MECHANISTIC STUDIES INTO THE REACTIONS OF DIAZONIUM AND RELATED COMPOUNDS

by

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Thesis presented for the degree of

DOCTOR of PHILOSOPHY

University of Edinburgh

September 1974

TO MY PARENTS

Douglas William and Isabella Seaton McKenzie Murray

AND MY BROTHER

William Graeme Murray

I declare that this thesis is my own composition, that the work of which it is a record has been carried out by myself, and that it has not been submitted in any previous application for a Higher Degree.

The thesis describes results of research carried out in the Department of Chemistry, University of Edinburgh under the supervision of Professor J. I. G. Cadogan since the 1st October, 1971, the date of my admission as a research student.

The following is a statement of postgraduate courses attended during the last three years: Summer School in Mass Spectrometry, University of Sheffield, 26-30 March 1972; Recent Developments in the Theory of Concerted Processes, Dr. A. J. Bellamy (five lectures); Organometallic Processes in Organic Chemistry, Professor P. L. Pauson (five lectures); Industrial Research and Development, Dr. B. Gravenor (five lectures); E. U. Chemistry Department Seminars (twenty-five periods).

ACKNOWLEDGEMENTS

I should like to express my gratitude to Professor J. I. G. Cadogan for suggesting the topic of research and to Professor Cadogan and Dr. J. T. Sharp for their guidance and encouragement in all aspects of this work.

I would also like to record my thanks and appreciation to various other members of Edinburgh University Chemistry Department: to Dr. R. M. Paton for advice and assistance related to e. s. r. studies; to Mr. David Thomas for instruction in the operation of the MS-902 mass spectrometer; to Mr. Colin Baxter, Mr. Tom Naisby and Mr. Alan Anderson for invaluable technical assistance; and to Mrs. C. G. Ranken for her skill and patience in typing the manuscript.

Finally I would like to thank the Carnegie Trust for the generous award of a Studentship during the tenure of which this work was carried out.

ABSTRACT

Experiments using ^{15}N-labelled N-nitrosoacetanilide (NNA) and related compounds have shown that the complex reaction leading to benzyne and/or phenyl radicals does not involve the reversible extrusion of nitrogen. The contrasting observation that nitrogen exchange did occur in the formation of benzenediazonium ions by the *in situ* nitrosation of ^{15}N-labelled acetanilide is attributed to the generation of unlabelled benzenediazonium ions by the reaction of phenyl radicals with the nitrosating agent. The reaction of 4-chlorobenzoyl nitrite with 1-phenylazo-2-naphthol and related hydroxyazo compounds provides a new route to the benzenediazonium ions which can be trapped by azo coupling or allowed to decompose to phenyl radicals. It is suggested that the nitrosation of the hydrazone form of the hydroxyazo compound, followed by rearrangement, provides the primary source of the diazonium ions but that these are again regenerated in the system as a result of the reaction between phenyl radicals and nitrosating agent.

An investigation into the mechanism of formation of benzyne from N-nitrosoacetanilide and benzenediazonium acetate has been carried out. Reaction of 2,4,6-[$^{2}H_3$]N-nitrosoacetanilide, formed by *in situ* nitrosation of 2,4,6-[$^{2}H_3$]acetanilide (99% [$^{2}H_3$]) in the presence of tetraphenylcyclopentadienone (tetracyclone) and acetic acid in benzene, gave biphenyl, from which no deuterium had been lost and 1,2,3,4-tetraphenylnaphthalene which had lost one g atom of deuterium. Similar results were obtained from reaction of 2,4,6-[$^{2}H_3$]benzenediazonium fluoroborate (99% [$^{2}H_3$]) with potassium acetate in benzene. The corresponding reaction using anthracene as a benzyne trap gave identical results. These observations exclude the operation of a 'pre-equilibrium' type of E_1cb mechanism in the formation of benzyne from the benzenediazonium acetate ion-pair, but do not allow a distinction to be made between E_1cb (irreversible) or concerted E_2 mechanisms, particularly in view of the low (1.5-1.8) isotope effects observed with 2-[$^{2}H_1$]benzene-

diazonium salts.

The observation that 1, 1-diphenylethylene and a series of related alkenes act as promoters for the formation of benzyne from benzenediazonium acetate even in the presence of furan, which otherwise promotes the competing radical reaction, has led to an explanation of the dual role played by tetracyclone during the decomposition of N-nitrosoacetanilide and related compounds.

Preliminary reports on some aspects of the work mentioned above have been published:

"Conversion of 1-Phenylazo-2-naphthol into the Benzenediazonium Ion: Another Route to Phenyl Radicals," J. I. G. Cadogan, Charles D. Murray, John T. Sharp, Chem. Comm., 1973, 572.

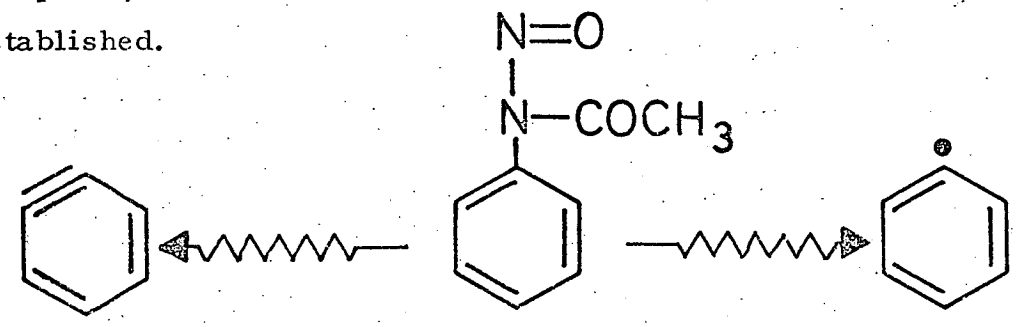
"The Role of [^{2}H]-Labelling in the Determination of the Mechanism of Formation of Benzyne from Benzenediazonium Acetate," J. I. G. Cadogan, Charles D. Murray, John T. Sharp, Chem. Comm., 1974, 133.

CONTENTS

INTRODUCTION : CONTENTS

INTRODUCTION

During the last century, the mechanism of the decomposition of N-nitrosoacetanilide has been the subject of widespread interest and study. The origin of biphenyl, formed in high yield when the reaction is carried out in benzene, puzzled the early workers until Hey suggested, amid controversy and scepticism, that 'electrically-neutral' phenyl radicals were responsible. More recently the discovery of 'cine-substituted' products arising out of the decomposition of certain t-butylacylarylnitrosamines has led to the complicity of a second short-lived intermediate, benzyne, being established.



Attempts to rationalise the reactions of N-nitrosoacetanilide in terms of these two concomitant decomposition pathways has proved to be a stimulating intellectual exercise. There follows a brief review of radical, benzyne and acylarylnitrosamine chemistry and, because of current interest in the precise mechanism of benzyne formation, a section on base-initiated β-elimination reactions.

1. FREE RADICALS

Historical Background

The history of free radical chemistry dates from Gomberg's discovery[1] in 1900 of the first authenticated free radical, triphenylmethyl, produced during the attempted synthesis of hexaphenylethane by treating solutions of triphenylmethyl chloride with silver or zinc. Despite many years of scepticism, based on the doctrine that carbon must at all times be quadrivalent, Paneth and Hofeditz[2] invoked the intermediacy of methyl radicals in the gas phase pyrolysis of lead tetramethyl in a current of hydrogen gas.

$$[CH_3]_4Pb \longrightarrow 4CH_3^{\bullet} + Pb$$

Soon after this discovery, the production of neutral radicals from the thermal decomposition of organic substances was established as a general process.[3]

In 1934, Grieve and Hey[4] suggested that the reactive species responsible for the formation of biphenyl in the decomposition of N-nitrosoacetanilide in benzene was an electrically neutral free phenyl radical. Soon the concept of a free radical chain mechanism was used by Hey and Waters[5] to rationalize the "anti-Markownikov" addition of hydrogen bromide to an olefin in the presence of trace amounts of peroxide.

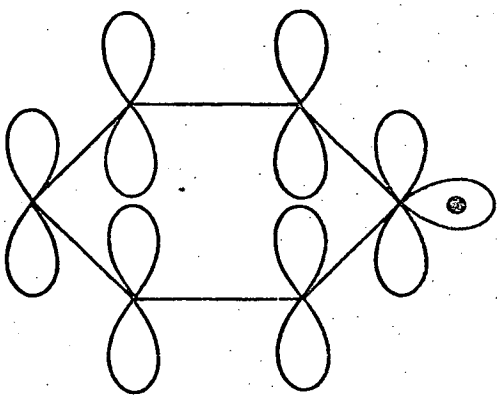
$$CH_3{\cdot}CH{:}CH_2 + HBr \xrightarrow{\text{normal}} CH_3{\cdot}CHBrCH_3$$

$$CH_3{\cdot}CH{:}CH_2 + HBr \xrightarrow{\text{peroxide}} CH_3CH_2CH_2Br$$

Succeeding years have seen great advances in the field of free radical chemistry, not only in the elucidation of reaction mechanisms but, more significantly, in the widespread use of these reactions in the industrial synthesis of rubbers and plastics by radical polymerisation processes. The subject of free radicals has been reviewed by a number of authors.[6]

Reactivity

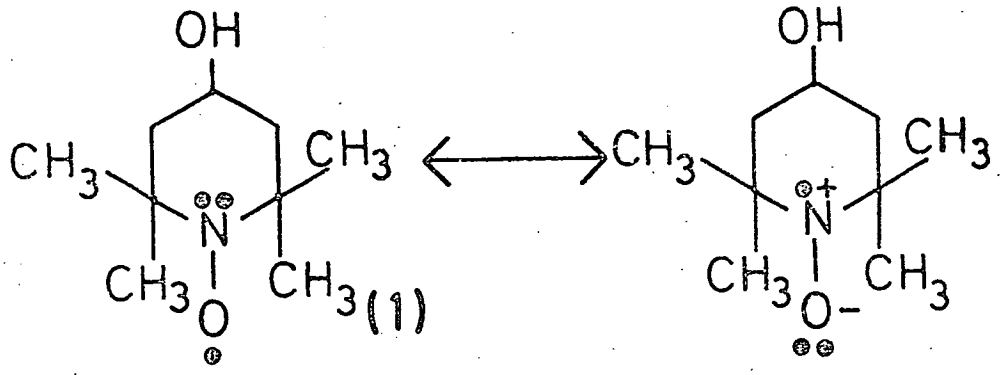
A free radical is an atom, molecule or complex which contains one or more unpaired electrons. The origin of radical reactivity lies in the tendency of the unpaired electron to form a strong electron pair bond with a substrate, the driving force of the reaction being the formation of a new bond. In the absence of a substrate, however, many radicals possess inherent thermodynamic stability. The distinction between radical stability and reactivity can be clearly illustrated in the case of the phenyl radical. Thus in a vacuum a single phenyl radical would show little tendency to fragment or rearrange, but in the presence of a substrate, it shows high reactivity due to the highly localised single electron contained in an sp_2 orbital orthogonal to the π-orbital system.



The acetoxyl radical on the other hand is unquestionably unstable, as illustrated by its rapid fragmentation to carbon dioxide and a methyl radical.[7]

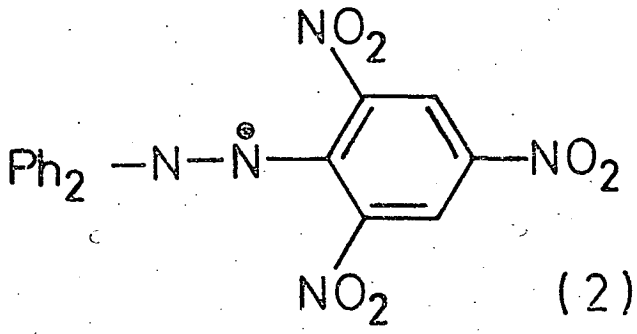
$$CH_3CO_2^{\bullet} \longrightarrow CH_3^{\bullet} + CO_2$$

In contrast, the nitroxyl radical (1) is not only stable but also unreactive towards many non-radical substrates, a consequence of delocalisation across the N-O bond, and to some extent steric shielding of the radical centre.



(1)

Similarly the diphenylpicrylhydrazyl radical (2) is stable in the solid state for years,[8] yet it cannot be described as unreactive since it finds wide use as a radical scavenger. It becomes essential, therefore, to specify reaction conditions when classifying



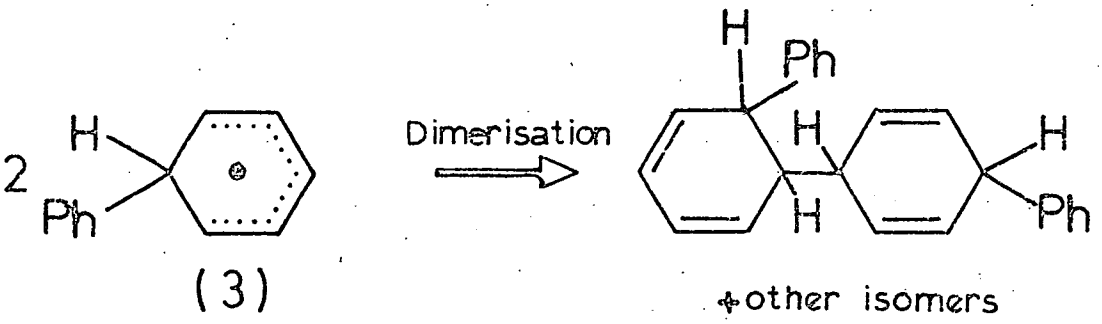
(2)

radicals in terms of stability or reactivity. Perhaps a more convenient way to classify radicals is in terms of their lifetime under normal reaction conditions, since this is determined not only by the intrinsic thermodynamic stability of the radical but also by its reactivity towards its environment. Thus the phenyl radical is short-lived - but not unstable - since its high energy content ensures rapid reaction with its surroundings.

Radical Reactions

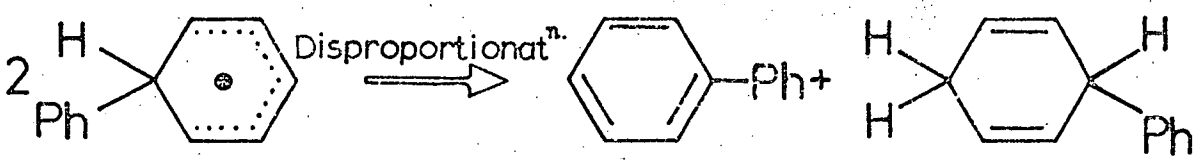
The reactions of free radicals in solution can be divided into three main categories: radical-radical reactions, in which the radical centre is lost; unimolecular reactions in which instability of the reactive intermediate induces fragmentation or rearrangement; and radical-molecule reactions in which a new radical species is always formed.

Radical-radical reactions are characteristic of "long-lived" radicals, stabilised through delocalisation, and also of "short-lived" radicals formed in high local concentration. The simplest reaction in this category is that of <u>combination</u>, the pairing of two radicals to form a neutral molecule. A special case of combination, <u>dimerisation</u>, involves two identical radicals. Thus dimerisation of the mesomeric phenylcyclohexadienyl radical (3) forms several isomers of tetrahydroquaterphenyl.[9]



(3)

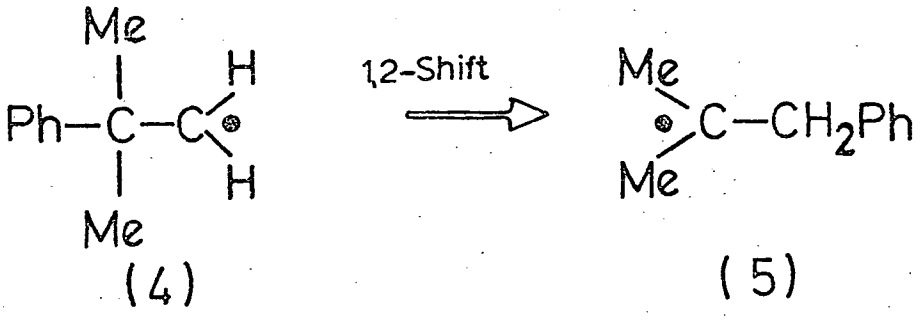
Radical <u>disproportionation</u> involves the collision of two radicals resulting in the abstraction of an atom, usually a hydrogen β to the radical centre, by one radical from another thereby leading to the formation of two stable molecules. Thus disproportionation of the phenylcyclohexadienyl radical gives biphenyl and dihydrobiphenyl.[9]



Unimolecular reactions occur when radicals are formed that are unstable relative to other molecular arrangements and may, as a consequence, decompose or rearrange.

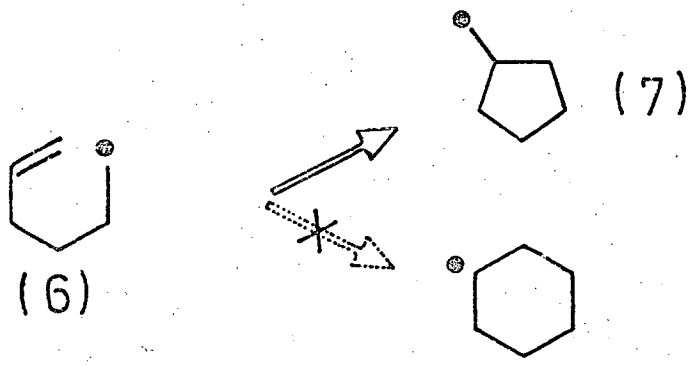
<u>Radical rearrangement</u>, which can involve migration of a group (H, halogen, aryl) or skeletal rearrangement, was first observed by Kharasch[10] during studies of the neophyl radical (4). He concluded that the formation of various 'rearranged' products could be best explained in terms of a 1, 2-aryl shift in the free neophyl

radical (4) to give the 3° radical (5).



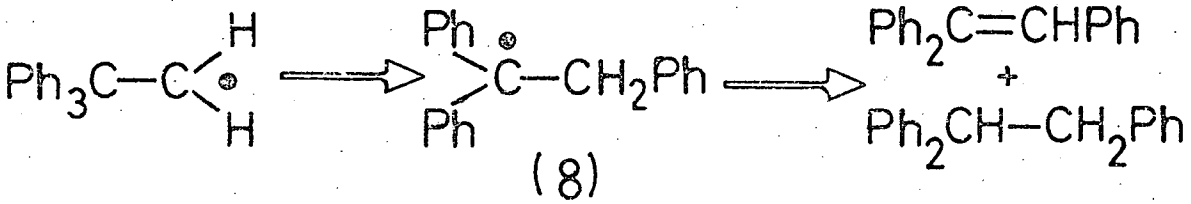
(4) (5)

Such a rearrangement is in accord with the popularly accepted order of radical stability, $3^{\circ} > 2^{\circ} > 1^{\circ}$. Intramolecular cyclisation of the hex-5-en-1-yl radical (6), however, follows the 'less exothermic' path and leads almost exclusively to the 1° cyclopentylcarbinyl radical (7).[11]



(6) (7)

Rearrangements are frequently followed by disproportionation or dimerisation. Thus rearrangement of the 2, 2, 2-triphenylethyl radical gives rise to (8) which can then disproportionate.[12]

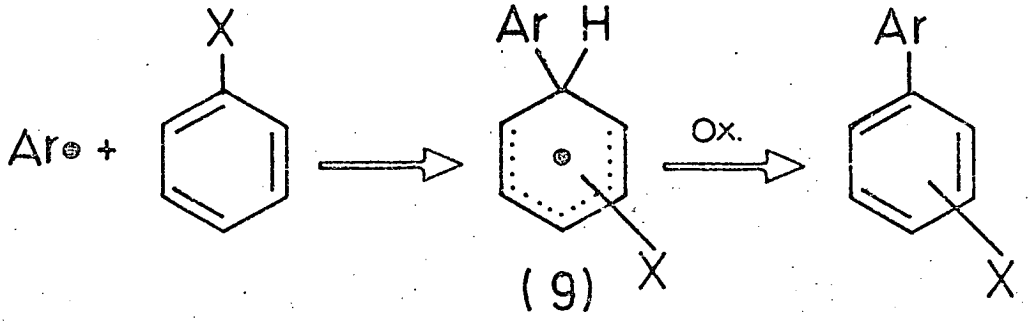


(8)

Radical <u>decompositions</u> proceed with <u>fragmentation</u> into a simpler radical and an unsaturated molecule, as in the case of the acetoxyl radical mentioned earlier.[7]

Radical-molecule reactions are preferred for those radicals

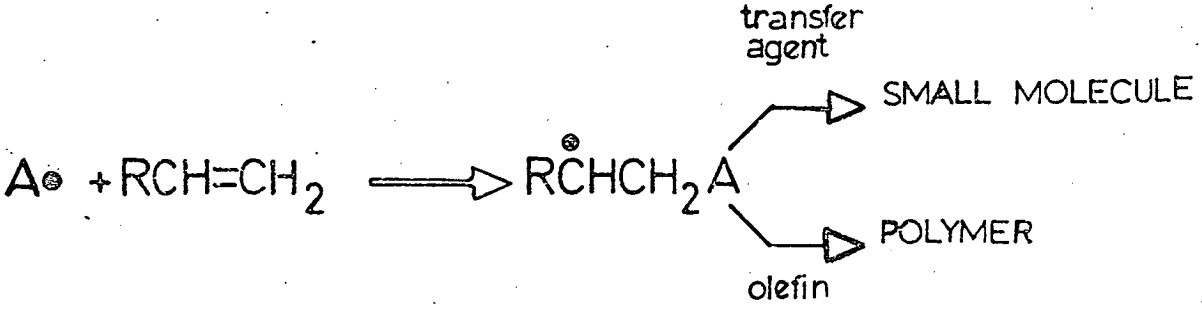
which are both stable and highly reactive, e.g. methyl and phenyl. The most common and probably the best documented reaction in this category is that of homolytic aromatic substitution, a process reviewed by Augood and Williams,[13] Hey,[14] and more recently by Perkins.[15] It was Grieve and Hey[4] who in 1934, realising that the product distribution in arylation reactions could not be rationalised in terms of the polar influences of directing groups, explained the anomaly by postulating a mechanism "involving the formation and transient existence of free phenyl radicals." The absence of a kinetic isotope effect in the arylation of deuteriated or tritiated aromatic compounds[16,17] indicates that aryl radical addition is the rate determining step. The arylcyclohexadienyl radical thus formed is dehydrogenated in a subsequent fast step.



(9)

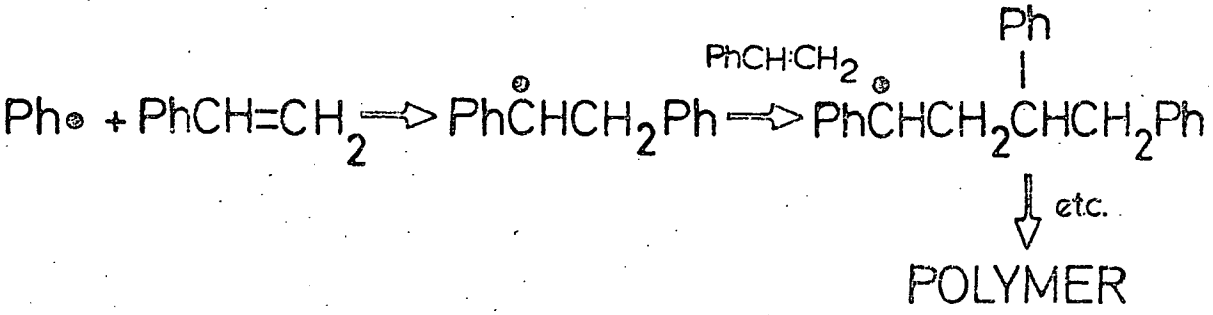
Dimerisation of the σ–complex (9) can lead to the formation of a number of isomeric and stereoisomeric derivatives of tetrahydroquaterphenyl.

When generated in the presence of non-aromatic unsaturated compounds, radicals undergo addition reactions. The new radical produced by addition of a radical to an olefin can undergo two main alternative reactions:



Reactions with molecules containing readily abstractable atoms

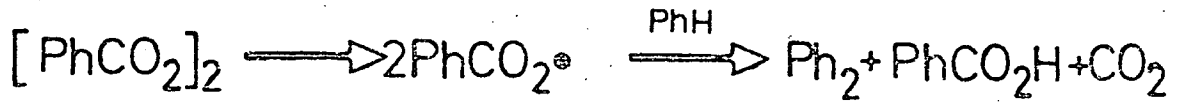
(transfer agents), such as halogens, alcohols and amines constitute a most important synthesis of small molecules *via* radical chains.[18] On the other hand, radical addition to styrene produces a weakly reactive benzylic radical which will itself add to olefin rather than abstract, thus giving a polymeric product.



Generation of Aryl Radicals in Solution

Aryl radicals can be formed from non-radical precursors *via* the photolytic or thermal homolysis of covalent bonds, and also *via* redox reactions. Absorption of electromagnetic radiation by a molecule can lead to homolysis of a covalent bond. At 270mμ, for example, the quantum size is equivalent to 420 kJ mol^{-1}, enough to break most bonds provided that the energy is not dissipated in other ways. Thus iodobenzene, diphenyl mercury and tetraphenyl lead can be photolytically decomposed to phenyl radicals.[19] Irradiation of dilute benzene solutions of other metal perphenyls $SnPh_4$ and $AsPh_3$ at 2537Å also leads to the generation of phenyl radicals.[20]

In solution, thermal homolysis can be induced at temperatures below 150° in those molecules which contain weak bonds with dissociation energies less than 160 kJ mol^{-1}. Dibenzoyl peroxide readily decomposes at 80°[21] in benzene with production of biphenyl, carbon dioxide and benzoic acid.



The complexity of this decomposition, however, has been emphasized by De Tar's[22] investigations from which he has shown that over one hundred reactions contribute to the overall decomposition. The genesis of both phenyl and benzoyloxyl radicals contributes to this complexity.

The decomposition of dibenzoyl peroxide in the presence of polycyclic hydrocarbons such as naphthalene[23] and substituted anthracenes[24] leads to ester formation, presumably via benzoyloxyl radical addition. Other routes to benzoyloxyl radicals and hence to phenyl radicals include the thermolysis of lead tetrabenzoate,[25] phenyliodosobenzoate[26] and silver halide dibenzoates.[27]

Azo compounds represent another valuable source of aryl radicals. Phenylazotriphenylmethane was shown by Wieland[28] in 1922 to evolve nitrogen at 80°, presumably with accompanying liberation of free triphenylmethyl and phenyl radicals, and Hey[29] later showed that decomposition in benzene led to the formation of

$$Ph\text{-}N{:}N\text{-}CPh_3 \longrightarrow Ph^{\bullet} + N_2 + Ph_3C^{\bullet}$$

$$Ph^{\bullet} + PhH \xrightarrow{X} Ph_2 + XH$$

biphenyl, an observation which he took to finally confirm the ability of the free phenyl radical to react with neutral aromatic compounds.

1-Aryl-3,3-dimethyltriazenes decompose to give aryl radicals[30] in the presence of acetic acid or hydrogen chloride according to the equation:

$$ArN{:}N\text{-}NMe_2 + PhR \xrightarrow{HCl} ArPhR + N_2 + NHMe_2HCl$$

A third major route to aryl radicals involves one electron

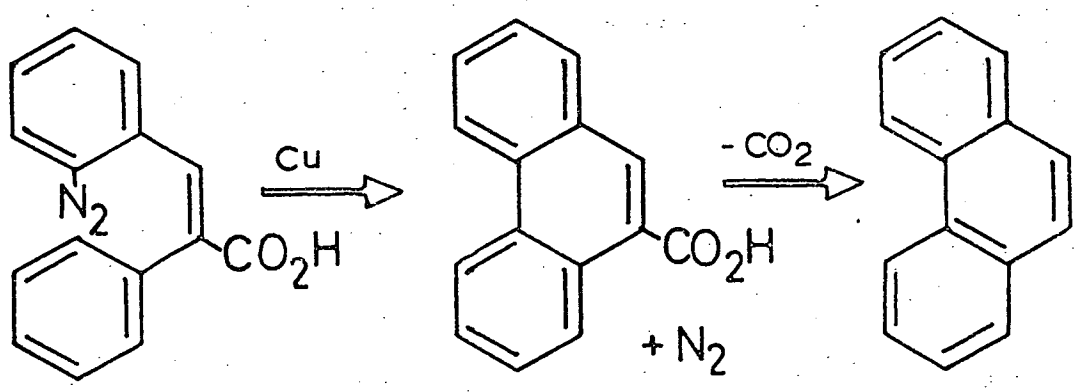
reduction of diazonium salts, a process that can be effected either polarographically[31] or chemically. The reaction of diazotised anilines with benzene in the presence of sodium hydroxide was discovered as a route to biaryls by Gomberg[32] in 1923 although it was Hey[4] who established the intermediacy of phenyl radicals in the reaction. The mechanism of this reaction is very similar to that proposed recently by Rüchardt[33] for the decomposition of N-nitrosoacetanilide, a reaction which serves as another valuable source of aryl radicals and one that will be dealt with in detail in a later section. Formally the Gomberg reaction can be written as:

$$ArN_2^+Cl^- + PhH \xrightarrow{NaOH(aq)} PhAr + N_2 + NaCl + H_2O$$

Phenyl radicals can also be readily obtained by the action of zinc powder on benzenediazonium salts suspended in acetone.[34] This

$$PhN_2^+Cl^- + Zn^\bullet \longrightarrow Zn^+ + Ph^\bullet + N_2 + Cl^-$$

method represents an excellent technique for the phenylation of anthracene and meso-substituted anthracenes. A similar process involves interaction of diazonium salts with copper.[35] It is now accepted that the copper or copper salt catalysed reactions such as the Sandmeyer and Meerwein reactions and the Pschorr cyclisation occur via single electron redox transfers.[36] Thus in the reaction bearing Pschorr's name, reaction of diazotised o-amino-α-phenylcinnamic acid with copper powder results in the transfer of one electron from copper to the diazonium function, followed by nitrogen extrusion and cyclisation to the phenanthrene-9-carboxylic acid, which in the final stage is decarboxylated.



A more recent and arguably more facile route to aryl radicals involves the in situ diazotisation of aniline with pentyl nitrite,[37] a reaction which probably proceeds via the following mechanism:

$$ArNH_2 + C_5H_{11}ONO \longrightarrow ArN{:}NOC_5H_{11} + H_2O$$

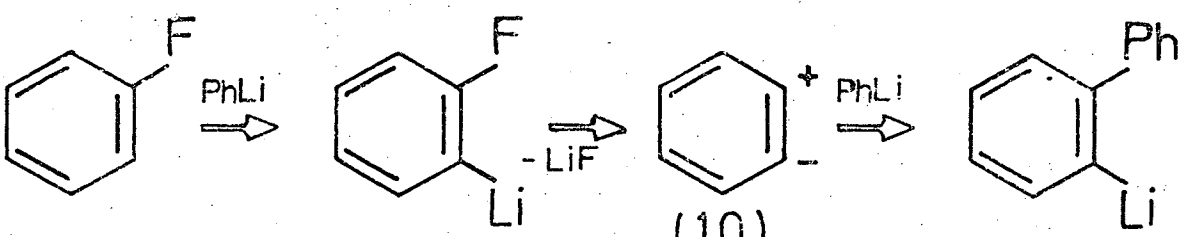
$$ArN{:}NOC_5H_{11} \longrightarrow Ar^{\bullet} + N_2 + C_5H_{11}O^{\bullet}$$

2. BENZYNE

Historical Background

Although biphenyl was isolated as a product from the reaction of bromobenzene and sodium over one hundred years ago,[38] the complicity of benzyne, or dehydrobenzene, in the reaction was not suggested at the time. Indeed it was not until 1942[39] that serious consideration was given to the possibility that such a species could exist as a genuine reactive intermediate.

It was Wittig[39] who suggested the formation of a permanently charged 1, 2-dehydrobenzene (10) species in the reaction of phenyl-lithium with fluorobenzene. Two crucial observations prompted this suggestion: first, the rate of the reaction was greater than that observed for other halogenobenzenes;[40] and second, 2-lithiobiphenyl was identified as the primary product of the reaction.[39] The mechanism proposed by Wittig is shown in Scheme 1.

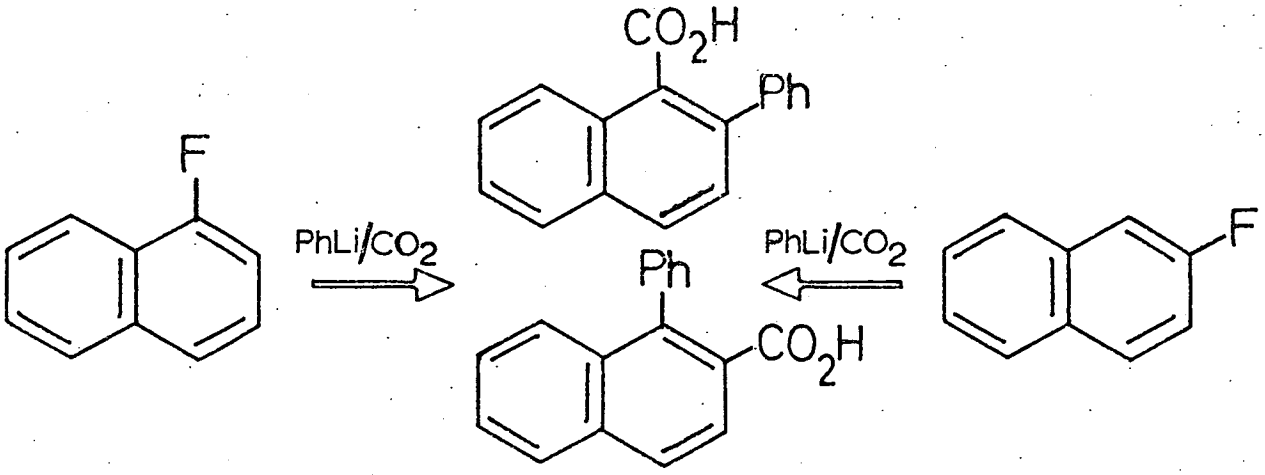


Scheme 1

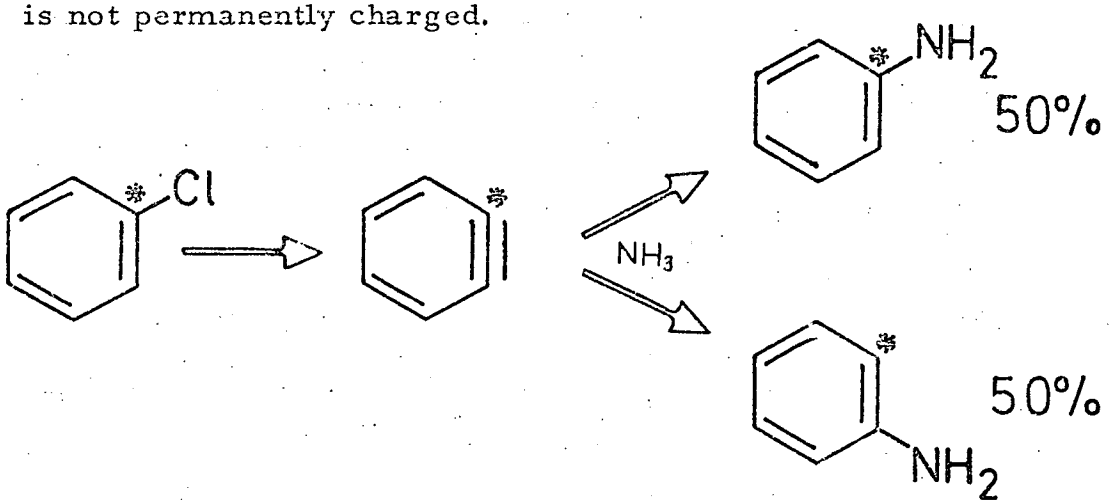
Subsequent decomposition of the 2-lithiobiphenyl afforded biphenyl. The increase in reaction rate was rationalised in terms of the increased acidity of the o-hydrogens in fluorobenzene.

That dehydrobenzene and related aryne species do not exist in the permanently charged form, suggested by Wittig, was later established by the independent studies of Huisgen and Rist[41, 42] and Roberts.[43] The former workers examined the products of the reaction of 1- and 2-fluoronaphthalenes with phenyl-lithium, followed by treatment with carbon dioxide. They found the same ratio of phenyl-substituted naphthoic acids in the products of both reactions. Cine-substitution was clearly incompatible with a

Wittig-type structure.



The decisive and better known reaction, however, was that of Roberts,[43] whose observation that equal amounts of 1-^{14}C aniline and 2-^{14}C aniline were produced from the amination of 1-^{14}C chlorobenzene provided compelling evidence that benzyne is not permanently charged.

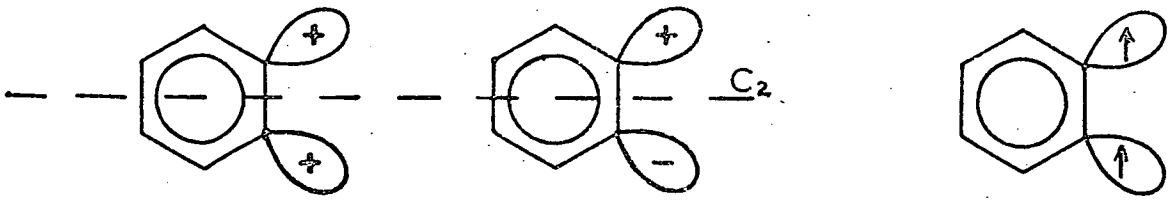


Although Roberts concluded warily that this result simply indicated an intermediate in which the 1- and 2-positions of the ring are, or can become, equivalent, the existence of benzyne was no longer in doubt.

Structure

Removal of two adjacent hydrogen atoms from benzene results in two sp_2-like orbitals, orthogonal to the π-orbital system, each containing a "free" electron. Interaction of these

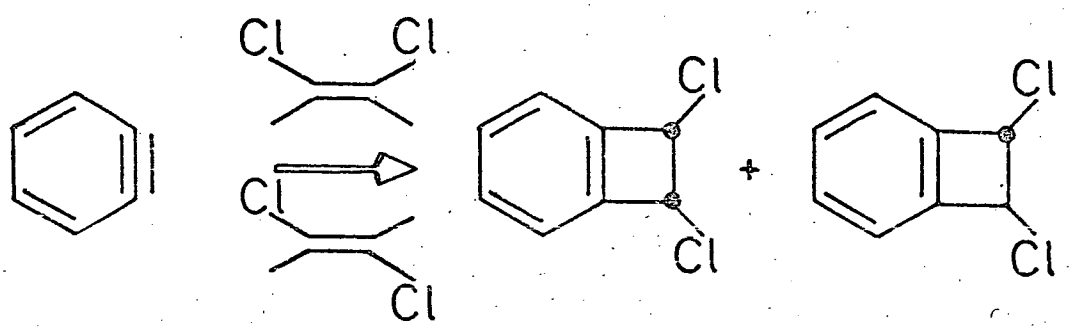
two orbitals can give either a singlet or triplet state.



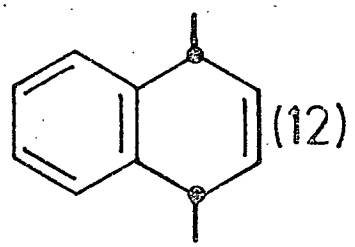
(S) (A) (11)

Although Rees[44] and Tabushi[45] have forwarded speculative suggestions that benzyne may under some reaction conditions exist in the triplet state (11), it is now generally agreed[46] that the ground state is a singlet. Hoffmann[47] has reached this conclusion as a result of theoretical calculations based on a variety of molecular orbital methods. More recently, Wilhite and Whitten[48] have used ab initio self-consistent field calculations to predict conclusively that the ground electronic state of o-benzyne is a singlet. Hoffmann,[47] appreciating that two singlets are possible, one symmetric (S) with respect to a C_2 axis and one asymmetric (A), has calculated that the symmetric singlet is the more stable by 1.52eV.

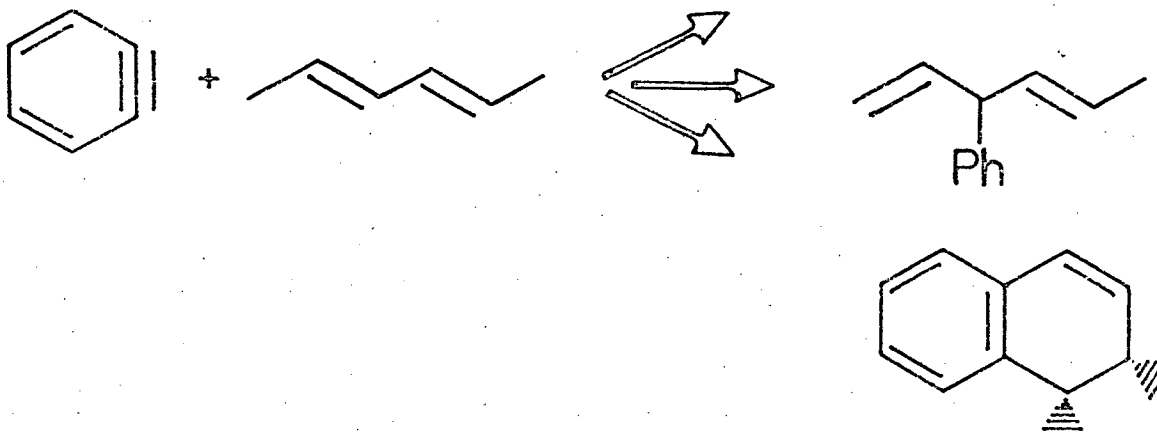
Empirically, a choice exists between these two singlet forms on the basis of the Woodward and Hoffmann rules on conservation of orbital symmetry.[49] Symmetry considerations predict that a non-concerted [2+2] cycloaddition will be preferred for the symmetric benzyne (S), while the [2+4] addition should be stereospecific. The opposite results are predicted for the asymmetric structure (A). Such predictions follow from the fact that if the molecule is a ground-state singlet with two electrons in the lower S orbital, then its electronic structure at the reactive site resembles another (partial) π-bond, i.e. it is like an olefin. Thus Jones[50] has found moderate loss of stereochemistry in the reaction of benzyne with each of cis- and trans-1, 2-dichloroethylene in accord with Hoffmann's calculations which point to benzyne being S.



In contrast, the Diels -Alder reaction of benzyne with trans, trans-2,4-hexadiene[50] proceeds with retention of stereochemistry.

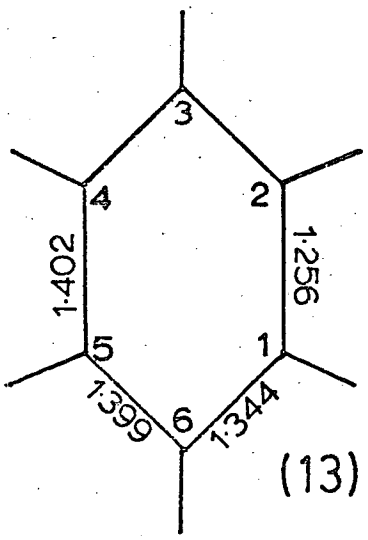


(12)



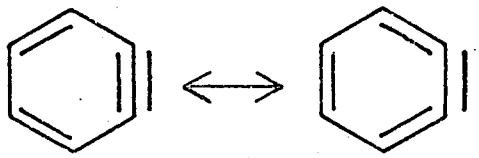
The [2+4] cycloaddition product, cis-1,4-dimethyl-Δ^2-dihydronaphthalene (12) constituted 85% of the total products. These results are consistent with a symmetric singlet ground state of benzyne.

A theoretical study of the structure and physico-chemical properties of 1, 2-benzyne by Haselbach[51] has indicated a structure (13), considerably different from that of benzene.



(13)

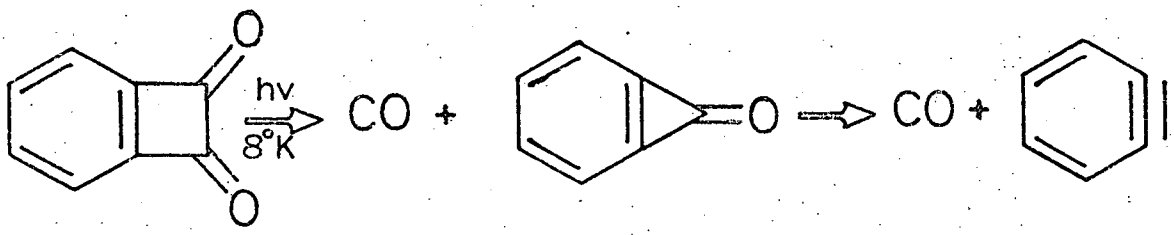
Of special interest in this structure is the length of the strained "triple" bond, it being only 0.05Å longer than that in acetylene. This value is in accord with Hoffmann's[47] bond length calculations. The C(2)-C(3) and C(1)-C(6) bonds are also shortened by about 0.05Å compared to benzene, thus indicating considerable π- electron delocalisation. Haselbach concludes that a sizeable resonance contribution comes from the cumulene structure (14b).



(14a) (14b)

On the basis of the above overall geometry, Haselbach has calculated the heat of formation of benzyne. His value of Δ Hf, 450 kJ mol^{-1}, is in good agreement with an estimate from mass spectrometric studies (ΔHf = 495 kJ mol^{-1}).

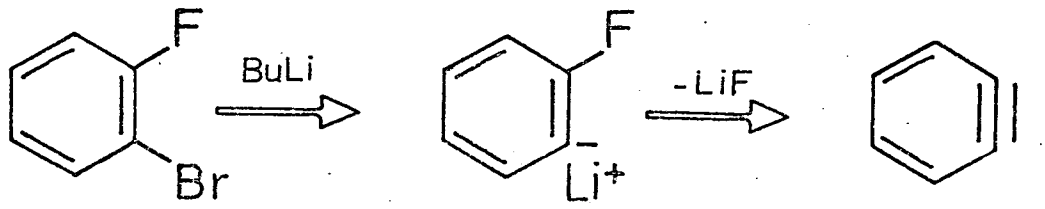
Chapman[52] has recently recorded the infrared spectrum of benzyne, generated by irradiation of benzocyclobutenedione, matrix-isolated in argon at 8°K:



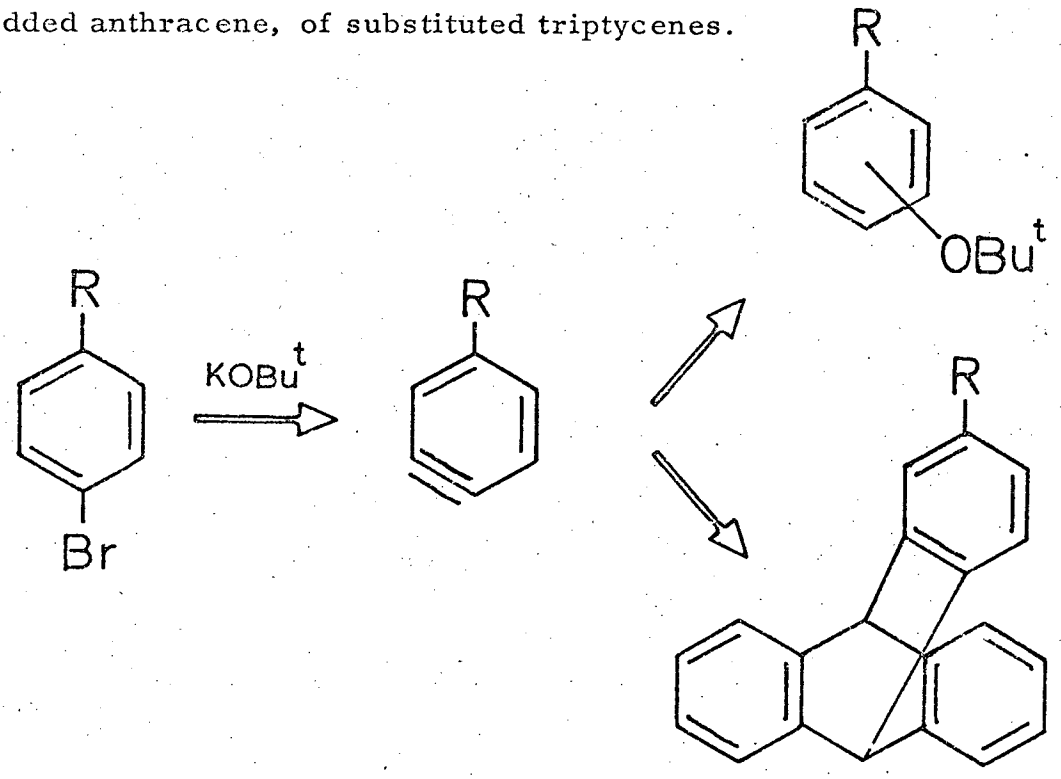
He concludes that the carbon-carbon bond frequencies indicate that 14a is energetically favoured relative to 14b, and that the molecule, therefore, has a high degree of cyclohexatriene character as far as the π-system is concerned.

Sources of Benzyne

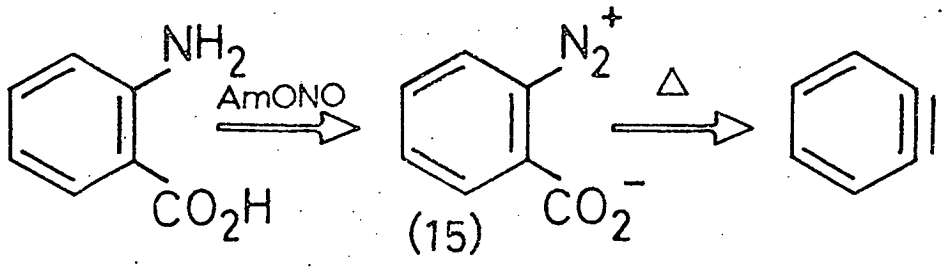
The classical pathway to benzyne involves the decomposition of o-anionised benzene derivatives prepared by the action of organometallic bases on substituted benzene.[53]



o-Dihalobenzenes will also liberate benzyne by reaction with lithium amalgum[54] and magnesium.[55] The reaction of halogenated aromatic substrates, in strongly basic media, such as ammonia, is of little synthetic value, the aryne being intercepted via nucleophilic attack by base. A simple and convenient route to substituted arynes from aryl halides has, however, been reported.[56] Thus reaction of the halide with potassium t-butoxide in an inert solvent gives arynes in good yield, as indicated by the isolation of mixtures of aryl t-butyl ethers, or, in the case of reactions carried out with added anthracene, of substituted triptycenes.

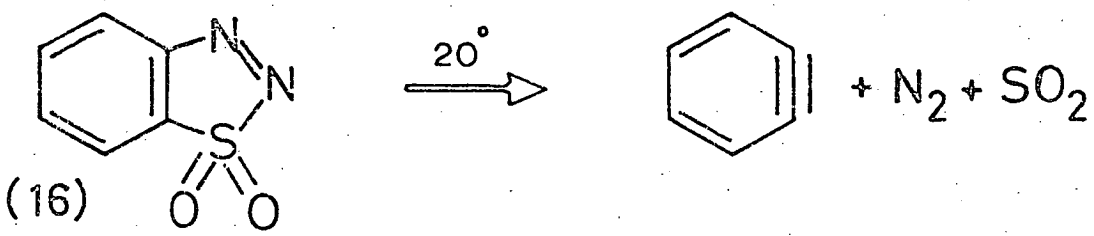


In a search for other aromatic compounds likely to yield benzyne under mild conditions, in the absence of organometallic agents, Stiles[57] and Friedman[58] found that in situ diazotisation of anthranilic acid generated the zwitterion, benzenediazonium carboxylate (15), which readily eliminated nitrogen and carbon dioxide to form benzyne.

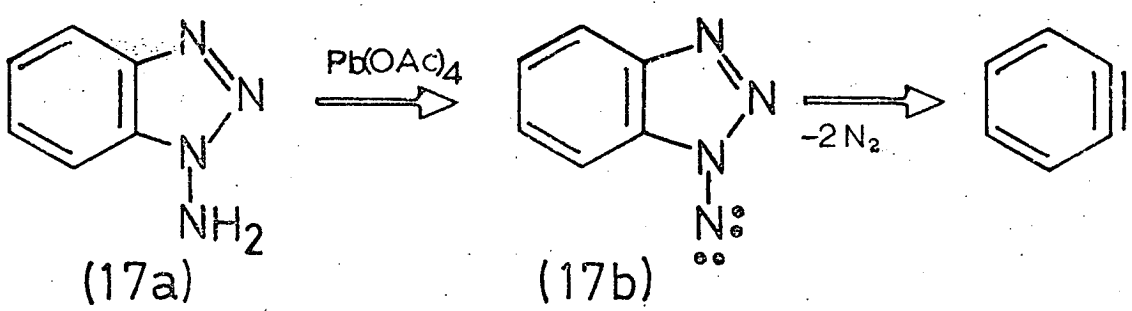


Benzyne, prepared by this method, was trapped by anthracene to give triptycene in 30% yield. An analogous reaction involved the decomposition of diphenyliodonium-2-carboxylate to benzyne at 160°. [59]

The loss of small stable molecules from a substituted aromatic nucleus was soon recognised as an excellent route to benzyne. Thus 1, 2, 3-benzothiadiazole-1, 1-dioxide (16) fragmented under mild conditions to benzyne, sulphur dioxide and nitrogen. [60]



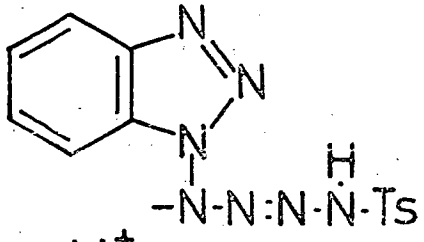
In 1968 Rees [61] developed a new route to benzyne *via* the oxidation of 1-aminobenzotriazole (17a) with lead tetraacetate, under very mild conditions. Oxidative removal of the amino



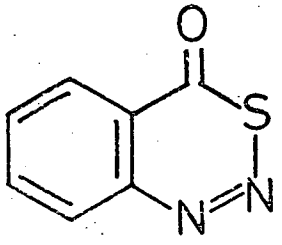
hydrogens is believed to form the nitrene (17b) which can subsequently fragment to benzyne with loss of two nitrogen molecules. Similarly, deoxygenation of 1-nitrosobenzotriazole, a reaction which also may proceed *via* the nitrene (17b), affords benzyne in reasonable yield. [62]

An intriguing feature of this reaction is that in the absence of an aryne trap, biphenylene, the dimer of benzyne, is formed in 85% yield. That this is a direct result of a high local concentration of benzyne is possible although slow addition of the lead tetraacetate to the amine solution also affords biphenylene in good yield (60%). Rees has advanced two other possible explanations of this phenomenon: firstly, he suggests that benzyne may be generated in a triplet state and as such would be expected to be less reactive towards nucleophiles; and secondly, he considers the possibility that a lead-benzyne intermediate may be formed in which the probability of dimerisation is enhanced.

More recently, Rees[63] has established that the lithium salt of 1-(benzotriazol-1-yl)-4-p-tolylsulphonyltetrazene (19) decomposes immediately to benzyne when dissolved in tetrahydrofuran or acetonitrile. This method benefits from the absence of an oxidising agent and from the low temperature suitable for decomposition.



(19)



(20)

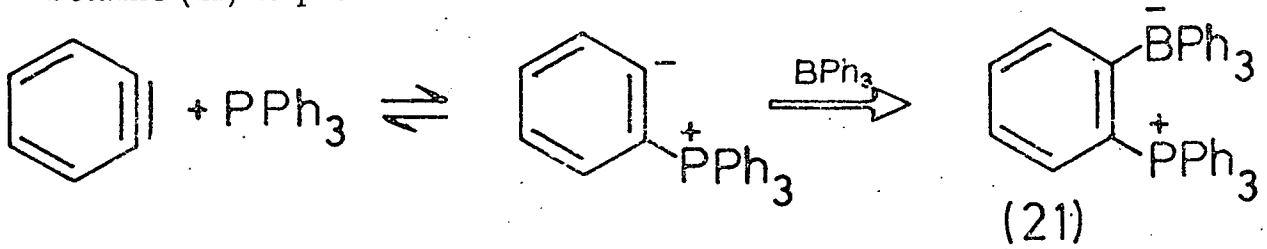
Other routes to benzyne developed during the last few years include the photolysis of phthaloyl peroxide through Pyrex[64] and the thermolysis of 4-oxo-3,4-dihydro-3,1,2-benzothiadiazene (20).[65]

The decomposition of N-nitrosoacetanilide and related compounds, as a route to benzyne, will be fully discussed in a later section.

Reactions of Benzyne

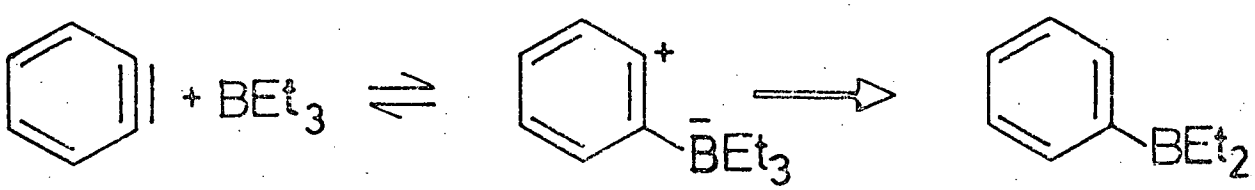
Benzyne is a highly reactive hydrocarbon species, known to participate in a wide range of reactions,[46] including polar additions,

cycloadditions, insertion reactions and the 'so-called' 'Ene'-reaction. Monodentate attack by both nucleophiles and electrophiles is known and such reactions are the subject of an extensive review.[46] Thus nucleophilic attack by triphenylphosphine on benzyne results in the formation of 9-phenyl-9-phosphafluorene;[66] but in the presence of an electrophile, such as triphenylboron a betaine (21) is produced.[67]



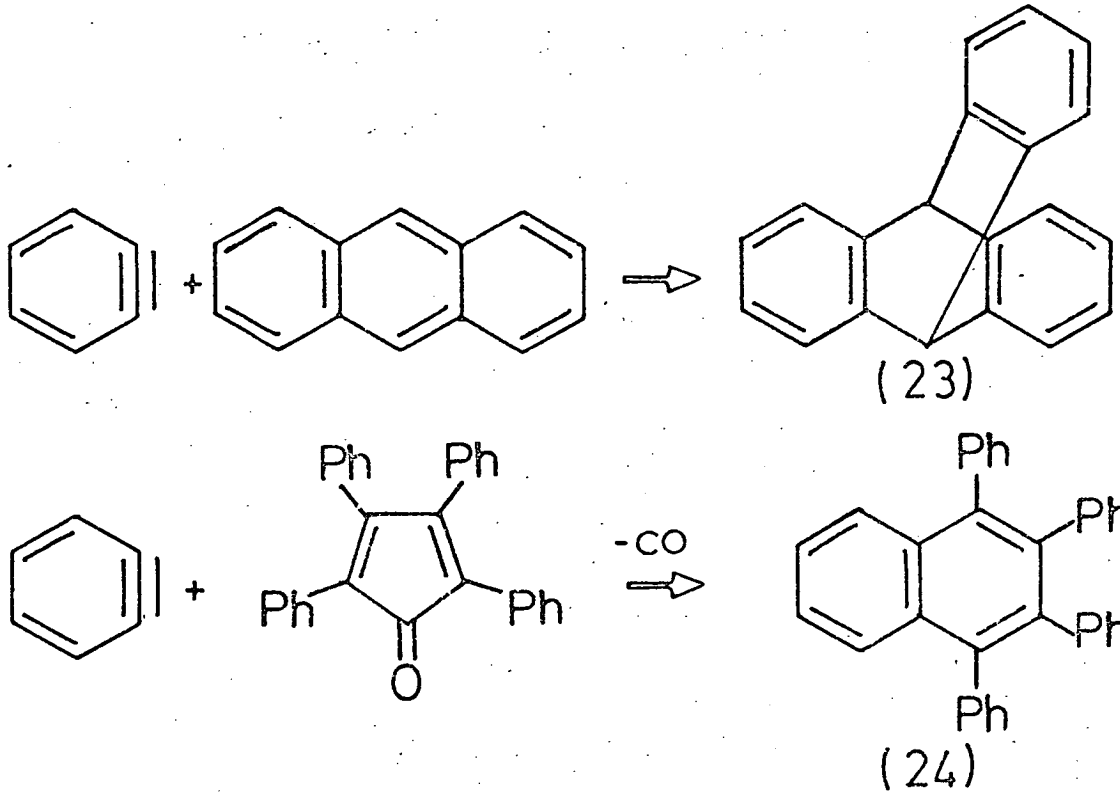
(21)

Electrophilic attack on benzyne, although less common, can occur as in the reaction with triethylboron.[67]



Benzyne will readily undergo cycloaddition reactions leading to four, five- and six-membered rings. Since Wittig employed furan as a benzyne trap in 1955,[54] many dienes have been shown to undergo Diels-Alder reactions with arynes. Thus with furan, anthracene[57] and tetraphenylcyclopentadienone,[68] benzyne gives 1,4-dihydronaphthalene-1,4-endoxide (22), triptycene (23) and tetraphenylnaphthalene (24).

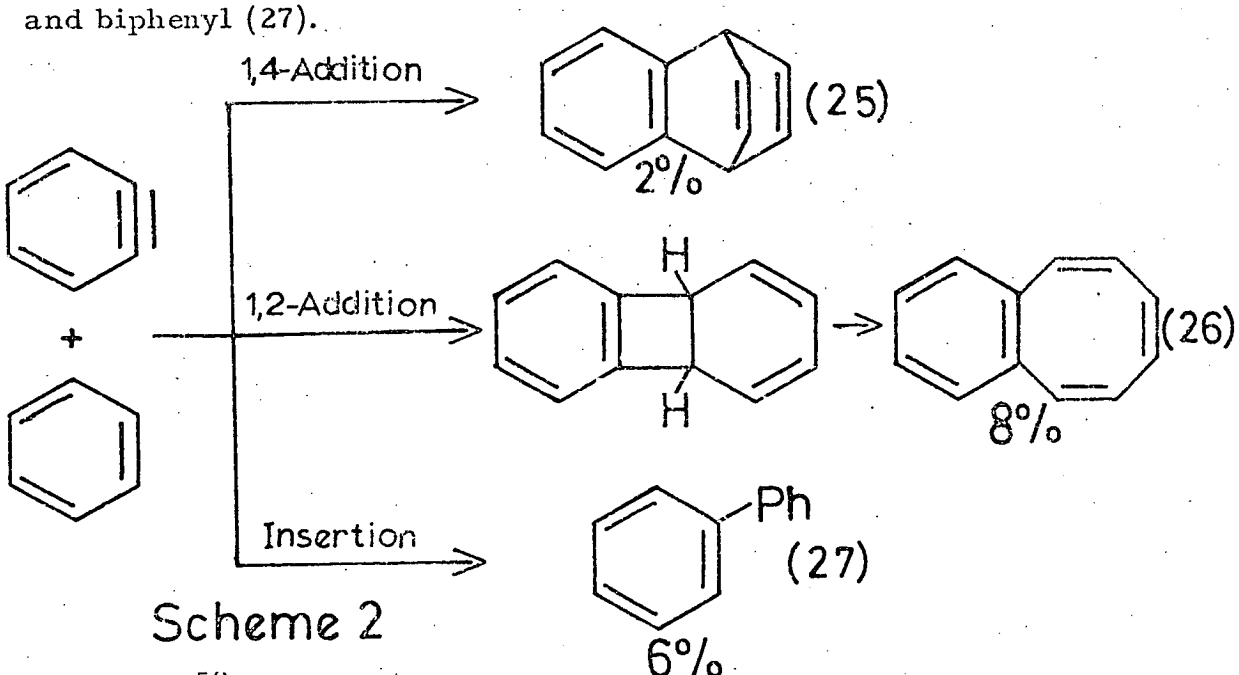
(22)



(23)

(24)

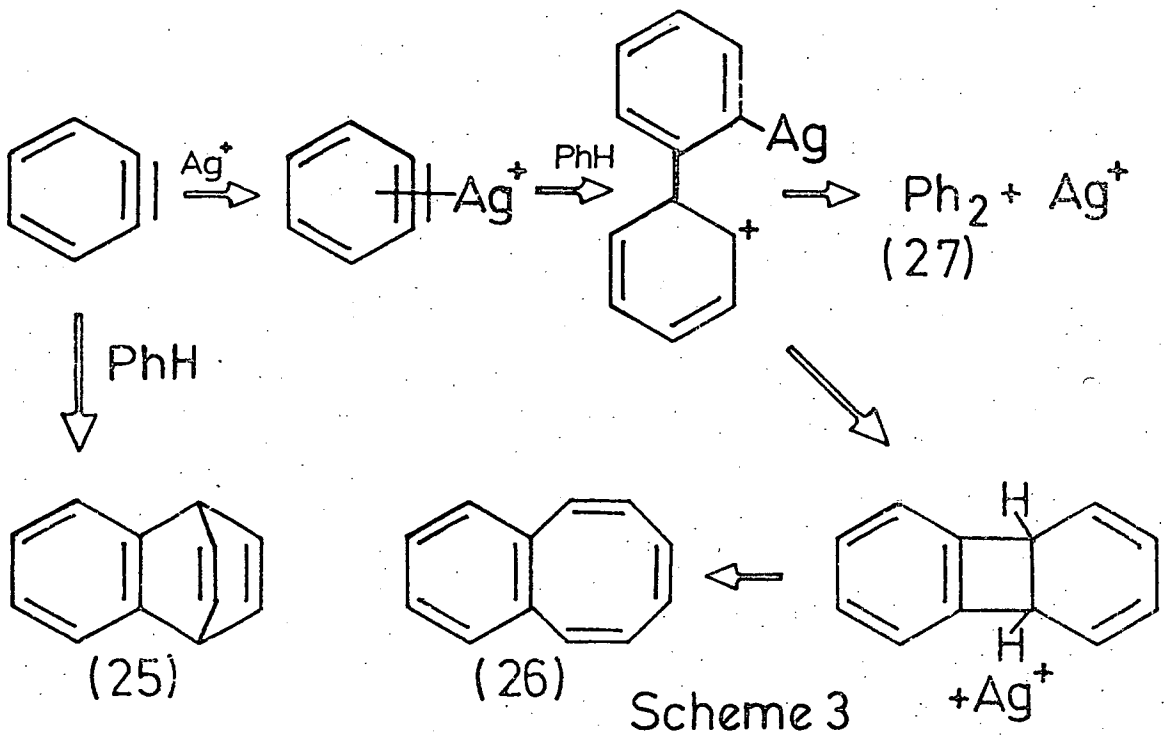
The tendency of dehydrobenzene to undergo cycloadditions is so marked that it will even attack benzene if no other reactive substrate is present. Thus decomposition of benzenediazonium-2-carboxylate in benzene[57] afforded three hydrocarbons, identified as benzobicyclo[2, 2, 2]octatriene (25), benzocyclooctatetraene (26) and biphenyl (27).



Scheme 2

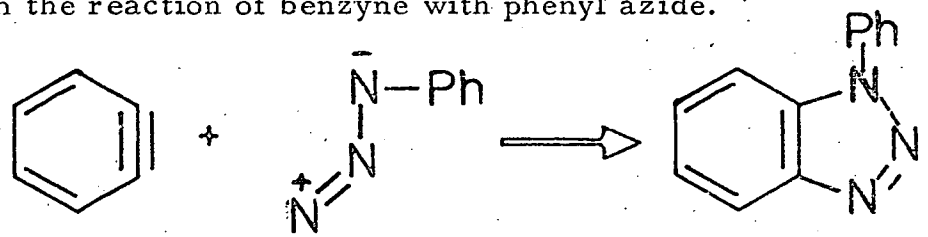
Friedman[58] later showed, however, that the product distribution in this reaction varied according to the concentration of silver ion. In the absence of Ag^+, Friedman isolated the 1,4-adduct in 17% yield,

along with biphenylene (2%). This prompted his suggestion that silver ion, present as a contaminant in Miller and Stiles' benzyne precursor, was complexing with benzyne, thereby forming a species more electrophilic than benzyne itself. Repetition of his reaction in the presence of trace amounts of silver salts led to a decreased yield of benzobicyclo[2, 2, 2]octatriene and a corresponding increase in the total yield of other products. Friedman suggested the mechanism shown in Scheme 3 to explain these results:



Scheme 3

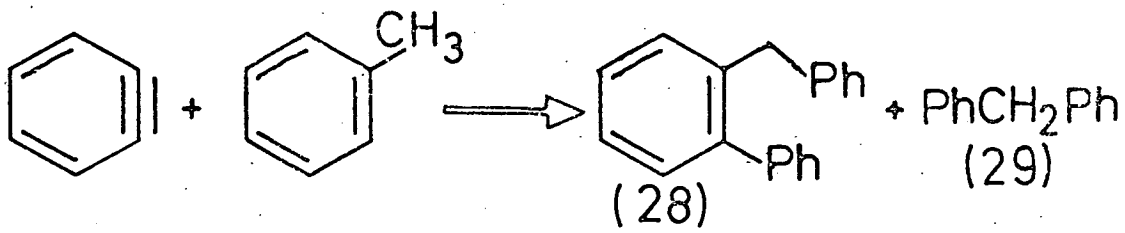
Benzyne will also undergo 1, 3-cycloadditions with 1, 3-dipolar species.[46] Thus a high yield of 1-phenylbenzotriazole results from the reaction of benzyne with phenyl azide.[69]



Other azides react in an analogous manner[70, 71] as do benzonitrile oxide[72] and a number of diazoketones.[73]

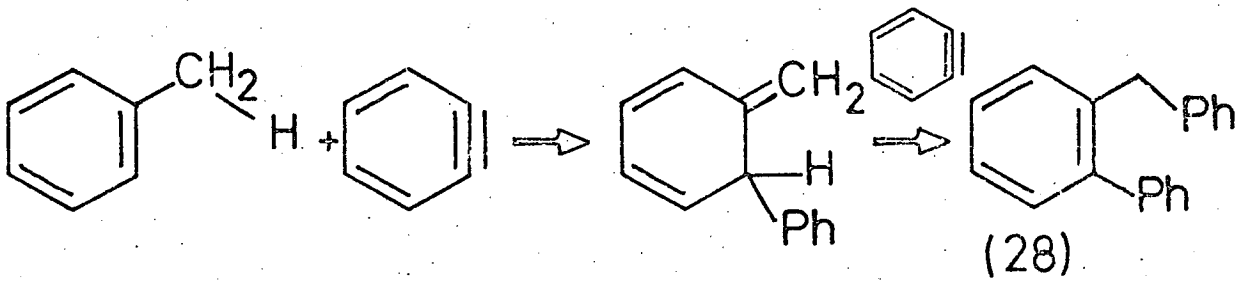
Whereas tetrafluorobenzyne reacts with benzene and alkylbenzenes to give the [4+2] cycloadducts exclusively[74] (tetrafluoro-

benzobicyclo[2, 2, 2]octatrienes), benzyne is less selective and in addition to the cycloadduct, products of insertion and 'ene' reactions have been identified.[75] Thus benzyne reacts with toluene to give o-benzylbiphenyl (28) and diphenylmethane (29).

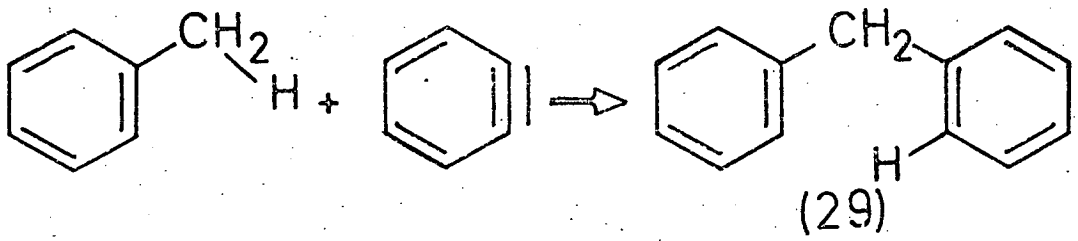


+1,4-Cycloadducts

The origin of o-benzylbiphenyl can be explained as the result of two successive 'ene' reactions, the first examples ever reported involving benzyne and an aromatic substrate.



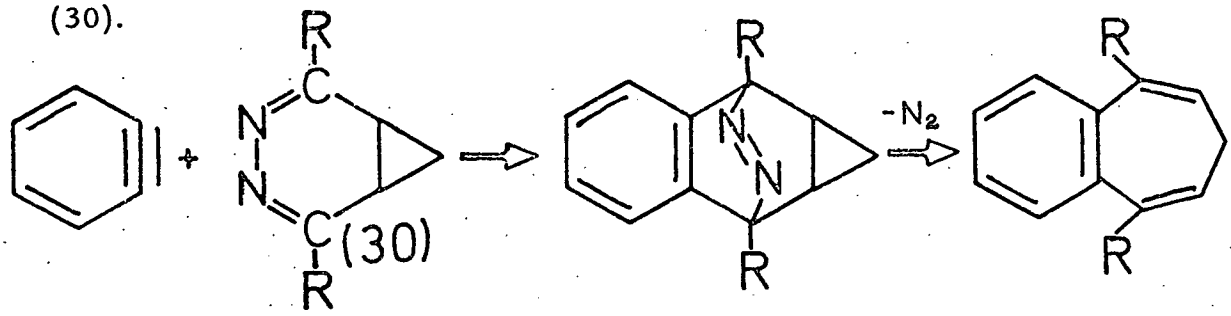
Diphenylmethane is believed to arise from the insertion of benzyne into the benzylic C-H bond.



The formation of this product is of special interest in view of the fact that very few insertion reactions of benzyne have been reported.[46] Benzyne can also react by hydrogen abstraction in the absence of other reactive substrates. Thus in cyclohexane, benzene is obtained[76] in 45% yield and in tetrahydrofuran, benzene (5%) and biphenyl (0.5%) are formed.[77]

The value of benzyne in the synthesis of new organic compounds has been fully realised in recent years. Thus Moerck and Battiste[78]

have developed a new route to cyclohepta-1, 3, 5-trienes by the reaction of benzyne with 2, 5-disubstituted-3, 4-diazanorcaradienes (30).



A new direct route to substituted naphthalenes and naphthols through the reaction of benzyne with dienolate anions has also been devised by Sammes and Wallace.[79]

3. ACYLARYLNITROSAMINES

Historical Background

In 1876, Fischer[80] reported the formation of an unstable yellow solid, N-nitrosoacetanilide when acetanilide was treated with nitrous fumes in acetic acid. An alternative route to acylarylnitrosamines was later developed by von Pechmann and Frobenius[81] who acetylated solutions of alkaline benzenediazonium salts, an observation which inspired Hantzsch[82] to suggest a tautomeric equilibrium between benzenediazoacetate and N-nitrosoacetanilide.

$$Ph{\cdot}N(NO)Ac \rightleftharpoons Ph{\cdot}N{:}N{\cdot}OAc$$

Kuhling[83] and Bamberger[84] studied the reactions of arenediazotate salts with aromatic substrates in the presence of acetyl chloride and acetic acid, a reaction which Gomberg[32a] developed as a synthetic route to biaryls. Bamberger[85] later showed that decomposition of N-nitrosoacetanilide in benzene gave biphenyl as a major product. This observation, in turn, led Grieve and Hey[4] to investigate this reaction as a general route to biaryl synthesis. Decomposition of N-nitrosoacetanilide in a series of substituted aromatic solvents yielded products whose origin could not be rationalised on the basis of established aromatic substitution patterns, the reaction proceeding invariably at the ortho- or para-position irrespective of substituent. Thus Grieve and Hey invoked the intermediacy of electrically neutral free phenyl radicals in these reactions. Subsequent kinetic studies of the decomposition,[4, 86] established that in a wide range of solvents, acetic acid excepted, the rate of first order evolution of nitrogen was unchanged. This led to Hey's suggestion that homolysis of the benzenediazotate was rate-determining.

$$Ph{\cdot}N(NO)Ac \rightleftharpoons Ph{\cdot}N{:}N{\cdot}OAc \xrightarrow{Slow} Ph^{\bullet} + N_2 + AcO^{\bullet}$$

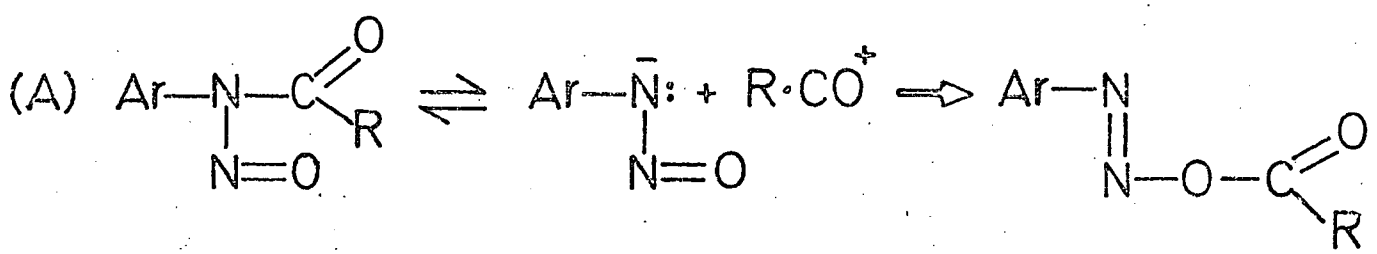
Thus the first partial mechanism had been proposed for the decomposition of N-nitrosoacetanilide. In the following thirty years, however, extensive study of acylarylnitrosamine chemistry was to establish the true complexity of the reaction.

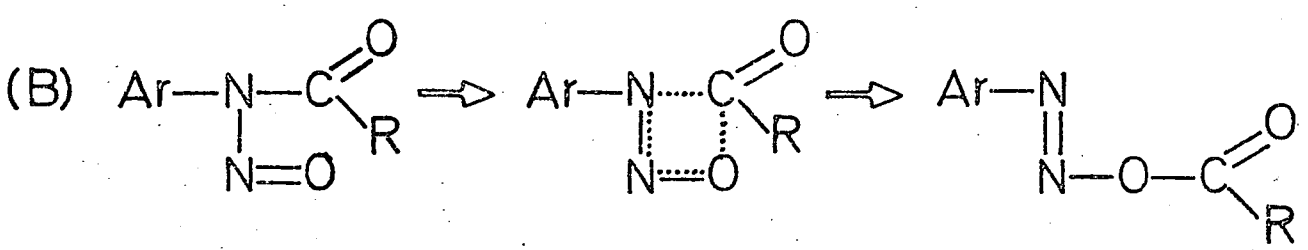
Elucidation of Mechanism

The mechanism of Hey and Butterworth[86] was challenged eleven years later by Huisgen and Horeld[87] who noted that N-nitrosoacetanilide coupled with β-naphthol at the same rate as nitrogen was eliminated in the absence of the phenol. In order to explain this they suggested that the intermediate common to both these reactions must be the covalent diazoacetate. As a consequence, they proposed a mechanism in which homolysis was fast and the rearrangement, rate-determining.

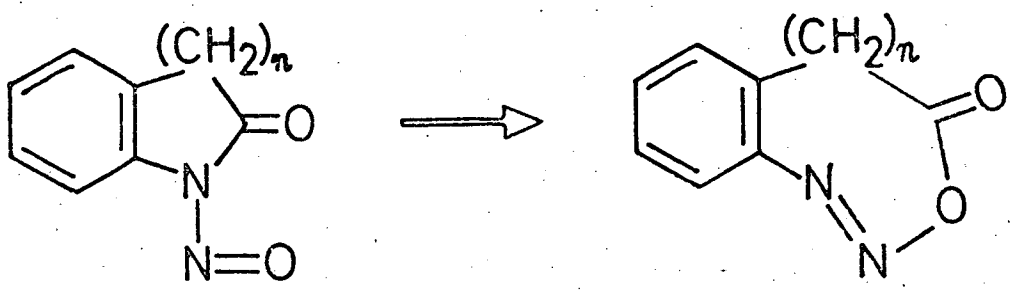
$$Ph{\cdot}N(NO)Ac \xrightarrow{Slow} Ph{\cdot}N{:}NOAc \xrightarrow{PhH} Ph_2 + N_2 + CH_3CO_2H$$

Attention was next centred on the mechanism of rearrangement of the acylarylnitrosamine to the diazo ester. Hey[88] concluded from his previous kinetic studies that only two mechanisms were possible: a "unimolecular" mechanism, A, involving ionic dissociation and recombination of the ions, and an "intramolecular" mechanism, B, in which the oxygen of the nitroso group functioned as a nucleophile.





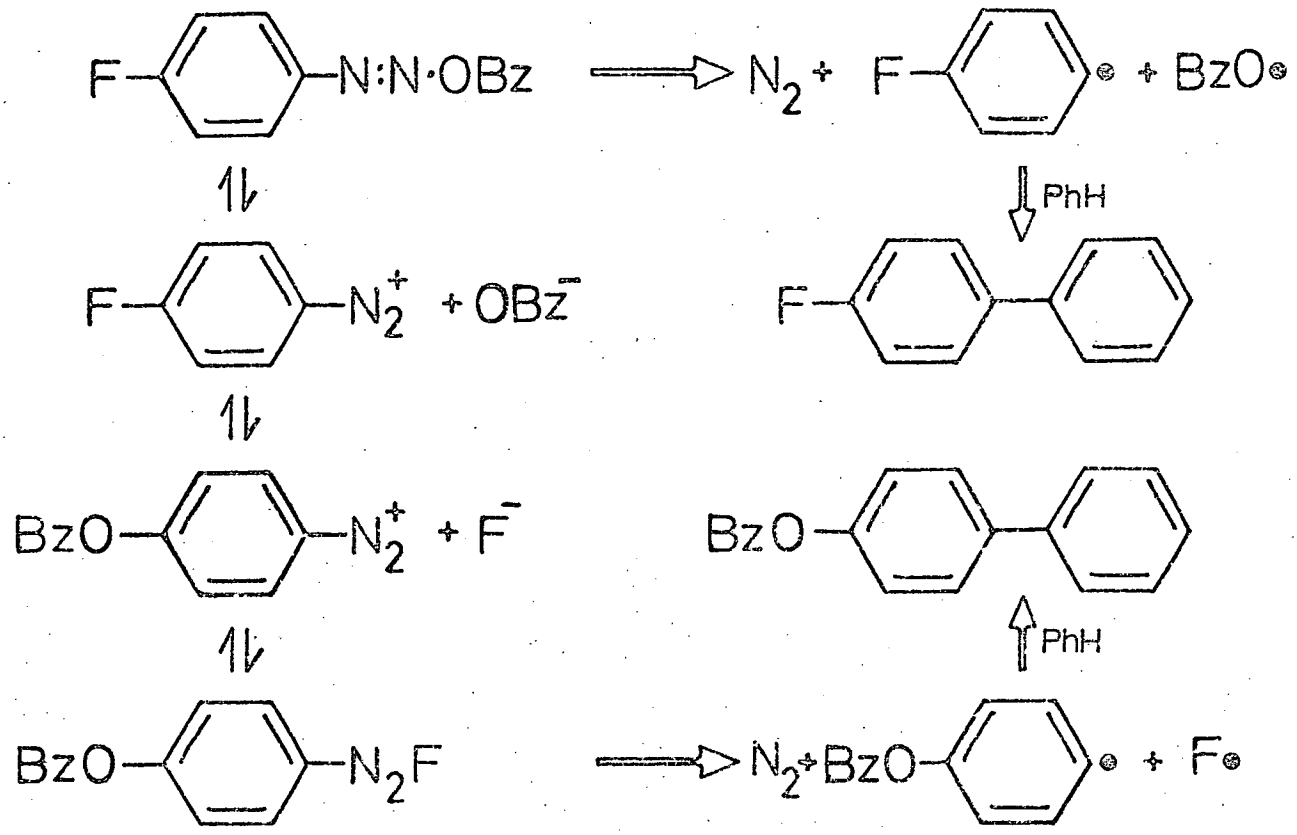
By varying Ar and R as well as the solvent, Hey looked for variations in the reaction rate which were to be expected if an ionic mechanism was operating. Similar values of the first order rate constant, however, were found for all nitrosamides and Hey concluded that an intramolecular mechanism was indicated, a conclusion fully endorsed by the independent studies of Huisgen.[89] Compelling evidence for mechanism B was later provided by Huisgen[90] who examined the rearrangements of N-nitrosobenzolactams (31) to cyclic diazoesters. Only when n was greater



(31)

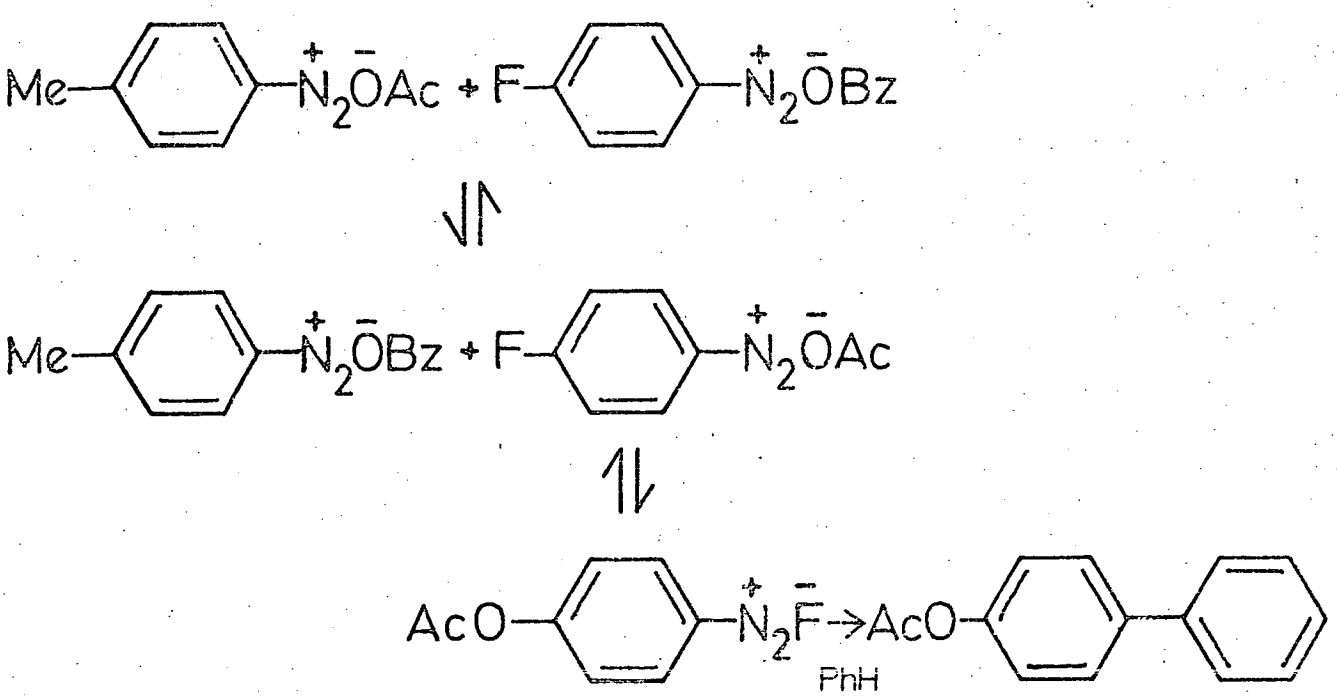
than or equal to three, did rearrangement occur, a result consistent with ring strain considerations, since, for the trans-configuration, a nine-membered ring will be the smallest unstrained structure.

The next major advance in the elucidation of the overall mechanism was the demonstration by Suschitzky[91] that a concurrent dual mechanism for the breakdown of acylarylnitrosamines occurred when an ortho- or para-fluorine atom was present. Thus decomposition of N-(4-fluorophenyl)-N-nitrosobenzamide in benzene gave not only the 4-fluorobiphenyl via homolytic substitution by the p-FC_6H_4• radical, but also an equal amount of 4-benzoyloxybiphenyl. Corresponding results were obtained with fluorine in the ortho-position (but not meta) and with other acyl groups. Suschitzky rationalized these observations by postulating the existence of arenediazonium acetate ion pairs in which the fluorine is rendered labile towards nucleophilic attack by the anionic partner (Scheme 4). That ion-pair formation was not restricted to a few acylarylnitrosamines was demonstrated by allowing each of a series of substituted



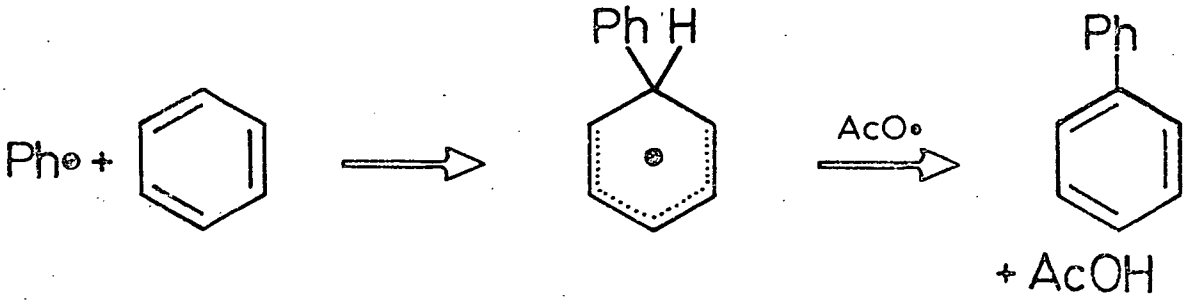
Scheme 4

N-nitrosoacetanilides to decompose in benzene containing p-fluoro-N-nitrosobenzanilide. Without exception, the mixed product, 4-acetoxybiphenyl was formed, confirming the formation of ion pairs by both nitrosamides with subsequent ion exchange (Scheme 5).

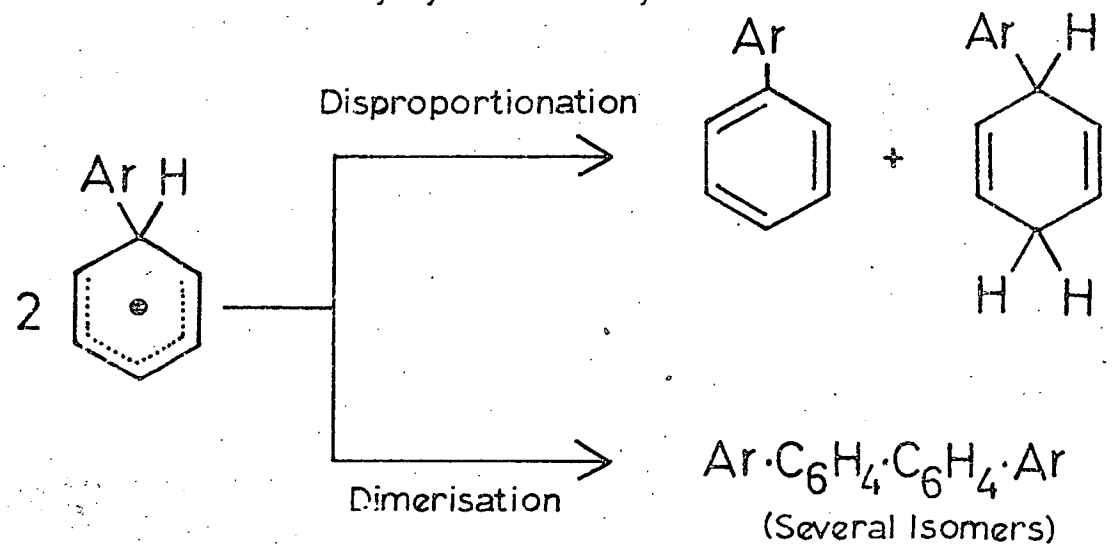


Scheme 5

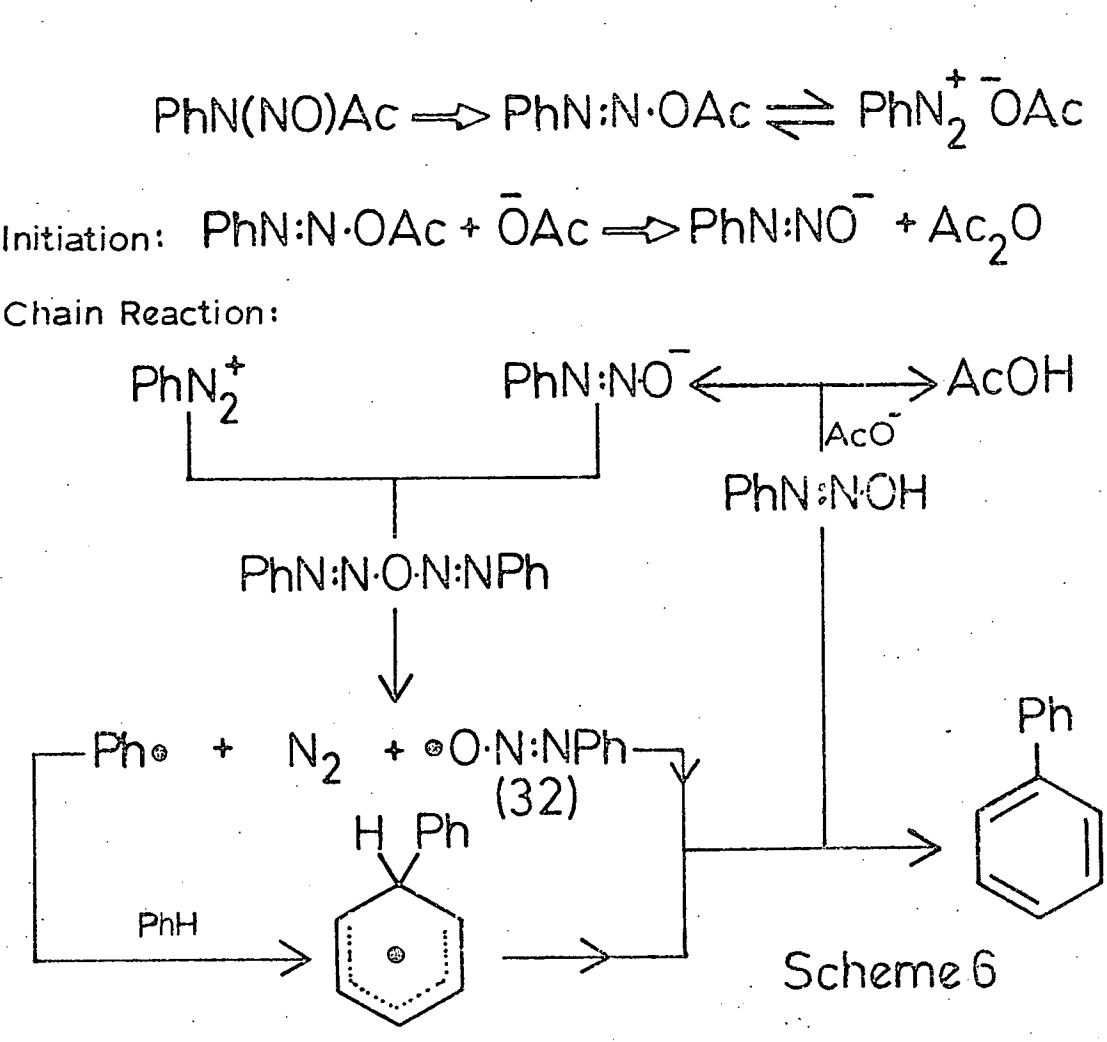
By 1964, two outstanding problems clouded an otherwise satisfactory understanding of acylnitrosamine decomposition. Firstly, the origin of acetic acid, present in high yield in all reactions, was unexplained. Suschitzky[91] had suggested that acetic acid was formed via hydrogen abstraction by acetoxyl radical from the phenylcyclohexadienyl radical. Such a scheme,



however, was incompatible with the known instability of the acetoxyl radical,[92, 93] whose rapid fragmentation to a methyl radical and carbon dioxide was established. The absence of significant amounts of carbon dioxide in the decomposition had also been noted by several workers.[87, 92] Secondly, the lack of quateraryls and dihydrobiaryls in the reaction[94] was puzzling since diaroyl peroxides were known to decompose in benzene to give products derived from disproportionation and dimerisation of arylcyclohexadienyl radicals.[9]

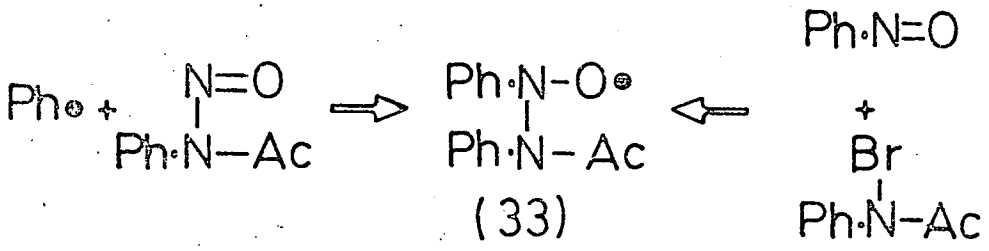


The complete absence of such products defied substantiated explanation until 1964 when Rüchardt and Freudenberg[95] advanced what appeared to be a complete explanation of the mechanism (Scheme 6), and one which could be successfully extended to the Gomberg reaction.[96] They suggested that a long-lived π-type free radical, (phenylazo)oxyl (32), functioning as a chain carrier, was capable of rapid oxidation of the phenylcyclohexadienyl radical

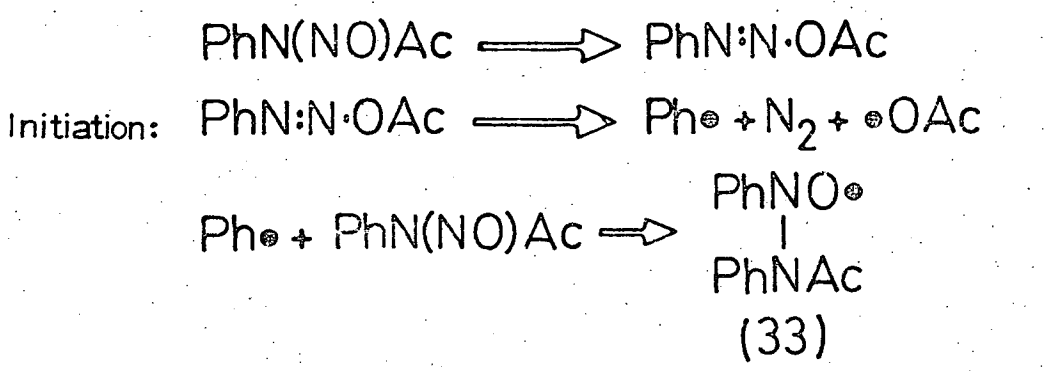


before disproportionation or dimerisation could occur. That acetate ions and not acetoxyl radicals were involved readily explained the genesis of acetic acid and lack of carbon dioxide. Finally, their mechanism invoked the intermediacy of ion pairs, which Suschitzky had shown to be present.[91] Qualified support for this mechanism followed[97] with the observation of a long-lived e. s. r. signal, which Rüchardt assigned to his diazotate π-radical (32).

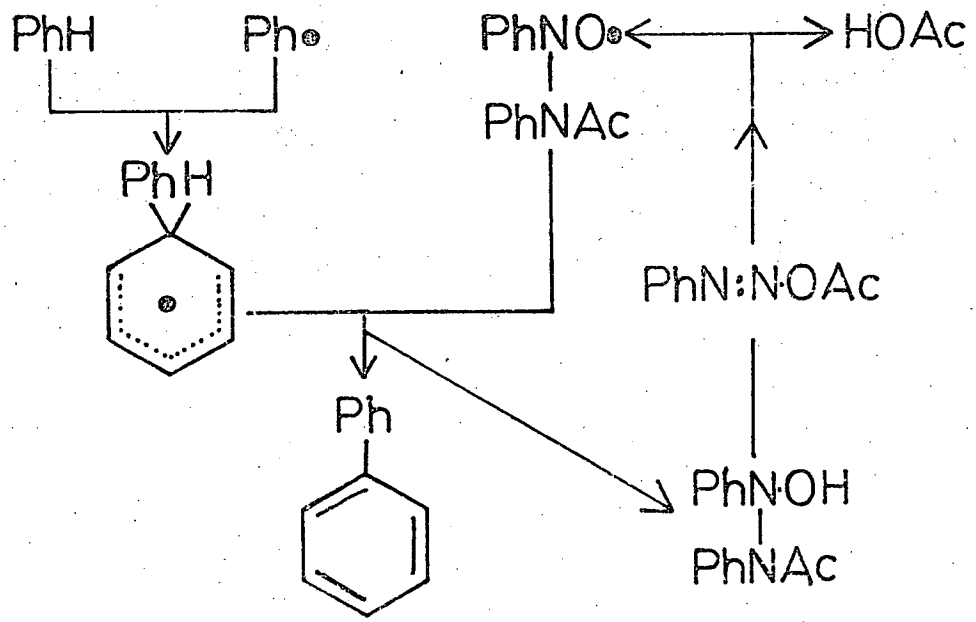
The origin of this e. s. r. signal, however, was soon called into question by Hey[98] who contended that the observed signal was that of a nitroxide, (N-phenylacetamido)phenyl nitroxide (33) (PAPN), produced by phenyl radical addition to N-nitrosoacetanilide.



Confirmation of this hypothesis followed when Chalfont and Perkins[99] synthesised the nitroxide (33) from nitrosobenzene and N-bromoacetanilide and showed its e.s.r. signal to be identical to that observed by Rüchardt. Two further independent syntheses confirmed this assignment.[100] As a result of these new developments, Chalfont and Perkins[99] proposed a modified mechanism in which the PAPN radical adopts the role of oxidant and chain carrier (Scheme 7).



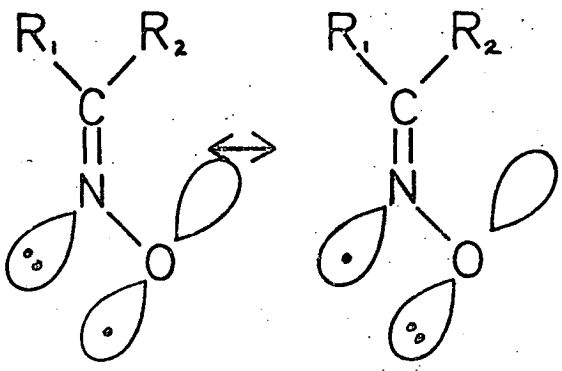
Chain Reaction:



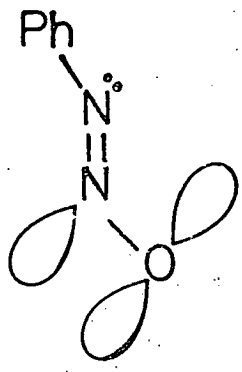
Scheme 7

A subsequent e.s.r. study of the reaction, conducted by Cadogan, Paton and Thomson,[101] however, revealed that the Perkin's signal was not present in all solvents and that the intensity of the signal was weak in those solvents having an easily abstractable hydrogen atom. Of major significance, however, was their

observation that a second signal, consisting of nine lines arranged as a triplet of triplets, was present in all solvents, a signal which was attributable to the (phenylazo)oxyl radical (32). Cadogan concluded that the PAPN radical was not the major chain carrier but rather a minor side-product. As a result of this new evidence, Cadogan suggested that Rüchardt's original mechanism (Scheme 6) was still tenable with the one exception that the (phenylazo)oxyl radical is a σ- rather than a π-radical, this being suggested by analogy with the values of splitting constants already known for the related σ-iminoxy radical[102] (34).



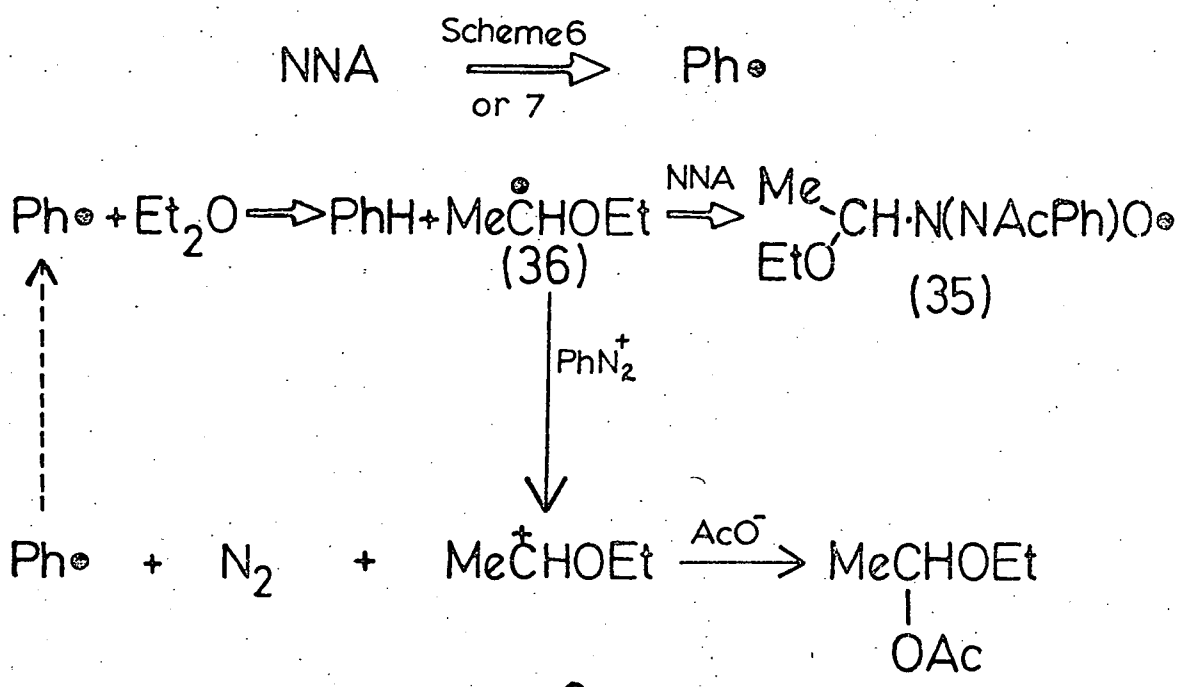
(34)



(32)

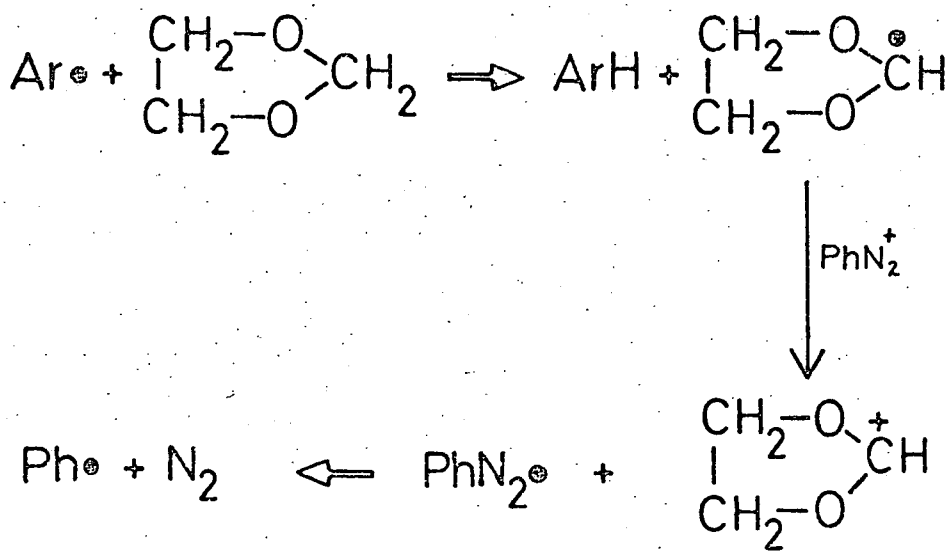
Thus the large a_N value of 30.7 gauss, observed by Cadogan, was consistent with the unpaired electron occupying a molecular orbital in the plane of the phenyl ring and, therefore, orthogonal to the molecular π-system. Furthermore, variation of the <u>para</u>-substituent on the aryl ring had little effect on the a_N value, unlike the case of a π-nitroxide radical where Hammett behaviour is exhibited.

Further insight into the mechanism resulted from an e.s.r. study of the decomposition of NNA in diethyl ether[103] which gave no signal corresponding to the σ-PhNNO$\cdot$ radical but instead an intense signal believed to arise from the nitroxide radical (35). Such a structure pointed to the intermediacy of the 1-ethoxyethyl radical (36), and hence to the mechanism outlined in Scheme 8. Thus electron transfer between the diazonium cation and the α-ethoxyethyl radical produces a phenyl radical, which then acts as the chain



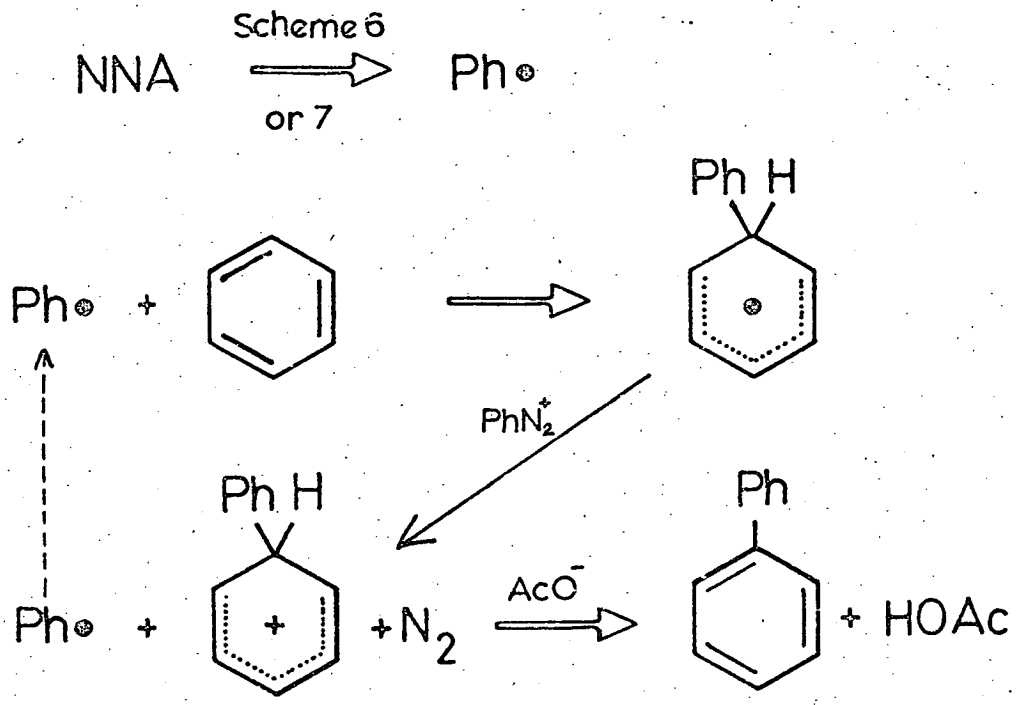
Scheme 8

carrier, and the α-ethoxyethyl carbonium ion which is scavenged by acetate to give 1-ethoxyethyl acetate (known from previous work[104] to be formed in 22% yield). Prior to this a similar redox mechanism had been proposed by Rüchardt and Werner[105] in the Meerwein reaction of diazonium salts in 1, 3-dioxolan, the propagation steps from which are shown in Scheme 9.



Scheme 9

By analogy with the two previous mechanisms, Cadogan[106] has suggested that a redox-transfer reaction, in which a phenyl radical acts as the chain carrier, may well operate in the decomposition of N-nitrosoacetanilide in benzene (Scheme 10),



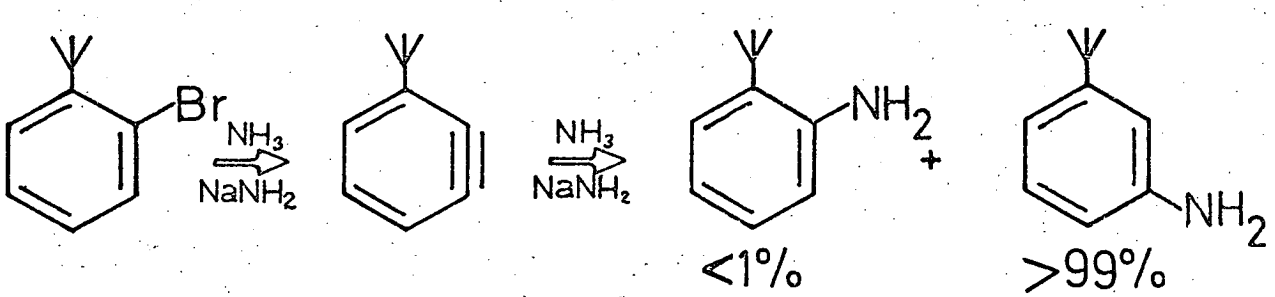
Scheme 10

particularly in the dilute solutions usually employed in these reactions. Thus once initiation has occurred via scheme 6 or 7 (or both), the redox-transfer gives rise to a phenyl radical and the phenylcyclohexadienyl cation, the immediate precursor of biphenyl.

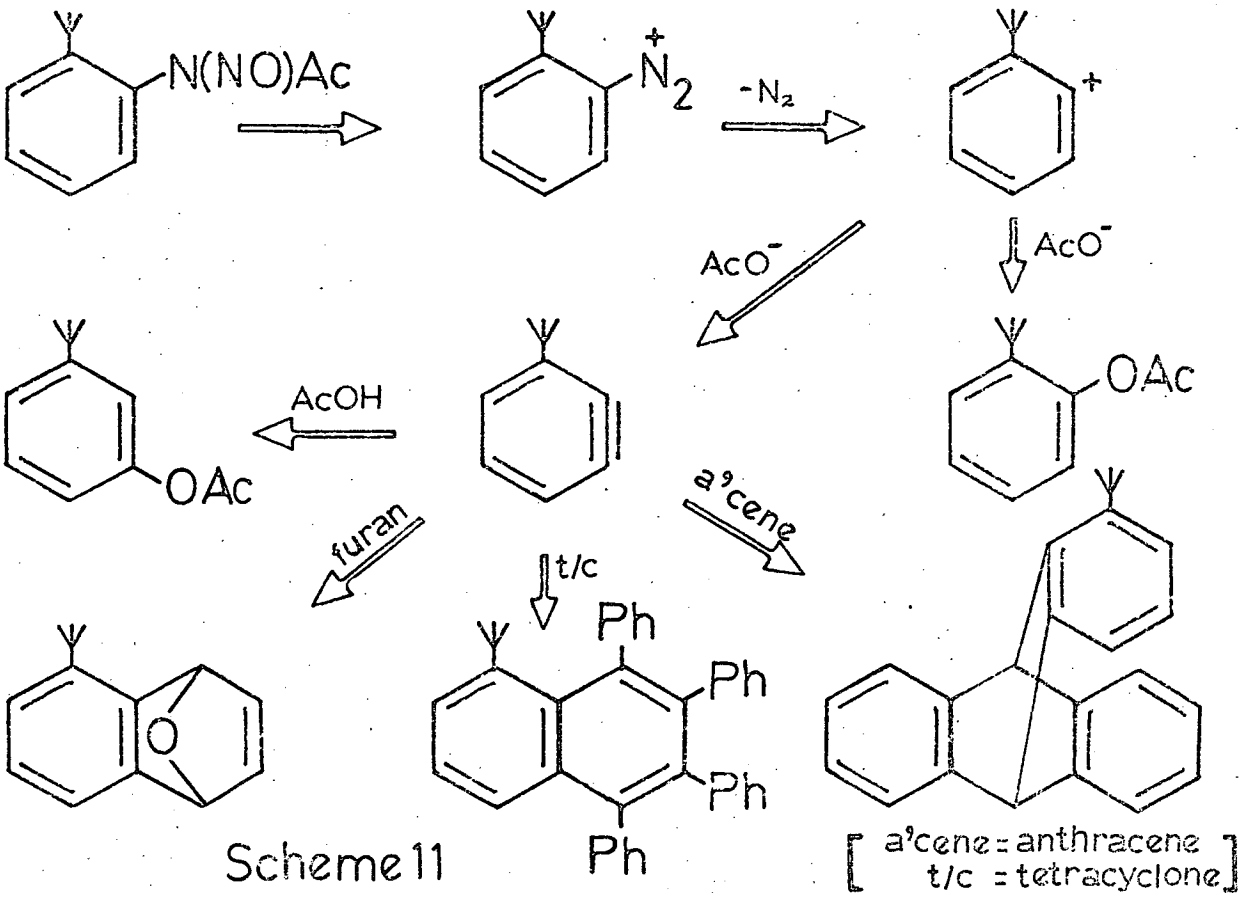
Aryne Participation

In 1954, Cadogan, Hey and Williams[107] reported that while 4-t-butyl-N-nitrosoacetanilide decomposed in benzene to give the expected biaryl, 4-t-butylbiphenyl, the o-isomer yielded a mixture of isomeric t-butylphenyl acetates with only a trace (2%) of biaryl, a result later confirmed by Rondestvedt.[108] Ten years later, Cadogan and Hibbert[109] in a reinvestigation of this reaction found that only the ortho- and meta-t-butylphenyl acetates were present

(46%) in the ratio 2:1. When this reaction was repeated in the presence of anthracene, 2-t-butyltriptycene was isolated in 9% yield, and the ester mixture (20%) was found to contain relatively more 2-t-butylphenyl acetate. Cadogan and Hibbert proposed the intermediacy of 3-t-butylbenzyne to account for these observations. The participation of an aryne intermediate was conclusively established[110] by competition experiments involving anthracene and 9, 10-dimethoxyanthracene and by the isolation of aryne adducts in the presence of furan and tetraphenylcyclopentadienone (tetracyclone). That the addition of aryne traps suppressed the formation of the m-isomer, leaving the level of 2-t-butylphenyl acetate unaltered, suggested that only the m-isomer was formed via the dehydro-aromatic intermediate. Consequently the 2-t-butylphenyl acetate was believed to arise from a mechanism in which a carbonium ion was formed (Scheme 11). That the meta-isomer should be formed preferentially from the aryne intermediate was explained on the basis of steric shielding by the bulky t-butyl group - a suggestion borne out by investigating the reaction of o-bromo-t-butylbenzene with sodamide in liquid ammonia.[110]



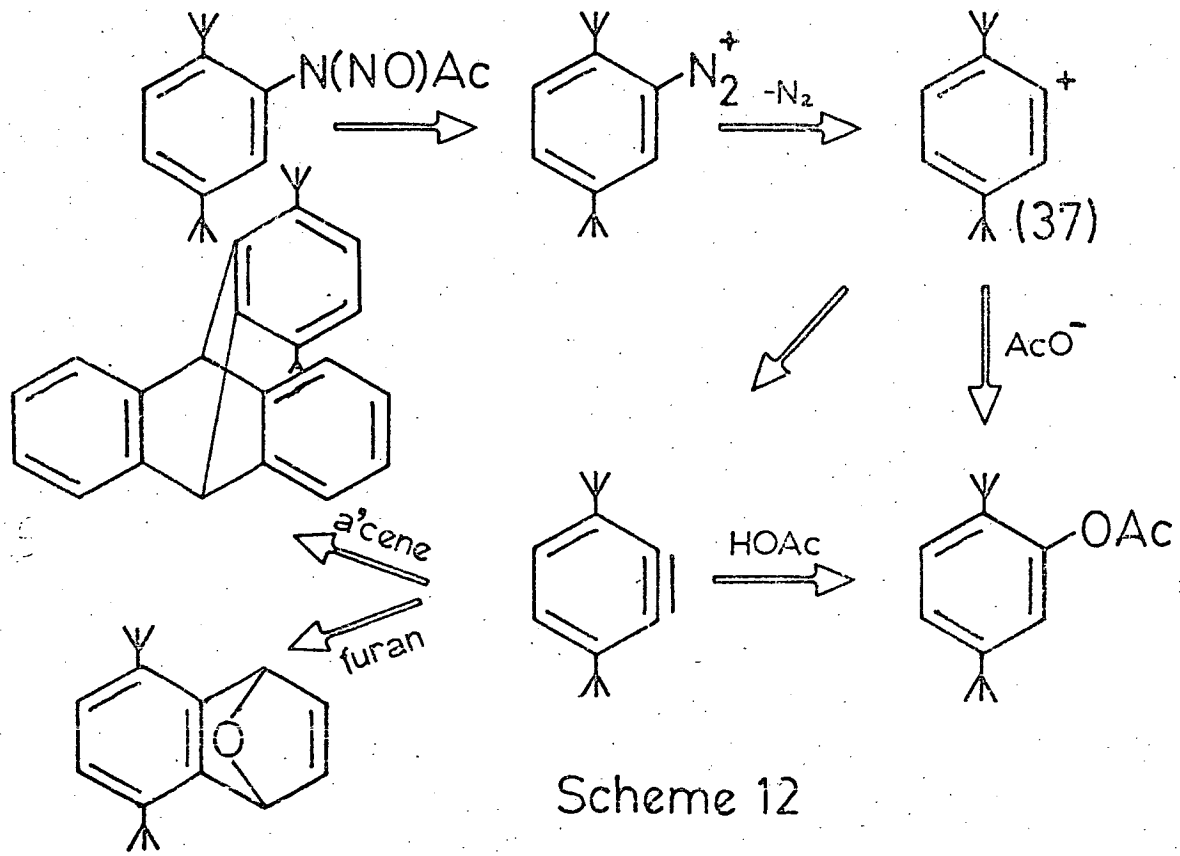
Thus the 3-isomer was formed to the virtual exclusion of the other, a result which can be best explained on steric grounds, since a corresponding reaction using o-bromomethylbenzene gave almost equal amounts of isomeric anilines, thereby discounting an electronic effect. The following scheme was proposed by Cadogan for the decomposition of 2-t-butyl-N-nitrosoacetanilide. That t-butylbenzyne should react with acetic acid, unlike benzyne itself, was explained on the basis of other reactions being energetically



Scheme 11

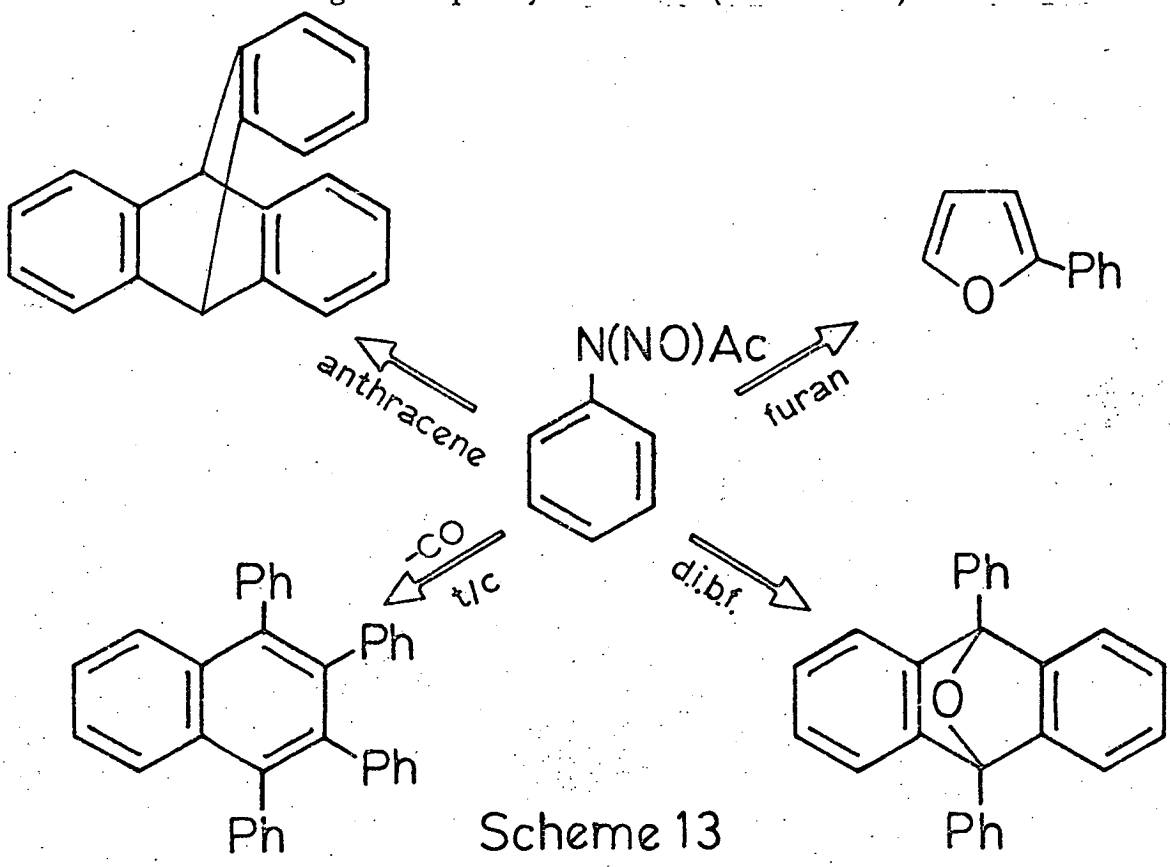
[a'cene = anthracene
t/c = tetracyclone]

unfavourable because of the steric impediment. This argument was strengthened by the observation that 2, 5-di-t-butyl-N-nitrosoacetanilide reacted almost exclusively with acetic acid to give 2, 5-di-t-butylphenyl acetate.[110] In the presence of furan and anthracene, small yields of adduct were obtained (Scheme 12).



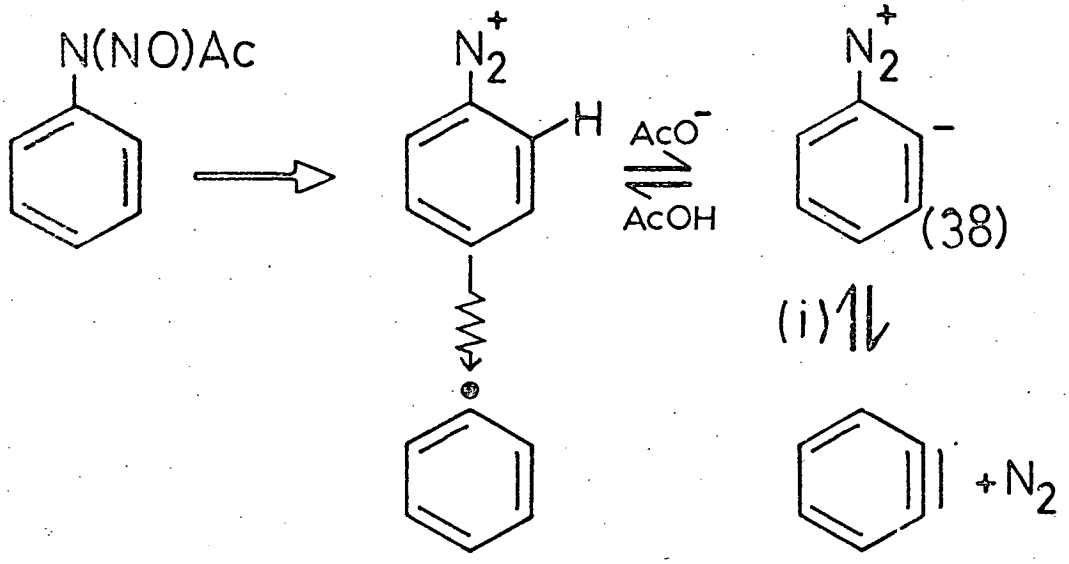
Scheme 12

Brydon[111] soon demonstrated, however, that the ability of t-butyl substituted N-nitrosoacetanilides to form arynes did not constitute a special case when he showed that N-nitrosoacetanilide itself gave not only varying amounts of radical derived products, but also benzyne adducts with tetracyclone (t/c), anthracene and 1, 3-diphenylisobenzofuran (d.i.b.f.), but, very surprisingly, not with furan which gave 2-phenylfuran. (Scheme 13)



Scheme 13

Of special interest was Brydon's observation that while N-nitroso-acetanilide in benzene gave 50% biphenyl, only trace amounts were isolated from the reaction carried out in the presence of tetra-cyclone. Radical or carbonium ion interception by the diene to give tetraphenylnaphthalene was ruled out by control experiments.[111] Thus Cadogan considered the possibility that an equilibrium may exist between the intermediate precursors to the radical and aryne derived products.[112] (Scheme 14) He considered the reversibility of (i) unlikely, however, and so concluded that the intermediate in the decomposition of N-nitrosoacetanilide was a benzynoid species, probably the betaine (38), capable of reacting with reactive dienes

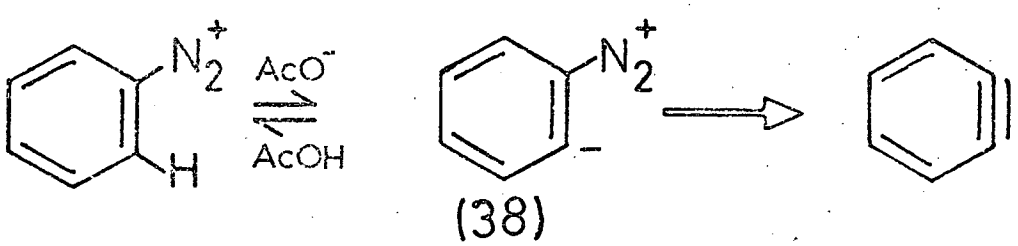


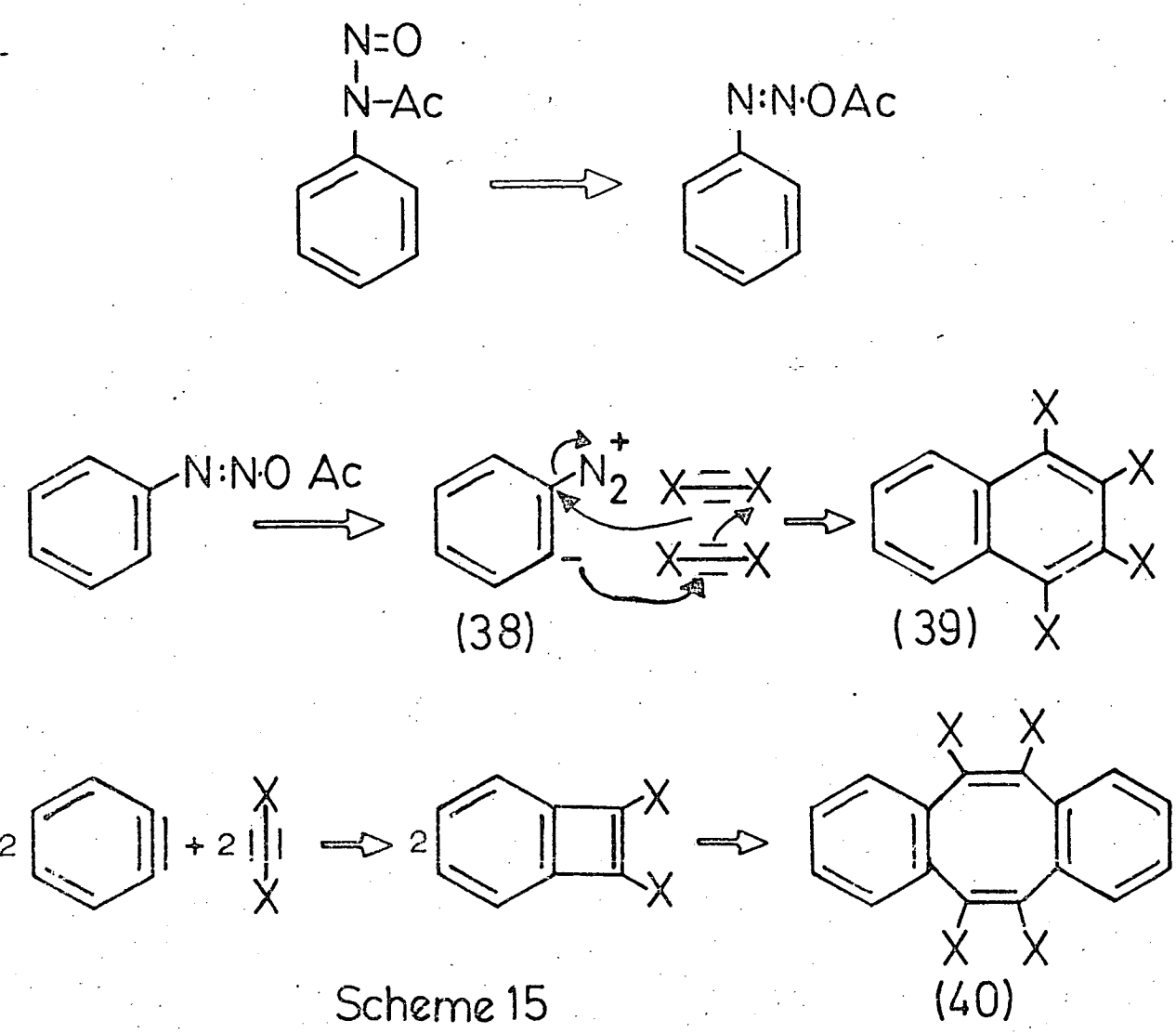
Scheme 14

but not with furan.

Cook,[112] however, presented compelling evidence for the intermediacy of a true benzyne intermediate by showing that for a series of arynophile pairs, identical competition ratios were obtained from authentic benzyne, and benzyne from N-nitroso-acetanilide. Furthermore, Cook[113] showed that while N-nitroso-acetanilide gave 1, 2, 3, 4-tetramethoxycarbonylnaphthalene (39) when allowed to decompose in benzene in the presence of dimethyl-acetylenedicarboxylate (DMAD), (X≡X), authentic benzyne gave the dibenzocyclooctatetraene (40). (Scheme 15). This he interpreted as evidence for the betaine (38) previously considered by Cadogan.[112]

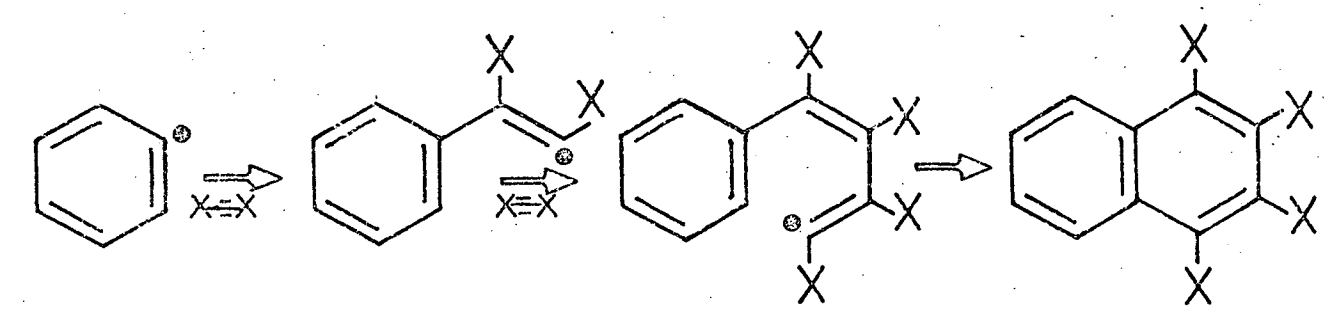
In the light of this latter information, Cadogan proposed that an E_1cb mechanism best represented the route to benzyne from N-nitrosoacetanilide.[111] (Elimination reaction mechanisms will be dealt with in more detail in the next section).



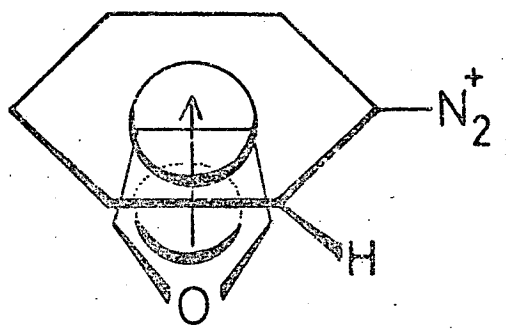


Scheme 15

Recent investigation[114] into the precise origin of (39) in the reaction of N-nitrosoacetanilide with D. M. A. D. has established that the substituted naphthalene is formed via a novel annelation reaction involving a phenyl radical and two molecules of D. M. A. D. Thus a shadow of doubt was once again cast over the intermediacy of the betaine.

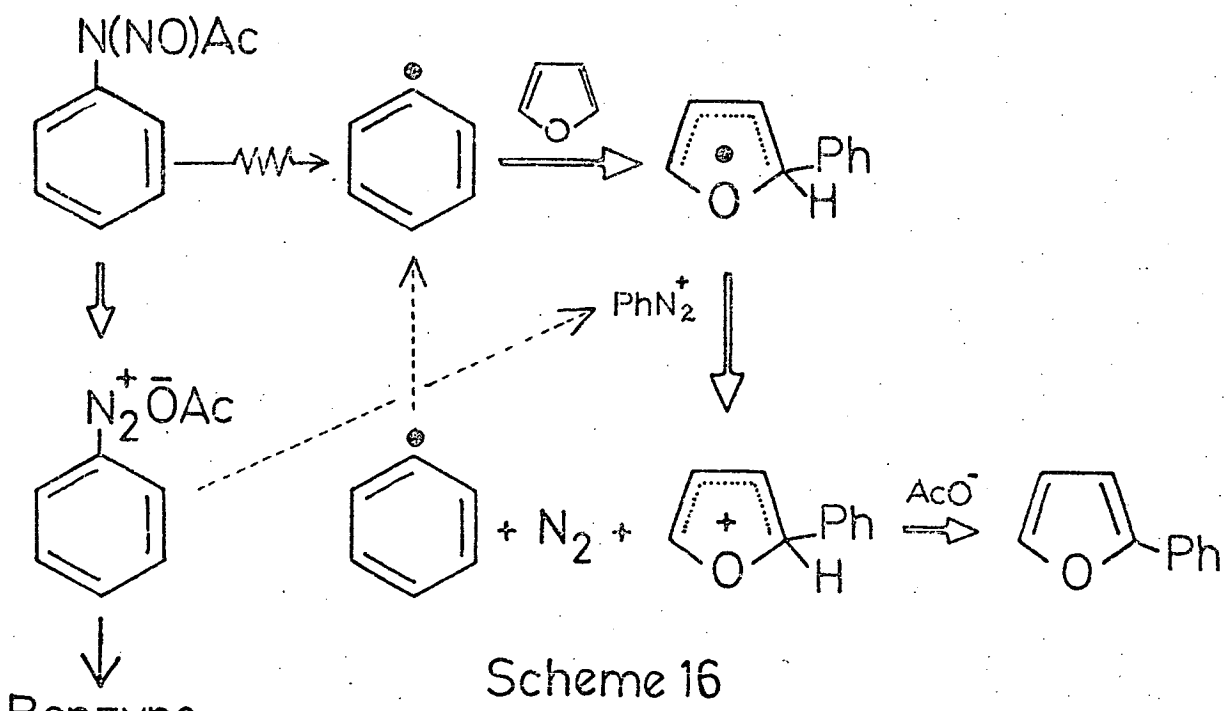


Cook's discovery that a true benzyne intermediate was involved in the decomposition of N-nitrosoacetanilide threw the anomalous behaviour of furan into question. Although Mitchell[115] and Rüchardt[116] were later to isolate the furan-benzyne adduct in low yield, no explanation existed for the high yield of 2-phenylfuran formed in this reaction or for the effect furan had on suppressing the formation of benzyne adducts with other arynophiles.[113] Mitchell established that the rate ratio $K^{furan}_{benzene}$ for the phenylation of equimolar mixtures of furan and benzene was high for those radical sources incorporating the benzenediazonium cation as the radical precursor. He advanced two possible explanations for this: firstly, the furan formed a π-complex (41) with the diazonium cation thereby rendering the ortho-proton less acidic, or secondly, a redox scheme, analogous to that proposed



(41)

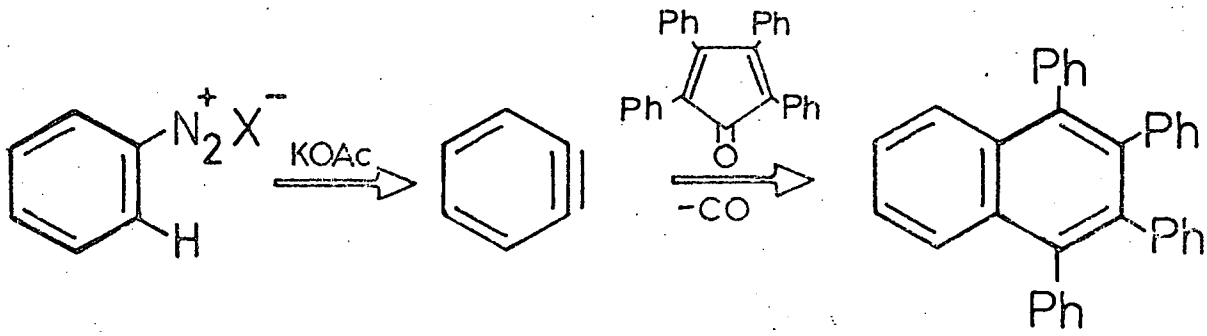
for the decomposition of N-nitrosoacetanilide in benzene[106] and diethyl ether[103] applied in this case. (Scheme 16).



Scheme 16

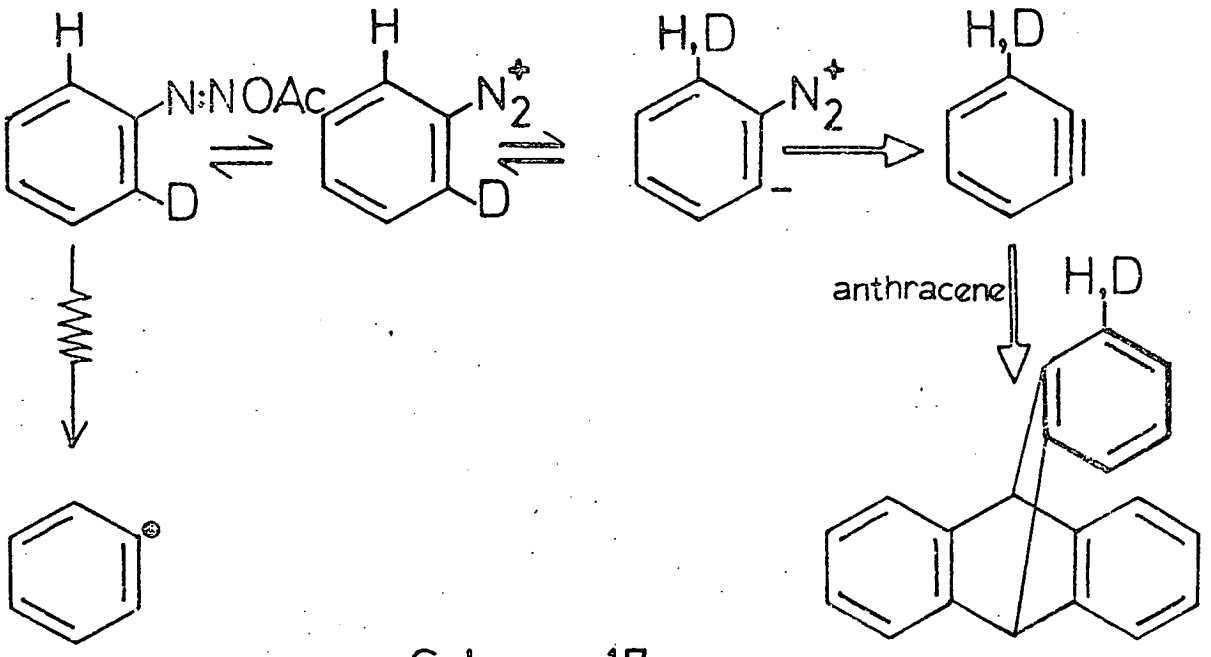
Thus Scheme 16 invokes the known affinity of the furan nucleus for electrophilic species and illustrates how removal of the diazonium cation in the fast redox chain reaction serves to suppress the formation of a benzyne/benzynoid species and hence of aryne adduct.

In 1970, Rüchardt[117] reported that the decomposition of arenediazonium salts in the presence of acetate ion gave good yields of arynes and he interpreted this result in terms of an E_2 elimination mechanism, initiated by the weakly basic acetate ion.



He suggested that the success of this reaction precluded the "arynoid intermediate" previously described by Cadogan,[103, 112] although he advanced no reason for this conclusion.

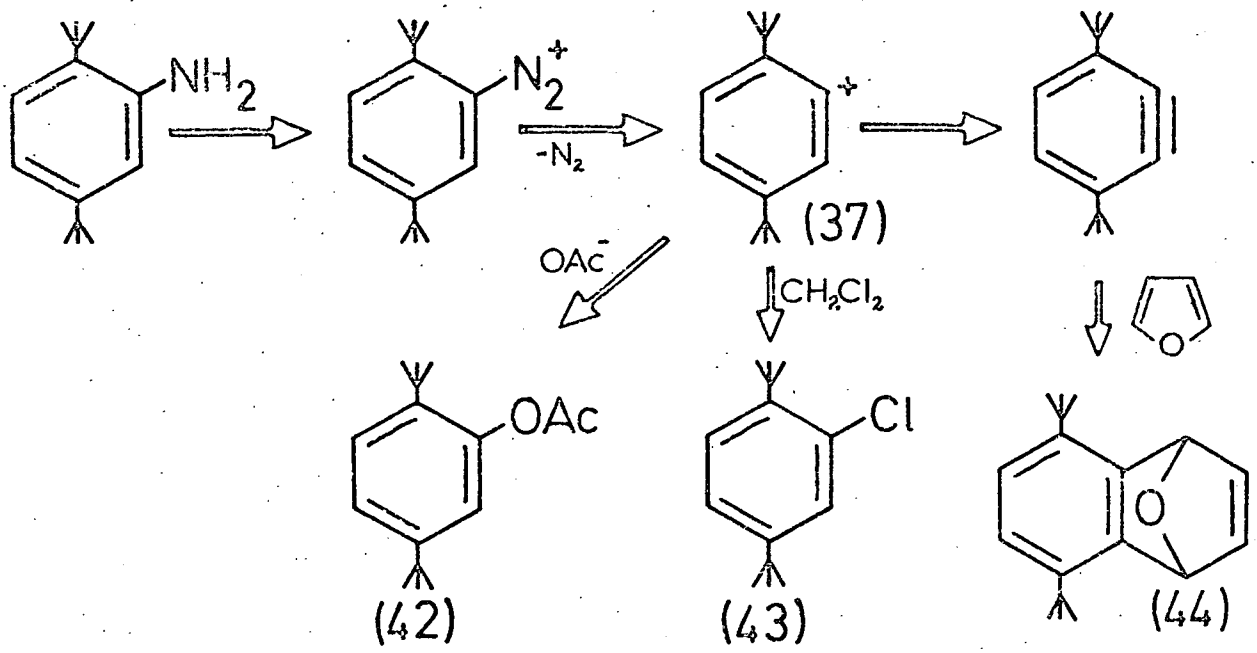
More recently, Heaney,[118] has presented evidence for the E_1cb mechanism previously suggested by Cadogan.[111, 119] He reported extensive loss of the isotopic label in the reaction of o-deuteriobenzenediazonium chloride with potassium acetate in the presence of acetic acid, and correctly concluded that such a result was incompatible with an E_2 mechanism, which would have resulted in the retention of more than half of the deuterium content. Heaney concluded that benzyne is formed from the benzenediazonium ion by an E_1cb mechanism (Scheme 17), in which extensive removal of the ortho-deuterium can occur before decomposition to benzyne.



Scheme 17

New Synthetic Approaches

In view of the detailed study devoted to the mechanism of aryne formation from N-nitrosoacetanilide and related compounds, it is not surprising that new synthetic routes to arynes have been developed as a consequence. Thus Franck and Yanagi[120] established that in situ diazotisation of 2, 5-di-t-butylaniline in methylene chloride in the presence of a carboxylic acid and furan, afforded the 2, 5-di-t-butylphenyl ester (42), 2, 5-di-t-butylchlorobenzene (43) and 5, 8-di-t-butyl-1, 4-dihydronaphthalene-1, 4-endoxide (44). Franck suggested a mechanism (Scheme 18) closely related to that of Cadogan[110] for the decomposition of 2, 5-di-t-butyl-N-nitrosoacetanilide in furan, in which an intermediate carbonium ion (37) is partitioned between substitution and elimination pathways. This was particularly interesting because Brydon[121] had previously discovered that diazotisation of other substituted anilines did not give benzyne adducts in significant yield (<1%), thus re-emphasizing the anomalous behaviour of the t-butyl-substituted acylarylnitrosamines. It was soon established[122, 123] that aryne formation from



Scheme18

diazonium precursors was suppressed by even trace amounts of water, which is a product of the in situ diazotisation of anilines with pentyl nitrite.

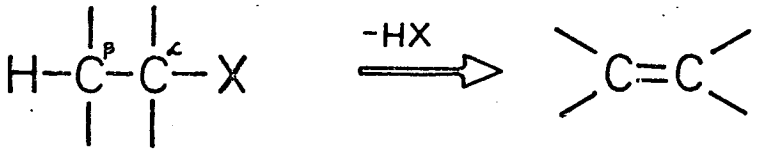
$$ArNH_2 + RONO + PhH \longrightarrow Ar{\cdot}Ph + ROH + N_2 + H_2O$$

Thus while acetate is basic enough in anhydrous benzene to remove an ortho-proton from the diazonium cation, solvation of the anion occurs in the presence of water thus leading to reduced basicity. That an aryne can be successfully formed from the diazotisation of 2, 5-di-t-butylaniline can be explained by the increased acidity of the o-proton in the aryl cation (37) counterbalancing the effect of water. To overcome the suppressive effect of water, the diazotisation was carried out in the presence of acetic anhydride, which could function both as a dehydrating or acetylating agent. If the latter occurs, the nitrosation by pentyl nitrite would then give N-nitrosoacetanilide in situ. This hope was vindicated when aryne

adducts were obtained with tetracyclone (32%) and anthracene (10%).[124] A recent development of this reaction, in which nitrosation of acetanilide is effected by treatment with 4-chlorobenzoyl nitrite has realised aryne adducts in yields up to 80%.[115, 124]

4. BASE-INITIATED ELIMINATION REACTIONS

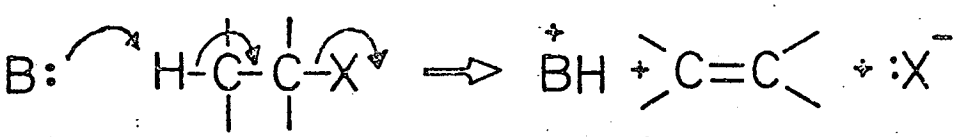
The most common type of elimination reaction is the base-initiated β-elimination of H-X from adjacent carbon atoms in an organic molecule. Thus a proton is lost from one of two adjacent carbon atoms and a leaving group (X) from the other. The atom bearing the substituent -X is designated the α-carbon.



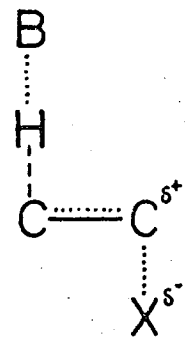
Three general types of base-promoted eliminations have been characterised,[125] namely, anionic, concerted and cationic processes. The borderlines between these mechanisms, however, are not sharp and it is often difficult to conclude unambiguously which mechanism is operative. Throughout this section, the use of isotopic labelling will be emphasized as a diagnostic tool in the elucidation of elimination mechanisms. It should not be forgotten, however, that many other measurements, e.g., adicity dependence, stereoselectivity and reactivity, leaving group effects, solvent effects and Hammett behaviour, are often essential to a complete mechanistic understanding.

The E_2 Mechanism

The concept of base-initiated elimination reactions was first introduced by Ingold[126] in 1927 to explain the formation of olefins from tetra-alkyl ammonium salts. Ingold proposed that the elimination proceeded via a single, concerted step in which β-hydrogen abstraction by base was accompanied by loss of the leaving group. Thus, in the transition state, the C-H and C-X bonds are both partially broken and the new C-C bond is partially formed.



The reaction follows second-order kinetics, first order in base and first order in substrate, and is classified as a bimolecular elimination (E_2). Although the E_2 mechanism proceeds via a single-stage process with no detectable intermediates, the subtle balance between the timing of bond-making and bond-breaking can vary with reactant structure, thereby giving rise to a spectrum of sub-mechanisms, differing in transition-state character.[125] Thus the E_2 mechanism, although concerted, need not be entirely synchronous, and it is possible to invoke three general types of E_2 transition state.[127] In structure (45), C-X rupture is far advanced



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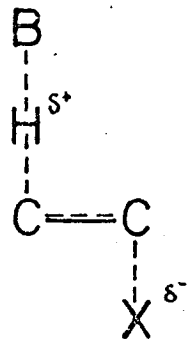

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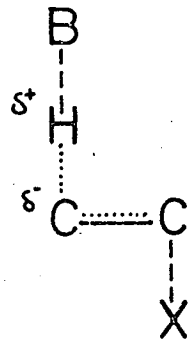
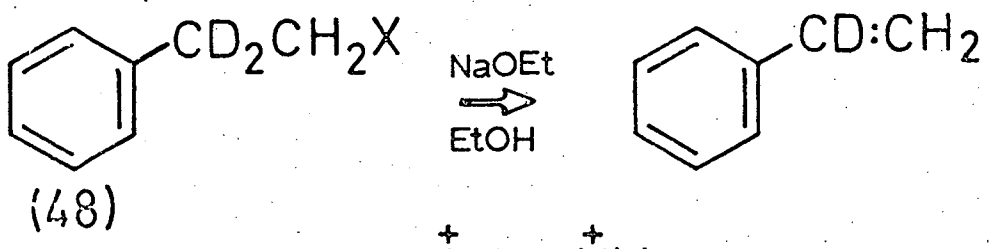


(47)

and the transition state resembles a carbonium ion. At the other extreme, an E_1cb-like (see later) transition state (47), with carbanionic character, can be pictured. The 'central transition state,' in which C-X and C-H rupture are equally advanced, is represented by structure (46). Using this variable transition state theory, Cram, Greene and DePuy[128] have been able to explain variations in the relative rates of bimolecular eliminations from the threo and erythro isomers of 1, 2-diphenyl-1-propyl derivatives resulting from variations in eclipsing effects in the transition state as the nature of leaving-group, base and solvent were changed.

The use of deuterium isotope effects in the elucidation of reaction mechanisms has proved to be an invaluable tool. The deuterium isotope effect of a synchronous three-centre proton transfer should be the theoretical maximum[129] (about seven) at room temperature (in the absence of quantal tunnelling[130]) when

the base and substrate exert equal control over the proton in the transition state. Several elimination reactions believed to proceed via a concerted mechanism exhibit this maximum isotope effect.[125] Any fall in the k_H/k_D ratio below this maximum indicates an approach of the mechanism towards one of the limits in which proton transfer has only just begun or is nearly finished in the transition state. Saunders[131] has used deuterium isotope effects in order to obtain a direct measure of the extent to which bonds are broken in the transition state of E_2 reactions of β-deuteriated-2-phenylethyl derivatives (48). He observed a variation in k_H/k_D values with leaving group, in the order $Br > OTs > \overset{+}{S}Me_2 > \overset{+}{N}Me_3$.



(48)

$X = Br, OTs, \overset{+}{S}Me_2, \overset{+}{N}Me_3.$

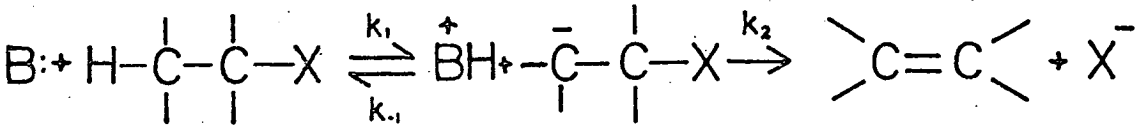
$k_H/k_D = 7{\cdot}1,\ 5{\cdot}7,\ 5{\cdot}1,\ 3{\cdot}0.$

Reference to Hammett ρ values shows a decrease in the order $\overset{+}{N}Me_3 > \overset{+}{S}Me_2 > OTs > Br$, and since a large ρ value implies a high degree of carbanion character, which is most easily achieved by a high degree of proton transfer, it is very probable that the extent of proton transfer in the transition state runs in the order $Br < OTs < \overset{+}{S}Me_2 < \overset{+}{N}Me_3$.

The range of k_H/k_D values (2-8) for well-documented E_2 processes[132] emphasizes the need for detailed study of a reaction system before concluding which particular mechanism is operative. The observation of a sizeable k_H/k_D, coupled with a substantial leaving effect (indicating a high degree of C-X bond breaking in the transition state) can, however, be interpreted as compelling evidence for an E_2 mechanism.

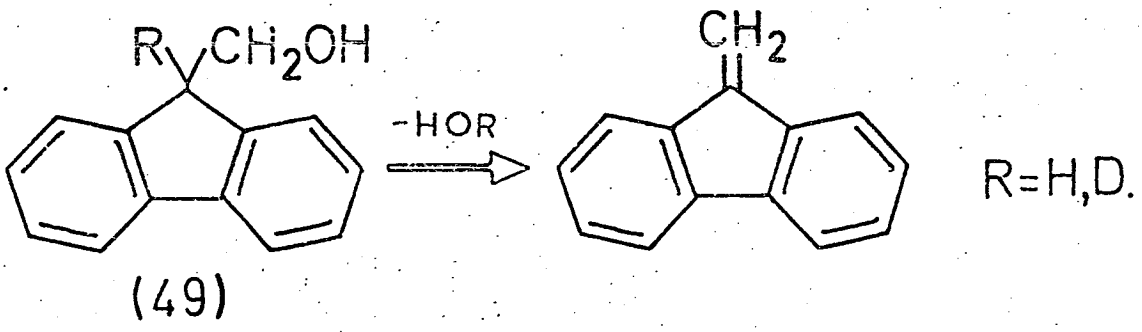
The E_1cb mechanism

The possibility of a two stage carbanion mechanism was first suggested by Hughes and Ingold[133] in 1933. Instead of simultaneous removal of the β-proton and loss of the leaving group, the proton is removed first to give a discrete carbanion intermediate and the leaving group is lost in a subsequent step.



Carbanionic eliminations fall into two distinct mechanistic categories: one in which $k_{-1} > k_2$, in which case a fast equilibrium is established between the carbanion and substrate, $(E_1cb)_R$; and another in which carbanion formation is slow and irreversible $(E_1cb)_I$, with subsequent rapid loss of the leaving group. In this case $k_2 \gg k_{-1}$. Both mechanisms obey second-order kinetics, but a kinetic demonstration of the reversible mechanism is possible since the reaction rate will show an inverse dependence on the concentration of the conjugate acid of the base.[134]

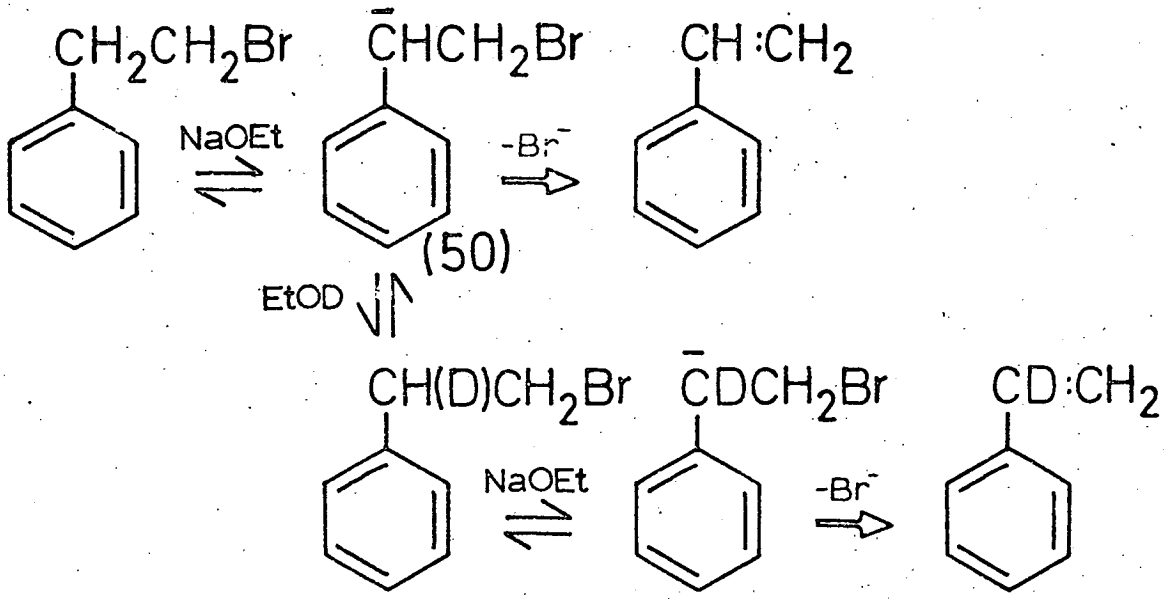
The use of isotope effects in elucidating the course of elimination reactions can be very useful, as already noted. McLennan[134] has argued that small primary isotope effects are to be expected for E_1cb reactions. While this is true of a pre-equilibrium carbanion mechanism, since deuterium exchange should occur before olefin formation becomes appreciable, the same does not apply for the irreversible E_1cb reaction.[132] O'Ferrall[135] has demonstrated that this is so and shown that a wide range of values is possible depending on the stability of the carbanion and the strength of the attacking base. He has recorded a k_H/k_D value of 7.5 for the loss of water from 9-fluorenylmethanol in t-butyl alcohol, a reaction he has shown to proceed via a carbanionic mechanism in which formation of a carbanionic intermediate is rate determining. No exchange accompanies elimination of ROH in this reaction,



(49)

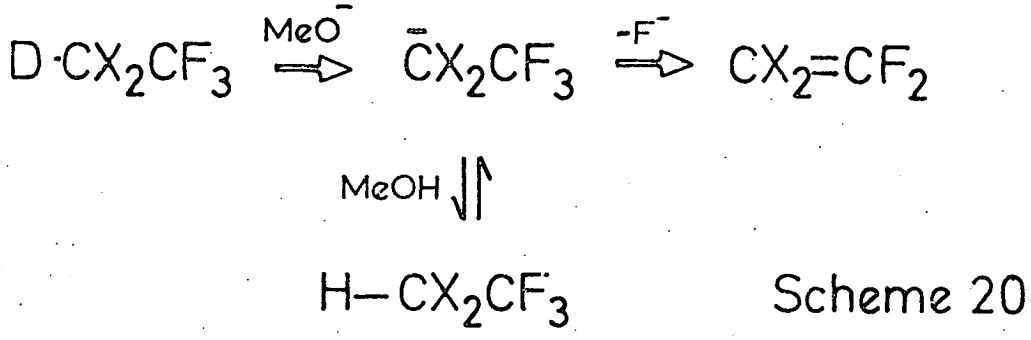
thereby excluding an $(E_1cb)_R$ mechanism. The choice of substrate is interesting here since (49) possesses a very poor leaving group (OH) as well as a hydrogen atom rendered acidic by the potential formation of an aromatic dibenzocyclopentadienide carbanion. Thus a carbanionic mechanism should be favoured.

The most frequently used criterion for the $(E_1cb)_R$ mechanism has been deuterium exchange in the unreacted substrate or product. Skell and Hauser,[136] who first suggested the value of this technique, have used it in the study of the base-initiated elimination of HBr from 1-phenyl-2-bromoethane a substrate believed at the time to possess a structure conducive to a carbanionic mechanism. They argued that if the first step in the reaction was the reversible formation of the anion (50), then the conversion, when carried out in deuteriated solvent, should be accompanied by incorporation of isotopic label into both substrate and product (Scheme 19).



Scheme 19

When the reaction was carried out in 'heavy' alcohol, however, both the unreacted halide and the styrene product were found to be free of deuterium. Thus a reversible carbanionic mechanism was discounted for this reaction. Hine,[137] however, has observed that deuterium exchange, in the reaction of 2, 2-dihalo-1, 1, 1-trifluoroethane with base, occurs much faster than elimination, suggesting an $(E_1cb)_R$ mechanism for this reaction (Scheme 20).

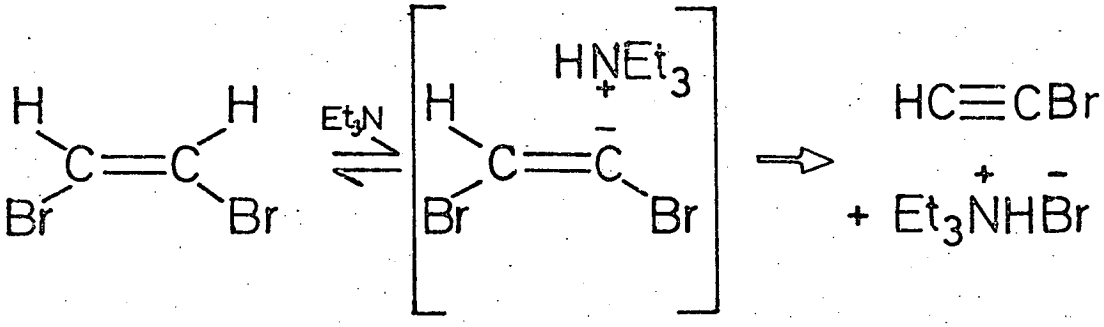


Scheme 20

Kŏbrich[138] has suggested that base-initiated eliminations from olefins proceed more readily via carbanions than their saturated counterparts because of the greater electronegativity of an sp_2 hybridised carbon over an sp_3. As with olefin-forming eliminations an E_1cb mechanism should be favoured when the leaving group is strongly bonded to carbon, and electron withdrawing groups are present to stabilise the carbanion. Thus it seems that all olefins with hydrogen and halogen substituents on the same unsaturated carbon atom, can undergo base catalysed H-D exchange.[138] This assertion has recently been challenged by Marchese,[139] however, who claims to have observed a concerted mechanism in the reaction of cis-β-bromo-4-nitrostyrene. Lack of exchange and a low kinetic isotope ratio (2. 2) has led him to postulate an E_2 mechanism although he concedes that his results are also consistent with an $(E_1cb)_I$ reaction.

In recent years, a third type of E_1cb mechanism has been invoked to explain some anomalous experimental results in carbanionic elimination reactions. This is the pre-equilibrium ion-pair or tightly solvated anion elimination $(E_1cb)_{IP}$, first

suggested by Kwok, Lee and Miller[140] in 1969, as a result of studies into the mechanism of dehydrobromination of cis-1, 2-dibromoethylene with triethylamine. Addition of $Et_3\overset{+}{N}D\ \bar{X}$ had no effect on the reaction rate, nor did it lead to deuterium exchange, thereby excluding an $(E_1cb)_R$ mechanism. Second order kinetics were obeyed and a substantial k_{Br}/k_{Cl} element effect was observed. The isotope effect, k_H/k_D, for elimination, however, was found to be unity, and Kwok noted that observed values of isotope rate effects for E_2 and $(E_1cb)_I$ reactions normally fall in the range k_H/k_D = 2-7.[132] On the basis of a few assumptions, he has shown that the isotope rate effect for the ion pair mechanism should be close to unity. Thus he has proposed the following scheme. The intimate ion pair (51) can either collapse

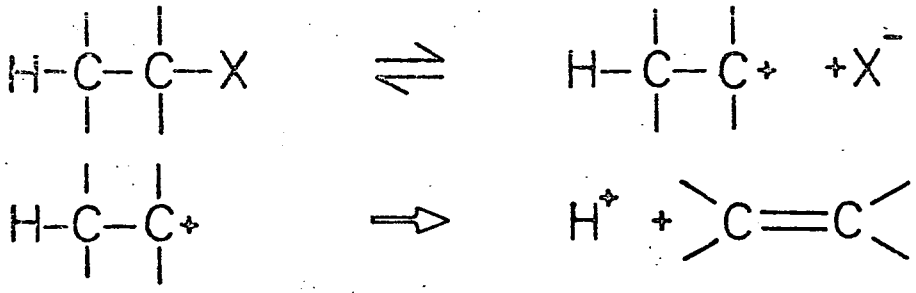


(51)

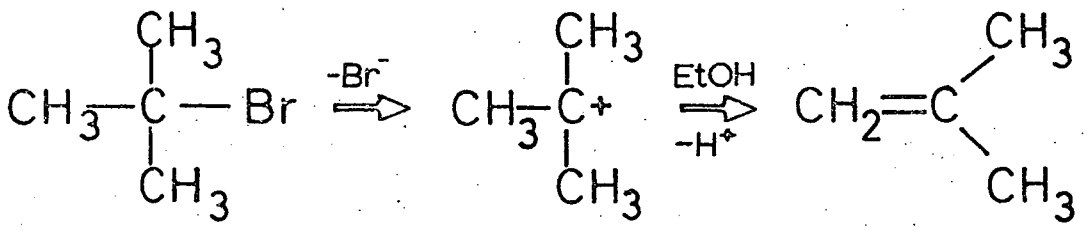
back to reactants or fall apart to give products. Triethylammonium ions, however, cannot be exchanged with those in the solvent 'pool.' In conclusion, Kwok has suggested that other 'low isotope effect' eliminations may proceed via the $(E_1cb)_{IP}$ mechanism.

The E_1 Mechanism

In 1935, Hughes[141] suggested a third type of elimination mechanism, in which initial slow ionisation of the substrate is followed by proton loss from the resulting carbonium ion. Three main factors favour this unimolecular or E_1 mechanism: a substrate capable of giving a stable carbonium ion; an ionising solvent; and



the absence of nucleophiles or strong bases. Formation of a carbonium ion will be favoured when the α-carbon is secondary or tertiary and, more particularly, when an α-phenyl or α-vinyl group is present. Evidence for the E_1 mechanism is derived mainly from kinetic studies, the reaction being first order in substrate but insensitive to addition of base.[125] Thus kinetic study has established that dehydrobromination of 2-bromo-2-methylpropane proceeds via an E_1 mechanism.[142] The relatively stable tertiary



(52)

carbonium ion (52), formed in this reaction, also undergoes unimolecular nucleophilic attack by ethanol, this constituting the major pathway (80%). Because the rate-determining step in an E_1 mechanism involves rupture of the C-X bond, a substantial element effect is observed.[132] The isotope rate effect, k_H/k_D, for the elimination will, of course, be unity. There follows a summary of the mechanistic classification of β-elimination reactions.

Symbol	k_H/k_D	Kinetic Order	Element Effect
E_2	2-8	2nd	Substantial
$(E_1cb)_R$	1.0	2nd	Substantial
$(E_1cb)_I$	2-8	2nd	Small
$(E_1cb)_{IP}$	1-2	2nd	Substantial
E_1	1.0	1st	Substantial

PROGRAMME OF RESEARCH

The isolation of aryne adducts from the decomposition of N-nitrosoacetanilide in benzene in the presence of various arynophiles provided evidence that benzyne, as well as phenyl radicals, was formed during the reaction. A puzzling feature of the decomposition emerged from the observation that while in the absence of an arynophile, high yields of biphenyl had been reported (up to 80%), an equally high yield of aryne adduct was isolated in the presence of tetraphenylcyclopentadienone (tetracyclone), suggesting that the decomposition had been diverted away from the radical pathway to that leading to benzyne. One of the objects of this research was, therefore, a thorough investigation into the role played by tetracyclone during the decomposition.

Furthermore, the precise mechanism of benzyne formation had not been fully established. In particular, the possible intermediacy of a betaine precursor to benzyne, originally proposed by Cook but recently questioned by Baigrie, merited investigation since evidence for this species would indicate an E_1cb mechanism, as originally suggested by Cadogan.

EXPERIMENTAL

SYMBOLS AND ABBREVIATIONS

b. p.	boiling point
m. p.	melting point
e. s. r.	electron spin resonance
n. m. r.	nuclear magnetic resonance
i. r.	infra-red
g. l. c.	gas-liquid chromatography
t. l. c.	thin-layer chromatography
m. s.	mass spectroscopy
s	singlet
d	doublet
t	triplet
q	quartet
m	multiplet
M^+	mass of molecular ion
m/e	mass/charge ratio
m/100m	moles per 100 moles of starting material
w/v	weight per volume

Gas Liquid Chromatography

For analytical and quantitative g.l.c. investigations, a Pye 104 chromatograph, with flame ionisation detector was used together with 2 m x 2.2 m.m i.d. packed columns. Quantitative measurements were made following the technique of Hibbert[143] after calibration of the instrument with known mixtures of authentic samples and internal standards. All authentic samples and internal standards were purified before use. For preparative g.l.c. a Pye 105 model 15 was used. In all cases the carrier gas was nitrogen, the flow-rates and split ratios being as recommended by the manufacturers. The following stationary phases, supported on 100-120 mesh celite were employed; neopentylglycolsuccinate (NPGS), polyethyleneglycol adipate (PEGA), silicone grease (SE-30) and polyethyleneglycol (CAR).

Column Chromatography

The alumina used for column chromatography was Laporte Industries Ltd., activated aluminium oxide, type H, (Brockmann activity = 1). Dry column chromatography was carried out after the method of Loev and Goodman[144] using chromatographic alumina, treated with Woelm fluorescent indicator for short wave u.v. (254 nm), and deactivated to Brockman activity 3-4. The columns were made up in "C" gauge, 2 in nylon tubing supplied by Walter Coles and Co. Ltd., London. After development, the columns were sliced and the products washed off with ether or chloroform.

Thin Layer Chromatography

Thin layer chromatograms were obtained on 0.3 mm layers of alumina (Merck, aluminium oxide G) or silica gel (Merck, silica gel G). Components in the developed chromatograms were detected by their fluorescence in u.v. light or by their reaction with iodine.

Nuclear Magnetic Resonance Spectroscopy

A Perkin-Elmer model R-10 and a Varian E. M. 360 spectrometer which operated at a frequency of 60MHz and a probe temperature of 33° were used. Spectra of isotopically labelled compounds were recorded using a Varian HA-100 instrument operating at 100 MHz and a probe temperature of 28°. Chemical Shifts were recorded at tau (τ) values in parts per million using tetramethyl silane as internal reference (τ=10. 0). Spectra were recorded in 10-15% w/v solutions, usually in deuterochloroform or carbon tetrachloride. The ^{15}N spectrum was recorded on a Brucker HX90 at Queen Mary's College.

Infrared Spectroscopy

Perkin-Elmer models 337 and 257 were used for infrared spectroscopy, liquid samples being examined as thin films and solid samples as nujol mulls.

Mass Spectroscopy

Mass spectra were recorded using an A. E. I. MS-902 double focussing mass spectrometer and a V. G. Micromass 12, single focussing mass spectrometer/gas chromatograph, using helium as the carrier gas. Exact mass measurements were conducted on the MS-902 instrument. The use of m. s. /g. l. c. analysis to confirm the presence of compounds in reaction mixtures was frequently made. In such cases the mass spectrum of the sample from the reaction mixture was compared with that of an authentic sample. The prominent peaks in the mass spectrum, together with their relative intensities, are given for each of the compounds confirmed by this technique in the Appendices (page 106).
The isotopic enrichment of compounds was calculated after the method of Biemann,[145] the following assumptions being inherent in the technique.

(1) The intensities of the isotope peaks at M+1 and M+2 are the same in both standard and labelled compounds.

(2) There is no 'M+1' peak due to ion molecule collisions.

(3) The electron energy does not change from standard to labelled compound.

(4) There are no background or other impurities present that contribute to the peaks being measured. While for some of the samples (both standard and labelled) an electron energy of 12eV was used (at which the molecular-ion peak is still intense enough to be measured accurately, while the fragmentation resulting in the loss of one or more hydrogens is negligible) it was found that identical results were obtained from spectra run at 70eV.

Electron Spin Resonance Spectroscopy

E. s. r. spectra were obtained using a Decca Radar Limited XI spectrometer, with a Newport Instrument 8-inch magnet system and Hilger and Watts Microspin magnet controls.

Elemental Analysis

Microanalyses were carried out on a Perkin-Elmer Elemental Analyser 240 by Mr. J. Grunbaum, University of Edinburgh.

Melting Points

Melting points of all compounds were determined using a Kofler hot-stage apparatus.

Solvents and Reagents

Benzene, cyclohexane and cyclohexene were purified by distillation of the sodium-dried solvent from calcium hydride in an atmosphere of dry nitrogen. Furan was passed down a short alumina column, distilled from lithium aluminium hydride and stored over molecular sieve. Dichloroethane was distilled from phosphorus pentoxide. Aniline was distilled from zinc dust at atmospheric pressure and stored at -15°. Acetanilide was purified by recrystallisation from ethanol. Unless otherwise stated, 'petrol' refers to light petroleum ether (b. p. $40-60^{\circ}$).

1 PREPARATION OF ACYLARYLNITROSAMINES.

a N-Nitrosoacetanilide.

Acetanilide (10 g, 74 mmol), fused potassium acetate (10 g, .10 mol) and phosphoric oxide (1 g) were stirred in a mixture of acetic acid (70 ml) and acetic anhydride (30 ml) at 0° for 10 min. Nitrosyl chloride (6.0 g, 92 mmol), in a 30% w/v solution in acetic anhydride, was added dropwise over 30 min. The solution was stirred for a further 30 min and then poured onto ice-water (500 ml). The N-nitrosoacetanilide separated out as a yellow solid, which was filtered off, washed thoroughly with cold water, and pressed several times between filter paper. The yellow powder was dried over phosphoric oxide at 0.05 mm for 3 h and stored at -15°. The product (9.6 g, 79%) melted with decomposition at 50°. (Lit.[146] m.p. 50°).

b 4-t-Butyl-N-nitrosoacetanilide.

This compound was prepared from 4-t-butylacetanilide by the method described by Harger.[147] The product (80% yield) was collected as a yellow powder, m.p. 49° (decomp). (Lit.[147] 40°).

In both cases, the absence of an N-H absorption (3400-3000 cm^{-1}) indicated the complete conversion of the amide.

2 PREPARATION OF ARYNE TRAPS.

a Tetraphenylcyclopentadienone (tetracyclone) was prepared by the condensation of benzil and dibenzyl ketone after the method of Johnson and Grummit[148] and was collected as dark purple crystals in almost quantitative yield from benzene : ethanol (1:1), m. p. 218-220° (lit[148] 218-220°).

b 2, 5-Diphenyl-3, 4-(*a*, *a*-naphthylene)cyclopentadienone (acecyclone) was prepared by the condensation of acenaphthenequinone and dibenzyl ketone with subsequent dehydration of the carbinol in acidified acetic anhydride, as described by Allen and Van Allan.[149] Recrystallisation from acetic acid afforded black crystals, m. p. 287-289° (lit[149] 289°).

c Methyl-2-oxopyran-5-carboxylate (methyl coumalate) was prepared by heating a sulphuric acid solution of coumalic acid with methanol, after the method of Bahl and Kemp.[150] Coumalic acid was obtained through treatment of malic acid with sulphuric acid as described by Wiley and Smith.[151] The ester was collected as white crystals, m. p. 69-72° (lit[150] 69-70°).

d 2-Oxo-1, 2H-pyrane (*a*-Pyrone).

Decarboxylation of coumalic acid as described by Zimmerman[152] afforded crude *a*-Pyrone which on distillation gave a colourless oil, b. p. 102°/23 mm (lit[152] 110°/26 mm).

e Other cyclopentadienones were prepared after the method of Allen and Van Allan[153] by the condensation of benzil with the appropriate ketone.

Prepared in this way were:

2, 5-diethyl-3, 4-diphenylcyclopentadienone m. p. 102-103° (Lit[153] 103°).

2, 5-dimethyl-3, 4-diphenylcyclopentadienone m. p. 183-184° (Lit[153] 181-182°).

2-methyl-3, 4, 5-triphenylcyclopentadienone m. p. 197-198° (Lit[153] 196°).

3 PREPARATION OF ARYNE ADDUCTS.

a 9, 10-Diphenyl-9, 10-epoxy-9, 10-dihydroanthracene was prepared by the Diels-Alder reaction of benzyne with 1, 3-diphenylisobenzofuran after the method of Wittig et al.[154] Recrystallisation from cyclohexane afforded colourless crystals, m. p. 188-189° (lit[154] 188-188.5°).

b 1, 4-Dihydronaphthalene-1, 4-endoxide was prepared from furan according to the method described by Wittig.[155] Recrystallisation from petrol gave colourless crystals, m. p. 55-56° (lit[155] 55-56°).

c Methyl naphthalene-2-carboxylate.

Methyl coumalate was allowed to react with anthranilic acid and pentyl nitrite as described by Bahl.[156] Fractional distillation of the crude oil gave methyl naphthalene-2-carboxylate in 70% yield, b.p. 105-107°/0.1 mm, m.p. 77° (lit[156] 78-79°).

4 PREPARATION OF AZO COMPOUNDS.

a 1-Phenylazo-2-naphthol was prepared by the coupling of benzenediazonium chloride with sodium β-naphthoxide at 0° as described by Vogel.[157] Recrystallisation of the filtered product from ethanol afforded red needles, m. p. 133° (lit[157] 131°).

b 4-Phenylazo-1-naphthol was prepared from sodium α-naphthoxide using a procedure analogous to that for the preparation of 1-phenylazo-2-naphthol. Violet needles were obtained from acetic acid, m. p. 204-206° (lit[158] 205-206°).

c 2-Phenylazo-1-naphthol.

1, 2-Naphthaquinone and phenylhydrazine hydrochloride were condensed in acetic acid after the method of Zincke.[159] Recrystallisation from ethanol gave brown crystals, m. p. 137-138° (lit[159] 137-138°).

d 1-Phenylazo-4-methoxynaphthalene.

Diazomethane, prepared from p-tosylsulphonylmethylnitrosamide as described by Vogel,[157] was reacted with 4-phenylazo-1-naphthol after the method of Smith.[160] Recrystallisation from methanol afforded the product in 80% yield, m.p. 82° (lit[160] 82°).

e 1-Phenylazo-7-methoxy-2-naphthol.

2-Hydroxy-7-methoxynaphthalene, prepared by the methylation of the 2,7-dihydroxy compound as described by Fischer,[161] was coupled with benzenediazonium chloride after the method of Vogel.[157] Dark red crystals were obtained from ethanol, m.p. 120-121° (lit[161] 121°).

5 PREPARATION OF NITROSATING AGENTS.

a Nitrosyl chloride.

This compound was prepared by the method of Morton and Wilcox[162] by the action of hydrochloric acid on sodium nitrite. The gas was passed through towers containing sodium nitrite, potassium chloride and calcium chloride before being dissolved as a 30% w/v solution in acetic anhydride or carbon tetrachloride, and was stored at -15° in sealed flasks.

b 4-Chlorobenzoyl nitrite.

Nitrosyl chloride (8.0 g, 0.12 mol) was added dropwise over 30 min to a well-stirred suspension of the silver salt of 4-chlorobenzoic acid (24.8 g, 0.09 mol) in carbon tetrachloride (200 ml) at -10° in an atmosphere of dried nitrogen. The mixture was stirred for a further 20 min at this temperature and subsequently for 1 h at room temperature. The stoppered reaction flask was then transferred to a nitrogen dry box where the yellow solution was filtered over celite. Evaporation of the filtrate on the rotary evaporator, fitted to a calcium chloride drying tower, afforded a dark yellow oil which on distillation gave a pale yellow solid, b.p. 62°/0.7 mm (lit[124] 70°/1 mm). This compound was dissolved in benzene (16% w/v) and stored at -15°.

6 PREPARATION OF ISOTOPICALLY LABELLED COMPOUNDS.

a Deuteriated materials.

(i) 2,4,6-[$^2H_3$]Aniline hydrochloride was prepared by the repeated reaction of aniline hydrochloride with deuterium oxide in a sealed Pyrex tube, using the method of Best and Wilson.[163] N.m.r. (D_2O): τ 2.50 (s, 2H, 3- and 5-H). Standard acetylation gave 2,4,6-[$^2H_3$]acetanilide m.p. 114-115°, m.s. showed a deuterium content of 99% [$^2H_3$]. N.m.r. ($CDCl_3$): τ, 7.86 (s, 3H, Me); 2.72 (s, 2H, 3- and 5-H); 1.72 (bs, 1H, NH).

(ii) 2,4,6-[$^2H_3$]Benzenediazonium fluoroborate was prepared from the corresponding [$^2H_3$] aniline by diazotisation in aqueous hydrochloric acid followed by treatment with aqueous sodium fluoroborate, and after repeated crystallisations from acetone/ether, had m.p. 96-97° (decomp: Kofler). The literature[157] m.p. is 119-120°. Since m.p. values from repeated preparations were consistent as were analyses, the samples were assumed to be pure. The product on treatment with alkaline β-naphthol gave a quantitative yield of 1-phenylazo-2-naphthol shown by m.s. to contain 99% [$^2H_3$].

(iii) 2-[$^2H_1$]Aniline was prepared from N,N-[$^2H_2$]-2-bromoaniline[164] after the method of Heaney.[165] Distillation afforded a colourless oil (45%), b.p. 52°/4 mmHg. N.m.r. ($CDCl_3$): τ, 2.6-3.6 (complex, 4H, aromatic); 6.5 (bs, 2H, NH_2).

(iv) 2-[$^2H_1$]Benzenediazonium fluoroborate was prepared using a procedure analogous to that for the preparation of the trideuteriodiazonium fluoroborate, and was obtained in 61% yield after recrystallisation from acetone : ether (4 times), m.p. 96-97° (decomp). A sample of the fluoroborate was coupled with an aqueous alkaline solution of β-naphthol and the resulting 1-phenylazo-2-naphthol showed a deuterium content of 92% [$^2H_1$].

(v) 2-[$^2H_1$] Benzenediazonium chloride was prepared by the method described by Vogel.[157] The salt was recrystallised (4 times) from acetone : ether and the colourless crystals were dried over P_2O_5. Owing to the explosive nature of the product, it was used without further characterisation. The deuterium content of the resulting 1-phenylazo-2-naphthol was 94% [$^2H_1$].

b N-15 Labelled materials.

(i) ^{15}N-Nitrosoacetanilide was prepared from ^{15}N-labelled acetanilide (96%-^{15}N) using a procedure identical to that for the preparation of the unlabelled compound, m.p. 49-51° (decomp).

(ii) ^{15}N-Aniline hydrochloride.

^{15}N-Benzamide, prepared in 80% yield from labelled ammonium chloride (99%-^{15}N) by the method of Lewis,[166] was treated with chlorine and sodium hydroxide to give the labelled aniline via a Hoffmann Degradation. Steam distillation afforded a pale yellow oil which was extracted with ether. The aniline hydrochloride was precipitated by the introduction of anhydrous hydrogen chloride. The yield of product was 64%, m.p. 196-198 (lit[157] 198-200).

(iii) ^{15}N-Benzenediazonium fluoroborate was prepared from the corresponding aniline hydrochloride by diazotisation in aqueous hydrochloric acid followed by treatment with aqueous sodium fluoroborate. Recrystallisation from acetone : ether (4 times) afforded colourless crystals, m.p. 96° (decomp).

(iv) ^{15}N -1-Phenylazo-2-naphthol was prepared by the coupling of ^{15}N-labelled benzenediazonium fluoroborate with an alkaline solution of β-naphthol. Recrystallisation of the filtered product from ethanol afforded the labelled compound in 90% yield, m.p. 133°. Analysis by m.s. showed a 99% enrichment of the nitrogen label in the product. N.m.r. ($CDCl_3$): δ_N = 110.8 ppm (relative to NO_3^- in NH_4NO_3).

7 MISCELLANEOUS PREPARATIONS.

a 1, 2-Dibenzoylphenylethylene.

This was prepared by the condensation of benzil and acetophenone after the method of Japp and Klingemann.[167] M. p. 126-128° (lit[167] 129°).

b 2, 3-Diphenylinden-1-one.

This compound was prepared by the reaction of phenylmagnesium bromide with benzalphthalate as described by Allen.[168] The product, obtained in 56% yield, had m. p. 149-150° (lit[168] 149-151°).

c 1-Nitroso-2-naphthol.

Treatment of 2-naphthol with an alkaline solution of sodium nitrite after the method of Marvel and Porter[169] afforded the product in 85% yield, m. p. 105-106° (lit[169] 106°).

d 1, 2, 3, 4-Tetraphenylcyclopent-2-enone.

Reduction of tetracyclone with lithium aluminium hydride in dibutyl ether gave the dihydro compound. The product, collected as colourless prisms from acetic acid, had m. p. 161° (lit[170] 161°).

e 1-Phenylazo-2, 3, 4, 5-tetrachlorocyclopentadiene.

Tetrachlorocyclopentadiene was coupled with benzene diazonium chloride using the method of Griffiths and Lockwood.[171] Recrystallisation from petrol gave orange crystals, m. p. 132-133° (lit[171] 132-133°).

f 1, 1-Diphenylethylene.

This was prepared by the reaction of phenylmagnesium bromide and ethyl acetate as described by Allen.[172] On distillation the pure product boiled at 122-124°/5 mm (lit[172] 113°/2 mm).

8 REACTIONS OF 4-CHLOROBENZOYL NITRITE AND ACETANILIDE WITH BENZYNE TRAPS.

a Tetracyclone

4-Chlorobenzoyl nitrite (1.6 g, 8.6 mmol) in benzene (50 ml) was added over 30 min to a mixture of acetanilide (0.675 g, 5 mmol) and tetracyclone (1.9 g, 5 mmol) in boiling benzene (100 ml). The mixture was boiled under reflux for 12 h and maleic anhydride (1 g) added to remove unreacted tetracyclone. Dry column chromatography of the reaction mixture on alumina (80 g), eluting with cyclohexane (150 ml), afforded biphenyl (0.9 g, 12 m/100 m) which after recrystallisation from petrol had m.p. and mixed m.p. 70-70.5° (lit[173] 70°) and tetraphenylnaphthalene (T.P.N.) (1.52 g, 71 m/100 m) which after recrystallisation from acetic acid had m.p. and mixed m.p. 204-204.5 (lit[174] 204-204.5°). The position of the T.P.N. band was determined by its fluorescence under u.v. light (350 nm). The i.r. (Nujol) spectra of both biphenyl and T.P.N. were identical to those of authentic samples.

b Anthracene.

4-Chlorobenzoyl nitrite (1.6 g, 8.6 mmol) in benzene (50 ml) was added over 30 min to a mixture of acetanilide (0.675 g, 5 mmol) and anthracene (0.9 g, 5 mmol) in boiling benzene (100 ml). The mixture was boiled under reflux for 12 h, concentrated by evaporation, and maleic anhydride (1 g) and chlorobenzene (20 ml) added. Refluxing was continued for a further 2 h. Chromatography of the reaction mixture on alumina, eluting with benzene, gave biphenyl (0.18 g, 24 m/100 m) and triptycene (0.20 g, 16 m/100 m). Recrystallisation of the triptycene from petrol afforded colourless crystals, m.p. and mixed m.p. 256° (lit[115] 256°). The i.r. (Nujol) spectrum was indistinguishable from that of an authentic sample. In a repeat of this experiment the yield of 9-phenylanthracene (5 m/100 m) was established by g.l.c. (1% SE 30, 230°) analysis using triptycene as the internal standard.

c Acecyclone.

4-Chlorobenzoyl nitrite (0.95 g, 5.1 mmol) in benzene (25 ml) was added over 30 min to a mixture of acetanilide (0.41 g, 3 mmol) and acecyclone (1.07 g, 3 mmol) in boiling benzene (75 ml). The mixture was boiled under reflux for 5 h, concentrated and applied to an alumina column. Elution with petrol gave biphenyl (0.040 g, 9 m/100 m) and 7,12-diphenylbenzo[k]fluoranthene (0.72 g, 59 m/100 m). Recrystallisation of the benzyne adduct from acetic acid gave colourless crystals, m.p. 273-274° (lit[149] 273-274°).

d 1,3-Diphenylisobenzofuran.

To a solution of acetanilide (0.34 g, 2.5 mmol) and 1,3-diphenylisobenzofuran (0.68 g, 2.5 mmol) in boiling benzene (50 ml), 4-chlorobenzoyl nitrite (0.8 g, 4.3 mmol) in benzene (15 ml) was added over 30 min. The mixture was boiled under reflux for 12 h and the volume reduced to 20 ml by evaporation. When cool, powdered zinc (6.5 g, 0.1 mol) and acetic acid (17 ml) were added and the solution stirred at 85° for 8 h. Chromatography on alumina gave biphenyl (.22 g, 57 m/100 m) and 9,10-diphenylanthracene (0.041 g, 5 m/100 m), which on recrystallisation from acetic acid had m.p. and mixed m.p. 246-248° (lit[154] 246-247°) and an i.r. spectrum identical to that of an authentic specimen.

e *α*-Pyrone.

4-Chlorobenzoyl nitrite (0.95 g, 5.1 mmol) in benzene (25 ml) was added over 30 min to a solution of acetanilide (0.41 g, 3 mmol) and *α*-pyrone (0.29 g, 3 mmol) in boiling benzene (75 ml). The reaction mixture was boiled under reflux for 5 h. Quantitative examination of the reaction mixture by g.l.c. (5% NPGS, 130°) using bibenzyl as internal standard gave: biphenyl (28 m/100 m) and naphthalene (23 m/100 m). Mass spectral/g.l.c. analysis of the biphenyl and naphthalene peaks gave spectra identical to those of authentic samples.

f Methyl coumalate.

To a solution of acetanilide (0.41 g, 3 mmol) and methyl coumalate (0.46 g, 3 mmol) in boiling benzene (75 ml), 4-chlorobenzoyl nitrite (0.95 g, 5.1 mmol) in benzene (25 ml) was added over 30 min and refluxing continued for a further 5 h. Quantitative examination of the reaction mixture by g.l.c. (5% NPGS, 130°) using bibenzyl as internal standard gave: biphenyl (26 m/100 m) and carbmethoxy naphthalene (18 m/100 m). Mass spectral/g.l.c. analysis of the product peaks gave spectra identical to those of authentic samples.

g Furan

4-Chlorobenzoyl nitrite (0.95 g, 5.1 mmol) in benzene (25 ml) was added to a solution of acetanilide (0.41 g, 3 mmol) and furan (0.204 g, 3 mmol) in boiling benzene (75 ml), and refluxing continued for a further 5 h. Quantitative examination of the reaction mixture by g.l.c. (5% NPGS, 130°) gave a biphenyl yield of 54 m/100 m. No peak corresponding to 1,4-dihydro-1,4-epoxynaphthalene was found. (0.1 m/100 m) would have been detected.

h 2,5-Diethyl-3,4-diphenylcyclopentadienone.

4-Chlorobenzoyl nitrite (0.8 g, 4.25 mmol) in benzene (20 ml) was added over 30 min to a solution of acetanilide (0.34 g, 2.5 mmol) and 2,5-diethyl-3,4-diphenylcyclopentadienone (0.68 g, 2.5 mmol) in boiling benzene (60 ml). The reaction mixture was boiled under reflux for 12 h and maleic anhydride (1 g) added to remove unreacted trap. Dry column chromatography of the reaction mixture on alumina, eluting with cyclohexane, afforded biphenyl (0.019 g, 5 m/100 m) and 1,4-diethyl-2,3-diphenyl naphthalene (0.50 g, 60 m/100 m). Recrystallisation from acetic acid gave colourless crystals, m.p. 141-142°. [Found: C, 92.52; H, 7.10. $C_{26}H_{24}$ requires C, 92.86; H, 7.14].

The mass spectrum showed a parent ion at m/e 336. N.m.r. ($CDCl_3$): τ, 1.8-3.0 (m, 14H, aromatic): 7.16 (q, 4H, CH_2); 8.84 (t, 6H, CH_3).

i 2-Methyl-3, 4, 5-triphenylcyclopentadienone.

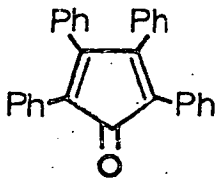
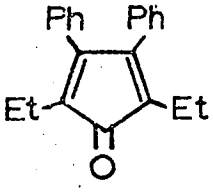
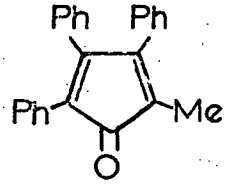
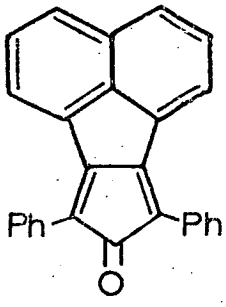
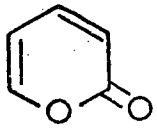
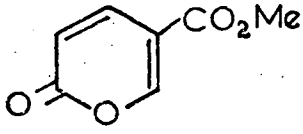
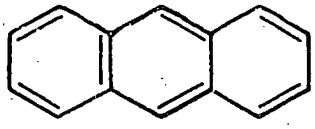
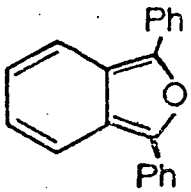
4-Chlorobenzoyl nitrite (0.93 g, 5.0 mmol) in benzene (20 ml) was added over 30 min to a solution of acetanilide (0.41 g, 3.0 mmol) and 2-methyl-3, 4, 5-triphenylcyclopentadienone in boiling benzene (75 ml). The reaction mixture was boiled under reflux for 12 h and maleic anhydride added as before. Isolation of products as described in the previous experiment gave biphenyl (0.031 g, 7 m/100 m) and 1-methyl-2, 3, 4-triphenylnaphthalene (0.71 g, 64 m/100 m). Recrystallisation from petrol (b.p. 60-80°) afforded colourless needles, m.p. 165-166°. [Found: C, 93.91; H, 5.89. $C_{29}H_{22}$ requires C, 94.04; H, 5.96]. The mass spectrum showed a parent ion at m/e 370. N.m.r. ($CDCl_3$): τ, 1.8-3.2 (m, 19H, aromatic); 7.48 (s, 3H, CH_3).

j In the absence of a trap.

To a solution of acetanilide (0.41 g, 3.0 mmol) in boiling benzene (75 ml), 4-chlorobenzoyl nitrite (0.93 g, 5.0 mmol) in benzene (25 ml) was added over 30 min. Refluxing was continued for 5 h and quantitative analysis of the reaction mixture by g.l.c. (5% NPGS, 130°) using bibenzyl as internal standard gave the yield of biphenyl (63 m/100 m).

TABLE 1

Products from the reaction of 4-chlorobenzoylnitrite with acetanilide in the presence of benzyne traps.

Arynophile	Biphenyl (m/100 m)	Adduct (m/100 m)
	12	71
	5	60
	7	64
	9	59
	28	23
	26	18
	24	16
	57	5
	54	-
—	63	-

9 REACTIONS OF ^{15}N-LABELLED COMPOUNDS.

The experiments in this section were carried out to investigate the possibility of ^{15}N exchange during the decomposition of the diazonium compound. The reactants, therefore, were partially decomposed and the reaction terminated by treatment with aqueous alkaline β-naphthol, or with sodium β-naphthoxide dissolved in a benzene solution containing crown ether. The reaction mixtures were then stirred for a further 30 min before work up.

a Partial Decomposition of ^{15}N-Labelled NNA formed in situ in Benzene.

(i) In the absence of a trap.

4-Chlorobenzoyl nitrite (0.3 g, 1.6 mmol) in benzene (5 ml) was added dropwise to a solution of acetanilide (0.11 g, 0.8 mmol), (96%-^{15}N) in benzene (20 ml) at 45°, under an atmosphere of dry nitrogen, and stirring was continued for 15 min. A solution of sodium β-naphthoxide (0.17 g, 1.0 mmol) in water (10 ml) was added to the reaction mixture with vigorous stirring. Extraction with ether gave an orange solution, from which 1-phenylazo-2-naphthol (0.040 g, 20 m/100 m) was isolated by dry column chromatography on alumina, eluting with carbon tetrachloride. Mass spectral analysis of the recrystallised product showed a nitrogen-15 isotope content of 93%-^{15}N indicating a 3% loss of the label. In a parallel experiment at 65°, the 1-phenylazo-2-naphthol, isolated in 5% yield, showed a nitrogen-15 isotope content of 53% indicating 43% loss of the label. The origin of the peaks at m/e 248 and 249 was confirmed by exact mass measurements (Found: M^+ 249.092092. $C_{16}H_{12}{}^{14}N^{15}NO$ requires 249.091993; Found: M^+ 248.085645. $C_{16}H_{11}{}^{14}N^{15}NO$ requires 248.084168; Found: M^+ 248.092935. $C_{16}H_{12}{}^{14}N_2O$ requires 248.094958).

(ii) In the presence of tetracyclone.

4-Chlorobenzoyl nitrite (0.15 g, 0.80 mmol) in benzene (3 ml) was added to a solution of acetanilide (0.05 g, 0.37 mmol) (96%-^{15}N) and tetracyclone (0.014 g, 0.37 mmol) in benzene (10 ml) as described

in the previous experiment. After 15 min sodium β-naphthoxide (0.083 g, 0.5 mmol) in water (5 ml) was added with vigorous stirring. 1-Phenylazo-2-naphthol (0.014 g, 15 m/100 m) was isolated by dry column chromatography and showed a ^{15}N content of 90%.

b Partial Decomposition of ^{15}N-Labelled Benzenediazonium Fluoroborate.

(i) In various solvents.

^{15}N-Labelled benzenediazonium fluoroborate (0.071 g, 0.37 mmol) (99%-^{15}N) was added to solvent (20 ml) with vigorous stirring under an atmosphere of nitrogen at 60°. After 15 min, sodium β-naphthoxide (0.083 g, 0.50 mmol) in water (5 ml) was added. The organic layer was extracted with ether, washed with sodium hydroxide and dried over magnesium sulphate. Dry column chromatography afforded 1-phenylazo-2-naphthol. Reactions were carried out in the following solvents and solvent mixture; benzene, water, acetone, methanol and benzene : water (2:1). In all cases the ^{15}N content of the azo product was 99%.

c Partial Decomposition of ^{15}N-Labelled NNA in Benzene.

(i) In an atmosphere of nitrogen.

^{15}N-Labelled N-nitrosoacetanilide (0.050 g, 0.30 mmol) (96%-^{15}N) was added to benzene (20 ml) under an atmosphere of dry nitrogen and the reaction mixture stirred for 5 min at 50°. The reaction mixture was then flushed with a solution of sodium β-naphthoxide (0.08 g, 0.50 mmol) in water (10 ml). Ethereal extraction of the organic products followed by dry column chromatography afforded 1-phenylazo-2-naphthol (0.025 g, 30 m/100 m) (96%-^{15}N).

(ii) In the presence of 4-Chlorobenzoyl nitrite.

^{15}N-Labelled N-nitrosoacetanilide (0.050 g, 0.30 ml) (96%-^{15}N) was added to a solution of 4-chlorobenzoyl nitrite (0.15 g, 0.80 mmol) in benzene (20 ml). 1-Phenylazo-2-naphthol, (0.027 g,

32 m/100 m) isolated as described above showed a ^{15}N content of 88%.

d Decomposition of ^{15}N-Labelled NNA formed in situ in Benzene under an atmosphere of Argon.

A solution of acetanilide (0.05 g, 0.37 mmol) (96%-^{15}N) in benzene (20 ml) was degassed (5 times) and the reaction vessel flushed out with argon. The mixture was stirred for 10 min at 50° and then 4-chlorobenzoyl nitrite (0.15 g, 0.80 mmol) added through a syringe, the reaction flask being fitted with a liquid paraffin bubbler. Stirring was continued for a further 5 min and the solution flushed with sodium β-naphthoxide (0.08 g, 0.50 mmol) in water (5 ml). Extraction of 1-phenylazo-2-naphthol (0.014 g, 15 m/100 m) was as described before and m.s. showed the ^{15}N content to be 87%.

e Reaction of ^{15}N-Labelled 1-Phenylazo-2-naphthol with 4-Chlorobenzoyl Nitrite.

4-Chlorobenzoyl nitrite (0.10 g, 0.54 mmol) in benzene (1 ml) was added from a syringe to a well-stirred solution of 1-phenylazo-2-naphthol (0.05 g, 0.20 mmol) (99%-^{15}N) in benzene (20 ml) at 50°. After 8 min, sodium β-naphthoxide (0.07 g, 0.40 mmol) in benzene (10 ml) containing crown ether was added with vigorous stirring and the reaction quenched with water (20 ml). The regenerated azo compound (0.01 g, 20 m/100 m) was isolated by dry column chromatography and showed a ^{15}N content of 51%. In a parallel experiment carried out under an atmosphere of argon using degassed solvents, the isolated 1-phenylazo-2-naphthol (0.015 g, 30 m/100 m) showed a ^{15}N content of 38%. The reaction carried out under an atmosphere of nitrogen was repeated several times and on one occasion a ^{15}N content of 30% was observed in the regenerated azo compound.

10 NITROSATIONS USING 4-CHLOROBENZOYL NITRITE.

a Nitrosation of Hydroxy-azo Compounds.

(i) 1-Phenylazo-2-naphthol.

4-Chlorobenzoyl nitrite (2.5 g, 13.6 mmol) in benzene (25 ml) was added dropwise to a well-stirred solution of 1-phenylazo-2-naphthol (1.7 g, 6.8 mmol) in benzene (150 ml) over a period of 2 min, the reaction being carried out under an atmosphere of dry nitrogen. The red colour due to the dissolved azo compound was rapidly discharged. Stirring was continued for a further 1 h and the solvent removed by evaporation. Addition of ether (100 ml) to the residual oil induced the precipitation of a brown solid (0.3 g) which showed up as four spots on t.l.c. Successive recrystallisations of this solid from acetone : petrol failed to purify the sample. The remainder of the reaction mixture was chromatographed on alumina eluting with petrol : ether. Biphenyl (0.25 g, 24 m/100 m) was collected as the only major product and after recrystallisation from petrol it had m.p. and mixed m.p. 70-71° (i.r. spectrum). A parallel experiment carried out in boiling benzene gave biphenyl (30%).

(ii) 2-Phenylazo-1-naphthol.

4-Chlorobenzoyl nitrite (0.30 g, 1.6 mmol) in benzene (5 ml) was added dropwise to a well-stirred solution of 2-phenylazo-1-naphthol (0.20 g, 0.8 mmol) in benzene (20 ml) at 50°, as above. Rapid decolorisation of the solution ensued, and g.l.c. investigation of the reaction mixture showed that the azo compound had been completely consumed. Further examination of the reaction mixture by g.l.c. (1% SE30, 140°) showed the presence of biphenyl. Dry column chromatography on alumina, eluting with cyclohexane, afforded biphenyl (0.021 g, 17 m/100 m). M.p. 70-70.5°.

(iii) 4-Phenylazo-1-naphthol.

A solution of 4-chlorobenzoyl nitrite (0.30 g, 1.6 mmol) in benzene (5 ml) was added to a solution of 4-phenylazo-1-naphthol

(0. 20 g, 0. 08 mmol) in benzene (20 ml) as in the previous reaction. Biphenyl (0. 033 g, 27 m/100 m) was isolated by dry column chromatography, m. p. 70-70. 5°.

(iv) 1-Phenylazo-4-methoxynaphthalene.

4-Chlorobenzoyl nitrite (0. 15 g, 0. 80 mmol) in benzene (5 ml) was added to a well stirred solution of 1-phenylazo-4-methoxy-naphthalene (0. 10 g, 0. 38 mmol) in benzene (20 ml), as described above, and the reaction followed by g. l. c. over 48 h. The peak corresponding to the azo compound persisted throughout the reaction while no trace of biphenyl was observed. A similar result was obtained for the reaction of 4-chlorobenzoyl nitrite with azobenzene.

b Nitrosation of Hydroxy-azo Compounds followed by Treatment with Naphthoxide Salts.

(i) 2-Phenylazo-1-naphthol.

A solution of 4-chlorobenzoyl nitrite (0. 22 g, 1. 20 mmol) in benzene (5 ml) was added dropwise over 2 min to a solution of 2-phenylazo-1-naphthol (0. 10 g, 0. 40 mmol) in benzene (20 ml) at 50°. Almost immediately, sodium β-naphthoxide (0. 10 g, 0. 60 mmol) in water (15 ml) was added with vigorous stirring. The reaction mixture was extracted with ether and the organic layer evaporated off. Dry column chromatography of the residue on alumina, eluting with carbon tetrachloride, afforded 1-phenylazo-2-naphthol (0. 053 g, 53 m/100 m) m. p. 133-134°. The i. r. (Nujol) spectrum was indistinguishable from that of an authentic sample.

(ii) 1-Phenylazo-2-naphthol.

4-Chlorobenzoyl nitrite (0. 22 g, 1. 20 mmol) in benzene (5 ml) was added to a solution of 1-phenylazo-2-naphthol (0. 10 g, 0. 38 mmol) in benzene (20 ml) at 50°. Sodium 7-methoxy-2-naphthoxide (0. 13 g, 0. 60 mmol) in water (15 ml) was then added as described in the previous experiment. Examination of the reaction mixture by g. l. c. and g. l. c. /m. s. (1% SE30, 250°) showed 1-phenylazo-7-methoxy-2-naphthol to be present as a major product.

c Nitrosation of Nitroso Compounds followed by Treatment with Sodium β-Naphthoxide.

(i) o-Methylnitrosobenzene.

4-Chlorobenzoyl nitrite (0.19 g, 1.0 mmol) in benzene (3 ml) was added dropwise over 2 min to a solution of o-methylnitrosobenzene (0.06 g, .5 mmol) in benzene (30 ml) at 50°. The reaction mixture was stirred for a further 5 min before the addition of sodium β-naphthoxide (0.08 g, 0.5 mmol), dissolved in benzene (5 ml) containing crown ether. The solution was then stirred for 1 h over which period the orange colour deepened. Chromatography of the reaction mixture on alumina afforded 1-(o-methylphenyl)azo-2-naphthol (0.021 g, 16 m/100 m) m.p. 135° (lit[175] 135°), M^+: 262.

(ii) Nitrosobenzene.

4-Chlorobenzoyl nitrite (0.34 g, 1.86 mmol) in benzene (5 ml) was added to a solution of nitrosobenzene (0.10 g, 0.93 mmol) in benzene (30 ml) as described in the previous experiment. Treatment of the reaction mixture with a solution of sodium β-naphthoxide afforded a red solution, chromatography of which gave 1-phenylazo-2-naphthol (0.056 g, 23 m/100 m), m.p. 134°.

d Nitrosation of 1-Phenylazo-2, 3, 4, 5-tetrachlorocyclopentadiene.

4-Chlorobenzoyl nitrite (0.28 g, 1.5 mmol) in benzene (5 ml) was added dropwise to a well-stirred solution of 1-phenylazo-2, 3, 4, 5-tetrachlorocyclopentadiene (0.31 g, 1 mmol) in benzene (30 ml) at 50°. Stirring was continued until t.l.c. showed the hydrazone to be consumed. Biphenyl (0.036 g, 17 m/100 m) was isolated by dry column chromatography and after recrystallisation from petrol had m.p. 70-70.5°. In a blank reaction in which the hydrazone was heated in benzene for 18 h at 50° no biphenyl was formed.

e Nitrosation of 1-Phenylazo-2-naphthol in t-Butylbenzene.

1-Phenylazo-2-naphthol (0.20 g, 0.80 mmol) was dissolved in t-butylbenzene (20 ml) and the mixture heated with stirring to 50°,

under an atmosphere of dry nitrogen. 4-Chlorobenzoyl nitrite (0.22 g, 1.20 mmol) in benzene (1 ml) was added dropwise over 1 min and the reaction mixture stirred for a further 2 h. The ratios of the isomeric t-butylbiphenyls, established by g.l.c. (1% SE30, 138°) were: 2-20%; 3-57%; 4-23%. The total yield of t-butylbiphenyls was approximately 20%.

f Decomposition of Phenylazotriphenylmethane in the Presence of 4-Chlorobenzoyl Nitrite.

Phenylazotriphenylmethane (0.24 g, 0.62 mmol) was added to a solution of 4-chlorobenzoyl nitrite (0.34 g, 1.86 mmol) in benzene (10 ml) at 50°, the reaction mixture being well-stirred. After 1 h, sodium β-naphthoxide (0.40 g, 2.48 mmol) in benzene containing crown ether was added. 1-Phenylazo-2-naphthol (0.021 g, 27 m/100 m) was isolated by dry column chromatography and had m.p. 133-134°, after recrystallisation from ethanol.

11 DECOMPOSITIONS OF DEUTERIATED COMPOUNDS.

All decompositions described below were carried out under dry nitrogen. Potassium acetate was fused immediately before use.

a Reaction of 4-Chlorobenzoyl Nitrite with 2,4,6-[$^2H_3$]Acetanilide in Benzene in the Presence of Acetic Acid and Tetraphenylcyclopentadienone (tetracyclone).

4-Chlorobenzoyl nitrite (0.30 g, 1.6 mmol) in benzene (2 ml) was added dropwise over 10 min to a mixture of 2,4,6-[$^2H_3$]acetanilide (0.152 g, 1.1 mmol) (99% [$^2H_3$]), tetracyclone (0.32 g, 1.1 mmol) and acetic acid (0.13 g, 2.2 mmol) in benzene (20 ml) and the reaction mixture was stirred at room temperature for 3 h and subsequently at 50° for 2 h. Work up using dry column chromatography, eluting with cyclohexane, gave biphenyl (0.032 g, 20 m/100 m), m.p. and mixed m.p. 70-71° (i.r. spectrum) and tetraphenylnaphthalene (0.055 g, 11 m/100 m), m.p. and mixed m.p. 203-204°.

Mass spectral analysis showed 99% [$^2H_3$] retention in the biphenyl and 99% [$^2H_2$] in the tetraphenylnaphthalene.

b Decomposition of Benzenediazonium Fluoroborate in Benzene in the Presence of Tetracyclone and Deuterioacetic Acid.

To a mixture of tetracyclone (0.192 g, 0.5 mmol), potassium acetate (0.098 g, 1 mmol) and deuterioacetic acid (0.06 g, 1 mmol) in benzene (10 ml), benzenediazonium fluoroborate (0.192 g, 1 mmol) was added in three batches, with 30 min between each addition. The temperature of the well-stirred reaction mixture was maintained at 60° for a further 1 h. The reaction mixture was chromatographed on alumina (30 g), eluting with cyclohexane. Biphenyl (0.34 g, 22 m/100 m) and tetraphenylnaphthalene (0.023 g, 6 m/100 m) were isolated and shown to contain no deuterium.

c Decompositions of 2,4,6-[$^2H_3$]Benzenediazonium Fluoroborate.

(i) In the presence of tetracyclone.

To a mixture of tetracyclone (0.38 g, 1 mmol), potassium acetate (0.20 g, 2.4 mmol) and acetic acid (0.036 g, 0.6 mmol) in benzene (12 ml), trideuteriobenzenediazonium fluoroborate (0.39 g, 2 mmol) (99% [$^2H_3$]) was added, as in the previous reaction, to give biphenyl (0.044 g, 14 m/100 m) (99% [$^2H_3$]) and tetraphenylnaphthalene (0.305 g, 35 m/100 m) (99% [$^2H_2$]).

(ii) In the presence of anthracene.

To a mixture of anthracene (0.18 g, 1 mmol), potassium acetate (0.20 g, 2.4 mmol) and acetic acid (0.036 g, 0.6 mmol) in benzene (12 ml) was added the benzenediazonium fluoroborate (0.39 g, 2 mmol) (99% [$^2H_3$]) in three batches with 30 min between each addition. The temperature was maintained at 60° and stirring continued for a further hour. The volume of the reaction mixture was reduced on the rotary evaporator and chlorobenzene (17 ml) and maleic anhydride (0.2 g) were added. The mixture was boiled under reflux for a further 24 h. Chromatography of the reaction mixture

on alumina (50 g) eluting with cyclohexane afforded biphenyl (0.041 g, 5 m/100 m) m.p. and mixed m.p. 69-70°, and triptycene (0.022 g, 5 m/100 m) which was shown to be pure by g.l.c. after recrystallisation from petrol (b.p. 60-80°) containing a little benzene, m.p. and mixed m.p. 255-256°. The biphenyl and triptycene obtained showed deuterium contents of 99% [$^2H_3$] and 99% [$^2H_2$]. respectively.

d Decomposition of 2-[$^2H_1$]Benzenediazonium Fluoroborate.

(i) In benzene in the presence of tetracyclone.

Reaction, as described above, of a mixture of tetracyclone (0.19 g, 0.5 mmol), potassium acetate (0.10 g, 1.2 mmol), acetic acid (0.02 g, 0.03 mmol) and 2-[$^2H_1$]benzenediazonium fluoroborate (0.195 g, 1 mmol) (92% [$^2H_1$]) in benzene (10 ml) at 60° gave biphenyl (0.015 g, 10 m/100 m) and tetraphenylnaphthalene (0.21 g, 29 m/100 m) showing deuterium contents of 92% [$^2H_1$] and 55% [$^2H_1$] respectively.

(ii) In dichloroethane in the presence of tetracyclone.

To a mixture of tetracyclone (0.19 g, 0.5 mmol), potassium acetate (0.10 g, 1.2 mmol) and acetic acid (0.2 g, 0.03 mmol) in 1,2-dichloroethane (10 ml), 2-[$^2H_1$]benzenediazonium fluoroborate (0.195 g, 1 mmol) (92% [$^2H_1$]) was added in 3 batches with 30 min between each addition. The temperature of the well-stirred reaction mixture was maintained at 60° for a further 1 h. Tetraphenylnaphthalene (0.061 g, 15 m/100 m), isolated by dry column chromatography was shown to have a deuterium content of 55% [$^2H_1$].

(iii) In benzene in the presence of anthracene.

Reaction of a mixture of anthracene (0.09 g, 0.5 mmol), potassium acetate (0.10 g, 1.2 mmol) and acetic acid (0.02 g, 0.03 mmol) in benzene (10 ml) and 2-[$^2H_1$]benzenediazonium fluoroborate (0.195 g, 1 mmol) (92% [$^2H_1$]) as described above, gave biphenyl (0.023 g, 15 m/100 m). Triptycene was isolated by preparative g.l.c. (3% SE30, 230°). The yield of triptycene (6 m/100 m) was established by quantitative g.l.c. examination of the reaction mixture

(5% SE30, 220°) using fluoranthene as internal standard. Biphenyl had 92% [$^2H_1$] and triptycene had 58% [$^2H_1$].

(iv) In benzene in the absence of a trap.

Reaction in benzene (10 ml), of a mixture of potassium acetate (0.05 g, 0.6 mmol), acetic acid (0.01 g, 0.015 mmol) and 2-[$^2H_1$]benzenediazonium fluoroborate (0.1 g, 0.5 mmol) (92% [$^2H_1$])gave biphenyl (0.028 g, 36 m/100 m) (92% [$^2H_1$]).

e Decomposition of 2-[$^2H_1$]Benzenediazonium Chloride.

(i) In dichloroethane in the presence of anthracene.

To a mixture of anthracene (0.27 g, 1.5 mmol), potassium acetate (0.30 g, 3.6 mmol) and acetic acid (0.06 g, 0.09 mmol) in dichloroethane (20 ml), 2-[$^2H_1$]benzenediazonium chloride (0.42 g, 3.0 mmol) (92% [$^2H_1$])was added in 3 batches over a period of 1 h. The reaction mixture was vigorously stirred and the temperature maintained at 60°. Stirring was continued for a further 4 h. The products were isolated by column chromatography on alumina (75 g), eluting with petrol. The triptycene fraction was purified by treatment with maleic anhydride in chlorobenzene. Recrystallisation from petrol (b.p. 60-80°) gave colourless crystals (m.p. and mixed m.p. 255-256°). The yield of triptycene was established in a separate experiment by quantitative g.l.c. examination of the reaction mixture (5% SE30, 220°) using fluoranthene as internal standard. The yield of 9-phenylanthracene (11 m/100 m) was established using the calculated yield of triptycene as a standard. The deuterium content of the triptycene and 9-phenylanthracene products were found to be 59% and 92% [$^2H_1$] respectively.

A similar experiment carried out under conditions identical to those of Buxton and Heaney[176] was as follows: to a mixture of anthracene (0.45 g, 2.5 mmol), potassium acetate (0.9 g, 9 mmol) and acetic acid (0.05 g, 0.8 mmol) in dichloroethane (25 ml), 2-[$^2H_1$]benzenediazonium chloride (0.5 g, 3.5 mmol) (94% [$^2H_1$])was added in three batches over a period of 1 h. The reaction mixture was vigorously stirred throughout and the temperature maintained

at 70°. The mixture was then heated under reflux for 16 h, filtered and the solvent removed. The products were isolated by column chromatography on alumina (75 g) eluting with petrol. The triptycene sample was purified as before and the yield (12 m/100 m) established by quantitative g.l.c. The yield of 9-phenylanthracene (12 m/100 m) was calculated as above. The triptycene showed a deuterium content of 58% [$^2H_1$]. The 9-phenylanthracene showed a deuterium content of 94% [$^2H_1$].

f Control Experiments and Calculation of the Isotope Effect.

Three competitive experiments using benzenediazonium fluoroborate, its 2,4,6-[$^2H_3$]-analogue, tetracyclone, potassium acetate and acetic acid in benzene were carried out as described above. The mixture of 1, 2, 3, 4-tetraphenylnaphthalene and its [$^2H_2$] analogue was analysed by m.s. (Table 2). The mean value of k_H/k_D so obtained, indicates the magnitude of the isotope effect leading to the slightly greater ease of formation of benzyne from the undeuteriated benzenediazonium fluoroborate.

TABLE 2

Reactions of PhN_2BF_4 and 2,4,6-[$^2H_3$] $C_6H_2N_2BF_4$ in the presence of Tetracyclone.

	Molar Ratios		
ArN_2BF_4 : T.C.	1	0.5	0.2
2,4,6-[$^2H_3$]ArN_2 : 2,4,6-[$^1H_3$]ArN_2	0.97	1.07	0.97
$^2H_2$-T P N : ^1H-TPN	0.75	0.79	0.73
k_H/k_D	1.29	1.36	1.33

Because the mono-deuteriated substrates employed in the diagnostic experiments above contained between 6- and 8% non-deuteriated

material, it now becomes possible to correct for the fact that relatively more ^{1}H benzyne will be formed from the non-deuteriated component. In practice, this correction factor is low. Thus in the five experiments, isotope rate effects calculated on the assumption that the D- and H-precursors partition equally into benzyne and non-benzyne paths were 1.49, 1.49, 1.71, 1.69 and 1.61. Allowing for the effect summarised in Table 2, these figures become 1.53, 1.53, 1.83, 1.78 and 1.70 giving a spread of 1.5-1.8.

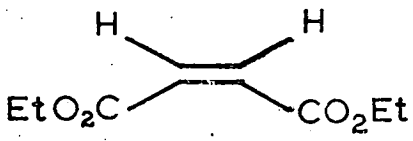
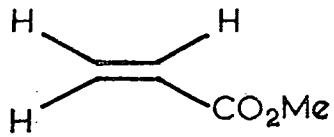
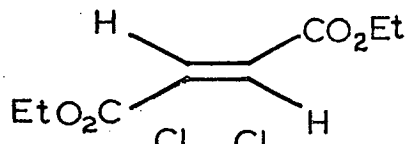
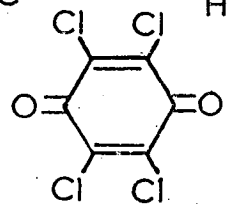
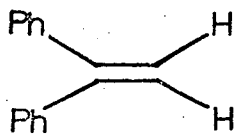
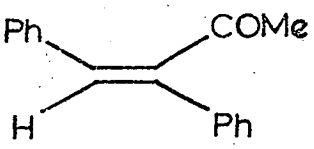
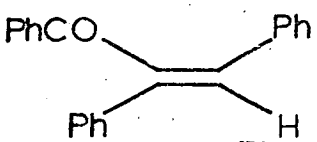
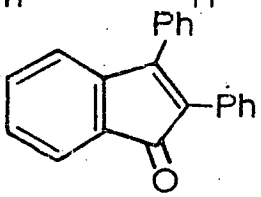
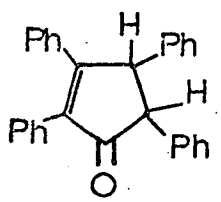
12 DECOMPOSITION OF IN SITU PREPARED N-NITROSO-ACETANILIDE IN THE PRESENCE OF ANTHRACENE AND VARIOUS ADDENDA.

a General Method.

4-Chlorobenzoyl nitrite (1.6 g, 8.6 mmol) in benzene (40 ml) was added over 30 min to a refluxing solution of acetanilide (0.675 g, 5 mmol), anthracene (0.9 g, 5 mmol) and the addendum (5 mmol) in benzene (100 ml). The reaction mixture was then boiled under reflux for 12 h and concentrated. Maleic anhydride (1 g) and chlorobenzene (25 ml) were added and the solution was boiled for 3 h. G.l.c. analysis (5% SE30, 220°) of the reaction mixture using fluoranthene as internal standard gave the yield of triptycene. The results obtained are summarised in Table 3.

TABLE 3

Triptycene Yields in the Decomposition Reactions of in situ N.N.A. in the Presence of Anthracene and Various Addenda.

Addendum	Triptycene (m/100m)
	18
	17
	18
	10
	5
	17
	18
	15
	14
—	17

13 REACTIONS OF N-NITROSOACETANILIDE IN THE PRESENCE OF VARIOUS ADDENDA.

a Reactions in Furan.

(i) 2, 6-Di-t-butylphenol.

N-Nitrosoacetanilide (1. 2 g, 7. 3 mmol) and 2, 6-di-t-butylphenol (1. 5 g, 7. 3 mmol) were dissolved in furan (20 ml) which had been freshly distilled from lithium aluminium hydride and the solution was stirred for 1 h at room temperature. The reaction mixture was then heated slowly to the boiling point and refluxing continued for a further 1 h. Examination of the reaction mixture by g. l. c. (5% NPGS, 135°) using naphthalene as internal standard gave the yield of 2-phenylfuran to be 52 m/100 m. The identity of the 2-phenylfuran product was confirmed by mass spectral/g. l. c. analysis, (Appendix 1). No peak corresponding to 1, 4-dihydro-1, 4-epoxynaphthalene was found (0. 1 m/100 m would have been detected). In a parallel experiment carried out in the absence of the substituted phenol, quantitative g. l. c. analysis gave the yield of 2-phenylfuran to be 78 m/100 m. Distillation of the bulk of this reaction mixture afforded a sample of 2-phenylfuran, b. p. 99-101°/11 mm (lit[177] 107-108°/18 mm), whose i. r. (film) spectrum was indistinguishable from that of an authentic sample.

(ii) 2, 6-Di-t-butyl-4-methylphenol.

N-Nitrosoacetanilide (1. 2 g, 7. 3 mmol) and 2, 6-di-t-butyl-4-methylphenol (1. 6 g, 7. 3 mmol) were dissolved in furan (20 ml) and the solution stirred for 1 h. The reaction mixture was then heated as described above. Examination of the reaction mixture by g. l. c. (5% NPGS, 135°) analysis, using naphthalene as internal standard, gave the yield of 2-phenylfuran to be 18 m/100 m. As in the previous experiment, no peak corresponding to 1, 4-dihydro-1, 4-epoxynaphthalene was observed.

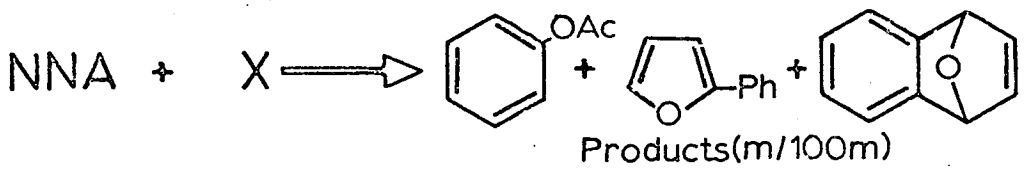
(iii) 2, 3-Diphenylinden-1-one.

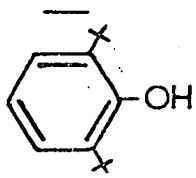
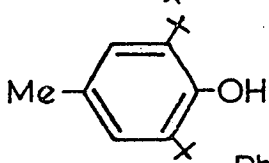
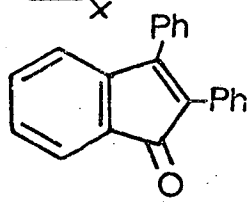
N-Nitrosoacetanilide (1. 2 g, 7. 3 mmol) and 2, 3-diphenylinden-

1-one were dissolved in furan (20 ml) and the solution stirred for 1 h. After heating, in the manner described above, examination of the reaction mixture by g.l.c. (5% NPGS, 135°) analysis showed the presence of phenylacetate (9 m/100 m), phenylfuran (40 m/100 m) and 1,4-dihydro-1,4-epoxynaphthalene (19 m/100 m). The presence of these compounds was confirmed by mass spectral/ g.l.c. analysis (Appendices 1 and 2).

TABLE 4

Reactions of NNA in Furan



X	Products(m/100m)		
—	-	78	-
	-	52	-
	-	18	-
	9	40	19

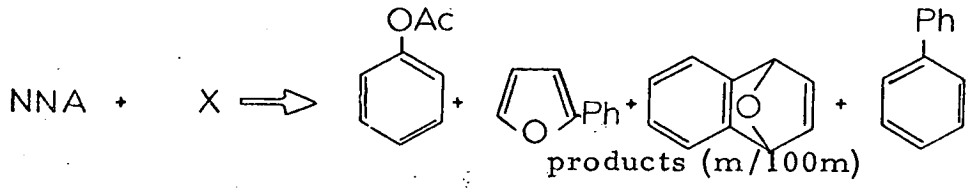
b Reactions in Benzene:Furan

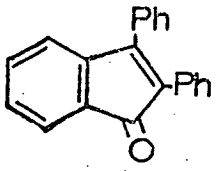
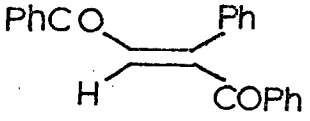
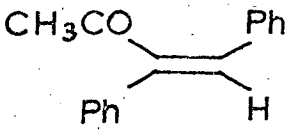
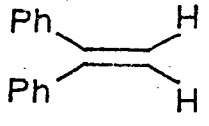
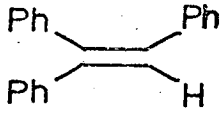
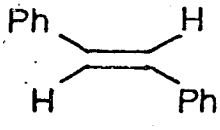
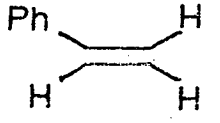
(i) General Reaction

N-Nitrosoacetanilide (0.6 g, 3.6 mmol) was added to a solution of the addendum (3.6 mmol) in furan (3 ml) and benzene (9 ml) with vigorous stirring at 60°. The reaction mixture was then stirred at this temperature for a further 2 h. Quantitative g.l.c. (2% CAR, 135°) analysis of the reaction mixture, using naphthalene as internal standard, gave the yields of phenylacetate, phenylfuran, 1,4-dihydro-1,4-epoxynaphthalene and biphenyl. In all cases g.l.c. peak assignments were verified by g.l.c./m.s. The results obtained are summarised in Table 5.

TABLE 5

Reactions of NNA in Benzene:Furan at 60°



X	products (m/100m)			
——	4	50	7	10
	21	8	37	2
	18	13	43	4
	11	30	23	6
	25	6	46	2
PhCO·COPh	7	42	11	10
	15	25	27	6
	17	18	32	5
	22	9	42	2

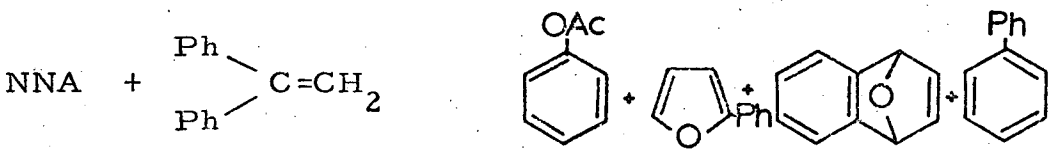
The molar ratio of furan:NNA in these reactions was 12:1

(ii) Conditions for the maximum yield of 1,4-dihydro-1,4-epoxynaphthalene in the presence of 1,1-diphenylethylene.

The dependence on diphenylethylene concentration:

In three parallel reactions, N-nitrosoacetanilide (0.4 g, 2.4 mmol) was added to separate mixtures of 1,1-diphenylethylene in furan (3 ml) and benzene (9 ml) at 60° with stirring. The molar ratios of diphenylethylene to NNA in the three solutions were 1.0, 0.5, and 0.1. Product yields were calculated by internal standard calibration as described in the previous experiment. The results are shown below in table 6.

TABLE 6



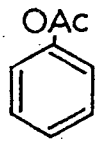
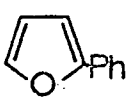
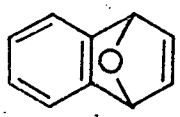
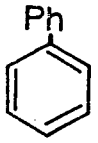
molar ratio	products (m/100 m)			
1.0	23	5	44	1
0.5	23	5	43	1
0.1	17	15	29	4

The dependence on furan concentration

In four parallel reactions, N-nitrosoacetanilide (0.3 g, 1.83 mmol) was added to well-stirred mixtures of 1,1-diphenylethylene (0.16 g, 0.9 mmol) in furan and benzene. The molar ratios of furan to NNA were 0.9, 2.6, 9 and 26. In each reaction, benzene was added in such quantity as to raise the total solvent volume to 7 ml. Product yields were obtained in the same manner described in the previous reactions except for triphenylethylene yields which were calculated using fluoranthene as standard (2% CAR, 220°). In all of these reactions, trace amounts (~1%) of triphenylethane were also produced. The identities of the triphenylethylene and triphenylethane products were established by g.l.c./m.s. analysis

(Appendix 3). The results obtained are summarised in table 7.

TABLE 7

moles furan / moles NNA					$Ph_2C{:}CHPh$
			m/100 m		
0.9	20	1	29	9	8
2.6	22	2	39	6	7
9.0	22	6	43	5	6
26	18	16	40	2	7

c Reactions in Benzene.

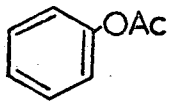
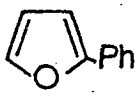
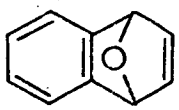
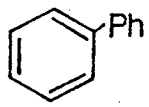
(i) 1, 1-Diphenylethylene.

N-Nitrosoacetanilide (0.3 g, 1.8 mmol) was added to a solution of 1, 1-diphenylethylene (0.16 g, 0.9 mmol) in benzene (6 ml) at 60° with vigorous stirring. The reaction mixture (A) was stirred at this temperature for a further 2 h. G.l.c. examination (2% CAR, 140°) showed that biphenylene was not a reaction product. The yields of phenylacetate, biphenyl and triphenylethylene were calculated as described previously and g.l.c. peak assignments were verified by g.l.c./m.s. through comparison with authentic samples. The recovery of diphenylethylene was calculated by g.l.c. (2% CAR, 135°) using naphthalene as internal standard.

For the purpose of comparison with previous experiments, two parallel reactions were carried out using the same batch of acylarylnitrosamine used above (reaction A) : B, as above in the absence of diphenylethylene; and C, as for A in the presence of furan (1 ml). The results of these three experiments are summarised below in table 8.

TABLE 8

Decomposition of NNA in the presence of various addenda

Product	Yield (m/100 m nitrosamide) A	B	C
	8	6	19
	-	-	8
	-	-	28
	13	36	4
$Ph_2C{=}CHPh$	18	-	8
Accountance(%NNA)	39	42	67
Recovered $Ph_2C{=}CH_2$	10%	-	62%

(ii) 1, 1-Diphenylethylene and anthracene.

N-Nitrosoacetanilide (0.6 g, 3.6 mmol) was added to a mixture of 1, 1-diphenylethylene (0.32 g, 1.8 mmol) and anthracene (0.65 g, 3.6 mmol) in benzene (15 ml) at 30° and 80° with vigorous stirring. After 2 h examination of both reaction mixtures by g.l.c. (1% SE30, 220°) showed that only trace amounts (<2%) of triptycene had been formed, phenylated reactants being the major products. In a blank reaction carried out in the absence of diphenylethylene, the yield of triptycene was shown to be 3%.

d Reaction in Cyclohexene : Furan.

N-Nitrosoacetanilide (0.6 g, 3.6 mmol) was added to a solution of furan (3 ml) and cyclohexene (9 ml) at 60° with vigorous stirring. After 2 h, quantitative g.l.c. analysis as described above gave the following product yields: phenylacetate (38 m/100 m), 2-phenylfuran (5 m/100 m) and 1,4-dihydro-1,4-epoxynaphthalene (22 m/100 m).

14 COMPETITION REACTIONS.

In the reactions described in this section, pentyl nitrite and anthranilic acid were allowed to react with pairs of benzyne traps in benzene. G.l.c. analysis was used to establish adduct yields from which competition ratios were calculated where appropriate. Adduct yields were established using the following conditions and internal standards : triptycene (5% SE30, 220°, fluoranthene); carbmethoxynaphthalene (5% NPGS, 160°, bibenzyl); tetraphenylnaphthalene (1% SE30, 252°, 9, 10-diphenylanthracene) and 9, 10-diphenylanthracene (1% SE30, 252°, tetraphenylnaphthalene).

a Anthracene and methyl coumalate.

Anthranilic acid (1.0 g, 7.5 mmol) in hot benzene (50 ml) was added over 45 min to a solution of pentyl nitrite (1.5 g, 13 mmol), anthracene (5.3 g, 30 mmol) and methyl coumalate (4.6 g, 30 mmol) in boiling benzene (75 ml). Heating was continued for a further 4 h. Adduct yields, calculated as described above were: triptycene (40 m/100 m) and carbmethoxynaphthalene (18 m/100 m); this gives a competition ratio, K^{trip}_{carb}, of 2.2.

b Tetracyclone and anthracene.

Anthranilic acid (1.0 g, 7.5 mmol) in hot benzene (50 ml) was added over 45 min to a solution of pentyl nitrite (1.5 g, 13 mmol), anthracene (5.3 g, 30 mmol) and tetracyclone (11.5 g, 30 mmol) in boiling benzene (75 ml). Heating was continued for a further 4 h. The yield of tetraphenylnaphthalene was 91 m/100 m. No peak corresponding to triptycene was observed (0.1 m/100 m would have been detected).

c 1, 3-Diphenylisobenzofuran and anthracene.

Anthranilic acid (0.17 g, 1.25 mmol) in hot benzene (10 ml) was added over 30 min to a solution of pentyl nitrite (0.25 g, 2.1 mmol), anthracene (0.89 g, 5 mmol) and 1, 3-diphenylisobenzofuran (1.35 g, 5 mmol) in boiling benzene (20 ml). The reaction mixture was heated for a further 4 h. Acetic acid (20 ml) and powdered

zinc (6 g) were then added and the mixture was stirred for 8 h at 85°. The yield of 9, 10-diphenylanthracene was 73 m/100 m. No peak corresponding to triptycene was observed.

d Tetracyclone and 1, 3-diphenylisobenzofuran.

Anthranilic acid (0. 17 g, 1. 25 mmol) in hot benzene (10 ml) was added over 30 min to a solution of pentyl nitrite (0. 25 g, 2. 1 mmol), tetracyclone (1. 92 g, 5 mmol) and 1, 3-diphenylisobenzofuran (1. 35 g, 5 mmol) in boiling benzene. Heating was continued for a further 4 h. The molar ratio of adducts was calculated from a calibration graph of tetraphenylnaphthalene against 9, 10-diphenyl-9, 10-epoxy-9, 10-dihydroanthracene. The competition ratio $K^{tetr.}_{diph.}$ was found to be 1. 2.

15 MISCELLANEOUS REACTIONS.

a Partial Decomposition of 2, 4, 6-[$^2H_3$] N-nitrosoacetanilide, formed in situ, followed by treatment with sodium β-naphthoxide.

4-Chlorobenzoyl nitrite (0. 15 g, 0. 80 mmol) in benzene (2 ml) was added by syringe to a well-stirred mixture of 2, 4, 6-[$^2H_3$] acetanilide (0. 05 g, 0. 37 mmol) (99% [$^2H_3$])and acetic acid (0. 044 g, 0. 74 mmol) in benzene (10 ml) at 45°, under an atmosphere of dry nitrogen. Stirring was continued for 15 min and a solution of sodium β-naphthoxide (0. 085 g, 0. 5 mmol) in water (10 ml) was added to the reaction mixture with vigorous stirring. Extraction of the cooled mixture with ether, followed by dry column chromatography of the crude organic product, afforded 1-phenylazo-2-naphthol (0. 019 g, 20 m/100 m). Mass spectral analysis of the recrystallised product indicated 99% [$^2H_3$]-enrichment in the coupled product. Reaction in the absence of acetic acid gave an identical result.

b Decomposition of Benzenediazonium Fluoroborate in Benzene in the Presence of 18-crown-6-ether.

Benzenediazonium fluoroborate (0. 39 g, 2 mmol) was added

in 3 batches over 45 min to a solution of acetic acid (0.04 g, 0.06 mmol), potassium acetate (0.24 g, 2.4 mmol) and 18-crown-6-ether (0.82 g, 2.2 mmol) in benzene (10 ml) at 20°. The reaction mixture was stirred for 5 h. Biphenyl was identified as the only major product by g.l.c. (1% SE30, 150°) and t.l.c. (alumina ; carbon tetrachloride) analysis. Dry column chromatography on alumina, eluting with carbon tetrachloride, afforded biphenyl (0.12 g, 38 m/100 m) which on recrystallisation from petrol had m.p. and mixed m.p. 70-70.5°. In a parallel experiment conducted in the absence of crown ether, biphenyl was isolated in 50% yield. When the reaction was repeated in the presence of tetracyclone (0.38 g, 1 mmol), only a trace amount of T.P.N. was formed.

c Decomposition of Phenylazotriphenylmethane in the Presence of Potassium Acetate and Tetracyclone.

Phenylazotriphenylmethane (0.7 g, 2 mmol), tetracyclone (1.5 g, 4 mmol) and potassium acetate (0.4 g, 4 mmol) were added to benzene (50 ml) and the mixture stirred under an atmosphere of dry nitrogen for 3 h at 80°. G.l.c. (1% SE30, 250°) and t.l.c. (alumina; cyclohexane) analysis of the reaction mixture showed that tetraphenylnaphthalene was not a product (0.2 m/100 m would have been detected). In a parallel reaction carried out at 50° for 10 h a similar result was obtained.

d Reaction of 4-Chlorobenzoyl Nitrite and Acetanilide with Tetracyclone in Cyclohexane.

4-Chlorobenzoyl nitrite (0.95 g, 5 mmol) in cyclohexane (20 ml) was added over 30 min to a mixture of acetanilide (0.41 g, 3 mmol) and tetracyclone (1.15 g, 3 mmol) in boiling cyclohexane (40 ml). The mixture was boiled under reflux for 16 h. G.l.c. analysis (5% NPGS, 203°) showed that all the acetanilide had been consumed. Dry column chromatography of the reaction mixture on alumina, eluting with cyclohexane, afforded tetraphenylnaphthalene (0.53 g, 41 m/100 m), which on recrystallisation from acetic acid

had m. p. and mixed m. p. 203-204°.

e Decomposition of N-Nitrosoacetanilide in Benzene in the Presence of Anthracene.

N-Nitrosoacetanilide (1.0 g, 6.1 mmol) was allowed to decompose in benzene (10 ml) containing anthracene (1.1 g, 6.1 mmol) at 50° for 12 h. The reaction mixture was then boiled under reflux for 1 h. G.l.c. (1% SE30, 200° and 5% SE30, 205°) analysis, using fluoranthene as internal standard, established the following product yields. 9-Phenylanthracene (26 m/100 m), triptycene (3m/100 m) and biphenyl (10m/100 m). Repetition of this experiment gave identical results and thus disagrees with those obtained by Cook[113] who reported a 56% yield of 9-phenylanthracene.

f Reaction of Bromobenzene with Potassium t-Butoxide in the Presence of β-Naphthol.

A reaction mixture containing bromobenzene (1.57 g, 0.01 mol), potassium t-butoxide (5.0 g, .044 mol) and β-naphthol (1.4 g, 0.1 mol) in dimethylsulphoxide (50 ml) was placed in a rocking autoclave and a pressure of 250 atmospheres of nitrogen established. The high pressure reactor was set in motion and the temperature gradually increased to 80° over 12 h. Investigation of the reaction mixture by g.l.c. (1% SE30, 250°) showed that 1-phenylazo-2-naphthol had not been formed. t-Butylphenyl ether was shown to be the major product, as reported by Cram[178] for the reaction in the absence of β-naphthol.

g. Decomposition of 4-t-Butyl-N-Nitrosoacetanilide in Benzene: Furan in the Presence of Diphenylethylene

4-t-Butyl-N-nitrosoacetanilide (0.79 g, 3.6 mmol) was added to a well-stirred solution of 1,1-diphenylethylene (0.65 g, 3.6 mmol) in furan (3 ml) and benzene (9 ml) at 60°, and stirring continued for 2 h. A parallel control reaction was carried out in the absence of diphenylethylene. Biphenyl (0.1 g) was added to both reaction mixtures and peak area ratios, measured relative to biphenyl, were calculated by g.l.c. (2% CAR, 160°) for the product peaks in both

reaction mixtures. The identity of the four products, 4-t-butylphenylacetate, 2-(4-t-butylphenyl)-furan, 6-t-butyl-1,4-dihydronaphthalene-1,4-endoxide and 4-t-butylbiphenyl was confirmed by g.l.c./m.s. comparison with authentic samples. Assuming a linear relationship between peak area ratio and component concentration, the following conclusions may be drawn. In the presence of diphenylethylene the yields of acetate and endoxide products increased by factors of 6 and 10 respectively relative to the control reaction while a decrease in the yield of both t-butylphenylfuran (6-fold) and t-butylbiphenyl (4 fold) occurred.

16 E.S.R. STUDY OF THE DECOMPOSITION OF N-NITROSOACETANILIDE AND DIBENZOYL PEROXIDE IN THE PRESENCE OF VARIOUS ADDENDA.

a General Procedure:

A measured volume of benzene was added to a known weight of N-nitrosoacetanilide (or in one case, dibenzoyl peroxide) and the addendum in a small beaker. The solution was transferred to a sample tube and degassed on a vacuum line by a process of repeated freezing, evacuation and thawing. The time taken between the mixing of solids and solvent and recording the first spectrum was about five minutes. All spectra were recorded at room temperature except for the decomposition of dibenzoyl peroxide which was effected at 60°. The sample tubes used were of quartz or pyrex and were of 3 or 5 mm internal diameter.

b Determination of g-Values

Measurements were made by comparison with a saturated sodium carbonate solution of Fremy's salt (potassium nitrosodisulphonate) for which $a_N = 13.091 \pm 0.004$ gauss[179] and $g = 2.00550 \pm 0.00005$[180]. A sealed capillary tube containing this solution was either placed inside or attached to the outside of the sample tube.

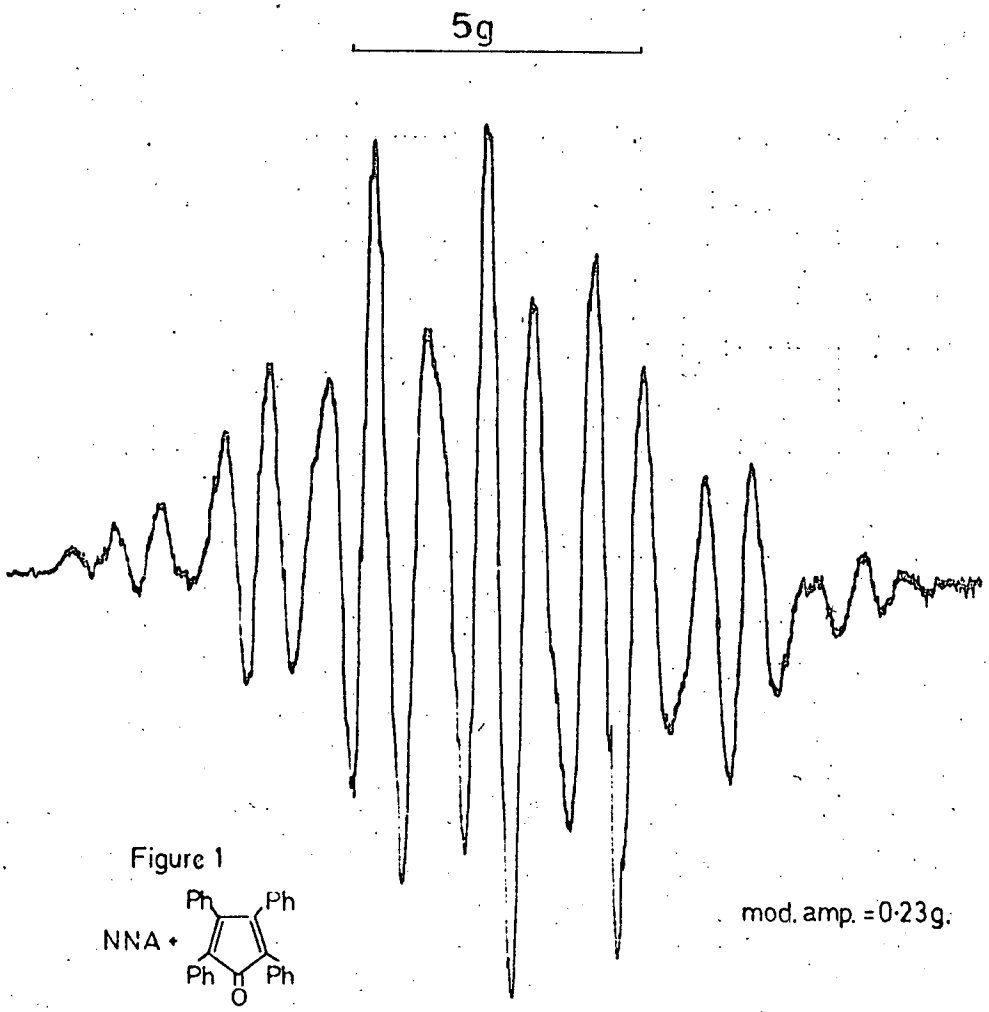


Figure 1

NNA +

mod. amp. = 0·23g.

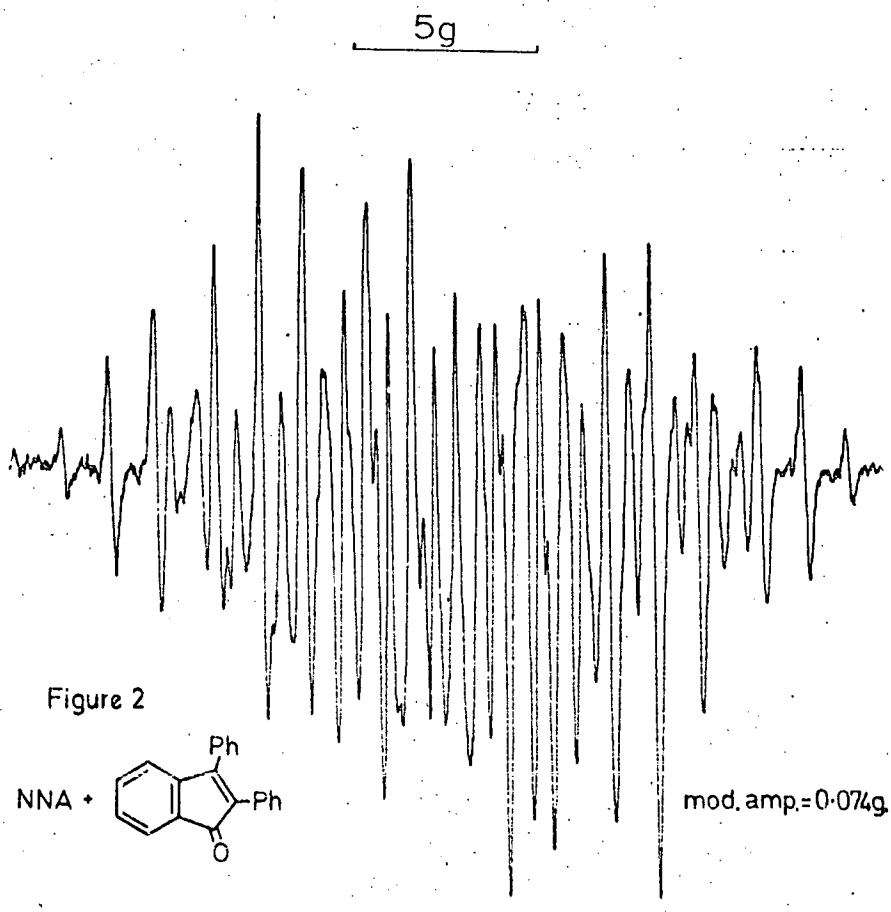


Figure 2

NNA +

mod. amp. = 0·074g.

The concentration of the reference solution was chosen so as to facilitate accurate determination of the separation of the hyperfine lines of both standard and sample. The g-values were calculated from the relationship:

$$g = \frac{h}{\beta H_C} = \frac{h}{\beta(H_{FS} + \Delta F)}$$

where H_C and H_{FS} are the centres of the sample and Fremy's salt signals respectively, and ΔF is the separation of these in gauss. H_{FS} was calculated from its g value thus:

$$H_{FS} = \frac{h}{\beta g} = \frac{6.6252 \times 10^{-27} \times 9270.26 \times 10^{6}}{2.00550 \times 0.92732 \times 10^{-20}} = 3302.47$$

F was measured from the superimposed signals and was defined as positive when the centre of the sample signal was at higher field than that of the standard.

There follows a brief description of the e. s. r. signals observed during the decomposition of the radical precursors in benzene in the presence of various addenda. Due to incomplete resolution, these spectra have not yet been fully analysed.

c Decomposition of N-Nitrosoacetanilide in the Presence of various Addenda.

(i) Tetraphenylcyclopentadienone

N-Nitrosoacetanilide (0. 033 g, . 2 mmol) and tetraphenylcyclopentadienone (0. 05 g, . 13 mmol) were dissolved in benzene (3 ml) and the solution degassed. An intense symmetrical signal was produced with a g-value of 2. 0032. The spectrum is shown in Fig. 1.

(ii) 2, 3-Diphenylinden-1-one

N-Nitrosoacetanilide (0. 1 g, . 6 mmol) and 2, 3-diphenylinden-1-one (0. 17 g, . 6 mmol) were dissolved in benzene (3 ml)

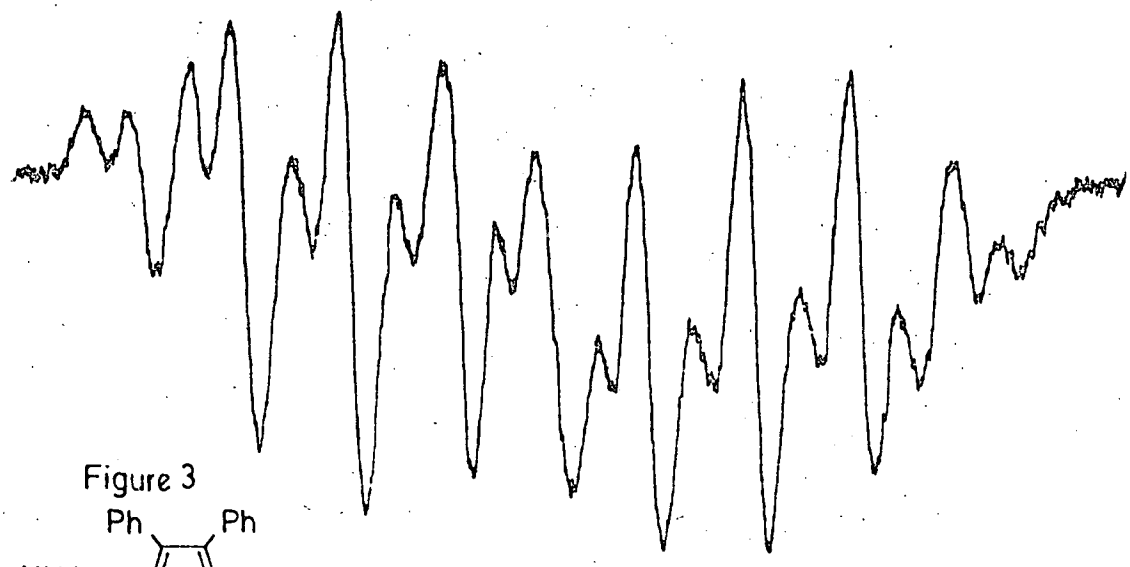
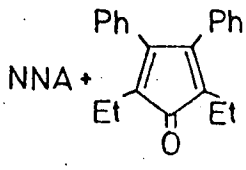


Figure 3



t=1h.

mod. amp.=0·23g.

5g

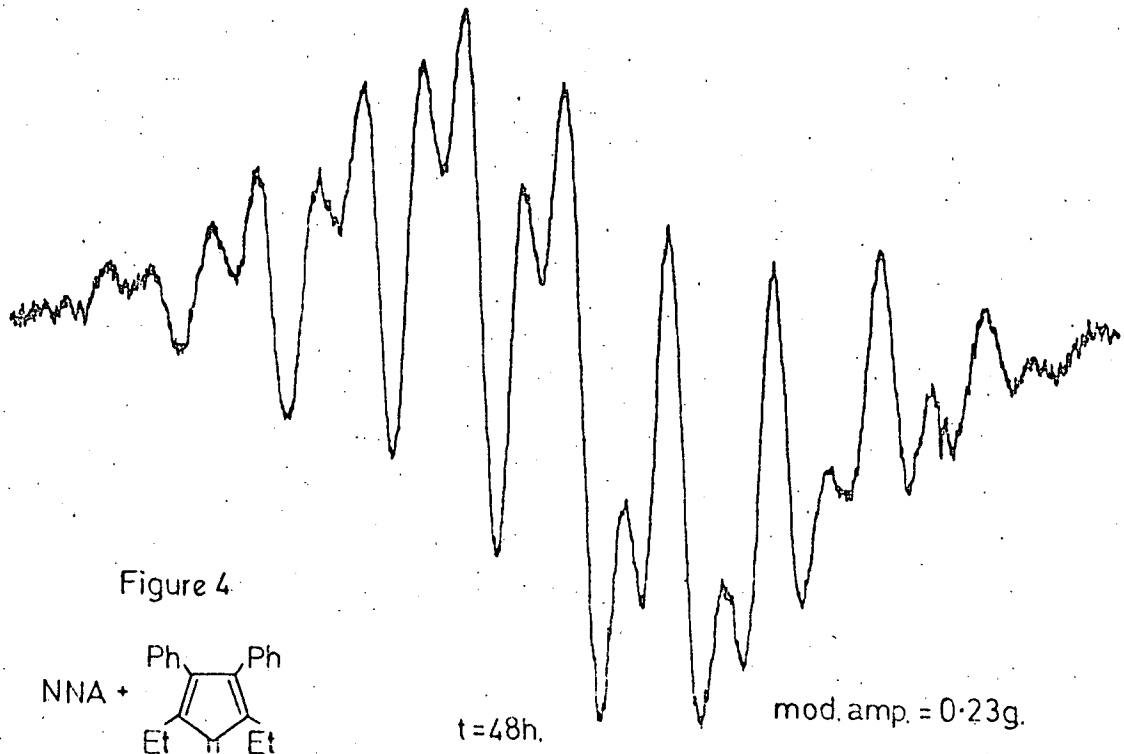


Figure 4

t=48h.

mod. amp. = 0·23g.

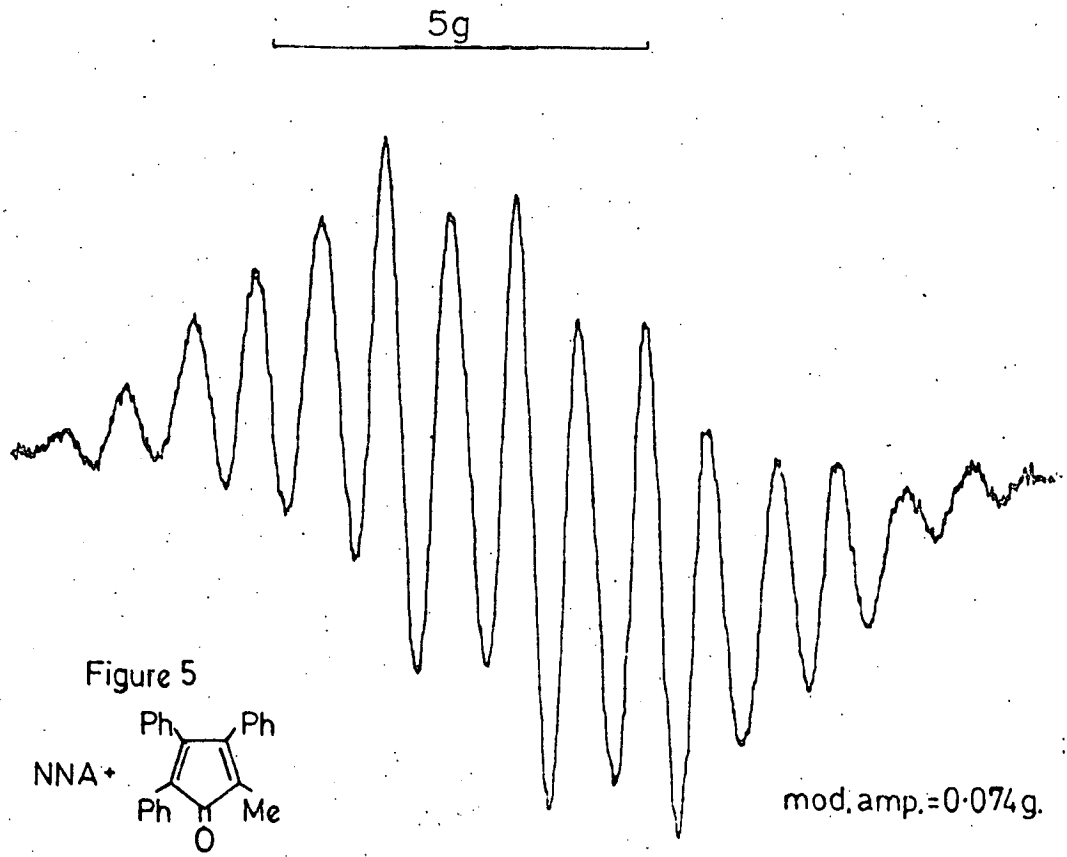


Figure 5

NNA +

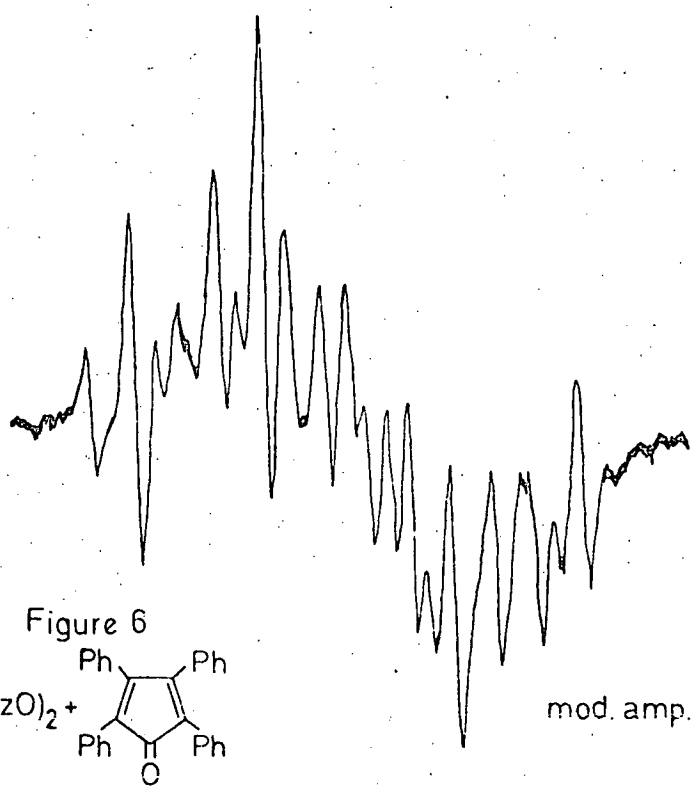


Figure 6

$(BzO)_2$ +

and the solution degassed. An intense symmetrical spectrum was obtained (Fig. 2), and a g-value of 2.0027 calculated.

(iii) 2,5-Diethyl-3,4-diphenylcyclopentadienone

N-Nitrosoacetanilide (0.05 g, .3 mmol) and the cyclopentadienone (0.07 g, .24 mmol) were added to benzene as above. Although a symmetrical signal was produced with a g-value of 2.0031, the peak intensities varied with time suggesting that more than one species was present with similar g-values. (Figs 3 and 4).

(iv) 2-Methyl-3,4,5-triphenylcyclopentadienone

N-Nitrosoacetanilide (0.04 g, .24 mmol) and the cyclopentadienone (0.08 g, .24 mmol) were dissolved in benzene (3 ml) and the solution degassed. A symmetrical signal was produced with a g-value of 2.0031. (Fig. 5).

(v) Anthracene

N-Nitrosoacetanilide (0.033 g, .2 mmol) and anthracene (0.11 g, .6 mmol) were dissolved in benzene as described previously. No signal was detected.

d Decomposition of Dibenzoyl Peroxide

(i) In the presence of tetraphenylcyclopentadienone

Dibenzoyl peroxide (0.05 g, .2 mmol) and the cyclopentadienone (0.05 g, .13 mmol) were dissolved in benzene (3 ml) and the solution degassed. The sample was heated to 60° and the spectrum showed an intense unsymmetrical signal, suggesting the presence of more than one radical species. The spectrum is shown in Fig. 6.

17 DETERMINATION OF ISOTOPIC ABUNDANCE IN DEUTERIO- AND ^{15}N-LABELLED SAMPLES

a ^{15}N-Content

The ^{15}N-content of 1-phenylazo-2-naphthol samples was determined mass spectroscopically, by scanning the molecular weight region and comparing the relative peak heights with those of a sample of known isotopic enrichment. Approximately ten scans were recorded for each sample and average intensities were calculated. Peak heights in both labelled and unlabelled samples were measured from spectra run at 70eV. A typical calculation is outlined below.

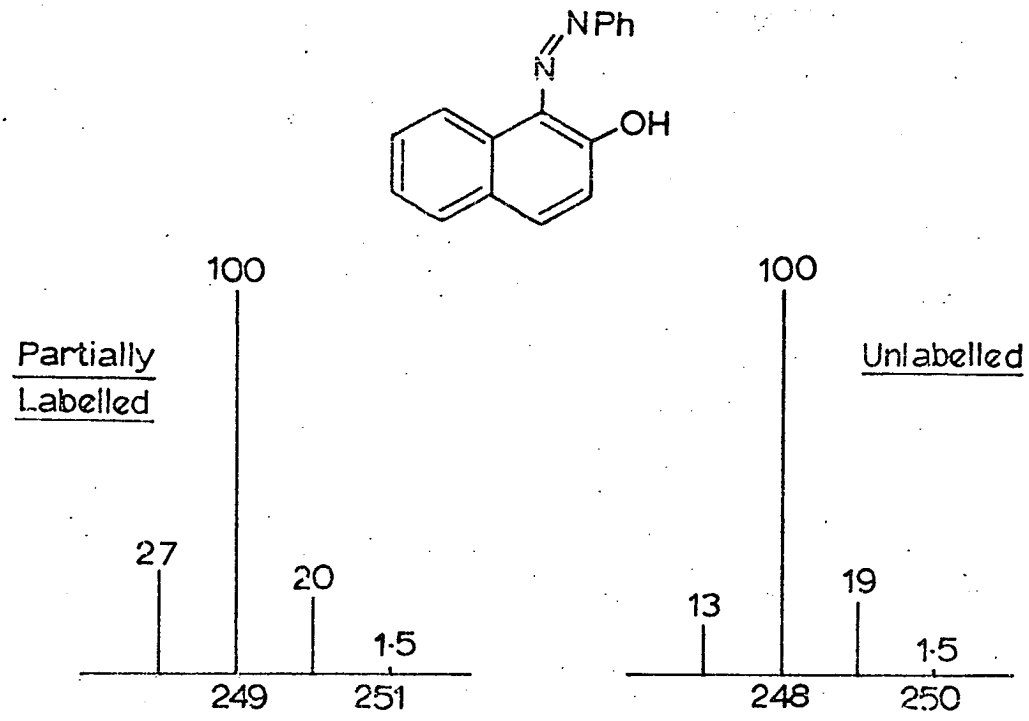
1-Phenylazo-2-naphthol, isolated from a typical partial decomposition reaction using N-nitrosoacetanilide prepared from acetanilide (96% [^{15}N]) and 4-chlorobenzoyl nitrite, gave the following parent peak intensity pattern:

Mass:	M-1	M	M+1	M+2	(M=249)
Intensity:	27	100	20	1.5	

Peak heights are scaled to give the base peak a value of 100, and M denotes the molecular weight peak. An unlabelled sample gave the following spectrum:

Mass:	M-1	M	M+1	M+2	(M=248)
Intensity:	13	100	19	1.5	

In the partially-labelled sample, the peak at mass (M-1) must be due to the molecular weight peak of the unlabelled species and also the (M-1) contribution from the labelled species. Similarly, the peak at mass (M) contains contributions from the molecular weight peak of the labelled compound and the (M+1) contribution from the unlabelled compound. The following quadratic



equations can, therefore be written:

$$100 = x + .19y$$

$$27 = y + .13x$$, where x and y are the parent peak contributions from labelled and unlabelled species respectively. Solution of the equations gives: $x = 97.3$; $y = 14.3$. Thus the ^{15}N-enrichment of the sample is 87%, indicating a 9% loss of the isotopic label.

b Deuterium Content

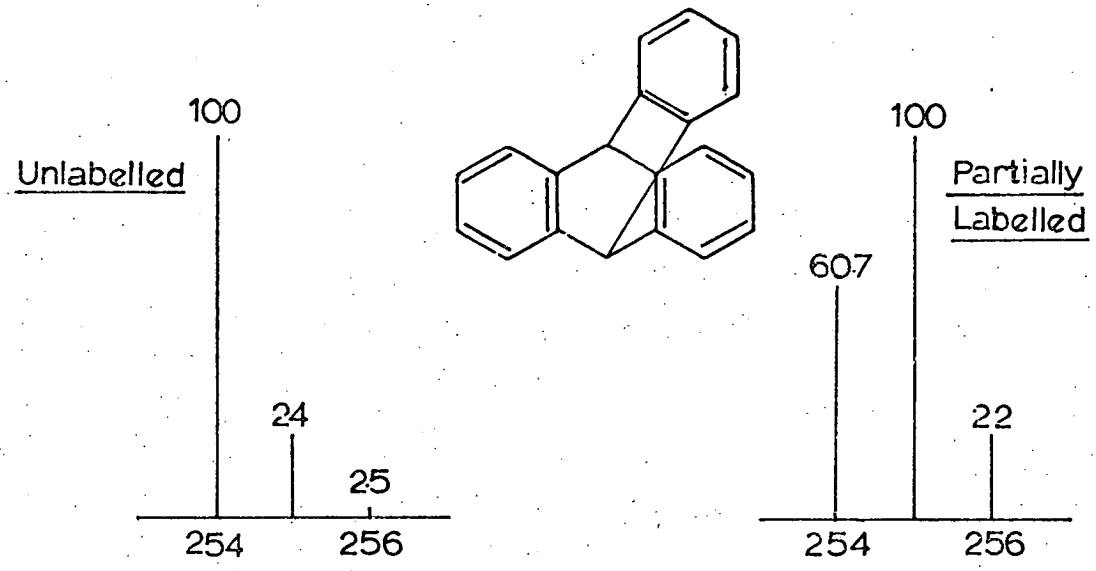
A similar procedure was used for deuterio-labelled samples: peak heights in both labelled and unlabelled samples being measured from spectra run at 70eV and 12eV. In the latter case no fragments of mass M-1, M-2 etc. were formed. The calculation of the deuterium content of a triptycene sample formed via the decomposition of o-deuteriodiazonium chloride (94% [$^2H_1$]) in dichloroethane in the presence of anthracene is outlined below. Spectra were recorded at 12eV.

Peak heights in the unlabelled standard (M denotes the molecular weight peak):

Mass:	M	M+1	M+2	
Intensity:	100	24.0	2.5	(M=254)

Peak heights in the partially-labelled sample:

Mass:	M	M+1	M+2	
Intensity:	60.7	100	22.0	(M=254)



In the partially-labelled sample, the entire peak at mass (M) must be due to unlabelled species. The peak at (M+1) must be due to the mono-deuterio labelled species plus the (M+1) contribution from the unlabelled compound.

Thus 100 = contribution from labelled compound +(60.7 x 0.24)

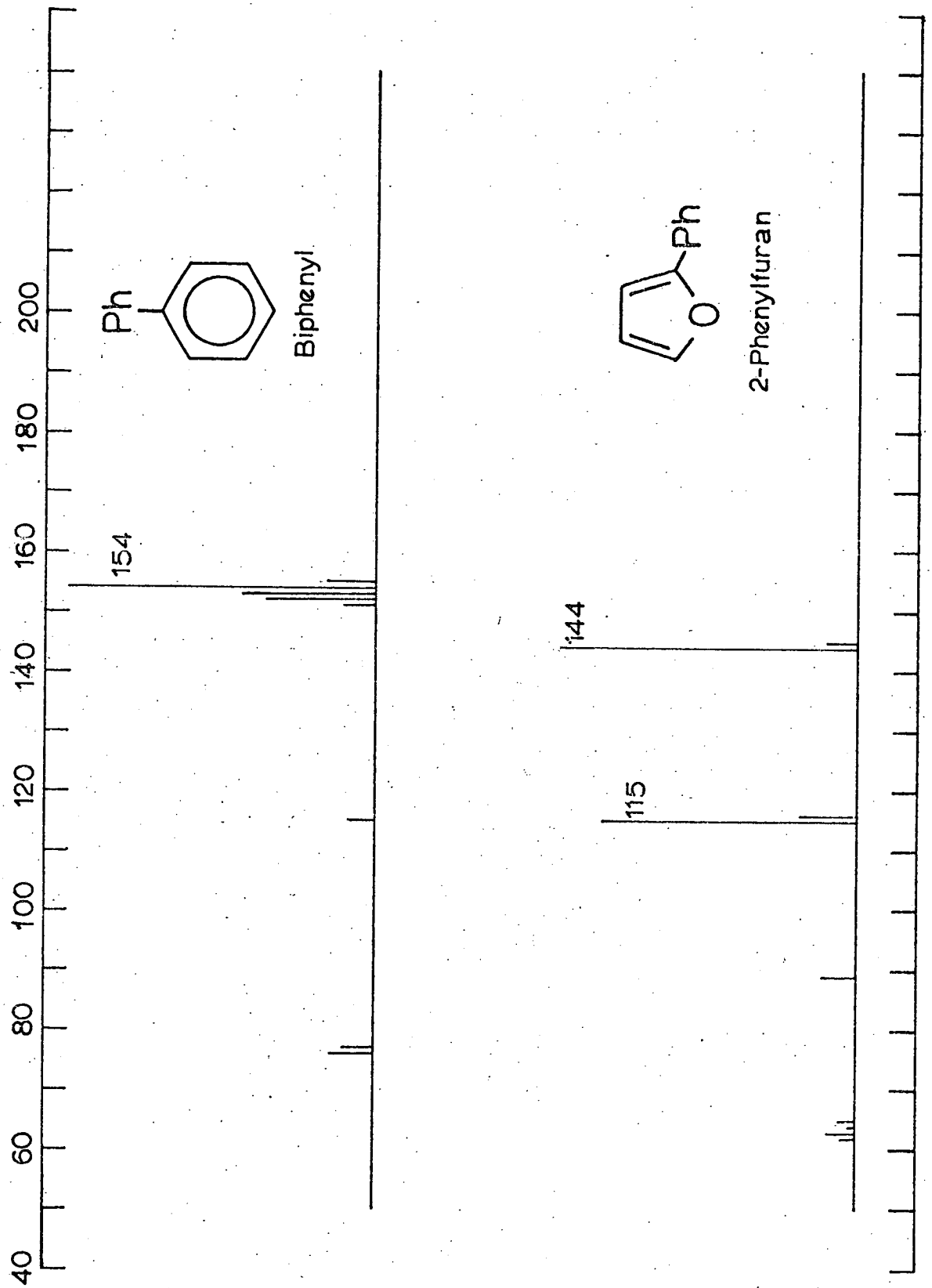
∴ Peak height of singly-labelled compound = 85.4

The sum of the corrected intensities is 60.7 + 85.4 = 146.1.

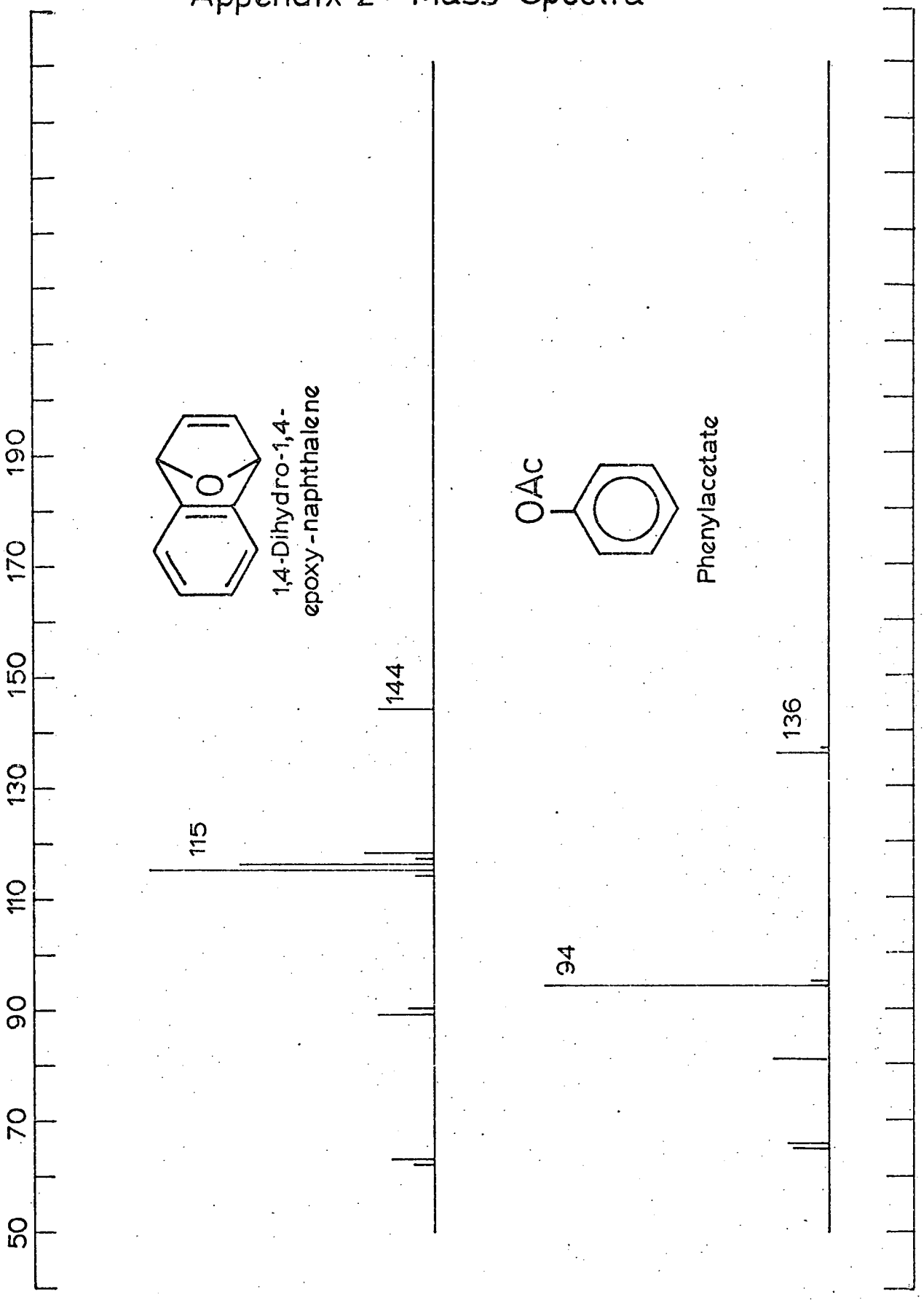
This gives a mole per cent value of labelled compound of 59%, indicating a 35% loss of the label.

The (M+2) intensity allows a cross-check on the calculation. Theoretically, the (M+2) peak height = [.24 (85.4) + .025 (60.7)] i.e. 22.0. This figure agrees with the recorded value.

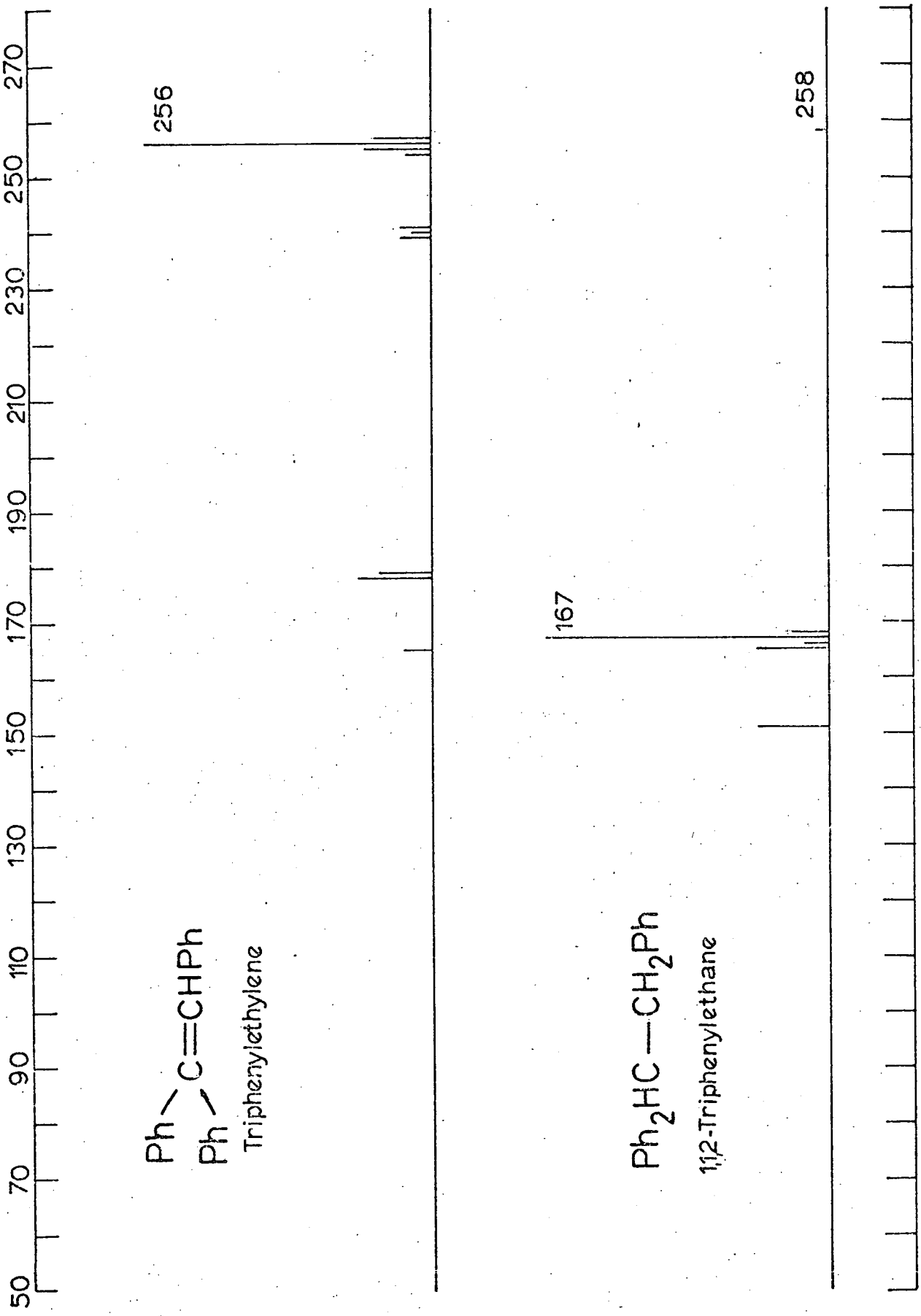
Appendix 1: Mass Spectra



Appendix 2: Mass Spectra



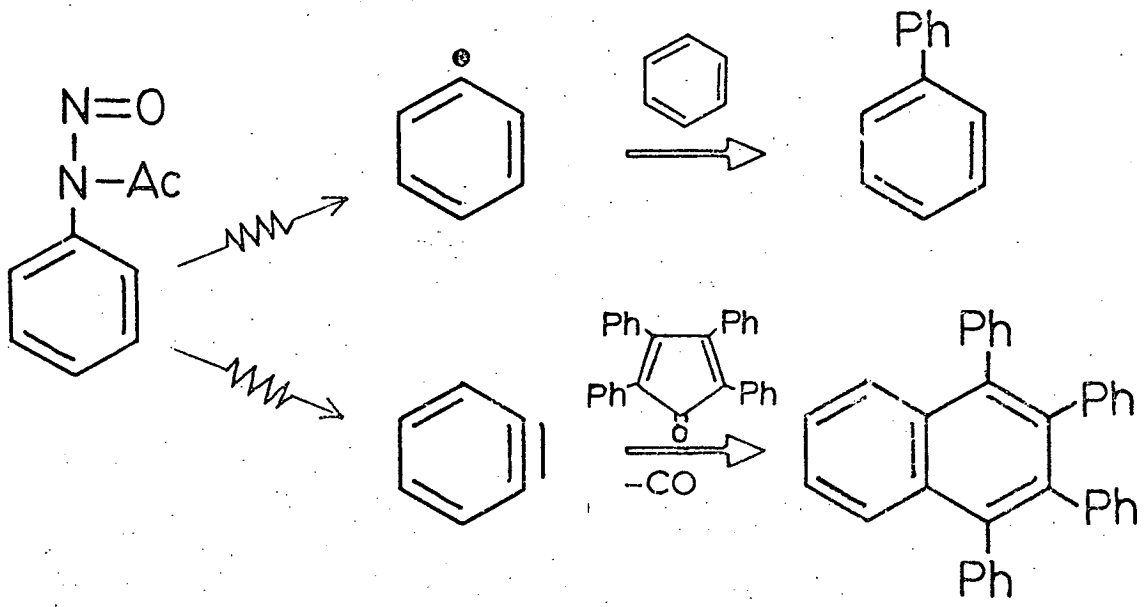
Appendix 3 : Mass Spectra



DISCUSSION OF RESULTS : CONTENTS

THE QUESTION OF NITROGEN EXCHANGE IN THE CONVERSION OF BENZENEDIAZONIUM ACETATE, OR ITS PRECURSORS INTO BENZYNE.

It is now well established that the decomposition of N-nitrosoacetanilide (NNA) in benzene can proceed via two possible routes[111,112] to give either phenyl radicals or the reactive intermediate benzyne. Attack of phenyl radicals on the solvent, followed by

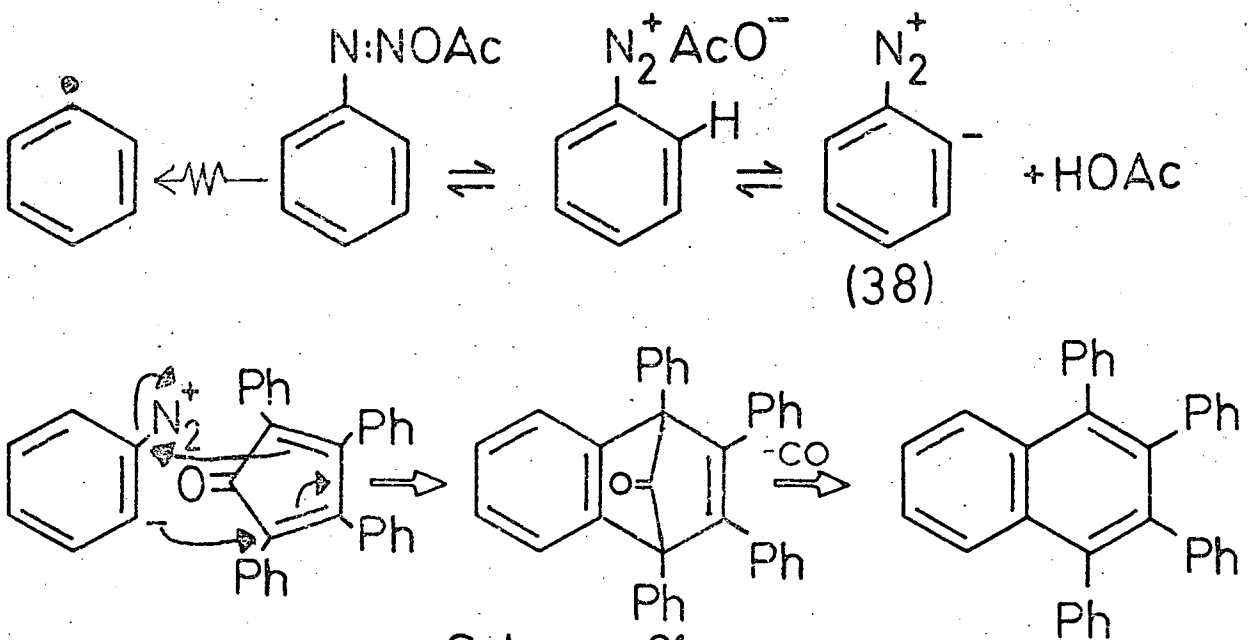


oxidation of the intermediate cyclohexadienyl radical affords biphenyl while benzyne can be conveniently detected through its reaction with 'aryne-traps' such as tetraphenylcyclopentadienone (tetracyclone).

An intriguing feature of the decomposition emerged from the observation that while in the absence of a trap, yields of biphenyl of up to 80% had been recorded[4], an equally high yield of adduct was isolated in the presence of certain arynophiles. Thus decomposition of NNA in the presence of tetracyclone and its 2, 5-di(p-methylphenyl) derivative afforded the corresponding tetra-arylnaphthalenes in 68% and 82% yield respectively[111] with only trace amounts of biphenyl. Other less effective arynophiles, however, such as anthracene, gave poor yields of the adduct, triptycene (5%). More recently, Mitchell[115] isolated triptycene

in 16% yield from a high dilution reaction of NNA, formed by in situ nitrosation of acetanilide by 4-chlorobenzoyl nitrite, in benzene in the presence of anthracene. Repetition of this reaction has allowed the yields of the radical-derived products, biphenyl (24%) and 9-phenylanthracene (5%) to be established. Such observations indicate that in the presence of certain arynophiles, such as tetracyclone, decomposition of NNA is diverted from the radical pathway into that leading to benzyne.

Formation of a benzyne adduct at the expense of phenylated products implies the intermediacy of a precursor common to both decomposition routes. With this in mind, Brydon[121] suggested that the balance between a radical and aryne pathway could be explained by invoking the intermediacy of a dipolar species (38) formed by reversible proton abstraction from the diazonium cation. He argued that the betaine would form a benzynoid adduct with

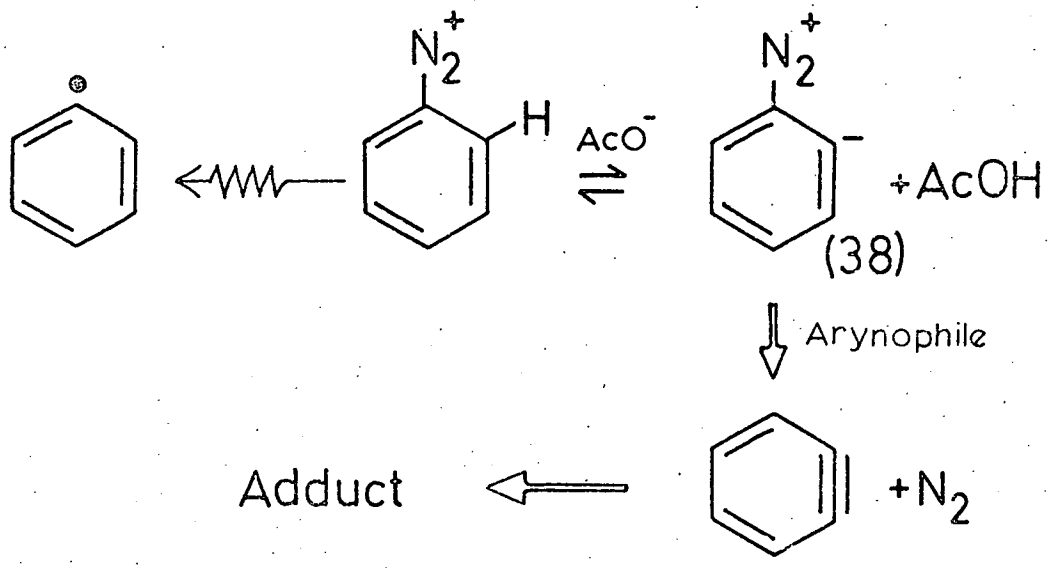


Scheme 21

highly polarisable cyclic dienes, such as tetracyclone, but in the absence of such arynophiles the radical route would be preferred (Scheme 21).

Cadogan and Cook later showed,[111, 113] however, that both NNA and authentic benzyne sources gave aryne adducts at the same

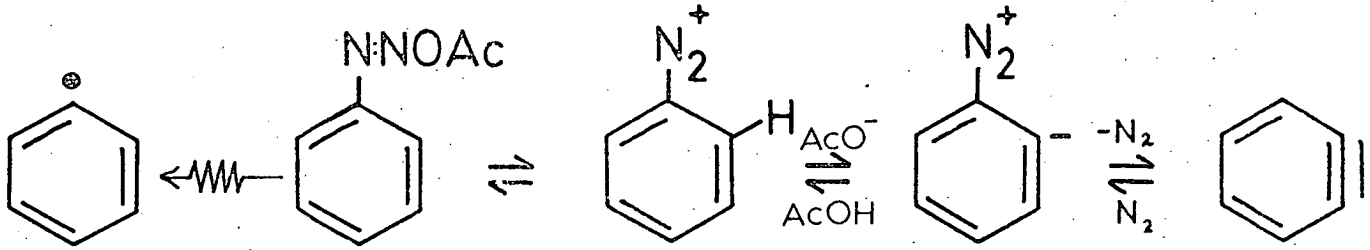
rate, thereby implying the complicity of a true benzyne species during the decomposition of NNA. Cook suggested that the betaine (38) could still be the elusive common intermediate but he proposed a mechanism (Scheme 22) to explain the 'tetracyclone-like' effect, in which a true benzyne was involved.



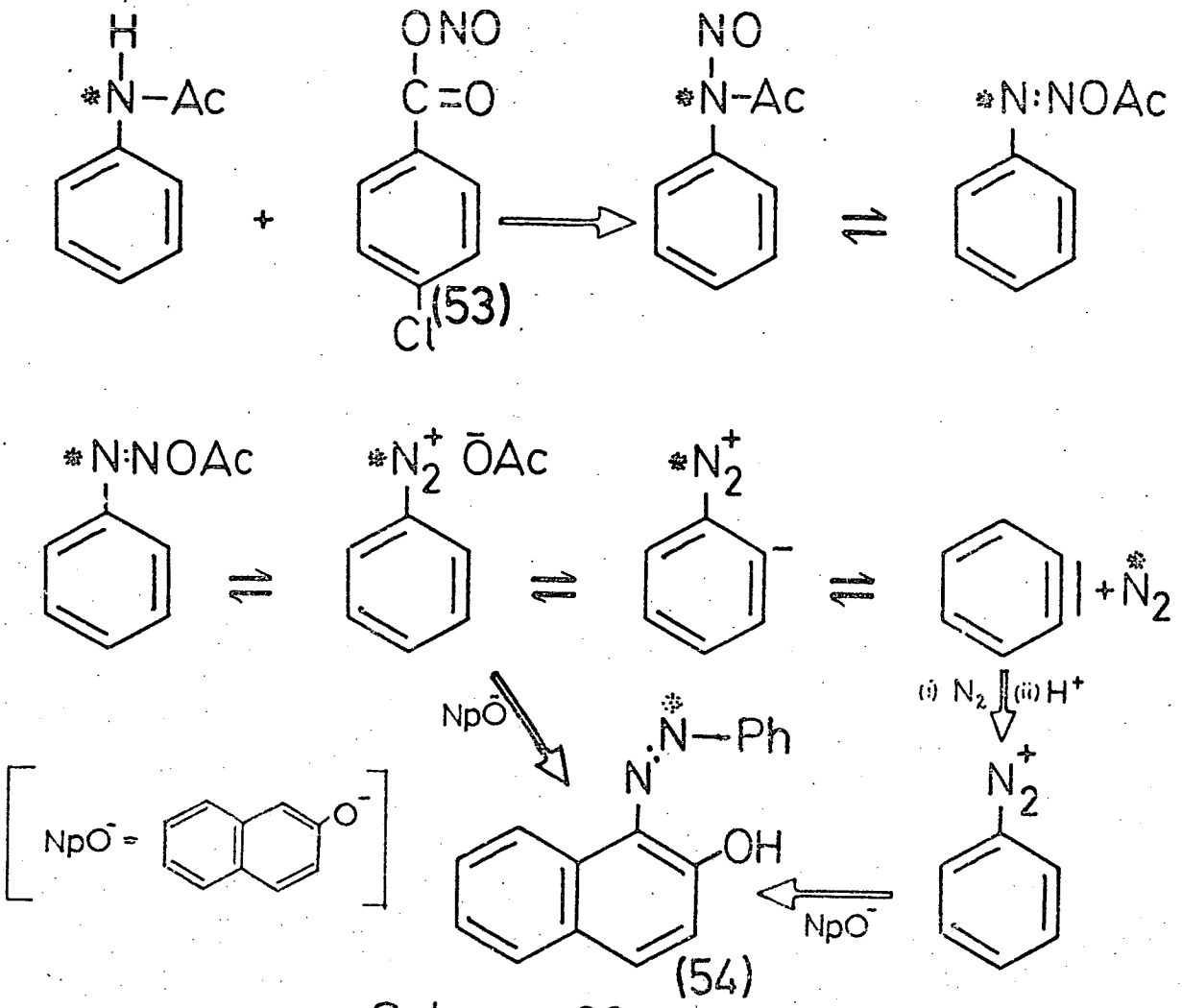
Scheme 22

Thus arynophile-induced decomposition of the betaine leads to aryne and hence adduct formation, while in the absence of the appropriate arynophile, the equilibrium shifts in favour of phenylation. Cook took as evidence for the intermediacy of (38) his observation that decomposition of NNA in benzene in the presence of dimethylacetylenedicarboxylate (D. M. A. D.) gave 1, 2, 3, 4-tetramethoxycarbonylnaphthalene while authentic benzyne gave dibenzocyclooctatetraene (see Introduction, p.38). He argued that in the presence of D. M. A. D., the betaine was intercepted before it could decompose to benzyne. Cadogan and Baigrie have recently shown, however, that the tetramethoxycarbonylnaphthalene results from a phenyl radical induced annelation process.[114] Thus at the outset of the work described in this thesis no satisfactory explanation existed for the role played by tetracyclone and analogous arynophiles during the decomposition of NNA.

If tetracyclone functions only as an efficient aryne trap and if, therefore, it fulfils no other role in the overall mechanism (other possible aspects of the tetracyclone behaviour will be considered later), then a possible explanation of the empirical observations is that loss of nitrogen from the betaine is reversible. Under these circumstances it can be argued that the high yield of benzyne adduct in the presence of tetracyclone is a consequence



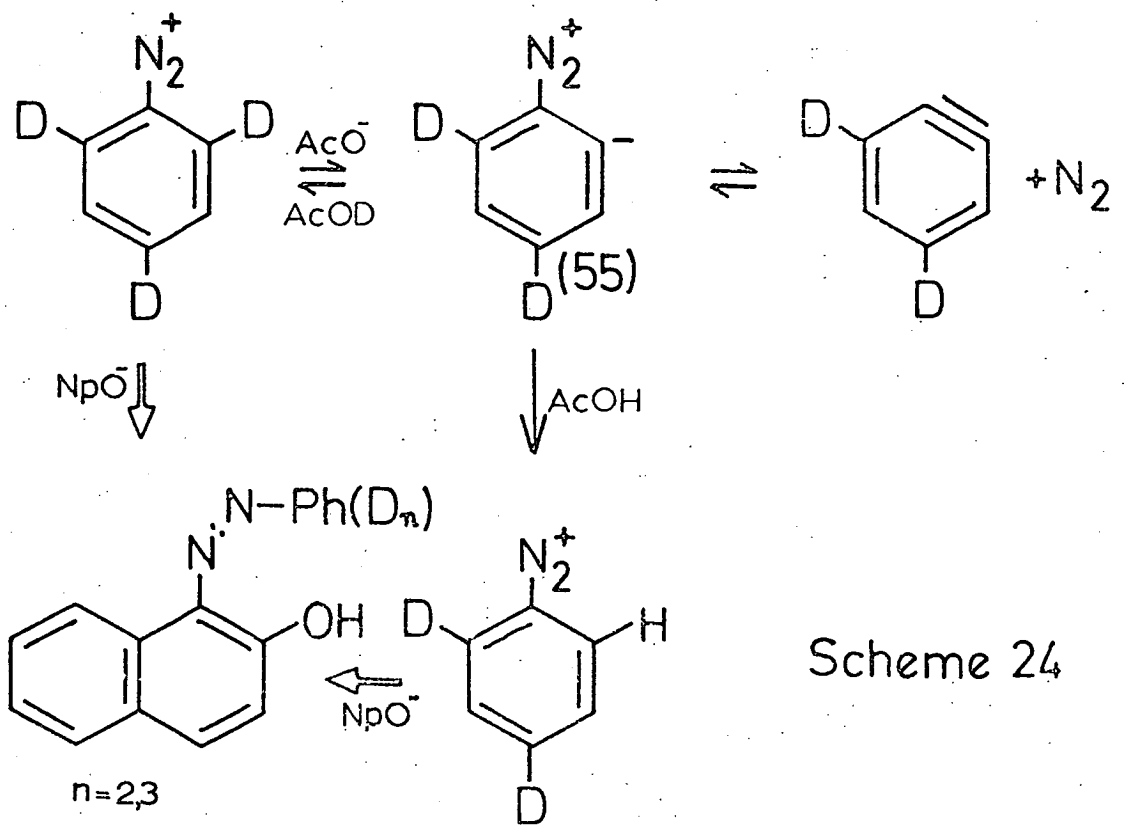
of the extreme arynophilicity of the aryne trap, while decomposition of NNA in benzene in the presence of a weaker arynophile (or in the absence of any trap at all) proceeds predominantly via the radical pathway. In order to investigate the potential reversibility of the benzyne-forming step, ^{15}N-labelled NNA, formed by in situ nitrosation of labelled acetanilide (96% [^{15}N]) by 4-chlorobenzoyl nitrite (CBN) (53) was allowed to decompose in benzene at 45° and 65° under an atmosphere of nitrogen. The reaction mixture was treated with a solution containing sodium β-naphthoxide after a predetermined time and the retention of nitrogen label in the resulting diazonium coupled product, 1-phenylazo-2-naphthol (54), determined by mass spectrometry. For the reaction at 45° the azo product showed a ^{15}N-isotope content of 93% indicating a 3% loss of the label while at 65° a 43% loss of the label was observed. These results, therefore, were consistent with a mechanism involving reversible loss of nitrogen from the betaine, as shown in Scheme 23. The position became less clear, however, when a comparable loss of nitrogen label was found for a corresponding reaction in the presence of tetracyclone. If scheme 23 accurately represents the decomposition mechanism and if tetracyclone



Scheme 23

functions as a powerful arynophile, then a much reduced loss of ^{15}N-label should have been observed for this reaction since tetracyclone would compete for the benzyne more efficiently than molecular nitrogen. The possible complicity of benzyne in the nitrogen exchange process was, therefore, further tested using deuterio-labelled NNA.

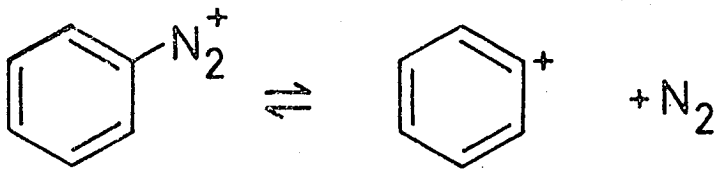
Partial decomposition of the trideuterio-acylarylnitrosamine formed by *in situ* nitrosation of 2,4,6-[$^2H_3$]*N*-nitrosoacetanilide (99% [$^2H_3$]) followed by treatment of the reaction mixture with aqueous naphthoxide gave an azo product which showed no loss of label. Now if Scheme 24 accurately describes the acetate ion induced decomposition of the diazonium cation then loss of deuterium should have been observed in the azo product since, under the



Scheme 24

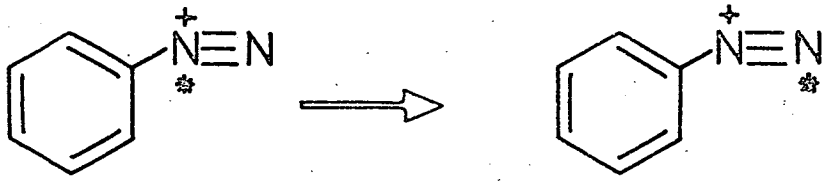
experimental conditions, reprotonation of the dideuterio-betaine (55) would involve hydrogen as well as deuterium. Further doubt was thrown on the feasibility of nitrogen incorporation by benzyne when the generation of benzyne from bromobenzene and potassium t-butoxide in the presence of β-naphthol at a pressure of 250 atmospheres of nitrogen failed to give any trace of 1-phenylazo-2-naphthol.

The possibility that nitrogen isotope exchange was the result of a reaction of free molecular nitrogen with some other highly energetic and unselective electrophilic species such as the aryl cation was next considered. Like the analogous reaction

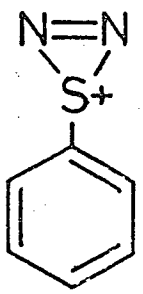


involving benzyne, such a process could well be a model for the

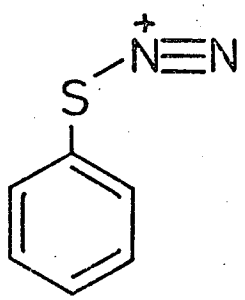
crucial step in the natural fixation of nitrogen. Insole and Lewis[181] have reported that when ^{15}N-benzenediazonium fluoroborate is subjected to hydrolysis at 35° until about 80% of the diazo compound is converted to phenol, the residual diazo compound shows rando-



misation of the isotopic label. That this resulted from the reaction of aryl cation with free molecular nitrogen, however, was discounted on the basis that an analogous reaction in which decomposition of benzenediazonium fluoroborate under 700 psi of carbon monoxide led to no detectable amount of benzoic acid. Lewis argued that if the isoelectronic and more powerful nucleophile, CO, gave no reaction with the phenyl cation, then a similar process involving nitrogen would be even more unlikely. Three years later, Owsley and Helmkamp[182] reported a reaction between benzenesulphenium ion, $C_6H_5S^+$, and molecular nitrogen under mild conditions. Although no pure products were isolated from this reaction, the presence of nitrogen in product mixtures was inferred from analyses and infra-red spectra. Initial incorporation of nitrogen by the sulphenium ion was believed to give either a cyclic (56) or linear (57) structure.



(56)



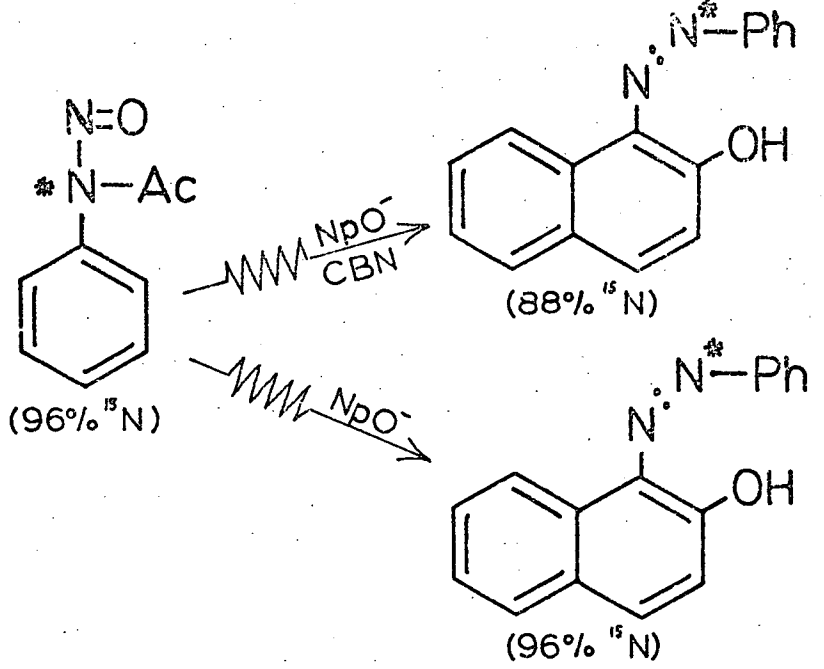
(57)

This work gave added significance to the investigation of diazonium salt decompositions under the same conditions as exchange had been observed using N-nitrosoacetanilide as the diazonium precursor. Thus labelled benzenediazonium fluoroborate (99% [^{15}N])

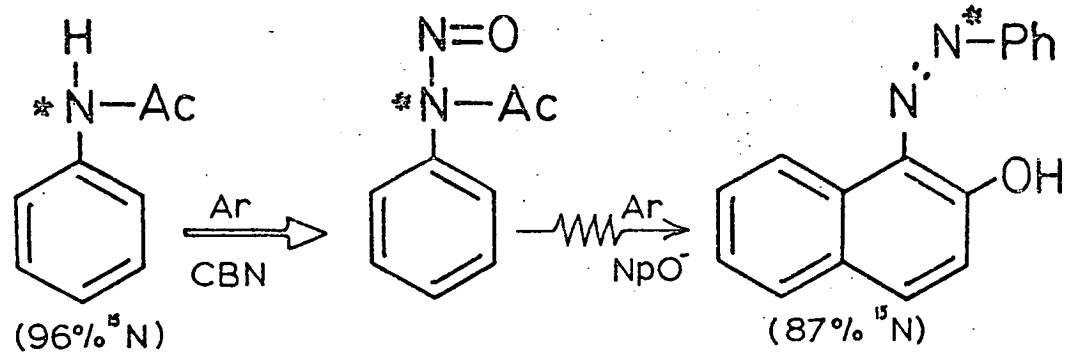
was partially decomposed in benzene, water, acetone, methanol and a mixture of benzene:water (2:1) at 60° and the reaction mixtures treated with aqueous sodium β-naphthoxide. In all cases the ^{15}N-content of the azo product was 99%.

The Role of 4-Chlorobenzoyl Nitrite in the Exchange Reaction: A New Route to Phenyl Radicals.

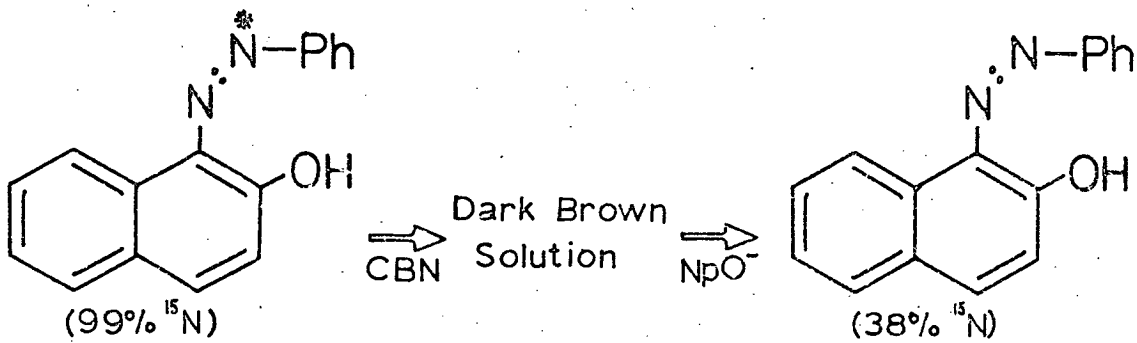
As a continuation of the investigation into the observed isotopic exchange in the original reactions, the complicity of the nitrosating agent, CBN, the only other source of unlabelled nitrogen in the system was investigated. Thus preformed NNA (96% [^{15}N]) was partially decomposed in benzene and the reaction mixture treated with naphthoxide. Complete retention of the label was found in the azo product, while in a parallel reaction in the presence of CBN partial loss of the label was observed. These observations strongly suggested that the source of ^{14}N in the azonaphthol was the nitrosating agent and not molecular nitrogen.



Compelling evidence that atmospheric nitrogen was not implicated in the exchange came from the observation that substantial loss of the isotopic label resulted from the decomposition of NNA prepared in situ in degassed benzene under an atmosphere of argon.



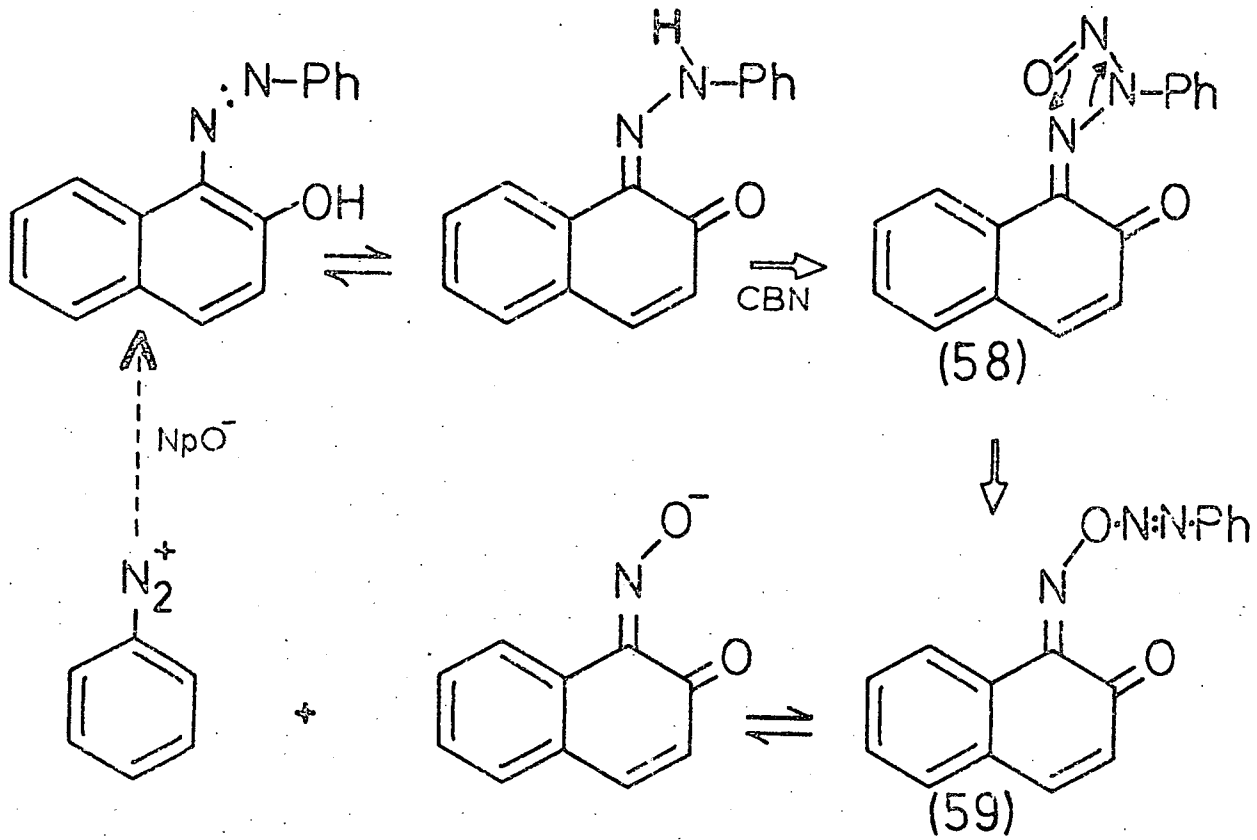
The situation became more involved when the reaction of CBN with 1-phenylazo-2-naphthol in benzene at room temperature or 80° led to rapid decomposition of the azo compound, immediate decolourisation of the solution accompanying the addition of nitrosating agent. Subsequent addition of aqueous alkaline β-naphthol led to the instant regeneration of the azo-naphthol. Furthermore, when the reaction was repeated using ^{15}N-labelled azo compound, extensive loss of the label (61%) was



observed. It is worth mentioning at this point that Huisgen has also reported the decolourisation of a solution of 1-phenylazo-2-naphthol in glacial acetic acid on addition of sodium nitrite,[183] a reaction that will be discussed in more detail later.

Since 1-phenylazo-2-naphthol exists partially in the hydrazone form,[184] it is possible that nitrosation proceeds via the nitrosohydrazone (58) which can then rearrange through the diazo-ether (59) to the diazonium cation (Scheme 25) by analogy with the nitrosation and decomposition of acetanilide. Evidence for this mechanism obtained from the observation that while instant

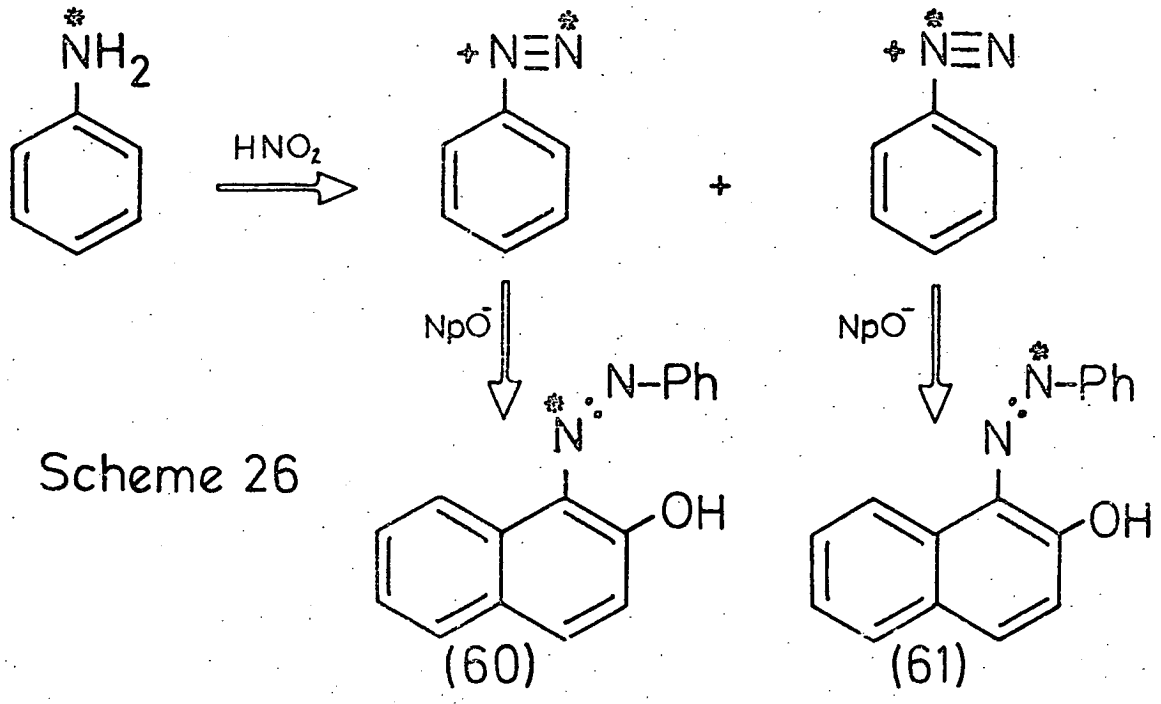
decolourisation accompanied the addition of CBN to benzene solutions of the isomeric 4-phenylazo-1-naphthol and 2-phenylazo-1-naphthol no reaction occurred between the nitrosating agent and either 1-phenylazo-4-methoxynaphthalene or azobenzene, neither of which can assume a hydrazone structure. While Scheme 25



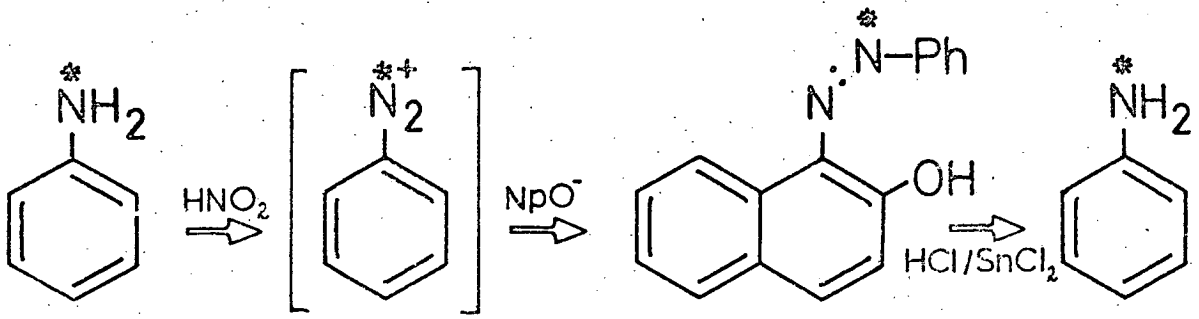
Scheme 25

accounts for the decomposition and subsequent regeneration of the azo compound on treatment with naphthoxide solution, however, it does not on its own account for the loss of the nitrogen label. A possible explanation was that during the preparation of the labelled azo compound (via diazotisation of labelled aniline in the presence of β-naphthol) randomisation of the label, analogous to that described by Lewis and Insole,[181] had occurred thereby leaving the absolute isotopic content unaltered but the position of the label variable (Scheme 26). If this had indeed happened, then it can be seen from Scheme 25 that loss of the label should be

Scheme 26



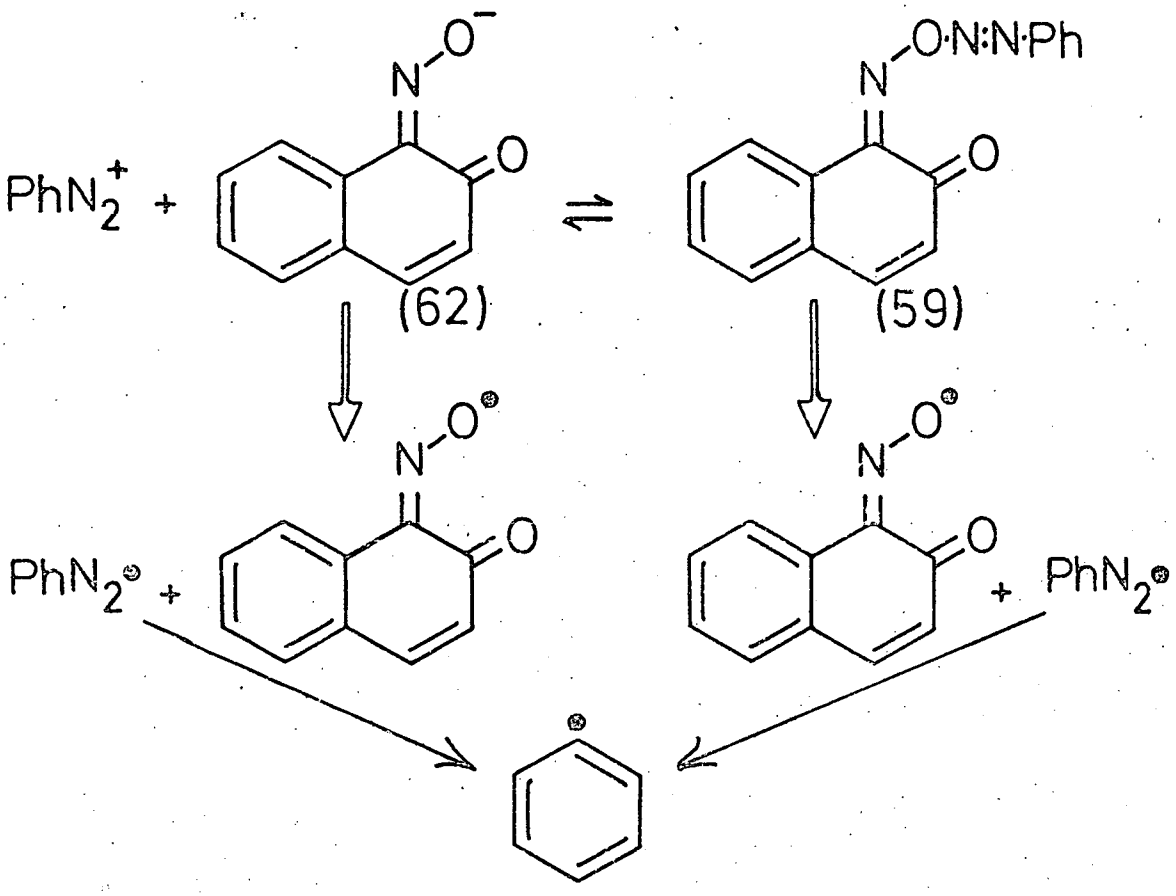
observed in the final product formed by nitrosation of (60) but not (61). Holt and Bullock,[185] however, have established the lack of interchange between the nitrogens of a diazonium ion during the diazotisation reaction by treating labelled aniline with acidified sodium nitrite, coupling the diazonium salt and regenerating the aniline by reduction of the azo compound. Complete retention of



the label was observed. That Scheme 26 did not apply was conclusively established when an n. m. r. spectrum of the azo compound gave only one ^{15}N-resonance.

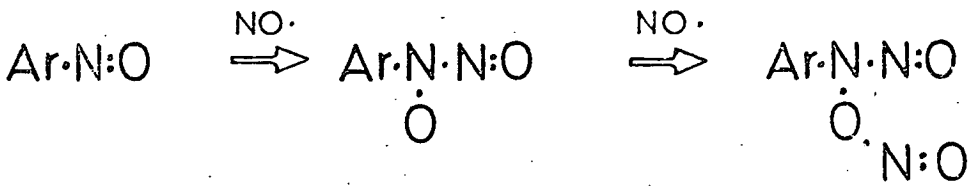
Further insight into the reaction obtained from the observation that nitrosation of 1-phenylazo-2-naphthol without subsequent addition

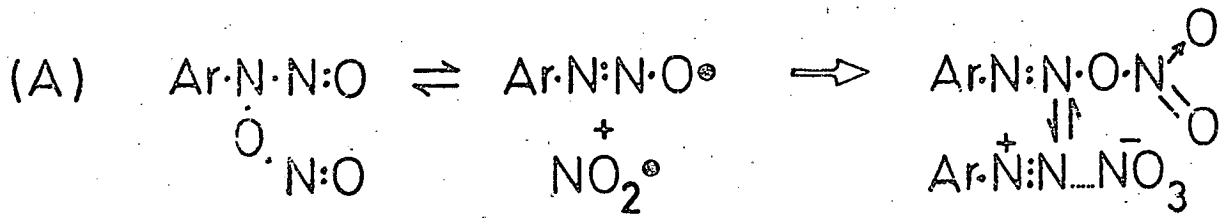
of the diazonium trap gave biphenyl as the only major isolable product in 30% yield. Phenyl radicals are presumably formed *via* homolysis of the covalent diazoether (59) or by decomposition of the diazenyl radical formed by a one electron transfer reaction involving the diazonium cation and (62).

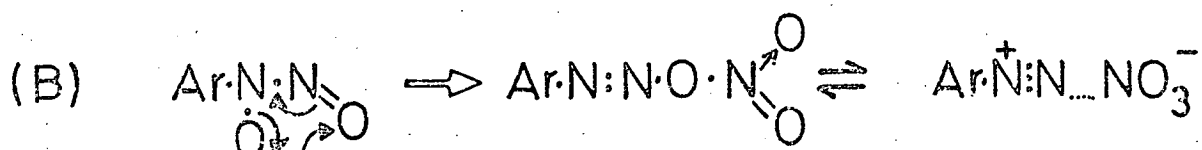


That biphenyl was formed by way of phenyl radical attack on solvent followed from the formation of a mixture of isomeric t-butylbiphenyls of the correct, i. e. radical derived, isomeric composition (2-, 20%; 3-, 57%; 4-, 23%),[107] when the reaction was carried out in t-butylbenzene rather than benzene. Thus nitrosation of both acetanilide and 1-phenylazo-2-naphthol results in the formation of phenyl radicals; both act as sources of the diazonium cation; and in the decomposition of both nitrosated labelled compounds, loss of the isotopic label is observed when the diazonium moiety is trapped by sodium β-naphthoxide.

Almost eighty years ago, Bamberger showed that nitric oxide will convert nitrosobenzene into benzenediazonium nitrate and that sodium nitrite will do the same.[186] More recently, Tedder and Theaker[187] have forwarded mechanisms to explain the formation of diazonium salts by the direct interaction of nitrous derivatives with aromatic compounds. They have suggested a simple addition mechanism, followed by either a dissociation and readdition (A) or an intramolecular rearrangement (B):

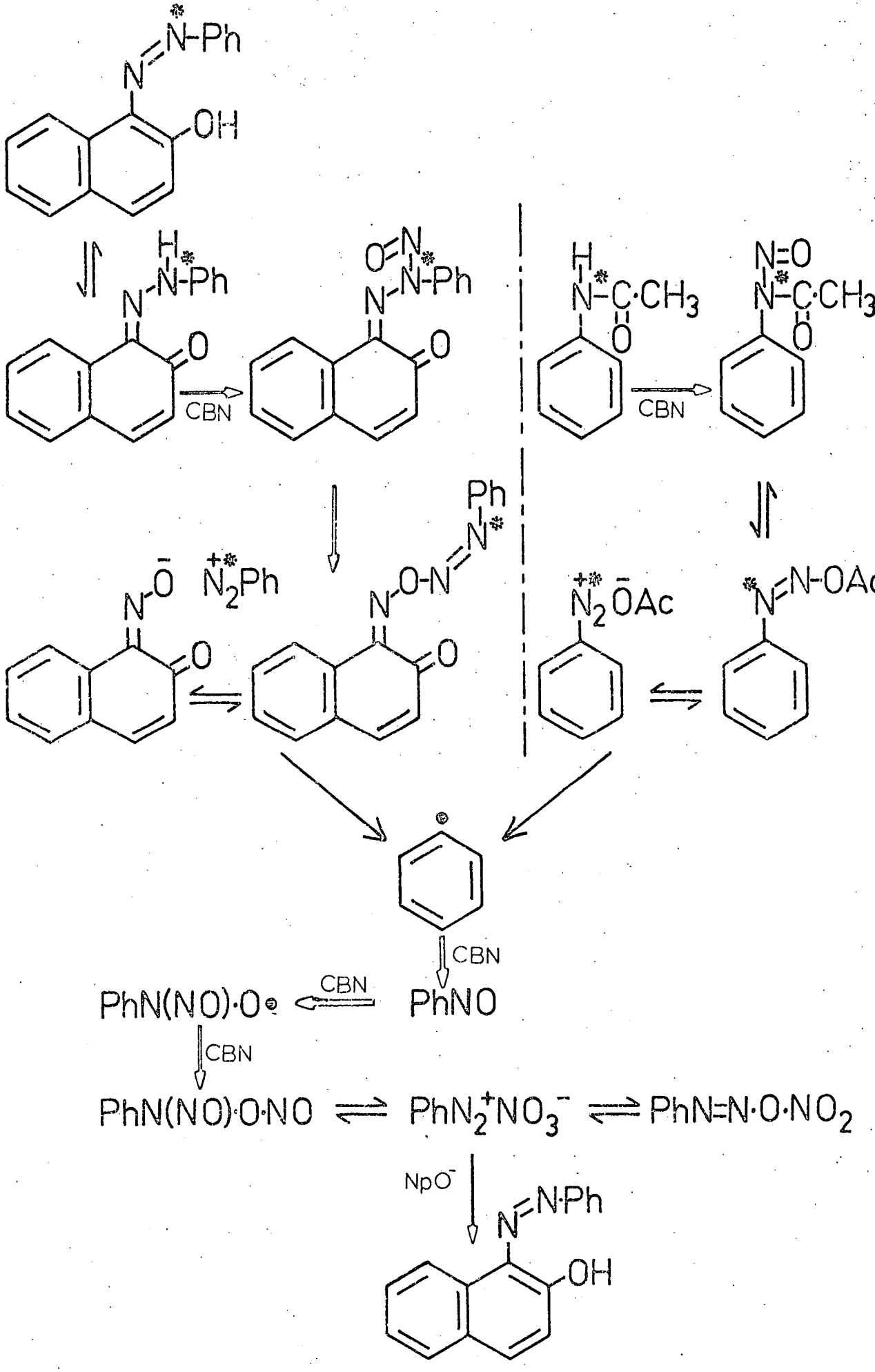






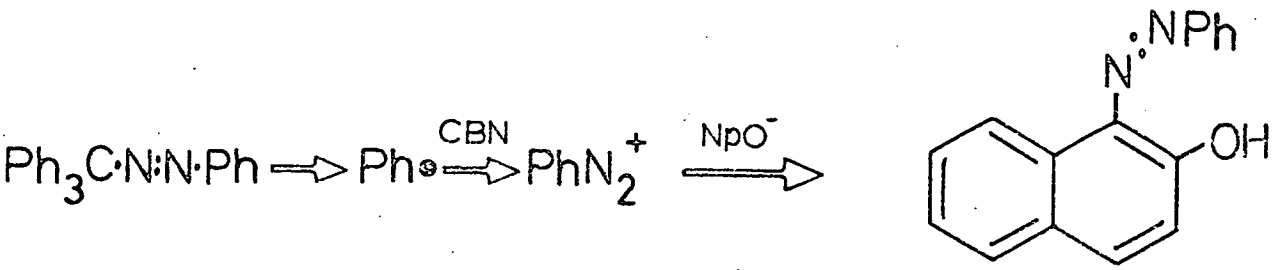
Scheme 27

The formation of the diazonium cation in this way affords a route to the unlabelled species - since both nitrogen atoms come from the nitrosating agent - and as such might explain the phenomenon of 'nitrogen exchange ' if phenyl radicals, formed via nitrosation of acetanilide or 1-phenylazo-2-naphthol, interact with CBN to give nitrosobenzene which in turn is further nitrosated to the diazonium salt according to Scheme 27. That such a mechanism was tenable followed when decomposition of phenylazotriphenylmethane in benzene in the presence of 4-chlorobenzoyl nitrite,


N-Ph
OH
CBN
CBN
CBN
CBN
CBN
PhN(NO)·O⊖
PhNO
PhN(NO)·O·NO
PhN2+NO3−
PhN=N·O·NO2
NpO−
N-Ph
OH

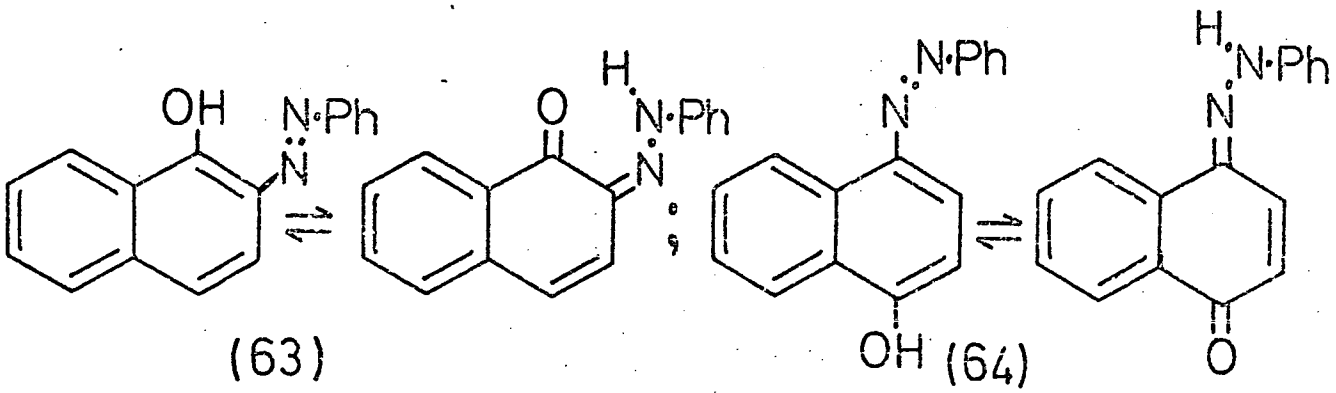
Scheme 28

followed by treatment with sodium β-naphthoxide, afforded 1-phenylazo-2-naphthol in 27% yield. Moreover the reaction of



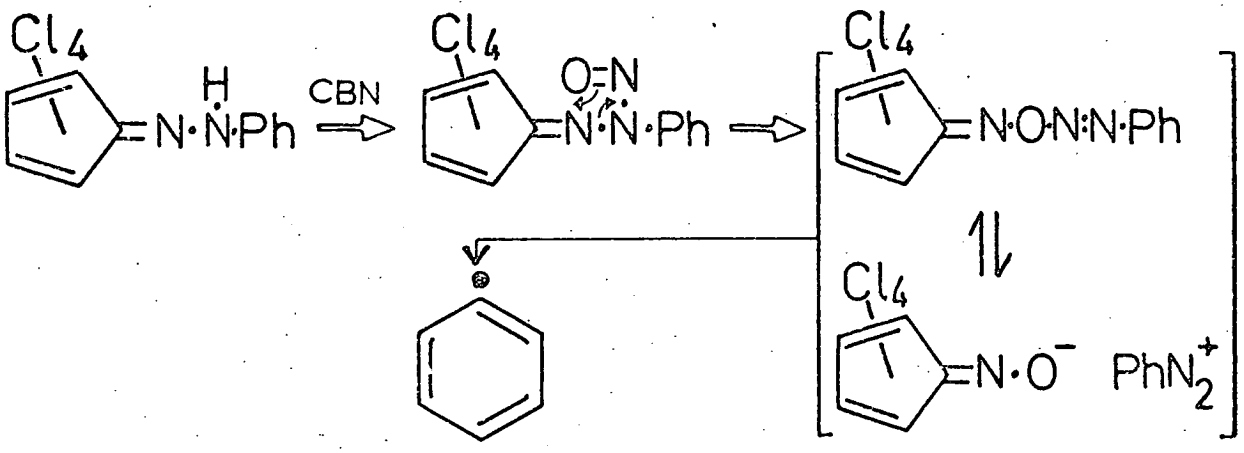
CBN with nitrosobenzene and p-methylnitrosobenzene gave the corresponding benzenediazonium cations (23% and 16% respectively) as shown by subsequent reaction with aqueous sodium β-naphthoxide. Thus in those reactions in which partial loss of the ^{15}N-label was observed, the experimental results can be accommodated by the formation of the diazonium ion, by way of Scheme 25 in the case of the azonaphthol and by way of Scheme 23 for NNA, some of which survives to be trapped by sodium β-naphthoxide to give the labelled azo compound, while the remainder decomposes with loss of the label to give phenyl radicals which subsequently react via Scheme 27 to give the unlabelled diazonium cation. A complete mechanism is shown opposite (Scheme 28).

Attempts to isolate the β-naphthol moiety were unsuccessful, it being converted into an unresolved complex tarry mixture. Further confirmation of the proposed reaction path, however, was provided by several other experimental observations. Thus the reaction of CBN with 2-phenylazo-1-naphthol (63) and 4-phenylazo-1-naphthol (64) in benzene gave biphenyl in yields of 17% and 27% respectively, illustrating the generality of the reaction for hydroxyazo

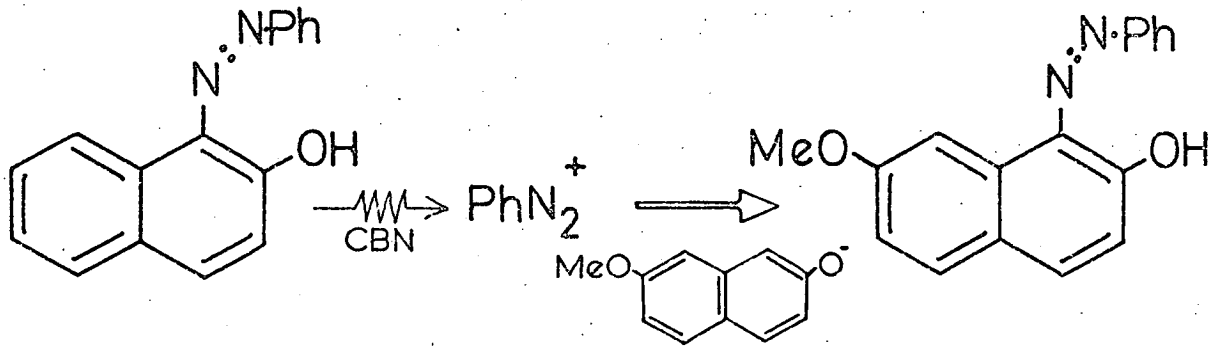


(63) (64)

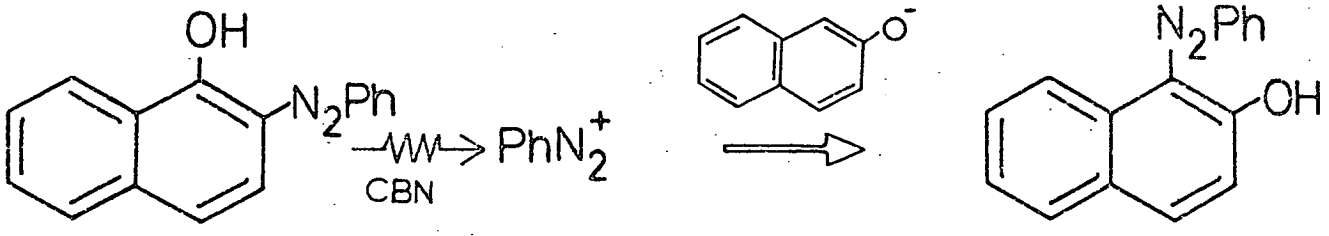
compounds capable of existing partially in the hydrazone form. Furthermore, nitrosation of 1-phenylazo-2, 3, 4, 5-tetrachlorocyclopentadiene, which Griffiths[171] has shown to exist exclusively as the hydrazone, afforded biphenyl as the major reaction product (17%), presumably via the following mechanism:



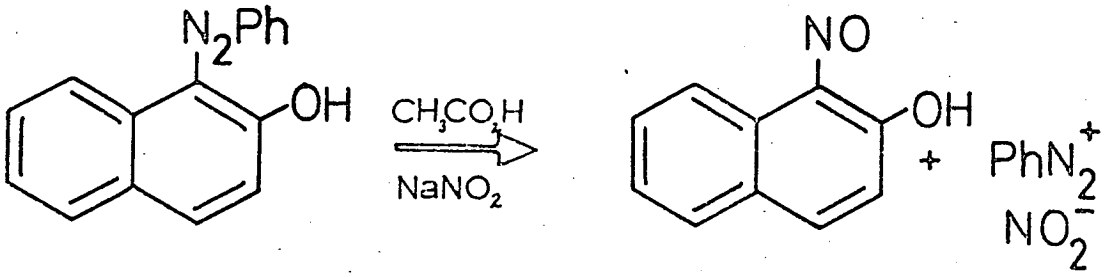
Finally, the origin of the coupled azo product was firmly established when reaction of 1-phenylazo-2-naphthol with CBN, followed by treatment with sodium 7-methoxy-2-naphthoxide afforded 1-phenylazo-7-methoxy-2-naphthol; while reaction of



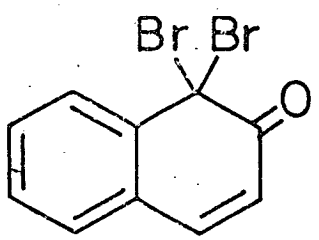
2-phenylazo-1-naphthol with nitrosating agent followed by treatment with sodium β-naphthoxide gave 1-phenylazo-2-naphthol.



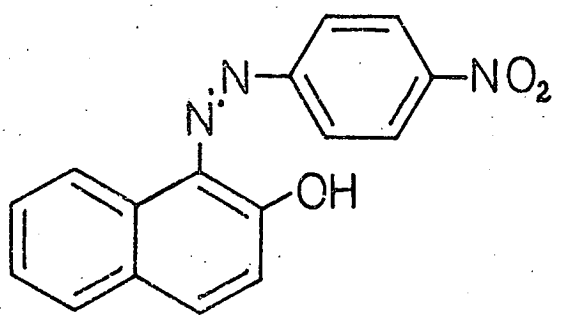
As mentioned previously, Huisgen[183] has observed decolourisation of a solution of 1-phenylazo-2-naphthol in glacial acetic acid on addition of sodium nitrite and has suggested that this is due to displacement of the arylazo moiety by a nitroso group.



More recently, Bunce[188] has reported the displacement of diazonium cations from o-arylazophenols with electrophiles. Thus the arylazo group was lost completely when 1-phenylazo-2-naphthol was treated with bromine in acetic acid in the presence of sodium acetate, evidence being obtained for the 1, 1-dibromo compound (65). Likewise nitration of the azo compound in acetic acid gave 1, 6-dinitro-2-naphthol and reaction with p-nitrobenzenediazonium chloride in dioxan-aq. NaOH gave (66).

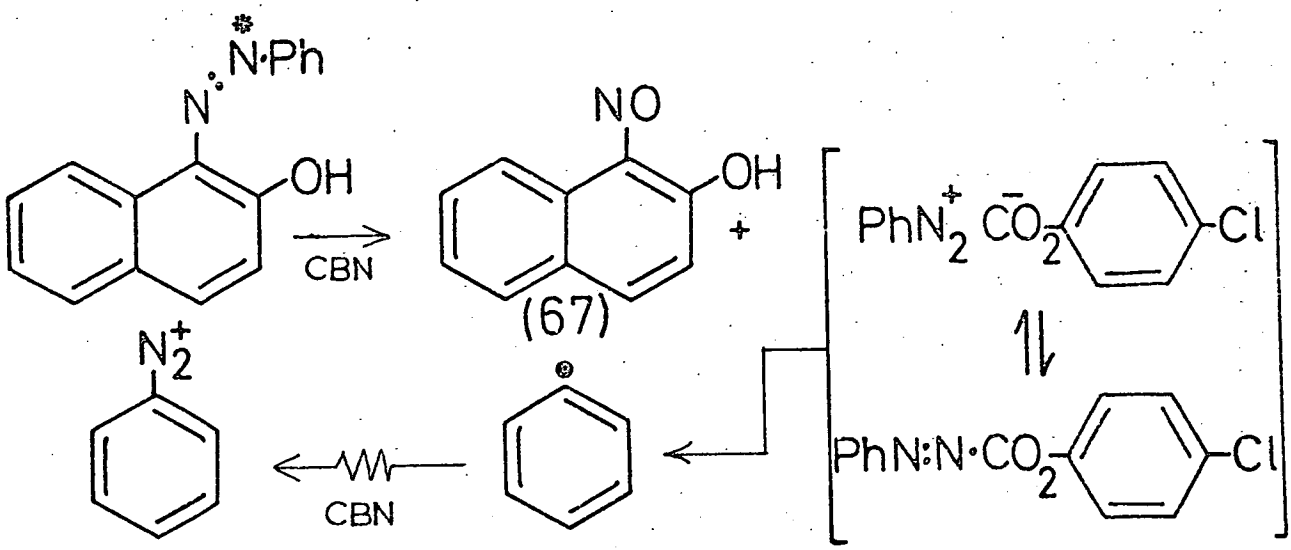


(65)



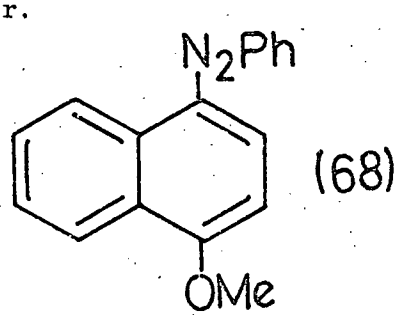
(66)

That a similar electrophilic displacement of the arylazo group operates in the case of CBN nitrosations cannot be discounted. Loss of the isotopic label could conceivably arise via a mechanism analogous to that proposed in Scheme 27, in which phenyl radicals, formed by homolysis of the covalent benzenediazonium-4-chlorobenzoate, interact with excess nitrosating agent to give the unlabelled diazonium cation (Scheme 29).



1-Nitroso-2-naphthol (67), however, was not present as a reaction product although it may react further under the reaction conditions. Since (67) could also be a product of the reaction outlined in Scheme 28, the knowledge of whether 1-nitroso-2-naphthol was present or not would have given no positive indication of which mechanism was operating.

Evidence against a mechanism involving electrophilic displacement comes from the observation that while a solution of 4-phenylazo-1-naphthol was rapidly decolourised on addition of nitrosating agent, the analogous methoxy compound (68) gave no such reaction and even after 48 h, there was no trace of biphenyl. Such a difference is not to be expected on the basis of a difference in activating ability of the -OH and -OMe substituents and points to a mechanism proceeding *via* nitrosation of the hydrazone tautomer as outlined earlier.

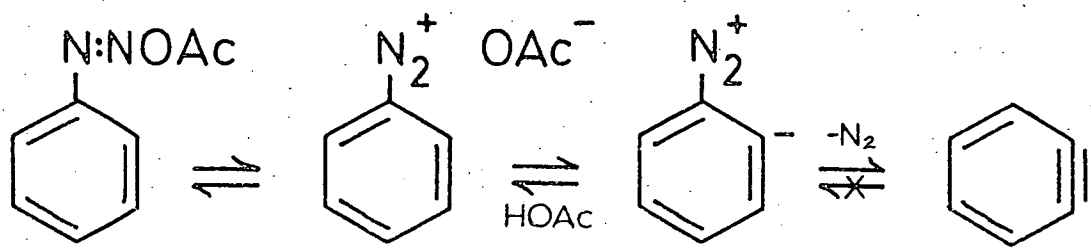


(68)

Development of the reaction discussed above has led to the discovery that nitrosation of 1-phenylazo-2-naphthol with the milder reagent, pentyl nitrite, affords biphenyl in 65% yield,[195] presumably *via* an analogous mechanism.

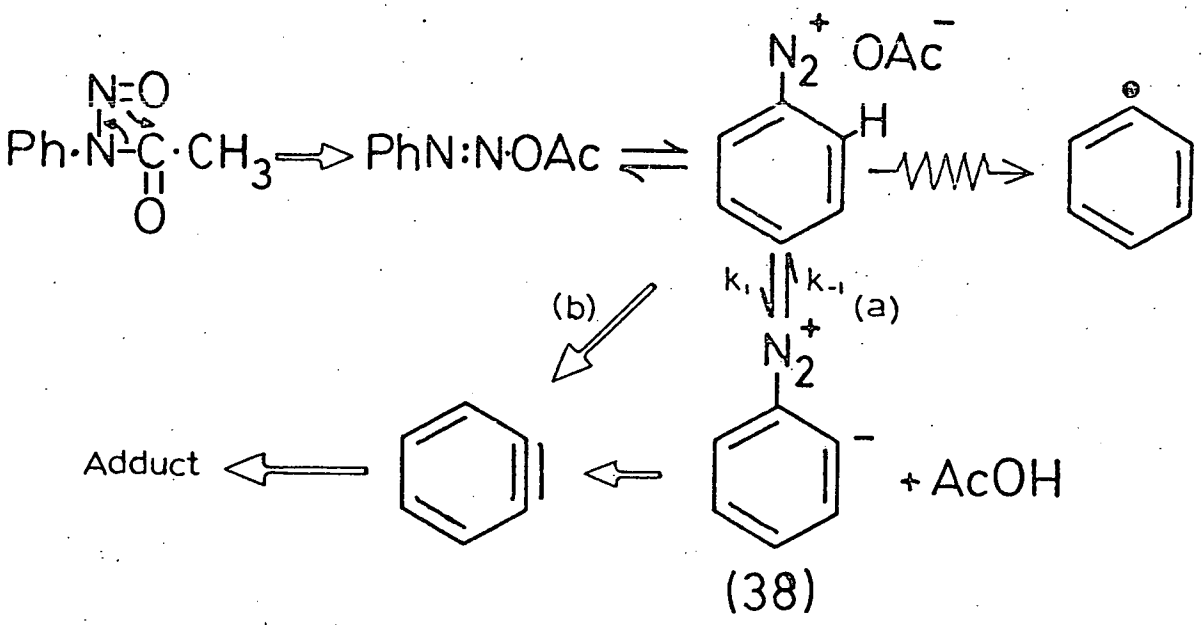
THE ROLE OF [^{2}H]-LABELLING IN THE DETERMINATION OF THE FORMATION OF BENZYNE FROM N-NITROSO-ACETANILIDE AND BENZENEDIAZONIUM ACETATE

In attempting to understand the role played by tetracyclone during the decomposition of N-nitrosoacetanilide, the possibility of reversible loss of nitrogen from the benzyne precursor has been investigated, the evidence suggesting that such a process does not occur:



Although it had been previously established that benzyne is formed during the decomposition of NNA *via* acetate induced elimination from the benzenediazonium ion, there remained the question of the precise nature of the elimination. That this shouldbe established might prove essential to an understanding of the 'tetracyclone effect.' The elimination could proceed stepwise *via* a carbanionic E_1cb process (Scheme 30, route a), involving either a fully reversible 'pre-equilibrium' where $k_{-1} \neq 0$, $(E_1cb)_R$, or an irreversible first stage where $k_{-1} = 0$, $(E_1cb)_I$. Both E_1cb mechanisms involve prior formation of the conjugate base of the diazonium ion, followed by unimolecular loss of the nitrogen leaving group. Alternatively, the reaction could proceed by way of a fully concerted E_2 elimination (Scheme 30, route b) without the intermediacy of the betaine.

As mentioned in the Introduction (page 36), an E_1 elimination operates in the case of sterically hindered diazonium salts. Thus in the case of o-t-butyl-N-nitrosoacetanilide, sterically assisted unimolecular loss of nitrogen from the o-t-butylbenzenediazonium cation occurs to give the o-t-butylphenylcarbonium ion and hence o-t-butylbenzyne. In the case of NNA itself, however, and other



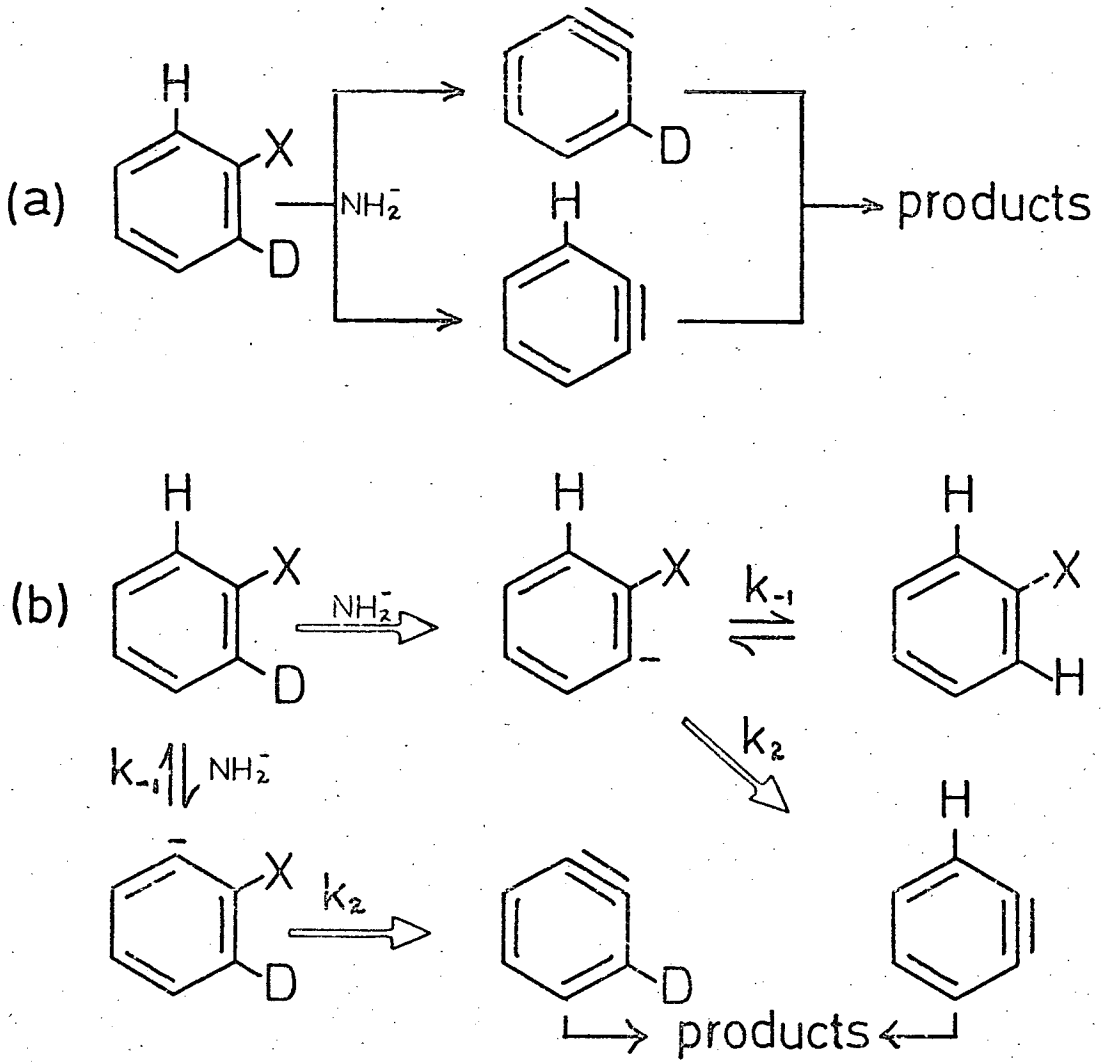
(38)

Scheme 30

substituted derivatives not subject to such steric acceleration of the loss of nitrogen, abstraction by acetate of the acidic proton ortho- to the diazonium function occurs before nitrogen is lost.

That the decomposition pathway involved the betaine intermediate (38) was originally postulated by Cadogan to account for the anomalous reaction of NNA in the presence of dimethylacetylenedicarboxylate.[122] Subsequent clarification of this anomaly,[114] however, threw doubt on the intermediacy of the betaine. In theory, some insight into the mechanism of formation of benzyne from NNA and hence into the potential existence of the betaine is possible by examining reactions involving deuteriated substrates.

Roberts[189] had previously used this technique in his investigation into the mechanism of amination of halobenzenes, a process known to proceed via a benzyne intermediate. Roberts considered two possible mechanisms for the 1, 2-elimination of hydrogen halide from a phenyl halide: a concerted mechanism (Scheme 31, route a) and a stepwise process (Scheme 31, route b). He proposed that if a concerted mechanism applied, then an isotope effect approaching the range 6-7 should be observed, while if the stepwise process was operating the k_H/k_D value should be significantly less, its absolute value depending on the k_2/k_{-1} ratio.

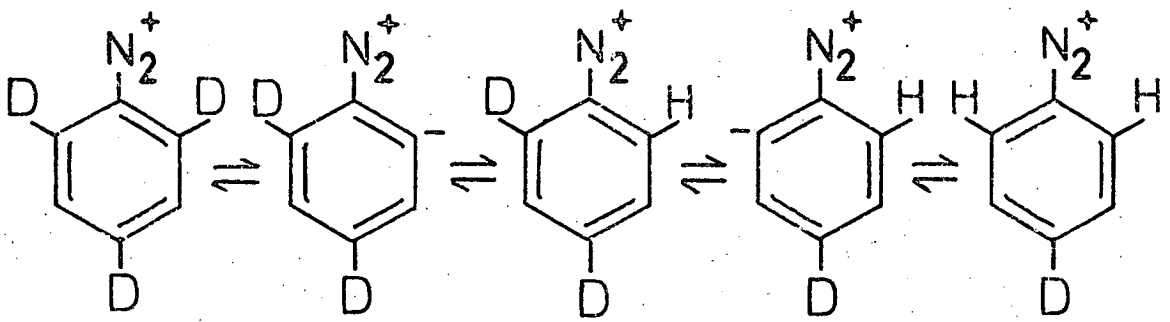


Scheme 31

Furthermore, he predicted that exchange of hydrogen for deuterium in the unreacted halobenzene would indicate the complicity of a carbanionic intermediate. Thus amination of o-deuteriofluorobenzene was found to proceed with extremely rapid exchange, indicating an $(E_1cb)_R$ mechanism. The stepwise mechanism was also proposed for the chlorobenzene analogue, hydrogen exchange for deuterium again being demonstrated and an isotope effect of 2.7 observed. For bromobenzene, however, a k_H/k_D value of 5.5 was computed, which Roberts took to indicate a concerted E_2 mechanism. Bordwell has recently shown,[132] however, that a high isotope effect is not indicative of an E_2 process and has demonstrated that $(E_1cb)_I$ eliminations can also show sizeable k_H/k_D values.

In an attempt to gain insight into the mechanism of benzyne formation from NNA and related benzenediazonium salts, a series

of experiments using deuteriated substrates was undertaken. Thus reaction in benzene of 2,4,6-[$^2H_3$]N-nitrosoacetanilide (99% [$^2H_3$]) formed by in situ nitrosation of labelled acetanilide by 4-chlorobenzoyl nitrite in the presence of tetracyclone and acetic acid gave 1,2,3,4-tetraphenylnaphthalene which had lost only one g-atom of deuterium (99% [$^2H_2$]), together with biphenyl, produced via the competing radical phenylation of benzene, from which no deuterium had been lost (99% [$^2H_3$]). This result clearly excludes a 'pre-equilibrium' E_1cb mechanism since this would require the loss of more than one g-atom of deuterium during benzyne formation on the assumption that the [$^2H_3$] diazonium cation would undergo rapid H-D exchange with the acetic acid via the betaine (69) (Scheme 32). In the same way, such a mechanism would also lead to the loss of deuterium from biphenyl resulting from radical phenylation of the solvent.



(69)

Scheme 32

An alternative entry to the benzyne pathway involves reaction of 2,4,6-[$^2H_3$]benzenediazonium fluoroborate in the presence of potassium acetate. Thus decomposition of labelled diazonium salt in benzene in the presence of tetracyclone and acetic acid, gave biphenyl (99% [$^2H_3$])and tetraphenylnaphthalene (99% [$^2H_2$]) while in a separate experiment using anthracene as the aryne trap, the diazonium salt gave triptycene (99% [$^2H_2$]) and biphenyl (99% [$^2H_3$]). In accord with these experiments were the results of the reverse case involving the reaction of undeuteriated benzenediazonium fluoroborate with potassium acetate and tetracyclone in benzene in the presence of acetic [^2H] acid. Both the

resulting biphenyl and benzyne adduct contained no deuterium which could be detected by mass spectroscopy, emphasizing the absence of hydrogen-deuterium exchange during the reaction. Compelling evidence against the operation of the $(E_1cb)_R$ mechanism obtained when partial decomposition of 2,4,6-[$^2H_3$]N-nitroso-acetanilide, formed *in situ*, followed by treatment with sodium β-naphthoxide, afforded 1-phenylazo-2-naphthol with 99% [$^2H_3$]-enrichment.

That an $(E_1cb)_R$ mechanism was not operating was further illustrated by the results of experiments involving mono *ortho*-deuteriated substrates. Thus decomposition of 2-[$^2H_1$]benzene-diazonium fluoroborate (92% [$^2H_1$]) in the presence of potassium acetate and tetracyclone in benzene gave a benzyne adduct which showed a deuterium content of 55%, indicating 37% loss of the isotopic label. Complete retention of the label was found in the biphenyl product. When this reaction was repeated using 1, 2-dichloroethane as solvent, an identical result was found for the isotopic content of the benzyne derived product. Reaction of the diazonium salt (92% [$^2H_1$]) using anthracene as the arynophile afforded triptycene (58% [$^2H_1$]) and 9-phenylanthracene (92% [$^2H_1$]). In the absence of a benzyne trap, biphenyl (92% [$^2H_1$]) was obtained.

Exactly comparable results emerged from experiments using 2-[$^2H_1$] benzenediazonium chloride (94% [$^2H_1$]) in dichloro-ethane in the presence of acetic acid and anthracene, the deuterium contents of the triptycene and 9-phenylanthracene products being 58% and 94% respectively. A summary of the results from the above experiments involving deuterio-labelled diazonium salts is given in table 9.

It should be noted at this point that the above results are at variance with those from an experiment carried out contemporaneously by Buxton and Heaney,[118] who have reported that the reaction of 2-[$^2H_1$]benzenediazonium chloride (81% [$^2H_1$]) with potassium acetate and acetic acid in 1, 2-dichloroethane in the presence of anthracene

Table 9

Reactions of deuteriated benzenediazonium salts in the presence of potassium acetate, acetic acid and a benzyne trap.

Solvent	Diazonium Salt	Isotopic Enrichment	Isotopic Retention in Product		
			Trap	Aryne	Radical
PhH	$PhN_2^+BF_4^-$	99% [$^2H_3$]	Tetracyclone	99% [$^2H_2$]	99% [$^2H_3$]
PhH	$PhN_2^+BF_4^-$	99% [$^2H_3$]	Anthracene	99% [$^2H_2$]	99% [$^2H_3$]
PhH	$PhN_2^+BF_4^-$	92% [$^2H_1$]	Tetracyclone	55% [$^2H_1$]	92% [$^2H_1$]
$C_2H_4Cl_2$	$PhN_2^+BF_4^-$	92% [$^2H_1$]	Tetracyclone	55% [$^2H_1$]	-
PhH	$PhN_2^+BF_4^-$	92% [$^2H_1$]	None	-	92% [$^2H_1$]
PhH	$PhN_2^+BF_4^-$	92% [$^2H_1$]	Anthracene	58% [$^2H_1$]	92% [$^2H_1$]
$C_2H_4Cl_2$	$PhN_2^+Cl^-$	94% [$^2H_1$]	Anthracene	58% [$^2H_1$]	94% [$^2H_1$]

gave 9-phenylanthracene (36% [$^2H_1$]) and triptycene (18% [$^2H_1$]). This result was correctly interpreted as being indicative of extensive removal of the ortho-deuterium before decomposition of the diazonium salt to phenyl radicals or benzyne. An E_1cb mechanism in which a fast equilibrium exists between the diazonium ion and the betaine was proposed. These results are now known to be in error,[176] however, repetition of the work having led to results identical to those mentioned above.

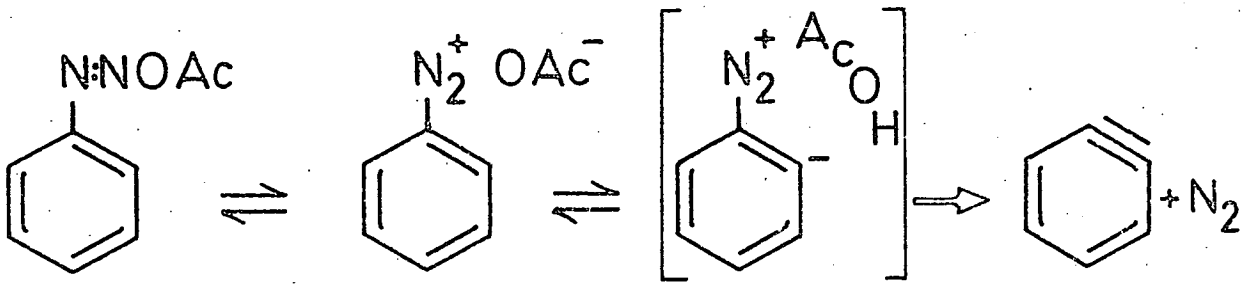
In the experiments with 2-[$^2H_1$]benzenediazonium salts already outlined, slightly more than half the original deuterium content was retained in the aryne adduct and calculations indicate isotope effects in the range 1.5-1.8 (making the assumption that [$^2H_1$]benzyne is

trapped as efficiently as [$^1H_1$]benzyne). Such a value is slightly lower than that normally observed[132] for either a fully concerted E_2 or irreversible E_1cb mechanism (Introduction, page 52). The value may, however, simply reflect a transition state in which proton transfer has only just begun or is nearly finished. That an isotope effect greater than unity was observed at all provides compelling evidence against an E_1 mechanism.

Two influences should effect the course of the elimination: firstly, the ease with which the ortho-hydrogen can be removed; and secondly, the rate at which a molecule of nitrogen can depart. An E_1cb mechanism should be favoured when the leaving group is strongly bonded but the hydrogen is very acidic. Conversely, as loss of leaving group becomes more facile, the concerted mechanism may be preferred. The subtle balance between these two effects is clearly illustrated by Roberts' work on the amination of halobenzenes. The acidity of the ortho-hydrogen atoms in the phenyl halides investigated will follow the order F>Cl>Br>I, on the basis of halogen electronegativities, while the leaving group rate sequence will be I>Br>Cl>F. Thus in the case of fluorobenzene, a very acidic hydrogen together with a poor leaving group should and does favour an E_1cb mechanism. With bromobenzene, however, the acidity of the proton is reduced (relative to fluorobenzene) while the leaving group is less strongly bonded: thus a concerted mechanism should be preferred. Applying these arguments to the β-elimination from the diazonium ion: the very strongly activating diazonium group will lead to the facile removal of the ortho-proton, and so should favour a carbanionic mechanism; but the excellent leaving ability of nitrogen should favour a concerted mechanism. Thus even on these qualitative grounds a choice between the $(E_1cb)_I$ and E_2 mechanisms is not possible.

In recent years a third type of carbanionic mechanism, the 'pre-equilibrium' ion-pair (tightly solvated anion) elimination mechanism has been invoked[140] to explain a number of 'low isotope effect' β-elimination reactions, but an analogous mechanism cannot operate

in the above case since a betaine-acetic acid complex (70) is involved rather than an ion-pair.



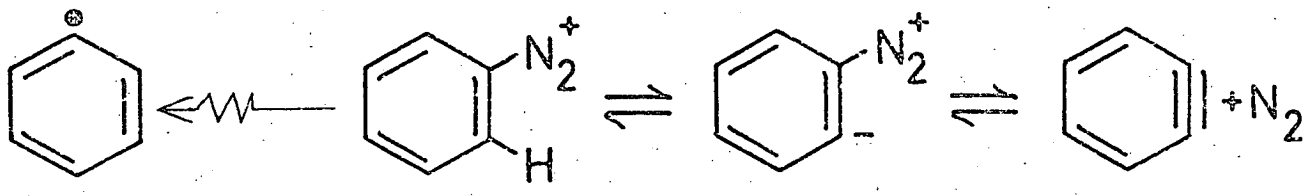
(70)

In order to draw a parallel between this mechanism and that proposed by Kwok it is necessary to propose some type of complex contained within a solvent cage such that the 'intimate zwitterion-acetic acid pair' (70) can only either collapse back to reactants or fall apart to give products without acetic acid molecules being exchanged with those in the solvent pool. That such a complex could exist, however, is only speculation.

On the basis of the above evidence, therefore, it is not possible to draw a distinction between the concerted and irreversible carbanion mechanisms. In theory, the existence of a significant leaving group isotope effect(for N_2) in the diazonium function would indicate partial breakage of the C-N bond in the transition state and hence an E_2 mechanism. Conversely the absence of a leaving group effect would tend to suggest an $(E_1cb)_I$ mechanism.

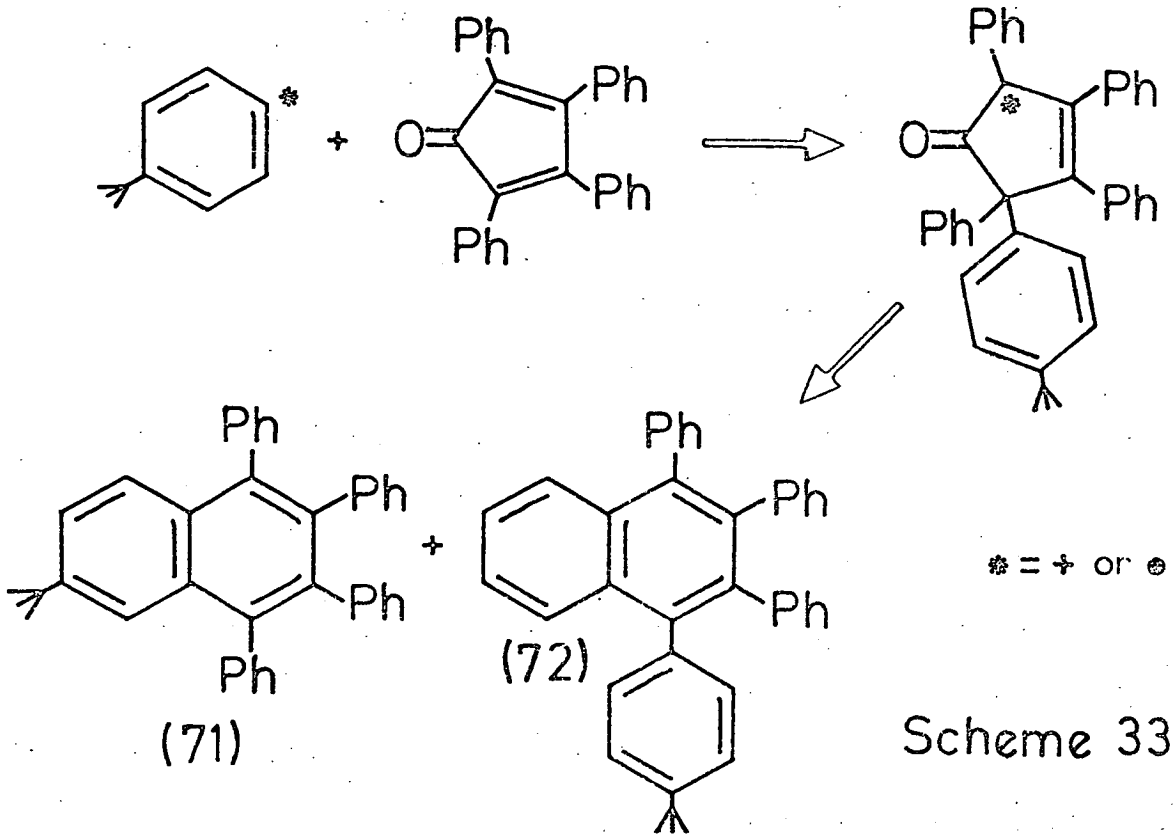
THE ROLE PLAYED BY TETRACYCLONE DURING THE DECOMPOSITION OF N-NITROSOACETANILIDE: THE MECHANISM OF 'BENZYNE PROMOTION'

Having established that benzyne formation *via* acetate ion induced *o*-proton elimination from the diazonium cation does not proceed by way of a reversible E_1cb mechanism, and that nitrogen loss from a possible benzyne precursor is irreversible, it became apparent that the 'tetracyclone effect ',whereby benzyne adduct formation proceeds at the expense of the phenyl radical chain reaction, could not simply be a consequence of the high arynophilicity of tetraphenylcyclopentadienone. Such a mechanism would require an equilibrium to exist between the precursors of both the phenyl radical and benzyne intermediates (in the event of the reaction proceeding *via* a betaine intermediate).



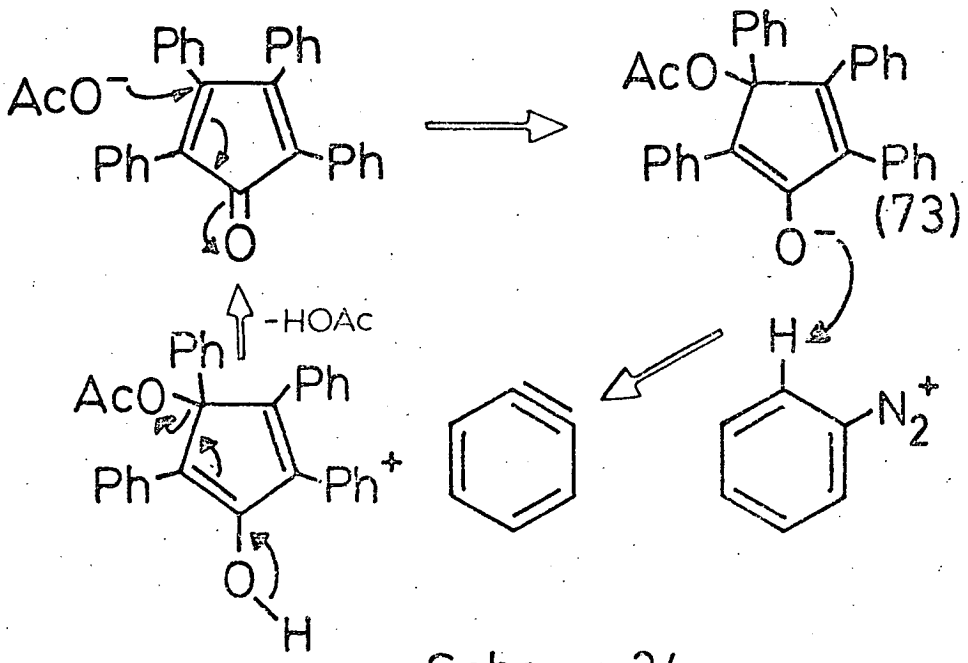
It followed that tetracyclone must fulfil some other role in the overall decomposition. That a high yield of tetraphenylnaphthalene could be explained on the basis of a reaction involving free radical or carbonium ion attack on tetracyclone had been previously considered and discounted by Cadogan *et al*[123] who demonstrated that decomposition of *p*-t-butyl-*N*-nitrosoacetanilide in benzene, in the presence of tetracyclone, gave only 6-t-butyl-1, 2, 3, 4-tetraphenylnaphthalene (71). If the reaction involves monodentate attack by a radical or cationic species, then the isomeric 1-(*p*-t-butylphenyl)-2, 3, 4-triphenylnaphthalene (72) would also have been produced (Scheme 33).

More recently, Cadogan has tentatively suggested[123] that the diversion from the'normal' radical route to that leading to benzyne, observed during NNA decomposition in the presence of tetracyclone,



Scheme 33

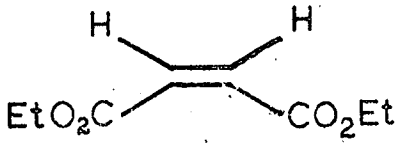
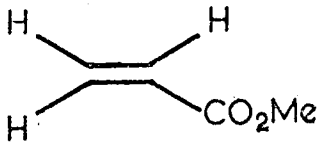
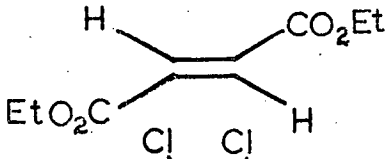
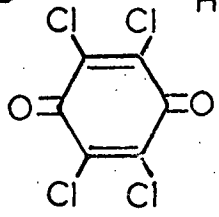
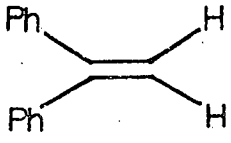
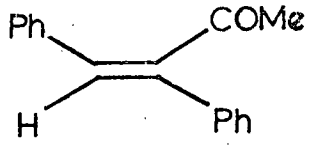
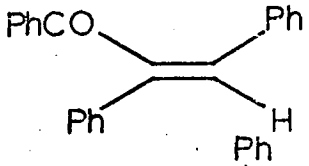
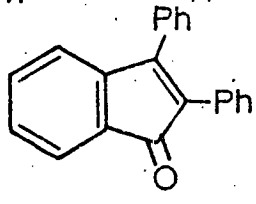
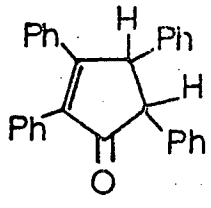
might result from an interaction between tetracyclone and the benzenediazonium-acylate ion-pair, in which acetate attack on the arynophile gives rise to an intermediate (73) capable of removing the proton ortho to the diazonium moeity more efficiently than acetate (Scheme 34). Such a scheme would only require a small



Scheme 34

TABLE 3

Triptycene Yields in the Decomposition Reactions of in situ N.N.A. in the Presence of Anthracene and Various Addenda.

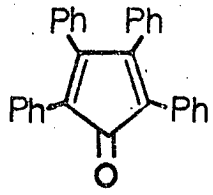
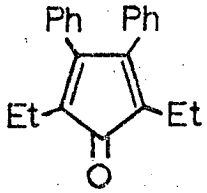
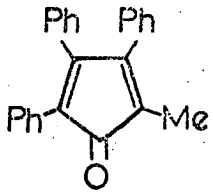
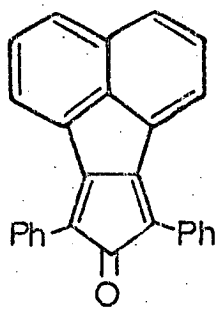
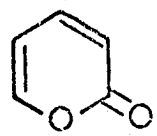
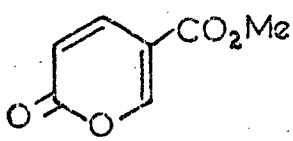
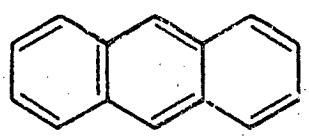
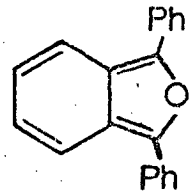
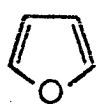
Addendum	Triptycene (m/100m)
	18
	17
	18
	10
	5
	17
	18
	15
	14
—	17

equilibrium concentration of the intermediate (73). In order to test this hypothesis, a set of reactions was undertaken in which N-nitrosoacetanilide, prepared in situ, was allowed to decompose in benzene in the presence of anthracene and each of a series of compounds possessing similar structural characteristics to tetracyclone without themselves being arynophilic. In the absence of these 'tetracyclone analogues' the decomposition gives triptycene (17%) and the phenyl radical derived products, 9-phenylanthracene (5%) and biphenyl (24%). It was hoped, therefore, that if tetracyclone functions in the manner described in Scheme 34, then addition of a compound bearing an analogous structure might similarly induce aryne formation, and so give an increased yield of triptycene. The results of these experiments are shown opposite in Table 3. Without exception, no significant increase in the yield of benzyne adduct was observed. This was particularly disappointing in the case of the closely related 2, 3-diphenylinden-1-one and dihydro-tetracyclone systems which one might reasonably expect to function in a manner analogous to tetracyclone.

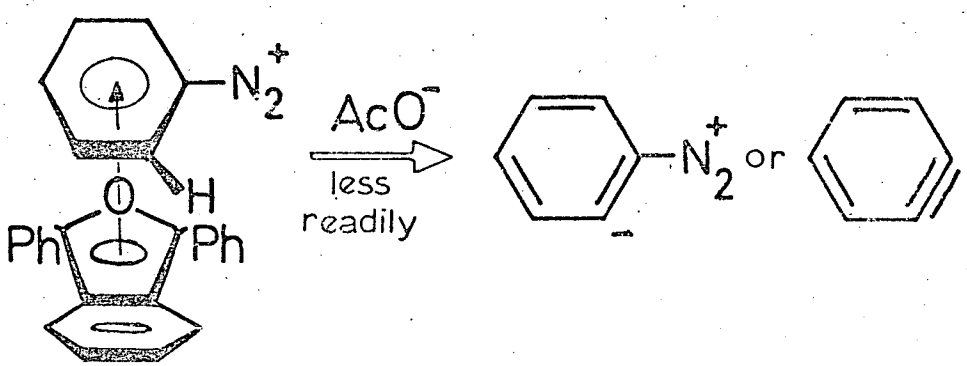
Before further investigation was undertaken into the possible role played by tetracyclone in the decomposition of N-nitrosoacetanilide it was decided that a study of NNA decompositions in the presence of other arynophiles under identical reaction conditions might furnish some useful information. Thus NNA, formed by in situ nitrosation of acetanilide, was allowed to decompose in benzene at 80° in the presence of a series of established arynophiles As can be seen from Table 1 (on the next page) those compounds with the basic tetra-substituted cyclopentadienone structure gave good yields of aryne adduct while in all other cases the major product was that resulting from the free radical chain reaction. Reaction in the presence of furan gave a predictably high yield of biphenyl, a consequence of the fast redox chain reaction discussed in the Introduction (page 41). That an equally high yield of radical derived product should result from the reaction of NNA with 1, 3-diphenylisobenzofuran, however, was rather puzzling since an

TABLE 1

Products from the reaction of 4-chlorobenzoylnitrite with acetanilide in the presence of benzyne traps.

Arynophile	Biphenyl (m/100 m)	Adduct (m/100 m)
	12	71
	5	60
	7	64
	9	59
	28	23
	26	18
	24	16
	57	5
	54	-
—	63	-

analogous redox scheme cannot be written in this case due to the absence of an appropriate hydrogen atom attached to the furan nucleus. Furthermore, a competition reaction in which authentic benzyne (from anthranilic acid/pentyl nitrite) was generated in the presence of tetracyclone and 1, 3-diphenylisobenzofuran gave a competition ratio $K^{tetr.}_{diph.}$ of 1. 2 illustrating comparable arynophilicities. A possible explanation, however, is that the intermediate diazonium ion, formed from NNA, forms a π-complex (74) with the isobenzofuran, thereby reducing the acidity of the o-protons and hence preventing the formation of the benzyne/benzynoid intermediate, as previously considered by Cadogan and Mitchell[115, 190] as a possible explanation of the analogous reactions in the presence of furan and 2, 5-dimethylfuran.

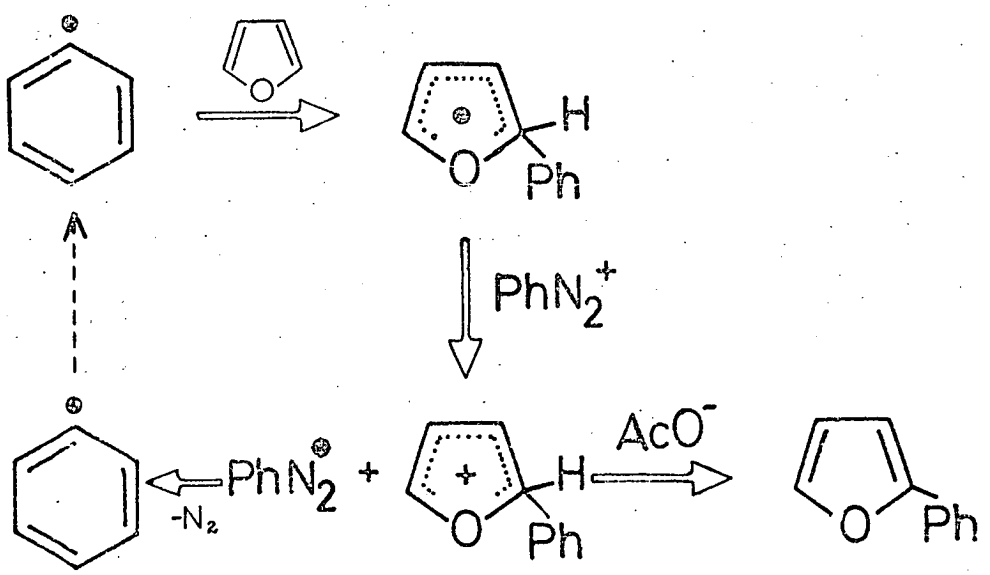


(74)

If nothing else, the above series of reactions did establish that there is something special about the substituted cyclopentadienone system which might hold the key to the problem. If tetracyclone is involved chemically in the mechanism, other than as an arynophile, then at first sight there are two possible explanations for its special effect. It may function in such a way as to inhibit the chain reaction, thereby allowing the diazonium-acylate ion pair to be diverted into a benzyne forming route; or, conversely, it may act directly so as to enhance benzyne formation at the expense of phenylation as already considered in Scheme 34.

As a new approach to the problem, it was decided to return to the decomposition of NNA in furan, a reaction known to give a

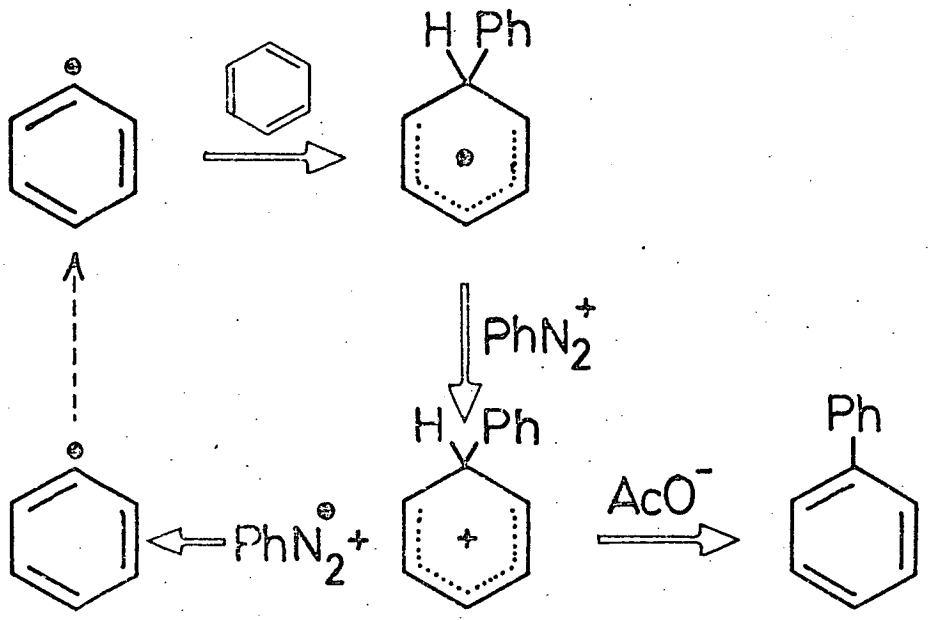
high yield of phenylfuran, the radical derived product, but only small amounts of the benzyne-furan adduct, 1,4-dihydro-1,4-epoxy-naphthalene. It was argued that if this reaction could be persuaded to follow a benzyne forming path in preference to the radical route, then greater insight might be obtained into the function of tetracyclone. Cadogan[111,113] has observed that the presence of furan in reactions which normally afford good yields of adduct, greatly suppresses the formation of benzyne. Thus the reaction of N-nitrosoacetanilide with tetracyclone in benzene gave tetraphenylnaphthalene in 80% yield while the same reaction in furan gave only 1% of the adduct. It can be seen, therefore, that while tetracyclone enhances benzyne formation, furan acts as an inhibitor. Cadogan[111] suggested that this special furan effect was probably due in part to a fast redox chain reaction, involving the diazonium cation and phenylfuranyl radical, which served to suppress the formation of a benzyne/benzynoid species (Scheme 35). Confirmation for such a scheme



Scheme 35

followed from Mitchell's measurements[115] of rate ratios from competition reactions involving furan and benzene with various sources of phenyl radicals and benzyne/benzynoid species. He found that phenylation of furan was extremely fast in those cases where the diazonium cation was known to be present.

A similar redox chain reaction has been suggested by Cadogan[106] to constitute the main product forming process in the decomposition of NNA in benzene (Scheme 36). It can be seen

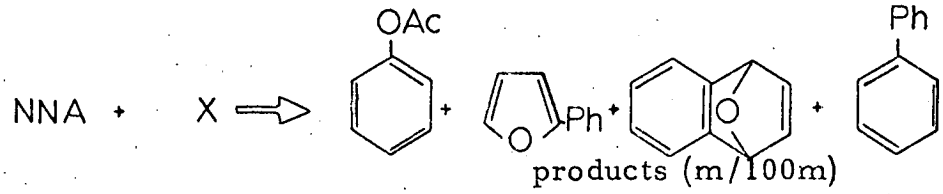


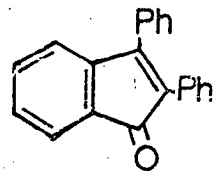
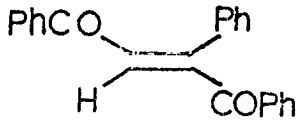
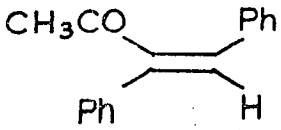
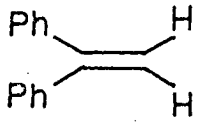
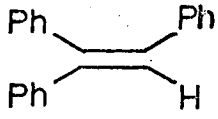
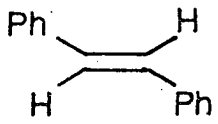
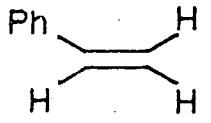
Scheme 36

from this and the previous scheme that the diazonium cation is removed via fast redox processes, thereby decreasing possible diazonium-acetate interaction leading to benzyne formation. If this is so, then addition of free radical inhibitors to the reaction should counteract this effect and enhance benzyne formation. Decomposition of N-nitrosoacetanilide in furan (initially at room temperature and subsequently at 30°), in the presence of 2, 6-di-t-butylphenol and 2, 6-di-t-butyl-4-methylphenol, however, gave no trace of the desired 1, 4-dihydro-1, 4-epoxynaphthalene although a marked decrease in the yield of 2-phenylfuran was observed, relative to the reaction in the absence of inhibitor. A similar reaction in the presence of 2, 3-diphenylinden-1-one, however, afforded the furan-benzyne adduct in 19% yield (Table 4). Furthermore, when the reaction in the presence of diphenylindenone was repeated at 60° in furan:benzene (1:3), the adduct was formed

TABLE 5

Reactions of NNA in Benzene:Furan at 60°

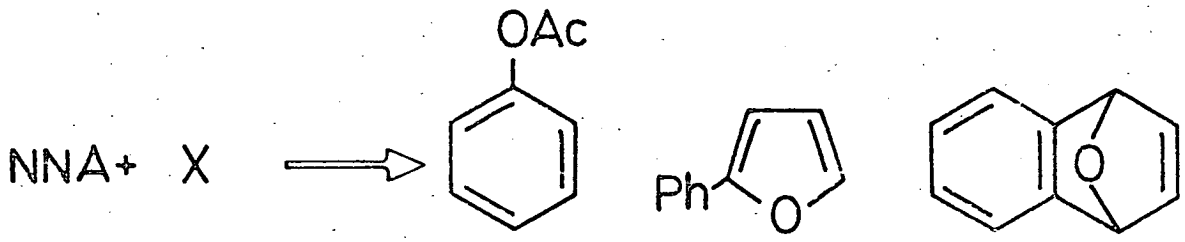


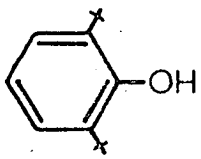
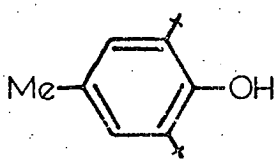
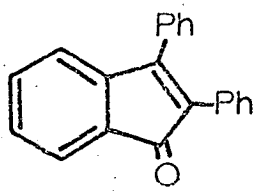
X				
—	4	50	7	10
	21	8	37	2
	18	13	43	4
	11	30	23	6
	25	6	46	2
PhCO·COPh	7	42	11	10
	15	25	27	6
	17	18	32	5
	22	9	42	2

The molar ratio of furan:NNA in these reactions was 12:1

Table 4

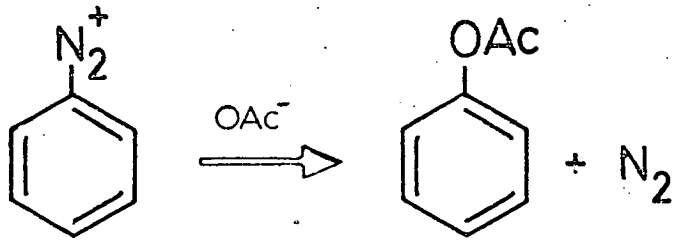
Reactions of NNA in Furan



X	products(m/100m)		
—	-	78	-
	-	52	-
	-	18	-
	9	40	19

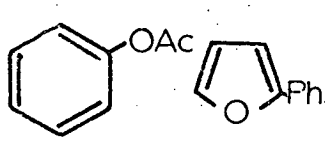
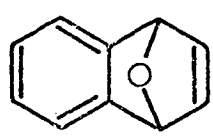
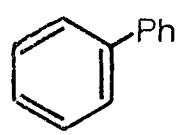
in 37% yield. This compares with a 7% yield when the reaction was repeated at 60° in the absence of the ketone. A possible explanation of this observation was that the added indenone had in some way inhibited the fast redox reaction shown in Scheme 35 and thus promoted benzyne formation. This result prompted a new set of experiments in which NNA was decomposed in furan:benzene in the presence of various other 'tetracyclone analogues.' The yields of phenyl acetate, 2-phenylfuran, 1,4-dihydro-1,4-epoxynaphthalene (naphthalene endoxide) and biphenyl are shown opposite in Table 5. Styrene, 1,1-diphenylethylene, trans-diphenylethylene and trans-dibenzoylphenylethylene were all found to have a marked benzyne-promoting effect. Even when the reaction was carried out using cyclohexene as both solvent and promoter a sizeable yield of benzyne

adduct was obtained. It is worth noting that as the yield of adduct increases, so also does that of the phenyl acetate, formed, presumably, via nucleophilic attack by acetate on the diazonium cation:



That phenyl acetate results from the reaction of benzyne with acetic acid is unlikely since cine-substitution has never been observed in substituted phenylacetates derived from the corresponding acylarylnitrosamines, except in the special case of the t-butyl substituted N-nitrosoacetanilides. Table 5 illustrates the profound effect that addition of diphenylethylene has on the product distribution, the yield of phenyl radical derived products falling from 60% to a mere 8% while the adduct yield increased by almost 40%. Further study of this particular system showed that sizeable yields of endoxide were still obtained when the concentration of olefin was reduced 2- and even 10-fold.

Table 6

moles $Ph_2C{:}CH_2$ / moles NNA			
1.0	23	5	44	1
0.5	23	5	43	1
0.1	17	15	29	4

The dependence of product yields on furan concentration was also very interesting. Thus when NNA was decomposed in furan:benzene mixtures in the presence of diphenylethylene, with

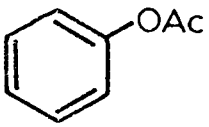
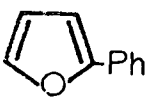
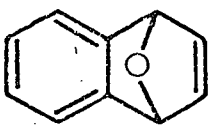
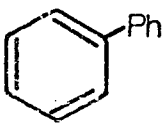
furan:NNA molar ratios of 0.9, 2.6, 9 and 26, the adduct yield was found to vary only within the limits 29-43%, illustrating how efficiently furan can trap benzyne in spite of being substantially less arynophilic than tetracyclone. (In a competition reaction in which authentic benzyne was generated in the presence of tetracyclone and furan, the aryne was quantitatively scavenged by the ketone, there being no trace of the furan-benzyne adduct.) In all reactions in which diphenylethylene was used as a benzyne promoter, triphenylethylene was identified as a reaction product. Also present, but in smaller amounts, was its saturated counterpart, triphenylethane. The origin of these products will be discussed in more detail later.

If diphenylethylene is functioning as a benzyne promoter by inhibiting the radical chain reaction, then it can be argued that repetition of the reaction in the absence of an aryne trap might afford other benzyne derived products, such as biphenylene, the dimer of benzyne, and as such represent a new synthetic route to this elusive class of compounds. In practice no biphenylene was identified from this reaction and, as can be seen from Table 10, the fall in NNA accountance in the absence of furan (A) corresponds exactly to the yield of endoxide when furan was present (B). This suggests that benzyne is being formed but is then 'lost' as unidentified products.

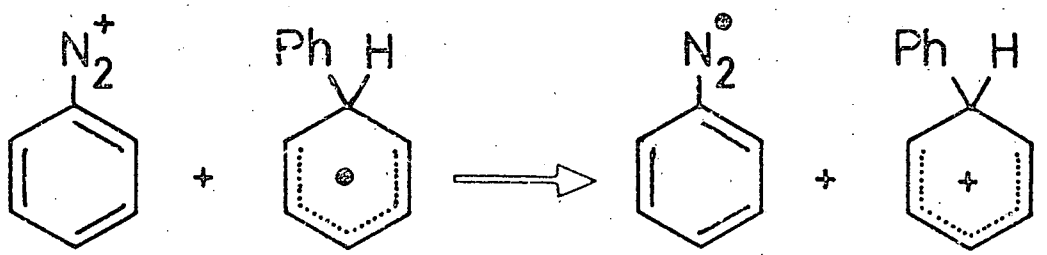
Many questions arose in the light of this promoting effect by the above mentioned compounds. Where did tetracyclone fit into this new picture? Did it function in a manner analogous to diphenylethylene? What was the exact mechanism of the promoting effect and why had a similar effect not been observed when NNA was decomposed in the presence of anthracene and the 'tetracyclone analogues'?

Table 10

Decomposition of NNA in the Presence of Diphenylethylene

Product	Yield (m/100m nitrosamide) A	B
	8	19
	-	8
	-	28
	13	4
$Ph_2C{:}CHPh$	18	8
Accountance (% NNA)	39	67

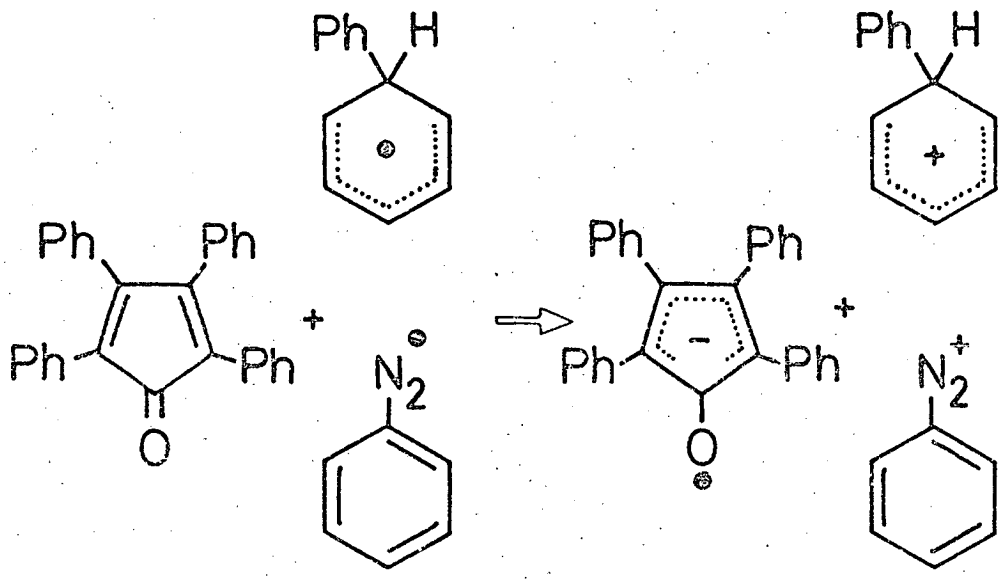
If tetracyclone functions by inhibiting the free radical chain reaction, then there are several ways in which this might be achieved. From Scheme 36 it can be seen that the propagation step in the radical reaction involves oxidation of the phenylcyclohexadienyl radical by diazonium cation:



(75)

In theory, such a process might be inhibited in three ways. Firstly, any process serving to remove the phenylcyclohexadienyl radical, whether by hydrogen abstraction or one-electron transfer to the

corresponding cation will leave the diazonium species free to decompose by way of the benzyne route. Secondly, scavenging of phenyl radicals will have the same effect by preventing the formation of the reducing radical. Thirdly, oxidation of the phenyldiazenyl radical (75) back to the diazonium cation would likewise inhibit the free radical chain reaction. If a one-electron redox reaction is occurring then it is likely to involve tetracyclone with either the phenylcyclohexadienyl or phenyldiazenyl radical (Scheme 37). In both cases electron transfer should give rise to



Scheme 37

the radical anion of tetraphenylcyclopentadienone, a species well characterised by previous e. s. r. studies.[191, 193] Thus decomposition of NNA in benzene in the presence of tetracyclone in the cavity of an e. s. r. spectrometer gave an intense symmetrical signal, consisting of 17 lines spread over 15 gauss. (Figure 1 in Experimental Section). Ray et al,[191] however, have reported the e. s. r. spectrum of the authentic radical anion of tetracyclone, obtained by alkali metal reduction in tetrahydrofuran, to be comprised of 39 lines spread over only 5 gauss (Figure 7). Their analysis was supported by computer simulation and they claimed that their assignment of this signal to the tetracyclone radical anion was in accord with McLachlan molecular orbital calculations.[192] Broser

et al[193] found similar results for a series of tetracyclone analogues.

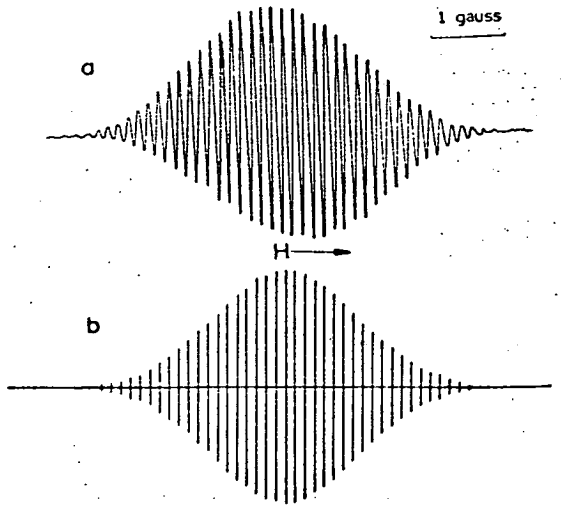
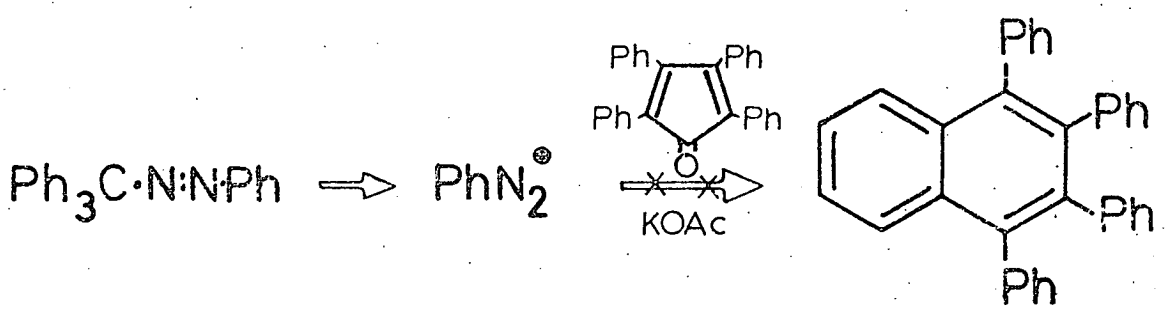


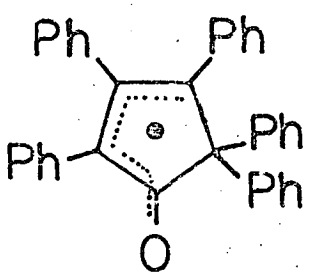
Figure 7: ESR spectrum of tetracyclone radical anion
[a: experimental; and b: theoretical]

That the diazenyl radical was not implicated with tetracyclone in a benzyne forming route was conclusively demonstrated when decomposition of phenylazotriphenylmethane in benzene in the presence of potassium acetate and tetracyclone failed to give any tetraphenylnaphthalene. This is perhaps not surprising in view of the known instability, and hence short life-time, of the diazenyl radical.[194]

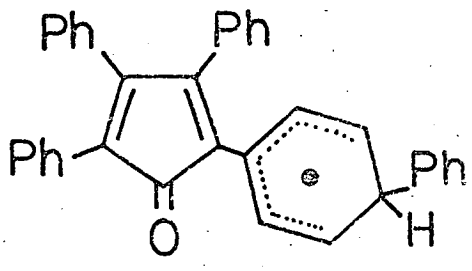


The occurrence of an e. s. r. signal was, however, of major significance. It persisted over several days and was, therefore, obviously due to some very long-lived free radical. Both the hyperfine structure and the g-value of 2.0032 strongly suggested a hydrocarbon radical. Although incomplete resolution of the spectrum prevented a detailed analysis, it may be that the origin of the signal lies in the addition of a phenyl radical to tetracyclone.

Brydon[121] has allowed dibenzoyl peroxide to decompose in the presence of tetracyclone and has isolated a product consistent with a benzoylated tetracyclone structure. That the dibenzoyloxyl radical attacks the arynophile before decarboxylation to a phenyl radical occurs, emphasises the ease with which radical addition to tetracyclone can occur. Further evidence for this reaction obtained from the observation of an intense unsymmetrical signal (suggesting the presence of more than one radical species) when dibenzoyl peroxide was decomposed in benzene in the presence of tetracyclone in the cavity of an e. s. r. spectrometer (Figure 6 in Experimental Section). These observations tend to suggest that the 'tetracyclone effect' may well result from the ability of the arynophile to scavenge phenyl radicals and thereby enhance benzyne formation. Radical attack is possible at various positions in the tetracyclone molecule, either on the cyclopentadienone nucleus (e. g. 76) or the substituent phenyl rings (e. g. 77). At the present



(76)



(77)

time, sufficient information is not at hand to assign one particular structure to the e. s. r. signal.

If tetracyclone does function in this way, then decomposition of NNA in the presence of those other arynophiles which gave high yields of aryne adduct should also lead to the observation of e. s. r. signals. In accord with this prediction, reaction in the presence of 2, 5-diethyl-3, 4-diphenylcyclopentadienone and 2-methyl-3, 4, 5-triphenylcyclopentadienone gave intense symmetrical signals (Figures 3, 4 and 5) with g-values very similar to that measured for the tetracyclone case. Furthermore, the analogous reaction with 2, 3-diphenylinden-1-one, previously found to have a

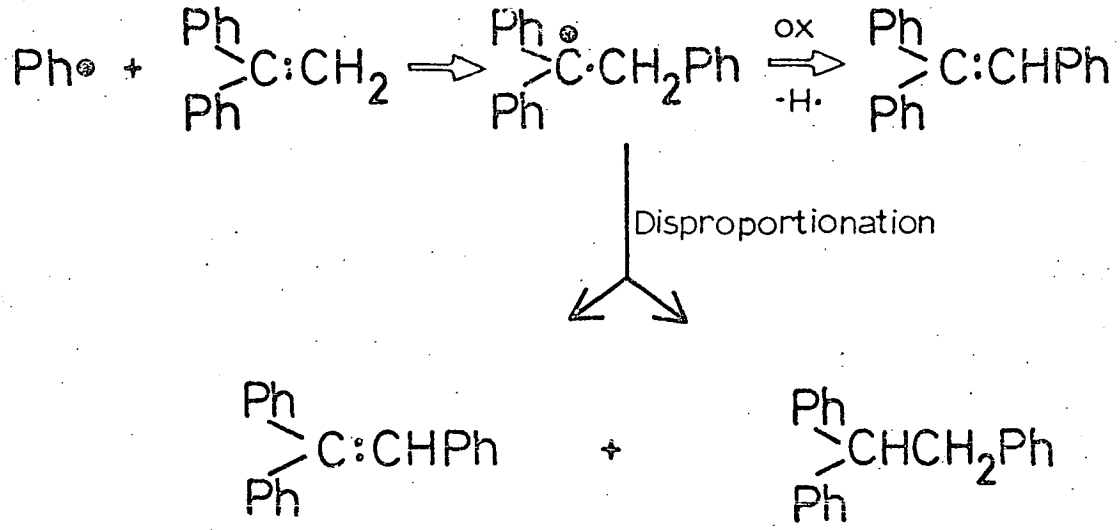
profound 'benzyne-promoting' effect, also gave an intense, long-lived e. s. r. signal. A summary of the g-values, measured for these signals, is given below in Table 11.

Table 11

Decomposition of NNA in Benzene: g-values of e. s. r. signals in the presence of various substituted ketones.

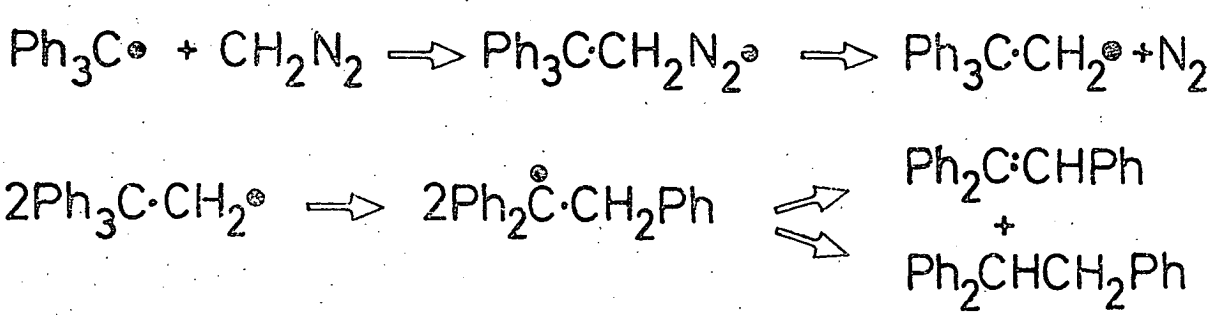
Ketone	
tetraphenylcyclopentadienone	2. 0032
2, 3-diphenylinden-1-one	2. 0027
2, 5-diethyl-3, 4-diphenylcyclopentadienone	2. 0031
2-methyl-3, 4, 5-triphenylcyclopentadienone	2. 0031

Although decomposition of NNA in the presence of diphenylethylene gave no e. s. r. signal, the isolation of triphenylethylene as a minor reaction product is consistent with a mechanism involving inhibition of the radical chain via scavenging of phenyl radicals. The triphenylethyl radical, formed via such a process can either disproportionate to give the observed triphenylethylene and triphenylethane products or else undergo hydrogen atom abstraction by some other radical species to form the substituted olefin. (Scheme 38).



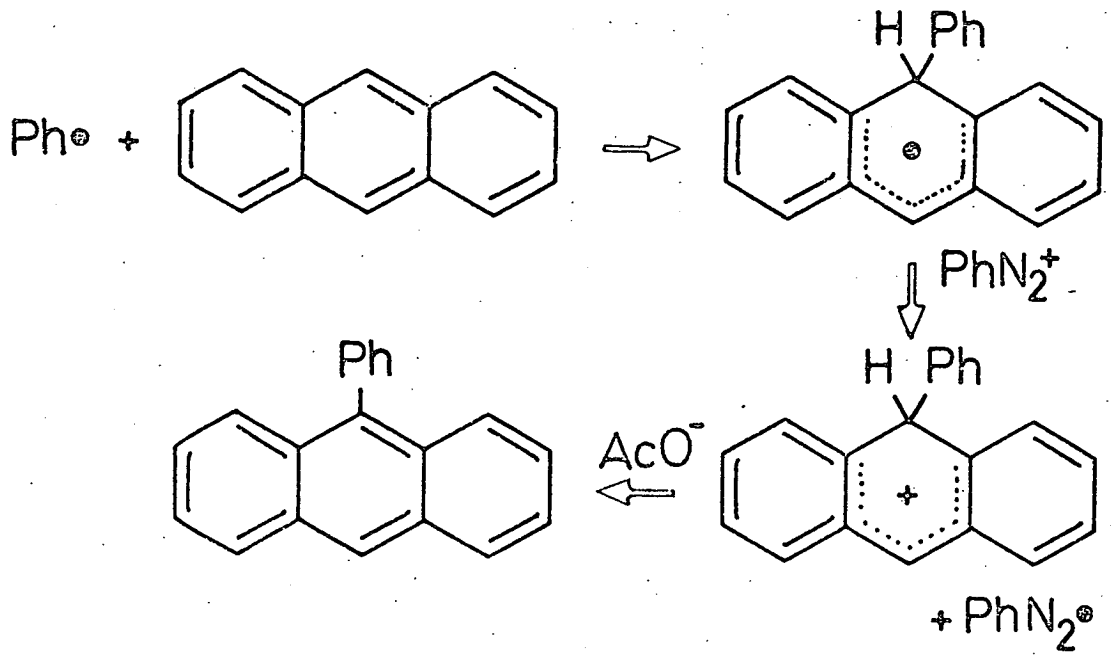
Scheme 38

Disproportionation of the 1, 1, 2-triphenylethyl radical has been previously reported by Denney and Newman[12] who were studying the reaction of triphenylmethyl with diazomethane. They explained the genesis of triphenylethylene (30%) and triphenylethane (7%) by postulating a mechanism in which formation of a 2, 2, 2-triphenylethyl radical is followed by an intramolecular rearrangement to the more stable 1, 1, 2-triphenylethyl species which can then disproportionate. (Scheme 39).



Scheme 39

A clearer picture of the benzyne-promoting effect was now beginning to emerge. That decomposition of NNA in benzene in the presence of anthracene gave a low yield of adduct (3%) and no e. s. r. signal can be explained on the basis that while phenyl radical addition to anthracene occurs readily (reaction in a 20:1 benzene:anthracene mixture gives 9-phenylanthracene (26%) and biphenyl 10%), the 9-phenylanthracyl radical formed by initial radical attack, can undergo redox transfer with the diazonium cation, by analogy with the phenylcyclohexadienyl radical, and thereby enhance propagation of the chain mechanism. (Scheme 40). Thus while anthracene (like benzene) can be thought of as an efficient phenyl radical scavenger, the radical so formed can further react with diazonium cation to give the corresponding diazenyl radical, thereby propagating the free radical mechanism. Conversely, phenylation of those compounds found to be benzyne promoters gives rise to either highly stable radicals (as in the case of tetracyclone and diphenylindenone) or else less stable radicals which



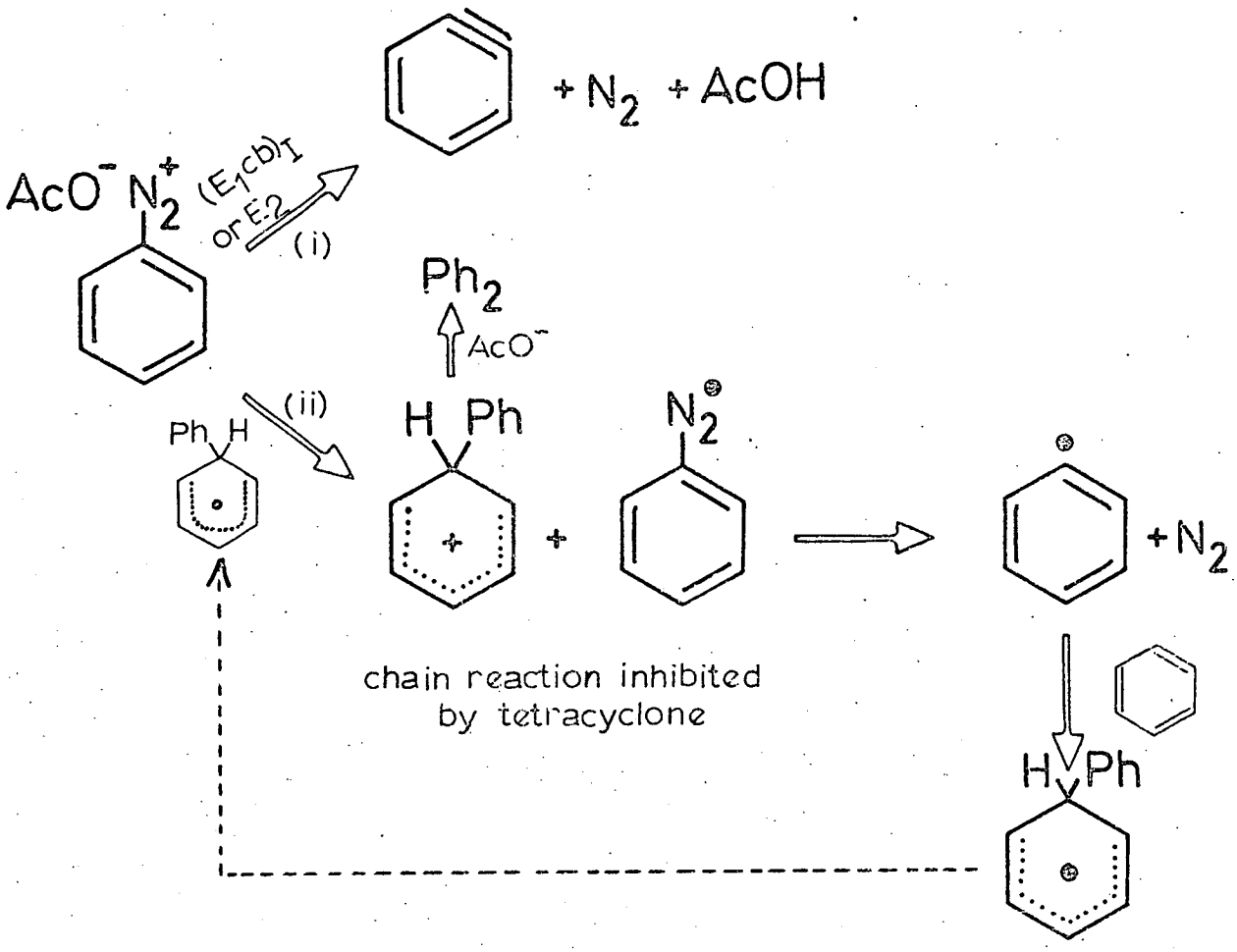
Scheme 40

subsequently follow a reaction path other than the redox process with diazonium (as for diphenylethylene). That decomposition of NNA in the presence of both diphenylethylene and anthracene gave a very low yield of triptycene (2%) presumably follows from the fact that the reaction outlined in Scheme 40 is sufficiently fast to counteract the chain inhibiting reaction preferred by diphenylethylene.

Diphenylethylene was also found to function as a benzyne-promoter with a related acylarylnitrosamine when decomposition of 4-t-butyl-N-nitrosoacetanilide in the presence of furan and the promoter, gave a 10-fold increase in the yield of 6-t-butyl-1,4-dihydro-1,4-epoxynaphthalene (relative to the no-promoter case) and a corresponding decrease in the yield of phenylated products.

In summary, the ability of certain compounds, such as tetracyclone, to divert the decomposition of N-nitrosoacetanilide from the 'normal' radical route (Scheme 41, route (ii)) to that leading to benzyne (route (i)) is believed to arise from a mechanism in which inhibition of the free radical chain reaction induces the

decomposition of the benzenediazonium-acylate ion-pair to proceed via a benzyne forming pathway. (Scheme 41).



Scheme 41

Thus, for the first time a comprehensive scheme can be written for the entire decomposition reaction.

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