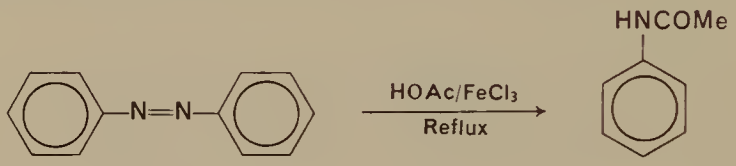
B. Cleavage of Azo Compounds

A recent case of the reductive cleavage of an aliphatic azo compound is the hydrogenolysis of the symmetrical and optically active *SS*-(−)-1,1′-diphenylazoethane (**72**) to *S*-(−)-α-phenylethylamine on treatment with zinc dust in aqueous ethanol and glacial acetic acid at 50°C[97] (equation 36).



(72) (36)

Azobenzene undergoes cleavage to aniline with a number of reagents, such as metal–acid combinations; and on catalytic hydrogenation over platinum. It may also suffer reductive cleavage to other products depending upon the reagent and the reaction conditions employed. For instance, when a solution of azobenzene (**12**) in acetic acid, containing ferric chloride, is boiled under reflux in the dark for an extended period of time, the product is acetanilide[98] (equation 37).



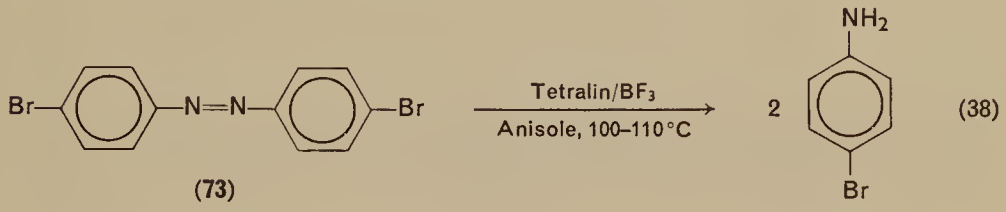
(12) (37)

Monosubstituted azobenzenes having an electron-releasing group (+M) in the 4 position, e.g. —OH or —OEt, which increases the electron density of the azo linkage, are cleaved to the amines by zinc dust and acetic acid[45]. This was also the case with disubstituted compounds, for instance 4,4′-dihydroxyazobenzene was reduced to *p*-aminophenol. In addition, unsymmetrically 4,4′-disubstituted azobenzenes in which one substituent is electron-attracting and the other electron-releasing undergo similar cleavage; 4-hydroxyazobenzene-4′-carboxylic acid giving the corresponding anilines, the electron-releasing effect of the —OH group predominating here. In contrast, 4-hydroxy-, 4-ethoxy-, and 4-acetoxy-4′-nitroazobenzene did not suffer cleavage with zinc and acetic acid, conversion to the 4-aminoazo derivatives taking place instead. This result was attributed to conjugation between the electron-releasing substituent in the 4 position and the electron-attracting nitro group, whose electron density would thereby be increased, making it a more favourable site for attack than the azo group.

Stannous chloride or tin and concentrated hydrochloric acid are reagents still frequently used to effect reductive cleavages for structural studies.

Recent examples of their use for this purpose are the reduction of 2,2′-diiodoazobenzene (**34**) to *o*-iodoaniline[44]; and the conversions of 2,2′-dichloro-3,3′-dimethyl- and 5,5′-dichloro-2,2′-dimethylazobenzene[76], and 4,4′-difluoro-3,3′-dimethylazobenzene[78] to the appropriate haloaminotoluenes.

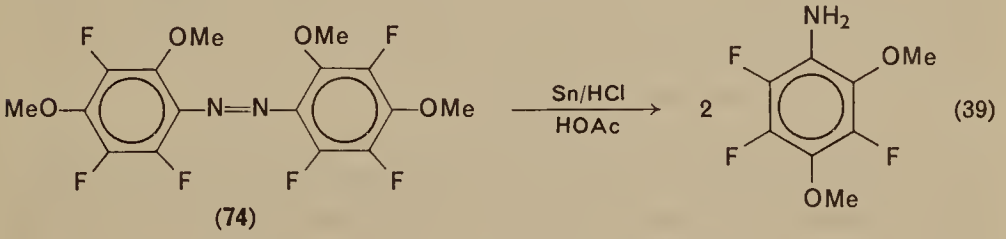
Tetralin in the presence of boron trifluoride has been reported to cause predominant reductive cleavage with certain disubstituted azobenzenes. After being exposed to this reagent in anisole at 100–110°C for 3 h, 4,4′-dimethyl- and 4,4′-dibromoazobenzene (**73**) afforded *p*-toluidine and *p*-bromoaniline (equation 38), respectively, each in 25% yield[49].



(73) (38)

Treatment of the highly sterically hindered 2,2′,4,4′,6,6′-hexaphenylazobenzene (**19**) with aluminium amalgam in aqueous ether causes cleavage of the azo group to yield 2,4,6-triphenylaniline[51].

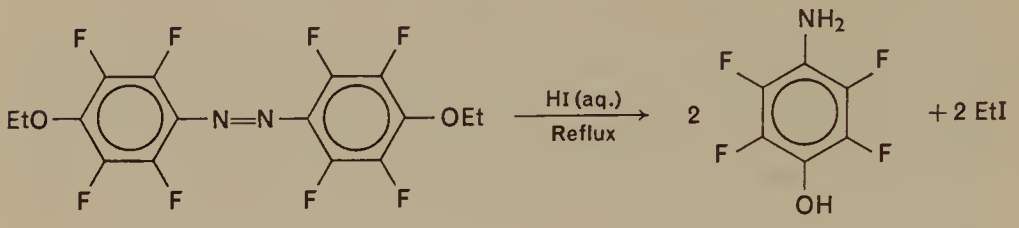
Some recent work has been done on the reductive cleavage of polyhalogenated azobenzenes. Burdon and co-workers[52] reduced decafluoroazobenzene (**20**) and similar compounds to the corresponding amines in glacial acetic acid by refluxing with tin and 11N-hydrochloric acid. In this way, hexafluoro-2,2′,4,4′-tetramethoxyazobenzene (**74**) was cleaved to 2,3,5-trifluoro-4,6-dimethoxyaniline (equation 39). Birchall and colleagues[53]



(74) (39)

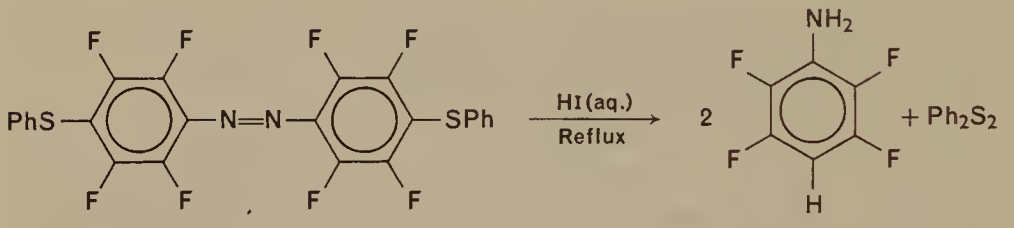
have applied aqueous hydriodic acid under reflux conditions to cleave **20** to pentafluoroaniline (57%). This interesting reagent, which appears to be more effective than tin and hydrochloric acid for reductive cleavage of fluoroazoarenes, was also used to fission nonafluoro-4-hydroxyazobenzene to 4-aminotetrafluorophenol and pentafluoroaniline; and to cleave similar derivatives to the appropriate amines, diamines and aminophenols. When

aqueous hydriodic acid was used on dialkoxyazobenzenes cleavage to the aminophenol and alkyl iodide took place as expected. For instance, octafluoro-4,4′-diethoxyazobenzene (**75**) gave almost quantitative yields of 4-aminotetrafluorophenol (**76**) and ethyl iodide (equation 40). However,



(**75**) (**76**) (40)

when octafluoro-4,4′-bisphenylthioazobenzene (**77**) was refluxed with this reagent an easy and unexpected cleavage to 4*H*-tetrafluoroaniline (**78**) and diphenyl disulphide occurred (equation 41). A mechanism involving

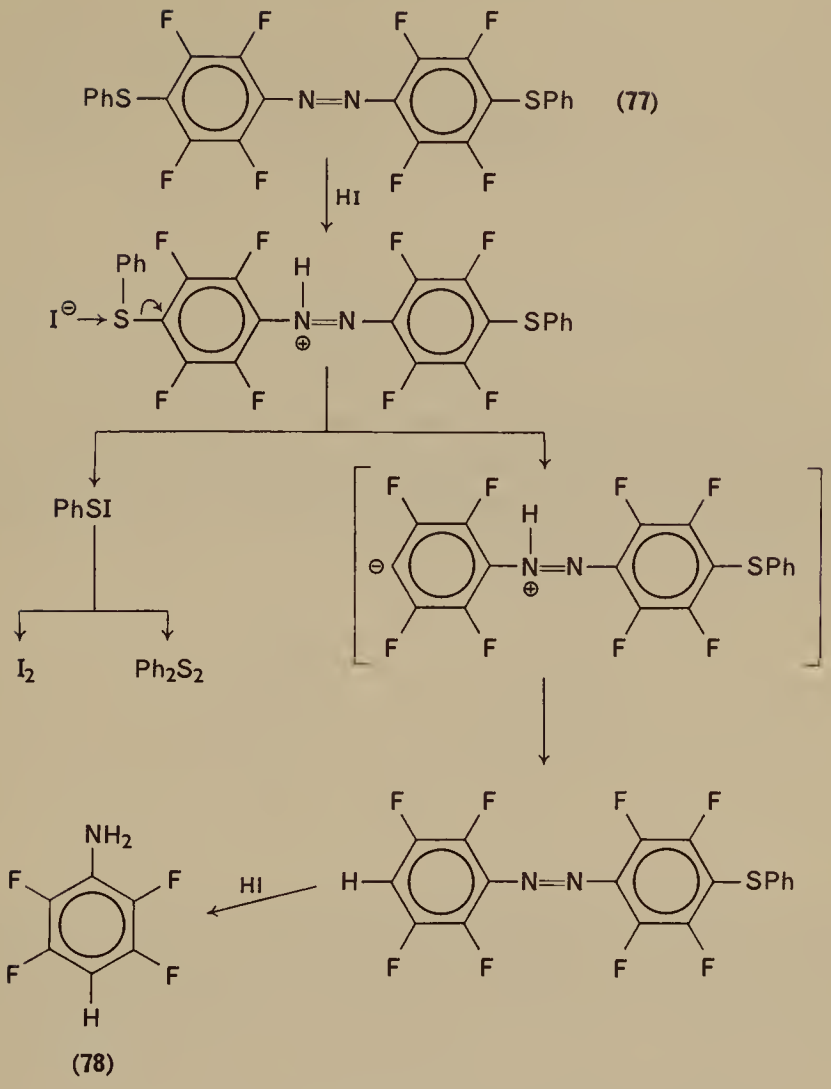


(**77**) (**78**) (41)

nucleophilic attack of iodide on sulphur was proposed (Scheme 2), the facile cleavage of the C—S bond in **77** being explained in terms of stabilization of the departing species by the inductive effects of the positively charged nitrogen atom and the fluorine atoms. It was arbitrarily assumed that fission took place before reduction.

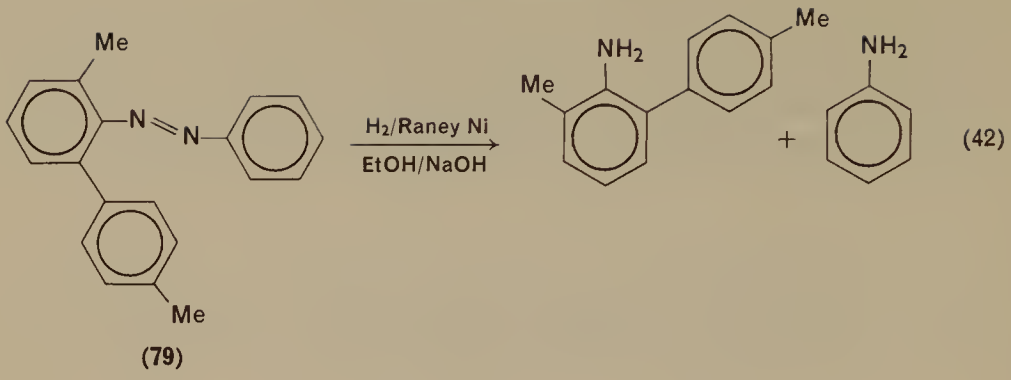
McBee and co-workers[79] found that exhaustive catalytic hydrogenation of decachloroazobenzene (**71**) over 5% palladium on charcoal led to reductive cleavage to pentachloroaniline. It will be recalled (Section III, A, 2, a) that similar hydrogenation of highly fluorinated azobenzenes produced pure hydrazo derivatives. However, when the hydrogenation of **71** was stopped before completion decachlorohydrazobenzene (**70**) was obtained, but the aniline was always present.

Reductive cleavages giving rise to mixtures of anilines have been reported in connection with studies carried out to establish the structures of various unsymmetrically substituted azobenzenes. For instance, Bozzini and



SCHEME 2.

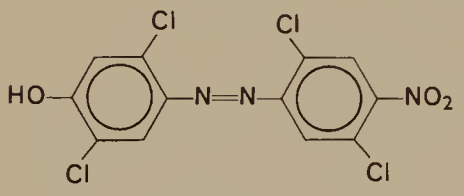
Stener[56] have cleaved 2-methyl-6-*p*-tolylazobenzene (**79**) to the anilines by hydrogenation in ethanol at room temperature in the presence of Raney nickel and sodium hydroxide (equation 42). Similarly cleaved was 2-methyl-6-phenylazobenzene. Hydrogenation over 5% palladium on charcoal has also been employed to reduce 2-methoxy-2′,6′-di-*p*-tolylazobenzene to the corresponding anilines[57]. Unsymmetrically substituted hydroxyazobenzenes, obtained as products of Wallach rearrangements, have been identified by means of reductive cleavage. For example, 3-methyl-3′-nitro-, 5,5′-dichloro-2,2′-dimethyl-4-hydroxy-, and 2,2′,5,5′-tetrachloro-4-



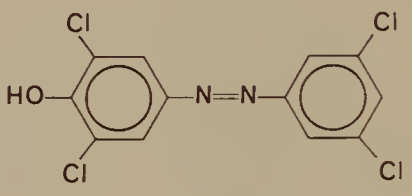
(42)

(79)

hydroxy-4′-nitroazobenzene (**80**) were cleaved with excess tin and concentrated hydrochloric acid[58]. Cleavage of 2,2′-dichloro-4-hydroxy- and 3,3′,5,5′-tetrachloro-4-hydroxyazobenzene (**81**) to the corresponding chloroaminophenols and chloroanilines has been carried out using excess stannous chloride in hydrochloric acid[75].



(80)

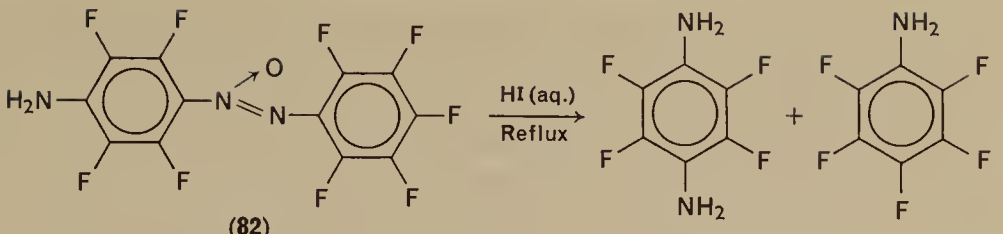


(81)

Electrochemical reduction of 4-amino- and 4-hydroxyazobenzene gives mainly cleavage (via a four-electron process) to the aniline and diamine or aminophenol; however the precise mechanisms involved still need clarification[91,99].

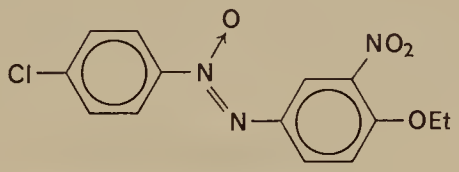
C. Cleavage of Azoxybenzenes

In general, azoxybenzenes have been cleaved to the corresponding amines by using essentially the same reducing agents as those applied to azobenzenes for this purpose. For instance, 2,2′-diethyl- and 2,2′-iodoazoxybenzene (**33**) have been cleaved with excess stannous chloride and hydrochloric acid[41,44]. 2,2′,5,5′-Tetra-t-butyl- (**55**) and 2,2′,5,5′-tetraethoxyazoxybenzene were reduced to the 2,5-disubstituted anilines by boiling under reflux with excess zinc dust and glacial acetic acid[77,92]. Decachloroazoxybenzene was converted to pentachloroaniline by hydrogenation over palladium[79]. Refluxing of 4-aminononafluoroazoxybenzene (**82**) with aqueous 55% hydriodic acid has been reported to yield pentafluoroaniline and tetrafluoro-*p*-phenylenediamine[53] (equation 43).



(82) (43)

Reductive cleavages of unsymmetrically substituted azoxybenzenes bearing a nitro group, which was also reduced, have been reported. Thus, 2,2′,5,5′-tetrachloro-4-nitro-NNO-azoxybenzene was converted to 2,5-dichloro-1,4-diaminobenzene with tin and hydrochloric acid[50]; and 4-ethoxy-3-nitro-4′-chloro-ONN-azoxybenzene (**83**) was transformed into *p*-chloroaniline and 3-amino-4-ethoxyaniline by the action of zinc and hydrochloric acid[100].



(83)

V. CONCLUSIONS

The majority of the recently reported investigations on the reduction of hydrazo, azo and azoxy compounds have been concerned with hydrazo-, azo- and azoxybenzenes; and of these far more studies were carried out on symmetrically substituted compounds than on unsymmetrical derivatives. There has apparently been little interest in reductions of other azo- and azoxyarenes.

Many agents have been employed for reductions of azo and related compounds, but the preferred means seem to be lithium aluminium hydride, zinc dust in alkaline or acidic medium, and hydrogenation; the growth in the use of the latter generally (with involvement of some new catalysts) having been quite remarkable. Reaction conditions are important and have been stressed here because, in the opinion of the author, this aspect has not previously received sufficient attention.

The effect of substituents on the course of reduction has been touched on in some investigations, particularly with regard to azobenzenes, however more systematic studies are clearly required for a fuller understanding of

the factors involved. Mechanistic investigations, with the notable exception of electrochemical reductions, are lacking, hence there is a need for detailed studies in this area as well.

Although symmetrically substituted azobenzenes have usually been synthesized via reduction of the appropriate nitrobenzenes, and more recently by oxidation of anilines, reduction of azoxybenzenes still offers a useful alternative route to these substances. Wallach rearrangement and allied reactions of azoxybenzenes are another source of azo compounds, but again relatively little is known of the nature of the mechanisms involved here. Reductive cleavage reactions, mainly of azo and azoxybenzenes, continue to be used in connection with structural determinations.

VI. ACKNOWLEDGMENTS

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CHAPTER 16

Ionic reactions involving hydrazo, azo and azoxy groups

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I. INTRODUCTION

The reactivity of compounds containing a nitrogen–nitrogen bond depends to a marked extent on the degree of oxidation of the bond. The ionic reactions of compounds with hydrazo, azo and azoxy groups are therefore most conveniently considered separately, with cross comparison as appropriate. On one hand, the chemistry of hydrazine derivatives is dominated by their basic properties and their ability to act as strong nucleophiles, while azoxy compounds show essentially no basic properties (except in concentrated acid solution) and reactions which have been described are limited to rearrangements, oxidation and reduction. The greater reactivity of hydrazo compounds is paralleled by the availability of a much richer chemistry since they have been the subject of intense interest since the last century; study of azoxy compounds is relatively recent a derivative largely of their carcinogenic and physiological properties. Azo compounds take a middle position, showing an intermediate reactivity. An exception to this is the group of azo compounds with strongly electron withdrawing substituents. These may act as electrophilic agents and consequently their reactions are treated separately.

II. HYDRAZINE DERIVATIVES

A. Acid–Base Reactions

1. Basicity

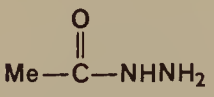
Perhaps the most characteristic reactions of hydrazine and its derivatives are those in which the hydrazo group acts as a nucleophile. Simple hydrazines are relatively strong amine bases, the basicity of hydrazine itself being ca. 1·5 units less than that of ammonia. Substitution of the hydrogens by alkyl groups however has a relatively small effect on the basicity of hydrazine (see Table 1)[2]. In contrast to the effect observed with simple ammonia derivatives, multiple alkyl substituents actually cause a reduction in the basicity of hydrazines and in general the symmetrically substituted hydrazines (hydrazo compounds) are somewhat stronger bases than the corresponding unsymmetrically substituted materials.

TABLE 1. pK_a Data of substituted hydrazines

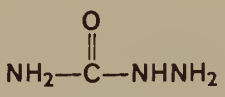
Hydrazine	pK_a
NH_2NH_2	8·07
$MeNHNH_2$	7·87
Me_2NNH_2	7·21
MeNHNHMe	7·52
Me_2NNHMe	6·56
Me_2NNMe_2	6·30
$PhNHNH_2$	5·10

Aryl substitution causes a marked diminution in basicity, although the pK_a difference between hydrazine and phenylhydrazine is not as great as the difference between ammonia and aniline since the terminal amino group of phenylhydrazine is available for protonation. Electron-withdrawing groups in the aryl ring reduce the basicity of the aryl hydrazine moiety. Because of the interpolation of the —NH— group, the effect of substituents ($\rho = -1{\cdot}21$) is markedly less than that observed for the corresponding anilines[3]. In hydrazobenzene the basicity is reduced further since now protonation must occur on a nitrogen adjacent to an aryl ring. Monoacyl derivatives such as acethydrazide (**1**) and semicarbazide (**2**) also retain their basic properties ($pK_a = 3{\cdot}24$ and 3·66 respectively) in contrast to the

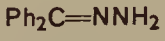
corresponding amine derivatives (amides or ureas), which have pK_a's < 0. Simple hydrazones, which are unsubstituted on the terminal nitrogen have pK_a's in the same region (pK_a of benzophenone hydrazone (3) = 3·85)[4].



(1)

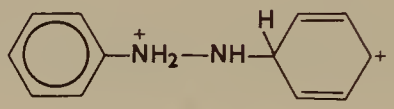


(2)



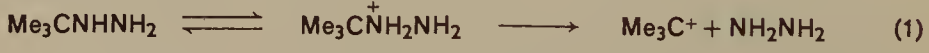
(3)

Diprotonation of hydrazine derivatives has been observed in superacid media. However it appears that in the case of hydrazobenzene, both protonations are not on nitrogen and a *C,N*-diprotonated species **4** has been suggested[5].



(4)

Hydrazines are normally stable in dilute acid solution and can usually be isolated as salts of the stronger acids. In more concentrated acid however extensive rearrangement and cleavage of the hydrazine may result. Thus hydrazobenzene is converted to benzidine in concentrated acid while more highly substituted hydrazine derivatives undergo cleavage to yield amines and oxidation products[6]. In general the ease of cleavage increases as the number and size of the substituents on hydrazine is increased. Thus *N,N*-diphenylhydrazine reacts with concentrated acid only at elevated temperatures whereas *N,N'*-dimethyl-*N,N'*-diphenylhydrazine reacts with 1 M-acid at room temperature. Dealkylation under acidic conditions may also occur in those cases in which the alkyl moiety can form a stable carbonium species; an example is given in equation (1)[7].

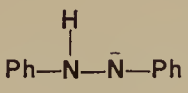


(1)

2. Acidity

Hydrazine itself and its simple derivatives show essentially no acidic properties in aqueous solution. However since a sodium salt of hydrazine can be formed on reaction with sodamide it is inferred that hydrazine is a stronger acid than ammonia[8]. Sodium and the less explosive barium salts of hydrazine have been used in synthesis (see Section II, B, 3) as sources of a highly reactive form of hydrazine. Hydrazobenzene forms mono (**5**) and

dianions (**6**) far more easily on reaction with Grignard reagents or alkali metals (see III, C).



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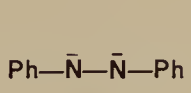
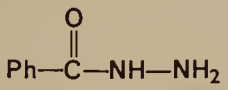


(6)

Hydrazine derivatives with electron withdrawing substituents can be ionized in basic solution. Thus the pK_a of benzhydrazide **7** is ca. 13, while *p*-nitrophenylhydrazones **8** and 2,4-dinitrophenylhydrazones **9** have pK_a's in the region 11–14. Since the anions formed are deeply coloured the latter have been used as acid base indicators in this region[9–12]. Tetraalkylhydrazinium salts **10**[13] and more particularly their acyl derivatives **11**[14] may readily lose a proton to form zwitterionic species.



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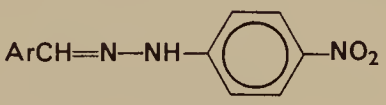

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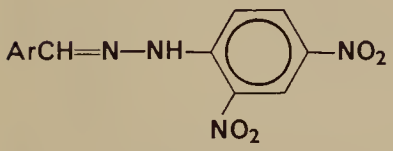

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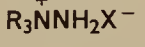

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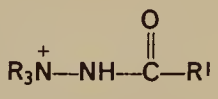
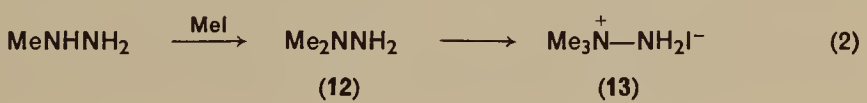


(11)

B. Alkylation

1. Site of alkylation

Although it has been clearly demonstrated that alkylation lowers the basicity of substituted hydrazines (see II, A, I) there is not a corresponding decrease in nucleophilicity. In fact it has been generally observed that the site of alkylation in methylhydrazine with most alkylating agents is the substituted nitrogen atom[15] (equation 2). In the presence of excess methylating agent alkylation may proceed to the trisubstituted derivative **13** implying

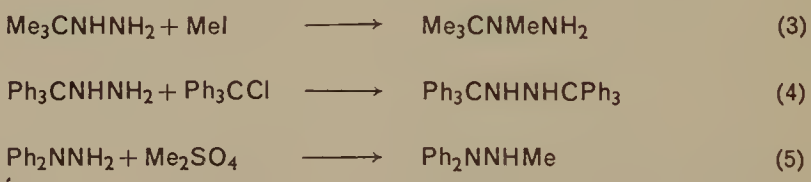


(12) (13) (2)

that the alkylation also occurs at the substituted nitrogen of 1,1-dimethylhydrazine (**12**)[14]. The substituted nitrogen of arylhydrazines may also be alkylated with simple alkylating agents, provided that the aryl substituent is not electron withdrawing. Thus Hinman[2] has shown that phenylhydrazine on treatment with excess methyl iodide gives 1,1-dimethyl-1-phenylhydrazinium iodide **14**.

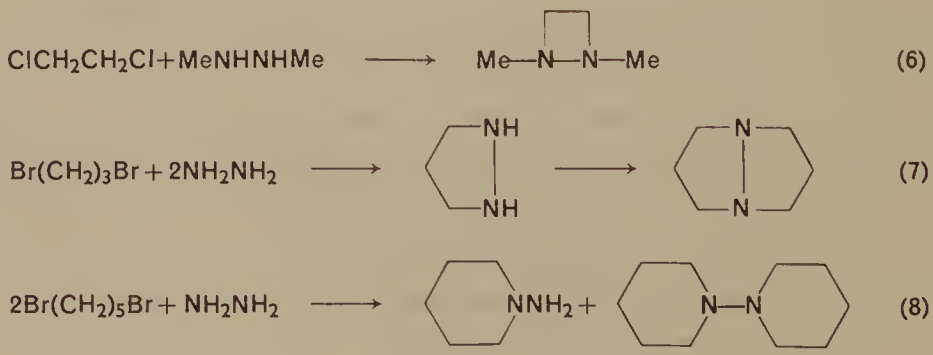
(14)

Even when there is considerable crowding at the hydrazine centre (equation 3) alkylation still gives the unsymmetrical product. However with more sterically hindered alkylating agents (equation 4) or with *N,N*-diarylhydrazines (equation 5) alkylation occurs at the unsubstituted nitrogen[16].



2. Alkylation with subsequent cyclization

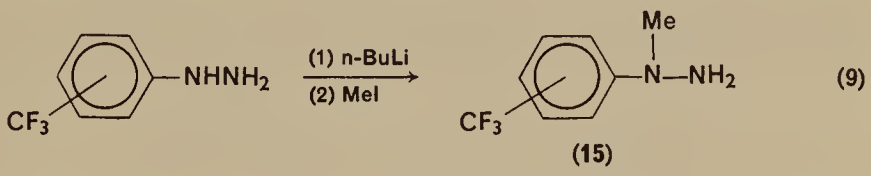
When bifunctional alkylating agents are used, cyclic products are normally obtained; the major product isolated is however dependent on the relationship of the functional groups to one another. Thus 1,2-dialkylhydrazines react with 1,2-dihaloethanes to give 1,2-diazetidines (equation 6). With 2 moles 1,3-dibromopropane hydrazine gives 1,5-diaza-bicyclo-



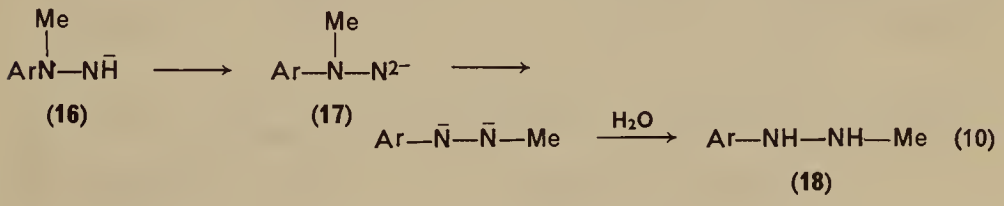
{3,3,0}-octane (equation 7)[17], while 1,5-dihalogenalkanes give 1,1′-dipiperidine, with 1-aminopiperidine as an intermediate (equation 8)[8].

3. Alkylation of hydrazo anions

Arylhydrazines readily form a monoanion on treatment with 1 mole n-butyllithium. The anion can then be alkylated, with for example, methyl iodide to give exclusively the *N*-aryl-*N*-methyl isomer (equation 9)[19].



Presumably the anion is formed exclusively by proton abstraction at the substituted nitrogen; the anion can then be stabilized by the adjacent aromatic ring. Further examples of the use of the conjugate base of hydrazine are also found in Section III, C. When **15** is treated with 1 mole of the alkyllithium, the mono anion **16** is formed; a further mole converts **16** to the dianion **17** which rearranges to the hydrazobenzene derivative **18**

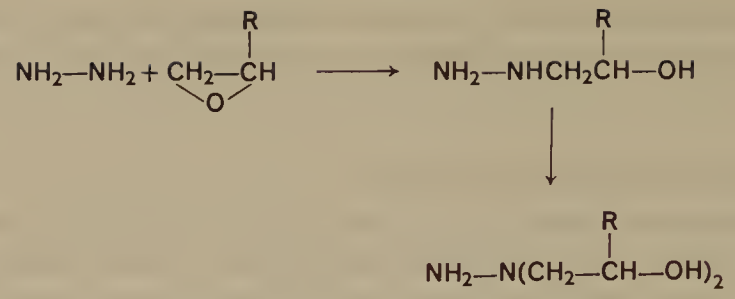


(equation 10). These subsequent reactions do not interfere with the utility of the initial alkylation since (a) the mono anion **16** does not itself rearrange and (b) the rearrangement of **18** is in any event slow[19].

4. Other alkylating agents

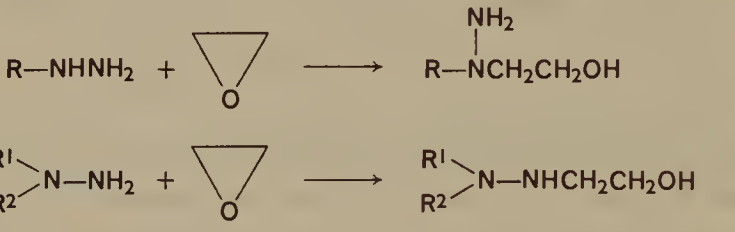
Hydrazines may be alkylated under more severe conditions (typically at 100°C) with epoxides; it is however usually possible to stop the reaction at the monoalkylated stage. Nucleophilic attack by the hydrazine occurs at the least hindered site in the epoxide (equation 11); when disubstitution does occur, the unsymmetrical product is the sole or major material formed.

Monoalkylhydrazines favour alkylation at the substituted nitrogen (equation 12); on the other hand 1,1-disubstituted hydrazines may give



(11)

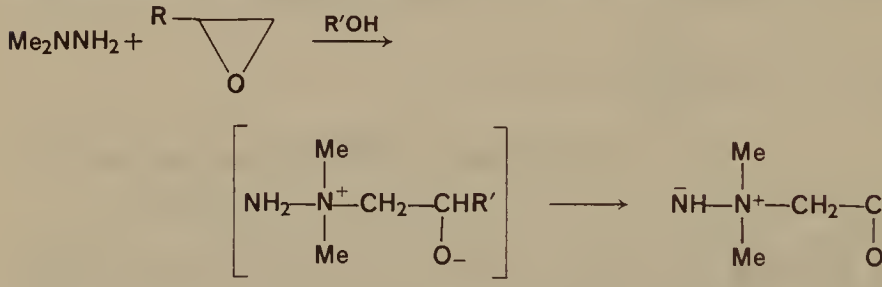
substitution on the $-NH_2$ group (equation 13)[20]. However it has more recently been shown[21, 22] that epoxides may react in polar solvents such as



(12)

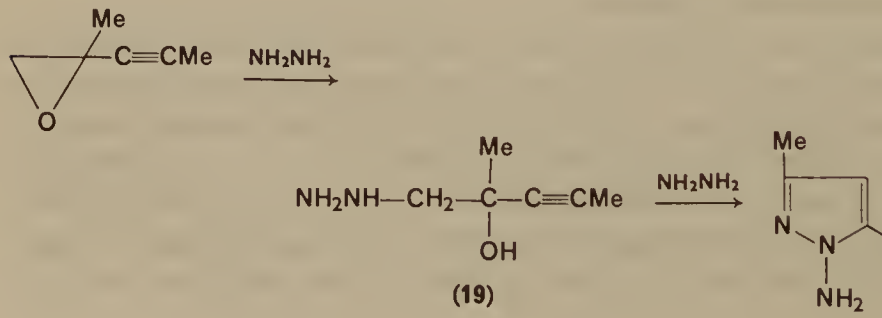
(13)

alcohols to form 1,1-dimethyl-1-(β-hydroxyethyl)-aminimides (equation 14); this in fact provides one of the most important routes to these materials.



(14)

If the substituted hydrazine formed has another functional group then subsequent cyclization may be observed. Equation (15) gives an example[23]; note that in this case the isolable intermediate **19** is formed by initial attack

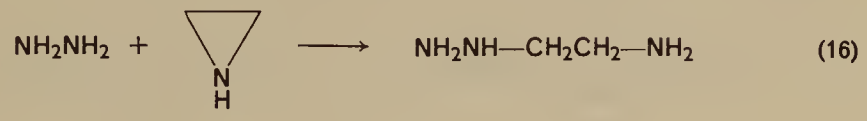


(15)

(19)

at the epoxide ring rather than at the (unactivated) alkyne centre (see also Section II, D).

The reaction with aziridines proceeds similarly, (2-aminoethyl) hydrazines being produced in good yield (equation 16)[23].

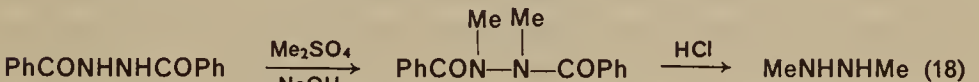


(16)

More reactive alkylating agents such as dimethylsulphate are generally unsatisfactory since they give rise to poly-alkylation. However when highly deactivated hydrazine derivatives are used as substrates (e.g. benzaldazine **20** or 1,2-dibenzoylhydrazine **21**), these reagents may be used to form pure mono or dialkylated materials (see equations (17) and (18) for examples)[25].

(17)

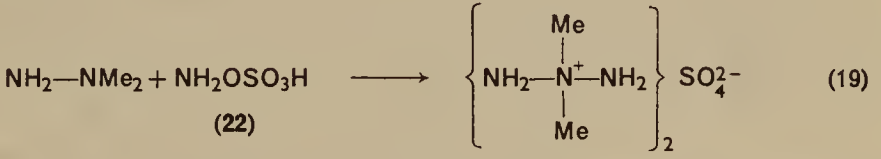
(20)



(18)

(21)

In a related reaction the aminosulphonic acid (**22**) has been found to react at the substituted nitrogen to yield 2,2-dimethyltriazinium sulphate (equation 19)[26].



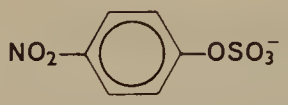
(19)

(22)

5. The α effect

Hydrazine and its derivatives are amongst the materials known to show, towards some substrates, enhanced nucleophilic reactivity known as the 'α-effect'[27]. All of the nucleophiles involved have available an unshared pair of electrons on an electronegative atom which is adjacent to the nucleophilic atom. The anomalous reactivity is usually quantified in terms of deviations from the Brønsted relation or from the oxybase scale[28]. Careful studies by Bruice and co-workers have established that hydrazine does not however

show enhanced reactivity towards sp^3 carbon (for example, in the alkylation reaction with methyl iodide)[29] or in proton abstraction from carbon acids[30]. The α-effect shown by hydrazine is also small with the substrates *p*-nitrophenyl sulphate (**23**)[31] and phosphate (**24**)[32].



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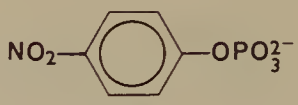
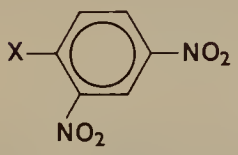


(24)

When the site attacked by hydrazine involves an sp^2-hybridized carbon (e.g. an acyl or vinyl centre), then the hydrazine can show a nucleophilicity which is several orders of magnitude greater than expected on the basis of its pK_a value; this can be used to advantage in a competitive situation to ensure reaction with hydrazine. Glycylglycine is a simple amine which has approximately the same pK_a as hydrazine; a comparison of the rates of reaction of hydrazine and of glycylglycine with a given substrate ($k_{\text{hydrazine}}/k_{(\text{glycylglycine})}$) is thus a measure of the magnitude of the α-effect shown by hydrazine. It has been found[33] that this ratio varies in a systematic way with the Brønsted β value for the reaction concerned, i.e. that the α-effect shown by hydrazine is greatest in those reactions in which there is a large degree of bond formation in the transition state. The substrates studied include halodinitrobenzenes **25**, esters **26** and the carbonium ion Malachite Green **27**[34].



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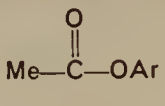

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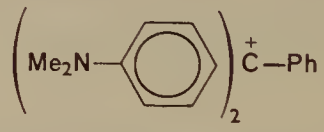


(27)

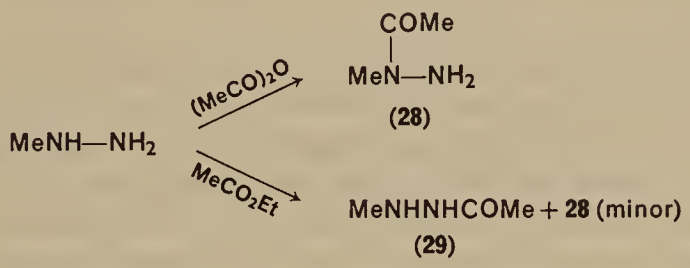
In general it has been found that the α-effect shown by a substituted hydrazine decreases as the basicity of the hydrazine is reduced. Thus the effect shown with $PhNHNH_2$ is smaller than that shown by NH_2NH_2 itself while semicarbazide, $NH_2CONHNH_2$, shows little enhanced reactivity. The origin of the increased nucleophilic reactivity of hydrazine has received much attention but remains controversial. It has been proposed that electron-repulsion between the unshared pairs of electrons may be relieved in transition state[35], while a further explanation based on MO perturbation theory has also been presented[36].

C. Acylation

1. Site of acylation

The position of acylation of an unsymmetrically-substituted hydrazine is even more sensitive than is alkylation to the nature of the reagent used. It is often possible, by controlling the reagent to obtain almost pure products uncontaminated by possible materials resulting from attack at the other site. In general acylation is also more sensitive to steric crowding both in the hydrazine and in the acylating agent.

The acylation of methylhydrazine was examined in detail by Hinman and Fulton[37] and in general their results have been confirmed by Theur and Moore[38]. It was found that the more reactive acetic anhydride led to the formation of largely 1-methyl-1-acetylhydrazine **28**; however with ethyl-acetate (which is a markedly less reactive reagent due to the poorer leaving group, ethoxide ion), **28** was formed as a minor product; most of the acylation occurred on the unsubstituted nitrogen, yielding 1-methyl-2-acetyl hydrazine (**29**) as product.

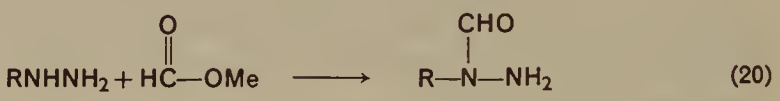


This result is surprising since it cannot be reconciled with the reactivity-selectivity principle[39] which predicts that the less reactive reagent would acylate the more nucleophilic centre (the substituted nitrogen). It was proposed[37] that the transition state for the reaction occurs later on the reaction pathway with ethyl acetate—the transition state is therefore tighter and thus more sensitive to steric crowding.

A more detailed study of the equilibria involved has been reported by Condon[40]. The ratio of **28**:**29** formed using acetic anhydride in pyridine or triethylamine as solvent was ca. 38 while in acetic acid as solvent the ratio was >100. With ethyl acetate as acetylating agent however the ratio was 0·30. Separate experiments indicated that the formation of these ratios was kinetically controlled. Equilibration between the two isomers does however occur more slowly (at ca. $\frac{1}{6}$ the rate of the initial acylation step) to give an equilibrium ratio of **28**:**29** of 0·39 at 27°C and 0·49 at 87°C. Diacetylation of **28** and **29** also occurred slowly in the presence of an excess of the reagent

to yield 1,2-diacetyl-1-methylhydrazine. Both isomers (**28** and **29**) undergo diacetylation at much the same rate; this is $<\frac{1}{50}$ the rate of the initial acetylation of methylhydrazine when ethyl acetate is used as reagent and $\sim\frac{1}{6}$ the initial rate with acetic anhydride.

It has been suggested[40] that the two reagents might react via different reaction pathways with the anhydride reacting via nucleophilic displacement ($B_{AC}2$ type) and the ester via addition-elimination. Since the reactivity–selectivity principle applies only to reactions with the same mechanism, this suggestion would appear to overcome the difficulty. However, the importance of steric effects in the reagent and substrate cannot be overlooked. Thus formylation using methyl formate as the reagent occurs on the substituted nitrogen of 1-alkylhydrazines, contrary to the effect observed with other esters (equation 20)[41]. Only when the alkyl group R is very large



$$RNHNH_2 + HC(=O)OMe \longrightarrow R{-}N(CHO){-}NH_2 \qquad (20)$$

(e.g. R = cyclohexyl) does formylation on the unsubstituted nitrogen predominate.

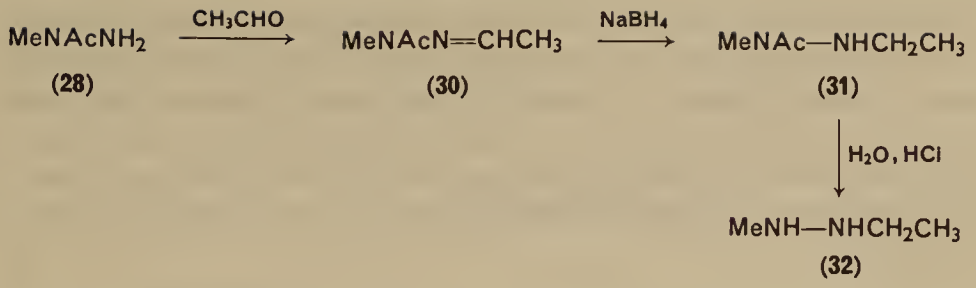
Detailed studies have been carried out on the kinetics of the reaction of hydrazine with ethyl[42] and phenyl[43] acetates in aqueous solution. In general the observed rate of reaction (k_{obs}) increases rapidly as the hydrazine concentration is increased and this has been interpreted in terms of the involvement of more than one molecule of hydrazine in the transition state (at higher hydrazine concentrations). Studies at various pH's show that both hydrazine free base (NH_2NH_2) and the protonated species ($\overset{+}{N}H_3NH_2$) can catalyse the reaction of hydrazine by general base and general acid mechanisms respectively. The observed rate of hydrazinolysis can be expressed as follows:

$$k_{obs} = k_1(NH_2NH_2) + k_2(NH_2NH_2)^2 + k_3(NH_2NH_2)(\overset{+}{N}H_3NH_2)$$

and the sensitivity of each of the individual rate constants k_1, k_2 and k_3 to structural change in the ester has been described[43].

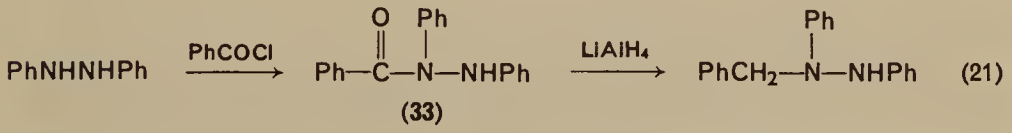
2. Use of protecting groups

Since by careful control of the reaction conditions the 1-acetyl isomer **28** can be obtained readily in 96% purity (76% yield is reported)[44], it has been used as an intermediate for synthesis. An example is shown in the conversion of **28** to **32**; on reaction with acetaldehyde, the hydrazone **30** is ob-



tained. This is subsequently reduced with sodium borohydride; in the final step de-*N*-acetylation is accomplished to give 1-methyl-2-ethylhydrazine (**32**). This provides an efficient route to **32** which cannot be obtained readily by direct alkylation of the hydrazine (see Section II, B).

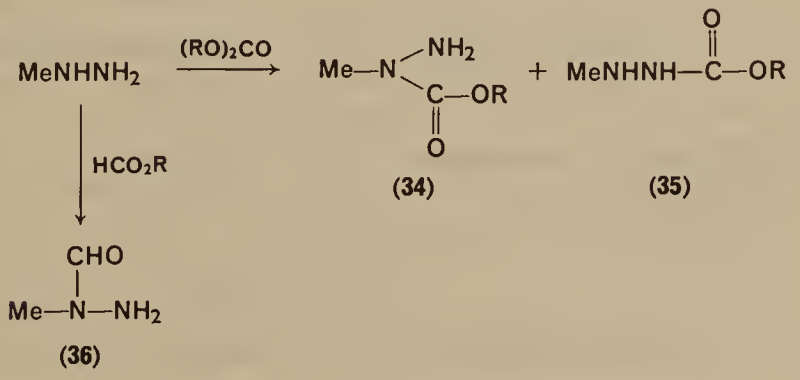
A further example of the formation of a monoalkylated product via prior hydrazide formation is given in equation (21)[45]. Because of the deactivating effect of the acyl group in **33**, monoacylation in contrast to monoalkylation can readily be achieved. Ollis and co-workers[46] have reviewed the various



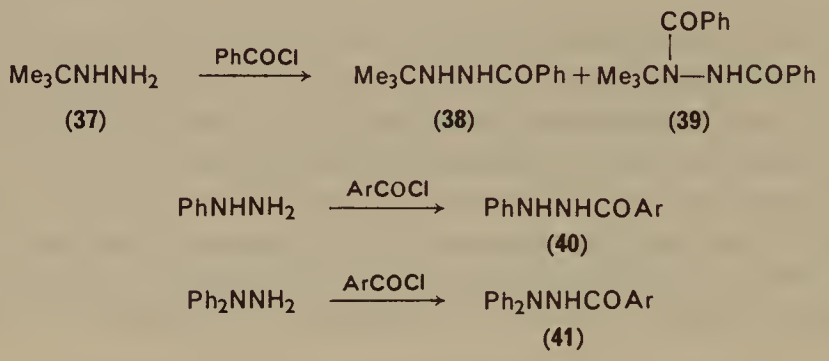
protecting groups which may be used to direct acylation exclusively to one or other of the hydrazine nitrogen atoms.

3. Other acylating agents

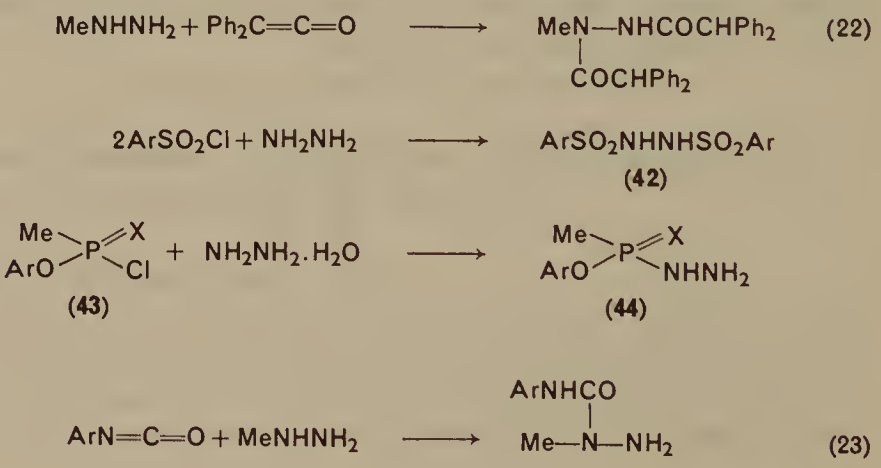
Acylation of methylhydrazine with dimethyl and diethyl carbonate has also been examined[47]. In this case substitution takes place in the 1- and 2-positions to form **34** and **35** (R = Me or Et). However the use of the less hindered reagents methyl or ethyl formate led to the formation of 1-formyl-1-methylhydrazine (**36**) exclusively.



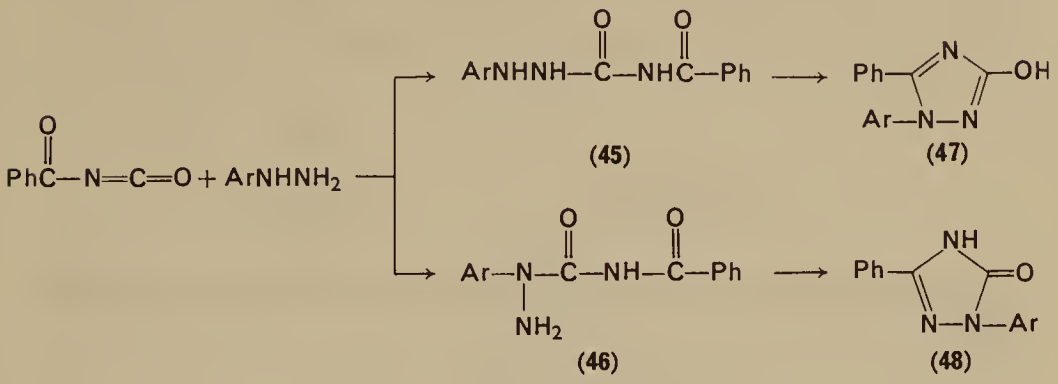
In general when an unsymmetrical hydrazine has a bulky alkyl substituent or an aryl substituent then acylation may occur predominantly at the unsubstituted nitrogen, even with the most reactive reagents. Thus treatment of t-butylhydrazine (**37**) with benzoyl chloride leads to the formation of **38** (together with some diacylated material, **39**). Benzoylation of phenylhydrazine and 1,1-diphenylhydrazine also leads to the 2-substituted isomers (**40** and **41**).



Other acylating reagents which have been used include diphenylketene which gives a disubstituted product with methylhydrazine (equation 22), and sulphonyl chlorides, which give disubstitution products **42** only when the reagents are used in excess[49]. Phosphonic and thiophosphonic acid hydrazides (**44**, X = O or S) are formed on reaction of the corresponding chlorides (**43**) with hydrazine hydrate[50]. Phenyl isocyanate, phenyl isothiocyanate and isocyanic acid also acylate *N*-alkylated hydrazides, substitution occurring, as expected, at the substituted nitrogen (equation 23). Benzoyl isocyanate reacts similarly[51]; however because of the presence of the extra

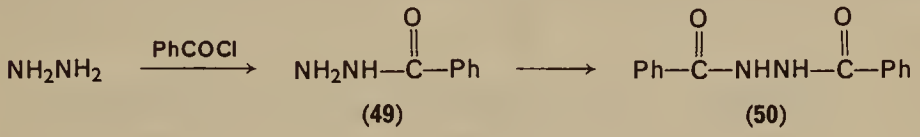


functional group subsequent cyclizations (to form triazoles **47**, **48**) of the initially formed 1- and 2-arylsemicarbazides (**45**, **46**) also occur.

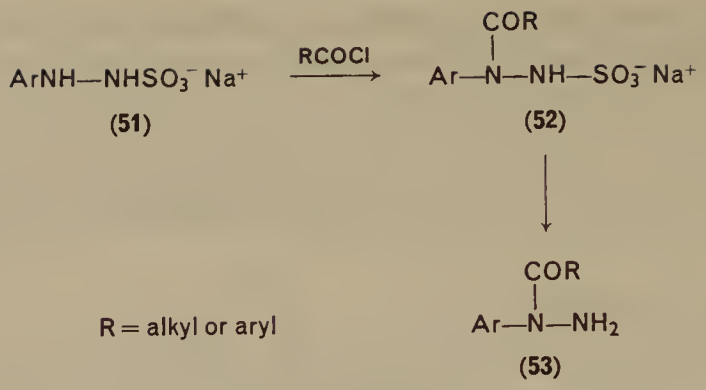


4. Diacylation

Treatment of hydrazides with a second mole of the acylating agent can lead to diacylation which normally occurs on the second nitrogen atom. Thus hydrazine with 2 moles of benzoyl chloride gives the symmetrical 1,2-dibenzoylhydrazine (**50**). This is readily explained in terms of the electron-

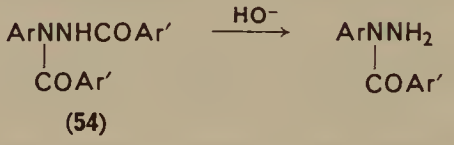


withdrawing effect of the benzoyl group in **49** in reducing the nucleophilicity of the adjacent nitrogen. The second acylation step is normally a good deal slower (>10-fold with the less reactive acylating agents) so that it is possible to stop the reaction at the monoacyl stage. Since the neutral **49** shows nucleophilic reactivity exclusively through the unsubstituted nitrogen, the acyl group may be used to direct the position of attack of incoming reagents. Examples of this have previously been given in Section II, C, 2; equation (24) provides a further interesting example[52]; acylation of the sodium salt leads to the 1-aryl-1-acyl material (**52**) and ultimately the hydrazide (**53**) which is difficult to prepare by direct acylation of the corresponding hydrazine. The hydrazide may also be reduced with lithium aluminium hydride to the corresponding 1-aryl-1-alkylhydrazine. The same hydrazide (**53**) can also be prepared by diacylation of an arylhydrazine; 1-aryl-2-aroylhydrazine (**50**) is initially formed and converted to **54** with excess reagent. The terminal



(24)

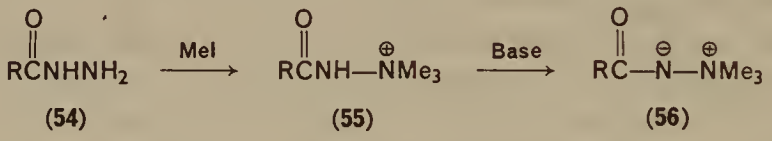
acyl group can then be removed selectively in the presence of base (equation 25)[53].



(25)

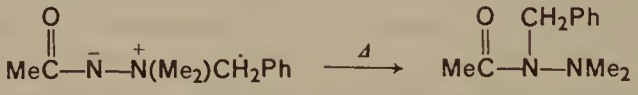
5. Reactions of hydrazides

Hydrazides undergo nucleophilic reactions almost invariably at the unsubstituted nitrogen; the electron withdrawing acyl group deactivating the adjacent nitrogen. Thus alkylation may proceed to the trialkyl stage **55**;



treatment of **55** with base gives the aminimides **56**. The chemistry of the latter group of compounds is interesting and varied[14]; for example rearrangement to isocyanates (equation 26) or alkyl group migration can occur (equation 27) on heating.

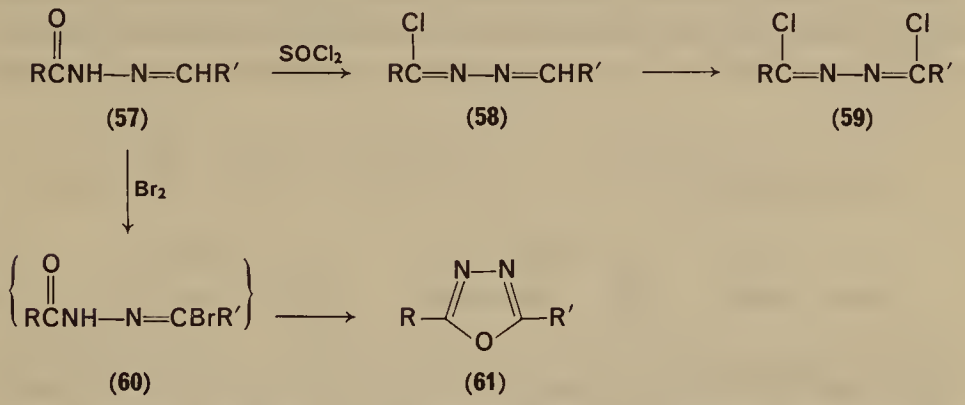
(26)



(27)

The terminal nitrogen in **54** is also sufficiently reactive to form benzylidine and alkylidene derivatives **57**; the latter can be converted to monochloro

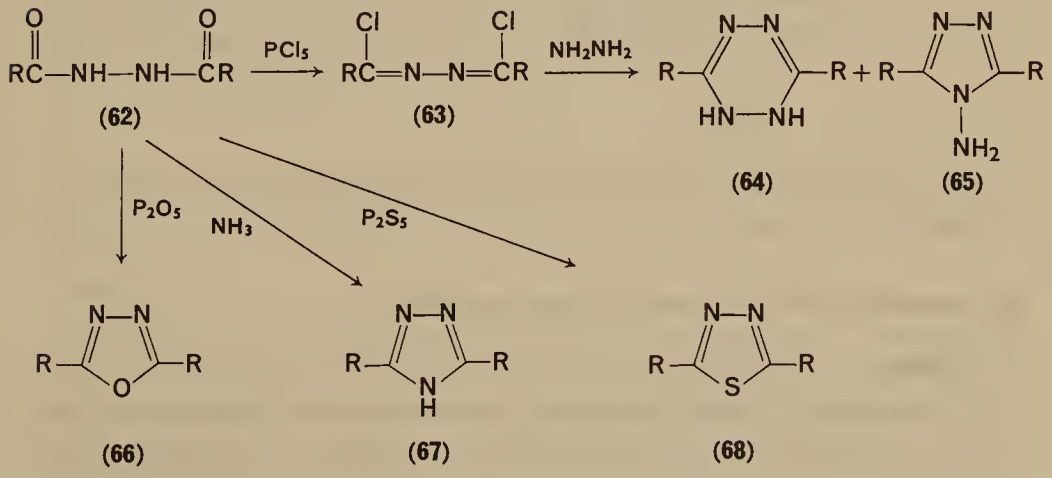
derivatives **58** by treatment with thionyl chloride in benzene[54, 55] and dichloro derivatives **59** (treatment of **58** with chlorine in glacial acetic acid)[55].



(57) (58) (59) (60) (61)

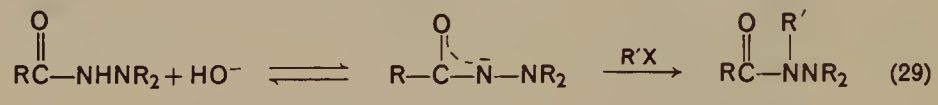
Direct bromination of **57** in acetic acid leads to the oxadiazole **61**, most likely via the intermediacy of the hydrazonyl bromide **60**[55].

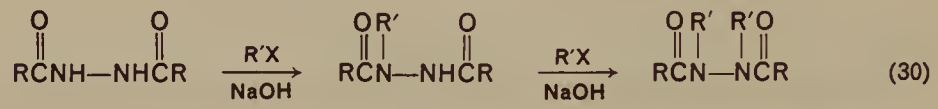
The symmetrically diacylated hydrazines (of type **62**) can be used as starting materials for the synthesis of a wide variety of heterocycles containing (at a minimum) two nitrogen atoms. Thus treatment of **62** (R = aryl) with PCl_5 gives the 1,4-dichloro-1,4-diaryl-2,3-diaza-1,3-butadienes **63**[51]. Both chlorides in **63** may be displaced (the initial step involving a unimolecular S_N1-type loss of Cl^-)[48] to give, for example on reaction with hydrazine the tetrazines **64** and triazoles **65**[55]. The triazole **67** may be formed directly on prolonged heating with ammonia while treatment of **62** with phosphorus pentoxide[57] (or using phosphorus oxychloride, thionyl chloride etc.)[58, 59] and phosphorus pentasulphide leads to the 2,5-diaryloxadiazoles (**66**) and thiadiazoles (**68**) respectively.



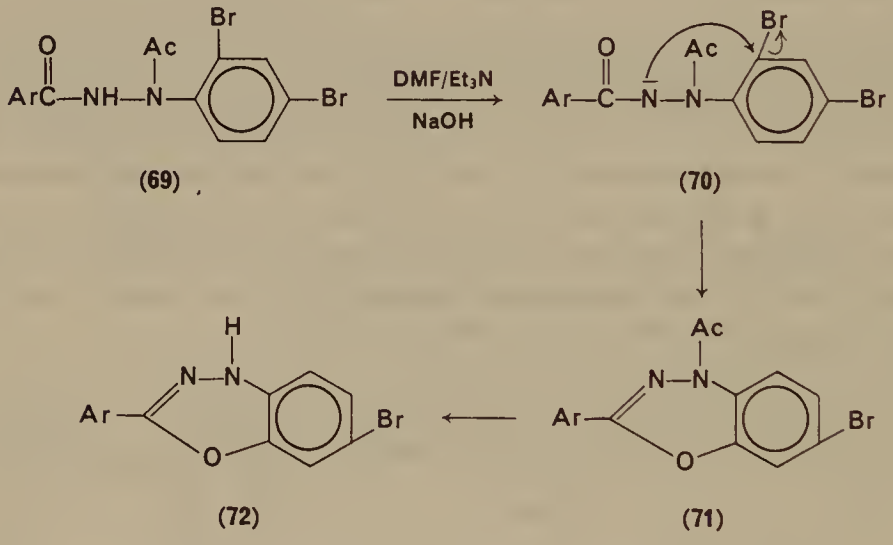
(62) (63) (64) (65) (66) (67) (68)

Under basic conditions the NH group adjacent to the carbonyl of the hydrazide may be ionized and alkylation under these conditions usually leads to substitution on this nitrogen (equation 29)[60]. Diacylated hydrazides can give mono or dialkylated products under these conditions (equation 30); the best yields of dialkylated products are obtained when R′ = Me[61].





The hydrazide conjugate base is a strong nucleophile in intramolecular reactions. An example is the displacement of halide from the *ortho*-positions of an adjacent aromatic ring (even if the latter is not activated for nucleophilic attack). (equation 32)[62]. The *N*-acyl intermediate **71** is normally deacylated *in situ* to the 4-*H*-1,3,4-benzoxadiazines **72**. The formation



of heterocyclic compounds from hydrazides by this route has been reviewed[63].

D. Reaction with Activated Alkenes and Alkynes

1. Alkenes

Alkenes and alkynes which have strongly electron-withdrawing substituents react readily with hydrazine and its derivatives. When 1 mole of

the alkene is used, the normal mono-alkylation product is formed, usually in high yield[64]. Thus 2-cyanoethylhydrazine (**73**) is obtained from the reaction of acrylonitrile with hydrazine. When 2 moles of hydrazine are used the major alkylation product is, as expected, unsymmetrical (**74**); the symmetrical material (**75**) is formed in <10% yield. When monoalkyl-

$$NH_2NH_2 + CH_2{=}CHCN \longrightarrow NH_2NHCH_2CH_2CN$$
(73)

$NH_2N(CH_2CH_2CN)_2$ (74) $NCCH_2CH_2NH{-}NHCH_2CH_2CN$ (75)

hydrazines are used as substrates (**76**, R = Me, cyclohexyl, $PhCH_2CH_2$), alkylation occurs on the substituted nitrogen giving (**77**) in 95–100% yield. When the vinyl group is not activated (as in styrene **78**) reaction is much

$$RNHNH_2 + CH_2{=}CHCN \longrightarrow RN(NH_2)CH_2CH_2CN$$
(76) (77)

more sluggish; however styrene does react with the sodium salt of hydrazine (**79**) to yield (**80**)[65].

$$PhCH{=}CH_2 + Na^{+}\bar{N}HNH_2 \longrightarrow PhCH_2CH_2NHNH_2$$
(78) (79) (80)

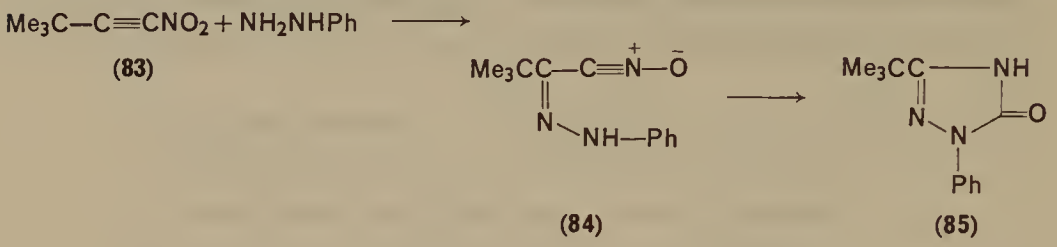
The salt **79** is however highly explosive and thus difficult to handle. It is possible to carry out much the same type of reactions using the barium salt of hydrazine; this is readily prepared and is relatively easy to handle[66]. In addition to the normal mono-substituted products, some reaction may occur with 2 moles of the substrate. Thus with styrene and benzonitrile as substrates **81** and **82** are also formed.

$PhCH_2CH_2NH{-}NHCH_2CH_2Ph$ (81) $PhC(=NH){-}NHC(=NH)Ph$ (82)

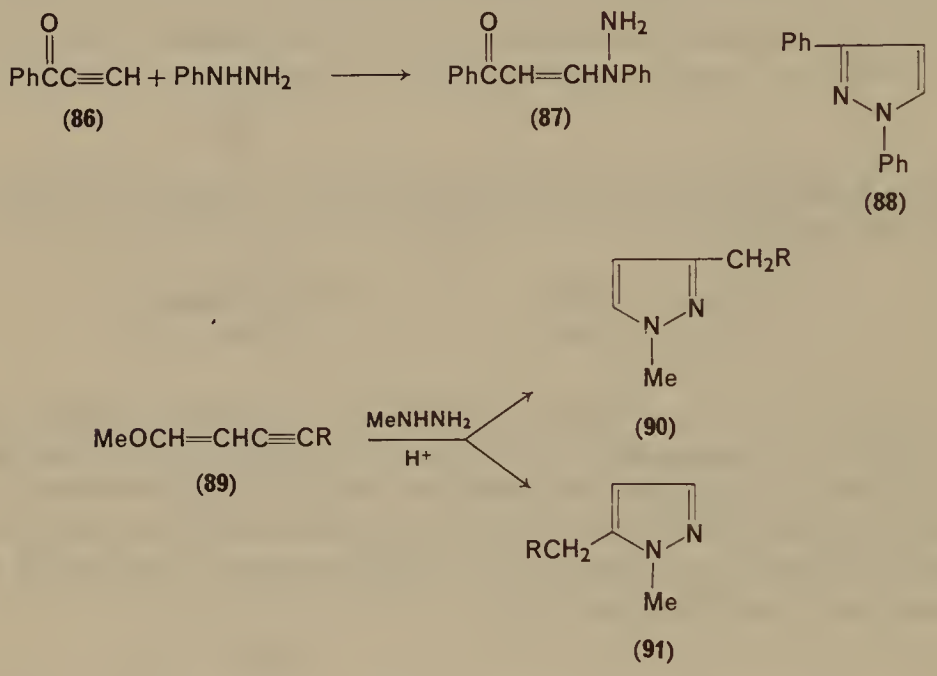
2. Alkynes

Alkyne derivatives may also react with hydrazines; a particularly interesting example is the preparation of 1,2,4-triazolin-5-one **85** from t-butylnitroacetylene **83** by reaction with phenylhydrazine, where the intermediacy of the nitrile oxide **84** has been proposed[67]. Subsequent cyclization

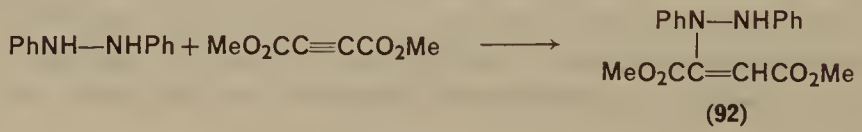
also occurs in the reaction of phenylhydrazine with 1-phenyl-2-propyn-1-one (**86**); in this case treatment of the intermediate **87** with acid gives the



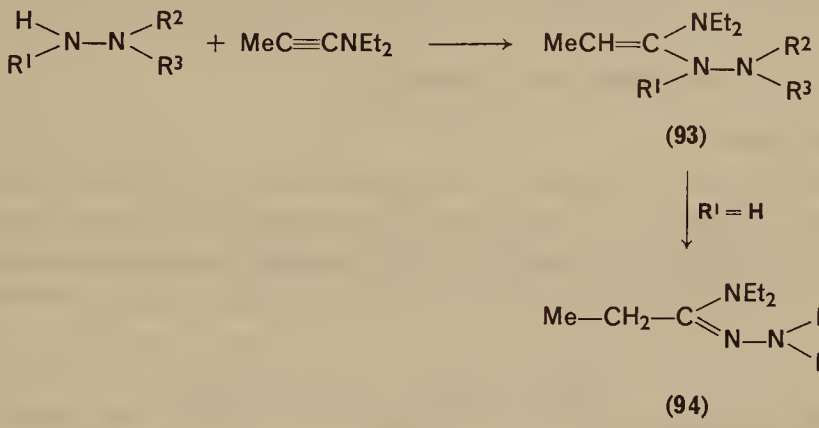
pyrazole (**88**)[68]. Reaction of methoxybutenynes (**89**) with methylhydrazine under acidic conditions leads to a mixture of products **90** and **91**, apparently formed by competitive attack at the alkyne and alkene centres[69].



Hydrazobenzene also reacts with activated acetylenes; in this case the intermediate *N*-anilino enamines (**92**) are isolable and were found to undergo a variety of subsequent cyclizations (to form pyrazoles, indazoles and quinazolines)[70].

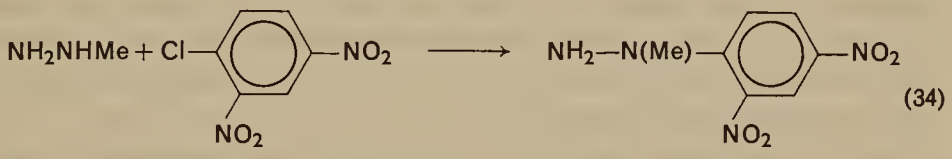


The addition of substituted hydrazines to ynamines leads to two kinds of products, amidrazones (**94**) and *gem*-enamino enehydrazines (**93**), see equation 33. Compounds **93** are formed only when the hydrazine used is trisubstituted, otherwise tautomerization to the more stable hydrazone form **94** occurs[71].

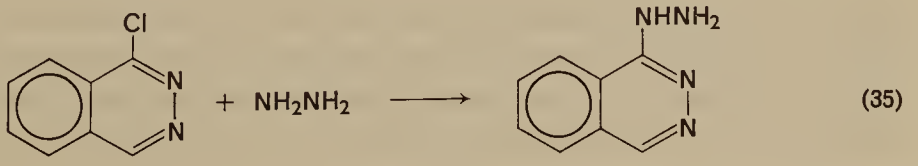


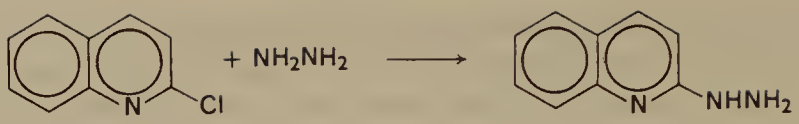
3. Nucleophilic aromatic substitution

Arylation of hydrazines also occurs readily when a good leaving group (e.g. halide ion) and electron-withdrawing groups are present in the aromatic nucleus. Thus methylhydrazine reacts exothermally with 2,4-dinitrochlorobenzene (equation 34). As in simple alkylations, the substituted nitrogen is the nucleophilic centre[72, 73]; only when the aryl group is



highly hindered (for example by 2,6-disubstitution) does the unsubstituted nitrogen react preferentially[74]. Substitution occurs particularly readily in heterocyclic systems (see, for example, equations 35 and 36). A large number of these displacements have been reported[75]; the substituted





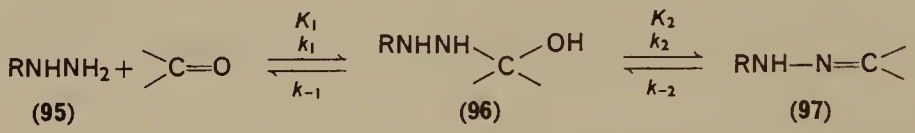
(36)

hydrazines which are formed have been used as intermediates in the synthesis of fused heterocyclic systems.

E. Reactions with Aldehydes and Ketones

1. Mechanism

It has been well established that the condensation of hydrazines with carbonyl compounds to yield hydrazones proceeds in a step-wise manner (equation 37) with the formation of a tetrahedral addition intermediate (**96**). A change-over in the rate determining step for such reactions is

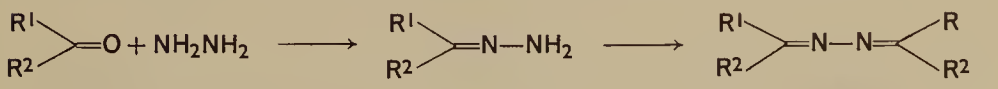


(95) (96) (97) (37)

normally observed in the weakly acidic pH range, with dehydration of the intermediate **96** (k_2) becoming rate determining at high pH values[76, 77]. The dehydration step may be either pH or buffer independent (for the more basic hydrazines such as hydrazine itself) or exhibit acid or base catalysis (with, for example semi-carbazide)[78]. In general the equilibrium constants for the formation of the intermediates **96** have been found to vary very little with the nature of the hydrazine; on the other hand the dehydration equilibrium constants K_2 are sensitive to the nature of the hydrazine used, decreasing with increasing pK_a of the hydrazine, in all cases the formation constants for the hydrazones being large ($>10^3$).

Because of this relative stability of the hydrazone linkage in **97** towards hydrolysis (compared with, for example the corresponding imines), hydrazones have been widely used as solid derivatives to characterize carbonyl compounds.[79] The most satisfactory reagents for this purpose are phenylhydrazine (**95**, R = Ph) and *p*-nitrophenylhydrazine (**95**, R = *p*-$NO_2C_6H_4$); semicarbazide (**95**, R = NH_2—$\overset{\overset{O}{\|}}{C}$—) and Girard's reagents (**95**, R = $Me_3^+NCH_2CO$—) have also been used and have the advantage of being water soluble[80]. 2,4-Dinitrophenylhydrazine (**95**, R = 2,4-$(NO_2)_2C_6H_3$) also reacts readily with aldehydes and ketones; however some of the simple

aldehydes can give derivatives with widely differing m.p.'s depending on the mode of preparation (this has been attributed to the retention of traces of the catalysing acid, rather than to the formation of *syn* and *anti* isomers of the hydrazone)[81]. Hydrazine itself is not suitable for the formation of derivatives for characterization since reaction may occur with a second mole of the carbonyl compound to form 1,4-substituted-2,3-diazabuta-1,3-dienes **99** (equation 38). When R^1 and R^2 are aliphatic groups then the inter-



(98) **(99)** (38)

mediate hydrazone **98** cannot be isolated and disproportionation to **99** occurs[82]. However when R^1 or R^2 is an aryl group, particularly with an electron-withdrawing substituent (e.g. $R^1 = p\text{-}NO_2C_6H_4$) the hydrazone **98** can be isolated. Benzophenone hydrazone (**98**, $R^1 = R^2 = Ph$) is also relatively stable; in this case it is difficult to form the corresponding azine[83].

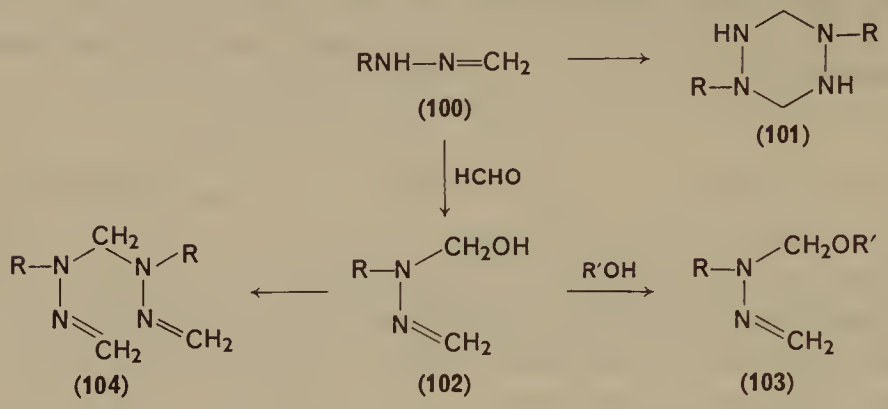
2. Reaction with formaldehyde

Mono substituted hydrazines, such as methylhydrazine, might be expected to react with carbonyl compounds at the more nucleophilic substituted nitrogen (by analogy with its alkylation and reaction with the more reactive acylating agents). Such a mode of reaction most likely does occur in solution but the carbinolimine intermediate (analogous to **96**) which is formed cannot undergo dehydration to give a stable product; instead the intermediate would be cleaved to regenerate the starting materials. Neither symmetrically disubstituted, nor trisubstituted hydrazines normally react with carbonyl compounds in the absence of a reagent to trap the carbinolamine for the same reason. However 2 moles of 1,1,2-trimethylhydrazine form an adduct with formaldehyde[84] (equation 39).

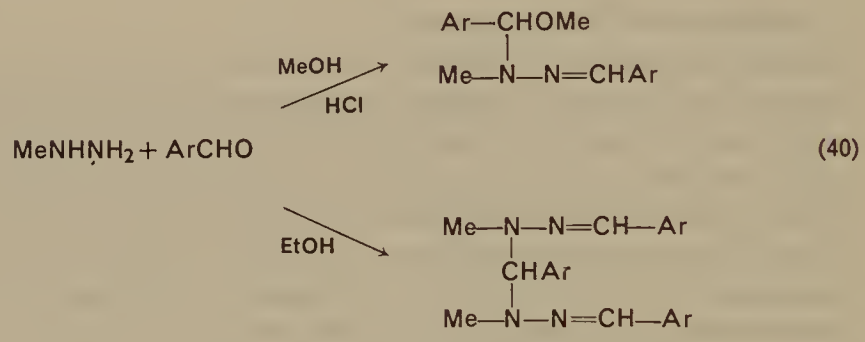
$$Me_2NNHMe + CH_2O \longrightarrow Me_2N{-}NMeCH_2NMe{-}NMe_2 \qquad (39)$$

Indeed the reaction of the simplest carbonyl compound, formaldehyde, with hydrazines is quite complex, several subsequent cyclizations occurring. Thus it has been shown[85] that the condensation of alkylhydrazines with formaldehyde leads to the corresponding formaldehyde alkylhydrazones (**100**). These dimerize (under acidic catalysis) via a step wise ionic mechanism to yield 1,4-dialkylhexahydro-1,2,4,5-tetrazines (**101**). When the alkyl

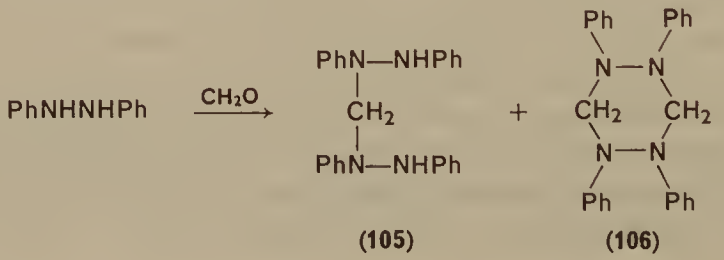
group, R, is unbranched dimerization is rapid and the hydrazones **100** cannot be isolated in a pure state. In the presence of excess formaldehyde in alcoholic (R′OH) solution further condensations take place leading to *N*-alkyl-*N*-alkoxymethylhydrazones **103** and the dimer **104**. Similar



reactions have been observed when methylhydrazine is treated with excess aromatic aldehyde under forcing conditions (see equation 40)[84].

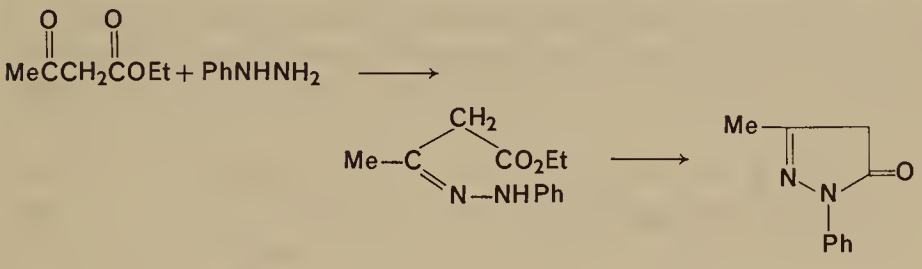


The reaction of hydrazobenzene with formaldehyde and other simple aliphatic aldehydes proceeds similarly except in this case no hydrazone-type products can be formed. The principal products isolated from the reaction of hydrazobenzene and formaldehyde are *bis*-(1,2-diphenylhydrazino) methane (**105**) and the hexahydrotetrazine (**106**)[86].

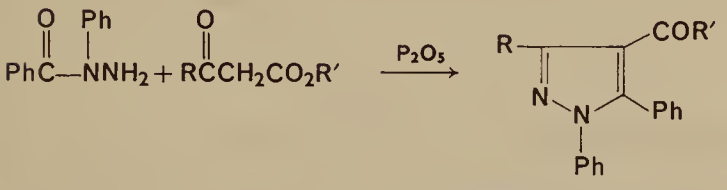


3. Reactions of bifunctional reagents

When either the hydrazine or the carbonyl substrate has more than one reactive site then the hydrazone which is formed initially may cyclize; several examples are given in equations (41–44). Cyclization is normally acid catalysed (for a detailed compilation see reference 65), but oxidizing agents such as lead tetra-acetate or bromine have also been widely used (see Section II, E, 4).

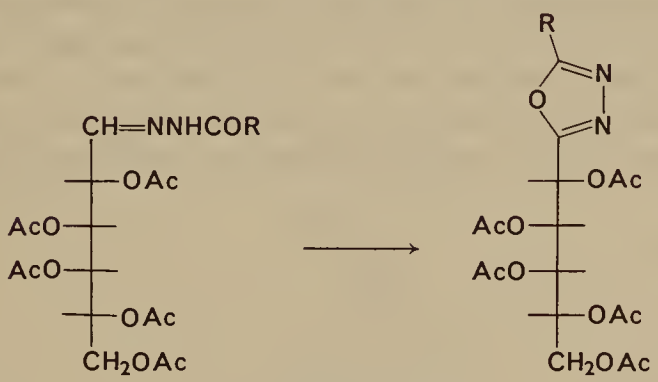


(41)



(42)

(Reference 87)



(43)

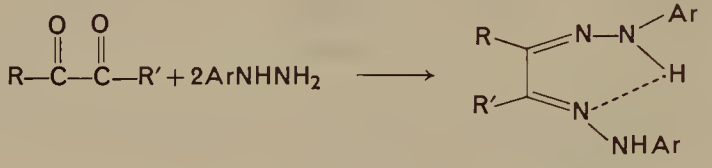
(Reference 88)

(44)

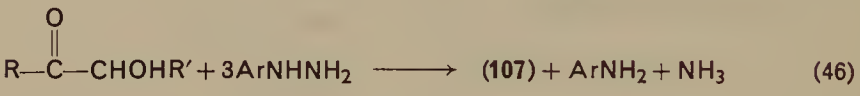
(Reference 89)

The formation of pyrazolines by acid catalysed reaction of phenylhydrazine with α,β-unsaturated ketones (equation 44) represents an important route to these materials. A mechanism for the cyclization has been proposed[89] on the basis of the substituent effects in Ar and Ar′ involving protonation of the imine nitrogen followed by rate determining cyclization to give an intermediate 3-pyrazoline.

When two carbonyl groups are adjacent in the substrate then 2 moles aryl hydrazines may react to form osazones (equation 45)[90]. Osazones are also formed from α-hydroxy ketones (equation 46); in this case 3 moles of the aryl hydrazine are consumed and the by-products include aniline and ammonia. The osazones are usually crystalline materials and have been widely used as derivatives for carbohydrates. The mechanism of their

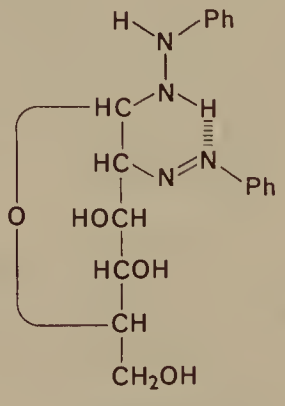


(107) (45)



(46)

formation however remains controversial[91], particularly so since phenylhydrazine is apparently acting as an oxidizing agent. The structure of the osazones has also received some attention and a quasi-aromatic hydrogen bonded structure (**107**) has been proposed[92]. The aromatic groups apparently stabilize this ring structure since in the presence of excess methylhydrazine, hexoses react to form hexahydrazones. However this chelate



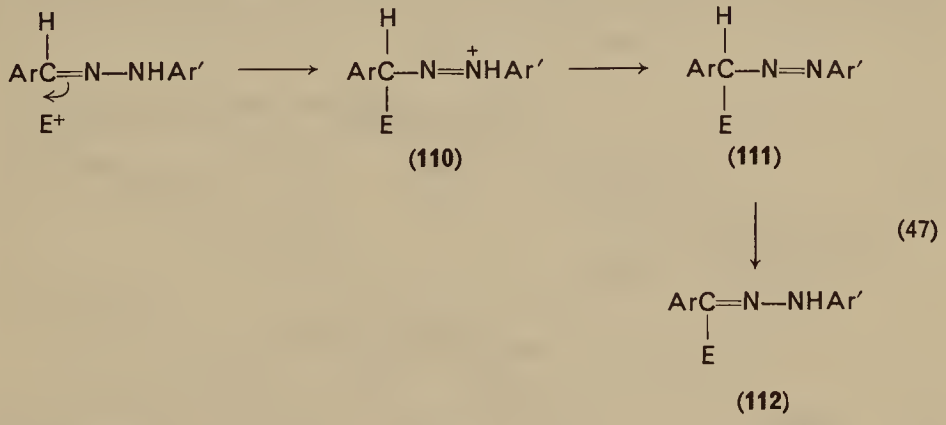
(108)

structure (**107**) is by no means generally accepted and it has been claimed on the basis of i.r., u.v. and chemical evidence that the C_2 phenylhydrazine residue has a phenylazo and not a phenylhydrazone structure. In the solid state structure **108** has therefore been proposed for the osazone formed from D-glucose; this structure readily explains the formation of a mono-*N*-benzoylated product[93].

4. Reactions of arylhydrazones[79]

Arylhydrazones have a rich chemistry of their own and may be converted to derivatives which serve as substrates undergoing cycloadditions, internal cyclization and displacement reactions. The most characteristic reaction of aldehydic arylhydrazones is electrophilic substitution. There has been much controversy as to the position on the hydrazone which is attacked by the incoming electrophile, but from studies in recent years it appears that the carbon atom is the favoured site. Thus hydrazones may be regarded as analogous to enamines, the dipolar structure **109** accounting for the

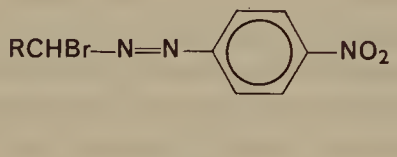
nucleophilicity of carbon. The suggested mechanism of electrophilic substitution is outlined in equation (47) (E^+ = electrophile)[94, 95]; a key step is the formation of the azo intermediate **111** en route to the more stable hydrazone tautomer **112**.



(47)

It is not always possible to isolate the intermediate **111**, since in most cases the intermediates have a very short lifetime under the conditions used for the formation of **112**. However such azo materials have now been reported

for reaction with bromine (**113**)[96], chlorine (**114**)[97], benzenediazonium ion (see II, F), α-carbonyl azo compounds (**115**)[98], lead tetraacetate (**116**)[99] and potassium nitrosobisulphate (**117**)[100]. Kinetic studies have shown[94, 95, 101] that the substituents in the *N*-aryl ring (Ar′) have a far larger effect on reactivity of the hydrazone than do those in the Ar ring; this is explained in terms of the formation of the stabilized species **110** in which most of the charge is localized on the nitrogen adjacent to Ar′.



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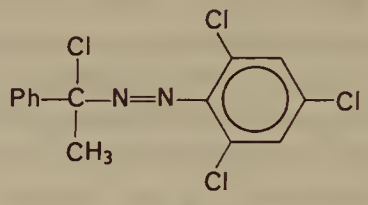

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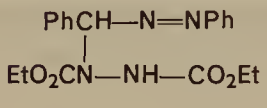
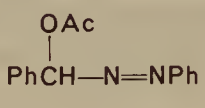


(115)



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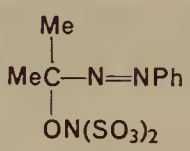
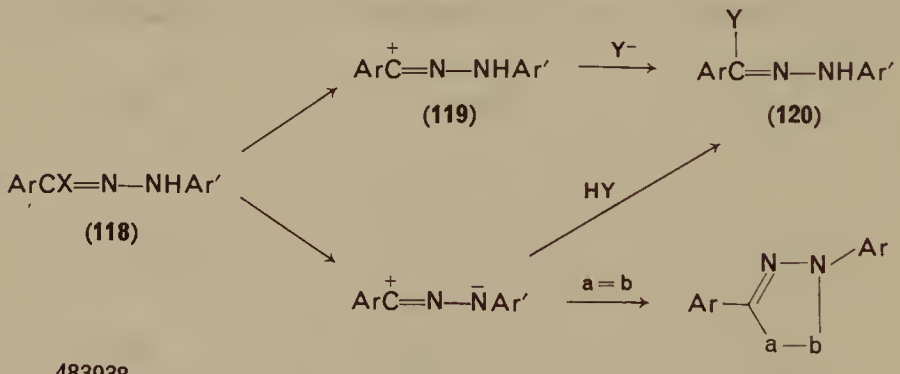


(117)

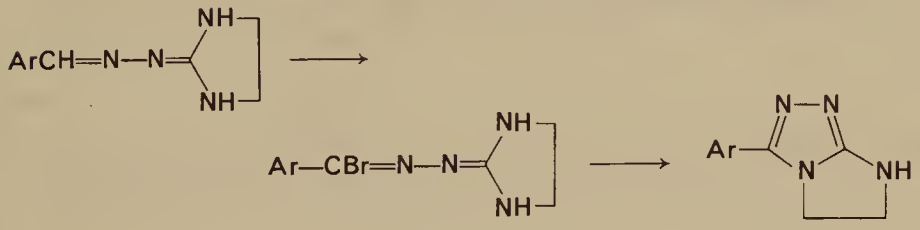
Hydrazonyl halides **118** are the normal ultimate products formed on treatment of aldehyde hydrazones with halogen (usually in acetic acid as solvent); if the *N*-aryl ring is not deactivated then substitution will occur in this ring as well. The halide group is labile and may be lost either via an uncatalysed (formation of **119**) or base catalysed (where the products are 1,3-dipolar ions **121**) pathway[12]. Both species (**119** and **121**) react with



nucleophiles to form, for example, hydrazonyl azides (**120**, $Y = N_3$) by reaction with azide ion[102], amidrazones (**120**, $Y = NR_2$) by reaction with

amines[103] and hydrazides (**120**, Y = OH) by reaction with water[104]. The 1,3-dipolar ion **121** also undergoes cycloadditions with a large variety of compounds containing double and triple bonds to form 1,3-diaryl pyrazoline derivatives (**122**)[105].

When the *N*-aryl group of the hydrazonyl halide (Ar′) itself contains a nucleophilic moiety then internal cyclization may occur; in fact halogenation of the starting hydrazone often results in the formation of the cyclic material directly without the isolation of intermediates. Some examples of these cyclizations are presented in equations (48)–(52); further examples are provided in reference 106.

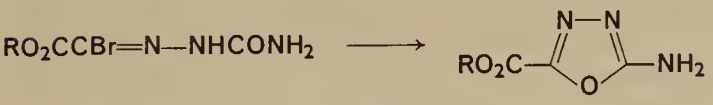


(48)

Reference 107

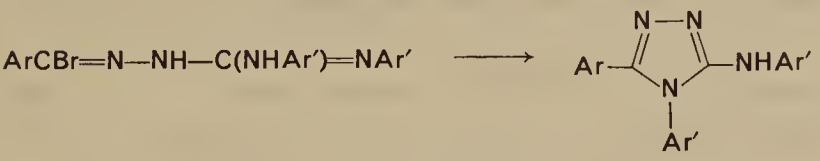
(49)

Reference 108



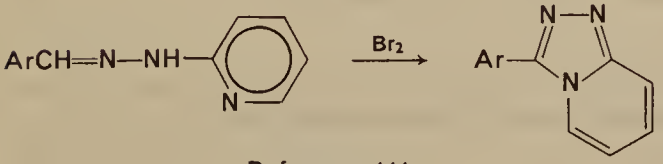
(50)

Reference 109



(51)

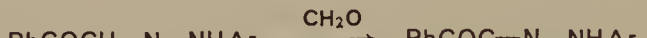
Reference 110



(52)

Reference 111

The hydroxymethylation of glyoxal arylhydrazones has been extensively studied by Hahn[112] (equation 53). Aminomethylation, which is analogous to the Mannich reaction, has also been described for arylhydrazones of phenylglyoxal[113] and of nitroformaldehyde[114]; primary amines react further to give 1,2,4-triazines (equation 54). Phenyl azide reacts with hydrazones under basic conditions to form *N*-amino formazans (equation 55)[115].



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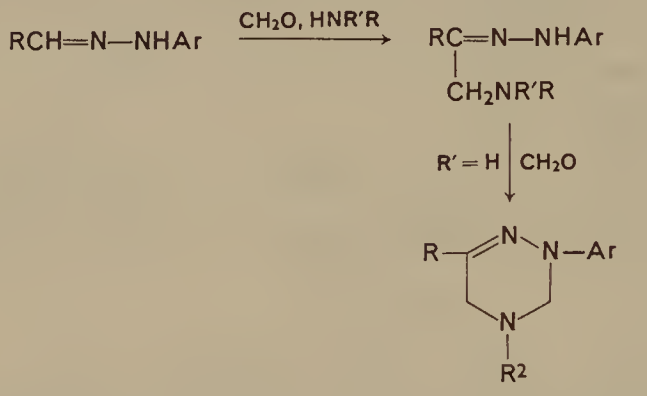

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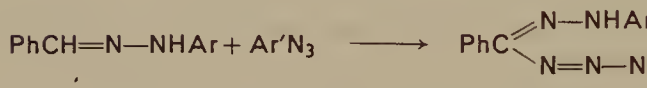
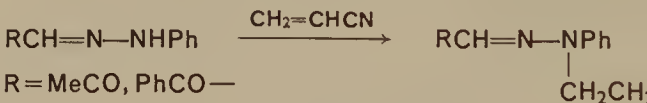
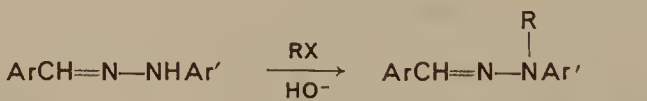


(55)

Direct alkylation or acylation of hydrazones is considerably more difficult than reaction with the corresponding hydrazines but reaction appears to occur on the amino nitrogen (when this is mono-substituted). Thus reaction of phenylhydrazones of methyl or phenyl glyoxal with acetonitrile leads to *N*-substituted products (equation 56); benzaldehyde phenylhydrazone fails to react under those conditions[116]. Direct alkylation



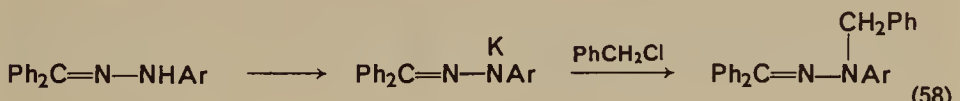
(56)



(57)

of *N*-aryl hydrazones (equation 57), unlike the *N*-alkyl analogues[117], does not occur with simple alkylating agents. However if the Ar′ group contains electron-withdrawing groups (e.g. Ar′ = *p*-$NO_2C_6H_4$ or 2,4-$(NO_2)_2C_6H_3$)

then alkylation of the conjugate base in the presence of hydroxide ion is possible[118]. Hauser and co-workers[119] have also reported that the conjugate bases of hydrazones can be formed in the presence of potassium amide in liquid ammonia, even when Ar′ = Ph. The hydrazone anions then undergo smooth alkylation using the normal alkyl halide reagents (equations 58 and 59). Benzoylation and acetylation of *N*-arylhydrazones has also been



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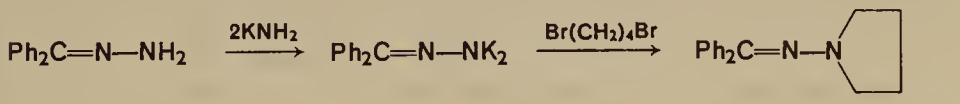


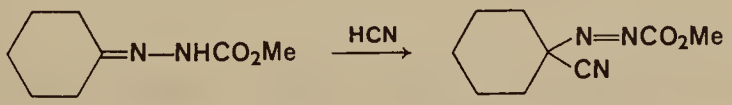
(59)

reported (equation 60)[118]; in this case also the products formed (**123**) are *N′*-substituted.

(60)

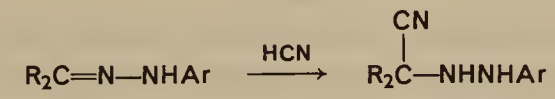
(123)

Nucleophilic attack on hydrazones has also been reported but this occurs much less frequently than the corresponding reactions with electrophiles. Examples are restricted to the cyanide anion as nucleophile and a mechanism involving attack by the nucleophile on the protonated hydrazone is indicated (equations 61–63)[120, 121].



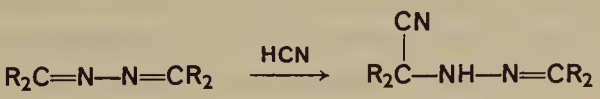
(61)

(124)



(62)

(125)

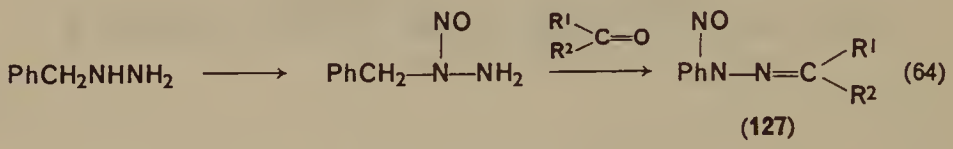


(63)

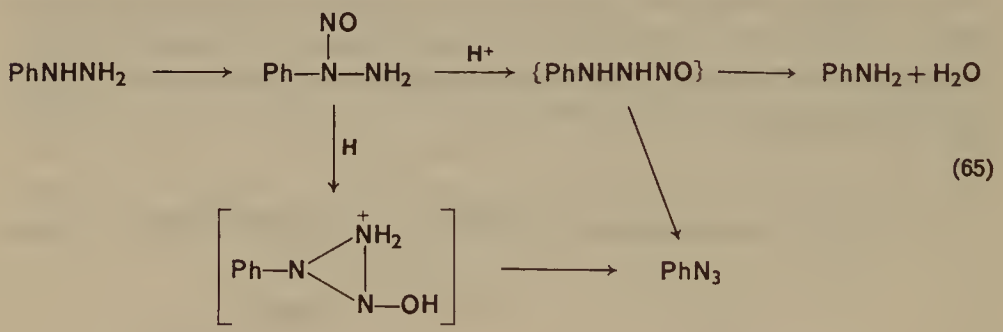
(126)

F. Nitrosation

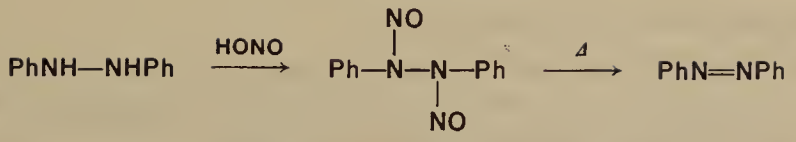
The nitrosation of hydrazines was extensively investigated both by Bamberger and Busch and their co-workers[122, 123]. Both alkyl and arylhydrazines undergo reaction but the initial products formed may undergo facile rearrangements involving migration of the nitroso group from one site to another. Chemical tests (as used by the earlier workers) are therefore not particularly informative as to the structures of the adducts. Alkylhydrazines (equation 64) appear to undergo reaction at the substituted nitrogen (as expected by analogy with the corresponding alkylation reactions (Section II, B), since the adduct formed reacts with aldehydes and



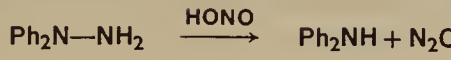
ketones to form nitrosohydrazones (**127**). A similar reaction has been observed for arylhydrazines but in this case the adducts formed also show some *N'*-nitroso characteristics; for example treatment with acid results in the formation of aryl azides. A possible mechanism involving initial nitrosation at the substituted nitrogen followed by complete or partial migration of the nitroso group on treatment with acid, is outlined in equation (65)[124, 125].



Disubstituted hydrazines react differently; symmetrically disubstituted hydrazo compounds form isolable mono or dinitroso adducts on reaction with nitrous acid (equation 66). Denitrosation of the adducts occurs readily on heating to give azo compounds—the overall reaction then involves oxidation of the hydrazone[126, 127]. The reaction of *N,N*-disubstituted hydrazines with nitrosating agents results in *N—N* bond cleavage (equation 67).

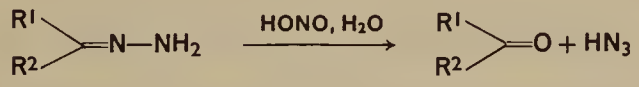


(66)

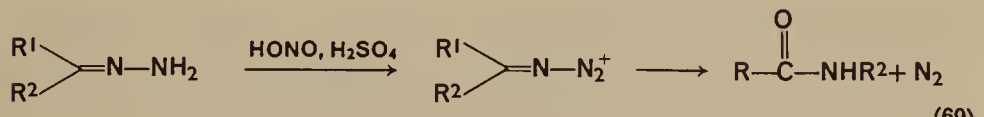


(67)

Extensive decomposition also occurs when *N*-unsubstituted hydrazones or semicarbazones are treated with nitrous acid. In the presence of water in glacial acetic acid, the product obtained in good yield is the corresponding aldehyde or ketone (equation 68). In concentrated acid, rearrangement (of the Schmidt type) takes place and the products formed are amides (equation 69)[128].

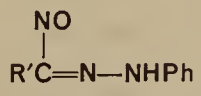


(68)



(69)

The structure of the nitroso compounds formed on reaction of *N*-substituted hydrazones with nitrosating agents (such as nitrous acid or alkyl nitrite) has long been the subject of debate[122, 129, 130, 131]. Besides the *N*-nitroso structure **127** *C*-nitroso formulations **128** and more recently azo alkane **129** have also been considered. The structure **128** is least likely since only aldehyde hydrazones could form this adduct whereas ketone hydrazones clearly react to form similar nitroso compounds[122]. Structure **129**



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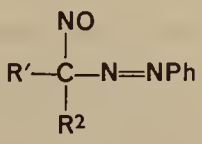
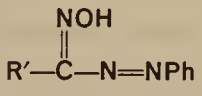


(129)

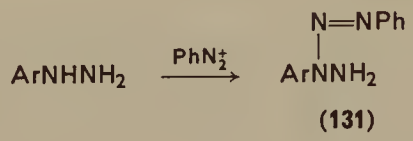


(130)

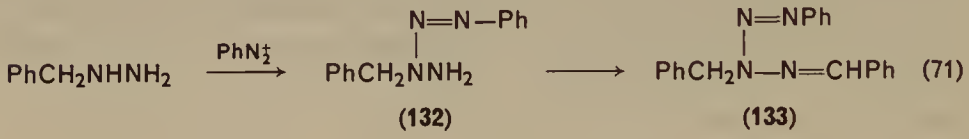
a priori might be favoured because it has been well established[79, 94] that other electrophiles react with hydrazones at carbon to give azo intermediates (see Section II, E, 4) and also because of the facile rearrangement of the nitrosohydrazones to arylazo oximes **130** (when $R^2 = H$). However, recent n.m.r. and u.v. data[130] supports the *N*-nitroso formulation **127**, originally proposed by Busch[123].

G. Reactions with Aryldiazonium Ions

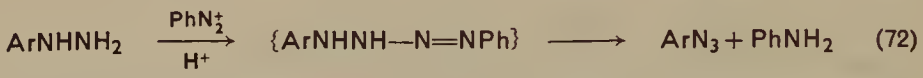
The electrophilic benzenediazonium ion reacts preferentially with alkyl and aryl substituted hydrazines in acetic acid at the substituted nitrogen to give 1,3-disubstituted tetrazenes (equations 70 and 71)[132–134]. Under more strongly acidic conditions, an arylazide and aniline are formed (equation



(70)

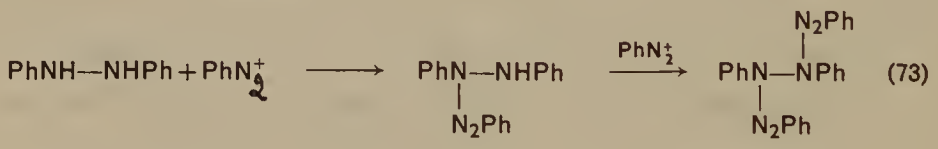


(71)



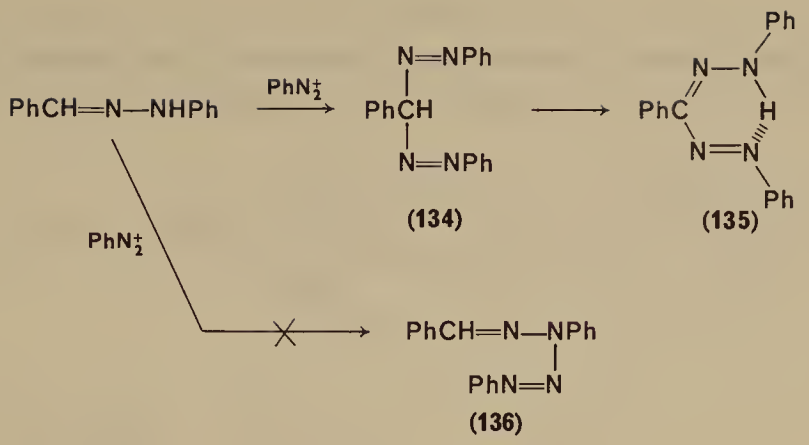
(72)

72) presumably via the intermediacy of a 1,4-diaryltetrazene. This duality of behaviour parallels that observed in the corresponding nitrosation reactions (Section II, F). Structural analysis for **132** includes conversion to a benzylidene derivative **133**; the latter is stable and does not rearrange to the isomeric formazan (see below). On the other hand **131** does not give the corresponding aldimine derivative cleanly; after a complex workup the only identifiable product isolated was the corresponding formazan (see also below). Hydrazo compounds may couple with one mole (or in the presence of excess reagent 2 moles) of aryl diazonium ion to give 1,3-trisubstituted tetrazenes (equation 73). In this case the mode of substitution on the tetrazene inhibits the normal rapid formation of azides[135].



(73)

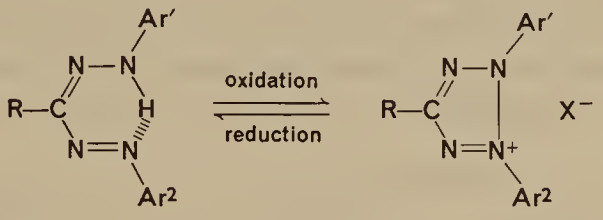
The structure of the initial product formed on the reaction of benzenediazonium ion with *N*-arylhydrazones has also been the subject of some controversy. The ultimate product isolated is the formazan **135**. However if the coupling reaction is carried out under mild conditions in neutral solution then an intermediate bright yellow material may be isolated; this on heating or treatment with base is easily converted to the isomeric formazan **135**. Originally it was proposed[132] that reaction initially occurred at the amino nitrogen of the hydrazone (by analogy with the corresponding reaction with



(74)

arylhydrazines) to form the tetrazines **136**. The formation of **135** would then involve an intramolecular[136] phenylazo group migration. However more recent spectral[137, 138] and kinetic work[94] has demonstrated that carbon is the nucleophilic centre of the hydrazone and that the intermediates actually have the *bis*-arylazo structure **134**. The conversion of **134** to the formazan **135** is then an azo-hydrazone tautomerization.

There are few structural limitations in the synthesis of formazans and consequently a large variety of materials have been reported[139]. Perhaps the most important use of formazans arises from their ready reversible conversion to tetrazolium salts (equation 75). The salts are generally



(75)

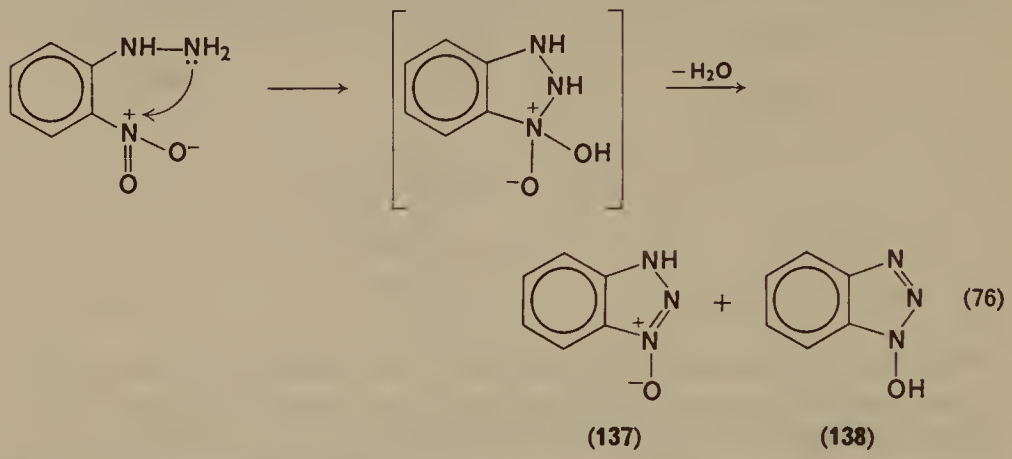
colourless and water soluble and are readily converted back to the highly coloured formazans; they have therefore been used as biological staining agents. The chemistry of formazans and tetrazolium salts has been the subject of two excellent reviews[139, 140].

H. Reactions with Nitro groups

1. Intramolecular

o-Nitrophenylhydrazines undergo an intramolecular condensation when heated in the presence of base to give mixtures of benzotriazole oxides **137**

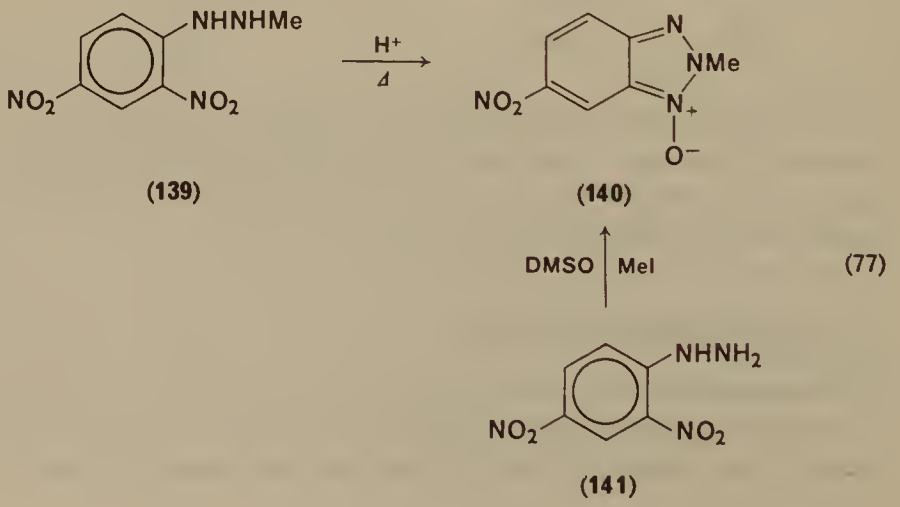
and *N*-hydroxybenzotriazoles **138**[141, 142]. The reaction most likely involves nucleophilic attack by the terminal nitrogen of the hydrazine moiety, followed by dehydration (equation 76). Whether **137** or **138** is the major



(137) **(138)**

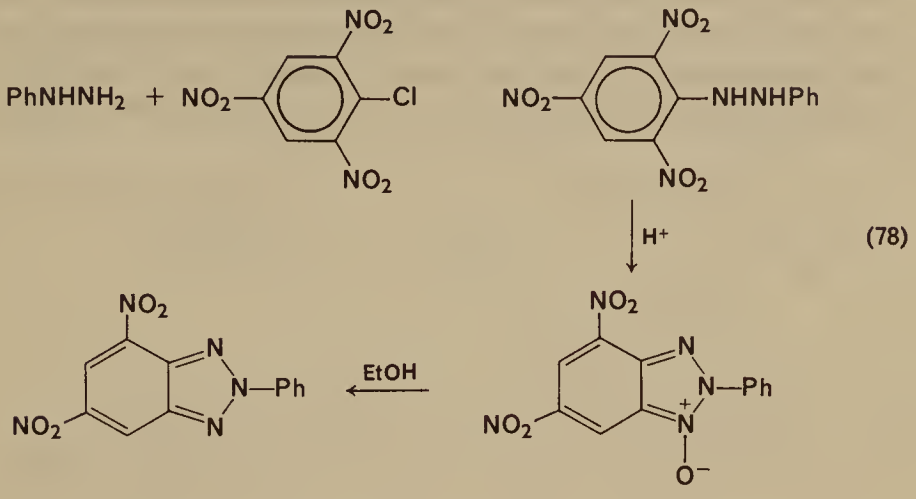
product is dependent on the reaction conditions and substitution in the aryl ring. The position of equilibrium has been shown to lie in favour of **137** in aqueous solution (the 4- and 6-nitro derivatives also exist in this form); however in ethanol **138** is the major species when the aryl ring of the product is unsubstituted or has a 6-nitro substituent, while the two isomers are present in approximately equal concentrations when the ring has a 4-nitro substituent[143].

Further examples of this type of cyclization are given in equation (77); the *N*-methyl derivative **140** is obtained either on heating **139** in acidic solution or on treating the unsubstituted hydrazine **141** with methyl iodide in DMSO[144]. The benzotriazole *N*-oxides (**140**) are readily reduced to the



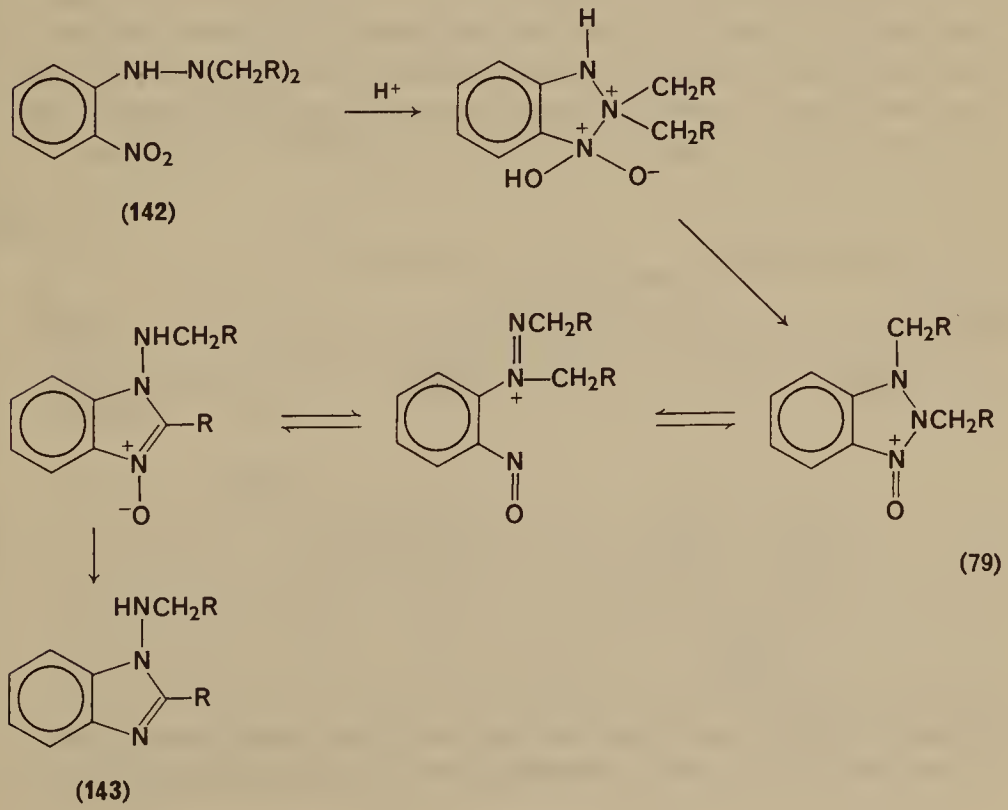
(139) **(140)** **(141)**

corresponding triazoles; this sequence therefore provides a convenient route to these materials. Equation (78) outlines the formation of a 2-aryl-benzotriazole from picryl chloride and phenylhydrazine[145].



(78)

When the terminal nitrogen of the hydrazine is disubstituted (**142**) then the cyclization (under acidic conditions) takes a different course and *N*-



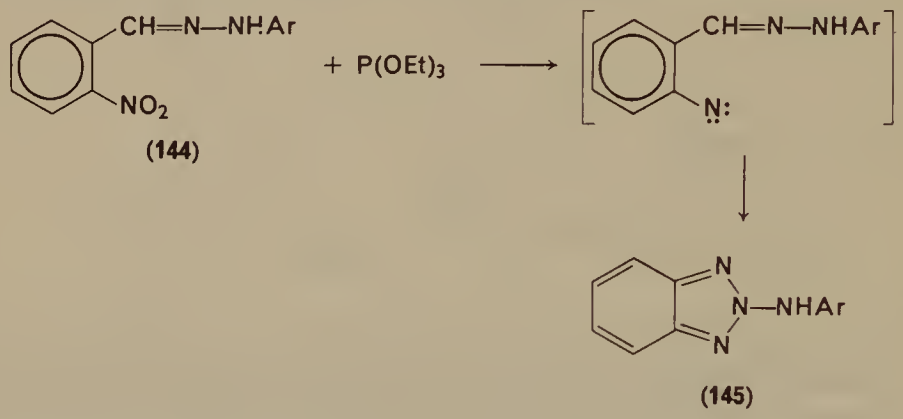
(142)

(79)

(143)

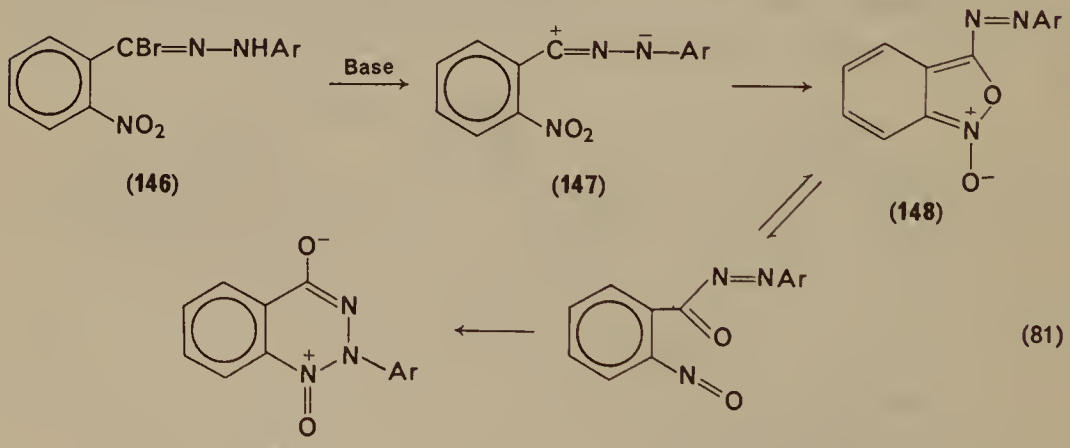
amino benzimidazoles **143** are formed in good yield[146]. A mechanism has been proposed (equation 79) involving initial nucleophilic attack on the nitro group by the substituted nitrogen of the hydrazine moiety.

Cyclizations involving nitro groups have also been observed in hydrazine derivatives. Thus treatment of *o*-nitrobenzylidene phenylhydrazine (**144**) with triethylphosphite gives the 2-aminoindazole derivatives (**145**) in good yield (equation 80)[147]. Cyclization also occurs on treatment of the *o*-nitro-



(144) (145) (80)

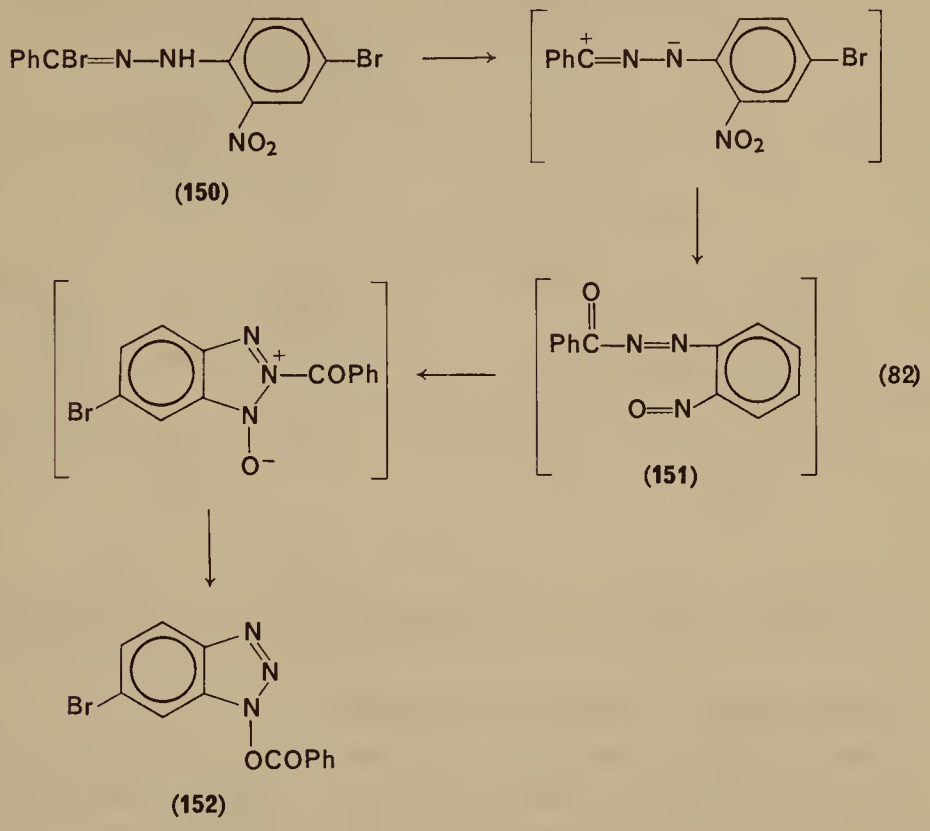
phenyl hydrazonyl bromides (**146**) with base, conditions known to lead to the formation of the 1,3-dipolar intermediate **147**. The product was formulated by Gibson[148] as the 3-arylazo-anthranil-1-oxide (**148**). More recent work by Kerber[149], however, favours the alternative azimine structure **149**; a possible route leading to its formation is outlined in equation (81).



(146) (147) (148) (149) (81)

A kinetic study has shown that the reaction involves rate determining formation of the 1,3-dipolar ion intermediate; the nitro group participates *after*

the slow step[150]. An *o*-nitro group in the *N*-aryl ring may also react with a nitrilimine intermediate produced from the hydrazonyl bromide **150** under anhydrous conditions[151, 152]. The final product formed is the benzoate of 6-bromo-1-hydroxybenzotriazole (**152**). A mechanism has been proposed



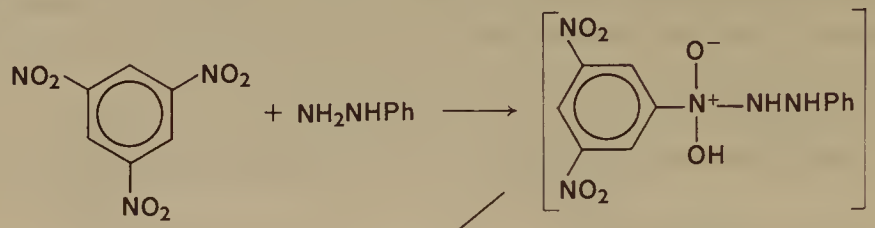
(82)

(equation 82) involving the intermediacy of an *o*-nitroso azo compound **151** (compare with equation 81); cyclization is followed by an acyl group migration.

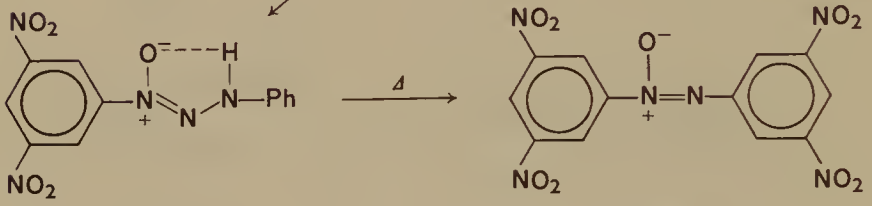
2. Intermolecular

An intermolecular reaction between phenylhydrazine and a nitro substituent has also been observed[153]. The first step apparently involves nucleophilic attack by the terminal nitrogen of the hydrazine to form the intermediate **153** (a similar reaction was previously reported for trinitrobenzene with amines)[154]. Dehydration leads to the observed product formulated as **154**. On heating the azoxy compound **155** is formed by dimerization with loss of nitrogen and benzene. The corresponding reaction

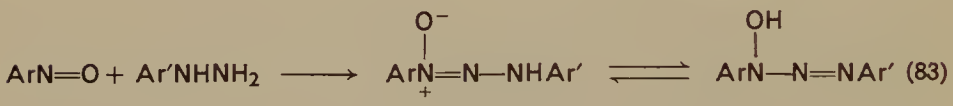
of aryl hydrazines with nitroso benzene (equation 83) has been known for some time[155]; the initial nucleophilic step is similar to that proposed above.



(153)



(154) (155)

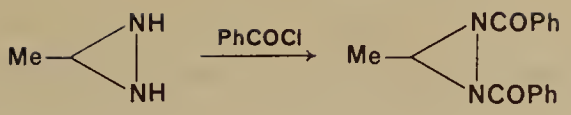


l. Cyclic Hydrazo Compounds—Diaziridines

The three-membered heterocycle containing two nitrogen atoms (diaziridines) has not received a great deal of study. It appears however that its reactions largely parallel those of the acyclic analogue, except of course that the strained small ring may be relatively easily cleaved.

Acylation of 3-methyldiazirine (**156**) proceeds normally with the formation of the diacylated material in the presence of excess benzoyl chloride (equation 84)[156]. Mono-acylations are observed on reaction of *N*-substituted diaziridines with nitrourea, phenylisocyanate and tosyl chloride (equation 85)[156]. Arylation of diaziridines has also been reported[144]; besides fluorodinitrobenzene (equation 86) other reagents which have been used include 2,4,6-trinitro-anisole and picryl chloride; the only other 1-aryldiaziridine which had been made, but not isolated, is 1-phenyl-3,3-pentamethylene diaziridine[157].

Diaziridines which have a free —N—H group can be readily isomerized
|
(for example on heating in toluene) to the corresponding hydrazones (see



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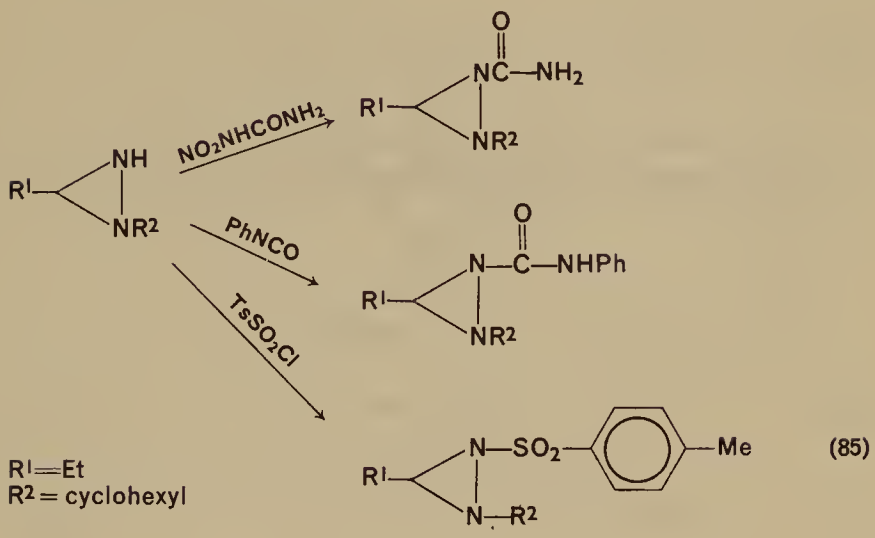
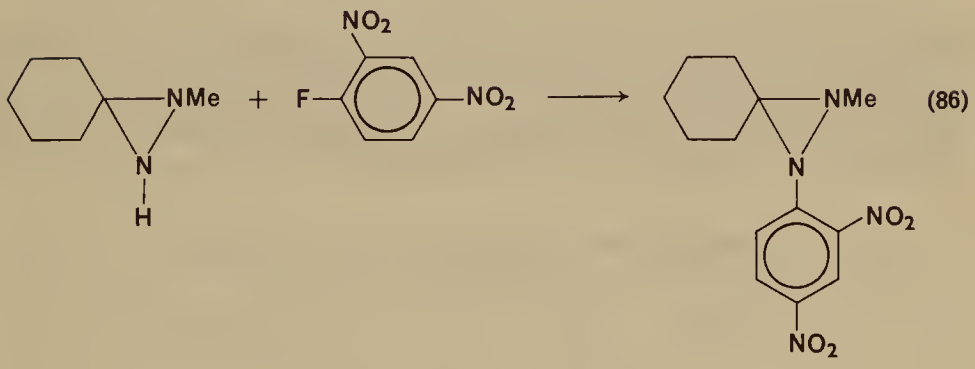


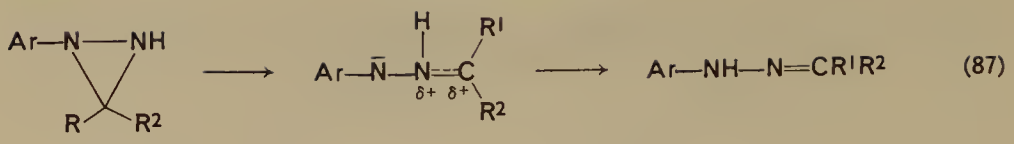
(85)



(86)

equation 87 for an example)[138]. *N,N'*-Disubstituted aziridines may behave differently and benzotriazole-1-oxides (**157**) are isolated as the final products in those cases where an *N*-(*o*-nitroaryl) group is present; the suggested reaction mechanism involves the formation of a similar dipolar intermediate (**156**) on ring opening (equation 88)[144].

Diaziridines also react with alkenes which are substituted by electron-withdrawing groups in a manner analogous to the corresponding hydrazo compounds (Section II, D, 1). Miller[158] has reported that 3-methyl-3-ethyldiaziridine adds to acrylonitrile and to butenone to give 1-(β-cyano-



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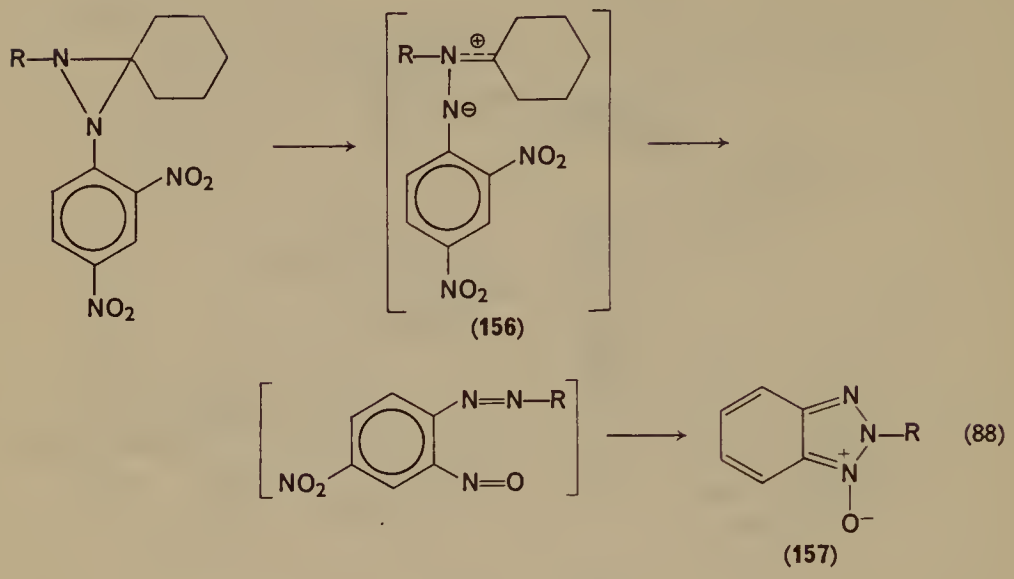
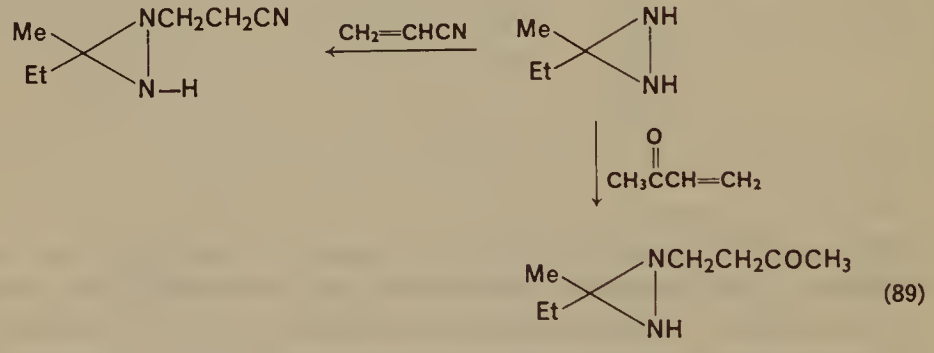


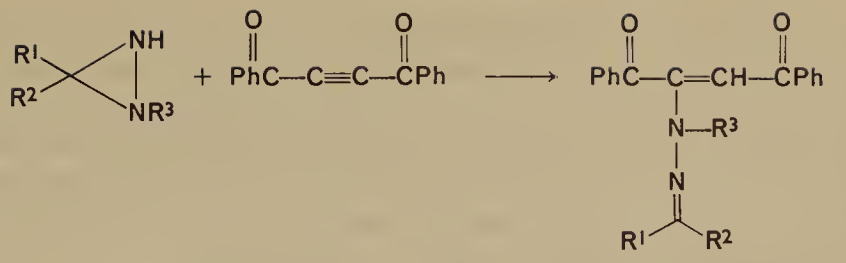
(88)

ethyl)-3-ethyl-3-methyldiaziridine and 1-(β-acetylethyl)-3-ethyl-3-methyldiaziridine respectively (equation 89). 1,3,3-Trialkyldiaziridines have been shown to react similarly with esters of ethenesulphonic acids[159]. In general the reaction of diaziridines with electrophilic acetylenes is accompanied by



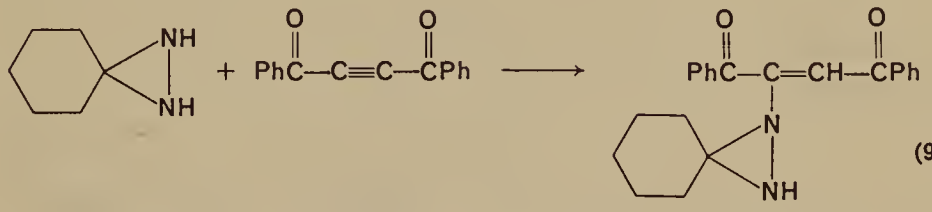
(89)

ring fission with the formation of hydrazones[160]. Typically the addition of dibenzoylacetylene to 1,3-dialkyl and 1,3,3- trialkylderivatives results in the formation of 2-(alkylidenehydrazino)-1,4-diphenylbutene-1,4-diones (equation 90). It is clear from the evidence presented[160] that it is the alkylated nitrogen of the diaziridine which acts as the nucleophilic site. In one case



(90)

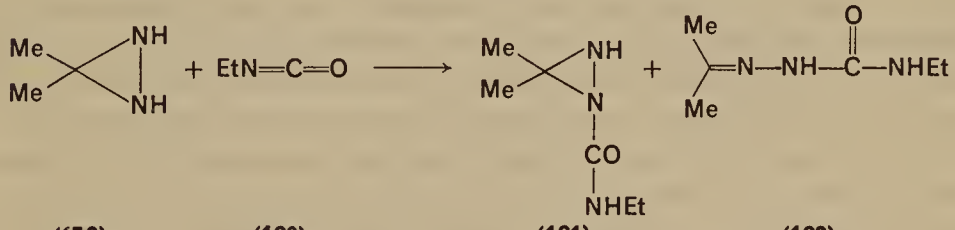
(equation 91) a diaziridine was found to give an addition product in which the ring was intact; however on mild heating **158** was readily isomerized to the corresponding hydrazone.



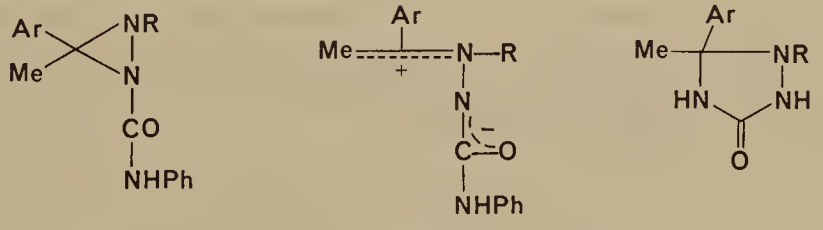
(91)

(158)

The adducts formed between diaziridines and isocyanates (equation 85) may undergo further reactions involving either an external nucleophile or an isomerization to form an open-chain or cyclized material. In addition to the expected substituted diaziridine **161**, the reaction of 3,3-dimethyldiaziridine (**159**) with ethylisocyanate (**160**) yields the semicarbazone **162**[161].



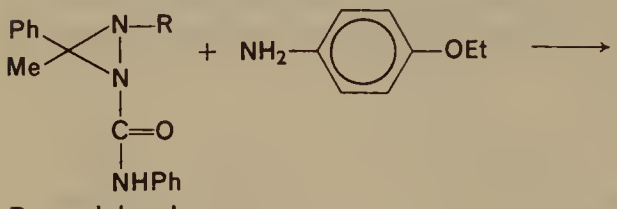
(159) **(160)** **(161)** **(162)**



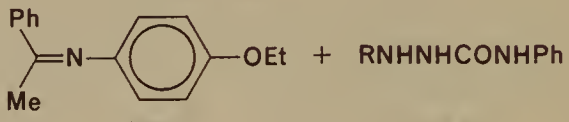
(163) **(164)** **(165)**

R = cyclohexyl.

The 1,3,3-trisubstituted diaziridine adduct **163** is isomerized to the more stable material **165**, which contains a five-membered ring, on mild heating[162]. The adduct **163** may also undergo reaction with *p*-phenetidine (at 100°C under nitrogen)[163]. In this case the products formed are the imine **166** and a semicarbazide **167**, and reaction mechanisms involving either direct nucleophilic attack on the diaziridine ring at carbon or trapping of an intermediate zwitterion (such as **164**) can be envisaged.



R = cyclohexyl.



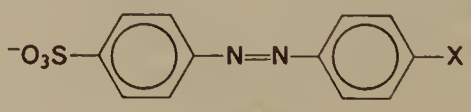
(166) **(167)**

III. AZO COMPOUNDS

A. Reaction with Acids

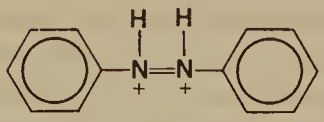
1. Basicity

Arylazo compounds are in general very weak bases and in the absence of special structural features are not protonated to any appreciable extent in aqueous solution. They are thus much weaker bases than the corresponding hydrazines. Protonation does occur in concentrated acid media and typically the pK_a values of substituted azobenzenes are in the region −6·0 to −1·0. Azobenzene itself is a particularly interesting example since the *cis* and *trans* isomers appear to have distinctly different pK_a values (−2·25 and −2·95 respectively)[163]. The relative basicities of substituted azobenzenes of type **168** have been correlated by means of the Ho function (using σ or σ^+ values) to give a ρ value of ca. −2·0[164]. The substituents therefore have an effect similar to that observed in the case of substituted anilines except that the sensitivity to substitutent variation is somewhat smaller ($\rho = -2{\cdot}7$ for protonation of substituted anilines)[165].



(168)

The structure of the protonated species formed from azobenzene has been the subject of debate. Two limiting structures are conceivable with either the proton being associated with a particular nitrogen atom or alternatively straddling the —N=N— bond, being equally bound to both nitrogen atoms[163, 166, 167]. Different types of σ values are used to correlate pK_a data for the *cis* and *trans* series (σ^- for *cis* and σ^+ for *trans*) and this has been interpreted in terms of a structure for *cis* azobenzenes in which the aryl rings are rotated out of the plane of the azo linkage and thus able to interact with the lone pair electrons on nitrogen[166]. The dipropionated *trans* azo-

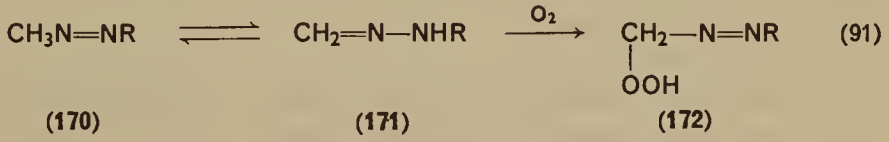


(169)

benzene **169** has also been observed by Olah in SbF_5—FSO_3H—SO_2 (magic acid) media at –80°C[5].

2. Tautomerism

Basicity data are not available for the aliphatic azo analogues since on dissolution in concentrated acid these undergo ready isomerization to the more stable hydrazone tautomer (equation 91). The cyclic analogues 1-pyrazolines are also tautomerized to the 2-pyrazoline form (equation



(91)

(170) **(171)** **(172)**

(92)

92)[168]. The possibility of the existence of tautomerism between phenylhydrazones (**171**, R = Ph) and phenylazoalkanes (**170**, R = Ph) and the question as to which is the more stable form if such an equilibrium existed remained unsettled[169, 170] until physical methods became available which could unambiguously distinguish between them. Disregarding resonance contributions it can be calculated that the hydrazone form **171** is favoured over the azoalkane by ca. 9 kcal mol^{-1}. Using i.r. and n.m.r. data Bellamy

and Guthrie[171, 172] showed that in non-polar solvents, the equilibrium between **170** and **171** lies almost completely on the side of the hydrazone. This view has since been confirmed by a number of workers, notably by Karabatsos[173, 174] and by Yao[175, 176]. O'Connor and co-workers[177–179] had earlier claimed that the reverse reaction (hydrazone → azoalkane) could be carried out under mild conditions in these solvents. However when oxygen was excluded, these reactions could not be repeated[171] so that it seems likely that the azo linkage formation observed by O'Connor was the result of reaction of the hydrazo form with oxygen (a reaction known to produce azo hydroperoxides **172**; the latter can be readily deoxygenated[180]).

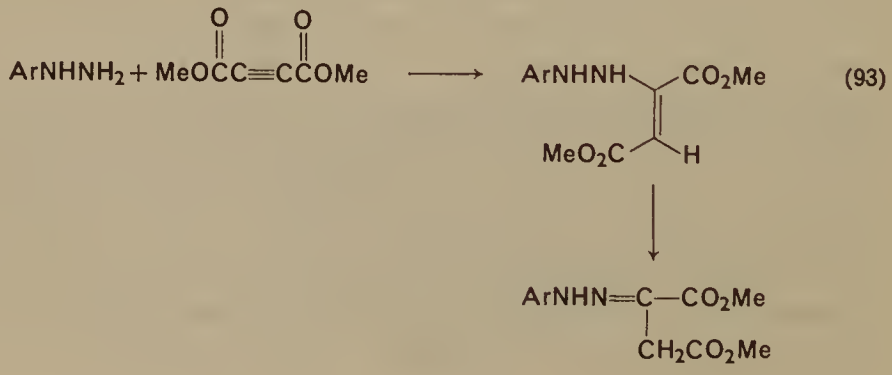
The situation may be different in polar solvents in the presence of strongly basic or acidic catalysis, and several studies have shown that equilibria may be set up under these conditions between hydrazone and azo forms with several per cent azo alkane (**171**) present[181]. In addition, azo compound may undergo a second tautomeric proton shift to form the ene-hydrazines (**173**)

$$RCH_2—CH_2—N{=}NR^1 \rightleftharpoons RCH{=}CH—NH—NHR$$

(173)

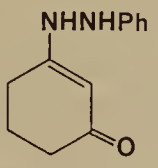
when hydrogens are available on the carbon atoms α- and β- to the azo linkage. In general in the absence of special structural features this form is less stable than either the azo or hydrazone forms[182]; however small equilibrium concentrations of the ene-hydrazine have also been observed in strongly acidic or basic solution[181]. In spite of its low equilibrium concentration, the ene-hydrazine form is postulated as the reactive species in the Fischer indole synthesis[183].

Special structural features may in some instances sufficiently stabilize the ene-hydrazine isomer to permit its isolation. Thus aryl hydrazines react with dimethylacetylenedicarboxylate to yield 1:1 adducts which exist as imine-enamine tautomers (equation 93)[184], while the ene-hydrazine



(93)

174[185, 186], and azo compound **175**[187] have been shown to exist in equilibrium with the hydrazone forms in solution.



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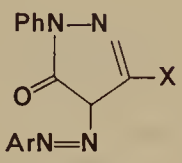
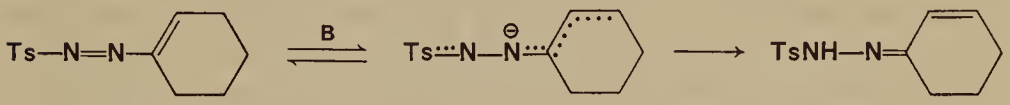


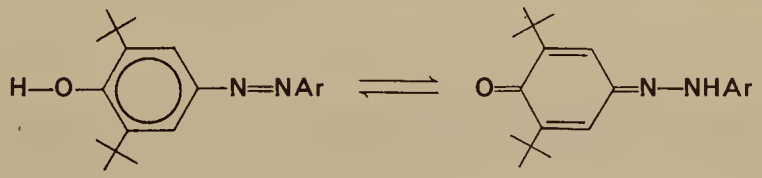
(175)

The spontaneous and base catalysed azo to hydrazo conversions of 1-tosylazocyclohexene **176** have also been investigated and a mechanism for the base catalysed process has been suggested involving the release of an allylic proton in the slow step (equation 94)[188].



(176) (94)

A study on the substituent effects on the azo-hydrazone tautomerism of 4-arylazo-2,6-di-(t-butyl)phenols (equation 95) has shown that the azo form is generally the more stable, although the hydrazone form may be stabilized by substituents capable of H-bonding to the —NH— group[189, 190]. This is



(95)

obviously a special case since the azo form is stabilized by the second aromatic nucleus[191].

B. Alkylation

The direct alkylation of azobenzenes with reagents such as alkyl halides is normally difficult, on account of the poor nucleophilicity of the azo linkage. However using more powerful alkylating agents such as methane trifluoromethane sulphonate or methylfluorosulphonate, mono-alkylated salts are readily obtained in 60–90% yield (equation 96)[192]. The effect of ring substituents on the ease of diazonium salt formation is quite marked.

$$PhN{=}\ddot{N}Ph + MeOSO_2R \longrightarrow Ph\overset{+}{N}(CH_3){=}NPh \quad (96)$$

$R = F, CF_3$

Generally when the substituents are not unalike then quaternization gave mixtures of the two structural isomers. When electron-withdrawing groups are present (e.g. with *p*,*p*′-dichloroazobenzene and *p*,*p*′-dinitroazobenzene) no reaction is obtained whereas with *p*-chloroazobenzene just one of the possible isomeric methylated salts is obtained; as expected the product here results from attack by the nitrogen adjacent to the phenyl (rather than *p*-chlorophenyl) ring.

Other methods which have been reported for the alkylation of azobenzene derivatives also involve concomitant reduction so that the products formed are actually alkylated hydrazine derivatives. The reaction of carbanionic reagents with azobenzenes has been investigated in detail by Kaiser and co-workers[193], who reported that under appropriate conditions ionic addition across the double bond could be achieved. A side reaction which interferes in ether solution is the transfer of an electron from the carbanion to the azo group, resulting in reduction of the azo linkage (and isolation of the oxidative dimer of the carbanion)[194]. In liquid ammonia, however, the major reaction of alkali metal salts of active hydrogen compounds with azobenzenes is the formation of tri-substituted hydrazines

$$Ph_2CH_2 + MNH_2 \rightleftharpoons Ph_2CH^-M^+ \xrightarrow[(2)\ NH_4Cl]{(1)\ PhN{=}NPh} Ph_2CHN(Ph)\text{—}NHPh \quad (97)$$

(177)

(equation 97). The highest yields of product are obtained by using sodium or potassium cations for relatively short reaction times; this was rationalized in terms of the formation of **177** as a kinetically controlled product. The presence of the anion **178** on the reaction pathway was indicated by a trapping reaction involving benzoyl chloride (in which case **179** was isolated among the products). The alkylation (equation 97) appears to be

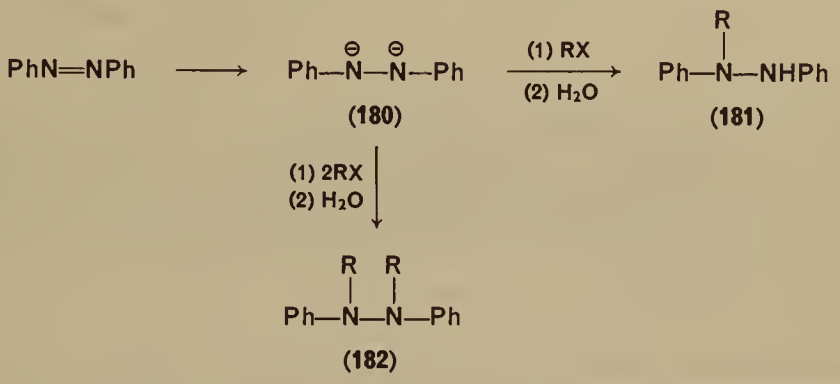
$$Ph_2CHN(Ph)\text{—}\overset{\ominus}{N}Ph \xrightarrow{PhCOCl} Ph_2CHN(Ph)\text{—}NPh(COPh)$$

(178) **(179)**

quite general and good yields of the hydrazines were obtained using a wide variety of active methylene compounds (e.g. 2-methylquinoline, 2-phenyl-

acetanilide, picolines, etc.) and with substituted azobenzenes.

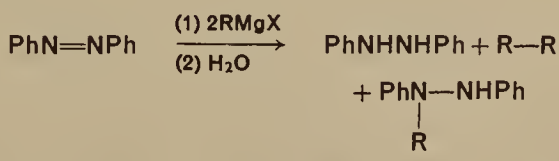
An alternative alkylation procedure (which also results in the reduction of the azo linkage) makes use of the ready formation of hydrazobenzene dianions (**180**) on treatment of azobenzenes with lithium, sodium or potassium[195, 196]. The di-anion may be mono-alkylated (**181**) with alkyl halides; dialkylation (**182**) is also possible, particularly with less hindered alkylating agents. Typically liquid ammonia is used as solvent[197] for these



reactions but aprotic solvents such as tetrahydrofuran have also been successfully used. Phenyllithium has also been used to arylate azobenzene. However the yield of 1,1,2-triphenylhydrazine is only 20%, most of the

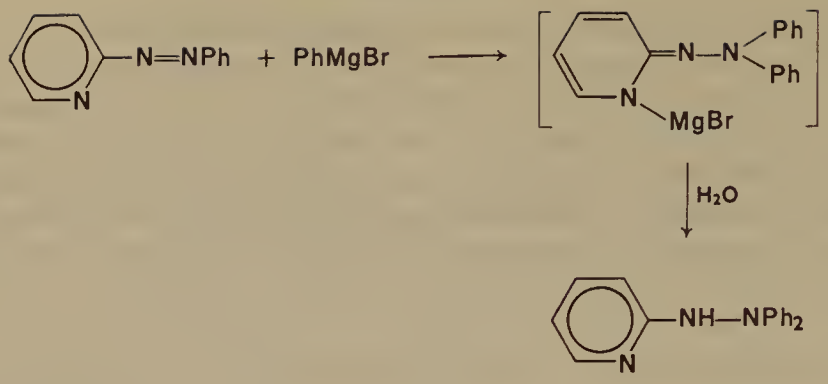
(98)

substrate being reduced to hydrazobenzene (equation 98)[198]. Grignard reagents react similarly to form dianions, and ultimately reduction products; the organic moiety of the Grignard reagent is usually dimerized or else disproportionation occurs (equation 99)[199]. Some alkylation (or



(99)

arylation) products are also observed[200]. One example in which the arylated product represents >80% of the product formed is illustrated in equation (**100**)[201]. It has been shown that *ortho*-substituted azobenzenes, unlike *m*- and *p*-isomers, undergo aromatic arylation with arylmagnesium bromides at the free *o*-positions to the azo group. Thus 2-methoxy and 2-methylazobenzene give 2-methoxy-2′,6′-diaryl and 2-methyl-6-arylazobenzene res-



(100)

pectively[202]. Some reduction of the azo linkage also occurs as a side reaction. 2-2′-Disubstituted symmetric azobenzenes do not undergo the arylation, while the presence of a large *o*-substituent also reduces the amount of C-arylation, presumably by reducing the coplanarity of the azo group with the reacting ring.

C. Reaction with Peracids

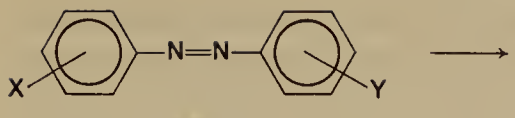
The reaction of peracids with azo compounds is one of the most characteristic reactions of the latter and has been studied in some detail[203–205]. In most cases the primary oxidation product is the corresponding azoxy compound, and a reaction mechanism involving electrophilic attack by the reagent on the azo linkage has been proposed. Several workers have shown that the stereochemistry of the starting azo compound is retained in the azoxy product, i.e. that *cis* and *trans* azobenzenes gives isomeric azoxy benzenes on treatment with peracids (equations 101 and 102)[206, 207]. Since

(101)

(102)

two possible azoxy compounds may be formed when the aryl rings of the starting azobenzene are not symmetrically substituted, four isomeric azoxy compounds are therefore possible.

The ratio of the two azoxy compounds (**184** and **185**) obtained from a given unsymmetrically substituted azobenzene (**183**) is dependent on the relative electron withdrawing or donating powers of the substituents X and Y[208]. In general if these are not too different (e.g. X or Y = *p*-Br, Cl, H, Me) then both materials are obtained, the predominant isomer having the



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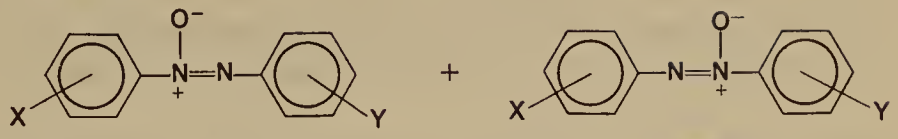
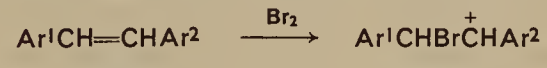


(184) (185)

azoxy group adjacent to the ring which carries the strongest electron-donating substituent[209]. With strongly electron donating or withdrawing substituents (X or Y = *p*-NO_2 or *p*-MeO) the difference in the nucleophilicities of the two nitrogens is such that only one azoxy isomer is isolated.

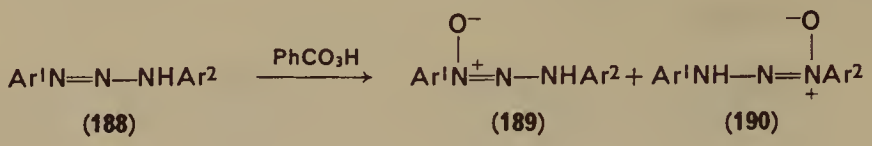
Some detailed kinetic studies have shown that the reaction of substituted azobenzenes with perbenzoic acid follows good second-order kinetics when the peracid is purified to eliminate the presence of benzoic acid (which acts as a catalyst). Light must also be excluded since this promotes the decomposition of the peracid. A good correlation has been reported when log k_2 (for the reaction of the substituted azobenzenes with perbenzoic acid) *vs.* the corresponding Hammett σ values (ρ is ca. $-1{\cdot}6$)[207]. Interestingly when the azobenzene is multiply substituted (in either ring, *m*- or *p*-positions) then simply the sum of the σ values of the various substituents is used to obtain a good correlation. This implies that the transition state for the reaction is symmetrical, the incoming electrophile being approximately equally bonded to both nitrogens; the product determining step (which determines which azoxy isomer is obtained from an unsymmetrically substituted azobenzene) evidently occurs *after* the rate determining step. This contrasts with the observed behaviour of the carbon analogues, *trans*-stilbenes **186**, towards electrophiles. In the bromination of stilbenes it has been unequivocally demonstrated that the carbonium ion intermediate formed **187** is always oriented towards the aryl ring (say Ar^2) providing the greatest stabilization (i.e. that containing the most electron donating substituent[210]).



(186) (187)

The formation of 1,3-diaryltriazene-1-oxides **189** and **190** by the reaction of diazoaminobenzenes with perbenzoic acid appears to follow the same pattern as that observed for azobenzenes[211]. An electron releasing substi-

tuent in Ar^1 directs the oxygen to the nearest nitrogen atom; thus a plot of the log of the isomer ratios (**189**:**190**) against the difference in the σ^+ values



for the substituents in Ar^1 and Ar^2 gives a good correlation (with $\rho = -1{\cdot}3$). Kinetic studies show that again good correlations are obtained when $\log k_2$ is plotted against the sum of the σ's (Brown and Okamoto σ^+ values are used) of substituents in Ar^1 and Ar^2. A mechanism is therefore proposed[211] in which the oxygen atom from peroxybenzoic acid is bonded to both nitrogen atoms at 1- and 3- in the transition state; this rapidly collapses to give the isomeric *N*-oxides in a ratio determined by the nature of the substituents. The ρ value obtained for the bimolecular reaction in the case of the diazoaminobenzenes is smaller ($\rho = -0{\cdot}87$) than that reported for azobenzenes ($\rho = -1.6$), reflecting the fact that an extra nitrogen atom is available in the former series to share in the delocalization of charge in the transition state.

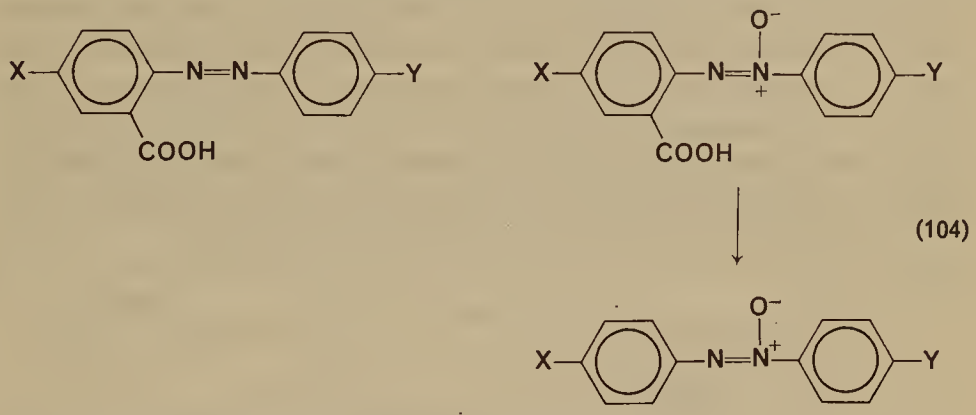
Azo compounds with mixed aryl and alkyl substituents normally react with peracids to form azoxy compounds with the oxygen adjacent to the aryl rather than the alkyl group (equation 103)[212]. Apparently resonance

(103)

stabilization provided by the adjacent phenyl group during the reaction is more important than the greater ground state nucleophilicity of the nitrogen adjacent to the alkyl group.

The presence of *ortho* substituents in one of the aryl rings can have a profound effect on the position of attack of the peracid reagent[213]. In general the azoxy compound formed predominantly (or exclusively) in this case has the oxide group remote from the *ortho*-substituent, independent of the other substituents present. The *o*-substituents which show this behaviour were *o*-(Me, MeO, Cl, CO_2H, CO_2Me and OAc). An exception is the *o*-HO group which favours oxidation of the nitrogen adjacent to the *o*-substituted ring, possibly by directing the incoming reagent by the formation of an H-bond between the *o*-HO group and the remote nitrogen, thus reducing the latter's nucleophilicity[214]. The formation of an azoxy benzene with >98% isomeric purity in the case of the *o*-COOH substituted azo-

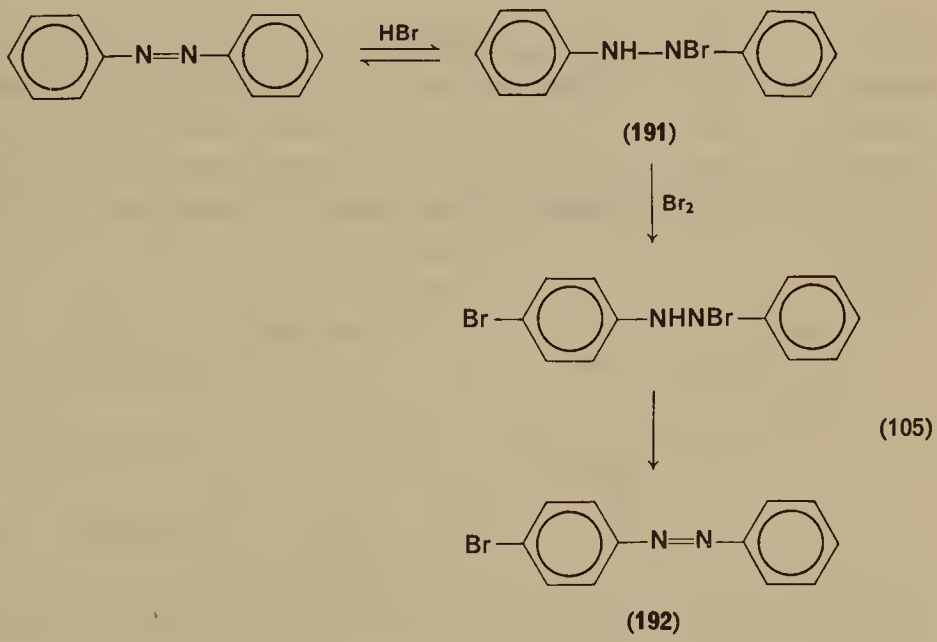
benzenes is particularly interesting since the carboxyl group can be readily removed. This pathway (equation 104) therefore provides a two-step synthesis of unsymmetrically substituted azoxybenzenes which is regioselective. A single product is also obtained by this route when the *p*-substituents X and Y are reversed (in contrast to the mixed products which would result from direct oxidation of the azobenzenes without the *o*-substituent).



(104)

D. Electrophilic and Nucleophilic Substitution

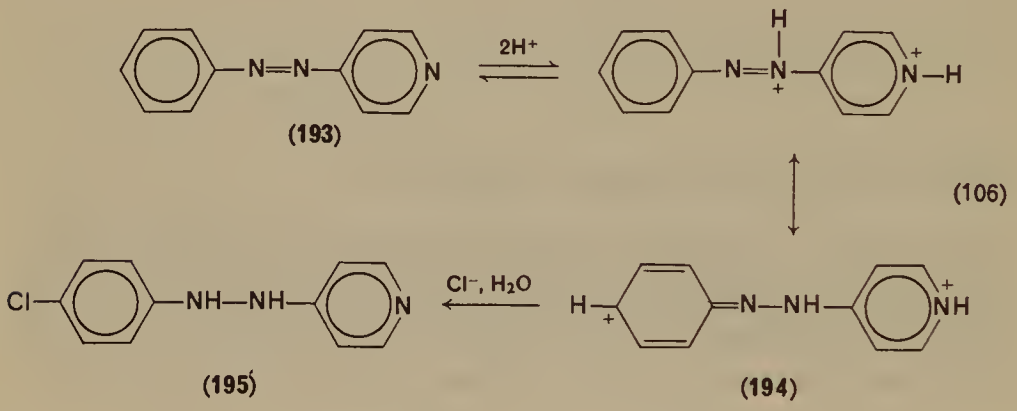
The presence of the azo group has a strong deactivating effect on a neighbouring aryl ring. It is difficult therefore to substitute the aryl azo ring using the normal electrophilic reagents. Indirect or catalytic methods are thus generally used. A possible example which may involve reversible electrophilic addition to the azo linkage is shown in equation (105).



(105)

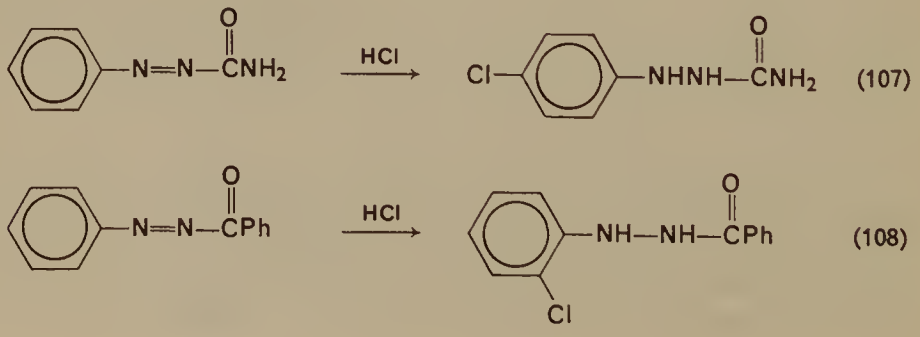
Robertson and Hitchings[215] have shown that bromination of azobenzene in acetic acid is catalysed by the presence of HBr. A possible mode of involvement of the catalyst (equation 105) involves the formation of the adduct (**191**), one of the aryl rings of which is then activated towards electrophilic attack by bromine. Dehydrobromination then gives the observed product *p*-bromoazobenzene (**192**).

Alternatively the mechanism of this reaction may not involve bromine acting as an electrophile but rather as an oxidizing agent on the final product; introduction of the halogen may have occurred via nucleophilic attack on the protonated azobenzene. This latter mode of reaction appears quite general and is illustrated by the reaction scheme outlined in equation (106). 4-Phenylazopyridine (**193**) on treatment with hydrochloric acid in



(106)

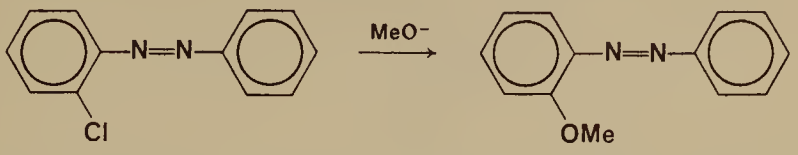
methanol gives the *p*-chlorophenylhydrazo compound **195** in good yield. A possible mechanism involves protonation of the azo linkage, followed by nucleophilic attack by Cl^- at the *p*- (or *o*-) position of the *N'*-phenyl ring. Note that the resonance form **194**, a substituted hydrazone, should be particularly stabilized. Further examples are given in equations (107)[217] and (108)[218].



(107)

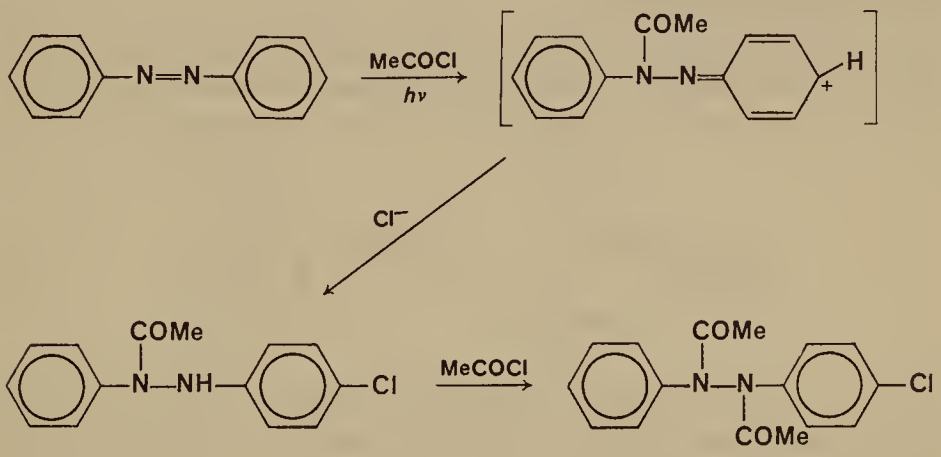
(108)

The azo group, being electron-withdrawing, activates the aryl rings to direct nucleophilic attack by strong nucleophiles. Thus *o*-chloroazobenzene reacts with methoxide ion in methanol to give *o*-methoxyazobenzene by displacement of chloride ion [equation (109)].

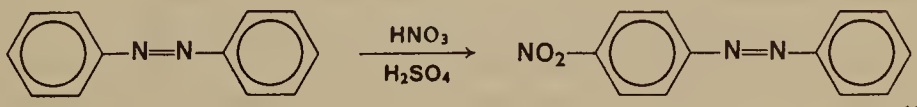


(109)

A similar mechanism involving nucleophilic halide ion attack on an activated aromatic nucleus is probably also involved in the formation of *p*-chloro-*N*,*N'*-diacetylhydrazobenzene on acetylation of azobenzene with acetyl chloride. Substitution probably occurs via the mono-acylated intermediate **196**[220].

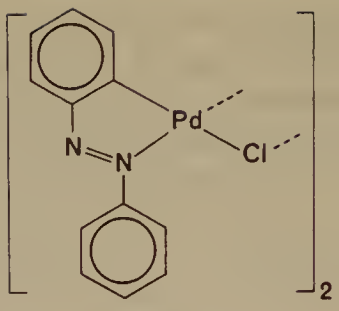


The direct nitration of azobenzene occurs, but is slow (equation 110)[221]. When the *p*-positions are filled (e.g. when *p*,*p'*-dichloroazobenzene is used as susbstrate) some *o*-substitution occurs but a major part of the substrate may be converted to the corresponding azoxy compound[222]. Substitution of chlorine into the *ortho*-positions of azobenzene has been observed in the



(110)

chlorination of azobenzene catalysed by palladium chloride[223]. The reaction is homogeneous and the intermediacy of a complex such as **197** has been

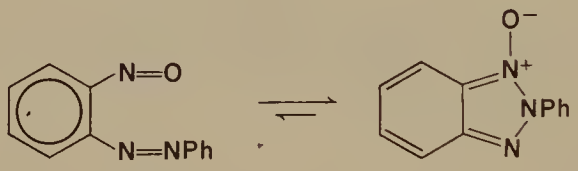


(197)

implied. *Ortho* substitution alone occurs and long reaction times give multiple substitution; for example after 16 h, the product composition is 2-Cl (12%), 2,6- (22%), 2,2′ (30%), 2,6,2′ (33%), 2,6,2′,6′ (3%). Longer reaction times yield up to 40% tetrachlorinated material.

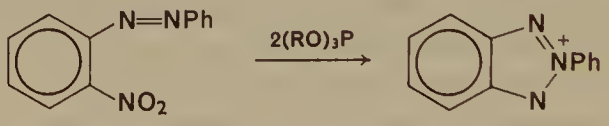
E. Intramolecular Reactions

Spontaneous cyclization occurs when a nitroso function is generated adjacent to an azo linkage. Thus *o*-nitroso azobenzenes have been shown to exist in the form of 2-aryl-benzotriazole-1-oxides (equation 111)[224]. The



(111)

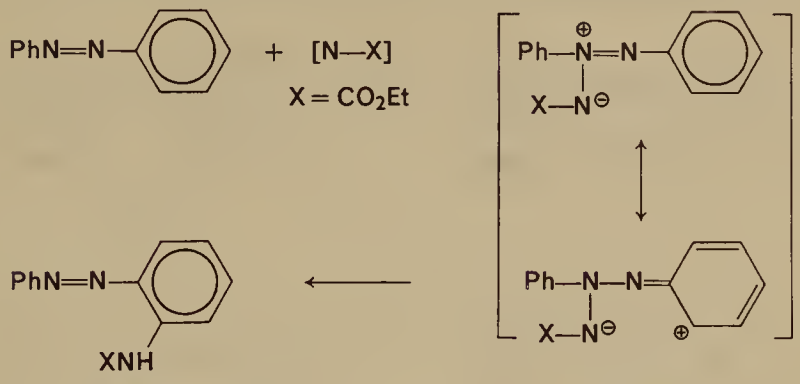
generation of an electrophilic nitrene species adjacent to the azo group also results in cyclization (equation 112); the products in this case are the corresponding azimines[225, 226].



(112)

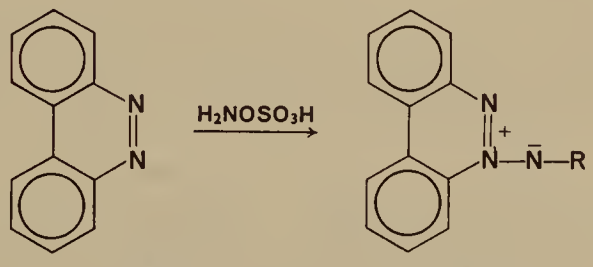
Since azobenzenes can be isolated in good yield from reactions in which aryl nitrenes are produced as intermediates, it has been suggested[229] that the reactivity of these species towards azobenzene in intermolecular reactions is not high. In an attempt to carry out such an intermolecular reaction with azobenzene Kerber[230] found that the main product isolated from the reaction of ethyl azidoformate (on thermolysis) with azobenzene was ethyl-2-(phenylazo) carbanilate (**198**) which could conceivably have

been formed by the rearrangement of the azimine (**199**). Such rearrangements are not likely for steric reasons in the cyclic analogues (equation 112).



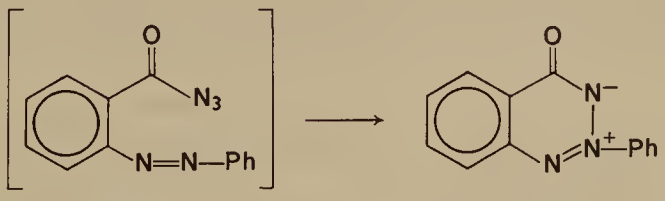
(198) (199)

The formation of the azimine **201** (in low yield) has however been reported from the amination of benzocinnoline **200** with hydroxylamine *O*-sulphonic acid[231]. An *o*-acyl nitrene has also been proposed as an



(200) (201)

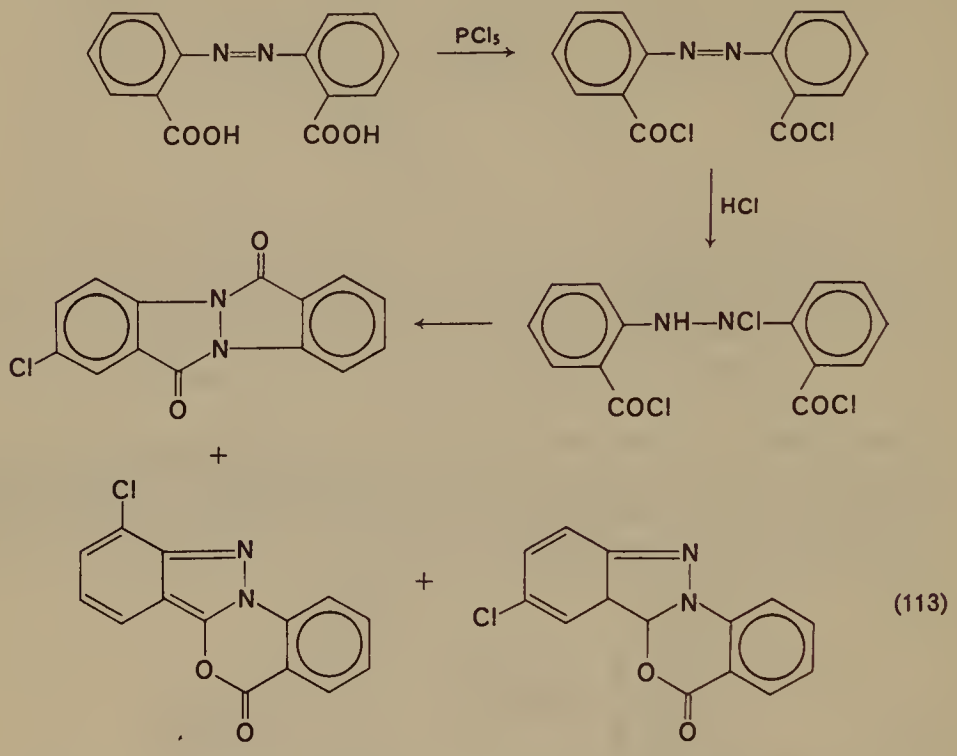
intermediate in the cyclization of the acylazido compound **202**. In this case however several side reactions intervene and the azimine is isolated in low yield[230].



(202) (203)

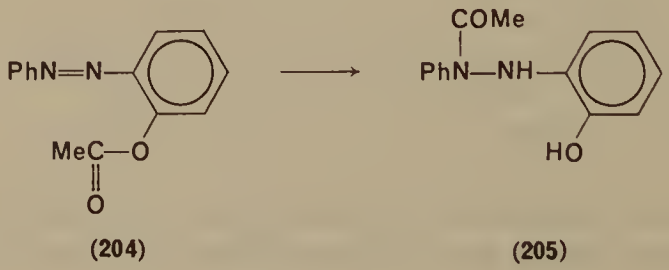
Treatment of azobenzene 2,2′-dicarboxylic acid with phosphorus pentachloride (which is known as the Freundler reaction[232]) has been

shown to give three isomeric major products all of which involve the interaction of the *o*-carboxy group with the azo linkage[233]. In each case nuclear chlorination accompanies cyclization (see equation 113).



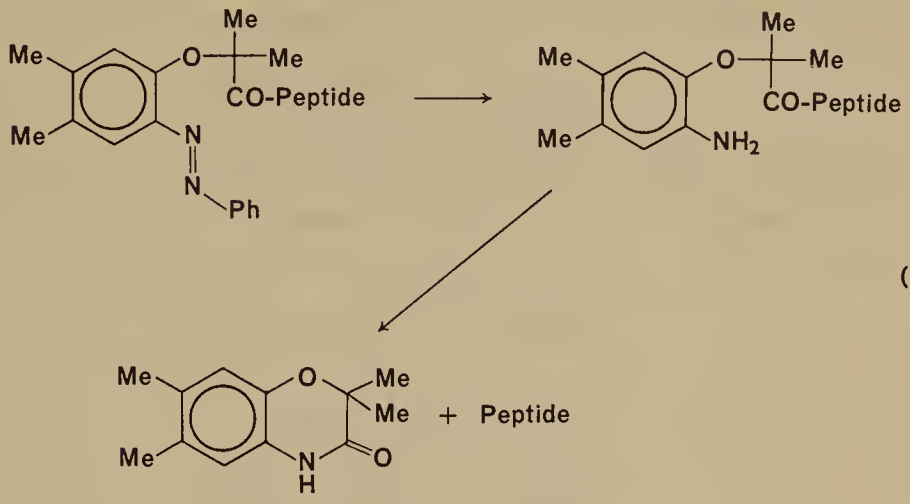
(113)

An unequivocal direct intramolecular acylation of azobenzene has not been reported, but facile acyl transfer can occur under reducing conditions. Thus treatment of the *o*-acetoxybenzene derivative **204** with sodium amalgam results in the formation of the *N*-acyl material **205**[234]. In this case it is like that reduction to the hydrazo compound preceded the intramolecular acyl transfer. The poor nucleophilicity of the azo group even when adjacent to an acyl linkage has led to the use of substituted phenylazo compounds as *N*-protecting groups in peptide synthesis. An example is given in equation (114)[235]. To remove the blocking group it is necessary to



(204) **(205)**

cleave reductively the azo bond. Intramolecular nucleophilic attack (aided by the *gem*-dimethyl groups) by the amino group can then occur to release the peptide.



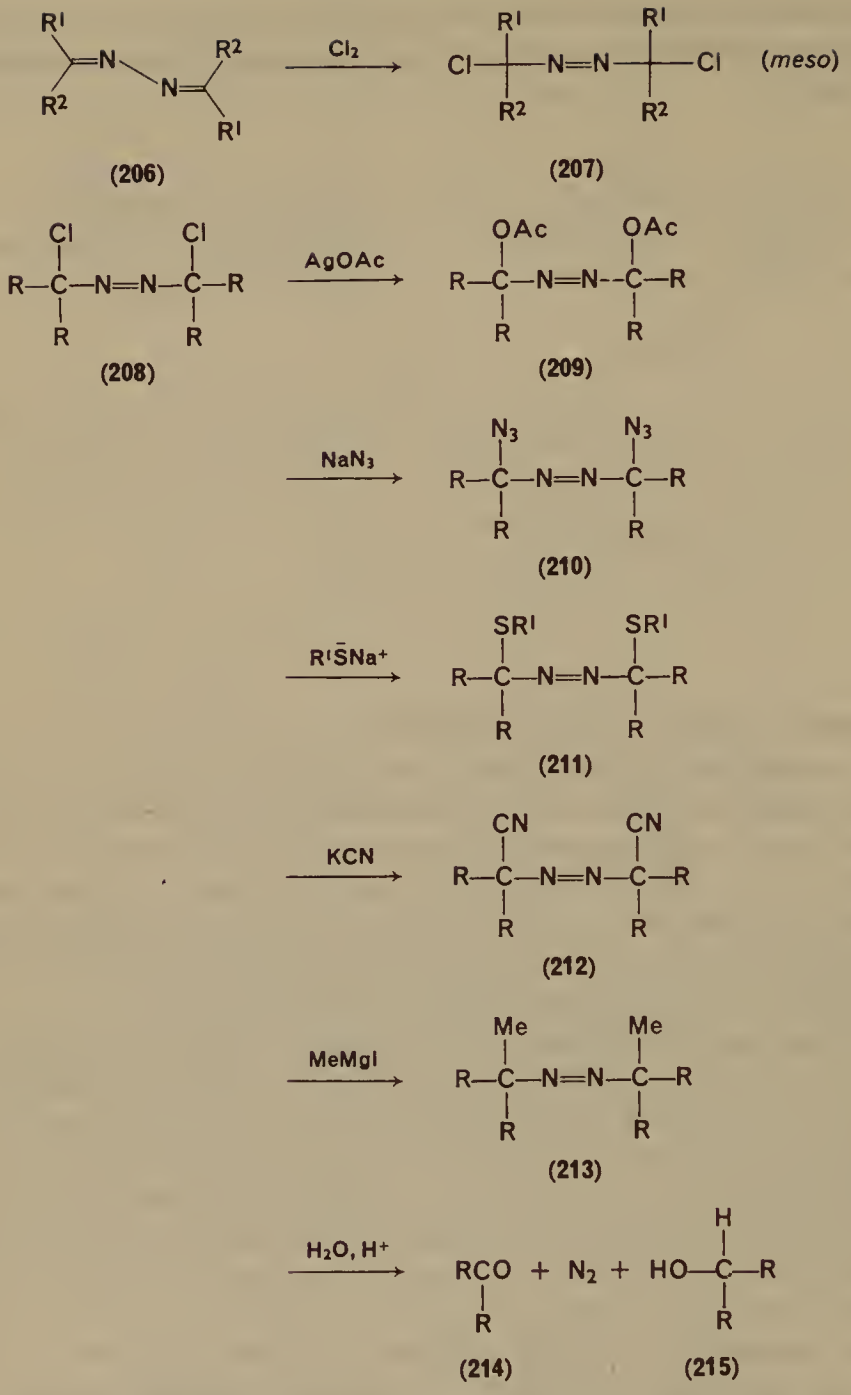
(114)

F. Reactions Adjacent to the Azo Group

In general azoalkanes undergo smooth photochemical or thermal decomposition to produce radical pairs with the loss of nitrogen. This has been a widely studied reaction and azoalkane derivatives (such as the azo-bisnitriles) have found acceptance as radical initiators. α-α′-Dichloroazoalkanes (**207**) may react similarly to produce free radical species but, more interestingly, recent studies have shown that the chloride is labile and could be replaced (by an ionic mechanism) by other nucleophiles.

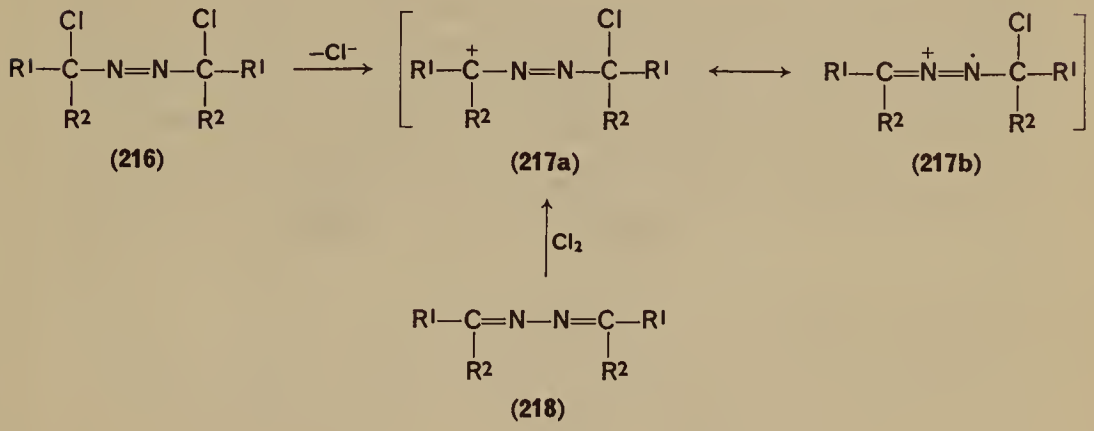
The α,α′-dichloroazoalkanes are best prepared by the 1,4-chlorination of the corresponding 2,3-diazabuta-1,3-dienes at −60°C in the absence of solvent[236, 237]. The chlorination reaction, which has been shown to be ionic (rather than free radical) proceeds stereospecifically so that symmetric ketazine **206** isomers give, for example *meso*-α,α′-dichloroazoalkanes[238].

The chloride groups can be replaced by acetate (**209**) azide (**210**) mercaptide (**211**) and cyanide (**212**)[237] and, in the presence of excess methylmagnesium bromide[239] or methylmagnesium chloride[240], the alkyl products **213** are obtained in 15–50% yield. Efforts to introduce alkyl or aryl groups using methylmagnesium iodide[239, 240] or phenylmagnesium bromide[237] or phenyllithium[240] led only to ketazine formation. However Ruchardt and co-workers[241] have recently shown that t-azoalkanes can be prepared in good yield (80–100%) from α,α′-dichloroazoalkanes (of type **208**) using excess trialkyl or triphenyl aluminium in petroleum ether at −70 to 0°C.

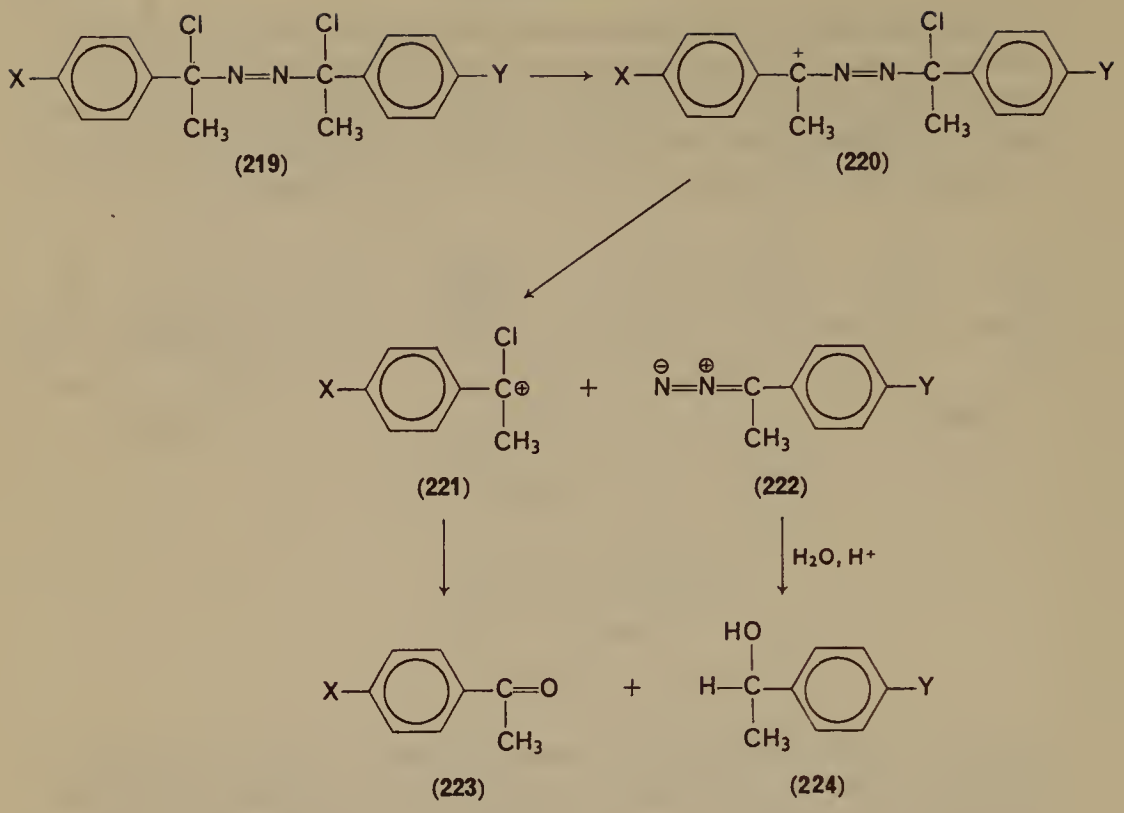


In aqueous organic solvent mixtures the dichloro materials **208** react rapidly to give as principal products a ketone (**214**), alcohol (**215**) and nitrogen; in addition smaller amounts of unsaturated materials and alkyl chlorides have been reported among the products[237].

It appears that the replacement reactions share a common mechanistic pathway in which the rate determining step is a unimolecular C—Cl bond fission to form an aza-allene type cationic intermediate **217**. It is likely that the ionic chlorination also proceeds through the formation of such an intermediate[238]. Benzing[237] has shown in kinetic studies, using sym-

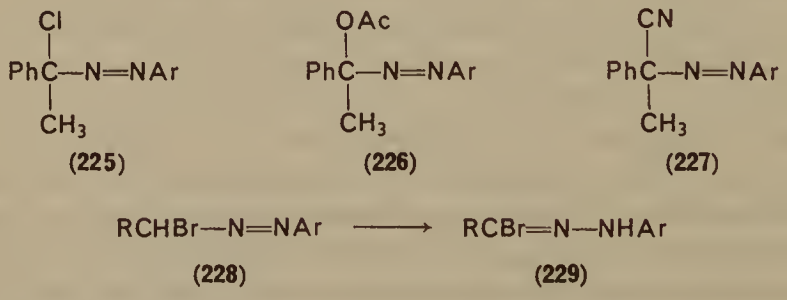


metrically disubstituted aliphatic substrates (**216**, $R^1 = R^2 = Me$) that the solvolysis reaction (in 85% aqueous acetone) is very sensitive to the ionic strength of the medium. Moreover the rate of solvolysis is depressed by the addition of Cl^-, which is presumably reacting with an intermediate (such as **217**) which is sufficiently long lived to discriminate between the various nucleophiles in solution. When unsymmetrical diaryl substrates (**219**) are used, the chloride ion which is first displaced is that adjacent to the aryl group with the more electron donating substituent. Because of the unsymmetrical nature of **220** the second substituent Y has a relatively small effect on reactivity. Thus a Hammett plot of $\log k_{obs}$ vs. σ is curved for monosubstituted substrates (**219**, Y = H), electron-donating substituents having a much larger effect than electron-withdrawing substituents $\rho = -2{\cdot}5$ and $-1{\cdot}1$ respectively)[242]. The azocarbonium ion intermediate **220** undergoes further reaction to form the diazoalkane **222** and ketone **223**. The diazoalkane intermediates (which are stable in basic solution) have been identified spectrally and, in some cases, by actual isolation. Rapid nitrogen loss in acid occurs to form the corresponding alcohols **224**. The ketone and alcohol formed when $X \neq Y$ however are not those expected if the azocarbonium ion **220** decomposes directly to give the diazoalkane **222** and carbonium ion **221**. In all cases the most stable materials (i.e. with Y electron-withdrawing and X electron donating) are formed. An extra step is therefore involved in the reaction sequence, and the migration of Cl^- in **220** to the carbonium ion



centre (possibly via a bridged intermediate) has been suggested[241]. The formation of such a bridged intermediate would, of course, also explain the observed stereospecific chlorination of the ketazines **206**[240].

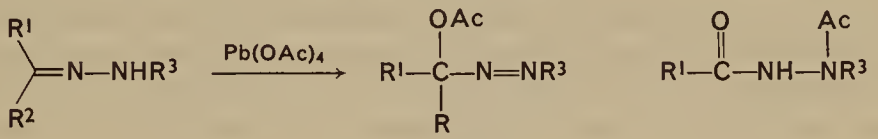
Two examples of compounds with a single halo group to the azo linkage are also known. Moon[97] has reported the synthesis of **225** (Ar = 2,4,6-$Cl_3C_6H_2$—) at −60°C by chlorination of the acetophenone 2,4,6-trichlorophenylhydrazone in chloroform. Although the replacement reactions were not studied in detail, it is probable that they parallel those for the corres-



R = sugar moiety.

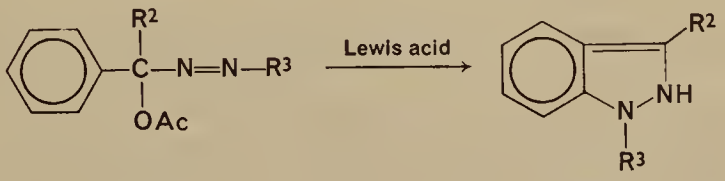
ponding α,α′-dichloroazoalkanes **216**; the azo acetate **226** and the cyano compound **227** are formed by reaction with sodium acetate and potassium cyanide respectively. The α-bromo compound **228** has also been reported, but the only further reaction which has been reported is the tautomerism to the more stable hydrazonyl bromide **229**[96].

Azoacetates **230** are readily formed on treatment of the corresponding hydrazones with lead tetracetate[243]. The reaction appears to be general for ketone hydrazones but examples are also available in which such acetates are obtained from aldehyde hydrazones[99, 244]. In the latter case (R = H) tautomerism to the hydrazone is possible and the products isolated are generally *N*-acylhydrazides (after O → N acyl group migration); an alternative direct mechanism of formation of the products **231** via a nitrilimine intermediate has also been suggested.



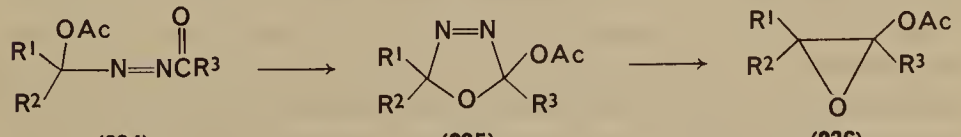
(230) **(231)**

The azoacetates **230** may undergo deacylation or reaction with suitable groups in R^1 or R^3. Thus on treatment with Lewis acids, azoacetates **232** are cyclized to 3-alkyl-1-arylindazoles **233**[245]. Cyclization is limited however to



(232) **(233)**

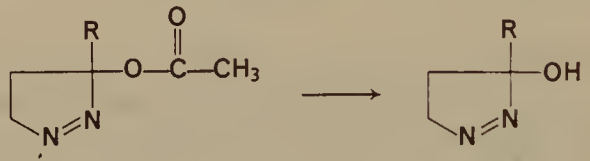
those systems in which R^3 contains electron withdrawing groups[246]. The azoacetates **234** are particularly reactive and may cyclize at room temperature to Δ^3-1,3,4-oxadiazolines (**235**); the latter lose nitrogen on heating yielding epoxides (**236**)[247, 248]. An ionic mechanism has been



(234) **(235)** **(236)**

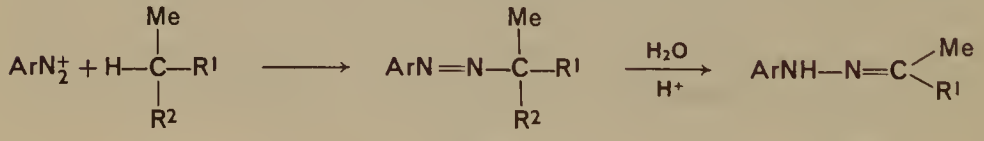
suggested for the cyclization in which the loss of acetate is rate determining[247] (this is analogous to the mechanism suggested for the solvolysis of the α,α′-dichloroazoalkanes above). Cyclic azoacetates **237** have also been isolated and characterized[249]; on hydrolysis in mildly basic solution deacetylation occurs and the α-hydroxy azo materials are formed. The latter can be reacylated with e.g. 2,5-dinitrobenzoyl chloride. On treatment with acid or base however **238** (or **237**) undergoes ring opening to form ketonic products. The latter appears to be a general mode of decomposition for azo acetates since compounds **230** on treatment with base in ethanol are reported to yield ethyl acetate, a ketone (R^1R^2CO), nitrogen and a hydrocarbon (R^3H)[250]. Several other cyclizations which may involve the intermediate formation of azo acetates (which were not isolated) have also been reported[243].

Azo compounds with a variety of substituents α- to the azo linkage are also formed as intermediates during the Japp–Klingemann coupling of aryl diazonium salts with active methylene compounds. The intermediate azo materials **239** can normally be isolated if the coupling is carried under neutral conditions; otherwise R^2 is expelled and the final products isolated



(237) (238)

are hydrazones (**240**)[251, 252]. An interesting reversal of the coupling re-



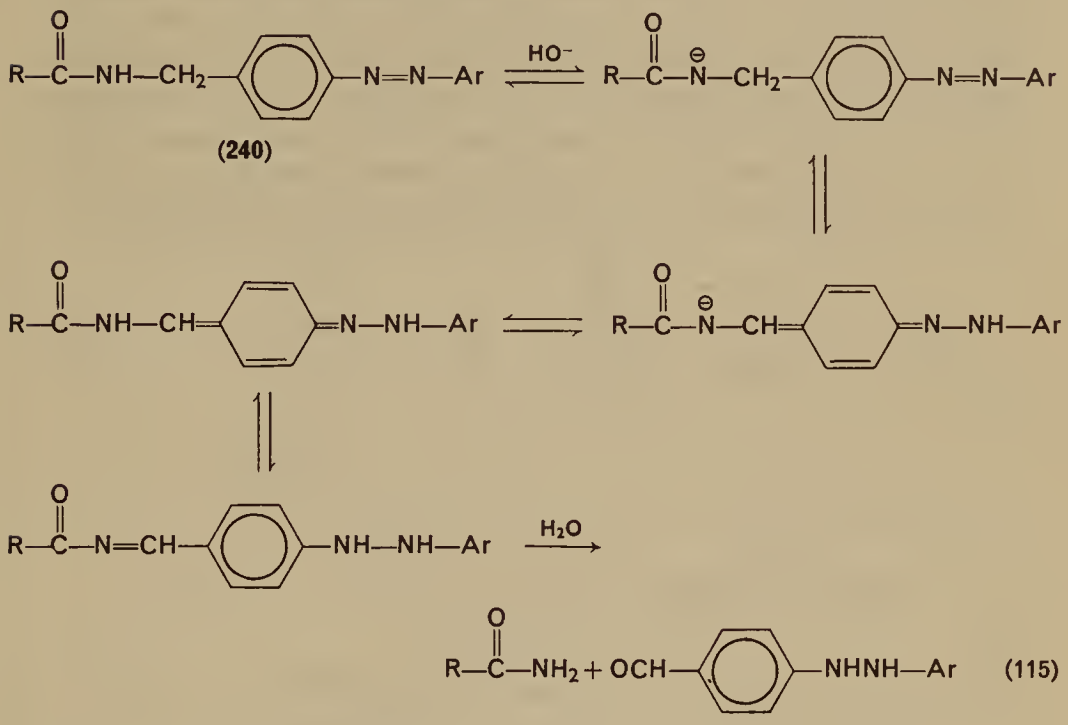
(239) (240)

R^1 = CONHPh, $CONH_2$, CO_2Et
R^2 = CN, NO_2, COPh, COMe

action, to reform the diazonium salt, occurs when **239** is treated with BF_3[251].

A particularly interesting example in which a remote azo group influences the course of a reaction has been reported by Stodola[253]. The amides **240** are hydrolysed by hydroxide, but contrary to most amide cleavages, the reaction is characterized by alkyl-nitrogen bond fission. Moreover the azo

group undergoes reduction during the course of the reaction. The mechanism proposed is outlined in equation (115); part of the driving force for the reaction stems from the tautomerism of the azo to hydrazo from followed by hydrolysis of the resultant imine. The reaction appears quite general with Ar = aryl; R may be alkyl or aryl.



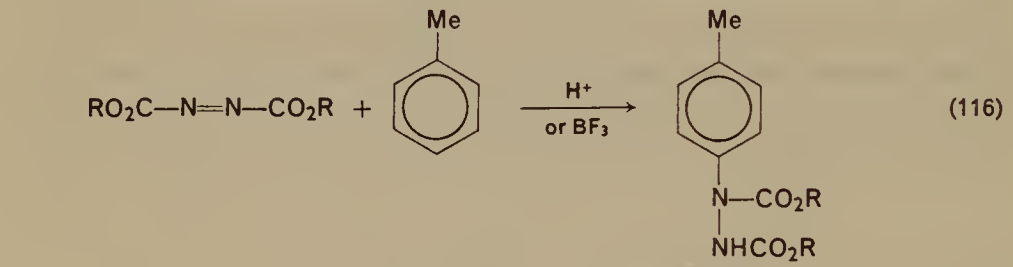
(115)

G. *Electrophilic Azo Compounds*

Azo compounds with strongly electron withdrawing groups such as —CN, —CO_2R or —COR, attached directly to the azo linkage can be highly reactive towards nucleophilic reagents. They are thus unlike 'normal' azo compounds (such as azobenzene) and are treated separately. Besides those reactions which proceed by an ionic pathway (and these include most of the electrophilic reactions), carbonyl azo compounds also undergo free radical reactions and concerted cycloadditions; their chemistry has also been reviewed[254, 255].

Some of the ionic reactions which have been observed are summarized in equations 116–128. Electrophilic substitution of an activated aromatic nucleus (equation 116) is quite general; the reaction is catalysed by Lewis acids[256, 257]. With aromatic amines, however, attack at nitrogen can be favoured leading to triazine formation (from primary and secondary amines)[258] or de-*N*-alkylation with tertiary amines, such as *N*,*N*-dimethyl-

aniline[259] (see also equation 117)[260]. Similar substitution reactions have also been reported with activated alkenes (equation 118)[261]. With diazoalkanes electrophilic attack by the azo group also occurs yielding, on loss of nitrogen, oxadiazolines or hydrazones (equation 119)[262]. Alkylation of activated methylene compounds, usually as sodium salts or in the form of Grignard's, leads to the formation of substituted hydrazines (equation 120)[263]. Electrophilic attack on aldehydic hydrazones (as with other electrophilic reagents, see Section II, E) is on carbon to yield initially azo hydrazines. The latter readily tautomerize and are converted to triazoline derivatives (equation 121)[264]. Thioureas react with diethylazo-dicarboxylate to form isolable intermediates which are cleaved by triphenylphosphine; the overall reaction provides a good route to carbodiimides (equation 122)[265].



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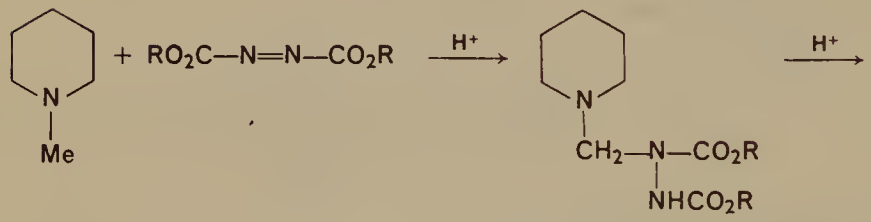

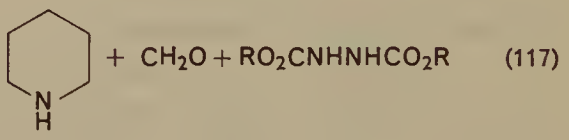

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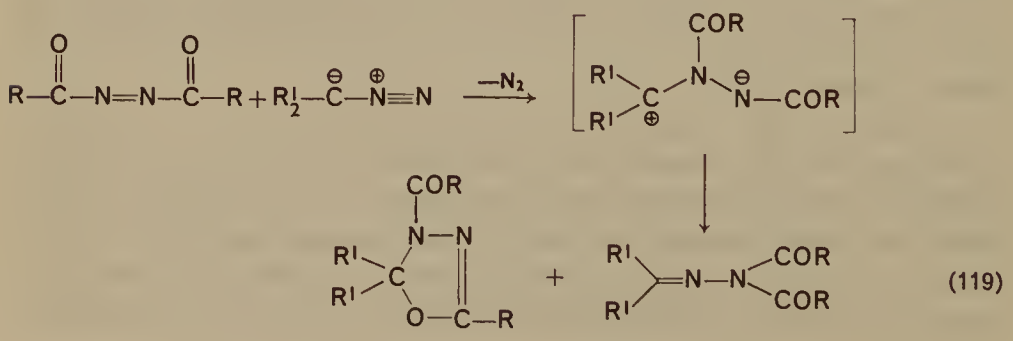
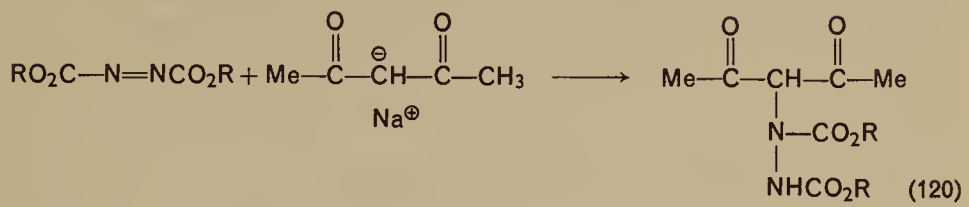


(119)

Addition of triarylsilanes and germanes has also been reported to occur via dipolar intermediates (equation 123)[266].



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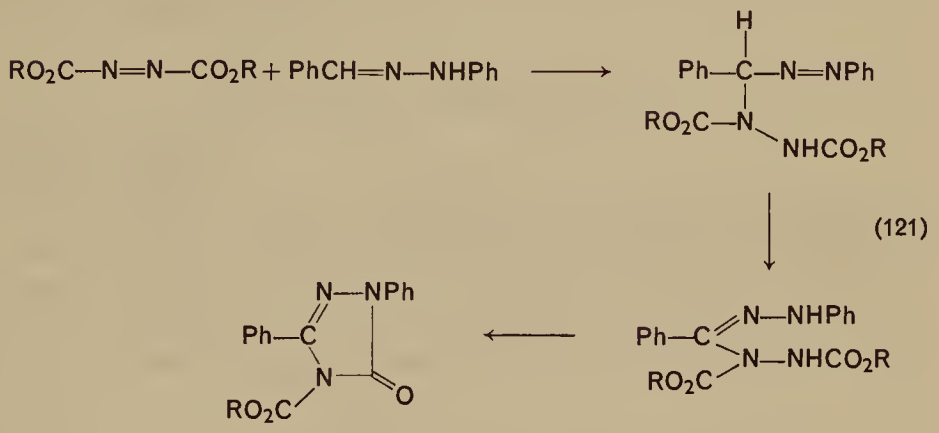

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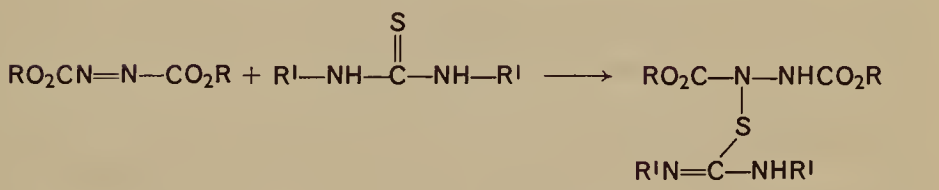
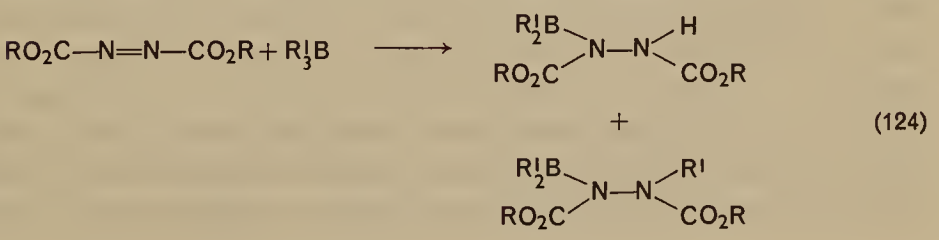


(122)

(123)



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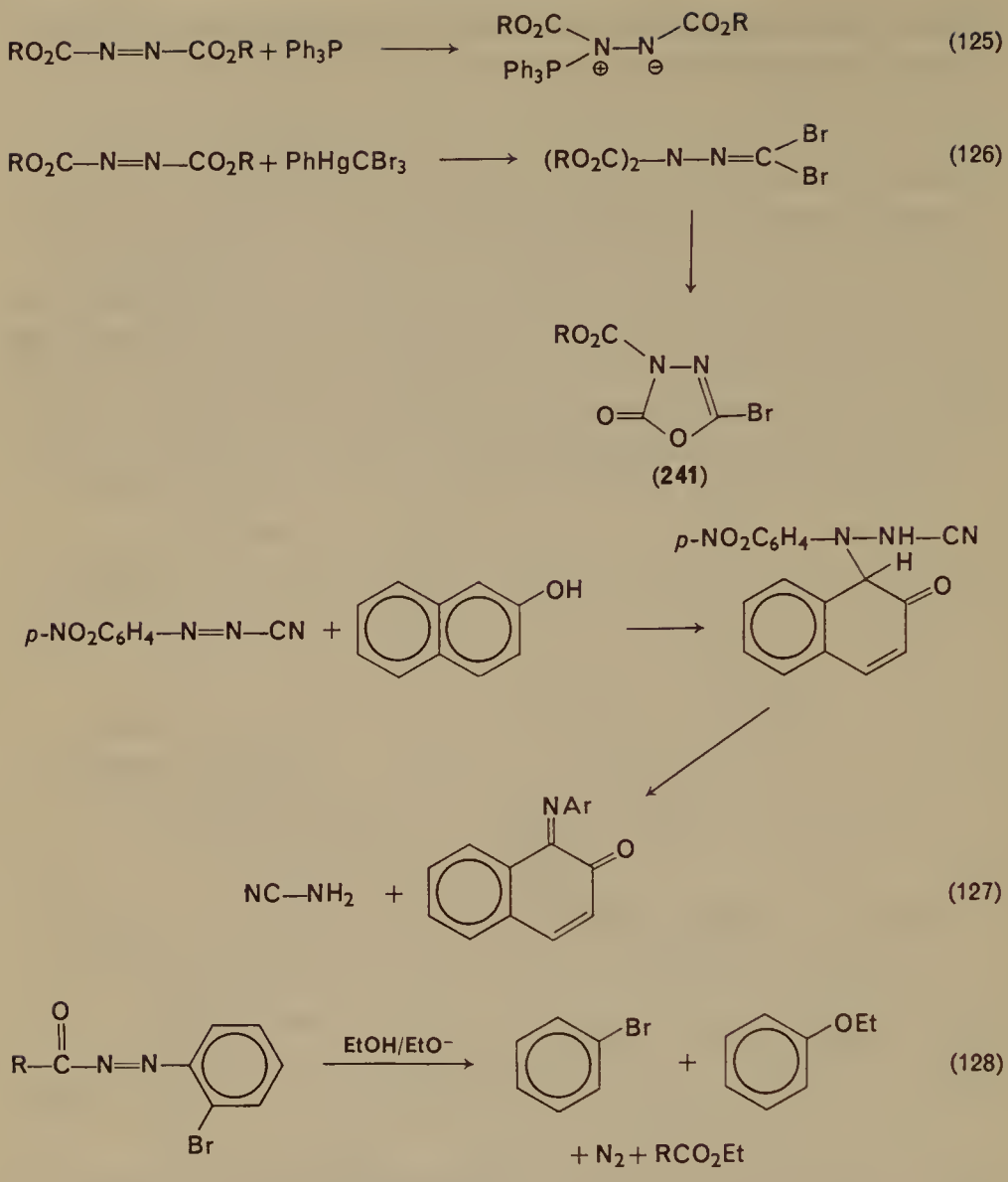


Dialkyl *trans*-azodicarboxylates react with organo-boranes to form hydroboration products; in addition homolytic alkylboration of the unsaturated system occurs (equation 124)[267]. Triphenylphosphine forms an adduct with dimethylazodicarboxylates (equation 125); although not actually isolated the adduct was shown to act as a 1,3-dipole in cycloadditions[268]. Azobenzene forms similar adducts, but in this case it is possible to isolate them as stable perchloric acid salts[269]. Surprisingly, dibromocarbene obtained from phenyl tribromomethyl mercury (which is expected to be an electrophilic carbene) also reacts with dialkylazodiesters

to give, on rearrangement, the α,α-dibromohydrazines (equation 126). Pyrolysis of the latter give the oxadiazolines **241** in high yield.

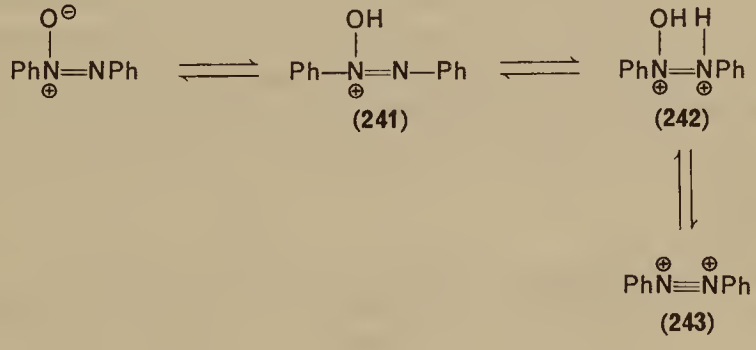
In most cases both nitrogen atoms originally present are retained in the product. However reactions in which N—N bond cleavage or loss of nitrogen occurs are also known. Thus the reaction of trans-*p*-nitrobenzeneazocyanide with β-naphthol yields 1-(*p*-nitrophenyl)-1-imino-naphthalen-2(1*H*)-one; an electrophilic first step is proposed followed by the elimination of cyanamide (equation 127)[271]. Treatment of α-carbonylazo compounds with base usually leads to rapid nitrogen evolution and both ionic (involving phenyl-anion or benzyne intermediates) and free radical pathways have been suggested (equation 128)[272–274].

IV. AZOXY COMPOUNDS

A. Acidity and Basicity

The basicity of azoxy compounds is even less pronounced than that of the corresponding azo materials; protonation does not occur except in concentrated acid media. Buncel and Lawton have reported a pK_a for azoxybenzene itself of −5·15[275]. Electron withdrawing substituents reduce the basicity further; substituted azoxybenzenes have pK_a's in the range −5·5 to −9·8.

The site of protonation of azoxybenzenes has also been debated[276], but the consensus is that the oxygen site is favoured (241). It is possible that the hydrogen is also bonded to the adjacent nitrogen since the n.m.r. signal of this proton shows that it is highly deshielded. Diprotonation (**242**) is also observed in superacid media; in this case an equilibrium concentration of the dehydrated dication **243** is also observed[5].



(241) (242) (243)

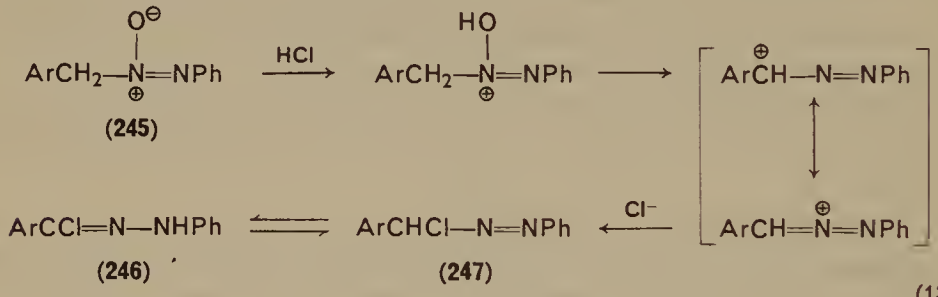
Since the azoxy group is electron withdrawing it might be expected that aliphatic azoxy compounds might show some acidic properties due to the ionization of the adjacent C—H bond (equation 129). However the pK_a's

(244) (129)

of these materials are >14 since simple azoxy compounds of type **244** are not appreciably ionized in basic solutions[277].

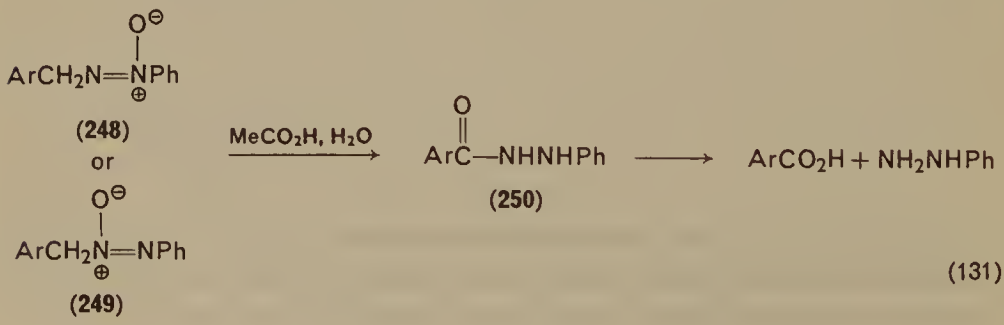
B. Reactions in Acid

On treatment with acid, aromatic azoxy compounds undergo Wallach rearrangement (see Chap. 18) aliphatic azoxy compounds can also react in acid and the products formed depend on the nature of the alkyl substituents present. When the *N*-benzyl material **245** is treated with hydrochloric acid under anhydrous conditions, the product isolated is the corresponding hydrazonyl chloride **246**. A possible mechanism is suggested (equation 130) involving initial protonation followed by dehydration; chloride ion then



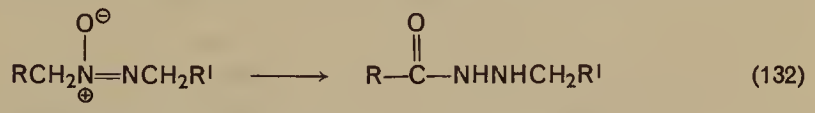
(245) (246) (247) (130)

reacts with the azocarbonium ion intermediate to form the α-chloroazo alkane **247** which tautomerizes to the more stable hydrazonyl chloride form. If the reaction is carried out in aqueous solution then the intermediate azocarbonium ion is trapped by water and hydrazides result (equation 131)[277]. When the reaction is carried out in acid under vigorous conditions then further hydrolysis of the hydrazide **250** occurs and the corresponding acid and phenylhydrazine are isolated (equation 131)[279].



(248) or (249) (250) (131)

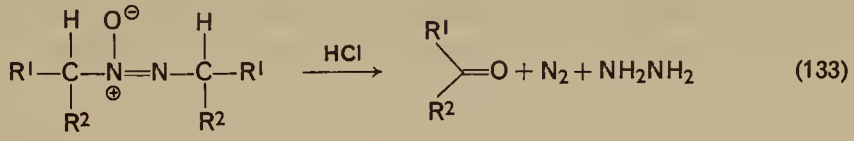
The formation of the hydrazide **250** occurs when either of the azoxy isomers **248** or **249** are treated with aqueous acid. However when both of the substituents present are primary alkyl groups then migration of oxygen to the nearest carbon occurs (equation 132)[278]. This observation raises the



(132)

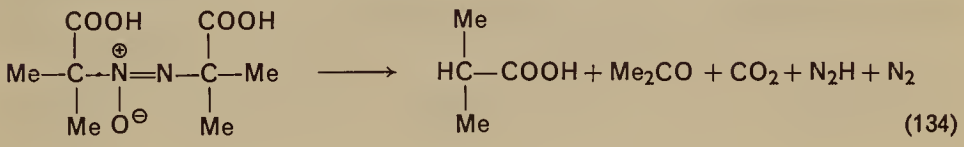
possibility that the migration might be intramolecular, but this does not appear to have been tested.

When the substituents are secondary alkyl groups then hydrazides of type **250** cannot be formed. In this case the observed products on treatment with acid are the corresponding ketone, nitrogen and some hydrazine (ca. 0·6 mol) (equation 133). A complex mixture of products was also obtained



(133)

on heating of the dicarboxy material **251** (equation 134). It appears from the

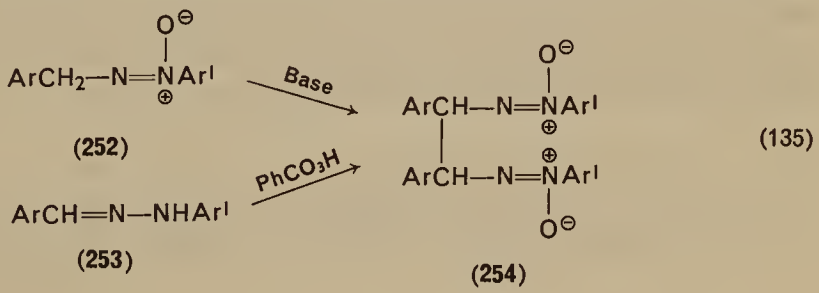


(134)

products formed that two competing parallel reactions occur but the decarboxylation must accompany further reactions since azoxypropane, if formed would have been stable under the reaction conditions[277].

C. Reactions in Base

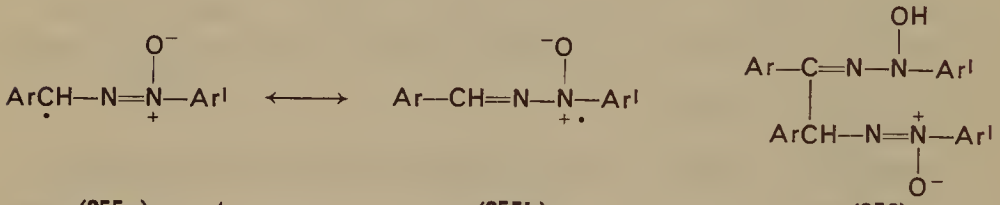
When the azoxy compounds **252** are treated in basic solution (even in the absence of air) an interesting oxidative dimerization takes place (equation **135**). The same products were isolated by Bergmann and co-workers[281]



(135)

on treatment of arylaldehyde and acylhydrazones with perbenzoic acid and originally formulated as oxazirines. Other proposals for the structure of the product included one with a *cis*-configuration of the azoxy group (in contrast to the *trans* arrangement in the starting azoxy compound **252**)[278]. However Woodward and Wintner[280] have clearly demonstrated that the product has the dimeric structure **254** and exists in a mixture of *dl* and *meso* forms. It was also demonstrated that **254** could be formed on treatment of *bis*-arylazo dimers of aldehyde hydrazones with peracids. The formation of **254** from **252** in the presence of base is accompanied by the isolation of reduction products from **252**.

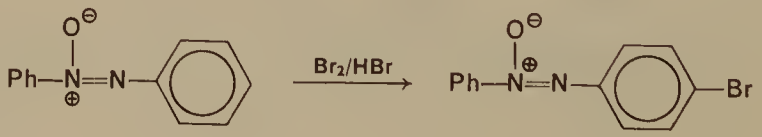
The mixture of *dl* and *meso* isomers of **254** can be enriched in one of the isomers by rapid cooling of a carbon tetrachloride solution and subsequent filtration. Equilibration (to a ca. 1:1 mixture) occurs rapidly even at room temperature. A free radical mechanism is suggested for the equilibration process (formation of **255**), tautomerization via **256** being ruled out by the fact that deuterium exchange does not occur at the methine carbons.



(255a) **(255b)** **(256)**

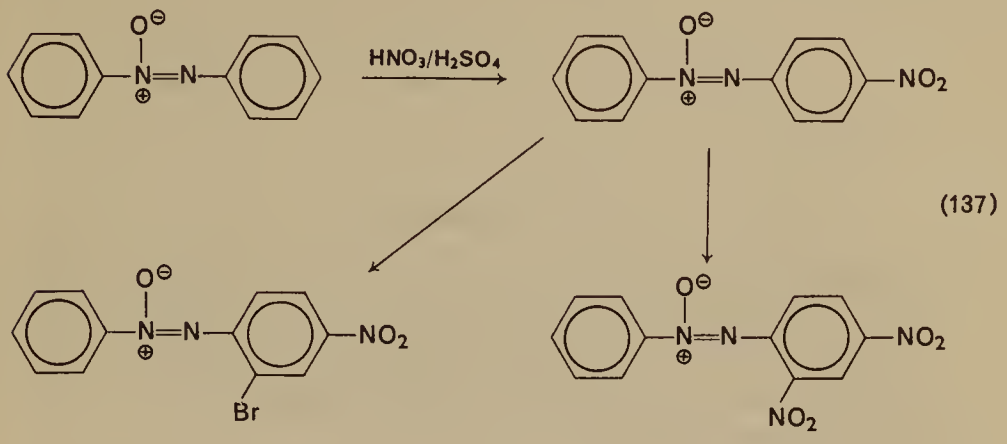
D. Electrophilic Substitution

The azoxy group is strongly electron withdrawing and deactivates an adjacent ring towards aromatic substitution. Thus normal aromatic substitution of azoxybenzene by bromine does not occur in the absence of catalysis[278]. Hydrogen bromide or $FeBr_3$ is required (equation 136) and it is likely that a mechanism involving nucleophilic attack by bromide ion on the protonated substrate is operative (as in the case of bromination of azobenzene itself). Substitution then invariably occurs in the ring remote from the NO group; this has been used as the classical method of structural determination of aromatic azoxy compounds.



(136)

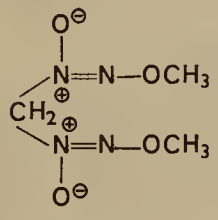
Nitration of azoxybenzene also produces a product in which the ring remote from the NO group is substituted (equation 137). Further substitution (nitration or bromination) also occurs in this ring, despite the presence of the nitro group[282].



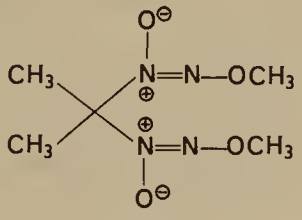
(137)

E. Alkylation

The presence of two azoxy groups has a strong acid strengthening effect on an adjacent methylene group and various alkylations have been carried out using the *bis*-methoxazonyl compound **257**[283]. In à typical alkylation



(257)



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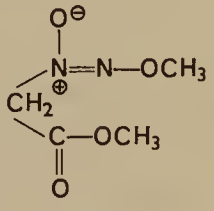
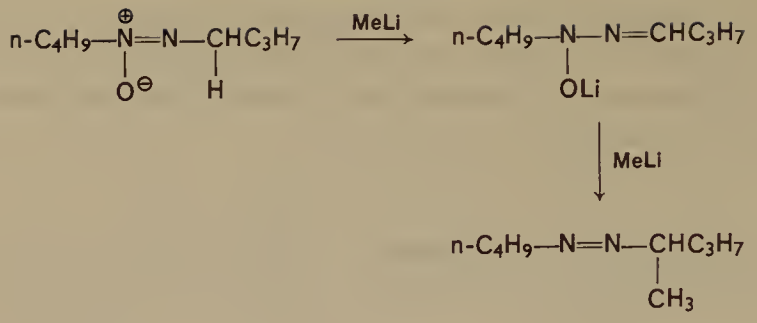


(259)

procedure using sodium hydride and methyl iodide a 55% yield of **258** was obtained. The mixed ester **259** can be similarly alkylated and both materials readily exchange deuterium at the methylene position in the presence of base.

Alkylation of simple aliphatic azoxy compounds with alkyllithium salts can also result in the formation of mono-C-alkyl products, except that in this case concomitant reduction occurs and the products are azo materials (equation 138)[284].



(138)

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CHAPTER 17

Syntheses and uses of isotopically labelled hydrazo, azo and azoxy compounds

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I. INTRODUCTION

The presentation of this chapter is divided into two major sections. The first deals with examples of the syntheses of isotopically-labelled hydrazo, azo and azoxy compounds. In the second section we consider the uses of these labelled compounds for the elucidation of reaction mechanisms, structure, etc. Our discussion will be restricted to those classes of compounds containing the functional groups —NH—NH—, —N=N— and —N(O)=N—, joined to carbon atoms comprising various organic residues.

Hydrazo, azo and azoxy compounds are often interconvertible by simple oxidation and reduction reactions. Nevertheless, the section on syntheses is conveniently subdivided into subsections dealing with these three classes of compounds separately. Therefore, despite the fact that a given labelled azo compound may be a precursor for a particular hydrazo, or azoxy compound, the synthesis appears in the section dealing with the compound of ultimate interest, in this case in the section on hydrazo, or azoxy, compounds. Because of their importance, the syntheses of azo compounds will be dealt with first. Since a variety of isotopic labels may be incorporated into these compounds, e.g. ^{15}N, ^{2}H, ^{14}C and ^{18}O, this section has been further subdivided on the basis of label type. In many cases the labelled compounds are prepared by standard synthetic procedures and the reader is referred to more general articles[1–3] which discuss such procedures in greater detail.

The second major section, on the uses of these labelled hydrazo, azo and azoxy compounds, is by no means intended to be exhaustive in scope but rather illustrative of some of the more significant areas in which these labelled compounds have been of interest. The order of presentation in this section follows the sequence given in the synthetic section.

The reader will perceive that the two major sections of this chapter differ in their approach and emphasis; this is in accordance with the current status of development of the respective areas. Thus the syntheses of isotopically labelled compounds in the hydrazo, azo, and azoxy series generally follow along well-established, classical, lines. In contrast, utilization of these labelled compounds range over numerous and varied areas of organic chemistry. On the one hand we have the classical tracer type experiments for elucidation of reaction mechanisms, as for example the use of labelled hydrazo and azoxy compounds in study of the benzidine and Wallach rearrangements. However, contrastingly, in the thermolysis of azo compounds we witness some of the most intensive studies of primary and secondary isotope effects, which when coupled with theoretical evaluation of force field changes, allow one to reach a high degree of comprehension of transition state structure.

II. SYNTHESES OF ISOTOPICALLY LABELLED COMPOUNDS

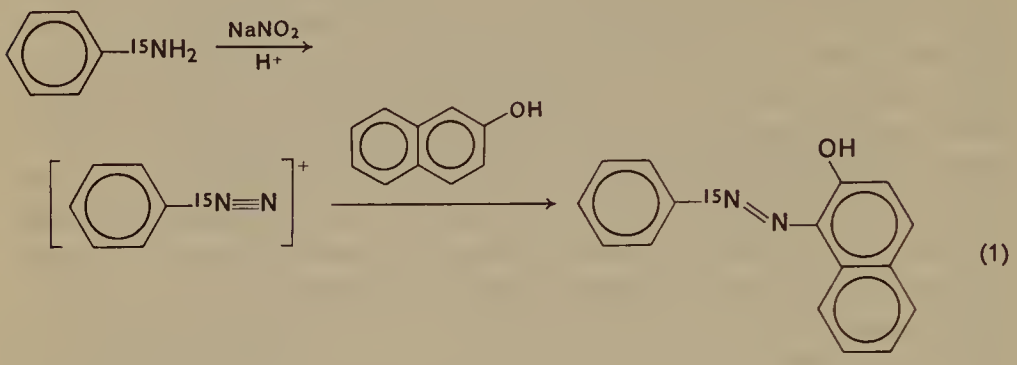
A. Syntheses of Labelled Azo Compounds

1. ^{15}N-Labelled azo compounds

Aromatic azo compounds containing the ^{15}N label on the azo function may be prepared by one of several reactions applicable to the preparation of isotopically normal aromatic azo compounds. A convenient method involves the coupling of suitably labelled aryl diazonium ions with phenol and aniline derivatives. The position of the ^{15}N label in unsymmetrical azo compounds can be pre-determined during the preparation of the diazonium salt. Thus, diazotization is effected either by employing a ^{15}N-labelled aromatic amine and an isotopically normal nitrite salt, or by using a normal aromatic amine and an ^{15}N-labelled nitrite salt[4–8]. These procedures are illustrated for the preparation of 1-(phenylazo-2-^{15}N)-2-naphthol (**1**) and 1-(phenylazo-1-^{15}N)-2-naphthol (**2**), starting with aniline-^{15}N (equation 1)[4, 7], and potassium nitrite-^{15}N (equation 2)[8], respectively*.

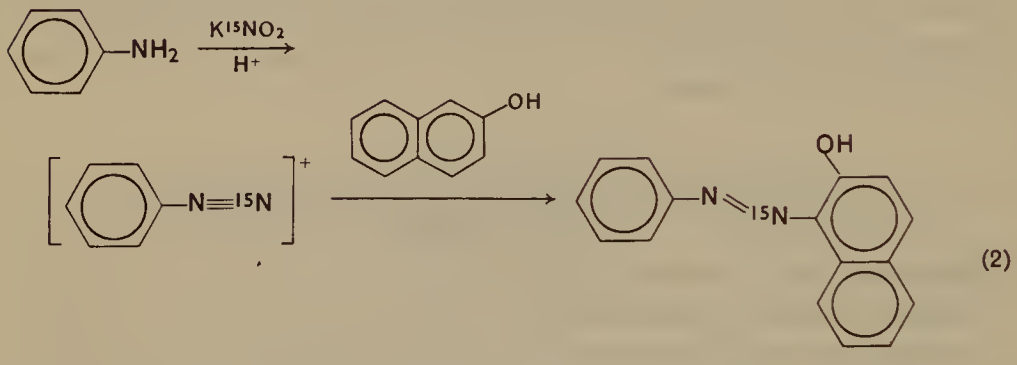
* Azo and azoxy compounds can exist as the *cis* or *trans* isomers, the *trans* being normally the more stable thermodynamic forms[1]. In this account the *trans* configuration will generally be assumed to hold, both for the aromatic and aliphatic derivatives, even though the stereochemistry may not always be explicitly shown.

Labelled aromatic amines are readily obtained by nitration with nitric acid-^{15}N and reduction of the resulting nitro compound[5]. Labelled nitrite salts such as sodium nitrite-^{15}N may be prepared by passing the gas evolved on heating nitric acid-^{15}N with arsenious oxide into aqueous sodium carbonate under nitrogen gas[5].



(1)

(1)



(2)

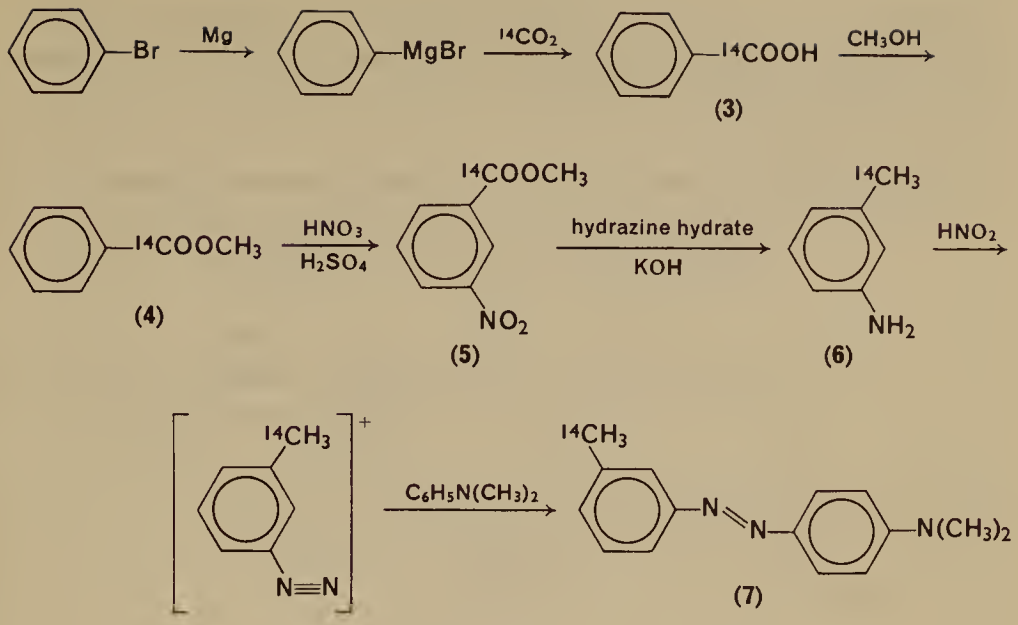
(2)

2. Azo compounds containing labelled carbon atoms

A wide variety of aromatic azo compounds containing the radioactive ^{14}C label, in the aromatic ring or on a side chain, are available via coupling reactions involving suitably labelled starting materials[9–12]. Examples of such reactions are shown below for the preparation of 3-methyl-^{14}C-4′-dimethylaminoazobenzene (**7**)[9], *N*-monomethyl-4-aminobenzene-ring-^{14}C (**9**)[11], and 3,3′,4,4′-tetrachloroazobenzene-*U*-^{14}C (**11**)[12]*.

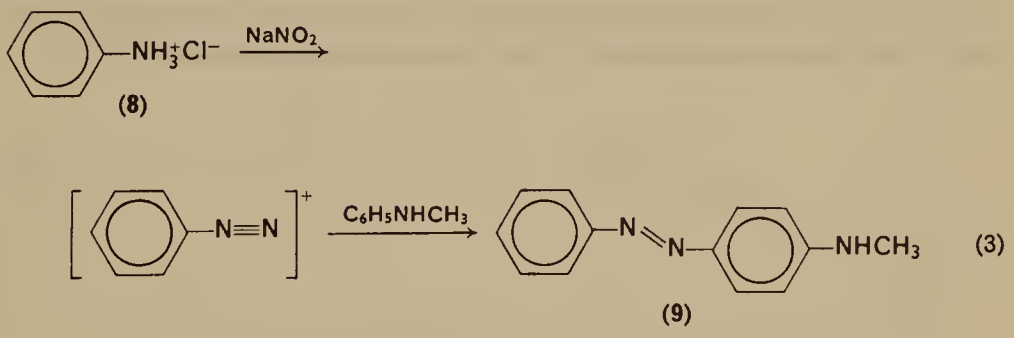
Compound **7** was obtained by diazotization of 3-methyl-^{14}C-aniline (**6**) followed by coupling with *N*,*N*-dimethylaniline[9]. This reaction, along with the preparation of the labelled aniline **6** from bromobenzene, is summarized in Scheme 1.

* Uniform labelling of the benzene ring carbons is denoted by '*U*'.



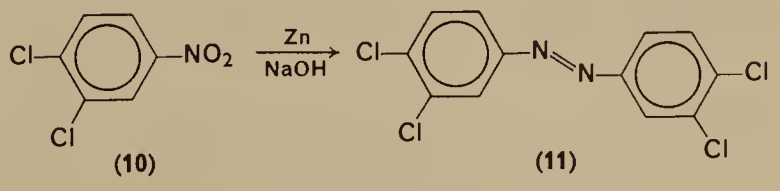
SCHEME 1.

The ^{14}C-labelled *p*-aminoazobenzene **9** was prepared by diazotization of aniline-*U*-^{14}C hydrochloride (**8**) and coupling with *N*-methylaniline as in



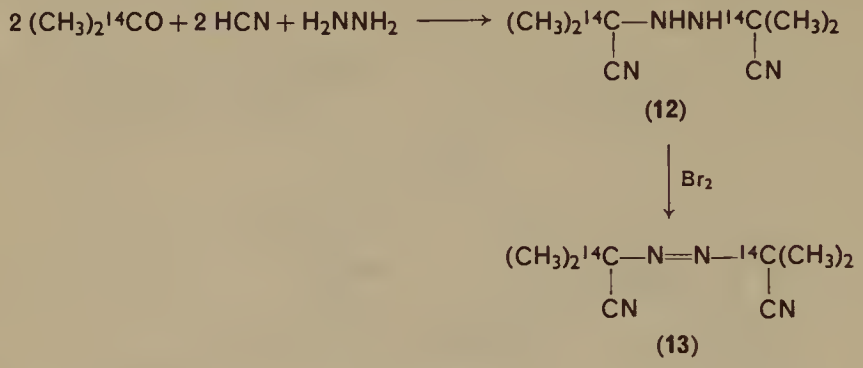
(3)

equation 3[11]. Reductive coupling of 3,4-dichloronitrobenzene-*U*-^{14}C (**10**) using zinc and alkali gave **11**, as shown in equation 4[12].



(4)

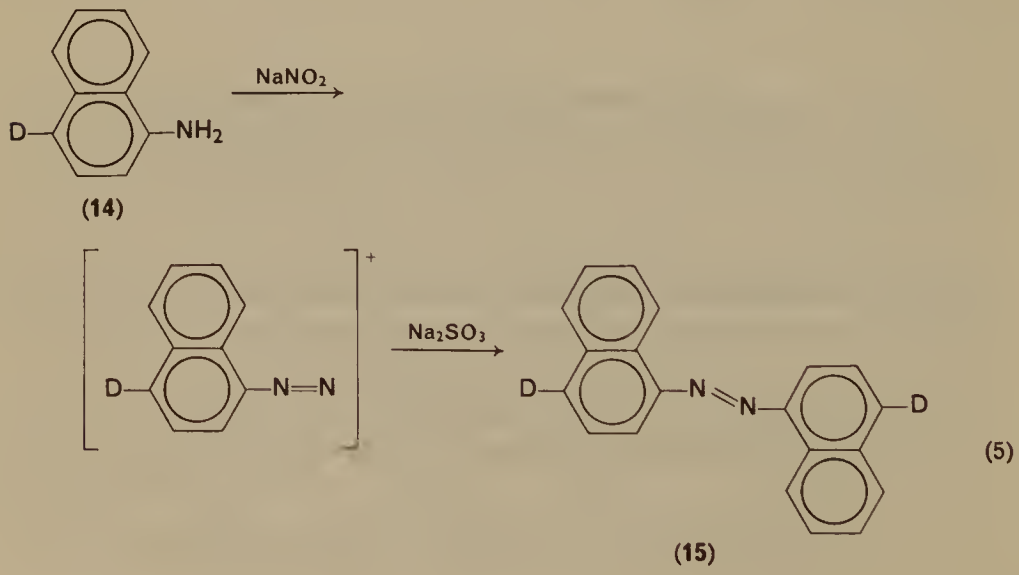
Aliphatic azo compounds containing a ^{14}C label have also been prepared. The synthesis of 2,2′-^{14}C-azobisisobutyronitrile (**13**) from ^{14}C-labelled acetone is shown in Scheme 2[13].



Scheme 2.

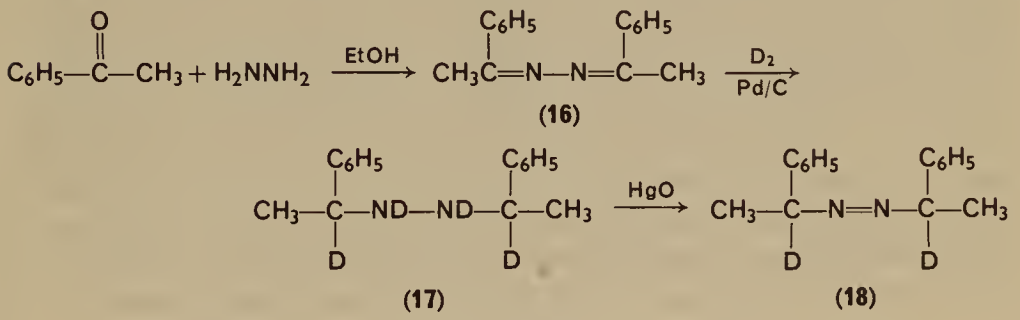
3. Deuterium labelled azo compounds

The syntheses of aromatic azo compounds containing deuterium on the aromatic ring may be accomplished by diazotization of an appropriately deuterated aryl-azo compound and coupling the diazonium ion in a buffered reducing medium of sodium sulphite, potassium ferrocyanide, ammoniacal cuprous oxide, or in cuprous chloride under acidic conditions. This reaction is illustrated in equation 5 for the preparation of 4,4′-dideuterio-1,1′-azonaphthalene (**15**) from 4-deuterionaphthylamine (**14**)[5].



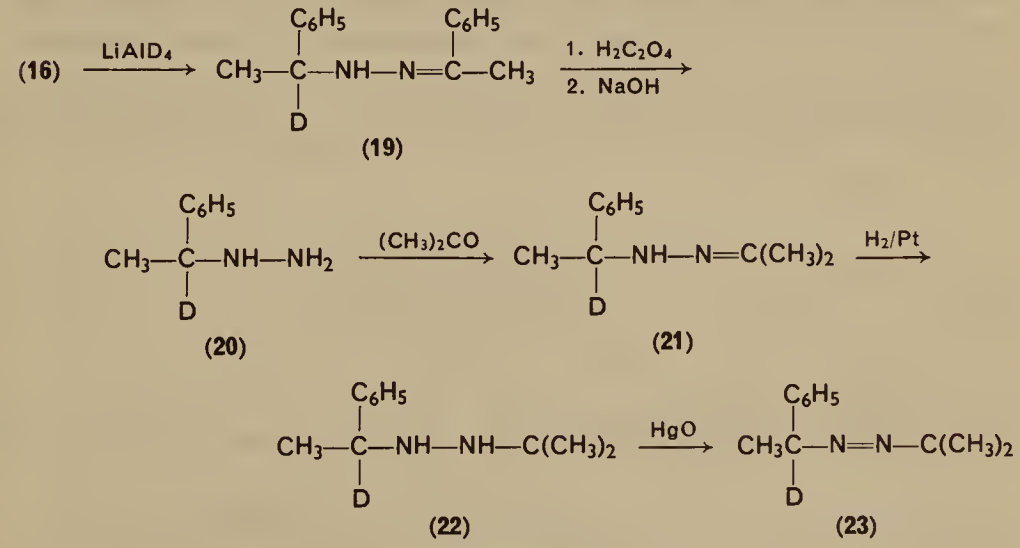
(5)

Aliphatic azo compounds containing a single deuterium atom attached at the *alpha* carbon position may be prepared by catalytic reduction of the appropriate azine with D_2, followed by oxidation of the resulting hydrazine with mercuric oxide. The azines are obtained by condensation between appropriately substituted aldehydes or ketones and hydrazines. Scheme 3 summarizes these reactions for the preparation of symmetrical 1,1′-diphenylazoethane-1,1′-d_2 (**18**)[14] from acetophenone and hydrazine.



SCHEME 3.

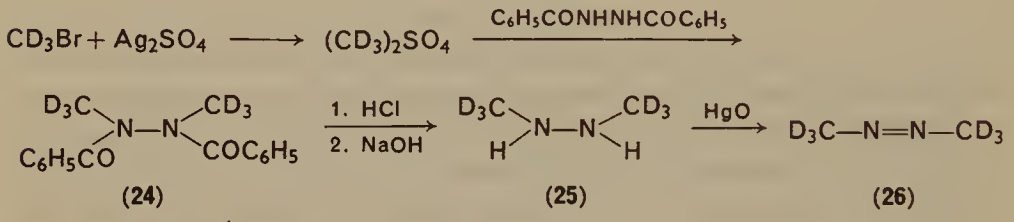
The preparation of unsymmetrical aliphatic azo compounds containing a single deuterium label at the *alpha*-carbon position is somewhat more complicated. For example, in synthesizing 1-methyl-1′-phenylazoethane-1′-*d* (**23**)[15], acetophenoneazine (**16**) was partially reduced with $LiAlD_4$ under controlled conditions to the corresponding deuterated hydrazone (**19**). The latter was treated with oxalic acid to give the acid salt of the α-phenylethylhydrazine. Neutralization of the salt and vacuum distillation



SCHEME 4.

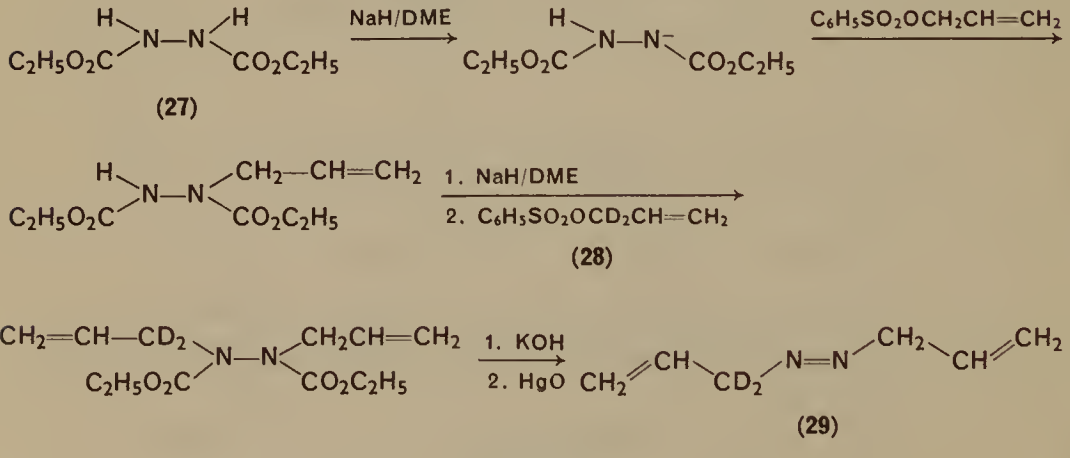
yielded the free deuterated α-phenyl-α-*d*-ethylhydrazine (**20**). Condensation of **20** with acetone afforded hydrazone **21**, which was catalytically reduced to the corresponding hydrazo compound **22**, and subsequently oxidized to the azo compound **23** (Scheme 4).

Several aliphatic azo compounds containing more than a single deuterium atom in the α-carbon positions have been synthesized[16–19]. The simplest of these compounds, azomethane-d_6 (**26**), cannot be obtained through the azine since the condensation of formaldehyde with hydrazine hydrate gives rise to polymers. However the procedure outlined in Scheme 5 was shown to be satisfactory[17]. Dimethyl-d_6 sulphate, obtained from the reaction of methyl-d_3 bromide and silver sulphate, was reacted with 1,2-dibenzoyl-hydrazine in the presence of base to afford 1,2-dibenzoyl-1,2-dimethyl-d_6-hydrazine (**24**). The latter was then refluxed in acid and steam-distilled leaving the 1,2-dimethyl-d_6-hydrazine monochloride salt. On isolation of the corresponding hydrazo compound (**25**) with aqueous alkali, and oxidation with yellow mercuric oxide, the required **26** was obtained.



Scheme 5.

Unsaturated aliphatic azo compounds containing two deuterium atoms in the α-carbon position have been synthesized by the stepwise allylation of hydrazoesters[18]. Scheme 6 summarizes the synthesis of 3,3′-azo-1-propene-

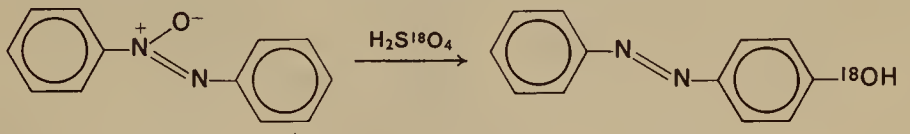


Scheme 6.

3,3-d_2 (**29**) by allylation of diethyl hydrazodicarboxylate (**27**) in dimethoxyethane (DME) using allyl-1,1-d_2-benzenesulphonate (**28**) and the isotopically normal allyl benzenesulphonate.

4. ^{18}O-Labelled azo compounds

Aromatic hydroxyazo compounds containing a labelled oxygen atom may be obtained upon rearrangement of the corresponding isotopically normal azoxy compound in concentrated sulphuric acid-^{18}O[20,21]. This transformation of azoxybenzene (**30**) to *p*-hydroxyazobenzene-^{18}O (**31**) is shown in equation 6. However, some hydroxyazo compounds have been found to undergo oxygen-18 exchange in acid solution[22].

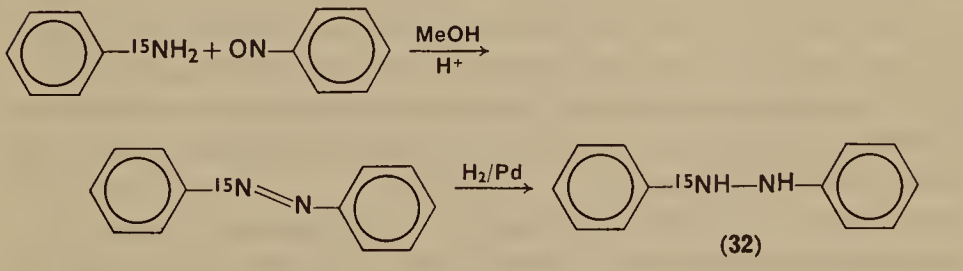


(30) (31) (6)

B. Syntheses of Labelled Hydrazo Compounds

1. ^{15}N-Labelled hydrazo compounds

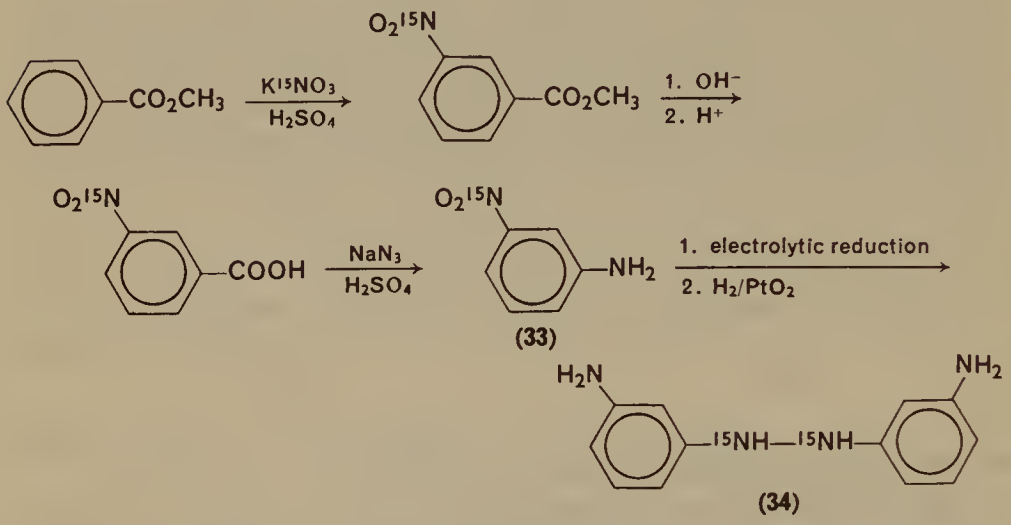
Aromatic hydrazo compounds possessing the ^{15}N label on the hydrazo group are readily prepared by reduction of the corresponding azo compounds. The latter may be obtained by condensation of ^{15}N-labelled aryl amines with isotopically normal nitrosobenzene (or vice versa) under acidic conditions[23], or by reductive coupling of ^{15}N-labelled aromatic nitro compounds by means of zinc and alkali (equation 4)[24], or by coupling reactions involving ^{15}N-labelled diazonium salts (equations 1, 2 and 5)[5,24,25]. The former reaction, which is restricted to benzene and its derivatives, is illustrated in equation 7 for the preparation of hydrazobenzene-^{15}N (**32**).



(32) (7)

Electrolytic reduction of *m*-nitroaniline-$^{15}NO_2$ (**33**) and catalytic reduction of the resulting azo derivative to yield ^{15}N-labelled 3,3-diamino-

hydrazobenzene (**34**) (Scheme 7) is yet another example of a method which may be employed[26]. The labelled nitro compound was obtained by nitration of methyl benzoate with potassium nitrite-^{15}N in sulphuric acid. The ester was subsequently hydrolysed and converted to **33** by reaction with sodium azide, as shown in Scheme 7.

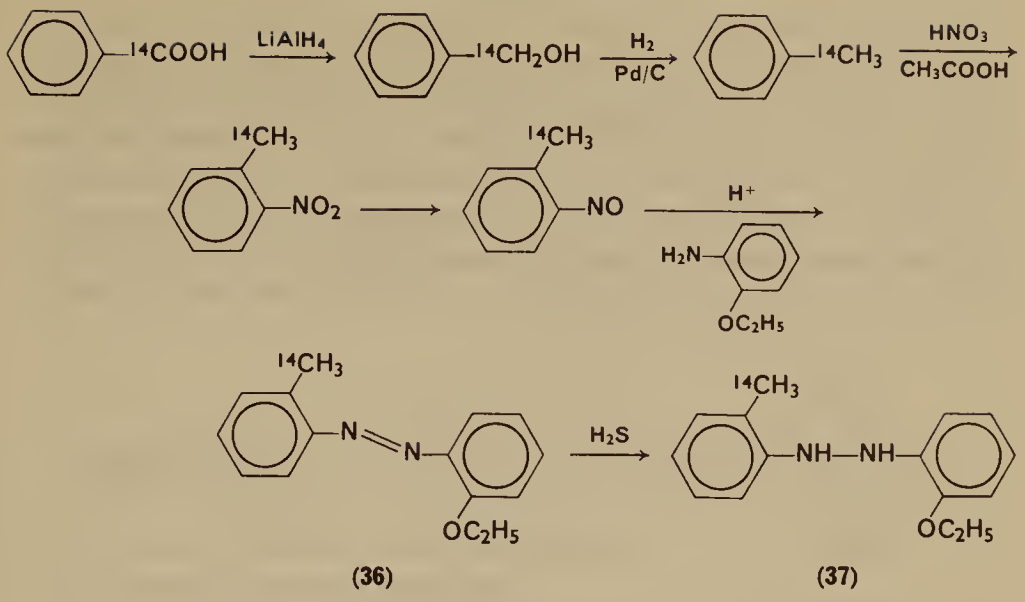


SCHEME 7.

2. Hydrazo compounds containing labelled carbon atoms

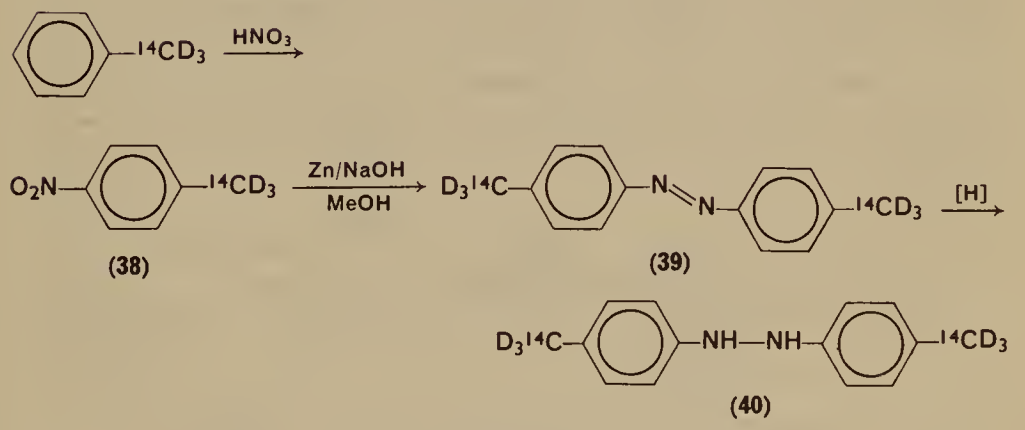
Aromatic hydrazo compounds containing a ^{14}C-labelled side-chain have been prepared from appropriately labelled benzene derivatives. Scheme 8 illustrates the synthetic procedure followed by Wheland and Schwartz[27] in the synthesis of 2-^{14}C-methyl-2′-ethoxyhydrazobenzene (**37**), starting with ^{14}C-labelled benzoic acid. Reduction of the acid, first with $LiAlH_4$ and followed by hydrogen, gave toluene-1-^{14}C. Nitration of the labelled toluene and separation of the mixture of isomers afforded the *ortho* nitro derivative, which was reduced to the labelled 2-nitrosotoluene (**35**). Coupling of **35** with 2-ethoxyaniline under acidic conditions gave the corresponding azo compound **36**, which on reduction with hydrogen sulphide in alcoholic ammonia yielded **37**.

Hammond and Clovis[28] synthesized 4,4′-di(trideuteriomethyl-^{14}C-hydrazobenzene (**40**) from toluene-α-d_3-1-^{14}C by reductive coupling of the corresponding *para* nitro derivative (**38**) with zinc and alkali, followed by reduction of the resulting azo compound **39** (Scheme 9).



(36) (37)

SCHEME 8.



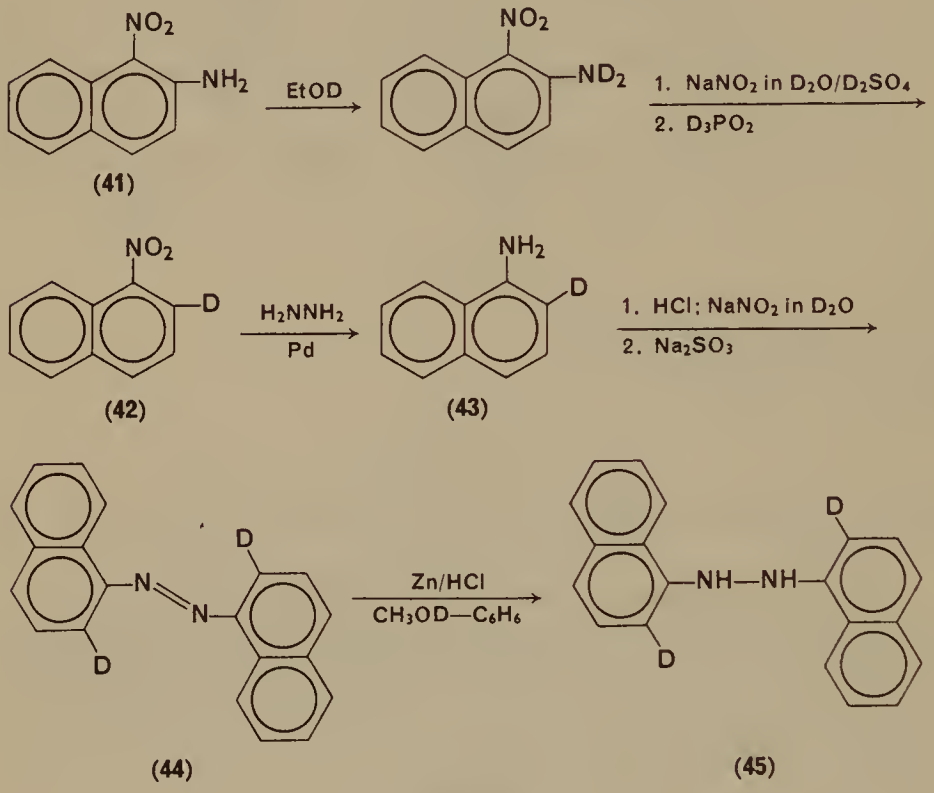
(38) (39) (40)

SCHEME 9.

3. Ring deuterated hydrazo compounds

A variety of ring-deuterated aromatic hydrazo compounds have been prepared by means of coupling reactions involving appropriately labelled aryl derivatives[5, 24, 29–33]. The syntheses of the deuterated starting materials are often quite involved, as may be seen in Scheme 10 for the preparation of 1,1′-hydrazonaphthalene-2,2′-d_2 (**45**) from 1-nitro-2-aminonaphthalene[32]. The amino hydrogens in the reactant were first exchanged with deuterium by treatment with EtOD, as a precaution against exchange with ring

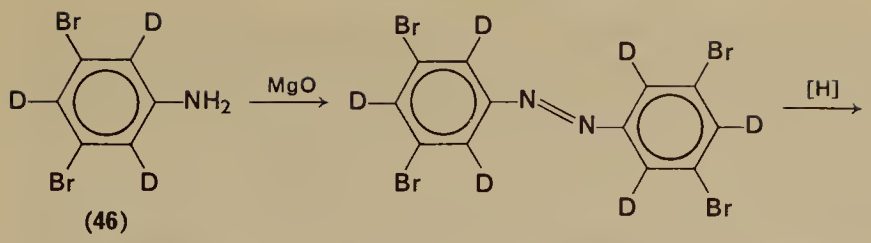
deuterium in the following reaction. The deuterated amino group in **41** was substituted with a deuterium atom (**42**) by formation of the diazonium salt in D_2O/D_2SO_4 and subsequent removal of the diazonium group with D_3PO_2. The nitro moiety of **42** was reduced to yield the amino compound **43** by refluxing with hydrazine hydrate in the presence of palladised asbestos as catalyst. Conversion of **43** to the amine hydrochloride, followed by diazotization and coupling, gave the azonaphthalene **44**. Reduction of **44** with zinc dust and ammonium chloride in methanol–benzene afforded the

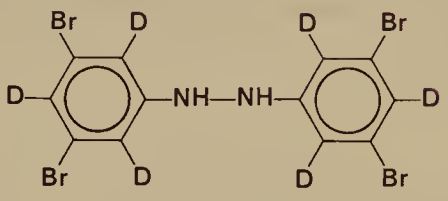


SCHEME 10.

deuterated hydrazo compound (**45**). Confirmation of the orientation of the deuterium atoms in **45** follows from examination of its rearrangement products[34] (see Section III, B, 1).

Substituted hydrazobenzenes containing deuterium labels have been prepared by the MgO oxidation of the appropriately labelled substituted aryl amines and reduction of the resulting azo compounds[35]. This sequence is illustrated in equation 8 for the preparation of 3,3′,5,5′-tetrabromohydrazobenzene-2,2′,4,4′,6,6′-d_6 (**47**) from 3,5-dibromoaniline-2,4,6-d_3 (**46**).



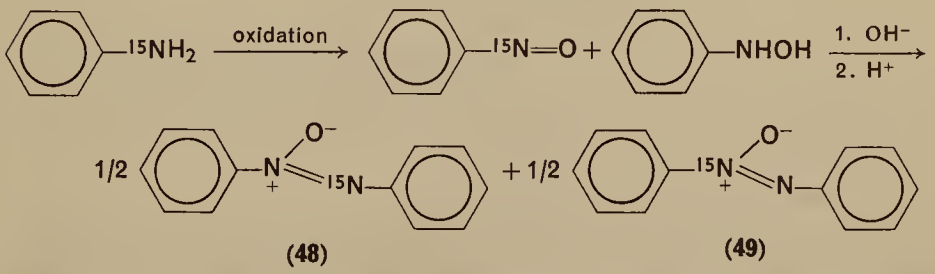


(8)

C. *Syntheses of Labelled Azoxy Compounds*

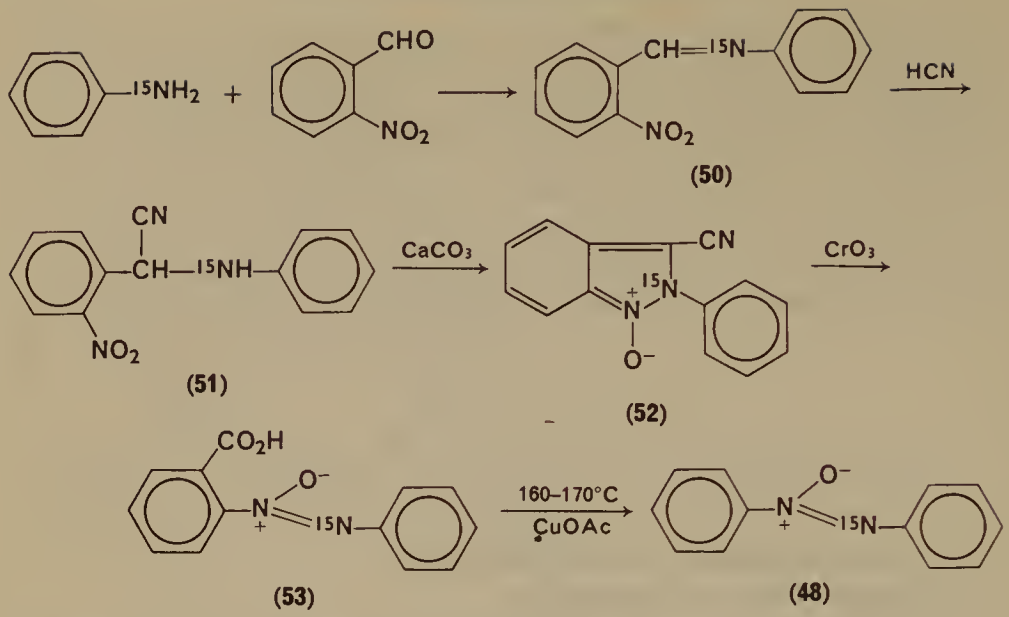
1. ^{15}N-Labelled azoxy compounds

Aromatic azoxy compounds containing a ^{15}N label in the azoxy function may be synthesized by condensing suitably labelled aryl nitroso compounds with aryl hydroxylamines in the presence of base. In the case of azoxybenzene, it has been found[36] that the label obtained in this manner from ^{15}N-labelled nitrosobenzene and isotopically normal phenylhydroxylamine is equally distributed between the two nitrogen atoms of the azoxy function (equation 9). The mechanism of this reaction will be discussed in Section III, C, 1.



(9)

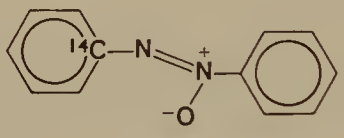
Unsymmetrically labelled azoxybenzene-^{15}N has been synthesized[37,38] from aniline-^{15}N according to the elegant method of Behr[39] (Scheme 11). Aniline-^{15}N was condensed with *o*-nitrobenzaldehyde to yield the anil derivative **50**. Addition of hydrogen cyanide gave **51** which when heated in alcohol in the presence of calcium carbonate afforded the indazole oxide **52**. Oxidation of **52** with chromic oxide in acetic acid yielded the corresponding carboxylic acid **53**, which was subsequently decarboxylated to give ^{15}N-labelled azoxybenzene (**48**).



SCHEME 11.

2. Azoxy compounds containing labelled carbon atoms

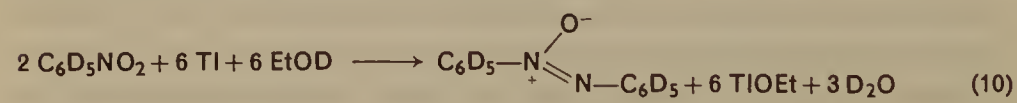
Azoxybenzene-1-^{14}C (**54**) has been synthesized[40,41] by condensing aniline-1-^{14}C and *o*-nitrobenzaldehyde, according to the reactions outlined in Scheme 11.



(54)

3. Ring deuterated azoxy compounds

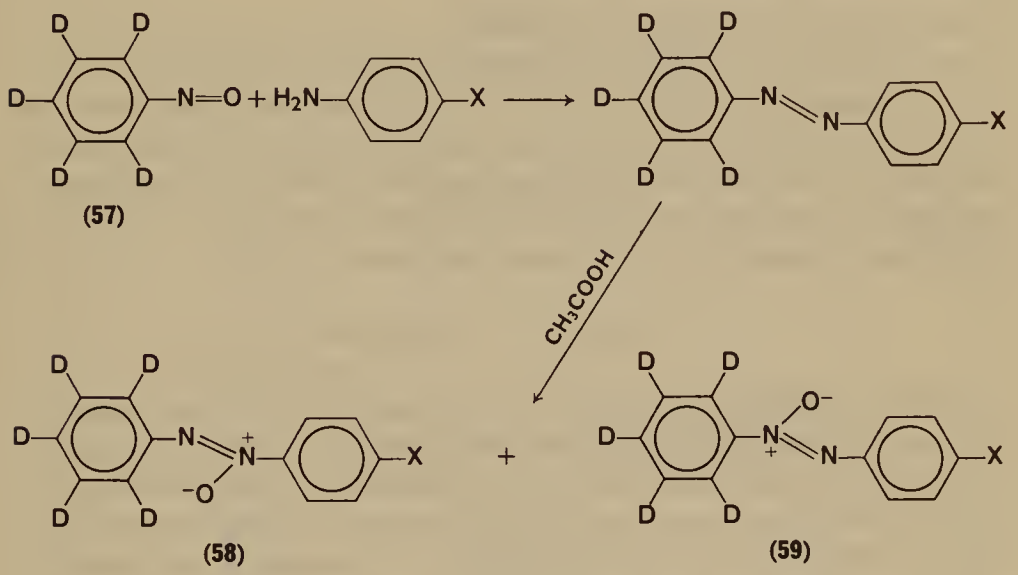
Azoxybenzene-d_{10} (**56**) may be prepared directly in reasonably good yield by reduction of nitrobenzene-d_5 (**55**) with thallium[42]. The reaction is carried out simply by refluxing the aromatic nitro compound in deuterated ethanol with excess thallium. The metal dissolves, due to the formation of thallium(I) ethoxide, and is subsequently separated from the azoxy product **56** by precipitation as thallium iodide (equation 10)[43].



(10)

(55) (56)

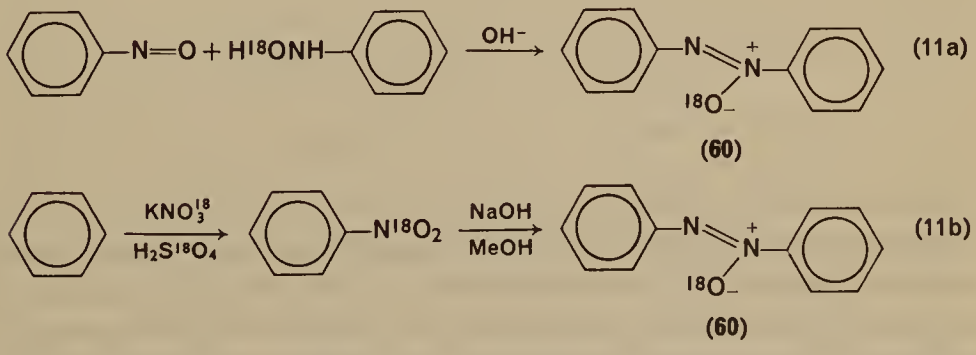
The syntheses of a number of azo and azoxy compounds with *para* substituents on one ring, and which are completely deuterated in the unsubstituted benzene ring, have recently been reported[44] (Scheme 12). The azo compounds were obtained by condensing nitrosobenzene-d_5 (**57**) with an appropriately substituted aniline, and the corresponding azoxy compounds by oxidation with peracetic acid. The α- and β-azoxy isomers*, structures **58** and **59** respectively, were separated by column chromatography.



SCHEME 12.

4. ^{18}O-Labelled azoxy compounds

Azoxybenzene containing an ^{18}O-labelled azoxy-oxygen (**60**) has been obtained by condensation of nitrosobenzene with ^{18}O-labelled phenyl-



* The α-isomer for a substituted azoxyarene may be denoted as the one with the N(O) function adjacent to the *less* highly substituted aryl group[45].

hydroxylamine[46,47] in the presence of base (equation 11a), and also by reduction of ^{18}O-labelled nitrobenzene with alkali[48] (equation 11b). In the latter case, ^{18}O-labelled nitrobenzene was obtained upon nitration of benzene with ^{18}O-labelled potassium nitrate in ^{18}O-labelled sulphuric acid.

III. UTILIZATION OF ISOTOPICALLY LABELLED COMPOUNDS

A. Studies with Labelled Azo Compounds

1. Rearrangement of diazonium salts

The possibility of exchange or interconvertibility of the nitrogen atoms in aryl diazonium ions (equation 12) will clearly have important bearing on interpretation of results of tracer studies using ^{15}N-labelled azo compounds which are derived from labelled diazonium salts. This is also the case for reactions of hydrazo and azoxy compounds, when derived from the corresponding labelled azo compound precursors.

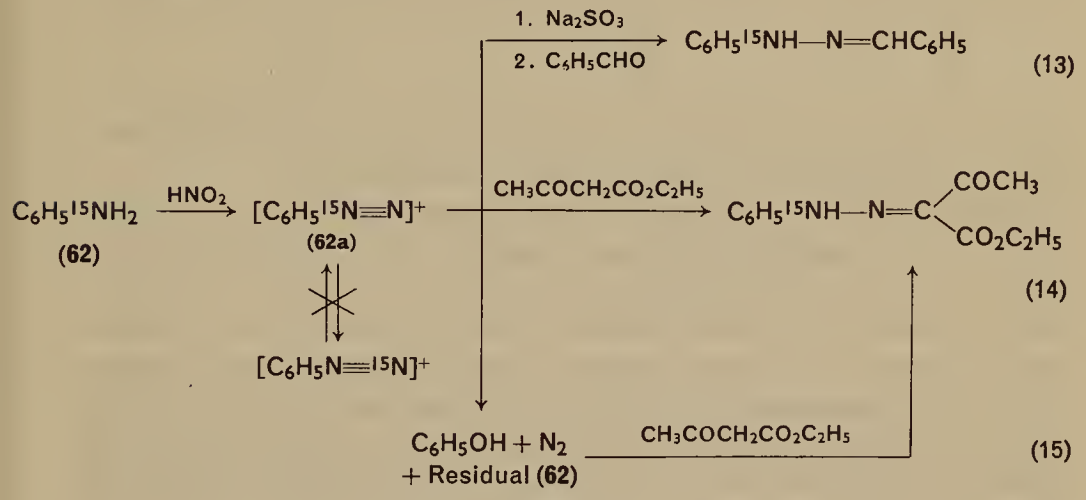
$$[Ar—{}^{15}N{\equiv}N]^+ \rightleftharpoons [ArN{\equiv}{}^{15}N]^+ \qquad (12)$$

Evidence has been presented[49,50] that rearrangement of the diazonium ion occurs during hydrolysis of benzenediazonium fluoroborate, albeit to a very limited extent. Moreover, the rearrangement was detected only after ca. 80% reaction and was reported to be slower than hydrolysis by a factor of 70, as based on mass spectral analysis of the nitrogen gas recovered in decomposition of the unreacted diazonium salt with sodium azide. Two possible intermediates were suggested for this rearrangement process; species **61a** with the two nitrogens indistinguishable, and species **61b** corresponding to a caged pair with non-equivalent but interconvertible nitrogens. The former structure was preferred.

(61a) **(61b)**

However the results of other experiments with ^{15}N-labelled compounds have indicated that the nitrogens in the diazonium ion are non-equivalent and do not interchange[4,5,51]. For example mass spectral analysis of the amines obtained upon reductive cleavage of 1-(phenylazo-2-^{15}N)-2-naphthol (**1**), which had been prepared from aniline-^{15}N (equation 1), showed that the label remained with the aniline[4].

Nuclear magnetic resonance studies[51] using ^{15}N-labelled compounds likewise lead to the conclusion that the benzenediazonium ion does not undergo rearrangement during reduction, coupling or hydrolysis (see equations 13, 14 and 15 respectively of Scheme 13). Quantitative evaluation of the relative amounts of ^{14}N and ^{15}N in the products of these reactions was obtained by measuring the area under the doublet due to ^{15}N—H, and of the singlet due to ^{14}N—H. In each case the ^{15}N content of the reaction product was identical with that of the precursor, namely aniline-^{15}N (**62**).

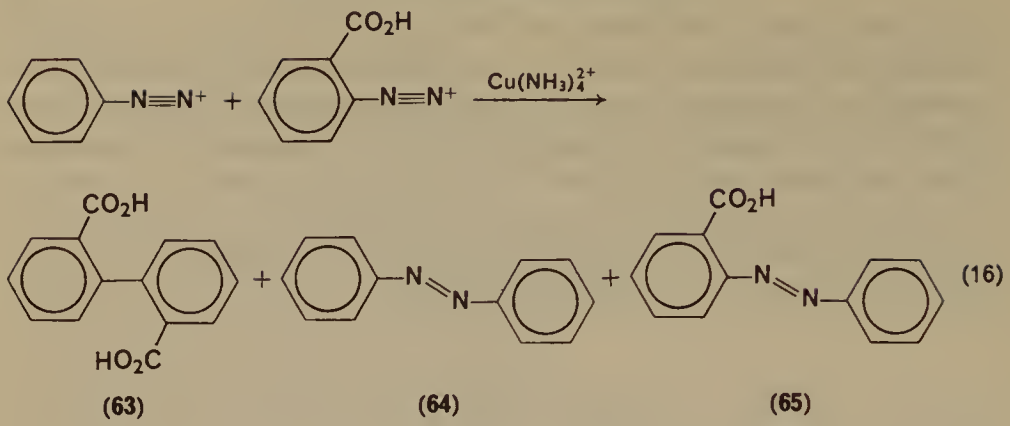


Scheme 13.

2. Diazonium ion coupling

Studies employing isotopically labelled compounds have been useful in providing information regarding the mechanism of diazonium coupling reactions[5, 6, 34, 52–54]. It has been found that, in the presence of ammoniacal solutions of copper salts, mixtures of two aryl diazonium salts afford unsymmetric azo compounds, when the diazonium salts contain substituents which differ in their electronic effects[1, 55].

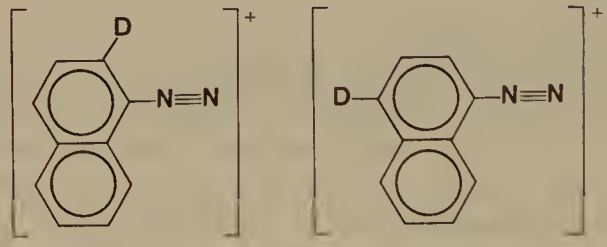
The reduction of a mixture of the diazonium salts of anthranilic acid and aniline with $Cu(NH_3)_4^{2+}$ yields not only the expected symmetrical species, diphenic acid (**63**) and azobenzene (**64**), but also the unsymmetrical azobenzene-2-carboxylic acid (**65**), as shown in equation 16. It was assumed at first that the nitrogens in **65** were derived from the diazotized aniline. The reasoning was that the product **64** from diazotized aniline contains nitrogen and the product **63** from diazotized anthranilic acid does not. However, by labelling first one, and then the other, diazonium salt (by diazotization with



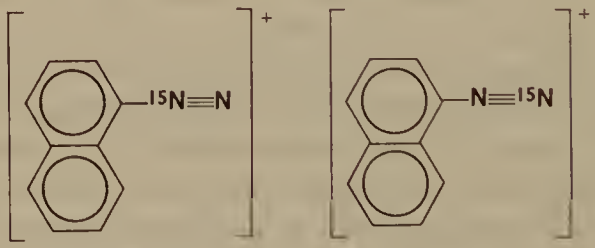
(63) (64) (65)

labelled potassium nitrite) it was shown[6] that the nitrogens in **65** were actually derived from the diazonium salt of anthranilic acid.

Banthorpe and co-workers[5,34] have investigated the azo products obtained by the reductive coupling of labelled 1-naphthyldiazonium ions (see above, Section II, A, 3). In experiments employing 1-naphthyldiazonium ions labelled with deuterium at the 2- or 4-positions (structures **66** and **67** respectively), it was found that in either case the original orientations of the deuterium label relative to nitrogen were unchanged in both aryl groups of the azo product. Similar experiments employing 1-naphthyldiazonium ions labelled with ^{15}N in the α or β positions (structures **68** and **69** respectively) demonstrated that once more the label was completely retained in the azo products.



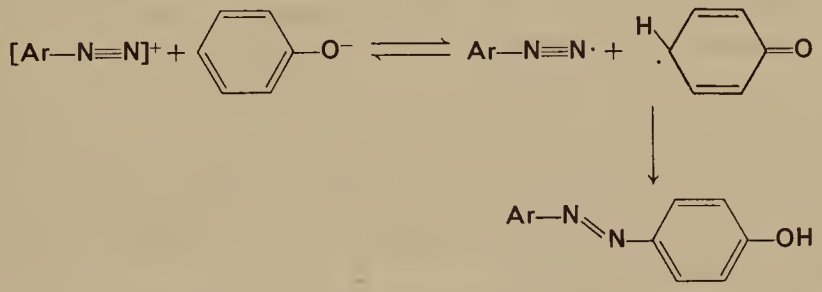
(66) (67)



(68) (69)

On the basis of the above results one may exclude certain mechanisms, such as formation of the azo compounds via reaction of a diazo radical with naphthalene (as formed by reaction of a naphthyl radical with solvent), or by coupling between azenes (as formed by extrusion of nitrogen from a tetrazole derivative). However, further studies are required to establish the actual reaction mechanism.

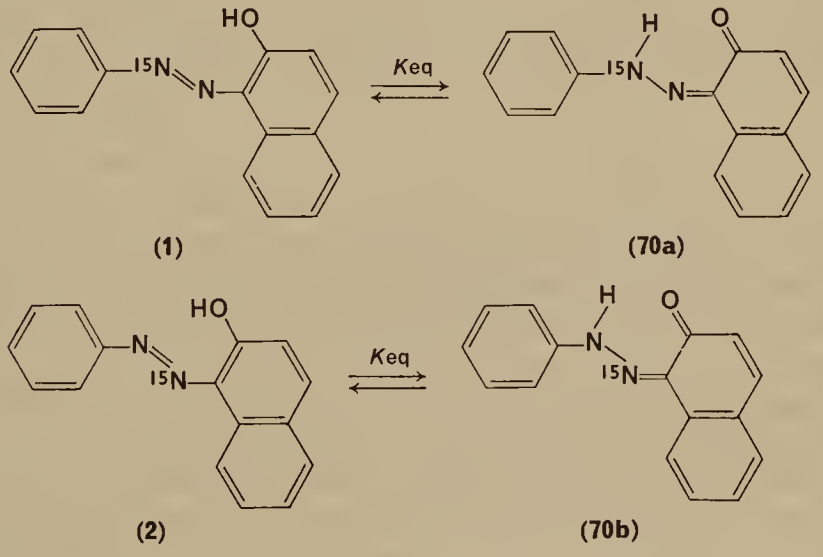
It is noteworthy that recent n.m.r. studies[54] of diazonium coupling reactions employing the ^{15}N-labelled benzenediazonium ion have indicated that reaction occurs in two steps. The first step involves an electron transfer process, while the second involves coupling of the two radicals.



(17)

3. Azo-hydrazone tautomerism

The fact that the ^{15}N isotope possesses a spin quantum number of 1/2 has permitted utilization of n.m.r. spectroscopy for the elucidation of azo-hydrazone tautomerism (see also Chapter 18). We may illustrate the principles involved by means of the labelled compounds **1** and **2**, participating in the equilibrium shown in Scheme 14:



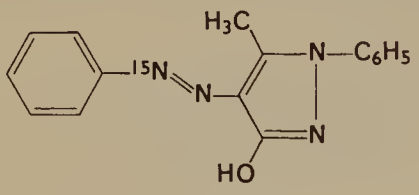
Scheme 14.

Whereas the ^{15}N—H proton resonance of the hydrazone form exhibits a low field doublet with $J_{15N-H} = 90$–100 Hz[8, 56], the OH proton resonance of the hydroxyl form is a low field singlet. Assuming a fast intramolecular proton transfer between the azo-hydroxy and hydrazoquinoid forms, the tautomeric equilibrium constant, K_{eq} = [azo form]/[hydrazone form], may be derived directly from equation 18[8]:

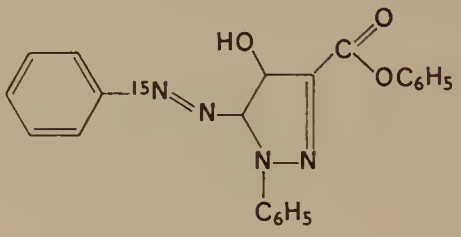
$$K_{eq} = \frac{J_{15N-H} - J_{obs}}{J_{obs}} \tag{18}$$

J_{15N-H} is the derived value of the spin–spin coupling constant and J_{obs} is the value as observed experimentally. The relationship of equation 18 holds when the proton in the hydrazone-form is bonded to the ^{15}N atom and if there is no long-range spin–spin splitting between the ^{15}N atom and the proton of the hydroxyl group. This proviso is illustrated by the observation of a large coupling constant for **1** in methylene chloride solution, which is in accord with a preponderance of the hydrazone-form **70a**[7]. In contrast, the spectrum of **2** exhibited only a singlet due to OH, identical to that of the isotopically normal compound[8].

Nuclear magnetic resonance studies have been carried out by Yoder and co-workers[57] on ^{15}N-labelled azo heterocycles, in order to establish their structures unambiguously. For example, the spectral data for 5-methyl-4-phenylazo-1-phenyl-3-pyrazolone and 3-carboethoxy-1-phenyl-5-phenylazo-4-pyrazolone showed them to exist primarily in the azo forms, **71** and **72**

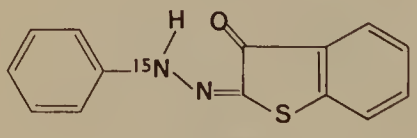


(71)



(72)

respectively. In contrast, 2-phenylazothianapthen-3-one and 1,3-diphenyl-4-phenylazobarbituric acid in DMSO solution were found to exist predominantly in the hydrazone forms, **73** and **74**, respectively.



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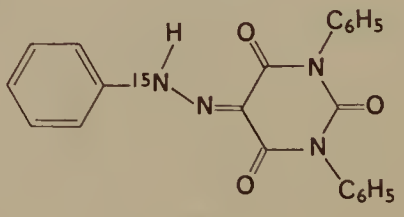


(74)

4. Thermolysis of azoalkanes

The past decade has witnessed considerable interest in the thermal decomposition of azo compounds. Important information has been derived from the determination of secondary α-deuterium isotope effects (α-effects), as well as from primary heavy atom isotope effects. Of particular interest is the timing of the bond cleavage processes in the unimolecular reaction, that is whether cleavage of the two carbon–nitrogen bonds occurs simultaneously (equation 19), or in step-wise fashion (equation 20, 21).

$$R—N{=}N—R' \longrightarrow R\cdot + R'\cdot + N_2 \quad (19)$$

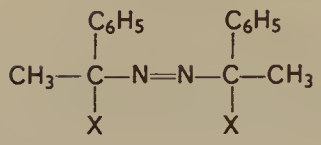
$$R—N{=}N—R' \longrightarrow R—N{=}N\cdot + R'\cdot \quad (20)$$

$$R—N{=}N\cdot \longrightarrow R\cdot + N_2 \quad (21)$$

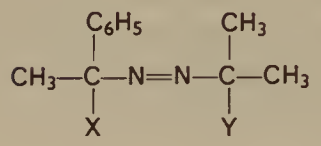
Of equal significance are the parallel theoretical studies relating the variation in the magnitude of these isotope effects with molecular structure[58]. Wolfsberg and Stern[59,60] have concluded that the magnitude of the α-effect for such unimolecular reactions is a function of the variation in the transition state force fields at the isotopically labelled position. Measurement of the α-deuterium isotope effect, coupled with measurement of the primary isotope effect for the C—N bond, permit calculation of the transition state force constants[61,62]. This enables one to probe the question of whether a transition state is reactant-like or product-like, and to evaluate the effect of molecular structure on transition state geometry. Classically, such information on structure–reactivity relationships in the azoalkane series has been derived from studies of rate constants and of activation parameters for various structural environments[63–65]. The secondary deuterium isotope effect thus constitutes a sensitive criterion of reaction mechanism.

The first extensive study of α-deuterium isotope effects in the pyrolytic decomposition of azoalkanes was carried out by Seltzer and coworkers[14,15,16], for the series 1,1′-diphenylazoethane (**75**), 1-methyl-1′-phenylazoethane (**76**), α-phenylethylazomethane (**78**), and their deuterated analogues.

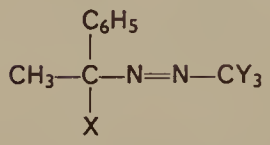
The reaction rates for the thermolytic decomposition of this series of compounds were determined by following the changes in absorbance due to reactant with time or by determination of the rate of N_2 evolution, in a solution of ethylbenzene or diphenyl ether containing 0·13M-benzoquinone for the higher temperature experiments[14–16]. Isotope effects obtained at various temperatures are summarized in Table 1. It should be noted that the deuterium isotope effect given is the value per deuterium atom, and



(75) X = H
(18) X = D



(76) X = Y = H
(23) X = D, Y = H
(77) X = H, Y = D



(78) X = Y = H
(79) X = D, Y = H
(80) X = H, Y = D

refers in each case to the ratio of the specific rate constants of the protio species and of the corresponding deuterated species, though only the latter is identified in the Table.

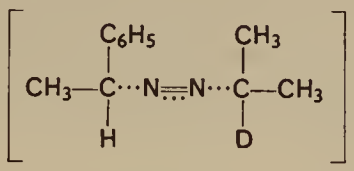
TABLE 1. Isotope effects for thermal decomposition of azoalkanes

Compound	Temp. (°C)	k_H/k_D per D atom	k_{14N}/k_{15N}	Reference
18	105·28	1·127	1·0229	14, 61
23	143·20	1·148	1·0152	15, 61
77	143·20	1·036		15
79	161·00	1·13	1·0132	66, 61
80	161·00	0·97		66

The observed secondary deuterium isotope effect in the case of **18** was taken to be indicative of a *symmetrical*, one step, cleavage, as given by equation 19. This conclusion is based in part on analogy with SN1 reactions for which the α-effect when corrected to 105°C takes the value 1·12 per deuterium atom. Therefore, in the reaction of **18** an overall α-effect of 1·12 would be expected if only one carbon–nitrogen bond breaks in the slow step, and the second in a following fast step. However if both C—N bonds break simultaneously then an α-effect of 1·12 *per D atom* is expected and is

experimentally observed. Similarly the α-effect observed for **23** was also interpreted in terms of simultaneous rupture of the two C—N bonds[15].

However the α-effect for **77** is indicative of a much smaller degree of bond stretching at the isopropyl C—N bond, in accord with the transition state as represented by **81**. This unsymmetrical structure is consistent with



(81)

consideration of relative stabilities of the respective radicals formed in this process. The delocalizing ability of a phenyl group is known to be larger than that of a methyl group, thereby allowing greater degree of radical character in the incipient α-phenylethyl than in the incipient 2-propyl radical in the transition state.

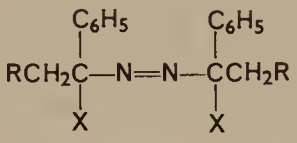
In contrast to the above situations, the α-effects obtained for **79** and **80** were interpreted in terms of the two-stage decomposition process (equations 20 and 21). The α-effect value, $k_H/k_D = 1{\cdot}13$, observed for **79** is that expected for the stretching of a benzylic C—N bond. However, the k_H/k_D value of 0·97 observed for **80** demonstrates that there is no weakening in the methyl C—N bond during the slow step. On the contrary, the slight inverse effect is indicative of a tightening of the methyl C—N bond in the transition state as the methylazo radical departs, resulting in a slight increase in the H—C—N bending force constant[16].

Further evidence for this conclusion derives from the ^{13}C isotope effect in the decomposition of **78**, as determined by mass spectral examination of the methane collected when **78** was decomposed in n-hexane. (The measurements were made with the substrate of natural abundance of ^{13}C). The low isotope effect observed, $k_{12}/k_{13} = 1{\cdot}0068$, showed that the C—N bond does not rupture in the transition state of the rate determining step. Plausibly, the two-stage mechanism arises as a result of the large difference in resonance stabilization energy of the benzylic radical as opposed to the methyl radical.

Primary nitrogen isotope effects have also been determined[61] in the decomposition of **75**, **76** and **78**, by the mass spectral analysis of the recovered nitrogen, using compounds of natural abundance of ^{15}N. These isotope effects (Table 1), coupled with the α-deuterium effects and the carbon-13 isotope effect obtained for **78**, enable the calculation of consistent values for the force field changes in the conversion of the reactant molecule into the activated complex. The general significance of such an 'exact' analysis

of the isotope effects using the methods of Wolfsberg and Stern[59,60] is discussed in a recent review[58].

Scheppele, Seltzer and co-workers[62,66] have determined the secondary deuterium isotope effects for thermal decomposition in the series *meso*- and *dl*-1,1′,2,2′-tetraphenylazoethane (**82**), 1,1′-diphenylazobutane (**83**), and 2,2′-dimethoxy-1,1′-diphenylazoethane (**84**). The results are presented in Table 2, which includes also the data for compound **18**, and the relevant Taft strain parameter E_S. A brief discussion of the results is given here, though the reader is referred to the original references for thorough evaluation of the problem.



(82a) R = C_6H_5, X = H, *meso* and *dl*

(82b) R = C_6H_5, X = D, *meso* and *dl*

(83a) R = C_2H_5, X = H

(83b) R = C_2H_5, X = D

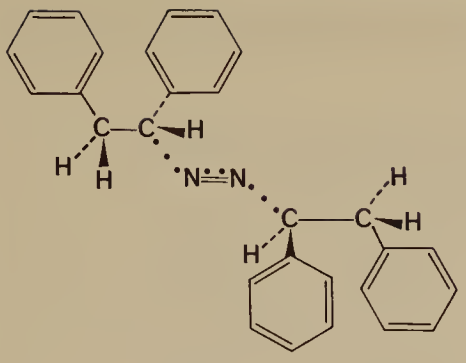
(84a) R = CH_3O, X = H

(84b) R = CH_3O, X = D

TABLE 2. Isotope effect and strain energies for thermal decomposition of azoalkanes[14,62,66]

Compound	k_H/k_D per D atom	*R*	E_S
18	1·127		
meso-**82b**	1·112	C_6H_5	−0·38
dl-**82b**	1·101	C_6H_5	−0·38
83b	1·100	C_2H_5	−0·36
84b	1·097	OCH_3	−0·19

The interesting hypothesis has been advanced[66] that the α-effect might serve as a useful probe in detecting the occurrence of anchimeric assistance (participation) by a neighbouring phenyl group. In the decomposition of the diastereoisomers of **82**, two possible transition states were considered for the formation of the 1,2-diphenylethyl radicals; structure **85** representing the 'classical' transition state and structure **86** in which the developing *p*-electron is stabilized by π-electrons of the neighbouring phenyl groups. It was reasoned that decomposition via **85** would result in greater hybridization change at C-α than decomposition via **86**, where interaction between the β-phenyl and C-α would partially compensate for the reduction in the



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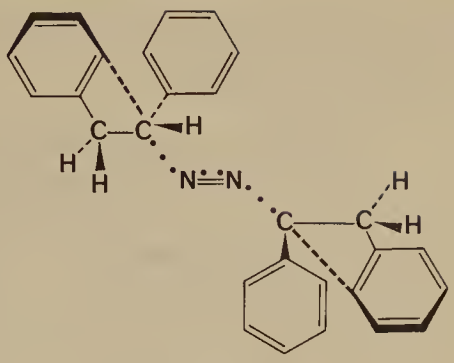


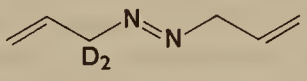
(86)

H—C—N bending force constant. Thus a larger α-effect would be expected for decomposition via **85**, comparable to the value obtained for **18**. In practice, a lower α-effect was observed (Table 2), suggesting reaction via **86**.

The steric and electronic effects of the methoxy substituents in **84** place opposite demands on the reactant-like, radical-like, character of the transition state and might be assumed to cancel each other. Therefore an α-effect similar to that obtained for **18** might be expected. The experimental value is lower[62], for which no definitive explanation is currently available.

The kinetic isotope effect observed in the thermal decomposition of ring-deuterated 1,1′-diphenylazoethane, $k_H/k_D = 1{\cdot}030 \pm 0{\cdot}007$, is thought to be of classical mechanical ($v_{1e}^{\neq}/v_{2e}^{\neq}$) origin[67].

Secondary deuterium isotope effects have also been determined for the gas phase thermolysis of azoalkanes[18,68,69]. Crawford and co-workers[18,19] studied the deuterated azoalkanes 3,3′-azo-1-propene-3,3-d_2



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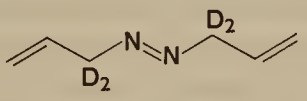

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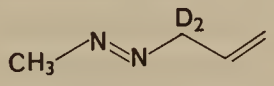


(89)

(**87**), 3,3′-azo-1-propene-3,3,3′,3′-d_4 (**88**) and methylazo-3-propene-3,3-d_2 (**89**). It is seen from the results given in Table 3 that the α-effects for **87** and **88** appear to be too low for reaction by the one-step mechanism, and too high for the two-step mechanism[18]. However, additional evidence obtained from the nitric oxide inhibited rates of thermolysis of **89**, as well as by study

of other symmetrical and unsymmetrical azoalkanes, is consistent with a two-stage mechanism[19].

TABLE 3. Isotope effects for thermal decomposition of azoalkanes in the gas phase

Compound	Temp. (°C)	k_H/k_D obsd.	k_H/k_D corr. per D atom
87	161·65	1·14 ± 0·04	1·08
88	161·65	1·26 ± 0·04	1·08
89	126·00	1·28 ± 0·05	—

5. Polymerization studies

Suitably labelled azo compounds have been used in elucidating the mechanism of radical polymerization reactions[70]. For example, 2,2′-^{14}C-azobisisobutyronitrile (**13**) has been employed in evaluation of the relative importance of chain termination by disproportionation (equation 22) and by combination (equation 23) reactions[13]. Each polymer chain will contain

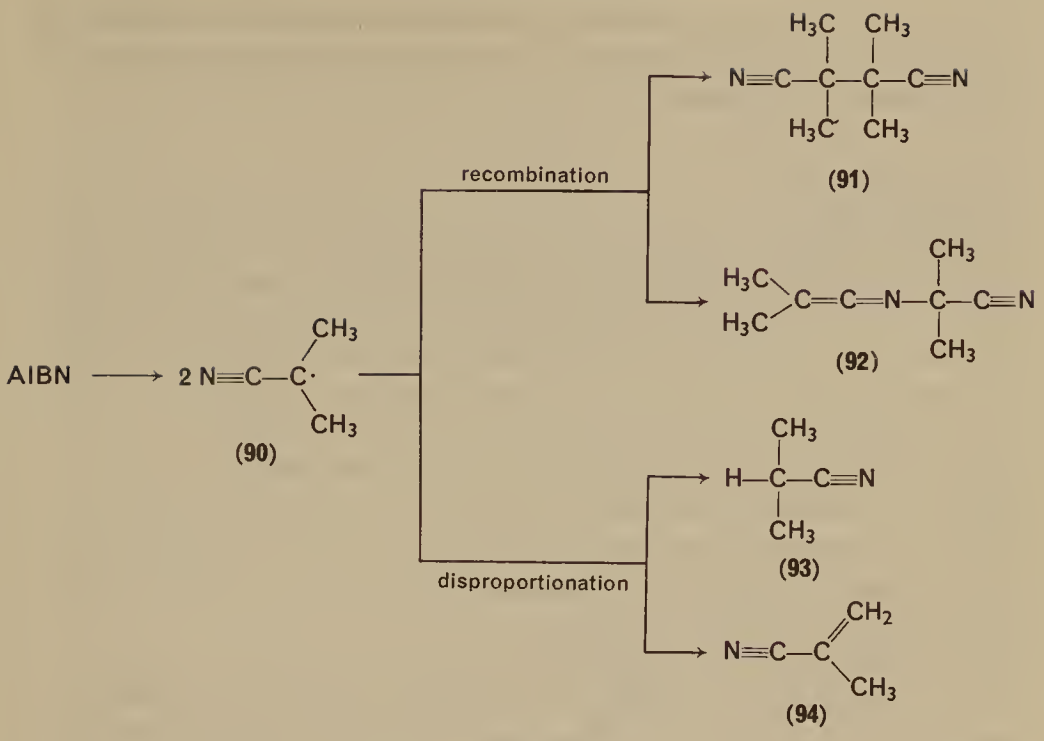
$$2\,RCH_2\dot{C}HX \longrightarrow RCH{=}CHX + RCH_2CH_2X \quad (22)$$

$$2\,RCH_2\dot{C}HX \longrightarrow RCH_2CHXCHXCH_2R \quad (23)$$

one initiator molecule if termination occurs by disproportionation, while two initiator molecules will be present if termination occurs by combination. The average number of initiator fragments per molecule of polymer, as obtained by measuring specific activities, showed that in the polymerization of methyl methacrylate at 25°C the probability of termination by disproportionation is twice as great as by combination.

Labelling experiments have also been carried out in studies pertaining to the photochemical and thermal decomposition of 2,2′-azobisisobutyronitrile (AIBN) itself[71]. The initially formed pair of cyanoisopropyl radicals (**90**) may recombine to form tetramethylsuccinodinitrile (**91**) and dimethyl-*N*-(2-cyano-2-propyl)ketenimine (**92**), or disproportionate to form isobutyronitrile (**93**) and methylacrylonitrile (**94**), as shown in Scheme 15.

Relevant information was obtained by use of the ^{14}C-labelled AIBN, **13**. The photochemical decomposition of **13** was performed in dilute solutions, under conditions used in polymerization reactions, and the product was examined at various stages of reaction using isotopic dilution techniques.



SCHEME 15.

The results showed that disproportionation occurred to a greater extent than recombination. In fact, recent p.m.r. studies have demonstrated that, in fluid solutions, 95% of the products are formed via recombination reactions after complete conversion[72]. In addition to fluid solutions, the photolysis of AIBN has been studied in nonfluid media such as glassy benzyl benzoate, in frozen mixtures and in the crystalline solid state, and the effect on product distribution has been determined. In glassy solutions, 71 to 91% of the products were formed by recombination of the cyanoisopropyl radicals. However, in frozen mixtures of benzene or benzyl benzoate containing small crystals of AIBN, or in the crystalline solid state, the situation was almost the reverse of that in the fluid or glassy solutions, with up to 90% or more of the products derived from disproportionation reactions. Also the failure to observe significant amounts (maximum 9%) of cross-disproportionation products in the reaction of mixtures of crystalline AIBN and AIBN-d_{12} indicated that in the solid state the disproportionation products are formed from geminate radical pairs[72]. Similar studies using deuterated AIBN indicated that disproportionation in the solid state is limited by rotational diffusion about the —C—C≡N axis

and not by atom transfer[73]. Recently, the lattice parameters of AIBN-d_{12} and AIBN have been determined to establish the geometry of the lattice in which the reaction occurs[74].

6. Miscellaneous

a. The cage effect. Deuterated alkyl azo compounds have been utilized in demonstrating the existence of a cage effect[68, 75, 76]. For example, mass spectral analysis of ethane formed during the gas phase photolysis of mixtures of azomethane and azomethane-d_6 showed a parent peak height ratio which was in agreement with the theoretical concentration ratio, $[CH_3CD_3]^2/[C_2H_6][C_2D_6] = 4$. This is the ratio expected for a random recombination of methyl radicals. In a similar reaction carried out in a solution of isooctane, less than 0·3% of the total ethane formed was CH_3CD_3. This result demonstrated directly and unequivocally the ability of the solvent to hold the reactive molecules together in a 'cage' facilitating recombination before diffusion occurs.

b. Mechanism of NO scavenging. Continuous mass spectral analysis of the products formed during the photolysis of mixtures of azomethane-d_6 and nitric oxide indicated the formation of the species $(CD_3)_2NOCD_3$[77]. A mechanism in which a nitric oxide molecule scavenges three methyl radicals in successive steps has been suggested and is shown in Scheme 16.

$$CD_3N{=}NCD_3 \xrightarrow{h\nu} 2\,CD_3 + N_2$$
$$CD_3 + NO \longrightarrow CD_3NO$$
$$CD_3 + CD_3NO \longrightarrow (CD_3)_2NO$$
$$CD_3 + (CD_3)_2NO \longrightarrow (CD_3)_2NOCD_3$$
$$CD_3 + CD_3 \longrightarrow C_2D_6$$

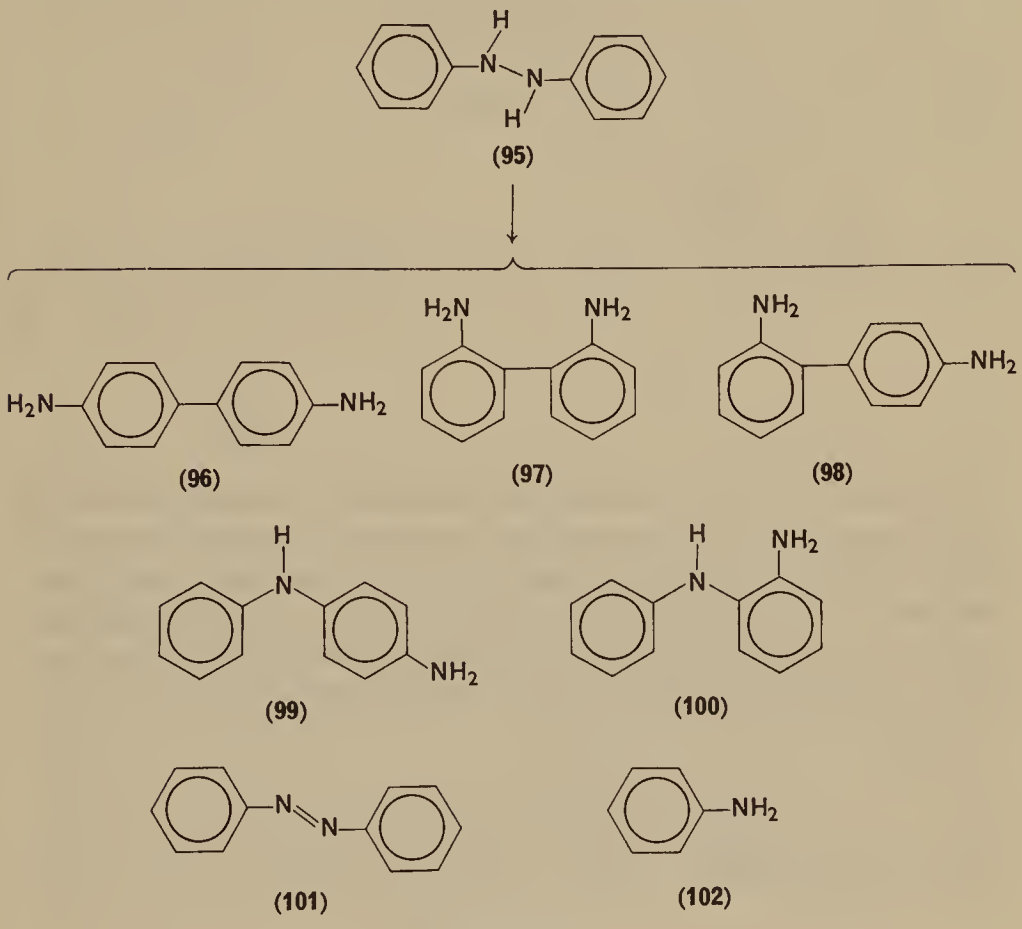
SCHEME 16.

c. Biological studies. Radio-labelled azo compounds have been used extensively in a variety of biological studies. For example, 3,3′,4,4′-tetrachloroazobenzene-^{14}C (**11**) has been employed in the study of soil microorganisms which are capable of transforming some chlorinated aniline-based herbicides into azobenzene derivatives[12]. Also, several radioactively labelled *N*-methylaminoazo dyes (e.g., compound **9**) have been employed in *in vivo* studies designed to establish the role in the carcinogenic process induced by these dyes[10, 11].

B. Illustrative Studies with Labelled Hydrazo Compounds

1. Isotopes and the benzidine rearrangements

Isotopic tracer studies have been used extensively in elucidating the mechanism of the benzidine rearrangement (cf. Chapter 18). Scheme 17 summarizes the wide variety of products which may be obtained from hydrazobenzene (**95**). These include actual rearrangement products such as the *para* and *ortho*-benzidines (**96**, **97**), diphenylines (**98**), *para* and *ortho*-semidines (**99**, **100**), as well as oxidation and disproportionation products such as azo compounds (**101**) and fission amines (**102**)[29].

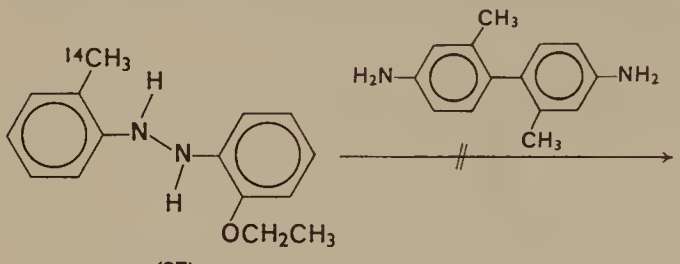


Scheme 17.

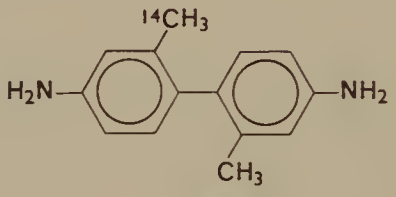
The majority of the isotopic studies have been concerned with the acid-catalysed rearrangement, and that situation is reflected in the present account, although thermal and photochemical processes are also considered briefly.

a. The acid-catalysed rearrangement. Tracer studies employing labelled

hydrazo compounds have provided definitive evidence that the acid-induced rearrangement occurs by an intramolecular mechanism. One of the first studies of this type was performed by Wheland and Schwartz[27]. These workers rearranged 2-^{14}C-methyl-2′-ethoxyhydrazobenzene (**37**) in the presence of an excess of 2,2′-dimethylbenzidine, the symmetrical product expected if the reaction proceeded by an intermolecular process (equation 24). Radioactive assay of the recovered 2,2′-dimethylbenzidine showed that less than 0·03% of the ^{14}C-labelled **103** was present.

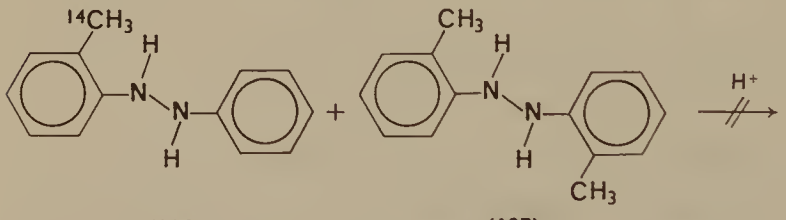


(37)

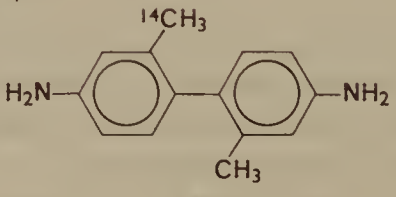


(103) (24)

In another study[78], 2-^{14}C-methylhydrazobenzene (**104**) was reacted in the presence of an equimolar quantity of 2,2′-dimethylhydrazobenzene (**105**), which in previous experiments had been shown to rearrange at a comparable rate. Examination of the recovered 3,3′-dimethylbenzidine showed it to contain less than 0·03% of ^{14}C, thus eliminating the formation of cross products via an intermolecular mechanism (equation 25):

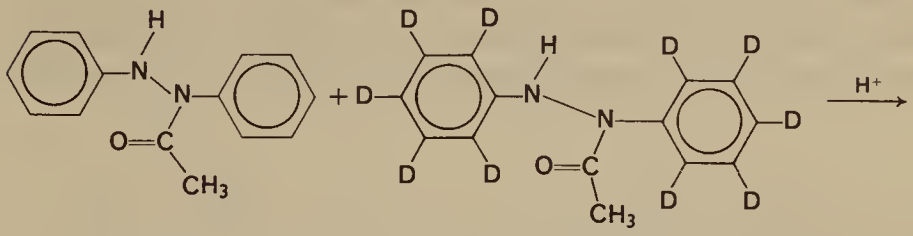


(104) **(105)**

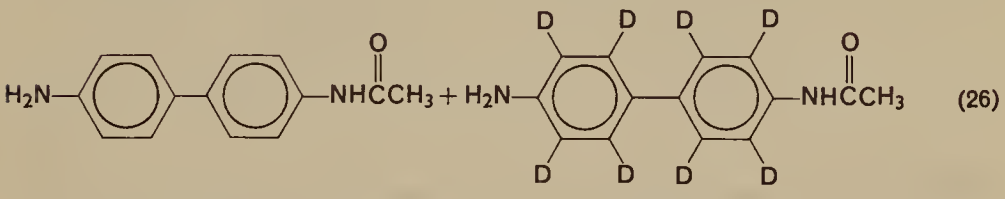


(106) (25)

An unusual variation on the theme of testing for cross products has been reported recently[33]. Mass spectral analysis of the *N*-acetylbenzidine product, obtained upon rearrangement of *N*-acetylhydrazobenzene (**107**) in the presence of an equivalent amount of the decadeuterio analogue **108**, revealed parent peaks corresponding to the isotopically normal species (**109**) and the octadueterio species (**110**) only, with no evidence of cross



(107) (108)

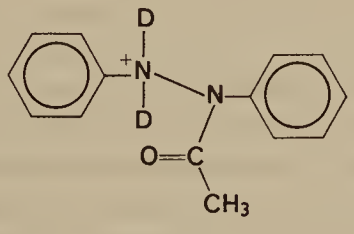


(109) (110)

(26)

product formation (equation 26). Exchange of the ring protons with solvent did not occur under the rearrangement conditions, pointing to the absence of protonation at the unsubstituted carbon atoms of the benzene rings. A small solvent isotope effect was observed, $k_{H_2O}/k_{D_2O} = 1{\cdot}27$, in accord with reaction proceeding via **111** in the deuterated acid medium. It is interesting that a small, but reproducible, secondary isotope effect, $k_H/k_D = 1{\cdot}07$, was reported for the rearrangement of **108**. The sum of the evidence favoured heterolytic cleavage of the N—N bond in **111** as the rate-determining step. Thus the *N*-acetyl group 'usurps' the catalytic role of the second proton in the acid-catalysed rearrangement of hydrazobenzene[33].

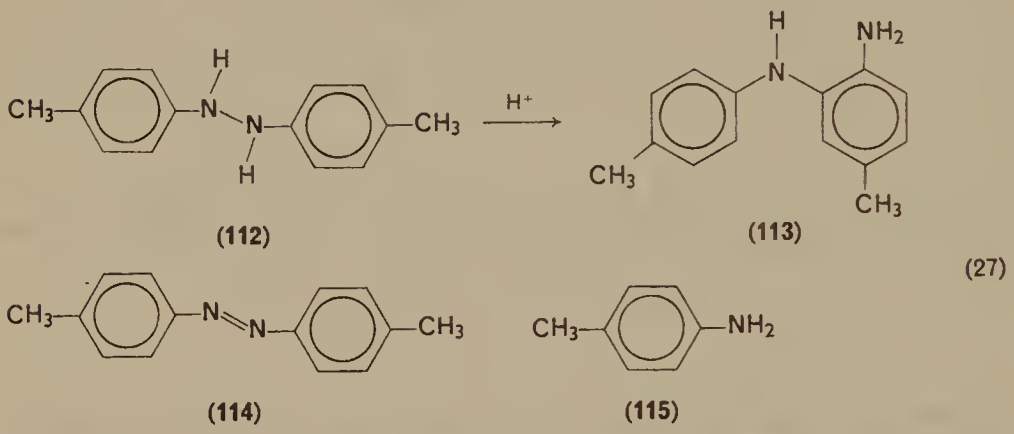
The isotopic dilution technique, using substrates in which the side-chain contains a radioactive label, facilitates product identification and in some



(111)

cases provides an alternative (and superior) method to analysis by conventional spectroscopic techniques. In the example to be cited, the results have a bearing on the disproportionation reaction in which one molecule of hydrazobenzene becomes oxidized to the azobenzene and the second reduced to yield the two anilines: $2\,ArNHNHAr' \rightarrow ArN{=}NAr' + ArNH_2 + Ar'NH_2$.

p-Hydrazotoluene (**112**) in acidic ethanol rearranges to yield the *o*-semidine, 2-amino-4,5′-dimethyldiphenylamine (**113**), with simultaneous disproportionation to 3,3′-dimethylazobenzene (**114**) and *p*-toluidine (**115**),

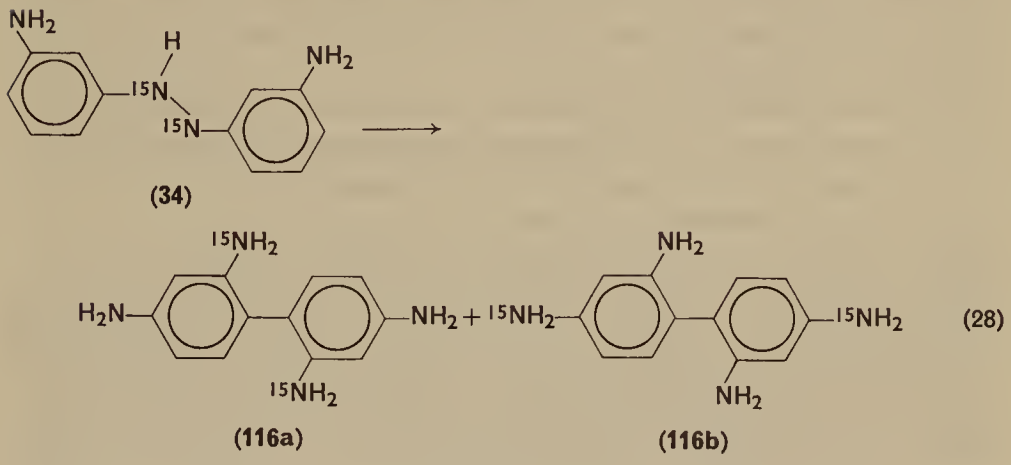


(112) (113) (114) (115) (27)

as illustrated in equation 27[28]. Spectroscopic analysis indicated formation of **113**, **114** and **115**, accounting respectively for 40, 20 and 40% by weight of the original amount of **112**.[79] It is apparent that a stoichiometric disproportionation should yield equal *weights* (or a 1:2 molar ratio) of **114** and **115**. Reaction of the labelled compound corresponding to **112**, *p*-hydrazotoluene-4,4′-^{14}C, and determination of the product distribution using isotopic dilution techniques, indicated the same proportions of **113** and **114** as obtained by the spectroscopic method; however a lower value, 28·8% by weight of the original amount of **112**, was obtained for **115**[28]. In addition it was shown that the presence of deuterium in the methyl group of 4,4′-di(trideuteriomethyl)hydrazobenzene-4,4′-^{14}C (**40**) had no effect on the rate of reaction or product distribution as compared with the isotopically normal compound **112**[28]. The mechanism of the disproportionation process, and its relationship to the rearrangement process, remains one of the mysterious aspects of the benzidine problem[29].

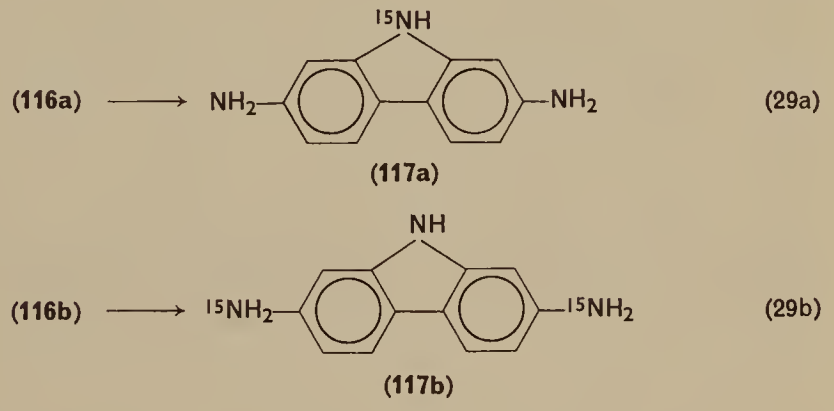
An ingeniously devised isotopic tracer study has been reported by Hammond and Clovis[26]. Rearrangement of 3,3′-diaminohydrazobenzene

(**34**) containing an excess of ^{15}N in the hydrazo linkage should afford the 2,2′-diaminobenzidine products **116a** and **116b** by *ortho* and *para* coupling respectively (equation 28)[26]:



(28)

The relative significance of *ortho* and *para* coupling could be evaluated by converting the rearrangement product into the corresponding 2,7-diaminocarbazole in which half of the *ortho* amino groups are removed:



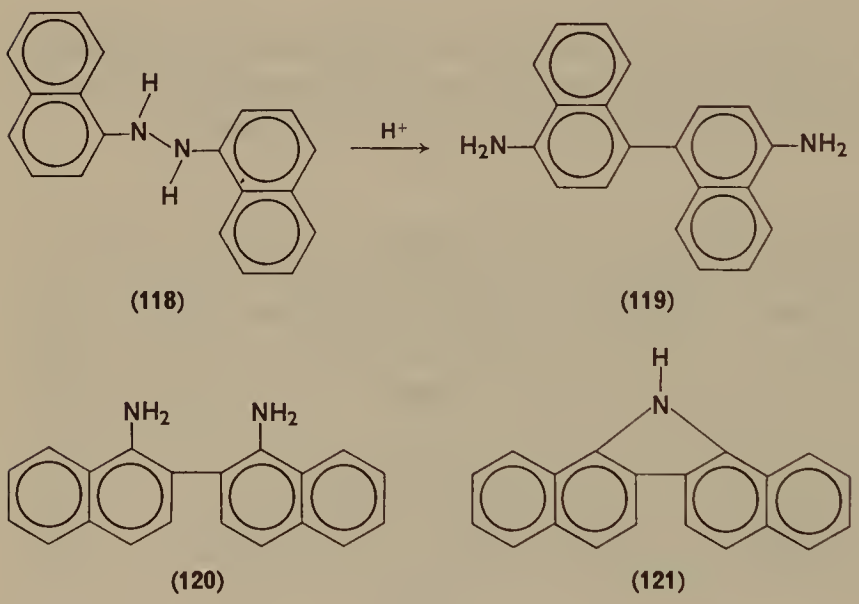
(29a)

(29b)

It follows that exclusive *ortho* coupling in reaction of **34** would lead to loss of one half the label in formation of **117a** (equation 29a). On the other hand if there is exclusive *para* coupling then all of the original label will be retained in the carbazole **117b** (equation 29b). The actual data, obtained by mass spectral analysis of the carbazole product, revealed an intermediate

situation. Surprisingly, though, the results indicated that the amount of *ortho* coupling *increased* with increasing acid concentration. Moreover, the increase in *ortho* coupling occurred in the acid region in which the dependence of reaction rate on acid concentration was invariant. It could therefore be concluded that the rate-determining step differs from the product-determining step and that a metastable intermediate is produced in the rate-determining step.

To determine the effects of deuterium substitution in reactions occurring via a one-proton mechanism, Banthorpe and co-workers[32] studied the acid-catalysed rearrangement of 1,1′-hydrazonaphthalene (**118**) and its 2,2′- and 4,4′-dideuterio derivatives, in 60% aqueous dioxane and 95% aqueous ethanol. It was found that in the dioxane medium 2,2′- or 4,4′-dideuteration did not affect the rate of reaction. Also dideuteration in the 4,4′-positions had no effect on product ratio in either reaction medium; the products formed included the 4,4′-ring coupled naphthidine (**119**), the 2,2′-ring coupled product dinaphthyline (**120**), and dibenzocarbazole (**121**), equation 30). However, although deuteration in the 2,2′-positions did not



(118) (119) (120) (121) (30)

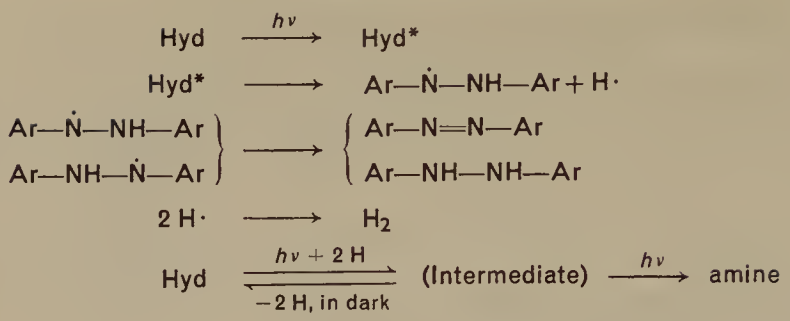
alter the ratio of 4,4′- to the total 2,2′-ring coupled compounds, it did affect the relative amounts of the latter, thereby resulting in a greater yield of the carbazole **121** as shown in Table 4. The change in product ratio with deuteration was thought to indicate that proton loss occurred in the rate-determining step of a branch reaction occurring after the main rate determining step for the rearrangement.

TABLE 4. Rearrangement products from deuterated and isotopically normal 1,1′-hydrazonaphthalene[29]

	Products (%)		
	4,4′-linked **119**	2,2′-linked **120**	carbazole **121**
Protium compound	63·6	17·0	16·7
2,2′-Dideuterionaphthalene (**45**)	63·1	6·5	29·5
4,4′-Dideuterionaphthalene (**44**)	62·5	18·1	18·5

b. Non-catalytic rearrangements. Labelling experiments have indicated that the thermally induced reactions of aryl hydrazo compounds proceed via an intramolecular mechanism[23]. For example, no randomization of the ^{15}N label was detected in the azobenzene product after reaction of an ethanolic solution of ^{15}N-hydrazobenzene (**32**) in a sealed tube at 150°C for 48 h[23]. Furthermore, studies of the thermal rearrangement of 2,2′- and 4,4′-dideuterionaphthalenes showed that the rate of reaction was substantially retarded by the presence of *ortho* deuterium atoms but little, if at all, by *para* deuterium atoms[80a]. Thus it appears that in the thermal reaction the aromatic protons are lost at a different stage along the reaction co-ordinate as compared with the acid catalysed reaction[32].

Photochemical reactions of aryl hydrazo compounds yield primarily the corresponding azo compounds and fission amines[24]. Experiments using labelled hydrazo compounds have also verified an intramolecular mechanism for this reaction[24, 80b]. This makes implausible an earlier claim that the reaction proceeds by a free radical mechanism involving the formation of anilinyl radicals ($PhNH^{\cdot}$) that give nitrenes, which then couple to form azo products[81]. Subsequently another mechanism was proposed[80b], also involving fission to anilinyl radicals, which by hydrogen abstraction from the substrate would form hydrazyl radicals, $Ph\dot{N}—NHPh$. The hydrazyl radicals would then undergo bimolecular reaction to give the azo product and the starting material. However, as recently pointed out by Banthorpe and co-workers[24], such a mechanism would require the formation of equivalent amounts of azo compounds and fission amines. Also, the formation of semidines would be expected in reactions involving anilinyl radicals[82]. Neither of these requirements are met experimentally. The reaction mechanism[83] outlined in Scheme 18 appears to satisfy the available experimental evidence. It should be noted that in this Scheme the arylazo compound and fission amines are formed in separate reactions. On absorp-



SCHEME 18.

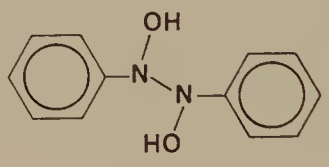
tion of ultraviolet radiation the hydrazo substrate (Hyd) is raised to an excited state. The latter decays to a mono-radical species, which subsequently disproportionates to give the azo product. The amine product is derived through an unidentified intermediate[83].

In conclusion of this section, it is apparent that current understanding of the thermal and photochemical reactions is not at par with that of the acid-catalysed process and further work in these areas should be worthwhile (see also Chapter 18).

C. Uses of Labelled Azoxy Compounds

1. Mechanism of the nitrosobenzene–phenylhydroxylamine condensation

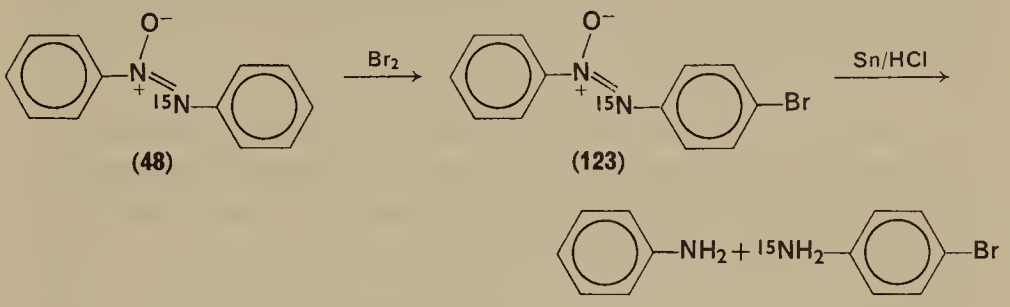
Reaction of ^{15}N-labelled nitrosobenzene with isotopically normal phenylhydroxylamine (equation 9) has been found to yield azoxybenzene-^{15}N in which the label is equally distributed between the two nitrogen atoms[36]. This result has been interpreted in terms of formation of a symmetrical *N,N'*-diol intermediate, **122**.



(122)

It is interesting to note the manner by which the distribution of the label in ^{15}N-azoxybenzene is determined (Scheme 19). Bromination of the azoxybenzene **48** gives 4-bromoazoxybenzene (**123**), with the halogen entering the ring furthest removed from the N(O) function[84], since the latter acts as a deactivating group in electrophilic substitution. Reductive cleavage of **123** with tin and hydrochloric acid yields the two anilines which can readily

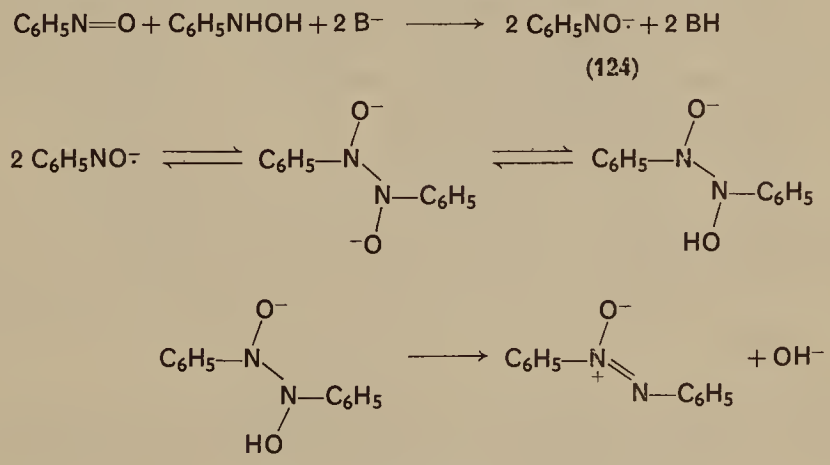
be separated on acetylation. Degradation of the respective acetanilides to ammonia followed by oxidation (NaOBr) yields molecular nitrogen which is then analysed by mass spectrometry.



SCHEME 19.

Returning to the nitrosobenzene–phenylhydroxyamine problem, it is also found that the reaction of nitrosobenzene and ^{18}O-labelled phenylhydroxylamine (equation 11a) yields azoxybenzene which contains one half the label of the original starting material[46,47]. This result was taken to implicate reversible formation of the symmetrical intermediate **122**.

Recent e.s.r. studies have demonstrated formation of nitrosobenzene radical anions in basic solutions of nitrosobenzene and phenylhydroxylamine[85,86]. Based on this evidence, a mechanism for the condensation has been proposed which does not involve formation of the *N*,*N*′-diol intermediate **122**. This mechanism, as outlined in Scheme 20, would however also account for the ^{15}N and ^{18}O results noted above. According to this scheme, the nitrosobenzene radical ions (**124**) dimerise to form an inter-

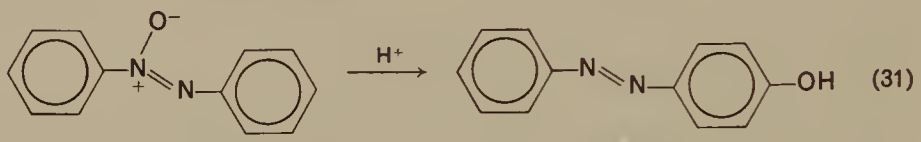


SCHEME 20.

mediate bis-anion, which becomes protonated by solvent and then loses hydroxide irreversibly to yield azoxybenzene. This mechanism also accounts for the observation that mixed condensations between XC_6H_4NO and YC_6H_4NOH yield all the possible azoxybenzenes, namely $XC_6H_4N(O)=NC_6H_4X$, $XC_6H_4N(O)=NC_6H_4Y$, $YC_6H_4N(O)=NC_6H_4X$ and $YC_6H_4N(O)=NC_6H_4Y$[87].

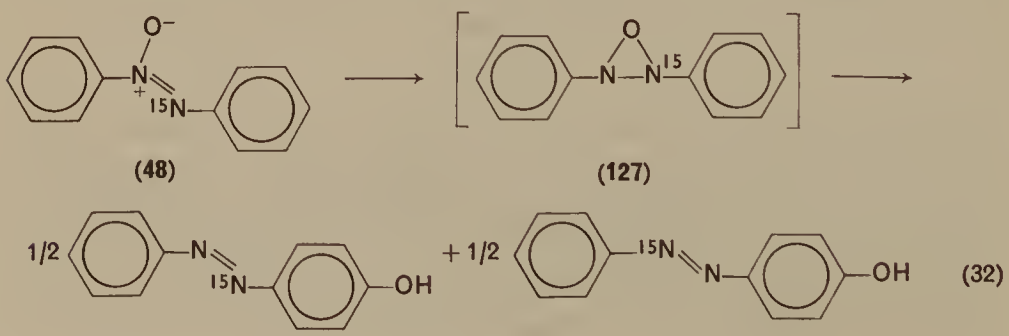
2. Mechanism of the acid-catalysed Wallach rearrangement

Aromatic azoxy compounds undergo an acid-catalysed transformation to hydroxyazo products. This general reaction is known as the Wallach rearrangement[88] and is illustrated by equation 31.



(125) (126) (31)

Studies involving labelled azoxy compounds have been highly informative concerning the mechanism of the rearrangement[89]. The first was reported by Shemyakin and co-workers[37,38], who reacted the unsymmetrically labelled ^{15}N-azoxybenzene (**48**) in 83% H_2SO_4 (8·5 days at 22–24°C) and examined the fate of the label in the *p*-hydroxyazobenzene product. Degradation by Scheme 19 and mass spectral analysis of the N_2 produced showed the label to be equally distributed between the nitrogen atoms of the *p*-hydroxyazobenzene. A similar examination of the unreacted azoxybenzene showed that the original ^{15}N label was undisturbed, thereby precluding a pre-equilibrium step in which the N atoms become equalized in the reactant. Based on these results Shemyakin and co-workers[37,38] postulated that the reaction mechanism involved formation of the symmetrical *N,N*-oxide intermediate **127**, which would then be attacked at either ring with equal ease (equation 32).



(48) (127) (32)

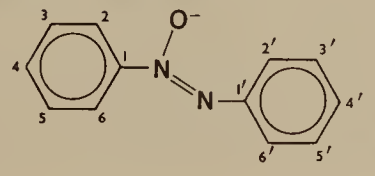
A complementary study[40] was performed with azoxybenzene-1-^{14}C (**54**) (83% H_2SO_4, at 90°C, for 30 min). Examination of the two anilines obtained upon reductive cleavage of the *p*-hydroxyazobenzene product confirmed the earlier results obtained with the ^{15}N-labelled compound **48**, that the entry of hydroxyl into the two phenyl rings occurs with approximately equal ease. However the actual data (azoxybenzene 0·3550; acetanilide 0·1730; *p*-hydroxyacetanilide 0·1627 μCi/mmol) point to the occurrence of a slight excess of 4′-substitution.

Isotopic tracer studies employing ^{18}O-azoxybenzene (**60**) have further demonstrated that the Wallach rearrangement proceeds by an intermolecular pathway. Working independently, Shemyakin's[36] and Oae's[48] groups showed that the *p*-hydroxyazobenzene obtained upon rearrangement of **60** in isotopically normal sulphuric acid (as well as chlorosulphonic acid) retained none of the original label. This result was confirmed by reaction of isotopically normal azoxybenzene in labelled acid medium, yielding the labelled *p*-hydroxyazobenzene[20, 21, 48].

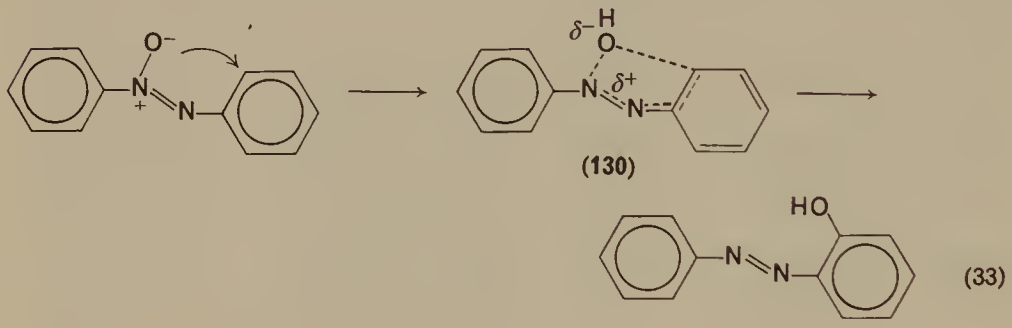
TABLE 5. Oxygen-18 tracer studies of the Wallach rearrangement

Reaction	Azoxyarene[a]	Atom-% ^{18}O in H_2SO_4	Hydroxyazo product	Atom-% ^{18}O	Ref.
1	4-bromo	0·99	4-bromo-4′-hydroxy	0·99	21
			4-bromo-2′-hydroxy	0·05	
2	4′-bromo	0·99	4-bromo-4′-hydroxy	0·99	21
3	4′-nitro	1·02	4-nitro-4′-hydroxy	0·96	20
4	4-methyl	0·38	4-methyl-4′-hydroxy	0·27	22
			4-methyl-2′-hydroxy	0·05	
5	4-methyl	0·99	4-methyl-4′-hydroxy	1·02	21
6	4′-methyl	0·99	4-methyl-4′-hydroxy	0·96	21
7	2,2′-dimethyl	0·91	2,2′-dimethyl-4′-hydroxy	0·95	21
8	3,3′-dimethyl	0·91	3,3′-dimethyl-4′-hydroxy	0·90	21
9	3,3′-dinitro	1·78	3,3′-dinitro-4′-hydroxy	1·75	20
10	4,4′-dimethyl	0·91	4,4′-dimethyl-2′-hydroxy	0·67	21

[a] The positions of azoxybenzene are numbered as follows: —



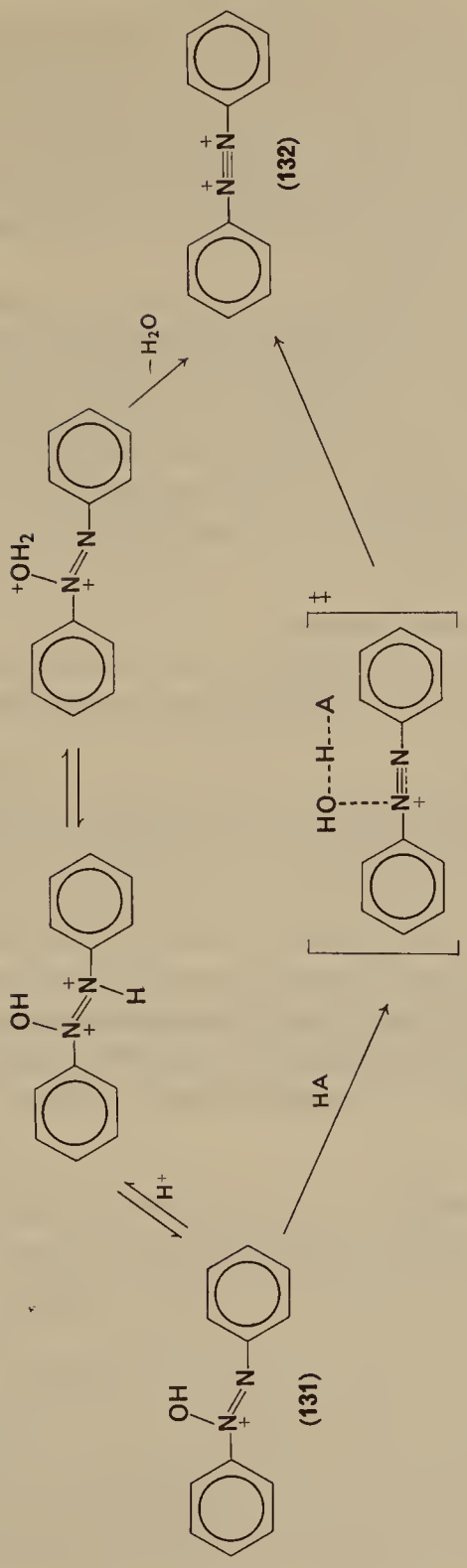
Although the acid-catalysed rearrangement of unsubstituted azoxybenzene yields the *para* hydroxyazobenzene exclusively (equation 31), substituted azoxybenzenes may result in *ortho* or *para* rearrangement, or a combination of both[89,90]. The reaction of a number of substituted azoxyarenes have been studied in labelled sulphuric acid[20,21,48]. The rearrangement products, and the atom-% ^{18}O, are given in Table 5[89]. The results show that, within experimental error, the *para* rearrangement products have the oxygen isotopic composition of the medium (note however the disagreement between reactions 4 and 5). In the case of the *ortho* rearrangement the oxygen is derived from the parent azoxy compound, except for 4,4′-dimethylazoxybenzene (reaction 10)[20]. In the latter case the 4,4′-dimethyl-2′-hydroxyazobenzene produced contains only 74% of the ^{18}O label of the medium. This appears to be the only case of an *ortho* rearrangement in which the oxygen is not exclusively derived from the parent azoxybenzene as given by isotopic labelling studies. From these results it was concluded that, whereas *para* rearrangement consistently occurs via an intermolecular mechanism, the *ortho* rearrangement may proceed either by inter- or intramolecular mechanism, depending on the nature of the substituents. In the case of *p,p′*-dimethylazoxybenzene both mechanisms operate simultaneously. Oae[48] has proposed that the mechanism of the *ortho* rearrangement involves formation of an intimate ion pair as shown in equation 33.



(130)

(33)

The potential usefulness of an approach which is alternative to that involving isotopic labelling is demonstrated by the results of kinetic studies of the Wallach rearrangement[91–93]. This work has been discussed in some detail in Chapter 18 and only the broad conclusions need be given here. A continued increase in rate of rearrangement of azoxybenzene, beyond the monoprotonation state (**131**), points to a two-proton process overall. This requirement is accommodated by Scheme 21 postulating the formation of a symmetrical dicationic intermediate, **132**[91,94], which will then undergo nucleophilic attack by solvent (or HSO_4^-) at either of the *para* carbons with



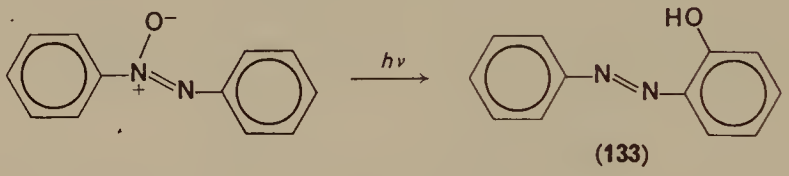
SCHEME 21.

equal ease. It is clear that the mechanism of Scheme 21 is in accord with the ^{15}N-labelling experiments which point to equalization of the two nitrogen atoms in the *p*-hydroxyazobenzene product, but not in the unreacted azoxybenzene recovered after partial reaction. The absence of a kinetic isotope effect in the rearrangement of azoxybenzene-d_{10}[95] shows that the aromatic proton is removed after the rate-determining step, which is also in accord with Scheme 21.

Kinetic studies of some substituted azoxyarenes indicate that a one-proton mechanism can also prevail. It appears in this case that nucleophilic attack occurs directly on the monoprotonated species, **131** (see ref. 89b). It is noted that such a mechanism does not predict equalization of the ^{15}N label, since there is no reason to suppose that **131** must necessarily be attacked with equal facility on either ring. As of to date, parallel kinetic and ^{15}N labelling experiments in such systems have not been reported.

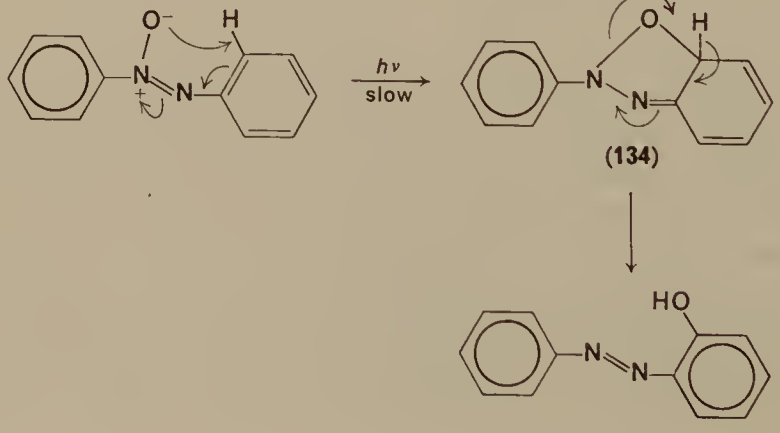
3. Photochemical rearrangements

Under the influence of u.v. radiation, azoxybenzene and its derivatives undergo transformation to the *ortho*-hydroxyazo products[45]:



(133) (34)

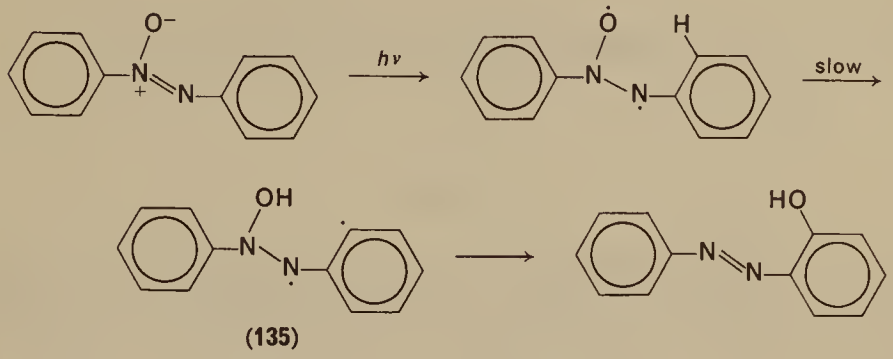
The photochemical *ortho* rearrangement has also been examined by isotopic studies. Labelling experiments similar to those carried out for the acid catalyzed reaction, employing ^{18}O and ^{15}N, have shown that the oxygen atom migrates to the ring furthest removed from the N(O) group,



(134) (35)

by an intramolecular pathway[37,38]. A possible mechanism for this reaction is illustrated in equation 35[96].

Alternatively one may propose a free radical mechanism, involving hydrogen abstraction from the *ortho* position of a distant aromatic ring in the rate-limiting step to give the intermediate **135**, which then undergoes a hydroxyl transfer to product, as depicted in Scheme 22.



(135)

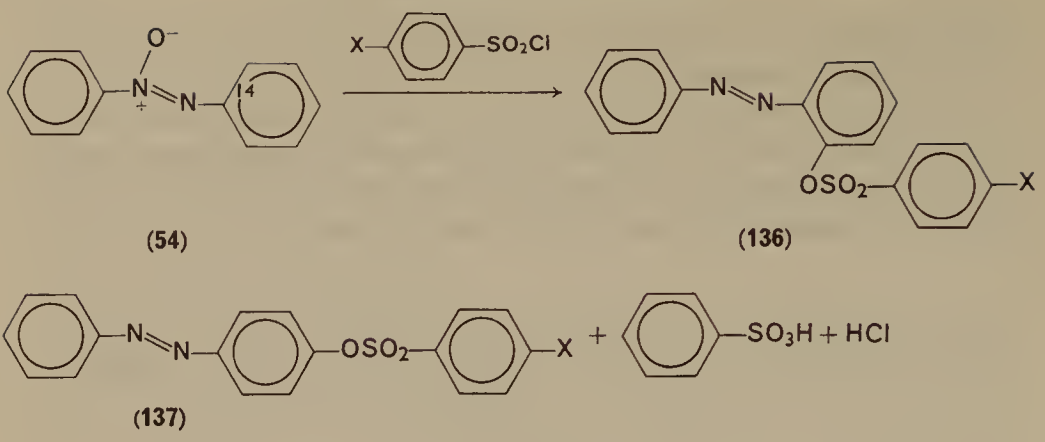
SCHEME 22.

Now assuming that intermediate **135** has a finite lifetime and is capable of returning to the ground state, the hydroxyl protons should exchange with solvent thereby incorporating the label of the medium into the starting material. However, irradiation of azoxybenzene-d_{10} in ethanol (and of isotopically normal azoxybenzene in CH_3CN/D_2O) to partial conversion and examination of the unreacted substrates showed no such exchange[42]. In addition, reaction via Scheme 22 would be expected to demonstrate a large primary isotope effect for the abstraction of an aromatic ring proton. However only a small, secondary, isotope effect is observed[42].

4. Reaction of azoxybenzene with arenesulphonyl chlorides

Azoxybenzene reacts with arenesulphonyl chlorides to yield the *ortho* and *para*-arenesulphonyloxyazobenzenes (**136** and **137**), arenesulphonic acid, and HCl, as shown in Scheme 23. The ratio of *ortho* to *para* products obtained in reactions using various sulphonyl chlorides was determined by means of isotopic dilution techniques employing azoxybenzene-1-^{14}C (**54**) as reactant[41]. The results are summarized in Table 6.

It is evident from Table 6 that the relative importance of *ortho* to *para* migration is dependent on the nature of the *para* substituent in the sulphonyl chloride. Rearrangement to the *ortho* position is most favoured with



SCHEME 23.

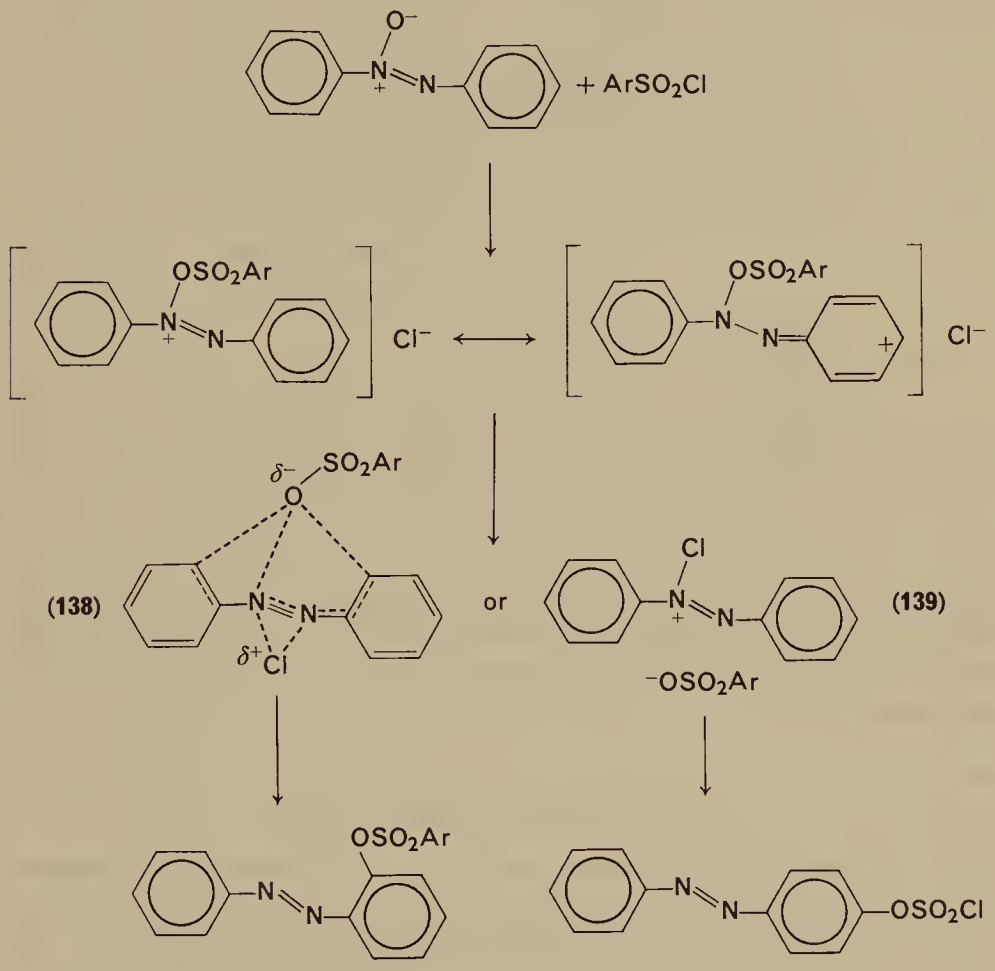
electron withdrawing substituents, while rearrangement to the *para* position is favoured with electron releasing substituents. In addition, analysis of the *ortho* product obtained upon reaction of **54** with *p*-nitrobenzenesulphonyl chloride revealed two noteworthy results. Firstly, the sulphonyloxy group migrates to both the phenyl rings. Secondly, two-thirds of the migration occurs to the *ortho* position of the ring farthest removed from the N(O) function, and one-third to the *ortho* position of the ring closest to the N(O) function. The isotopic analysis was carried out by reductive cleavage (Scheme 19) and determination of the specific activity

TABLE 6. Distribution of reaction products from reaction of azoxybenzene-1-^{14}C with sulphonyl chlorides in nitrobenzene[41]

Sulphonyl chloride (reaction conditions)	Arenesulphonyloxyazobenzene	
	% *ortho*	% *para*
p-$O_2NC_6H_4SO_2Cl$ (110°C, 25 h)	59·7	24·8
p-$BrC_6H_4SO_2Cl$ (110°C, 30 h)	28·8	36·8
p-$CH_3C_6H_4SO_2Cl$ (110°C, 50 h)	0·6	61·4
CH_3SO_2Cl (110°C, 50 h)	—	63·8

of the resulting amines. Experiments carried out using ^{18}O-labelled *p*-substituted arenesulphonyl chlorides have shown that the *ortho* rearrange-

ment occurs via an intramolecular process, suggestive of an oxygen-bridged ion pair intermediate. On the other hand, *para* rearrangement occurs by an intermolecular process, indicating a mechanism somewhat similar to the Wallach rearrangement; a nucleophilic process involving a solvent-separated ion-pair (**139**) has been proposed (Scheme 24)[41]:



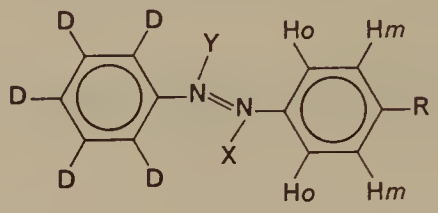
SCHEME 24.

5. Spectroscopic identification of α and β azoxy isomers

McBee and co-workers[44] have synthesized a number of *para* substituted azo and azoxy compounds which are completely deuterated in the unsubstituted phenyl ring (see Scheme 12, Section II, C, 3). The n.m.r. spectra of the α- and β-azoxyarene isomers showed subtle differences in the

resonance frequencies when compared with the corresponding azo compounds (Table 7). The difference in the observed chemical shifts can be

TABLE 7. Difference in chemical shift between pentadeuterioazo- and azoxybenzenes containing various substituents[44]



R	X	Y	Δ (azoxy-azo) Hz
CH_3	O		20
OCH_3	O		22
Br	O		22
CH_3		O	20
OCH_3		O	24
Br		O	16

utilized in differentiating between α- and β-azoxy isomers. The results substantiate structural assignments based on the use of the lanthanide shift reagent $Eu(fod)_3$[97] as well as conclusions drawn from mass spectral measurements[44].

IV. ACKNOWLEDGMENTS

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CHAPTER 18

Rearrangements of hydrazo, azoxy and azo compounds

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I. GENERAL INTRODUCTION

The rearrangements of hydrazo, azoxy and azo compounds, although not very large in number, constitute a class of reactions which have been extensively studied. Most involve aromatic substrates, and most involve acid catalysis, and their study has contributed greatly to our present understanding of aromatic rearrangements and of acid-catalysed reactions in general.

Of the rearrangements of hydrazo compounds, undoubtedly the best known reaction is the benzidine rearrangement, which has fascinated chemists for a long time. At least five different mechanisms for this process have been proposed, and at the time of writing the actual mechanism cannot be regarded as settled. The most frequently studied is the acid-catalysed reaction; related thermal and photochemical reactions are known, and processes involving similar rearrangements are important synthetically, for instance in the Fischer Indole Synthesis.

Proceeding to the azoxy series, the principal transformation here is the Wallach rearrangement of azoxybenzenes. The past decade has witnessed an upsurge in activity concerned with this reaction. Three general mechanisms have been proposed for the acid-catalysed rearrangement. A related photochemical process is known. Aliphatic azoxy compounds also rearrange, but this reaction has not been widely studied.

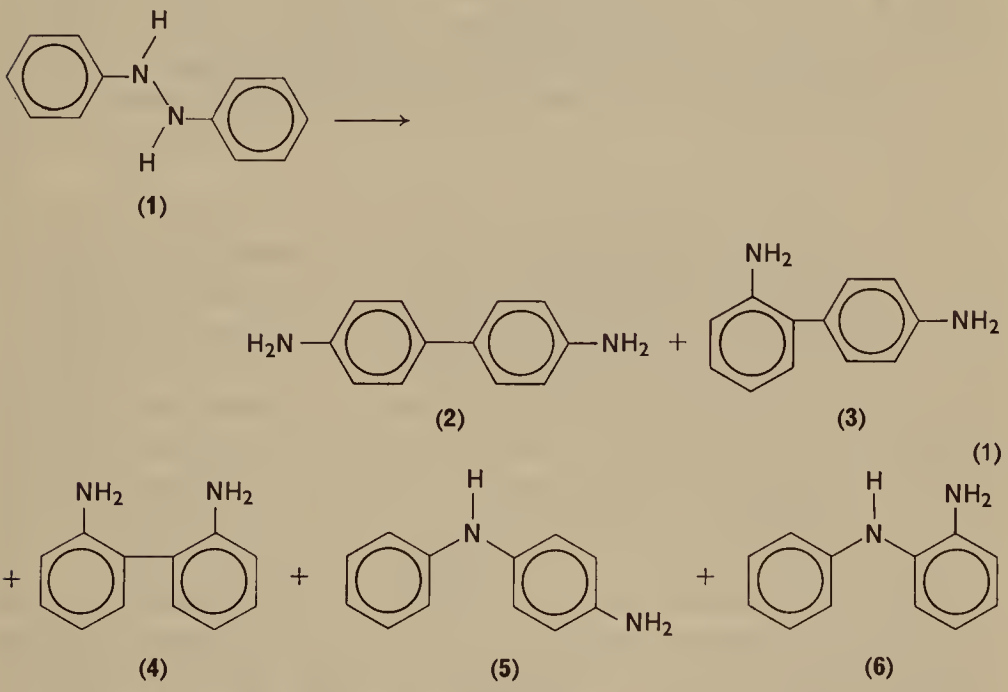
Certain azo compounds and protonated azo compounds tautomerize; although not a true rearrangement this process has been widely studied, in part due to the importance of these compounds in the dyestuff industry

and their use as indicators. Only few examples of true azo rearrangements are currently known.

II. REARRANGEMENTS OF HYDRAZO COMPOUNDS

A. The Benzidine Rearrangements

The term 'benzidine rearrangement' refers to the reaction which aromatic hydrazo compounds undergo, under acid-catalysed conditions or thermally, to yield compounds in which the hydrazo C—NH—NH—C grouping has rearranged, resulting in C—C or C—NH—C bonds with aryl-amino substitution (equation 1):



The various products formed from hydrazobenzene (**1**) and related compounds are known as benzidines (**2**), diphenylines (**3**), *ortho*-benzidines (**4**) and *para*- and *ortho*-semidines (**5** and **6**).

This reaction has been extensively reviewed and we do not propose to cover in exhaustive detail in this chapter the work carried out before 1965 or so, already treated by several authors[1–7]. We will conduct a general survey, concentrating more on the most recent mechanistic studies, with particular emphasis on the different possibilities for reaction intermediates and transition states.

Most of the work reported on the benzidine rearrangement has been directed at elucidation of the acid-catalysed reaction, and in this account emphasis is given to that aspect. The thermal and photochemical reactions are also considered, however, though more briefly. The rearrangement of heterocyclic hydrazo compounds is conveniently dealt with in a separate section. Lastly, we discuss briefly certain rearrangements which bear resemblance to the benzidine rearrangement, such as the Fischer Indole reaction.

1. The acid-catalysed benzidine rearrangement

a. Reaction products. The acid-induced rearrangement is usually performed in ethanol or dioxane solution on the addition of aqueous HCl or H_2SO_4. Acetic acid, and HCl in benzene or toluene, are also used[8]. Azo-compounds have also been used as substrates by treating them with $SnCl_2$ in concentrated HCl (the Jacobson method[9]); reduction followed by rearrangement generally results, although reductive cleavage may also occur.

Initially, only **2** was detected in the reaction of **1**[10], and only later was **3** also found[11]. Typically, the rearrangement of **1** in acidic ethanol leads to ~70% of **2** and ~30% of **3**. However, if solid **1** is treated with dry HCl gas, all the products given in equation 1 are observed[12] in the ratio **2**:**3**:**4**:**5**:**6** = 1·0:1·25:1·08:0·09:0·84. Products analogous to **4**, **5** and **6** are generally formed from substituted hydrazobenzenes, the predominant product depending on the substitution pattern. Paper chromatographic product analyses[13] suggest that at least traces of all possible products may be present in the reaction of most substrates, although many give only one major product.

The products obtained from the reactions of a large number of substituted hydrazobenzenes, together with the range of acidity over which the reaction was studied, and the observed order of the reaction in H^+, are collected together in Table 1, which is based on tables given by Banthorpe and Ingold[1,18]. It is apparent from the Table that (i) compounds with one *o*- or *m*-substituent give a predominance of benzidines, with small amounts of disproportionation products (fission amines, azo compounds, products from which the substituent has been lost, etc.), except for 3,3′-diamino-hydrazobenzene which is probably a special case; (ii) compounds with four *meta* substituents also give mainly benzidines, but now diphenylines and *ortho*-benzidines are formed as well, along with disproportionation products; (iii) compounds with either one or two *para* substituents give no benzidines at all, yielding instead mainly *ortho*-semidine and dispropor-

TABLE 1. Reaction products and observed order in H^+ for the rearrangements of substituted hydrazobenzenes

Compound R—NH—NH—R′		Products (% of total)[a]						Range $[H^+]$[b], M	Solvent[c]	Order in $[H^+]$	Ref.
R	R′	(2) 4,4′	(3) 2,4′	(4) 2,2′	(5) *N*,4′	(6) 2,*N*′	Dispr.				
Ph	Ph	73(79)	27(11)	—	—	—	(5)	0·05–1	A	2	14, 15, (16)
2-$CH_3C_6H_4$	2′-$CH_3C_6H_4$	100	—	—	—	—	—	0·01–0·5	A	1·3–2	17
2-$CH_3OC_6H_4$	Ph	100	—	—	—	—	—	0·002–0·3	A	1·1–2	18
2-$CH_3OC_6H_4$	2′-$CH_3OC_6H_4$	95	—	—	—	—	5	0·0001–0·05	A	1	18
2-FC_6H_4	2′-FC_6H_4	86	—	—	—	—	14	0·1–0·8	A	2	18
2-ClC_6H_4	2′-ClC_6H_4	94	—	—	—	—	6	0·8–2·8	A	2	18
2-BrC_6H_4	2′-BrC_6H_4	95	—	—	—	—	5	0·2–2·0	A	1·2–1·9	18
2-IC_6H_4	2′-IC_6H_4	100	—	—	—	—	—	0·7–1·6	A	1	18
2-PhC_6H_4	2′-PhC_6H_4	90	—	—	—	—	10	0·9–1·6	A	2	18
2-$CH_3C_6H_4$	3′-$CH_3C_6H_4$	100	—	—	—	—	—	0·05–0·1	A	2	19
3-$H_2NC_6H_4$	3′-$NH_2C_6H_4$	—	—	40	—	—	—	0·01–0·0442	B	1	20
4-$CH_3C_6H_4$	4′-$CH_3C_6H_4$	—	—	—	—	40	60	0·005–0·07	A	2	14, 21, 22
4-$CH_3OC_6H_4$	Ph	—	—	—	24	55	20	7×10^{-6}–5×10^{-3}	A	1	18
4-$CH_3CONHC_6H_4$	Ph	—	+	—	++	+++	70	0·007–0·1	A	1	18
4-FC_6H_4	4′-FC_6H_4	—	—	—	—	18·5	80	0·04–0·2	A	1–2	23
4-ClC_6H_4	Ph	—	19	—	20	30	31	0·07–1·0	A	2	18
4-ClC_6H_4	4′-ClC_6H_4	—	—	—	—	22	75	0·1–1·0	A	2	18
4-BrC_6H_4	4′-BrC_6H_4	—	—	—	—	30	70	0·1–0·5	A	2	18
4-PhC_6H_4	Ph	—	30	—	20		40	0·004–0·6	A	2	23
4-PhC_6H_4	4′-PhC_6H_4	—	—	—	—	25	75	0·006–0·02	B	1·8	24
4-$O_2NC_6H_4$	Ph	—	+++	—	20	+++	40	2·0–4·0	A	2	18
4-t-BuC_6H_4	4′-t-BuC_6H_4	—	—	—	—	47	53	0·01–0·05	B	2	25
3-t-BuC_6H_4	4′-ClC_6H_4	—	—	—	—	54	46	0·01–0·1	B	1·9	25
4-$CH_2{=}CHC_6H_4$	4′-$CH_2{=}CHC_6H_4$	—	—	100	—	—	—	0·001–0·05	B	1	26
3,5-$(CH_3)_2C_6H_3$	3′,5′-$(CH_3)_2C_6H_3$	27	30	11	—	—	8	2:1 H_2SO_4/H_2O v/v	H_2O	—	16
3,5-$Br_2C_6H_3$	3′,5′-$Br_2C_6H_3$	19	26	8	—	—	18	2:1 H_2SO_4/H_2O v/v	H_2O	—	16
3,5-$Cl_2C_6H_3$	3′,5′-$Cl_2C_6H_3$	36(60)	21(14)	16(+)	—	—	16(+)	2:1 H_2SO_4/H_2O v/v	H_2O	—	16 (27)

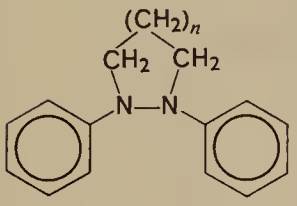
TABLE 1 (*cont.*)

Compound R—NH—NH—R′		Products (% of total)[a]						Range $[H^+]$[b], M	Solvent[c]	Order in $[H^+]$	Ref.
R	R′	(2) 4,4′	(3) 2,4′	(4) 2,2′	(5) *N*,4′	(6) 2,*N*′	Dispr.				
$3,5\text{-}F_2C_6H_3$	$3',5'\text{-}F_2C_6H_3$	69	10	2	—	—	7	2:1 H_2SO_4/H_2O v/v	H_2O	—	16
$3,5\text{-}(CH_3)_2C_6H_3$	$3',5'\text{-}Br_2C_6H_3$	49	20	2	—	—	11	2:1 H_2SO_4/H_2O v/v	H_2O	—	16
α-Naphthyl	α-Naphthyl	61	—	39[d]	—	—	—	5×10^{-6}–0·03	A	1	28
α-Naphthyl	β-Naphthyl	—	—	100[e]	—	—	—	0·01–0·15	A	1	29
β-Naphthyl	β-Naphthyl	—	—	100[f]	—	—	—	0·01–0·2 0·001–0·02	A C	1–1·2 1–2	30, 26
α-Naphthyl	Ph	44	—	56	—	—	—	1×10^{-4}–0·4	A	1–2	31
β-Naphthyl	Ph	—	—	100	—	—	—	8×10^{-4}–0·6	A	1·1–2	32
Ph—NMe—NHPh		+	+	—	—	—	—	3×10^{-4}–0·06	D	1·1–1·9	33
$Ph\text{—}NCOCH_3\text{—}NHPh$		83	—	—	—	—	—	2–6 M-$HClO_4$ in H_2O		1	34
$Ph_2N\text{—}NPh_2$		'high yield'	—	—	—	—	—	CF_3CO_2H in CH_2Cl_2		—	35
$Ph_2N\text{—}NHPh$		+++	—	—	—	—	—	'HCl in warm aq. EtOH'		—	36

[a] Plus signs indicate relative amounts, when the actual yield was undetermined.
[b] $HClO_4$ unless noted. Usually at 0°C.
[c] A = 60:40 dioxan:water; B = 95:5 ethanol:water; C = 75:25 acetone:water; D = 25:75 methanol:water.
[d] 20% in the form of 1,2:7,8-dibenzocarbazole.
[e] 35–40% in the form of 1,2:5,6-dibenzocarbazole.
[f] 6% in the form of 3,4:5,6-dibenzocarbazole.

tionation products, with scattered instances of the other possibilities*; (iv) *ortho*-benzidines are only formed in large amount by compounds with additional unsaturation, such as a naphthalene ring or vinyl groups; (v) such *N*-substituted compounds as have been studied give predominantly benzidine products.

An interesting example of case (v) above arises from the work of Wittig and co-workers[37], who studied the rearrangement of **7** in 2N-HCl ($n = 1$–4, 8). With $n = 1$ reduction occurred, but with $n = 2$, 43% of **8** and 20% of **9**



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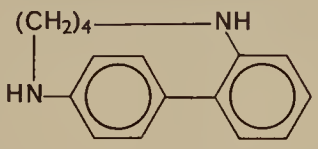

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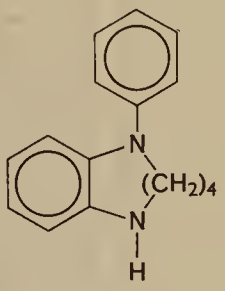

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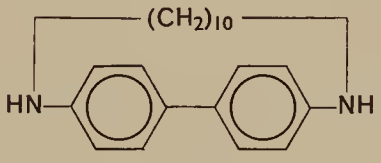


(10)

were produced, while with $n = 3$ or 4 products like **8** resulted. With $n = 8$, 4% of **10** was produced. Products such as **8** or **10** will be strained.

Table 1 refers to mainly aqueous acidic media. Products and product ratios are often different in aqueous and non-aqueous media, as the selected examples from the work of Lukashevich[3,8] in Table 2 indicate.

Jacobson has reported products[9] from a large number of substituted hydrazobenzenes, as obtained by the method of reduction of the azo-compound ($SnCl_2$/HCl), with rearrangement following; space limitations preclude discussion of this material, which in any case is regarded as of less value than that presented up to now[1]. However, a recent case involving the Jacobson method is of special interest; Allan[38] has shown that 4-chloro- and 4-methoxyazobenzene give detectable amounts of both 2,*N*′- and

* Banthorpe, Hughes and Ingold[4] summarized the situation: 'A 4-substituent, if strongly electron-donating, leads to 2,*N*′-linking, if not, to 2,4′-linking, and if both strongly donating and attracting (halogens), to both modes of linking; an electron-donating substituent, if at 4, orientates linking towards 2, and if at 2, towards 4, with a strength paralleling that of its electron donation.'

TABLE 2. Rearrangement products of some substituted hydrazobenzenes in non-aqueous media[3]

Compound; substituents in Ph—NH—NH—Ph	Conditions[a]	Products (% of total)					
		Benzidines	Diphenylines	*ortho*-Benzidines	*ortho*-Semidines	Anilines	Azo-compound
None	A	36·4	29·6	12·8	12·5	0·4	0·4
	B	33·6	30·6	7·5	16·0	1·5	1·6
	D	75·5	19·0	—	2·3	1·3	1·3
	E*	56·5	23·8	—	2·6	8·1	8·0
2,2′-Dimethyl	A	44·7	25·0	—	1·5	10·5	11·5
	B	41·1	30·4	—	9·5	6·8	6·0
	E*	87·0	10·9	—	0·7	0·5	0·5
4,4′-Dimethyl	C	—	—	—	76·1	8·5	8·2
	E*	—	—	—	58·1	23·0	16·1
3,3′-Dimethyl	C	32·6	18·1	16·5	23·0	1·5	1·6
	E*	79·2	11·0	—	3·0	2·0	2·3
2,2′-Dimethoxy	B	14·0	18·2	—	18·5	20·0	18·1
	D	65·7	16·9	—	2·6	4·7	4·5
2,2′-Diethoxy	C	48·7	18·8	—	9·2	2·8	2·4
	D	76·0	8·0	—	4·4	2·5	2·5

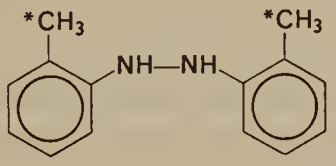
[a] A = HCl in benzene/toluene at −10°C; B = HBr in ether at −10°C; C = HCl in ether at −10°C; D = HCl in 99·9% ethanol at 0°C; E* = HCl in 95·0% aq. ethanol at 0°C (aqueous medium).

N,2′-coupled *ortho*-semidines, when modern chromatographic methods of product detection are used. This may be significant from a mechanistic viewpoint, as we shall see later on. The actual results obtained are given in Table 3[38] (cf. ref. 18).

TABLE 3. Rearrangement products of 4-chloro- and 4-methoxyhydrazobenzene obtained by the Jacobsen method[38]

Coupling pattern of products	4-chloro	4-methoxy
2,4′	~40	9
2,2′	0·5	~0·01
N,4′	14	11
2,*N*′	8	~65
N,2′	8	+
dispr.	28	13·75

b. Kinetic and other mechanistic studies. The benzidine rearrangement has been shown to be *intramolecular* in several ways, mainly involving the lack of formation of any crossed products when two different substrates are reacted in the same solution. Thus equimolar amounts of decadeuterio-*N*-acetyl-hydrazobenzene and the equivalent undeuterated compound produce less than 0·2% of the crossed products (containing 4 atoms of D; the *para* proton is derived from the medium)[34]; reaction of **11** in the presence of *ortho*-hydrazotoluene produced none of **12**[39]; mixtures of 1,1′-



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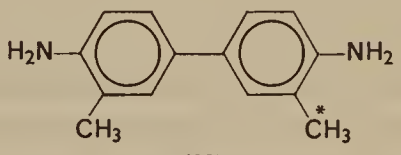


(12)

and 2,2′-hydrazonaphthalene give no evidence of products obtainable from the rearrangement of 1,2′-hydrazonaphthalene[40]; and mixtures of 2,2′-dimethoxy- and 2,2′-diethoxyhydrazobenzene lead only to dimethoxy and diethoxy products, and not to 3-ethoxy-3′-methoxybenzidine[41]. Thus the benzidine rearrangement is accepted as being an intramolecular process[1–7].

The reaction is also known to proceed by two parallel pathways*, one

*The history and development of ideas and observations leading to this proposal are discussed at length in refs. 1 and 2.

first order and the other *second order* in H^+. Thus the rate law for the rearrangement of hydrazobenzene is of the form of equation 2, where S is the substrate (hydrazobenzene) and P represents all possible products. With the mechanism being partially represented by equations 3 and 4, $k_2 = K_1 k_1'$ and $k_3 = K_1 . K_2 . k_2'$.

$$\frac{-\mathrm{d}[S]}{\mathrm{d}t} = k_2[S][H^+] + k_3[S][H^+]^2 \tag{2}$$

$$S + H^+ \underset{\text{fast}}{\overset{K_1}{\rightleftharpoons}} SH^+ \xrightarrow[\text{slow}]{k_1'} (P) \tag{3}$$

$$S + H^+ \underset{\text{fast}}{\overset{K_1}{\rightleftharpoons}} SH^+ \underset{\text{fast}}{\overset{K_2}{\rightleftharpoons}} SH_2^{2+} \xrightarrow[\text{slow}]{k_2'} (P) \tag{4}$$

In Table 1 are listed the observed orders of the reaction in H^+ for different substrates, together with the range of acidity over which the reaction was studied. The order in H^+ ranges from 1 to 2 at the extremes, with several of fractional order and several in the ranges quoted. The reaction order values can be obtained as follows[2]. Rewriting equation 2 as equations 5 and 6,

$$\frac{-\mathrm{d}[S]}{\mathrm{d}t} = k_T[S] \tag{5}$$

$$k_T = k_2[H^+] + k_3[H^+]^2 \tag{6}$$

we can see that a plot of $\log k_T$ vs. $\log[H^+]$ (or $-H_0$)[23] will be a curve, with slope close to 1 initially and close to 2 finally. A more useful plot is that of $k_T/[H^+]$ vs. $[H^+]$, which will be linear with intercept k_2 and slope k_3, allowing both rate constants to be obtained; some data obtained in this way are given in Table 4.

The data in Table 4 illustrate the correlation between the occurrence of fast reactions and the one-proton mechanism, as might have been expected; generally speaking, electron-donating *o*- and *p*-substituents enhance the rate, and electron-withdrawing ones reduce it.

With the quantity of kinetic data now available for various substituted benzidines (e.g. Table 4 and ref. 23), one might expect various linear free energy relationships to apply. It is seen that, from equations 2–4 above, $k_3 = K_1 . K_2 . k_2'$, and one might expect log k_3 to be a linear function of $(pK_1 + pK_2)$, if log k_2' is itself a linear function of $(pK_1 + pK_2)$, as seems reasonable. Unfortunately, neither pK_1 nor pK_2 can be measured, since the rearrangement is too fast to permit the observation of protonated species[23]. However, the pK's of similarly substituted anilines can be used instead[23]; these will certainly be linear functions of the pK's of the hydrazo-

TABLE 4. Rate constants for the rearrangements of some hydrazobenzenes RNHNHR′ by the one- and two-proton reaction[1,2]

R	R′	$k_2 \times 10^{3\,a}$	$k_3 \times 10^{3\,a}$
2-ClC_6H_4	2-ClC_6H_4	—	0·000034
2-FC_6H_4	2-FC_6H_4	—	0·0027
4-ClC_6H_4	4-ClC_6H_4	—	0·013
Ph	Ph	—	1·7
2-$CH_3C_6H_4$	2-$CH_3C_6H_4$	0·21	8·5
3-$CH_3C_6H_4$	3-$CH_3C_6H_4$	—	17
4-PhC_6H_4	Ph	—	680
4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	—	1400
β-naphthyl	Ph	0·50	5·0
α-naphthyl	Ph	20·0	130
β-naphthyl	β-naphthyl	460	—
α-naphthyl	β-naphthyl	1000	—
α-naphthyl	α-naphthyl	1800	—
4-$CH_3OC_6H_4$	Ph	~8500	—

[a] Rate constants calculated at 0°C in 60:40 dioxane:water with $HClO_4$ as the catalysing acid. k_2 is in $sec^{-1}\ M^{-1}$, k_3 is in $sec^{-1}\ M^{-2}$.
References for individual compounds as in Table 1.

benzenes, if protonation is on nitrogen, as is generally assumed. It seems evident that at least one nitrogen will be protonated in the two-proton process and it is usually assumed that the second proton goes on the other nitrogen[1,2]. Similarly nitrogen should be protonated in the one-proton process[1,2].

However, a plot of log k_3 for substituted hydrazobenzenes[23] vs. ($pK_1 + pK_2$) for similarly substituted anilines[42] is not linear; the plot is quite random, with no obvious trends even among quite similar compounds. A similar plot of log k_2 against pK_1[23] (one-proton process) also displays considerable scatter, but here it is evident that the effect of substituents on rate is much greater than the effect on basicity. Plots of this type have been found to be linear by Onishi[43], who corrected his observed rates for the steric effects of the *ortho* substituents used, via Taft's E_s parameters.

Another possible linear free energy relationship for the two-proton process is a plot of log $k_3 - pK_1 - pK_2$ ($\equiv$ log k_2') against σ or σ^+ for the different substituents. Again the pK's of the corresponding anilines must be used. These plots are reported to give 'poor Hammett correlations' with $\rho = -6{\cdot}0 \pm 1{\cdot}8$[23]. Three substituted *N*,*N*′-dimethylhydrazobenzenes are reported to have their rates correlated by σ^+ values with a ρ of $-11{\cdot}9$[44].

The correlations with σ^+, rather than σ, and the large negative ρ value indicate large development of positive charge in the transition state, as might have been expected.

Activation parameters for the benzidine rearrangement are composite functions of equilibrium and rate constants, and so are not particularly helpful in elucidating the mechanism. For the two-proton process, values of ΔH^* between 19 and 22 kcal/mol, ΔS^* between −10 and +3 e.u., and ΔV^* between −7 and 0 cm^3/mol are reported[1,43]. For the one-proton process, values of ΔH^* are about 5 kcal/mol lower[1]; values of ΔV^* lie between −2 and −12 cm^3/mol[43] though no ΔS^* values are reported.

Adding salts to aqueous acidic reaction media markedly increases the rate of the benzidine rearrangement[28,45,46]. This is held to reflect the creation of charge as the transition state is reached[4]. The polarity of the medium affects both the rate[28] and the products formed (see Tables 1 and 2 above). The rate behaviour is complex. The rearrangement rates, at constant pH, of hydrazobenzene in ethanol/water[46] and of 2,2′-hydrazonaphthalene in dioxan/water[30] both decrease to a minimum value as water is added to the non-aqueous solvent component, and then increase again as more water is added. Banthorpe, Hughes and Ingold[4] feel that this behaviour reflects preferential solvation of a highly polar transition state by the more polar aqueous component. The rate acceleration at low water contents is due to the increased activity of catalytic protons in these media[4].

c. General vs. specific acid catalysis. The question arises as to whether one of the proton transfers to hydrazobenzene is rate determining or not. Rate-determining proton transfers exhibit general acid catalysis—all acid species present catalyse the reaction to the extent of their proton-donating abilities—whereas fast proton transfers occurring before the rate-determining step involve specific hydrogen ion catalysis. Cohen and Hammond measured the rate of rearrangement of hydrazobenzene in 50% aqueous ethanol at constant pH, catalysed by varying amounts of organic buffer acids[47]. They considered the results to indicate catalysis by undissociated acids. However, as Banthorpe points out[1], a Brønsted relationship could not be demonstrated, and the sensitivity of the rate to the changing medium polarity, as the amount of added acid was changed, was not taken into account. In a subsequent study, general acid catalysis of the rearrangement of 4-methoxyhydrazobenzene could not be demonstrated[48].

Another test for general vs. specific acid catalysis is based on the supposition that rate constants are linear functions of h_0 for specific acid catalysis, and of $[H^+]$ for general acid catalysis (the Zucker–Hammett hypothesis)[49]. Benzidine rearrangement rates are linear functions of h_0 and this is held to support a specific acid catalysis mechanism[1,2]. However the supposition

involved is subject to doubt since it has been pointed out that both types of mechanism can in fact lead to linear correlations with h_0[49, 133].

A third approach to the problem involves the use of solvent isotope effects. If a proton transfer is rate-determining, replacing the catalysing acid H_3O^+ by D_3O^+ will cause a rate decrease[54]. On the other hand, concentrations of protonated species will be higher in D_3O^+ solutions than in H_3O^+ solutions of equal concentration, since D_3O^+ in D_2O is a stronger acid than H_3O^+ in H_2O[50]. This means that the reaction will be faster if pre-equilibrium proton transfer is involved, because of the increased concentration of the protonated intermediate.

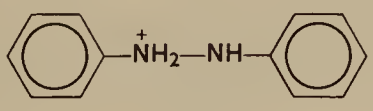
Results obtained for the benzidine rearrangement by Banthorpe, Hughes and Ingold[4] for several substrates, with reaction orders in H^+ varying between 1 (1,1′-hydrazonaphthalene) and 2 (hydrazobenzene), show solvent isotope effects, k_D/k_H, between 2·1 and 4·8. From their data it is possible to define a rate-enhancement factor per added proton, f_m, as the positive root of equation 7, where x = order in H^+ and $y = k_D/k_H$. The value

$$(x-1).f_m^2 + (2+x).f_m = y \qquad (7)$$

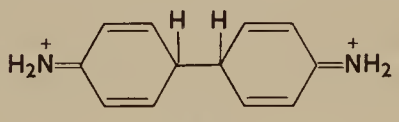
of f_m is 2·0 ± 0·1, averaged over six cases, which is strong evidence for the occurrence of both proton transfers before the rate-determining step.

Ring deprotonation has been shown not to be rate determining through isotope effect studies. Deuterium substitution into hydrazobenzene, at the 4,4′-positions, and at all positions but these, and into 1,1′-hydrazonaphthalene, at the 2,2′- and 4,4′-positions, did not affect the observed rate constants[4]. Deprotonation of benzidine precursors must therefore be fast processes, occurring after the rate-determining step.

d. Reaction intermediates. The only authenticated examples of isolable intermediates in the benzidine rearrangement, prior to 1970, were the monohydrochloride salts of some hydrazobenzenes, e.g. **13**, which can be obtained in good yield by adding HCl in ether to a molar excess of the hydrazobenzene[48, 51]. However, in 1972 Olah and co-workers[52] prepared



(13)



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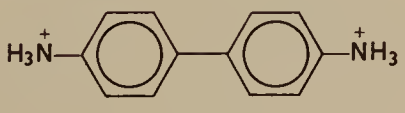


(15)

and characterized by n.m.r. spectroscopy in superacid media the species **13–15**. Compound **13** was prepared as described above; **15** was formed as a yellow precipitate (di-HCl salt) by the treatment of hydrazobenzene with HCl in SO_2 or SO_2ClF solution at −78°C, followed by solvent evaporation; and **14** could be observed by n.m.r. when hydrazobenzene was treated with FSO_3H/SO_2, FSO_3H/SO_2ClF or HF/SO_2 at −78°C. Diprotonated hydrazobenzene was not observed in any form, however[52].

e. Requirements for an acceptable mechanism. It is appropriate at this stage to review the experimental evidence thus far presented, almost all of which should be accounted for by an acceptable mechanism.

An acceptable mechanism should be able to rationalize all of the different types of bonding found in the observed products (see equation 1 and structures **2–6** therein), as well as the disproportionation products observed in some cases (Tables 1–2). It is worth noting here that the different products observed from the same substrate are not formed from one another, i.e. they are all stable under the reaction conditions. Even the carbazoles formed from some hydrazonaphthalenes (see Table 1) are not formed under the rearrangement conditions from the 2,2′-diaminodinaphthalenes which might have been regarded as their immediate precursors[4,28]. Thus either all products are formed from the same intermediate (which occurs at or after the rate-determining step), or the transition states leading to the different products are themselves different.

The observed intramolecularity must be accounted for, as must the two parallel pathways leading to product, one first order and the other second order in H^+. The rate-determining step apparently occurs after mono- or diprotonation of the substrate, but before deprotonation of the protonated product. Assuming that intermediates **13** and **14** are on the reaction pathway, it appears that the rate-determining step occurs at some point between these two intermediates in the reaction course.

The fact that ring-deuterated substrates react without deuterium loss or scrambling[4,34] is important, as is the lack of deuterium incorporation into the ring positions of product benzidine when hydrazobenzene is rearranged in the presence of D_2SO_4 or $SbF_5/DF/SO_2ClF$[52].

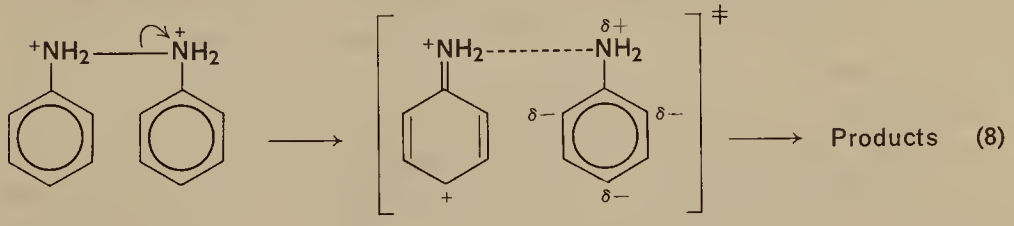
Finally, the effects of substituents, solvent polarity, and added salts on the reaction rate, as discussed above, should also be satisfactorily accounted for.

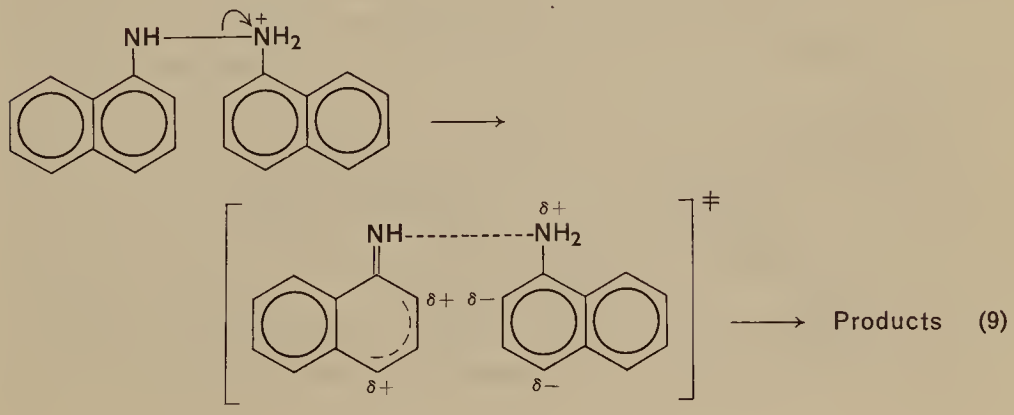
f. Theories of mechanism. This fascinating reaction has been a fruitful source for mechanistic speculation over the years. At the present time there can be considered to be five different theories. They may be designated as Dewar's π-complex theory, the caged-radical mechanism, Lukashevich's mechanism, the polar transition state theory of Banthorpe, Hughes and

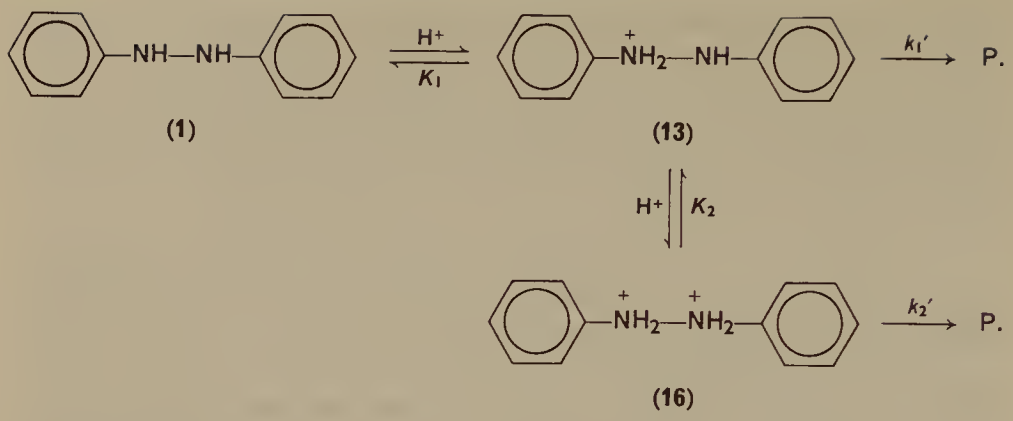
Ingold, and lastly, the C-protonated intermediate mechanism. The polar transition state theory differs from the others in that it proposes the formation of the product skeleton during the rate-determining step, rather than via an intermediate. At the time of writing the fifth mechanism is sufficiently in flux that its evaluation can only be considered as tentative. A discussion of these rival theories follows.

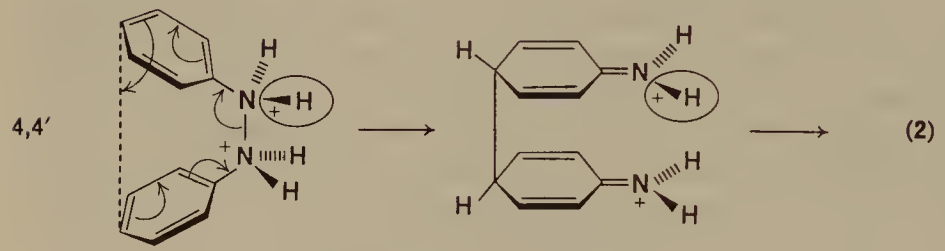
g. The polar-transition-state theory. A simplified form of the mechanism proposed by the exponents of this theory is given in Scheme 1. Initially, hydrazobenzene is protonated on nitrogen, giving **13**. A second protonation on nitrogen would yield the dication **16**. Either **13** or **16** can react in the five ways illustrated, leading to the five products **2–6**. The circle around one proton and one positive charge in the structures in Scheme 1 is intended to illustrate the fact that this position is a lone pair in the one-proton mechanism. Thus the extra proton is visualized as promoting the reaction by encouraging the N—N bond to break, in order to minimize the repulsion of the adjacent positive charges. According to this scheme we have five different concerted reactions; the transformation **16** → **14**, for example, occurs without the incidence of another intermediate.

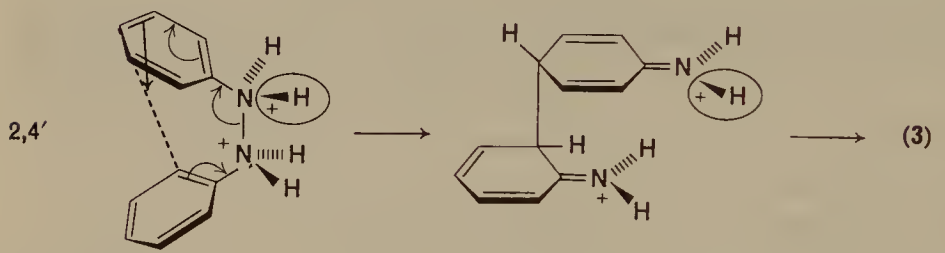
Scheme 1 is actually a drastic simplification. Banthorpe prefers to write the diprotonated transition state as in equation 8, and the monoprotonated one as in equation 9, for example. He writes: 'For each mechanism the

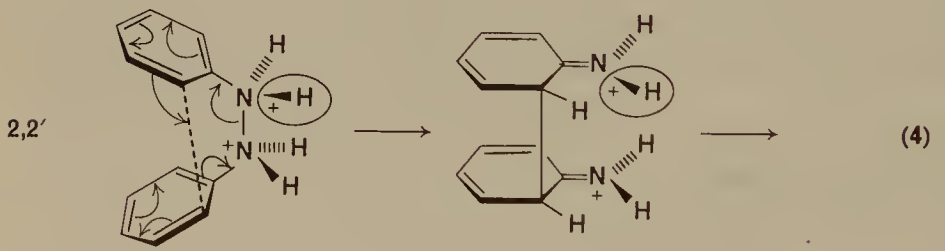


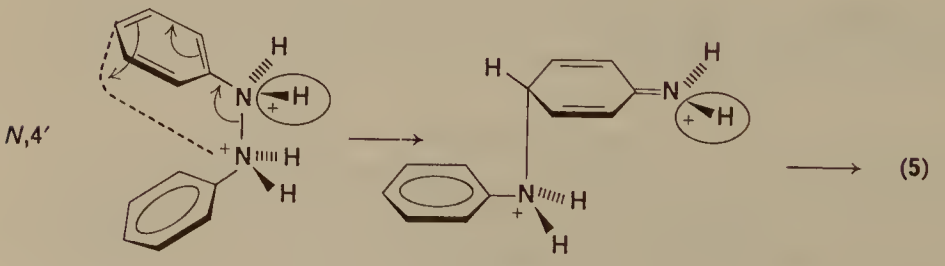




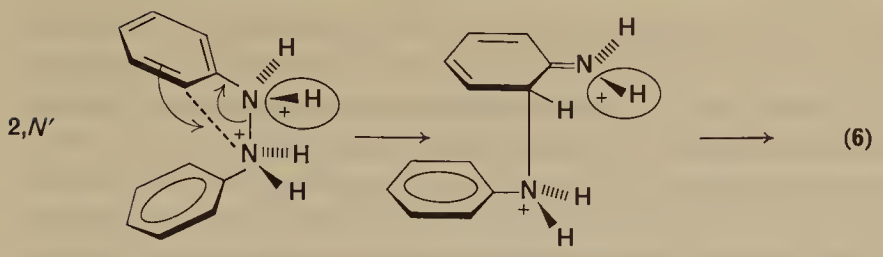








SCHEME 1.



SCHEME 1 (*cont.*)

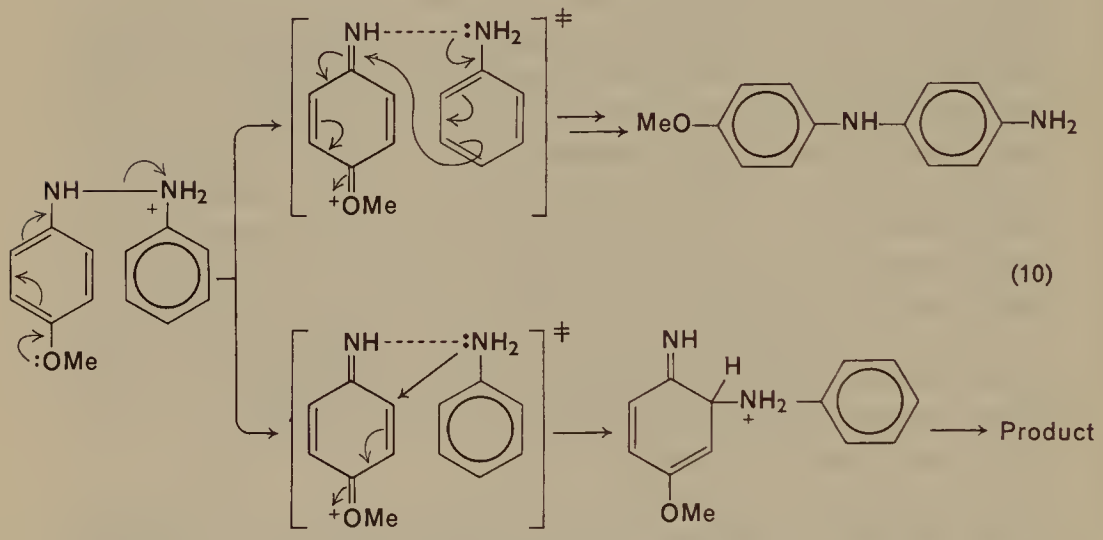
incipient cation is formed adjacent to an incipient neutral species capable of undergoing activated electrophilic attack at the 2- and especially 4-ring positions. Thus a strong electrostatic interaction between potential bonding sites, together with the polar character of the N—N bond in the transition state allowing a low bending-constant of the C—N bond, permits energetically-cheap changes of shape to meet the stereochemical requirements for rearrangement, and a concerted movement of the electronically distinct quasi-fragments into coplanarity is possible. This may be assisted by electrokinetic interactions between the π-orbitals of the rings (such as occur in graphite), and also by the low effective dielectric constant of the medium at the atomic distances involved. The weakly directed electrovalences develop into well-directed covalencies and internal substitution occurs to lead to rearrangement products[1].'

It can be seen that this mechanism accounts for all of the 'requirements for an acceptable mechanism' above. The kinetic data can be rationalized qualitatively (though perhaps not quantitatively—see the poor linear free energy relationships discussed above) in terms of the known inductive and mesomeric effects of substituents on rates and nitrogen basicities. Charge distributions in the transition states are also held to account for all the products. A few examples will serve to illustrate this theory.

Hydrazobenzene itself on rearrangement gives mainly benzidine, with about 30% diphenyline. This is in line with the known susceptibility of benzene rings to attack at the 4-position, and to a lesser extent at the 2-position. Hydrazonaphthalenes give mainly 2,2′-bonded *ortho*-benzidine; in these cases 'folding over' of the rings (as in Scheme 1) is less pronounced, for steric reasons, leading to more 2,2′-bonding, as these positions are simply closer together.

4-Methoxyhydrazobenzene reacts via the one-proton mechanism to give *ortho*- and *para*-semidines and disproportionation products, but no 2,2′-

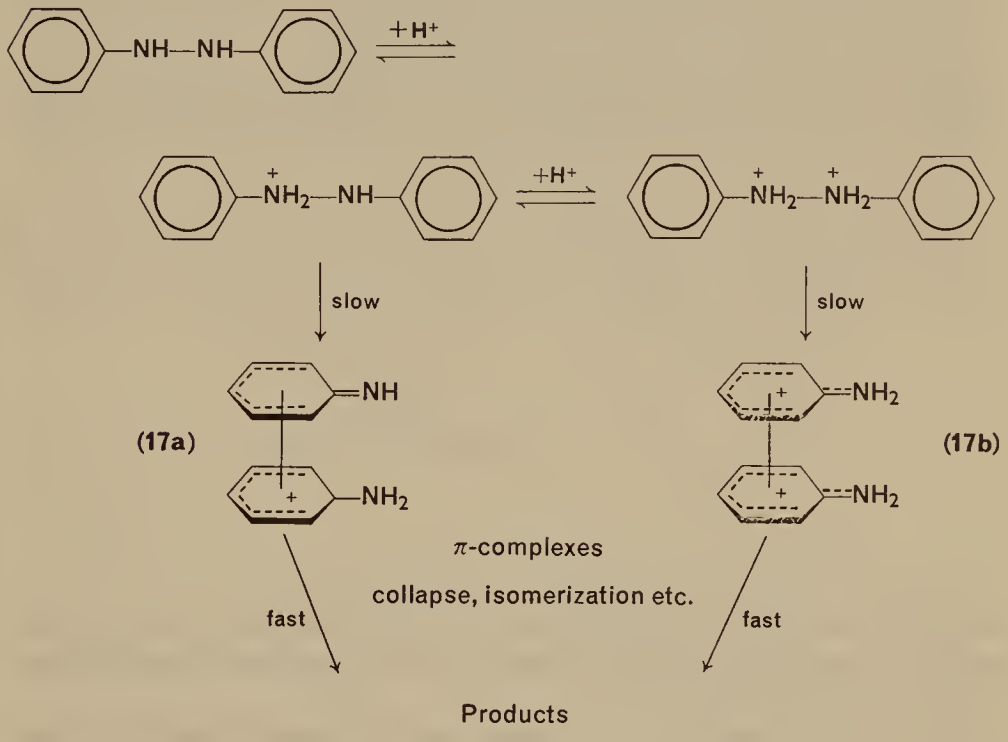
or 2,4′-linked products (see Table 1 above). The reaction can be visualized to occur as in equation 10. Note that the *ortho*-semidine product predicted is 2,*N*′-bonded and not *N*,2′-bonded. The bonding required to form an *N*,4′-bonded *para*-semidine appears rather questionable, as has been remarked upon by Shine[11]: 'the synchronous breaking of the N—N bond and making of the *N*,4′-bond requires too great a molecular distortion to be reasonable'[2]. One of the difficulties with this mechanism is that it is sometimes difficult intuitively to account for the large molecular distortions proposed. It is also worth noting that in equation 10 the single proton is



placed on the less basic of the two nitrogen atoms[42]. Presumably, since protonation of the more basic site does not lead along the favourable delocalization pathway of equation 10, it can be regarded as resulting in much slower reaction, or as being reversible (or as leading to disproportionation). Thus reaction via protonation of the less basic site is favoured.

Replacing the 4-OMe group by CH_3 or Cl weakens the electron release of the substituent, requiring the presence of the second proton for bond heterolysis, and leading to less 2,*N*′- and more 2,4′-bonding, as the situation approaches that found in benzidine itself (4,4′-bonding is of course not possible with a 4-substituent). This is in substantial agreement with experiment. 2-Substituted hydrazobenzenes have been treated in a similar fashion[4].

h. The π-complex theory. This theory, originally proposed by Dewar in 1946[53] before many of the facts concerning the benzidine rearrangement were known, has been substantially modified since that time[5]. As the basis of the theory, the π-complex is worthy of consideration because of the intuitively attractive idea that such interaction between the benzene rings will help the massive geometric change required of the molecule during reaction. The theory as it stands today may be summarized by the following scheme:

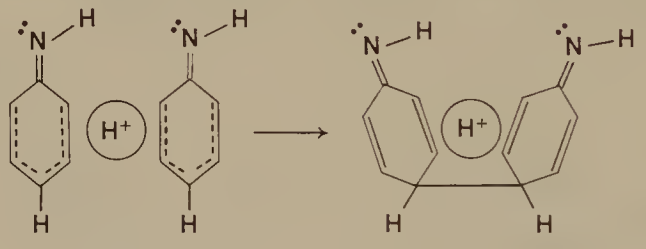


According to this Scheme, π-complexes **17a, b** would be formed as intermediates, which may isomerise or collapse to products directly. The isomers would be rotated or displaced π-complexes.

The π-complex theory of Dewar is supported by a number of other authors[34, 55, 56]. However, Banthorpe feels that π-complexes are unnecessary in these reactions and has recently criticized the validity of the π-complex concept[54]. On the other hand, Dewar believes the polar transition state concept to be unsound[5b]. Perhaps the two concepts are not mutually

exclusive after all, since one can envisage the π-complexes to be formed via polar transition states. It may also be that structures of the π-complex type represent energy minima (intermediates) in some cases, and energy maxima (transition states) in others. It would appear that in the case of the cyclic *N,N'*-polymethylene hydrazo compounds, quoted above, coplanarity of the two benzene rings would be impossible to achieve[37]. However, it is not clear what degree of coplanarity is required for formation of a π-complex. Shine[2] feels that settling the question of whether or not π-complexes are involved 'is the major remaining task in the mechanism of the benzidine rearrangement'. However this opinion may turn out to be premature, in view of the fact that another major contending theory (the C-protonated intermediate) has since then come to the foreground.

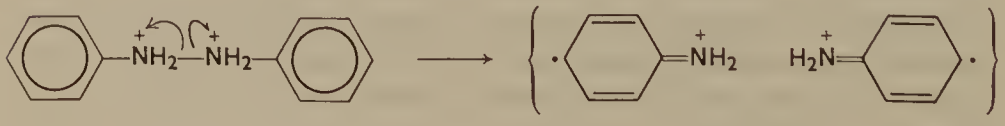
Another type of π-complex, the 'proton sandwich' **18** proposed by Ferstandig as a possible intermediate[57], has received little attention, and



(18)

such as it has received has been critical[1,5]. Similarly, the charge-transfer complex proposed by Murrell[58] has not received sufficient consideration among workers in the field.

i. The caged-radical theory. A theory often discussed in relation to the benzidine rearrangement involves dissociation of the *N,N*-diprotonated intermediate **16** into two cation radicals, e.g. **19**, which are prevented from diffusing apart by a solvent molecule 'cage'. Recombination in various ways inside this cage would lead to the observed products. This theory



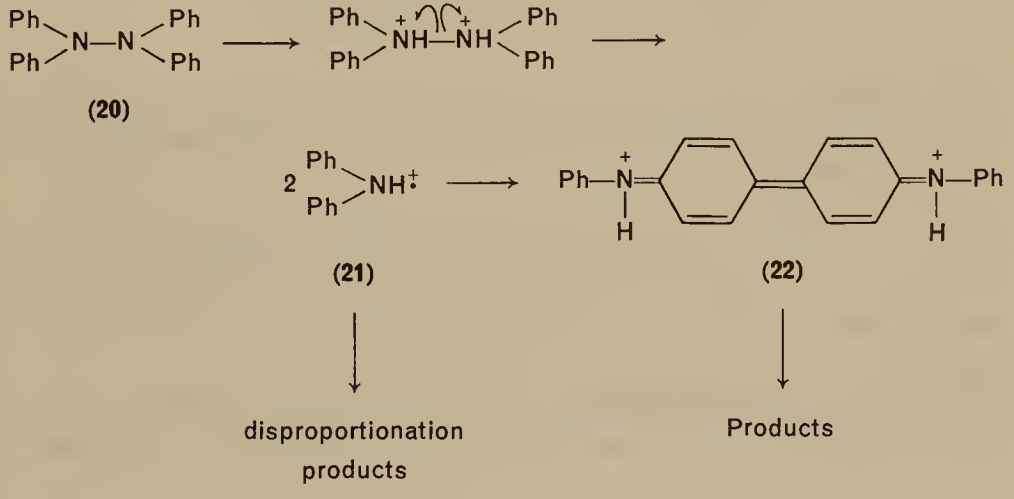
(16) **(19)**

accounts well for the observed disproportionation products (Table 1), e.g. equation 11, but reaction of this type represents escape of radicals from

$$2\,PhNH_2^{+\cdot} + PhNHNHPh \longrightarrow PhN{=}NPh + 2\,PhNH_3^{+} \longrightarrow 2\,PhNH_2 \qquad (11)$$

the cage, and it is very difficult to reconcile 'escaped' radicals with the lack of formation of 'crossed' products during the simultaneous rearrangement of different hydrazobenzenes. Also, attempts to detect radicals by e.s.r. spectroscopy[24, 59], trapping experiments[60] and the CIDNP technique[60] have been wholly unsuccessful. Thus this theory is improbable, at least under the normal conditions of acid catalysis in partially aqueous media.

However, Parker and co-workers[35] have recently provided evidence for the formation of the cation radical **21** during the rearrangement of tetraphenylhydrazine (**20**) in trifluoroacetic acid or trifluoroacetic acid/dichloromethane at room temperature, presenting convincing evidence for its



presence in these solutions by e.s.r. spectroscopy, and by comparison of the u.v. spectrum with that of authentic **21** prepared electrochemically[35]. The presence of **22** was also confirmed. Thus cation radicals can be formed, at least for this substrate, under the non-aqueous conditions used. It is reasonable that radicals would be more likely to occur under these con-

ditions than under those of aqueous acid normally used for the reaction, which may help to explain some of Lukashevich's data (Table 2).

j. Lukashevich's theory. Lukashevich[3,8] has consistently advocated a theory involving a transition state like **23** for the rearrangement. It is

$$Ar—NH—\overset{+}{N}H_2—Ar \cdot H_3O^+$$

(23)

suggested that this is required by the failure to isolate diacid salts of hydrazo compounds; Lukashevich feels that diprotonation 'cannot occur', but that 'continued action of acid is necessary'.

Reaction via **23** would be general acid catalysed, since one can write:

$$ArNHNHAr + HA \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ArNH\overset{+}{N}H_2Ar + A^-$$

$$ArNH\overset{+}{N}H_2Ar + HA \xrightarrow{k_2} ArNH\overset{+}{N}H_2Ar \cdot HA \longrightarrow \text{products}$$

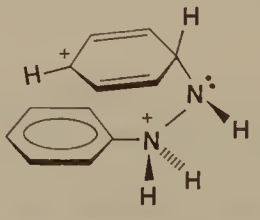
The rate of reaction, obtained by the steady-state approximation, is given by equation 12. If $k_{-1} > k_2[HA]$ the reaction is second-order in acid, and if $k_{-1} < k_2[HA]$, it is first order. The second condition should apply at

$$\text{Rate} = k_1 k_2 [HA] \frac{[ArNHNHAr][HA]}{k_{-1} + k_2[HA]} \qquad (12)$$

high [HA], and the first at low [HA], which is exactly the opposite of that observed experimentally. Lukashevich's theory has also been criticized on other grounds[1,2].

k. The C-protonated intermediate theory. Very recently a mechanism based on a proposal made by Hammick and Mason in 1946[61] has been revived, and is advocated by several authors: Lupes[7], Allan[38,62], Wepster[63] and Olah and co-workers[52]. The following is a synthesis of these authors' proposals.

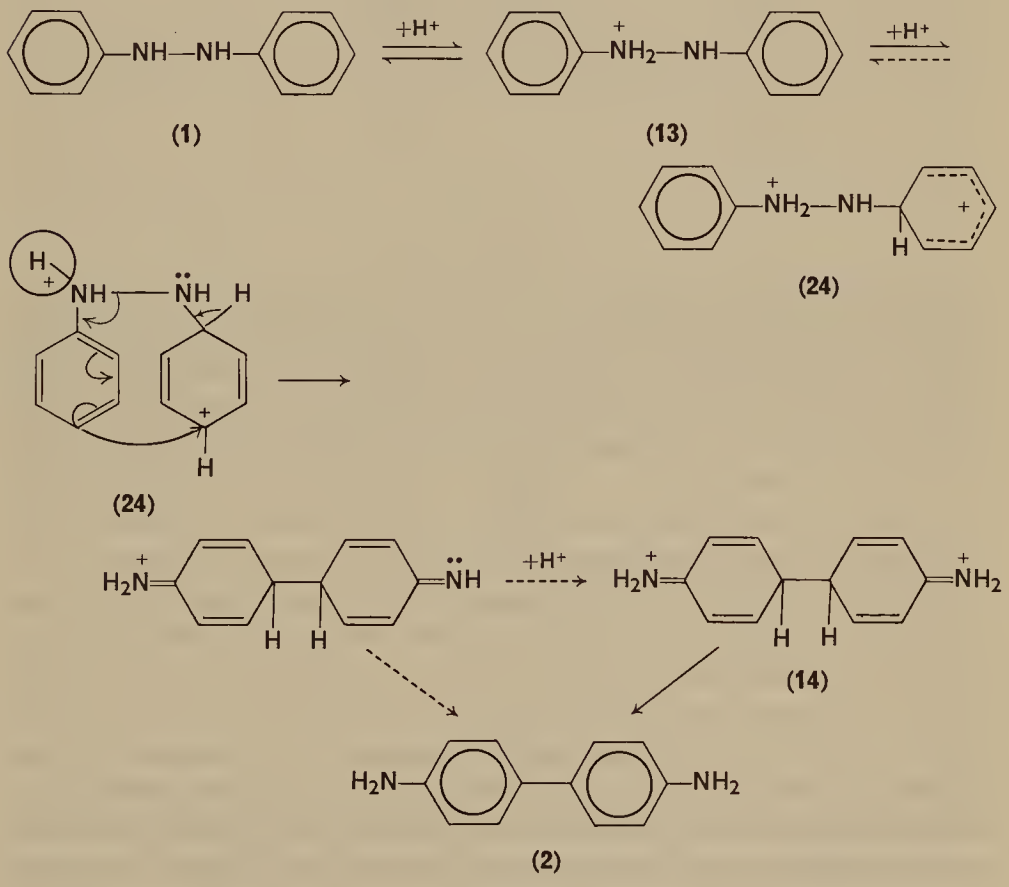
The basis of this mechanism is that one of the protonations occurs on carbon rather than on nitrogen, e.g. to give **24**. This serves two purposes.



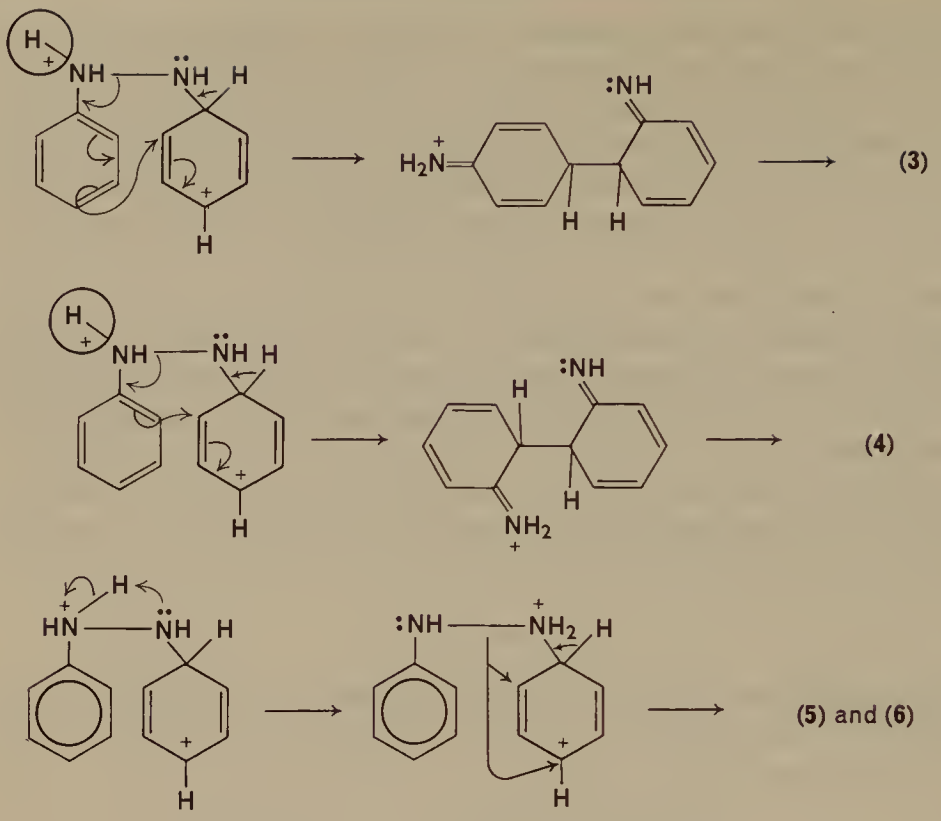
(24)

Firstly, the geometry of the molecule is now such that the two *para* ring positions are much closer to one another than is possible in the *N*-protonated structure. Another sp^3 centre has been introduced, making the structure more flexible. This facilitates benzidine and *p*-semidine formation. Secondly, a pair of electrons has been 'removed' from the aromatic system, to form the new C—H bond. The energy required to destroy this aromaticity should represent a large part of the activation energy of the reaction. Also the electron-pair of the new C—H bond is available to act in a nucleophilic fashion. Allan[62] and Lupes[7] favour protonation of the carbon directly adjacent to the protonated nitrogen, rather than that shown in **24**, but this is now thought to be less likely[52, 64, 65], at least as far as carbon basicity is concerned.

All of the reaction products can be accounted for by this mechanism as is indicated in Scheme 2, which is based on Olah's schemes[52]. The products result from an initial nucleophilic attack of the C—H electron-pair on the



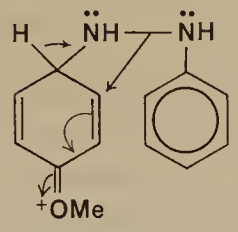
SCHEME 2.



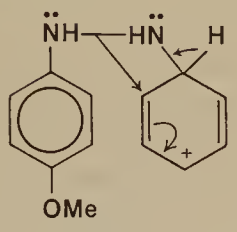
(25)

SCHEME 2 (*cont.*)

adjacent C—N bond, causing the N—N bond to break. This may or may not be the rate-determining step (see below). The first-formed products, while not really aromatic, are at least conjugated or cross-conjugated, and subsequent fast proton transfers lead to the final products. The scheme indicates, in the same manner as Scheme 1, that only one proton (the one on carbon) is necessary for benzidine, diphenyline and *ortho*-benzidine formation, although the second proton, and the resulting positive charge, on nitrogen undoubtedly facilitates N—N bond cleavage. It seems, however, that two protons are necessary for semidine formation, at least according to Scheme 2, and that only the structure **25**, with adjacent C and N protonated, leads to these products. Interestingly, Table 1 shows that most compounds which give semidines also react via the 2-proton pathway. However, 4-methoxyhydrazobenzene is an important exception, and we can visualize a one-proton-catalysed process for this occurring as in **26** and **27** below. Of these **26** will be the more important, though **27**, leading to *N*,2′-linkage, should still be possible. Banthorpe[65] points out that the non-detection of this mode of linkage (as well as the non-formation of 2,4′



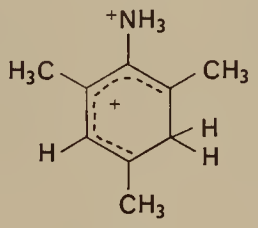
(26)



(27)

and 4,2′-diphenylines) is a factor against this mechanism; the polar transition state theory predicts exclusive 2,*N*′-linkage. However, Allan[38] has now found such products in two cases—see Table 3. Further investigation of this aspect would be worthwhile.

In accord with this theory is the lack of correlation of log rates with nitrogen basicities, which was noted above. If carbon, rather than nitrogen, is protonated then no correlation would be expected. In particular the fact that the rate of the one-proton process is affected to a very much greater degree than the nitrogen basicity by changes in substituents is thought provoking. Another point which needs to be considered is the apparent inability to measure the pK_{BH^+} values of hydrazo compounds[64], despite the fact that hydrochloride salts can be prepared and characterized. Additionally the total inability to detect any *N*,*N*-diprotonated hydrazobenzene, even under conditions where the phenylhydrazine dication, $PhNH_2^+NH_3^+$, is quite stable[52], is noteworthy. Both pK_1 and pK_2 values for phenylhydrazine have been measured by u.v. spectroscopy[66]. This would suggest that the C_1 position remote from the protonated nitrogen is more basic than the second nitrogen. Olah found that most aryl amines gave only anilinium ions under his highly acidic conditions ($SbF_5/FSO_3H/SO_2$)[52], but he was able to prepare and characterize the N,C-diprotonated ion **28** from mesidine. This amine is not protonated at the carbon adjacent to the NH_3^+, however, but at a position *meta* to it.



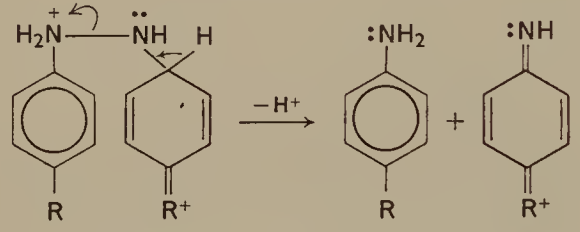
(28)

One difficulty with this theory is concerned with the nature of the rate-determining step. If intermediates like **24** are formed in a pre-equilibrium, then why are the C_1 or $C_{1'}$ positions protonated preferentially? Since no deuterium exchange of ring protons has ever been observed under the

conditions, this particular position appears to be substantially more basic than the others. Yet there seems no reason to expect this—in fact one might expect the *ortho* and *para* ring positions to be more basic[67].

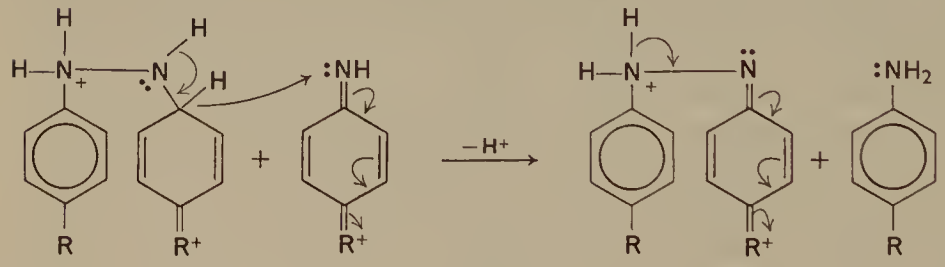
The above difficulty disappears if the C-protonation is in fact rate determining. Now if this second protonation were slow, then the reaction would be general acid catalysed. The body of evidence seems to indicate that this is not so[1,2], but of late some of the interpretations have been questioned, e.g. the H_0 correlations (see above). The solvent isotope effect evidence had seemed convincing, but very recently Banthorpe and Winter[64], studying the solvent isotope effects on the two-proton-catalysed reaction of 2,2′-dichloro- and 2,2′-dibromohydrazobenzene, and 4-chlorohydrazobenzene, found values of only 2·0, 2·3 and 3·0, respectively. These values are much lower than those previously found for this reaction (see above). Banthorpe and Winter concluded that, at least for these compounds, 'the second protonation could become rate-determining'. Thus even the solvent isotope effect evidence is not conclusive. The problem of general vs. specific acid catalysis should be studied further since it may well hold the key to the question of whether or not the C-protonated intermediate theory is tenable.

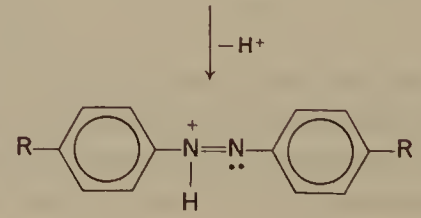
One should also examine whether or not the C-protonated intermediate theory can accommodate the disproportionation that accompanies many



(13)

(29) (30)





(14)

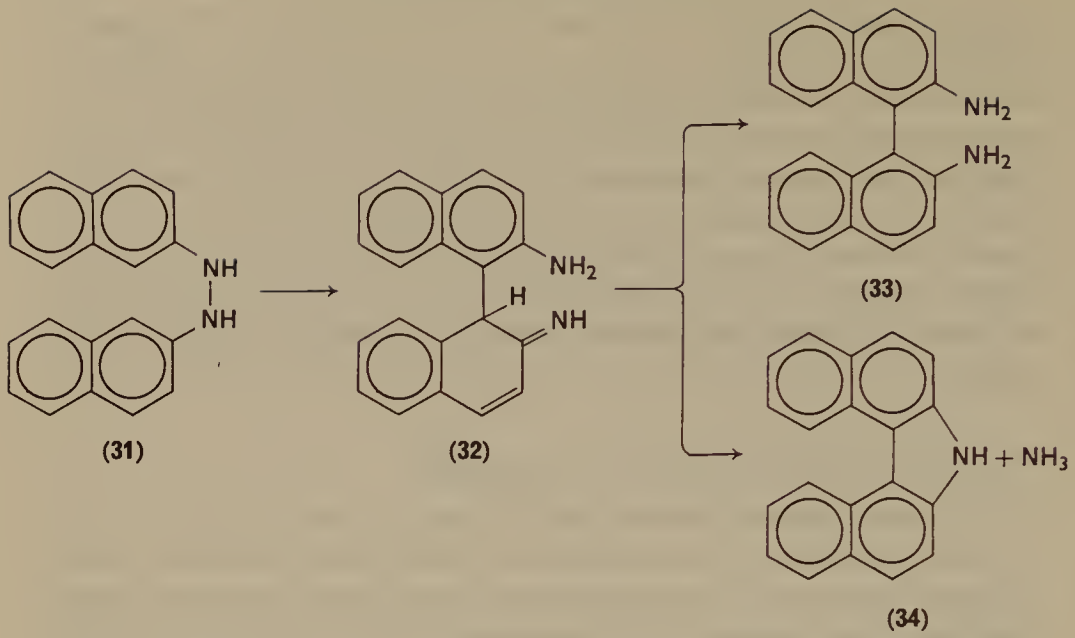
benzidine rearrangements. The following, rather speculative, suggestion may be considered. The dication **29** may disproportionate, especially if the 4-positions are blocked, giving amine and **30**, as in equation 13. The species **30** can function as a hydride ion acceptor, equation 14. Overall two molecules of (protonated) amine and one of (protonated) azo-compound result, from two molecules of **29**. The electron-pair of the new C—H bond is used in both processes. Various states of protonation of the nitrogens other than those indicated in equations 13 and 14 are also possible. However, without further experimental evidence it is difficult to decide on the feasibility of these reactions.

2. The thermal benzidine rearrangement

a. Products. Several hydrazo compounds have been found to rearrange and disproportionate when heated, in a solvent or in the melt, in the absence of acid. This process is termed the 'thermal' or 'uncatalysed' benzidine rearrangement. 2,2′-Hydrazonaphthalene was found to give 2,2′-diamino-1,1′-binaphthyl when heated in aqueous alcoholic NaOH[68], and in neutral ethanol[69], showing that the process is thermal and not base-catalysed.

The products of this reaction are similar to those of the acid-catalysed reaction, but the product distribution sometimes differs appreciably[2, 70–72]. 2,2′-Hydrazonaphthalene (**31**) and *N*-2-naphthyl-*N*′-phenylhydrazine give 70–90% 2,2′-diamines (e.g. **33**) and 10–30% carbazoles (e.g. **34**) when heated at 110°C either alone or in ethanol, acetone, acetonitrile or benzene; a small amount of disproportionation also occurs. The carbazole **34** has been shown not to be formed from **33** under the reaction conditions, which argues for the presence of a structure such as **32** as the first-formed product[2]. Under similar conditions 1,1′-hydrazonaphthalene gives carbazole and disproportionation products, with variable amounts of 2,2′- and 4,4′-diamine, depending on the solvent. *N*-1-Naphthyl-*N*′-phenylhydrazine gives mainly 4,4′- and 1,1′-diamines. Hydrazobenzene itself gives mainly diphenyline and *ortho*-semidine, with some disproportionation, rather than mainly benzidine as in acid solution[70–72]. Generally speaking, apart from the 2-naphthyl compounds the thermal rearrangement is not as clean as the acid-catalysed one, tars sometimes being produced[70] in the former; oxygen has to be excluded. 4-Methyl-, 2,2′-dimethyl-, 4,4′-dimethyl- and 2,2′-dimethoxyhydrazobenzene also rearrange when heated alone. The major reaction is disproportionation, but some *ortho*- and *para*-semidines are formed[13, 73].

b. Mechanism. The thermal rearrangement has also been shown to be

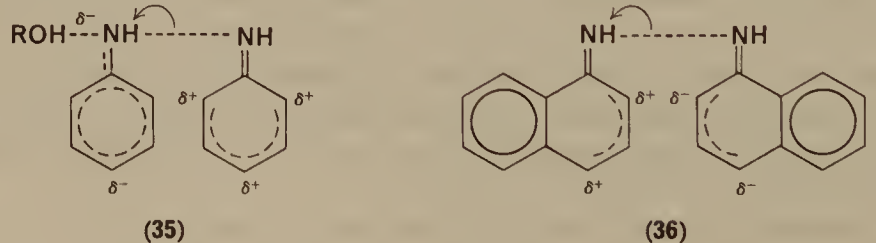


(31) (32) (33) (34)

intramolecular[72]. Tests for radical formation have shown that a radical mechanism is unlikely[2]. The reaction is first order in substrate[1,2,74]; the rates are greater in polar than in non-polar solvents, and greatest in hydroxylic solvents[2]. The rate decreases with decreasing alcohol acidity for a series of alcohols[75]. A linear plot of log (rate constant) vs. the Grunwald–Winstein Y value for the alcohol solvents indicates that the rate is related to the ionizing power of the solvent[75]. Thus Shine and Trisler proposed that thermal rearrangements in alcohols were of the acid-catalysed type, with the alcohol acting as a general acid, and that the transition state was polar[75].

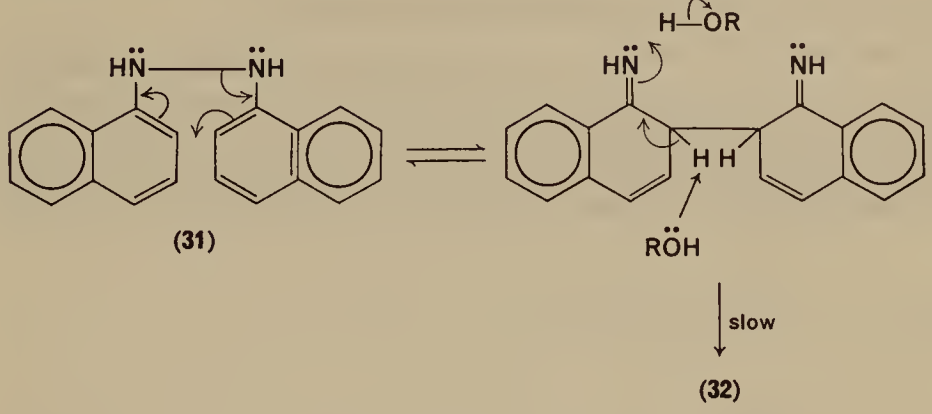
It has been proposed that the thermal reaction also goes via a polar-transition-state mechanism, at least in alcohol solvents, with quasi-anionic and quasi-cationic portions, e.g. **35** and **36**; factors similar to those discussed above (Section II, A, 1, g) account for the observed products, rates, solvent effects and so on[1,4].

However, ring deuteration at the 2- and 4-positions of 1,1′-hydrazonaphthalene leads to kinetic isotope effects (k_H/k_D) of 2–6 for reaction of



(35) (36)

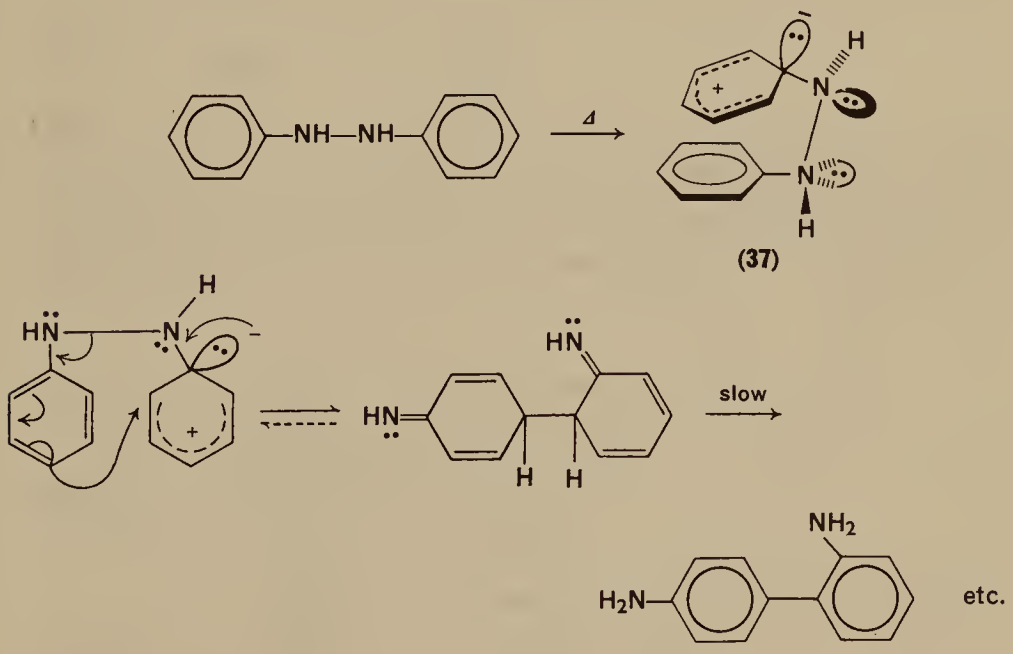
this substrate in ethanol, acetone and acetonitrile[70]. This means that proton loss from the ring is probably involved in the rate-determining step, which is an important difference from the acid-catalysed reaction. A mechanism which suggests itself is one of the Claisen ester type, with ring-proton loss being rate-determining:



(31) (32)

On formation of **32**, further reaction gives the observed diamine **33** and carbazole **34**.

Lupes[7] has proposed that the thermal rearrangement involves structures like those discussed above for the 'C-protonated intermediate theory', only now involving charge separation as in **37**. Presumably this would then react as shown below:

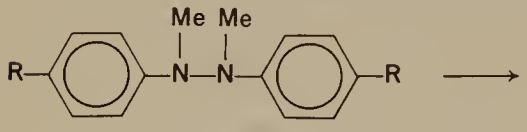


(37)

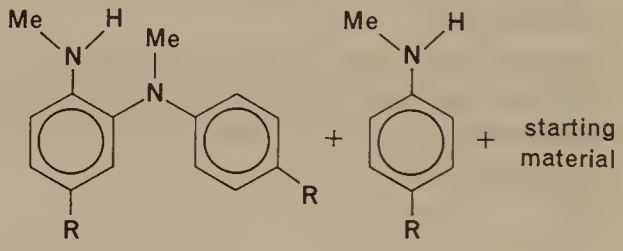
Generally speaking the thermal benzidine rearrangement has not been studied nearly as extensively as the acid-catalysed one, and much work remains to be done before a full understanding is achieved, especially for the reaction in non-polar solvents.

3. The photochemical benzidine rearrangement

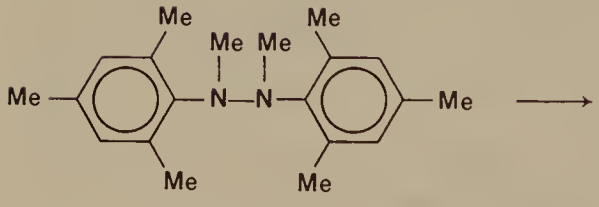
Hydrazobenzenes which are not substituted on nitrogen usually dehydrogenate and decompose when irradiated[76], although a 0·25% yield of *ortho*- and *para*-semidines resulting from the irradiation of hydrazobenzene has been reported[77]. However, Shine and co-workers[78] have found that *N*,*N*-dimethylhydrazobenzenes undergo some rearrangement when irradi-

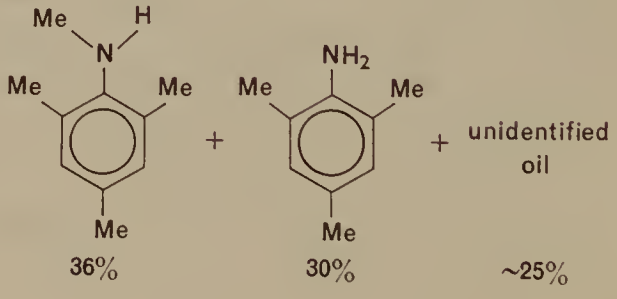


R = Me
= OMe
= C_6H_5



19%	+	74%
65%	11%	17%
24%	35%	34%



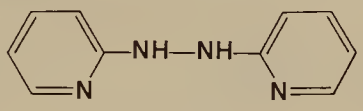


36% 30% ~25%

ated at 300 nm over several hours at 25°C in cyclohexane. The products obtained are indicated above[78]; in general they do not closely correspond to the products of the acid-catalysed rearrangement[78]. Extension of this work to other systems should prove interesting.

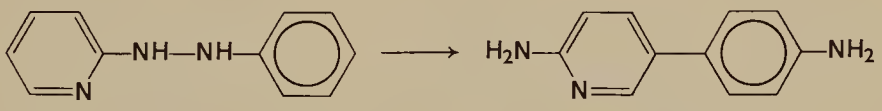
4. Heterocyclic hydrazo compounds

Hydrazo compounds with two heterocyclic rings, such as 2,2′-hydrazopyridine (**38**), do not rearrange in acid. For instance, **38** was recovered unchanged after heating for several hours with concentrated HCl[79a].



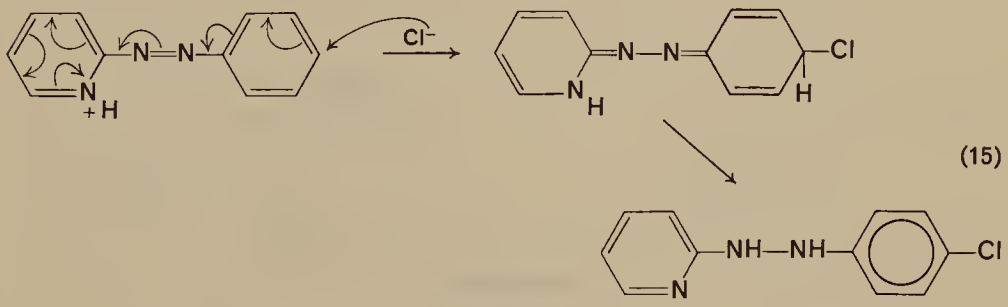
(38)

Presumably this is because the heterocyclic nitrogens are protonated, and so protonation of the hydrazo group becomes more difficult. Phenylhydrazopyridine (**39**) and -picoline each rearrange to the extent of 25% under the same conditions[79a], giving benzidine-type products (e.g. **40**).



(39) **(40)**

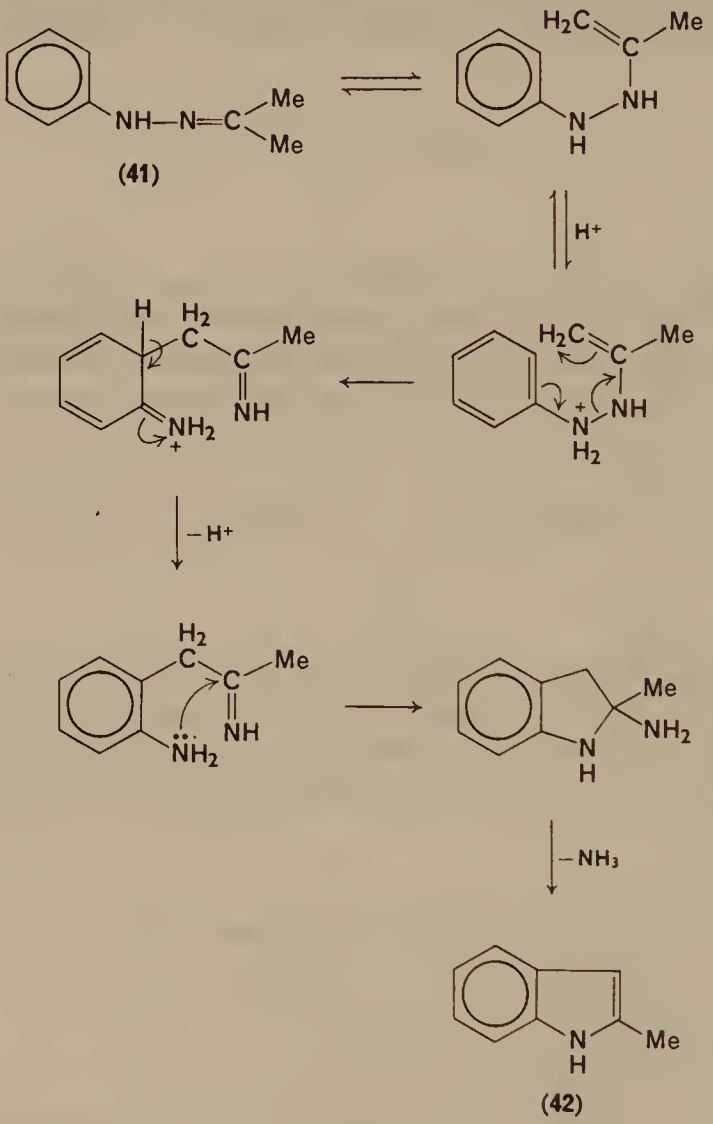
Many other products arising from disproportionation and reductive chlorination were also found, but no azo compounds. These would presumably react with HCl (equation 15); the resulting chloro compound formed on tautomerization would again disproportionate, giving amine and chloroaniline.



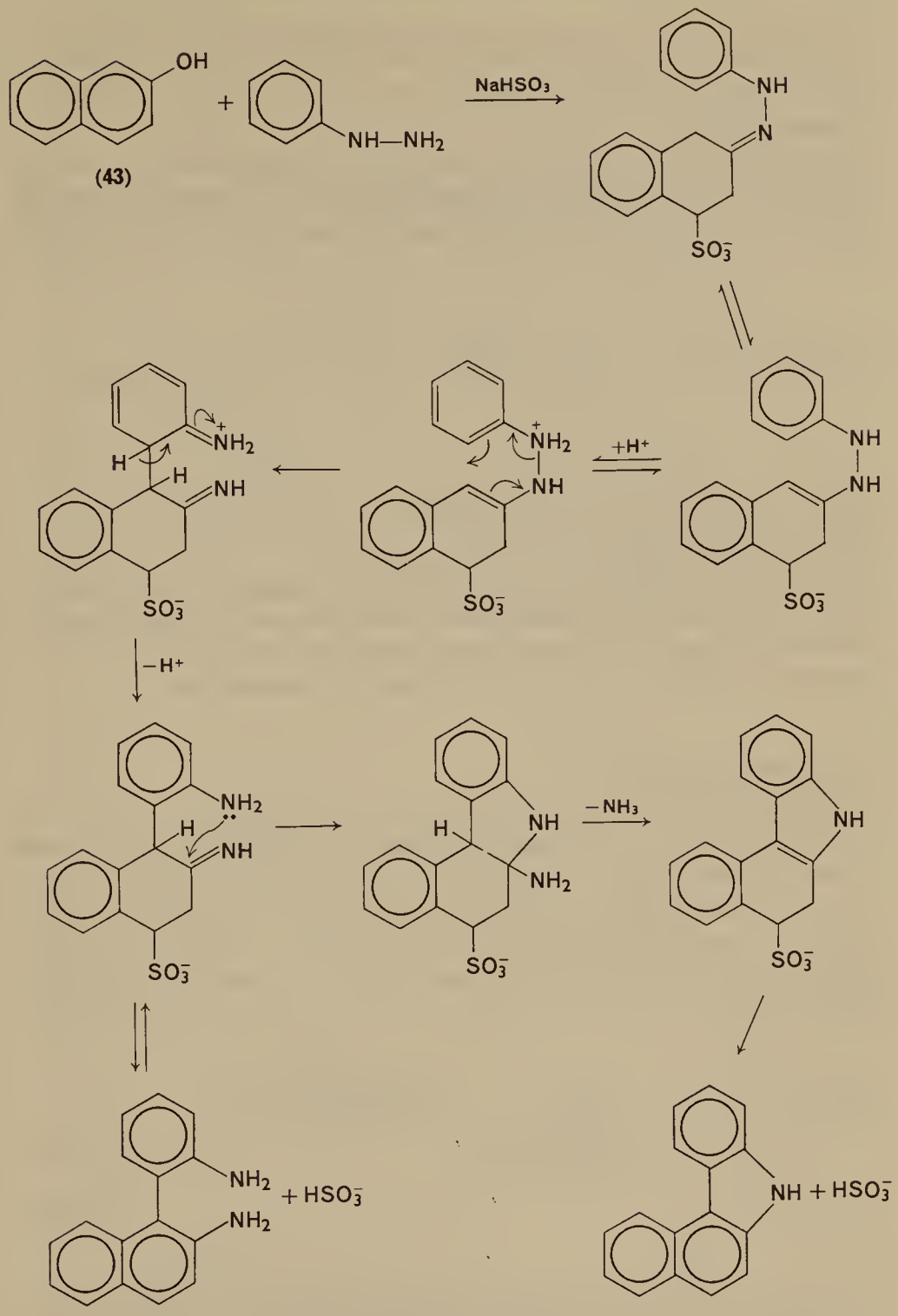
(15)

B. Related Rearrangements

Processes in which reactions similar to the benzidine rearrangement occur are the Fischer Indole reaction—the conversion of phenylhydrazones (**41**) to indoles (**42**)[79b]—Scheme 3, and some examples of the Bucherer reaction—for instance during the reaction of α- or β-naphthol (**43**) with phenylhydrazine and sodium bisulphite which produces amines and carbazoles[79c]—as shown in Scheme 4.



SCHEME 3.



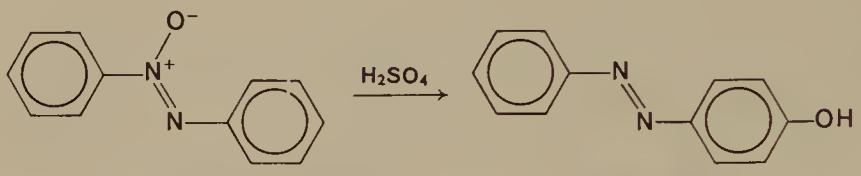
SCHEME 4.

III. REARRANGEMENTS OF AZOXY COMPOUNDS

A. The Wallach Rearrangement

1. Introduction

Aromatic azoxy compounds rearrange when treated with certain strong acids. The prototype of this class of rearrangement is that of azoxybenzene, **44**, to *p*-hydroxyazobenzene, **45**; it was first investigated by Wallach and



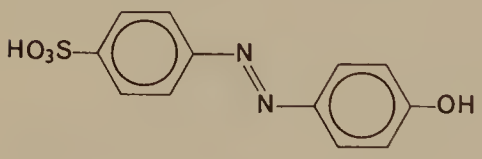
(44) **(45)**

Belli[80], and this class of rearrangements has since become known by the name of the discoverer.

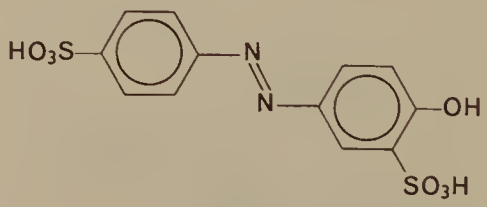
Since this reaction has also been reviewed[81–83], again we will concentrate on the more recent mechanistic studies of the process. A formally related, but mechanistically not similar, photochemical rearrangement is covered in another chapter[84] and will not be extensively discussed here.

2. Reaction products

The products of this rearrangement depend to some extent on the reaction conditions. At relatively low acidities (less than ca. 90% H_2SO_4 in the case of azoxybenzene) and at low substrate concentration (10^{-3}–10^{-5}M, as used in kinetic studies by u.v.–visible spectroscopy) one generally obtains the product **45** quantitatively, but at higher substrate concentrations other products (azobenzene, etc.) may appear, possibly as a result of bimolecular redox processes.



(46)



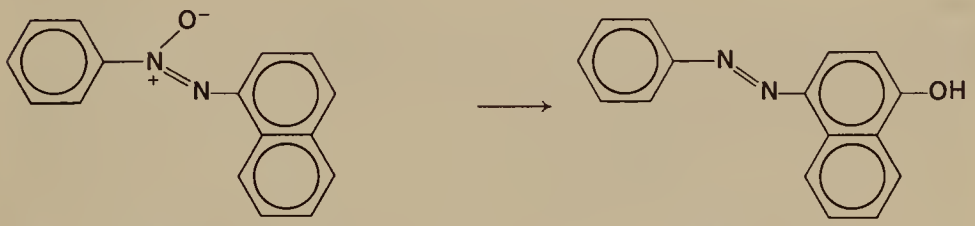
(47)

If the sulphuric acid concentration is high, sulphonation of the first-formed product may occur; this process has been extensively investigated[85–89].

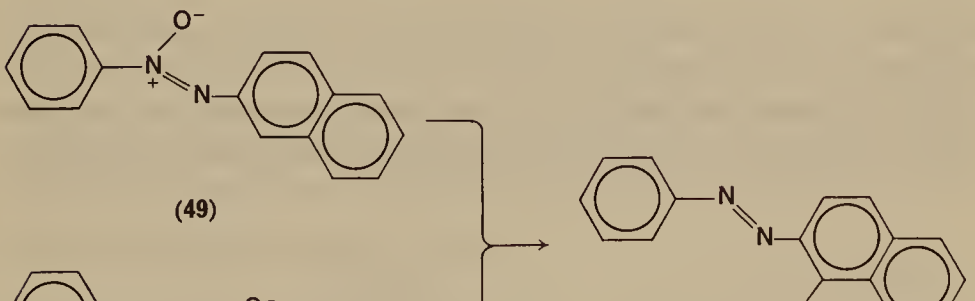
Above 95% H_2SO_4, sulphonation of **45** leads to **46**, and in fuming H_2SO_4 **46** is again sulphonated. The second sulphonation product was tentatively identified as **47**. The protonation equilibria involved and the mechanisms of the sulphonation processes have been discussed[88,89]. These reactions present a complication in study of the Wallach rearrangement itself at these acidities, but it is nevertheless possible to follow the rearrangement rate by using an appropriate technique[85]. Another process precluding the observation of some rearrangements at high acidity may also occur, namely ring protonation and subsequent break-up of the molecule.

A fairly large number of substituted azoxybenzenes and azoxynaphthalenes have been studied. In most cases the products contain a *p*-hydroxy group; in some cases an *o*-hydroxy group, and in at least one case the OH enters a ring-substituted methyl group, giving a primary alcohol. In a number of cases (*vide infra*), the major product of reaction is the azoarene.

The azoxynaphthalenes **48–53** give the products **54–58** as shown[90,91]. A spectrophotometric study showed that the reactions proceed in high yield; however in some cases (e.g. **50**) side products also form. It is seen that OH enters the 4-position of a 1-naphthyl group if this position is

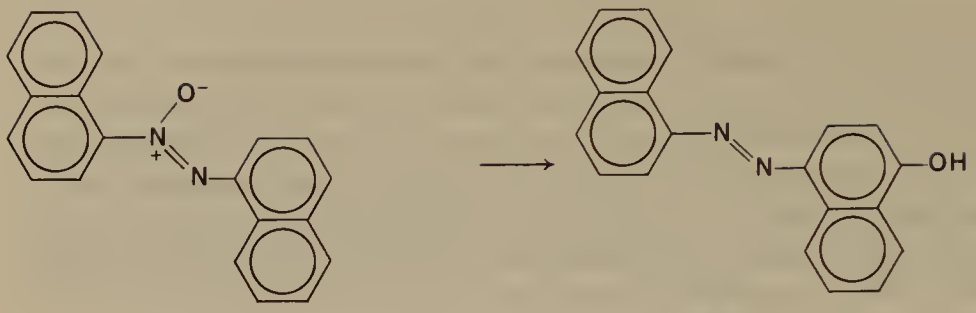


(48) (54)

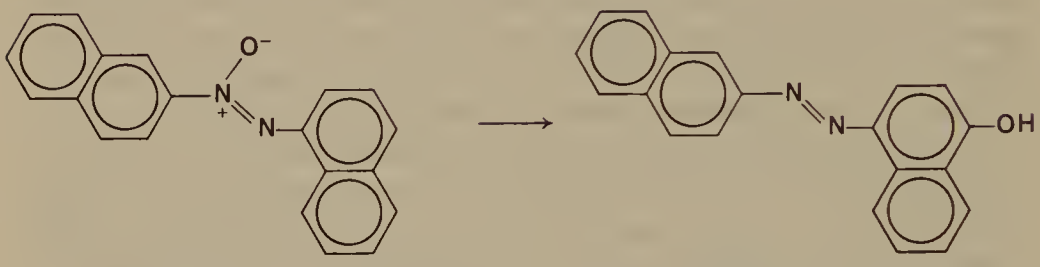


(49)

(50) (55)



(51) (56)



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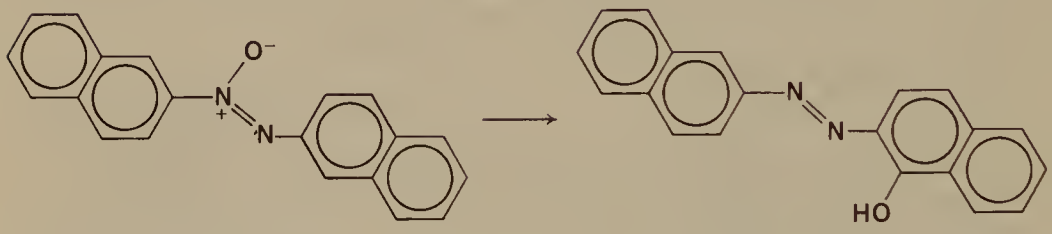
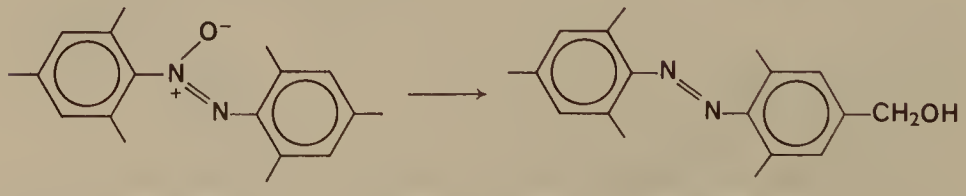


(53) (58)

available, and otherwise the 1-position of a 2-naphthyl group. Phenyl substitution was not observed.

Hexamethylazoxybenzene (**59**) gives the primary alcohol **60** on treatment with 60–98 % H_2SO_4; at 25 or 45°C the reaction is almost quantitative[91–92].



(59) (60)

The compound 4,4′-dimethylazoxybenzene* 'gave a 20% yield of a product soluble in alkali and a 75% yield of an alkali-insoluble product'[93]. The latter product was thought to be an alcohol similar to **60**, though the former was not thought to be 4,4′-dimethyl-2-hydroxyazobenzene[93]. However, a 47% yield of this compound was obtained from 4,4′-dimethylazoxybenzene by Gore and Hughes[94]. Shemyakin and co-workers[95], and Newbold and Akhtar[96], also observed this product; the latter workers reported formation of the azoarene product in addition. 2,2′-Dimethyl- and 3,3′-dimethylazoxybenzene both give a product with a 4-OH group[93–94]. 2- and 3-Methylazoxybenzene are reported to rearrange to 2- and 3-methyl-4-hydroxyazobenzene, respectively, according to one group[93], but the former compound is reported to yield 4-hydroxy-2′-methylazobenzene according to another[99].

Hahn and Jaffé reported that both 4-methyl- and 4′-methylazoxybenzene give 2-hydroxy-4′-methylazobenzene quantitatively in 20% EtOH/80% aqueous H_2SO_4 mixtures[97]. This is in disagreement with other reports[93, 95, 98], according to which both isomers are stated to give 4-hydroxy-4′-methylazobenzene. Oae and collaborators found that 4-methylazoxybenzene gave both 2- and 4-hydroxy-4′-methylazobenzene, though only about 1% of the 2-isomer was obtained[99].

Further work seems necessary to establish the balance of *ortho* and *para* substitution before definitive conclusions can be made. Overall, it seems that the hydroxyl group migrates to a vacant *para*-position if one is available; however in the case of the 4-methyl compounds, OH appears in the 4′- or 2′-position. If both *para*-positions are blocked, OH either appears in an *ortho*-position or enters one of the *para*-methyl groups. If all *ortho*- and *para*-positions are blocked by methyl groups, only the latter process is observed.

The products observed for azoxybenzenes with substituents other than annelated rings, or methyl groups, are summarized in Table 5. In all but a few cases the OH group enters a 4-position in the ring removed from the substituents. If both 4-positions are blocked, OH enters a 2-position, and considerable amounts of azoarene occur in most of these cases. If OH enters a 2-position, it again seems to prefer the substituent-free ring, except

* Numbering system for azoxybenzene:

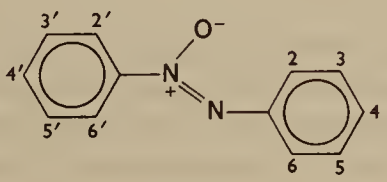


TABLE 5. Products of rearrangement of substituted azoxybenzenes

Substituents in azoxybenzene	Substituents in hydroxyazobenzene product	Ref.
4-NO_2	4-NO_2, 4′-OH	100
4′-NO_2	4-NO_2, 4′-OH	100, 101
4-OCH_3	4-OCH_3, 4′-OH	97
4′-OCH_3	4-OCH_3, 4′-OH	97
3-NO_2	'Probably 3′-NO_2, 4-OH'	102
3′-NO_2	'Probably 3′-NO_2, 4-OH'	102
4-Br	4′-Br, 4-OH (and 4-Br, 2-OH)	97, (95)
4′-Br	4′-Br, 4-OH	95, 97
4′-Cl	4′-Cl, 4-OH	103
4 or 4′-Ph	4-Ph, 4′-OH and 4-Ph, 2′-OH	104
4 or 4′-OPh	4-OPh, 4′-OH and 4-OPh, 2′-OH	104
2,2′-di-C_2H_5	2,2′-di-C_2H_5, 4-OH	96
2,2′-di-F	2,2′-di-F, 4-OH	96
2,2′-di-Cl	2,2′-di-Cl, 4-OH	96, 103, 105
2,2′-di-Br	2,2′-di-Br, 4-OH	96
2,2′-di-I	Oxygen lost, azoarene only product	96, 106
2,2′-di-OMe	No reaction	96
3,3′-di-F	3,3′-di-F, 4-OH	96, 105
3,3′-di-Cl	3,3′-di-Cl, 4-OH	103, 105
3,3′-di-Br	3,3′-di-Br, 4-OH	105
3,3′-di-I	3,3′-di-I, 4-OH	96
3,3′-di-NO_2	3,3′-di-NO_2, 4-OH	94, 96, 101
4,4′-di-F	4,4′-di-F, 2-OH + much azoarene	96
4,4′-di-Cl	4,4′-di-Cl, 2-OH + much azoarene	96, 105
4,4′-di-Br	4,4′-di-Br, 2-OH + much azoarene	96
4,4′-di-I	Oxygen lost, azoarene only product	96
4,4′-di-i-Pr	4-i-Pr, 4′-OH (4′-i-Pr lost)	96
4,4′-di-t-Bu	4-t-Bu, 4′-OH (4′-t-Bu lost)	96
4,4′-di-OMe	No reaction	96
2-NO_2, 3′-CH_3	2-NO_2, 3′-CH_3, 4-OH	107
3-CH_3, 3′-Cl	3-CH_3, 3′-Cl, 4-OH	107
2-NO_2, 4-Br	2-NO_2, 4-Br, 4′-OH	108
2,2′,5,5′-tetra-Cl, 4-NO_2	2,2′,5,5′-tetra-Cl, 4-NO_2, 4′-OH	109
3,3′,4,4′-tetra-Cl, 6-NO_2	3,3′,4,4′-tetra-Cl, 6-NO_2, 6′-OH	109

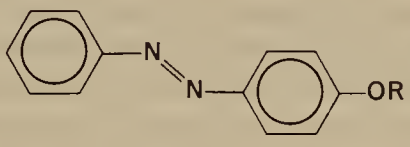
in one case where some 4-bromo-2-hydroxyazobenzene was observed as a rearrangement product of 4-bromoazoxybenzene[95]. Neither 2,2′- nor 4,4′-diiodoazoxybenzene give rise to azophenol, yielding the azoarene instead[96]. Both 2,2′- and 4,4′-dimethoxyazoxybenzene are unreactive,

though the reason for this is unclear. In two cases iso-propyl and tert-butyl groups are lost, being replaced by OH; the reason for the anomalies is again unclear.

It is noteworthy that the entry of OH, into one ring or another, does not appear to be controlled to any great extent by the electronic demands of the substituents. For instance, in two unsymmetrically substituted compounds the OH group enters the ring remote from both CH_3 and Cl (which have opposite inductive effects), while in two compounds OH enters the ring remote from both NO_2 and Cl (which have opposite mesomeric effects). It may be stated now that the mechanistic theories of this reaction, discussed below, do not seem capable of explaining all of these observations. Much further work remains to be done on substituted azoxybenzenes before this problem can be resolved.

3. Products in acids other than sulphuric

The Wallach rearrangement takes place in a number of acidic media besides aqueous H_2SO_4, which is the medium used for practically all of the results discussed above. In chlorosulphonic acid the rearrangement of azoxybenzene proceeds readily to yield **61**, rather than **45**; the reaction proceeds at a conveniently measurable rate at 25°C[110]. Several substituted

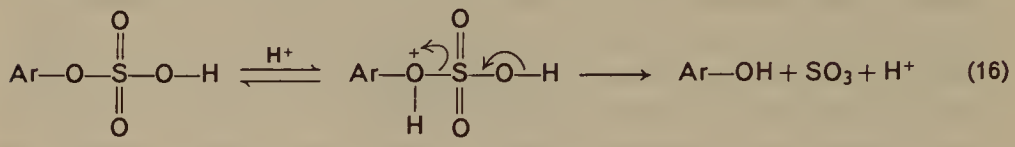


(61) $R = SO_2Cl$
(62) $R = SO_2F$
(63) $R = SO_2Ar$
(64) $R = SO_2OH$

azoxybenzenes yield azoaryl chlorosulphates with $ClSO_3H$ at −8°C in CCl_4 (Lukashevich's method)[103, 111]. The rearrangement also takes place readily in fluorosulphonic acid, yielding **62**[110]. Substituted azoxybenzenes with an open *para* position also give fluorosulphates with FSO_3H in CH_2Cl_2 at 0–25°C; if difluoramine is added compounds with both *para*-positions open give 4,4′-diaminoazobenzenes[112]. Azoxybenzene and some substituted azoxybenzenes have been found to give **63** and similar products with several arenesulphonic anhydrides in acetonitrile or benzene in excellent yields[113]. Interestingly, azoxybenzene has been found to be unreactive at 25°C in both methanesulphonic acid and concentrated perchloric acid[110].

The observation of **61–63**, substituted with the nucleophile of the medium

rather than with OH, poses the question whether or not the reaction in H_2SO_4 involves H_2O or HSO_4^-. This question was investigated by Buncel and Strachan[114], who synthesized **64** and subjected it to the reaction conditions; they found, however, that the process shown in equation 16 is



(16)

faster than the rearrangement itself. Therefore, the question regarding the nature of the attacking nucleophile in H_2SO_4 could not be definitively answered[114]. However, since HSO_4^- is known to be the predominant species in such solutions[133], it is also likely to be the attacking reagent.

4. Isotopic substitution studies

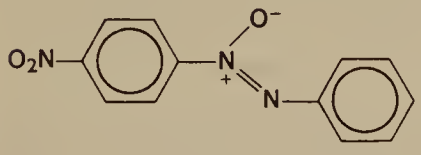
Isotopic tracers have been particularly useful to the study of the mechanism of the Wallach rearrangement. A large number of studies have been performed[95, 99, 101, 103, 113, 115–20]; the results obtained by one group have been summarized[121]. What follows is a consensus of the results obtained by several groups.

a. para-*Hydroxy product.* Studies with ^{15}N and ^{14}C labels have shown that the two nitrogen atoms, which are non-equivalent in azoxybenzene, become equivalent in the product. Thus, the OH group is equally likely to appear in either ring when no substituents are present. This indicates that a symmetrical intermediate is involved in the reaction. Unreacted azoxybenzene, recovered from reaction mixtures, retains its label (^{15}N or ^{18}O) undisturbed, showing that oxygen exchange, or migration of oxygen from one nitrogen to the other, does not occur under the reaction conditions (see below on this point). Labelling with ^{18}O shows that the product OH group is solvent-derived, which means that the reaction is intermolecular, as the different products obtained in different acids (see above) would also seem to indicate. Substituted azoxybenzenes also give products with medium-derived hydroxy groups; the products were shown not to undergo oxygen exchange with the medium[99].

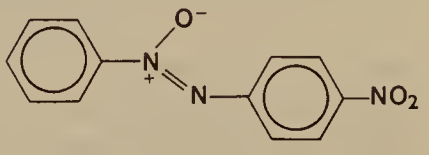
Azobenzene was shown not to be a reaction intermediate by its addition to a reaction mixture containing ^{15}N-labelled azoxybenzene; the *para*-hydroxy product showed no dilution of label[116]. Fully deuterated azoxybenzene undergoes the Wallach rearrangement at the same rate as the undeuterated material, showing that aromatic proton loss does not form part of the rate-determining step of the reaction[120].

b. ortho-*Hydroxy product.* *ortho*-Hydroxyazobenzene, observed as a minor product by Shemyakin and co-workers[101], was shown to contain the same oxygen atom as the azoxybenzene reactant; thus the rearrangement leading to *ortho*-product appears to be intramolecular. Mono- and di-substituted reactants give the same result[95,99]. In only one case, that of 4,4′-dimethylazoxybenzene, was incorporation of oxygen from the medium observed[95], to the extent of 70%. Parallel inter- and intramolecular mechanisms for this compound were thus proposed[95].

c. Oxygen migration in the reactant. One case of $\beta \rightarrow \alpha$ isomerisation, **65** to **66**, has been observed in sulphuric acid[101,117]. The oxygen isotope

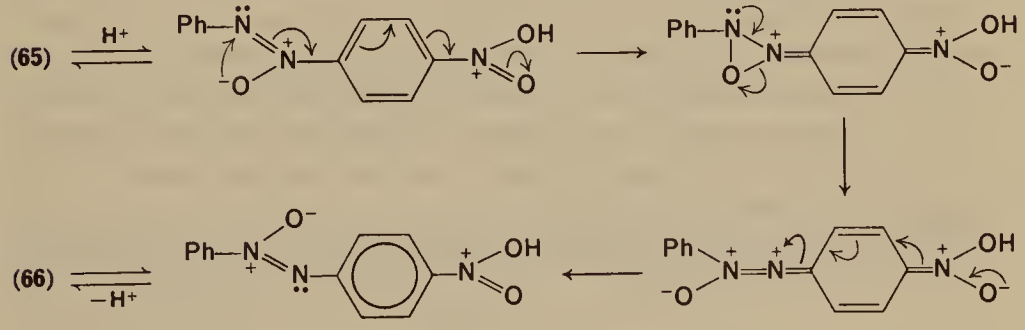


(65)



(66)

in **66** was the same one as that of **65**, whereas that in the 4-hydroxy-4′-nitroazobenzene rearrangement product was derived from the medium. The $\beta \rightarrow \alpha$ isomerization is therefore intramolecular. The following mechanism for the process has been proposed[81]:

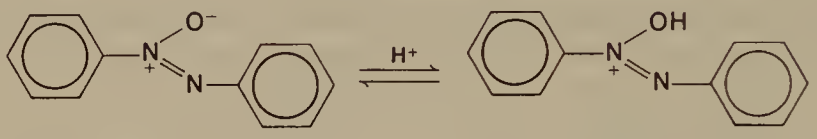


The isomerization **65** → **66** has been confirmed in other work[122–123]. The only other established cases of this type of isomerization are the transformation of 4′-carboxyazoxybenzene into the 4-carboxy isomer in hot chromic acid[124], and the isomerization of bisazoxybenzene in sulphuric acid at 0°C[125]. Evidently a strong electron-withdrawing group in the 4′-position is required for the reaction; see the proposed mechanism above. Apart from these few cases, however, it is generally believed that this type of isomerization does not occur under Wallach rearrangement conditions.

5. Reaction intermediates

Much controversy has surrounded the question of intermediates in the Wallach rearrangement[81,82,121,123]. Mechanistic studies have been handicapped by the fact that no direct observational evidence of reaction intermediates was available until quite recently.

It has been demonstrated by several groups that azoxy-compounds are essentially entirely monoprotonated on oxygen, as a result of protolytic equilibria (e.g. **44** ⇄ **67**), at the acidities at which the Wallach rearrange-



(44) **(67)**

ment normally occurs[92,123,126–128]. For instance, the pK_{SH^+} value (defined as the H_0 value at which the substrate is half protonated) for azoxybenzene itself[126] is −5·15, whereas the rearrangement of **44** does not occur at an appreciable rate at 25°C at acidities below about −6 on the H_0 scale[126]. pK_{SH^+} values for substituted azoxy compounds range between −4·6 and −7, except for compounds with nitro-substituents, which are weaker bases still. Processes equivalent to **44** ⇄ **67** are undoubtedly the first stage of the Wallach rearrangement sequence.

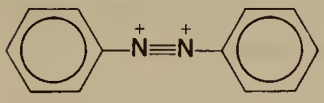
The monoprotonation of azoxybenzene on oxygen was confirmed by direct observation, by Olah and co-workers[52]. Structure **67** was observed and fully characterized by n.m.r. spectroscopy in FSO_3H/SO_2 solutions at −78°C. Monoprotonated 4,4′-dichloroazoxybenzene was also observed. The n.m.r. spectra indicated possible hydrogen bonding between the OH group and the nitrogen lone pair[52].

Diprotonated azoxybenzene **68**, in *syn* and *anti* forms, was also observed

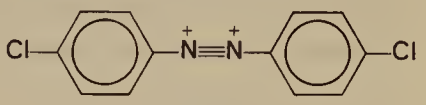
(68, *syn*) **(68**, *anti*)

in $SbF_5/HF/SO_2$ solution at −78°C[52]. The observation of this species is interesting because it shows that the next most basic site in **67** is the other

nitrogen, rather than the oxygen atom or one of the ring carbons. When solutions containing **68** were warmed to −50°C for 5 min and again cooled to −78°C, the n.m.r. spectra had changed; the characteristic OH and NH signals of **68** had disappeared and a large H_3O^+ peak had formed, together with aromatic proton signals characteristic of the dicationic species **69**.



(69)

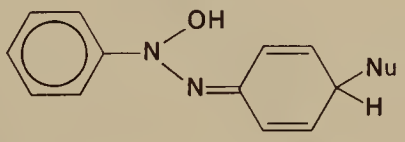


(70)

Structure **70**, from 4,4′-dichloroazoxybenzene, was also observed, but diprotonation was not seen in this case. Quenching of solutions containing **69** in water gave 4-hydroxyazobenzene[52].

Structure **69** presents itself, therefore, as a most promising candidate for the symmetrical intermediate required for the Wallach rearrangement. It had first been proposed as a reaction intermediate by Gore* in 1959[122] and has been strongly advocated by Buncel and associates[81, 126]. Such a reaction intermediate has been accepted with some reservation by Jaffé and collaborators[129] and by Shine[82].

The direct observation of **69**, however, does not necessarily require that the intermediate be involved in the reaction. Two other possibilities have been proposed. One is the species **71** (Nu = nucleophile), proposed by Duffey and Hendley[120, 123]. Arguments have been given by the authors

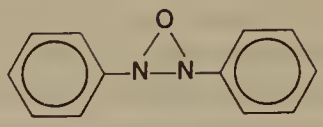


(71)

that, despite their lack of symmetry, structures like these can satisfactorily account for the observations. It seems that this type of structure is indeed involved in some Wallach rearrangements[91, 131] and we will be returning to this subject in a later section.

The other major possibility for a reaction intermediate is **72**, first proposed by Shemyakin and associates[130], advocated in monoprotonated form (on oxygen) by Oae and co-workers[99, 118], and advocated in diprotonated form (on oxygen or nitrogen) by Jaffé and collaborators[129]. Olah[52] has pointed out that the lack of observation of protonated **72** under conditions where

* Gore actually formulated the dicationic intermediate as Ph—$\overset{+}{\underset{\cdot\cdot}{N}}$—$\overset{+}{\underset{\cdot\cdot}{N}}$—Ph whereas the triple bond formally present in **69** was preferred by Buncel and Lawton due to the high bond energy of N≡N (see Section III, A, 7, b).



(72)

it should be stable argues against the *N*,*N*-oxide intermediate. We will consider the other evidence, for and against, in a later section.

6. Kinetic studies

The rate of the Wallach rearrangement as a function of medium acidity has been studied by several groups. The first kinetic study with azoxybenzene was reported by Buncel and Lawton and was later extended to include hexamethylazoxybenzene and six azoxynaphthalenes[85,91,126,131–132]. Hahn, Lee and Jaffé reported similarly on azoxybenzene, 4- and 4′-bromo-, and 4- and 4′-methylazoxybenzene[129], while Duffey and Hendley did so for azoxybenzene, 4- and 4′-nitro-, 3- and 3′-nitro-, 4- and 4′-bromo, 4-hydroxy-, 3,3′-dinitro- and 3,3′-dimethoxyazoxybenzene[123]. The results have in general been quite informative.

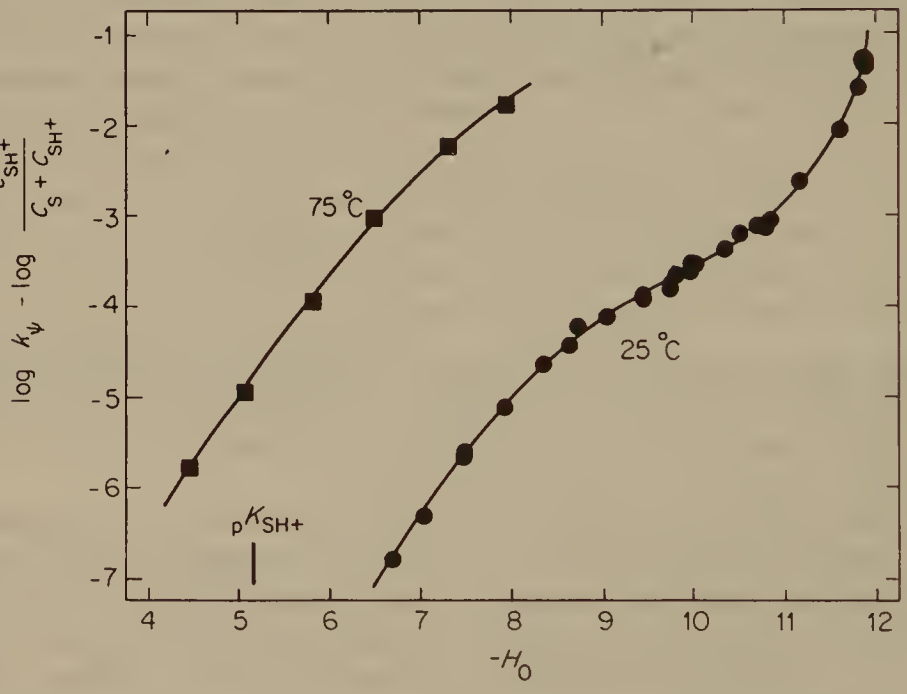


FIGURE 1. Graphs of $\log k_\psi - \log(C_{SH^+}/C_S + C_{SH^+})$ vs. $-H_0$ for the Wallach rearrangement of azoxybenzene in sulphuric acid at 25°C (●) and 75°C (■). Reprinted with permission from Cox, *J. Am. Chem. Soc.*, **96**, 1059 (1974). Copyright by the American Chemical Society.

The results for azoxybenzene, studied by all three groups, are in broad agreement; the log (rates), corrected for the fact that azoxybenzene is not entirely monoprotonated at the lower acidities by the term $\log(C_{SH^+}/C_S + C_{SH^+})$, are plotted as a function of $-H_0$ in Figure 1[85,126]. (This means that we are regarding protonated azoxybenzene, rather than the unprotonated material, as the reacting substrate in the rearrangement.) It is immediately apparent that the rate continues to increase with acidity, even when the substrate is entirely monoprotonated (the pK_{SH^+} value is indicated in Figure 1). A qualitatively similar result is obtained with all the substrates studied, by the several different groups involved. This means that *more than one proton is involved in the reaction*, as was found for many cases of the benzidine rearrangement. As in that case also, the question arises as to whether or not the second proton transfer is involved in the rate-determining step of the reaction, particularly since it is quite evident that the graphs in Figure 1 are not linear. This question of general *vs.* specific acid catalysis can properly be understood by applying the principles of kinetic analysis to the system.

The kinetic scheme for specific acid catalysis can be partially depicted as follows, with S = substrate (azoxybenzene) and X^{2+} a kinetic intermediate:

$$S + H^+ \underset{}{\overset{K_{SH^+}}{\rightleftharpoons}} SH^+$$

$$SH^+ + H^+ \overset{K_{SH_2^{2+}}}{\rightleftharpoons} SH_2^{2+}$$

$$SH_2^{2+} \xrightarrow[\text{slow}]{k_0} X^{2+} \xrightarrow[\text{fast}]{} \text{Product}$$

Defining, as usual[49,126], C_S, a_S, etc. as the concentration and activity, respectively, of S, etc.; k_ψ as the observed pseudo first-order reaction rate constant; k_0 as the rate constant for the rate-determining step; K's as equilibrium constants for *de*protonation of protonated species; f's as activity coefficients ($f_\ddagger$ as that of the transition state); and h_+ as the acidity function applicable to the protonation equilibrium between mono- and diprotonated bases BH^+ and BH_2^{2+}, we have:

$$\text{Rate} = -\frac{d(C_S + C_{SH^+})}{dt} = k_\psi(C_S + C_{SH^+}) = k_0 \frac{a_{SH_2^{2+}}}{f_\ddagger}$$

Assuming that S is largely monoprotonated to SH^+, but essentially not diprotonated to SH_2^{2+}, under the reaction conditions, we have, from the

definitions of $K_{SH_2^{2+}}$, h_+ and a:

$$a_{SH_2^{2+}} = \frac{a_{SH^+} \cdot a_{H^+}}{K_{SH_2^{2+}}}; \quad a_{H^+} = h_+ \cdot \frac{f_{BH_2^{2+}}}{f_{BH^+}} \quad \text{and} \quad a_{SH^+} = C_{SH^+} \cdot f_{SH^+}$$

$$k_\psi(C_S + C_{SH^+}) = \frac{k_0}{K_{SH_2^{2+}}} \cdot C_{SH^+} \cdot h_+ \cdot \frac{f_{BH_2^{2+}} \cdot f_{SH^+}}{f_{BH^+} \cdot f_\ddagger}$$

$$\log k_\psi - \log \frac{C_{SH^+}}{C_S + C_{SH^+}} = -H_+ + \log \frac{k_0}{K_{SH_2^{2+}}} + \log \frac{f_{BH_2^{2+}} \cdot f_{SH^+}}{f_{BH^+} \cdot f_\ddagger} \qquad (17)$$

In the case of general acid catalysis, the second proton transfer would be the rate-determining step and the kinetic scheme is

$$S + H^+ \overset{K_{SH^+}}{\rightleftharpoons} SH^+$$

$$SH^+ + HA \xrightarrow[\text{slow}]{k'_0} X^{2+} \xrightarrow[\text{fast}]{} \text{Product}$$

$$\text{Rate} = -\frac{d(C_S + C_{SH^+})}{dt} = k_\psi(C_S + C_{SH^+}) = k'_0 \cdot \frac{a_{SH^+} \cdot a_{HA}}{f_\ddagger}$$

$$\log k_\psi - \log \frac{C_{SH^+}}{C_S + C_{SH^+}} = \log a_{HA} + \log k'_0 + \log \frac{f_{SH^+}}{f_\ddagger} \qquad (18)$$

If the acid HA is fully dissociated, however, we have

$$a_{HA} = a_{H^+} = h_+ \cdot \frac{f_{BH_2^{2+}}}{f_{BH^+}}$$

In this case equation 19 takes the place of equation 18, and is indistinguishable in practice from equation 17.

$$\log k_\psi - \log \frac{C_{SH^+}}{C_S + C_{SH^+}} = -H_+ + \log k'_0 + \log \frac{f_{BH_2^{2+}} \cdot f_{SH^+}}{f_{BH^+} \cdot f_\ddagger} \qquad (19)$$

Thus our analysis shows that the mechanistic cases of general acid catalysis (equation 19) and specific acid catalysis (equation 17) cannot be distinguished if the acid HA is fully dissociated. Buncel and Lawton[126] felt unable to decide which mechanism was more likely, although later Buncel and Strachan[85] thought that general acid catalysis was more probable.

However, it was pointed out by Cox and co-workers[91, 133] that all that is necessary to observe rate correlations according to equation 18 is to work at acidities where the acid is *not* fully dissociated. This is, in fact, the case for the whole acidity range in Figure 1 for the rearrangement of azoxybenzene. It may be noted[123, 133] that above 67% H_2SO_4 the undissociated

sulphuric acid molecule is a better proton donor than H_3O^+, and above about 96% H_2SO_4, the protonated sulphuric acid molecule, $H_3SO_4^+$, is better still. It appears that neither equation 17 nor equation 19 is applicable, as the Figure 1 plot shows multiple curvature*; however, equation 18 does apply, since plots of $\log k_\psi - \log(C_{SH^+}/C_S + C_{SH^+})$ against $\log a_{H_2SO_4}$ are accurately linear below 96·5% H_2SO_4 for azoxybenzene[133]. In addition, the plot is also linear, above 80% H_2SO_4, for hexamethylazoxybenzene and at least two of the azoxynaphthalenes[91]. Below 80% H_2SO_4 another mechanism applies for some substrates; this will be considered in a later section. Above 96·5% H_2SO_4 in acidity, the correlation with $\log a_{H_2SO_4}$ ceases to apply, as can be seen from Figure 2; the rate continues to increase, but

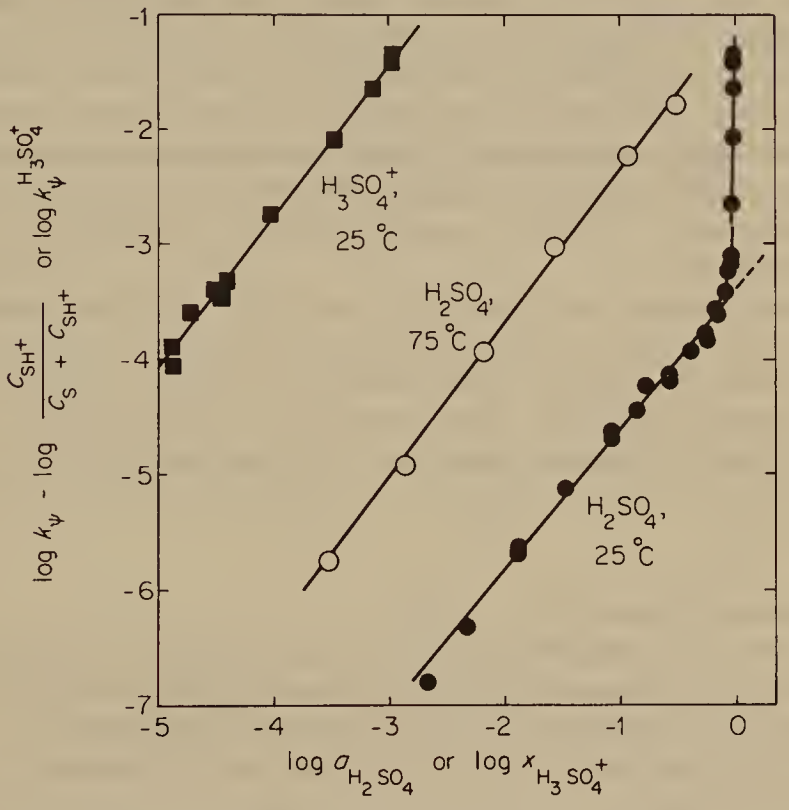


FIGURE 2. Graphs of $\log k_\psi - \log(C_{SH^+}/C_{SH^+})$ at 25°C (●) and 75°C (○) vs. $\log a_{H_2SO_4}$, and of $\log k_\psi^{H_3SO_4^+}$ at 25°C (■) vs. $\log X_{H_3SO_4^+}$, for the rearrangement of azoxybenzene in H_2SO_4. Reprinted with permission from Cox, *J. Am. Chem. Soc.*, **96**, 1059 (1974). Copyright by the American Chemical Society.

* Acidity functions have been shown to be linear functions of one another[134], so the Figure 1 curves, plotted against H_0 rather than H_+, should still be linear if these equations were obeyed, although the slope would probably not be one.

$\log a_{H_2SO_4}$ does not. However, the log (rate) data above this point for azoxybenzene (the only compound so far studied kinetically at this high an acidity) is an accurately linear function of $\log a_{H_3SO_4^+}$[133]. The slopes in these plots are close to unity (Figure 2).

Thus the Wallach rearrangement, with some exceptions to be discussed below, is a *general-acid-catalysed* reaction. The strongest acids of the system, undissociated H_2SO_4 and $H_3SO_4^+$, are required; the solvated proton is not a strong enough acid to catalyse the reaction. The reason that the rearrangement does not occur in perchloric acid (see Section III, A, 3) is that the only acidic species present in this system is the solvated proton in the acid range so far studied (up to 78% $HClO_4$)[133].

Hahn, Lee and Jaffé[129] found that the rearrangement rates for the 4′-bromo- and -methylazoxybenzene isomers were very close to those for the 4-isomers. The medium used in that work was 20% ethanol/80% aq. H_2SO_4 for which H_0 values are known.[135] On the other hand, Duffey and Hendley's data[123], obtained for the aq. H_2SO_4 medium, show large reactivity differences among different nitro-substituted azoxybenzenes. Approximate Hammett ρ values could be calculated, of −3·3 for 3- and 4-substituted compounds, and −0·7 for 3′- and 4′-substituted compounds, in 90% H_2SO_4 solutions.

Activation parameters, derived from pseudo first-order rate constants, are a composite function of rate and equilibrium processes. In addition they contain an unknown contribution from activity coefficient terms such as those in equations 17–19, and another unknown term for the variation of acidity function, or species activity, with temperature. Several studies have, however, reported such apparent activation parameter values[123, 126, 129].

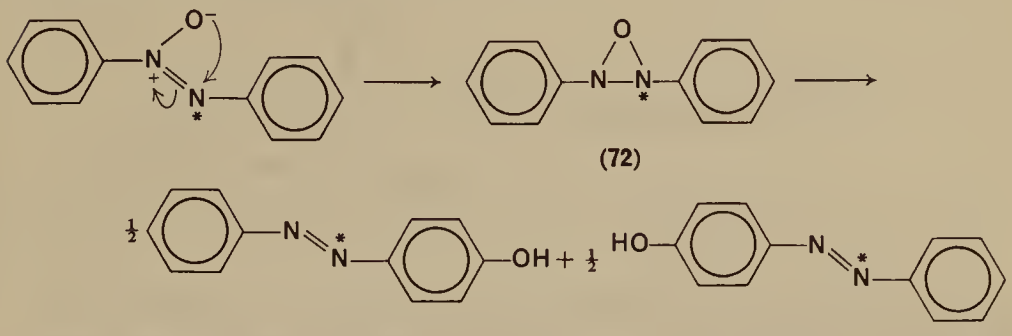
7. Theories of mechanism

Apart from early theories, such as the decomposition of azoxybenzene into phenol and diazosulphonic acid followed by recombination[80], that have since been disproved[81], three theories for the mechanism of the Wallach rearrangement currently exist. These may be referred to as the *N*,*N*-oxide intermediate mechanism; the dicationic intermediate mechanism, and the quinonoid intermediate mechanism*. These three mechanisms will be discussed in turn. All refer to the rearrangement resulting in *para*-substituted products. Mechanisms for the rearrangement leading to

* On occasion the three mechanisms have been designated, respectively, as the Shemyakin–Oae–Jaffé (SOJ) mechanism, the Gore–Buncel–Lawton (GBL) mechanism, and the Duffey–Hendley (DH) mechanism.

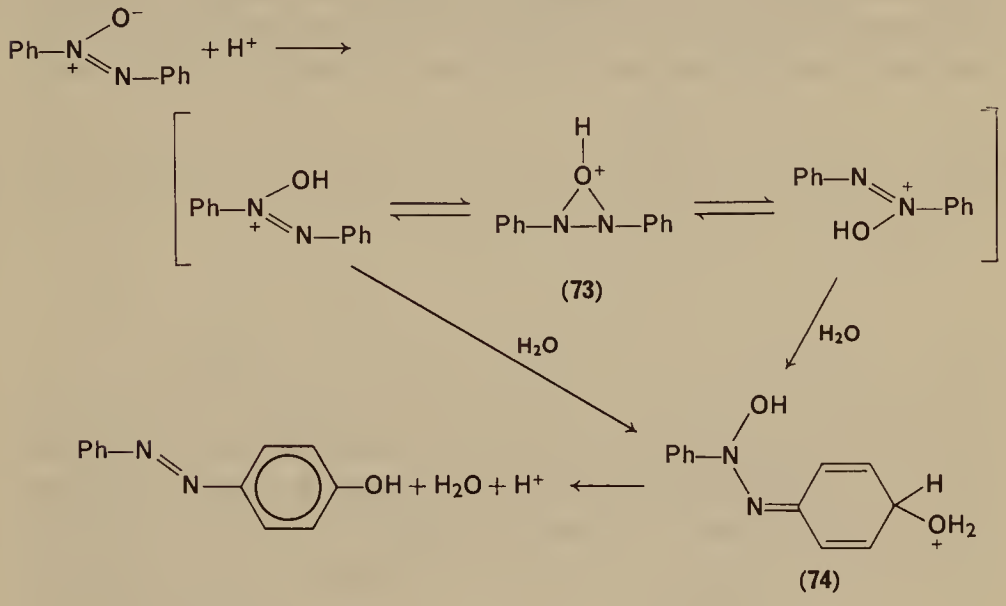
ortho-substituted products are not so well understood at the present time and will be discussed separately.

a. The N,N-*oxide intermediate mechanism.* In order to explain the results of ^{15}N-labelling experiments, Shemyakin and collaborators[130] proposed the formation of **72**, as a symmetrical intermediate, which would be attacked with equal ease on either ring:



(72)

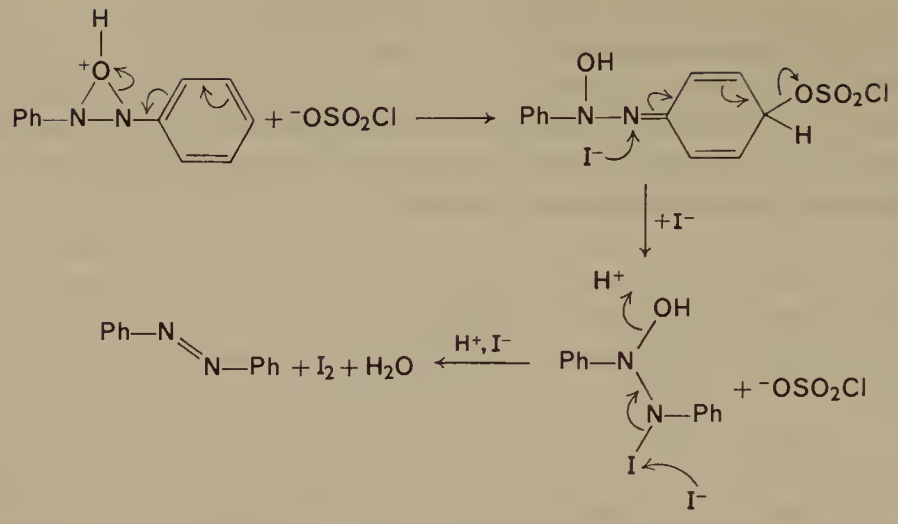
Oae and co-workers elaborated on this idea by introducing the requirement of protonation and proposed the following scheme[99,118]:



(73)

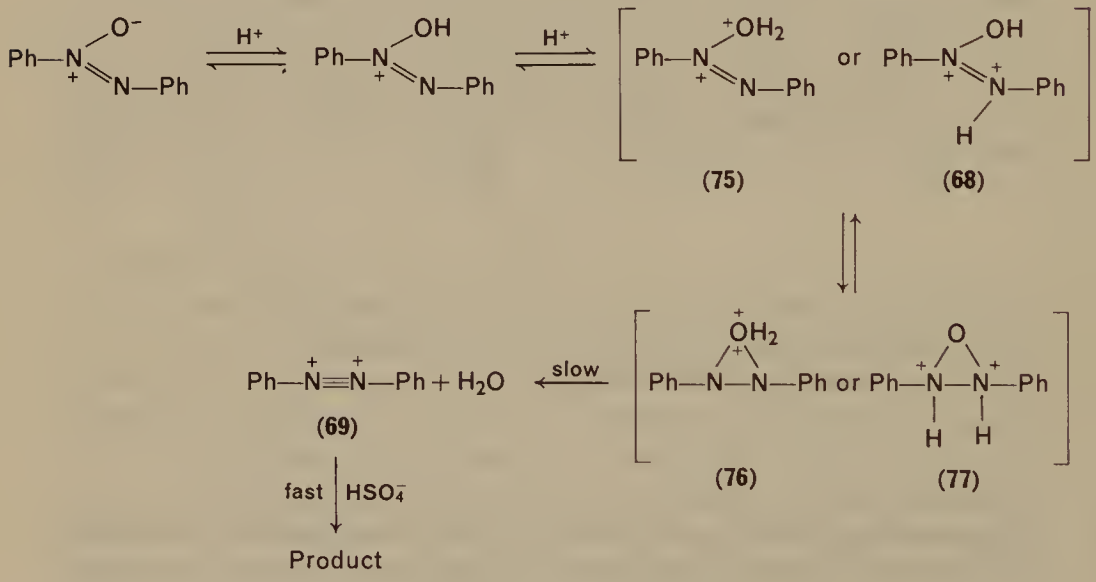
(74)

Circumstantial evidence in favour of **72**, given by Shemyakin and co-workers[117], was that addition of iodide ion to a reaction mixture of azoxybenzene in chlorosulphonic acid at −8°C caused azobenzene formation, at the expense of the *p*-hydroxyazobenzene product, to the extent of 50%. This was suggested to be evidence in favour of **72**, because N,C-oxides and some C,C-oxides are readily reduced by HI to the unsaturated com-



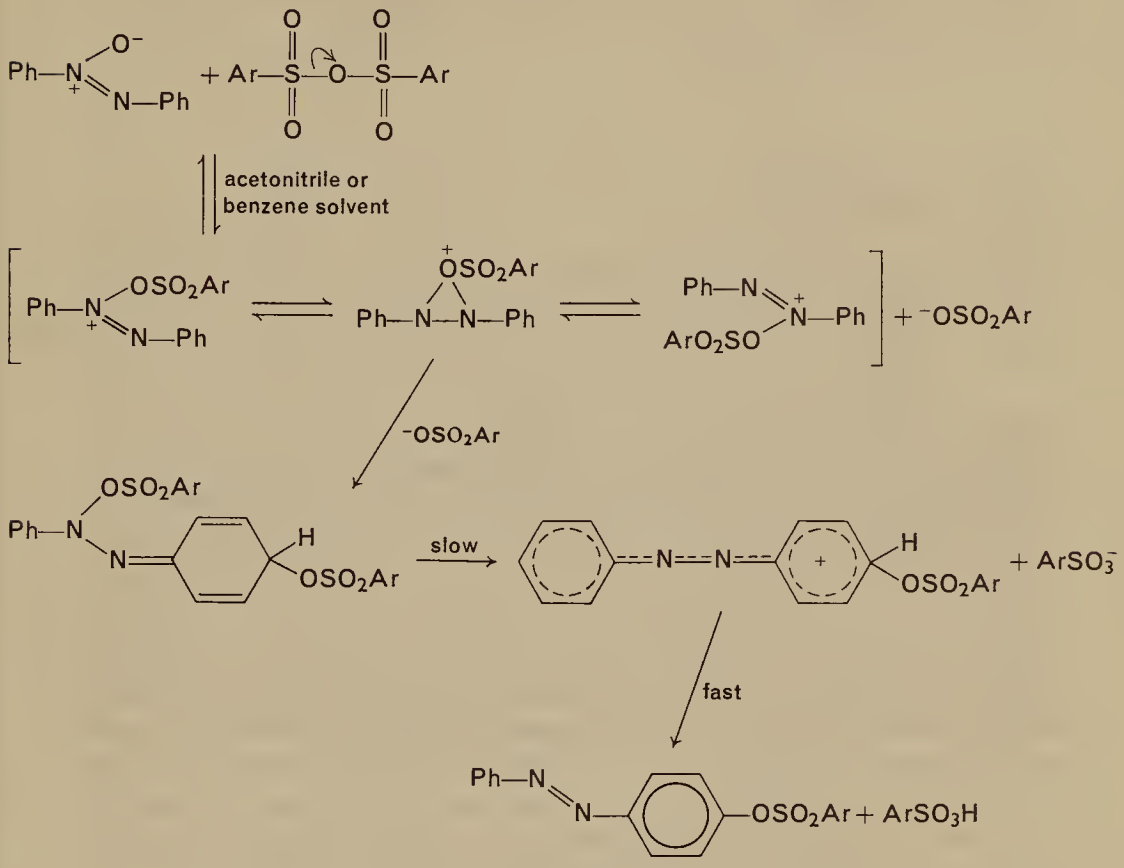
pounds, while nitrones are unaffected. Shine[82] has given a possible mechanism for this reaction, which is consistent with Oae's scheme (see above). However, the iodide results are also consistent with the dicationic intermediate mechanism, as will be seen later.

Jaffé and collaborators[129] accommodate the diprotonation requirement by the proposal of diprotonated N,N-oxide intermediates, **76** or **77**, which would break down to yield the dicationic intermediate, **69**; product forma-



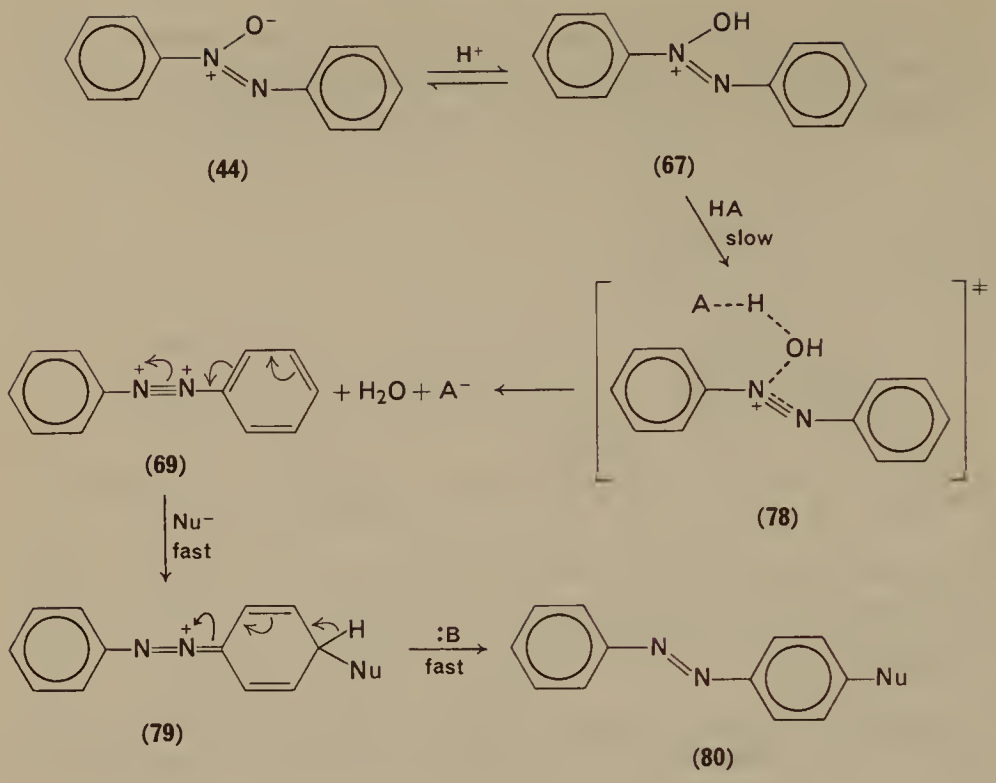
tion would follow as previously. This mechanism, though attractive, is not in accord with the lack of isomerization and reactant label scrambling noted above, unless it were modified such that the symmetrical intermediate (**76** or **77**) were not formed in a pre-equilibrium stage.

Considerable evidence has been put forth that a related reaction, that of azoxybenzene with arenesulphonic anhydrides, proceeds via an *N,N*-oxide intermediate[113], according to the following reaction scheme:



b. The dicationic intermediate mechanism. The main feature of this mechanism is the postulate of the involvement of the dicationic intermediate **69** which was first introduced by Gore[122]. The scheme given below was originally proposed by Buncel and Lawton[126], together with a similar mechanism in which the second protonation is an equilibrium rather than the slow step of the reaction. Later Buncel and Strachan[85] favoured the mechanism shown.

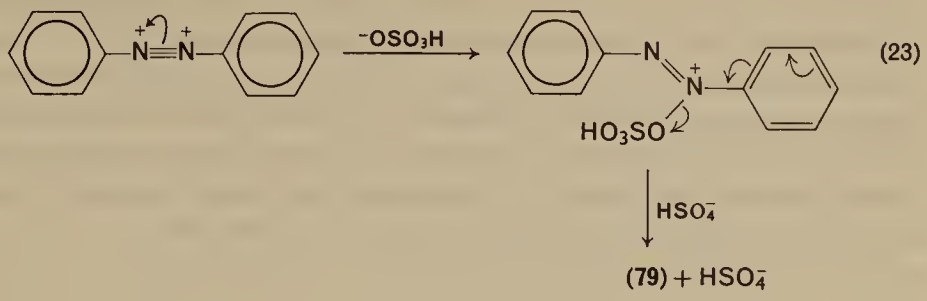
This reaction pathway seems to fit the kinetic and other data currently available. The first stage is protonation of **44** on oxygen to give **67**, a well-established process for which the pK_{SH^+} is known. Next **67** reacts with a general acid HA, which in the present case will be H_2SO_4 or $H_3SO_4^+$, but not H_3O^+ (see Section III, A, 6). Proton transfer is a concerted process with water loss and participation of the nitrogen lone pair, as shown in the



transition state **78**, and leads to formation of dication **69** in an essentially irreversible process. Dication **69** then undergoes fast nucleophilic attack by Nu^- (probably HSO_4^-) giving **79**, which is readily deprotonated by base B: (probably again HSO_4^-) and rearomatized to give the product **80**. If the product is the hydrogen sulphate, it speedily loses SO_3 to give the phenol (see Section III, A, 3); the phenolic product undoubtedly exists in the monoprotonated, or even diprotonated[88], form in these solutions. In acids other than sulphuric, Nu^- and B: will correspond again to the species derived from the medium. (Though B: and Nu^- may be the same species, e.g. HSO_4^-, the different notation is used in the scheme in order to emphasize the different functions fulfilled by these species.)

It is easily seen that this mechanism accounts for both the two-proton requirement as well as for general acid catalysis. It can reasonably be assumed that the formation of **69** is irreversible, because of the low water activity in the 80–100% H_2SO_4 media used[136]. Hence the observed lack of isomerization of 4- and 4′-substituted compounds and the recovery of unreacted labelled **44** with the label undisturbed are also accounted for. Should the dication be attacked on nitrogen first rather than carbon, by a nucleophile such as HSO_4^-, then subsequent nucleophilic attack on the

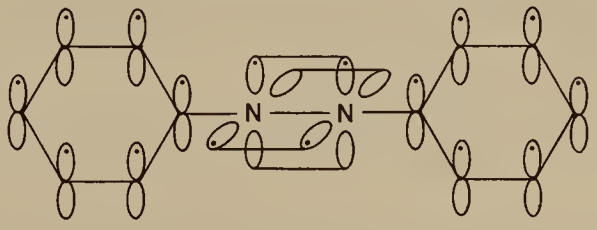
para carbon will be greatly aided by the presence of a good leaving group (HSO_4^-) rather than a poor one (OH^-):



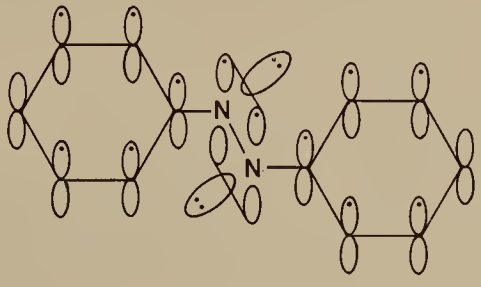
(23)

It may be noted that the reactions shown in equation 23 should be faster than the formation of **69** from **67** in the above scheme. Under these conditions there will be no oxygen exchange with the medium (see Section III, A, 4, a), while the nitrogen equalization is readily accounted for.

Intermediate **69** has been the subject of some scrutiny. Although stable at low temperatures in non-aqueous very strong acids[52], it has not been observed under Wallach rearrangement conditions. Attempted observation by cryoscopic techniques in 100% H_2SO_4 yields parameters which are characteristic only of the aftermath of rearrangement and sulphonation processes[85–86]. Extensive molecular orbital calculations[81,137–138] on the dicationic species point to a linear diphenylacetylene-like structure rather than a bent azobenzene-like structure. The orbital diagrams for the two systems (14π- and 12π-electrons respectively) are given by **81a** and **81b**.

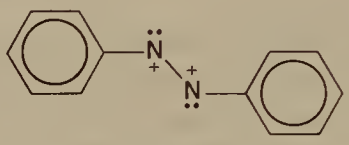


(81a)



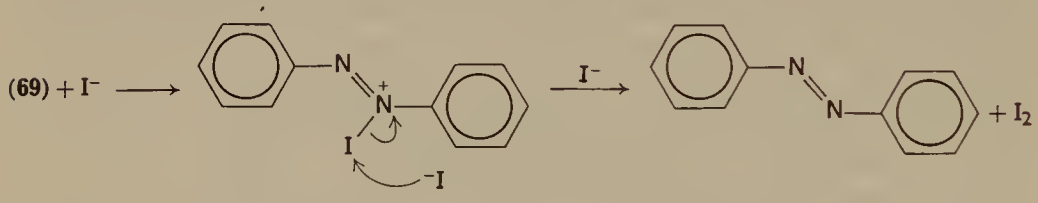
(81b)

The 'di-nitrenium' type of structure **82**, originally proposed by Gore, is probably not representative of the electronic configuration of the dication. This would explain why the Wallach rearrangement is not closely similar to the Bamberger rearrangement, as might have been expected[82]. The Bamberger rearrangement, of phenylhydroxylamines to aminophenols, probably involves a nitrenium ion intermediate[82, 139]. These calculations also show that much of the positive charge is present at the *p*-carbons in **69**, and that a lesser amount resides on the *o*-carbons. This would allow for small amounts of *ortho*-hydroxy products observed in some cases.



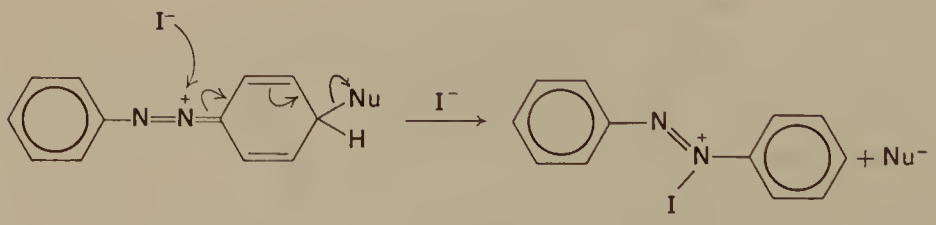
(82)

It will be recalled that the reported formation of azobenzene in presence of iodide ion has been invoked as evidence for the N,N-oxide intermediate. Now iodide ion, if present in solution, could lead to azobenzene in two other ways. If **69** is attacked by I^- on nitrogen, as in equation 23, then **83** would result; the latter should be susceptible to nucleophilic attack on iodine by another I^- ion, leading to azobenzene:



(83)

Alternatively, if structure **79** has a significant lifetime, it could be attacked by I^- to yield the intermediate **83**, which would once more react with I^- to



(79) **(83)**

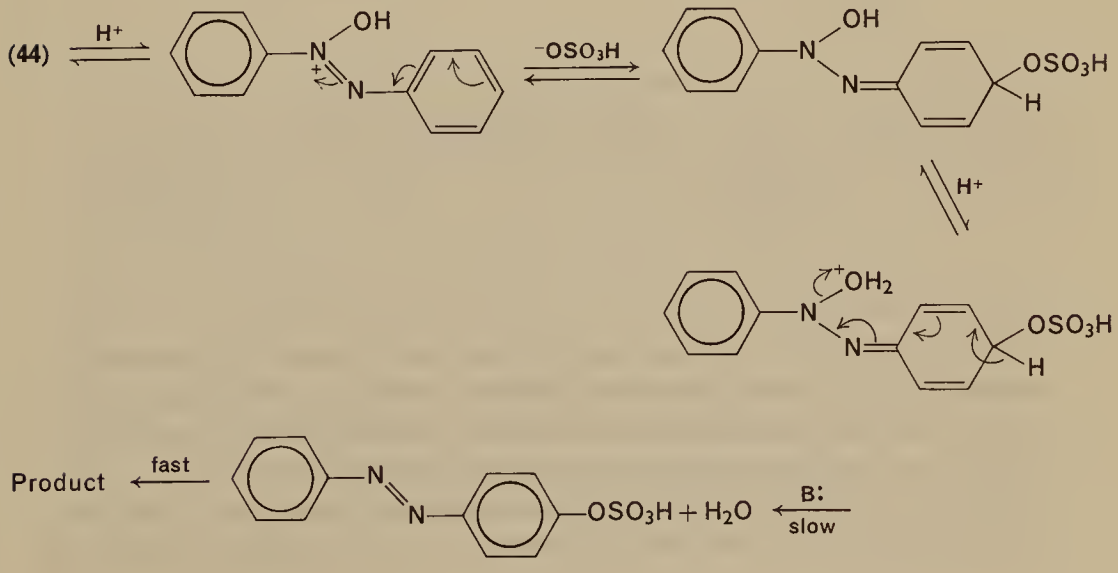
give azobenzene. Thus the observed reduction by iodide ion[117] can also be accommodated within the framework of the dicationic intermediate mechanism.

The second protonation of **67** on oxygen, necessary to obtain **69**, is a *rate* process, not an equilibrium protonation. It seems likely that the $pK_{SH_2^{2+}}$ value of azoxybenzene is of the order of 7–10 units more negative than the pK_{SH^+} value[88]; however the second protonation will occur on nitrogen, to give **68**, and not on oxygen[52]. No evidence for a second protonation has been observed in 100% H_2SO_4[85], 78% $HClO_4$, FSO_3H or $ClSO_3H$[110], as indicated by the identity of the u.v.-visible spectra in these systems. It may be possible, however, that some of Jaffé's studies[129] involve small amounts of the diprotonated substrates at the highest acidities studied, which were below −12 on the H_0 scale, and may account for some of the levelling off of rates observed in this region[140].

In summary, it appears that the GBL mechanism is followed by all substrates at acidities greater than 80% H_2SO_4, and probably by many substrates in more dilute acids also. However, another mechanism is possible in more dilute acid solutions, and is discussed in the next section.

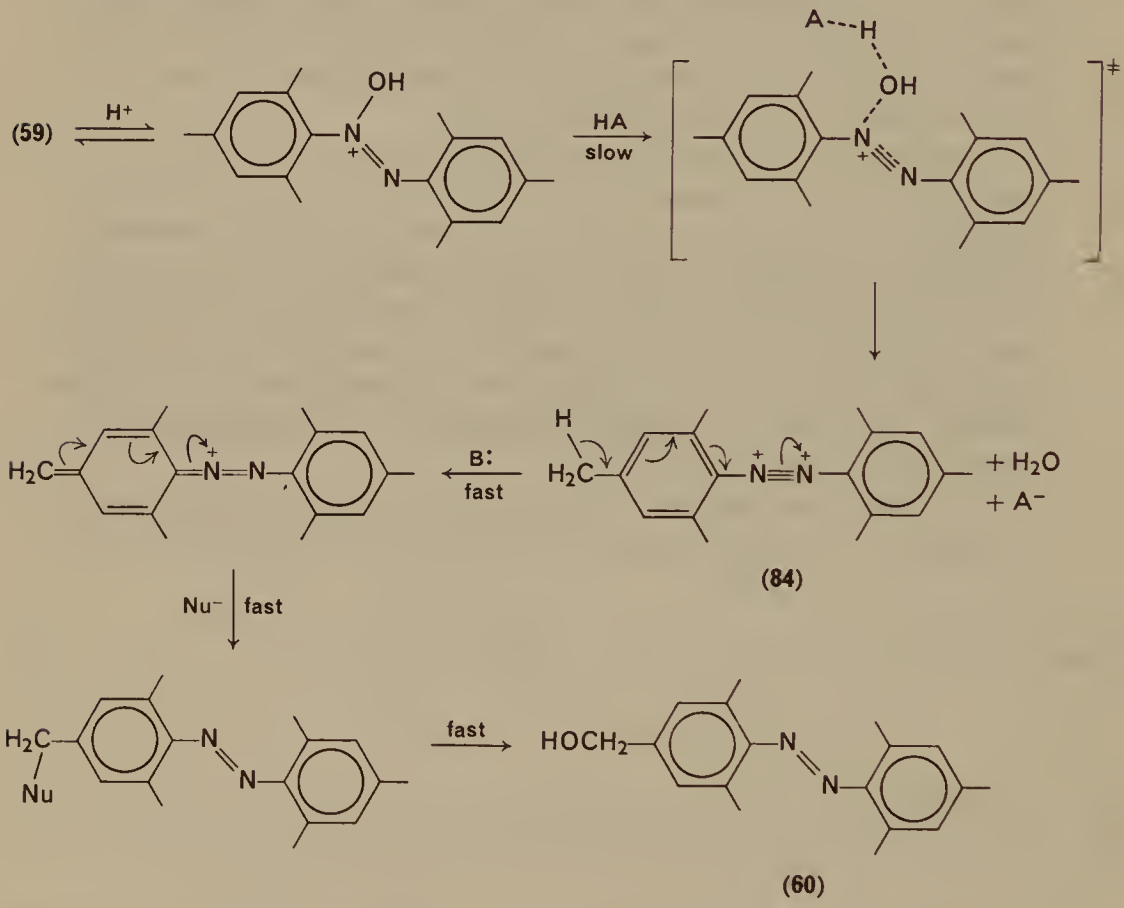
c. The quinonoid intermediate mechanism. Duffey and Hendley[123] have proposed a mechanism for the rearrangement of azoxybenzene in sulphuric acid which bears some relation to an original suggestion by Gore[122], and involves the postulate of quinonoid structures as the key intermediates, according to the scheme below.

In support of this mechanism the authors have shown[123] that bromide ion is liberated at about the same rate from either 4- or 4′-bromoazoxybenzene



in alcoholic alkali at 117°C. In this way the necessity for a symmetric intermediate, as indicated by the isotopic tracer experiments, would appear to be no longer a requirement.

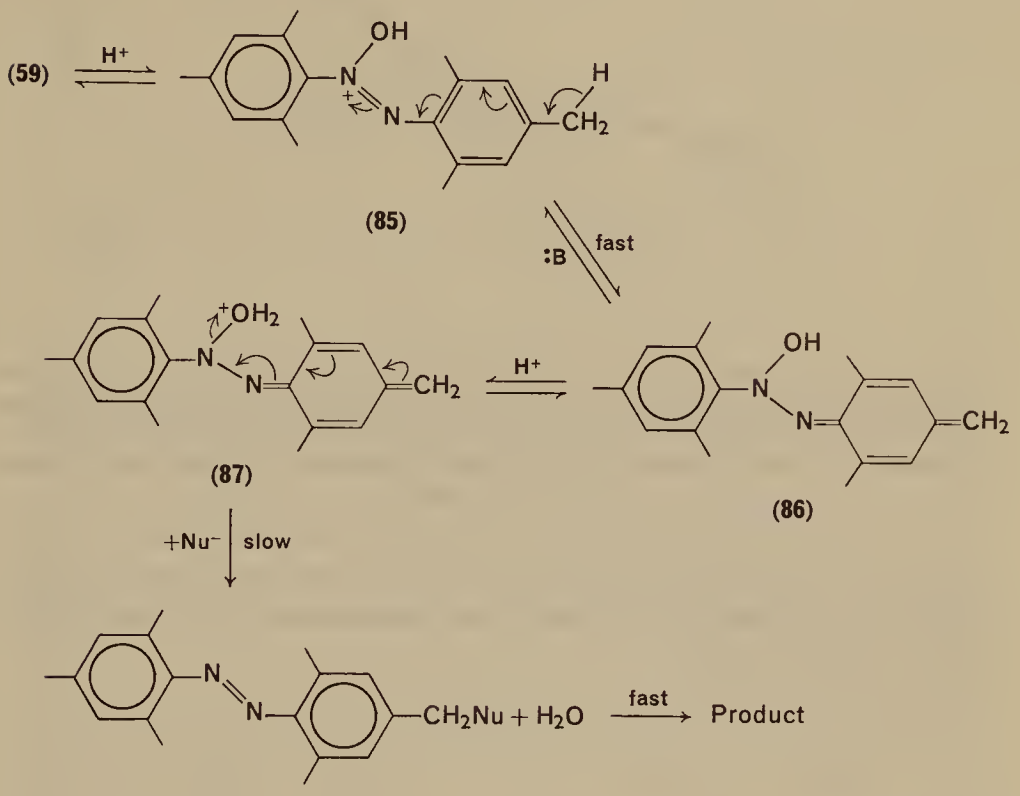
Evidence for this type of mechanism has been derived from a recent kinetic study of the rearrangement of hexamethylazoxybenzene (**59**), yielding the alcohol **60** (see Section III, A, 2)[91,132]. This indicated that two mechanisms for this process were in operation, depending on the acid concentration. Above 80% H_2SO_4, the log (rate) plot was a linear function of $\log a_{H_2SO_4}$, showing that the dicationic mechanism is obeyed, according to the following scheme[91,92,132]:



Dication **84** does not undergo nucleophilic attack directly, but one of the protons of a *p*-methyl group is lost (these protons have now become quite acidic), and eventually **60** results as shown. The process is some 6 to 10 times faster than the rearrangement of azoxybenzene[132].

Below 80% H_2SO_4 in acidity, however, the log (rate) plot is not linear in $\log a_{H_2SO_4}$; in fact the acidity dependence is rather shallow between 60

and 80% H_2SO_4[132]. On the other hand in the 60–80% H_2SO_4 region the log (rate) plot was found to be a linear function of $2\log a_{HSO_4^-}$ (of unit slope), which means that two bisulphate ions are involved before, or during, the rate-determining step. The following mechanism was thus proposed for the low acid region[91,132]:



According to this scheme, initial protonation of **59** to **85** ($pK_{SH^+} = -4{\cdot}75$)[92b] is followed by fast reversible proton loss to bisulphate ion (B:), giving **86**. There follows a second protonation to yield **87**; presumably the substrate exists in this form at the acidities studied, since practically no acidity dependence, apart from that required for **59** $\rightleftharpoons$ **85**, is apparent. The rate-determining step is nucleophilic attack, presumably concerted with water loss, by another bisulphate ion (Nu^-) on **87**, resulting eventually in the observed product **60**. The kinetic equation derived for this process[132] requires that the log rate be a linear function of $2\log a_{HSO_4^-}$, as is observed. In Figure 3 the experimental points are compared with theoretical curves for the two mechanisms; the agreement is satisfactory.

The DH mechanism was also found to apply to the rearrangements of some azoxynaphthalenes at acidities below 80% H_2SO_4[131]. Kinetic analysis

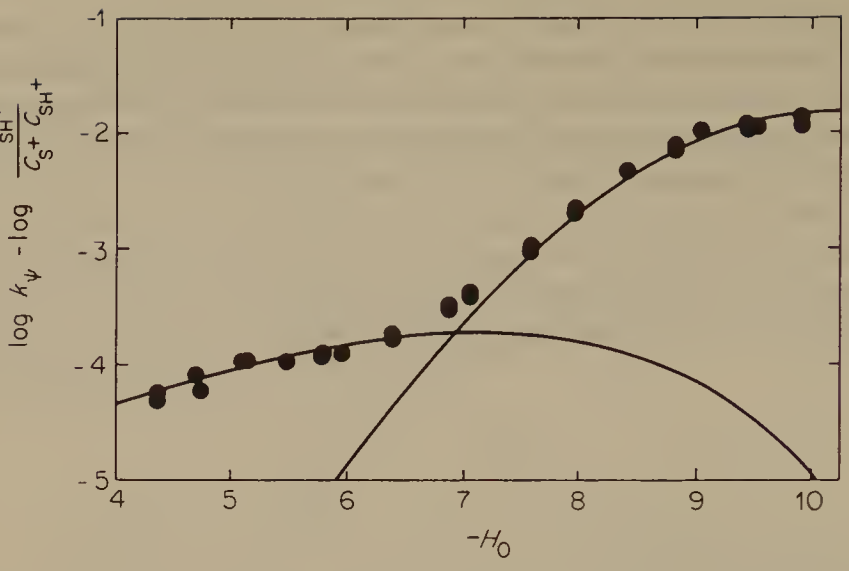
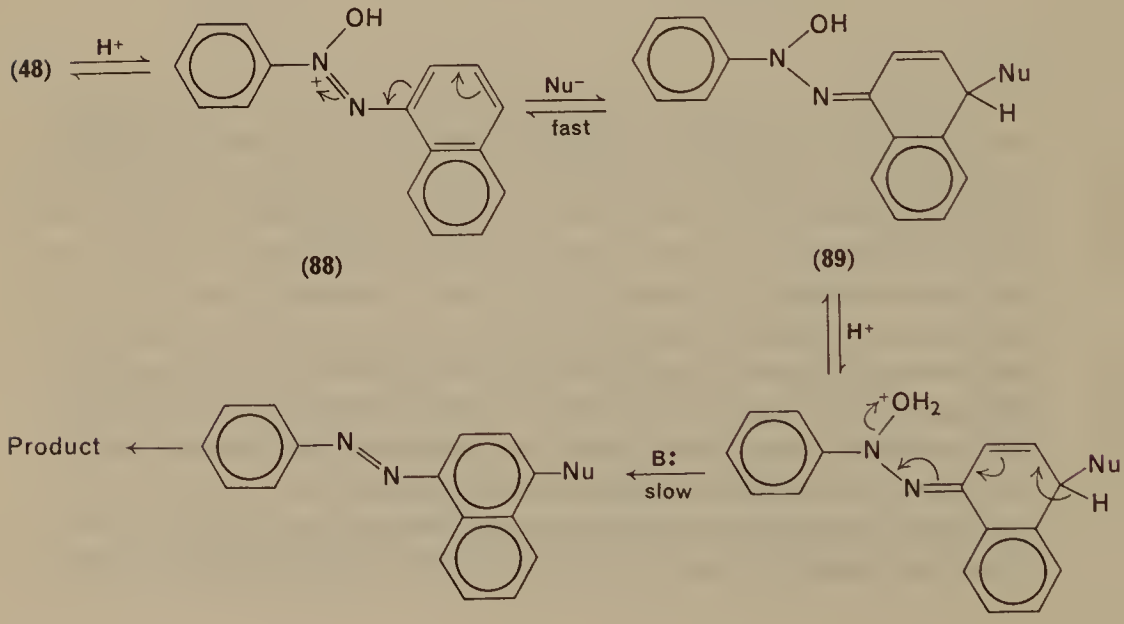
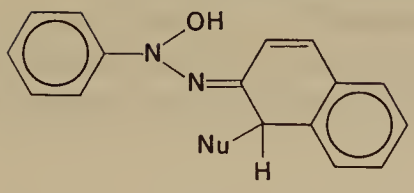


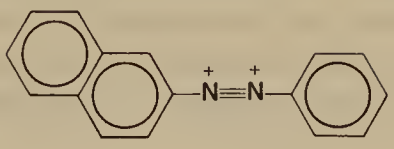
FIGURE 3. Comparison of theory with experiment in the Wallach rearrangement of hexamethylazoxybenzene in sulphuric acid at 45°C. Experimental points are compared with the upper curve, drawn assuming correlation with $\log a_{H_2SO_4}$ only, and the lower curve, drawn assuming correlation with $2\log a_{HSO_4}$ only. (Data from ref. 132.)

of the rate data showed again that two bisulphate ions were involved. The mechanism proposed[131] for a typical compound at acidities below 80% H_2SO_4 is shown below.

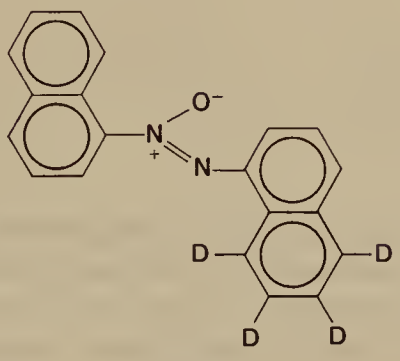




(91)



(92)



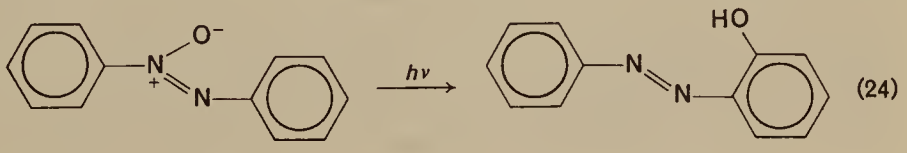
(93)

It is thought that the DH mechanism is applicable (at low acidities) to reactions in which the intermediates, such as **86** and **89**, can be stabilized in some way. For instance, in **89** and **91** the aromaticity of one of the naphthyl rings is retained, while **86** is a quinonoid-type structure stabilized by hyperconjugation. Note that one of the azoxynaphthalenes studied, **50**, cannot form structures like **89** or **91**, since the naphthyl ring is not suitably located with respect to the oxygen-carrying nitrogen. Although a quinonoid type of structure involving attack at phenyl is possible, energetically this appears to be unfavourable. Hence, as with azoxybenzene, the dicationic intermediate mechanism is followed, forming **92**, which is then attacked at the most favourable site.

One obvious test of this mechanism is to synthesize an isotopically labelled compound such as **93** and to determine whether or not it reacts as is predicted. Another prediction is the observation of a primary isotope effect involving ring deuterium. Tests of these are under way[141a].

8. Rearrangements giving *ortho*-hydroxy products

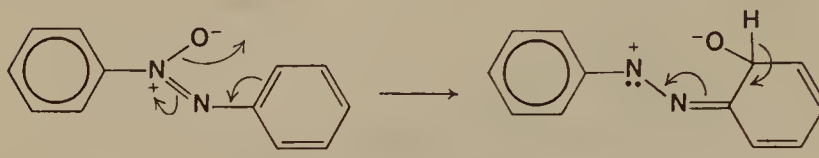
When irradiated, azoxybenzenes undergo a photochemical rearrangement to yield *ortho*-hydroxy products, e.g. **44** → **94**. Isotopic tracer studies



(24)

(44) (94)

show this rearrangement to be intramolecular[81]. A detailed discussion is not presented here since the reaction is covered in another Chapter[84] and a review is available[141b]. Badger and Buttery[142] proposed a cyclic mechanism for the process:



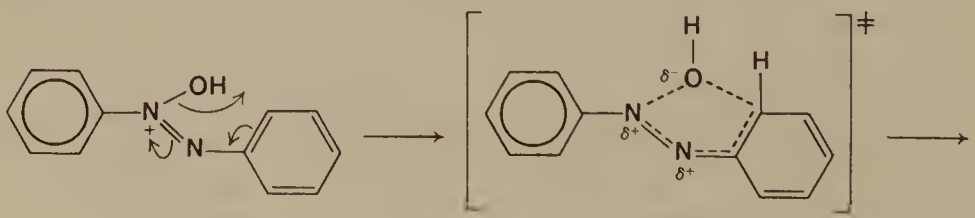
(94)

Tanikaga[143] proposed that the excited state involved is a $\pi \rightarrow \pi^*$ singlet (triplet states lead to azobenzene[144]). Evidence in favour of Badger and Buttery's mechanism was given by Bunce and co-workers[145], who found that a hydrogen abstraction/hydroxyl transfer mechanism was rendered unlikely by the failure of the azoxy oxygen to abstract hydrogen atoms more weakly bound than aromatic ones, in variously substituted azoxybenzenes.

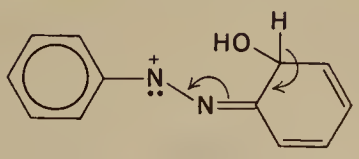
As we have seen, some of the acid-catalysed reactions leading to *ortho*-hydroxyazo products are also intramolecular (see Section III, A, 4, b). However in other cases, for instance the acid-induced rearrangement of azoxynaphthalenes **49**, **50** and **53**, the reactions appear to follow normal intermolecular pathways[131].

It would appear that at least three mechanisms are possible for the acid-induced intramolecular *ortho* rearrangement. In two of these the oxygen is nucleophilic (equations 25 and 26), and in one it is electrophilic (equation 27). Oae and collaborators[99] favour the pathway given in equation 25 but consider that **90** would be an intimate ion-pair intermediate, rather than a transition state.

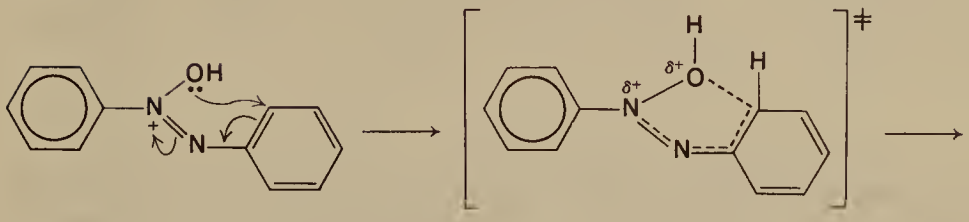
Recently, Jaffé and co-workers[146a] have obtained evidence for a photochemical process involving the monoprotonated azoxybenzene substrate. This is a most interesting result, worthy of further investigation.

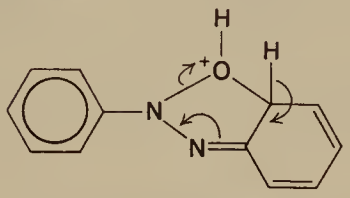


(90)

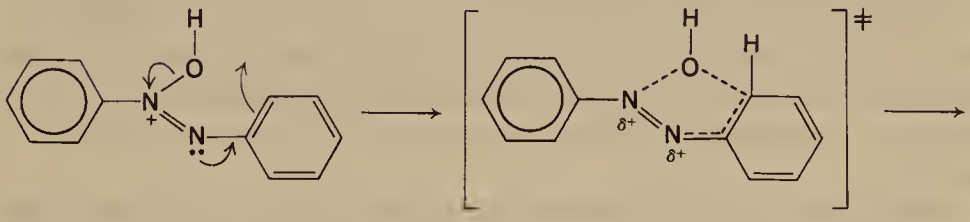


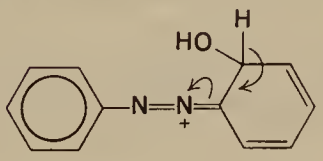
(94) (25)





(94) (26)

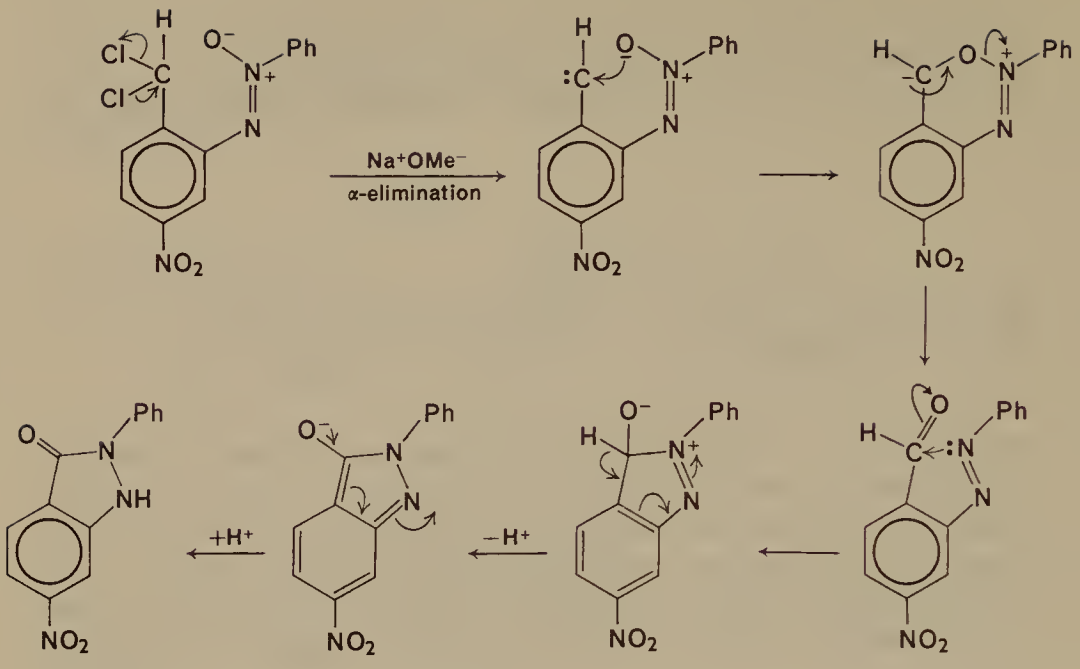




(94) (27)

B. Other Aromatic Azoxy Rearrangements

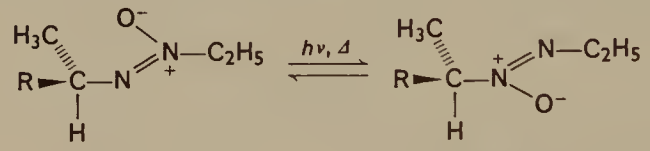
Apart from the Wallach rearrangement, the only other rearrangement undergone by aromatic azoxy compounds appears to be the formation of an indazolone derivative when 4-nitro-2-(benzeneazoxy)-benzylidene dichloride is treated with alkoxide[146b]. The interesting reaction pathway shown below has been given by Rembges and Kröhnke[146b] and involves, overall, migration of the azoxy oxygen onto an aldehydic carbon and ring closure.



C. *Aliphatic Azoxy Rearrangements*

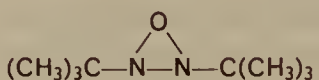
Compared to aromatic azoxy compounds, very little is known about the rearrangements which the aliphatic analogues undergo. Also no work appears to have been done on Wallach-type rearrangements involving heterocyclic analogues of azoxybenzene. However, several reactions are of interest.

Azoxyalkanes undergo migration of oxygen from one nitrogen to the other when irradiated[147]. Thus irradiation of **95** or **96** (R = alkyl) produces a



(95) **(96)**

photostationary mixture, **95**:**96** = 1:1·28, presumably via an intermediate

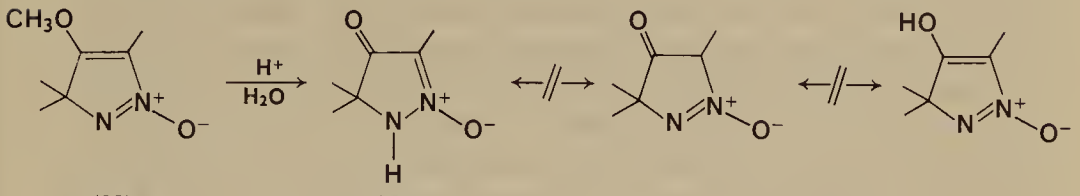


(97)

cyclic *N*,*N*-oxide. It is recalled that the oxadiaziridine **97** is formed when azoxy-t-butane is irradiated[148].

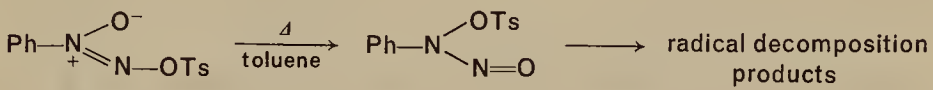
The possibility of nitrone-azoxy group tautomerism arises in some situ-

ations. However the product obtained by acid hydrolysis of **98** could unambiguously be assigned the structure **99**[149], which apparently rules out this kind of isomerism.



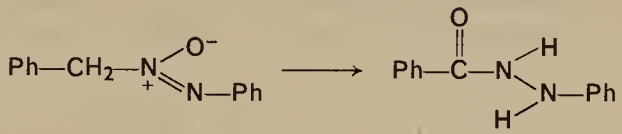
(98) **(99)**

Tosyl migration to *N*-oxide oxygen has been demonstrated by Shemyakin and associates, during the decomposition of *β*-phenylazoxy tosylate (**100**), by using ^{18}O tracer techniques[150]:



(100)

Benzylazoxybenzene (**101**) rearranges to *N*-benzoyl-*N'*-phenylhydrazine (**102**) under various conditions of acid catalysis[151–152]:



(101) **(102)**

Similarly, primary aliphatic azoxy compounds give *N*-acyl-*N'*-alkyl-hydrazines in hot hydrochloric acid[153]. A number of *cis*-aryl-alkyl and *cis*-dialkyl azoxy compounds were found to undergo similar rearrangements by Gillis and Schimmel[154], as shown in Table 6. The mechanism of these transformations is quite unknown at the present time.

TABLE 6. Rearrangement products of some alkyl azoxy-compounds[154]

Reactant	Product
cis-*p*-Z-$C_6H_4CH_2N{=}N(O)C_6H_5$ Z = H, CH_3O, C_6H_5, NO_2	*p*-Z-$C_6H_4CONHNHC_6H_5$ Z = H, CH_3O, C_6H_5, NO_2
cis-*p*-Z-$C_6H_4CH_2N{=}N(O)CH_3$ Z = H, CH_3, Br, NO_2	*p*-Z-$C_6H_4CONHNHCH_3$ Z = H, CH_3, Br, NO_2
p-$CH_3C_6H_4CH_2N(O){=}NCH_2C_6H_5$	*p*-$CH_3C_6H_4CONHNHCH_2C_6H_5$
p-$CH_3C_6H_4CH_2N{=}N(O)CH_2C_6H_5$	*p*-$CH_3C_6H_4CH_2NHNHCOC_6H_5$

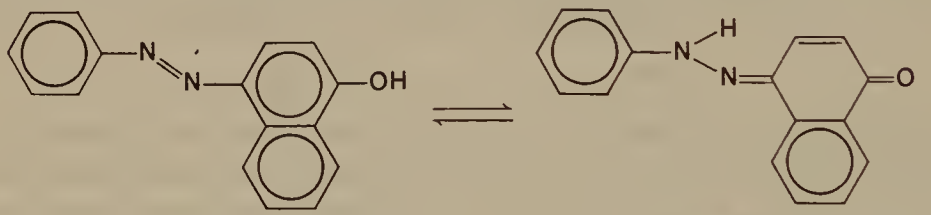
IV. REARRANGEMENTS OF AZO COMPOUNDS

A. Scope of Presentation

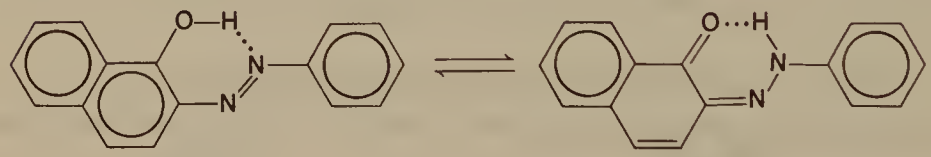
Azo compounds containing hydroxy and amino substituents can in principle exist in two or more tautomeric forms (e.g., **103** ⇄ **104** below). This is the main 'rearrangement' which azo compounds undergo, apart from *cis–trans* isomerism which is covered in another chapter[155], although the transformation is correctly classified as tautomerism. Owing to its general interest, the topic is reviewed in the presentation below; the literature on this topic is extensive and previous summaries of various facets have been given[156–160]. Aromatic azo compounds are emphasized in the following account; most of the published work refers to these, owing to their importance in the dyestuff industry and as acid–base indicators. The section is ended with a consideration of 'true' azo rearrangements, of which there are currently very few known.

B. Azo–Hydrazone Tautomerism of Aromatic Azo Compounds

In 1884 Zincke and Bindewald[161] found that the same product was obtained from both the coupling of benzenediazonium ion with 1-naphthol, and the condensation of phenylhydrazine with naphtha-1,4-quinone. The product could be represented as **103** or as **104**, and a mobile equilibrium was suggested[161]. Similarly **105** ⇌ **106** was thought possible. From com-



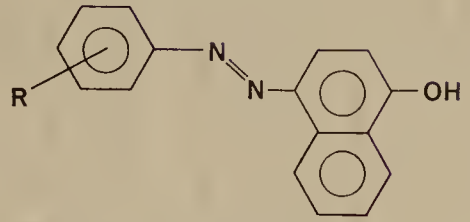
(103) (104)



(105) (106)

parison of the spectra of solutions of 4-phenylazo-1-naphthol with those of its *O*- and *N*-methyl derivatives, Kuhn and Bär concluded that the mobile equilibrium **103** ⇌ **104** was set up in all solutions studied, favouring **103** in pyridine and **104** in glacial acetic acid[162]. However, in the case of 2-phenylazo-1-naphthol, the hydrazone form **106** was found to predominate over the azo form **105**[162].

TABLE 7. The effect of phenyl substituents on the amount of azo tautomer present in 4-phenylazo-1-naphthol in various solvents[165]

Substituent R in 	% Azo tautomer present in					
	Benzene	Acetone	Acetonitrile	Acetic acid	Pyridine	DMF
Hydrogen	72	78	78	50	100	52
o-Chloro	0	100	92	0	92	54
m-Chloro	92	100	86	0	98	52
p-Chloro	86	100	88	66	92	48
o-Nitro	86	88	98	100	58	36
m-Nitro	82	92	90	100	68	44
p-Nitro	88	92	100	90	50	8
o,*p*-Dichloro	100	100	88	92	78	18
o,*m*-Dichloro	100	86	88	92	66	18
o,*o*-Dichloro	100	86	89	88	68	18
o,*p*-Dichloro	88	—	—	100	16	16
o,*o*-Dinitro	64	64	72	100	30	30
o-Chloro, *p*-nitro	100	96	96	88	12	8

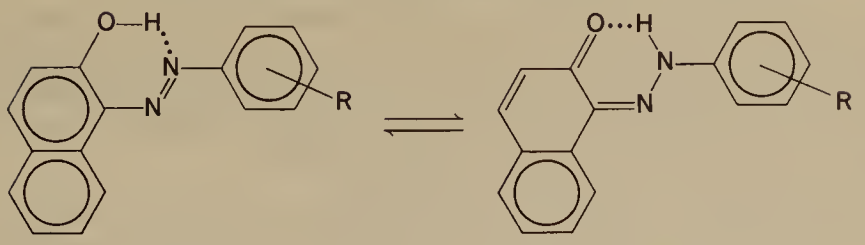
Increasing solvent polarity displaces the equilibrium towards the quinone hydrazone form for *para*-hydroxy compounds, but at the same time hydrogen-bonding solvents stabilize the azo form. Thus solvents stabilizing the hydrazone form were found to be more effective in the order hexane < ethanol < benzene < chloroform < 50% aq. ethanol < acetic acid[163]. Increasing alkalinity stabilizes the azo form[164]. A more recent report states that the position of tautomerism depends on the prototropic properties of the solvent[165]; the percentages of azo form present in a number of different solvents for several substituted 4-phenylazo-1-naphthols are shown in Table 7[165].

The opposite effect to that in *para*-hydroxy compounds is observed in *ortho*-hydroxy compounds, and has been ascribed to steric effects causing reduced solvation of the hydrazone form[163]. However, solvent effects are smaller in the *ortho*-hydroxy systems, and the preference for the hydrazone form **106** which is observed is probably due to the presence of an intramolecular hydrogen bond[156, 166] as shown. This hydrogen-bonding effect is strong enough to make deuterium exchange of the OH hydrogen difficult, even in boiling D_2O[156, 167].

Reeves and Kaiser have studied a series of 4′-substituted 2- and 4-arylazo-1-naphtholsulphonates in a range of protic and aprotic polar solvents[168]. They found that the position of equilibrium between tautomers did not correlate with bulk solvent properties. For solvent-sensitive dyes, the hydrazone form dominates in those neat solvents which can form a three-dimensional structure, whereas the azo form dominates in those that cannot. In binary water/alcohol mixtures, increasing alcohol content increases the percentage of azo tautomer. Similar results were obtained in DMF/- and DMSO/water mixtures. The results were explained in terms of selective solvation of the hydrophobic dyes by the organic co-solvent[168].

For 4-phenylazo-1-naphthol derivatives it is found that, in general, electron-donating substituents in the benzene ring stabilize the azo form (**103**), while electron-withdrawing ones stabilize the hydrazone form (**104**)[156, 169–171]. The situation is not clear-cut, however, as can be seen from the results in Table 7[165]. Somewhat similar results were obtained for the 2-phenylazo-1-naphthol series, probably as a result of the fact that the hydrogen bond in structures like **106** is weakened by electron-withdrawing substituents, since such substituents will have the effect of reducing the electron density on nitrogen[156, 169–171].

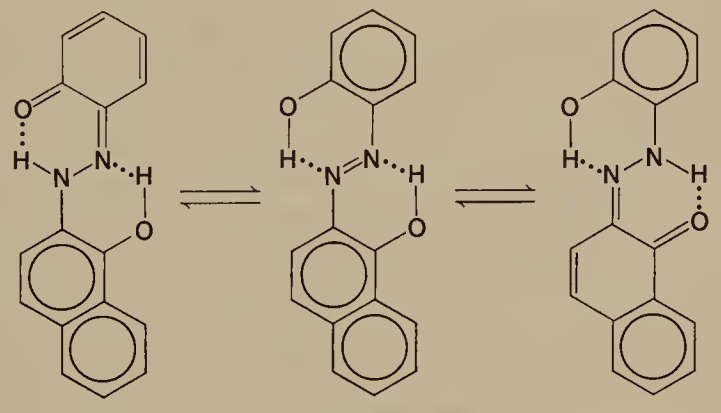
It was reported that in the solid state, adsorbed on filter paper, *p*-chloro and *o*-nitro substituents favour the azo form, **107**, while *m*-chloro and *o*-methyl favour the hydrazone form, **108**[172]. However, in direct contrast, diffuse reflectance spectra in sodium chloride showed that *p*-Cl and *o*-NO_2



(107) (108)

substituents favoured **108**, and *p*-NO_2 and *o*-OH favoured **107**[173]. Electronic and vibrational spectra indicate that crystalline azo compounds in the 1-arylazo-2-naphthol series exist as intermolecularly hydrogen-bonded hydrazone-like aggregates[174]. Dimerization of ionic arylazonaphthols in water also occurs[175]; the study of this aggregation is complicated by the concurrent azo-hydrazone tautomerism also taking place[176].

Nuclear magnetic resonance studies of 4-phenylazo-1-naphthol and 1-phenylazo-2-naphthol, substituted with a methoxy group in the *para* position of the phenyl ring, enabled Saeva[177] to evaluate the tautomerization equilibrium constants, K_{eq} = [hydrazone]/[azo]. For **103** ⇄ **104**, K_{eq} changes from 0·84 to 0·25 between −20°C and +20°C in acetone-d_6, while for **107** ⇄ **108**, K_{eq} changes from 1·54 to 0·95 between 20 and 50°C. The thermodynamic parameters at 20°C for the former system are $\Delta H^0 = -4{\cdot}5$ kcal/mole, $\Delta S^0 = -18{\cdot}1$ e.u., $\Delta G^0 = 807$ cal/mol; and for the latter, $\Delta H^0 = -3{\cdot}1$ kcal/mol, $\Delta S^0 = -9{\cdot}7$ e.u., $\Delta G^0 = -250$ cal/mol. The enthalpy term favours the hydrazone form in both systems; however the smaller ΔH^0 for **107** ⇄ **108** probably reflects the partial hydrogen-bonded stabilization of the azo tautomer relative to the hydrazone tautomer which is present in **107** but not in **103**[177]. The entropy term, however, favours the less polar azo form for both systems; the more negative value for **103** ⇄ **104** probably reflects the fact that the hydrazone form is more polar relative to

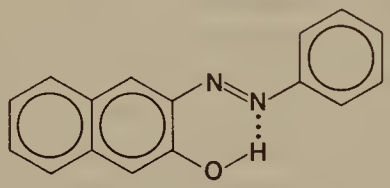


(109) (110) (111)

the azo form in the 4-phenylazo-1-naphthol system than in the 1-phenylazo-2-naphthol case. Thus the fact that the latter exists mainly as the hydrazone and the former as the azo form is due to the dominance of, respectively, the entropy term for **103** ⇄ **104** and the enthalpy term for **107** ⇄ **108** in the free-energy differences between the tautomers[177].

Hückel molecular orbital calculations have shown that the larger the ring bearing the oxygen atom, the more stable is the hydrazone form[178]. This form is also favoured by inter- and intramolecular hydrogen bonding, by electron-withdrawing substituents, and by hydrogen-bonded dimer formation. Calculations for diphenols such as **110** agree with experiment in predicting that each tautomeric form is almost equally probable; the ratios were **109**:**110**:**111** = 0·872:1·00:0·95 (expt.); = 0·905:1·00:0·945 (calc.)[179].

Compounds such as 2-phenylazo-3-naphthol and 8-phenylazo-1-naphthol exist mainly as the azo tautomers, **112** and **113**, possibly as



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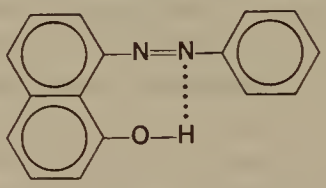
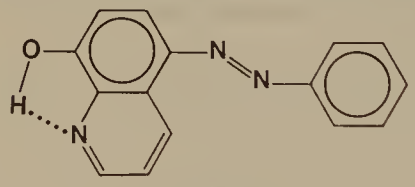


(113)

hydrogen-bonded species[156]. The predominance of the azo form is probably due to the fact that a C=O bond cannot be formed without destroying the aromaticity of both naphthalene rings. Other examples of intramolecular hydrogen bonds which stabilize the azo form are in compounds **114** and **115**[156]. The lower frequency and intensity of vibrations of the CO group of quinone-hydrazone tautomers suggest that zwitterionic structures such as **116** are important contributors[156].



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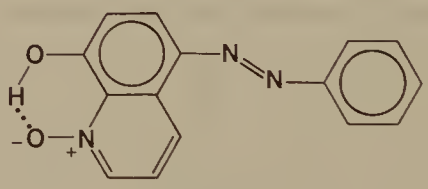

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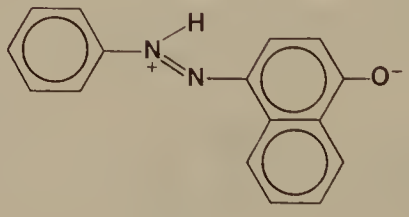

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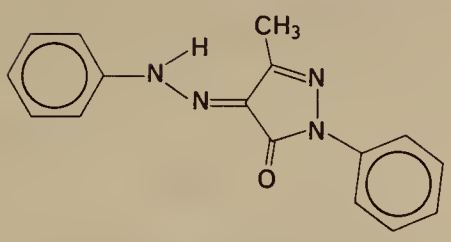

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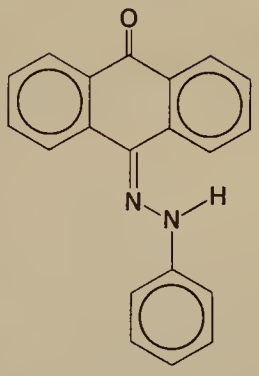
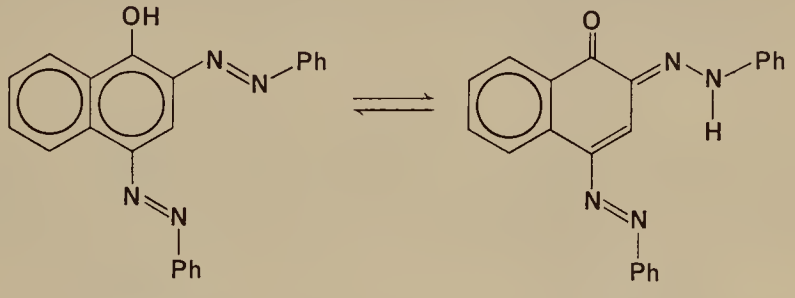


(118)

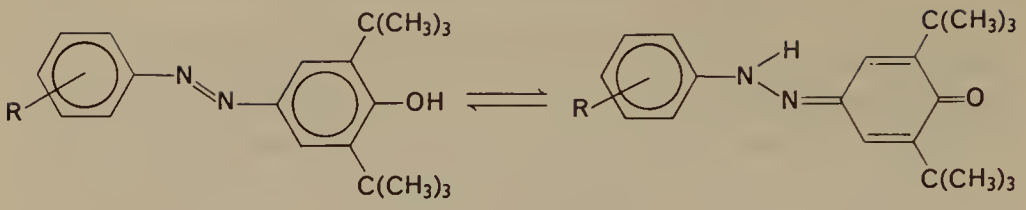
From n.m.r. spectroscopic studies of ^{15}N-substituted azo-compounds, Vecera and co-workers[180] find that 1-phenyl-3-methyl-4-phenylazo-5-pyrazolone exists in the tautomeric form **117** in chlorinated hydrocarbon solvents, in agreement with earlier work[181]; 2-phenylazoresorcinol exists in the azo form in DMF; 4-phenylazo-1-naphthol prefers the azo form (**103**) in DMF between 0 and –40°C; and the phenylhydrazone of 9,10-anthraquinone exists only as **118** in all the solvents and at all the temperatures studied[180]. The equilibrium constant for **119** ⇌ **120** was found to favour



(119) (120)

120 in methylene chloride, especially at low temperatures[180]. A similar, though less pronounced, situation prevailed for 1-phenylazo-2-naphthol[180].

Both *ortho*- and *para*-hydroxyazobenzene appear to exist practically entirely in the azo form[156]; the only evidence for possible small amounts of the hydrazone form appears to be the observation of some weak fluorescence[182]. However, the situation is complicated by the occurrence of *cis–trans* isomerism and aggregation[176]. Two cases in which the hydrazone is important are: (*i*) the detection by n.m.r. spectroscopy of azo-hydrazone tautomerism in complexes of Co(III) with different arylazophenols[183]; and (*ii*) the tautomerization of various 3,5-di-t-butyl-4-hydroxyazobenzenes, **121** ⇄ **122**[184], in accord with the known tendency of hindered phenols to

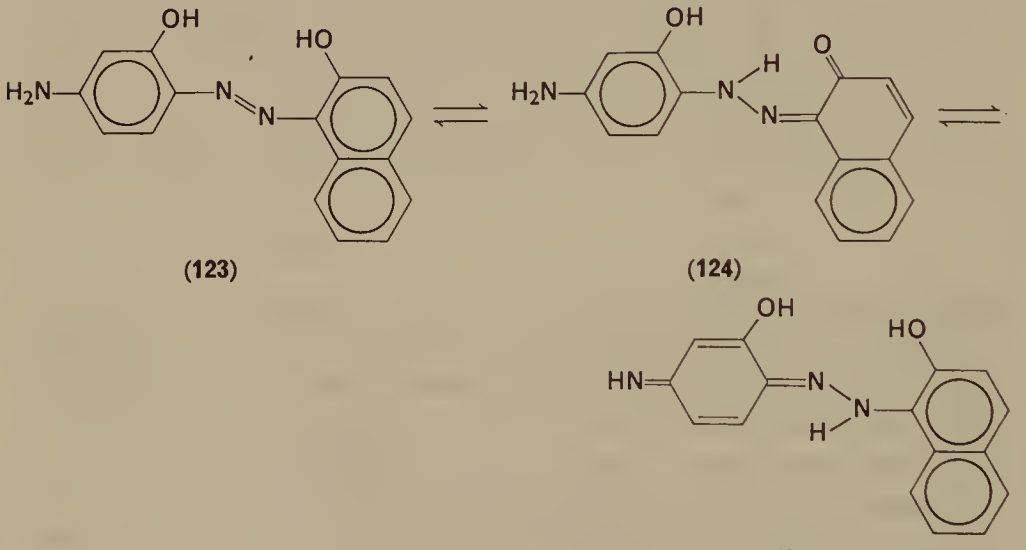


(121) (122)

form quinones[185]. Electron-withdrawing R substituents increase the percentage of **122**[186].

In contrast, the condensation products of the benzenediazonium ion with polycyclic phenols, e.g. with anthrols, exist almost entirely in the quinone–hydrazone form, of which **118** is an example[156, 180]. This shift from predominant azo to predominant hydrazone on passing from the benzene series to the naphthalene and the anthracene series was also found in a study of monolayers of azo compounds with long alkyl groups[187].

Potentially tautomeric *p*-aminoazobenzenes and related molecules appear to be either true azo compounds or to be strongly on the azo side of postulated tautomeric equilibria, regardless of solvent polarity, according to Skulski and collaborators[188]. The evidence regarding *o*-aminoazobenzenes is inconclusive, though it seems that derivatives of anthracene can tautomerize[156]. An interesting case of a system consisting of three tautomers is given by **123**, **124**, and **125**[189].



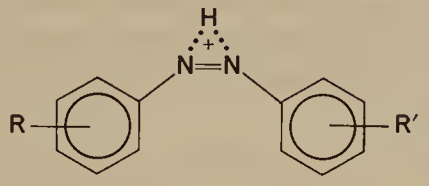
(123) (124)

(125)

C. *Tautomerism of Protonated Aromatic Azo Compounds*

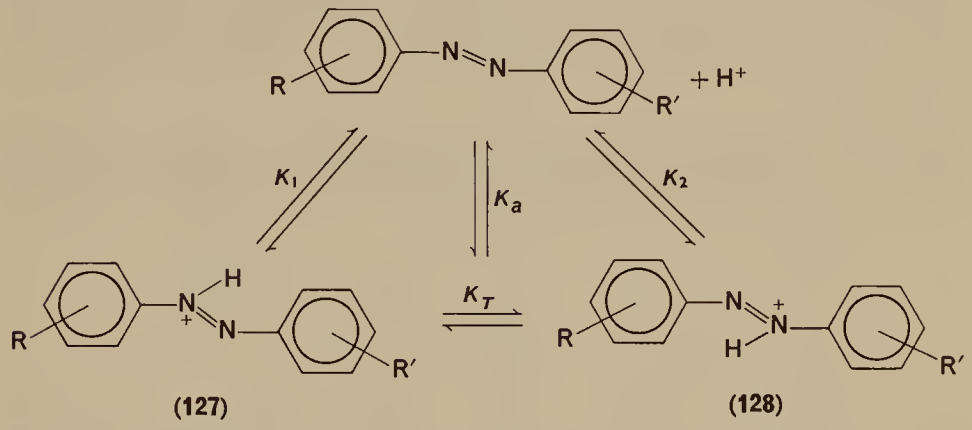
Azo compounds are protonated on the azo function in fairly strong acid solutions; the pK_{BH^+} values range between 0 and -7[190]. The structure of

the protonated species has been a subject of some controversy. Jaffé and co-workers[190, 191] preferred the structure **126**, with the proton attached to



(126)

both nitrogens of a *cis*-azobenzene, on the basis of the near-linear correlation between observed pK_{BH^+} values and the sum of substituent σ^+ values which was found for unsymmetrical azo compounds[190]. This structure has received some support[192]. However in other work it has been found that *trans*- and *cis*-azobenzene give rise to conjugate acids which differ both in absorption spectrum and base strength[193], and subsequent detailed investigations of the protonation behaviour, by Haselbach[194] and by Wepster and co-workers[195], have shown that the unsymmetrical structures



(127) **(128)**

127 ⇌ **128** are in fact much more probable for protonated azobenzenes. Jaffé's observations are explained by the close similarity in the two ρ values; one for protonation on the nitrogen adjacent to the substituent-containing ring, and the other for protonation on the other nitrogen[156, 195]. Unsymmetrical protonation is also consistent with other observations[195, 196].

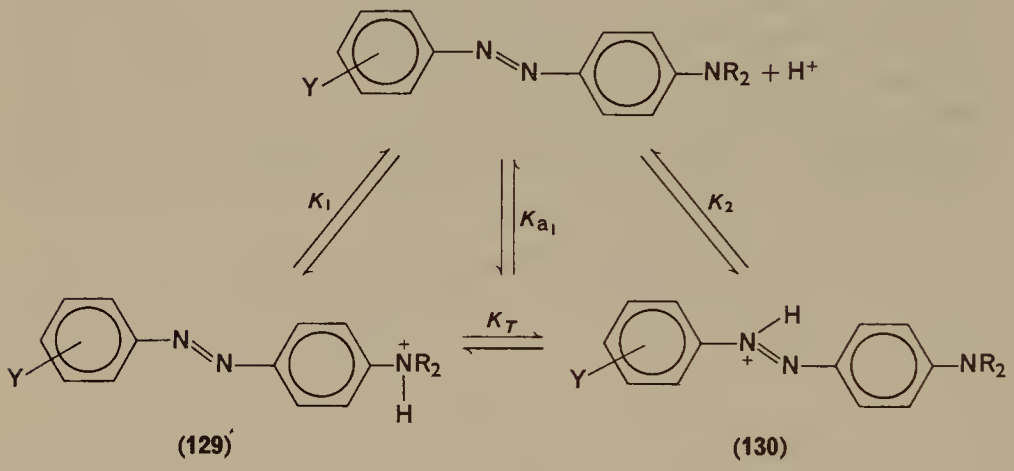
Four equilibrium constants are involved in these systems: the effective basicity constant $K_a = K_1 . K_2/K_1 + K_2$, and the tautomeric equilibrium constant for the two azonium ions, $K_T = K_2/K_1$. The relevant σ–ρ equations are given by equations 28 and 29[156]. It is known that the values of ρ_1 and

$$pK_1 = (pK_1)_0 - \rho_1 \sigma \tag{28}$$

$$pK_2 = (pK_2)_0 - \rho_2 \sigma \tag{29}$$

ρ_2 are 1·7 and 3·0, respectively[194], and, since $(pK_1)_0 = (pK_2)_0$, it can be estimated that with a substituent of $|\sigma| = 0{\cdot}5$ in the azobenzene molecule the concentration of one of the tautomeric forms will be less than 20%. If this σ-constant, or the difference between those of two substituents in the different rings, is unity, then one tautomer will be present in greater than 95% concentration[156].

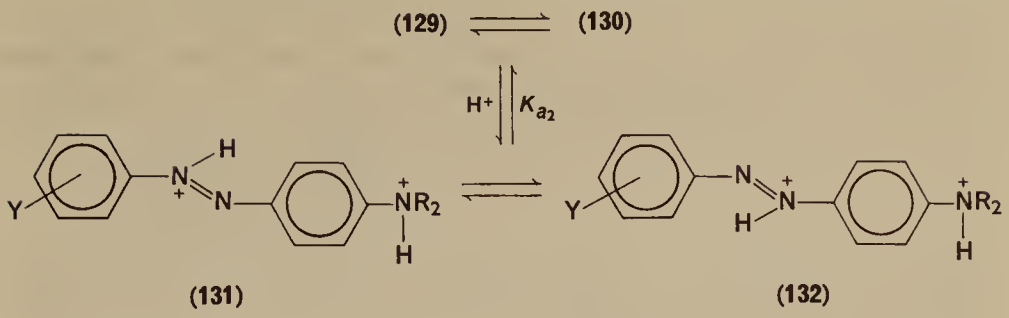
The situation for azo-compounds containing an amino substituent is even more complex. Such derivatives may be protonated either on the substituent or on the azo group, to give a tautomeric mixture, as shown in Scheme 5.



Scheme 5.

The u.v.-visible spectra of amino-azo compounds contain two peaks, one attributable to **129** (for instance by comparison with the spectra of the corresponding trimethylammonium derivatives[160] or *N*-oxides[196]) and one attributable to **130** (for instance by comparison with azoanisoles[197] and azothioanisoles[198]). It is probable that all *p*-amino azo compounds undergo these prototropic equilibria; early suggestions involving exclusive *azo*-protonation[199], and later ones involving exclusive *amino*-protonation[200,201], have been superceded[159,202a]. Protonation of the azo nitrogen adjacent to the amino substituent[202b] is held to be much less likely[156,159], both from the consideration of σ–ρ correlations[156] (see above) and by Hückel molecular orbital calculations[203].

In stronger acids, a further protonation equilibrium may occur:



In the general case there will be two diprotonated species (**131** ⇄ **132**) in the equilibrium mixture[156]. Values of pK_{a_1}, in 50% aqueous ethanol, lie between 1·8 and 2·5[197, 199b, 201, 204–206, 208]; and values of pK_{a_2} between −2·1 and −8·5 are reported, in aqueous H_2SO_4[197, 199b, 201] or in aqueous H_2SO_4 containing 20% ethanol[191c, 207].

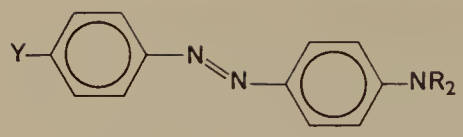
Much effort has been expended in endeavours to determine the position of the tautomeric equilibrium of the first conjugate acid, **129** ⇌ **130**, and the influence of substituents on it[191c, 204, 207–211]. Space considerations preclude a detailed discussion of experimental methods and results—see in particular refs. 156, 202a, and 208. Some typical results are given in Table 8

TABLE 8. Equilibrium constants[a] for some substituted *N*,*N*-dialkylaminoazobenzenes in 1M-hydrochloric acid[208]

Compound	pK_{a_1}	K_T	pK_1	pK_2
133	2·00	0·78	1·64	1·75
134	2·89	5·4	2·82	2·09
135	2·38	0·14	1·46	2·38
136	2·17	1·1	1·89	1·85
137	3·09	7·8	3·04	2·12
138	2·43	0·14	1·57	2·43
139	1·88	1·0	1·58	1·58
140	2·65	7·2	2·60	1·71
141	2·15	0·14	1·23	2·15

[a] Defined as in Scheme 5.

for the compounds **133–141**[208]. As can be seen, in many cases pK_1 and pK_2 are closely similar, leading to values of K_T between 0·1 and 10 in all cases. In other words both tautomers are normally present; the concen-



(133) Y = H, R = Me (136) Y = H, R = Et
(134) Y = Me, R = Me (137) Y = Me, R = Et
(135) Y = Cl, R = Me (138) Y = Cl, R = Et

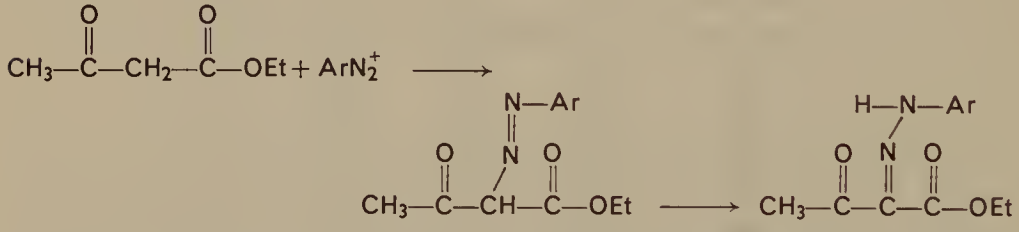
(139) Y = H, $R_2 = (CH_2)_4$
(140) Y = Me, $R_2 = (CH_2)_4$
(141) Y = Cl, $R_2 = (CH_2)_4$

tration of the lesser does not fall below 10% of the total, at least for the compounds of Table 8 in 1M-HCl.

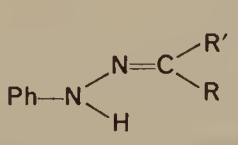
The position of equilibrium between **129** and **130** shifts as the acid concentration is changed. Thus measurements of K_T at one acidity[208,209] do not necessarily agree with measurements for the same compounds at a different acidity[191c]. This is because the activity coefficients for the different chemical species **129** and **130** vary differently as the medium is changed[156]. Bershtein and Ginzburg have investigated this phenomenon[207,211,212] and have found that the value of K_T is a linear function of the H_0 value of the solution. Linear correlations of K_T at fixed acidity with various Hammett substituent constants were also found[156].

D. Tautomerism of Aliphatic Azo Compounds

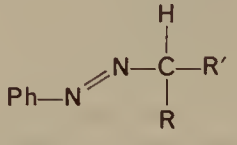
Aliphatic azo compounds are also known to exist in tautomeric forms. One of the first cases to be observed arises in the reaction between active hydrogen compounds and diazonium ion, the so-called Japp-Klingemann reaction[213]:



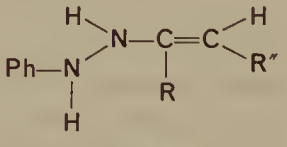
Phenylhydrazones have been the subject of some study, following the pioneering observations by Freer[214]. Three possible tautomers can be visualized: the hydrazone (**142**), the azo (**143**), and the ene-hydrazine (**144**)



(142)



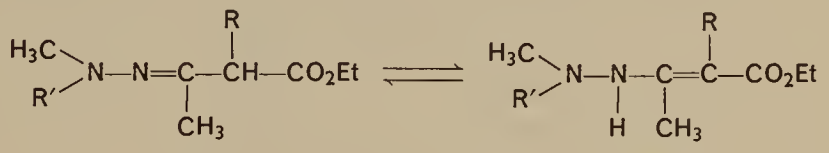
(143)



(144)

forms. It was thought[215] that **142** was the only stable form until Grammaticakis[216] concluded from spectral studies that small quantities of the azo tautomer **143** were also present. Polarographic studies led Arbuzov and Kitayev[217] to the conclusions that: (*a*) phenylhydrazones of aliphatic ketones existed as the ene-hydrazines (like **144**) in the solid state and in freshly prepared solutions; (*b*) aldehyde and aromatic ketone hydrazones were in the form **142**; and (*c*) reaction in solution led to the most stable tautomer in the sequence **144** → **142** → **143**[217]. A series of i.r., u.v.-visible and n.m.r. studies led O'Connor[218] to conclude, on the other hand, that: (*a*) freshly prepared phenylhydrazones of aliphatic ketones and aldehydes exist as the hydrazones, **142**; (*b*) these phenylhydrazones tautomerize rapidly to benzeneazoalkanes, **143**; and (*c*) no detectable amount of the ene-hydrazine tautomer, **144**, was present in neutral non-polar organic solvents, although the possibility of its presence in polar solutions could not be ruled out[218]. O'Connor's conclusions regarding the tautomeric change **142** → **143** have been shown to be unfounded, however, and it appears that the process observed was actually an autoxidation[219]. Bellamy and Guthrie[220] found, in fact, that phenylazoalkanes (**143**) could be converted to phenylhydrazones (**142**) under a variety of conditions, and suggested that the hydrazone is the thermodynamically stable form[220]. Tautomerism of this type was also observed by Corley and Gibian[221] during the thermal decomposition of α-phenylazoethane and was thought to be acid-catalysed[221].

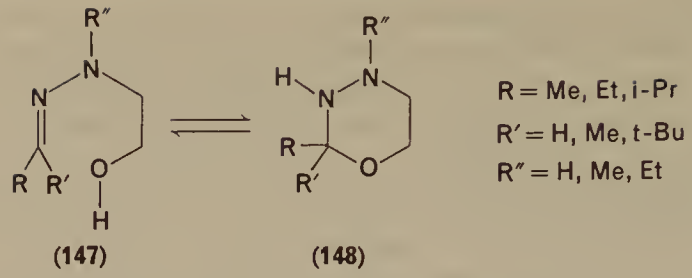
Favorskaya, Yakimovich and collaborators[222–224] have found that the reaction products of ethyl cyclopentanone-2-carboxylate and some α-acylbutyrolactones with unsymmetrically disubstituted hydrazines exist as tautomeric mixtures, with the ene-hydrazine form predominating over the hydrazone form[222]. Reaction with α-alkylacetoacetic esters also leads to a tautomeric mixture, e.g. **145** ⇌ **146**[223]. Here **145** predominates; the



(145) **(146)**

equilibrium position is not highly dependent on the chain length of the substituent R[223]. The reaction products of β-keto esters with 1,1-dimethylhydrazine are also hydrazone/ene-hydrazine tautomeric mixtures[224].

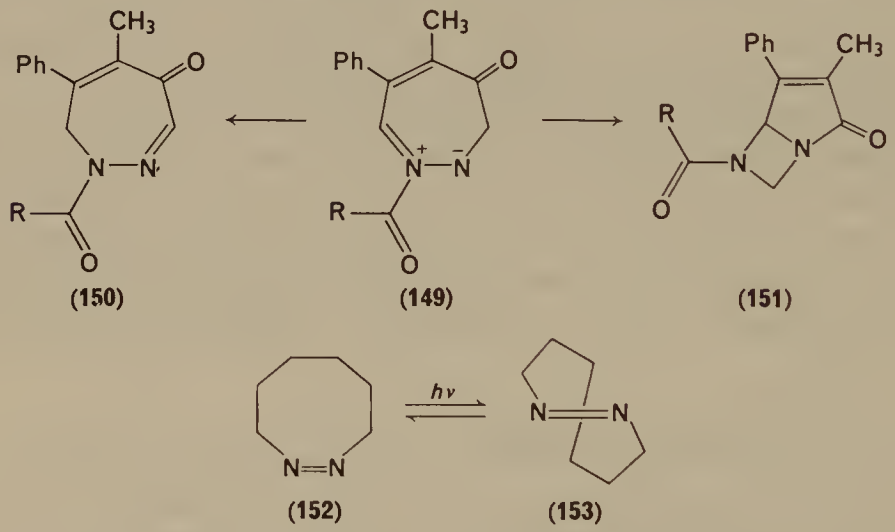
Potekhin[225] has studied the ring-chain tautomerization process **147** ⇌ **148**. The tetrahydro-1,3,4-oxadiazine **148** was formed in most cases; the equilibrium concentration of the hydrazone form increased with increasing



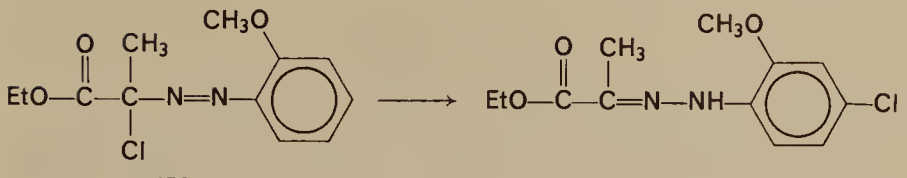
number and size of 2-substituents and decreasing size of 4-substituents[225]. As in the previous case, however, an azo tautomer does not appear to be present.

E. Some Further Azo Rearrangements

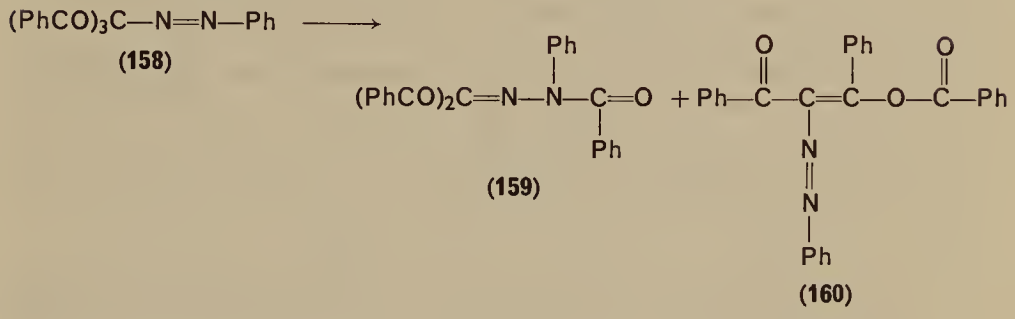
True azo rearrangements, that is, rearrangements involving the azo linkage itself, are uncommon. Thus, the many interesting skeletal rearrangements of the type studied by Moore and co-workers[226,227], for instance **149** → **150** + **151**[227], and the *cis–trans* interconversions, e.g. **152** → **153**[228], cannot be regarded as true azo rearrangements.



Baldwin, Brown and Höfle[229] have found that allylic diazenes, e.g. **154**, undergo a sigmatropic rearrangement to azo compounds, e.g. **155**. This is



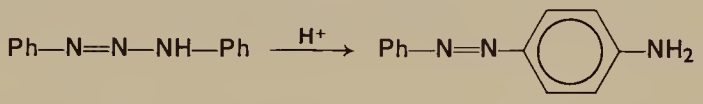
(156) (157)



(158) (159) (160)

a most interesting reaction and is worthy of further investigation. Moon[230] has found that **156** rearranges to **157** on heating in acetic acid; the mechanism is unknown. Curtin and Poutsma report that refluxing **158** in dioxane for 30 min leads to **159** and **160**[231].

The rearrangement of diazoaminoaromatics to aminoazobenzenes, e.g.



(161) (162)

161 → **162**, probably involves dissociation of **161** into aniline and diazonium ion, followed by diazo coupling. This type of rearrangement has been discussed by Banthorpe in previous volumes of this series[232].

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CHAPTER 19

Radical reactions of azo, hydrazo and azoxy compounds

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I. INTRODUCTION

This chapter will deal with radical reactions of azo, hydrazo and azoxy compounds. Included in it will be processes which either involve the formation of radicals as presumed intermediates or reactions of azo, hydrazo and azoxy compounds with radicals. Save for the recent upsurge

of studies of the decomposition of azoalkanes—and of medium-size cyclic azo compounds in particular—few systematic investigations of radical reactions have been reported. Compounds which incorporate these functional groups as part of aromatic heterocycles will not be included. Many of the reactions described herein have not been *established* as involving radical intermediates. An attempt has been made to cover the literature up to December 1971. Mention of radical reactions of azo, hydrazo and azoxy compounds are scattered in reviews and monographs dealing with nitrogen chemistry. Although earlier work has been included, the present review will deal in large part with recent studies. Photolytic reactions will not be in integral part of this summary and are covered in another chapter of this Volume.

II. RADICAL REACTIONS OF AZO COMPOUNDS

A. The Thermal Decomposition of Azoalkanes

The problem whether an azo compound decomposes into three fragments in one step (equation 1) or in two discrete steps (equation 2) was first examined by Ramsperger[1]. He compared the decomposition rates for

$$R{-}N{=}N{-}R' \longrightarrow R^{\cdot} + N_2 + {}^{\cdot}R' \qquad (1)$$

$$R{-}N{=}N{-}R' \longrightarrow R^{\cdot} + {}^{\cdot}N{=}N{-}R' \longrightarrow N_2 + {}^{\cdot}R' \qquad (2)$$

(1) R,R′ = Me; **(2)** R,R′ = i-Pr; **(3)** R = Me, R′ = i-Pr

dimethyl (**1**), diisopropyl (**2**) and methyl isopropyl (**3**) diimides and chose the former interpretation:

'If the decomposition of these azo compounds occurs by the breaking of a single bond, then we may expect the heat of activation of **3** to be very nearly that of **2** for the reaction will occur at the weaker isopropyl bond.... If, however, the reaction occurs by the simultaneous rupture of both bonds, then we may expect an intermediate heat of activation, and this is the experimental result.'

The activation energies of gas-phase decomposition were found[2] to be 51·2 and 40·9 kcal mol^{-1} for **1** and **2**, respectively, and the value 47·5 kcal mol^{-1} found for **3** was very close to the arithmetic mean of above values.

This conclusion was however, rather controversial. Subsequent investigations[3] have revealed that the stoichiometry of the reaction is not in accord with equation (3) and the products are complex.

$$CH_3N{=}NCH_3 \longrightarrow C_2H_6 + N_2 \qquad (3)$$

The formation of a large quantity of methane indicates concomitant induced chain decomposition[4]. In a thermolysis inhibited from induced reactions by added nitrogen monoxide, the activation energy of the true unimolecular decomposition of **1** was found to be 55·5 kcal mol^{-1} [5]. The magnitude of the value of E_a for **2** has also been questioned[6]. A Polanyi plot[7] for the activation energy for thermal decompositions of dimethyl (**1**)[5], diethyl (**4**)[8], di-*t*-butyl (**5**)[6a], and diallyl (**6**)[9] diimides showed a plain linear relationship represented as:

$$E_a = 0{\cdot}996D(R{-}H) - 48{\cdot}4 \text{ kcal mol}^{-1} \qquad (4)$$

R—N=N—R (**4**) R = Et; (**5**) R = *t*-Bu; (**6**) $R = CH_2{=}CHCH_2$

leaving the value for diisopropyl diimide **2** well below the line[9]. The activation energy for **2** that would be expected from equation (4) is 46 ± 1 kcal mol^{-1}, a value which if observed would have led to the completely opposite conclusion.

On the other hand, a reinvestigation of gas-phase pyrolysis of **2** has shown that with propylene as an inhibitor there was no detectable induced chain decomposition. Ramsperger's value of activation energy was confirmed within 0·15 kcal mol^{-1} ($E_a = 40{\cdot}75$ kcal mol^{-1})[10].

While the large Arrhenius factors ($\log A > 15$) observed have been regarded as support for the three fragments decomposition[11], a compilation of gas-phase pyrolysis rate data was interpreted in favour of one-bond decomposition mechanism[12]. While this type of reactivity comparison has been used[13] as a rough measure for speculating on the decomposition mode, its inadequacy to make a definitive choice between the two mechanisms has been emphasized[14].

The gas-phase pyrolysis of the simplest diimides which produce resonance stabilized radicals was investigated by Crawford and co-workers[6b,9,15].

$CH_2{=}CHCH_2N{=}N{-}R$ (**7**)

(**a**) R = Me
(**b**) R = *n*-Pr
(**c**) R = *t*-Bu

If the one-step mechanism is operative, the decomposition rate of each 3-alkylazopropene may be expected to be nearly a mean of those for the corresponding dialkyl diimide[3b,5,6a,10] and **6**. For the two-step mechanism, the rate would be expected to be one-half (statistical factor) of that for **6**. These predicted values with appropriate allowance were compared with the observed decomposition rates for **7a–c** and were all found to be within the expected range for a two-step mechanism; the difference between their relative rates were attributed to steric effects.

	E_a (kcal mol^{-1})	log A	ΔS^* (eu)	Rates			
				Obs. × 10^6 (122.3°C)	Rel. rate	Calc × 10^6 (one-step)	(two-step)
7a	35·5	14·36	4.6	4·90	0·138	0·0001 ~ 0.069	1·8 ~ 180
7b	35·6	14·80	6·6	12·0	0·339	0·0021 ~ 0·29	1·8 ~ 180
7c	29·8	12·72	−2·8	174	4·92	0.14 ~ 14	1·8 ~ 180
6	36·1	15·54	9·8		1·00		

A generalized Polanyi equation, which is applicable to the unsymmetrical diimides R—N=N—R′, may be given as

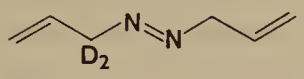
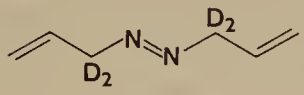
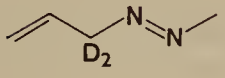
$$E_a = \alpha D(R - H) + \alpha' D(R' - H) - C \qquad (5)$$

in which α and α' may be taken as a measure for the degree of dissociation of R—N and R′—N bonds in the transition state. If $\alpha + \alpha' = 1{\cdot}0$ and $C = 48{\cdot}4$ were assumed from equation (4), then the allyl diimides **6–7c** fit only if $\alpha = 1{\cdot}0$–$0{\cdot}9$ and $\alpha' = 0$–$0{\cdot}1$, values which imply an insignificant stretching of the alkyl-N bond associated with a fully stretched allyl-N bond in the transition state. Examination of the thermochemistry of **7b** also supports the view for the transition state wherein the allyl-N bond is almost completely ruptured. The calculated ΔH° value (37 kcal mol^{-1}) for the one-bond dissociation reaction from

$$CH_3CH_2CH_2N{=}NCH_2CH{=}CH_2 \longrightarrow C_3H_7N{=}N^{\cdot} + CH_2{=}CHCH_2^{\cdot}$$

group additivity value[12] was very close to the ΔH^* found for **7b** (36.3 kcal mol^{-1}).

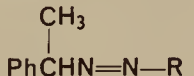
Further evidence for the two-step mechanism was furnished by an examination of secondary deuterium isotope effects. The $\Delta\Delta G^*$ values obtained by assuming a two-step mechanism were found to be more consistent within themselves and with those generally found ($\Delta\Delta G^*$ 80–120 kcal mol^{-1})[16].

		k_H/k_D	$\Delta\Delta G^*$/D (cal mol^{-1})	
			Two-step	One-step
	**6**-d_2	1·14 (162 °C)	121	56
	**6**-d_4	1·26 (162 °C)	99	50
	**7a**-d_2	1·28 (126 °C)	98	98

A vast amount of data has been accumulated from studies of the thermolysis in solution, mainly for the decomposition of benzyl-type diimides. First, the effect of a substituent on the kinetics of the decomposition was utilized in the mid-50's by Cohen[17] and Overberger[18] and their groups to infer the mechanism. They observed an activation energy decrease about 4 kcal mol^{-1} each time a phenyl group replaced a methyl group, or 6–7 kcal mol^{-1} each time a phenyl group replaced a hydrogen on the α-carbons of diimides. The effect was found to be additive for the replacements on both sides of the diimide linkage, thus giving a strong support for the synchronized two-bond rupture.

Somewhat later, Seltzer described kinetic isotope effect experiments which provided a decisive clue in the first of a series of papers[19].

Analysis of α-deuterium kinetic isotope effects on the pyrolyses of α-phenylethyl diimides **8**, **9**, and **10** revealed an interesting shift of the



(**8**) R = —CHPh(CH$_3$)

(**9**) R = —CH(CH$_3$)$_2$

(**10**) R = —CH$_3$

decomposition mode from a completely synchronized two-bond fission in **8** to a decidedly stepwise decomposition in **10**, **9** falling somewhere in between.

The observed k_H/k_D values, 1·13–1·18/D for **8**-d_2, **9**-α-d, and **10**-α-d, fit the average secondary deuterium isotope effect, 1·12 at 105°C, for various ionic unimolecular bond fission, the observed effect for **8** being consistent with a synchronous two-bond fission mechanism. In the decomposition of **10**,

		k_H/k_D	T(°C)	reference
PhCDN=NCDPh (Me, Me)	**8**-d_2	1·18	105	19a
PhCDN=NCHMe$_2$ (Me)	**9**-α-d	1·14$_8$	143	19b
PhCHN=NCDMe$_2$ (Me)	**9**-α'-d	1·03$_6$	143	19b
PhCDN=NCH$_3$ (Me)	**10**-α-d	1·13	161	19c
PhCHN=NCD$_3$ (Me)	**10**-α'-d_3	0·97	161	19c
PhCHN=N^{13}CH$_3$ (Me)	**10**-^{13}C	1·0068*	161	19c

*k_{12C}/k_{13C}

the observed effects indicate that the CH_3—N bond is not stretched in the transition state, rather somewhat tightened possibly because of a three electron bond resonance[14] in the resultant methylazo radical.

The interpretation of the observed isotope effects for **9** is not straightforward. Assuming a stepwise bond breaking, the observed isotope effect, k_H/k_D 1·04, for **9**-α'-d is too large to be correlated with any hyperconjugative stabilization of a transient isopropylazo radical[20].

$$\text{R—N=N—R}' \xrightarrow{k_1} \text{R—N=N}^{\cdot} + {}^{\cdot}\text{R}'$$

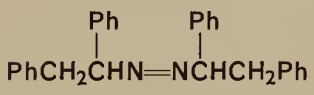
$$\text{R—N=N}^{\cdot} \xrightarrow{k_2} \text{R}^{\cdot} + \text{N}_2 \qquad k_1 < k_2$$

Furthermore, according to a detailed kinetic analysis, the above sequential first order reaction should show a considerable induction period which is much longer than the very short observed one. The only possibility left for consideration was a transition state wherein two C—N bonds are stretched *simultaneously but to unequal degrees*. The shift of the mechanism in **8**–**10** was attributed to the different stability of the alkyl radicals R from the diimides

Me
|
PhCH—N=N—R.

Exact force field calculations were performed to test the validity of the above interpretation[19d]. All kinetic isotope effects including that for ^{15}N which were measured[19d] for **8–10** at its natural abundance, were excellently reproduced by choosing an appropriate set of perturbed force constants in each transition state. The consistent setup of the transition states featured, *inter alia*, benzylic C—N stretching force constant decreased by 98% associated with isopropyl C—N stretching force constant decreased by 20% in the transition state of **9**, and benzylic C—N stretching force constant decreased by 98% associated with increased methyl C—N stretching force constant increased by 13% in the transition state of **10**.

The secondary α-deuterium isotope effect was examined for the

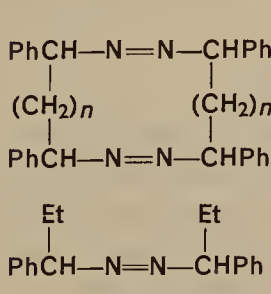


(11)

	k_H/k_D (106·5°C)	E_a (kcal mol^{-1})	ΔS^* (eu)
meso	1·224	33·1	7·6
dl	1·202	33·2	8·2

decomposition of two diastereomers of **11**-α,α′-d_2[19e]. The activation parameters for both diastereomers are very close to those for **8** (E_a 32·6 kcal mol^{-1}, ΔS^* 7·0 eu) and consistent with a synchronous two-bond fission mechanism. The somewhat smaller isotope effects compared to **8** were rationalized in terms of either a more reactant-like transition state caused by steric effects[21] or participation of a neighbouring phenyl group.

In the cyclic bisdiimides **12–14**, the decomposition at one azo site was shown to be independent of the other. Thus, the observed activation energies[22] and α-deuterium isotope effect[23] were found to be consistent with one —N=N— synchronous rupture in the transition state. Decomposition of a mixture of **13** and **13**-α-d_4 gave no appreciable amount of cross-over product. The elimination of the second nitrogen molecule,



	E_a (kcal mol^{-1})	k_H/k_D*
(12) $n = 6$	34·8	
(13) $n = 8$	34·4	1·18
(14) $n = 10$	33·7	
	32·2	

*Observed at 113 °C for α-d_4 derivative

therefore, may be considered to follow only after the recyclization of the biradical initially formed.

Another important guide as to whether a radical initiator decomposes by a one-bond or a two-bond mechanism was introduced by Pryor and Smith[24]. In azo decomposition in solution, a simplified scheme for the two modes of decomposition may be expressed as shown in equations (6)

$$\text{R—N=N—R}' \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [\text{R—N=N}\cdot\ \cdot\text{R}']\text{cage} \xrightarrow{k_D} \text{'free' radicals} \qquad (6)$$

$$\text{R—N=N—R}' \xrightarrow{k_1} [\text{R}\cdot\ \text{N}_2\ \cdot\text{R}']\text{cage} \xrightarrow{k_D} \text{'free' radicals} \qquad (7)$$

and (7). The observed rate constant for equation (6) is given as

$$k_{obs} = k_1 k_D/(k_{-1} + k_D) \qquad (8)$$

The temperature dependence of the rate constant for the diffusion process k_D, may be written in Arrhenius expression

$$k_D = A_D \exp(-E_D/RT) \qquad (9)$$

If one assumes that the energy barrier for diffusion E_D, is linearly correlated to the energy barrier E_V, for the self-diffusive flow of the solvent molecule, $E_D = \alpha E_V$, then the rate constant for the diffusion process as a function of the solvent viscosity will be given by equation (10)

$$k_D = A_D(A_V/\eta)^\alpha \qquad (10)$$

where A_V represents the pre-exponential factor in the temperature dependence equation for solvent viscosity, equation (11)[25].

$$\eta = A_V \exp(-E_V/RT) \qquad (11)$$

Combination of equation (8) with equation (10) gives an equation relating the observed rate constant for one-bond decomposition (equation 6) and the solvent viscosity.

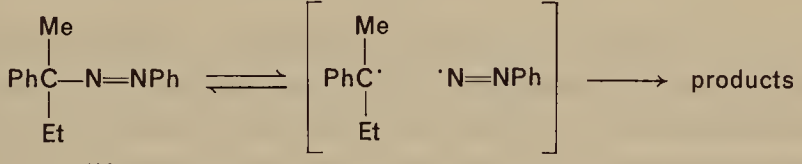
$$1/k_{obs} = 1/k_1 + (k_{-1}/k_1 A_D)(\eta/A_V)^\alpha \qquad (12)$$

This equation predicts a linear relationship between $1/k_{obs}$ and $(\eta/A_V)^\alpha$.

For the synchronous two-bond decomposition (equation 7), k_{-1} is expected to be near zero since it is unrealistic to expect recombination of two radicals to a nitrogen molecule. Therefore, the observed decomposition rate is identical to k_1 and should not be dependent on the solvent viscosity.

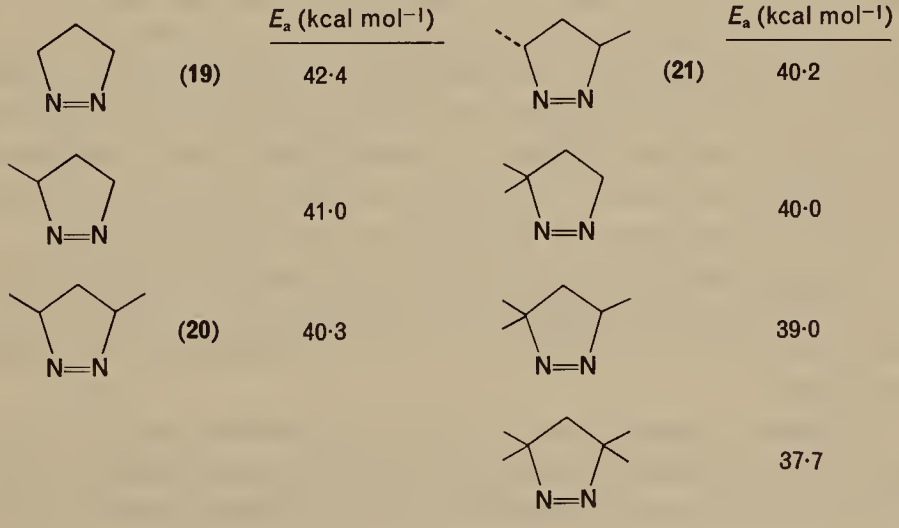
The prediction was tested for the decomposition of azocumene **15**, phenylazotriphenylmethane (PAT) **16**, and *p*-nitrophenylazotriphenylmethane (NAT) **17** along with some non-azo initiators. Decomposition rates of PAT and NAT in *n*-alkanes ranging from C_5 to C_{18} showed a regular dependence on the solvent viscosity clearly indicating one-bond fission, whereas that of **15** remained independent of the solvent viscosity indicating two-bond fission. Results consistent to relevant data in the literature were also obtained for non-azo initiators. The effect was found to be intrinsic to the viscosity based on solvent molecules surrounding the radical pair but not to the viscosity based on bulk measurements. Thus, viscosity enhancement by dissolution of polystyrene into a solvent did not reduce the decomposition rate of NAT.

An initial one-bond scission was also demonstrated in the solution photolysis of phenylazo-2-phenyl-2-butane **18**. The quantum yield for the disappearance of starting azo compound was clearly correlated to the solvent viscosity and when an optically active **18** was used, a substantial degree of racemization was observed[26].



(18)

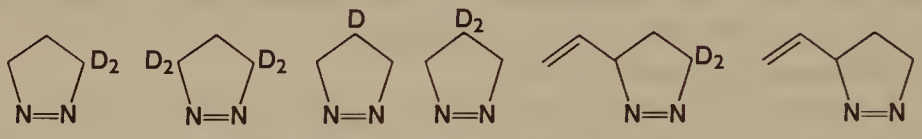
Crawford and co-workers, through a series of investigations, suggested a synchronous two-bond fission for the vapour-phase thermolysis of 1-pyrazolines to cyclopropanes and propenes[27,29].



It was shown that the introduction of a methyl group into the 3- and 5-positions of 1-pyrazoline **19** results in a decrease of activation energy additively and regularly by 0·7–1·4 kcal mol^{-1} per methyl[27].

An interesting inversion of geometry observed in cyclopropanes derived from **20** and **21** was explained in terms of π_u-cyclopropane intermediate[28] which cyclizes in a preferential conrotatory manner (*vide infra*).

Kinetic isotope effects on the pyrolysis of deuterated 1-pyrazolines were also found to be consistent with a synchronized two-bond fission



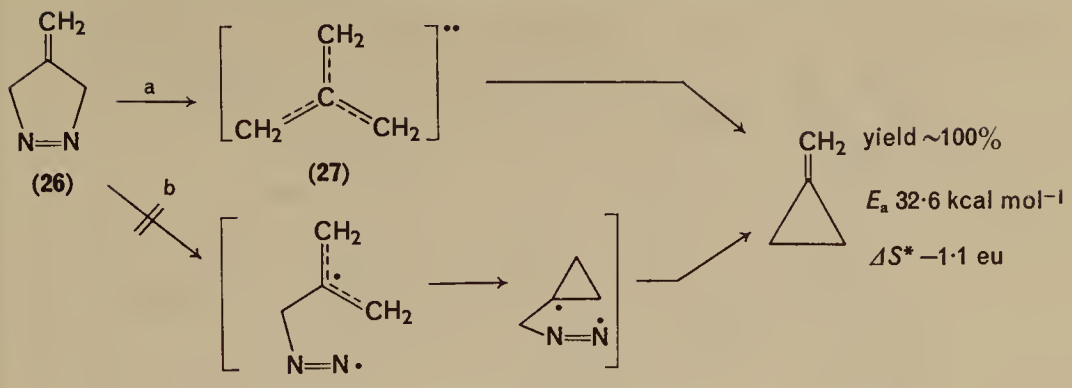
			(22)	(23)	(24)	(25)
k_H/k_D	1·26	1·55	1·06	1·14	1·21	
						E_a 32·2 kcal mol^{-1}
T(°C)	105	105	105	105	134·3	

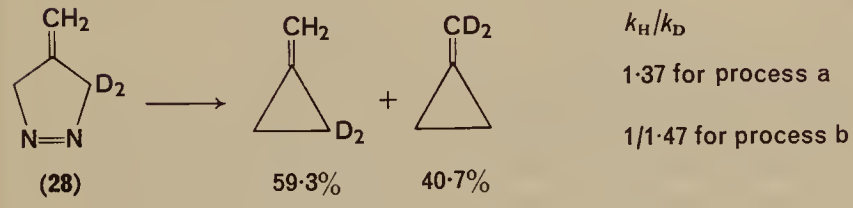
mechanism[29]. Higher than normal[30] β-deuterium effects in **22** and **23** were attributed to the importance of hyperconjugation in a trimethylene intermediate biradical[28]. A 10 kcal mol^{-1} decrease of E_a by the introduction of a vinyl group at one α-position coupled with deuterium effect at the other α-position suggested that the simultaneous two-bond fission is also operative in the decomposition of 3-vinyl-1-pyrazoline **25**[29b].

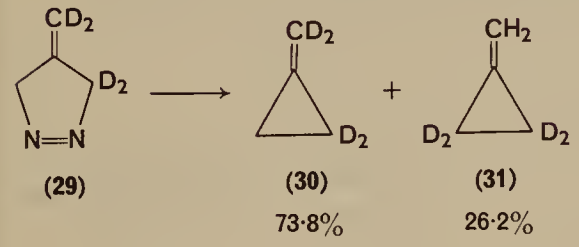
An important hydrocarbon species, trimethylenemethane **27**, was suggested to be formed *via* a simultaneous two-bond fission of methylene pyrazoline **26**[31]. If the observed distribution of the products from the dideuterio-compound **28** were to be governed by isotope effect on a C—N bond fission in process b, an unreasonable value 1/1·47 has to be taken for k_H/k_D from the product ratio. Furthermore, through process b, the same ratio of products **30** and **31** should result from tetradeuterio-compound **29**. The calculated isotope effects for **28** and **29** assuming process a, on the other hand, were found to be consistent with each other.

A direct observation of trimethylenemethane during a low temperature photolysis of **26** was accomplished by e.s.r. spectroscopy. The e.s.r. signal of the triplet species was reported to persist for a month at liquid nitrogen temperature[32].

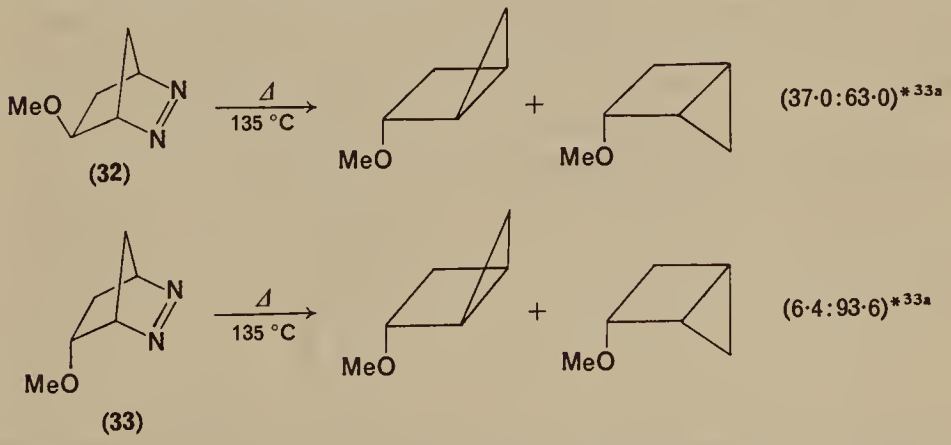
A puzzling stereochemical inversion somewhat related to that observed in the decomposition of 3,5-dimethyl-1-pyrazolines **20** and **21**[27] was found in the gas-phase pyrolysis of the diazanorbornene systems



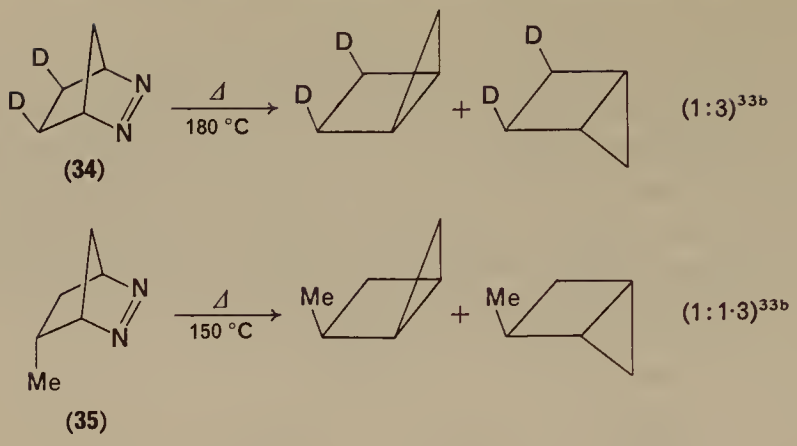




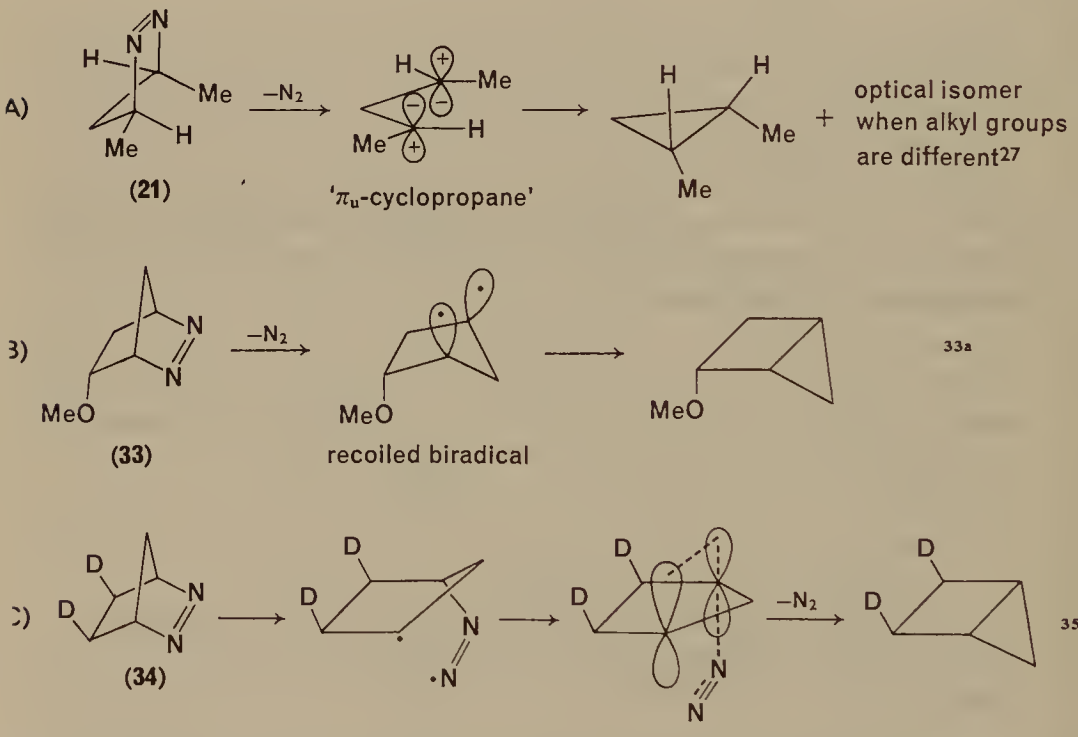
32–35[33]. This inverse stereospecificity is still held in vapour or solution photolysis[33a,34], whereas solid photolysis of **32–35** gave cyclopropanes of retained geometry preferentially[33].



* The equilibrium ratio of the thermal isomerization of the above products at the decomposition temperature was 12·9:87·1.

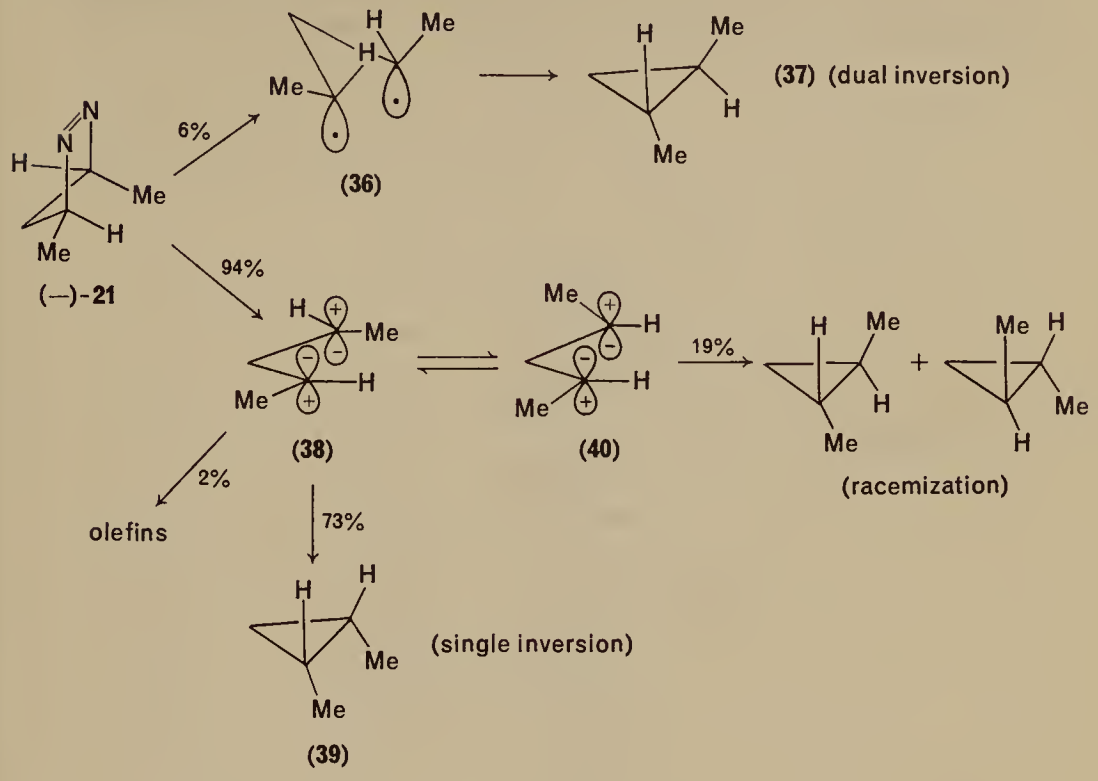


None of the following proposed mechanisms (A–C) for dimethylpyrazolines and diazanorbornenes conforms to both experimental facts at the same time since, while an inversion at one carbon end associated with a retention at the other end was observed for 1-pyrazolines, inversions at both carbon ends were observed in the bicyclic compounds.



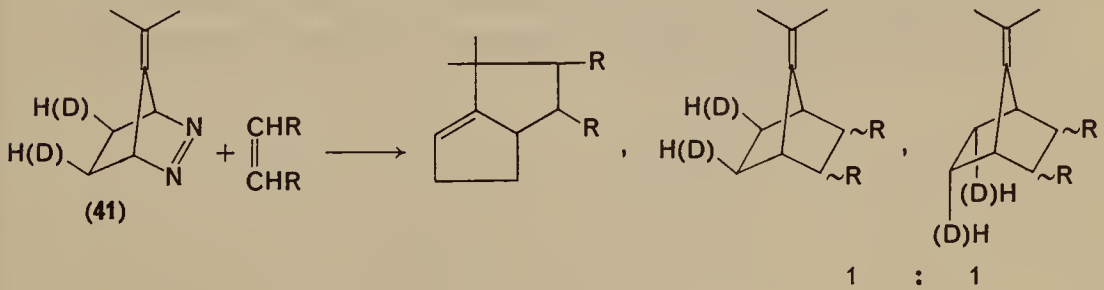
Pyrolysis of an optically pure **21** gave 73% of *cis*-dimethylcyclopropane **39**, a single inversion product, and 25% of *trans* isomer **37** of which dually inverted optical isomer accounted for a 24% excess (6% of total products)[36].

On the basis of these results, Mishra and Crawford[27,29,36] depicted the following scheme.



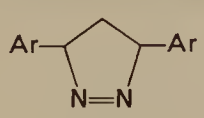
The possibility that the intermediate π-cyclopropane **38** is formed *via* the pyramidal biradical **36** and also that the dual inversion path involves a two-step mechanism as suggested by Roth and Martin were left open[35]. Although the conformational equilibrium, **38** ⇄ **40**, was not mentioned explicitly, a similar equilibrium in 1,4-biradicals generated from two isomers of dimethyldiazabicyclo[2.2.2]octane has been reported to be almost complete before collapsing into the products[37].

When a bicyclic diimide **41** was pyrolysed slowly in the presence of an appropriate olefin, cycloadducts of the intermediate 1,3-diradical were



obtained[38]. The trapped species was shown to be a practically planar cyclic biradical with no stereospecificity in the adducts.

In connection with the above investigations, thermal and photolytic decompositions of 3,5-diaryl-1-pyrazolines in solution with different

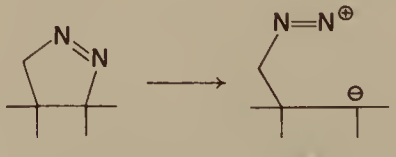


Ar=C_6H_5—[39c]	*trans*	*Δ* (in PhH)	89	11
		hν (in MeOH)	88	12
Ar=*p*-$MeOC_6H_4$—[39b]	*trans*	*Δ* (in PhMe)	93·3	6·7
		hν (in THF)	99·3	0·7
	cis	*Δ* (in PhMe)	57·4	43·0
		hν (in THF)	42·8	57·2

stereochemical consequences have been reported[39]. In contrast to the preponderant retention of geometry in cyclopropanes derived from *trans*-isomers, the *cis*-isomer lost its geometry almost completely.

Some alteration in the above mechanism for simple pyrazolines might be due because of perturbation by phenyl groups on the intermediate biradical.

Cyclopropane formation from 1- or 2-pyrazolines prepared by the action of diazomethane derivatives on olefins activated by electron-withdrawing substituent(s) has long been known[40]. Although the pyrolysis to cyclopropanes had been reported[41] to be stereospecific with retention of the geometry of initial or intermediate 1-pyrazolines, subsequent investigations[42]



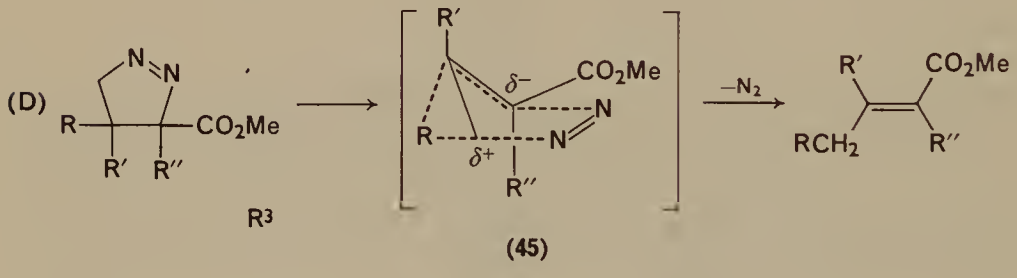
(42)

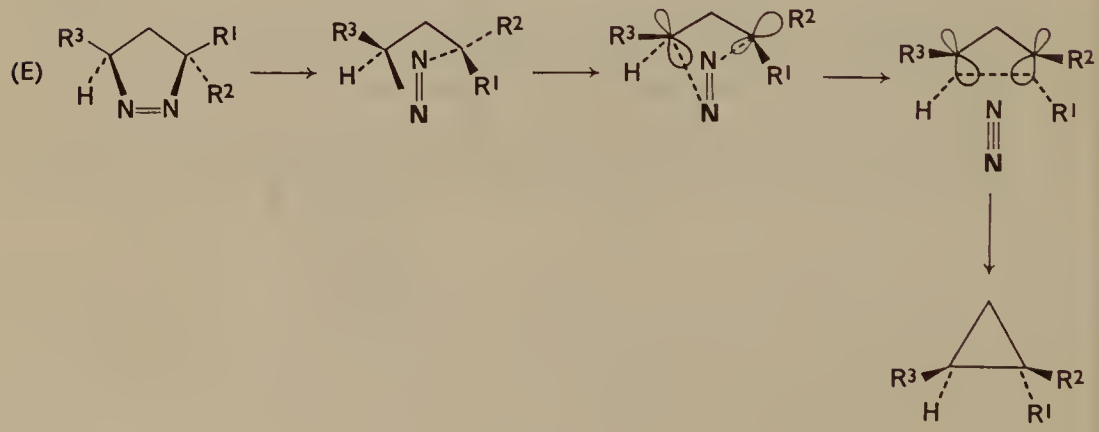
	%	%	%	%
(43) (vapour)	47	19	0	29	6
(44) (neat)	11	72	13	0	4
(vapour)	18	74	6	0	2

have revealed that the formation of cyclopropane through thermolysis of 1-pyrazolines bearing electron-withdrawing substituent(s) at the carbon adjacent to the N=N linkage, proceeds partly with loss of geometrical specificity to varying degrees, the rest being *inverted* at one site [42f]. Photolyses gave cyclopropanes of preferentially retained geometry[42c, f, g]. Although the reaction had been interpreted in terms of 1,3-biradical formation[43] or a heterolytic C—N bond fission to give a dipolar diazonium ion **42**[42c,44], the complex mixture of products observed by McGreer and co-workers[41d–g] has complicated the picture.

While cyclopropane formation is partially non-stereospecific in these decompositions, concomitant olefin formation was found to be essentially stereospecific and the ratio of olefin to cyclopropane was found to be dependent on the solvent polarity.

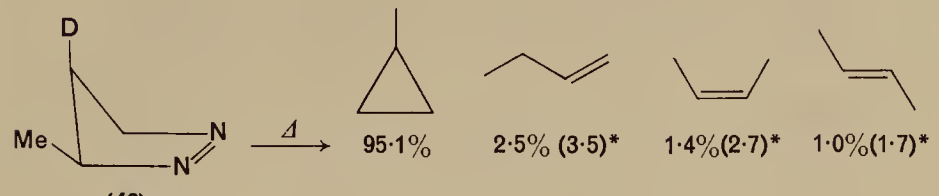
These facts have led to consideration of a dual pathway for the reaction; a concerted migration–elimination which accompanied a partial charge separation (mechanism D) for the olefin-forming reaction and a biradical-formation similar to Crawford's or twisted transition '$_{\sigma}2_s + {}_{\sigma}2_a$' mechanism (mechanism E)[41f,45] for the cyclopropane-forming reaction. In the transition state **45**, only a C-4 substituent *trans* to stretching C—N bonds can migrate to C-5 synchronously, and the observed stereospecificity for





each olefin product could be interpreted in terms of the preferred conformation of the starting pyrazolines.

This mechanism for the olefin-forming reaction, however, is not valid for the decomposition of simple alkylpyrazolines. Pyrolysis of deuterated 3-methyl-1-pyrazolines **46** and **47** gave olefins of essentially the same structural and isotope distributions[46].



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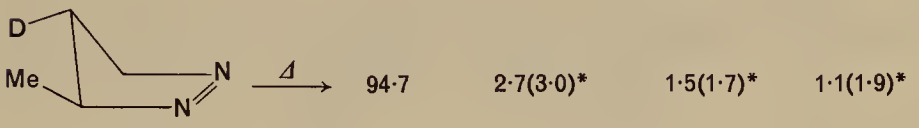
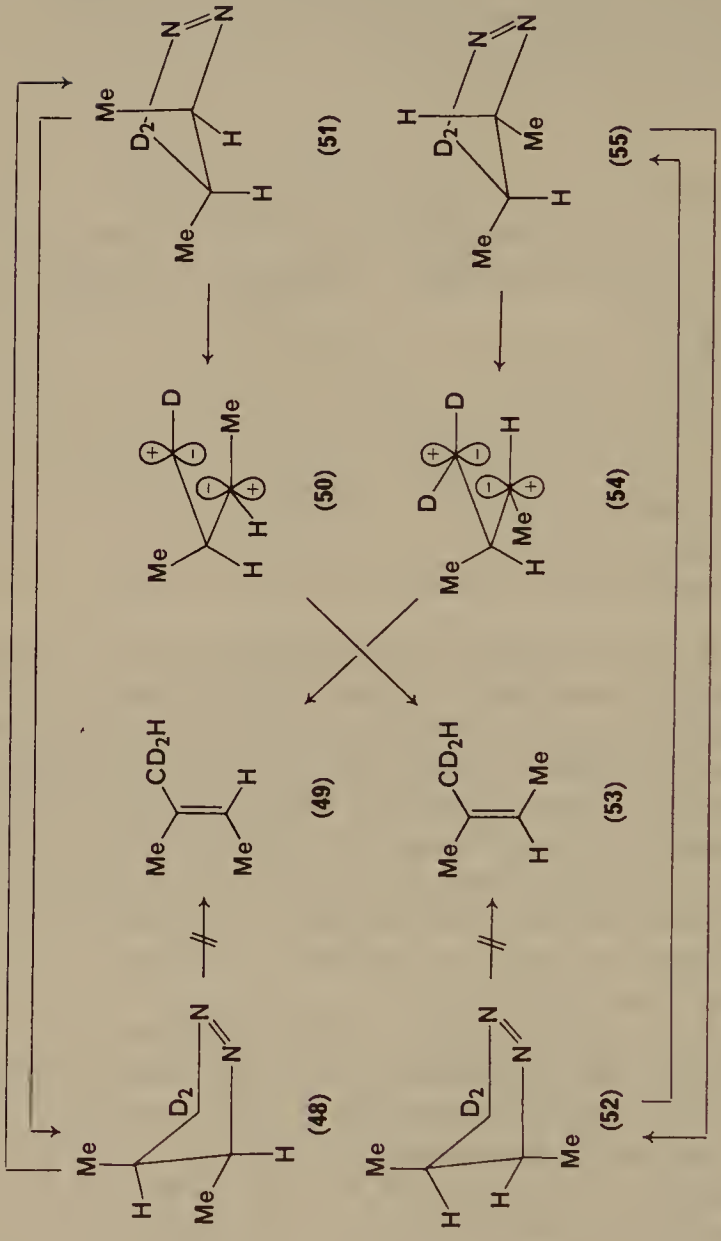


(47)

Moreover, if only a quasi-equatorial hydrogen on C-4 was assumed to be migrating, the structure of 3-methyl-2-butenes produced by thermolysis of 3,4-dimethylpyrazolines **48** and **52** would be **49** and **53**, respectively. The product correlation was found to be completely opposite to this expectation. *cis*-Dimethylpyrazoline **48** gave **53** in more than 94% stereospecificity while the *trans*-isomer **52** gave **49** in more than 96% specificity[47]. This olefin-forming reaction was interpreted *via* π-cyclopropane intermediates **50** and **54** which were formed through the preferred conformations **51** and **55**, respectively, assigned to the starting pyrazolines.

Another fact which makes the situation more perplexing is that the π-cyclopropane (0,0-trimethylene)[28] is by no means a favoured intermediate in the thermal isomerization of cyclopropane **56**[48]. If a π-cyclopropane pathway is energetically favoured over a biradical pathway, the racemization of (−)-**56C** will be much faster than its geometrical isomerization to (±)-**56T**. The rates at 377°C were found to be $k_r = 4{\cdot}21 \times 10^{-5}$ sec^{-1} and $k_i = 3{\cdot}16 \times 10^{-5}$ sec^{-1}, suggesting an intervention of biradical intermediate **58** for both processes. It was pointed out that the

* Values in parentheses are for H-migration/D-migration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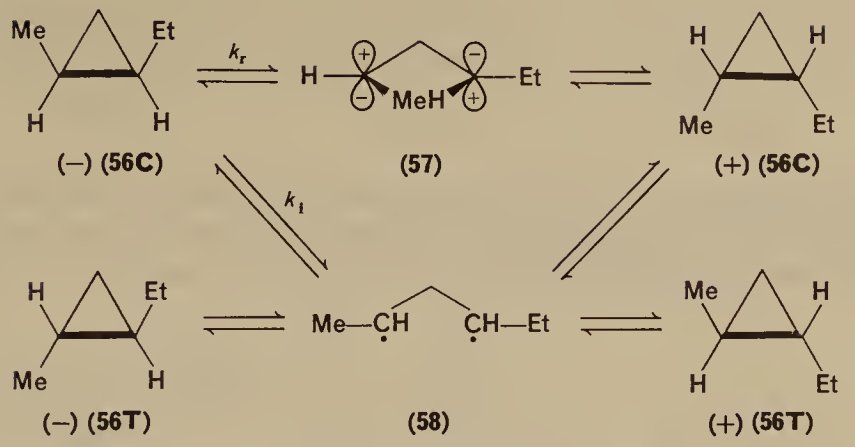
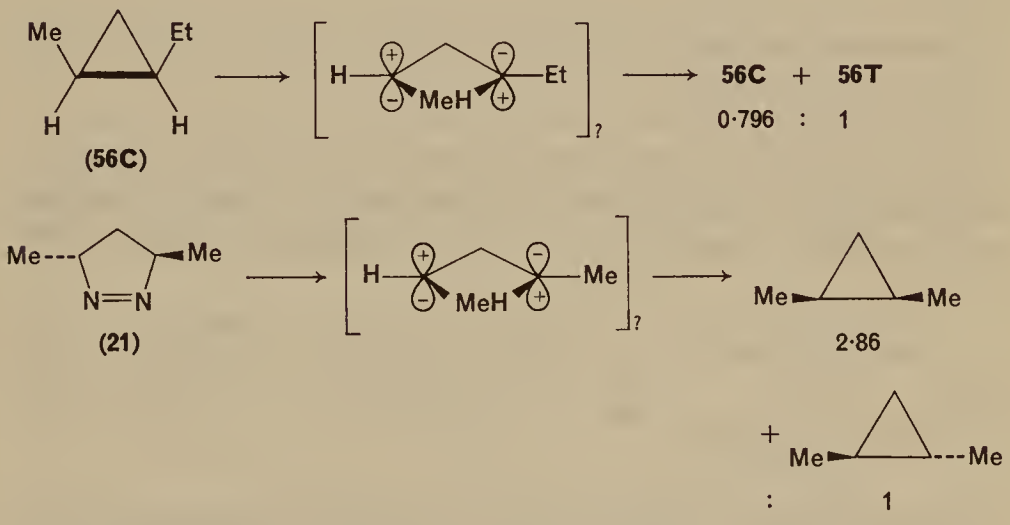
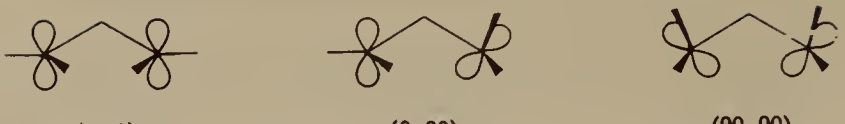


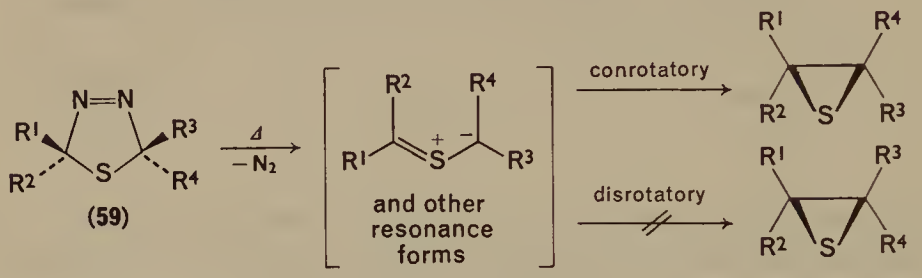
difference of *cis/trans* product selectivity for the isomerization of cyclopropane **56C** and for the decomposition of pyrazoline **21** suggests the intermediates in two reactions are not identical.



It is important to note that the very basis of the above discussions may not be valid. Thus the conclusion derived by Hoffmann that (0,0)-configuration (π-cyclopropane) is the most stable geometry for trimethylene biradical is still a matter of discussion[49a]. A nearly (0,90) conformation of the transition state has been determined through examination of a potential-contour map of the reaction coordinate depicted by an extensive SCF-MO computation[49b].

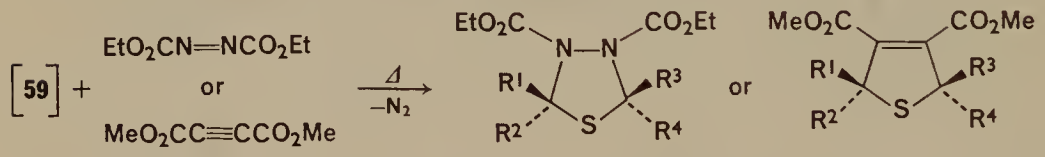


Thiocarbonyl ylides *A* produced by the thermolysis of thiadiazolines **59a–d** have been reported to cyclize to thiiranes in conrotatory manner with nearly 100% stereospecificity[50a]. A (4s + 2s) cycloaddition of this



	R¹	R²	R³	R⁴
(a)	Et	H	H	Et
(b)	Et	H	Et	H
(c)	*t*-Bu	H	H	*t*-Bu
(d)	—$(CH_2)_5$—		—$(CH_2)_5$—	

transient intermediate with diethyl azodiformate or dimethyl acetylenedicarboxylate was also shown to proceed with complete or prevailing stereospecificity, consistent with orbital symmetry requirements[50b].

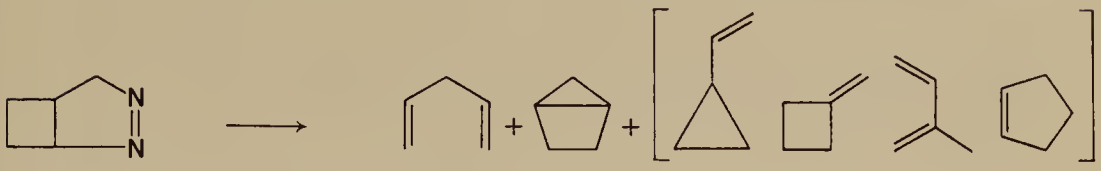


The decomposition of **59c** provided an impressive demonstration of orbital symmetry control; the formation of severely hindered *cis*-di-*t*-butylthiirane was completely stereospecific.

Photolytic decomposition of **59d** to give cyclohexanone azine without evolution of nitrogen is also consistent with the photochemical allowedness of cheletropic elimination of sulphur[50c, d].

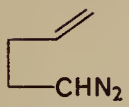
In bicyclic pyrazolines fused at the 3,4-position, two concurrent decomposition modes have been demonstrated by product analysis and by comparison of the products with those of the corresponding

Bamford–Stevens reaction[50e]. Decomposition of **59e** gave 1,4-pentadiene and bicyclo[2.1.0]pentane along with four minor products[51].



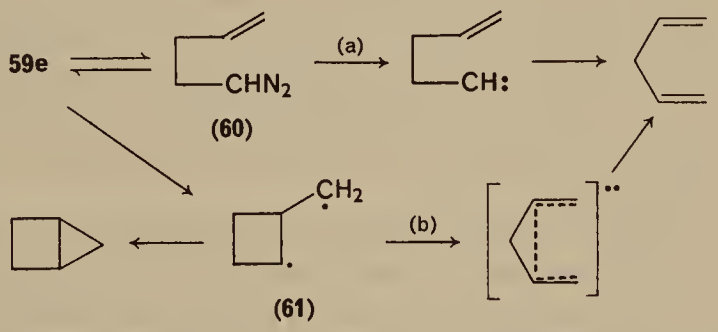
(59e)

	%	%
Δ (gas phase) 267 °C	75·3	14·5
Δ (gas phase) 389 °C	64·7	15·9
hν (direct)	26·8	58·9
hν (sensitized)	10·3	89·7
(B.—S. reaction)	88·7~92·2	0



(60)

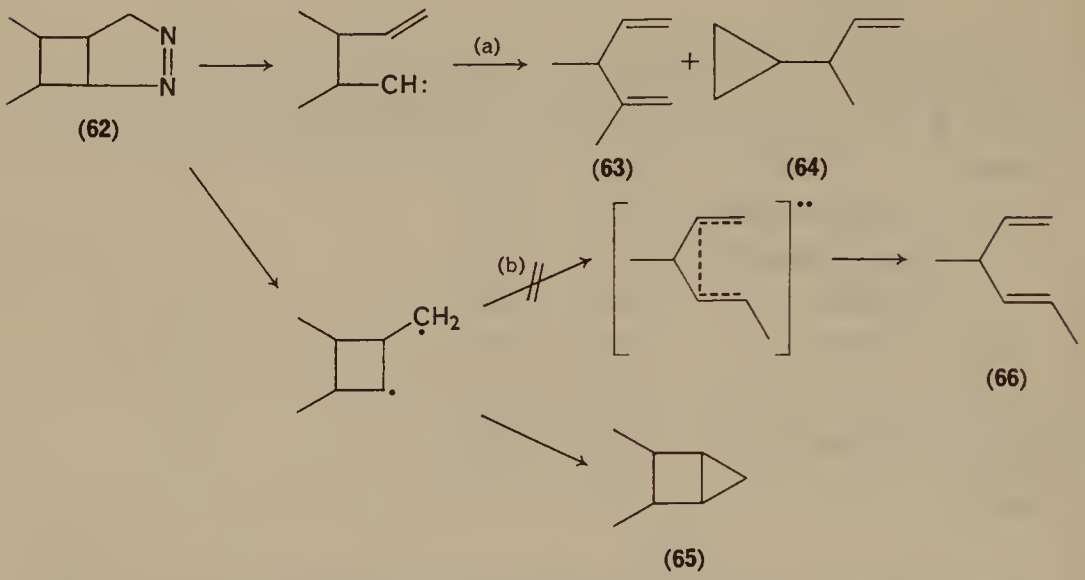
A large amount of pentadiene in the pyrolysis products can most easily be explained as arising from carbene species formed *via* a diazo compound **60**. On the other hand, the absence of bicyclopentane in the products of the Bamford–Stevens reaction (in contrast to its predominant formation in photolyses of **59e**) coupled with the temperature dependence of its ratio to 1,4-pentadiene, strongly suggest that it was formed *via* a different intermediate, namely biradical **61**.



(61)

1,4-Pentadiene could also be formed from biradical **61** *via* a rearrangement to di-π-methane biradical (path b). Thermolysis of two isomeric dimethyl derivatives **62** was examined to assess this possibility. If only the carbene species intervenes—the pathway leading to diene—the structure of resultant diene from **62** will be **63**, whereas methylhexadiene **66** is expected to be

produced *via* the path (b). The results clearly excluded path b as the diene-forming reaction[52].



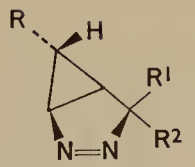
		(65) (*cis-syn*)	(65) (*cis-anti*)	(63)	(64)	(66)
(62) (*cis-syn*)	$\xrightarrow{\Delta}$	13·1%	<1%	56·8%	23·2%	0%
(62) (*cis-anti*)	$\xrightarrow{\Delta}$	<1	10·1	52·8	28·4	0

Substitution at the 4-position in **59e** provided information that (1) isomerization of the biradical species to the carbene species is negligible, and (2) single inversion of geometry is preferred for the formation of bicyclo[2,1,0]pentane derivatives[52a]. This propensity for the single inversion has again led to a doubt as to the intermediacy of π_u-cyclopropane which in this case, should suffer a serious destabilization by the strained cyclobutane fusion and thus should allow some non-stereospecific processes to become predominant.

The same type of carbene formation was suggested for the thermal and photolytic decompositions of cyclopropane-fused pyrazolines **67**[53].

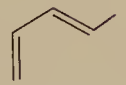
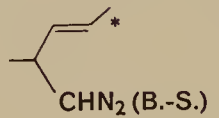
Most of the products can be viewed as arising from intervening carbene species, while preferential formations of 1,3-pentadienes **68** and **69** from **67a** and **67b** respectively and of 2,4-hexadienes **70** and **71** from **67c** and **67d** respectively, imply a concurrent diradical or concerted path with retained configuration at C-4 and inversion of geometry at C-6.

Although the role of bicyclobutanes, potential biradical products corresponding to bicyclopentanes from **59e** and **62**, was not discussed[53],



(67)

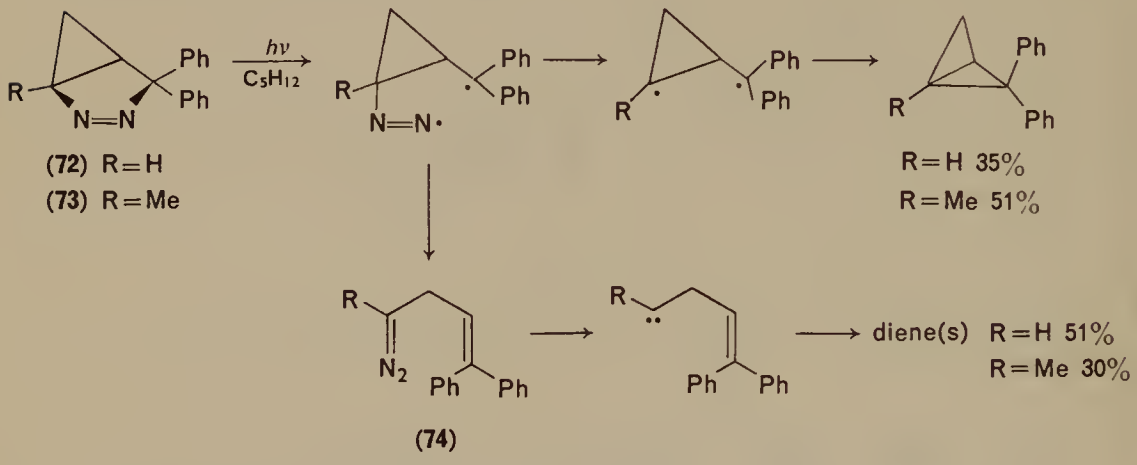
	R	R¹	R²
(a)	H	H	Me
(b)	H	Me	H
(c)	Me	H	Me
(d)	Me	Me	H

67a	$\xrightarrow[\text{or } h\nu]{\Delta}$	 (68)	98%	 (69)	2%			
67b	$\xrightarrow[\text{or } h\nu]{\Delta}$		3		97			
67c	$\xrightarrow[190°C]{\Delta}$	56·4%		23·4%		7·8%	12·8% (70)	(71)
	$\xrightarrow{h\nu}$	57·7		5·8		15·0	21·5	
67d	$\xrightarrow[188°C]{\Delta}$		43·6%		27·1%	2·3	4·8	22·2%
	$\xrightarrow{h\nu}$		47·6		23·5	4·6	12·4	11·9
		61·6	13·3	3·6	0·5	9·7	8·8	2·6

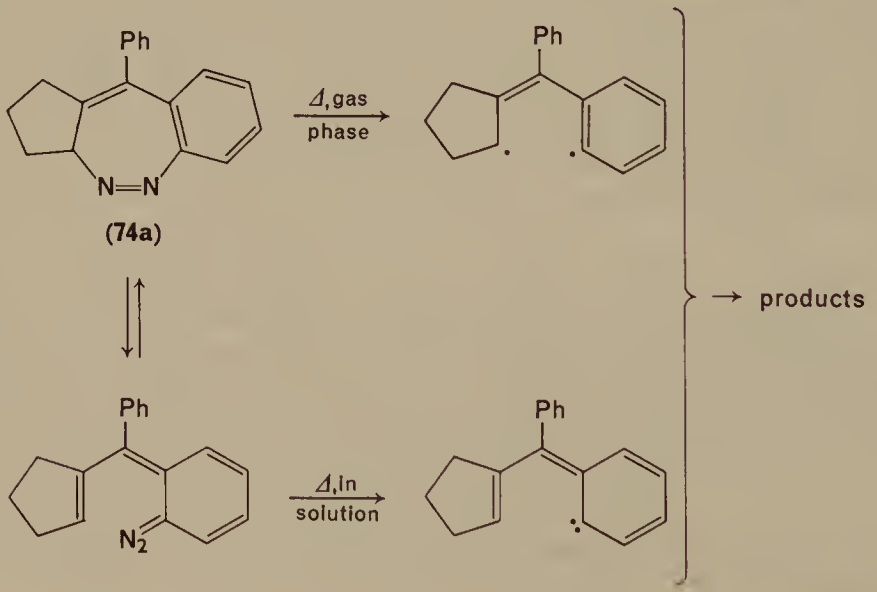
CHN_2 (B.-S.)

* $84 \pm 2\%$ *trans*

it has been identified as one of the major products in the photochemical decomposition of the diphenylpyrazolines **72** and **73**[54]. Close inspection of the latter reaction by n.m.r. monitoring showed a transient accumulation of an unknown species which was tentatively assigned to the diazo olefin **74**. An overall scheme of the reaction akin to those presented above was proposed.

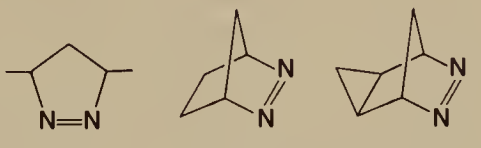


A similar diazo olefin formation was also suggested for the thermal decomposition of **74a**[54a].

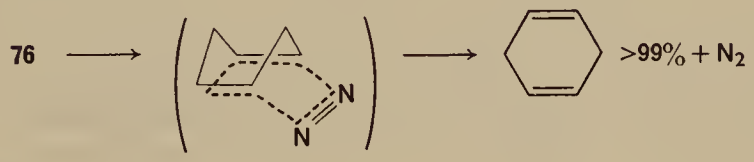


A true electrocyclic mechanism (retro Diels–Alder reactions including retro homo Diels–Alder cases) without intervention of discrete radical species has been inferred for some cyclic diimides which decompose with anomalous ease.

Thus, an enormously high reactivity observed in the tricyclic compound **76** was attributed to the participation of cyclopropane in the transition state[55]. The high product specificity of **76** is remarkable as is its low

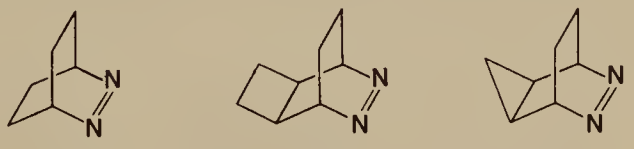


		(75)	(76)
E_a (kcal mol^{-1})	40·3	37·3	18·9
rel. rate (−3·5 °C)	0·01	1·0	$1·6 \times 10^{11}$



activation energy compared to the parent diimide **75**.

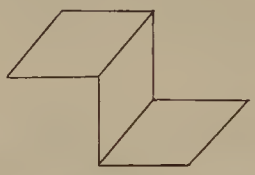
An even more dramatic difference was observed between **77** and **79**. Both tricyclic compounds, **78** and **79**, gave corresponding monocyclic dienes as the sole product in more than 98% yields[56]. Although it was tempting



	(77)	(78)	(79)
E_a (kcal mol^{-1})	44·6	39·2	14·9[57]
ΔS^* (eu, T)	+10·5 (240 °C)	+11 (150 ~ 175 °C)	−21 (−3·5 ~ 12 °C)
rel. rate (−3·5 °C)	1·0	$6·4 \times 10^4$	$1·1 \times 10^{17}$

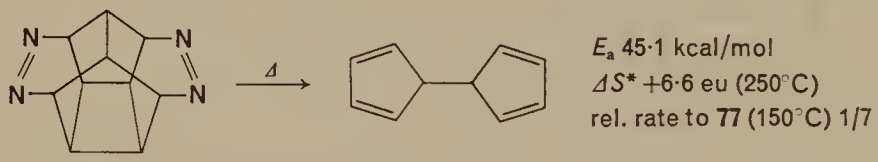
to interpret the significant rate increase and the high product specificity in **78** as cogent evidence for the participation of cyclobutane ring,

examination of the stability of potential biradical products and of kinetic parameters shown above has led to a preference for the biradical mechanism. Subsequently it was found that at least part of the products 1,4-cyclooctadiene, is attributable to the rearrangement of **80** at the decomposition temperature of the diimide[56b].



(80)

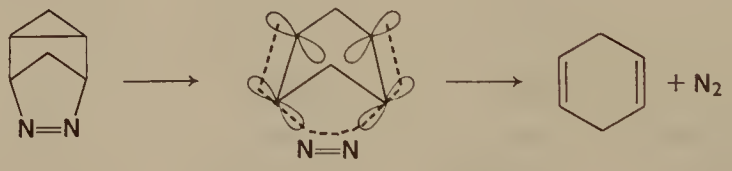
Cyclobutane participation in the thermal decomposition of the cage molecule **80a** was decisively ruled out on the basis of kinetic studies.



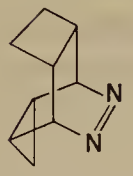
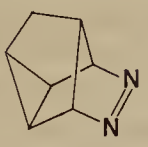
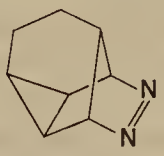
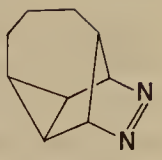
(80a)

The decreased reactivity of **80a** as compared to **77** has been attributed to the rigid structure of this molecule.

Cyclopropane participation discussed above is exerted by an overlap between the developing p-orbitals at carbon atoms releasing a nitrogen molecule and the cyclopropane orbitals opening with outward rotation.



Therefore, a cyclopropane ring fused in the endo direction with respect to the nitrogen bridge (e.g. in **81**) can exert no effect on the decomposition[58]; the angle between the planes containing the cyclopropane ring and the C—N=N—C moiety is also critical for the effective participation[59] (diimides **82–84**).

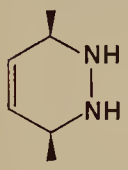
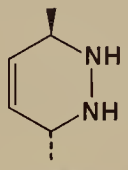
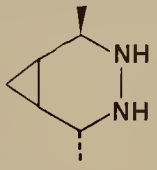
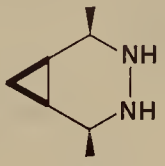
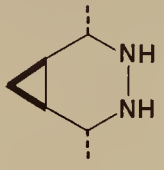





(78)

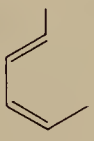
	(81)		(82)	(83)	(84)
E_a (kcal mol^{-1})	41·4	39·2	36·5	23·3	19·6
ΔS^*(eu, T)	+10·3	+11	+8·3	−5	−6
	(199 °C)	(150 ~ 70 °C)	(150 °C)	(33 ~ 50 °C)	(−5 ~ 9 °C)
rel. rate (−3·5 °C)	$8{\cdot}8 \times 10^2$*	$6{\cdot}4 \times 10^4$*	9·2†	$5{\cdot}2 \times 10^8$†	$1{\cdot}9 \times 10^{11}$†

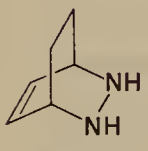
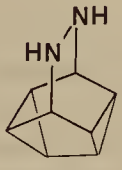
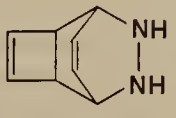
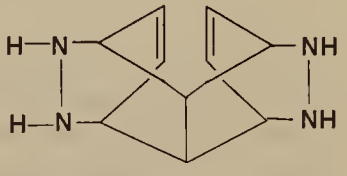
*relative to **77** †relative to **75**

It can be seen from the above results that the orientation of the cyclopropane ring in **82** is too steep to overlap effectively with breaking C—N bonds.

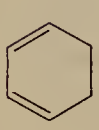






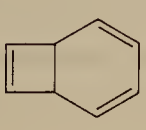
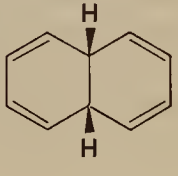
(85) (86) (87) (88) (89)

(90)[60b,c,d] (91)[60e,f,g] (92)[60h] (92a)[60i]

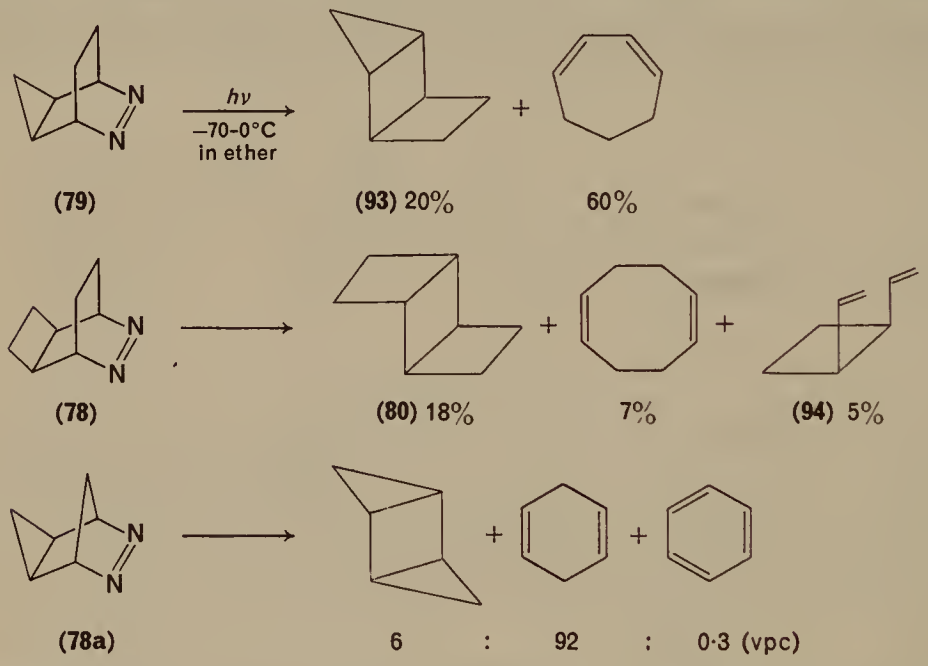


Similar retro Diels–Alder decompositions are exemplified by extremely rapid nitrogen elimination observed when hydrazo compounds **85–92a** were subjected to oxidation[60]. Although the intermediate diimides have not been isolated, the product specificity observed for each case speaks well of a true electrocyclic mechanism *via* the corresponding diimides.

Quite unexpectedly, low temperature photolysis of each diimide prepared *in situ* by oxidation of **87–89** gave quantitative yield of the *same* diene as was obtained from its thermal counterpart[61]. This apparent violation of orbital symmetry prediction was explained in terms of stereochemical 'extra-symmetric' control[62].

On the other hand, the low temperature photolysis of **79** was reported to result in the loss of product selectivity observed in its thermolysis[63]; similar results were also obtained with its homologs **78** and **78a**[64].



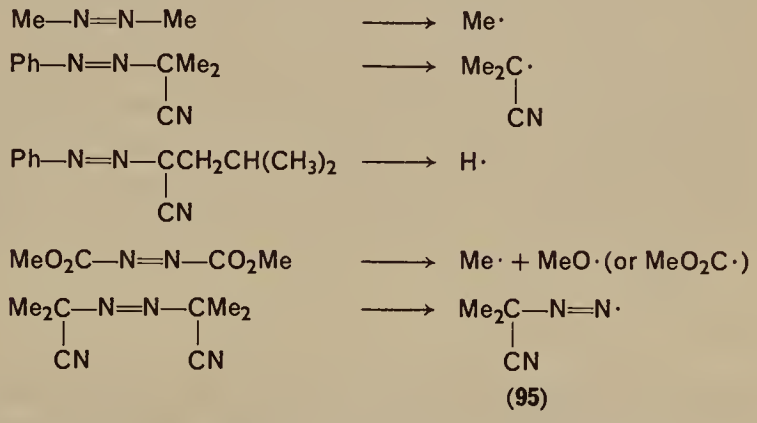
An exclusive stereospecificity for the products, **80, 93** and **94**, is noteworthy in view of preferential retention of geometry, or loose stereospecificity reported for photolyses of pyrazolines and diazanorbornenes.

Activation volume has been shown to give a measure to the decomposition mode. Through a series of investigations of a pressure effect on the decomposition of various initiators, Neuman and co-workers have generalized that values of activation volume will be about +4 ml mol^{-1} for initiators which decompose into three fragments in one step and values more than +10 ml mol^{-1} are expected when the initially dissociated radical pair is able to regenerate the original substrate within the solvent cage[65].

Pertinent data shown below are quite compatible with previously accepted view of the decomposition mode.

	ΔV^* (ml mol^{-1})	P (atm)
$PhCMe_2N{=}NCMe_2Ph$	+5·0 ~ +4·3	~6100
p-$MeC_6H_4CMe_2N{=}NCMe_2C_6H_4Me$-$p$	+4	~4100
p-$NO_2C_6H_4N{=}NCPh_3$	+18 ~ +21	~3840
$(CH_3)_3CON{=}NOC(CH_3)_3$	+4·3	~6200

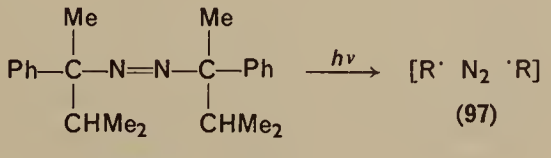
The recent development of magnetic resonance spectroscopy including chemically induced dynamic nuclear polarization (c.i.d.n.p.) has opened new avenues to investigate the mechanistic details of azo decomposition. The first report along these lines was provided by Ayscough and co-workers. They observed e.s.r. signals during photolysis of several diimides in the solid state at −196°C and assigned the observed spectra to radicals shown in the following equations[66].



(95)

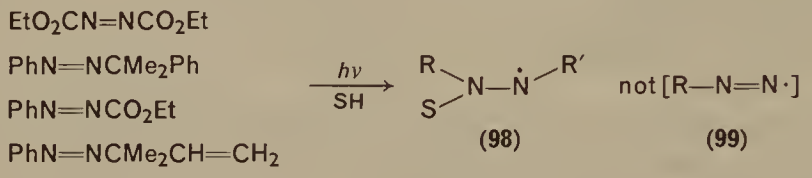
The interpretation in terms of asymmetric one-bond fission for azobisisobutyronitrile is not unambiguous because of the complex and ill-defined feature of the spectrum assigned to the diazenyl radical **95**.

A weak signal of triplet species observed for the photolysis of bis(2-phenyl-3-methyl-2-butyl) diimide **96** at −196°C in a benzene matrix was assigned to the weakly interacting triplet radical pair **97**[67].

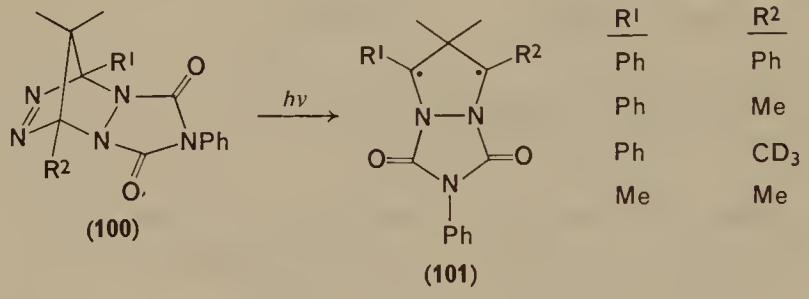


(96) **(97)**

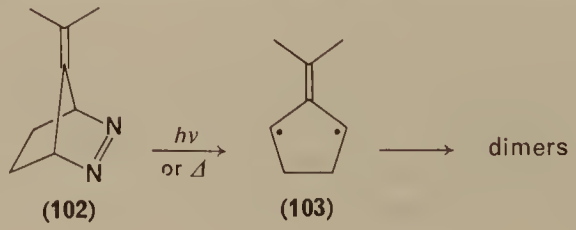
The e.s.r. spectrum observed during photolysis of azodiformate ester and once assigned to a diazenyl radical **99**[68] is now attributed to a solvent participated hydrazyl radical **98**. The same type of solvent participated radicals were also shown to be formed during the photolysis of phenylazocumene, ethyl phenylazoformate, and phenylazo-3-methyl-3-but-2-ene in cyclohexane or isopentane-methylcyclohexane[69].



The formation of 1,3-biradical species during the decomposition of a cyclic diimide was directly proven by e.s.r. Four derivatives of diimide **100** gave well-defined e.s.r. signals corresponding to the triplet biradical **101** upon irradiation of a solid sample at −196°C (at 4 K in case of R^1, R^2 = Me)[70].



The thermal and photolytic decompositions of 7-isopropylidenediazanorbornene **102** gave four isomeric products in the same distribution. Both reactions were interpreted to give rise to an initial formation of a triplet biradical **103** which dimerized to the products. Evidence for the scheme was adduced through the observation of an e.s.r. signal during low temperature photolysis and of strong c.i.d.n.p. signals emitted from the dimer products during pyrolysis[71]. A theory which predicts the observation



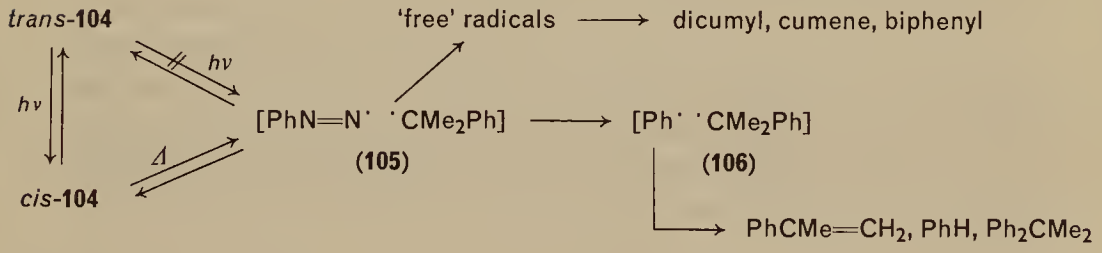
of c.i.d.n.p. during a dimerization process of two triplet biradicals but not for triplet–singlet or singlet–singlet combination supported the interpretation[72].

A highly instructive example of c.i.d.n.p. investigation on the decomposition of azo compounds was given in a recent paper by Porter and Closs and their co-workers[73].

$PhN{=}NCMe_2Ph$

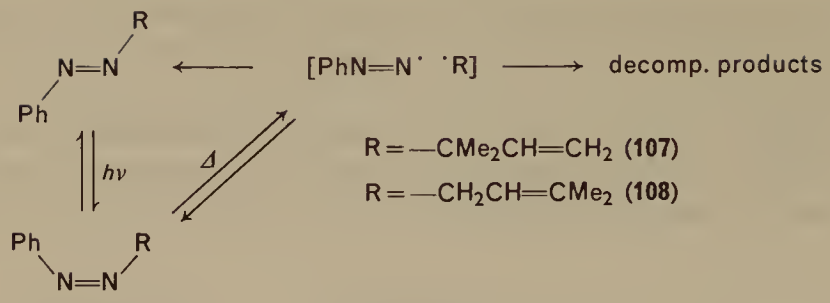
(104)

When a benzene solution of *trans*-**104** was irradiated inside an n.m.r. spectrometer probe, enhanced absorption (A) and emission (E) signals were observed for dicumyl (weak A), cumene (AE multiplet), 2,2-diphenylpropane (E), α-methylstyrene (E), benzene (E), and methyl group of *trans*-**104** itself (E). Major products were 48% dicumyl and 20% biphenyl. That the decomposition is essentially a thermolysis of *cis*-**104** which was formed by photoisomerization of *trans*-**104** was demonstrated by the identity of c.i.d.n.p. spectrum observed during thermolysis of *cis*-**104** at 40°C and by absence of decomposition when *trans*-**104** was photoisomerized at −40°C[74]. These results clearly indicate an initial dissociation of *cis*-**104** to a radical pair **105** which undergoes either recombination to *trans*-**104** or further decomposition to products.



A secondary radical pair **106** was assumed because of greater specific polarization of α-methylstyrene as compared to that of *trans*-**104**, a fact which suggests a different and much longer-living precursor for the styrene than that for *trans*-**104**. The same two-step decomposition with the transient formation of phenyldiazenyl radical has been deduced from the observed c.i.d.n.p. spectra during the thermolysis of PAT[74a].

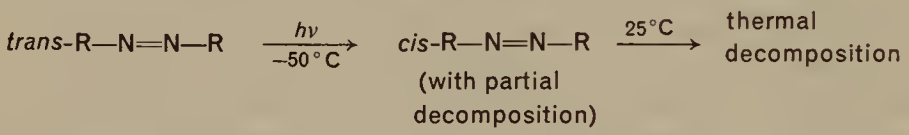
Several lines of evidence also support the same mechanism for photodecomposition of unsymmetric diimides **18** and **107**.



(*a*) Racemization of optically active **18** during the photolysis at room temperature and the solvent viscosity dependence of its quantum yield[26].

(*b*) Observation of concurrent structural isomerization of *trans*-**107** to **108** during the photodecomposition at room temperature[75a] and facile thermal decomposition of *cis*-**107** to result in the same transformations[74].

A low temperature photochemical isomerization of *trans*- to *cis*-diimides and subsequent facile thermal decomposition of the latter has also been studied by u.v. and n.m.r. spectroscopy[75b]. The large decrease of activation energy brought about by isomerization to the *cis*-isomer has been attributed mainly to steric factors.



R = *t*-Bu, Me_2CCN, CH_2CO_2Bu-*t*, 1-cyanocyclohexyl

Ea(*trans*)–Ea(*cis*) = 20 kcal mol^{-1} (for R = *t*-Bu)

cis-Phenylazo-2-isobutane (**109**), on the other hand, undergoes thermal isomerization to the *trans*-isomer with little decomposition to hydrocarbon products at room temperature[76]. In this case, the slow decomposition accompanying irradiation is thought to be a truly photolytic decomposition of *cis*- and/or *trans*-**109** rather than a simple thermal decomposition of the *cis*-isomer.

B. Radical Reactions of Azocarbonyl Compounds

Azo compounds which are activated by one or two electron-attracting groups directly bound to the —N=N— linkage, can react with a wide variety of compounds, and differ from simple azoalkanes and azoarenes in their pronounced reactivity. Our discussion of this type of compounds will be confined to thermal decomposition, some cycloadditions, substitutive additions and oxidations.

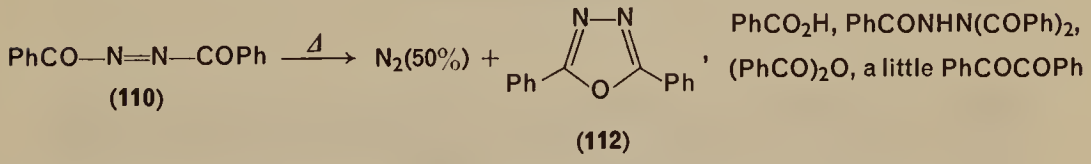
An excellent review accounting for all types of reactions reported up to 1966 has been presented[77].

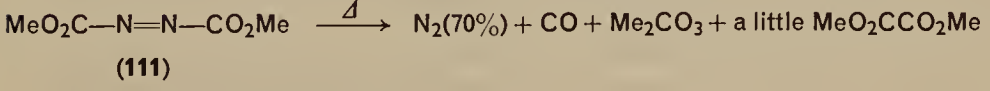
I. Thermal decomposition

Azodiformate esters in their *trans* form are fairly stable to heat and irradiation, although the parent azodiformic acid is extremely unstable and sensitive to general acid catalysis[78]. Thus, azodiformic acid salts when neutralized or acidified, liberate diimide which undergoes subsequent characteristic reactions[79].

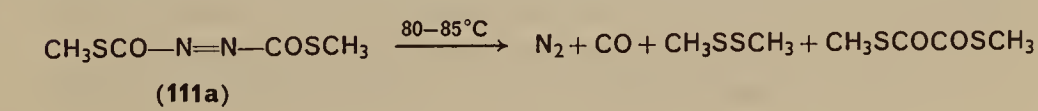
Thermal decomposition of azodiformate esters and azodiacyls has been observed at various temperatures depending on the nature of the substrates and the solvents[80]. The thermolysis of these compounds has not been as well scrutinized as that of azoalkanes. This is because of the complexity of the course of reaction and of its kinetics[80]. While azoalkanes decompose with a clean first order rate to give mainly recombination and disproportionation products of corresponding alkyl radicals, alkoxycarbonyl or acyl radicals formed by the decomposition of azodiformates or azodiacyls, tend to induce secondary reactions. In general, recombination of two radicals by the thermal extrusion of nitrogen molecule is very ineffective.

In 1929, Stolle and Reichert reported the thermolysis of azodibenzoyl (**110**) and dimethyl azodiformate (**111**, MAD) from which they obtained 2,5-diphenyl-1,3,4-oxadiazole **112** and dimethyl carbonate, respectively, as the main product. The recombination products, benzil and dimethyl oxalate were very minor[80a].

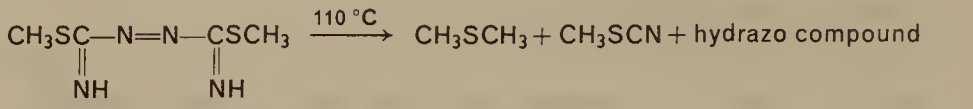




On the other hand, the thiol ester analogue **111a** decomposed under rather mild conditions to give nitrogen, carbon monoxide and dimethyl disulphide; the acyl coupling product was also isolated[80g]. Similarly, the

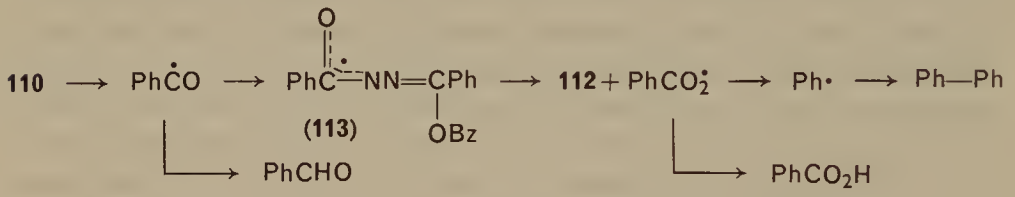


imino analogues **111b** underwent explosive decomposition at 110°C, dimethyl sulphide and methylthiocyanate were among the products identified.



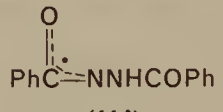
(111b)

Thermal decomposition of **110** in various solvents was studied further by Leffler and Bond[80]. In benzene at 110°C, product **112** dominated over the other products, $PhCO_2H$, PhCHO, Ph—Ph, and $BzNHNBz_2$. In ethanol, the decomposition occurred at room temperature and more than 50% of



(113)

$PhCO_2H$ and PhCHO were isolated. The same products were also observed in the oxidation of benzhydrazide or *N,N'*-dibenzoylhydrazine in aromatic solvents, and were supposed to be formed *via* a radical **114** akin to **113**.



(114)

Benzil, the presence of which would constitute unequivocal evidence for the formation of benzoyl radicals, could not be detected either in the azo thermolysis or the hydrazide oxidation[80f].

In spite of the very ineffective coupling of the acyl moieties in the thermolysis of simple azodiacyls[81], the formation of up to 45% of the diacyl from the thermal decomposition of **115** led to the suggestion that the utility of the thermal decomposition of azodiacyls for the synthesis of 1,2-diketones seems to be greater for more complex structures than for simpler ones[80e].

(115)

Thermal decomposition of azodiformate esters is more complex and less well defined[82].

The product composition varies considerably between the thermal and photolytic decompositions. A predominant radical recombination has been reported for the photolysis of azodiacyls in benzene solution. Whether

$$PhCON{=}NCOPh \xrightarrow[PhH]{h\nu} Bz{-}Bz\ (29\%),\ \mathbf{112}\ (22\%),\ BzNHNBz_2\ (13\%)^{80f}$$

$$ArCON{=}NCOAr \xrightarrow[PhH]{h\nu} ArCOCOAr,\ ArCONHN(COAr)_2,\ ArCO_2H^{83}$$

Ar = *p*-ClC_6H_4	40%	40%	20%
o-ClC_6H_4	55%	25%	trace

the photolysis involves the decomposition of an excited *trans* and/or *cis*-azo compound or the thermal decomposition of ground state *cis*-isomer[84] is unknown. An initial formation of triplet biradical was assumed in connection with the photolysis of azodiformate esters in ethereal and alcoholic solutions or in the presence of olefins[85]. Although the products of these reactions are consistent with this view, e.s.r. spectroscopy could only show the presence of degraded alkyl radical[86] or solvent participated hydrazyl radical **116**[87].

$$SH \longrightarrow S\cdot \xrightarrow{EtO_2CN{=}NCO_2Et} EtO_2C\dot{N}{-}N(CO_2Et)(S)$$

(116)

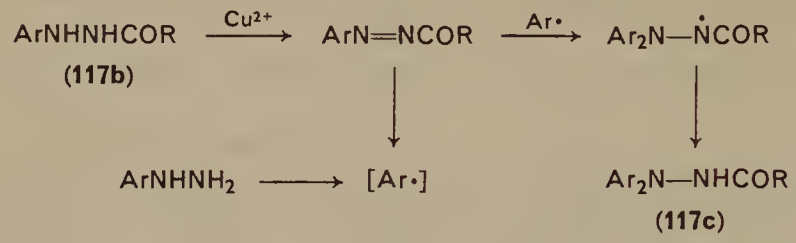
The thermolysis of triphenylmethylazocarboxylates **117** in benzene and cumene has been reported[88]. The formation of all the products that contain an alkoxy group (total 42–48% for R = Me and 42% for R = Ph) could be explained by coupling of the alkoxycarbonyl radical with a trityl radical or a substituted trityl radical formed in a secondary reaction by the attack of alkoxycarbonyl radical(s) on the phenyl ring(s).

$$Ph_3CN{=}NCO_2R\ (\mathbf{117})\ (R = Me, Ph) \xrightarrow{\Delta}$$

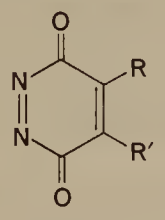
$$Ph_3CH, Ph_3CCO_2R, Ph_2CHC_6H_4CO_2R{-}p, Ph_2C(CO_2R)C_6H_4CO_2R{-}p, PhCH(C_6H_4CO_2R{-}p)_2$$

Other reaction modes of alkoxycarbonyl radicals[89a], such as hydrogen abstraction to yield formate esters, dimerization to oxalate esters, or addition to solvent molecule, were not appreciable.

A reaction which most likely involves radical species is the Gatterman–Tafel 1,1-diarylhydrazine synthesis[89b]. When 2-acyl arylhydrazines (**117b**) are oxidized with ammoniacal copper sulphate, the 1,1-diaryl-2-acyl hydrazines (**117c**) are obtained in excellent yields. The addition of an aryl

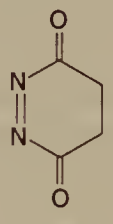


radical generated from the intermediate azo carbonyl compound to undecomposed azo carbonyl compound followed by hydrogen abstraction can account for the formation of the observed product. The aryl radical can be generated by oxidation of the arylhydrazines in the presence of **117b**.



(118)

R,R′=H,H; F,F; R + R′ = benzo-



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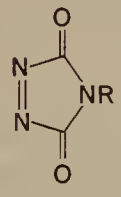
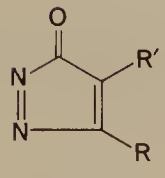


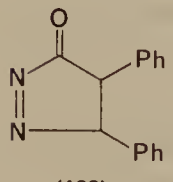
(120)

R = H, Alkyl, Aryl



(121)

R, R′ = Me, H; Ph, H; Ph, Ph; R + R′ = benzo-



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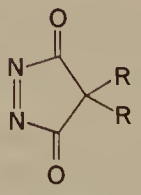
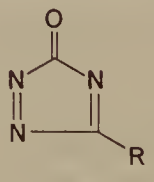


(123)

R = Alkyl

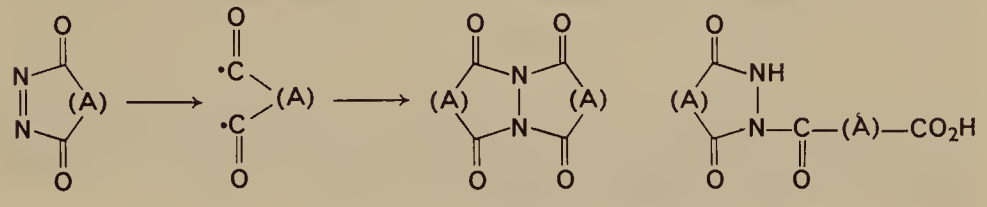


(124)

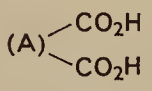
R = Alkyl, Aryl

Recently six- and five-membered cyclic α-carbonylazo compounds **118–124** have been generated in search for a class of dienophiles with a high reactivity[90a–q]. These compounds, because of their *cis*-configuration, have shown marked reactivity and instability as well.

Thermal decomposition products were identified for some of them. The carbonyl biradical formed by extrusion of nitrogen molecule may either add to the parent azo compound to form hydrazide derivatives **125** and **126** or split off carbon monoxide to form a stable molecule.



(125) **(126)**



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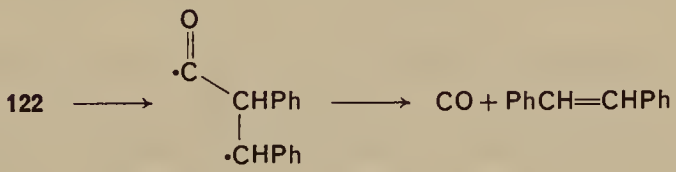
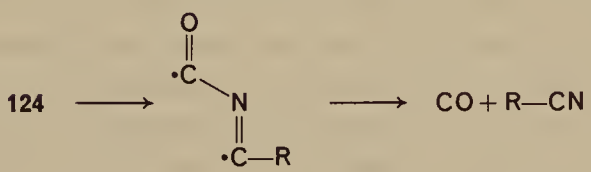
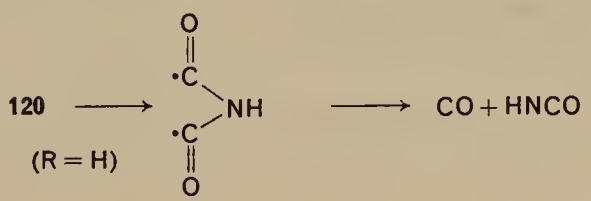






Although it has been reported[91] that the thermal decomposition of azosulphone **128** in non-polar solvents leads to the formation of the sulphone **129**, a study of the decomposition of phenyl phenylsulphonyldiimide **128** (R = Ph) by Overberger and Rosenthal has shown this not to be

true[92]; subsequently, Kice and Gabrielsen disclosed yet more complicated feature of the reaction[93]. The thermal decomposition of **128** (R = Ph or Me) in non-polar solvents gave products which can easily be interpreted as arising *via* a mechanism involving initial homolytic dissociation into free radical intermediates.

$$\text{PhN=NSO}_2\text{R}\ (\textbf{128}) \xrightarrow[\text{in PhH}]{\Delta} \text{PhN}_2^{\bullet} + {}^{\bullet}\text{SO}_2\text{Ph} \longrightarrow \text{Ph}^{\bullet} + \text{N}_2 + {}^{\bullet}\text{SO}_2\text{Ph}$$

$\longrightarrow$	PhPh	$PhSO_2H$	PhN=NPh	$PhSO_2Ph$ (**129**)	
(R = Ph)	45–50%	27%	2%	5%	92
(R = Me)	32%	not checked	3%	—	93a

In a polar solvent such a acetonitrile, **128** (R = Me) gave 71% of acetanilide as a sole product[79a], which was thought to arise *via* an initial heterolytic dissociation[94] into sulphinate and benzenediazonium ions.

$$\text{PhN=NSO}_2\text{Me} \xrightarrow[\text{in MeCN}]{\Delta} \text{PhN}_2^{+} + \text{MeSO}_2^{-}$$

$$\text{PhN}_2^{+} \xrightarrow{-\text{N}_2,\ \text{MeCN}} \text{PhN}{=}\overset{+}{\text{C}}\text{Me}$$

$$\text{PhN}{=}\overset{+}{\text{C}}\text{Me} + \text{MeSO}_2^{-} \longrightarrow \text{PhN=C(Me)—OSOMe} \longrightarrow \text{PhNHCOMe}$$

On the other hand, the azosulphone **130**, when decomposed in benzene, evolved more than 60% of SO_2, yielding benzaldehyde phenylhydrazone and *N*-benzyl-*N'*-benzalphenylhydrazine as principal products[93]. The reaction was shown to be of a radical chain mechanism which involved benzylphenyldiimide as an intermediate.

$$\underset{(\textbf{130})}{\text{PhCH}_2\text{SO}_2\text{N=NPh}} \xrightarrow{\text{PhCH}_2^{\bullet}} \text{PhCH}_2\text{SO}_2\text{N}\overset{\bullet}{\text{N}}\text{Ph}(\text{CH}_2\text{Ph}) \longrightarrow \text{PhCH}_2^{\bullet} + \text{SO}_2 + \text{PhCH}_2\text{N=NPh}$$

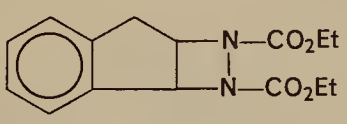
or

$$\textbf{130} \xrightarrow{\text{R}^{\bullet}} \underset{(\textbf{131})}{\text{Ph}\dot{\text{C}}\text{HSO}_2\text{N=NPh}} \xrightarrow{-\text{SO}_2} \text{Ph}\dot{\text{C}}\text{HN=NPh} \xrightarrow{\textbf{130}} \textbf{131} + \text{PhCH}_2\text{N=NPh}$$

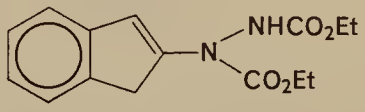
The thermal or photolytic decomposition of azobissulphones has not been investigated. Although Bock has described that *N,N'*bis(*p*-toluenesulphonyl)hydrazine decomposed even at −50°C upon oxidation[95], a successful preparation of bisphenylsulphonyldiimide has been claimed[96].

2. Reactions with olefins

Uncatalysed reactions of azodiformate esters and azodiacyls with olefins have been known since 1926[97]. The reactions are divergent and their actual nature is often unclear. For example, the reaction product of indene and diethyl azodiformate (EAD) had originally been assigned[97] two possible structures **132** and **133**, of which the latter was preferred by Alder[98] because of the conversion of the adduct to 2-indanone on treatment with acid. Later, Huebner and co-workers[99] proposed the azetidine structure **132**, taking account of the absence of NH absorption in its i.r. spectrum

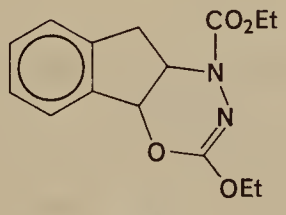


(132)

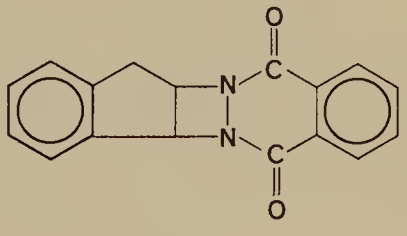


(133)

and an ABXY pattern of the aliphatic ring proton signals of its p.m.r. spectrum. Finally, Huebner and co-workers and Koerner von Gustorf and co-workers[100] revised the assignment to the third structure **134** which is consonant with both spectral characteristics and dissimilarity of LAH reduction mode from that of an azetidine type adduct **135**[101].



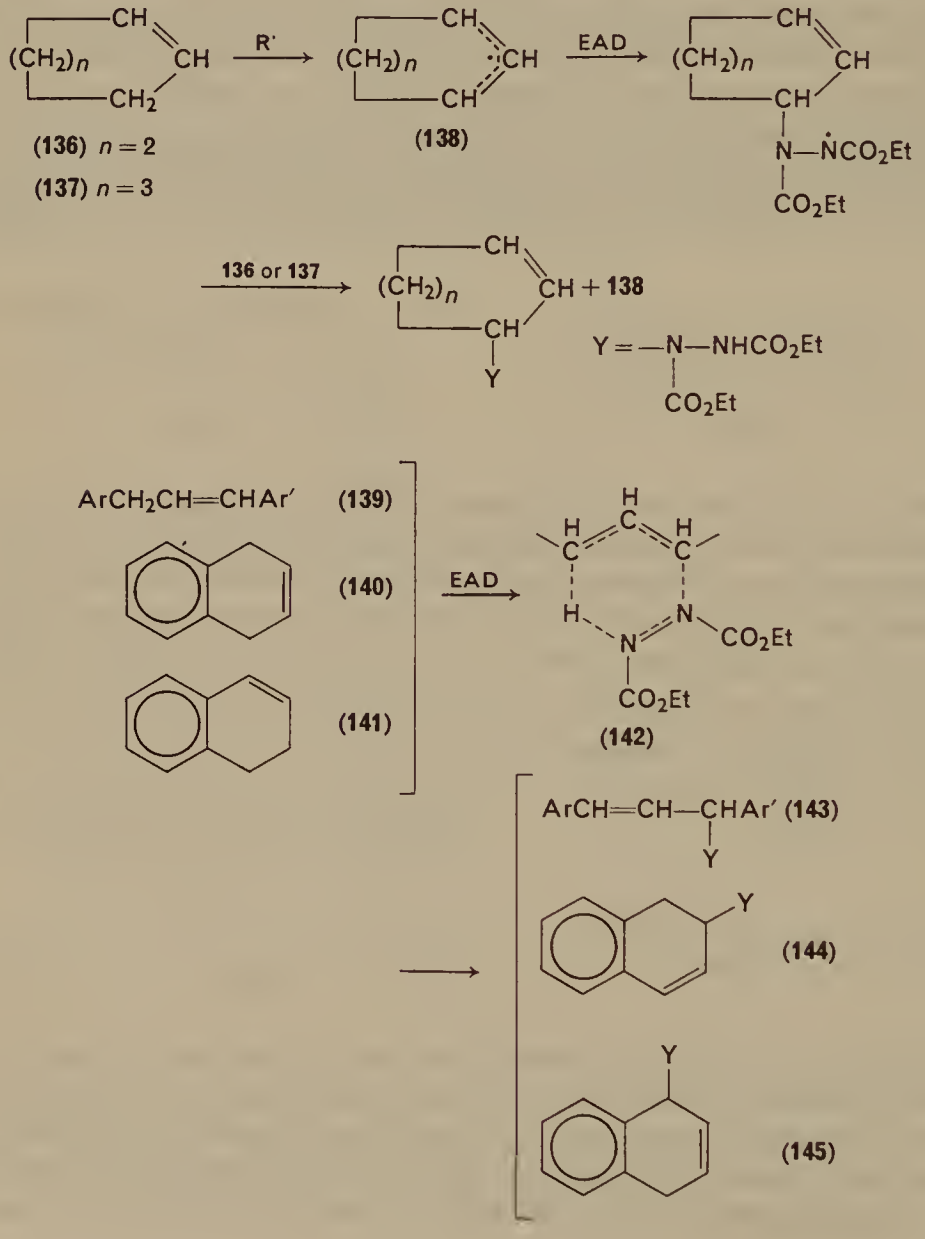
(134)



(135)

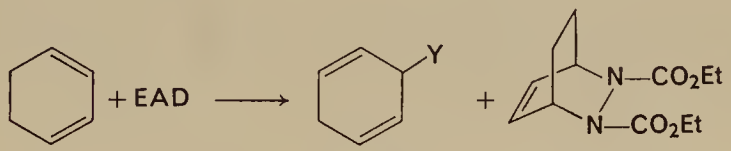
Simple olefins and some enamines and vinyl ethers undergo substitutive addition with α-carbonylazo compounds. The nature of the reaction had first been studied extensively by Huisgen and his group. They found that with EAD, some olefin reactions could be accelerated by radical initiators and were retarded by radical inhibitors. Reactions of olefins which could be

assisted by initiators were those of cyclopentene and cyclohexene. The reactions of 1,3-diarylpropenes **139** and dihydronaphthalenes **140** and **141** were not affected by radical initiators nor by acidic or basic catalysts[102]. A double bond migration was observed in the products of the latter group along with a deuterium kinetic effect (k_H/k_D 2·8–4·1) in the reaction of 1,4-dihydronaphthalene-1,4-d_2 and a slight solvent effect in the reaction of 1-*p*-tolyl-3-phenylpropene[102b]. The following mechanisms have been proposed.



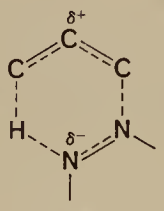
A small amount of **144** isolated from the reaction product of **141** and EAD indicated a concurrent free radical process in the latter reaction.

Substitutive addition also occurs with some 1,3-dienes when the Diels–Alder adduct is not favoured. Thus, in contrast to the normal Diels–Alder reaction of cyclopentadiene, 1,3-cyclohexadiene and cycloheptatriene undergo this type of reaction with EAD. The reaction of cycloheptatriene with EAD was not affected by added radical initiators nor inhibitors and is believed to proceed *via* the cyclic mechanism, although the required shift of double bond had not been demonstrated[103]. 1,3-Cyclohexadiene gave the substitutive adduct **146** and small amounts of the Diels–Alder adduct[104]. The large negative value of the activation entropy and the moderate



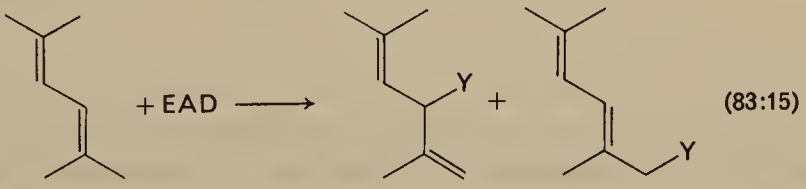
(146) ~80% **(147)** 5–15%

solvent effect observed were interpreted in terms of a modification **148** of the cyclic transition state **142**[106]. Competition with Diels–Alder



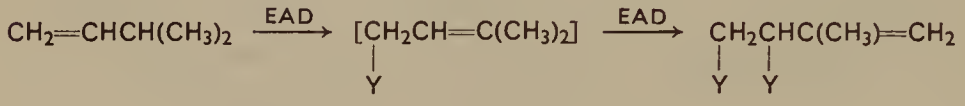
(148)

reaction has also been observed with highly alkylated acyclic dienes and trienes[105b,107]. Evidence of a concurrent free radical process has been inferred from the formation of **149** from the reaction of 2,5-dimethylhexa-2,4-diene with EAD[105].

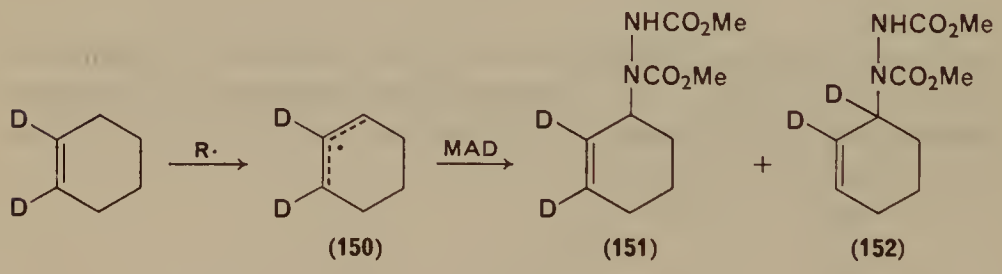


(149)

Although it is tempting to generalize the demonstrated radical nature of the reaction of EAD with cyclopentene or cyclohexene to every simple olefin, Thaler and Franzus have shown that the reaction of cyclopentene was in fact, a special case among C_4 and C_5 monoolefins[106]. In these acyclic monoolefins, it was shown that the rate is enhanced by alkyl branching which is capable of stabilizing the developing positive charge of the rate determining intermediate **148**, and the rates of *cis*-olefins are slower than those of the corresponding *trans*-isomers because of unfavourable geometry of the transition state. With this knowledge, it is understandable that some of the monoadducts are more reactive than their parent olefins, thus giving diadduct preferentially.

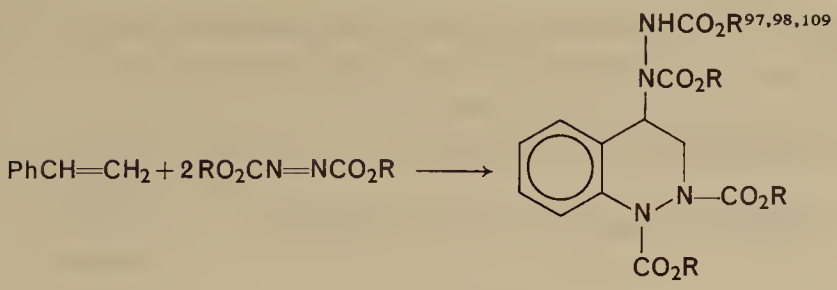


The preference for a radical chain mechanism in reactions of EAD with cyclic monoolefins has been attributed to a higher free radical reactivity of an allylic hydrogen in cycloolefins[108] and the lower reactivity towards cyclic substitutive addition because of their *cis* configuration. The radical nature of the reaction of cyclohexene was also demonstrated by Ahlgren and coworkers[85c]. The thermal or photolytic reaction of MAD with cyclohexene-1,2-d_2 gave a mixture consisting of equal amounts of **151** and **152**; an obvious intermediate is the allylic radical **150**.

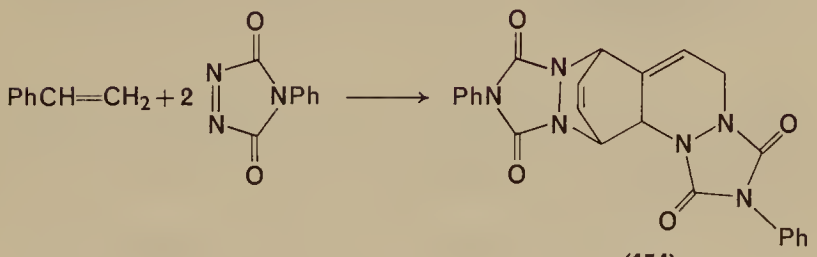


(150) (151) (152)

The reactions of α,α′-azodicarbonyl compounds with styrene give 2:1 adducts[90d,97,98,109]. The product is either **153** or **154** depending on the nature of the azo compound.

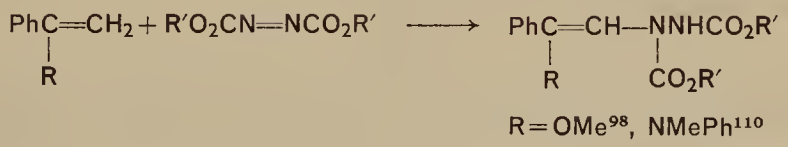


(153)

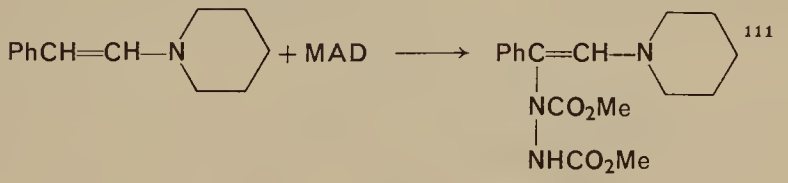


(154)

Some styrenes which have an alkoxy or *sec*-amino substituent on the side-chain react with azodiformates to give a direct substitutive adduct *via* an undefined mechanism.



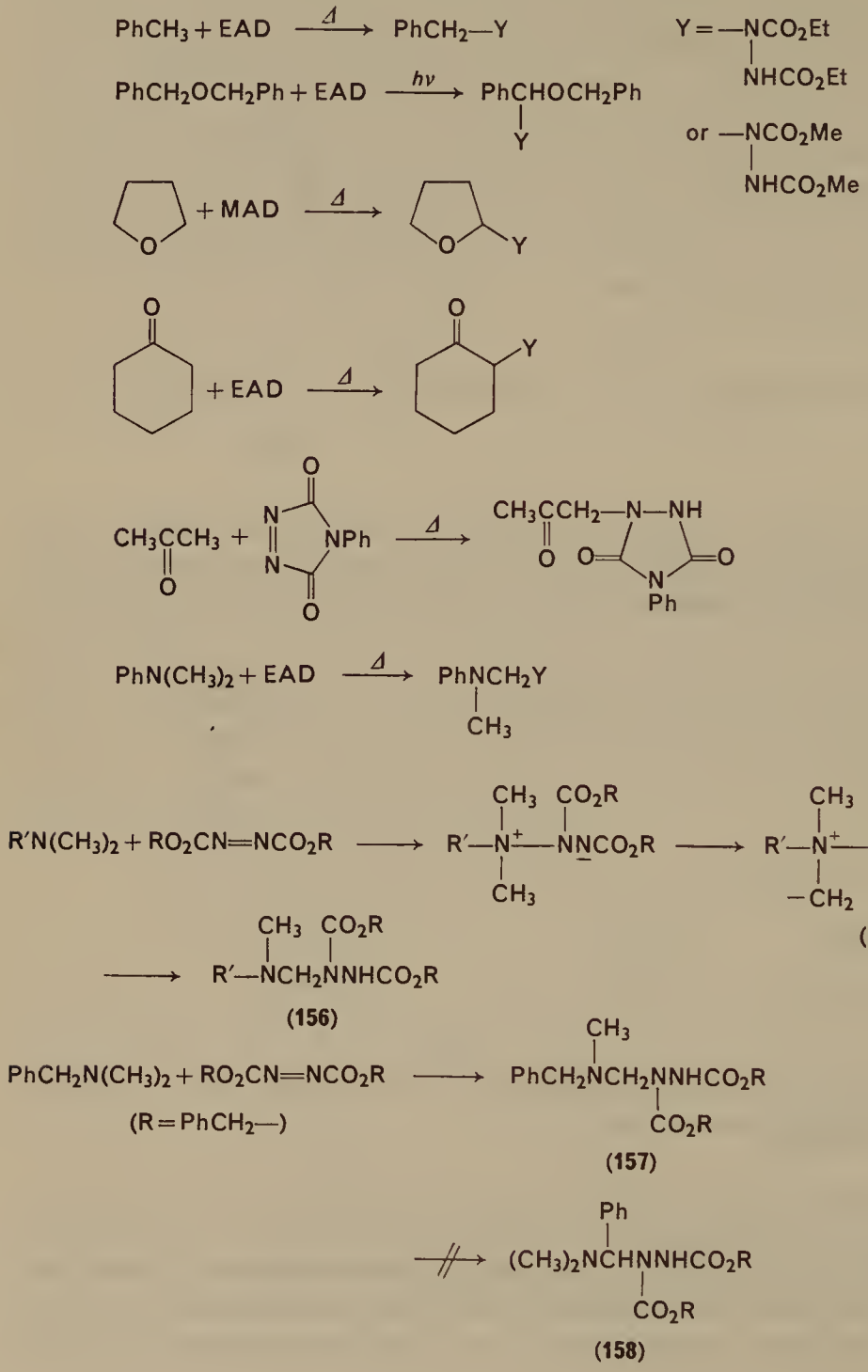
R = OMe[98], NMePh[110]



3. Reactions with alkylbenzenes and oxygen- and nitrogen-containing compounds

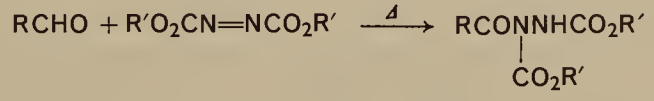
Azidoformate esters and azodiacyls, either by heat or by irradiation, react with alkylbenzenes[112], esters[112,113], ketones[113,114], and tertiary amines [114,115] to give substitutive adducts. The reactions were shown to be assisted by free radical initiators[112,113,114], and gave products which are consistent with a radical process; an α-hydrogen abstraction from the

substrates followed by addition of resulting radicals to the N=N double bond of azo compounds and by a final hydrogen abstraction.

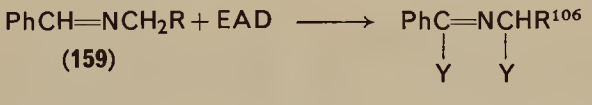


The reaction of tertiary amines with azodiformate esters is not well defined. It was not affected by a radical inhibitor[114], but the suggested mechanism involving an ylid rearrangement **155** → **156** does not seem to accommodate the fact that the sole product from benzyldimethylamine was **157** instead of **158**[115].

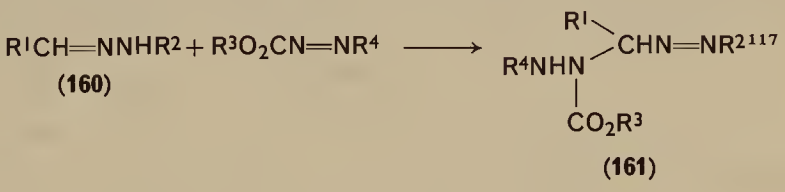
Aldehydes have been reported to react with azodiformates *via* a radical process[112c,114,116].



A formal resemblance to the cyclic substitutive adduct formation with olefins was noted in the reactions of benzaldimines **159** and hydrazones **160**.

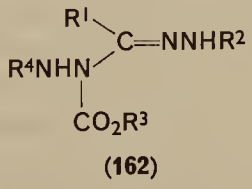


(159)



(160) (161)

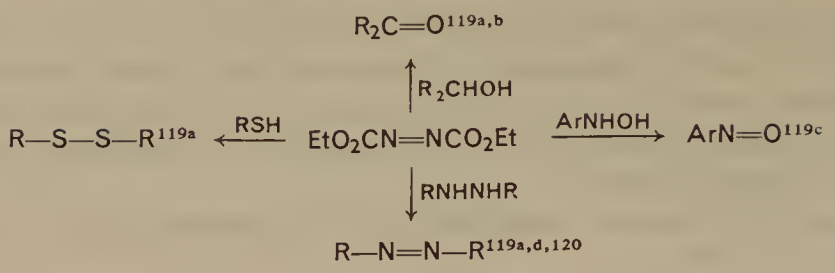
The earlier assignment of the structure of the latter adduct as **162** has been revised to **161** on the basis of spectral evidence and an independent synthesis of the hydrazines **162**[118].



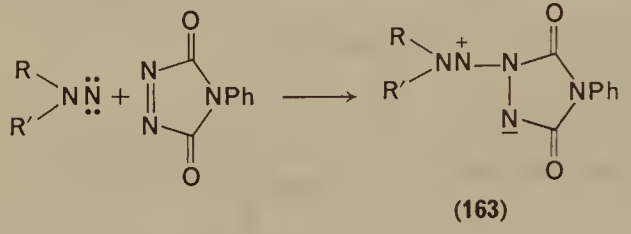
(162)

4. Oxidation with α-Azocarbonyl compounds

Although the irradiation of EAD in isopropanol had been reported to give acetone[85a], it was not until recently that these types of compounds were shown to be valuable oxidizing agents. While the radical nature of these oxidations has not been demonstrated, they are reported here for the sake of completeness[119]. Mercaptans, hydroxylamines, alcohols and hydrazines were oxidized to the corresponding disulphides, nitroso, carbonyl and



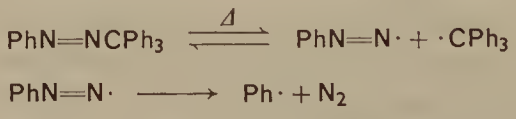
azo compounds respectively. Similarly, the long-known reaction of 1,1-disubstituted hydrazines may involve a radical process in the initial stages[120]. The presumed *N*-aminonitrenes are intercepted by the α-azo carbonyl compounds to either give rearranged products or stable amino azimine adducts (**163**)[121].



R	R′
Me	Me
Et	Et
—$(CH_2)_5$—	
$PhCH_2$	$PhCH_2$
Ph	Ph
Ph	Me

C. Radical Reactions of Azoarenes

Azobenzene is extremely stable to heat and irradiation; it does not decompose even at 600°C in the vapour phase [122] and only geometrical isomerization has been observed during ultra-violet irradiation in neutral media[123]. Although *cis*-azobenzene is not thermally stable being isomerized to the *trans*-isomer by heat[124], no decomposition has been observed. The generation of the phenyl radical may however be facilitated by replacement of one of the phenyl groups of azobenzene with more weakly bound groups such as triphenylmethyl[74,76,125].



Addition of free radicals to the central double bond of azoarenes on the other hand, is sufficiently exothermic to result in the formation of

1,2-diarylhydrazyl radicals which may be stabilized by subsequent transformations.

When azobenzene was heated with benzaldehyde in the presence of a catalytic amount of *t*-butyl peroxide, benzanilide, 1,2-diphenylbenzhydrazide and an unidentified oil were formed. Apparently a radical chain reaction is responsible for the formation of the main product[126].

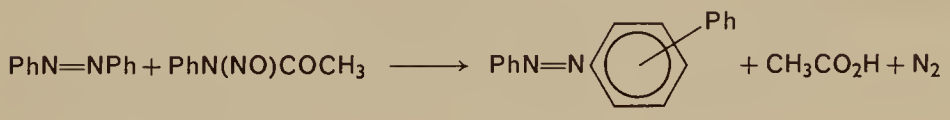
$$(t\text{-BuO})_2 \longrightarrow t\text{-BuO}\cdot$$

$$PhCHO + t\text{-BuO}\cdot \longrightarrow Ph\dot{C}O + t\text{-BuOH}$$

$$PhN{=}NPh + Ph\dot{C}O \longrightarrow Ph\dot{N}{-}NPh(COPh)$$

$$Ph\dot{N}{-}NPh(COPh) + PhCHO \longrightarrow PhNHNPh(COPh) + Ph\dot{C}O \quad (\sim 80\%)$$

A homolytic phenylation on the phenyl ring of azobenzene has been reported to be particularly facile[127]. As is shown, the phenyl ring of azobenzene is as strongly activated to radical phenylation as that of nitrobenzene.



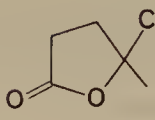
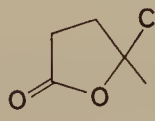
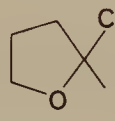
(55–60%)

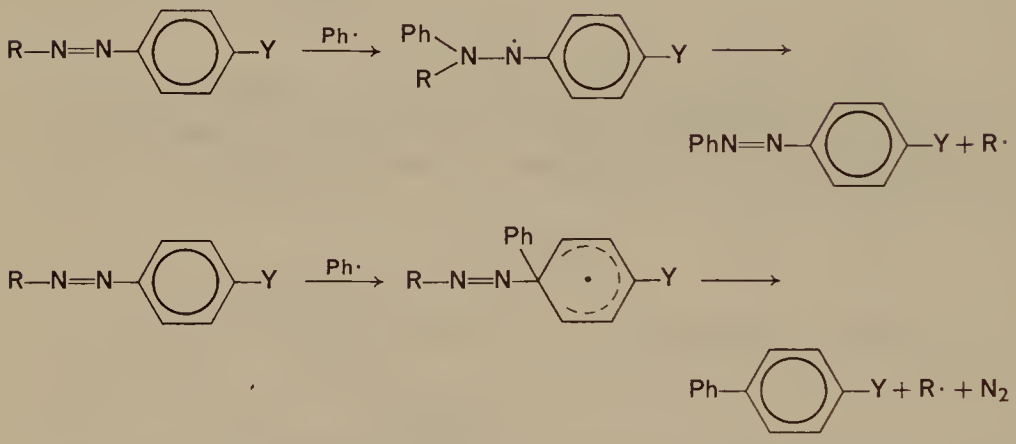
	relative rate to PhH	partial rate factors		
		o-	*m*-	*p*-
PhN=NPh	10·0	9·7	0·95	8·8
$PhNO_2$	5·0	9·4	1·2	9·1

Homolytic substitutions by phenyl radical follow somewhat different courses in γ-phenylazo-γ-valerolactone and related compounds **164**[128]. Thus, while **164** are stable in degassed benzene at 85°C, they decompose under the same conditions in the presence of excess benzoyl peroxide to give azobenzene and biphenyls. Although the formation of biphenyl in the decomposition of **164a** and **164c** was obscured by concurrent reaction of the phenyl radical with the solvent, the formation of *p*-nitrobiphenyl from **164b** clearly demonstrates a unique radical substitution in which the leaving group is an azo function. The reaction of *p*,*p*′-dinitroazobenzene with phenyl radical was also shown to produce *p*-nitrobiphenyl.

$$R{-}N{=}N{-}C_6H_4Y \xrightarrow{Ph\cdot} Ph{-}N{=}N{-}C_6H_4Y + Ph{-}C_6H_4Y$$

(164)

(a) R =  , Y = H	37%	—
(b) R =  , Y = *p*—NO_2	24%	48%
(c) R =  , Y = H	14%	—



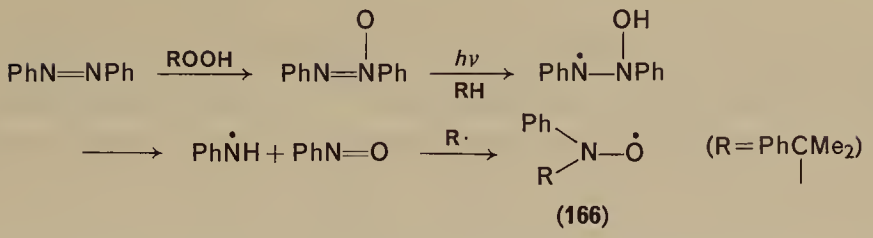
When azobenzene was irradiated in cumene, a stable e.s.r. signal was observed[129] and was attributed to a cumyl hydrazyl radical (**165**).

$$PhN{=}NPh + RH \xrightarrow{h\nu} \begin{matrix} Ph \\ R \end{matrix}\!\!>\!N{-}\dot{N}Ph \qquad (R = PhCMe_2)$$

(165)

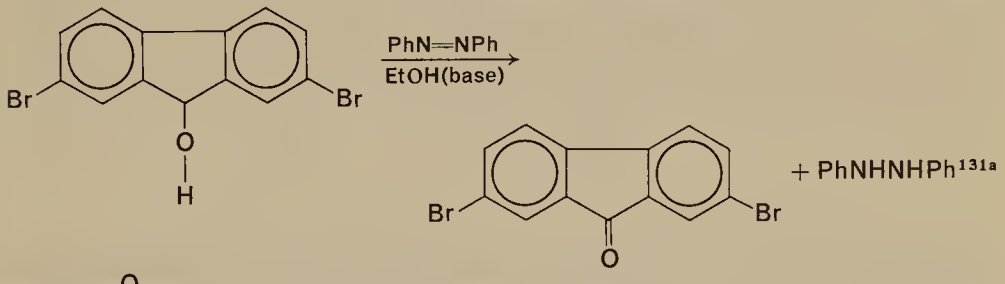
Recently this paramagnetic species has been re-investigated by Ingold[130]. The e.s.r. signal was not generated upon photolysis of azobenzene in pure cumene; instead, the same spectrum as reported appeared when (1) azobenzene in peroxide-containing cumene or (2) azoxybenzene in pure cumene was photolysed or (3) azocumene was mixed with nitrosobenzene in benzene. From this and other evidence, it was concluded that the radical formed is phenylcumyl nitroxide (**166**).

Azobenzene can be homolytically reduced by hydrogen donors to



(166)

hydrazobenzene and/or aniline. An interesting application of this well known reduction is the use of azobenzene as a preparative oxidizing agent[131].



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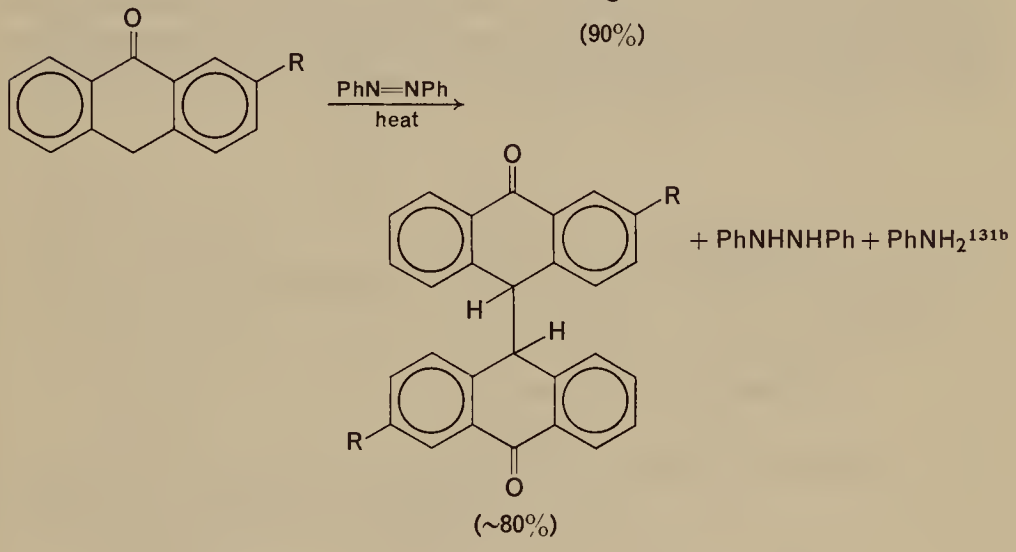

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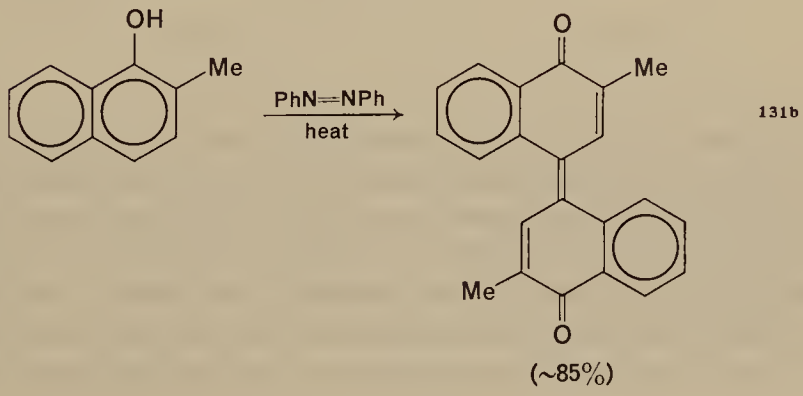
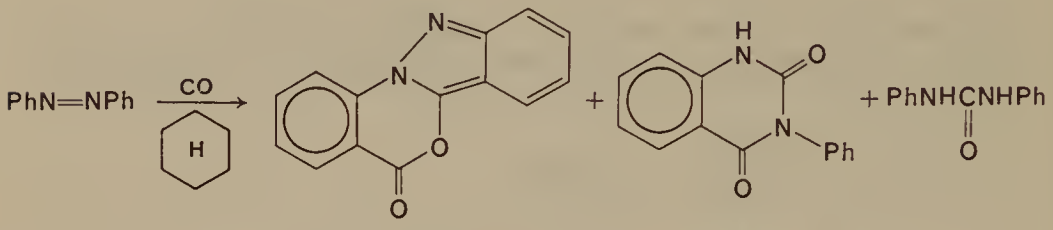


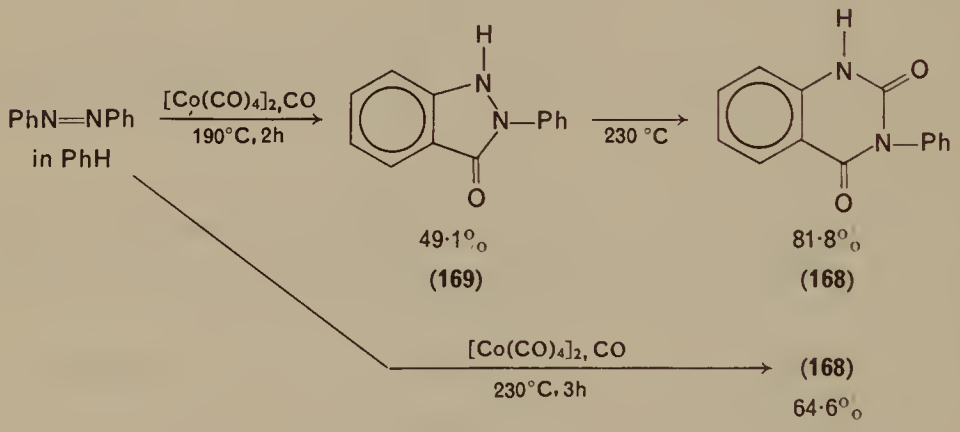
(~85%)

An oxo-reaction of azobenzene catalysed by nickel tetracarbonyl was found to give mainly a lactone (**167**) along with smaller amounts of a quinazolinedione (**168**) and diphenylurea[132]. A similar reaction catalysed by cobalt tetracarbonyl has been investigated under greater scrutiny.



(**167**) (**168**)

With an initial pressure of 150 atm of carbon monoxide, the reaction may be controlled either to give mainly the quinazolinedione (**168**) or indazolone (**169**) which is shown to be the precursor of **168**[133]. When azobenzene was



substituted with electron-donating substituents at *para*-position, a regio-specific attack of carbon monoxide on the substituted phenyl ring occurred. The lactone **167** and diphenylurea were thought to arise *via* paths different from the above reaction course; the formation of the former compound as the main product was found to be specific for the reaction catalysed by nickel tetracarbonyl and the formation of the latter was facilitated in hydrogen donating solvents with smaller amounts of cobalt tetracarbonyl[134].

III. RADICAL REACTIONS OF HYDRAZO COMPOUNDS

A. Oxidation

Hydrazo compounds are easily oxidized to the corresponding azo compounds and numerous oxidation methods have been developed in connection with the preparative aspects of azo chemistry. Although radical processes are conceivable in most of these reactions, few investigations have been carried out to elucidate the nature of the reaction.

Pratt and McGovern have studied the manganese dioxide oxidation of hydrazobenzenes in boiling benzene[135]. Little substituent effect was observed, an indication of a radical process rather than an ionic one.

$$p\text{-}RC_6H_4NHNHC_6H_4R'\text{-}p \longrightarrow p\text{-}RC_6H_4N{=}NC_6H_4R'\text{-}p$$

R	R′	Half life (min.)	R	R′	Half life (min.)
MeO	H	34	Me	Me	39
H	H	40	H	H	40
Cl	H	46	Cl	Cl	44
Me	H	55			

The mechanism was proposed as follows:

$$ArNHNHAr' + MnO_2 \longrightarrow ArNH\dot{N}Ar' + HO{-}Mn^{3+}{=}O$$
$$\longrightarrow ArN{=}NAr' + Mn^{2+}(OH)_2$$

Some of the product could result from disproportionation of the intermediate radical.

$$2ArNH\dot{N}Ar' \longrightarrow ArN{=}NAr' + ArNHNHAr'$$

The proposed mechanism of the reaction was also supported by the fact that phenylcarbinols[136] and diphenylmethanes[137] have been reported to be oxidized under similar conditions *via* homolytic processes. Furthermore, the relative reactivity of bibenzyl, *N*-benzylaniline and hydrazobenzene toward manganese dioxide oxidation was shown to parallel their reactivity toward the oxidation by diphenylpicrylhydrazyl (DPPH), which had been proved to be homolytic.

$$\underset{\textbf{(170)}}{PhCH_2CH_2Ph} \xrightarrow{MnO_2 \text{ or DPPH}} PhCH{=}CHPh$$

$$\underset{\textbf{(171)}}{PhCH_2NHPh} \longrightarrow PhCH{=}NPh$$

$$\underset{\textbf{(172)}}{PhNHNHPh} \longrightarrow PhN{=}NPh$$

Reactivity **170** $\ll$ **171** $<$ **172**

Homolytic hydrogen transfer to diphenylpicrylhydrazyl was reported to be very sluggish at 80°C with **170** as a hydrogen donor, whereas **171** was readily dehydrogenated at 40°C and **172** was converted to azobenzene almost instantaneously at room temperature[138]. The difference in reactivity between donors containing CH and NH bonds was interpreted in terms of configurational liability of nitrogen atom. The trivalent nitrogen of **171** and **172** can easily assume an sp^2 configuration in the transition state, thus resembling the configuration with the resulting intermediate radical. This resemblance, which apparently is not expected for the transition state of the CH bond dissociation, was thought to be the reason for the lower activation energy of NH bond dissociation.

This marked reactivity of NH bonds in hydrogen transfer as compared to that of CH bonds seems to be a general phenomenon as illustrated by diethyl 1,4-dihydrolutidine-3,5-dicarboxylate which was also dehydrogenated instantaneously.

2,2′-Hydrazo(2-methylpropionitrile) **173** decomposes with evolution of nitrogen when heated in various solvents in the presence of 2,2′azobis(2-methylpropionitrile) **174** or benzoyl peroxide[139]. A free-radical oxidation

$$\underset{\textbf{(173)}}{2P^{\cdot} + RNHNHR} \longrightarrow 2PH + \underset{\textbf{(174)}}{RN{=}NR}$$

$$RN{=}NR \longrightarrow 2R{\cdot} + N_2$$

$$2R^{\cdot} + RNHNHR \longrightarrow 2RH + RN{=}NR$$

P· = initiator radical R = cyanoisopropyl

of the hydrazo compound **173** to **174**, with thermal decomposition of the latter regenerating free radical species, was thought to be involved. When styrene was heated in the presence of **173**, nitrogen evolution was observed and the rate of polymerization was accelerated.

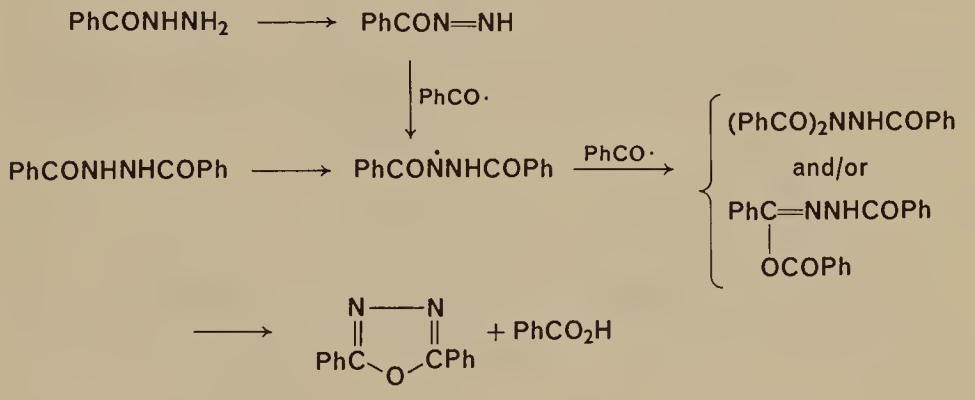
Autooxidation of hydrazobenzene in a strongly basic medium, DMSO-t-BuOK system, yielded azobenzene smoothly with the uptake of oxygen.

In 80% DMSO solution, strong e.s.r. signal assigned[140] to the radical anion **176** of azobenzene, was observed. A reaction mechanism proceeding *via* dianion **175** which was oxidized stepwise to the product, was proposed[141].

$$\mathrm{PhNHNHPh} \xrightarrow{2\text{t-BuO}^-} \underset{(175)}{\mathrm{PhN{-}^{-}N{-}^{-}Ph}} \xrightarrow{O_2} \underset{(176)}{\mathrm{PhN{-}^{-}\dot{N}Ph}} \xrightarrow{O_2} \mathrm{PhN{=}NPh}$$

The behaviour of the benzoyl radical generated by silver oxide oxidation of benzoylhydrazide and *N*,*N'*-dibenzoylhydrazine was compared with that generated from thermal and photolytic decomposition of benzoyldiimide. Oxidation of the hydrazines gave substantial amounts of 2,5-diphenyl-1,3,4-oxadiazole and benzoic acid which were also formed from thermal and photolytic reactions of the diimide. Unlike the photolytic decomposition, the radical dimerization product, benzil, was not detected.

The reaction was explained by a specific coupling of the benzoyl radical with the dibenzoylhydrazyl radical which was formed either by oxidation of 1,2-dibenzoylhydrazine or by addition of the benzoyl radical to benzoyl diimide[142].



In connection with the above oxidation, *N*-aryl-*N'*-arenesulphonylhydrazines were obtained in fair to excellent yields by oxidizing benzene solutions of arylhydrazines with stoichiometric amounts of silver oxide in the presence of SO_2[143]. No incorporation of solvent molecules took place.

$$\mathrm{ArNHNH_2} \longrightarrow \mathrm{ArNH\dot{N}H} \longrightarrow \mathrm{ArN{=}NH} \longrightarrow \mathrm{Ar\cdot + N_2 + H\cdot}$$

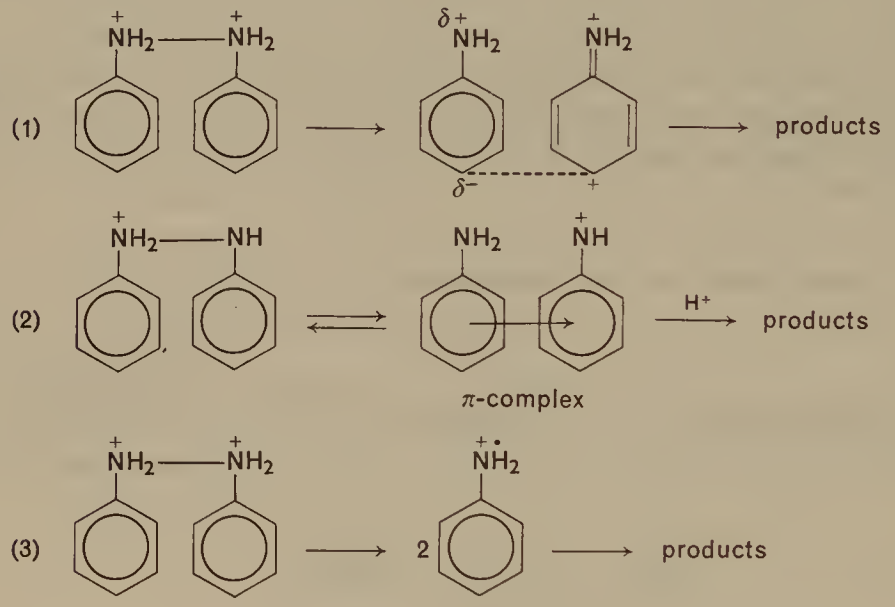
$$\mathrm{ArNH\dot{N}H + SO_2 + Ar\cdot} \longrightarrow \mathrm{ArNHNHSO_2Ar}$$

The reaction seems to be of some preparative importance because of its general applicability.

A mechanism of similar nature was also suggested for the anomalous formation of *N*-phenyl-*N*-benzenesulphonylhydrazine from reaction of phenylhydrazine and dimethylsulphamyl chloride[144].

B. The Benzidine Rearrangement

The mechanism of the benzidine rearrangement has long been the subject of controversy which seems not to be completely settled at this time. The rearrangement has been viewed to proceed *via* (1) a polar transition state, (2) a π-complex or (3) a radical mechanism.



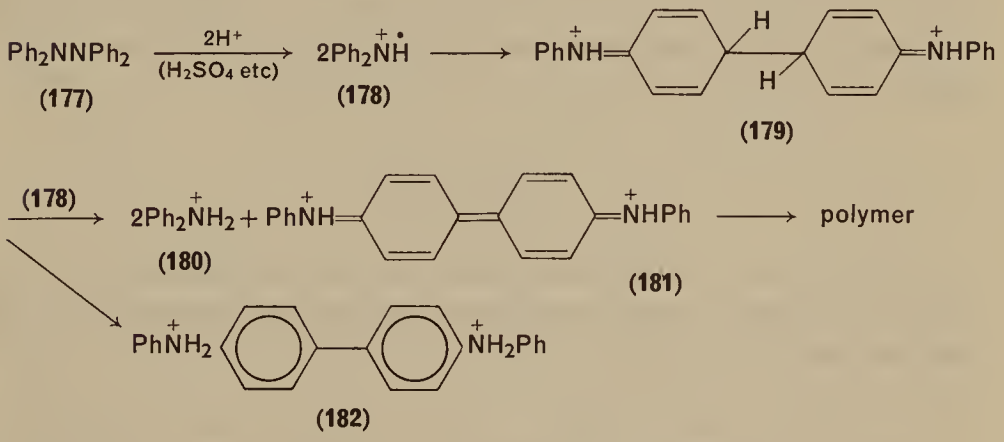
Of these, the polar transition theory has received the strongest experimental support, *inter alia*, the intramolecular character of the reaction. Yet, the oldest one, the radical mechanism, continues to retain some consideration with occasional modifications of its original form (3). The reader is referred to pertinent chapters in this series and other reviews for the complete view of the present situation on the subject[145–148].

In 1903, Tichwinsky suggested that the benzidine rearrangement involved dissociation of the hydrazo compound to give radicals, followed by various coupling reactions of the radicals. This argument was supported by the

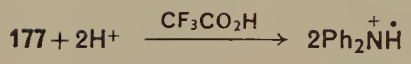
formation of benzidines from the electrochemical or lead dioxide oxidation of aromatic amines[149–151].

Later, an accumulation of data on the intramolecularity of the rearrangement have led to rejection of the radical mechanism for two reasons. First, if radicals are formed, cross-coupling products would be expected when a mixture of hydrazines was subjected to rearrangement, because it is unlikely that cation radicals of like-charge would remain in their original solvent cage without diffusion. The second difficulty is that the radical mechanism cannot accommodate the one-proton mechanism. Although homolysis could easily be induced owing to the repulsion of adjacent charges in the two-proton mechanism, the transition state in the one-proton mechanism would have little such tendency. These arguments, on the one hand, and the following facts, on the other, have rendered the subject still of deep interest and controversy.

Chemical and physico-chemical evidence suggests a radical dissociation mechanism in the case of tetraphenylhydrazine. Thus, the formation of polymeric product and diphenylamine along with the corresponding benzidine on the rearrangement of tetraphenylhydrazine **177** was attributed to the attack of cation radical **178** on the primary product **179**[152].



Recently a cation radical **183** as an intermediate of the rearrangement of **177**, was identified by u.v., e.s.r. and voltammetry comparisons of the reaction solution with an electrochemically oxidized solution of **177**. The cation radical was shown to rearrange to **182** *via* the dication **181**. Although the oxidation and reduction processes (**183** → **181** → **182**) remain unexplained, the safest assumption to account for the formation of **183** was an electron transfer between **177** and the cation radical **178**.



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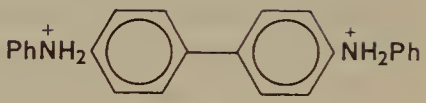
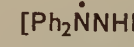


(182)

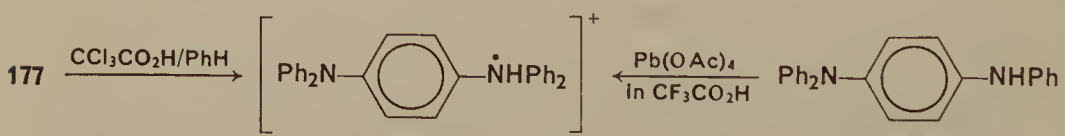
The mechanism differs from the 'in-cage' radical mechanism previously considered for the rearrangement of hydrazoarenes and it was suggested that the difference lies in the stability of cation radicals corresponding to **178** and is not of an essential nature[153].

There had been observed yet another radical species in the tetraphenylhydrazine–acid system. Instead of the violet colouration of **183** obtained in a trifluoroacetic acid (or TFA–methylene chloride) solution of tetraphenylhydrazine, a green colour was observed in trichloroacetic acid–benzene solution; this dual colouration had been attributed to **183** and **184**, respectively, in an earlier study by Russian chemists[154].



(184)

Later, the species in the latter green solution was identified as **185** by comparison of its u.v. and e.s.r. spectra with those of oxidized solution of semidine **186**[155].

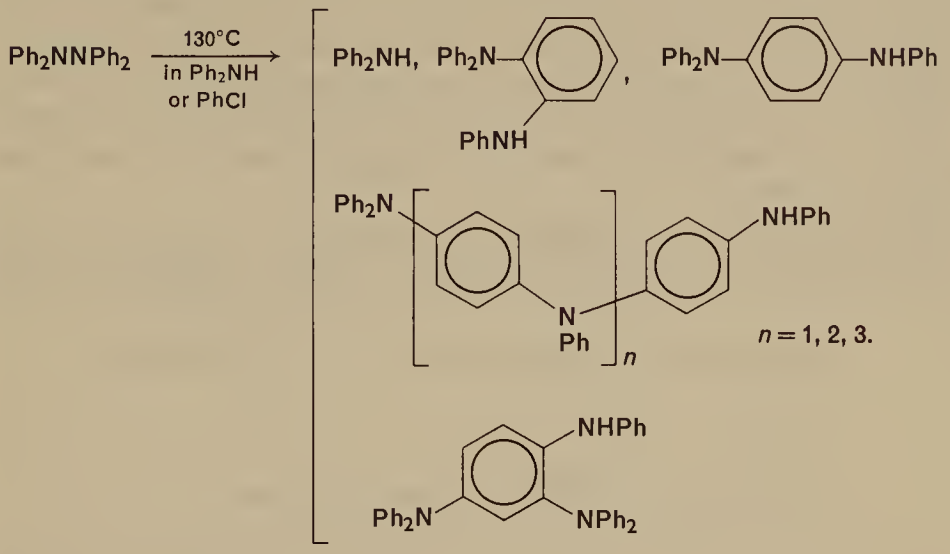


(185) (186)

The role or fate of this species in the benzidine rearrangement is not clear.

A thermal uncatalysed rearrangement of tetraphenylhydrazine was reported to give a complex mixture of products. The radical description

involving an initial homolysis of the N—N bond for the reaction seems to be a reasonable postulate in view of its complexity[156].

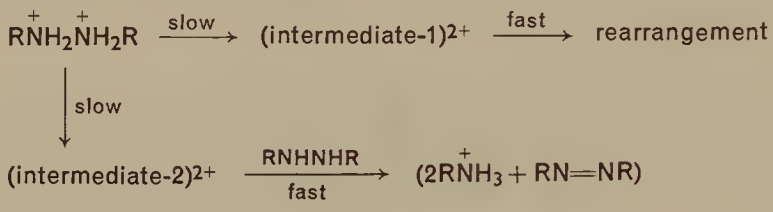


No convincing evidence for the intermediacy of radical species has so far been presented in the case of rearrangement of hydrazoarenes. The decreased stability of the monoarylaminyl radicals compared to that of diarylaminyl might not permit their detection by conventional methods.

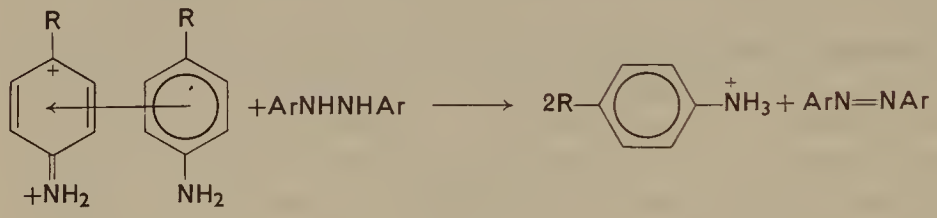
When 4,4′-divinylhydrazobenzene was subjected to acid catalysed rearrangement in aqueous alcohol, a polymeric product, likely to be polyvinylaniline, was obtained[157]. The result has been viewed[146] as involving an initial homolytic fission to give an aminyl radical conjugated with the vinyl group. 4,4′-Dimethylhydrazobenzene gave 2-amino-4′,5-dimethyldiphenylamine (an *o*-semidine), *p*-azotoluene, and *p*-toluidine as the main products on acid rearrangement. Some radical species was suspected to be involved because an added Wurster base was oxidized to a Wurster radical cation during the rearrangement reaction[158]. Suggested candidates for the oxidant are *p*-CH_3—$C_6H_4\dot{N}H$ and *p*-$CH_3C_6H_4\dot{N}H_2^+$. As evident in the case of 4,4′-dimethylhydrazobenzene, the benzidine rearrangement is generally accompanied by a disproportionation reaction to varying extents. Since the same kinetics were observed for both the rearrangement and the disproportionation, a common rate-determining step was assumed for both reactions. Thus, as has been true for the rearrangement, no general agreement has yet been reached for the mechanism for the disproportionation[146,147]. There are several points of interest: (1) The ratio of rearrangement to disproportionation seems to be

independent of both substrate and acid concentrations[159,160]; (2) in hydrazoarenes substituted at both the 4- and 4′-positions, disproportionation predominates; even in 4-substituted hydrazoarenes, the extent of disproportionation sometimes exceeds that of rearrangement[158,159–161]; (3) the oxidation–reduction process is intermolecular, yet no crossed azo product nor solvent trapped product has been observed[158,159]; (4) some oxidizing species is present in the reaction mixture[158]; (5) efforts to adduce evidence for the intermediacy of radical species have not been successful[158,162–164].

The oxidation–reduction was discussed in terms of a π-complex or radical pair mechanism by Shine and Stanley[159]. Here, intermediate-1 was



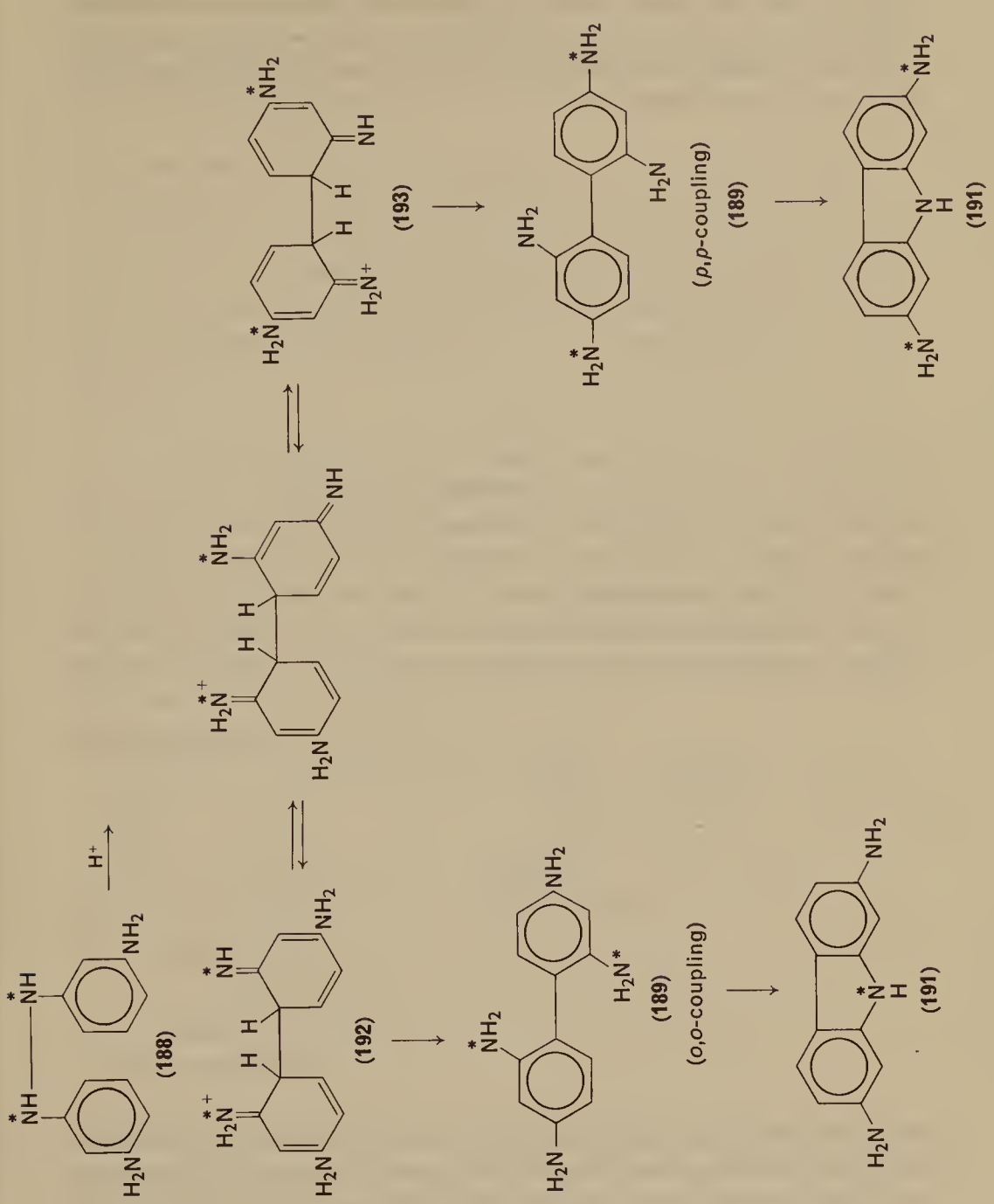
visualized for the polar transition route, while intermediate-2 was suggested to be a pair of cation radicals or a modified π-complex such as **187**.



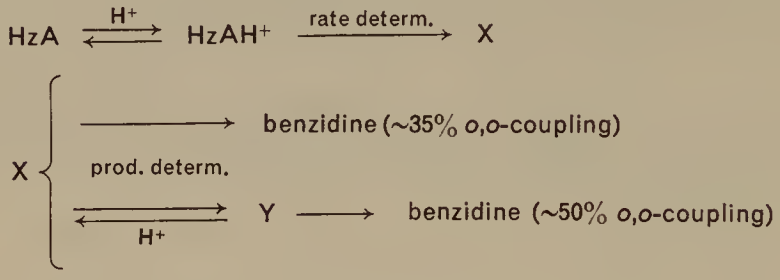
(187)

The most serious drawback to the radical mechanism is that one must postulate that most of the cation radicals diffused out of the cage (in the case of 4,4′disubstituted hydrazoarenes) and yet were deactivated only *via* reduction by the parent hydrazine.

An acid-catalysed rearrangement of 3,3′-diaminohydrazobenzene (HzA, **188**) isotopically labelled at two hydrazo-nitrogens was studied by Clovis and Hammond[165]. The rearrangement was first order in the proton concentration and gave 2,2′-diaminobenzidine (**189**) as the sole isolable product; **189** was subsequently converted to 2,7-diaminocarbazole (**190**) for analysis of the isotope content. If the reaction had proceeded by *p,p*-coupling, the resulting diaminocarbazole would retain all of ^{15}N initially labelled, and *o,o*-coupling would lead to conservation of 50% of

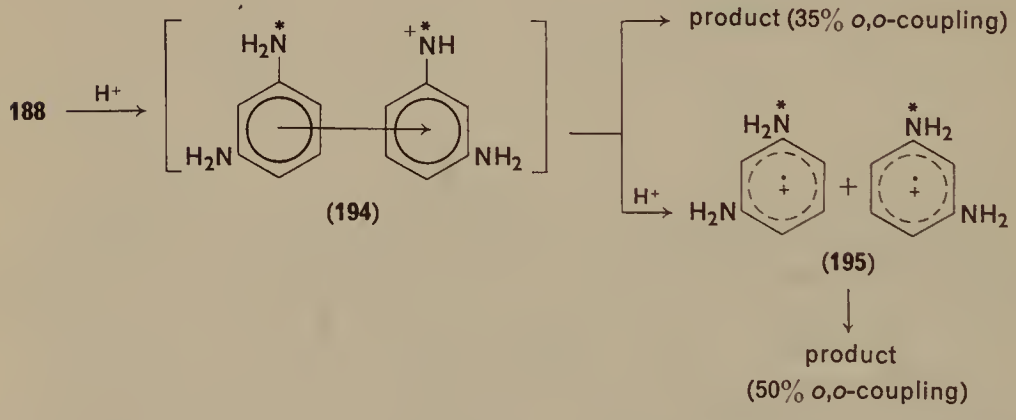

(188)
(192)
(193)
(189)
(o,o-coupling)
(189)
(p,p-coupling)
(191)
(191)

^{15}N in the carbazole. Interestingly, the percentage of *o,o*-coupling was found to be dependent on the acid concentration, ranging from a minimum value of 35% *o,o*-coupling at zero free proton concentration to a maximum of 50% *o,o*-coupling at very high acid concentration. This suggested a dual path in the product-determining step. (The *o,p*-coupling value could not



be estimated from the data. Therefore, both values referred to as *o,o*-coupling include also the *o,p*-coupling value; however, this does not alter the essential point of the argument.) The polar transition theory predicts a maximum of 50% of *p,p*-coupling, that is at best **192** and **193** are equivalent. The observed maximum of 65% does not conform to this.

A more plausible explanation was given in terms of a modified π-complex scheme involving a concurrent radical pathway, If, in the



π-complex **194**, 20% of the *ortho* carbon atoms and 80% of the *para* carbon atoms of the unsymmetrical ring attacked equally the *ortho* and *para* carbon atoms of the symmetrical ring, the observed requirement of 35% *o,o*-coupling would be satisfied. Addition of a proton to **194** would result in the formation of a pair of cation radicals **195** which would lead to complete randomization.

Although this rationalization has many questionable points—e.g. the unsymmetrical π-complex **194** might in fact be symmetrical because of fast proton transfer from $—NH_2$ to $—\overset{+}{\underset{\bullet}{N}}H$ groups—it is hard to visualize any alternative explanation.

C. Uncatalysed Thermal Reactions

Hydrazobenzenes were reported to undergo disproportionation reaction upon heating or irradiation of their solution. The thermal reaction was found to be of first order and aryl nitrenes, formed either directly or *via* the radical (Ar—$\dot{N}$H) were suggested to be intermediates. Another theory depicted the reaction in terms of an intermolecular oxidation-reduction without rupture of the N—N bond since no symmetrical azobenzenes were obtained in the thermolysis of 4-methylhydrazobenzene[166]. A first-order

$$ArNHNHAr \longrightarrow ArN{=}NAr + 2H\cdot$$

$$ArNHNHAr + 2H\cdot \longrightarrow 2ArNH_2$$

rate would be expected if the former step is the rate-determining one. Subsequently, the latter view was supported by an isotope labelling experiment[167]. No randomization was observed during the thermal disproportionation of hydrazobenzene-^{15}N in ethanol; the same results were obtained from photolytic disproportionation[168].

Considering the kinetic data obtained by Stieglitz and Curme[166a,b], the following scheme was proposed for both reactions[146].

$$PhNHNHPh \longrightarrow PhNH\dot{N}Ph + H\cdot$$

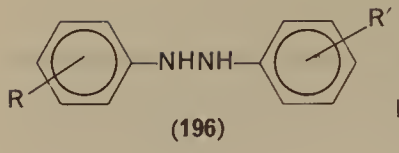
$$\text{or } 2Ph\dot{N}H$$

$$PhNH\dot{N}Ph \longrightarrow PhN{=}NPh + H\cdot$$

$$PhNHNHPh + H\cdot \longrightarrow PhNH_2 + Ph\dot{N}H$$

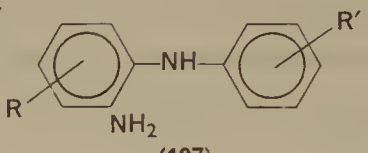
$$PhNHNHPh + Ph\dot{N}H \longrightarrow PhNH_2 + PhNH\dot{N}Ph$$

Concurrent rearrangements to an unspecified degree were detected during thermolysis of hydrazobenzenes[169]. The detected products were the corresponding *o*- and *p*-semidines, **197** and **198** from **196a–c** and 4,4′- and 2,2′-semidines from 1,1′-hydrazonaphthalene. A homolytic fission of the N—N bond to produce a pair of radicals was presumed to be the main process for the rearrangement. The recombination of the paired radicals



(196)

(a) R = R′ = H
(b) R = R′ = 2—CH_3
(c) R = H, R′ = 4—CH_3



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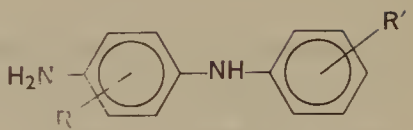


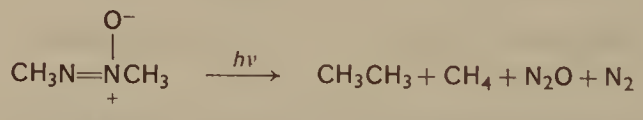
(198)

was shown to occur exclusively within the original solvent cage in which it was formed since no intermolecular products were detected in the rearrangement of **196c**.

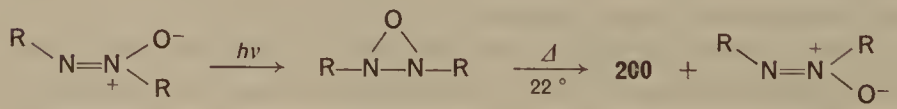
IV. RADICAL REACTIONS OF AZOXY COMPOUNDS

Despite the fact that azoxy compounds have been known since the nineteenth century, relatively little of their chemistry has been investigated[170]. Interest in azoxy compounds has centred on their structure and the existence of isomers. Only recently has our knowledge of this type of compounds been extended to aliphatic analogues, presumably because of the biological activity of naturally occurring azoxyalkanes.

In contrast to azoalkanes which lose nitrogen upon thermolysis, a comparable loss of nitrous oxide is apparently not favoured. This remarkable difference (also observed in their mass spectra[171]) has been rationalized in terms of molecular orbital arguments which suggest that the extrusion of nitrous oxide is at least partly forbidden[172]. Even though it has been reported that the photolysis of azoxymethane (**199**) produces nitrous oxide[173], recent investigations[174] indicate that photolysis can lead to oxaziridines (**201**); the use of preparative photolysis resulting in

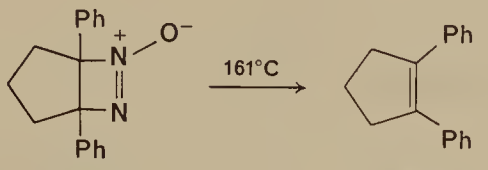


(199)



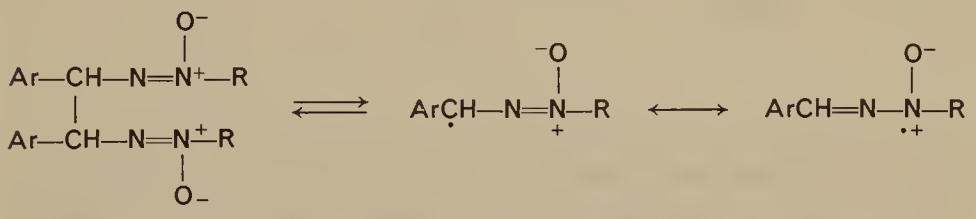
(200) (201) (202)

oxygen migration and isomerization[174,175] is a further indication of the unusual stability of azoxy compounds. Indeed it has been suggested that labile azo compounds be stored as their *N*-oxide derivatives[172]. The bicyclic *cis*-azoxy compound **203** does lose nitrous oxide to yield 1,2-diphenyl-1-cyclopentene (**204**) upon thermolysis although the radical nature of this reaction has not been established[175,176].



(203) **(204)**

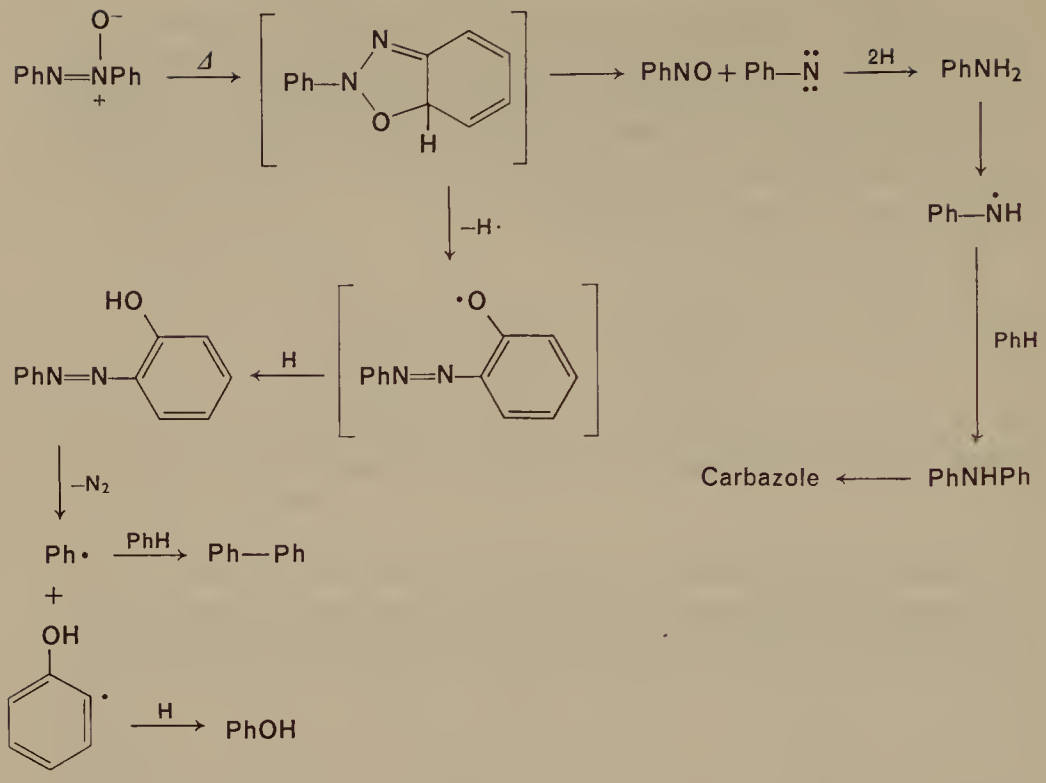
Woodward and Wintner[176] have shown that isomerization (*dl* ⇌ *meso*) of **205** proceeds *via* radical **206**. The pyrolysis of azoxybenzene which had been reported to yield aniline, azobenzene (and nitrosobenzene)[177], was



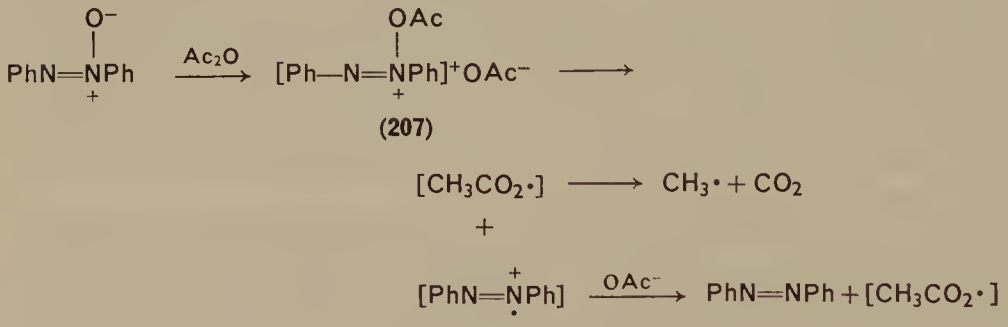
(205) **(206)**

reinvestigated[178]; at 600°C in benzene, biphenyl (34%), aniline (30%), phenol (15%) and diphenylamine (10%) were the major products. The scheme below was suggested to account for these products. In cyclohexane, phenol (31%) and aniline (37%) were the major constituents while biphenyl (9%) and diphenylamine (7%) decreased markedly; this is consistent with the proposed scheme[181].

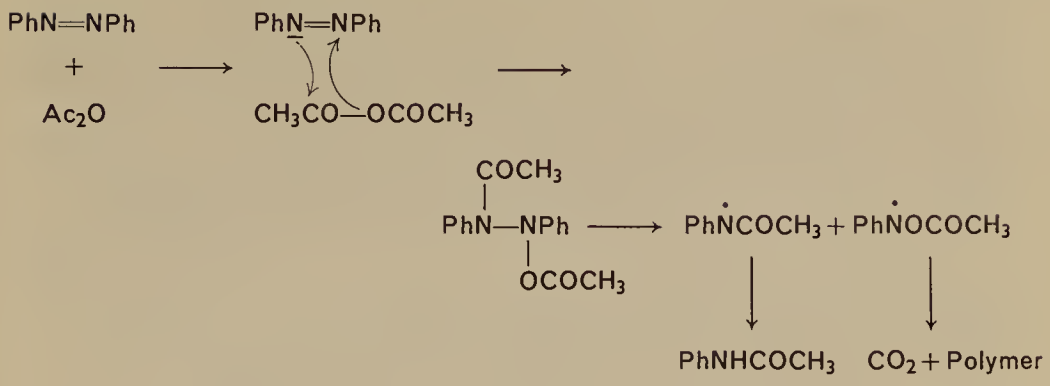
The reaction of azoxybenzene with acetic anhydride gave azobenzene, acetic acid and acetanilide in addition to carbon dioxide, carbon monoxide and methane[179]. The surprising formation of acetanilide along with carbon dioxide and methane could be rationalized in terms of a radical breakdown of the initial salt **207** to the radical cation of azobenzene thence to azobenzene. Acetanilide was formed in good yield from azobenzene and acetic anhydride in independent experiments which also showed that



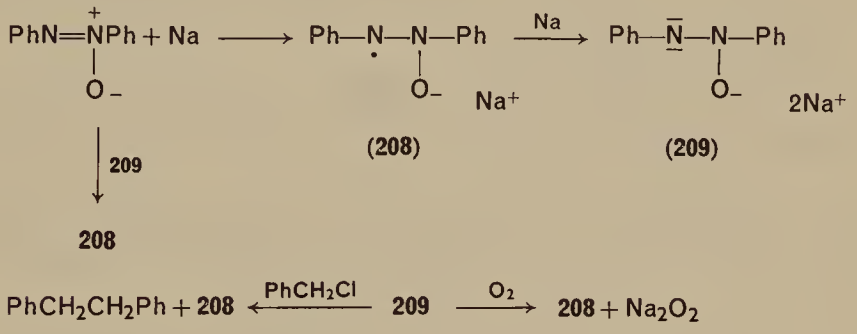
radical scavengers had a deleterious effect on the yield of acetanilide. The following path was suggested for the reaction[179]. In contrast, a similar reaction of azoxybenzene with arylsulphonyl chloride[180] resulted in a Wallach-type rearrangement[181]. The reaction seems best explained *via* ionic processes.



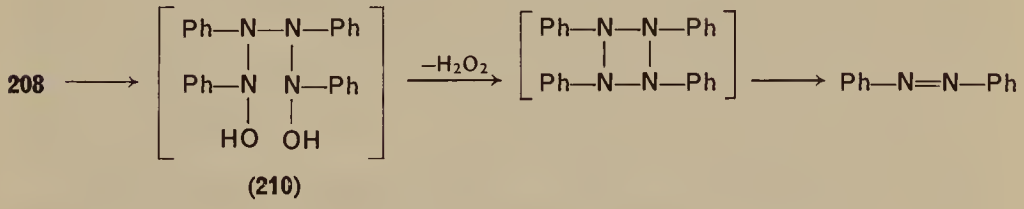
Lastly, the action of alkali metals on *cis*- and *trans*-azoxybenzene gives a deep-blue colour initially which changes to a reddish brown[182]. The deep blue colour was shown to be due to the anion radical **208** by e.s.r. and the



reddish brown colour to **209**. The radical anion **208** could also be obtained by the action of oxygen, benzyl chloride or azoxybenzene on **209**. With



water, **208** gave azobenzene and hydrogen peroxide, perhaps *via* dimer **210**.



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CHAPTER 20

The photochemistry of the hydrazo, azo and azoxy groups

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I. THE HYDRAZO GROUP

A. Aliphatic Hydrazo Compounds

There appears to have been no recent work on the photochemistry of aliphatic hydrazo compounds. A study of the photolysis of 1,2-dimethyl-

hydrazine (**1**) vapour was reported by Kay and Taylor[1] in 1942. The overall reaction is given in equation 1.

$$\underset{(1)}{3\ MeNHNHMe} \xrightarrow{h\nu} H_2 + N_2 + CH_4 + NH_3 + MeNH_2 + (MeN{=}CH_2)_2 \quad (1)$$

The starting material (**1**) was reported[1] to have an absorption continuum from 280 nm to beyond 200 nm with a maximum at 245 nm (ε ca. 1000 l/mol-cm) so that irradiation at 254 nm was very suitable. Variation of the wavelength of irradiation had little effect, except that at 190 nm both ammonia and methylamine decomposed. The overall quantum yield for the decomposition of the dimethylhydrazine (**1**) was about 0·3.

From the presence of hydrogen and methane, with a trace of ethane, it was suggested that hydrogen atoms and methyl radicals were present. These species could have arisen from the alternative primary processes given in equations 2 and 3.

$$MeNHNHMe + h\nu \longrightarrow \begin{cases} H\cdot + R\cdot & (2) \\ CH_3\cdot + R'\cdot & (3) \\ 2\ MeNH\cdot & (4) \end{cases}$$

The nature of the radicals R· and R′· were not specified, but by analogy with the photolysis of hydrazine[2] at 206·2 nm, where N—H bond cleavage occurs as the primary process with a quantum yield of 0·97, R· probably has the structure **2** and R′· structure **3**.

$$\underset{(2)}{MeN\cdot NHMe} \qquad \underset{(3)}{MeNHNH\cdot}$$

Subsequent reactions of the radicals were presumed to give rise to the observed products. The dissociation shown in equation 4 was not considered to be a major process as it was thought that methylamine would then become the major product. Clearly the photochemistry of 1,2-dimethylhydrazine (**1**) and of other aliphatic hydrazo compounds should be given further study.

B. Aromatic Hydrazo Compounds

The photochemistry of aromatic hydrazo compounds depends very much on the substituents attached to the hydrazo group. Three main

types of reaction can be identified, namely N—N bond fission, disproportionation and rearrangement.

1. Photolysis giving N—N bond fission

The photolysis of tetraphenylhydrazine[3] appears to lead solely to diphenylamino radicals in solution and in a rigid matrix at 77 K. Several

$$Ph_2NNPh_2 \xrightarrow{h\nu} 2\,Ph_2N\cdot \qquad (5)$$

e.s.r. studies of the radicals have been made at 77 K[3–6]. Grinberg and coworkers[4] showed that the dissociation occurred from an n, π^* excited state, by using linearly polarized light.

In a similar manner, triphenylhydrazine gave radicals on photolysis at 77 K (equation 6). When the radical products shown in equations 5 and 6,

$$Ph_2NNHPh \xrightarrow{h\nu} Ph_2N\cdot + PhNH\cdot \qquad (6)$$

formed at 77 K, were warmed to 'melt' the rigid matrix, the radical pairs recombined to form the original starting material [6].

In some early work on the photolysis of hydrazobenzene, Weiss[7] proposed that the primary process was dissociation of the N—N bond. This is not supported by more recent work as discussed in Section 2 below.

2. Photochemical disproportionation

The major photoproducts of hydrazoarenes are the corresponding azo compounds and fission amines[7–11] (equation 7). These products have been

$$Ar^1NHNHAr^2 \xrightarrow{h\nu} Ar^1N{=}NAr^2 + Ar^1NH_2 + Ar^2NH_2 \qquad (7)$$

reported from the photolysis of hydrazobenzene[7–9] and several of its *p*-substituted derivatives[10,11], and from phenylhydrazo-2-naphthalene and 1,1′-hydrazonaphthalene[11]. The yield of azo compound was found to be greater than expected on the basis of simple disproportionation.

It was suggested[7] that homolytic fission of the N—N bond occurred in the initial step, but this has been shown to be incorrect. No appropriate e.s.r. signals were found when hydrazobenzene was photolysed in a rigid matrix at 77 K[6]. Furthermore, on warming the irradiated mixture to a fluid state, hydrazobenzene was not reconstituted, in contrast to tetraphenylhydrazine, for example[6]. Also when using ^{15}N-labelled hydrazo compounds, no scrambling of the tracer was found in the products[8] and no isotope

effect was found when unchanged hydrazo compound was isolated either at the beginning or near the end of the photolysis[11]. Similarly, irradiation of 4-chlorohydrazobenzene or 4-methoxyhydrazobenzene did not produce any detectable disubstituted or unsubstituted azobenzene[9].

It is now generally accepted that the initial photochemical event is the homolysis of an N—H bond to produce a hydrazyl radical (**4**) (equation 8)[9,11,12].

$$\mathrm{PhNHNHPh} \xrightarrow{h\nu} \underset{(4)}{\mathrm{PhN{\cdot}NHPh}} + \mathrm{H{\cdot}} \qquad (8)$$

Hashimoto and co-workers[9] have proposed the following steps in the mechanism subsequent to the formation of the hydrazyl radical (**4**):

$$\left.\begin{matrix}\mathrm{PhN{\cdot}NHPh}\\ \mathrm{PhNHN{\cdot}Ph}\end{matrix}\right] \longrightarrow \begin{matrix}\mathrm{PhN{=}NPh}\\ \mathrm{PhNHNHPh}\end{matrix} \qquad (9)$$

$$2\mathrm{H{\cdot}} \longrightarrow \mathrm{H_2} \qquad (10)$$

$$\mathrm{PhNHNHPh} + 2\mathrm{H{\cdot}} \longrightarrow 2\,\mathrm{PhNH_2} \qquad (11)$$

This scheme explains the excess of azo compound over amine and also the formation of molecular hydrogen[9].

In a more thorough study of the mechanism, Shizuka and co-workers[12] found that piperylene, a good triplet quencher, had no effect on the quantum yield of formation of azobenzene from hydrazobenzene. This suggested that dissociation of the N—H bond originated from the lowest excited singlet state of hydrazobenzene. Strangely a negligible yield (<0·5%) of aniline was found in their experiments[12]. They proposed that azobenzene was formed by the processes of equations 8 and 9; the latter reaction was considered to be diffusion-controlled. Formation of hydrogen was more reasonably thought to involve the solvent (e.g. cyclohexane, equation 12).

$$\mathrm{C_6H_{12}} + \mathrm{H{\cdot}} \longrightarrow \mathrm{C_6H_{11}{\cdot}} + \mathrm{H_2} \qquad (12)$$

In the absence of oxygen the quantum yield for formation of azobenzene was independent of the concentration of hydrazobenzene, the light intensity or the wavelength of irradiation (254 or 280 nm), and was found to have a value of 0·07. However, in the presence of oxygen the quantum yield was very much greater and decreased as the light intensity increased. A chain

$$\mathrm{PhN{\cdot}NHPh} + \mathrm{O_2} \longrightarrow \mathrm{PhN{=}NPh} + \mathrm{HO_2{\cdot}} \qquad (13)$$

$$\mathrm{PhNHNHPh} + \mathrm{HO_2{\cdot}} \longrightarrow \mathrm{PhN{\cdot}NHPh} + \mathrm{H_2O_2} \qquad (14)$$

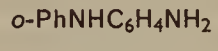
reaction was proposed to explain the results and was found to agree with the kinetic data. Hydrogen peroxide was in fact detected in the reaction mixture.

Concerning the primary processes of the photolysis Shizuka and co-workers[12] argue for a predissociative intersystem crossing $S_1(\pi, \pi^*) \rightarrow {}^3\sigma_0$(N—H) involving cleavage of the N—H bond of hydrazobenzene by analogy with β-bond fission in other benzene derivatives[13,14]. Such a transition would be spin forbidden[14] but this may explain the moderately low quantum yield for the dissociative step (equation 8). Shine and co-workers have shown that the lowest excited singlet state of hydrazobenzene and 2,2′-hydrazonaphthalene is a π,π^* state[15].

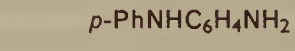
Shine and Cheng[16] report unpublished work by Baldwin and Harris which indicates that the dehydrogenation of hydrazobenzene to azobenzene is almost quantitative at 290 nm, whereas some scission to amines occurs at 250 nm. It is difficult to explain, however, the negligible yield of aniline obtained by Shizuka[12] when irradiating at 254 nm.

3. The photobenzidine rearrangement

The acid-catalysed rearrangement of hydrazobenzene is well known (Chapter 18) but irradiation of hydrazoarenes has been shown to give mainly the azo compound and amines, with only very small amounts of rearrangement products[9–11]. From hydrazobenzene, *o*-semidine (**5**) and *p*-semidine (**6**) were each found in 0·25% yield[9] and a trace of semidines was found after irradiation of 4-methoxyhydrazobenzene[10]. Banthorpe[11] reported less than 0·2% rearrangement products from a number of hydrazoarenes, including 1,1′-hydrazonaphthalene[11].



(5)

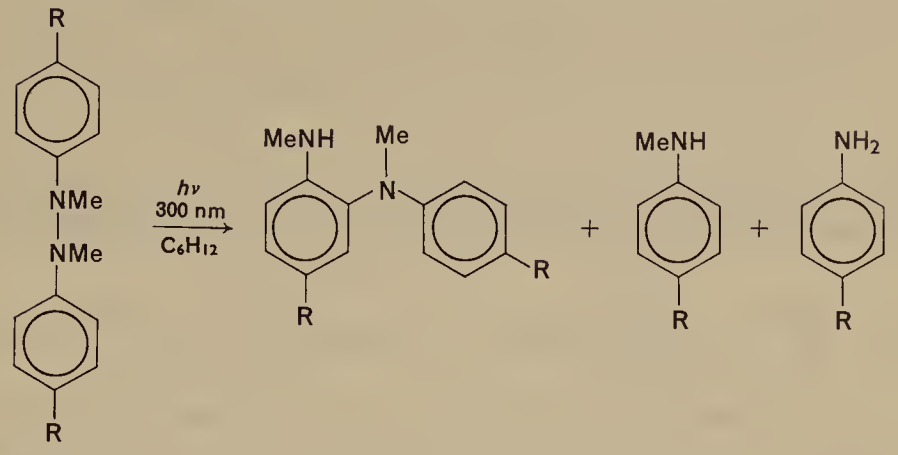


(6)

In contrast, *N*,*N*′-dimethylhydrazobenzenes undergo a photobenzidine rearrangement[16,17] (equations 15–18).

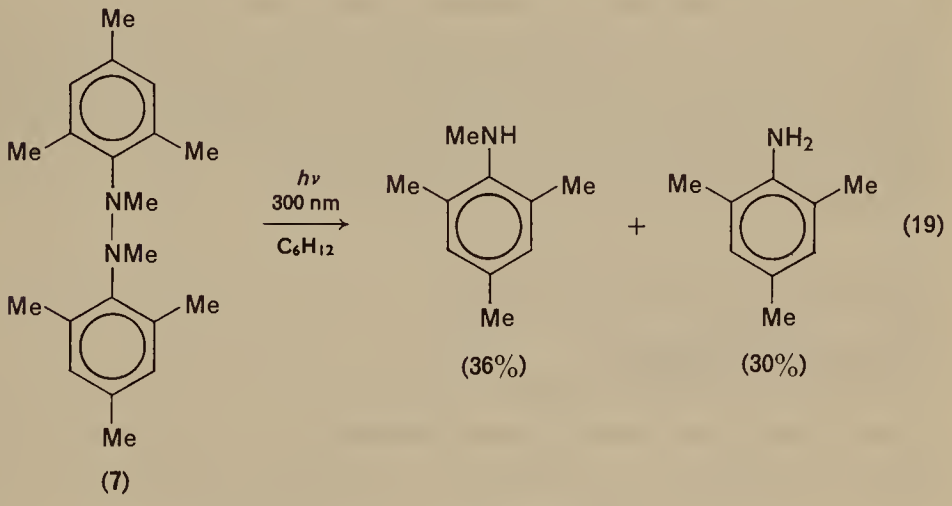
N,*N*′-Dimethylhydrazomesitylene (**7**) was also irradiated but it was unable to rearrange. Irradiations were carried out at 300 nm in hexane (equation 15) or cyclohexane (equations 16–19). No data on the mechanism of the rearrangements was given but it has been suggested that *N*-methylarylamino radicals could be formed as precursors to the fission products[16]. Whether or not these same radicals are involved in the rearrangement is not known.

$$PhNMeNMePh \xrightarrow[\text{hexane}]{h\nu,\ 300\ nm} PhNHMe\ (24\%) + p\text{-}Me_2NC_6H_4NHPh\ (46\%) \qquad (15)$$



R = Me	19%	+*	–	(16)
R = OMe	65%	11%	–	(17)
R = Ph	24%	35%	+*	(18)

Svanholm and Parker[18] have reported a novel photobenzidine rearrangement of a cation radical. Whereas tetraphenylhydrazine absorbs light at

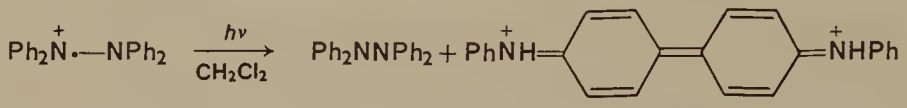


(7)

295 nm and dissociates into diphenylamino radicals (Section I, B, 1 above), the tetraphenylhydrazine cation radical (**8**, λ_{max} 465 nm) rearranges when irradiated in quartz or Pyrex vessels to give an equimolar mixture of tetra-

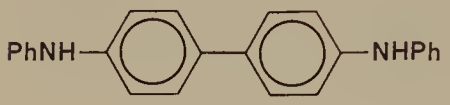
*Yield not determined

phenylhydrazine and the oxidized form of *N,N'*-diphenylbenzidine (**9**), from which *N,N'*-diphenylbenzidine (**10**) was obtained on treatment with

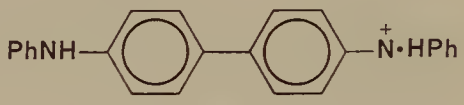


(8) (9) (20)

base. It was suggested that excitation of **8** results in a unimolecular rearrangement to **11**. The nature of the subsequent steps was ambiguous.



(10)



(11)

II. AZO COMPOUNDS

There is a marked difference in the photochemical behaviour of aliphatic and aromatic azo compounds. Aliphatic azo compounds usually undergo photodissociation to give free radicals and nitrogen, whereas aromatic azo compounds are stable towards C—N bond fission. Both types may undergo *cis–trans* photoisomerization, although this is not always readily observable. Certain aromatic azo compounds have been found to undergo photochemical cyclodehydrogenation. Mixed aliphatic–aromatic azo compounds more closely resemble the purely aliphatic series in their photochemical behaviour. Some differences in the photochemistry of cyclic and acyclic azoalkanes justifies their treatment separately.

A. Acyclic Aliphatic Azo Compounds

1. General introduction

The photochemistry of acyclic aliphatic azo compounds has been studied quite actively for many years, particularly as a clean source of alkyl radicals[19] (equation 21). Although the lowest energy absorption band is

(21)

weak[20] (ε as low as 5 or less) it is conveniently placed in the near ultraviolet, suitable for irradiation with mercury lamps (366 or 313 nm). The radicals produced from irradiation at 366 nm behave as thermally equilibrated free radicals and undergo the common reactions such as recombination, dis-

proportionation, hydrogen abstraction and addition[21]. The use of short-wavelength irradiation is known to produce vibrationally excited radicals[22]. At the other end of the u.v.-visible spectrum it has been shown that azoethane may be photolysed using a ruby laser at a wavelength where it is transparent (694 nm) if two photons are absorbed simultaneously[23].

Photolysis of acyclic azoalkanes in the gas phase at low pressures produces alkyl radicals with near unit efficiency[20]. In solution, however, geminate recombination of the radical pair within the solvent cage occurs to a considerable extent[24] (equations 22 and 23) thus reducing the efficiency of the

$$RN{=}NR + h\nu \longrightarrow [R\cdot N_2\ R\cdot] \quad (22)$$

$$[R\cdot N_2\ R\cdot] \longrightarrow [RR + N_2] \quad (23)$$

production of free radicals. Cage recombination of radicals has also been observed in the gas phase photolysis of azomethane in the presence of propane[25] at densities up to 0·26 g/cm^3. In the solid state the crystal lattice appears to favour disproportionation of the radicals rather than recombination[26].

A second ethane-producing reaction in the gas phase photolysis of azomethane (equation 24) has been shown to make negligible contribution to

$$CH_3N{=}NCH_3 + h\nu \longrightarrow C_2H_6 + N_2 \quad (24)$$

the yield of ethane, except at high temperatures or very low irradiation intensities[27]. The reaction, an intramolecular split in which no radicals are released, has a quantum yield of about 0·01 over a wide range of temperatures[27,28] and is unaffected by oxygen[27,28], 1,4-hexadiene or sulphur dioxide[28]. At low intensities of irradiation the steady-state concentration of radicals is low and so the rate of the recombination reaction (equation 25) is small relative to the intramolecular split. At high temperatures the hydrogen abstraction reaction (equation 26) becomes more important, thus reducing the yield of ethane from reaction 25, but enhancing the relative importance

$$2CH_3\cdot \longrightarrow C_2H_6 \quad (25)$$

$$CH_3\cdot + CH_3N{=}NCH_3 \longrightarrow CH_4 + CH_2\cdot N{=}NCH_3 \quad (26)$$

of reaction 24, particularly at higher partial pressures of azomethane. The intramolecular split appears to be less significant in the photolysis of higher azoalkanes[19].

Although most of the work on the photolysis of acyclic aliphatic azo compounds has been concerned with the reactions of the free radicals

produced, some considerable effort has been made toward understanding the mechanism of the decomposition step. It is only recently that a sensible pattern has begun to emerge and it appears that the precise details of the mechanism depend very much on the particular azo compound concerned. For example, whereas with most *trans* acyclic azoalkanes it appears that dissociation occurs from an electronically excited state of the azo compound, with azo-2-methyl-2-propane and some others a rapid *thermal* dissociation occurs from the *cis* isomer which is formed photochemically[29]. The question of whether dissociation occurs in one or two steps is considered in a later section (II, A, 7).

In the following sections the photochemistry of acyclic aliphatic azo compounds is reviewed in detail. Considerable attention is given to aspects relating to the mechanism of decomposition, the nature of the excited states involved and to photoisomerization. Secondary reactions are also considered briefly.

2. Gas-phase kinetics

For convenience the formation of nitrogen is taken as the measure of decomposition, other side reactions generally being negligible. The photolysis of azomethane in the gas phase at pressures below one atmosphere proceeds with unit quantum efficiency[30,31], although at greater pressures the quantum yield does decrease[30]. All other azoalkanes show a reduction of the quantum yield of decomposition with increased pressure at pressures considerably less than one atmosphere. The pressure effect is more pronounced the more complex the azoalkane.

It is generally accepted that the effect of pressure is caused by collisional deactivation of an excited state of the azo compound in competition with dissociation[32]. In the simplest mechanism (equations 27–29) A represents an azoalkane molecule in the ground state, A* an unspecified excited state of A and M another molecule which could be an azoalkane or another

$$A + h\nu \longrightarrow A^* \tag{27}$$

$$A^* \xrightarrow{k_{28}} 2R\cdot + N_2 \tag{28}$$

$$A^* + M \xrightarrow{k_{29}} A + M \tag{29}$$

added gas molecule such as carbon dioxide[32,33]. If the rate constants of reactions 28 and 29 are k_{28} and k_{29} respectively then it can be readily shown that

$$1/\Phi_{N_2} = 1 + (k_{29}/k_{28})[M] \tag{30}$$

where Φ_{N_2} is the quantum yield of nitrogen and $[M]$ is the molarity of the added gas molecules. The assumption is made that all types of molecules will be equally effective in producing collisional deactivation of A*. This is not true[32] but correction of this aspect does not affect the subsequent arguments.

Stern–Volmer[32] plots of $1/\Phi_{N_2}$ against $[M]$ or the gas pressure should be linear giving an intercept of unity and a slope of k_{29}/k_{28}. Generally speaking these conditions are fulfilled although some departures from this simple scheme may be seen in Table 1. The rate constants, k_{28}, for the decomposition of the excited states, shown in Table 1, represent minimum values in that the diffusion controlled rates for k_{29} are the maximum possible values for collisional deactivation. It may also be noted that the rate of decomposition of the excited azoalkane is dependent on the complexity of the alkyl groups. Presumably accumulation of the vibrational energy required to dissociate the azo compound takes longer with the more complex azoalkanes which have more vibrational degrees of freedom. Collisional deactivation would then be favoured[28].

a. *Stern–Volmer intercepts.* Intercepts greater than unity may be explained by adding an extra step (equation 31) to the mechanism, where $A^{\dagger}$ is a

$$A^* \xrightarrow{k_{31}} A^{\dagger} \tag{31}$$

non-dissociative state of the azo compound. Equation 31 could represent *trans* → *cis* isomerization or conversion to a non-dissociating n,π^* triplet state (see later). Internal conversion to the ground state would seem unlikely in the gas phase as the resulting vibrationally excited ground-state molecule would have more than enough energy to dissociate thermally[42]. If the rate constant for reaction 31 is k_{31}, then equation 30 may be rewritten as

$$1/\Phi_{N_2} = 1 + k_{31}/k_{28} + (k_{29}/k_{28})[M] \tag{32}$$

The intercept of the Stern–Volmer plot now becomes $(1 + k_{31}/k_{28})$. The effect of temperature on the slope and intercept is discussed later.

There is some evidence that equation 31 does not itself represent an isomerization reaction, at least for azo-2-propane. At low pressures, presumably at room temperature, Steel and co-workers found that both the *cis* and *trans* isomers of this compound decomposed with unit quantum efficiency and that no isomerization occurred[33]. As the pressure was increased by adding an 'inert' gas (carbon dioxide), the quantum yield for

decomposition decreased while isomerization increased. Clearly the isomerization is related to a collision process similar to equation 29. At higher temperatures, where equation 31 appears to become more important[37], it may be that the state $A^{\dagger}$ is also important in isomerization, but no data are available at present to answer this question.

b. *Non-linear Stern–Volmer plots.* The Stern–Volmer plot for hexafluoroazomethane shows a marked departure from linearity when taken to moderate pressures (720 Torr)[40] and Wu and Rice suggest[40] that similar behaviour may be displayed by azoethane if its photolysis were studied at high enough pressures. This behaviour may be explained by invoking an additional dissociating excited state A** which is a precursor of state A*[40]. It is assumed that the rate constant k_{29} in equation 36 for the collisional

$$A + h\nu \longrightarrow A^{**} \quad (33)$$

$$A^{**} \xrightarrow{k_{34}} 2R\cdot + N_2 \quad (34)$$

$$A^{**} \xrightarrow{k_{35}} A^{*} \quad (35)$$

$$A^{**} + M \xrightarrow{k_{29}} A + M \quad (36)$$

deactivation of A** is the same as for A* (equation 29) and this is taken to be the collision frequency of A* or A** molecules. Equation 31 has been omitted from this treatment as the intercept was taken as unity.

TABLE 1. Gas-phase photolysis of *trans* azoalkanes and some fluoro derivatives at 366 nm. Data from Stern–Volmer plots.

Compound	Temp. (K)	Intercept	Gradient (k_{29}/k_{28}) (1/mol)	Linearity[a]	k_{28}[b] $\times 10^{-7}$ (sec^{-1})	Reference
MeN_2Me	[c]	1	0	+(760)	—	30, 31
EtN_2Et	300	1·04	92·5	+(180)	385	34
	[c]	1[d]	104	+(105)	342	35
	301	1·12	81·3	+(134)	439	36
	351	1·08	68·1	+(148)	566	36
	389	1·04	53·0	+(157)	765	36
	425	0·99	31·0	+(163)	1370	36
EtN_2Pr-n	[c]	1·1	980	+(40)	34	35
n-PrN_2Pr-n	[c]	1[d]	2200	+(17)	14	35
i-PrN_2Pr-i	307	1·35 ± 0·11	771 ± 77	+(45)	41	37
	334	1·38 ± 0·14	560 ± 84	+(56)	58	37

TABLE 1 (*cont.*)

Compound	Temp. (K)	Intercept	Gradient (k_{29}/k_{28}) (1/mol)	Linearity[a]	k_{28}[b] $\times 10^{-7}$ (sec^{-1})	Reference
	360	$1{\cdot}46 \pm 0{\cdot}17$	518 ± 90	+(66)	65	37
	376	$1{\cdot}72 \pm 0{\cdot}06$	426 ± 45	+(53)	81	37
	400	$1{\cdot}75 \pm 0{\cdot}03$	301 ± 30	+(51)	119	37
n-BuN_2Bu-n	298	1[e]	59,500	o[e]	0·53	38
	354	1[e]	33,100	o[e]	1·04	38
	380	$0{\cdot}8 \pm 0{\cdot}2$	18,500	+(50)	1·93	38
	435	1[e]	10,900	o[e]	3·51	38
i-BuN_2Bu-i	368	1[e]	61,700	o(7)[e]	0·57	39
	384	1[e]	33,900	o(8)[e]	1·06	39
	419	1[e]	22,100	o(15)[e]	1·70	39
	441	1[e]	16,200	o(13)[e]	2·38	39
	470	1[e]	10,600	o(13)[e]	3·76	39
	580	1[e]	5010	o(7)[e]	8·83	39
$CF_3N_2CF_3$	304	1[d]	244[f]	−(720)	[h]	40
	304		43[g]	−(720)	[h]	40
$C_2F_5N_2C_2F_5$	298	1·33	730	+(100)	36	32
	343	1·04[i]	543	+(90)	52	32
	378	1·12[i]	476	+(60)	62	32
	423	1·20	223	+(100)	141	32
	300	1[d,j]	560[j]	+(140)	47	41

[a] The linearity or otherwise, of the Stern–Volmer plot is denoted by + (linear), o (uncertain), − (non-linear). The number in parentheses refers to the maximum pressure in Torr at which measurements were made.

[b] k_{28} was calculated assuming k_{29} = collision frequency. Collision diameters of 0·7 nm were assumed for all except n-BuN_2Bu-n and i-BuN_2Bu-i (0·75 nm) and $C_2F_5N_2C_2F_5$ (0·8 nm).

[c] Ambient temperature, assumed to be 298 K.

[d] Intercept assumed to be unity.

[e] Insufficient data to determine intercept (assumed to be unity) or linearity.

[f] Determined from the limiting gradient at low pressures.

[g] Determined from the limiting gradient at high pressures.

[h] See later discussion in the text.

[i] Low accuracy due to insufficient points.

[j] Recalculation of the original data by Pritchard and co-workers[32] gave an intercept of 1·27 and gradient of 523 l/mol.

From their kinetic data Wu and Rice[40] have obtained the following values at 31°C for the rate constants: $k_{34} = 8{\cdot}2 \times 10^9$/sec, $k_{35} = 11{\cdot}4 \times 10^9$/sec and $k_{28} = 0{\cdot}9 \times 10^9$/sec. It may be noted that A** is shorter-lived with respect to decomposition than is A*. Thus at high pressure the longer-lived state A* would be deactivated by collision much more often than it

would decompose and the quantum yield expression approximates equation 37, where C is a constant. This argument cannot be used to explain

$$1/\Phi_{N_2} = C + (k_{29}/k_{34})[M] \tag{37}$$

intercepts greater than unity as referred to above because the intercepts were determined at low pressures where collisional deactivation was much less important. Essentially, at high pressure one is examining the decomposition of hexafluoroazomethane from the shorter-lived A** state (equation 34) with reactions 35 and 36 as competition.

At low pressure the situation is a little more complex, the quantum yield expression reducing to equation 38. If the slope of the Stern–Volmer plot

$$1/\Phi_{N_2} = 1 + [M](k_{35} + k_{28})k_{29}/(k_{34} + k_{35})k_{28} \tag{38}$$

is written as k_{29}/k, where $k = k_{28}(k_{34} + k_{35})/(k_{35} + k_{28})$, then $k = 1{\cdot}4 \times 10^9$/sec for hexafluoroazomethane[40]. The expression for k may be simplified to

$$k \simeq k_{28}(1 + k_{34}/k_{35}) \tag{39}$$

since k_{35} is significantly greater than k_{28}. It would appear that for most acyclic azoalkanes k_{35} is much greater than k_{34}. This simply means that dissociation from the state A** is much slower than conversion to A* and the kinetics again become simple with equation 30 being obeyed. These matters will be discussed later in connection with the nature of the excited states.

c. *Activation energies.* In a number of cases the pressure dependence of the quantum yield for the photolysis of azoalkanes has been studied over a range of temperatures (see Table 1). From the Arrhenius plots, log k_{28} or log (k_{29}/k_{28}) against $1/T$, activation energies for the dissociation of the excited state A* have been obtained and these are given in Table 2. It has been assumed that collisional quenching (equations 29 and 36) has zero activation energy. Some authors have also ignored the $\sqrt{T}$ dependence in k_{29}, but this has not introduced serious errors. It appears that the activation energy for dissociation increases as the complexity of the azoalkane increases. This apparent relationship may be spurious, however, because in some cases the Arrhenius plots were non-linear, particularly for azoethane and decafluoroazoethane. The explanation suggested[32,43] is that the rate of dissociative reaction (equations 28 or 34) reaches a limiting value at low temperatures. Here the thermal energy makes a negligible contribution towards the rate of the dissociation, all the necessary energy coming from the light. Part of the energy of the absorbed photon provides for a degree of vibrational excitation in the electronically excited state and this would be a function of the wavelength of the light used. Indeed a wave-

length dependence has been observed for the rate of decomposition with azoethane[34]. At high temperatures the thermal contribution to the vibrational excitation of the electronically excited state would become dominant and so from the slope at the high temperature limit of the data one may obtain a minimum value of the activation energy of the dissociation process. This corresponds to the upper values given in Table 2 for azoethane and its

TABLE 2. Arrhenius plots and activation energies from the gas phase photolysis of some *trans* azoalkanes and a fluoro derivative

Compound	Arrhenius plot for $\log(k_{29}/k_{28})$		Arrhenius plot for $\log(k_{31}/k_{28})$	Reference
	E_{28}[a] (kJ/mol)	linearity[b]	E_{31}[c] $- E_{28}$ (kJ/mol)	
EtN_2Et	9–21	–	–7[d]	36
i-PrN_2Pr-i	9·5 ± 1·5	+[e]	8·3 ± 3·0	37
n-BuN_2Bu-n	16	+		38
i-BuN_2Bu-i	20	+		39
$C_2F_5N_2C_2F_5$	8–21	–	–4[f]	32

[a] Activation energy for reaction 28.
[b] + means linear, – means non-linear over the temperature range in Table 1.
[c] Activation energy for reaction 31.
[d] Estimated from intercepts at 301 and 351 K.
[e] Pritchard and co-workers considered this plot to be non-linear[32].
[f] Determined from intercepts at 298 and 423 K.

decafluoro derivative. Only these compounds in Table 2 definitely gave non-linear Arrhenius plots for k_{28}. Pritchard and co-workers[32] have also included azo-2-propane in this category but the evidence is not compelling[37]. Just why azoethane and its perfluoro derivative should be the only azoalkanes to display this behaviour is not clear. Perhaps the explanation given above is not correct and the non-linear Arrhenius plot is due to competition between decomposition from states A* and A** (equations 28 and 34). The simple rate constant k_{28} would be replaced by k (equation 39) and a simple activation energy would then be meaningless.

With compounds having Stern–Volmer intercepts significantly greater than unity, the effect of temperature on the intercept allows the difference in activation energy between equations 31 and 28 to be determined. Values for $E_{31} - E_{28}$ are shown in Table 2. For azo-2-propane E_{31} is greater than E_{28}, while the opposite appears to be true for azoethane and its decafluoro

derivative. This is related to the observation that for azo-2-propane, the Stern–Volmer intercept increased with temperature but decreased for azoethane and decafluoroazoethane.

3. Photolysis in condensed phases

a. *Quantum yields in solution.* The quantum yields for decomposition of azoalkanes in solution are much lower than in the gas phase. Hutton and Steel[44] found that increased solvent polarity further decreased the quantum yield. For azomethane the quantum yields of decomposition in various solvents were $0{\cdot}17 \pm 0{\cdot}01$ (isooctane), $0{\cdot}07 \pm 0{\cdot}01$ (ethanol), $0{\cdot}05 \pm 0{\cdot}01$ (dimethylformamide) and $0{\cdot}01 \pm 0{\cdot}01$ (water). The reason for the solvent effect does not appear to have been investigated.

A comparison of quantum yields in the gas phase with those in solution further supports the requirement for the existence of a very short-lived dissociating state A**, otherwise decomposition would not occur in solution[33]. For example, in isooctane, which corresponds to a gas-phase pressure of about 1000 atmospheres[33], the quantum yield of decomposition for *trans*-azo-2-propane is 0·025. This may be compared with a calculated value of less than 2×10^{-4} based on quantum yields in the gas phase at moderate pressures and assuming only the simple mechanism (equations 27, 28 and 29). The kinetic behaviour in solution would be expected to resemble that of hexafluoroazomethane in the gas phase at high pressure, as described in the previous section. In effect, the conversion of A** to A* (equation 35) could be an important cause of the low quantum yield in solution, in addition to collisional deactivation of A** (equation 36). Solvent effects could probably be important in both processes, leading to the solvent polarity effect noted by Hutton and Steel[44].

Further evidence that dissociation from A** is the major pathway in solution comes from the effect of temperature on the quantum yield of decomposition of azoethane in n-heptane[45]. From the preceding argument it can be seen that in solution A* behaves like the non-dissociating state $A^{\dagger}$ (equation 31) because of efficient collision quenching of A* by solvent molecules. Thus we write

$$1/\Phi_{N_2} = 1 + k_{35}/k_{34} + (k_{29}/k_{34})[M] \qquad (40)$$

which is similar to equations 32 and 37. Now when one uses the quantum yield data of Kodama and co-workers for azoethane[45] to plot $\log(1/\Phi_{N_2} - 1)$ against $1/T$, a linear Arrhenius plot is obtained over the whole temperature range (−75 to +90°C) and an activation energy of −3·3 kJ/mol is inferred. This sign should be changed for comparison with the figure given by Kodama and co-workers (2·7 kJ/mol)[45]. These values are much lower than the activa-

tion energy obtained in the gas-phase studies (see Table 2), and can be attributed to either the k_{35}/k_{34} term or the k_{29}/k_{34} term in equation 40 ($E_{35} - E_{34}$ or $E_{29} - E_{34} = -3{\cdot}3$ kJ/mol). It is not certain which term is more important in equation 40, but either way the importance of dissociation from the state A** is reinforced because the Arrhenius plot is different from that in the gas phase. Probably equation 35 like equations 29 and 36 has negligible activation energy associated with it so that $E_{34} \simeq 3$ kJ/mol.

b. *The cage effect*. Whereas the above discussion has been concerned with the actual decomposition step, photochemical kinetic studies on azoalkanes in solution have shown that inefficiency in the production of free radicals is due to the cage effect (equation 23) as well as to collisional deactivation of excited states. For example, virtually all the ethane produced in the photolysis of azomethane in hexane arises from recombination of the radical pairs formed in their solvent cages (equations 41 and 42). This is shown by the failure of styrene, a good radical scavenger, to affect the product ratio

$$MeN{=}NMe + h\nu \longrightarrow [Me\cdot + N_2 + Me\cdot] \quad (41)$$

$$[Me\cdot + N_2 + Me\cdot] \longrightarrow [C_2H_6 + N_2] \quad (42)$$

C_2H_6/N_2 which was 0·75 at 0°C with irradiation at 366 nm. In contrast the added styrene caused the ratio CH_4/N_2 to decrease from values near 0·5 to nearly zero[24]. The methane is considered to be formed from free methyl radicals which have escaped from the solvent cage in which they were formed (equation 43), followed by reaction with the solvent (equation 44).

$$[Me\cdot + N_2 + Me\cdot] \longrightarrow 2Me\cdot + N_2 \quad (43)$$

$$Me\cdot + C_6H_{14} \longrightarrow CH_4 + C_6H_{13}\cdot \quad (44)$$

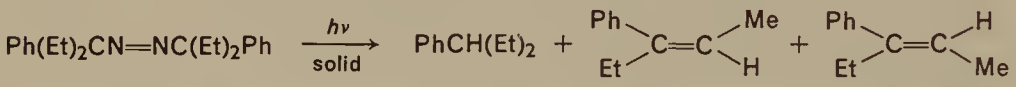
The efficiency of release of the free radicals is important as they are often used to initiate many polymerization and other chain reactions. Szwarc and co-workers[46] showed that the extent of cage recombination for azomethane, C_2H_6/N_2, was inversely proportional to the square root of the absolute temperature and proportional to the viscosity of the solvent. Kodama had earlier noted the importance of the solvent viscosity[47]. Irradiation at 254 nm gave the same results as at 366 nm, indicating that the extra energy supplied from the light did not facilitate the escape of radicals from the solvent cage[48]. Increased pressure decreases the yield of the radicals. Tanaka and co-workers[49] studied the photolysis of azoisobutyronitrile (**12**) in toluene up to pressures of 2000 kg/cm^2 and obtained an apparent activation volume of +7·6 cm^3/mol. Diphenylpicrylhydrazyl was used as the scavenger to measure the yield of free radicals.

In the solid state, the cage effect is also very pronounced. However, the major radical–radical reaction is disproportionation[26, 50–53] whereas in the liquid phase this is a minor reaction. Furthermore, it has been found that disproportionation involves only the geminate radical pairs, at least for azoisobutyronitrile (**12**)[52, 53]. For this compound over 91 % of the radical

$$(CH_3)_2C(CN)N{=}NC(CN)(CH_3)_2$$

(12)

reactions occur within the crystalline cage[53]. The rate of disproportionation is limited by a rotational diffusion which brings a methyl group on one of the isobutyronitrile radicals into a position formerly occupied by the nitrogen molecule[52]. McBride and co-workers have shown[26] that in the photolysis of crystalline azo-3-phenyl-3-pentane (**13**) at −78°C the crystal lattice has control over the stereochemistry of the olefinic disproportionation products **14** and **15** (equation 45). The ratio of the isomers **14** and **15** was about 1 to 3 compared with a thermodynamically predicted ratio of 1 to 1·6.



(13) **(14)** **(15)** (45)

4. The nature of the dissociating states

In the preceding sections the kinetic data demanded a number of mechanistic steps and in particular the existence of more than one dissociating excited state as well as a non-dissociative excited state. For irradiation above 300 nm, which is used by most workers, the initial act of absorption leads to an n,π^* singlet state[54]. This first excited singlet state probably corresponds to the short-lived state A** (equation 33). However, most attention has been given to the nature of the longer lived dissociative state corresponding to A* (equations 28 and 35) as this state appears to be the most important one in the decomposition of most azoalkanes in the gas phase. There has been some argument[19] as to whether this state is an electronically excited singlet, triplet or vibrationally excited ground state. Using data of Worsham and Rice[34] on azoethane, Calvert and co-workers[19] have argued against a vibrationally excited ground state being involved in the dissociative step. The activation energy for the thermal decomposition of azoethane is 203 kJ/mol[42] whereas Worsham and Rice[34] calculated that the minimum vibrational energy required to dissociate the particular electronic state involved was only about 84 kJ/mol. This value was obtained by application of Rice–Ramsperger–Kassel (RRK) theory (see reference 34 and

references therein) to the photolysis of azoethane at different wavelengths around 366 nm, and choosing a value for the activation energy which gave the best agreement between the calculations and the experimental results. Thus dissociation would seem to occur from an *electronically* excited state.

a. *Evidence favouring singlet decomposition in direct photolysis.* For azomethane and azoethane there seems to be a clear difference between direct and triplet-sensitized decomposition. Whereas most good triplet sensitizers like benzophenone do not sensitize the decomposition of azoalkanes, a clear case of triplet-sensitized decomposition of azomethane appears to have been shown by Rebbert and Ausloos[30] using acetone-d_6 in the gas phase. Singlet energy transfer appears to have been absent in this work as the *fluorescence* of the acetone-d_6 was not quenched, even at fairly high concentrations of azomethane where all the *phosphorescence* was quenched. The quantum yield of nitrogen was only about 0·3 at 30°C under conditions where all the acetone triplets were quenched by the azomethane and where triplet acetone accounted for 90% of the excitation. An increase occurred in the quantum yield with temperature and reached a maximum of about 0·35 at 100°C. Most significantly the quantum yield was noticeably affected by the total pressure, which indicated collision-quenching of an intermediate excited state. Clearly this excited state must have a much greater lifetime than that produced by direct irradiation because the quantum yield for direct irradiation of azomethane is unity up to total pressures of at least one atmosphere. A similar situation exists for acetone-d_6 sensitization of azoethane, the quantum yield of nitrogen being lower than for direct irradiation at comparable pressures[36, 55], even though azoethane is just as efficient as azomethane in quenching the acetone-d_6 triplets[30].

The obvious inference is that direct irradiation of azomethane and azoethane proceeds by dissociation of an excited singlet state. This conclusion was not clear at the time of the paper by Rebbert and Ausloos[30] owing to uncertainty about the triplet energy of acetone. A rather low value of 300 kJ/mol was accepted. It is now clear, however, that acetone has a triplet energy around 331–343 kJ/mol[31, 56, 57] which may be compared with 327 kJ/mol available from direct irradiation at 366 nm.

There is an inference in the paper by Collier, Slater and Calvert[19] that the acetone-photosensitized decomposition of azo-2-methyl-1-propane may have shown behaviour similar to that just described for azomethane and azoethane. Not much data were given but it is tempting to postulate a singlet decomposition for the direct photolysis of *trans* azoalkanes generally. Actually Calvert and co-workers[19] avoided the inference of a singlet mechanism as did Rebbert and Ausloos[30], but the arguments for and against the triplet decomposition mechanism will be taken up later.

b. *Evidence against A* being the first excited singlet state.* There are certain objections to the direct photodecomposition of azoalkanes in the gas phase proceeding from their first excited singlet states. Azoalkanes do not show any detectable fluorescence or phosphorescence[30] whereas it has been shown[19,33] that fluorescence should be observed if dissociation occurs from the first excited singlet state. If it is assumed that the dissociative state A* may be deactivated only by fluorescence (rate constant k_F), dissociation (equation 28, rate constant k_{28}) and collision (equation 29, rate constant k_{29}), then the quantum yield of fluorescence, Φ_F, may be obtained from equation 46. On the assumption that A* is the first excited singlet state, the

$$\Phi_F = k_F/(k_{29}[M] + k_{28} + k_F) \tag{46}$$

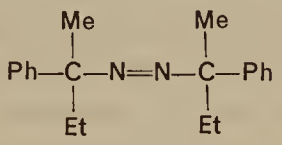
natural radiative lifetime ($1/k_F$) may be calculated from the absorption spectrum of the azo compound (ε, against $1/\lambda$) using the procedure of Strickler and Berg[58]. For example, for azo-2-propane[33] and azo-2-methyl-1-propane[19] k_F was estimated to be about 1×10^5/sec. Maximum values for k_{28} may be obtained from Stern–Volmer plots (see Table 1) and the maximum value for k_{29} would be given by the collision frequency (ca. 3×10^{11} l/mol-sec). Calculated values of Φ_F were found to be at least an order of magnitude above the detectable level[19,33] yet no emission was observed. Hence A* cannot be the first excited singlet state of the azo compound. Because of this many workers have favoured a triplet decomposition mechanism. This is discussed later in Section d.

On the other hand application of the above reasoning to the shorter-lived dissociative state A** allows it to be the first excited singlet state. This is because the conversion of A** to A* (equation 35) is very rapid if hexafluoroazomethane is any guide (see Section II, A, 2, b). At low pressures, where collisional deactivation would be negligible, the quantum yield of fluorescence from A**, Φ_F**, would be given by equation 47, where k_F has the same significance as in equation 46 and k_{35} is the rate constant for con-

$$\Phi_F{}^{**} = k_F/(k_{35} + k_F) \tag{47}$$

version of A** to A*. If k_F is assumed to be about 10^5/sec[19,33] and k_{35} about 10^{10}/sec[40] then Φ_F** would be about 10^{-5} which is virtually undetectable. Actually, for most azoalkanes k_{35} is probably greater than 10^{10}/sec, considering the low quantum yields for decomposition in solution (Section II, A, 3, a). Hence the value of Φ_F** is probably even lower than 10^{-5}. These considerations are consistent with A** being the first excited singlet state.

c. *Search for another dissociative singlet state.* The nature of A* is not certain. Although several workers favour a triplet state[19,30,33], the conclusions drawn from acetone-d_6 photosensitization of azomethane and azoethane[30] cause one to look for another dissociative singlet state. The existence of a 'forbidden' singlet state, lower in energy than the first excited singlet, has been suggested by Rau, although he favours a triplet state in the photodissociation[54]. Kosower and Severn[59] have suggested that there is some evidence for the existence of two closely spaced transitions in the circular dichroism (CD) curve of optically active azo-2-phenyl-2-butane (**16**). The maxima of two resolved CD bands of opposite sign were at about



(16)

380 nm for the stronger transition and at about 350 nm for the weaker one, while the ultraviolet absorption spectrum had a maximum at 375 nm (ε 37). One interpretation of these data was that the two CD bands were due to the $n_+ - \pi^*$ and $n_- - \pi^*$ transitions, the longer wavelength band being CD allowed but absorption forbidden, the shorter wavelength band being CD forbidden but absorption allowed. The authors appear to have confused the symmetry labels and accordingly the longer wavelength band should have been designated $n_+ - \pi^*$ and the other $n_- - \pi^*$[54,60,61]. It is of significance to the photochemistry of azoalkanes that the longer wavelength band is absorption forbidden. Jano[62] has also proposed the existence of two closely spaced vibronic states for *trans* azoalkanes generally, based on the assumption of closely spaced n_+, π^* and n_-,π^* singlet states, although here also his symmetry labels for the n_+ and n_- orbitals were incorrectly reversed[54,60]. Thus one might be tempted to assign the n_-,π^* singlet state to A** and the lower energy n_+,π^* singlet state to A*.

However convenient this interpretation may be for explaining the photochemistry of azoalkanes, the overwhelming opinion now seems to be that there is a large splitting between the n_+ and n_- orbitals[54,63]. Photoelectron spectra of azomethane have shown that the energy of the $n_-(B_u)$ lone pair orbital is 320 *k*J/mol below that of the $n_+(A_g)$ orbital[64]. Thus it seems that all the other spectroscopically accessible singlet states are of much higher energy than the first excited singlet state[61]. Severn and Kosower[63] now favour an explanation in which the two CD bands of opposite sign in **16** are due to the difference in polarizability of the highest and lowest vibrational states of the n_+,π^* electronic state. This is of no help in attempting to find another

singlet dissociative state for *trans* azoalkanes, and it is not at all clear whether such a 'forbidden' singlet state exists.

d. *A triplet decomposition mechanism.* In spite of previous comments the proposition that dissociation of *trans* acyclic azoalkanes occurs from a *triplet* state in the direct photolysis is by no means totally excluded. The absence of any detectable phosphorescence may be accounted for by the rapid rate of decomposition of the excited state compared with a relatively long radiative lifetime for the triplet state. The difference between the acetone-d_6 photosensitized and direct photolysis of azomethane and azoethane is a little more difficult to explain solely in terms of triplet decomposition. It could be that the energy transfer from the sensitizer to the azo compound is somewhat inefficient, the azo compound not receiving the full 331–343 kJ/mol from the acetone. This would reasonably be expected to affect the quantum yield at least for azoethane because of the noticeable wavelength dependence of the quantum yield for this compound in the region of 366 nm[34]. Alternatively it could be argued that energy transfer from the acetone-d_6 may occur to give one of two triplet states, only one being capable of dissociation. However, the difficulty with this explanation is that in the case of azomethane, the sum of the quantum yields of nitrogen and carbon monoxide (from decomposition of the acetone-d_6) at 133°C approached unity at low pressures[30]. For example, at the lowest pressures used Φ_{N_2} was 0·39 and Φ_{CO} was 0·52. This allows negligible room for inefficiency caused by populating a non-dissociating triplet state of the azo compound.

It does appear, nevertheless, from sensitization experiments, that *trans* azoalkanes do have two triplet states at levels similar to or below that of the first excited singlet state. The upper triplet is considered to be a π,π^* state[31,33] and it would seem that acetone is the only sensitizer capable of populating this state by triplet energy transfer. Steel and co-workers[33] have suggested that direct photolysis of azoalkanes leads to decomposition from this $^3(\pi,\pi^*)$ state. The triplet states of many other sensitizers are also quenched by *trans* azoalkanes, presumably leading to the n,π^* triplet state of the azo compound, with no decomposition. This is in contrast with cyclic azoalkanes where decomposition apparently can occur from the $^3(n,\pi^*)$ state[65,66]. With some *trans* azoalkanes the $^3(n,\pi^*)$ state may be important in photoisomerization. These last two matters will be discussed later. From quenching experiments an $^3(n,\pi^*)$ energy of 222 ± 13 kJ/mol has been estimated for azo-2-methyl-1-propane[19] and less than 230 kJ/mol for azo-2-methyl-2-propane[31].

e. *Spin correlation effects.* A number of attempts have been made to detect spin correlation effects in the supposedly triplet-sensitized photolysis

of azo compounds[31,67,68]. The reasoning was that decomposition of a triplet azo compound would lead to the formation of geminate radical pairs having parallel spin. It was hoped that the radicals would diffuse out of the solvent cage before spin inversion could occur thus reducing the extent of cage recombination. In fact, no difference was observed between the proportion of cage recombination in direct and sensitized photolyses. This was attributed to rapid spin inversion by the radicals[67] or to an effect of the nitrogen molecule[68]. However, Engel and Bartlett[31] have shown that the hydrocarbon sensitizers used were acting as *singlet* sensitizers. No spin correlation effect was found even with the acetone-d_6 photosensitized decomposition of azomethane[31] but as the azomethane concentration was fairly high (0·02 M) it is possible that singlet energy transfer was occurring here also. Thus no definitive answer has been obtained on the multiplicity of the dissociative state by studying spin correlation effects. It should be pointed out that such studies are carried out in solution and so one is comparing dissociation of the short-lived state A** with that of the state produced by energy transfer from the sensitizer. According to earlier argument A** is probably the first excited singlet state, so that spin correlation effects ought to be observable in acetone-photosensitized azomethane in solution, provided singlet energy transfer can be avoided. Unfortunately these studies have no bearing on the nature of the longer-lived dissociative state A* which is the important one in the gas phase.

The problem of singlet sensitization with commonly used triplet photosensitizers has been reviewed recently by Engel and Monroe[69]. In this connection one of the worst offenders was found to be triphenylene which regularly produced singlet sensitization, particularly when the concentration of the acceptor was fairly high.

f. *The intramolecular split.* As was briefly mentioned in Section II, A, 1, azomethane and to a lesser extent the higher azoalkanes undergo an intramolecular split in the gas phase in which photodecomposition occurs without the formation of free radicals (equation 24). For azomethane the quantum yield of this process, Φ_{im}, was found to be $0{\cdot}007 \pm 0{\cdot}001$[27] and independent of temperature between 25 and 218°C[28]. Toby and Nimoy[27] have speculated that the reaction involves intersystem crossing to a triplet state followed by isomerization to the *cis* isomer and then an intramolecular split of the *cis* triplet azomethane. However, one of the reaction products, either ethane or nitrogen, would have to be formed in its triplet state, As both these compounds have very high triplet energy levels such a process would be energetically unfavourable. Toby and co-workers[70] have attempted to avoid this problem by suggesting that the decomposition step (equation 24) actually occurs in the normal fashion (equation 21) giving two radicals

which then undergo rapid spin randomization and rapidly recombine due to their close proximity.

It must be emphasized that the proposal that triplet azomethane is involved in the intramolecular split is highly speculative and in view of the fact that oxygen has no effect on the reaction, it would have to be assumed that such a triplet state is very short lived[27]. Since there is a pressure effect on the quantum yield of nitrogen in the acetone-photosensitized decomposition of azomethane[30] (see Section II, A, 4, a), the π,π^* triplet state would appear to be too long-lived to be involved in the intramolecular split. This leaves only the n,π^* triplet state or an excited singlet state.

Considering the n,π^* triplet state as the precursor one could explain the low value of Φ_{im} in two ways. Either there is a low efficiency of conversion to the *cis* n,π^* triplet state with an appreciable degree of intramolecular split from this state or there is a high degree of conversion to the *cis* n,π^* triplet with a low degree of intramolecular split. The first alternative is ruled out because when using benzophenone as sensitizer the quantum yield of nitrogen was only 0·009, even though the azomethane quenched the benzophenone triplets with good efficiency and a considerable degree of *trans* → *cis* isomerization occurred ($\Phi > 0{\cdot}4$)[31]. Furthermore, the little decomposition which did occur was considered to have been caused by direct photolysis[31]. The second alternative is rejected because if significant conversion to a relatively non-decomposing n,π^* triplet state occurred then the quantum yield of nitrogen could not be unity which it is in the gas phase for azomethane[30].

Thus the intramolecular split would seem to originate from a singlet state, probably the first excited singlet state corresponding to A** (Sections II, A, 2, b and 4, b). In view of the short-lived nature of A** the absence of a temperature effect on Φ_{im} is not surprising. At shorter wavelengths of irradiation, Φ_{im} decreases[70]. This would be expected because the rate of dissociation from a more vibrationally excited state would increase relative to other processes like the intramolecular split[70]. Interestingly this suggests that in the gas phase photolysis of azomethane, a significant proportion of the decomposition occurs from A** otherwise there would be no direct competition between the normal dissociation and the intramolecular split.

g. *Conclusions.* The preceding discussions may be summarized as follows:

(*i*) The short-lived dissociative state A** probably corresponds to the first excited singlet state $^1(n_+,\pi^*)$ of the azo compound. This state is probably the important one in the solution-phase photolysis of most azoalkanes.

(*ii*) The longer-lived dissociative state A* could either be an as yet unidentified singlet state or the π,π^* triplet state. There are difficulties with each of these alternatives. It is certain, however, that the lower energy n,π^*

triplet state is unimportant in terms of dissociation, although it is important in photoisomerization (Section II, A, 5) and in the dissociation of cyclic azoalkanes (Section II, B, 2).

(*iii*) The intramolecular split appears to occur from a singlet state, probably A**, and not from a triplet state as suggested by Toby and co-workers[27,70].

5. Photoisomerization

Hutton and Steel appear to have been the first to demonstrate *trans* ⇄ *cis* photoisomerization in azoalkanes[44] using azomethane. More recently azo-2-propane[33,71], azo-1-propane[72], azo-1-pentane[72] and azo-1-octane[72] have been shown to exhibit photoisomerization in addition to decomposition. The *cis* isomers of the above compounds are thermally stable in contrast to those of certain aliphatic azo compounds discussed in Section II, A, 6.

Photoisomerization of azoalkanes does not appear to occur in the gas phase at low pressure and most studies appear to have been done in solution. Interestingly the use of polar solutions appears to suppress decomposition for azomethane[44] and azo-2-propane[33] making it easy to determine the composition of the photostationary state which is produced on extended irradiation. A list of some photostationary compositions is given in Table 3.

TABLE 3. Photostationary *cis–trans* compositions of some azoalkanes

Compound	[*cis*]/[*trans*]	Solvent	Reference
Azomethane[a]	0·10 ± 0·01	Methanol	44
Azo-1-propane[b]	0·18	Benzene	72
Azo-1-pentane[b]	0·34	Benzene	72
Azo-1-octane[b]	0.49	Benzene	72

[a] Irradiation was at 365 nm.
[b] Wavelength of irradiation was not stated.

It may be noted that these compositions are richer in *trans* isomer than *cis*. This is largely due to the higher extinction coefficient for the *cis* isomer at the wavelength of irradiation (usually 366 nm). In the *cis* azo group the lowest energy transition is n_-–π^* which is symmetry allowed, whereas in the *trans* azo group the lowest energy transition is n_+–π^* which is symmetry forbidden[54,61]. The ratio of *trans* to *cis* isomer in the photostationary state was independent of temperature for azomethane in methanol over the

range −40 to +30°C and *cis* isomer was formed from *trans* even in an ether glass or in pure solid *trans*-azomethane at −196°C[44].

a. *Quantum yields.* For aqueous solutions of azo-2-propane the quantum yields for irradiation at 366 nm were 0·38 ± 0·03 for *trans* → *cis* and 0·56 ± 0·03 for *cis* → *trans* which add to give approximately unity[33]. In isooctane solution Φ_{365nm} (*trans* → *cis*) = 0·50 with 0·01 M-*trans*-azo-2-propane[33]. In contrast, at low pressure in the gas phase the quantum yield for decomposition was approximately unity but decreased on increasing the pressure with an 'inert' gas (CO_2)[33]. For example, with the carbon dioxide pressure at 600 Torr, *trans*-azo-2-propane (0·25 Torr) had Φ_{350nm} (decomposition) = 0·18 and Φ_{350nm} (*trans* → *cis*) = 0·31 while the *cis* isomer (0·09 Torr) had Φ_{350nm} (decomposition) = 0·27 and Φ_{350nm} (*cis* → *trans*) = 0·48. One could rationalize the higher quantum yield for decomposition of *cis*-azo-2-propane compared with its *trans* isomer in terms of a higher energy in the ground-state *cis* isomer.

b. *Photosensitized isomerization.* The use of sensitizers to elucidate the nature of the excited states involved in the isomerization is complicated by the different behaviour of azomethane and azo-2-propane. Benzophenone photosensitization of the latter compound[33] gave Φ_{303nm} (*trans* → *cis*) = 0·06 ± 0·02, even though the triplet state of benzophenone was being quenched by the azo compound at a rate close to diffusion controlled. From the previous discussions (Section II, A, 4, d) the n,π^* triplet state of the azo compound would have been produced and one would presume then that isomerization from this state was inefficient. However, Engel and Bartlett[31] found that benzophenone photosensitized the *trans* → *cis* isomerization of azomethane with a quantum yield greater than 0·4, yet no sensitized isomerization occurred with azo-2-methyl-2-propane. It could be that efficient isomerization from the n,π^* triplet state occurs only with the simplest azoalkanes and is inhibited in proportion to the bulkiness of the alkyl groups.

c. *Mechanism of photoisomerization.* Just as with the mechanism of photodecomposition of acyclic azoalkanes, the mechanism of their photoisomerization is not fully understood. From the foregoing discussion, however, one can draw some conclusions.

(*i*) Decomposition and photoisomerization are directly competitive, at least for azo-2-propane. Collision of the excited azo molecule with another

$$A^* + M \longrightarrow A^{\ddagger} + M \quad (48)$$

$$A^{\ddagger} \longrightarrow cis\text{-}A \quad (49)$$

$$A^{\ddagger} \longrightarrow trans\text{-}A \quad (50)$$

molecule, M, deactivates the excited molecule for decomposition (equation 29) but forms instead an isomerizing state, $A^{\ddagger}$ (equations 48–50). This is clearly shown by the effect of increased pressure in the gas phase where the quantum yield of decomposition was reduced with a concomitant increase in the quantum yield of isomerization.

(*ii*) A common isomerizing state, produced from either the *cis* or *trans* azo compound, which then can give either isomer, is indicated by the observation that the sum of Φ (*trans* → *cis*) and Φ (*cis* → *trans*) is near unity.

(*iii*) This common state cannot be the n,π^* triplet state because of the low quantum yields for benzophenone-photosensitized isomerization of azo-2-propane, compared with direct excitation.

(*iv*) No energy barrier appears to exist for the conversion of this common state to the ground state *cis* or *trans* isomers for azomethane because the composition of the photostationary state is independent of temperature and *cis*-azomethane is formed even at −196°C.

The π,π^* triplet state appears to be the one most favoured for the isomerizing state[33,72]. Steel and co-workers have suggested that dissociation may occur from upper vibrational levels of this same state[33] which would correspond to A* (Section II, A, 2). The state designated $A^{\ddagger}$ would then be the same electronic state as A* but vibrationally deactivated by collision. If, however, A* were a singlet state then we would have to say that equation 48 represented intersystem crossing, collisionally enhanced, which is also a reasonable hypothesis. By analogy with ethylene, the first excited singlet and triplet states of acyclic aliphatic azo compounds probably have an equilibrium configuration with the alkyl groups at 90° to each other, that is, intermediate between *cis* and *trans* configurations[33,61,73]. This makes it easy to explain the formation of a common isomerizing state (see (*ii*) above). However, the molecular orbital calculations of Kearns[74] indicate that the n,π^* triplet state of aliphatic azo compounds would lead to *cis* or *trans* isomers with no activation energy, whereas the n,π^* singlet and π,π^* singlet and triplet states would have an activation energy for their isomerization. This is not easy to reconcile with the conclusions (*iii*) and (*iv*) given above. It would seem that either Kearns' calculations are incorrect or azomethane is unusual in having no activation energy for photoisomerization. The latter explanation may be favoured by the *cis* → *trans* quantum yield being greater than that for *trans* → *cis* for azo-2-propane. This suggests some slight barrier to the latter process compared with the former.

Concerning the isomerization process itself, it has been assumed[33,74] that rotation about the N=N bond occurs by analogy with the isomerization of ethylene derivatives. However, no attention appears to have been

given to the possibility of inversion of the configuration at a nitrogen atom in the plane of the double bond. Ljunggren and Wettermark[75] have made such theoretical calculations for the thermal isomerization of azobenzene and it was found that inversion was far more favourable energetically than rotation about the N=N bond.

6. Photolysis of some sterically bulky azo compounds

a. *Thermolysis of unstable* cis *isomers.* Mill and Stringham have reported[29] that certain acyclic azo compounds decompose by a different mechanism when irradiated in solution. The actual decomposition step involves thermolysis of an unstable ground-state *cis* isomer which is formed photochemically from the *trans* isomer. Such behaviour is also shown by many mixed aliphatic-aromatic azo compounds[76,77] (Section II, C, 1).

The compound most thoroughly studied by Mill and Stringham was azo-2-methyl-2-propane (**17**) although azoisobutyronitrile (**12**), 1,1′-dicyanoazocyclohexane (**18**) and 1,1′-bisacetoxy-2,2′-dimethyl-l,l′-azopropane (**19**) were also considered to have the same decomposition mech-

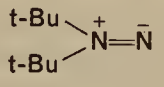
(17) (18)

i-Pr(AcO)HCN=NCH(OAc)Pr-i

(19)

anism. Irradiation of solutions of these four compounds in $CFCl_3$, acetone, methanol or pentane at wavelengths less than 400 nm (mercury lamp) in Pyrex vessels below −50°C produced an intense yellow colour after several hours, but only a trace of nitrogen. On warming the solutions to 25°C, the yellow colour disappeared and nitrogen was evolved[29]. In the more detailed study, irradiation of **17** at −80°C in CH_3OD produced mainly an isomer of **17**, together with a small quantity of isobutane and isobutylene. The absorption spectrum of this isomer had λ_{max} 447 nm in pentane at −60°C, 80 nm red-shifted with respect to the starting material. The n.m.r. spectrum of the isomer showed a singlet at $\delta = 1{\cdot}45$ p.p.m. compared with $\delta = 1{\cdot}12$ p.p.m. for the starting material at −70°C. Taking the starting material to be *trans*-**17** it was concluded that the isomer was *cis*-**17**. Further evidence came from the reversion of the isomer back to starting material on treatment with trifluoracetic acid at −80°C or on irradiation above 400 nm. There was no photodecomposition under the latter con-

ditions, perhaps because of the somewhat lower energy in the irradiating light compared with the 366 nm light normally used in the photolysis of azoalkanes. The rather long wavelength absorption maximum of the isomer is readily accounted for by the expected increase in the N—N—C bond angle, due to steric factors[78]. The possibility of the isomer being 1,1-di-t-butyldiazene (**20**) was ruled out on chemical grounds[29].

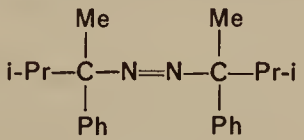


(20)

Thermal decomposition of the isomer (*cis*-**17**) had an Arrhenius factor of $10^{15\cdot6\pm0\cdot5}$/sec and an activation energy of 96 ± 8 kJ/mol which is 84 kJ/mol below that of the *trans* isomer[79], presumably due to steric strain in *cis*-**17**. It is noteworthy that the other three azo compounds, **12**, **18** and **19**, investigated by Mill and Stringham[29] also had bulky groups attached to the azo group. Compound **18** had been used by Fox and Hammond who were investigating spin correlation effects[68] (Section II, A, 4, e) in sensitized photolyses. However, if the decomposition is a thermal reaction then no spin correlation would be expected, even if genuine triplet-sensitized decomposition were achieved.

The quantum yield of nitrogen from 0·02 M-**17** in solution is 0·46[31] which is within experimental error of the quantum yield for its *trans* → *cis* isomerization[31]. This is further support for the mechanism. It is noteworthy that under similar conditions the quantum yield for decomposition of azomethane was only 0·15[31], a reflection of the difference in mechanism. The nature of the excited state involved in the photoisomerization of **17** is not certain (compare Section II, A, 5). However, the absence of decomposition when safe triplet sensitizers are used would rule out involvement of the n,π^* triplet state of the azo compound[31].

b. *Exceptions to the* cis *thermolysis.* There appears to be some disagreement over the behaviour of azoisobutyronitrile (**12**). McBride and coworkers[53] claim not to have observed the thermal decomposition of *cis*-**12** and prefer to regard photolysis of **12** as a direct photodecomposition. Also by way of contrast the sterically crowded azo-3-methyl-2-phenyl-2-butane



(21)

(**21**) appears to undergo normal photochemical dissociation. Bartlett and McBride[51] have irradiated this compound at −196°C in benzene, using 366 nm light, and found that a bright yellow colour was produced. The e.s.r. spectrum at −196°C indicated the presence of a triplet state in which the two paired electrons were separated by 0·6–0·7 nm. This is consistent with two free radicals trapped in the rigid cage and possibly separated by a nitrogen molecule. Thermal equilibrium would be expected between singlet and triplet radical pairs. The proportion of triplet was expected to be appreciable, as very little energy difference between the singlet and triplet spin configurations would be anticipated with such a distance separating the two unpaired electrons. The triplet state of the azo compound could not show such a large separation of the two electrons due to the small size of the azo group.

After 48 h in the dark at −196°C the yellow colour was still present and the e.s.r. spectrum showed some enhancement of an unsplit peak which may have been due to some diffusion apart of the radicals. A further 7 days at −196°C produced little additional change in either the shape or intensity of the e.s.r. spectrum. At higher temperatures (−150°C) the triplet signal disappeared in one hour but the unsplit peak was undiminished at −125°C after 25 min. However, it disappeared in 15 min at −75°C. At −35°C a triplet signal could just be detected under continuous irradiation. It would seem that the yellow colour was due to the radicals produced and not to an unstable *cis* isomer as in the case of azo-2-methyl-2-propane (**17**). Conversely, there seems to be no possibility that the formation of radicals could account for the low temperature behaviour of **17**, particularly as the solvents used by Mill and Stringham[29] would not have formed a rigid matrix at −80°C. The comparison between the behaviour of **17** and **21** points up the difficulty of generalizing about the mechanism of decomposition of acyclic azo compounds. It may be significant, however, that the *cis* thermal decomposition was discovered in fluid media whereas the triplet radical pair was formed in a crystalline matrix. Symons[80] found that photolysis of solid azoisobutyronitrile (**12**) at 77 K gave a trapped radical pair, detectable from its e.s.r. spectrum. At 25°C in benzene solution **12** had a quantum yield for decomposition of 0·47[81], virtually the same as azo-2-methyl-2-propane (**17**)[31], which strongly supports the *cis* thermal decomposition mechanism for **12** in solution (see part a above). Perhaps in a rigid matrix *trans* → *cis* photoisomerization is prevented while direct dissociation of the excited azo compound occurs instead.

c. *Unusual sensitization kinetics.* Engel and Bartlett found a kinetic behaviour for the triphenylene-photosensitized decomposition of azo-2-methyl-2-propane (**17**) which was difficult to explain[31]. A plot of $1/\Phi_{N_2}$ against

$1/[azo]^2$ was approximately linear, whereas the quenching of the excited triphenylene singlets showed normal Stern–Volmer kinetics. The implication would seem to be that an electronically excited azo molecule (**17**) has to interact with an azo molecule in the ground state in order to effect the conversion to *cis*-**17** which is required for decomposition. This matter requires further investigation since Engel and Bartlett did not consider any of their own explanations were satisfactory[31].

d. *Gas-phase photolysis.* The reactions considered so far in this section have been carried out in solution where collisions suffered by the excited azoalkanes are likely to favour *trans* → *cis* isomerization (Section II, A, 5). In the gas phase it is probable that azo-2-methyl-2-propane (**17**) decomposes from an electronically excited state A* (Section II, A, 2). This is because increased pressure from added gases reduces the quantum yield of decomposition[28,82] which is in accord with the normal collisional deactivation mechanism. At 25°C and 19·5 Torr, azo-2-methyl-2-propane (**17**) decomposed with a quantum yield of 0·63 at 366 nm in the absence of other gases[82]. Assuming an intercept of unity for the Stern–Volmer plot of $1/\Phi_{N_2}$ against the molarity of **17**, a gradient of 1500 l/mol may be calculated. This compares favourably with the values for other azoalkanes given in Table 1 (Section II, A, 2), particularly when one takes into account that branching of the alkyl group at the α-carbon atom appears to favour a lower gradient.

If a *cis* thermolysis mechanism operated in the gas phase one might have expected a low quantum yield at low pressures, increasing as the gas pressure was raised. It is possible that the thermal mechanism takes over the decomposition as the pressure is increased, but presumably with lower efficiency. However, because of the square dependence on the concentration of azo compound discussed in Section c above[31], the quantum yield of decomposition in the gas phase would be expected to fall well below its maximum value in solution (0·46) before rising again when the pressure of the azo compound became great enough. If inert gases were used to increase the pressure, no rise in the quantum yield would be expected. These predictions would be worth testing to see if the 'square dependence' operates in the gas phase as in solution.

7. Concerted or step-wise decomposition?

It has been suggested that the photodecomposition of acyclic azoalkanes is stepwise (equations 51 and 52) as an explanation for the low

$$RN{=}NR + h\nu \longrightarrow \underset{(22)}{[RN{=}N\cdot + R\cdot]} \quad (51)$$

$$RN{=}N\cdot \longrightarrow R\cdot + N_2 \quad (52)$$

quantum yields in condensed media[24, 45, 83] (equation 53) and in connection

$$[RN{=}N\cdot + R\cdot] \longrightarrow RN{=}NR \qquad (53)$$

with the intramolecular formation of ethane[84] (equation 54) from azo-

$$\underset{\textbf{(23)}}{2\,MeN{=}N\cdot} \longrightarrow C_2H_6 + 2N_2 \qquad (54)$$

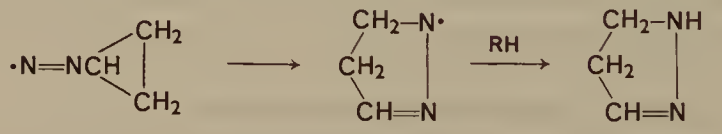
methane. There are thermochemical reasons, however, why a stepwise pathway would be unfavourable as equation 51 would be more endothermic than the overall decomposition reaction[42]. A lower energy pathway would be expected if both C—N bonds were broken simultaneously[42] as advantage would be taken of the large release of energy on forming the nitrogen molecule.

Flash photolysis of azomethane at room temperature has given no spectroscopic evidence of the MeN=N· radicals (**23**) on a millisecond time scale[85]. However, the lifetime of **23** would probably be very much shorter as its decomposition is estimated to be exothermic to the extent of about 120 kJ/mol[86], and probably very little activation energy would be required. On the other hand Rebbert and Ausloos[83] have suggested that **23** and $CD_3N{=}N\cdot$ may be stable enough at 4 K to undergo secondary photolysis.

More recently Szwarc and co-workers[87] have found evidence suggesting the formation of the cyclopropyldiazenyl radical (**25**) in the photolysis of 1,1,1-trifluoromethylazocyclopropane (**24**). The diazenyl radical (**25**)

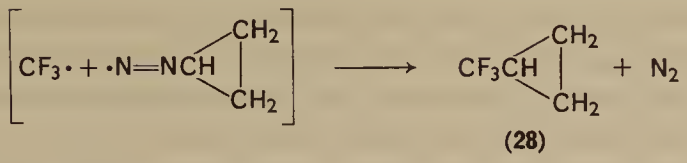
(24) (25) (55)

apparently rearranged to give 2-pyrazoline (**27**) rather than decomposing



(25) (26) (27) (56)

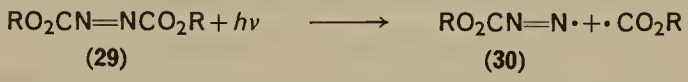
to cyclopropyl radicals because no cyclopropane was formed in the gas phase. The formation of trifluoromethylcyclopropane (**28**) in liquid-phase photolysis of **24** was accounted for by cage recombination with loss of nitrogen (equation 57). It was not possible, however, to determine whether



(28)

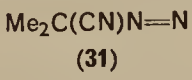
or not the decomposition of **24** gave the cyclic radical (**26**) directly, without the need for **25**.

When one turns to e.s.r. for evidence of diazenyl radicals one is confronted with conflicting viewpoints. On the one hand, Stilbs, Ahlgren and Åkermark[88] claim to have detected such radicals (**30**) from the photolysis of azoesters (**29**). Whereas no triplet states were detected, even at 77 K, the



(29) (30)

half-lives of the diazenyl radicals (**30**) were said to be about 1 min at 25°C. Such stability would seem to be quite amazing. In contrast Symons[80] claims that for photolysis of azoisobutyronitrile (**12**) in the solid state at 77 K the nitrogen is extruded in a one-step process, or else the 2-cyano-2-propyldiazenyl radical (**31**) decomposes rapidly, even at 77 K.



(31)

These conflicting results may in fact be due to the probable difference in the decomposition mechanism, depending on the medium in which the photolysis is carried out. It was suggested earlier (Section II, A, 6, b) that crystalline media may prevent some azo compounds from decomposing by the *cis* thermal mechanism which they may follow in fluid media. Perhaps the two-step mechanism is characteristic of the thermal pathway while the concerted decomposition occurs with true photodissociation. Ayscough, Brooks and Evans[89] photolysed a number of azo compounds at −196°C, including azoisobutyronitrile (**12**). The e.s.r. spectrum from **12** was interpreted as being that of the diazenyl radical (**31**), but this interpretation has been questioned[90]. The state of the sample was described as 'polycrystalline,[89] so that this example supports the proposition that the *cis* thermal decomposition mechanism is inhibited in the solid state. In contrast, Leermakers and co-workers[91] irradiated azoisobutyronitrile (**12**) in a glassy matrix at 77 K and found negligible decomposition compared with irradiation in solution at 25°C. On warming the irradiated glassy solution decomposition occurred. This behaviour was explained in the terms of the photolytic formation of the diazenyl radical (**31**), assumed to be fairly

stable at 77 K, but could be better explained by the *cis* thermal mechanism of Mill and Stringham[29]. As no e.s.r. measurements were made there was no evidence of the formation of radicals at 77 K in the glass matrix.

Probably the best evidence for the intermediate formation of diazenyl radicals comes from studies of the thermal decomposition of azo compounds[92,93]. Also the mixed aliphatic–aromatic azo compounds which undergo the *cis* thermal decomposition on irradiation show evidence of diazenyl radicals in the decomposition step (Section II, C, 1). There appears, however, to be no undisputed case where true photolytic dissociation of azo compounds occurs via the two-step mechanism.

8. 'Hot' radicals from short-wavelength photolysis

Evidence for the formation of 'hot' (vibrationally excited) free radicals in the photolysis of acyclic azoalkanes was found by Calvert and coworkers in the flash photolysis of azomethane[85] and azoethane[94] in quartz apparatus. In the case of azomethane about 1 % of the methyl radicals were reactive enough to form methane by hydrogen abstraction when the full spectral emission of the krypton flash was used. When a filtered flash was used, containing only wavelengths above 300 nm, only 0·5 % of the methyl radicals were able to form methane[85].

With azoethane[94] the disproportionation/recombination ratio was about halved to 0·11 ± 0·01 when Pyrex apparatus was used in place of quartz. This was explained in terms of a greater rate of disproportionation of 'hot' ethyl radicals, compared with their thermally equilibrated counterparts. Furthermore, with Pyrex apparatus the disproportionation products ethylene and ethane were produced in equal quantities as expected (equation 59) but in quartz apparatus the yield of ethylene was greater than that of

$$2\,C_2H_5\cdot \longrightarrow C_2H_4 + C_2H_6 \qquad (59)$$

ethane. This was explained by the decomposition of 'hot' ethyl radicals (**32**) (equation 60). The addition of 95 Torr of methanol vapour had little

$$\underset{(32)}{C_2H_5\cdot^*} \longrightarrow C_2H_4 + H\cdot \qquad (60)$$

effect on the quartz photolysis, in contrast to that in Pyrex, indicating the short life of the 'hot' ethyl radical.

In a more thorough investigation, Arin and Steel have studied the photolysis of azo-2-propane in the 200 nm region[22]. The most notable feature was the quantum yield of 0·97 ± 0·08 for decomposition, independent

of wavelength or intensity in the 200 nm region and independent of pressure, at least up to 400 Torr of carbon dioxide. The latter is in marked contrast to the behaviour of this compound when irradiated at 366 nm[37]. The absorption of azo-2-propane in the 200 nm region is more intense ($\varepsilon \simeq$ 1000 l/mol-cm) than in the 350 nm region and is thought to be due to an $n_+ \rightarrow \sigma^*$ transition[60].

When azo-2-propane was photolysed at 200 nm, hydrogen, methane, ethylene, isobutane and a trace of ethane were formed in addition to the more common $n \rightarrow \pi^*$ photolysis products, propylene, propane and 2,3-dimethylbutane. The additional products could be accounted for by the decomposition of 'hot' isopropyl radicals (**33**) (equations 61 and 62) together with subsequent reactions of the resulting hydrogen atoms and

$$\underset{\textbf{(33)}}{\text{i-}C_3H_7\cdot^*} \longrightarrow C_3H_6 + H\cdot \qquad (61)$$

$$\text{i-}C_3H_7\cdot^* \longrightarrow C_2H_4 + CH_3\cdot \qquad (62)$$

methyl radicals. Although the quantum yield for decomposition was independent of wavelength, the product ratios were wavelength dependent in the 200 nm region. The reason was discussed in terms of the excess excitation energy. The 'hot' isopropyl radicals had a mean energy of 146 ± 84 kJ/mol.

From the absence of a pressure effect on the quantum yield, the dissociative state in short-wavelength photolysis must be much shorter-lived than for long-wavelength photolysis. The exact nature of this state is uncertain but a vibrationally excited ground state(S_0^{vib}) was ruled out on the basis of calculation of the expected dissociative lifetime of S_0^{vib}. By default it may be presumed that dissociation occurs from an electronically excited state, although the possibility of *trans* → *cis* isomerization complicates the problem. The two configurations would be expected to have different dissociative lifetimes. If dissociation occurs from a common state for short and long-wavelength photolysis, the much shorter life of the dissociative state produced by short wavelengths may be explained by its much higher vibrational excitation[22]. In support of this argument it was pointed out[22] that the lifetime of the dissociative state of azoethane was halved on shortening the wavelength of irradiation from 378 to 352 nm[34].

Rebbert and Ausloos[83] have suggested that hot methyl radicals may be formed by the secondary photolysis of methyldiazenyl radicals (**23**) at 4 K. This may explain the considerable increase in the methane/nitrogen ratio from the photolysis of azomethane at 4 K, compared with higher temperatures.

9. Secondary reactions and unusual products

a. *Typical secondary reactions.* Although most of this review has been concerned with the primary events in the photodecomposition of acyclic aliphatic azo compounds, the secondary reactions involving the free radicals are usually of more interest to the practical photochemist. The most important secondary reactions are recombination and disproportionation of the free radicals. At low pressure and room temperature secondary reactions of the radicals with the azo compound are almost negligible[21] and under these conditions the photolysis of azoalkanes provides a clean source of alkyl radicals. At higher temperatures and pressures alkyl radicals abstract hydrogen atoms from the azo compound and add to the N=N bond. For example, in the photolysis of azoethane at 34 Torr at 97°C the following products were formed (yield relative to nitrogen = 1·0 in parentheses): $C_2H_4 + C_2H_6$ (0·166), butane (0·629), tetraethylhydrazine (**34**, 0·122), ethylazo-2-butane (**35**, 0·083) and ethanal diethylhydrazone (**36**, 0·073)[21]. By increasing the pressure up to 250 Torr with added propane an additional product, ethanal ethylhydrazone (**37**), was formed in low yield. The addition

$$EtN{=}NEt + h\nu \longrightarrow 2Et\cdot + N_2 \quad (63)$$

$$2Et\cdot \longrightarrow C_2H_4 + C_2H_6 \quad (64)$$

$$2Et\cdot \longrightarrow C_4H_{10} \quad (65)$$

$$Et\cdot + EtN{=}NEt \longrightarrow Et_2NN\cdot Et \quad (66)$$

$$Et\cdot + Et_2NN\cdot Et \longrightarrow Et_2NNEt_2 \quad (67)$$

(34)

$$Et\cdot + EtN{=}NEt \longrightarrow C_2H_6 + [CH_3CH{=}N{=}NEt]\cdot \quad (68)$$

$$Et\cdot + [CH_3CH{=}N{=}NEt]\cdot \longrightarrow s\text{-}BuN{=}NEt \quad (69)$$

(35)

$$Et\cdot + [CH_3CH{=}N{=}NEt]\cdot \longrightarrow CH_3CH{=}NNEt_2 \quad (70)$$

(36)

$$RH + [CH_3CH{=}N{=}NEt]\cdot \longrightarrow R\cdot + CH_3CH{=}NNHEt \quad (71)$$

(37)

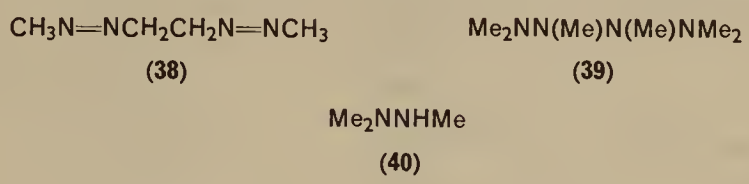
$$EtN{=}NEt \xrightarrow{\text{wall}} CH_3CH{=}NNHEt \quad (72)$$

$$RH + [CH_3CH{=}N{=}NEt]\cdot \longrightarrow R\cdot + EtN{=}NEt \quad (73)$$

of nitric oxide as a radical scavenger completely suppressed the formation of **34**, **35** and **36** but a small quantity of **37** was still formed, probably on the walls.

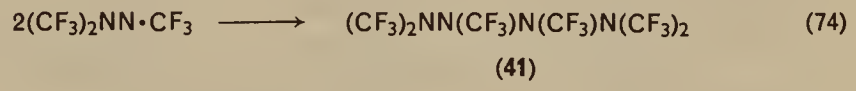
The products found may be explained by the following reaction scheme (equations 63–73)[21]. This scheme may also be applied to the thermal decomposition of azoethane but tetraethylhydrazine (**34**) is not a significant product, perhaps due to the high decomposition temperatures required[21].

Gray and Thynne[95] found tetramethylhydrazine and methylazoethane in the photolysis of azomethane. In addition, 1,2-bis(methylazo)ethane (**38**),



$CH_3N{=}NCH_2CH_2N{=}NCH_3$ (**38**) $Me_2NN(Me)N(Me)NMe_2$ (**39**) Me_2NNHMe (**40**)

hexamethyltetrazane (**39**) and possibly trimethylhydrazine (**40**) were tentatively identified from their mass spectra. Propane and butane were also found on prolonged photolysis, presumably from the photolysis of methylazoethane. No hydrazone derivatives were found in contrast with the photolysis of azoethane. In the photolysis of hexafluoroazomethane, Pritchard and co-workers[96] found that perfluorohexamethyltetrazane (**41**) was formed by dimerization of two hydrazo radicals (equation 74). No



$$2(CF_3)_2NN{\cdot}CF_3 \longrightarrow (CF_3)_2NN(CF_3)N(CF_3)N(CF_3)_2 \quad (74)$$

(**41**)

tetrazane product was found in the photolysis of perfluoroazoethane[41], presumably for steric reasons[96].

b. *Free radical studies.* The photolysis of azoalkanes has been used as the source of alkyl radicals in many studies of their rates of reaction and other properties. A particular virtue of photolysis compared with thermolysis is the ability to generate the radicals in a controlled manner at a variety of temperatures, particularly at ambient temperatures. This is of importance for studying gas-phase reactions in the atmosphere in relation to air pollution, for example[97]. The gas-phase photo-oxidation of azomethane, azoethane and azo-2-methyl-2-propane (**17**) has been reviewed by Hoare and Pearson[98]. Zollinger has briefly reviewed the photolysis and applications of aliphatic azo compounds[99]. A list of some common radicals, generated by photolysis of azoalkanes, is given in Table 4. Neither the list of radicals nor the bibliography is intended to be exhaustive.

TABLE 4. Some free radicals generated by photolysis of azoalkanes

Radical	Phase	Reference
Methyl	Gas	25, 28, 30, 35, 48, 83, 85
	Solution	24, 25, 46, 47, 48, 83, 100, 101, 102
	Solid	83, 103
Methyl-d_3	Gas	30, 83, 104
	Solution	83, 104
	Solid	83
Trifluoromethyl	Gas	96, 105
	Solution	46, 106
Ethyl	Gas	21, 35, 36, 107, 108
	Solution	45, 101, 102
Pentafluoroethyl	Gas	41
Propyl	Gas	35, 109, 110, 111
Isopropyl	Gas	22, 37
Butyl	Gas	38
Isobutyl	Gas	39, 97, 108
t-Butyl	Gas	28, 82, 108
Pentyl	Gas	112
1-Phenylethyl	Liquid SO_2	113
2-Phenyl-2-propyl	Solution and solid	50
3-Methyl-2-phenyl-2-butyl	Solution and solid	51
3-Phenyl-3-pentyl	Solution and solid	26
2-Phenoxy-2-propyl	Solution	114
2-Phenylthio-2-propyl	Solution	115
2-Cyano-2-propyl	Solution	53, 81, 116
	Solid	52, 53
3-Cyano-3-pentyl	Solution and solid	53
1-Cyanocyclohexyl	Solution	68
2-Ethoxycarbonyl-2-propyl	Solution	68, 117

c. *Unusual products.* In a few cases the photolysis of acyclic azo compounds leads to products which do not fit into the simple pattern outlined in Section a above. The formation of 2-pyrazoline (**27**) in the photolysis of 1,1,1-trifluoromethylazocyclopropane (**24**) was discussed in Section II, A, 7.

In the photolysis of azoisobutyronitrile (**12**) dimethyl-*N*-(2-cyano-2-propyl)ketenimine (**42**) was formed as one of the radical recombination products in addition to the expected tetramethylsuccinodinitrile (**43**) and the disproportionation products methacrylonitrile (**44**) and isobutyronitrile (**45**)[53, 81]. Products **42** and **44** are often not observed because the ketenimine

(**42**) is subject to thermal and photolytic decomposition[68, 118] to reform the 2-cyano-2-propyl radical while **44** is susceptible to polymerization[119].

$Me_2C{=}C{=}NC(CN)Me_2$ (**42**)

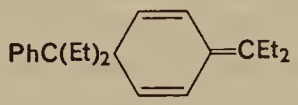
$Me_2C(CN)C(CN)Me_2$ (**43**)

$CH_2{=}C(CN)Me$ (**44**)

Me_2CHCN (**45**)

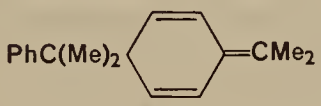
The photolysis of azo-3-phenyl-3-pentane (**13**) in degassed benzene solution at 5°C gave almost entirely radical recombination products, mainly 3,4-diethyl-3,4-diphenylhexane (**46**, 70–60%), but with some n.m.r.

$PhC(Et)_2C(Et)_2Ph$ (**46**)



(**47**)

evidence for the formation of a *para*-coupling product (**47**, 30–40%)[26]. This product (**47**) was photolabile and on further irradiation it was converted to **46**[26]. The photolysis of **13** in the solid state at −78°C was discussed in Section II, A, 3, b, where disproportionation was the dominant reaction. Nelsen and Bartlett[50] reported that a quinoid product (**48**), similar to **47**, was formed in about 2% yield in the photolysis of azo-2-phenyl-2-propane (**49**).



(**48**)

$PhC(Me)_2N{=}NC(Me)_2Ph$ (**49**)

B. Cyclic Aliphatic Azo Compounds

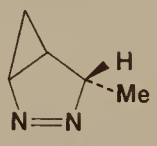
1. Introduction

Most cyclic aliphatic azo compounds give rise to direct and sensitized photoproducts which can be explained by the loss of nitrogen to form a biradical, followed by ring closure or olefin formation. The ring formation is of particular value in the preparation of small rings and highly strained systems. Examples are given in Sections II, B, 3 and 4, together with some exceptions to the general rule.

The position of the absorption maximum of the azo compound is very much dependent on the ring size and correlates with the N—N—C bond

angle[78]. Values for λ_{max} range from 315 nm for saturated five-membered rings to 385 nm for saturated six-membered rings, with conjugation increasing the absorption maximum further. Thus the 366 nm emission from mercury lamps is not effective for direct photolysis of the saturated five-membered rings, while the 313-nm line is quite satisfactory. In sensitized photolyses, some difficulties have been experienced when using sensitizers which do not absorb at wavelengths significantly greater than the absorption of the azo compound. Very high sensitizer concentrations have been employed to overcome the problem. Benzophenone-sensitized photolyses of the saturated five-membered rings do not suffer from this problem as 366-nm light can be used. The absorption intensity of cyclic azo compounds is greater than that of their acyclic counterparts because in the *cis* configuration the lowest energy absorption band of the azo group, n_+–π^*, is symmetry allowed while being forbidden for the *trans* configuration[60,61]. The extinction coefficient for the n_+–π^* transition in cyclic azo compounds is generally well in excess of 100 l/mol-cm, at least an order of magnitude greater than for *trans*-azoalkanes[54,60]. This ensures efficient use of the irradiating light in preparative photolyses, even in fairly dilute solutions.

Most investigators have not reported quantum yields, although the data available covers a wide range from values around unity in the gas phase to 0·01 in some solution photolyses. The quantum efficiency appears to depend on the wavelength of irradiation and the ring-size as well as the medium, but these matters will be discussed in more detail in Section II, B, 2. Not all photolyses in solution are inefficient: for example, the quantum yields for the 313 nm photolysis of *exo*- and *endo*-4-methyl-2,3-diazabicyclo[3.1.0]hex-2-ene (**50**) and (**51**) in pentane were found to be 0·75 and 0·53 respectively, *cis*- and *trans*-1,3-pentadiene being the products[120].



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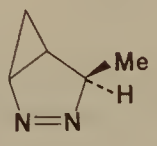


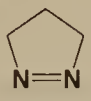
(51)

2. Mechanism and the primary processes

Cyclic aliphatic azo compounds have revealed the mechanistic secrets of their photochemistry more readily than have their acyclic counterparts for two main reasons. Firstly, many of the cyclic azo compounds fluoresce, although they do not phosphoresce, making possible direct study of their first excited singlet states. Secondly, both the singlet and triplet states of

cyclic azo compounds decompose, as shown by the differences in product ratios between direct and triplet-sensitized photolysis. This allows the indirect study of cyclic azo triplets through their photochemistry. It has been suggested that the reason why cyclic azo compounds decompose from their triplet state while acyclic azo compounds do not may be related to the rigidity in the cyclic compounds which prevents *cis* → *trans* isomerization as an energy relaxation pathway[66, 121]. It may be recalled that acyclic azo compounds failed to show a spin correlation effect with triplet sensitizers (Section II, A, 4, e). Cyclic azo compounds frequently show this effect.

a. *Gas-phase photolysis of* 1-*pyrazolines.* Mechanism studies of the photolysis of 1-pyrazoline (**52**) and its derivatives have been used to study the



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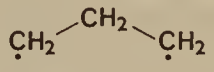
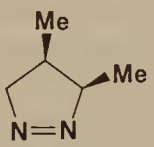


(53)

reactions of excited trimethylene biradicals (**53**) and also the energy partitioning and reactions of the vibrationally excited cyclopropane fragment[122]. In a detailed study of 1-pyrazoline (**52**) in the gas phase Loper and Dorer[122] found fluorescence and decomposition to be the only processes competing for excited **52** at shorter wavelengths (313 nm). The processes were dependent on the wavelength of irradiation, the total gas pressure and the presence or absence of oxygen. Similar investigations have been made by Trotman-Dickenson and co-workers[123] although only at a single exciting wavelength (313 nm) and without fluorescence measurements. Vibrational deactivation of excited singlet 1-pyrazoline (**52**) molecules by collision with inert molecules enhanced the quantum yield of fluorescence. This effect was particularly marked at shorter wavelengths where the quantum yield of fluorescence was decreasing steeply with wavelength. At wavelengths shorter than 308 nm no fluorescence could be detected and decomposition occurred with unit quantum efficiency in less than 10 nsec. Dorer and coworkers[124] have found that the product distribution in the direct photolysis of *cis* and *trans*-3,4-dimethyl-1-pyrazoline (**54** and **55** respectively) tends towards that found in triplet-sensitized photolysis as the wavelength in the



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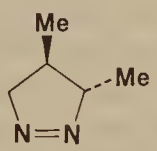
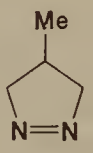


(55)

direct photolysis is shortened. Thus decomposition from both singlet and triplet states must be admitted in direct photolysis. The same need not be true in solution[65].

Two types of hydrocarbon products are formed. Cyclopropane or its derivatives are formed by closure of the 1,3-biradical, and since the cyclopropane is vibrationally excited it may undergo unimolecular decomposition to give propene. The 1,3-biradical may also give olefins directly. These products all have the same number of carbon atoms as the original 1-pyrazoline. A second class of product arises by cleavage and yields olefins, ethylene in the case of 1-pyrazoline (**52**). The cleavage reaction is a stereospecific singlet-state reaction of 1-pyrazolines[124–126] (but cf. reference 123). At shorter wavelengths and lower pressures the extent of cleavage increases[122]. This no doubt reflects a greater rate of cleavage from higher energy species which are, however, capable of collisional deactivation. The formation of 2-methylpropene, a 1,2-hydrogen migration product from the photolysis of 4-methyl-1-pyrazoline (**56**), is also considered to be a singlet-



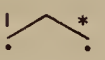
(56)

state product. Its yield decreases as the exciting wavelength is decreased. In triplet-sensitized photolysis of 1-pyrazolines, 1,2-hydrogen migration is a minor reaction, it if occurs at all [124–126].

The mechanism of the direct photolysis of 1-pyrazolines in the absence of oxygen may be described by equations 75–88 where P refers to a 1-pyrazoline molecule, superscripts refer to the multiplicity of an excited state, subscripts refer to the level of electronic excitation, an asterisk indicates a vibrationally excited species and M is a nonreacting molecule. The lifetime of the 'hot' first excited singlet state, $^1P_1^*$, has a maximum value of about 195 nsec when 1-pyrazoline (**52**) is irradiated at 335 nm, near the onset of absorption, but decreases to 10 nsec at 312 nm. On the other hand, the radiative lifetime is essentially independent of the exciting wavelength and is about 1·3 μsec. Thus the decrease in the lifetime of $^1P_1^*$ is due to faster rate constants for equations 77, 78 and perhaps 79. Vibrational deactivation of $^1P_1^*$ (equation 80) is significant and the lifetime of $^1P_1$ is lengthened to about 320 nsec, allowing for an increase in fluorescence (equation 81). The quantum yield of decomposition from $^1P_1$ (equation 82) is about 0·5, independent of pressure above 10 Torr up to at least 325 Torr with excitation at 333 nm.

$$^1P_0 + h\nu \longrightarrow {}^1P_1^* \quad (75)$$

$$^1P_1^* \longrightarrow {}^1P_0 + h\nu \quad (76)$$

$$^1P_1^* \longrightarrow \text{  } + N_2 \quad (77)$$

$$^1P_1^* \longrightarrow {}^3P_1^* \quad (78)$$

$$^1P_1^* \longrightarrow C_2H_4 + n \quad (79)$$

$$^1P_1^* + M \longrightarrow {}^1P_1 + M \quad (80)$$

$$^1P_1 \longrightarrow {}^1P_0 + h\nu \quad (81)$$

$$^1P_1 \longrightarrow \text{hydrocarbons} + N_2 \quad (82)$$

$$^1P_1 + M \longrightarrow P_0 + M \quad (83)$$

$$^3P_1^* \longrightarrow \text{propene} + N_2 \quad (84)$$

$$^3P_1^* + M \longrightarrow {}^1P_0 + M \quad (85)$$

Collisional deactivation of $^1P_1$ and the triplet $^3P_1^*$ to the ground state, $^1P_0$, (equations 83 and 85) does not appear to be very important as the sum of the quantum yields of fluorescence and decomposition approaches unity, particularly at short wavelengths of excitation. Equation 84 is suggested by Trotman-Dickenson[123] as an explanation for the pressure-independent formation of some of the propene. Closure of the singlet biradical (equation 86) would be expected to be rapid[123]. Rather unexpectedly the rate of isomerization of 'hot' cyclopropane (equation 88) is greater when longer exciting wavelengths are used. By application of Rice–

 (86)

 (87)

 (88)

Ramsperger–Kassel–Marcus (RRKM) theory (see ref. 122 and references cited therein) Loper and Dorer found that the most probable energy received

by the 'hot' cyclopropane was about 59 kJ/mol less at 313 nm compared with 333 nm. They conclude that at longer wavelengths the energy of the excited 1-pyrazoline is distributed to the fragments statistically while non-random energy distribution occurs at short wavelengths[122].

In the presence of oxygen the excited singlet state of 1-pyrazoline (**52**) is quenched with a collision efficiency of about 0·5. Only 10 Torr of oxygen is needed to quench more than 90% of the 1-pyrazoline singlets produced by 333 nm irradiation although, due to the shorter life of the singlet state, at shorter wavelengths the singlet quenching is less efficient. The nature of the state of 1-pyrazoline produced is uncertain and is designated $P^{\dagger}$ in the following additional mechanistic steps (equations 89–92). In the presence of only 10 Torr of oxygen $P^{\dagger}$ decomposes (equation 92) with unit efficiency

$$^1P_1{}^* + O_2 \longrightarrow P^{\dagger} + O_2 \quad (89)$$

$$^1P_1 + O_2 \longrightarrow P^{\dagger} + O_2 \quad (90)$$

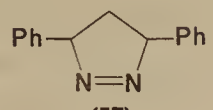
$$P^{\dagger} + M \longrightarrow {}^1P_0 + M \quad (91)$$

$$P^{\dagger} \longrightarrow \text{hydrocarbons} + N_2 \quad (92)$$

at 333 nm. With the further addition of pentane up to total pressures of about 400 Torr collisional quenching of $P^{\dagger}$ was demonstrated. From this data Loper and Dorer calculated the rate constant for the decomposition of $P^{\dagger}$ (equation 92) to be $7{\cdot}0 \pm 1{\cdot}6 \times 10^9$/sec. Using RRKM[122] theory this rate indicates that $P^{\dagger}$ has about 230 kJ/mol excess internal energy. Whether $P^{\dagger}$ is a vibrationally excited ground state, $P_0{}^*$, as assumed in the RRKM calculations, or whether it is a triplet state which undergoes intersystem crossing to $P_0{}^*$ is not clear[122].

b. *Condensed-phase photolysis of 1-pyrazolines.* Comparable mechanistic studies in solution have not been made on 1-pyrazolines, although many cases of spin correlation effects have been noted when comparing the products of direct and triplet-sensitized photolysis, particularly in relation to the stereospecificity of the reaction. Generally direct photolysis gives greater stereospecificity than triplet-sensitized photolysis. Several examples are described in Sections II, B, 3 and 4. For differing views on the mechanism of spin correlation effects see references 121 and 127.

Overberger and Anselme[128] reported evidence for the presence of a free radical but no triplet state in 3,5-diphenyl-1-pyrazoline (**57**) which was irradiated at 77 K in a Nujol or Fluorolube matrix. Andrews and Day[65, 129, 130] found that 1,3-pentadiene, a good triplet quencher, did not



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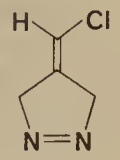
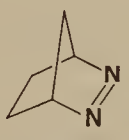


(58)

affect the product ratio in the direct photolysis of 4-chloromethylene-1-pyrazoline (**58**) in hexane. Therefore it was concluded that direct photolysis was proceeding via the singlet state. As will be seen in Section II, B, 2, c this may not be a valid argument because of very short triplet lifetimes. The 1,3-pentadiene, however, did quench the singlet state of **58** as indicated by fluorescence quenching. By means of a 'Saltiel plot'[131] of varying product composition against the triplet energy of a number of sensitizers it was estimated that the triplet energy of **58** was between 230 and 272 kJ/mol[130].

c. *Photolysis of bicyclic azo compounds.* The mechanisms of the photolysis of the bicyclic azo compounds 2,3-diazabicyclo[2.2.1]hept-2-ene (**59**) and 2,3-diazabicyclo[2.2.2]oct-2-ene (**60**) have been examined fairly thoroughly



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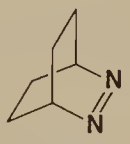
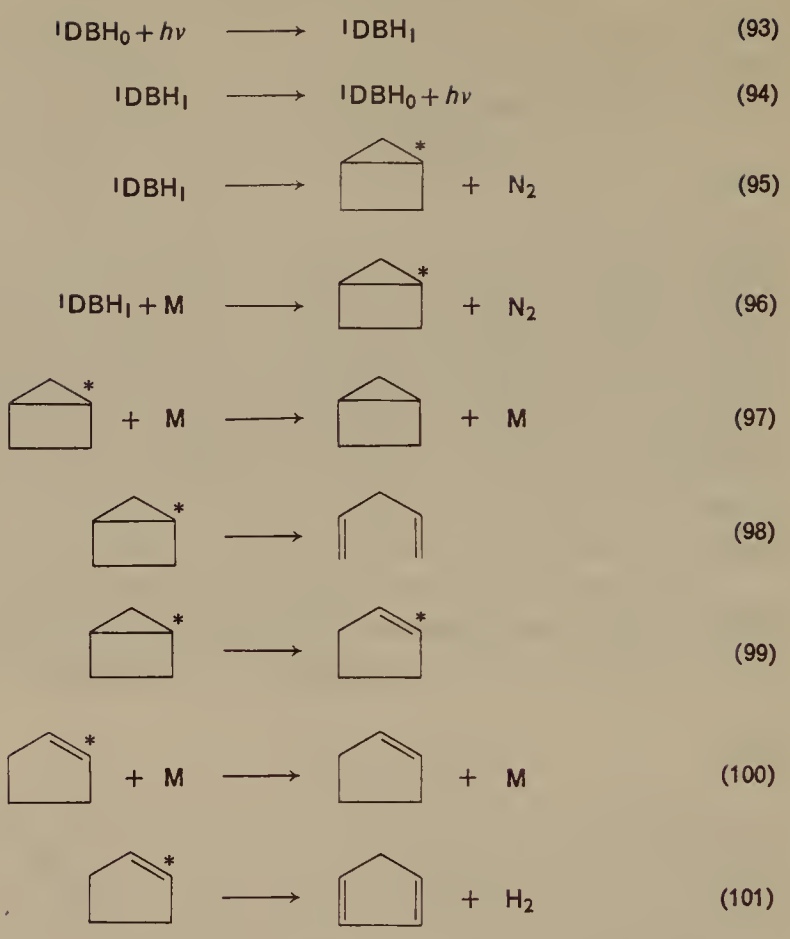


(60)

both in the gas phase and in solution[66, 132–134]. The two compounds show considerable difference in behaviour. For example, whereas both **59** and **60** fluoresce in the vapour phase only **60** fluoresces in solution. In contrast the quantum yield, Φ, of decomposition of **59** is slightly enhanced from 0.85 in the gas phase to unity in solution, whereas decomposition of **60** is quenched from $\Phi = 0{\cdot}50$ in the gas phase to $\Phi = 0{\cdot}08$ in solution.

The mechanism of direct photolysis of **59** is outlined in equations 93–101 where DBH is used to represent **59** and superscripts, subscripts, asterisks and M have the same significance as in equations 75–88. Intersystem crossing is not included in the mechanism because Clark and Steel[66] found that oxygen had no effect on the direct photolysis of **59**, while it quenched the triplet-sensitized photolysis (see below). Equation 96 is included to account for the fluorescence quenching with slight enhancement of decomposition[66, 132]. Oxygen, nitrogen and pentane all had similar effectiveness as quenchers. A detailed study of the unimolecular decomposition of the 'hot' hydrocarbon fragments (equations 97–101) has been made by Thomas,



Sutin and Steel[133]. No evidence has been found for the 1,3-cyclopentanediyl radical (**61**) as the addition of 1000 Torr of oxygen had no effect on the 1:1

(61)

relationship between C_5 hydrocarbons formed and **59** consumed[132]. If formed, **61** must have a lifetime of less than 10^{-10} sec[132]. Photodecomposition of **59** from a 'hot' ground state, $^1DBH_0$*, was rejected because its lifetime would be sufficiently long that essentially complete collisional deactivation would occur in solution[66].

By sensitized photolysis of **59** using triplet sensitizers of different triplet energies Engel[134] found the triplet energy, E_T, of **59** to be 250 ± 4 kJ/mol. With high energy sensitizers like benzophenone the quantum yield of

decomposition was unity. The lifetime of triplet **59** was so short that no reliable quenching data using stilbene or *trans*-1,3,5-hexatriene could be obtained. The maximum lifetime for triplet **59** in solution was 10^{-9} sec[66]. Thus the mechanism of triplet-sensitized photolysis of **59** is simple (equations 102–104) where S refers to the sensitizer. Triplet **61** would have to

$$^1S_0 + h\nu \longrightarrow {}^1S_1 \longrightarrow {}^3S_1 \tag{102}$$

$$^1DBH_0 + {}^3S_1 \longrightarrow {}^3DBH_1 + {}^1S_0 \tag{103}$$

$$^3DBH_1 \longrightarrow \text{(62)} \longrightarrow \text{(61)} \tag{104}$$

undergo spin inversion before cyclization. Oxygen had a significant quenching effect on decomposition of $^3DBH_1$ and **62** was suggested as a possible intermediate which could be quenched[66]. On the other hand it is hard to imagine that **62** could have the required lifetime of 5×10^{-8} sec. There was a marked discrepancy between the yield of hydrocarbons and the consumption of **59** in the presence of oxygen. This was thought to be due to reaction of oxygen with the biradical **61**. A minimum lifetime of 10^{-7} sec was assigned to triplet **61** which is in contrast to the 10^{-10} sec maximum estimated in direct photolysis[66].

The mechanism of the direct and triplet-sensitized photolysis of **60** is outlined in equations 105–116 where DBO is used to represent **60**. Virtually

$$^1DBO_0 + h\nu \longrightarrow {}^1DBO_1 \tag{105}$$

$$^1DBO_1 \longrightarrow {}^1DBO_0 + h\nu \tag{106}$$

$$^1DBO_1 \longrightarrow {}^3DBO_1 \tag{107}$$

$$^1DBO_0 + {}^3S_1 \longrightarrow {}^3DBO_1 + {}^1S_0 \tag{108}$$

$$^1DBO_1 + M \longrightarrow {}^1DBO_0 + M \tag{109}$$

$$^1DBO_1 + O_2 \longrightarrow {}^3DBO_1 + O_2 \tag{110}$$

$$^3DBO_1 + M \longrightarrow {}^1DBO_0 + M \quad (111)$$

$$^1DBO_1 \longrightarrow Q \quad (112)$$

$$^1DBO_1 + Q \longrightarrow {}^1DBO_0 + Q \quad (113)$$

$$^3DBO_1 \longrightarrow \square\square + \square\!\!/\!\!/ \quad (114)$$

(63) (64)

$$^1DBO_1 \longrightarrow \mathbf{63} + \mathbf{64} \quad (115)$$

$$^3DBO_1 \xrightarrow{?} {}^1DBO_0 \quad (116)$$

all the data for this mechanism and the following discussion comes from the work of Clark and Steel[66]. As can be seen the primary steps in the mechanism are more complex than for **59**, although only two hydrocarbon products **63** and **64** are formed. Considering direct photolysis in the gas phase, the quantum yield of fluorescence ($0{\cdot}56 \pm 0{\cdot}10$) is insensitive to pressure whereas decomposition ($\Phi = 0{\cdot}50 \pm 0{\cdot}05$ at 0·1 Torr) is markedly quenched above about 10 Torr. This indicates that the triplet $^3DBO_1$ is the major dissociating state in the gas phase. In fact, similar quenching characteristics were found in high energy triplet-sensitized photolysis of **60**. Decomposition from 'hot' $^1DBO_0$* was rejected for the same reasons as with **59**. The triplet energy of **60** was found to lie between 222 and 234 kJ/mol.

Direct measurements of the fluorescence lifetime of **60** by flash techniques gave values of 1·0 μsec in the gas phase and 0·33 μsec in 2,2,4-trimethylpentane[132]. As with **59** quenching experiments using *trans*-1,3,5-hexatriene in triplet-sensitized photolysis gave an upper value of 10^{-9} sec for the lifetime of triplet **60**. In solution the quantum yield of fluorescence on direct excitation was 0·2, not a very large decrease from its value of 0·56 in the gas phase. Thus we have the paradoxical situation of a longer-lived singlet, $^1DBO_1$, being less susceptible to collision-quenching by inert molecules (equation 109) than is the much shorter-lived triplet, $^3DBO_1$ (equation 111). There are, however, very efficient quenchers of singlet **60**. One of these is produced as a minor by-product in direct but not triplet-sensitized photolysis of **60** (equations 112 and 113) and is thought be to a hydrazine derivative formed by reduction of the azo group in **60**; its structure is not known. Oxygen also quenches $^1DBO_1$ efficiently to give the triplet state (equation 110) as shown by the fluorescence yield being quenched much more than that of the hydrocarbon products. Apparently in this case the short life of

the triplet state is a restricting factor on its quenching by oxygen. In benzophenone-sensitized photolysis of **60** in the presence of oxygen the same quenching behaviour was encountered as with **59**. 1,3-Pentadiene also quenches singlet **60**, although at only 1/2000 of diffusion controlled rate[129].

The hydrocarbon product ratio of 27% bicyclo[2.2.0]hexane (**63**) to 73% 1,5-hexadiene (**64**) in triplet-sensitized photolysis compared with 42% and 58% respectively on direct photolysis indicates that a mixture of triplet and singlet decomposition (equations 114 and 115) occurs on direct photolysis in solution. On the assumption that the sum of intersystem crossing and fluorescence quantum yields in solution is unity, as it is in the gas phase, Clark and Steel calculated that only 50–60% of the hydrocarbons **63** and **64** are formed by a triplet pathway in direct solution photolysis of **60**. Only 1·4% of $^3DBO_1$ molecules dissociate to give hydrocarbon products. The remainder must return to the ground state by an as yet unknown path (equation 116).

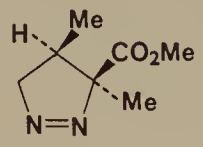
In retrospect it is perhaps not surprising that **59** does not photodecompose by a dual singlet and triplet pathway on direct irradiation. The rate of intersystem crossing for **60** is estimated to be $2{\cdot}4 \times 10^6$/sec and if a similar value applies to **59** this would be no competition for its singlet lifetime of 7 nsec in the gas phase or less than 0·1 nsec in solution. Some of the difference in behaviour of **59** and **60** may reflect the different energy of the absorption bands. Loper and Dorer found wavelength dependence studies on 1-pyrazoline (**52**) very rewarding[122]. The different ring size and greater flexibility in **60** compared with **59** may also be a factor.

3. General photolyses of compounds containing a five-membered azo ring

By far the largest group of azo compounds which have been studied and used photochemically are those containing a five-membered azo ring. Their usefulness in synthesis of three-membered carbocyclic rings and also some novel mechanistic features are shown in the following sections. Triplet-sensitized photolysis generally favours the cyclic products over olefins but at the risk of losing stereospecificity which is more characteristic of direct photolysis.

a. *1-Pyrazolines.* Photolysis of monocyclic 1-pyrazolines has been used widely to synthesize cyclopropane derivatives. Generally the stereochemistry of the pyrazoline is retained in the product, frequently more than in thermolysis. For example, Van Auken and Rinehart[135] found that the photolysis of methyl *trans*-3,4-dimethyl-1-pyrazoline-3-carboxylate (**65**) gave a 72% yield of the *trans*-cyclopropane **66** with about 98% retention of

configuration. It may be noted that the minor product **67** also has the *trans* configuration. Analogous results were obtained on irradiation of *cis*-**65**,



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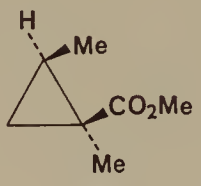

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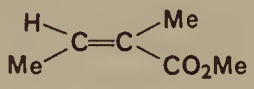
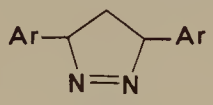


(67)

yielding *cis*-**66** and *cis*-**67**. Similarly in the photolysis of 3,5-diaryl-1-pyrazolines (**68**) Overberger and co-workers[128, 136, 137] found that *trans*-**68**



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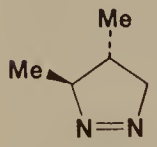
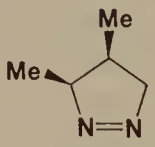
(70)

gave a high yield of *trans*-**69** although thermolysis also gave a high retention of configuration. There was much lower retention of configuration on photolysis and thermolysis of *cis*-**68**, there being a trend towards formation of the more stable *trans*-**69**[136]. Nevertheless, photolysis favoured *cis*-**69** when compared with thermolysis. Presumably the excited singlet diradical **70** generated by photolysis is more reactive towards cyclization than the ground-state singlet **70** formed by thermolysis. No olefinic products were formed from **68**.

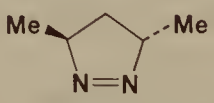
In the direct photolysis of dimethyl-1-pyrazolines Crawford and co-workers[125] found much less retention of configuration in the 1,2-dimethylcyclopropane products. Generally retention was worse for *cis* isomers and worse in solution compared with the gas phase. Yields of olefinic material were generally fairly low, except for *trans*-3,4-dimethyl-1-pyrazoline (**71**)



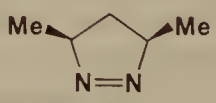
(71)



(72)

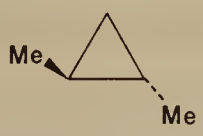


(73)



(74)

where about 35% of olefins was formed. In benzophenone-photosensitized decomposition of **71–74** virtually no olefins were formed and the ratio of *trans*-1,2-dimethylcyclopropane (**75**) to *cis*-1,2-dimethylcyclopropane (**76**)

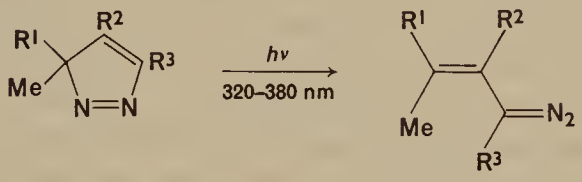


(75)

(76)

was the same for **71** and **72** (ca. 61 : 39) and for **73** and **74** (71 : 27), depending somewhat on the solvent for **73** and **74**. Clearly the triplet biradical generated using benzophenone survives long enough for complete equilibration before cyclization occurs, whereas in direct photolysis cyclization and equilibration are competitive.

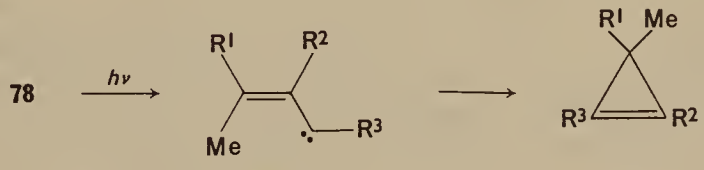
b. *3H-Pyrazoles.* The photochemistry of 3*H*-pyrazoles resembles that of 1-pyrazolines in the formation of cyclopropenes[138–140], although some exceptions will be noted. Closs and co-workers[138] have shown that the initial step is photochemical conversion of the 3*H*-pyrazole **77** to the



(117)

(77) (78)

diazoalkene **78** (equation 117). Subsequent photolysis converts **78** into the cyclopropene **79** via the carbene **80** (equation 118). The restricted wave-



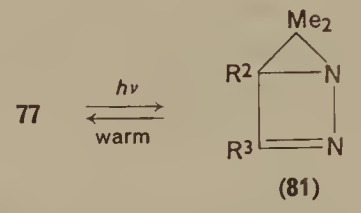
(118)

(80) (79)

length range (320–380 nm) largely prevented photolysis of the diazoalkene (**78**) which was red in colour and also had strongly increasing absorption in the region of 300 nm. A 50% yield of the diazoalkene **78** ($R^1 = R^3 = Me$, $R^2 = H$) was obtained and similarly from two other derivatives ($R^1 = R^2 = R^3 = Me$ and $R^1 = Me$, $R^2 = H$, $R^3 = Ph$). In another example (see below) the characteristic infrared absorption of the diazo group at 2010 cm^{-1} was found after a few minutes of irradiation[141]. It was not possible to tell whether the lower yield of diazoalkene (**78**) when wavelengths shorter than 320 nm were used was due to less **78** formed and more direct photodecomposition of

77 or to the faster rate of photolysis of **78** because of its higher extinction coefficient.

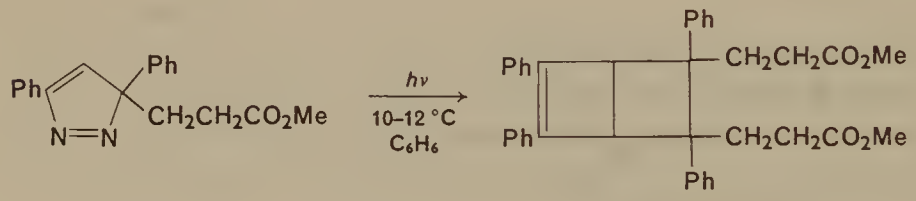
In fully alkylated derivatives of 77 ($R^1 = R^2 = R^3 = Me$; $R^1 = Me$, R^2, $R^3 = -(CH_2)_n-$, $n = 4$ or 5) irradiation in polar solvents such as dichloromethane or methanol at –50°C gave a bicyclic isomer (**81**) which reverted to



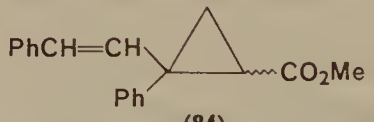
(81) (119)

77 on warming (equation 119)[138]. The choice between decomposition and isomerization was solvent-dependent at about –60°C with no decomposition occurring in methanol or dichloromethane but 70% decomposition and 30% isomerization occurring in pentane. Photosensitizers benzophenone, acetophenone and anthracene made no change to the ratio of decomposition to isomerization and so it was concluded that both reactions arose from a triplet state of the 3*H*-pyrazole (77).

There are other exceptions to the formation of cyclopropenes in the photolysis of 3*H*-pyrazoles. Moritani, Hosokawa and Obata[141] found that **82** gave the dimer **83** and two isomeric cyclopropanes **84** (equation 120). The stereochemistry of the cyclopropane ring was uncertain although it was shown to be opposite in the two isomers of **84** which were obtained.



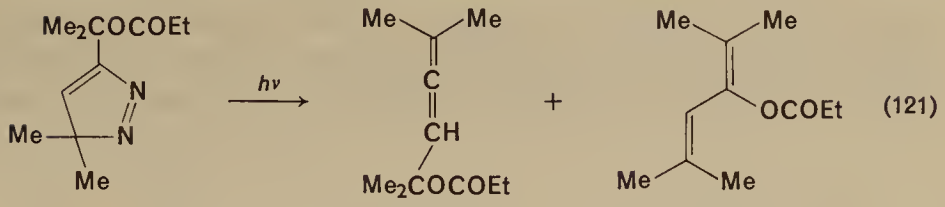
(82) (83) (7·5%)



(84) (120)

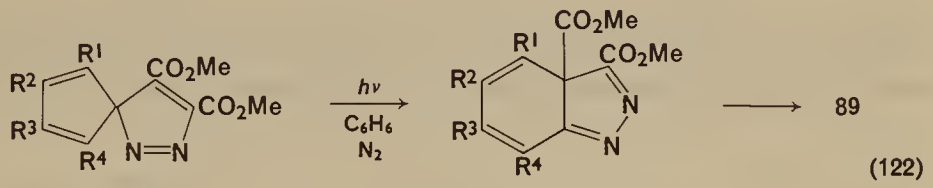
(7·5% *trans*-styryl + 6·5% *cis*-styryl)

Day and Whiting[142] found no cyclic products in the photolysis of **85** (equation 121). Instead the allene **86** and diene **87** were found. Dürr and Schrader[143] found that the spiro-3*H*-pyrazole **88** first underwent a photo-



(85) (86) (87) (121)

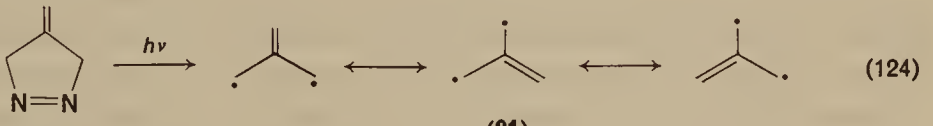
chemical ring expansion before the resulting 3*H*-indazole derivative (**89**) was photolysed to **90** (equations 122 and 123).



(88) (122)

(89) (90) (123)

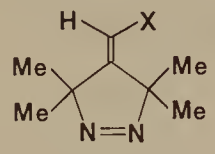
c. *Formation of the trimethylenemethyl biradical.* The photolysis of 4-alkylidene-1-pyrazolines is of particular interest as the theoretically interesting trimethylenemethyl biradical (**91**) or its derivatives, would be expected as the primary product (equation 124). Dowd[144] found that irradiation of 4-methylene-1-pyrazoline (**92**) at −185°C in hexafluorobenzene or perfluoromethylcyclohexane gave a triplet species as indicated



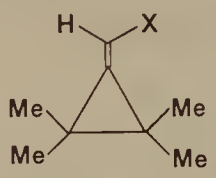
(92) (91) (124)

by its e.s.r. spectrum. This product was stable for at least a month after the irradiation when stored at liquid nitrogen temperatures. It had been predicted from theoretical calculations that **91** should be a ground-state triplet.

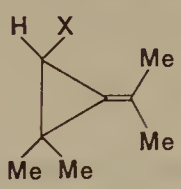
Irradiation of substituted derivatives of **92** produces methylenecyclopropane derivatives, some product being rearranged. For example, Andrews and Day[65, 130] have irradiated **93** (X = $EtCO_2$— or Cl—) and found mainly



(93)

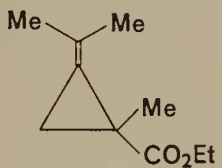


(94)

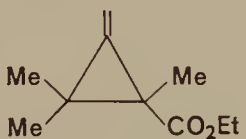


(95)

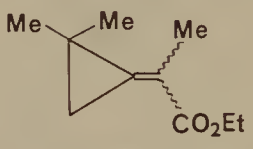
94 with some rearranged product **95**. Similarly, Sanjiki, Kato and Ohta[145] obtained small yields of all possible rearranged methylenecyclopropanes **96–98** on irradiation of **99** and **100**. When triplet sensitizers such as benzo-



(96)

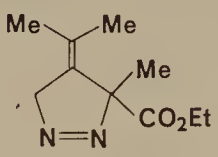


(97)

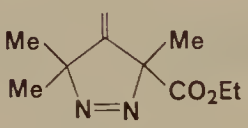


(98)

mixture of both isomers



(99)

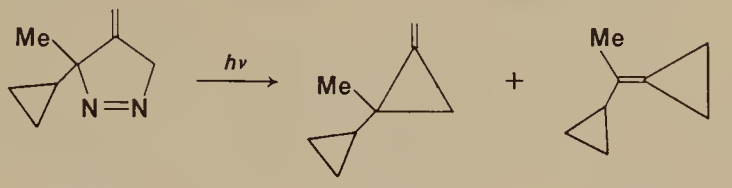


(100)

phenone and triphenylene were used in the above cases, a larger yield of the rearranged methylenecyclopropanes was generally obtained. In fact, **95** was the major product from **93**, and **96** the major product from both **99** and **100**. These results have been interpreted to mean that the direct photolysis proceeds via a short-lived excited singlet trimethylenemethyl biradical which undergoes ring closure faster than relaxation to a delocalized configuration (**101**). The triplet-sensitized decomposition, on the other hand, is considered to yield a longer-lived triplet biradical which allows time for rearranged product to be formed. Spin inversion of the triplet would be

(101)

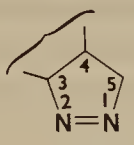
required before cyclization could occur. In contrast, the photolysis of 3-cyclopropyl-3-methyl-4-methylene-1-pyrazoline (**102**) showed negligible difference in product distribution in direct or benzophenone-sensitized photolysis (equation 125)[146].



(125)

(102) (71%) (29%)

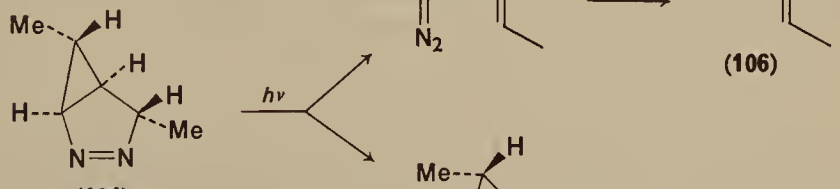
d. *Bicyclic and polycyclic systems.* This section deals with examples of the type **103** with ring fusion at C_3, C_4. 3,5-Bridged systems are discussed



(103)

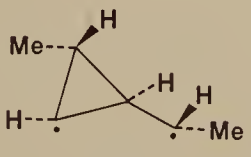
elsewhere. 2,3-Diazabicyclo[2.2.1]hept-2-ene (**59**) was discussed in Section II, B, 2, c in connection with the mechanism of photolysis. Some derivatives of **59** are discussed in Section II, B, 4, d where they are compared with derivatives of 2,3-diazabicyclo[2.2.2]oct-2-ene (**60**).

The simplest system of type **103** shows evidence of more than one mechanism in its photolysis. Eaton, Bergman and Hammond[120] have found evidence of carbenes in the photolysis of *exo*-4,*exo*-6-dimethyl-2,3-diazabicyclo[3.1.0]hex-2-ene (**104**) (equations 126–129). The major photoproduct is *trans*-2-methyl-1,3-pentadiene (**105**) which could be formed from either the carbene **106** or the biradical **107**. However, the formation of



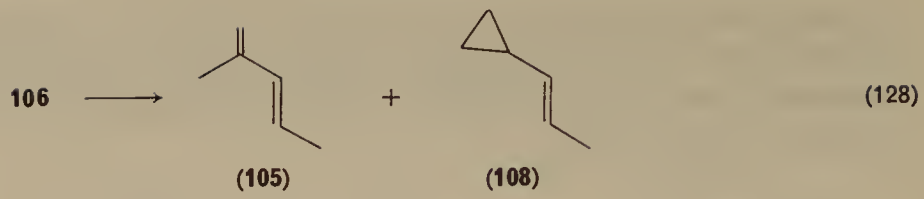
(126)

(104) **(106)**

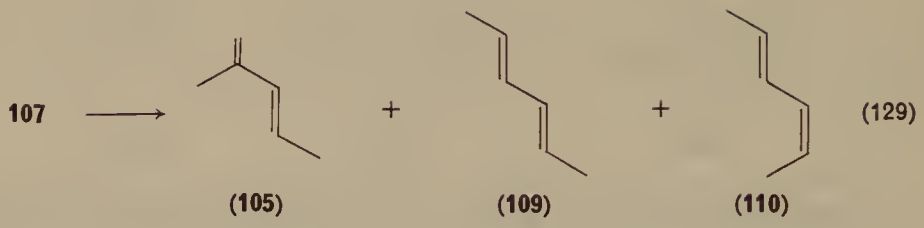


(127)

(107)

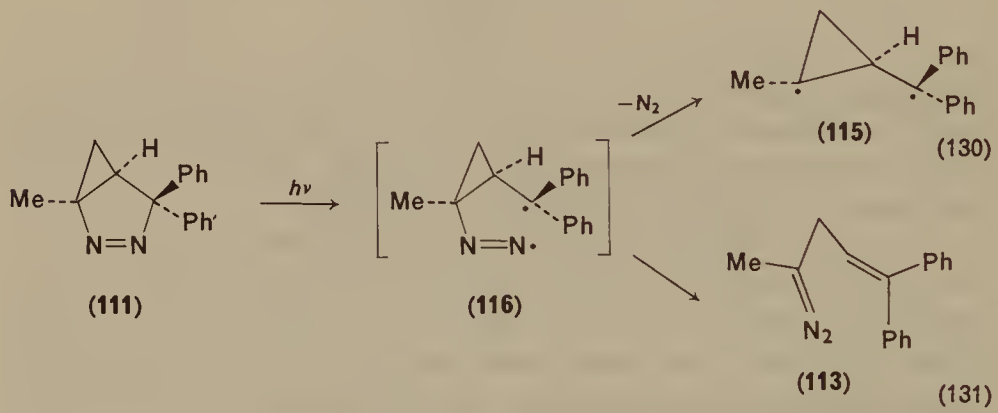


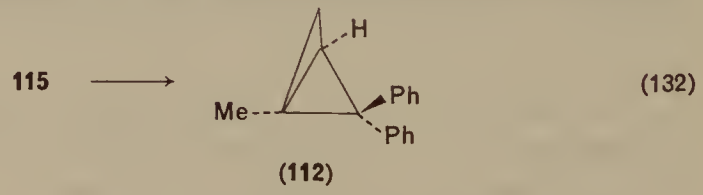
(128)



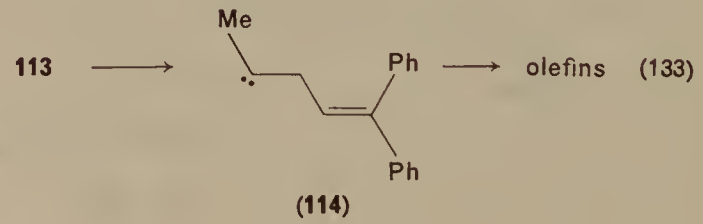
(129)

trans-1-cyclopropylpropene (**108**) unambiguously implicates the carbene intermediate (**106**) while the hexadienes **109** and **110** would be most reasonably expected to come from the biradical (**107**). Similar results were obtained in the photolysis of the *endo*-4 epimer of **104**.





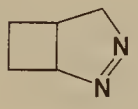
(132)



(133)

Gassman and Greenlee[147] claim that the presence of phenyl substituents dramatically changes the mechanistic picture, favouring the biradical pathway. Nevertheless, the carbene mechanism is still considered competitive as shown in equations 130–133. Irradiation of 4,4-diphenyl-1-methyl-2,3-diazabicyclo[3.1.0]hex-2-ene (**111**) gave the bicyclobutane **112** in 51% yield, together with about 30% of a mixture of four 1,3-dienes. The main evidence for the competition between equations 130 and 131 came from an n.m.r. study of the irradiated reaction mixture. When the photolysis of **111** was 95% complete, the solution contained 44–50% of **112**, only small quantities of olefinic material and 26–30% of a component which was tentatively identified as the diazo compound **113**. Attempts to isolate this product were unsuccessful. The olefinic material apparently arose from secondary reactions of **113** via the carbene **114** while the bicyclobutane **112** was formed from the biradical **115**, or perhaps even by a concerted elimination of nitrogen from the electronically excited azo compound (**111**), without the formation of **115**. In the actual decomposition steps (equations 130 and 131) a one-bond fission of the azo group to give **116** seems the best way to explain the formation of the proposed diazo compound (**113**), at the same time allowing for a competitive route to **112**. Hammond and coworkers[120] have suggested that the carbene mechanism may occur in some unstrained monocyclic systems and may account for small quantities of cleavage products.

The 2,3-diazabicyclo[3.2.0]hept-2-ene system (**117**) has been found to



(117)

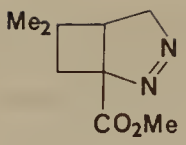

(118)


(119)

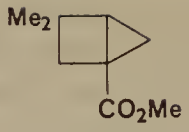

(120)

give bicyclo[2.1.0]pentane (**118**) and derivatives on thermolysis, direct photolysis and triplet-sensitized photolysis[148–151]. Generally thermolysis gave the worst yields of bicyclic product and triplet-sensitized photolysis the best. For example, in the thermolysis of the parent system (**117**)[148] the major product was 1,4-pentadiene (**119**, >65%) with only 15–17% of **118** and about 6% of vinylcyclopropane (**120**). Direct photolysis ($\lambda > 300$ nm) in cyclohexane gave **118** (59%), **119** (27%) and **120** (11%), while benzophenone-sensitized photolysis gave **118** (90%) and **119** (10%). Other olefins were formed in small yields on thermolysis and direct photolysis.

In the photolysis of methyl 6,6-dimethyl-2,3-diazabicyclo[3.2.0]hept-2-ene-1-carboxylate (**121**) it was found[149] that the bicyclopentane **122** was

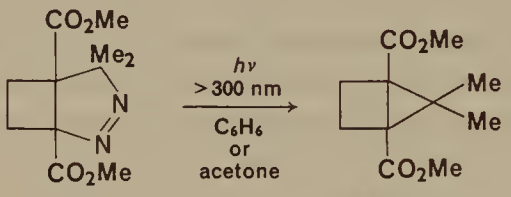


(121)



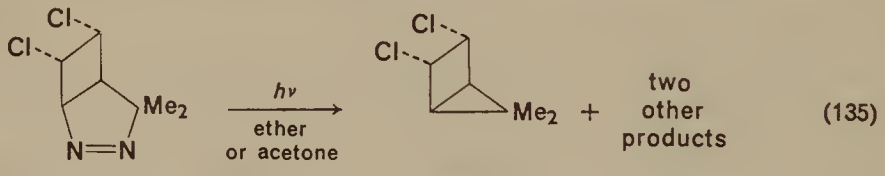
(122)

formed in 80% yield when acetone was used as the solvent, whereas a much more complex mixture was produced in pentane. This suggests that acetone was acting as a triplet sensitizer, absorbing the shorter wavelengths from the mercury lamp which were transmitted by the Pyrex filter. The sensitizing effect of acetone does not appear to have been observed by Franck-Neumann[150] in the photolysis of **123** (equation 134). On using benzophenone as photosensitizer, the yield of **124** increased to 88%.

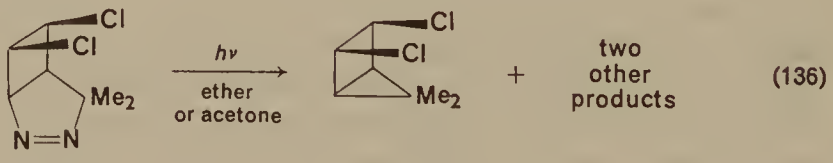


(123) (124) (*ca.* 50%) (134)

The stereochemistry of the four-membered ring is preserved as is shown by photolysis of **125** and its *endo* isomer (**126**) (equations 135 and 136)[150]. Interestingly, acetone as the solvent gave better results than ether, and when



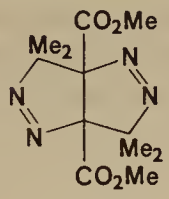
(125) (127) (135)



(126) (128) (136)

benzophenone was used as photosensitizer the yield of **127** was 97% and **128** was 80%.

Photolysis of the pyrazolopyrazole (**129**) yielded the bicyclobutane (**130**) in about 20% yield, together with two dienediesters[152]. In the 2,3-diaza-



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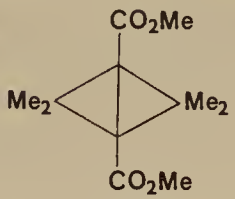
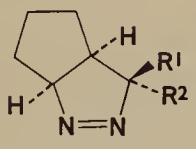


(130)

bicyclo[3.3.0]oct-2-ene system (**131**) the stereochemistry of the products depends on the method of decomposition[153]. Thermolysis of *exo*-**131**



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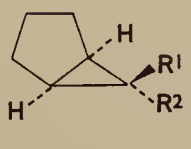

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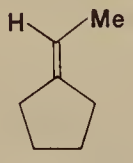
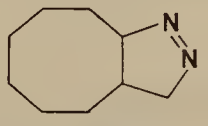


(133)

(134)

($R^1 = H$; $R^2 = Me$) and *endo*-**131** ($R^1 = Me$; $R^2 = H$) gives largely inversion of configuration, i.e. *endo*-**132** ($R^1 = Me$; $R^2 = H$) and *exo*-**132** ($R^1 = H$; $R^2 = Me$) respectively with up to 19% of the olefins **133** and **134**. Direct photolysis of *exo*-**131** and *endo*-**131** gives mainly retention of configuration with up to 16% of **133** and **134**. Benzophenone-photosensitized decomposition gives mainly *exo*-**132** from either *exo*-**131** or *endo*-**131** with a slight tendency towards retention of configuration in the case of *endo*-**131**. Only a trace of olefins was formed.

Configuration is also retained in very high yield on photolysis of 9,10-diazabicyclo[6.1.0]undec-9-ene (**135**)[154]. Direct photolysis of *trans*-**135**



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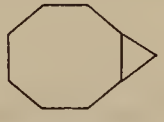
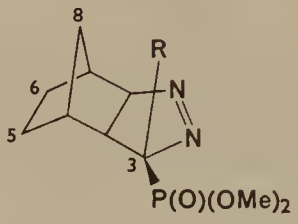


(136)

gave 96% *trans*-**136** and 4% *cis*-**136** while *cis*-**135** gave 100% *cis*-**136**. Benzophenone-sensitized photolysis of *trans*-**135** gave equal proportions of *cis*- and *trans*-**136** while *cis*-**135** gave 93% *cis*-**136** and 7% *trans*-**136**. No olefins were formed on photolysis in contrast to thermolysis of *cis*-**135** where 49% olefins were produced. Strangely thermolysis of *trans*-**135** gave 100% *trans*-**136**.

Pyrazoline rings may be conveniently built on to norbornene and norbornadiene and the photolysis of these compounds has been studied[155, 156]. For example, Callot and Benezra[155] have photolysed the two isomers **137** and **138** and also their 5,6-dehydro derivatives (R = Ph or Me). Direct



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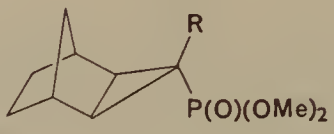

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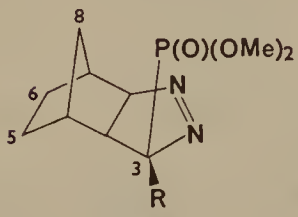

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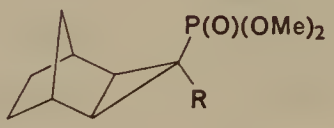


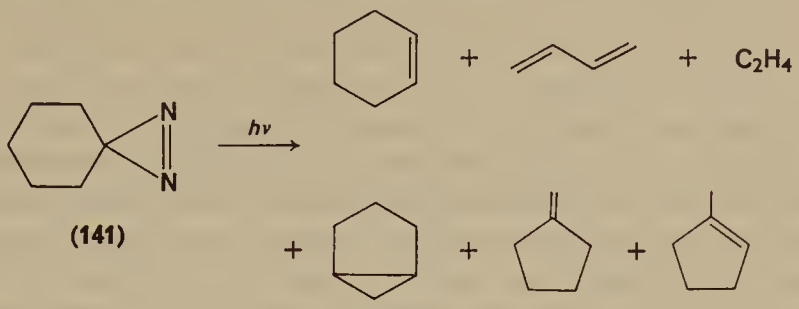
(140)

photolysis of **137** gave only **139** while **138** gave mainly **140** with 10–20% of **139**, i.e. general retention of configuration at C_3. The presence of a double bond at the 5,6 position did not alter the overall product pattern, although some side-products were formed. Benzophenone-photosensitized decomposition of **137** and **138** gave in each case a mixture of **139** and **140**. This would seem to indicate that the longer lifetime of the triplet biradical is more important than interaction between the C_8 methylene group and the bulky dimethylphosphono group for determining the stereochemistry of the products.

4. General photolyses of other cyclic azo compounds

a. *Three-membered azo rings.* Diazirines are isomeric with diazo compounds and their photochemistry appears to be similar in involving a carbene. Frey and Stevens[157] found that photolysis of cyclohexanespiro-3-diazirine (**141**) in the gas phase gave a number of products (equation 137), the major ones being cyclohexene and the fragmentation products butadiene and ethylene. The extent of fragmentation decreased as the gas pressure was increased, presumably by collisional deactivation of vibrationally excited cyclohexene molecules. The possibility that the diazirine

first underwent a photorearrangement to give diazocyclohexane was not considered to be significant.



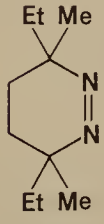
(141) (137)

b. *Six-membered azo rings.* The photolysis of the simple monocyclic perhydropyridazine system may be illustrated by 3,6-diethyl-3,6-dimethylperhydropyridazine (**142**)[121]. A comparison between the product yields from thermolysis, direct photolysis and triplet-sensitized photolysis is given in Table 5 for both *meso*-**142** and (±)-**142**. The decrease in retention of

TABLE 5. Yields of thermolysis and photolysis products of *meso*- and (±)-3,6-diethyl-3,6-dimethylperhydropyridazine (**142**).

Azo compound	Method	Product yield (%)[a]			% Retention of configuration in **144** and **145**
		143	**144**	**145**	
meso-	Thermal	49	43	2·5	>98
(±)-		51	3·5	42	>98
meso-	Direct *hv*	61	35	3·5	95
(±)-	($\lambda > 330$ nm)	60	4	33	97
meso-	Thioxanthone-	77	11·5	8	61
(±)-	sensitized[b]	75	8	12	65

[a] Small quantities of another unidentified product were also formed.
[b] Triplet energy = 274 kJ/mol[158].



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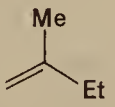
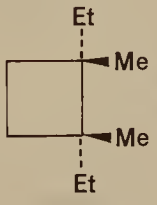
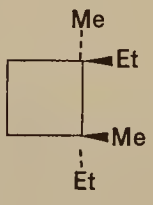


(143)



(144)

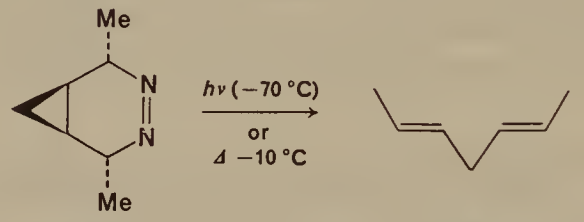


(145)

configuration in the sensitized photolysis conforms to the general pattern of behaviour shown by 1-pyrazolines but the increase in the yield of olefin (**143**) is in contrast to the 1-pyrazolines. Perhaps the greater separation of radical centres in the 1,4-biradical initially formed favours cleavage over cyclization, particularly in the longer-lived triplet. When benzophenone was used as sensitizer, negligible yields of **143**, **144** and **145** were obtained while other unidentified products were formed. The reason for this was not clear.

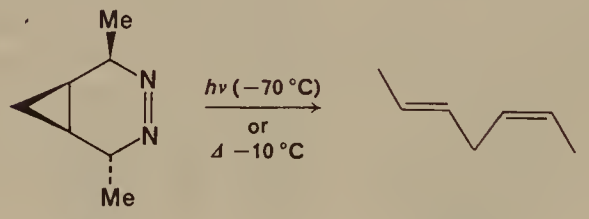
Turning now to bicyclic systems, both the photolysis and thermolysis of all three isomers of 2,5-dimethyl-3,4-diazabicyclo[4.1.0]hept-3-ene **146**, **147** and **148** gave the dienes **149**, **150** and **151** with greater than 99·5% stereospecificity[159] (equations 138–140). This is a clear violation of orbital symmetry rules[160]. However, Berson and Olin caution concerning the theoretical analysis of concerted reactions containing heteroatoms[159].

A case of inversion of configuration has been reported by Allred and



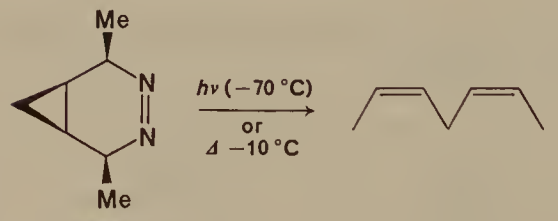
(138)

(146) **(149)**



(139)

(147) **(150)**



(140)

(148) **(151)**

Smith[161] in the direct photolysis of *exo*-5-methoxy-2,3-diazabicyclo-[2.2.1]hept-2-ene (**152**) and its *endo* isomer. The inversion is thought to

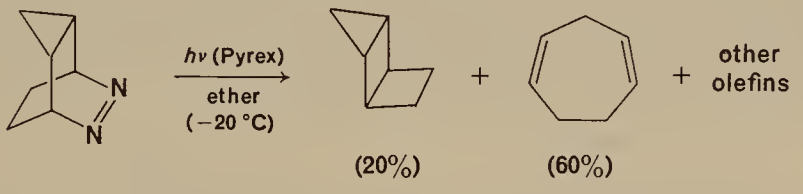
(152) (153) (154) (141)

occur by recoil as the nitrogen molecule is expelled, leading to the biradical **153** which cyclizes rapidly in the excited singlet state to give **154** (equation 141). In benzophenone or triphenylene-sensitized photolysis the *cis* product **155** was produced in similar yield (73–78 %) from both the *exo* and *endo* azo compounds. This was explained in terms of equilibration of the triplet biradicals **153** and **156** prior to cyclization (equation 142). In a crystalline

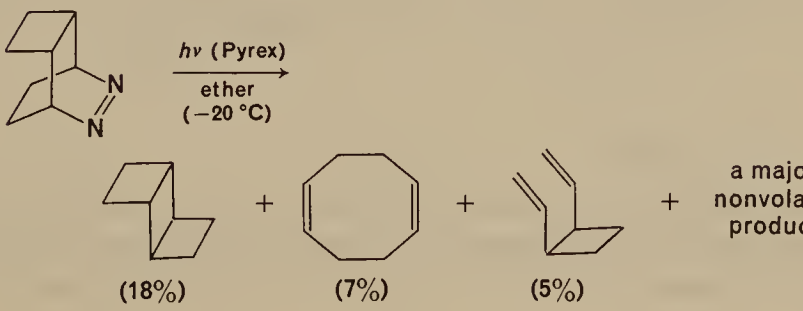
(156) (155) (142)

medium retention of configuration was observed on direct photolysis, particularly from the *exo* isomer (**152**) where **155** was obtained in 97% yield. Presumably the rigidity of the crystal matrix prevented inversion of the biradicals during their formation. On the other hand, a glassy matrix was apparently less restricting and a tendency toward inversion was again apparent.

Tanida and co-workers[162–164] have shown that inversion of configuration is the rule in the direct photolysis of a number of tricyclic azo compounds

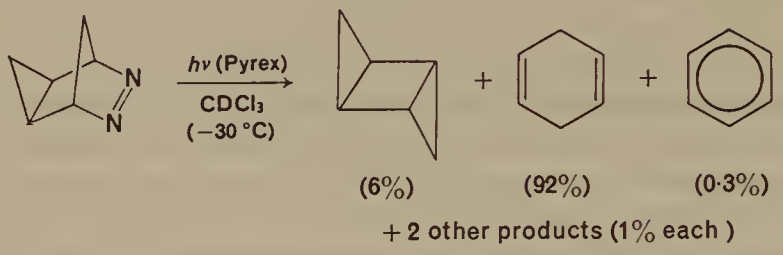


(20%) (60%) (143)



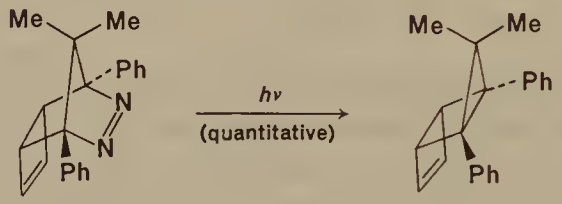
(18%) (7%) (5%) (144)

(equations 143–145) although the yields of tricyclic hydrocarbons were rather low. No products showing retention of configuration were found. Participation by the cyclopropane ring (equations 143 and 145) in the decomposition is forbidden by orbital symmetry rules in photolysis but



(145)

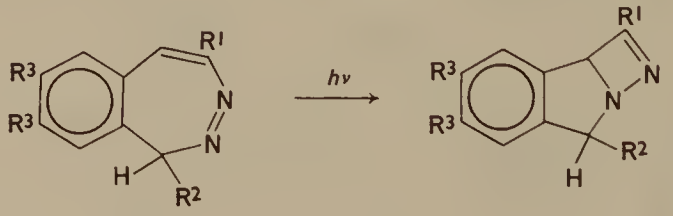
allowed in thermolysis[162, 164]. This is thought to be a reason for the great thermal instability of these azo compounds. A case of retention of configuration in a similar tricyclic system (equation 146) has been reported by



(146)

Paquette and Leichter[165] although they caution against drawing definite conclusions in the absence of low-temperature studies to see whether or not a *cis* isomer is involved.

c. *Seven-membered azo rings.* In the larger diazepine system photolytic extrusion of nitrogen does not always occur. Sharp and co-workers[166] found that the 1*H*-2,3-benzodiazepine **157** underwent valence tautomerism (equation 147) whereas 1,2-benzodiazepines underwent photolytic ex-

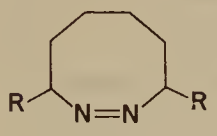


(147)

(157)

trusion of nitrogen[167]. The photoisomerization of **157** is reminiscent of the low-temperature photoisomerization of some 3*H*-pyrazoles studied by Closs and co-workers[138].

d. *Eight-membered azo rings.* Overberger and co-workers[168, 169] have reported on the photolysis of eight-membered cyclic azo compounds. In spite of the greater flexibility, no *cis–trans* photoisomerization of the azo group was observed, the only reaction being decomposition. In all the 3,8-disubstituted examples studied (**158**; R = Ph or Me) the major product of direct irradiation both in the solid state and in solution was the disproportionation product **159**, with smaller amounts of *cis*- and *trans*-1,2-disubstituted cyclohexanes (**160** and **161**). There was a slightly greater tendency for retention of configuration in **160** and **161** at –78°C in the solid state[168]. In benzophenone-sensitized photolysis of **158** (R = Ph) the dis-



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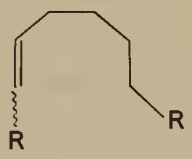

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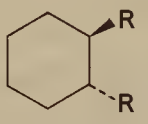

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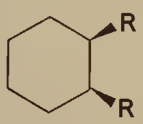
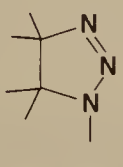


(161)

proportionation product **159** (R = Ph) was formed in over 95% yield with only a trace of the 1,2-diphenylcyclohexanes. Due to the distance between the radical centres in the expected triplet 1,6-biradical intermediate after it has rotationally equilibrated, it is not surprising that disproportionation is much more competitive than ring closure. A similar spin correlation effect was observed in the fluorene or biphenyl-sensitized photolysis of the unsubstituted azo compound (**158**; R = H) and the dimethyl derivative (**158**; R = Me). Ketonic sensitizers like benzophenone or acetophenone failed to act on these two compounds, even though the diphenyl derivative (**158**; R = Ph) had been successfully photosensitized with benzophenone. It may be recalled that a similar situation was found with the six-membered cyclic azo compound **142**[121]. This behaviour cannot be for a want of sufficient triplet energy[158], nor can it be due to purely singlet energy transfer from the successful sensitizers, though some was occurring, because of the observed spin correlation effect.

e. *Cyclic azo compounds containing other heteroatoms.* The photochemical behaviour of triazolines (**162**) is analogous to that of pyrazolines,



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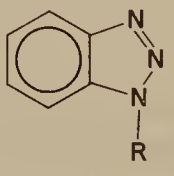
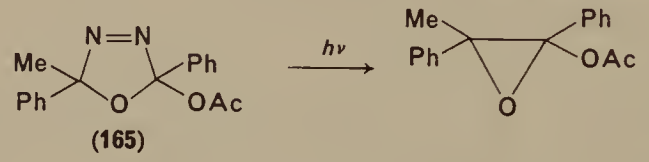


(164)

leading to the formation of aziridines (**163**) by extrusion of nitrogen[154, 170]. Retention of configuration in the direct photolysis also appears to be the rule with less stereospecificity in the triplet-sensitized photolysis[154, 170]. Quantum yields were about unity for direct photolysis at 313 nm in solution[170]. In contrast benzotriazoles (**164**) undergo slower photolysis yielding aniline derivatives (R = H or Me) or carbazole (R = Ph)[171], but no three-membered rings (cf. equation 123).

The photolysis of the 2*H*,5*H*-1,3,4-oxadiazole derivatives **165** and **166** leads to extrusion of nitrogen (equations 148 and 149)[172] whereas the



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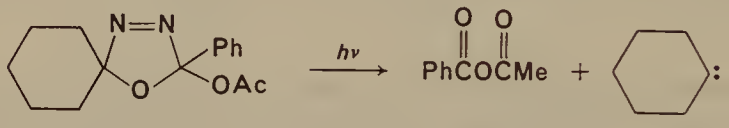
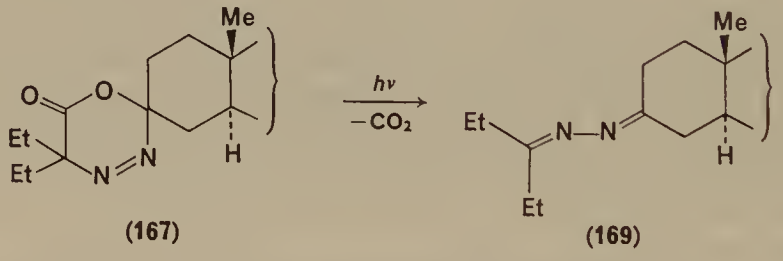
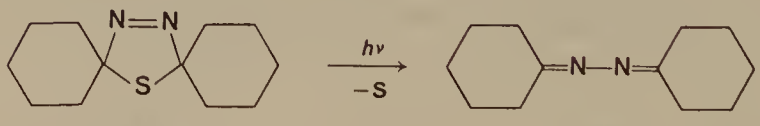


(166) (149)

2*H*,5*H*-1,3,4-oxadiazine-6-one **167**[173] and the 2*H*,5*H*-1,3,5-thiadiazole **168**[174, 175] eliminate carbon dioxide and sulphur respectively (equations 150 and 151) to form the azines **169** and **170** respectively. It is of interest that in



(167) (169) (150)



(168) (170) (151)

the thermal decomposition of **167** and **168** it is the nitrogen which is extruded. This difference is probably due to orbital symmetry factors[173, 174].

C. *Mixed Aliphatic–Aromatic Azo Compounds*

Until fairly recently the photochemistry of azo compounds with the azo group bonded to one aromatic and one aliphatic carbon atom was a neglected field. Due mainly to the work of Porter and co-workers several of these mixed azo compounds have been studied, some of which resemble aliphatic azo compounds while one resembles the aromatic series. Visible light may be used to effect photolysis as these azo compounds have λ_{max} greater than 400 nm, the *cis* isomer absorbing at longer wavelengths than the *trans* isomer[77]. All four compounds so far investigated undergo photoisomerization and all decompose, albeit by two different mechanisms.

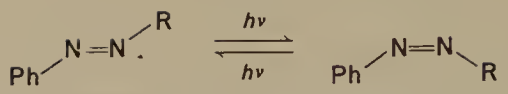
1. Decomposition via thermolysis of unstable *cis* isomers

In the azo compounds where the aliphatic group is of a benzylic or allylic type, irradiation leads to *trans* → *cis* isomerization, followed by thermal decomposition of *cis* isomer. Essentially this is the same mechanism as Mill and Stringham found for azo-2-methyl-2-propane (**17**)[29] (Section II, A, 6, a).

Photolysis of (2-phenyl-2-propylazo)benzene (**171**) in benzene at room temperature yielded biphenyl and 1,2-diphenyl-1,1,2,2-tetramethylethane (**172**) as the major products with only a trace of the disproportionation products 2-phenylpropene and 2-phenylpropane and the cage recombination product 2,2-diphenylpropane (equation 152)[77]. At temperatures below −40°C irradiation of **171** produced only *trans–cis* isomerization with no decomposition. The *cis* isomer was isolated by low-temperature chromatography and decomposed in benzene solution at 25°C to give the same

$$\underset{\textbf{(171)}}{PhN{=}NC(Me_2)Ph} + h\nu \xrightarrow[\text{benzene}]{} Ph{-}Ph\ (20\%) + \underset{\textbf{(172)}}{PhC(Me_2)C(Me_2)Ph}\ (48\%) + \text{traces of other products} \qquad (152)$$

products as in the photolysis of *trans*-**171**, together with a variable yield of *trans*-**171** (30–50%). The higher yields of *trans*-**171** were obtained in solvents with higher viscosity. This behaviour suggests the following mechanism (equations 153–156)[77]. A key feature of the mechanism is the one-bond dissociation of the azo compound to give the phenyldiazenyl radical. Direct evidence for the formation of this radical as an intermediate in the reaction has come from chemically induced dynamic nuclear polarization (CIDNP) studies[176]. It was estimated that the rate constant for the de-


(153)


(154)


(155)


(156)

composition of the radical (equation 157) was 10^7–10^9/sec. That this

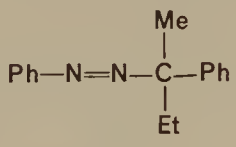
$$Ph—N=N\cdot \rightarrow Ph\cdot + N_2 \qquad (157)$$

rate of decomposition reflects a stabilizing effect of the phenyl group is shown by failure to find any evidence of the diazenyl radical in a CIDNP study of the aliphatic azo compound benzylazodiphenylmethane (**173**)[176–178].

$Ph_2CHN=NCH_2Ph$

(173)

The suggested decomposition mechanism (equations 153–156) is further supported by the photolysis of optically active (2-phenyl-2-butylazo)benzene (**174**)[77, 179]. Partial racemization accompanies the photodecomposition

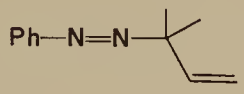


(174)

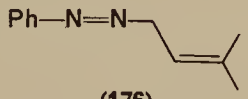
of optically active **174** and furthermore the quantum yield of its decomposition is dependent on the solvent viscosity, the quantum yield being low (0.029) in hexadecane and higher (0·051) in pentane. Racemization may be explained by equations **154** and **155** where inversion of the configuration of the radical R· may occur prior to reforming the azo compound. Solvents of higher viscosity presumably favour reformation of the azo compound rather than the escape of the caged radicals to form products (equation 156). At low temperatures (−78°C) no racemization accompanies the photoequilibration of (+)-**174**, again supporting the mechanism. In the thermal decomposition of optically active *cis*-**174** the degree of retention of configuration in the recovered *trans* isomer was viscosity dependent, being

greatest in low-viscosity solvents. It is quite possible, however, that some of the *cis* → *trans* thermal isomerization proceeds directly, without any bond fission.

The third example studied which shows the above general behaviour is (2,2-dimethyl-3-butenylazo)benzene (**175**)[180]. The *cis* isomer of **175** is more



(175)



(176)

thermally unstable than those of **171** and **174** and has the additional feature of yielding the rearranged azo compound **176** on thermal decomposition. A complex mixture of hydrocarbons is also produced.

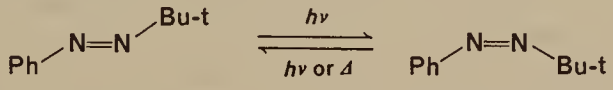
2. Photolysis of (t-butylazo)benzene

In contrast to the three examples discussed in the previous section the *cis* isomer of (*t*-butylazo)benzene (**177**) is thermally stable towards

PhN=NBu-t

(177)

decomposition[76], yielding only *trans*-**177**. In this respect it resembles azobenzene. However, photodecomposition of **177** does occur whereas azobenzene does not photodissociate. Irradiation of *trans*-**177** in pentane at temperatures from −85°C to +25°C shows a rapid *cis–trans* photoequilibration followed by a very slow conversion into benzene and *t*-butylbenzene. The photochemistry of **177** may be described by equations 158 and



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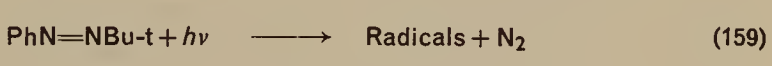


(159)

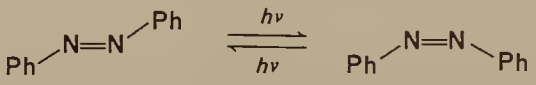
159. Presumably the main reason for the difference in mechanism is the difference in stability between the *t*-butyl radical and the more stable benzylic and allylic radicals. It should be recalled, however, that azo-2-methyl-2-propane (**17**) followed the *cis* thermal decomposition mechanism. Further work may elucidate this problem.

D. Aromatic Azo Compounds

The photochemistry of azobenzene and its derivatives has been reviewed very recently by Griffiths[181] and so only a very brief outline is presented here. Unless otherwise indicated the reader is directed to the references contained in Griffiths' review. Some later work and reactions not discussed by Griffiths are also included. Irradiation of aromatic azo compounds is generally carried out with visible light as the longest wavelength absorption band has its λ_{max} at greater than 400 nm. The major types of photoreactions characteristic of aromatic azo compounds are *cis–trans* isomerization, cyclization and addition to the azo group.

I. Photoisomerization

Azobenzene and many of its derivatives readily undergo *cis–trans* photoisomerization (equation 160) to yield a photostationary composition which is wavelength and temperature dependent. The presence of amino or



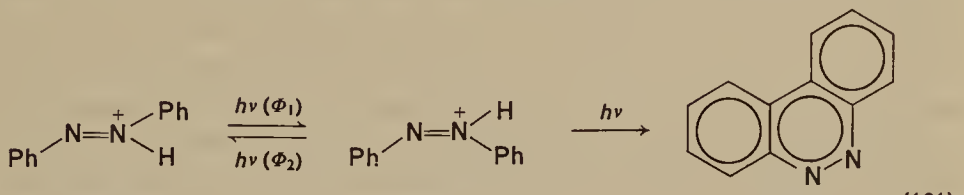
(160)

hydroxyl groups on the aromatic ring generally causes the *cis* isomer to be thermally unstable and it readily isomerizes back to the *trans* isomer. Such cases are difficult to study although flash spectroscopic techniques have been used[182, 183].

Recent photosensitization studies have indicated that the mechanism of the photoisomerization is rather complex, involving more than one triplet state[184]. By using a series of triplet sensitizers of different energy the n,π^* triplet energy of *cis*- and *trans*-azobenzene was estimated to be 188 and 184 kJ/mol respectively[185]. The marked difference in the composition of the photostationary state using high energy sensitizers when compared with direct irradiation[185] reinforces the earlier view of Jones and Hammond[186] that different mechanisms operate in the direct and triplet-sensitized photoisomerization. It may be that the lack of difference between direct and sensitized photostationary state compositions found by Fischer[187] was due to singlet energy transfer from the naphthalene or triphenylene sensitizers[69]. Mauser and Hazel have analysed the kinetics of the photoisomerization of azobenzene by means of a computer program involving n,π^* and π,π^* singlet and triplet states of both isomers[188].

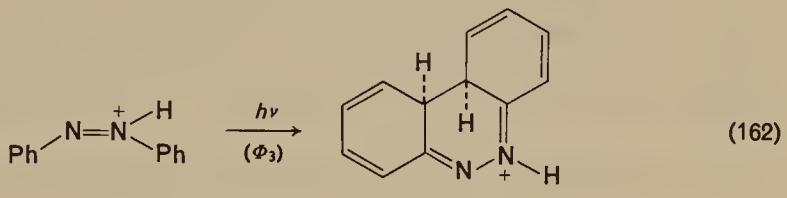
2. Cyclodehydrogenation

Irradiation of the conjugate acid of azobenzene and many of its derivatives leads to the formation of benzo[*c*]cinnoline (**178**) or its derivatives (equation 161). The reaction has been suggested as being suitable for a



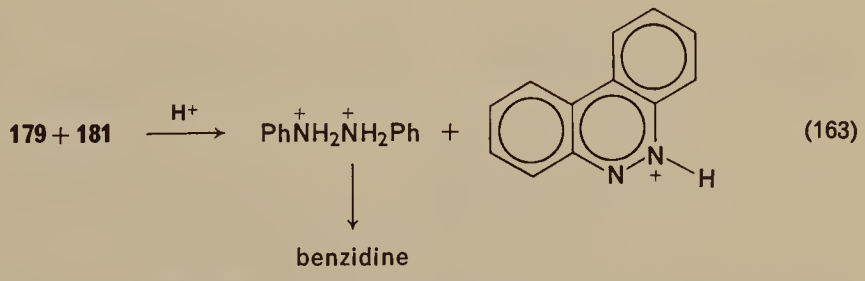
(180) (179) (178) (161)

student experiment[189]. Very recently the mechanism of the reaction has been reinvestigated by Mauser and co-workers[190], confirming the mechanism which had been proposed by Lewis and co-workers[191]. In 66% sulphuric acid the quantum yields for *trans* → *cis* (Φ_1) and *cis* → *trans* (Φ_2) isomerization were 0·27 and 0·25 respectively. The quantum yield of the cyclization step (Φ_3) (equation 162) was 0·02. It was found that the con-



(179) (181) (162)

jugate acid of *cis*-azobenzene (**179**) was at least 100 times more effective than its *trans* isomer (**180**) in dehydrogenating the conjugate acid of 10a,10b-dihydrobenzo[*c*]cinnoline (**181**) (equation 163)[190].



(163)

Investigations of the photocyclization of azobenzene in nonaqueous solvents in the presence of ferric chloride have led to the conclusion that the

ferric chloride acts as a Lewis acid, not as an oxidizing agent[192]. Likewise with aluminium chloride the overall mechanism is considered to be similar to that in strong sulphuric acid[193].

3. Photo-addition to the azo group

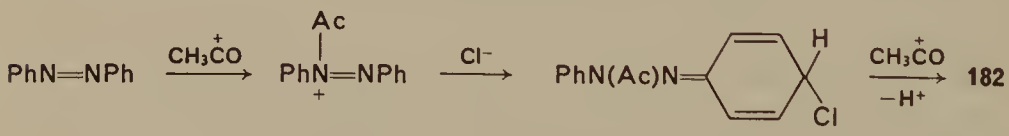
Photoreduction of azobenzenes was reviewed by Griffiths[181] where a distinction was drawn between two mechanistic types. In the first type the electronically excited azo compound abstracted hydrogen from a donor while in the second type a photochemically produced hydrogen donor reduced the azo linkage in a subsequent dark reaction. Because of very low quantum yields obtained for the first mechanistic type, caution in interpretation needs to be exercised as the reduction may have been caused by impurities. For example, 2-propanol was found to be the most effective solvent in promoting the first mechanism. The presence of acetone, a likely impurity, could lead to the formation of ketyl radicals by photoreaction of the acetone itself, i.e. the second mechanism. Suspicion is increased by the report that the photoreduction of azobenzene in 2-propanol was increased in the presence of a little oxygen and took place only at shorter wavelengths (nominally 366 nm using a filter)[194]. Careful experiments would be needed to rule out the possibility of the second mechanism occurring here.

A quite different addition to the azo group occurs when azobenzene is irradiated in acetyl chloride or in acetic anhydride containing hydrogen chloride (equation 164)[192,195]. No reaction occurs in the dark and an

$$PhN{=}NPh \xrightarrow[CH_3COCl]{h\nu} PhN(Ac)N(Ac)C_6H_4Cl\text{-}p \quad (84\%) \qquad (164)$$

(182)

ionic mechanism has been proposed (equation 165). A little *ortho*-substitution by the chloride ion also occurs[196].



(165)

III. AZOXY COMPOUNDS

The general photochemistry of azoxy compounds was reviewed in 1970 by Spence, Taylor and Buchardt[197] so only a brief treatment will be given here, together with some more recent work. Most investigations have con-

cerned aromatic azoxy compounds where the reactions observed are *cis–trans* photoisomerization, rearrangement involving the oxygen atom and photoreduction. Aliphatic azoxy compounds undergo photoisomerization and form oxadiaziridines when irradiated in solution. An example of mixed aliphatic–aromatic azoxy photochemistry is included with the aliphatic series.

A. Aliphatic Azoxy Compounds

Rather short wavelengths (ca. 220 nm) are required in the photolysis of aliphatic azoxy compounds. The gas-phase photolysis of the simplest member azoxymethane[198] leads to dissociation into radicals reminiscent of the behaviour of azoalkanes (Section II, A). Nitrogen, nitrous oxide, methane and ethane were the gaseous reaction products and their formation was explained by the occurrence of two primary dissociation pathways (equations 166 and 167). Equation 166 accounted for 83 % of the decomposition as indicated by the N_2/N_2O ratio which was independent of tem-

$$\mathrm{MeN(O^-)=NMe} + h\nu \longrightarrow 2\mathrm{Me}\cdot + \mathrm{N_2O} \qquad (166)$$

$$\mathrm{MeN(O^-)=NMe} + h\nu \longrightarrow \mathrm{Me}\cdot + \mathrm{N_2} + \cdot\mathrm{OMe} \qquad (167)$$

perature. No work appears to have been done on the primary processes of the reaction.

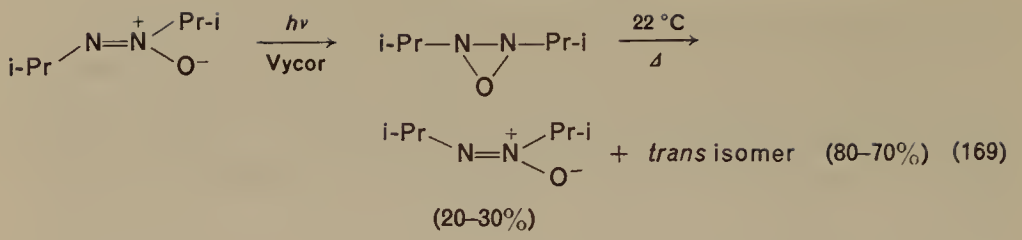
A rather different behaviour is displayed in the photolysis of higher azoxyalkanes in solution. Green and Hecht[199] found that oxadiaziridines **183–185** were formed on photolysis of the azoxyalkanes **186–188** in pentane at 10–20°C (equation 168). The oxadiaziridine **185** could be detected in the

$$\mathrm{R^1N(O^-)=NR^2} \underset{\Delta}{\overset{h\nu\,(\mathrm{N_2})}{\rightleftharpoons}} \mathrm{R^1{-}N(O){-}N{-}R^2} \qquad (168)$$

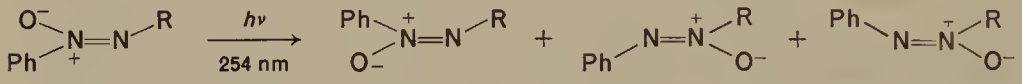
(**186**; $R^1 = R^2 =$ t-Bu)
(**187**; $R^1 = R^2 =$ n-Bu)
(**188**; $R^1 =$ Me, $R^2 =$ t-Bu)

(**183**; $R^1 = R^2 =$ t-Bu)
(**184**; $R^1 = R^2 =$ n-Bu)
(**185**; $R^1 =$ Me, $R^2 =$ t-Bu)

reaction mixture but was too unstable to be isolated. Swigert and Taylor[200] have used this cyclization of the azoxy group to prepare the first documented example of a *cis*-azoxyalkane (equation 169).



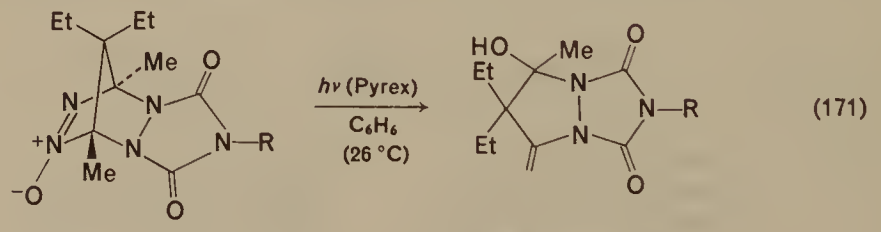
In mixed aliphatic–aromatic azoxy compounds Taylor and Riehl[201] found that a slow oxygen migration from the aryl nitrogen to the alkyl nitrogen occurred as well as rapid *trans* → *cis* photoisomerization (equation 170). In no case was oxygen observed to migrate from the alkyl nitrogen to



(R = Me or Et) (170)

the aryl nitrogen. Oxadiaziridines were considered to be intermediates in this reaction although no attempt was made to isolate them because of their expected thermal instability. Oxygen had no effect on the reaction which was interpreted to mean that an excited singlet state was involved. When a Pyrex filter was used, no oxygen migration occurred while facile *cis–trans* photoisomerization proceeded. Presumably under these conditions no oxadiaziridine was formed.

Photolysis of bicyclic azoxy compounds related to 2,3-diazabicyclo-[2.2.1]hept-2-ene (**59**) and 2,3-diazabicyclo[2.2.2]oct-2-ene (**60**) has been shown to lead to polymeric products[199, 202]. However, photolysis of **189** gave **190** (equation 171)[202]. Cross-ring perturbations by nitrogen were

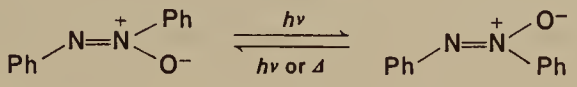


(**189**; R = Me or Ph) (**190**; R = Me or Ph) (171)

suggested as an explanation for the difference in behaviour compared with simple bicyclic azoxy compounds.

B. Aromatic Azoxy Compounds

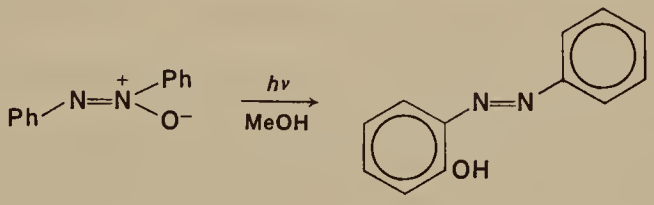
Azoxybenzene and its derivatives undergo *cis–trans* photoisomerization in solution (equation 172). The quantum yields of *trans* → *cis* and *cis* → *trans* isomerization have been reported as 0·11 and 0·64 respectively in



(172)

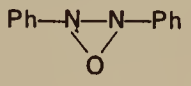
95% ethanol or heptane at 5°C and independent of the wavelength of irradiation in the region of the $\pi \rightarrow \pi^*$ absorption band[203].

In polar solvents such as methanol a much less efficient rearrangement also occurs involving migration of the azoxy oxygen atom into the *ortho* position of the more distant aromatic ring (equation 173). Mauser and



(173)

co-workers[204] have recently suggested that some diphenyloxadiaziridine (**191**) was formed in a side reaction at the beginning of the irradiation. In



(**191**)

cyclohexane the rearrangement (equation 173) did not occur but an intermediate, thought to be **191**, was produced which was decomposed by further irradiation.

Concerning the mechanism of the rearrangement it has been suggested[197] that the π,π^* singlet state of the azoxy compound is involved on the basis that benzophenone photosensitization causes reduction of the azoxy group to the azo group. However, Monroe and Wamser[205] have shown that the reduction of the azoxy group is actually caused by the ketyl radical produced from triplet benzophenone. Thus the reduction is not a photochemical reaction of the azoxy group. In general it may be observed that the sensitizers which were effective in reducing the azoxy group were carbonyl

compounds, good hydrogen abstractors, while the ineffective sensitizers were poor hydrogen abstractors. The nature of the excited state involved in the rearrangement remains uncertain.

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CHAPTER 21

Conformational analysis of hydrazines

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I. INTRODUCTION

The conformational aspects of hydrazines have been extensively studied during the past ten years*. Both theoretical calculations, using various methods with variable degrees of sophistication and experimental techniques (i.r., Raman, microwave, n.m.r., X-ray and, most recently, photoelectron spectroscopy) have contributed to the present-day general knowledge of this subject.

Most of the current research aims at the refinement and confirmation of subtle points of the subject. While the experimental facts are generally well established, and fit the results of the calculations, a clear understanding of the physical factors which govern the various conformational phenomena is still lacking. Various theories and rules have been advanced for the interpretation of the conformational behaviour of hydrazines, however, very often they give rise to the wrong predictions.

* Instead of extending the present chapter to cover azo, azoxy and hydrazine systems, the author has taken the liberty of treating only the last mentioned system in a comprehensive manner.

The present essay is not intended to be of an encyclopaedic nature. Only points which are of general importance and of a fundamental nature will be presented and discussed. We shall try to be critical and also attempt to suggest our own viewpoints whenever we deem alternative interpretations to be in place. Special attention will be paid to existing controversies.

Any treatment of conformational analysis must be based on two fundamental concepts, namely the thermodynamic and kinetic properties of the system under consideration. While the thermodynamic properties allow us to evaluate the relative stabilities and populations of the various conformers as a function of their geometry, the kinetic properties of the system tell us how fast these conformers are interconverting, i.e. a complete analysis must be based on the total conformational potential function. When two or more different conformational processes may occur simultaneously, the complete energy surface must be considered. Conformational potential functions are in some cases available from rotation–vibration spectroscopy. This technique is limited to structurally simple molecules and the results may depend on the particular potential function which has been selected to fit the experimental results. Nevertheless, this is the only experimental method by which *total* conformational potential function can be obtained. An evaluation of this technique has been recently published[1].

N.m.r. is a powerful tool for investigating conformational problems. It cannot produce the detailed conformational potential function but it can yield the conformational energy of the ground state (E_{min}) relative to that of the transition state (E_{max}), i.e. the energy barrier of a dynamic conformational equilibrium. For details on dynamic nuclear magnetic resonance (d.n.m.r.) spectroscopy, the reader is referred to a review by Binsch[2]. Another very important property of the E_{min} conformation (and sometimes also of the E_{max} conformation) can be obtained by n.m.r., namely its symmetry. This information is of the utmost importance in conformational analysis, as it bears directly on the geometry of the E_{min} conformation.

The n.m.r. technique has dramatically advanced the field of conformational analysis and is accompanied by lively controversies. The most serious problem is the correct identification of the kinetic process which is responsible for the observed spectral phenomena. This may become a difficult task in systems with multi-conformational processes. In some of these cases corroborative evidence either of theoretical or experimental nature was adduced in order to clarify the picture, but in several cases erroneous conclusions have been reached. Even so n.m.r. technique as applied to conformational analysis is still the most straightforward and simple method. Its principal limitation is the time scale which, together with the available temperature range (ca. −150 to 200°C), gives rise to a measur-

able range of activation energy of ca. 7–24 kcal/mol. Indeed, this is the range which is difficult to investigate by classical kinetics. However, the range below ca. 7 kcal/mol is inaccessible to *proton* magnetic spectroscopy.

The ground state conformational structure of hydrazine can, for convenience, be analysed in terms of two easily handled parameters, namely the geometry of the N atoms and the torsional (dihedral) angle about the N—N bond. Of course, a complete geometrical description also requires the knowledge of all bond distances and angles.

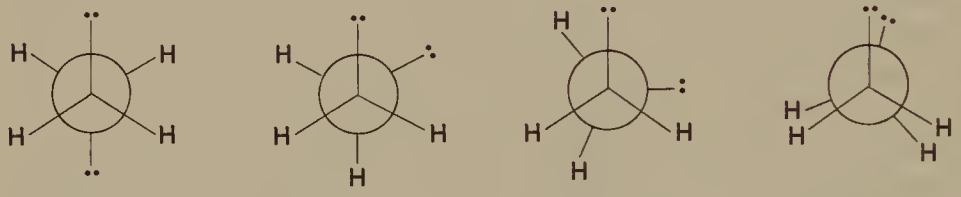
The two kinetic processes which are associated with the above two parameters are nitrogen inversion and torsion about the N—N bond. Depending on the substituents, the N atoms may assume geometries ranging from pyramidal to planar, with a rather broad range for the rates of inversion. Although no exact correlation exists, we usually associate slow inversion rates with a higher degree of pyramidality and faster inversion rates with a shallower nitrogen pyramid. Thus the inversion barrier of a nitrogen atom may be considered as the hybridization energy required to transform it from the non-planar ground state geometry to an sp^2 planar form. Therefore, the shallower the pyramid the less energy must be invested to produce its inversion[3].

Regardless of the configuration of the N atoms of hydrazine, one can define a torsional angle about the N—N bond in terms of a dihedral angle between the substituents of the two N atoms. In any such analysis it is of extreme importance to consider also the resulting dihedral angle between the non-bonding orbitals of the two N atoms, since theoretical treatments of hydrazine systems imply that the torsional angle is mainly determined by lone pair–lone pair interactions. Although this angle cannot be directly determined by experiment, it can be deduced from the dihedral angle of the nitrogen substituents and the configuration of the nitrogen atoms. The non-bonding orbital of the N atom is stereochemically active, although more diffused than a σ orbital, and can therefore be considered as a substituent. In our discussion we shall refer to the dihedral angle of the lone pairs in hydrazine as an inter-orbital angle (ϕ). Although the N—N bond in hydrazine is of a σ type the torsional barriers which are experimentally encountered are, in some cases, extremely high (ca. 24 kcal/mol) and actually approach the physical isolation time scale. It will be demonstrated that these torsional barriers are highly sensitive to the configuration of the N atoms.

In summary, conformational analysis of hydrazines is associated with a kinetic dichotomy (rotation–inversion) and a thermodynamic dichotomy (nitrogen configuration and N—N torsional angle). Although such treat-

ment is artificial inasmuch as the system may be described by one potential surface, nevertheless, it is convenient to analyse the conformational aspects of hydrazo systems in terms of the two separate properties, although the discussion in most cases must be unified. It should be mentioned here that evidence exists which indicates that the rotation and the inversion are two independent processes and that they do not share a common transition state[4].

The most interesting aspect of the conformation of hydrazo compounds is the torsional angle of the N—N bond. Assuming for the moment a pyramidal structure for the N atoms of hydrazine (*vide infra*) there are two diastereomeric staggered conformations (**1**) and (**2**) with C_{2h} and C_2 symmetries



C_{2h}-*trans* C_2-*gauche* C_2-orthogonal C_{2v}-eclipsed

respectively, also named *trans* and *gauche* respectively when referring to the lone pairs. Hydrazine has a substantial dipole moment of 1·83–1·85 D[5]. In fact the dipole moment of a series of substituted hydrazines such as phenylhydrazine, 1-methyl-1-phenylhydrazine, 1,1-diphenyl- and 1,2-diphenylhydrazines were found to be in the range of 1·53–1·87 D[5]. Since **1** possesses a centre of symmetry, and in view of the substantial dipole of hydrazine, it must be concluded that the *trans* conformer (**1**) cannot be the sole contributing conformational species. This observation prompted Penney and Sutherland[6] in 1934 to calculate the torsional potential function of hydrazine using the electron pair method, assuming $r_{N-N} = 1{\cdot}5$ Å and sp^3 hybridized atoms. Their potential function is schematically depicted in Figure 1. Accordingly, the lowest energy conformation of hydrazine should be described by the C_2 conformation (**3**) where the interorbital angle $\phi = 90°$. The high energy maximum ($\phi = 0°$) corresponds to the symmetrically eclipsed conformation (**4**) while a second maximum at $\phi = 180°$ corresponds to the trans conformation (**1**). The authors have claimed that the dominant factor which determines the torsional angle about the N—N bond is the interaction of the two non-bonding electron clouds, whereas all other types of interactions will shift the equilibrium angle only slightly. Although these results now account for the finite dipole moment of hydrazine, one may still

ask why the system does not adopt the *trans* conformation (**1**) which superficially seems to offer minimal interaction between the lone pairs.

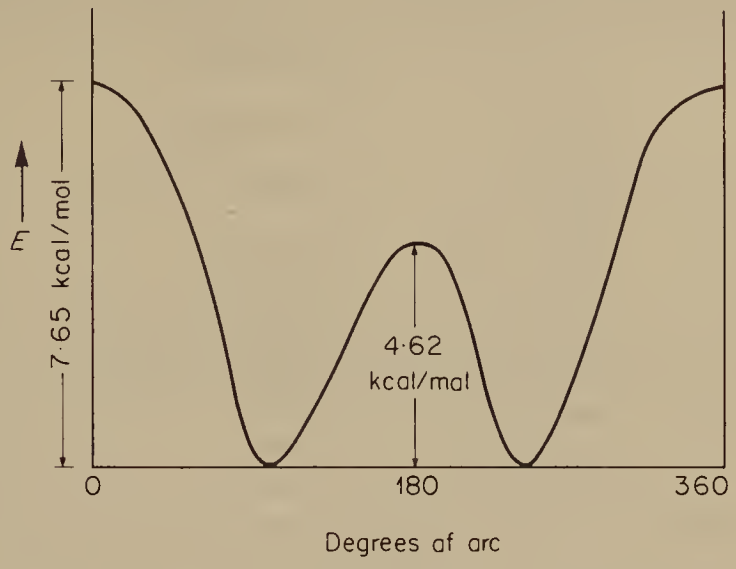


FIGURE 1. Torsional potential function of N_2H_4 (schematic)[6].

In 1966 Veillard[7], using non-empirical SCF–LCAO methods and also assuming essentially pyramidal N atoms, reached strikingly similar results in calculating the torsional potential function of hydrazine. Thus, the E_{min} conformation was found to have a diorbital angle, $\phi = 94°$ with a calculated dipole $\mu = 2{\cdot}333$ D. The energy maxima were found at $\phi = 0°$ ($E = 11{\cdot}5$ kcal/mol) and $\phi = 180°$ ($E = 4{\cdot}7$ kcal/mol). Additional calculations of the torsional function of hydrazine followed, and the results are summarized in Table 1. These calculations are based on essentially pyramidal N atoms and on experimental molecular coordinates (*vide infra*). Aside from the CNDO calculation[8], all others predict a minimum energy conformation of NH_2NH_2 at $\phi \approx 90°$, and maxima at 0° and 180°, Even the agreement among the relative energy values is reasonable a ide from the CNDO[8] and SCF, EH, LCAO–MO[9] calculations. Especially gratifying is the agreement among the three *ab initio* calculations[10–12]. Thus the original suggestion by Penney and Sutherland[6], made almost forty years ago, survived the current more sophisticated theoretical treatments.

Later, we shall examine to what extent the original proposal of Penney and Sutherland survived the experimental results. However, before doing so, it will be instructive to enquire into the question of the origin of the

TABLE 1. Calculated conformational parameters of hydrazine

E_{min} (degrees)	E_{max} (degrees; kcal/mol)	Method of calculation	Reference
90	0; 7·65	Electron pair	6
	180; 4·62		
94	0; 11·5	SCF–LCAO	7
	180; 4·7		
66, 180	0; 3·3	CNDO	8
	133; 2·5		
gauche	0; 1·3–3·6	SCF, EH	9
	180; 3·0–5·9	LCAO–MO	
ca. 90	0; 11·8	*ab initio*	10
	180; 3·70	LCAO–MO–SCF	
90	0; 11·05	*ab initio*	11
	180; 6·21		
97	0; 12·37	*ab initio*	12
	180; 3·68		

above torsional barrier of hydrazine. Several interpretations have been advanced. The widely quoted one is that of the original investigators[6] which attributes the shape of the torsional barrier to the lone pair–lone pair repulsive interaction. If one considers the above interaction in terms of a dipole–dipole interaction there should be a decrease in an approximately monotonic fashion from 0° to 180° with no apparent reason for an intermediate minimum. In fact such calculations have been recently carried out by Fourier decomposition of the total potential function of hydrazine[12]. Obviously the torsional barrier cannot only be interpreted in terms of dipole–dipole interaction.

The localized electron-pair theory, also known as valence-shell–electron-pair repulsion theory (VSEPR)[13–15], which has been successfully employed in structural chemistry, may also be invoked for the present problem. The underlying idea, related to the Pauli exclusion principle, is that electrons of like spins in different bonds or in non-bonding orbitals tend to draw apart. This type of interaction is considered to be more important than the electrostatic repulsive interaction among the electrons. Also, due to the more diffuse nature of the non-bonding orbital, lone pair–lone pair repulsive interaction is more energetic than lone pair–bond pair, which in turn is more energetic than bond pair–bond pair. Accordingly, repulsion should decrease as the interorbital angle ϕ in hydrazine increases from 0 to 180°. The situation may be saved by arguing that at 90°,

the interaction between the main non-bonding lobe of one N atom with the back non-bonding lobe of the second N atom is minimal (**5**), and that upon further rotation to 180° this interaction reaches a maximum (**6**), thus qualitatively accounting for the two maxima and one minimum in the torsional potential function of hydrazine (Figure 1) (the other lone pair–

(5)

(6)

bond pair and bond pair–bond pair interactions are neglected inasmuch as the lone pair–lone pair interactions are energetically the most important ones.) This is a simple conceptual and qualitative interpretation based on existing theory.

A different approach has been recently advanced by Allen[16, 10] and was summarized and further developed by Wolfe[17] (and references cited therein). The authors[17] have postulated a general rule for predicting the stereochemistry of systems containing adjacent lone pairs and/or polar bonds, i.e. 'when electron pairs or polar bonds are placed or generated on adjacent pyramidal atoms, *syn* or *anti* periplanar orientation is energetically disfavoured with respect to a structure which contains the maximum number of gauche interactions'. Exceptions to this 'gauche rule' will be mentioned. This rule correctly predicts the E_{min} conformation (**2**) (*gauche*) (or **3**) for hydrazine. The above concept is based on the quantum mechanical component analysis of torsional barriers[16, 10]. The total energy of the system E_T is a sum of four terms: V_{ne} (nuclear–electron attraction), V_{nn} (nuclear–nuclear repulsion), V_{ee} (electron–electron repulsion) and T (kinetic energy of the electrons). The total energy at a given diorbital angle is the sum of the attractive and the repulsive terms. The barriers are said to be attractive or repulsive dominant according to the energetic relationship between the attractive and the repulsive terms at the barrier configuration. This quantum mechanical analysis indicates that in the case of compounds containing lone pairs and polar bonds on adjacent atoms, energy minima are attained when the molecules adopt conformations which have the maximum number of gauche interactions between adjacent electron pairs and polar bonds. Component analysis was carried out for hydrazine[10], and is schematically depicted in Figure 2. The torsional function is the resultant of two opposing phase terms (surprisingly V_{ee} at 0° is smaller than V_{ee} at 180°).

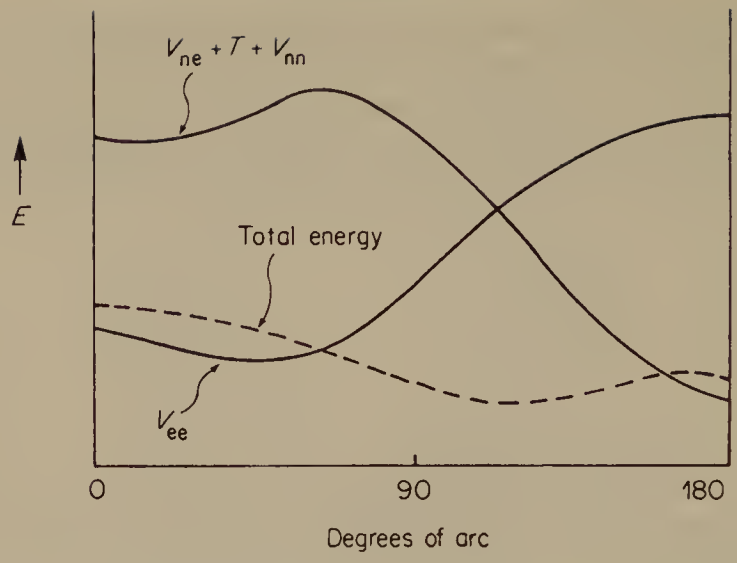
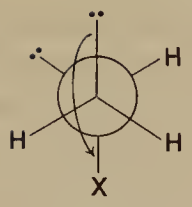


FIGURE 2. Decomposition of hydrazine total energy[10] (schematic).

Radom, Hehre and Pople (RHP)[18] attribute the conformational behaviour of hydrazine and substituted hydrazines partly to $n \rightarrow \sigma$ electron donation. In the case of hydrazine the non-bonding electrons on N are shifted to the σ bond of the adjacent N atom (7, X = H). Such an interaction is said to be most effective when the axis of the lone pair (sp^3) is coplanar with the said σ bond, a geometry which places the two lone pairs in a gauche disposition, 7. Thus both the RHP approach ($n \rightarrow \sigma$ donation)[18] and the 'gauche rule'[17] predict the same conformation (7) for hydrazine. But, while Wolfe[17] attributes a stabilizing character to the gauche lone pair–lone pair interaction in 7 (X = H), in the RHP model this interaction is a *consequence* of the *trans* lone pair–bond pair stabilizing interaction. The above two approaches are bound to yield contradictory results when the analysis of hydrazine with an electronegative X group (7) is attempted[12]. The 'gauche' rule[17] that requires a maximum number of gauche interactions among lone pairs and polar bonds will predict (8) to be more stable than (7) (X = electronegative group) which is in variance with the results of the RHP model. In fact, the latter approach argues that the stability of 7 over 8 is enhanced the more electronegative X is, due to more effective $n \rightarrow \sigma$ donation. The above donation concept is based on bond separation energies which constitute a measure of the interaction between bonds in a molecule. In the case of hydrazine itself the N—H bond must be considered electron attracting, while the nitrogen lone pair is the best donor of the first row elements.



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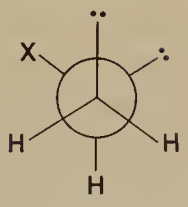


(8)

In a more complete analysis RHP[12] interpret the potential barrier of hydrazine, as well as of other molecules, in terms of the potential functions of three components, the usual threefold torsional function, a twofold function which expresses the $n \rightarrow \sigma$ electron donation and a onefold component which expresses the dipolar interaction. Although both RHP[12] and Allen[16] analyse the torsional function in terms of its components, the nature of these components in the two analyses is widely different. The components, and especially their angular dependence, are more comprehensible in the RHP approach when carrying out conformational analysis.

It now remains to examine the available experimental data and compare it with the results from theoretical calculations, and the various rules and theories. Considerable amount of experimental structural studies has been carried out on hydrazine itself. The permanent dipole of hydrazine is in qualitative agreement with the theoretical results inasmuch as the *trans* conformation **1** may not constitute the sole species which populates a possible equilibrium mixture.

X-ray[19] and diffraction[20] experiments were carried out on solid hydrazine in 1951 and 1961, respectively. Although unit cell dimensions and the symmetry of the crystal were established, no rigorous conclusions were reached by either group as to the molecular symmetry of solid hydrazine. Both the C_{2v} (eclipsed) and C_2 (gauche) symmetries are compatible with the experimental data, although the former is favoured. Electron diffraction studies of gaseous hydrazine yielded an N—N distance of $1{\cdot}47 \pm 0{\cdot}02$ Å[21] and $1{\cdot}449 \pm 0{\cdot}004$ Å[22], however, no conclusion could be reached as to the dihedral angle.

The vibrational and rotational spectra of hydrazine were studied by several groups with the aim of determining the various structural and conformational parameters. As stated by Durig[23], the agreement of the data and the analysis of the spectra leave much to be desired. If the molecule belongs to the point group C_2 it should have 12 nondegenerate fundamental vibration modes (four N—H stretching, six N—H bending, one N—N stretching and a torsional oscillation). Accidental overlap of resonances, inversion doubling and intermolecular association may result in a complex spectrum.

Scott[24] has found that the number of coincidences between Raman lines and infrared bands is consistent with C_2 symmetry and not with the centrosymmetric C_{2h} *trans* conformation. However, the *cis* (C_{2v}) conformation does not conflict seriously with the spectral data. Although the vibrational assignments of Scott[24] are somewhat different from those of Fresenius[25], both authors interpret the vibrational spectrum of hydrazine in terms of a C_2 conformation. From the infrared N—N torsional band, the potential barrier, $V_{rot} = 2800$ cal/mol, was calculated for the inter-conversion of the two enantiomeric gauche conformations ($\phi = 60°$)[24], which is in fair agreement with the calculated low barrier value ($\phi = 180°$) (Table 1).

Giguere[26] has also based the spectral interpretation on a C_2 symmetry ($\phi = 90°$) although the existence of a *cis* conformation ($\phi = 0$) could not be excluded on purely spectroscopic grounds.

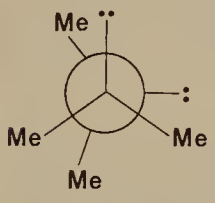
Durig[23] has also interpreted the infrared and Raman spectra of hydrazine and hydrazine-d_4 in terms of C_2 symmetry. Dilution experiments have indicated that at least part of one band in the N—H stretching region is due to hydrogen bonded species, while Wagner[27] has attributed the spectral changes with temperature to a change in the conformational equilibrium. Furthermore, from the analysis of the N—H stretching bands in the infrared and Raman spectra, Wagner[27] concludes, in variance with the previous mentioned works, that both in gaseous and liquid phase hydrazine consists of a 1:1 mixture of *trans* and C_2 species.

Catalano[28] has studied the infrared spectrum of hydrazine in N_2 matrix. All 12 bands have been observed and were assigned to the corresponding vibrational modes of a C_2 conformation. A band at 3207 cm^{-1} was assigned to a polymeric or dimeric species on the basis of matrix dilution. The bond angles and bond lengths derived from the spectrum are in excellent agreement with electron diffraction data[21,22].

The three torsional vibration bands in the region of 250–750 cm^{-1} arising from the transitions of n: $0 \rightarrow 1$, $0 \rightarrow 2$ and $1 \rightarrow 2$ were analysed by Yamaguchi[29,30]. Although the torsional angle could not be directly determined, the small symmetry, as deduced from the rotational spacing pattern, is compatible with a dihedral angle $\phi = 90°$. The rest of the structural parameters were found to be in excellent agreement with those derived from electron diffraction experiments[21,22]. The above-cited experimental techniques either assume (for the purpose of determining another parameter) or yield essentially pyramidal N atoms in hydrazines. In agreement with the latter mentioned results, microwave spectroscopy[31] of hydrazine also yielded a dihedral angle of 90° and a rotational barrier $V_{rot} = 3{\cdot}07$ kcal/mol, which is in close agreement with the value of 2·8 kcal/mol derived from N—N torsional band analysis[24].

In summary, X-ray and neutron diffraction experiments of *solid* hydrazine favour an eclipsed C_{2v} conformation, while infrared, Raman, microwave and electron diffraction spectroscopies, excluding the work of Wagner[27], point to a C_2 conformation in all phases, which is qualitatively compatible with the dipole moment and the theoretical calculations on hydrazine. A change in conformation in going from the liquid to the solid state is conceivable.

In hydrazo systems in general, the question arises as to what extent do substituents perturb the conformational properties of the parent hydrazine. When *alkyl hydrazines* are considered, one can argue that the only factor which may perturb the ground state conformational equilibrium is the non-bonded interactions. The kinetic aspects may consequently also be affected and will be discussed later. In order to predict the conformational thermodynamic properties of alkyl hydrazines, one may use the known conformational principles of the carbon systems and superimpose them on the general torsional function of hydrazine. In order to perform such an analysis on tetramethylhydrazine, the energy value of a *gauche* N—Me/N—Me interaction is necessary. Katritzky and co-workers[32] have found a value of 0·65 kcal/mol for the conformational free energy of 1-methylpiperidine, considerably less than the 1·8 kcal/mol for methylcyclohexane. If this value is taken as a basis, and noting from Figure 1 that $E_{60°} \approx E_{180°}$, it turns out that the *trans* (**11**) should be more stable than the *gauche* (**10**) by ca. 0·325 kcal/mol. However, from Figure 1, when the dihedral angle is increased from 60° to 90° (10 → 9), the molecule gains ca. 4 kcal/mol. The only serious steric interactions which are thereby generated are due to the dihedral angle of 30° between the two N—Me groups in **9**. Considering the butane torsional potential function[33] such an interaction cannot exceed 3·5 kcal/mol, and if it is granted that N—Me groups generate an even smaller non-bonded interaction, it must be concluded that **9** is the most stable conformation of tetramethylhydrazine. Thus, although one would



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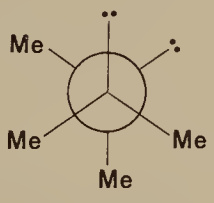

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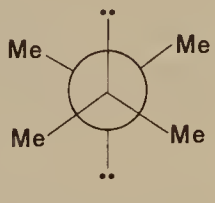


(11)

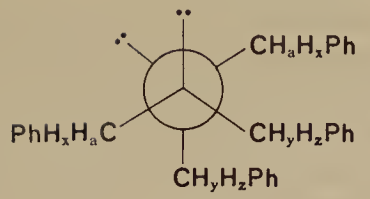
not hesitate to claim that a *trans* conformation such as **11**, is the most stable one in the analogous 2,3-dimethylbutane system, this is not so obvious in

the hydrazine case, where the energy associated with the interorbital angle is similar in magnitude to that due to non-bonding interactions of alkyl groups, and therefore is a decisive factor in determining the conformational equilibrium.

The above analysis demonstrates the unique conformational properties of the hydrazo systems. The infrared spectrum of tetramethylhydrazine[34] is claimed, on the basis of the number of bands and their relative intensities, to give support to an orthogonal model ($\phi = 90°$), although not in a rigorous manner.

An exciting and very recent development in the subject under discussion is the photoelectron spectroscopy (p.e.s.) of hydrazine and hydrazo systems[35a, 35b]. Since p.e.s. has a time scale comparable to u.v. and i.r., a superposition of the spectra of the individual conformational species in an equilibrium system is obtained. Ionization of electrons from lone pair orbitals occurs at lower energy than those from the σ bonds and the corresponding peaks were found to be fairly well resolved. Two ionization peaks are expected for a hydrazine, and these correspond to the symmetric and antisymmetric combination of the lone pair orbitals. It is the magnitude of this interaction which depends on the diorbital angle (ϕ) of hydrazine and therefore affects the magnitude of the splitting (Δ) between the two ionization peaks. An approximately cos ϕ relationship has been calculated for the above splitting resulting in about equal and maximum splitting at 0 and 180°, and nearly 0 at 90°. The authors[35a,b] have measured the p.e.s. of a series of structurally diverse hydrazines and the splitting varied from 0·40 eV for tetramethyl and tetraethylhydrazine to 2·45 eV for 9,10-diazadecalin[35a], indeed an impressive range. The general experimental trend of Δ as a function of the geometries, which were mainly deduced from n.m.r., corresponds to that which is expected from the calculations. Although the acyclic hydrazines have exhibited the smallest splitting, the exact angle could not be deduced on purely spectroscopic grounds (approximate calculations indicate that at $\phi = 90°$ the splitting should vanish; see authors'[35a] argument). However, p.e.s. indicates that tetramethyl and tetraethyl hydrazines are conformationally homogeneous within the detection capability (few percent), and the diorbital angle is most probably in the vicinity of 90°[35a, b].

Several other tetraalkyl hydrazines have been investigated by d.n.m.r. The low temperature (–120°) n.m.r. spectrum of tetrabenzylhydrazine has been analysed[4, 36], and is schematically depicted in Figure 3. A singlet was recorded at higher temperatures. The doublet at τ 5·47(2H) collapsed to give a singlet when the broad signal at τ 6·52(6H) was irradiated, indicating that the two belong to the same conformational species, and that the



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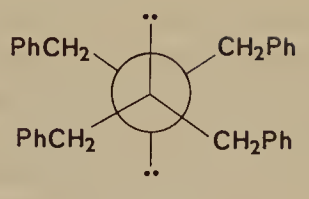


(13)

doublet is the A part of an AB (or AX) quartet. This pattern can be interpreted only in terms of a C_2 type conformation, i.e. **12**, since the *trans* conformation (**13**) (both N inversion and rotation are slow) should have exhibited *one* AB quartet, as all the benzyl groups are interchangeable via the centre of symmetry. The doublet in Figure 3 can be assigned to any pair of equivalent nuclei, *viz.* H_A, while the rest of the protons resonate together.

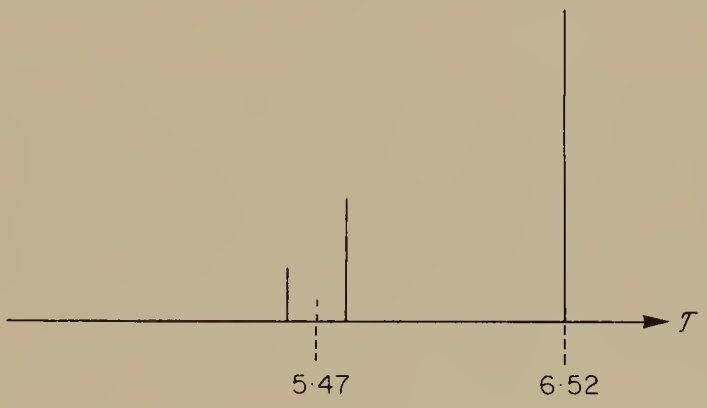


FIGURE 3. N.m.r. lines of tetrabenzylhydrazine at −120°C (schematic)[4].

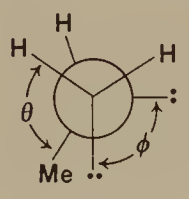
The n.m.r. spectrum therefore supports a conformation which belongs to a C_2 point symmetry, *viz.* **12**, but cannot yield the exact diorbital (dihedral) angle ϕ which by n.m.r. criteria must be defined as $0° < \phi < 120°$. The above experimental results are in general agreement with our previous analysis for tetramethylhydrazine inasmuch as the *trans* conformation can be definitely excluded*.

From n.m.r. studies of other tetra-alkylhydrazines, which will be analysed in the subsequent discussion, an interorbital angle, $0° < \phi < 120°$ can also be inferred[37].

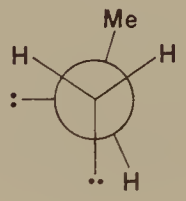
If indeed tetraalkylhydrazines exist in the C_2 conformation, our argument of non-bonded interactions would indicate that lower substituted alkyl-

* N.m.r. is a poor method for detecting low populated species. Thus if $K_{eq} < 0{\cdot}05$ the minor component (ca. 5%) would not usually be observed.

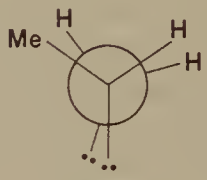
hydrazines will also prefer similar conformations. Methylhydrazine possesses a dipole moment of 1·68 D, similar to that of hydrazine[38]. The conformational problem of methylhydrazine is somewhat modified due to conformational asymmetry. If, indeed, the geometrical relationship between the two lone pair orbitals determines the conformational equilibrium, then the two diastereomeric conformers (**14**) and (**15**), ($\phi = 90°$), are expected to be the most stable ones.



(**14**)
'outer'



(**15**)
'inner'



(**16**)

The infrared[39,40] and the microwave[41] spectra of methylhydrazine have been measured and analysed. The torsional potential function was calculated[39] using infrared data and microwave values of $\theta = 84·5$ and $83·3°$[41], for the inner (**15**) and outer (**14**) conformations respectively. In spite of the uncertainties in the exact microwave values of θ, qualitatively, the potential function (Figure 4) looks reasonable and it is what we would expect on the basis of the previous argument. The present data imply that the outer

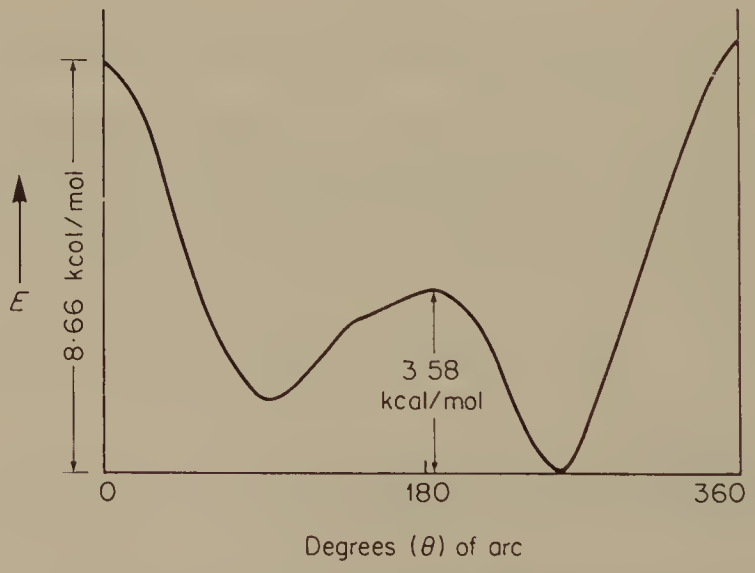


FIGURE 4. Torsional potential function (N—N) of methylhydrazine[39] (schematic).

rotamer (**14**) is less stable than the inner rotamer (**15**) provided, of course, that the spectral lines are correctly assigned. For this purpose Lattimer and Harmony[41] have presented a convincing argument based on calculations of dipole moments, and their components as a function of the dihedral angle, which enables them to assign the spectral lines to the appropriate conformers. Then, from the relative line intensities these authors have calculated the inner rotamer (**15**) to be more stable than the outer one (**14**) by 838 cal/mol, which corresponds to the presence of 19% of **14** at room temperature. There is no apparent physical reason for this rather large difference in stability. In fact, the above order of stability is in conflict with entropy calculations based on infrared data[42,43], and *ab initio* calculations (assuming orthogonal conformation)[18].

The findings of very recent *ab initio* calculations of the torsional potential of methylhydrazine[12] are in excellent agreement with the ones calculated from experiments (Figure 4)[39]. The potential minima are $\phi = 95°$ (outer configuration) and $\phi = 100°$ (inner configuration), the energy difference being 0·09 kcal/mol. The *cis* and *trans* barriers are 11·87 and 3·26 kcal/mol respectively. Indeed, aside from the somewhat larger calculated *cis* barrier and the equi-energy potential minima, the agreement is gratifying. Although relative stabilities of the inner and outer conformers are still uncertain, there is agreement as to their pronounced stability over other possible conformations. Thus, regardless of the exact horizontal location of the double minima in the potential function (Figure 4), the behaviour is completely analogous to that of hydrazine. At this stage one may conclude that in the absence of serious non-bonded interactions the dihedral angle of acyclic alkyl hydrazines can be deduced from the parent hydrazine.

It is now of interest to examine to what extent polar factors may affect the conformation of a hydrazine molecule. An interesting case is tetrafluorohydrazine. This compound was first reported by Colburn[44] and was extensively investigated by the above author and his co-workers as well as by others. The heat of dissociation of N_2F_4 to NF_2 radicals is only 19·8 kcal/mol[45]. The temperature and pressure of the various measurements are therefore critical for the observation of the appropriate species.

A CNDO calculation by Gordon[8] yielded a potential function, schematically depicted in Figure 5, indicating minima of almost equal energy at $\phi = 69°$ and 180°. The minimum at 180° is clearly in variance with the maximum observed in hydrazine at this angle. A semi-empirical calculation by Cowley[9] yields the following order of decreasing conformational stability: *gauche* > *cis* > *trans*, in disagreement with the above calculation[8]. Colburn[46] has measured the F^{19} n.m.r. spectrum of N_2F_4 in NF_3 and in N_2F_2 at −155°. In both solvents a singlet and an AB quartet ($J = 600$ c.p.s.) in the

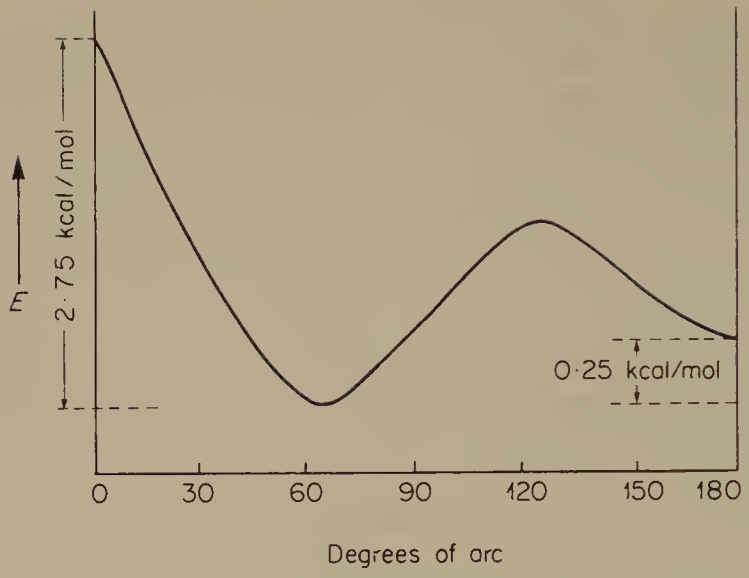
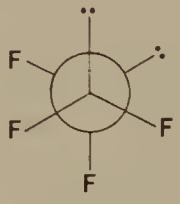


FIGURE 5. Torsional potential function of N_2F_4[8] (schematic).

ratio of 1:1 were observed. Clearly, the AB quartet must indicate that at −155° the nitrogen inversion is slow on the n.m.r. time scale, since conformations possessing planar (or fast inverting) N atoms could in no way give rise to an AB quartet. The spectrum is perfectly compatible with a mixture of the *trans* (**16**) and a C_2-conformation such as 17. Again, the

(16)



(17)

n.m.r. spectrum does not provide us with the exact equilibrium dihedral angle of **17**. The former C_{2h} species is responsible for the singlet while the latter C_2 species is responsible for the AB quartet. From the integral ratio the *gauche* **16** was found to be more stable than the *trans* **17** conformation by ca. 100–200 cal/mol. This situation is in agreement with the calculation by Gordon[8] inasmuch as the location of the minima at $\phi = 69$ and 180° were correctly predicted.

The rotational constants in a microwave spectrum of N_2F_4[47] are consistent with a C_2 species. Of course the centrosymmetric (**16**) cannot be

observed by the above spectral method, but from the consideration of the intensities due to the observed species it constitutes ca. 10% of a possible equilibrium mixture.

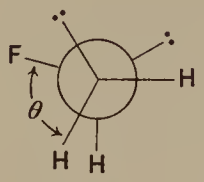
Bohn[48] carried out an electron diffraction study of N_2F_4 in the gas phase, and the radial distribution curve exhibited only a *single* F...F (non-bonding) distance at 3·38 Å (*trans*) which excludes the possibility of a *trans* conformation in the gas phase. A dihedral angle of 70 ± 3°, considerably smaller than in hydrazine (ca. 90°) and an N—N bond length of 1·53 ± 0·02 Å, significantly longer than in hydrazine (1·449 Å) were found, the N atoms being essentially pyramidal. The increase in the complementary dihedral angle F—F (50°) with respect to hydrazine (30°) was attributed to F...F non-bonding repulsion[48].

Finally, Durig[49] has studied the infrared and Raman spectra of N_2F_4. At −120°C liquid N_2F_4 exhibits 17 Raman lines of which five lines are in excess of the number anticipated for a C_2 species. It must therefore be concluded that the additional lines arise from a species having different symmetry properties. A dramatic alternate forbiddance between the Raman and infrared frequencies of the above extra lines has been observed below 800 cm^{-1} which is compatible with the centrosymmetric *trans* conformation. From the insensitivity of the intensity of the lines to the temperature, it was concluded that the two species are about equally populated. These results are in excellent agreement with the previously mentioned n.m.r. results at −155°[46], but in disagreement with the gas phase electron diffraction study[48]. They also agree with the CNDO calculations and the microwave spectrum inasmuch as the latter ascertained the presence of a C_2 species in the gas phase. The infrared, Raman and n.m.r. results present strong evidence that liquid N_2F_4 consists of an approximately equimolar mixture of the *trans* (**16**) and C_2 (**17**) conformers.

The change in isomer stabilities of N_2F_4 with respect to N_2H_4 was taken by Wolfe[17] as evidence that electron pair–polar bond interactions are stabilizing inasmuch as four such interactions prevail in **16** vs. only two in the C_2 conformation (**17**). The above change in stabilities finds no explanation in terms on $n \rightarrow \sigma$ donation[12], since by this argument the *gauche* **17**, which has *two trans* antiplanar arrangements for $n \rightarrow \sigma$ donation, would be even more stable than the *gauche* conformation of hydrazine itself. However, the inclusion of the torsional and dipolar components[12] in the conformational analysis of N_2F_4 may perhaps yield better results.

Calculation of the torsional potential energy function of monofluorohydrazine has produced an unequal double minima curve[12]. The minima occur at $\theta = 280°$ ($E = 0$) for the inner conformer (**18**) and at $\theta = 110°$ ($E = 7{\cdot}14$ kcal/mol) for the outer conformer (**19**). The remarkably large

difference between the two is attributed mainly to the optimal geometry for $n \rightarrow \sigma$ donation in **18**[12]. Indeed, the overwhelming stability of **18** over any other conformation is in accordance with the electronegativity of F

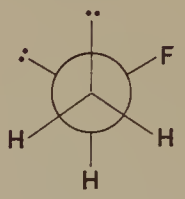


(19)

'outer'

(18)

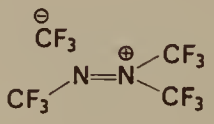
'inner'



(20)

and the relatively large value calculated for the bond separation energy of fluorohydrazine[18]. The 'gauche rule'[17] would favour conformation **20** which has the maximum number of lone pair–lone pair and lone pair–polar bond pair arrangements rather than **18** which has been favoured by the RHP approach[12].

Another interesting hydrazine structure is $N_2(CF_3)_4$, the most notable feature being the flatness of the nitrogen pyramid. Electron diffraction study[50] reveals $\measuredangle$ NNC = 119·0 ± 1·5° and $\measuredangle$ CNC = 121·2 ± 1·5°. Also the N—N bond distance of 1·402 ± 0·02 Å is appreciably shorter than the 1·449Å found in N_2H_4[21]. These results could be interpreted in terms of a contributing resonance structure (**21**) which is in accord with the known strong electronegative character of the CF_3 group. Since the electron



(21)

diffraction measurements have indicated a dihedral angle of 88 ± 4°, the authors[50] concluded that such a contributing structure is geometrically incompatible with effective resonance. However, MO descriptions of $N_2(CF_3)_4$ have revealed a strong delocalization of the lone pair on to the carbons[50]. In fact this is in accord with the general idea of $n \rightarrow \sigma$ donation[18], which, due to the strongly electron accepting property of the F_3C—N bond, outweighs the energy of pyramidalization of the nitrogen atoms.

The dynamic aspects of hydrazo systems bring us to the problem of the rotation inversion dichotomy. This problem becomes especially acute when

the phenomena are investigated by dynamic n.m.r. techniques, since, as previously mentioned, molecular symmetry properties may in some cases prevent unambiguous differentiation between the rotation about the N—N bond and the inversion of the nitrogen atoms. Another hopeless situation may arise when the rates of the two processes are similar.

The barriers to N inversion in some hydrazine systems were calculated by several groups and are presented, together with that for ammonia, in Table 2. According to the calculation of Dewar[51] and Rauk[52] and their co-

TABLE 2. Inversion barriers of nitrogen atoms (calculated)

Compound	Barrier (kcal/mol)	Reference
NH_3	3·7	51
	3·2	52
NH_2NH_2	10·3	51
	7·4	52
$CH_2CH_2N—NH_2$	22·3 (ring N)	51
	9·7 (NH_2)	51
	30·0 (ring N)	52
$CH_2CH_2N—H$	13·8	51
	21·4	52

workers, the inversion barrier of hydrazine is higher by 4·2–6·6 kcal/mol than that of ammonia. An analogous trend is also observed with the ring nitrogen in aziridine and 1-aminoaziridine. Thus, substitution of H by an N atom in an amine raises its barrier to inversion, as has been confirmed by many experiments*. In fact, the above phenomenon is general inasmuch as various electronegative groups, when attached to a nitrogen atom, raise the barrier to its inversion[53]. In the transition state of inversion the N atom adopts an essentially planar (sp^2) configuration and its substituents are placed in approximately one plane. The origin of the heteroatom effect on the nitrogen barrier is not completely clear, and the literature offers essentially two interpretations which are not necessarily exclusive of one another[3,54]. The first interpretation[3] invokes the inductive effect of the hetero substituent which, by virtue of its electronegativity increases the *p* character in the σ bond to N, and consequently shifts the *s* character to the non-bonding orbital. Consequently, since in the planar transition state this

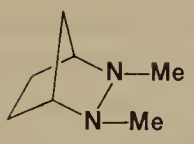
* See refs. 101–109 cited in reference 1.

orbital is transformed into a *p* orbital, more energy will be required for the inversion process. Griffiths and Roberts[54] have not been able to observe the inversion of the tertiary N atom in 1-benzyl-1,2,2,2-tetramethylhydrazinium iodide at –70°C (n.m.r.) which indicates that in this case the inductive effect does not play a major role in decreasing the rate of N-inversion. However, at this temperature the base itself also did not show any spectral changes. The second argument involves the enhanced repulsion in the inversional transition state between the non-bonding electrons of the N atom and the adjacent electronegative hetero atom bonded to it[55,54]. It is difficult to envisage this interaction in hydrazine and acyclic hydrazines where the non bonding orbitals may assume orthogonal relationships. Such an interaction may perhaps play a role in hydroxyl and halo amines which have more than one pair of non bonding electrons. Thus, at present, no clear cut experimental or theoretical results are available on the basis of which we can assess the relative importance of these two effects. Nevertheless, the experimental facts clearly indicate that nitrogen inversion rates in hydrazine are slower than in the corresponding amines.

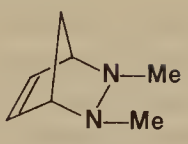
Although earlier[31] a low N inversional barrier of 2·83 kcal/mol was reported for hydrazine, more recently, analysis of the splitting of the infrared band at 937 cm^{-1} yielded an inversional barrier of 7·48 kcal/mol[56], in excellent agreement with the calculated value (7·4 kcal/mol, Table 2).

Structurally more complex hydrazo systems cannot be very well analysed by microwave, i.r. or Raman spectroscopies. On the other hand, these are the more interesting systems and the ones most frequently encountered by chemists. The experimental tool for their investigation is d.n.m.r., and many such studies have been carried out in recent years. As previously mentioned, the rotation–inversion dichotomy in hydrazine prevents, in many cases, the unambiguous identification of the spectral changes in the n.m.r. One solution to this problem is to select those systems in which one process becomes immeasurably slow on the n.m.r. time scale due to inherent structural factors and therefore the other kinetic process can be unambiguously correlated with the spectral changes. However, it should be realized that such an approach almost invariably also affects the observed process. This point will become clear in the subsequent discussion.

Consider the rigid bicyclic hydrazo system **22**, in which structural constraint prohibits the torsional process about the N—N bond. Compound **22**, **22a** and structurally related ones were subjected to d.n.m.r. studies[57,58]. The signals of the *N*-methyls were found to be temperature dependent (doublet → singlet). Obviously, these changes may only be correlated with N inversion. The enthalpies of activation, calculated from the appropriate



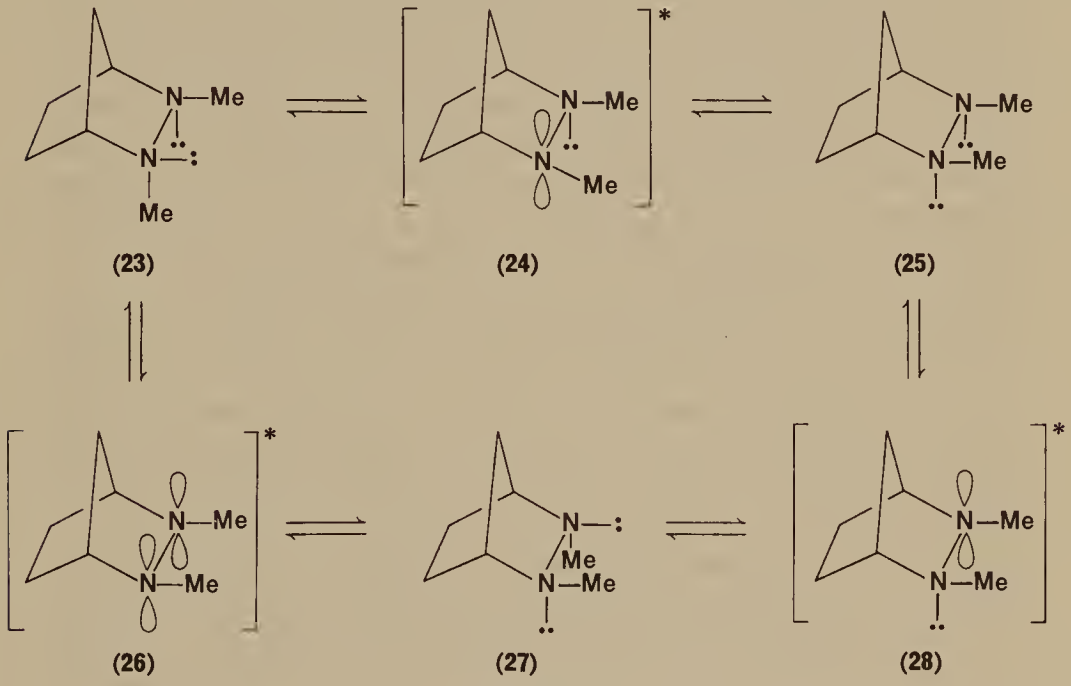
(22)



(22a)

spectral changes of **22** and **22a** are 14·5 and 13·2 kcal/mol respectively[57, 58]. These values are substantially higher than those calculated for hydrazine (7·4–10·3 kcal/mol; Table 2) and essentially twice as large as the experimentally measured ones, which in acyclic hydrazines barely exceed 10 kcal/mol (*vide infra*).

It is therefore instructive to enquire into the conformational details of this process. The very fact that at slow exchange rates two signals of the two N—Me groups were observed, and shown to originate from the same molecule[57, 58], indicate that the E_{min} conformation is asymmetric. Con-



(23) (24) (25)

(26) (27) (28)

SCHEME I

sidering essentially pyramidal N atoms, **23** (and its enantiomer **27**) is the structure which is compatible with the observation of two Me signals at slow inversion rate. It can readily be seen that enantiomerization is accompanied by the exchange of the Me groups, and no conformational process, other than double inversion, can bring about this exchange. The pathway

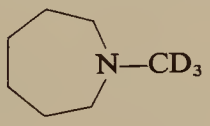
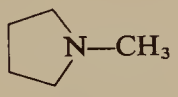
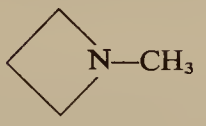
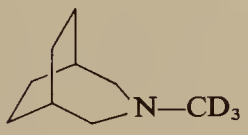
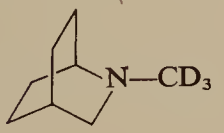
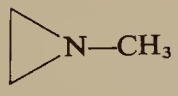
of the enantiomerization constitutes an interesting problem which was considered by the authors[57, 58]. The question can be formulated as follows: Is the interconversion **23** ⇌ **27** proceeding via two consecutive inversions (**23** ⇌ **24*** ⇌ **25** ⇌ **28*** ⇌ **27**) or is it a concerted one-step simultaneous double inversion of the two N atoms **23** ⇌ **26*** ⇌ **27**? The present experimental data cannot distinguish between the two paths. The consecutive pathway involves the *cis* intermediate (**25**) (or its di-endo isomer) which, although undetected by n.m.r. may still constitute a low concentration intermediate by which enantiomerization occurs. It is noted that the two methyls of **25** are equivalent. It is logical to assume that **26*** is a high energy transition state and the authors[57, 58] have consequently adopted the consecutive inversion mechanism.

We are still faced with the question of why the inversion barriers in **22** and **22a** are significantly higher than those of the corresponding acyclic alkyl hydrazines (*vide infra*). Ring strain in the inversional transition state is being frequently quoted as the factor responsible for the slowing down of the N inversion. When a comparison is made with the barrier of dibenzylmethylamine (**29**) (Table 3), it is clear that an *appreciable* inversion hindrance, due to ring strain, can be invoked only in the case of the aziridine (**35**). For the rest of the cyclic amines, a maximal value of ca. 2 kcal/mol may perhaps be assigned to ring strain, which still cannot account for the large N inversion barrier of **22** and **22a**. The reason for this increase must be sought in the fact that the rigidity of **22** does not only restrict the rotational process about the N—N bond but also imposes a restriction on the mode of inversion of the N atom with respect to its substituents, and perhaps more important, with respect to the adjacent lone pair. Thus, while the inversion process in acyclic hydrazines can follow a geometrical path which minimizes non-bonded and electronic interactions, such is not the case in a rigid system. One must also consider the fact that the interorbital angle in the *ground state* of cyclic and acyclic hydrazines is different. As was previously stated this angle is of great importance in determining the conformational stability. Therefore in this sense ring constraint may modify the *ground state* stability with respect to an acyclic system and consequently also affect the inversion barrier. We are emphasizing this point because it has served as a starting point for interesting new concepts in the conformational analysis of hydrazines[59, 60], which will be presented in the subsequent discussion.

Another conformational problem, also related to the kinetic aspects, is the dependence of the rotational barrier on the configuration of the N atoms of hydrazine, which was mentioned by Dewar[4]. One may discern three *extreme* types of hydrazo systems where the two N atoms are pyramidal (bipyramidal), one pyramidal and one planar (pyramidal-planar) and

two planar (biplanar). These structural variations depend, of course, on the substituents. Since the rotational barriers of the above three classes are widely different (*vide infra*) and since each of the above classes possesses unique symmetry properties, they will be discussed separately. Unfortunately, torsional potential functions for pyramidal–planar and biplanar hydrazines have not been calculated. It should be noted that the availability of the torsional potential functions for the above three structural types of hydrazines would have demonstrated the dependence of the N *inversion* barrier on the dihedral angle of hydrazine.

TABLE 3. Nitrogen inversion barriers[53]

Compound	ΔG^* (kcal/mol)
(29) $(PhCH_2)_2NCH_3$	6·5 (–137°C)
(30) 	6·4 (–140°C)
(31) 	7·9 (–107°C)
(32) 	8·2 (–105°C)
(33) 	8·8 (–92°C)
(34) 	8·4 (–98°C)
(35) 	19·2 (60°C)

II. CONFORMATIONAL PROCESSES IN BIPYRAMIDAL HYDRAZINES

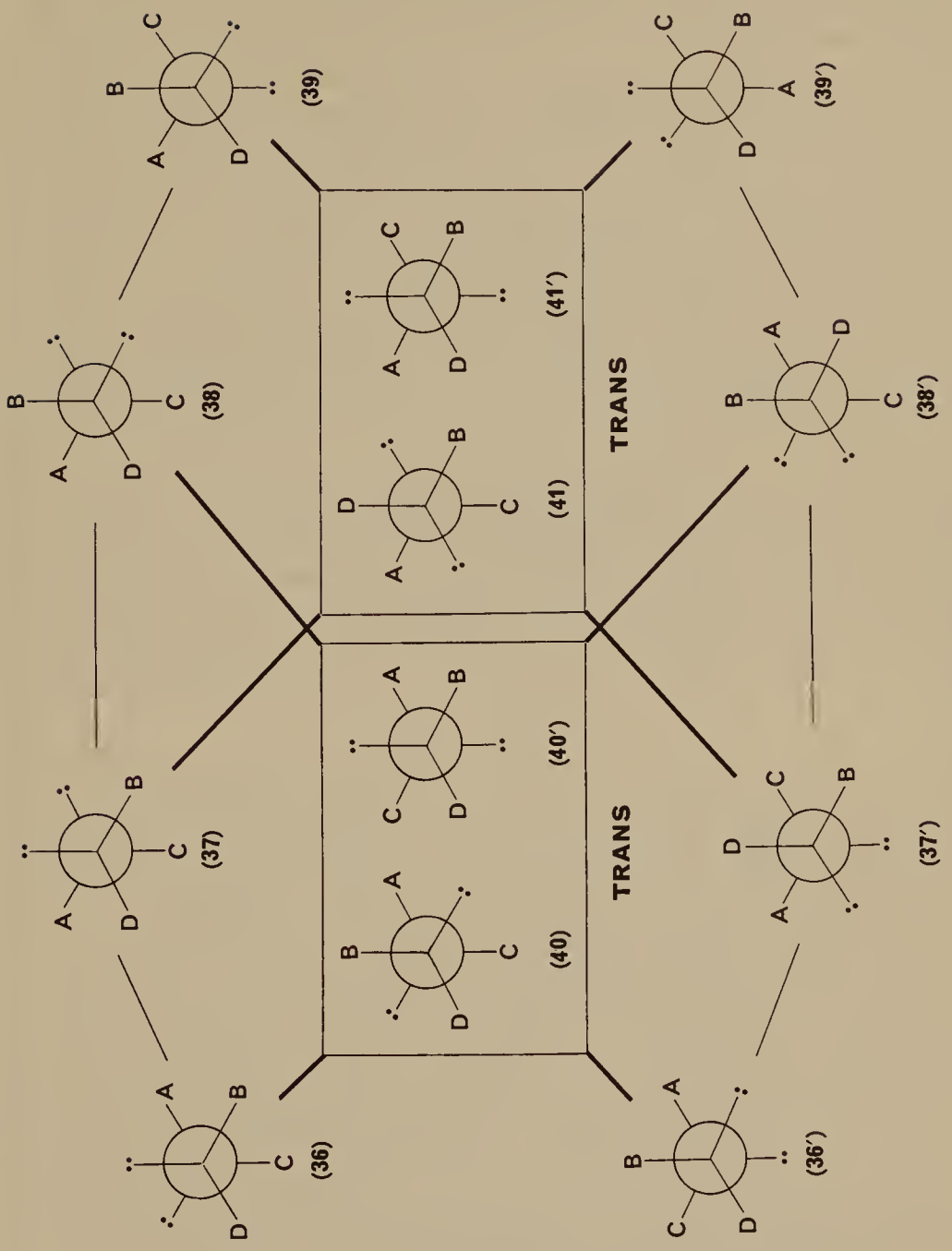
Simple alkyl hydrazines may be regarded as bipyramidal. The starting point for a conformational analysis of this type of hydrazine is the calculated torsional potential function. Although the E_{min} conformation requires a dihedral angle of 90°, a 60° angle will be used for convenience, in drawings, and we will comment on this discrepancy when necessary. As the above two conformations ($\phi = 60$ and 90°) have the same symmetry properties, d.n.m.r. analysis cannot distinguish between the two.

A bipyramidal hydrazine ABN–NCD can undergo two types of processes, inversion of the nitrogen pyramids, and rotation about the N—N bond. In the new approach introduced by Jones, Katritzky and co-workers[59, 60], two types of N inversion were recognized. A 'low energy' inversion which does not involve eclipsing of substituents (non-eclipsing inversion) and a 'high energy' inversion which does involve eclipsing of substituents (eclipsing inversion) during the process of N inversion*. There are also two types of rotational processes in acyclic hydrazines, namely a low energy one which involves eclipsing of only one pair of substituents and a high energy one which involves eclipsing of two pairs of substituents as well as the nitrogen lone pairs. Our general schematic representation differs from that of the original authors[59, 60]. The inversion and rotation analyses are represented by schemes 2 and 3 respectively. The lines connecting the various conformations represent equilibria, and their intersections have no physical significance, i.e. they are *not* common reaction points.

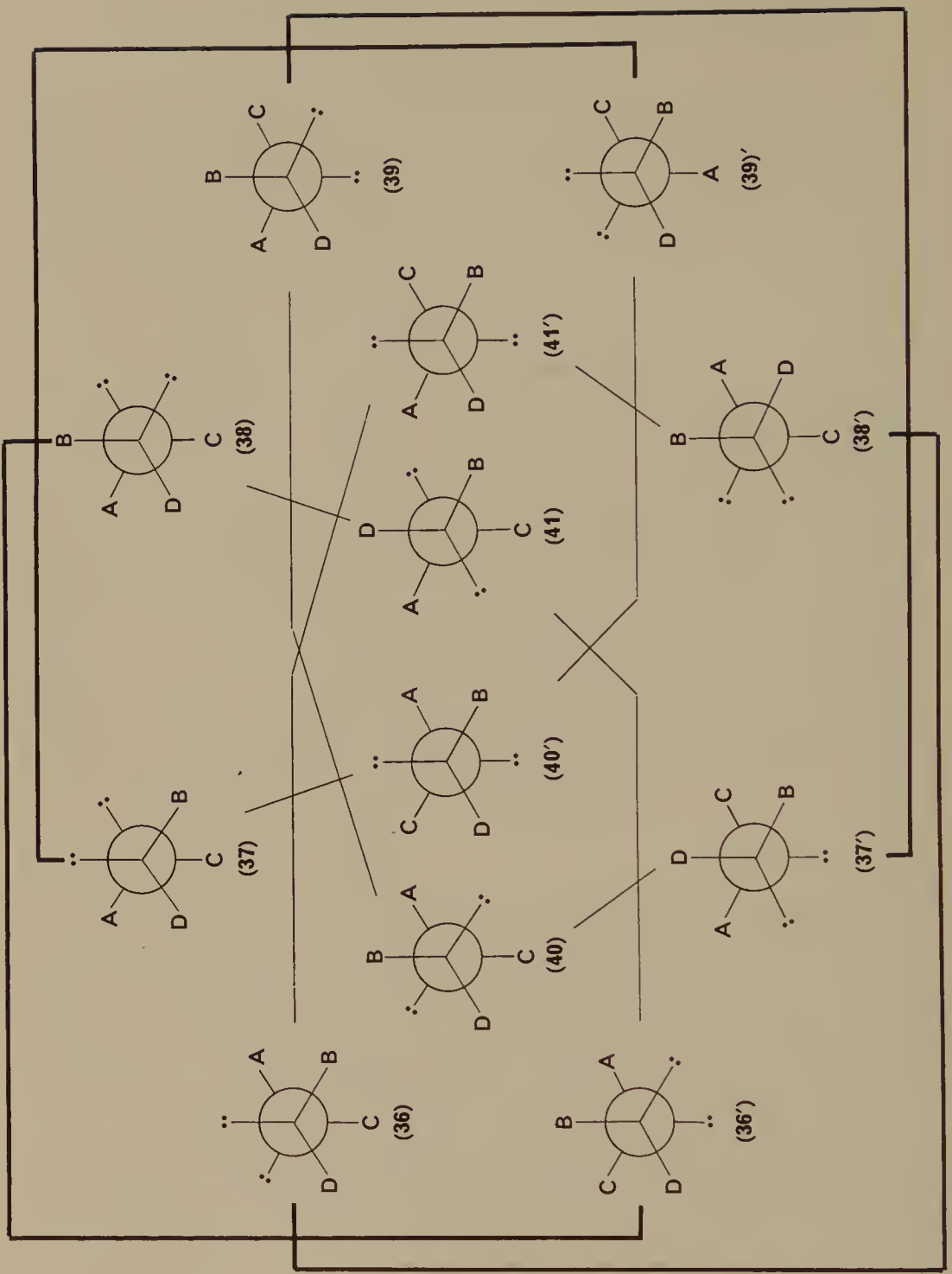
A. Inversion Scheme (Scheme 2)

There are four pairs of diastereomeric conformations with *gauche* lone pairs, **36–39** and their respective enantiomers are depicted by **36′–39′**. The interconversions within each of the above series are via non-eclipsing 'low energy' inversion (these are represented by lightly drawn connecting lines). According to the authors[59] this is a fast process. We may estimate that the barrier to such a mode of inversion will be similar to the inversion barrier of hydrazine (7·5 kcal/mol) which has been determined from infrared spectroscopy[56]. The second mode of inversion involves eclipsing of one pair of substituents, presumably in the transition state, and must necessarily lead to a *trans* conformation. Two pairs of such racemic

* The authors[59] have termed these processes as passing and non-passing inversions.



SCHEME 2. Inversion



SCHEME 3. Rotation

trans conformations (**40** + **40′**) and (**41** + **41′**) are possible (Scheme 2). According to the authors this eclipsing inversion requires more energy, and is represented by heavy connecting lines. From simple considerations, we may state that the barrier value for this type of inversion is higher than that of the non-eclipsing inversion by the amount of energy generated due to the eclipsing of substituents in the transition state. If the substituents are simple alkyl groups, a value of 3 kcal/mol is a maximal estimate that yields 10·5 kcal/mol for the barrier of an eclipsing N inversion. It is important to note that the barrier of the reverse process (*trans* → *gauche*) is lower, by the difference in the ground state stabilities of the *trans* and *gauche* conformations, than the forward process (*gauche* → *trans*). This difference is estimated at ca. 3–4 kcal/mol (Table 1). The rate determining step (RDS) of an inversional racemization process such as **36** ⇌ (**40** + **40′**) ⇌ **36′** (Scheme 2) is therefore the transformation *gauche* → *trans*.

Analysis of Scheme 2 reveals that **36**, **36′**, **38** and **38′** are all interconvertible by eclipsing inversion via the *trans* mixture (**40** + **40′**). A second set, namely **37**, **37′**, **39** and **39′** may similarly interconvert *via* the *trans* racemate **41** and **41′**. The members of each of the above two sets may interconvert by non-eclipsing inversion. Consequently racemization of any of the *gauche* conformations must necessarily occur by two eclipsing N inversions via a *trans* conformation.

B. Rotation Scheme (Scheme 3)

There are two distinct types of rotational processes. The first one is a low energy one and is associated with the interconversion between *gauche* and *trans* conformations *viz.* **36** ⇌ **41′** and **36′** ⇌ **41** (Scheme 3). This results from a torsional process of 120° from a gauche, or more accurately a 90° orthogonal conformation, which in the eclipsed transition state generated only one eclipsing interaction of groups. From the torsional potential function of hydrazine (Figure 1), we know that $E_{180°} - E_{90°} \simeq$ 3–4 kcal/mol, and by adding to this value one eclipsing interaction of simple alkyl groups (ca. 3 kcal/mol) we arrive at 6–7 kcal/mol as the barrier value of the 'low energy' torsional process. (We do not know to what extent the two lone pair–bond pair eclipsing interactions, also generated in this process, differ from those of the unsubstituted hydrazine). Again, the barrier of the rotational transformation *trans* → *gauche* (*viz.* **41′** → **38′** or **41** → **36′**) is lower than that of the reverse transformation (*viz.* **36′** → **41** or **38′** → **41′**) by the amount of the difference in the ground state stabilities of the two conformations involved. The lightly drawn lines (Scheme 3) all represent

such low energy torsional processes. It can be seen that each of the gauche conformers may be transformed into the appropriate *trans* conformers by the above torsional process.

The second torsional process, represented by heavily drawn connecting lines (Scheme 3) involves the eclipsing of all the substituents and also the two lone pairs. Considering the torsional potential function (Figure 1), $E_{0°} \cong 10$ kcal/mol and the two eclipsed interactions of simple alkyl groups (6 kcal/mol), one arrives at a value of ca. 16 kcal/mol for the barrier of this torsional process. Necessarily this kind of rotation does not involve the *trans* conformers and the various possible interconversions are depicted in Scheme 3. Of course, rotation alone can never bring about racemization. In fact, the pathways of rotational interconversions are closed loops of two diastereomeric *gauche* and one *trans* conformation.

In order to analyse a real conformational problem the two schemes must be superimposed. The symmetry properties of the various interconverting conformers will be affected by the pattern of substitution. In the following, we shall analyse some of the experimental data.

The conformational kinetics of tetrabenzylhydrazine were investigated by n.m.r. spectroscopy[4]. Referring to Schemes 2 and 3, since $A = B = C = D = CH_2Ph$ the *gauche* conformation is dissymmetric giving rise to only one racemate (**36** = **37** = **38** = **39** and **36′** = **37′** = **38′** = **39′**), and one achiral *trans* conformation (**40** = **40′** = **41** = **41′**). As previously mentioned, tetrabenzylhydrazine exhibits in the n.m.r. at −120°C *two* AB quartets[4] (Figure 3) which collapsed to a singlet at −100°C, indicating that it is the chiral *gauche* conformation with two kinds of benzyl groups (outer and inner) carrying prochiral protons which is being observed. The results of the various conformational operations on **36** are summarized in Table 4, keeping in mind that the conformational equilibrium is composed of two *gauche* enantiomeric and one achiral *trans* conformation.

Clearly, the n.m.r. results indicate that at −120° (2 × ABq) all the kinetic processes associated with N inversion and rotation are slow on the n.m.r. time scale, and the question is which pathway(s) leads to the observed spectral change, i.e. a singlet at −100°C. The barrier (8·2 kcal/mol) was assigned to the N inversion, without considering the two possible modes[4], while the rotation barrier was said to be equal or greater than 8·2 kcal/mol. Undoubtedly, topomerization of the benzyl protons requires N inversion. From Scheme 3 and Table 4 it is obvious that rotation alone cannot render the benzyl *protons* equivalent (path 5). This is also true when one rotation (120°) which leads to a *trans* conformer, followed by one inversion, are considered. Thus, if $k_{rot} > k_{inv}$ the appearance of the singlet in the n.m.r. spectrum at −100°C should be preceded by a single AB quartet, which is

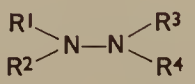
TABLE 4. Summary of conformational interconversions of $(PhCH_2)_2N—N(CH_2Ph)_2$ (Schemes 2 and 3; A = B = C = D = CH_2Ph)

Path No.	Pathway	Mode of interconversion	Type of interconversion	Topomerization[a]		N.m.r. signals
				Benzyl groups	Benzyl protons	
1	**36** ⇌ **37** ⇌ **38**	Non-eclipsing inv.	Degenerate	+	+	Singlet
2	**36** ⇌ *trans* ⇌ **38**	Eclipsing inv.	Degenerate	+	+	Singlet
3	**36** ⇌ *trans* ⇌ **36′**	Eclipsing inv.	Racemization	−	+	2 × Singlet
4	**36** ⇌ *trans* ⇌ **38′**	Eclipsing inv.	Racemization	+	−	1 × AB
5	**36** ⇌ *trans* ⇌ **38′**	Low energy rotation	Racemization	+	−	1 × AB

[a] Topomerization is denoted by + and no topomerization by − signs.

not the case. We must therefore conclude, in agreement with the original interpretation[4], that $k_{rot} \leqslant k_{inv}$. However, both the non-eclipsing and the eclipsing N inversions (paths 1,2; Table 4) bring about the topomerization of both benzyl groups and protons, i.e. a singlet in the n.m.r. spectrum*. The present system does not offer a way to distinguish between the two inversion modes. But, from the previous considerations of the energetics of the above two processes it can be assumed that it is the faster non-eclipsing inversion ($\Delta G^* = 8{\cdot}2$ kcal/mol) which is being spectrally detected. The 'high energy' rotational process (Scheme 3) need not be considered, since its spectral consequences can be achieved by the other much faster processes. Although in the case of tetrabenzylhydrazine such an analysis is not much more informative than that of the original author[4], the assignment of the barrier, and its value, to the non-eclipsing inversion mode is important for the subsequent analyses. Furthermore, our estimate of the barrier value of 7·5 kcal/mol for the non-eclipsing inversion is in good agreement with the observed one. The estimate of the low energy rotational barrier (6–7 kcal/mol) must be somewhat low since, from the above argument it is expected to be equal to or exceed 8·2 kcal/mol.

Fletcher and Sutherland[37] have studied the conformational behaviour of tetraalkyl hydrazines (**42**)–(**44**), which can be regarded as bipyramidal. The



(**42**) $R^1 = R^3 = CH_2Ph$; $R^2 = R^4 = Et$ $\quad \Delta G^*_{222} = 10{\cdot}7 \pm 0{\cdot}2$ kcal/mol
(**43**) $R^1 = R^3 = CH_2Ph$; $R^2 = R^4 = i\text{-}Pr$ $\quad \Delta G^*_{227} = 11{\cdot}2 \pm 0{\cdot}2$ kcal/mol
(**44**) $R^1 = R^2 = R^3 = CH_2Ph$; $R^4 = Et$ $\quad \Delta G^*_{220} = 10{\cdot}8 \pm 0{\cdot}2$ kcal/mol

n.m.r. spectra of **42** and **43** at −60°C exhibit one AB quartet for the benzyl protons which coalesces to a singlet at −51 and −46°C respectively. The authors have concluded that at these temperatures N inversion is fast and rotation is slow on the n.m.r. time scale. Accordingly, it is the rotational process which is responsible for the observed spectral changes[37]. The substitution patterns of **42** and **43** are identical and in terms of our two schemes (2 and 3), A = D = CH_2Ph, C = B = Et for **42** and A = D =

* Paths 3 and 4 (Table 4) by themselves do not account for the spectral observations.

CH_2Ph, C = B = iPr for **43**. The conformations of **42** and **43** can be classified as follows:

36 + **36′**: C_2 symmetry (enantiomeric)
37 + **37′**: C_1 symmetry (enantiomeric)
38 + **38′**: C_2 symmetry (enantiomeric)
37 = **39**; **37′** = **39′**
40 = **40′**: centrosymmetric (achiral)
41 + **41′**: C_2 symmetry (enantiomeric)

The benzyl *groups* are enantiotopic in each of the diastereomeric conformations except for **37** (and **37′**) and of course, they differ from each other in the various diastereomeric conformations. The benzylic protons are diastereotopic in every conformation. Thus, in the absence of any conformational exchange (very low temp) and assuming comparable enthalpies for the various *gauche* conformations, the system should exhibit several AB (or AX) quartets (we assume that the *trans* conformations are practically unpopulated and therefore undetectable in the n.m.r. spectrum). Since a single AB quartet was observed in the low temperature spectrum of **42** and **43**, a mechanism must exist which averages all the benzyl groups (but not the benzyl protons) among all the diastereomeric conformations and also those of **37** (and **37′**) which are diastereotopic. Symmetry analysis reveals that it is the non-eclipsing inversion sequence (Scheme 2) **36** ⇌ **37** ⇌ **38** ⇌ **39** (and the corresponding enantiomeric series) which has this property*. Indeed, this mode of inversion in tetrabenzylhydrazine is detectable only below −100°C[4], however, compounds (**42**) and (**43**) were not cooled to this temperature, which explains the observation of a single AB quartet. It is noted that formation of the *trans* conformer, either by eclipsing inversion or by rotation, will necessarily be followed by a faster eclipsing inversion which will lead to racemization and consequently topomerization of the benzyl protons. Therefore, the *trans* conformers (Schemes 2 and 3) do not intervene in the low temperature process which averages out only the benzyl groups of **42** and **43**. We believe this is an important point since it provides the experimental evidence for the existence of discreet modes of N inversion, i.e. non-eclipsing and eclipsing. Although the barrier value for the non-eclipsing inversion of **42** and **43** has not been determined, it must be lower than 10·7 kcal/mol, this being the value of the barrier of the next process[37].

* Strictly, the barriers for interconversion among the conformers **36**–**39** of compounds (**42**) and (**43**) are not equivalent, but may be considered as being very similar.

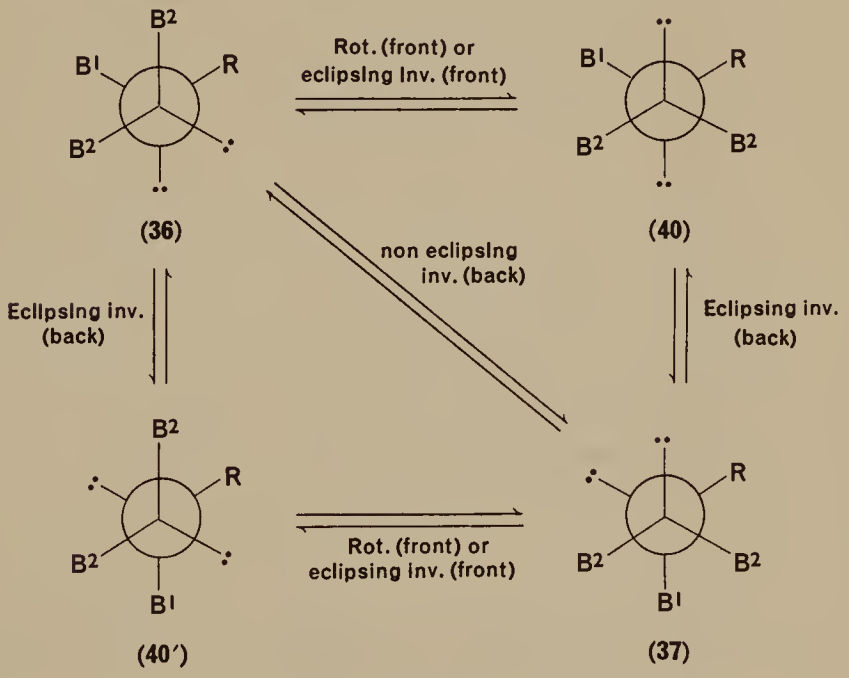
Now the question is, which process is responsible for the topomerization of the benzyl protons of **42** and **43** (singlet) at higher temperatures ($\Delta G^* = 10{\cdot}7$ and $11{\cdot}2$ kcal/mol respectively). Both eclipsing inversion *viz.* **36** ⇌ **40** ⇌ **36′** (Scheme 2) and low energy rotation followed by non-eclipsing inversion *viz.* **36** ⇌ **41′** ⇌ **38′** (Scheme 3) **38′** ⇌ **37′** ⇌ **36′** (Scheme 2) bring about topomerization of the benzyl protons. The RDS in the first sequence is the eclipsing inversion **36** → **40** (Scheme 2) while in the second sequence it is the 'low energy' rotation **36** → **41′** (Scheme 3), this being due to the already mentioned difference in the ground state stabilities between a *gauche* and *trans* conformation. Consequently, these experimental results do not allow any decision between the two pathways both of which satisfy the experimental observations. Although, as was previously mentioned, our estimate for the 'low energy' rotation barrier (6–7 kcal/mol) is most probably too low, one cannot say whether it exceeds the estimate of the eclipsing inversion barrier of 10·5 kcal/mol. The above conclusions do not necessarily agree with those of the authors[37] who have assigned the topomerization of the benzyl protons to a rotation process which was said to be accompanied by fast inversion. Indeed, fast eclipsing inversion must be operative at the coalescence temperatures of **42** and **43** but both rotation and eclipsing inversion may account for the spectral changes. Since the authors[37] did not distinguish between the two modes of N inversion, and since fast N inversion has already been invoked by them for the low temperature process, obviously no other process but rotation could account for equivalence of the benzyl protons.

Tribenzylethylhydrazine (**44**)[23] gives rise to an interesting conformational system, with a substitution pattern A = Et; B = C = D = CH_2Ph (Schemes 2 and 3). Formally this system possesses one asymmetric centre and the various conformations can be classified as follows:

36 + **37**: C_1 symmetry (enantiomeric)
38 + **39**: C_1 symmetry (enantiomeric)
40 + **40′** = **41** + **41′**: C_1 symmetry (enantiomeric)

Thus, the system is reduced to two racemates with *gauche* lone pairs, which can all be interconverted via the non-eclipsing inversion process **36** ⇌ **37** ⇌ **38** ⇌ **39** with the important consequence that both racemization and diastereomeric exchange occur by the same type of process (although the barriers may be slightly different). When the system is frozen, and assuming undetectable concentration of the *trans* racemate, the benzyl groups should exhibit a total of six different AB quartets, three in each

racemate. The interconversion within each of the racemic pairs via non-eclipsing N inversion leads to the topomerization of the diastereotopic benzyl *groups* of the achiral N atom and the benzyl *protons* of the chiral N atom. Therefore the exchange among the four conformers should reduce the predicted six AB quartets to one quartet and one singlet with intensity ratio of 2:1 respectively, and is the pattern observed in the n.m.r. spectrum of **44** below −53°C. Low energy rotation by itself can bring about exchange of diastereomers *viz.* **36** ⇌ **39** and **37** ⇌ **38** (Scheme 3)* but not racemization, and consequently it cannot induce the topomerization of the benzyl protons of the chiral N atom. Before definitely assigning the low temperature process to the non-eclipsing inversion mode it is necessary to check whether a combination of rotation and N inversion, where the former process is the RDS, may also account for the observation of a quartet and a singlet below −53°C. Consider the total equilibrium system of the enantiomeric pairs **36** and **37** and also **40** and **40′** of tribenzylethylhydrazine (**44**), shown in Scheme 4 (B = benzyl; R = ethyl).



SCHEME 4

* This is possible since as stated above the two racemates are equivalent.

All rotations are of the 'low energy' type. It can readily be seen that the equilibrium between the two enantiomers **36** ⇌ **37** can be achieved by three different paths:

(i) Non eclipsing inversion (**36** ⇌ **37**)
(ii) Rotation followed by eclipsing inversion (**36** ⇌ **40** ⇌ **37**) and the equivalent sequence, **36** ⇌ **40′** ⇌ **37.**
(iii) Two eclipsing inversions (**36** ⇌ **40** ⇌ **37**) and the equivalent sequence **36** ⇌ **40′** ⇌ **37.**

The enantiomers may also undergo a degenerate conversion by rotation and eclipsing inversion *viz.* **36** ⇌ **40**. The symmetry and spectral consequences of the conformational interconversions of this system are summarized in Table 5. The net results of all the interconversions (racemizations) are the same, i.e. **36** ⇌ **37**, they differ as far as the symmetries of the benzyl groups and protons are concerned.

It can readily be seen (Table 5) that the spectral consequences of both paths 1 and 2 are in accord with the experimental n.m.r. spectrum of **44** below −53°C, namely a singlet and a quartet with an intensity ratio of 1:2 respectively. It is possible to decide between the two pathways provided it is remembered that the barriers in going from the *trans* to the *gauche* conformations are significantly lower than those of the reverse process. If eclipsing N inversion is the RDS of path 2, then paths 2 and 3 must operate concurrently, since the latter is composed of two eclipsing N inversions. Mixing of the two paths would result in topomerization of all groups and protons, exhibiting two singlets at −53°C, which is not the case. If eclipsing inversion is not the RDS of path 2, then the rotational process may assume this role. Since both paths 2 and 4 contain a rotational step, they must also operate concurrently and give rise to a two-singlets spectrum. It is therefore concluded that the above conformational system (Scheme 4) does not follow path 2 below −53°C, although the spectral consequences are compatible with the experimental ones. Thus, we are left with the non-eclipsing inversion (path 1, Table 5) as the only logical conformational process which can account for the n.m.r. spectrum of **44** below −53°C. Similar analysis can be carried out on the second enantiomeric pair **38** and **39** (Scheme 2), and since the two diastereomeric pairs can equilibrate via the non-eclipsing inversions the low temperature spectrum will stay the same, i.e. a singlet and a quartet.

The conclusion is that even without previous knowledge of the barriers we may definitely state that it is the non-eclipsing inversion which operates below −53°C, while low energy rotation and N-eclipsing inversion are

TABLE 5. Summary of conformational interconversion of $(PhCH_2)_2N—N(Et)CH_2Ph$ (Schemes 2 & 3; A = B = C = CH_2Ph, D = Et)

Path No.	Pathway	Mode of interconversion[a]	Type of interconversion	Topomerization[b]			N.m.r. signals
				B_1 protons	B_2 groups	B_2 protons	
1	**36** ⇌ **37**	Non-eclipsing inv.	Racemization	+	+	−	Singlet + qt. 1:2
2	**36** ⇌ **40** ⇌ **37**	Rot. (f) + eclipsing inv. (b)	Racemization	+	+	−	Singlet + qt. 1:2
3	**36** ⇌ **40** ⇌ **37**	Eclipsing inv. (f) + eclipsing inv. (b)	Racemization	+	−	+	3 × Singlets
4	**36** ⇌ **40**	Rot. (b) + eclipsing inv. (f)	Degenerate	−	+	+	Singlet + qt. 2:1

[a] f and b denotes front and back nitrogen atom respectively.

[b] The signs + and − denote topomerization and no topomerization of the groups and protons.

higher energy processes. An important corollary to the above conclusion is that, indeed, two energetically distinct nitrogen inversion processes may occur in hydrazine as originally suggested by Jones, Katritzky and co-workers[59].

As to the appearance of two singlets (1:2) in the n.m.r. spectrum of **43** *above* −53°C, the authors[23] have suggested that a rotational process superimposed on the already fast N inversion is responsible for the observed spectral transformation. Inspection of Table 5 reveals that each of the paths 3 and 4 lead to topomerization of the benzyl protons (B^2 protons) and, when operating together with the non-eclipsing inversion process (path 1) will lead to the complete topomerization of all groups and protons and consequently to an n.m.r. spectrum of two singlets above −53°C. If the rotation step is the RDS of path 4, then paths 3 and 4 become distinctly different, recalling that the second step (*trans* → *gauche*) is always faster than the first step (*gauche* → *trans*). Thus again, the experimental results do not allow us to decide whether the spectral transformation from a singlet and a quartet below −53°C to two singlets above −53°C is associated with 'low energy' rotation or eclipsing N inversion. In fact, none of the systems which were hitherto analysed were suitable for distinguishing between these two processes.

Finally, Roberts and co-workers[61,54] have found that at −137°C the benzyl protons of benzyltrimethylhydrazine exhibit an AB quartet for the benzyl protons which coalesces to a singlet at −130°C ($\Delta G^* = 6{\cdot}8 \pm 0{\cdot}3$ kcal/mol). No chemical shift separation between the geminal N—Me signals could be observed in the low temperature spectrum. The symmetry properties of this molecule are similar to those of **44**, namely the total conformational system consists of two *gauche* racemates and one *trans* racemate. This equilibrium system is depicted in Scheme 5, and the results of the various conformational interconversions are summarized in Table 6.

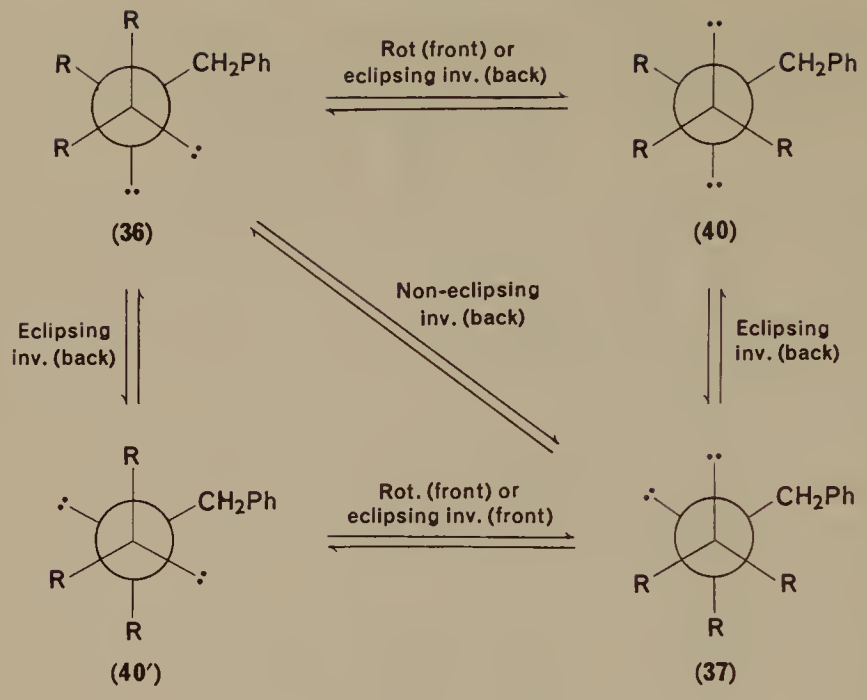
Under conditions of slow rotation and inversion a pair of enantiomers *viz.* **36** and **37** (Scheme 5) should give rise to a quartet for the benzyl protons, and three N—Me singlets. If we follow the previous arguments, the low ΔG^* value found for the coalescence of the quartet to a singlet must be related to a non-eclipsing inversion process, i.e. path 1. (Table 6). Path 2 (Table 6) is compatible with the spectral observations, but as previously argued the barrier to rotation and eclipsing N inversion are substantially higher (>10 kcal/mol) than the one which was experimentally determined (6·8 kcal/mol). Consideration of path 1 requires that below the coalescence temperature (−130°C) the geminal N—Me groups should have exhibited two, rather than the one signal which was observed. Accidental equivalence or a small chemical shift difference between these signals, and

TABLE 6. Summary of conformational interconversion of $PhCH_2(Me)N—N—Me_2$ (Schemes 2 & 3; A = Benzyl, B = C = D = Me).

Path No.	Sequence of interconversion	Mode of interconversion[a]	Type of interconversion	Topomerization[b]		N.m.r. signals
				Benzyl protons	Methyl groups	
1	**36** ⇌ **37**	Non-eclipsing inv. (b)	Racemization	+	+	3 singlets
2	**36** ⇌ **40** ⇌ **37**	Rot. (f) Eclipsing inv. (b)	Racemization	+	+	3 singlets
3	**36** ⇌ **40** ⇌ **37**	Eclipsing inv. (f) Eclipsing inv. (b)	Racemization	+	−	4 singlets
4	**36** ⇌ **40**	Rot. (b) Eclipsing (f)	Racemization	−	+	Quartet and two singlets

[a] f and b denote front and back N atoms respectively.

[b] Topomerization is denoted by + and no topomerization by −.



SCHEME 5. (R = Me)

extensive broadening[61], may account for this apparent inconsistency. The authors[61], have argued that the spectral transformation from an AB quartet to a singlet below −130°C is related to the slow inversion of the chiral N-atom while the achiral N-atom is still inverting at a fast rate at that temperature, and the geminal N—Me groups are therefore effectively enantiotopic. However, the authors have felt that there is actually no good reason for assigning appreciably different inversion rates to the two similarly substituted N-atoms and consequently suggested that the considerable line width of the N—Me signal at the temperature of observation may have obscured its splitting. Accepting this reservation, we conclude that the observed process in the temperature dependent spectrum of benzyltrimethylhydrazine is the non-eclipsing N inversion **36** ⇌ **37** (Table 6). The barrier value, 6·8 ± 0·3 kcal/mol[61], is in good agreement with that of tetrabenzylhydrazine, 8·2 kcal/mol[4] and the one predicted by us (7·5 kcal/mol).

At this stage the following statements can be made regarding the conformational processes which may take place in acyclic bipyramidal hydrazines:

(i) Non-eclipsing and eclipsing nitrogen inversions are discreet con-

formational processes as originally suggested by Jones, Katritzky and co-workers[59].

(ii) The experimental range of the barrier values of the non-eclipsing N-inversion is 6·8–8·2 kcal/mol.

(iii) Although eclipsing N-inversion and low energy rotation processes could not be distinguished experimentally, their barriers must be higher than that of the N non-eclipsing inversion and in the range of 10–11 kcal/mol.

(iv) There is no experimental evidence to suggest that the high energy rotational process (total eclipsing) in acyclic hydrazines was ever observed by d.n.m.r.

C. Cyclic bipyramidal hydrazines

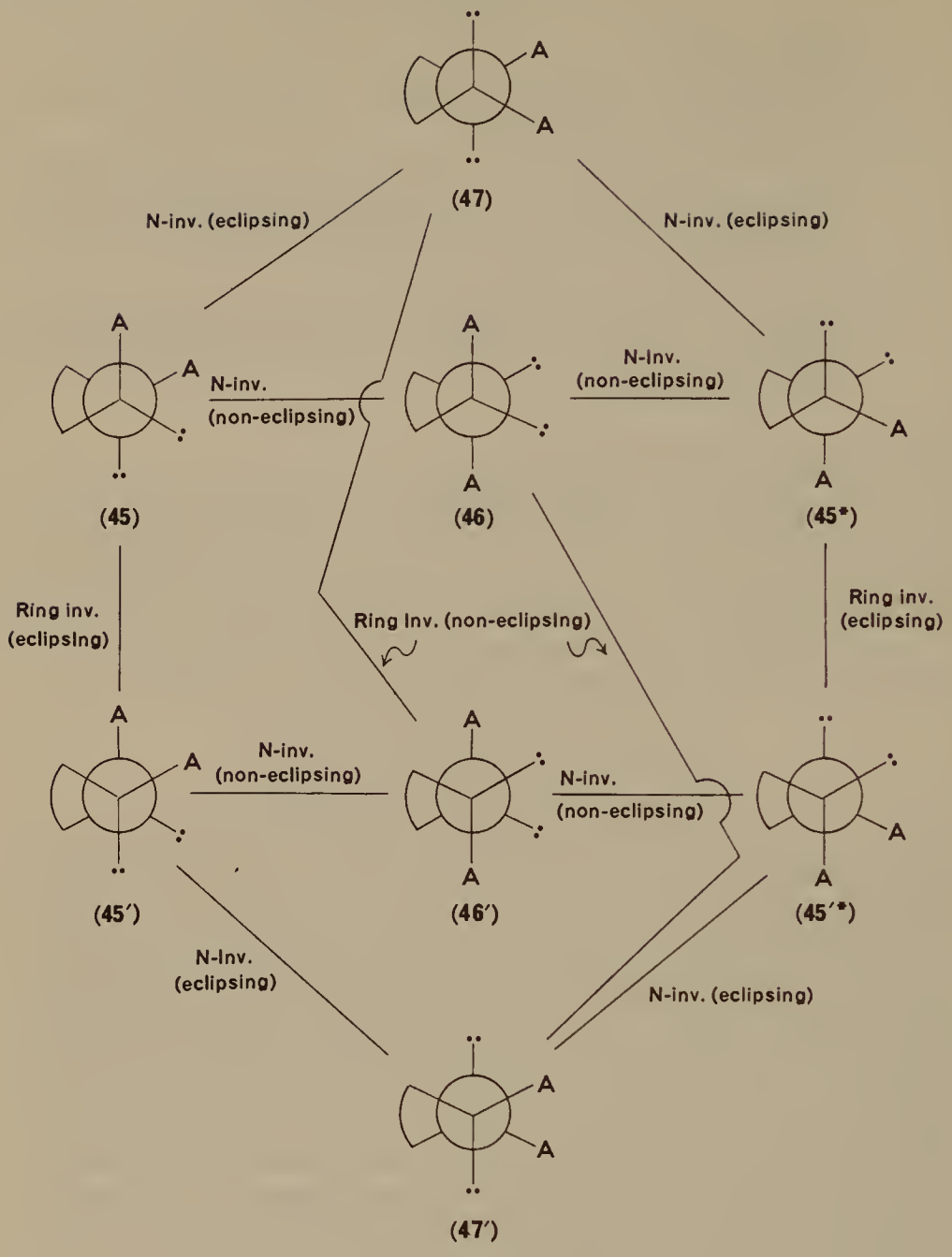
The restricted conformational freedom in cyclic and bridged bicyclic hydrazines somewhat simplifies the situation, although conflicting interpretations of experimental results have appeared in the literature. The general conformational equilibrium in terms of Newman Projections of *N,N*-disubstituted cyclic hydrazines is presented in Scheme 6 (A = alkyl group). A symmetry classification of the conformers is as follows:

45 + **45′**: C_1 symmetry (enantiomers)
46 + **46′**: C_2 symmetry (enantiomers)
47 + **47′**: C_2 symmetry (enantiomers)

The total equilibrium system consists of a *cis* and two *trans* conformations, all being chiral.

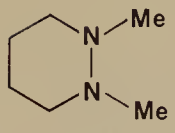
The degenerate transformations **45** $\rightleftharpoons$ **46** $\rightleftharpoons$ **45*** and **45′** $\rightleftharpoons$ **46′** $\rightleftharpoons$ **45′*** take place by non-eclipsing inversions of the N atom in each step, while the paths **45** $\rightleftharpoons$ **47** $\rightleftharpoons$ **45*** and **45′** $\rightleftharpoons$ **47′** $\rightleftharpoons$ **45′*** involve eclipsing of the two A groups in each of the N-inversion steps. The ring inversion in a cyclic hydrazine is accompanied by rotation about the N—N bond, but to a limited extent, depending on the ring size. **45** $\rightleftharpoons$ **45′** involves eclipsing of both the A groups and the lone pairs and can be considered of high energy, while ring inversion which transforms **47** $\rightleftharpoons$ **46′** and **46** $\rightleftharpoons$ **47′** is of the non-eclipsing type and is therefore of lower energy. Of course each ring inversion is also accompanied by eclipsing of the ring carbons, however, this may be considered as an inherent property of the cyclic system. This general description is based on the conformational principles advanced by Jones, Katritzky and co-workers[59, 60].

* The asterisk stands for a degenerate transformation.

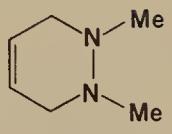


SCHEME 6

The conformational problem of the pyridazine derivatives **48** and **49** has been investigated by several groups[62, 59, 60, 35a]. Upon varying the temperature Anderson[62] has found the following n.m.r. spectral behaviour:



(48)



(49)

NMe:	singlet (room temp)	singlet (−70 to −150°C)	singlet (room temp)	singlet (−44°C)	2 × singlets (−111·5°C)
NCH_2:	multiplet (room temp)	AB q. (−70 to −150°C)	broad singlet (room temp)	AB q. (−44°C)	2 × AB q. (−111.5°C)

The above two compounds have the same symmetry properties. In terms of the general scheme (6), in the *cis* conformer (**45** + **45**′) which has no symmetry elements, all structurally equivalent groups and protons are diastereotopic and consequently **45** + **45**′ should exhibit two chemically shifted quartets (CH_2N) and two singlets (N**Me**). The *trans* conformers (**46** + **46**′) and (47 + 47′) which have a C_2 axis should each exhibit a singlet (N**Me**) and a quartet (CH_2N). This situation should prevail in the absence of any of the conformational processes, and also provided that all the diastereomerically related conformers are detectable by n.m.r.

Let us now examine the spectral consequences when the system is in a dynamic state. In relation to scheme 6, the N—**Me** groups of **48** and **49** become equivalent either by direct racemization **45** ⇌ **45**′ (eclipsing ring inv.) or by degenerate transformations such as **45** ⇌ **46** ⇌ **45*** (non-eclipsing N-inv.) and **45** ⇌ **47** ⇌ **45*** (eclipsing N-inv.).

Concerning **49**, the observation of two N**Me** singlets of *equal* intensities implies that the spectrally observed E_{min} conformation is the *cis* **45** (Scheme 6), as was suggested by Anderson[62]. Fortuitous equal concentration of the two *trans* conformers is quite improbable. The consequences of the interconversions of the various conformers of **49** which are described in Scheme 6 are presented in Table 7. The observation of two N**Me** singlets in the lowest temperature spectrum of **49** requires that the rates of all relevant conformational processes are slow at that temperature (−111·5°C). In order to explain the changes in the spectrum of **49** (between −111·5 and −44°C) we need a process which will render the N**Me** and NCH_2 groups equivalent but not the protons of the latter. It is evident from Table 7 that three such pathways, 1, 2 and 3 are compatible with the above requirements. Path 1 (Table 7) can be rejected on the ground of the high barrier, associated with the eclipsing ring inversion. Path 2 (2 × non-eclipsing N inv.), rather than Path 3 (2 × eclipsing N inv.), becomes therefore the most logical rate

TABLE 7. Summary of conformational interconversions of 1,2-dimethyl-1,2,3,6-tetrahydropyridazine (**49**) (Scheme 6)

Path No.	Sequence of interconversion	Mode of interconversion	Type of interconversion	Topomerization			N.m.r. signals
				Me groups	CH_2N groups	CH_2N protons	
1	**45** ⇌ **45′**	Eclipsing ring inv.	Racemization	+	+	−	Singlet + ABq
2	**45** ⇌ **46** ⇌ **45***	2 × non-eclipsing N-inv.	Degenerate	+	+	−	Singlet + ABq
3	**45** ⇌ **47** ⇌ **45***	2 × eclipsing N-inv.	Degenerate	+	+	−	Singlet + ABq
4	**45** ⇌ **46** ⇌ **47′** ⇌ **45′**	Non-eclipsing N-inv. Non eclipsing ring inv. Eclipsing N-inv.	Racemization	+	+	+	2 × singlets
5	**45** ⇌ **45′** ⇌ **46′** ⇌ **45′**	Eclipsing ring inv. 2 × non-eclipsing N-inv.	Racemization	+	+	+	2 × singlets

process to be associated with the averaging out of the NMe and CH_2N signals of **49**. The barrier found for this process (8·2 kcal/mol)[62] falls in the range of 6·8–8·2 kcal/mol which was previously assigned to this mode of N-inversion. Since the barrier to ring inversion in cyclohexene (5·3 kcal/mol) can be roughly related to that of the non-eclipsing ring inversion, i.e. **46** $\rightleftharpoons$ **47′**, it must be concluded that the above equilibration does take place at the coalescence temperature of the two NMe singlets of **49**. It does not affect the spectral pattern and the interconversion **47′** $\rightarrow$ **45′** is barred on the grounds of the previous argument. In agreement with previous suggestions, the inclusion of the hydrazo function in a ring (medium size) does not appreciably affect the nitrogen inversion rate (non-eclipsing).

The slower conformational rate process of **49** which requires the topomerization of the CH_2N protons can be described by paths 4 and 5 (Table 7), (It should be noted that ring inversion by itself is not sufficient for the topomerization of CH_2N protons; two N inversions are also required). The non-eclipsing N inversion in paths 4 and 5 must be considered to be fast at the temperature of the slow rate process. From simple considerations, the eclipsing N-inversion **47′** $\rightleftharpoons$ **45′** and the non-eclipsing ring inversion **46** $\rightleftharpoons$ **47′** must be considerably faster than the inversion of the ring (**45** $\rightleftharpoons$ **45′**) in which eclipsing interactions of both Me groups and lone pairs are generated. Consequently path 4 is the one which can be assigned to the transformation ABq $\rightarrow$ singlet in the n.m.r. spectrum of **49**. From previous arguments it is clear that the RDS in path 4 is the eclipsing N-inversion (**47′** $\rightleftharpoons$ **45′**) rather than the non-eclipsing ring inversion (**46** $\rightleftharpoons$ **47′**), and therefore the barrier must be assigned to the former process. The spectral interpretations of Anderson[62] differ from the above inasmuch as the low and high energy processes were assigned to ring and nitrogen inversion processes respectively. It is noted that although ring inversion of the non-eclipsing type most probably occurs both at low and high temperatures, in neither of them is it the rate-determining step.

Granting that the barrier of 12·3 kcal/mol found[62] for **49** can now be related to an eclipsing N-inversion, it constitutes the first definite experimental value for such a process.

It should be recalled that in the previously discussed acyclic hydrazines (**42**)–(**44**), the barrier (10·7–11·2 kcal/mol) could have been identified either with eclipsing N-inversion or low 'energy' rotation. Although the present value (12·3 kcal/mol) is in the proximity of the above range there is as yet no way of ascertaining whether the spectrally observed process in (**42**)–(**44**) is eclipsing N-inversion or 'low energy' rotation.

The spectral behaviour of the hexahydropyridazine derivative **48** differs from that of **49** in that only a single kinetic process was observed by d.n.m.r.

down to −150°C. To account for the failure to observe the two N—**Me** signals, Anderson[62] has argued that the diequatorial conformation (**47** + **47′**; Scheme 6) of **48** is the spectrally observed E_{min} species. The equilibrium **47** ⇌ **47′** was said[62] to occur by two N-inversions and a ring inversion via the diaxial conformers **46** and **46′**, undetectable due to their low concentration, thus accounting for the N**Me** singlet. Consequently, no conclusion could be drawn as to the nature of the spectrally observed process. The change in the conformational stability in going from **49** to **48** seems peculiar and it was in this connection that Jones, Katritzky and co-workers[59,60] re-investigated the conformational problem of the hexa and tetrahydro pyridazines and consequently introduced the new approach to the conformational analysis of hydrazines.

Dipole moment measurements and calculations on **48** and **49** have indicated that all the conformers are appreciably populated[59,60]. But, while in **49** the axial equatorial conformer (**45** + **45′**; Scheme 6) predominates, in **48** it is the diaxial conformer (**46** + **46′**; Scheme 6) which predominates in the equilibrium mixture. When considering **49** these results are in accord with the n.m.r. spectra and the conformational assignment made by Anderson[62]. However Anderson's assignment of the diequatorial (**47** + **47′**) as the E_{min} conformation of **48** (the spectrally observed one) conflicts with the dipole moment results[59,60]. The diaxial (**46** + **46′**) and the diequatorial (**47** + **47′**) conformers of **48** should exhibit identical n.m.r. patterns.

The p.e.s. of **48**[35a] shows three peaks which result from overlap of two pairs, indicating a substantial population of at least two different conformers with *trans* and *gauche* lone pairs*. From intensity considerations it was concluded that the latter predominates. Since both **45** and **46** (Scheme 6) possess *gauche* lone pairs, these results alone cannot allow for the differentiation between the axial–equatorial conformer (**45**) and the diaxial (**46**). However, when coupled with the n.m.r. results, which indicate a single signal for the N**Me** group of **48**, it must be concluded that indeed it is the *trans*-diaxial **46** which predominates and is the E_{min} conformation of **48**. Since both dipole moment measurements and p.e.s. results indicate a multi-conformational equilibrium system of **48**, a complex low temperature n.m.r. spectrum is anticipated. While one singlet for the N**Me** groups of **48** at −70°C has been observed by Anderson[62] in dichlorodifluoromethane, two singlets in a ratio of ca. 7:1 were recorded by Jones *et al.*[60] below −73°C in d_4-methanol. These were assigned to the two *trans* racemates (**46** + **46′**) and (**47** + **47′**) which exist in concentrations of 62 and 18 % respectively and

* The p.e.s. of **49** has not been determined.

leave the undetected *cis* conformer (**45** + **45′**) as 20% (from dipole moment considerations).

Referring to Scheme 6, the observation of the two NMe singlets implies that interconversion between the two *trans* conformers **47** and **46′** (**46** and **47′**) of **48** has been slowed down below −73°C. One can discern the following three pathways by which the two diastereomeric racemates may equilibrate:

(i) **47** ⇌ **46′** (non-eclipsing ring inv.)
(ii) **47** ⇌ **45** ⇌ **45′** ⇌ **46′** (eclipsing N-inv. + eclipsing ring inv. + non-eclipsing N-inv.)
(iii) **47** ⇌ **45** ⇌ **46**. (eclipsing N-inv. + non-eclipsing N-inv.).

(Spectrum-wise the equilibrations of **47** with **46** or **46′**, are identical).

We now have to decide which of the three pathways is the fastest one. One may immediately reject pathway (ii) since it involves a 'high energy' eclipsing ring inversion. The selection between pathways (i) and (iii) must also be in agreement with the experimental fact that although the a,e conformation (**45** + **45′**) of **48** is present in concentrations comparable to that of the *trans* (**47** + **47′**), its NMe signals have not been detected[60]. This implies that below −70°C it is in fast equilibrium with the *trans* conformer(s). Unfortunately, both pathways (i) and (iii) are in accord with this requirement (non-eclipsing N-inversion) and therefore an *experimental* distinction between the two is impossible.

The authors[60] have selected the direct non-eclipsing ring inversion (pathway i) as the process responsible for the equilibrium of the two *trans* conformers ($\Delta G^* = 11 \pm 1$ kcal/mol)*. It follows then that fast non-eclipsing N-inversion of **46** and **46′** is responsible for the required equilibration between the undetected *cis* conformation and the *trans* systems. The barrier value for an eclipsing N inversion (path iii) must be ⩾11 kcal/mol. The authors' conclusion was based on the argument that in the rigid bicyclic system (**22**), where eclipsing N inversion is the only conformational process possible, higher barrier values of 12–14 kcal/mol were encountered. This may also be in agreement with the barrier values of 12·3 kcal/mol which was assigned to the eclipsing N-inversion in (**49**). In our opinion the rather small differences between the barrier values of different compounds do not justify a rigorous identification of the actual process. If, however, it is the non-eclipsing ring inversion which is the spectrally measured process, it is interesting to note that the barrier value is very similar to that of the ring inversion of *cyclohexane*.

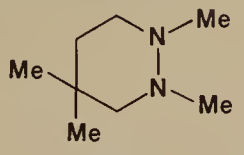
* There actually should exist two different barriers, for the forward and the reverse transformations.

It still remains to comment on the conformational stability of the two systems (**48**) and (**49**). From the n.m.r. data of **48** at −73°C the population ratio (**46** + **46′**):(**45** + **45′**):(**47** + **47′**) = 0·62:0·20:0·18[60]. The predominance of the diaxial conformers of **48** is striking and at variance with the accepted conformational concepts in cyclohexane. This was rationalized[60] in terms of the inter-orbital angle and the known, remarkably small, conformational free energy of N—Me (*N*-methylpiperidine) which is 0·65 kcal/mol[32], as compared to 1·8 kcal/mol in methylcyclohexane. Conformations **46** and **47** (of **48**) differ by three *gauche* butane (NMe) interactions. Consequently **46** is destabilized with respect to **47** by ca. 1 kcal/mol due to non-bonded interactions. To offset this value and therefore to account for the stability of **46** over **47** one must invoke the electronic energy due to the different interorbital angles in the above two conformers. Since, from Figure 1, $E_{60°} \cong E_{180°}$ it must be concluded that the interorbital angle in **46** is greater than 60°. Actually the low conformational free energy of N—Me piperidine is interpreted as a result of distortion of the N—Me away from the ring[32]. When applied to the diaxial **46** this would increase the magnitude of the diorbital angle toward 90°[60]. When the conformational stability of **45** (of **48**) was considered, it was argued[60] that similar distortion of the axial N—Me group away from the ring is unlikely since it would decrease the interorbital angle and also augment the non-bonded interaction between the two NMe groups.

The change in the conformational stability in going from **48** to **49** has been interpreted[60] in terms of a change in the non-bonded interactions due to the introduction of the ring double bond. Thus, the removal of the 1,3 axial–axial interaction in conformation (**46**) of compound (**49**) should hardly affect its geometry, since splaying the Me groups further apart will decrease the interorbital angle below 90° (or 60°). However, when the *gauche* conformation **45** is considered, the removal of axial–axial 1,3 interactions may now allow an increase in the dihedral angle between the two N—Me groups, which is also accompanied by an increase in the orbital angle towards 90°.

These results and analyses emphasize the different concepts associated with the conformational thermodynamics of carbocyclic and cyclic hydrazo systems.

It is of interest to enquire as to what extent ring substitution affects the conformational equilibrium of the hexahydropyridazine systems. The conformational equilibrium of 1,2,4,4-tetramethylhexahydropyridazine (**50**) has been studied by Jones, Katritzky and co-workers[59,60], and the total equilibrium system is presented in Scheme 7. It can be readily seen that conformers **53**, **54**, **58** and **59** generate 1,3-Me/Me-diaxial interactions



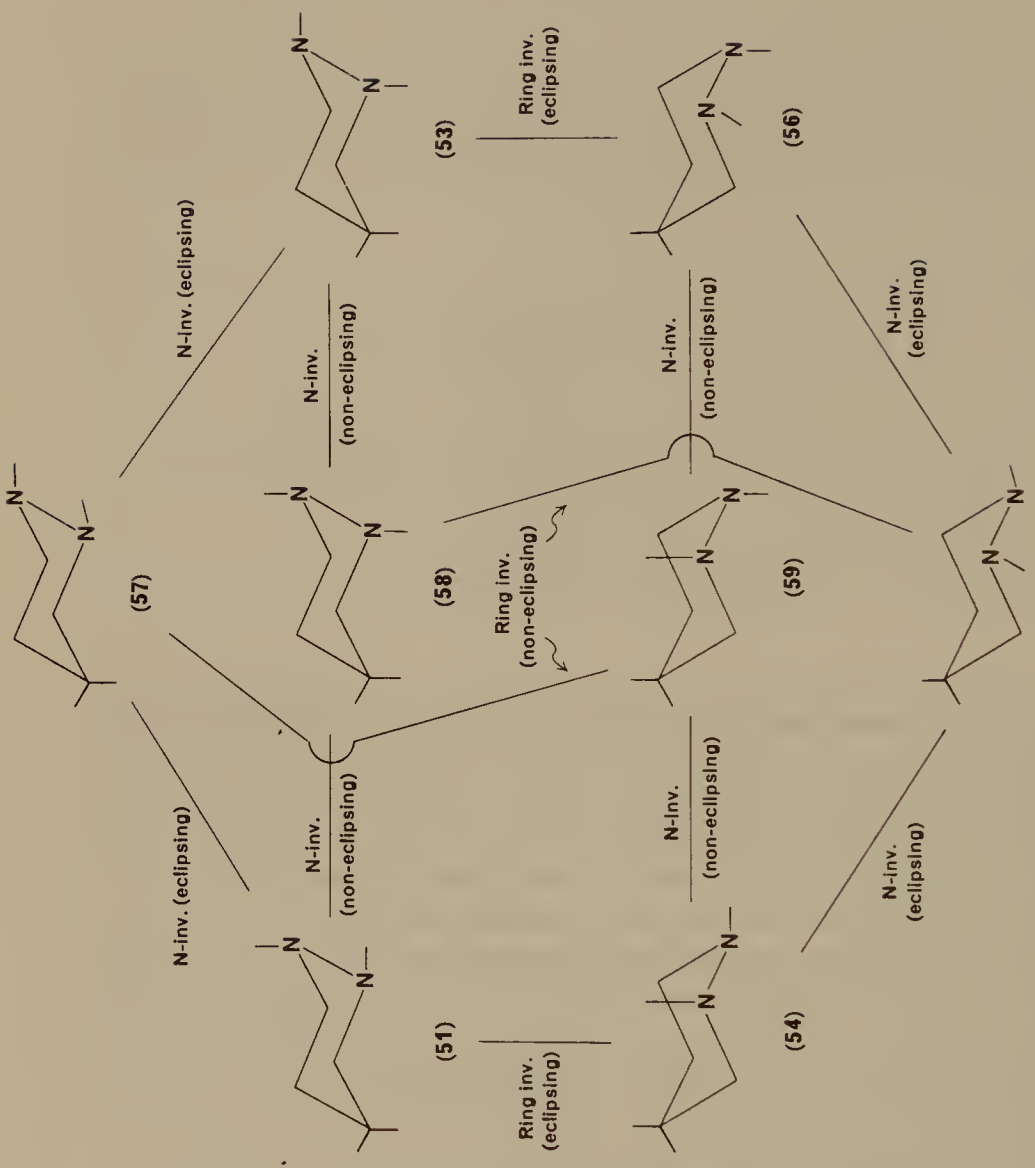
(50)

and are therefore assumed to be negligibly populated. This is also supported by dipole moment measurements and calculations[59,60]. The following n.m.r. spectral observations of **50** were made [59,60]:

	Temperature		
	Ambient	−45°C	−50°C
NCH_3	doublet (1:1)	doublet (1:1)	2 × doublets (2·7:1)
CCH_3	singlet	doublet (1:1)	
ΔG^* (kcal/mol)		11·5	ca. 10

Two kinetic processes were observed. When ignoring the high energy species, the observable ones are the axial–equatorial (**51** + **56**) and diequatorial (**57** + **60**) racemates. From the unequal intensity of the two NMe doublets below −50°C it follows that the observed conformers at this temperature are indeed the above two racemates, with the diequatorial one predominating, $K_{298} = (\mathbf{57} + \mathbf{60})/(\mathbf{51} + \mathbf{56}) = 1{\cdot}8$ (calculated assuming $\Delta S^\circ = 0$)[59,60]. The assignment of the peaks was made on the basis of the relative chemical shifts. These thermodynamic results were found to be in very good agreement with the dipole moment data. Thus, as in the unsubstituted system **48**, the a,e and the e,e conformers are of roughly comparable energy, while the a,a one has now been excluded from the equilibrium mixture.

It is interesting to examine the possible pathways which could account for the d.n.m.r. results of **50**. Topomerization of the C—Me groups can occur only by a process which involves ring inversion. Therefore, the observation of a C—Me doublet at −45°C indicates that those ring inversion processes which are accompanied by racemization, have been slowed down at that temperature. The observation of only one C—Me doublet and one NMe doublet requires that at −45°C diastereomeric exchange between the


(57)
N-inv. (eclipsing)
N-inv. (eclipsing)
N-inv. (non-eclipsing)
(53)
Ring inv. (eclipsing)
(56)
N-inv. (non-eclipsing)
N-inv. (eclipsing)
(58)
Ring inv. (non-eclipsing)
(59)
(60)
N-inv. (non-eclipsing)
N-inv. (non-eclipsing)
N-inv. (eclipsing)
(51)
Ring inv. (eclipsing)
(54)

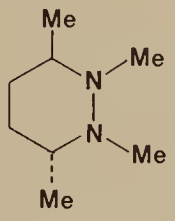
SCHEME 7

axial–equatorial and diequatorial conformers is still fast. The following two possibilities are compatible with the above requirements:

(a) Fast diastereomeric exchange by eclipsing N-inversion, i.e. **51** ⇌ **57** and **56** ⇌ **60**, when the non-eclipsing ring inversion **57** ⇌ **59** and **58** ⇌ **60** is slow.
(b) Eclipsing inversion **51** ⇌ **57** and **56** ⇌ **60** is slow, allowing for fast diastereomeric exchange **51** ⇌ **58** ⇌ **60** and **56** ⇌ **59** ⇌ **57** (since **57** and **60** are enantiomeric the spectral consequences of the exchange of either one of them, with **51** and **56**, are identical).

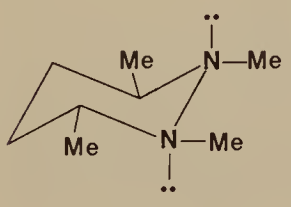
Jones, Katritzky and co-workers[60] have assigned the spectral changes at −45°C (ΔG^* = 11·5 kcal/mol) to the eclipsing N inversion, and the spectral changes at −50°C (ΔG^* = 10 kcal/mol) to the non-eclipsing ring inversion. However, experimentally, it is impossible to distinguish between the two possibilities.

The system of *trans*-1,2,3,6-tetramethylhexahydropyridazine (**61**) has been examined by n.m.r. and p.e.s.[35a]. The p.e.s. indicates a negligible



(61)

concentration of the diequatorial conformer (**62**) implying that either **63**



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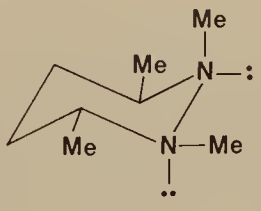
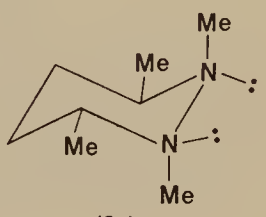


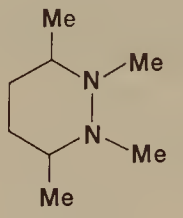
(63)



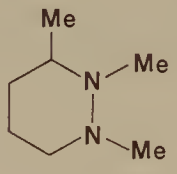
(64)

and/or **64**, both with *gauche* lone pairs, are the predominating conformer(s). The low temperature (−120°C) n.m.r. spectrum of **61** shows only two equal intensity N**Me** singlets, which is consistent with the a,e conformer **63**[35a] (all conformers with two axial C—Me groups are assumed not to be detectable by n.m.r.). Unlike the two previous systems, the transformations

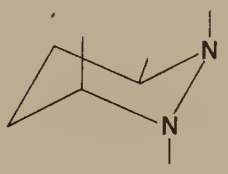
viz. **45** ⇌ **46** ⇌ **45*** (Scheme 6) are now associated with eclipsing interactions of the NMe and CMe groups. Similarly, the interconversion *viz.* **46** ⇌ **47′** (Scheme 6) is associated with two eclipsing interactions of the NMe and CMe groups of **61**. In light of the previous data on barriers it must be assumed that at −120°C all the conformational processes in **61** are slow on the n.m.r. time scale. In accordance with the conformational behaviour of the unsubstituted system **48**, it is the diaxial **64** which is expected to be the most stable one (in both cases the *trans* diaxial conformer possesses one extra *gauche* interaction in comparison to the a,e one). This apparent discrepancy can be explained in terms of the previously mentioned principles. Thus, while a distortion of the N—Me groups away from the ring in the *trans* a,a conformer of **48** is accompanied by stabilization (smaller 1,3 nonbonded interactions and a larger diorbital angle) a similar distortion in the *trans* conformer (**64**) is bound to decrease the dihedral angles between the NMe and CMe groups.



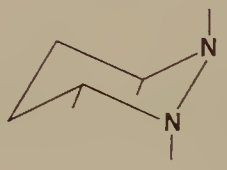
(65)



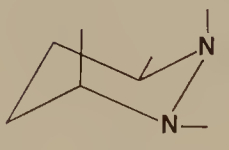
(70)



(66)



(67)



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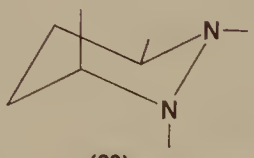
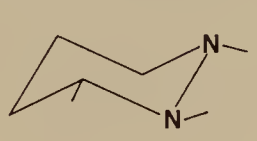


(69)

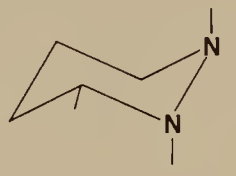
The p.e.s. of the *cis* isomer **65** does not exhibit peaks of significant intensities which could be assigned to the e,e conformer, i.e. lone pairs in *trans*-diaxial disposition[35a]. We are therefore left with conformers (**66**)–(**69**), all carrying *gauche* lone pairs, and therefore compatible with the p.e.s.

results. Since the molecule lacks any symmetry, the observation of two **NMe** singlets in the n.m.r. spectrum of **65** is of no help in selecting the E_{min} conformation. The most logical candidate, selected by the author[35a] is **69**, being the only one which is free of 1,3-diaxial Me—Me interactions.

The p.e.s. of the 3-methyl substituted derivative (**70**) indicates two pairs of ionization potentials in the ratio of 0·2:1, while the low temperature n.m.r. spectrum exhibited two sets of doublets for the CH*CH*$_3$ group in the ratio of 0·44:1 ($CDCl_3$) and 0·11:1(CF_3Cl)[35a]. From the magnitude of the peak separation in the p.e.s. it was concluded that the diequatorial conformer (**71**) (trans lone pairs) is still the minor component, although it is populated to an appreciably larger extent than in **65** and **61** where it does not exceed 4%. Since the present molecule also lacks any symmetry it is only possible to assign the low intensity peak in the n.m.r. spectrum of **70** to the di-equatorial conformation (**71**), while the major peak is assignable to any of the three conformers (**72**)–(**74**) (*gauche* lone pairs).



(71)



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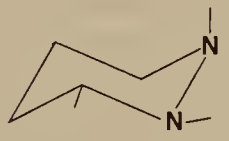
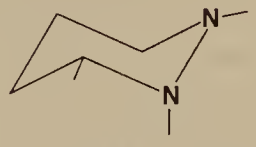
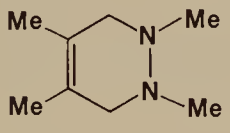


(73)



(74)

Compounds (**75**)[62,60], (**76**), (**77**)[63] all have a double bond in common in the 4 position. Their n.m.r. spectral behaviour is similar to the parent system **49**, and therefore the thermodynamic and kinetic properties must also be analogous to those of **49**, which have already been discussed.



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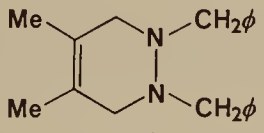
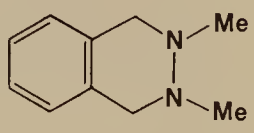


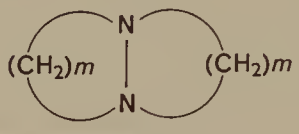
(76)



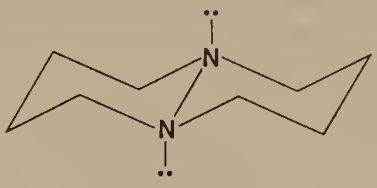
(77)

ΔG^* (kcal/mol):	12·3 (–14.5°C)		
	8.2 (–111.5°C)	11.5 (–37°C)	12.0 (–27°C)

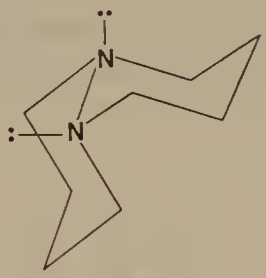
The bicyclic fused hydrazines of the general structure (**78**) constitute another conformationally interesting system. The diaza decalin (**78a**) can exist in the *trans* (**79**) and *cis* (**80**) conformations with *trans* and *gauche* lone pairs respectively. We shall first discuss the relative stabilities of the two. In the p.e.s.[35a] and n.m.r. spectra[64], a single conformer could be detected and it was unequivocally identified as the *trans* (**79**)*. This may imply that



(78a) $m = 4$



(79)

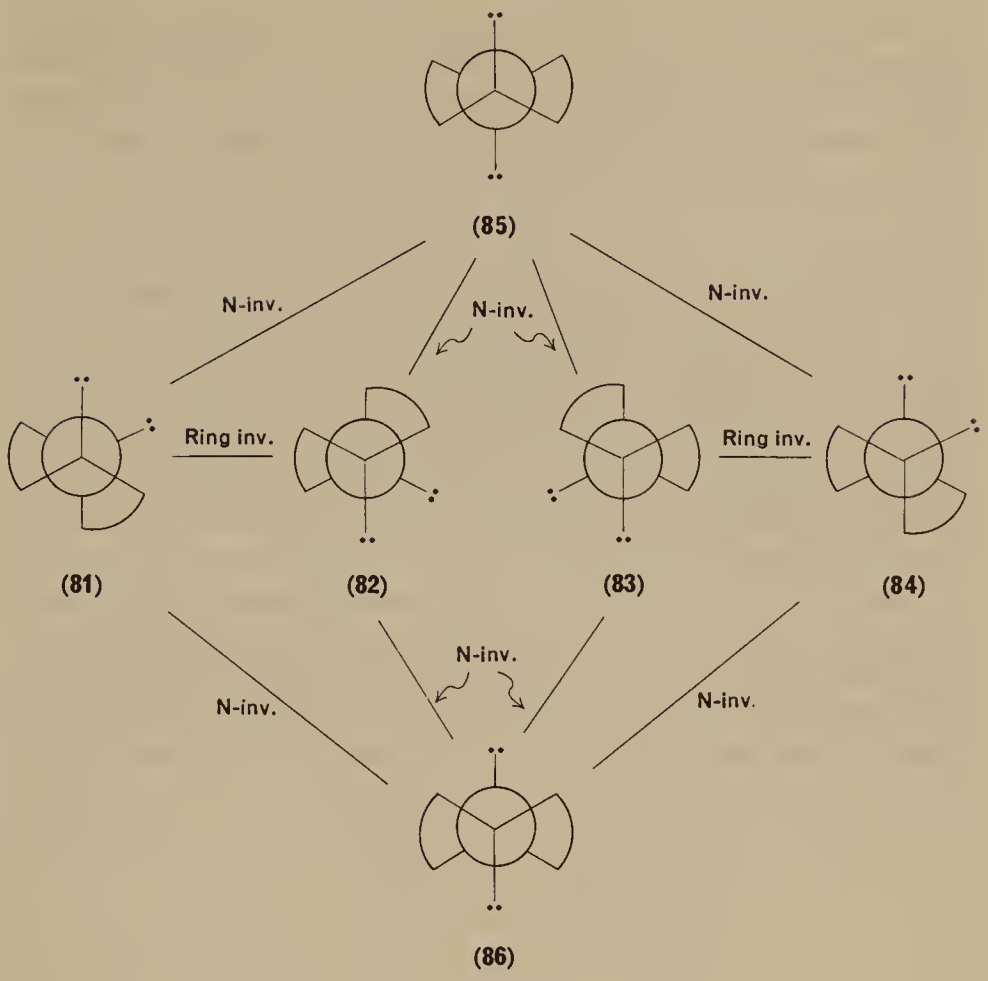


(80)

the difference in the energy of the lone pairs of **79** and **80** does not exceed ca. 2·7 kcal/mol, this being the enthalpy difference of *trans* and *cis* decalin[33].

The general conformational equilibrium of **78** is presented in Scheme 8. When the two rings of **78** are equivalent, then the *trans* conformation is achiral and **85** = **86** (Scheme 8). The *cis* conformation (C_2) is chiral, **81** and **82** are enantiomers while **81** = **83** and **82** = **84** (Scheme 8). The degenerate interconversion of the *trans* conformer may occur by the appropriate double N inversion, *viz.* **85** ⇌ **81** ⇌ **86**. All N inversions are accompanied by eclipsing of the ring methylenes. Racemization of the *cis* conformer may take place either by two N inversions *viz.* **81** ⇌ **85** ⇌ **84**, or by a decalin-type ring inversion *viz.* **81** ⇌ **84** (**81** ⇌ **82**). The latter process corresponds to a torsion (120°) about the N—N bond with concomitant eclipsing of the methylenes and the lone pairs. Since, as previously mentioned the E_{min} conformation of **78a** has the *trans* configuration[35a,64], the observed topomerization of the CH_2N protons (AB quartet → singlet) most probably

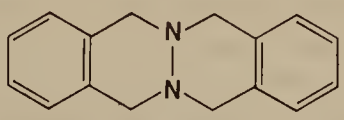
* Compound **78a** exhibits the largest ionization potential splitting of the lone pairs ($\Delta = 2{\cdot}45$ e.v.).



SCHEME 8

occurs via two consecutive N inversions*, where the low thermal stability of the intervening *cis* conformer excludes its detection by n.m.r.

The low temperature spectrum (−53°C) of the tetracyclic hydrazine (**87**) exhibits two equal intensity, rather than one AB quartet[63], which is compatible with *cis* (**81** + **82**) (Scheme 8) as the E_{min} conformation. Although

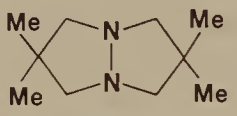


(87)

* No barrier value was reported by the authors[64].

in variance with the previously discussed system **78a**, this observation is consistent with the data and conclusions drawn for the cyclic hydrazines, (**49**), (**75**)–(**77**), all of which are unsaturated at the 4 position (with respect to the hydrazo system). The two AB quartets of **87** coalesce directly to a singlet ($\Delta G^* \cong 12{\cdot}4$ kcal/mol). Ring inversion *viz.* **81** $\rightleftharpoons$ **82** is accompanied by topomerization of only the CH_2N groups and not the protons, and would therefore lead to a single AB quartet for all eight CH_2N protons of **87**. The topomerization of the protons requires two N inversions *viz.* **81** $\rightleftharpoons$ **85** $\rightleftharpoons$ **82** which must be the spectrally observed process. The implication is that the *cis* decalin-type ring inversion has a barrier higher than the observed 12·4 kcal/mol. From the recent C^{13} d.n.m.r. study, the barrier to ring inversion in *cis* decalin has been determined as 12·6 kcal/mol[65]. Surely the eclipsing of the lone pairs in the transition state of the rings inversion in *cis* **87** generates more energy than that of the two H atoms in the analogous transition state of *cis* decalin. Consequently it is logical to anticipate that the barrier value for this type of process in *cis* **87** should exceed 12·6 kcal/mol, which was indeed borne out by the experiment.

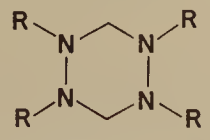
The low temperature n.m.r. spectrum of the 1,5-diazabicyclo[3.3.0]nonane system (**88**), exhibits a single AB quartet for the ring methylenes and a doublet for the Me groups at low temperature[66, 64]. This can only be



(**88**)

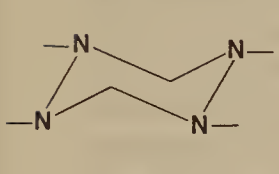
compatible with a *cis* conformation. *cis*-Bicyclo[3.3.0]octane is more stable than the *trans* isomer by 6 kcal/mol (ΔH)[33]. Apparently this difference in the stability is sufficient to overcome the eclipsing interaction of the two lone pairs in the *cis* conformation of **88**. It has been pointed out that some distortion can partially relieve this interaction, and from the magnitude of the splitting in the p.e.s. of **88** a diorbital angle of 10–30° has been estimated[35a]. The n.m.r. spectral changes ($\Delta G^*_{-55^\circ} = 12$ kcal/mol) were assigned to two consecutive N-inversions *viz.* **81** $\rightleftharpoons$ **86** $\rightleftharpoons$ **84** (Scheme 8)[66], which constitute a degenerate interconversion.

In hexahydrotetrazine (**89**), one of the questions is whether the two hydrazo moieties interact with each other or behave independently. Of the many conformations possible for 1,2,4,5-tetramethylhexahydrotetrazine (**89a**), only four (**90**–**93**) lack the 1,3 interaction of the NMe groups and should therefore be considered as the only ones which may be appreciably

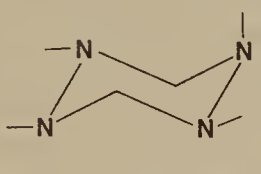


(89a) R = Me
(89b) R = Et

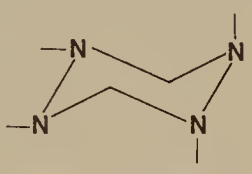
populated. Their n.m.r. spectral patterns are listed below. Anderson and Roberts[67] have recorded two singlets for the **Me** and $\mathbf{CH_2}$ groups of **89a** at ambient temperature; a 1:1 doublet (**NMe**) and an AB quartet ($\mathbf{CH_2}$N) were observed at −87°C (ΔG^* = 11·7 kcal/mol). Thus, of the four conformations only **92** and **93** have the proper symmetries compatible with the low temperature n.m.r. observation. The authors[67] have selected **93** as the spectrally observed E_{min} conformation on the grounds of identical interactions



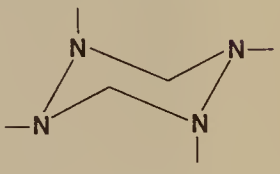
(90)



(91)



(92)



(93)

	Centrosymmetric	Asymmetric	Asymmetric	Centrosymmetric
Me Signals	1	4	2	2
CH_2N (ABq)	1	2	1	1

between the members of each pair of vicinal NMe groups. This assignment was challenged by Jones, Katritzky and Richards[68] who have chosen conformation **92**, for the reason that it possesses one *gauche* butane (NMe) and one *gauche* lone pair interaction less than **93**. Surprisingly, the authors[68] have assigned a destabilizing effect (0·9 kcal/mol) to the extra *gauche* lone pair interaction in **93** with respect to **92***. Overlooking this point, the authors have concluded that **92** is more stable than **93** by 1·2 kcal/mol and therefore it is the spectrally observed conformation (>95%).

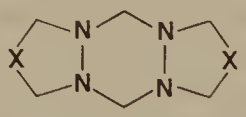
More convincing perhaps is the dipole moment argument[68]. The centrosymmetric conformation **93**, selected by Anderson and Roberts[67], lacks a dipole moment, while for **89a**, Jones and co-workers[68] have measured a value of 1·45 D vs. a calculated 1·31 D for conformation **92**. Although the

* It has already been pointed out that the $E_{60°} \cong E_{180°}$ (Figure 1).

above evidence seems to be quite conclusive, Nelsen and Hintz[64] have reopened the controversy by supporting (**93**). Apparently, while the tetramethyl derivative **89a** was found by n.m.r. to be conformationally homogeneous, in cyclopropane[67] and in chloroform[64], the tetraethyl derivative **89b**, examined[64] exhibited two AB quartets (CH_2N) in the ratio 15:85. Thus, it was argued that the appearance of the new conformer in **89b** can be rationalized only on steric grounds, i.e. Me/Me vs. Et/Et non-bonded interactions in **89a** and **89b** respectively. The conformation of the minor component of **89b** was said to be equivalent to that of **89a** on the basis of the similar $\Delta\nu_{AB}$ values (0·49 and 0·64 p.p.m. respectively) while $\Delta\nu_{AB}$ for the major component of **89b** was found to be 1·70 p.p.m., strikingly different from the above two values. Thus, the major component (the only observed one) of **89a** has decreased by 85% in going to **89b**. This can be rationalized only if **89a** exists in conformation **93**, and steric interactions in **89b** shift the equilibrium towards the sterically more stable **92**. Thus we are again left with conflicting results and arguments. Nelsen[64] has challenged the dipole moment results of Jones[68] on grounds of the chemical instability of the tetrazine system, which may have led to erroneous dipole moment results.

It should be noted that if, for some reason, the E_{min} geometry of **89a** is a twist boat rather than the assumed chair conformation, then the above controversy could be resolved. Consideration of the properties of the boat conformation of **93** reveals that while on one hand the methyls retain their original symmetry relationships, on the other hand such a conformation should possess a finite dipole moment since it is not centrosymmetric anymore.

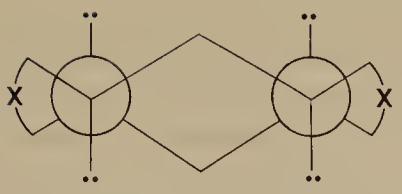
Nelsen[64] has further investigated the conformational problem of the tricyclic tetrazine system (**94**)*. Upon cooling **94a** and **94b** each exhibits,



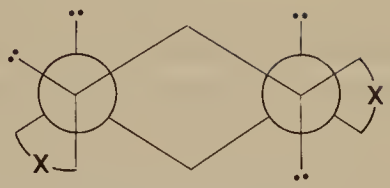
(94a) X = CH_2
(94b) X = CH_2CH_2
(94c) X = CH=CH

in the n.m.r. spectrum, a single AB quartet for the NCH_2N protons. From symmetry analysis (the centre ring must be a twisted boat) it was concluded that the spectrally observed conformations of the above two compounds are the ones depicted in **95**. The n.m.r. spectrum of the unsaturated system

* No activation or rate data have been presented[64].

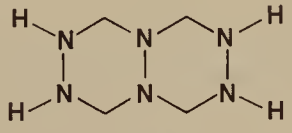


(95a) X = CH_2
(95b) X = CH_2CH_2



(96) X = CH=CH

94c exhibits two AB quartets, on the basis of which conformation **96** was deduced. It was again noted that the two AB quartets have strikingly different chemical shift separations $\Delta\nu_{AB} = 1{\cdot}53$ and 0·38 p.p.m. This effect was correlated with the geometry of the protons with respect to the lone pairs and is believed to arise from a through-space rather than a through-bond effect. As in the diazadecalin (**78a**), the two pairs of the adjacent non-bonding electrons in **94a** and **94b** are in the *trans* configuration. It is interesting that the *trans–syn–trans* configuration of perhydroanthracene, which corresponds to **95** is also the most stable one[33]. The *trans* arrangement of the two lone pairs and the two 1,3-diaxial interactions of the N lone pairs ('rabbit ear effect'[69]) in **95** are not sufficient to overcome the intrinsic stability of the perhydroanthracene-like system in which all the equatorial bonds radiate from the central ring. However as pointed out by Nelsen[64], the conformational balance must be delicate and conformation **96** (for **94c**) represents 'a compromise between destabilizing steric and electronic effects'. Indeed as has been previously demonstrated, unsaturation in the ring stabilizes the *cis* configuration of a cyclic hydrazo system.

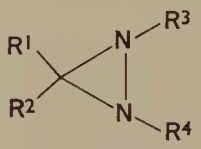


(96a)

Kintzinger and co-workers[66] have found that **96a** at 31°(D_2O) exhibits a single AB pattern for all the CH_2N protons. As previously argued this must be compatible with a *trans* conformation of type **85** (Scheme 8). The above spectral pattern coalesced to a singlet at 58° ($\Delta G^* = 16{\cdot}6$ kcal/mol) which corresponds to the degenerate interconversion of type **85** ⇌ **81** ⇌ **86** (Scheme 8). It would be of interest to compare this activation parameter with that of the *trans* diazadecalin **79** for which however no activation data have been reported[64]. Nevertheless the above barrier value is high when compared to the previously mentioned barriers for N inversion in bicyclic

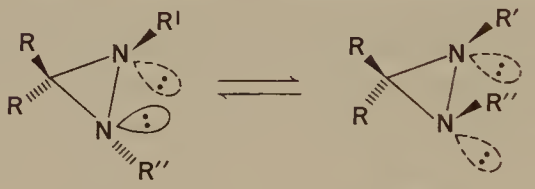
and tetracyclic hydrazines. This may perhaps be ascribed to the fact that the d.n.m.r. spectra of **96a** were measured in a water solution. Alternatively, it may be attributed to the torsion about the two outer N—N bonds, which accompanies the inversion of the N atoms at the juncture.

Mannschreck and co-workers[70,71] have examined the n.m.r. spectra of the diaziridine system (**97**). Obviously, the only conformational process



(97a) $R^1 = R^2 = H$; $R^3 = R^4 = Me$
(97b) $R^1 = R^2 = H$; $R^3 = R^4 = Et$
(97c) $R^1 = R^2 = H$; $R^3 = R^4 = i\text{-}Pr$
(97d) $R^1 = R^2 = H$; $R^3 = H$; $R^4 = t\text{-}Bu$
(97e) $R^1 = R^2 = Me$; $R^2 = H$; $R^4 = i\text{-}Pr$
(97f) $R^1 = R^4 = Me$; $R^2 = R^3 = CH_2Ph$
(97g) $R^1 = R^4 = Me$; $R^2 = CH_2Ph$; $R^3 = H$

which may affect the signals of the R groups is nitrogen inversion. The



(98) **(99)**

observation of one signal for the ring protons of **97a–97c** must imply that the E_{min} configuration about the N—N bond is *trans* (**98**) which places the diorbital angle $180° > \phi > 120°$. In the light of the eclipsing interactions of both the R groups and the two lone pairs, the instability of the *cis* (**99**) is obvious. The methylene protons of the ethyl group in **97b** and the methyls of the isopropyl groups in **97c** were found to be diastereotopic at all temperatures, and even fast equilibration **98** $\rightleftharpoons$ **99** is not expected to render these groups equivalent. Only a simultaneous double inversion of the two N atoms produces the proper symmetry for topomerization of these groups, and it is quite inconceivable that such a process could occur in this ring-strained system. Both **97d** and **97e** have the proper symmetry for detection of the N inversion process **98** $\rightleftharpoons$ **99**. In both compounds the ring substituents (H and Me) exhibit chemically shifted signals at ambient and high temperatures. Thus N inversion in diaziridine is very slow and the barrier value

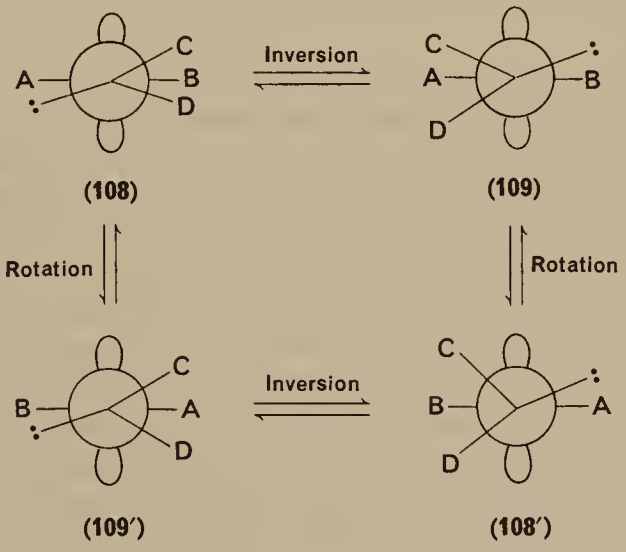
was estimated as >23 kcal/mol[70]. The barriers of **97f** and **97g** were determined by epimerization kinetics[71] ($\Delta G^*_{70°} = 27{\cdot}3$ and $27{\cdot}1$ kcal/mol respectively). Their high magnitude makes it actually possible to isolate the diastereomeric invertomers.

The barrier for N-inversion in *N*-methylaziridine in 19·2 kcal/mol (Table 3), and is substantially lower than that of the diaziridine system. If ring strain is already included in the N-inversion barrier of aziridine, then the excess of activation energy required for the N inversion in the diaziridine must be due to factors which are inherent in the hydrazo moiety of the latter system. This perhaps can be rationalized by assuming that the geometry of the transition state of N-inversion in diaziridine is similar to that of the product, namely the *cis* isomer, where an appreciable lone pair eclipsing interaction is being generated.

From i.r., Raman[74] and p.e.[35b] spectroscopies Rademacher has concluded that the E_{min} conformation of 1,1′-biaziridine is centro-symmetric ($\phi = 180°$), while that of 1,1-bipiperidine possesses a dihedral angle of 77°. In our opinion the difference in the conformational stabilities of the above two systems cannot be ascribed to non-bonded interactions.

III. PYRAMIDAL–PLANAR HYDRAZINES

Mesomerically electron withdrawing groups substituted on one of the N atoms of a hydrazine system are anticipated, as in amines, to deform the pyramidal configuration of the N atoms towards a planar one, due to



SCHEME 9

conjugation of the lone pair with the adjacent π system. Since most of the conformational studies have been carried out by n.m.r., we can safely assume that when an N atom of a hydrazine is bonded to π-electron-withdrawing groups, regardless of whether this N atom is truly planar, the rate of its inversion is too fast for detection by n.m.r. Actually, strong conjugation is required in order to render the N atom completely sp^2 planar[73].

In Table 8 the activation data for this class of hydrazines as determined by d.n.m.r. are collected.

TABLE 8. Pyramidal–planar hydrazines—activation data

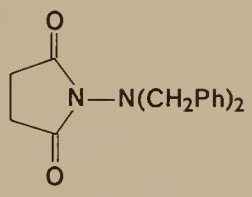
No.	Compound	ΔG^* (T) kcal/mol[a]	Reference
100	$(PhCH_2)_2NNH$(2,4-dinitrophenyl)	16·6 (59°C)	4
101	$(PhCH_2)_2NNH$(2,4,6-trinitrophenyl)	16·4 (50°C)	4
102	$(PhCH_2)_2NNHCOCH_3$(E)	15·5 (39°C)	4
		16·9 (50°C)	74
103	$(PhCH_2)_2NNHCOCH(CH_3)_2$($E$)	17·1 (68°C)	74
104	$(PhCH_2)_2NNHCOPh$	Singlet −60°C	4
105	$(PhCH_2)_2NNHCHO$	Two singlets −59°C	74
106	$(PhCH_2)_2NHNCOBu$-t	Singlet	74
107	$(i\text{-}Pr)_2NNHCHO$	Two singlets	75

[a] Aside from **107** all ΔG^* values were determined from the signals of the *N*-benzyl protons.

The symmetry properties of this general system give rise to a pair of racemates (**108** + **108′**) and (**109** + **109′**) (Scheme 9). It is logical to assume that the E_{min} conformation of this class of hydrazines is characterized by an orthogonal relationship between the lone pair orbitals. Racemization may occur by a combination of rotation and inversion. As was pointed out by Dewar and Jennings[4] and by Walter and Reubke[74], rotation in such a system necessarily involves eclipsing of the two lone pairs which, in bipyramidal hydrazines is known to raise the barrier substantially. According to Scheme 9, N inversion is free of eclipsing interactions of the substituents, and the two lone pair orbitals may retain a 90° angle during this process. It is assumed that the magnitude of this barrier should be similar to that of the non-eclipsing inversion of the N atoms in acyclic bipyramidal hydrazines (7–8 kcal/mol). Compounds **100–103** (Table 8) exhibit for the $PhCH_2$ protons a singlet at ambient temperature and an AB quartet at low tem-

perature. The symmetry of these systems modifies Scheme 9 to the extent that C = D and then **108** = **108′** and **109** = **109′** while **108** and **109** are diastereomerically related. The benzyl groups are rendered equivalent by the σ plane, while topomerization of the PhCH_2 protons requires a degenerate interconversion such as **108** $\rightleftharpoons$ **108′** via a combination of rotation and inversion. Regardless of whether **108** or **109** represents the E_{min} conformation, in view of the previous argument, the rate determining step must be the rotation about the N—N bond, and therefore this is the process observed by d.n.m.r. It is clear that the barriers measured are strikingly higher than those observed in the bipyramidal hydrazines.

A convincing proof that indeed the rotational process is the RDS has been presented by Dewar and Jennings[4]. Compound **110** did not exhibit the



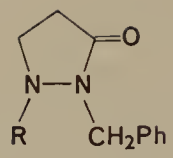
(110)

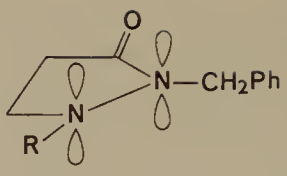
splitting of the benzyl protons even below −130°C. Only when the rate of inversion of the pyramidal N atom is high, would the rotational process, regardless of its barrier, produce no spectral changes, as is indeed the case.

Thus, while in the schemes proposed for the various conformational processes of bipyramidal hydrazines the barrier for rotation which involves eclipsing of the two lone pairs in the transition state could never be observed, in the case of pyramidal–planar hydrazines this barrier can be measured. Kinetically, this is the fundamental difference between the two structurally different hydrazine types.

It would be of interest to calculate the torsional potential function of this type of hydrazine which in principle would most probably have a minimum at 90° and two equal energy maxima at 0 and 180°.

The inversion of the pyramidal N atom in a pyramidal–planar hydrazine can possibly be observed in special ring structures where rotation about the N—N bond is impossible. Thus, Elguero and co-workers[76] have examined the d.n.m.r. spectra of **111**. Only slow N inversion can render the benzyl protons diastereotopic (ABq). The magnitudes of the barriers are quite similar to those found for the eclipsing N inversion in the bipyramidal hydrazines. This is somewhat surprising, since the inversional transition state (**112**) also generates a *cis* lone pair–lone pair interaction.





(112)

(111a) R = CH_2Ph; $\Delta G^* = 11{\cdot}7$ kcal/mol
(111b) R = CH_3; $\Delta G^* = 10{\cdot}7$ kcal/mol

In connection with acyl hydrazines, several groups[75, 74, 4] have also observed the isomerization about the N—CO bond, which is in fact analogous with the well-known phenomenon in amides. The configurations of the isomers were identified on the basis of the argument that the proportion of the *Z* isomer increases upon increasing the steric bulk of *R*[75, 74]. Most interesting, however, is the fact that all three authors have observed that only the *E* isomer exhibits an AB quartet for the benzyl protons, while the *Z* isomer gives rise to a singlet even at −60°C. This must indicate that rotation about the N—N bond in the *Z* isomers of acyl hydrazines is much

Z isomer *E* isomer

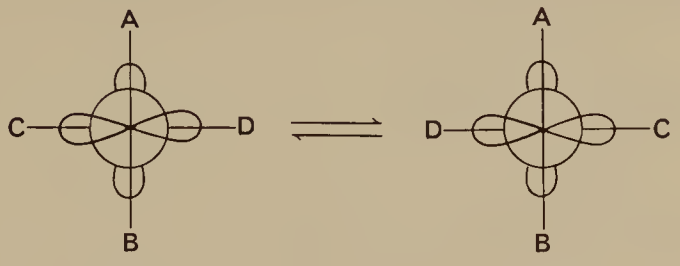
faster than in the corresponding *E* isomers. The singlet observed for the benzyl groups of **104** and **106** (Table 8) is due to the presence of only the more stable *Z* isomer, for which rotation (N—N) is fast. The two singlets observed in the cases **105** and **107** imply that in formyl hydrazines rotation about the N—N bond is fast in both the *E* and *Z* isomers. The experimental results appear to indicate that these phenomena arise from steric interactions which are more severe in the *E* than in the *Z* isomer. The magnitude of this steric acceleration of the rotation about the N—N bond is striking and according to Table 8 may even amount to 6–7 kcal/mol. It must be concluded that rotation about the said bond in pyramidal–planar hydrazines is extremely sensitive to the steric bulk of the substituents.

Although Anthoni and co-workers[75] have attributed the non-equivalence of the isopropyl methyl groups in various acyl and thioacyl hydrazines to N inversion, this seems unlikely in view of the previous arguments.

IV. BIPLANAR HYDRAZINES

Near planarity of both N atoms of hydrazine is most probably achieved when each of these atoms carries at least one mesomerically electron-withdrawing group. Thus, inversion rotation dichotomy is now eliminated and the only process which may possibly be detected by n.m.r. is rotation about the N—N bond (excluding slow rotation about N—CO bonds).

For a biplanar hydrazine with four different substituents, and assuming that for steric and electronic reasons the E_{min} conformation is orthogonal,



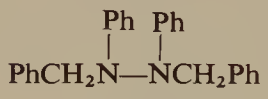
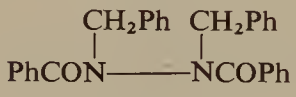
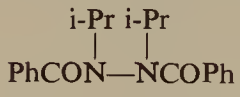
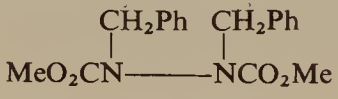
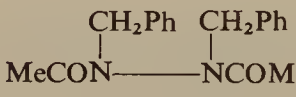
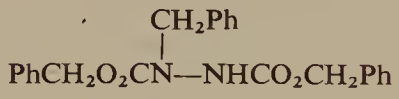
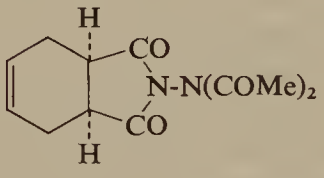
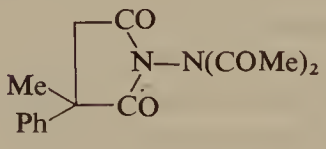
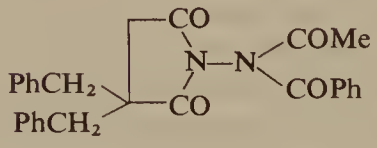
(113) **(113′)**

the conformational scheme amounts to two interconverting enantiomers **113** and **113′**. The interconversion process must involve rotation about the N—N bond with eclipsing of both groups and the lone pairs in the transition state. It should be noted that unlike in the pyramidal–planar hydrazine system, rotation about the N—N bond of **113** generates simultaneous eclipsing of two groups and two electron pairs. This fact, coupled with the closer proximity of the groups and lone pairs on the two N atoms, generates, very high rotational barriers (Table 9).

The symmetries of the systems in Table 9 allow for the detection of chirality when present, and the rotation, **113** $\rightleftharpoons$ **113′**, is accompanied by topomerization of the prochiral protons. In some of the systems the picture is complicated by amide-type isomerism which, however, does not affect the chirality of the molecules. Therefore, the topomerization of the prochiral protons in the biplanar hydrazines can be unambiguously identified with the torsional process about the N—N bond. Since this process is considerably slower than the rotation about the N—CO bond, it could in most cases be studied without interference from the other. Moriarty and co-workers have also invoked a slow conformational change about the O—CO bond of the carbamate moieties[77] but this was rejected by other workers[78,79].

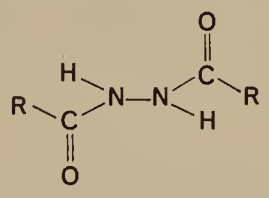
Apart from **1·1** and **119** the experimental rotational barriers (Table 9) are about 5–6 kcal/mol higher than those of the pyramidal–planar hydrazines (Table 8). The relatively low barrier value recorded for **114** can be

TABLE 9. Biplanar hydrazines—activation data.

No.	Compound	ΔG^* (T) (kcal/mol)	Reference
114		14·2 (13°C)	80
115		19·6 (117°C)	37
116		23·5 (147°C)	37
117		23·5 (192°C)	81
118		23·4 (188°C)	81
119		13·2 (4°C)	81
120		20–21 (120°C)	82
121		23	83
122		~20	83

interpreted on the basis of the higher degree of pyramidality of the N atoms of this compound due to steric interference with the effective π resonance. The still lower barrier of **119** could be taken as a measure of the sensitivity of the torsional process about the N—N bond to steric factors in the rotational transition state. It is not clear as to what extent the exchange of the relatively acidic N—H affects the process under consideration.

X-ray studies of *N,N'*-diformyl and *N,N'*-diacetyl hydrazine have yielded all-planar structures, depicted in **123**[84,85]. It is perhaps not surprising to find that each of the NCO_2R moieties is planar, but it is not obvious why the whole molecule is planar, although such an arrangement maximizes the electronic energy due to the eclipsing of the two lone pairs. Of course, the



(123a) R = H
(123b) R = Me

conformation of a molecule may be affected by crystal lattice forces. The authors[84,85] have argued that electron delocalization into the carbonyl groups, as reflected by the charge distribution and shorter N—C bond distance, are responsible for stabilizing the planar conformation. Although the diminution of electron population on the N atoms is expected to decrease the repulsive interaction between the lone pairs, these results are in apparent conflict with the data of Table 9. These data clearly indicate that the E_{min} conformation of similar molecules in solution are chiral and therefore cannot have a planar geometry such as **123**. A noteworthy structural feature of the above two hydrazines in the solid state is the strong intermolecular NH...O bonding (2·799 Å[84]), which, according to the author may amount to 6·1 kcal/mol. Perhaps the effectiveness of this bonding is related to the planar geometry.

An X-ray study of *N,N'*-bisuccinimidyl revealed an angle of 65° between the planes of the two rings[86]. Obviously, here, the configuration about the amide bond is rigid and the strong repulsion between the oxygen atoms also contributes to destabilization of a planar geometry.

An interesting controversy has developed around the conformational problem of di-carbamates of *cyclic* hydrazines of the type listed in Table 10. Phillips[87] was the first to report on the conformational behaviour of these compounds. The F^{19} n.m.r. spectrum of the diazetidine derivative (**124**)

TABLE 10. Cyclic biplanar hydrazines—activation data

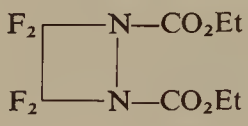
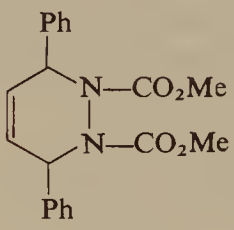
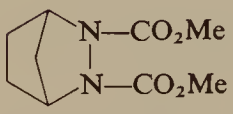
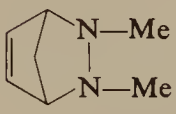
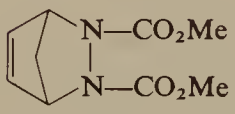
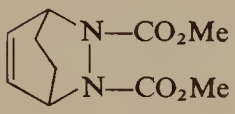
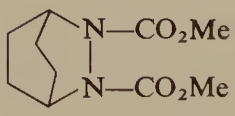
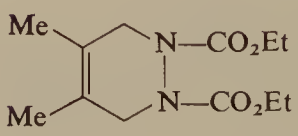
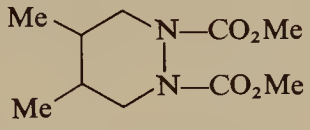
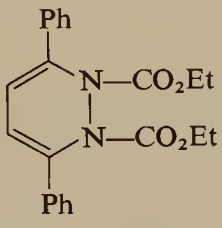
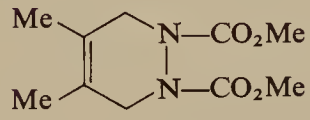
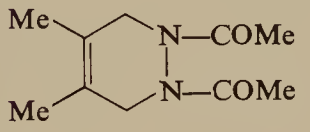
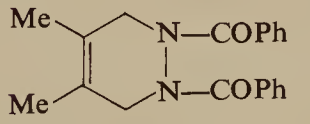
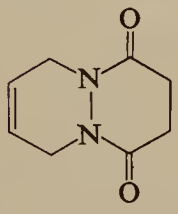
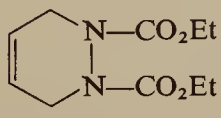
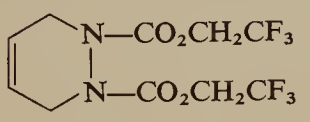
Compd No.	Structure	ΔG^* (T) (kcal/mol)	Reference
124		8·0 (E_a)	87
125		14·8 (−3°C) N—CO_2Me rot. 18·9 (97°C) ring inv.	88, 78
126		14·8 (−7°C)	57
22		16·0 (−11°C)	57
127		13·7 (−5°C)	89
128		16·4 (27·5°C)	89
129		19 (30°C)	89
130		19·7 (123°C)	90

TABLE 10 (*cont.*)

Compd No.	Structure	ΔG^* (T) (kcal/mol)	Reference
131		19·4 (74°C)	90
132		23	90
133		20·7 (138°C) 14·7 (−7·5°C)	78
134		>21·4 (160°C)	78
135		14·9 (8°C)	78
136		<10·4 (−60°C)	78
137		20 (25°C) 15·7[a] 14·3[a]	79
138		20 (25°C) 16[a] 16·5[a]	79

[a] Calculated by computer simulated d.n.m.r. spectra.

exhibits a singlet at 23°C and a quartet at −50°C. Phillips interpreted this in terms of N inversion *viz.* **124a** ⇌ **124b**, which implies that the N atoms possess an appreciable degree of pyramidality. In fact the essence of the

(124a) **(124b)**

subsequent controversies is centred around the question of the geometry of the N atoms in the cyclic dicarbamates. As was pointed out by Price and co-workers[78] the above spectral observations are also compatible with interconversion of two non-planar diazacyclobutane rings in which the N atoms are trigonal–planar, the molecule is dissymmetric, and therefore the geminal F atoms are diastereotopic.

Three conformational processes, which may be detected by n.m.r. can take place in dicarbamates of mono-cyclic hydrazines.

(i) *Inversion of the N atoms.* When such an inversion is capable of being detected by n.m.r., it implies that the nitrogen atoms are essentially pyramidal. As was pointed out by Anderson and Lehn[89,90] such an implication is incompatible with general structural concepts which require essential planarity of the —N—CO_2R moiety, like in amides, where N inversion is too fast to be observed by n.m.r.

(ii) *Rotation about the N—CO_2R bonds.* If the N atoms are planar (or nearly so), π conjugation is anticipated to raise the torsional barrier for the above process.

(iii) *Ring inversion.* This is associated with torsion about the N–N bond, the magnitude of which depends on the ring size. If the N atoms are planar, the transition state generates an eclipsing interaction of the N substituents (CO_2R) and the two lone pairs, much as in the acyclic biplanar hydrazines. Should this process be operative, the magnitude of the experimental barriers would also resemble those of the acyclic biplanar hydrazines (Table 8) rather than those of ring inversion of the corresponding carbocyclic systems.

On purely spectroscopic grounds one cannot decide whether the observed kinetic process in **124** (Table 10) is N inversion, as was originally suggested[87], or ring inversion. However, from the subsequent argument it seems most probable that the latter process is operative. The magnitude of the barrier is far smaller than those recorded for the acyclic members (Table 9). However this is not necessarily evidence in support of N inversion. If one recalls that

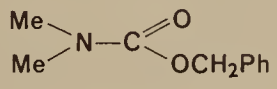
the *acyclic* biplanar hydrazine can adopt an orthogonal conformation (**113**), while the degree of puckering of the strained ring system **124** must be very small, then the small barrier in the latter can be rationalized on the ground of the small torsional angle which is required to reach the planar transition state of **124**. This is equivalent to saying that with respect to non-bonded interactions of groups and lone pairs, the ground state of **124** is high.

The first intensive study of the conformational properties of dicarbamates of cyclic hydrazines was initiated by Breliere and Lehn[88] who have reported that the ambient n.m.r. spectrum of **125** (Table 10) exhibits two unequal height (but equal area) signals for the OMe groups, which coalesce to a singlet at higher temperatures, and give rise to three OMe singlets at lower temperatures. The authors[88] have assigned the spectral changes in the low temperature region to hindered rotation about the N—CO_2Me bond ($\Delta G^* = 14{\cdot}8$ kcal/mol) and those at high temperature to ring inversion, thus implying that the N atoms are planar. Although the magnitude of the barrier of the latter process (18·9 kcal/mol) resembles that recorded for torsion about the N—N bond in the acyclic biplanar hydrazines (Table 9), two consecutive N inversions could not be excluded on purely spectroscopic grounds, since identical n.m.r. spectral changes are anticipated for both of these processes.

The above interpretation was challenged by Bushweller[91] who claimed different intensities (and areas) for the two OMe signals of **125** below 97°C and consequently assigned the high temperature process to torsion about the N—CO_2Me bond. The low temperature process was ascribed to ring inversion, which was said to be energetically more compatible with cyclohexene behaviour.

Daniels and Roseman[92] have carefully checked the disputed intensities ratio and have concluded that the areas under the OMe signals of **125** are indeed equivalent within the integration error, thus supporting the original interpretation[88].

Korsch and Riggs[82] have investigated several substituted tetrahydropyridazines analogous to **125**, and have also encountered barriers in the range of 18–19 kcal/mol which they have assigned to ring inversion. Price, Smallman and Sutherland[93] have confirmed the equality of the integrated areas of the two OMe signals of **125**. Furthermore, the d.n.m.r. spectrum of the following carbamate has yielded $\Delta G^*_{-3^\circ} = 15{\cdot}9$ kcal/mol.



This barrier can safely be assigned to rotation about the $Me_2N—CO_2CH_2Ph$ bond, and being similar to that of **125** (14·8 kcal/mol) supports, according to the author[93] a similar process in the latter system.

Allred and co-workers[57] have studied the bicyclic carbamate **126** (Table 10) and discovered that at low temperature the signals of the bridgehead protons and OMe groups each split into two absorptions. The rigid nature of **126** excludes ring inversion and therefore rotation about the N—N bond is also impossible. The two kinetic processes which may account for the spectral observations are consecutive N inversions, which implies pyramidal N atoms, and rotation about the $N—CO_2Me$ bond which in light of the relatively high barrier (14·8 kcal/mol) requires essentially planar N atoms with effective π conjugation. On the grounds of angle strain the authors[57] have rejected the latter possibility. This conclusion was further justified on the grounds of the similarity of the barrier values of **126** and **22** (Table 10). It was argued that since in the latter, N inversion is necessarily the process which is being spectrally observed, the same also holds true for **126**.

Indirectly, this conclusion challenges the interpretation of Breliere and Lehn[88] as to the nature of the low temperature conformational process in the mono-cyclic hydrazine **125**. It is interesting that identical barriers have been recorded for **125** and **126** below 0°C (Table 10).

Anderson and Lehn[89,90] have answered most of the criticisms and cleared the ambiguities. The equality of the areas under the two OMe signals of **125** has been reaffirmed. Model bicyclic compounds of the 2.2.1 heptane as well as of the 2.2.2 octane types were studied. The authors[89] have argued that if one of the observed rate processes in **127** and **128** (Table 10), as well as in similar systems, is N inversion, it should (a) be present in *both* **127** and **128**, and (b) give rise to an exchange process between two sites of equal populations. The low temperature n.m.r. spectra of **127** and **128** exhibit three and four signals respectively for the OMe groups. The signals are of unequal areas. Consequently the low temperature processes in the above two compounds do not fulfil condition (b). The higher temperature spectrum (28°) of **127** exhibits a sharp singlet for the OMe groups while at that temperature the corresponding signal of **128** is a doublet. Thus, condition (a) is not being fulfilled with respect to the high temperature processes in these compounds. Consequently[89], neither the 'low' nor the 'high' temperature processes can be assigned to N inversion. Thus, the observed rate process below 0°C in both compounds (**127**, **128**) is ascribed to rotation about the $N—CO_2Me$ bond, and it was argued that the N atoms are essentially planar as in amides.

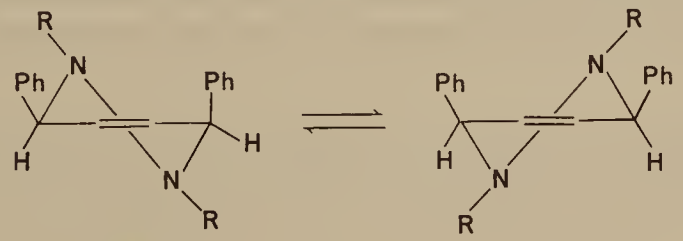
The high temperature process in 128 ($\Delta G^* = 16{\cdot}4$ kcal/mol) has been interpreted[89] in terms of 'ring flipping' *viz.* **128a** $\rightleftharpoons$ **128b**. This is possible

due to the partial conformational mobility of the bicyclo 2.2.2 octane (and octene) ring system, as compared to the rigid bicyclo-2.2.1-heptane structure.

(128a) **(128b)**

The n.m.r. spectrum below 30°C of the symmetrical structure **129** (Table 10) exhibits an ABX_3 pattern for the ethyl group. If one rejects the idea of the pyramidality of the N atoms, such an observation indicates molecular dissymmetry which is accounted for by a twisted conformation similar to **128a** and **128b**, and the process responsible for the topomerization of the diastereotopic protons is also 'ring flipping' of the type described above. With respect to the N—N bond this is a torsional process, associated with eclipsing of both the N substituents and lone pairs in the symmetrical transition state, thus accounting for the relatively high barrier values. In principle, this process is analogous to the ring inversion in **124** and **125** (Table 10). As was argued in the case of the diazetidine (**124**), the magnitude of the barrier is proportional to the angle of twist in the E_{min} conformation. This argument accounts for the diminished barrier of **128** and **129** with respect to the acyclic biplanar hydrazines (Table 9). It also provides for the difference between the barriers of **128** and **129**, since the latter system is less rigid than the former, thus allowing for a larger angle of twist (ca. 60°C) in the conformational ground state.

Returning now to the monocyclic system **125**, as well as to **130** and similar systems (Table 10), Anderson and Lehn[90], as well as others[78, 79], have argued that the E_{min} conformation of these compounds is of a cyclohexene-like half-chair geometry. Their argument is based on the correlation between the observed spin couplings of the various ring protons and the dihedral angle. The E_{min} geometry of **125** (and similar systems) is depicted by **125a** and its enantiomer **125b**. The chirality of the molecule could be inferred from the observation of an AB quartet for the ring methylene

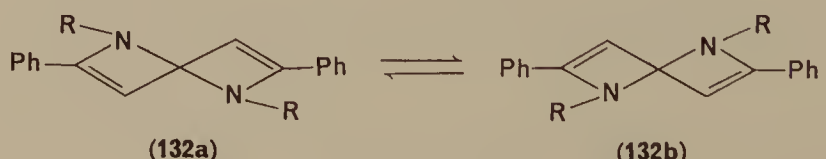


(125a) **(125b)**

protons of **130**. On the grounds of the similarity between the barrier values of **125** (14·8 kcal/mol) and those of **126** and **127** (14·8 and 13·7 kcal/mol respectively, Table 10) which were previously ascribed to rotation about the N—CO_2R bond, the authors[90] have also assigned the low temperature spectral changes in **125** as well as in **130** and **131** (and similar systems) to the above kinetic process, again implying planar N atoms. Various conformational arrangements originating from the restricted rotation about the N—CO_2R bond are possible, and a maximum of eight absorptions of the OMe groups of **125** are possible. The low temperature spectra of the mono-cyclic systems are quite complex. The smaller number of signals indicates that not all the conformers are significantly populated, and the authors[90] have not analysed this part of the spectrum in detail.

Ring inversion *viz.* **125a** ⇌ **125b** in the mono-cyclic system is now the only kinetic process which can be assigned to the spectral changes which take place at higher temperatures. The barrier values are in the range of 19–20 kcal/mol (**125**, **129**, **130**, **131**, **133**, **137**, **138**; Table 10) and approach those of the acyclic members (Table 8). The authors[90] are of the opinion that eclipsing of both the CO_2R and the lone pairs in the transition state as well as the negative entropy of activation (ca. −7 e.u.) contribute to these rather large barriers. In order to evaluate the relative importance of these factors it would be of interest to calculate the two-fold potential function of a biplanar hydrazine. The introduction of a biplanar hydrazine moiety into a cyclohexene system drastically modifies the kinetic conformational properties of the latter system. An approximately fourfold increase in the barrier to ring inversion has been recorded.

Even more interesting is the conformational behaviour of the dihydro pyridazine derivative **132** (Table 10) which at ambient temperature exhibits one ABX_3 n.m.r. pattern for the ethyl group. A barrier of ca. 23 kcal/mol has been calculated from the coalescence: $ABX_3 \rightarrow A_2X_3$[90]. These spectral observations clearly indicate that the E_{min} conformation of this molecule is chiral. The enantiomeric geometries **132a** and **132b** with planar carbamate moieties have been suggested by the authors. The spectrally observed changes were again assigned to ring inversion which is accompanied by topomerization of the prochiral ethyl protons. No precedent to such a high barrier can be found in the corresponding carbocyclic system. The additional



(132a) **(132b)**

eclipsing interactions of the CO_2Et and Ph groups in the inversional transition state of **132** have been invoked by the authors[90] in order to account for the increase in the barrier magnitude with respect to **125**.

Additional entries in this series have been studied (**133–136**; Table 10) as well as other similar systems. The ring methylene protons of **133–135** exhibit an AB quartet which in **133** and **135** coalesce to an A_2 system, and resist coalescence in **134**. These high temperature changes were also ascribed to ring inversion, in agreement with the original suggestion of Breliere and Lehn[88]. The low temperature process of **133**, detected by the non-equivalence of the OMe groups, was ascribed to rotation about the N—CO_2R bond assuming that the N atoms are trigonal–planar. However, a deformation towards a pyramidal configuration with little increase in energy was also considered by Price and co-workers[78]. Interesting is the high barrier of **134** (Table 10) which could perhaps be attributed to a higher 'degree of planarity' of the N atoms achieved by more effective π-type delocalization of the electrons onto the carbonyl groups of this compound. This could be taken as an indication that in the corresponding dicarbamates the N atoms are indeed somewhat deformed toward a pyramidal configuration.

According to the above authors[78] the severe non-bonding interactions of the N substituents in the planar transition state to ring inversion are responsible for the observed high barriers. Therefore, by replacing these non-bonded interactions by bonded ones as in **136** (Table 10), a lower barrier for ring inversion is expected. Indeed, the ring CH_2 protons of **136** exhibit a singlet in the n.m.r. spectrum down to –60°C. It should, however, be noted that such structural alterations also modify the ground state geometry. Specifically, the angle of twist of the unsaturated ring of **136** is estimated to be 10–20°, while that of the monocyclics (**133**)–(**135**) (Table 10) is close to 80°. This large difference may also account for the relatively low barrier to ring inversion of **136** as compared to the other monocyclic systems listed in Table 10.

The low barrier value of **135** (compared to **134**) is surprising, and similar to that of the N inversion in **22** (Table 10). One may argue that due to a less effective π conjugation of the lone pairs, the N atoms of **135** are appreciably pyramidal, therefore the rates of ring inversion and N inversion become similar.

Bittner and Gerig[79] recently discussed the detailed nature of the low temperature processes in the dicarbethoxy tetrahydropyridazine systems. In agreement with the previously discussed work, the above authors have assigned the high barriers ($\Delta G^* \cong 20$–22 kcal/mol) in **137**, **138** and in similar systems (Table 10), to ring inversion. The conclusions regarding

the low temperature process ($\Delta G^* = 14$–16 kcal/mol) are most interesting. From the low temperature H and F^{19}-n.m.r. spectra of **137** and **138** respectively (ethyl and trifluoroethyl resonances) and with the aid of computer simulated spectra, the authors have concluded that when ring inversion is slow, four distinguishable conformational forms are available for each of these compounds. Inasmuch as at −60°C the signals under consideration were of different intensities, the interchange among these conformational species is associated with several activation parameters. Two separate conformational equilibria, assuming planar carbamate moieties, (rotation about the N—CO_2R bond) and pyramidal N atoms (N inversion) were analysed and the relationship among the various barriers was found to disagree with those which were obtained from spectra simulation. Thus, neither rotation about the N—CO_2R bond nor possible inversion of the pyramidal N atoms can by itself account for the observed spectral changes at low temperatures[79]. The basic idea that led to the solution of this problem is the observation that the coalescence of the four signals of the ethyl groups in the spectra of **137** and **138** takes place in pairs, i.e. a coalescence of two sets of signals to one set of two signals which consequently, by raising the temperature, coalesce into a singlet. These observations were accommodated into a scheme of ten interchanging conformers with the following two important points:

(a) The N atoms are pyramidal to the extent that the CO_2R groups may be located in pseudoaxial and pseudoequatorial positions with respect to the ring.
(b) In spite of the above, the rotation about the N—CO_2R bond is sufficiently restricted as to give rise to barriers detectable on the n.m.r. time scale.

Analysis of this proposition reveals that N inversion or rotation about the N—CO_2R bond, each by itself, will average out the four-signal pattern into a two-signal system. An additional conformational motion, i.e. one of the above processes, will average out the remaining two singlets into a single line. Thus the total spectral changes are characterized by two distinct kinetic processes. Although the RDS could not be identified, the barrier values are very similar (Table 10).

The above analysis is based on certain assumptions regarding the chemical shifts. Accepting these assumptions, the tetrahydrapyridazines **137** and **138** and similar systems (Table 10) are characterized by N atoms which are not planar but are deformed toward pyramidality and possess an appreciable inversion barrier. This is at variance with other authors[78,89,90] who have assumed essentially planar carbamate moieties.

V. CONCLUSION

A distinct difference in the thermodynamic and kinetic conformational behaviour between hydrazo and carbon systems has emerged from experimental as well as theoretical results. The most important factor which governs the thermodynamic and kinetic conformational properties of hydrazines is associated with the two vicinal non-bonding orbitals. Energetically, this factor outweighs, in many cases, the energy associated with non-bonding interactions of atoms and groups within a hydrazine molecular framework. The *gauche* (90°) conformation is significantly stabilized with respect to other conformations. It is perplexing and not self-evident that the 180° *trans* disposition of the lone pairs in hydrazine is significantly destabilized with respect to the 90° *gauche* arrangement. When regarded as oriented dipoles, the lone pair orbitals should adopt the *trans* disposition and thus minimize their mutual repulsive interaction. This has been confirmed by recent calculations[12]. Consequently, there must exist another energy term(s) which outweighs that due to the repulsion between the lone pairs. While in the '*gauche* rule'[17] the conformational stability of hydrazine is treated in terms of attractive and repulsive torsional potential functions, in the RHP approach[12] the total conformational energy at a given dihedral angle is composed of the dipole–dipole interaction, $n \rightarrow \sigma$ donation and the usual three-fold torsional potential functions. The most important energetic factor which counterbalances the dipole–dipole interaction is the $n \rightarrow \sigma$ donation effect, which is based on the concept of bond separation energies[18]. In each of the above approaches different energy components are analysed. If the '*gauche* rule'[17] is taken as a rule of thumb without performing the detailed component analysis then it does not seem logical to compare its results with those of the analytical RHP approach[12]. Nevertheless, currently, the above two theoretical analyses are the only ones which attempt to explain on a quantitative basis, the various physical factors which may govern the conformational phenomena in hydrazines.

A point of interest is the low conformational free energy value of the NMe group, (0·65 kcal/mol), and presumably other *N*-alkyl groups, as determined in *N*-methylpiperidine[32]. It seems logical to apply the above value also to the N—Me group in the hydrazine system. Thus in conformational analysis of hydrazines the above energy term must be considered in conjunction with the general torsional potential function (Figure 1). The majority of results indicate that hydrazine and simple acyclic bipyramidal alkyl hydrazines tend to adopt a *gauche* conformation with respect to the two lone pairs. Such an arrangement may be perturbed by polar effects

(N_2F_4). After settling some of the controversies, a clear pattern emerges for bipyramidal cyclic hydrazines. Thus, while in those heterocyclics which contain a double bond in the 4 position, the N substituents tend to adopt a *cis* configuration; in the saturated ones, a *trans* diaxial configuration is found to be the most stable one. A similar situation prevails in the fused N—N bicyclics (unbridged), but the *trans* diequatorial (instead of diaxial) is now the preferred configuration in the simple saturated bicyclic systems. Ring substitution may perturb the above pattern.

N.m.r. is a superior and simple experimental method in conformational analysis, which can be applied to complex molecules where other types of spectroscopic methods frequently fail. In many cases conformational investigation by n.m.r. will yield both thermodynamic and kinetic information. Photoelectron spectroscopy emerges as a potent tool in conformational thermodynamic problems of hydrazines,[35a,b] and becomes especially powerful when used in conjunction with n.m.r.

The nature of the kinetic data presented justifies the division of the various hydrazo systems into three groups, depending on the approximate geometry of the two nitrogen atoms, i.e. bipyramidal, pyramidal–planar and biplanar. Both the analyses and the experimental barriers in these three groups are distinctly different. In general, when the N atoms of acyclic hydrazines deform toward a planar structure the torsional barrier seems to increase while the nitrogen inversional barrier decreases. As has been pointed out a theoretical calculation of the torsional potential barriers of pyramidal–planar and biplanar hydrazines would be welcome.

Finally, the new concepts which were recently introduced[59,60] concerning the conformational kinetics of hydrazines are illuminating, useful and clarify many ambiguities in this area. In this approach the rotation–inversion dichotomy was further divided into several kinetic paths available for each of the above processes. Every path is characterized by different eclipsing interactions associated with substituents and lone pairs. Analysis of the experimental results indicates that a hydrazine molecule is most probably capable of distinguishing among these paths and will follow the low energy one.

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Subject index

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