NEW REACTIONS OF DIAZONIUM AND RELATED COMPOUNDS

by

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To my Mother and Father

ABSTRACT

At the outset of this investigation two objectives were outstanding, to examine the scope and synthetic utility of a new route to benzyne, recently developed in these laboratories and to clarify the mechanism of the reaction of N-nitrosoacetanilide with dimethyl acetylenedicarboxylate. Investigation of the latter objective led to the development of a new annelation reaction involving reaction of aryl radicals with dimethyl acetylenedicarboxylate and further, to the development of some new facets of the chemistry of hydrazyl radicals. The work described in this thesis thus falls naturally into three sections.

In chapter one investigation of the substituent effects in the production of arynes from substituted anilines and acetanilides with 4-chlorobenzoyl nitrite is described. Yields of aryne adduct were higher when the preformed acetanilide rather aniline-acetic anhydride was used. meta-Substituted anilines and acetanilides both gave higher yields than the corresponding para-isomers which in turn were better than those from ortho derivatives, many of which gave no aryne adduct at all. While both the yields of adduct and the isomer ratios could be ascribed in many cases to the electronic influences exerted by the substituent, the many anomalous results obtained on this basis suggested that the substituent effects were subject to more subtle electronic influences and/or to other so far unassessed complicating factors. The ability of arynes generated by this method to undergo intramolecular nucleophilic attack by a suitable substituent incorporated on the aryne nucleus was also examined. Reaction of both 3-acetamidophenylacetic acid and 3-acetamidophenethyl alcohol with 4-chlorobenzoyl nitrite in benzene failed to yield the expected annelated products but gave instead the radical derived products. The failure of these reactions was ascribed to the poor nucleophilicity of the carboalkoxy and alkoxy groups under the reaction conditions.

In chapter two the mechanism of the reaction of N-nitrosoacetanilide with dimethyl acetylenedicarboxylate is outlined fully. The investigation led to the discovery of a novel reaction of phenyl radicals with dimethyl acetylenedicarboxylate which proceeded via intramolecular cyclization and in the remainder of this section an evaluation of extensions to this reaction via the use of aryl, heterocyclic and polycyclic radicals and other acetylenes is described in detail. The success of these reactions was found to be dependent on the nature of the acetylene and to a lesser extent on the reactivity of the parent peroxide.

Reactions of radicals with azo compounds were examined and discussed in chapter three. Reaction of phenyl radicals with azodiformic esters did not give annelated products analogous to those obtained from dimethyl acetylenedicarboxylate, but gave instead 1,4 diphenyl-1,2,3,4-tetracarboalkoxytetrazanes by dimerisation of the hydrazyl radical first formed by addition of the phenyl radical to the azo double bond. This reaction was found to be extremely susceptible to changes both in the nature of the attacking radical and in the azo substrate. These novel tetrazanes were found to exhibit the phenomenon of severe restricted rotation about the nitrogen-carboalkoxy bond.

ACKNOWLEDGEMENTS

I should like to extend my thanks to Professor J.I.G. Cadogan for his continual encouragement and enthusiasm during the tenure of my studentship and also to Dr. J.T. Sharp for the many helpful and interesting discussions during that period.

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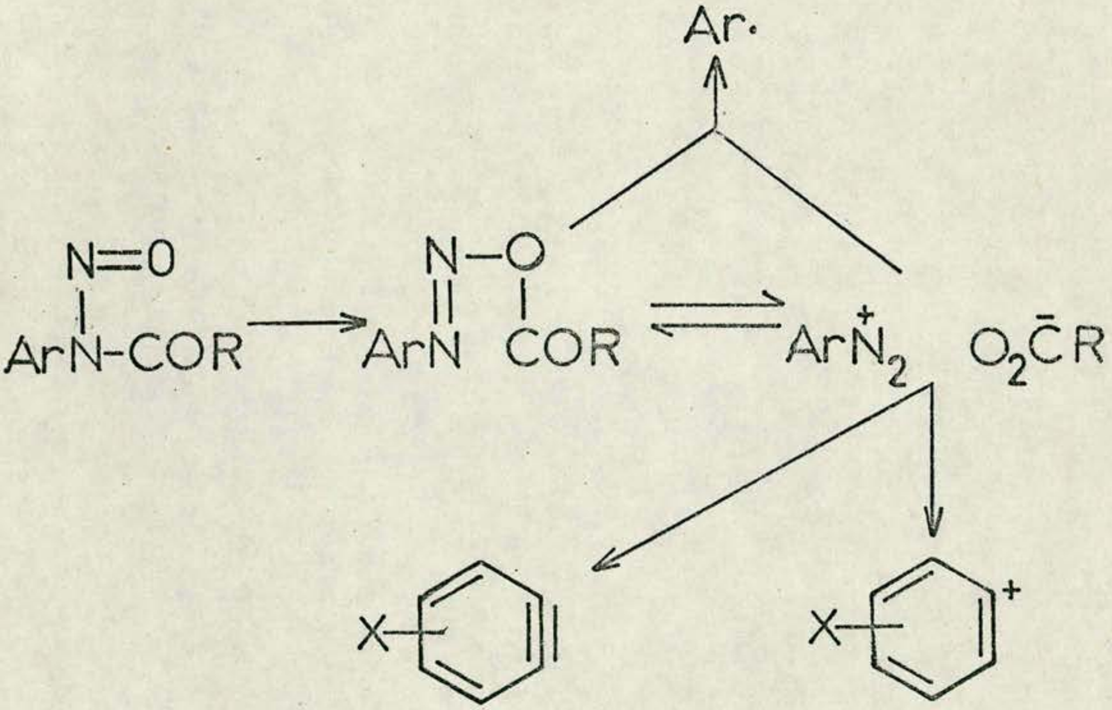
That acylarylnitrosamines rearrange in solution to give a diazonium cation and an acylate counter ion, has been known for some seventy years. The role of this ion pair in the subsequent generation of a family of reactive species, radicals both short- and long-lived, arynes and carbonium ions has proved to be the lynch pin in unravelling the mechanism of acylarylnitrosamine decompositions.



Insofar as the work described in this thesis is germane to the reactions of two of the species derived from the diazonium acylate ion pair, the background to both radicals and arynes will be discussed in a short review. Recent developments in the chemistry of acylarylnitrosamines will also be included.

1. ARYL RADICALS IN SOLUTION

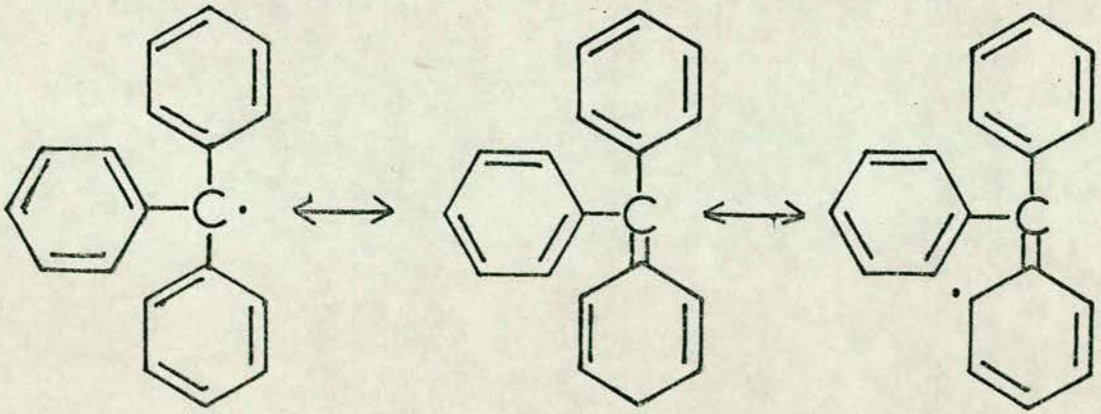
Early background. Like many innovations that directly challenge the credibility of entrenched beliefs, the postulation by Hey and Waters[1] of free radicals as transient intermediates in many commonplace reactions, occurring in solution at ordinary temperatures was met with at best mild disapproval and often fierce scepticism. The concept of an electrically neutral free radical had been extant for some forty years. The triphenylmethyl radical was postulated by Gomberg[2] in 1900 and the existence of the reactive methyl radical was invoked by Paneth and Hofeditz[3] to explain the results of gas phase pyrolyses of lead tetramethyl. Grieve and Hey[4] in 1934 had suggested the involvement of phenyl radicals in the decompositions of acylarylnitrosamines and one year later, Waters[5] tentatively suggested that radical as well as ionic addition reactions occurred with olefins. In general however, radicals were regarded as chemical freaks, being outwith the pale as species in normal chemical reactions.

Such was the intellectual power of the Hey-Waters tour de force, directing attention as it did to an alternative interpretation of the courses of chemical reactions, that it initiated much of the subsequent work in this field and led to the general acceptance of the free radical as a genuine reaction intermediate.

Reactivity. Radicals undergo many types of reaction: they are more numerous than non-radical reactions and frequently have no heterolytic counterparts. The reason for their great reactivity lies in the ability of the unpaired electron to readily form a strong electron pair bond, the driving force being the energy liberated in the formation of the bond. It is important that reactivity not be confused with instability for although many radicals are highly reactive, they possess inherent thermodynamic stability. Thus methyl radicals are stable despite an estimated mean lifetime of 10^{-3} sec at 2mm,[3] yet the acetoxy radical undergoes decarboxylation to give carbon dioxide and a methyl radical, a reaction which is exothermic by 50-60 k J mol^{-1}.[6]

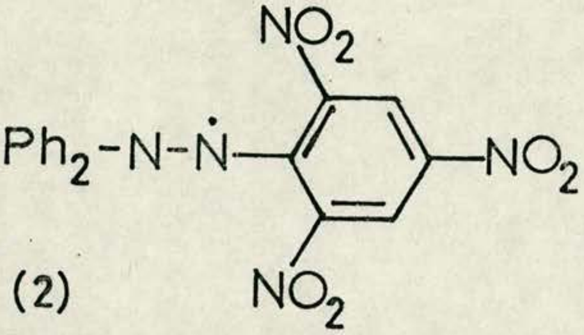
$$CH_3CO_2^{\cdot} \longrightarrow CH_3^{\cdot} + CO_2$$

Conversely, the triphenylmethyl radical (1) which is stabilised by electron delocalisation, thus allowing conjugation between the aryl nucleii undergoes a variety of combination reactions with iodine atoms, sodium atoms, and nitric oxide.



(1)

The diphenylpicrylhydrazyl radical (2) is readily obtained as a violet-black solid[7] and is stable

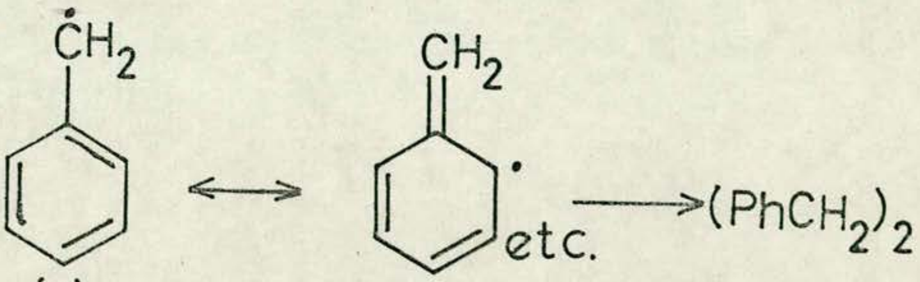

(2)

in the solid state for years, yet it finds wide use as a radical scavenger as it readily combines with radicals of all types.

The simplest reaction of radicals is <u>combination</u>:

e.g. $Ph_3C\cdot + Ph_2N\cdot\dot{N}Ph \longrightarrow Ph_2\dot{N}\cdot NPhCPh_3$

It is energetically favourable due to the heat of bond formation and frequently proceeds with little or no energy of activation. A special case of combination is <u>dimerisation</u> which involves combination of identical radicals. The phenomenon of combination is observed when the radical is long lived i.e. when it is stabilised by delocalisation and therefore capable of existing in high local concentration. Typical of this type is the benzyl radical (3).



(3)

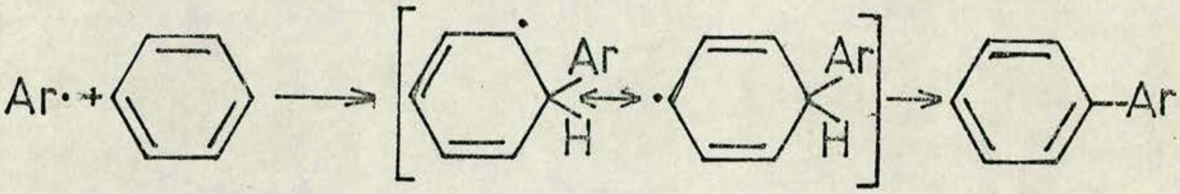
Combination reactions of short-lived radicals are relatively rare since radical-molecule reactions are statistically favoured. A notable example of this type is furnished in the Kolbe[8] reaction which allows the electrolytic conversion of a carboxylic acid containing n carbon atoms into a molecule containing 2n-2 carbons:

$$2RCO_2^- \xrightarrow{-2e} R\text{-}R + 2CO_2$$

Studies of the Kolbe reaction[9,10,11] have thrown light on the mechanism of radical <u>disproportionation</u>, which being a radical-radical process is usually unfavourable on statistical grounds. However, C-H bonds adjacent to carbon bearing an unpaired electron are known to be very weak with a bond energy of 168 k J mol^{-1},[12] so that the process is energetically well disposed. Thus electrolysis of β,β,β-tri(^{2}H) propionic acid and of α,α-di(^{2}H) propionic acid gives α,α-di(^{2}H) ethylene, showing that one propyl radical <u>abstracts</u> a β hydrogen from the other.

$$2CD_3{\cdot}CH_2{\cdot}CO_2^{\cdot} \longrightarrow 2CD_3{\cdot}CH_2^{\cdot} \longrightarrow CH_2{:}CD_2 + CD_3{\cdot}CH_2D$$
$$2CH_3{\cdot}CD_2{\cdot}CO_2^{\cdot} \longrightarrow 2CH_3CD_2^{\cdot} \longrightarrow CH_2{:}CD_2 + CH_3{\cdot}CHD_2$$

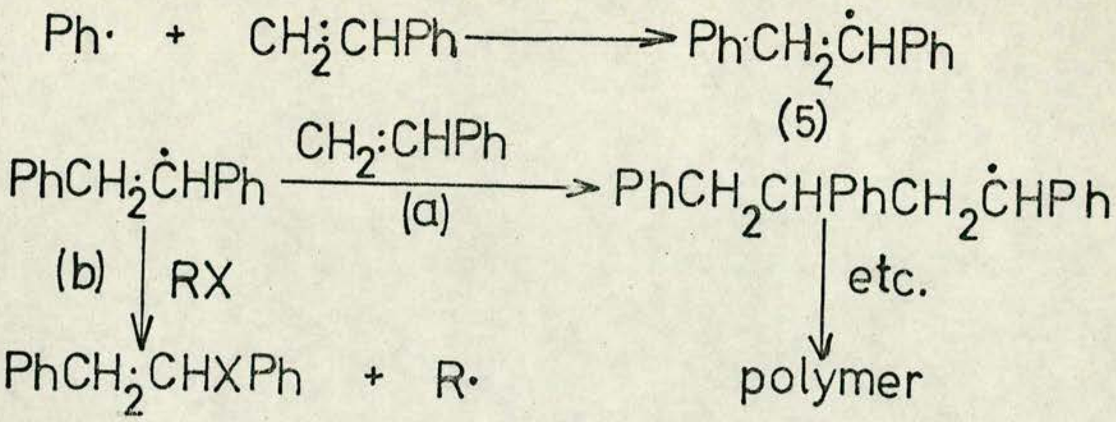
Of the various reactions of <u>homolytic aromatic substitution</u> which are known, such as alkylation, hydroxylation and mercuration, arylation has proved the most amenable to investigation. The theoretical study of arylation, whereby an atom (usually hydrogen) which is situated at an aromatic nucleus is replaced by a phenyl or other aryl radical via an intermediate arylcyclohexadienyl radical (4), has been directed both at the mechanisms of the various arylation reactions and towards an understanding of the influence of substituent groups in both the substrate and attacking radical on the rate and course of the substitution process.



(4)

Much of the pioneering work in this field has been done by Hey[4] and the subject has been comprehensively reviewed by Williams[13] and others.[14]

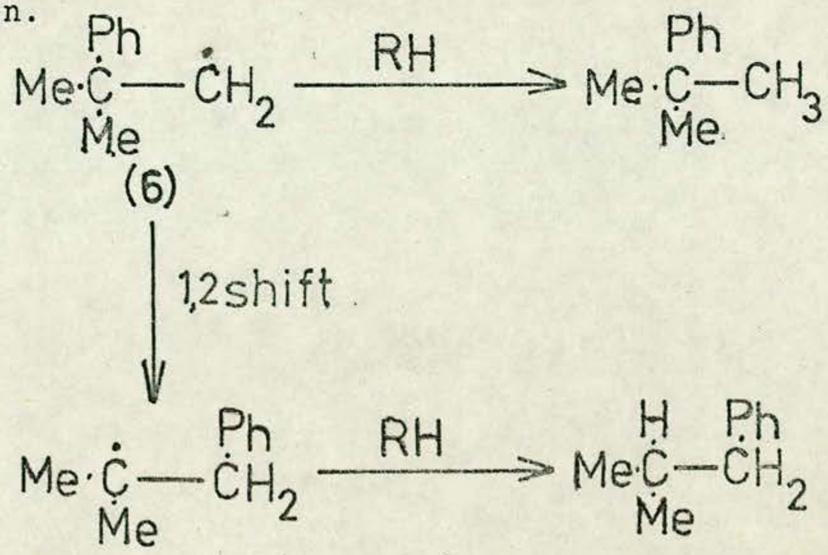
The addition reactions of radicals to olefins are of immense importance (a) as the propogation step of radical polymerisations and (b) as the first stage of the chain sequences that produce small molecules: e.g. addition of phenyl radicals to styrene. The first formed product is the 1,2 diphenylethyl radical (5) which can then undergo reaction via pathways (a) or (b).



(5)

It should also be pointed out that the anomalous addition of hydrogen bromide to allyl bromide, studied by Kharasch and co-workers[15] was found to proceed by peroxide initiation of a radical chain addition mechanism and hence affords an example of reaction via pathway (b).

A more uncommon radical reaction is that of radical rearrangement which may involve migration of groups (H, halogen, aryl) or skeletal rearrangements. These reactions were first observed by Kharasch and Urry[16] during studies of the neophyl radical (6). This radical was observed to rearrange to a significant extent, via a 1,2 aryl shift before undergoing the familiar reactions of dimerisation, disproportionation, and abstraction.



(6)

Much of the work in this field and related reactions such as fragmentation and displacement has been reviewed recently.[17,18]

Sources of aryl radicals

Homolytic fission of most bonds can be readily achieved by thermal or photochemical means. In solution, molecules containing weak bonds with dissociation energies below 168 k J mol^{-1} will undergo thermal dissociation at an appreciable rate below 150^{o}. Although this is a widely used basis for generation of phenyl radicals, the limitations inherent in this method restrict the choice of compound.

One of the most facile methods of producing aryl radicals is by decarboxylation of aroyloxy radicals, which can themselves be generated from a variety of sources. Thus decomposition of dibenzoyl peroxide in benzene occurs at 80^{o} with production of biphenyl, carbon dioxide and benzoic acid.[19,4]

$$(PhCO_2)_2 \longrightarrow 2PhCO_2^{\cdot} \xrightarrow{PhH} Ph_2 + PhCO_2H + CO_2$$

This gross oversimplification bears no resemblance to the true complexity of the reaction. In a mammoth quantitative product study of this reaction, De Tar[20] found that at a peroxide concentration of 0.3M, 101 reactions were found to contribute 0.05% or more to product formation. Apart from radical induced decompositions, the main determinant of product distribution from decomposing aroyl peroxides is the competition between loss of carbon dioxide from the aroyloxy radical and its reaction, by abstraction from, or addition to other species.

As shown some years back,[21] the benzoyloxy radical can be trapped by an efficient scavenger.

$$PhCO_2^{\cdot} \xrightarrow{I_2} PhCO_2I \xrightarrow{H_2O} PhCO_2H$$

The decomposition of benzoyl peroxide in naphthalene[22] and other polynuclear aromatic solvents[23,24] produces substantial yields of benzoates, probably <u>via</u> benzoyloxy addition.

Lead tetrabenzoate has been shown to decompose in aromatic solvents at 125° to give products derived by solvent phenylation,[25] as does phenyl iodosobenzoate.[26,27] Aryl radicals have also been generated by decomposition of silver halide benzoates,[28] by the electrolysis of benzoates in pyridine,[29] and by the oxidation of aroic acids.[30]

There are many recorded instances of the use of diazo-compounds of various types for the production of aryl radicals. Mono-aryl azo-compounds such as phenylazotriphenylmethane (7)[4] and 1,3 diphenyltriazen (8)[31] decompose to phenyl radicals and specific counter ions such as the trityl radical and anilino radical respectively.

$$\underset{(7)}{\mathrm{Ph{-}N{=}N{-}CPh_3}} \longrightarrow \mathrm{Ph\cdot} + \mathrm{N_2} + \mathrm{\cdot CPh_3}$$

$$\underset{(8)}{\mathrm{Ph{-}N{=}N{-}NHPh}} \longrightarrow \mathrm{Ph\cdot} + \mathrm{N_2} + [\mathrm{\cdot NHR}]$$

An alternative route from diazonium salts to phenyl radicals involves one electron reduction of the substrate.

$$\mathrm{PhN_2^+} + e \longrightarrow [\mathrm{PhN{=}N\cdot}] \longrightarrow \mathrm{Ph\cdot} + \mathrm{N_2}$$

This can be effected polarographically[32] or chemically: it occurs in the copper catalyzed reactions of diazonium fluoroborates,[33] and it is now accepted that the Sandmeyer, Gatterman and Meerwein reactions proceed in similar fashion.[34]

The classic method of aryl radical generation is the Gomberg reaction.[35] This is a heterogeneous reaction in which an aqueous solution of the appropriate diazonium salt, in contact with the aromatic substrate, is treated with sodium hydroxide or sodium acetate.

$$\mathrm{ArN_2Cl} + \mathrm{NaOH} + \mathrm{Ar'H} \longrightarrow \mathrm{ArAr'} + \mathrm{N_2} + \mathrm{NaCl} + \mathrm{H_2O}$$

Although often suffering from poor yields of biaryl and much polymer production, the method was widely used before simpler routes were devised. One such route employed the <u>in situ</u> diazotisation of aromatic amines with pentyl nitrite and was devised and developed by Cadogan and co-workers.[36]

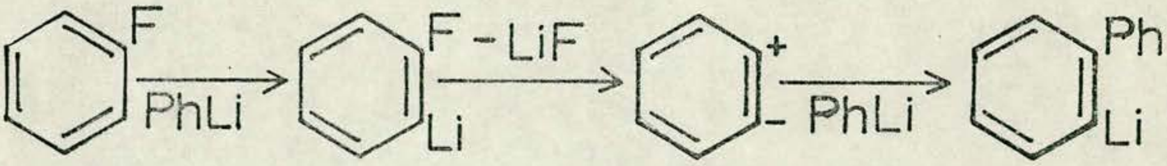
The production of phenyl radicals from acylarylnitrosamines will be discussed more fully in a later section.

Not only is photolysis a convenient means for radical production from some of the sources considered previously, but in many cases can provide routes to radicals unavailable by conventional thermolytic means. Phenyl iodide is thermally stable but is known to give a high yield of phenyl radicals upon irradiation with ultra violet in cumene. Similarly, diphenyl mercury and tetraphenyl lead have generated phenyl radicals on photolysis.[37]

2. ARYNES

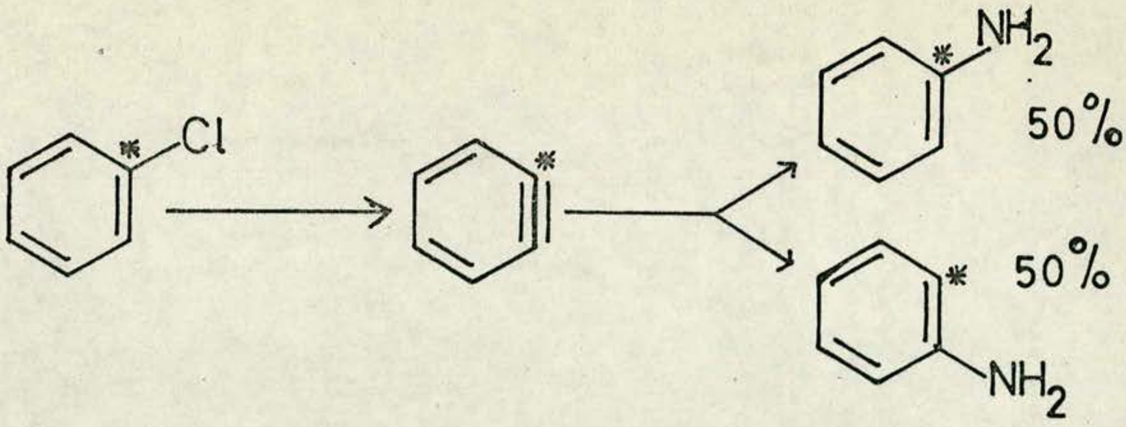
Background. Although there had been many chemical pointers to the existence of a 1-2 bifunctional intermediate, the development of the aryne concept can be dated from the early studies of nucleophilic aromatic substitution.

Wittig and co-workers[38] found that the reaction of halogenobenzenes with phenyllithium gave biphenyl, but that its rate of formation from fluorobenzene was greater than from other halogenobenzenes, thus excluding the possibility of straight displacement of fluoride by phenyl cation. The proper interpretation of this reaction was aided by the discovery that 2-lithiobiphenyl was the primary product of the reaction.[39] Wittig, in accounting for its formation, postulated the intermediacy of a 1,2 dipolar species (9) which was a formal canonical form of benzyne.

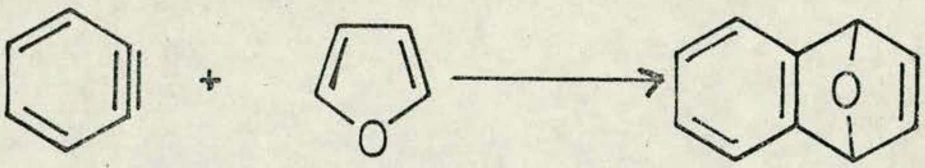


(9)

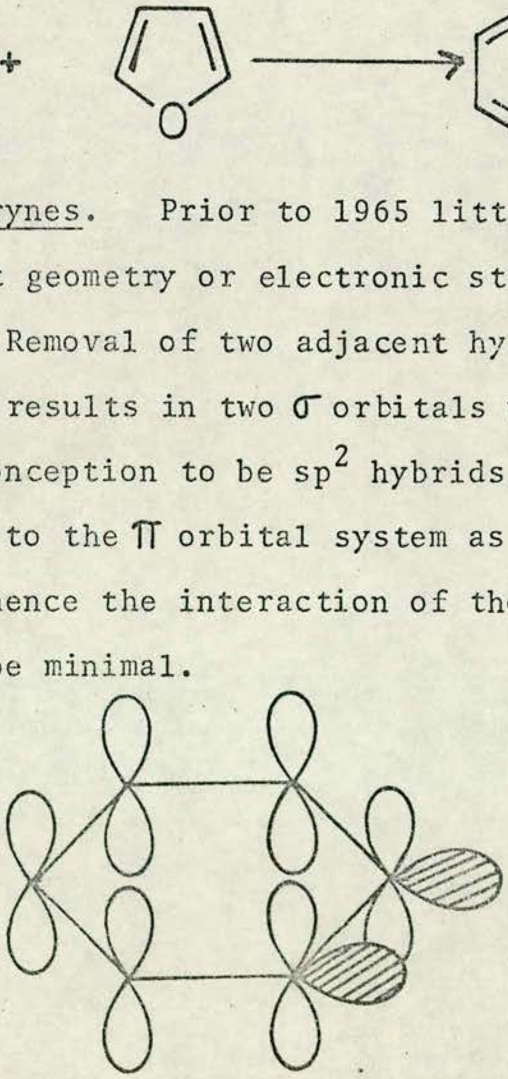
Many rearrangements were reported to occur during the amination of aryl halides by metal amides in liquid ammonia.[40] The participation of benzyne as an intermediate in these aminations was visualized by Roberts[41] who carried out the crucial amination of 1-^{14}C chlorobenzene. The formation of equal amounts of 1-^{14}C aniline and 2-^{14}C aniline proved that benzyne was an intermediate in these reactions.



Later work by Huisgen[42] on the reaction of aryl halides with phenyllithium confirmed the intermediacy of benzyne in these nucleophilic substitutions, although his results suggested that Wittig's structure for benzyne was erroneous. Any dubiety about the reality of benzyne was finally removed when Wittig succeeded in trapping the species as a Diels-Alder adduct of furan.[43]

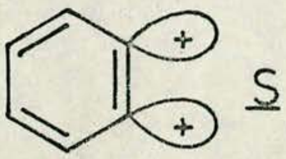


Structure of Arynes. Prior to 1965 little was known about the exact geometry or electronic structure of even 1-2 benzyne. Removal of two adjacent hydrogen atoms from benzene itself results in two σ orbitals which are taken by common preconception to be sp^2 hybrids. These orbitals are orthogonal to the π orbital system as depicted for 1,2 benzyne (10), hence the interaction of those two sets of orbitals will be minimal.



(10)

The newly formed σ orbitals can now interact to give a singlet or triplet state: the former can exist in either the bonding, symmetrical electronic configuration (11) or the antibonding, antisymmetrical configuration (12); the latter exists in the triplet, diradical configuration (13).



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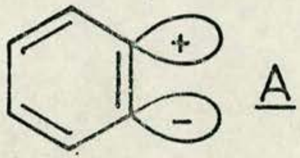

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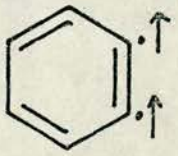
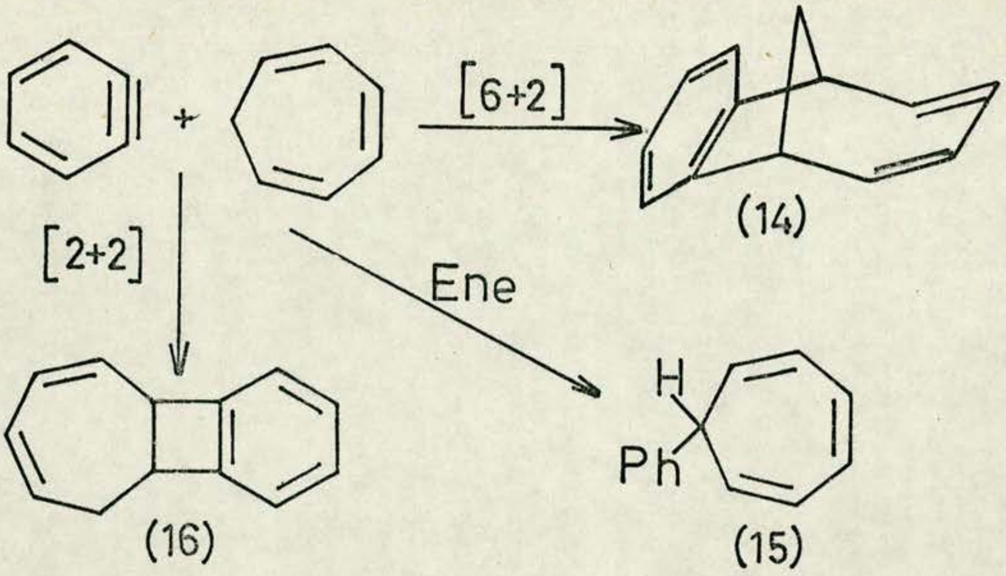

(13)

The early evidence regarding the nature of the ground state of benzyne was confusing and often contradictory: dehalogenation of o-dihalogenobenzene with disodiumtetraphenylethylene was thought to produce benzyne in an equilibrium state of singlet and triplet;[44] Rees[72] suggested that formation of biphenylene in high yield from 1-aminobenzotriazole was due to triplet benzyne and Tabushi[50a] claimed to have experimental evidence of triplet benzyne from trapping experiments with olefins. However, neither photolysis of 1,2,3 benzothiadiazole-1,1 dioxide in a hexfluorobenzene glass nor fluorolube glass led to the production of an e.s.r. signal consistent with structure (13).[45]

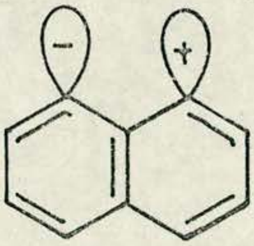
On the other hand it was shown by time-resolved mass spectroscopy during the flash photolysis of benzenediazonium-2-carboxylate that benzyne, carbon dioxide and nitrogen were produced simultaneously.[46] This observation was interpreted in terms of an excited state of the benzenediazonium-2-carboxylate decomposing in a concerted fashion to products in singlet states. The general acceptance of the singlet configuration as the ground state for 1,2 benzyne[47] meant that structures 11 and 12 were the only viable possibilities. In a comprehensive study of the stereochemistry of the [2+2] and [2+4] cycloadditions of benzyne, Jones and Levin[47] concluded that the reactive species, and hence the ground state was the symmetrical singlet (11), a conclusion that was supported by several theoretical studies.[48,49]

In contrast, Tabushi and co-workers[50b] reported that the S̲ and A̲ forms appeared to be equally reactive, on the basis that benzyne underwent [6+2] cycloaddition with heptatriene to give adduct (14) as well as the ene product (15), instead of the expected [2+2] and [2+4] cycloadducts (scheme 1), a product distribution which required a major contribution from A̲ benzyne on the basis of orbital symmetry considerations.[51] This assertion was refuted convincingly by two groups[52,53] who considered the major products to be the [2+2] adduct (16), formed by a stepwise route, and the ene product (15) in a 1:1 ratio.



Scheme 1

That these theoretical computations on the structures of arynes mirror reality, was demonstrated by Hoffman[48] who calculated that the ground state for 1,8 dehydronaphthalene should be the antisymmetrical state (17).

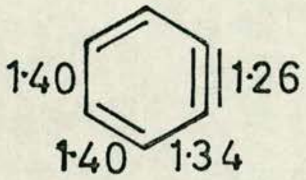


(17)

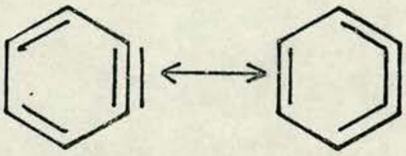
The selection rules previously derived for concerted cycloadditions[51] predicted that the intermediate should then undergo thermal, concerted 1,2 cycloadditions, an observation that was borne out experimentally by Rees.[54]

A theoretical study on the molecular geometry of 1,2 benzyne by Haselbach[55] indicated a bond length of

1.26Å for the strained triple bond, a value which was only 0.05Å greater than that of acetylene. The structural data obtained (18) indicated a considerable π electron delocalisation in 1,2 benzyne and supported Hoffman's suggestion[48] that a sizeable resonance contribution came from the cumulene structure (18a).

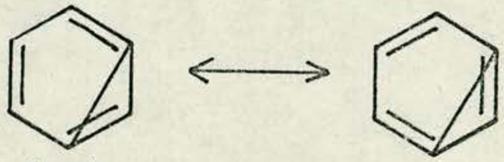


(18)



(18a)

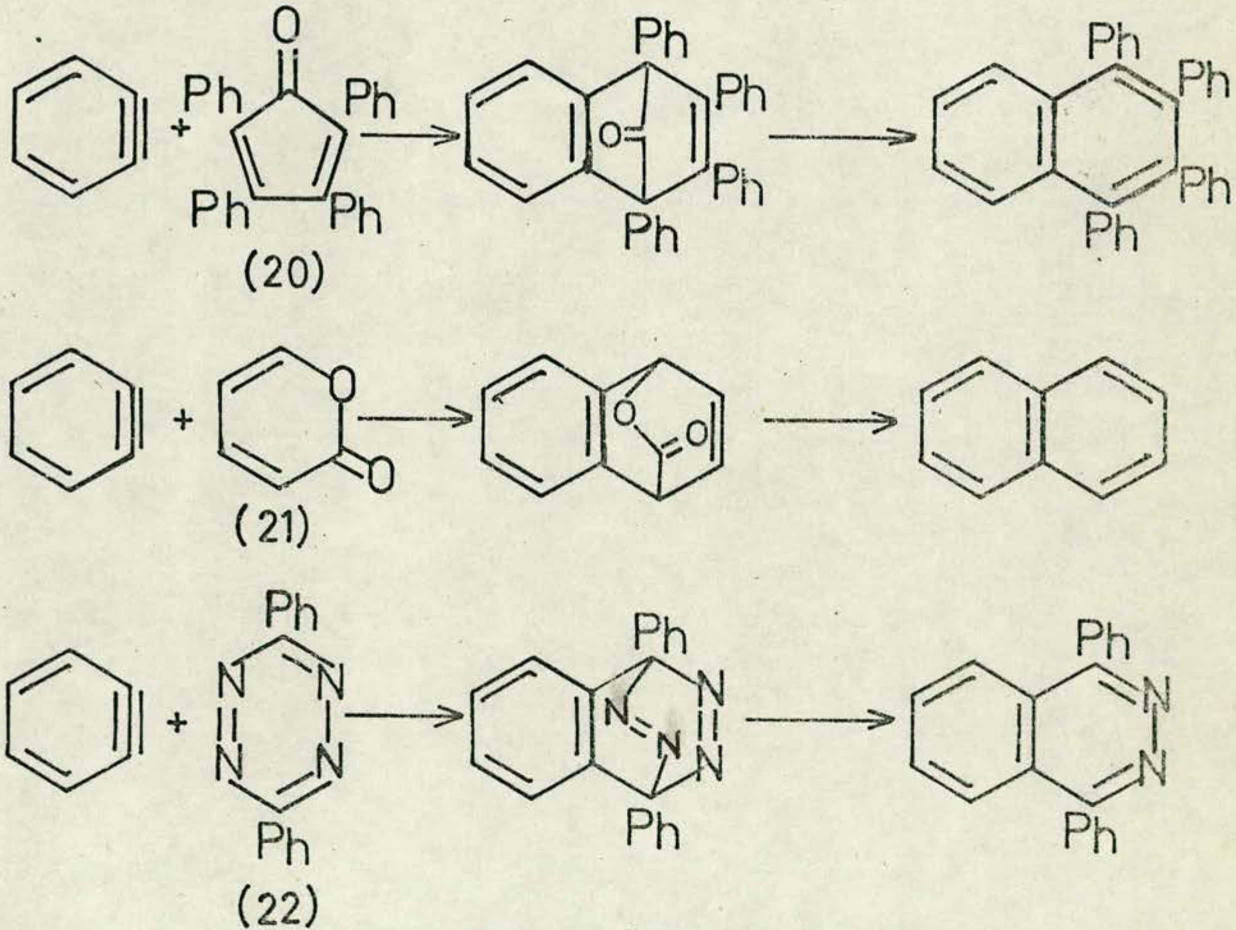
A similar study for 1,3 benzyne[56] concluded that the formation of (19), with a shortened distance across the ring owing to σ bond formation, was a distinct possibility. This assertion was in direct agreement with Hoffman[48] who also found evidence for partial 1,3 bonding.



(19)

Reactivity of Arynes. As might be expected from the foregoing discussion on the structure of arynes, they characteristically show properties expected of highly reactive acetylenes, undergoing cycloaddition reactions with conjugated dienes and 1,3 dipolar species.

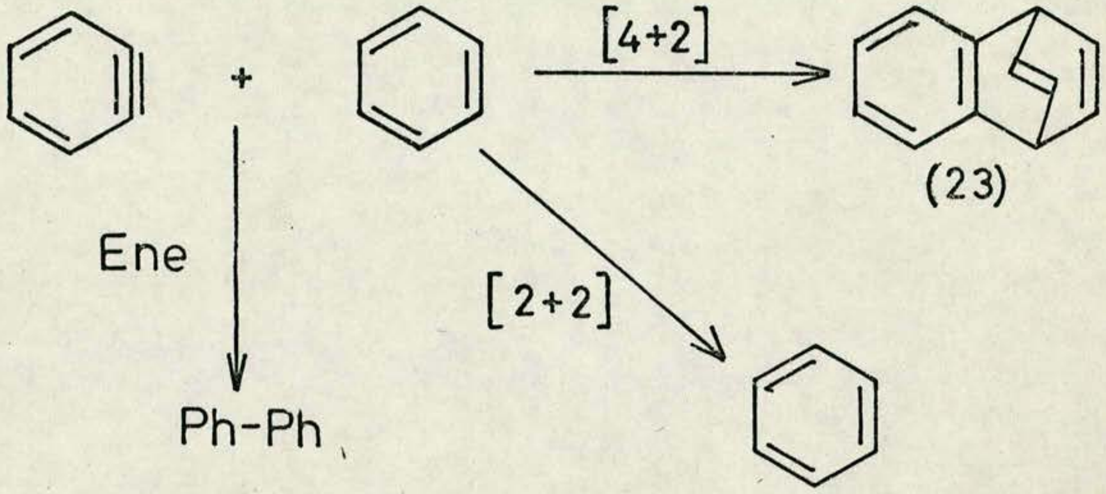
Since 1955 when Wittig trapped benzyne as a Diels-Alder adduct with furan,[43] so many dienes have been shown to undergo this reaction that it is now regarded as a diagnostic test for benzyne formation. Some of the products, such as those of 2,3,4,5-tetraphenylcydopentadienone (tetracyclone) (20),[57] 2-pyrone (21),[58] and diphenyltetrazine (22)[59] are not primary Diels-Alder adducts, but result from loss of a bridging group with formation of a fully aromatic system (scheme 2).



Scheme 2

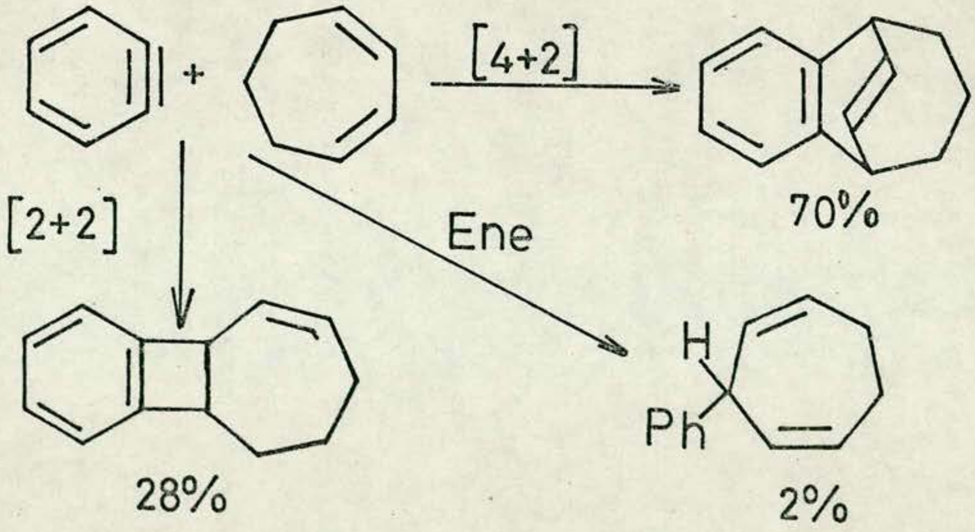
The reactivity of benzyne is so great that it will add across the π system in benzene, a reaction requiring 151 k J of resonance energy to overcome the aromaticity.

Friedman[60] showed that the major product was the [4+2] cycloadduct, benzobicyclo [2,2,2] octatriene (23) obtained in 17% yield (scheme 3).



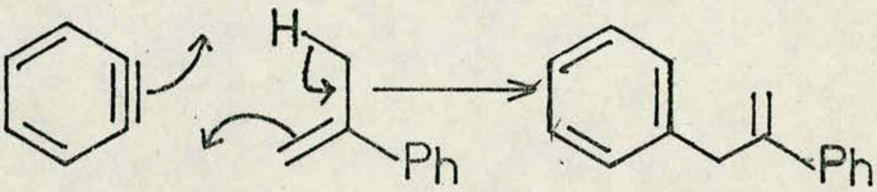
Scheme 3

Although the observed ground state for benzyne favours concerted [4+2] cycloaddition over the stepwise [2÷2] cycloaddition, effective competition of the latter (28%) with the former (70%) has been observed in benzyne addition to cyclohepta-1,3-diene (scheme 4).[52,53]



Scheme 4

Simple olefins with allylic hydrogen can react with benzyne by a concerted cycloaddition, analogous to the Diels-Alder reaction, known as the 'Ene' reaction:[61] reaction of benzyne with α methyl styrene gives 2,3-diphenylpropene (32%) as the major product, with minor products arising from [2+4] and [2+2] reactions.[62]

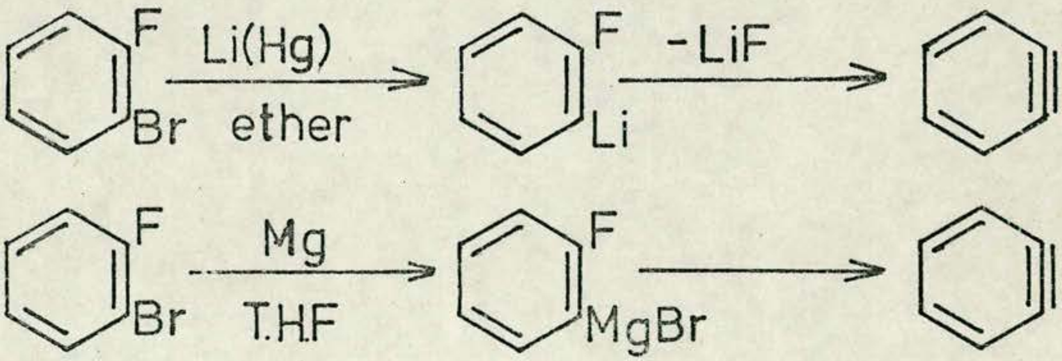


In a study of benzyne cycloadditions to cyclic olefine[63] it was found that the conformation of the polyolefin coreactant was of primary importance in the relative partitioning between [2+4], [2+2] or ene cycloadditions.

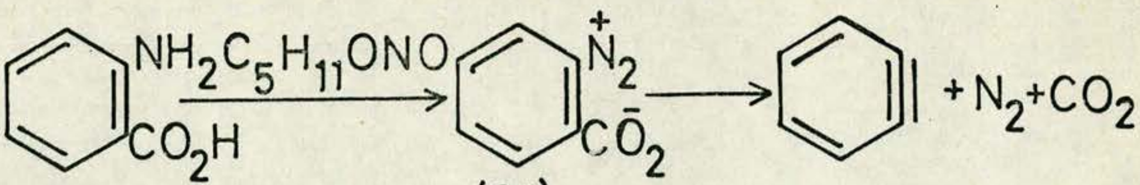
Although they are electrically neutral, arynes have a pronounced electrophilic character and consequently react with nucleophiles of all kinds. These reactions are reviewed extensively elsewhere.[64] When the nucleophile in question is part of a side chain on the aryne, a simple synthetic route to a variety of carbocyclic or heterocyclic systems is afforded. These intramolecular cyclisations have provided useful syntheses of many common ring systems and have been readily extended to more complex systems.[65,66]

Sources of Arynes. Since the early work of Wittig and Roberts, many routes to arynes have been developed utilising the reactivity of halogenated aromatic substrates in strongly basic media. This reaction has been used to generate dehydroaromatic derivatives of benzene, naphthalene, phenanthrene and a variety of heterocyclic systems.[64] A major drawback to this mode of production is the severe reaction conditions employed; arynes formed in the presence of strong base are often intercepted, undergoing nucleophilic attack by the base to give adducts. The limitations imposed on the synthetic usefulness of arynes prepared in this way activated research into developing milder sources of arynes.

A first means of circumventing strong organometallic agents was designed by Wittig[43] who employed metal-halogen exchange between 1,2-dihalogenobenzenes and lithium amalgam or magnesium to generate arynes in good yield.

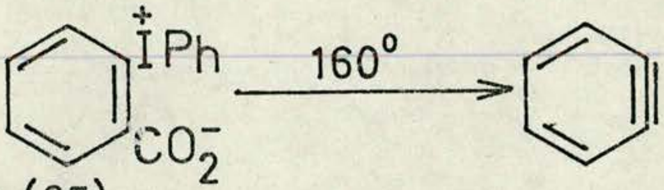


Benzenediazonium-2-carboxylate (24), generated from anthranilic acid and decomposed *in situ* below 80° was found to give benzyne in high yield.[67,68]



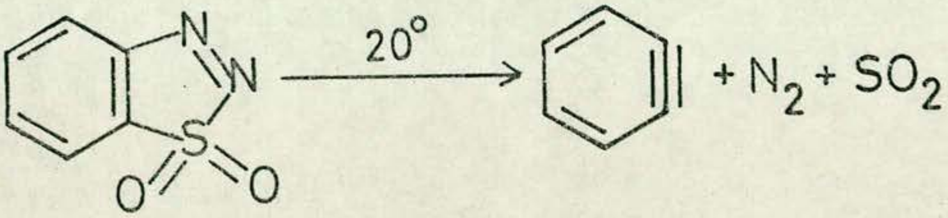
(24)

A similar but more stable zwitterionic compound, diphenyliodonium-2-carboxylate (25) also found use as a benzyne precursor.[69]



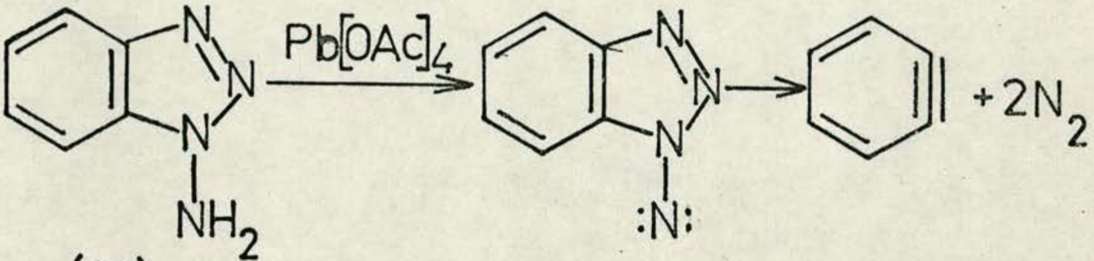
(25)

The principle underlying these facile productions of aryne i.e. compensation of ring strain in the aryne with the heat of formation of small, stable molecules was extended to the production of arynes by cleavage of cyclic systems. Relatively stable molecules like acid anhydrides afforded benzyne when pyrolyzed at 700°.[70] 1,2,3-benzothiadiazole-1,1-dioxide (26), although isolable as a crystalline compound, was found to be unstable and fragmented under mild conditions to benzyne, sulphur dioxide and nitrogen.[58]



(26)

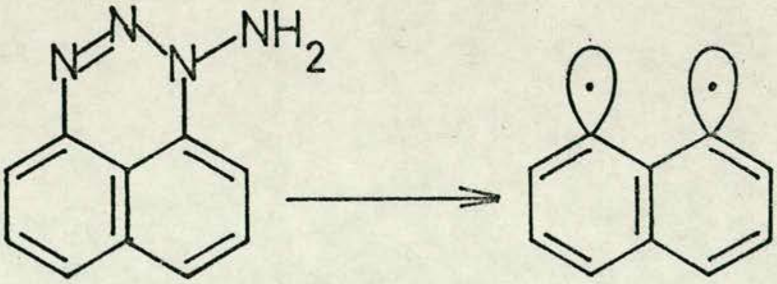
The complications associated with benzenediazonium carboxylate and benzothiadiazole dioxide were finally overcome with the development of 1-aminobenzotriazole (27). Oxidation of the triazole at or below room temperature gave the intermediate nitrene, which underwent rapid fragmentation to benzyne and nitrogen.[71,72]



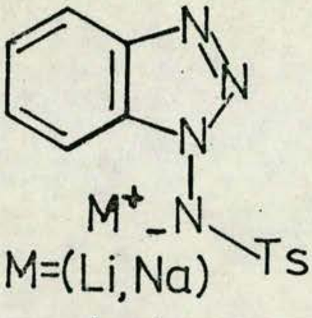
(27)

In the absence of efficient traps, biphenylene was produced in exceptionally high yield, a testimony to the great efficiency of the oxidation and fragmentation steps which leads to a high local concentration of benzyne.

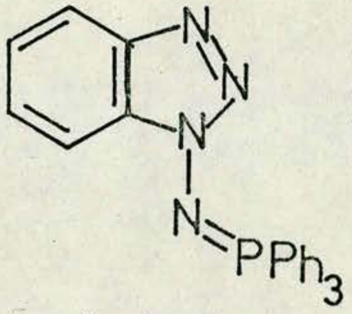
This route provided easy access to the interesting 'meta-aryne', 1,8-dehydronaphthalene.[54]



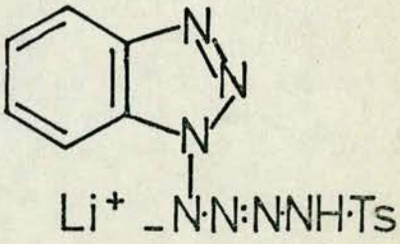
Alternative routes to arynes which precluded the use of lead tetraacetate were further developed by Rees and co-workers. Photolysis of the tosylamido salts (28) or the iminophosphorane (29) was found to give benzyne adducts in the presence of dienes, while benzyne was obtained from the isolable salt (30) simply on dissolution in tetrahydrofuran at room temperature.[73]



(28)



(29)



(30)

Recent work on the production of arynes from acylarylnitrosamines has resulted in a general method for the simple and efficient conversion of anilines and anilides into arynes.[74] The development of this field will be discussed more fully in the next section.

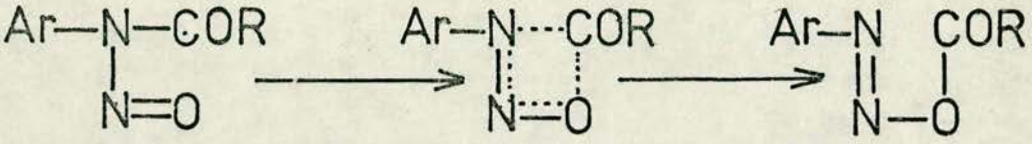
3. ACYLARYLNITROSAMINES

Background. Fischer first reported the preparation of *N* nitrosoacetanilide in 1876:[75] Bamberger[76] showed that the reaction of *N* nitrosoacetanilide with benzene gave biphenyl; and the use of acylarylnitrosamines in a general synthesis of biaryls was developed by Grieve and Hey.[4] Earlier work by Kuling[77] and Bamberger[8] on the decomposition of dry sodium arenediazotates in the presence of acetylating agents had been developed by Gomberg,[35] also as a synthetic route to biaryls. Attempts to rationalise the products of these reactions led Grieve and Hey to postulate the intermediacy of phenyl radicals.[4] Only during the early post-war years did the theories of homolytic aromatic substitution and hence the participation of phenyl radicals in the decompositions of acylarylnitrosamines become generally accepted. Once established however determined efforts were made to elucidate the precise mechanism of acylarylnitrosamine decomposition.

The Mechanism of Decomposition. Work by Huisgen and Horeld[79] established that the rate determining step in the decomposition was rearrangement to the phenyldiazoacetate form.

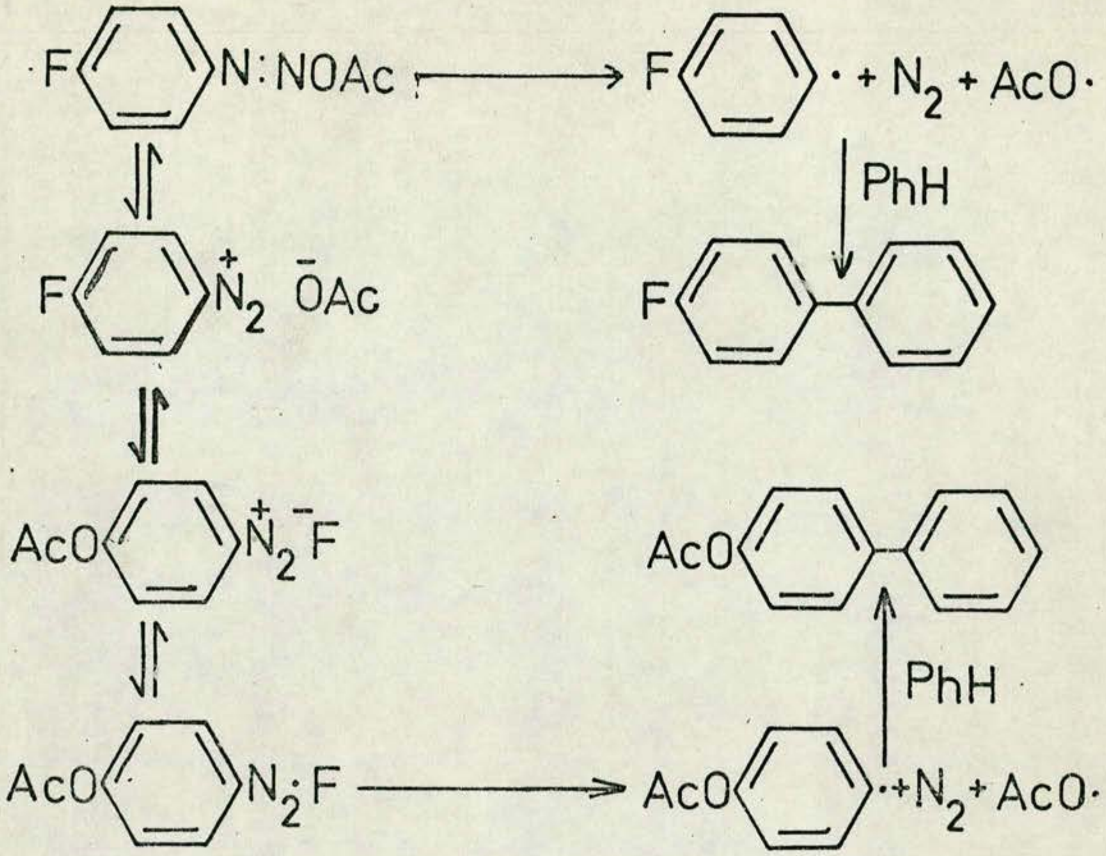
$$\mathrm{PhN(NO)Ac} \xrightarrow{\text{slow}} \mathrm{PhN{=}NOAc} \xrightarrow{\text{fast}} \mathrm{Ph}\cdot$$

This rearrangement was further shown by Hey[80] and Huisgen[81,82] to proceed via a cyclic transition state (31)



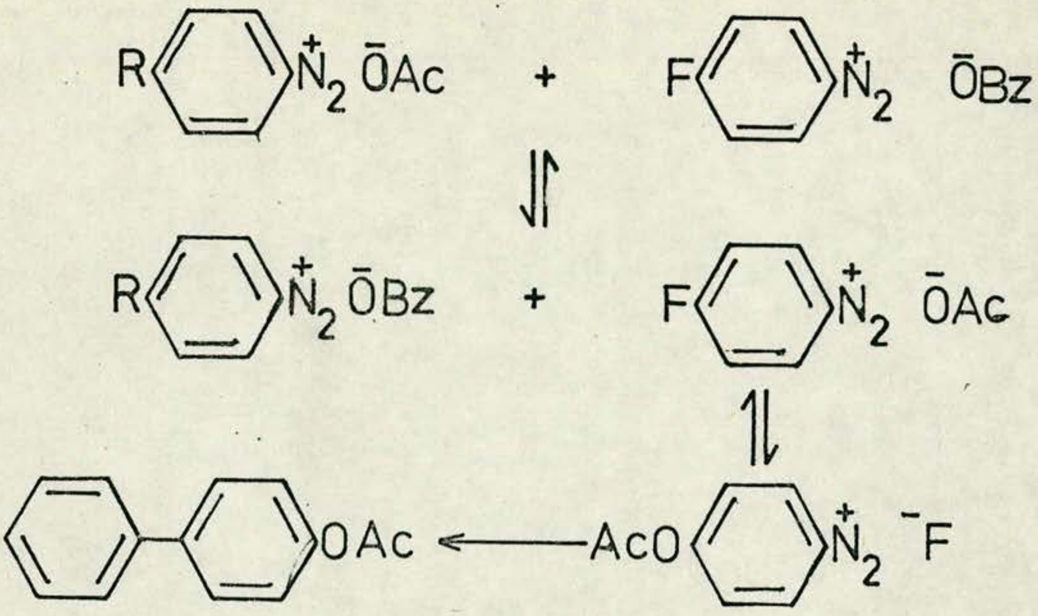
(31)

Suchitzsky and collaborators[83,84] made the crucial observation that arenediazonium-acetate ion pairs were present in solutions of acetylarylnitrosamines and that heterolysis of the covalent diazoester would be important even in non-polar solvents. Thus decomposition of 2- and 4-fluoro-N-nitrosoacetanilides and benzanilides in benzene yielded not only 2- and 4-fluorobiphenyls, but also comparable amounts of 2- and 4-acyloxybiphenyls.[83b] Neither fluorine in the meta position nor any other halogen in any position were displaced. These results indicated the formation of ion pairs from halogen-substituted N-nitrosoacylanilides, with subsequent displacement of only fluorine from the activated 2- and 4-fluorobenendiazonium cation; fluorine meta to the diazonium group, being less activated, could not be displaced (scheme 5).



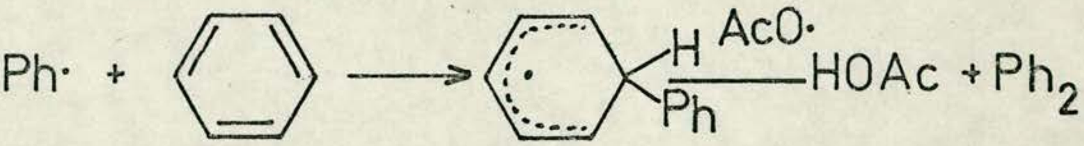
Scheme 5

The generality of this ion pair formation was demonstrated in mixed experiments using 4-fluoro-N-nitrosobenzanilide and other acetylarylnitrosamines. In every case the mixed product 4-acetoxy biphenyl was isolated, confirming formation of ion pairs by both nitrosamides, with subsequent exchange of partners (scheme 6).[83a]

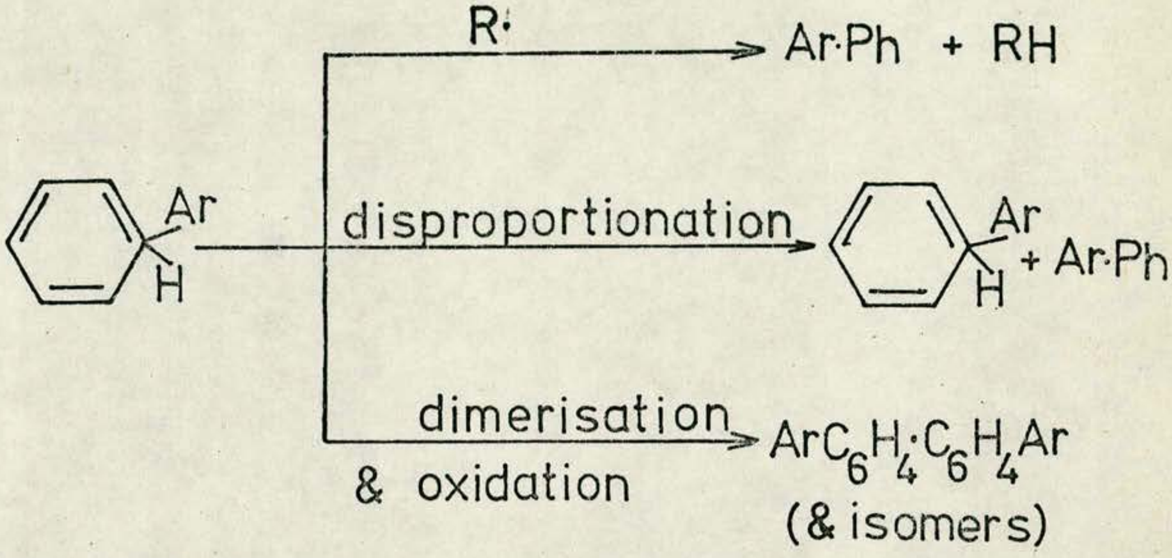


Scheme 6

Two anomalies were still unanswered: the origin of acetic acid which was always formed in high yield in these decompositions, and also the complete absence of dihydrobiphenyl and isomeric tetrahydroquaterphenyls. Formation of acetic acid via the acetoxy radical was suggested by Suschitzsky.[83]



This scheme was untenable since the instability of the acetoxy radical, fragmenting to a methyl radical and carbon dioxide, had been known for some years.[85] Moreover, no evidence existed to suggest that acetoxy radicals or their decomposition products were formed to any large extent; in fact the absence of significant amounts of carbon dioxide had been noted by many workers.[79, 85] Decomposition of diaroyl peroxides in benzene had been known to give, in addition to biaryl, dihydrobiaryls and tetrahydroquateraryls via disproportionation and dimerisation at the arylcyclohexadienyl radical.[86]



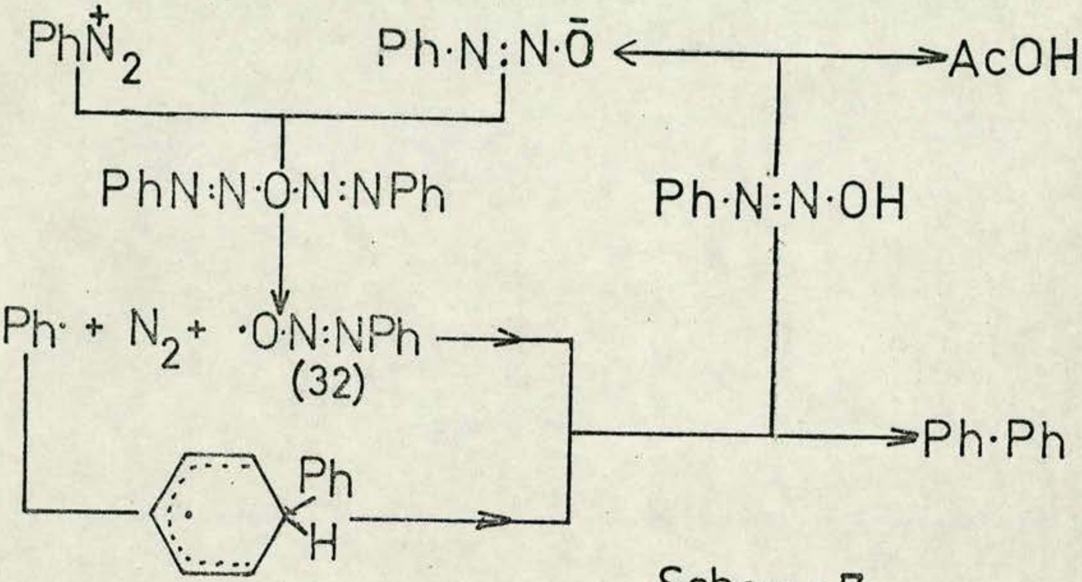
No feasible explanation could be advanced for the absence of these products in the decompositions of acylarylnitrosamines in benzene.

An elegant and apparently complete explanation for the mechanism of decomposition was proposed by Ruchardt and Freudenberg,[87] the key step of which involved a long-lived π-type free radical, (phenylazo)oxyl (32) as chain carrier (scheme 7).

$$\mathrm{PhN(NO)Ac} \longrightarrow \mathrm{Ph{\cdot}N{:}N{\cdot}OAc} \rightleftharpoons \mathrm{Ph\overset{+}{N}_2\ {}^{-}OAc}$$

Initiation: $\mathrm{PhN(NO)Ac} + \bar{\mathrm{O}}\mathrm{Ac} \longrightarrow \mathrm{PhN{:}N\bar{O}} + \mathrm{AcO_2}$

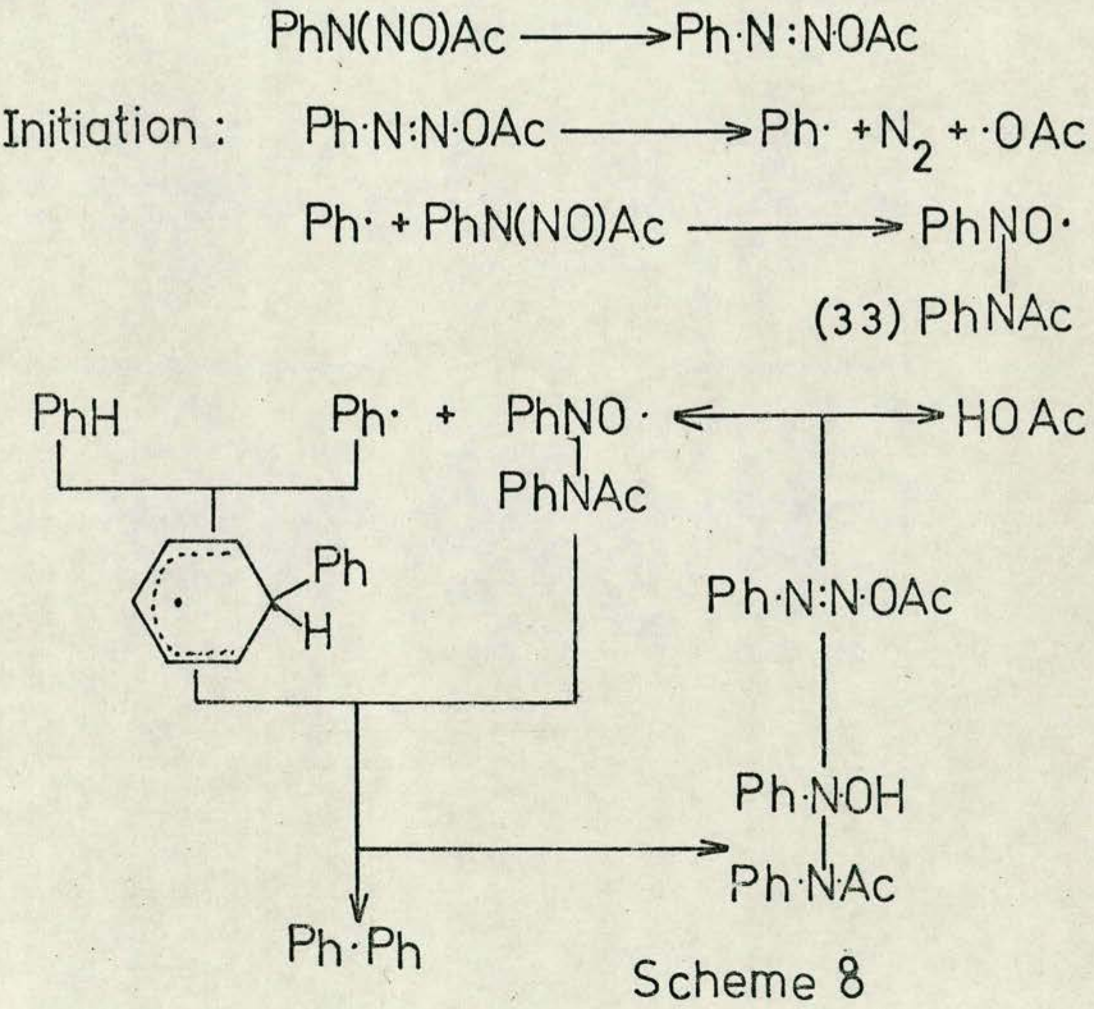
Chain Process :



Scheme 7

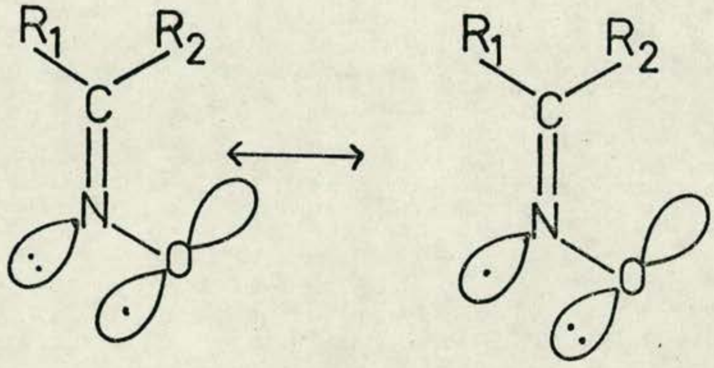
This scheme had many satisfactory features: the chain carrier was capable of oxidising the important phenylcyclohexadienyl radical, hence quaterphenyls and dihydro-derivatives were absent, acetic acid was formed by a chain process from acetate ions, and the chain mechanism proceeded via interaction of ion pairs which Suschitzsky[83] had shown to be present.

The experimental basis of Ruchardt's mechanism, the e.s.r. spectrum of the supposed (phenylazo)oxyl radical[87,88] was challenged by Hey and colleagues[89] who contended that the signal observed by Ruchardt was in fact that of the π-type radical, (N-phenylacetamido) phenyl nitroxide (PAPN) (33). Several independent syntheses of this radical[90] confirmed that the signal observed by Ruchardt was due to the PAPN radical. On the basis of these observations, Chalfont and Perkins proposed a new chain mechanism for the decomposition of N-nitrosoacetanilide in benzene, with the PAPN radical (33) as chain carrier (scheme 8).

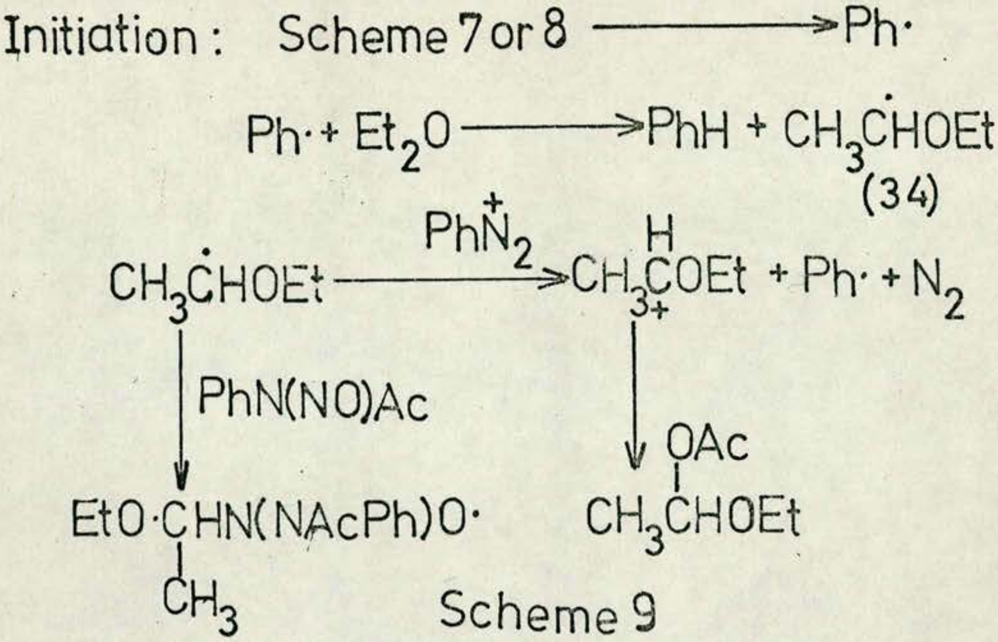


Scheme 8

A reappraisal of the e.s.r. evidence was undertaken by Cadogan[91] who was able to reconcile these conflicting views. He showed that the appearance of the PAPN signal was solvent dependent, being especially weak in solvents with easily abstractable hydrogens (e.g. totally absent in isopropyl benzene). In benzene the PAPN signal was very intense and almost completely masked another weak signal which Cadogan had detected in all the solvents used and which was attributed to the (phenylazo) oxyl radical (32). Cadogan concluded that the PAPN radical was not a significant, chain carrying radical and that the mechanism of Ruchardt was probably correct, with the important proviso that the chain carrying species was a σ-type (phenylazo)oxyl radical, from analogy with the splitting constants previously recorded for the closely related σ-iminoxy radicals.[92]

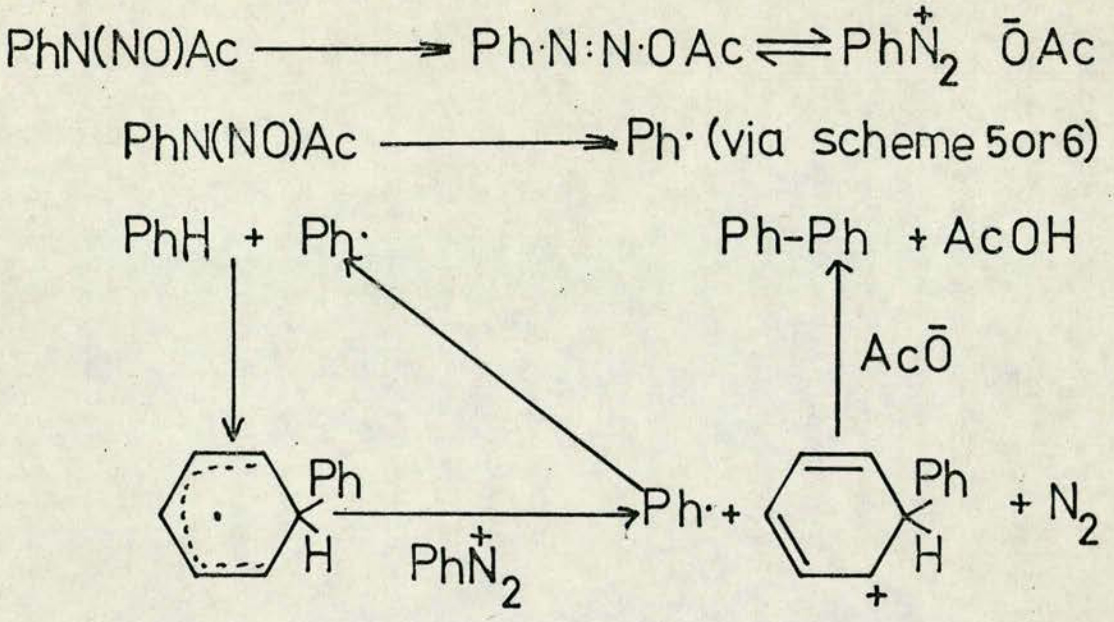


Following an e.s.r. study of the decomposition of N-nitrosoacetanilide in diethyl ether, in which evidence for the intermediacy of the 1-ethoxyethyl radical (34) was obtained, Cadogan[91] suggested a mechanism, outlined in scheme 9, which involved a redox transfer step with (34) and the diazonium cation, and which also involved the phenyl radical as chain carrier.



Scheme 9

The suggestion of a redox reaction between the diazonium cation and a radical such as (34) was extended to the case of N-nitrosoacetanilide decomposition in benzene. Cadogan[91] suggested that once initiation by scheme 7 or 8 had occurred, a redox reaction between the arylcycohexadienyl radical and diazonium cation occurred, giving rise to acetic acid, biaryl and nitrogen *via* a chain reaction involving the aryl radical as a chain carrier (scheme 10).

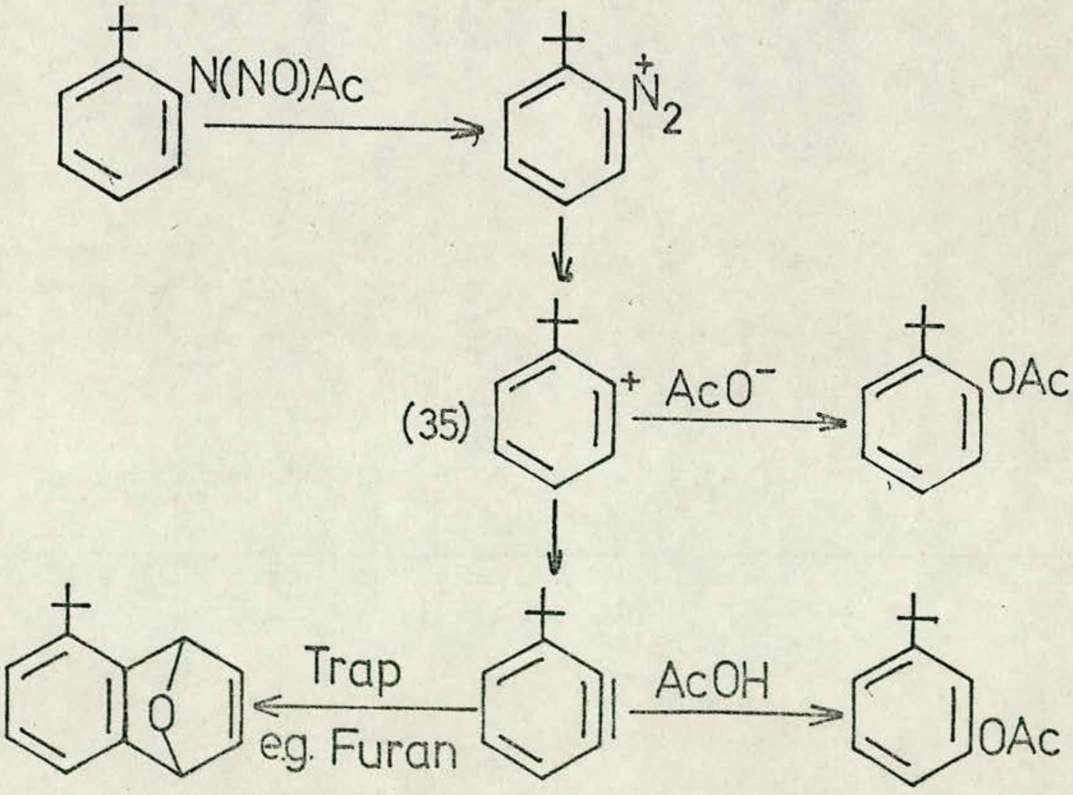


Scheme 10

This scheme was considered the most attractive representation of the decomposition of N-nitrosoacetanilide since it required 7 or 8 only as sources of phenyl radicals, and accommodated the data concerning the appearance and non-appearance of PhNNO· (32) and PAPN (33).

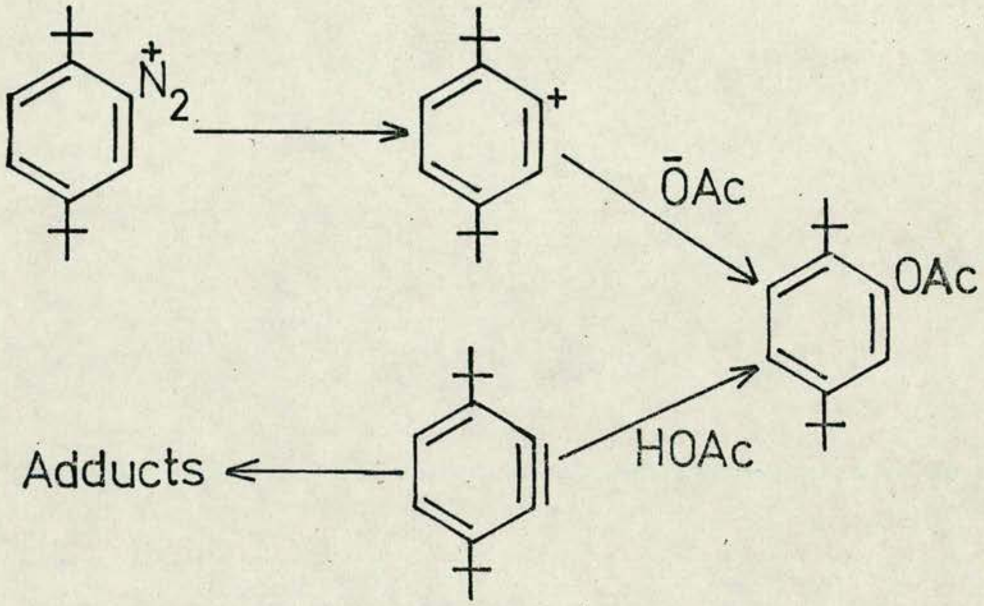
Arynes from Acylarylnitrosamines. While scheme 10 may best represent the decomposition of acylarylnitrosamines to phenyl radicals, it became apparent that there existed a concurrent and possibly distinct mode of decomposition giving rise to products which could best be rationalised in terms of aryne intermediates.

Cadogan and Hibbert[93] examined the decomposition of 2-t-butyl-N-nitrosoacetanilide, which had been shown earlier to give a mixture of isomeric t-butylphenyl acetates instead of the expected product, 2-t-butylbiphenyl.[94] They proved that only the 2-and 3-t-butylphenyl acetates were present and proposed the intermediacy of 3-t-butylbenzyne to account for the products.[93] This prediction was confirmed when the intermediate was trapped as a Diels-Alder adduct with tetracyclone, anthracene and furan.[93,95] These aryne traps were found to suppress the formation of 3-t-butylphenyl acetate, leaving the level of the 2- isomer unaltered, thus suggesting that only the 3- isomer was formed via 3-t-butylbenzyne.[95] Whereas the 3- isomer was envisaged as being formed by nucleophilic addition of acetic acid to 3-t-butylbenzyne, a process made more efficient by the suppression of other reactions through steric shielding of the t-butyl group, the formation of the 2-isomer was thought to occur by direct combination of the 2-t-butylphenylcarbonium ion (35) with acetate ion (scheme 11).



Scheme 11

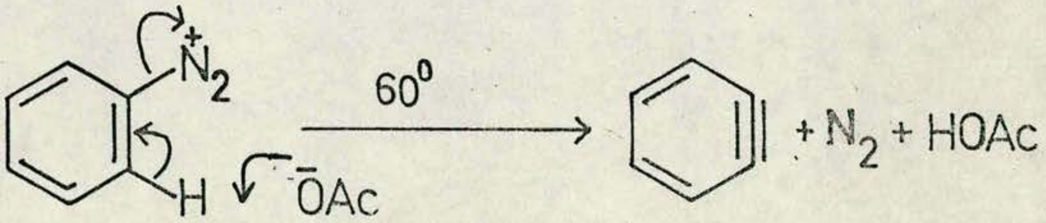
The decomposition of 2,5-di-t-butyl-N-nitrosoacetanilide in benzene leant further credence to these assumptions when high yields of acetate and fair yields of aryne adduct were obtained (scheme 12).[95]



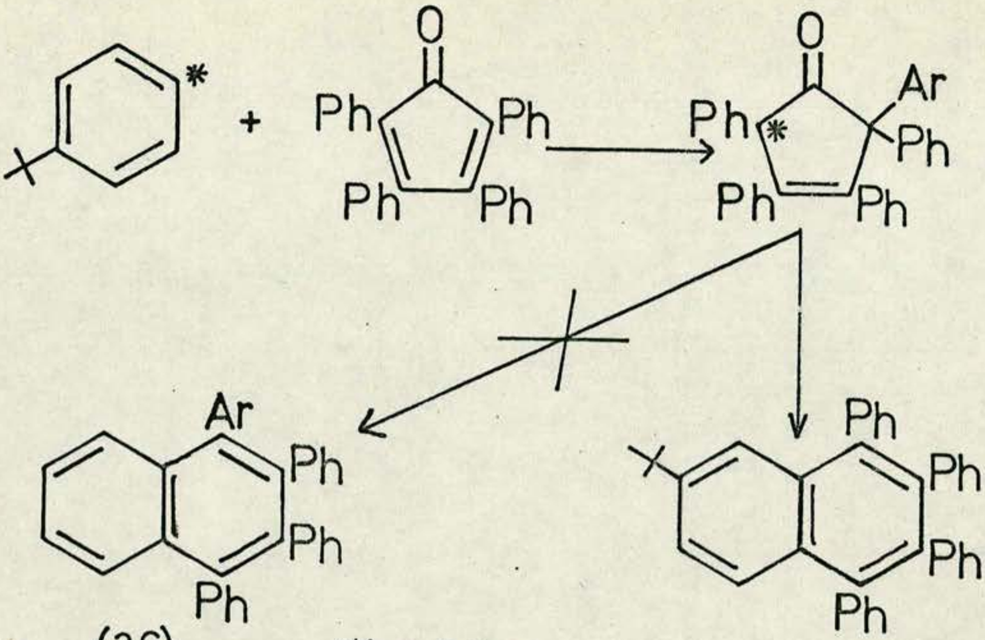
Scheme 12

The extension of this reaction to other acetylarylamines, including N-nitrosoacetanilide itself, undermined the belief that it was a special case arising through steric acceleration of the aryldiazonium cation to the corresponding carbonium ion. Thus N-nitrosoacetanilide was found to give aryne adducts with tetracyclone, anthracene and 1,2-diphenylisobenzofuran.[96] It was found however that decomposition in furan did not yield the expected 1,4-dihydro-1,4-epoxynaphthalene, but gave the radical derived product, 2-phenylfuran instead. Although this anomalous result cast doubts as to the intermediacy of a true aryne in these decompositions, recent work has resulted in the isolation of the corresponding Diels-Alder adduct, in low yield, from the decomposition of N-nitrosoacetanilide in both furan[97,98] and 2,5-dimethylfuran.[97]

It seemed clear that an aryne or arynoid species was involved in this reaction. Cook [99] showed that for a series of arynophile pairs, the competition ratios of authentic benzyne (from anthranilic acid/pentyl nitrite) and benzyne from N-nitrosoacetanilide were the same, confirming that a true benzyne species was involved. Following this work from St. Andrews, Ruchardt[100] showed that arynes could be prepared in good yields from aromatic diazonium salts and interpreted his results in terms of benzyne formation via an E_2 elimination process:



Furthermore, the possibility that the adduct produced in reactions of acylarylnitrosamines with tetracyclone was formed by attack of a unidentate species such as arylcarbonium ion or aryl radical was excluded when decomposition of 4-t-butyl-N-nitrosoacetanilide in the presence of tetracyclone[96] failed to realise the isomeric tetraarylnaphthalene (36) (scheme 13).



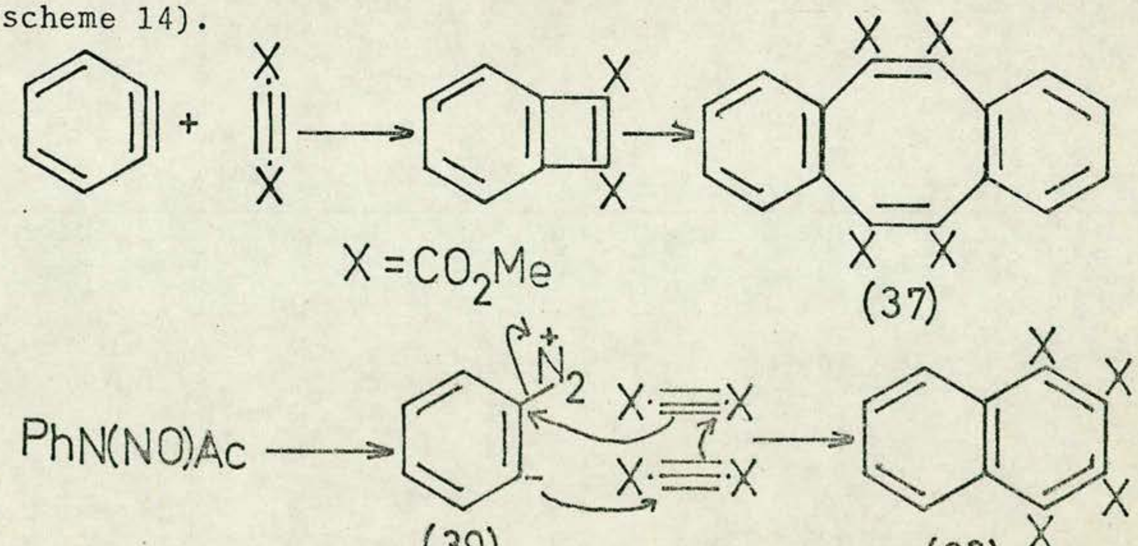
(36)

$* = +$ or $\cdot$

$Ar = 4\text{-}Bu^t\cdot C_6H_4\cdot$

Scheme 13

Cook [99] showed that authentic benzyne gave the dibenzocyclooctatetraene (37) when generated in the presence of dimethyl acetylenedicarboxylate (DMAD), yet N-nitrosoacetanilide gave 1,2,3,4-tetramethoxycarbonylnaphthalene (38). Cook rationalised these results by postulating the reaction of the intermediate betaine (39) with two molecules of the acetylene to give the naphthalene (38) (scheme 14).



$X = CO_2Me$

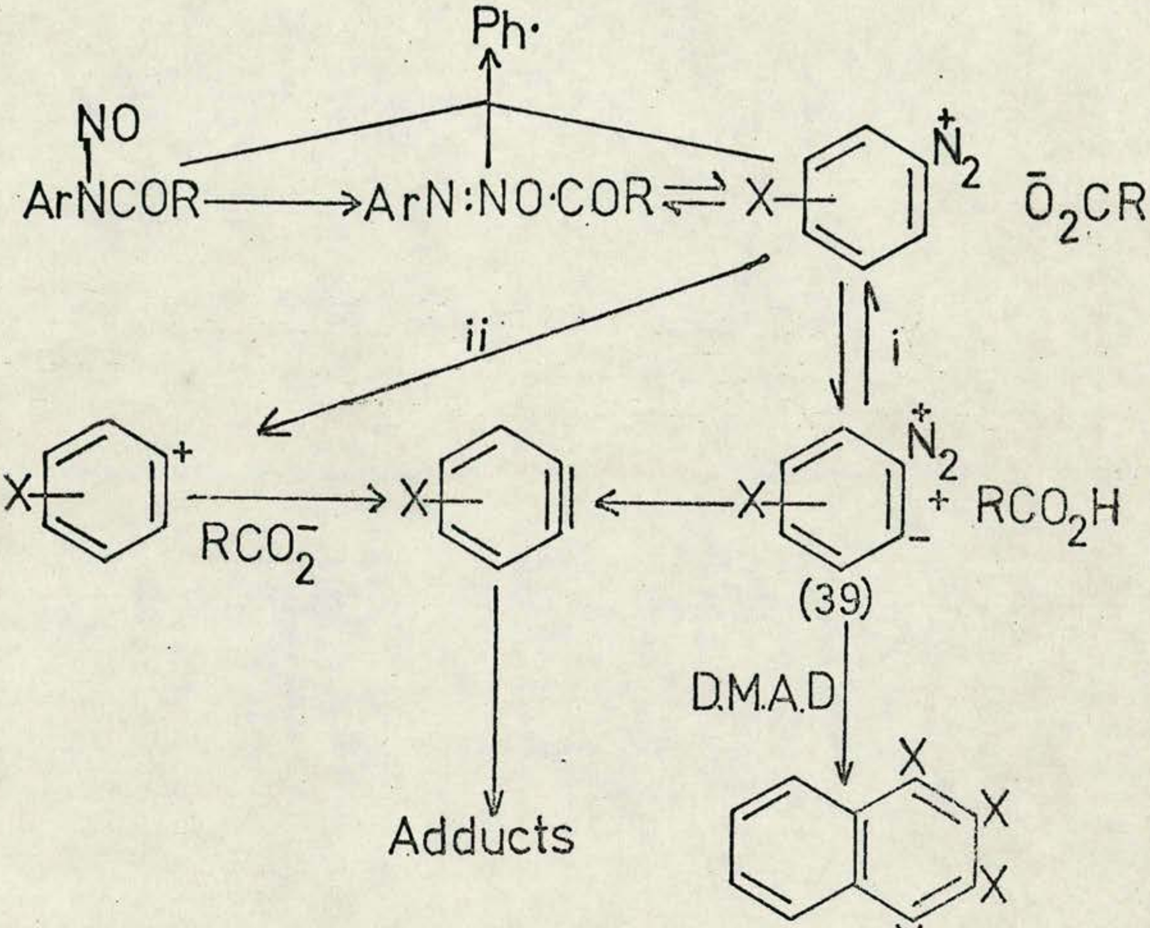
(37)

(39)

(38)

Scheme 14

To accommodate all these observations, a modified decomposition mechanism was suggested which was in competition with the known radical decomposition (scheme 15).



Scheme 15

(39)

This mechanism required that the betaine (39) be in equilibrium with the diazonium cation (route i).[99,101] Decomposition via route (ii) would only occur in the special case when X = 2-t-butyl in which steric acceleration of nitrogen loss was predominant.

A New Route to Arynes. The special effect of the 2-t-butyl group had been confirmed by the observation that *in situ* diazotisation of 2,5-di-*t*-butylaniline with butyl nitrite led to the corresponding aryne.[102,103] This case was thought to be unique however, since Brydon[103] found that diazotisation of other anilines in similar fashion gave no trace of aryne adduct.

It became clear that the failure of this method was due to the formation of water in the diazotisation process,

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

for it was known that aryne formation from both *N*-nitrosoacetanilide and benzenediazonium fluoroborate-potassium acetate was severely depressed by even small quantities of water.[96,133] The sensitivity of these reactions to water was attributed to the fact that solvation of the diazonium-acylate ion pair would greatly decrease the basicity of the acylate ion and possibly reverse equilibrium (i) in scheme 11. Since scheme 11 requires prior formation of an aryl carbonium ion when X = 2-*t*-butyl, the concomitant increase in the acidity of the *ortho* proton counterbalances the suppressive effect of the water and accounts for the successful formation of arynes from 2,5-di-*t*-butyl benzendiazonium salts.

To overcome the suppressive effect of water, aniline was diazotized with pentyl nitrite in the presence of acetic anhydride in the role of dehydrating agent. Aryne adducts were obtained with tetracyclone (32%), and anthracene (10%).[104] When acetanilide was diazotised under the same reaction conditions, aryne adduct was obtained in 21% yield. Optimisation of the reaction conditions was undertaken by Mitchell:[97] 4-chlorobenzoyl nitrite (PCBN) was developed as a more efficient nitrosating agent; suppression of the competitive benzenediazonium acetate decomposition[90,100] was effected using high dilution techniques, and preformed acetanilide was found to be more efficient than aniline.

In this way, addition of PCBN to preformed acetanilide in boiling benzene gave with tetracyclone, anthracene, 9,10-dimethoxyanthracene, and methyl methacrylate traps the corresponding aryne adducts, 1,2,3,4-tetraphenylnaphthalene (70%), triptycene (16%), 9,10-dimethoxytriptycene (14%) and, by the ene[61] reaction, ethyl-2-methylene-3-phenylpropionate (31%), respectively. Prior reaction of aniline with acetic anhydride, followed by addition of tetracyclone, then PCBN gave the aryne adduct in 51% yield.

4. PROGRAMME OF RESEARCH

Two simple procedures for the direct conversion of anilines and anilides into benzyne had been developed viz., use of aniline/acetic anhydride/pentyl nitrite or use of acetanilide/PCBN, the latter being more efficient. This investigation was initiated to determine the scope of these reactions (a) in converting substituted anilines or anilides into the corresponding arynes and (b) as a simple synthetic route to fused heterocyclic systems, via intramolecular cyclization.

The existence of a pre-benzyne, arynoid species had been proposed by Cook to account for the novel product obtained from the reaction of N-nitrosoacetanilide and dimethyl acetylenedicarboxylate. The ramifications of this proposal vis-a-vis the decomposition of the benzenediazonium-acylate ion pair made it imperative that this reaction be investigated with regard to both its synthetic scope and mechanistic implication.

EXPERIMENTAL

Page No.

1. PREPARATION OF ACETYLARLAMINES

2. PREPARATION OF SOME AROYL AND HETEROCYCLIC PEROXIDES

a Diaroyl peroxides

b Heterocyclic peroxides

3. PREPARATION OF AZO COMPOUNDS

Page No.

d Reactions of phenyl radicals with some other acetylenes

8. REACTIONS OF RADICALS WITH AZO COMPOUNDS

a Reactions of aroyl radicals with diethyl azodiformate

b Reactions of some sources of phenyl radicals with dimethyl azodiformate

Page No.

SYMBOLS AND ABBREVIATIONS

b.p.	boiling point
m.p.	melting point
g.l.c.	gas liquid chromatography
t.l.c.	thin-layer chromatography
R.f.	ratio of distance moved by the substance to the distance moved by the solvent front
h.s.l.c.	high speed liquid chromatography
i.r.	infrared
u.v.	ultraviolet
n.m.r.	nuclear magnetic resonance
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

Gas-Liquid Chromatography

For analytical and quantitative g.l.c. investigations, a Pye 104 chromatograph, with flame ionisation detector was used together with 2m x 2.2mm i.d. packed columns. Quantitative measurements were made after calibration of the instrument with known mixtures of authentic samples and internal standards. All authentic samples and internal standards were purified before use. 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 used: Apiezon L grease (APL), silicone oil (SIL), silicone grease (SE-30), neopentylglycol succinate (NPGS) and polyethyleneglycol 20M (CAR).

Column Chromatography

Alumina used for column chromatography was Laporte Industries Ltd., activated aluminium oxide, type H. Silica gel (100-200 Mesh) was supplied by Fisons Scientific Apparatus.

Alumina for dry column chromatography was prepared from chromatographic alumina, treated with Woelm fluorescent indicator for short-wave u.v. (254nm) and deactivated to Brockman activity 3-4 as described by Loev and Goodman.[142] The columns were made up in "c" gauge nylon tubing of variable diameter, supplied by

Walter Coles and Co. Ltd., London, S.E.1.

High Speed Liquid Chromatography

A Dupont 820 liquid chromatograph with a u.v. photometer detector and 1m x 2mm packed columns was used. Samples were examined by Dr. J. Done, Chemistry Department, University of Edinburgh.

Thin Layer Chromatography

Thin layer chromatograms were obtained on 0.3mm 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

Spectra were recorded on a Perkin-Elmer Model R-10 and a Varian EM 360 spectrometer which operated at a frequency of 60MHz and a probe temperature of 33°. Spectra of new compounds and variable temperature studies were recorded using a Varian HA -100 instrument operating at 100MHz and a probe temperature of 28°. Chemical shifts were recorded as tau (τ) values in parts per million using tetramethylsilane as internal reference (τ=10.0). Spectra were determined on 10-15% w/v solutions, usually in deuterochloroform, unless solubility or sample availability imposed limitations. ^{13}C spectra were recorded on a Varian XL -100 operating at 25.2 MHz and a probe temperature of 30°.

Mass Spectroscopy

Mass spectra and exact mass measurements were recorded on an A.E.I. MS-902 mass spectrometer. Reaction mixtures were analysed using an A.E.I. MS-20 mass spectrometer coupled to a Pye 104 gas chromatograph using helium as the carrier gas.

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.

Ultraviolet Spectroscopy

Ultraviolet spectra were recorded on a Unicam SP800 ultraviolet and visible spectrophotometer using a matched pair of 1-0cm quartz cells.

Elemental Analysis

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

Melting Points

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

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Solvents and Reagents

Ether and petrol were purified by distillation and dried over sodium wire. Unless otherwise stated 'petrol' refers to light petroleum ether (b.p. 40-60°). Benzene and cyclohexane were prepared when required, by distillation of the sodium-dried solvent from calcium hydride, in an atmosphere of dry nitrogen. Carbon tetrachloride and dichloromethane were dried over calcium chloride. All other reagents were purified by distillation or recrystallisation.

1. PREPARATION OF ACETYLARYLAMINES

a 3-Acetamidophenylacetic acid

3-Nitrobenzoyl chloride. This was prepared by the method described in Vogel.[105] The crude product was distilled to give a pale yellow, crystalline solid b.p. 126°/3mm Hg, m.p. 34° (lit. m.p.[106] 35°).

Diazomethane. An ethereal solution of diazomethane was prepared by the method of De Boer and Backer.[107] 4-Tolylsulphonylmethylnitrosamine was prepared from 4-toluenesulphonyl chloride and methylamine in sodium hydroxide solution. The nitrosamide was added to an ethanolic solution of potassium hydroxide to form diazomethane, which distilled over in ether and was stored as an ethereal solution at 5°. The ethereal solution was quantified by addition of an aliquot to a weighed amount of benzoic acid, then back titratrion of the excess acid with standard sodium hydroxide solution, using phenolphthalein as indicator.

3-Nitrophenylacetic acid. After the method described by Holmes,[108] 3-nitrobenzoyl chloride and diazomethane were condensed to form ω-diazo-3-nitroacetophenone, which was converted to the corresponding acid by treatment with silver oxide and sodium thiosulphate. Recrystallisation from ethanol afforded the product as yellow crystals, m.p. 118-120° (lit. m.p.[109] 116-118°).

3-Aminophenylacetic acid. This was prepared by reduction of 3-nitrophenylacetic acid with ammonium sulphide, using an adaptation of the method described in Vogel.[105]

3-Nitrophenylacetic acid (18.1g, 0.1 mole) was added slowly, with shaking, to 6N ammonia (sp. qr. ca. 0.95, 100ml). The flask was cooled and the mixture was saturated with hydrogen sulphide, keeping the temperature below 50°. The solution was boiled gently until it changed to a pale yellow colour, then filtered to remove sulphur. Glacial acetic acid (10ml) was added to the hot filtrate which was allowed to stand at 5° overnight. The precipitate was collected to give 3-aminophenylacetic acid as white needles (10.1g, 67%), m.p. 150-151° (lit. m.p.[106] 151°).

3-Acetamidophenylacetic acid. 3-Aminophenylacetic acid (7.6g, 50m mole) was dissolved in acetic anhydride (50ml) containing five drops of concentrated sulphuric acid. After warming at 80° for 30 min., the yellow solution was poured into ice water (200ml) and the cooled reaction mixture was then neutralised with 10% sodium hydroxide solution. The solution was concentrated to 40ml, acidified with a few drops of acetic acid, and cooled. The solid which separated was collected and recrystallised from water to give 3-acetamidophenylacetic acid (6.9g, 72%), m.p. 132-133° (lit. m.p.[110] 122-124°) (Found: C, 61.6; H, 5.7; N, 7.3; $^{m}/e$ 193. Calc.

for $C_{10}H_{11}NO_3$: C, 62.1; H, 5.7; N, 7.3%; $^{m}/e$ 193). I.r. (nujol) 3318 cm^{-1} (N-H), 1700 cm^{-1} and 1670 cm^{-1} (c = o). N.m.r. (d.m.s.o.d.^{6}): τ, 0.12 (s, 1H acidic); τ, 2.51 (s, 2H, aromatic); τ, 2.72-2.82 (m, 1H aromatic); τ, 3.07-3.14 (m, 1H aromatic); τ, 6.50 (s, 2H, CH_2); τ, 7.98 (s, 3H amide CH_3).

b 3-Acetamidophenethyl alcohol

3-Aminophenethyl alcohol. A suspension of 3-aminophenylacetic acid (6.04g, 40m mole) in dry tetrahydrofuran (200ml) was added dropwise over 1h to a solution of lithium aluminium hydride (3.64g, 0.1M) in boiling tetrahydrofuran (200ml). Excess lithium aluminium hydride was destroyed by cautious addition of ethyl acetate (20ml); the reaction mixture was shaken with 10% sodium hydroxide solution (50ml), and the precipitated aluminium salts were then filtered off. This precipitate was dissolved in dilute sulphuric acid (50ml), the aqueous solution was extracted with ether (3 x 50ml) and the organic layers were combined and dried (Mg. SO_4). The solvents were evaporated, yielding an amber oil which was distilled to give a yellow, oily solid (3.8g, b.p. 110-140^{o}/0.05 mm Hg). G.l.c. analysis (2% CAR, 170^{o}) of this solid indicated a mixture of two components. The solid was chromatographed on an alumina dry column (50 x 2cm), using ethyl acetate as solvent to give a yellow oil which solidified on scratching under ether.

The solid was collected and washed with a little cold ether to give white, fluffy needles (1.6g, m.p. 66-68^{o}) which on g.l.c. examination (2% CAR, 170^{o}; 5% NPGS, 190^{o}) proved to be pure 3-aminophenethyl alcohol. (Found: C, 69.9; H, 7.9; N, 10.4; $^{m}/e$ 137. $C_8H_{11}NO$ requires C, 70.1; H, 8.0; N, 10.2%; $^{m}/e$ 137). N.m.r. ($CDCl_3$ after shaking with D_2O): τ, 2.84-3.00 (m, 1H, aromatic); τ, 3.37-5.00 (m, 3H, aromatic); τ, 6.15-6.27 (t, 2H, $-CH_2OH$); τ, 7.19-7.31 (t, 2H, $PH-CH_2$). I.r. (nujol) 3375cm^{-1} (N-H), 3300-3100cm^{-1} (O-H broad).

3-Acetamidophenethyl alcohol. 3-Aminophenethyl alcohol (1.37g, 10m mol) was dissolved in acetic anhydride containing one drop of concentrated sulphuric acid, and the solution was boiled under reflux for 30 min. The reaction mixture was poured onto ice water (50ml) and the solution neutralised with 10% sodium hydroxide solution. The yellow solution was extracted with chloroform (3 x 25ml), the organic layer was washed with water and dried ($MgSO_4$). The chloroform was evaporated and the residual oil solidified on scratching under ether. The amorphous solid was recrystallised from aqueous ethanol to give 3-acetamidophenethyl alcohol as white plates (0.6g, m.p. 98-100^{o}). (Found: C, 66.8; H, 7.3; N, 7.8; $^{m}/e$ 179 $C_{10}H_{13}NO_2$ requires C, 67.0; H, 7.1; N, 7.8%; $^{m}/e$ 179). N.m.r. (d.m.s.o.d.^{6}): τ, 2.58-3.15 (m, 4H, aromatic); τ, 6.32-6.46 (t, 2H, CH_2OH); τ, 7.22-7.37 (t, 2H, $PH-CH_2$); τ, 7.95 (S, 3H, amide CH_3). I.r. (nujol) 3400cm^{-1}-3100cm^{-1} (N-H, O-H), 1668cm^{-1} (C=O).

c Other acetylarylamines

The method of preparation is exemplified by that of 2-nitroacetanilide: 2-Nitroaniline (6.9g, 50m mol) in acetic acid (10ml) and acetic anhydride (10ml) was heated at 120° for 15 min. The solid which separated when the hot solution was poured into ice water (500ml) was collected, washed with water, and recrystallised from benzene: petrol (6:1) to give 2-nitroacetanilide as fine, yellow needles (6.5g, 72%), m.p. 93° (lit. m.p.[106] 93°).

Prepared in similar fashion were:

2-ethoxycarbonylacetanilide	m.p. 65-66° (lit. m.p.[106] 66°)
2-methylacetanilide	m.p. 110° (lit. m.p.[106] 110°)
2-methoxyacetanilide	m.p. 85-86° (lit. m.p.[106] 87-88°)
2-acetamidobenzotrifluoride	m.p. 95° (lit. m.p.[111] 95-96°)
3-acetamidobenzotrifluoride	m.p. 103-104° (lit. m.p.[112] 100-102°)
3-fluoroacetanilide	m.p. 85° (lit. m.p.[106] 84-86°)
3-chloroacetanilide	m.p. 125° (lit. m.p.[106] 76-6°)
3-iodoacetanilide	m.p. 125° (lit. m.p.[106] 119-5°)
4-acetamidobenzotrifluoride	m.p. 155-156° (lit. m.p.[113] 208-211°)
4-*t*-butylacetanilide	m.p. 170° (lit. m.p.[106] 169-170°)
2-acetamidopyridine	m.p. 69-70° (lit. m.p.[106] 71°)
3-acetamidopyridine	m.p. 133-135° (lit. m.p.[106] 133°)

Acetanilide, m.p. 114-5°, 4-ethoxycarbonylacetanilide, m.p. 110° and 2,5 dimethoxyacetanilide, m.p. 91° were purified by recrystallisation of commercially available samples.

2. PREPARATION OF SOME AROYL AND HETEROCYCLIC PEROXIDES

a Diaroyl peroxides

These were prepared by the method described by Cooper[114] which is exemplified by the case of bis-4-methylbenzoyl peroxide: Thionyl chloride (40ml, 0.5 mole) and 4-methylbenzoic acid (13.6g, 0.1 mole) were boiled under reflux under anhydrous conditions for 24h. Excess thionyl chloride was evaporated and the residue was distilled to give 4-methylbenzoyl chloride (13.8g, b.p. 106-108°/11mm Hg). A solution of the acid chloride in chloroform (30ml) was added over 30min to a stirred solution of "20 volume" hydrogen peroxide (50ml) and 25% sodium hydroxide solution (20ml) at 0°, keeping the temperature below 10°. Stirring was continued for 1h, then the solution was concentrated to 30ml. Addition of methanol precipitated the peroxide, which was recrystallised from chloroform: petrol (1:3) to give bis-4-methylbenzoyl peroxide as lustrous white plates (5.1g, 40% based on acid), m.p. 136.5 (lit. m.p.[115] 136°).

Prepared in this way were:

bis-4-chlorobenzoyl peroxide m.p. 137° (lit. m.p.[115] 140°)
bis-3-chlorobenzoyl peroxide m.p. 121-123° (lit. m.p.[115] 122-123°)
bis-3-methylbenzoyl peroxide m.p. 50-51° (lit. m.p.[115] 54°)

Other peroxides kindly supplied by Professor J.I.G. Cadogan were:

bis-4-bromobenzoyl peroxide m.p. 142° (lit. m.p.[115] 151-152°)
bis-3-bromobenzoyl peroxide m.p. 127° (lit. m.p.[115] 131°)
bis-4-cyanobenzoyl peroxide m.p. 166° (lit. m.p.[115] 176°)
bis-2-nitrobenzoyl peroxide m.p. 136° (lit. m.p.[115] 147°)
bis-2-naphthoyl peroxide m.p. 133° (lit. m.p.[115] 140°)

b <u>Heterocyclic peroxides</u>

These were prepared using the carbodiimide synthesis of Greene and Kazan[116] and a typical example is that of bis-2-thenoyl peroxide: a solution of 2-thenoic acid (3.84g, 30m mole) in dichloromethane (50ml) was added dropwise to a stirred solution of dicyclohexylcarbodiimide (6.39g, 31m mol) in ether (20ml) at 0°, keeping the temperature below 5°. The solution was stirred for a further 30min at room temperature, then the dicyclohexylurea was filtered off and washed with dichloromethane (3 x 50ml). The organic layers were combined and ether was added to double the volume. The organic solution was washed successively with saturated ammonium sulphate (3 x 50ml), 10% sodium carbonate (2 x 50ml) and saturated sodium chloride (2 x 50ml); the solvent was evaporated at room temperature, and the yellow residue was recrystallised from chloroform: cyclohexane (1:9) to give bis-2-thenoyl peroxide as opaque, almost colourless leafs (3.35g, 88%), m.p. 99-100° (lit. m.p.[117] 100-101°).

Also prepared in this manner were:

bis-2-furoyl peroxide m.p. 86-87° (lit. m.p.[113] 86-87°)
bis-2-phenylbenzoyl peroxide m.p. 103-104° (lit. m.p.[119] 105-106°)

3. PREPARATION OF AZO COMPOUNDS

a Methyl azodiformate

This was prepared using a modification of Rabjohn's[120] method for the synthesis of ethyl azodiformate. Methyl chloroformate (47.2g, 0.5 mole) was added dropwise with stirring to a cooled solution of hydrazine hydrate (12.5g, (0.25 mole) in ethanol (120ml) at a rate sufficient to maintain the temperature between 15° and 20°. After one half of the chloroformate had been introduced, a solution of sodium carbonate (26.5g, 0.25 mole) in water (120ml) was added dropwise simultaneously with the remaining methyl chloroformate and the reaction mixture was allowed to stir for an additional 30min. The solution was concentrated to half its volume and the precipitated methyl hydrazodiformate was filtered off and washed well with water (200ml) to give methyl hydrazodiformate as a white crystalline mass (29.2g, 80%).

Chlorine was bubbled slowly into a mixture of the methyl hydrazodiformate (29g, 0.2 mole) in benzene (200ml) and water (200ml), stirred in an ice bath. The temperature was maintained below 15° and chlorine was introduced until the increase in weight amounted to 25g. The layers were separated, and the water layer was extracted once with benzene. The combined benzene solutions were washed successively with water (2 x 100ml), 10% sodium bicarbonate (4 x 100ml) and water (2 x 100ml) and then dried (Na_2SO_4). Benzene was evaporated and the residue was distilled to give methyl azodiformate as an orange red oil (22.6g, 77%), b.p. 98°/25mm Hg (lit. b.p.[106] 96°/25mm Hg.

b t-Butyl azodiformate

t-Butyl azodiformate was prepared as described by Carpino and Crowley.[121] t-Butyl hydrazodiformate was prepared from t-butyl carbazate and t-butyl azodiformate in pyridine. Oxidation of the hydrazo compound was effected with N-bromosuccinimide in dichloromethane, giving the product as lemon yellow crystals after recrystallisation from petrol m.p. 90-92° (lit. m.p.[121] 90-92°).

t-Butyl azodiformate was prepared by the nitrosation of t-butyl carbazate using sodium nitrite as described by Carpino et. al.[122]

c Phenylazoethoxycarbonyl

This was prepared by the method of Ingold and Weaver.[123] Phenylhydrazoethoxycarbonyl was first prepared from ethyl chloroformate and phenylhydrazine in ether, and was oxidised with potassium permanganate to give phenylazoethoxycarbonyl as a dark red viscous liquid b.p. 65-70°/0.02mm Hg (lit. b.p.[124] 130-132°/24mm Hg).

d 4-Phenyl-1,2,4-triazoline-3,5-dione

This was prepared by the method of Cookson et. al.[125] Ethyl carbazate was prepared by the condensation of hydrazine hydrate and diethyl carbonate, and was reacted with phenyl isocyanate in benzene to give the urea derivative, 4-phenyl-1-carbethoxysemicarbazide. Treatment of this semicarbazide with potassium hydroxide resulted in ring closure to give 4-phenylurazole, which was oxidised with t-butyl hypochlorite at room temperature to give 4-phenyl-1,2,4-triazoline-3,5-dione as large maroon crystals which decomposed between 165°-180° (lit. m.p.[125] 165-175°).

t-Butyl hypochlorite was prepared by the method of Teeter and Bell.[126]

4. MISCELLANEOUS PREPARATIONS

a Nitrosyl chloride

This compound was prepared by the method of Morton and Wilcox[127] from the action of hydrochloric acid upon sodium nitrite. The product was dissolved as a 30% w/v solution in acetic anhydride or carbon tetrachloride, and was stored at -15° in sealed flasks.

b Phenylazotriphenylmethane

This compound was prepared by the method of Gomberg,[128] as described by Brydon.[103] m.p. 110° (lit. m.p.[128] 110-111°).

c 4-Chlorobenzoyl nitrite

This was prepared after the method of Mitchell,[97,74] from nitrosyl chloride and silver 4-chlorobenzoate, b.p. 62°/0.7mm Hg (lit. b.p.[74] 70°/1mm Hg). This compound was dissolved in benzene (16% w/v solution) and stored at -20°.

d t-Butyl hyponitrite

This was prepared as described in Vogel,[105] b.p. 61° (lit. b.p.[105] 61°).

e 2,3,4,5-Tetraphenylcyclopentadienone

This compound was prepared by the condensation of benzil and dibenzyl ketone as described by Johnson and Grummit[129] and was obtained as dark purple crystals in almost quantitative yield from benzene: ethanol (1:1), m.p. 218-220° (lit. m.p.[129] 218-220°).

f N-Nitrosoacetanilide

This was prepared by the method of France et. al.[130] by the nitrosation of acetanilide with nitrosyl chloride. The yellow solid obtained from this reaction was dried over P_2O_5 in vacuo and used immediately.

g N,N'-Diethoxycarbonyl-N-phenylhydrazine

N'-Acetyl-N-phenylhydrazine. Acetic anhydride (10.2g, 0.1 mole) was added dropwise to phenylhydrazine (21.6g, 0.2 mole), stirred in an ice bath. The solution became brown and on cooling solidified to an orange crystalline mass which on recrystallisation from water gave N'-acetyl-N-phenylhydrazine (21.7g, 72%) as thin colourless plates m.p. 126-128° (lit. m.p.[131] 128-5°).

N'-Acetyl-N-ethoxycarbonyl-N-phenyl hydrazine. A solution of N'-acetyl-N-phenylhydrazine (9.0g, 60m mole) and ethyl chloroformate (6.5g, 60m mole) in benzene (80ml) was boiled for 1h. Excess benzene was evaporated and the residual brown oil was chromatographed on alumina (200g), eluting with ether. The first dark brown fraction was discarded; the remaining pale yellow oils were combined, and under ether trituration gave a cream solid. Recrystallisation from benzene gave the product as colourless crystals (8.4g, 63%), m.p. 71° (lit. m.p.[132] 72-73°). I.r. (nujol) 3190cm^{-1} (N-H), 1720cm^{-1} and 1660cm^{-1} (C = O).

N-Ethoxycarbonyl-N-phenylhydrazine. To a mixture of N'-acetyl-N-ethoxycarbonyl-N-phenylhydrazine (7.7g, 35m mol), concentrated sulphuric acid (9.5g) and water (85g) was added enough ethanol (70ml) to make the solution clear. The solution was boiled for 12h. and then concentrated to half volume. The cooled solution was made basic with 10% sodium hydroxide solution and then extracted with ether (4 x 50ml). The ethereal layers were combined and the solvent evaporated to give a thick brown oil, which was purified by chromatography on alumina (50g), eluting with ether. The product was obtained as an orange oil (4.2g, 71%) and was used without further purification.

N,N'-Diethoxycarbonyl-N-phenylhydrazine. To a stirred solution of N-ethoxycarbonyl-N-phenylhydrazine (5.4g, 30m mol) at 5° was added dropwise ethyl chloroformate (3.3g, 30m mol), keeping the temperature around 10°. After half the chloroformate had been added, a solution of sodium carbonate (1.6g, 15m mol) in water (15ml) was added dropwise simultaneously with the remaining chloroformate. When the addition was complete a further portion of water (15ml) was added and the mixture was allowed to stir for 30 min. Ethanol was evaporated and the aqueous layer was extracted with ether (3 x 50ml)

The solvents were evaporated and the residue was purified by chromatography on alumina (50g), eluting with ether, to give an orange oil. This oil was shaken under petrol for 15 min and left at -20° for 12h. An amorphous cream solid (4.5g) was filtered off and recrystallised from benzene: petrol (2:1) to give N,N'-diethoxycarbonyl-N-phenylhydrazine as a mass of colourless prisms (3.9g, 52%) m.p. 56-58° (lit. m.p.[132] 58-59°). N.m.r. ($CDCl_3$): τ, 2.43-2.90 (m, 5H, aromatic); τ, 5.56-6.00 (2q, 4H, $2OCH_2CH_3$); τ, 8.55-8.99 (t, 6H, $2OCH_2CH_3$). I.r. (nujol) $3240cm^{-1}$ (N-H), $1750cm^{-1}$ and $1700cm^{-1}$ (C = O).

5. REACTIONS OF SUBSTITUTED ANILINES WITH 4-CHLOROBENZOYL NITRITE IN THE PRESENCE OF 2,3,4,5-TETRAPHENYLCYCLOPENTADIENONE

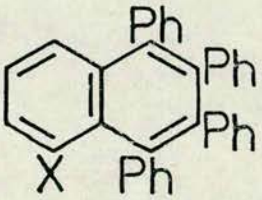
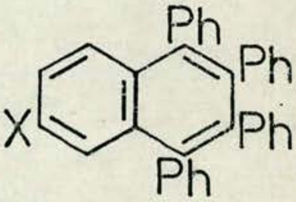
a General Method

To a stirred solution of the amine (5m mol), 2,3,4,5-tetraphenylcyclopentadienone (10m mol), and acetic anhydride (5m mol) in benzene (100ml) at its b.p. was added 4-chlorobenzoyl nitrite (1.6g, 8.5m mol) in benzene (50ml) during 1h. The solution was boiled under reflux for 12h, maleic anhydride (10m mol) was added, and the mixture was boiled to remove the excess of 2,3,4,5-tetraphenylcyclopentadienone. When the violet colour had disappeared (2h), alumina (5g) was added and the solvent was evaporated off, leaving the reaction mixture absorbed on the alumina. The mixture was added to the top of a dry column of alumina (50 x 2cm) and eluted with either cyclohexane or, in the case of more polar amines, carbon tetrachloride. Illumination of the column with u.v. light (254n.m.) showed the products as distinct bands which were separated from alumina with ether. Evaporation of the extracts yielded the products: (a) substituted biphenyls which were characterised by comparison of i.r., n.m.r. and mass spectra with thos of authentic samples where possible, (b) substituted 1,2,3,4-tetraphenylnaphthalenes, which were recrystallised from benzene: ethanol (1:2) and characterised similarly, and also by m.p. and mixed m.p. determinations (Table II).

The results obtained are summarised in Table I. Samples of authentic substituted tetraphenylnaphthalenes, for comparisons and mixed m.p. determinations, were supplied by Professor J.I.G. Cadogan.

TABLE I

Formation of arynes, as measured by 1,2,3,4-tetraphenylnaphthalene (T.P.N.) from PCBN - $XC_6H_4.NH_2$ - Ac_2O

	Aryne	Adduct %
		
X	5-X-T.P.N.	6-X-T.P.N.
2-CO_2Et	5	-
2-CF_3	0	-
3-CO_2Et	16	32
3-CF_3	48	8
3-NH_2-C_5H_4N	0	12
4-CO_2Et	-	48
4-CF_3	-	32
H	46	-

6. REACTIONS OF SUBSTITUTED ACETANILIDES WITH 4-CHLOROBENZOYL NITRITE

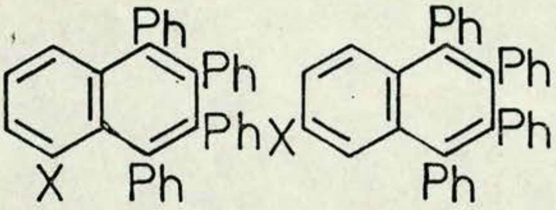
a In the presence of 2,3,4,5-tetraphenylcyclopentadienone

The reaction is exemplified by the case of 3-chloroacetanilide: to a solution of the anilide (0.789g, 5m mol) and 2,3,4,5-tetraphenylcyclopentadienone (3.84g, 10m mol) in dry benzene (100ml) at the b.p. was added during 1h, 4-chlorobenzoyl nitrite (1.6g, 8.5m mol) in benzene (50ml) under strictly anhydrous conditions. After 10h. at the b.p., excess of benzene was removed and maleic anhydride (1g, 10m mol) was added. The mixture was chromatographed as described in section 5a and the isolated product was recrystallised from benzene: ethanol (1:2) to give 5-chloro-1,2,3,4-tetraphenylnaphthalene (1.84g, 78%), m.p. and mixed m.p. 257°.[96] The results of similar experiments at the b.p. are summarised in Table II.

In the cases of 3-substituted anilines (section 5a) and 3-substituted acetanilides (section 6a), where both the corresponding 5- and 6-substituted tetraphenyl naphthalenes were possible products, the ratio of isomers was determined by ^{1}H n.m.r. spectroscopy. Thus in the case of a mixture of 5- and 6-ethoxycarbonyl-1,2,3,4-tetraphenylnaphthalenes, the ratio of 5-to 6-isomer was determined by direct comparison of the integral tracings for the quartets and/or triplets of the respective ethoxycarbonyl groups, the signals for the 5-isomer always

TABLE II

Formation of arynes as measured by 1,2,3,4-tetraphenylnaphthalene (T.P.N.) from PCBN - X - C_6H_4NHAc



	Aryne	Adduct %	m.p.^{o}	lit. m.p.^{o}	ref.
X	5-X-T.P.N.	6-X-T.P.N.			
3-F	75*	0	267		
3-Cl	78	0	257	257	96
3Br	77	0	232	235	133
3-I	57	6^{+}		206	134
3-CO_2Et	21.5	43			
3-MeO	59*	0	217-218		
3-CF_3	69.5*	11.5	187		
4-MeO	-	24*	274-275		
4-t-Bu	-	35	288-290	286-287	96
4-CO_2Et	-	46	220.5	218	134
4-CF_3	-	50*	248		
4-NO_2	-	0			
2-Me	0	-			
2-MeO	0	-			
2-CO_2Et	23	-	210	210	134
2-CF_3	0	-			
2-$NH_2.C_5H_4N$	0	-			
3-$NH_2.C_5H_4N$		18	218	220-222	135
2,5-$(MeO)_2$	49		199-200	175	134

* indicates new compounds

$^{+}$ the mixture could not be separated appearing downfield to those of the 6-isomer due to the greater interaction of the 5-substituent with the ring current of the unsubstituted naphthalene ring. In those cases where no extraneous signals outwith the aromatic region were present e.g. 3-halogen, 3-trifluoromethyl etc., the signal due solely to the 4-phenyl group of the 5-isomer was fixed by comparison of the spectrum of the mixture with that of the 6-isomer (obtained from the 4-substituted acetanilide). The integral tracing of this fixed signal was compared with that for the rest of the spectrum and the ratio of isomers was determined by simple computation.

In addition it was usually possible to obtain pure specimens of either isomer from a mixture of the two: a mixture of 5- and 6-ethoxycarbonyl-1,2,3,4 tetraphenylnaphthalene (1.40g) was chromatographed on an alumina dry column (20 x 4cm), developed with carbon tetrachloride, and the fluorescent segment was cut out; this segment was further divided into several fractions, each being examined by t.l.c. Those fractions containing only the 6-isomer were combined and the solid obtained was recrystallised from benzene:ethanol to give 6-ethoxycarbonyl-1,2,3,4 tetraphenylnaphthalene (0.85g) as a colourless crystalline solid m.p. 220-5°. Those fractions containing only the 5-isomer (which was eluted more slowly) were combined and the solid was recrystallised as before to give 5-ethoxycarbonyl-1,2,3,4-tetraphenylnaphthalene (0.34g), as a colourless powder m.p. 210°.

When necessary, the mother liquors were combined with those fractions still containing a mixture of isomers and the whole procedure was repeated

New tetraphenylnaphthalenes obtained in this way were: from 3-fluoroacetanilide, 5-*fluoro*-1,2,3,4-*tetraphenylnaphthalene*, m.p. 267°. (Found: C, 90.7; H, 5.0; $^{m}/e$ 450. $C_{34}H_{23}F$ requires C, 90.7; H, 5.1%; $^{m}/e$ 450). N.m.r. (CCl_4): τ, 2.55-2.75 (m, 2H); τ, 2.83 (s, 5H); τ, 2.92 (s, 5H); τ, 3.00-3.13 (m, 1H); τ, 3.25 br (s, 10H).

from 3-methoxyacetanilide, 5-*methoxy*-1,2,3,4-*tetraphenylnaphthalene*, m.p. 217-218°. (Found: C, 90.7; H, 5.7; $^{m}/e$ 462. $C_{35}H_{26}O$ requires C, 90.9; H, 5.6%; $^{m}/e$ 462). N.m.r. (CCl_4): τ, 2.73 (s, 1H); τ, 2.88 br (s, 7H); τ, 3.02 (s, 5H); τ, 3.30 br (s, 10H); τ, 6.68 (s, 3H, OMe).

from 4-methoxyacetanilide, 6-*ethoxy*-1,2,3,4-*tetraphenylnaphthalene*, m.p. 274-275°. (Found: C, 90.8; H, 5.8; $^{m}/e$ 462. $C_{35}H_{26}O$ requires C, 90.9; H, 5.6%; $^{m}/e$ 462). N.m.r. (CCl_4): τ, 2.50-2.58 (d, 1H); τ, 2.85 (s, 10H); τ, 3.00-3.11 (dd, 1H); τ, 3.15-3.30 br (s, 11H); τ, 6.38 (s, 3H, MeO).

from 3-acetamidobenzotrifluoride, 5-*trifluoromethyl*-1,2,3,4-*tetraphenylnaphthalene*, m.p. 187°. (Found: C, 83.8; H, 4.6; $^{m}/e$ 500. $C_{35}H_{23}F_3$ requires C, 84.0; H, 4.6%; $^{m}/e$ 500). N.m.r. (CCl_4): τ, 2.07-2.26 (m, 2H);

τ, 2.58-2.64 (d, 1H); τ, 2.68 (s, 5H); τ, 3.03 (s, 5H); τ, 3.10-3.50 br (s, 10H).

from 4-acetamidobenzotrifluoride, 6-trifluoromethyl-1,2,3,4-tetraphenylnaphthalene, m.p. 248°. (Found: C, 84.0; H, 4.7; $^m/e$ 500. $C_{35}H_{23}F_3$ requires C, 84.0; H, 4.6%; $^m/e$ 500). N.m.r. (CCl_4): τ, 2.12 (s, 1H); τ, 2.22-2.31 (d, 1H); τ, 2.47-2.58 (dd, 1H); τ, 2.82 (s, 10H); τ, 3.23 (s, 10H).

Previously known substituted tetraphenylnaphthalenes obtained in this way were: from 3-chloroacetanilide, 5-chloro-1,2,3,4-tetraphenylnaphthalene, m.p. and mixed m.p. 257°. N.m.r. and i.r. identical to that of an authentic sample.

from 3-bromoacetanilide, 5-bromo-1,2,3,4-tetraphenylnaphthalene, m.p. 232° and mixed m.p. 235°. N.m.r. and i.r. identical to that of an authentic sample.

from 4-t-butylacetanilide, 6-t-butyl-1,2,3,4-tetraphenylnaphthalene, m.p. and mixed m.p. 288-290°. N.m.r. and i.r. identical to that of an authentic sample.

from 3-iodoacetanilide, 5- and 6-iodo-1,2,3,4-tetraphenylnaphthalene. These were obtained as a mixture which could not be resolved, m.p. 178-179°. Mass spectrum: $^m/e$, 558 ($C_{34}H_{23}I$); 431 ($C_{34}H_{23}$).

from 2-ethoxycarbonylacetanilide, 5-ethoxycarbonyl-1,2,3,4-tetraphenylnapthalene, m.p. and mixed m.p. 210°. N.m.r. (CCl_4): τ, 2.30-2.40 (dd, 1H); τ, 2.48-2.55 (dd, 1H);

τ, 2.62-2.78 (dd, 1H); τ, 2.87 (s, 5H); τ, 2.99 (s, 5H); τ, 3.20-3.44 br (s, 10H); τ, 6.54-6.67 (q, 2H, $CH_3.CH_2O$); τ, 8.89-9.01 (t, 3H, CH_3CH_2O). Mass spectrum: $^m/e$, 504 ($C_{37}H_{28}O_2$); 431 ($C_{34}H_{23}$).

from 4-ethoxycarbonylacetanilide, 6-ethoxycarbonyl-1,2,3,4-tetraphenylnaphthalene, m.p. 220-5°. N.m.r. (CCl_4): τ, 1.72 (d, 1H); τ, 2.06-2.17 (dd, 1H); τ, 2.37-2.43 (d, 1H); τ, 2.82 (s, 5H); τ, 2.85 (s, 5H); τ, 3.23 (s, 10H); τ, 5.62-5.83 (q, 2H, CH_3CH_2O); τ, 8.61-8.77 (t, 3H, $CH_3.CH_2O$). Mass spectrum: $^m/e$, 504 ($C_{37}H_{28}O_2$), 431 ($C_{34}H_{23}$).

from 2,5-dimethoxyacetanilide, 5,8-dimethoxy-1,2,3,4-tetraphenylnaphthalene, m.p. 199-200°. N.m.r. (CCl_4): τ, 3.04 br (s, 10H); τ, 3.33 br (s, 10H); τ, 3.39 (s, 2H); τ, 6.76 [s, 6H $(CH_3O)_2$]. Mass spectrum: $^m/e$, 492 ($C_{36}H_{28}O_2$), 462 ($C_{35}H_{25}O$).

from 3-acetamidopyridine, 4,5,6,7-tetraphenylisoquinoline, m.p. 218°. (Found: C, 91.2; H, 5.3; N, 3.4; $^m/e$ 433. Calc. for $C_{33}H_{23}N$ C,91.4; H, 5.3; N, 3.2%; $^m/e$ 433). N.m.r. (CCl_4): τ, 1.06 (s, 1H); τ, 1.60-1.68 (d, 1H); τ, 2.62-2.69 (d, 1H); τ, 2.80 br (s, 10H); τ, 3.20 br (s, 10H).

All the experiments summarised in Table II were carried out under standard conditions at the b.p. of benzene. An experiment with 3-chloroacetanilide at room temperature overnight gave a comparable yield 69% (cf. 78% at b.p.) of the 5-chloro-1,2,3,4-tetraphenylnaphthalene.

b Utilising intramolecular addition to the aryne

(i) To a solution of 3-acetamidophenylacetic acid (1.93g, 10m mol) in dry benzene (250ml) at the b.p. was added during 2h 4-chlorobenzoyl nitrite (3.6g, 17m mol) in benzene (100ml). After 12h at the b.p., the solution was filtered to remove 4-chlorobenzoic acid. The red filtrate was extracted with 5% potassium bicarbonate solution (5 x 20ml), washed with water (2 x 20ml) and dried. Evaporation of the solvent left a brown, polymeric residue.

The combined aqueous extracts were acidified with dilute hydrochloric acid and the precipitate was filtered off. The mass spectrum of the crude solid indicated a mixture of 4-chlorobenzoic acid ($^m/e$ 158/156) and 3-phenylphenylacetic acid ($^m/e$ 212), the radical derived product. The mixture (1.7g) in methanol (40ml) was treated with an ethereal solution of diazomethane (40ml) to give an amber oil, after removal of solvents. Distillation of this oil gave methyl-4-chlorobenzoate (0.2g), b.p. 50°/0.05mm Hg, m.p. 43° (lit. m.p.[106] 46°).

A second fraction was distilled (0.8g), b.p. 80-90°/ 0.05mm Hg. Examination of this yellow oil by mass spec./ g.l.c. (2% N.P.G.S., 180°) indicated a mixture of two components with parent ions ($^m/e$ 212) and ($^m/e$ 226) respectively. The major component ($^m/e$ 226) corresponded to the expected methyl-3-phenylbenzoate, although all attempts to remove the minor component from the mixture failed.

(ii) To a solution of 3-acetamidophenethyl alcohol (0.358g, 2m mol) in dry benzene (40ml) at the b.p. was added during 30 min 4-chlorobenzoyl nitrite (0.6g, 3m mol) in benzene (20ml). After 12h at the b.p., the cooled solution was extracted with 5% potassium bicarbonate solution. The solutions were filtered to remove insoluble polymeric material and then separated. Evaporation of the organic layer gave an orange oil (0.3g) which, on examination by g.l.c. (2% CAR, 180°; 2% N.P.G.S., 180°) proved to be a mixture of two components. Mass spectrum/g.l.c. analysis of the first component gave a spectrum identical to that of the starting alcohol. Analysis of the second component gave ($^m/e$ 198) suggesting the radical derived product, 3-phenyl-phenethyl alcohol.

The expected aryne adduct, 2,3-dihydrobenzofuran was synthesised by an alternative route.[136] However, no peak corresponding to this product was found (0.1m/100m) would have been detected.

7. REACTIONS OF RADICALS WITH ACETYLENES

a Reactions of various sources of phenyl radicals with dimethyl acetylenedicarboxylate

(i) With Acetanilide - P.C.B.N. To a solution of acetanilide (5.4g, 40m mol) and dimethyl acetylenedicarboxylate (17g, 120m mol) in benzene (100ml) at the b.p. was added during 2h. P.C.B.N. (9.2g, 50m mol) in benzene (100ml). After 12h the solution was filtered; the solvent was evaporated, and excess of dimethyl acetylenedicarboxylate distilled off. The residue (9.2g) was chromatographed on an alumina dry column (90 x 5cm), developed with benzene, and the blue fluorescent band was cut out and the product washed from alumina with methanol. Evaporation of solvents gave a dark red oil which was dissolved in hot methanol to give 1,2,3,4-tetramethoxycarbonylnaphthalene (0.49, 4%), m.p. 146^{o} (lit. m.p.[99] 145-146^{o}), n.m.r. and i.r. identical to that of a sample obtained by Dr. J. Cook.[99]

The column was divided into another five segments and the products separated from alumina with ether. T.l.c. (alumina/benzene) and g.l.c. (2% CAR 175^{o}) examination of the fractions indicated three main products: fractions two and three were combined and the solvents evaporated to give a yellow solid which was recrystallised from methanol to give a mixture (2:1) of cis- and trans- dimethyl diphenylmaleate (0.85g, 7%), g.l.c. retention times (2% N.P.G.S., 175^{o}; 2% CAR, 180^{o}) being identical to those of authentic samples obtained by Dr. J. Cook;[99] the remaining fractions were combined and the solvents evaporated to give a yellow solid which was recrystallised from methanol to give phenyl -4-chlorobenzoate (0.6g), m.p. 103-104° (lit. m.p.[106] 100-101°). (Found: C, 67.1; H, 4.0. Calc. for $C_{13}H_9ClO_2$: C, 67.1; H, 3.9%). N.m.r. ($CDCl_3$): τ, 1.85-1.93 (d, 2H, aromatic); τ, 2.50-2.58 (d, 2H, aromatic); τ, 2.62-2.90 (m, 5H, aromatic).

(ii) With N-Nitrosoacetanilide. A solution of N-nitrosoacetanilide (1.64g, 10m mol) in dimethyl acetylenedicarboxylate (7.1g, 50m mol) was stirred at 0° under nitrogen for 15min then allowed to come gradually to room temperature. After 12h, the excess solvent was distilled off and the black tarry residue (4.5g) was chromatographed on an alumina dry column (50 x 3cm) to give 1,2,3,4-tetramethoxycarbonylnaphthalene (0.66g, 17%) as pale orange crystals after recrystallisation from methanol, m.p. and mixed m.p. 145°.

(iii) With Phenylazotriphenylmethane. A solution of phenylazotriphenylmethane (2.45g, 6m mol) in dimethyl acetylenedicarbonylate (7.1g, 50m mol) was stirred at 60° under nitrogen. After 8h, excess solvent was distilled off and the brown residue (3.1g) was chromatographed on an alumina dry column. No fluorescent blue band, characteristic of the tetramethoxycarbonylnaphthalene was observed, but a white solid (0.1g) isolated from the column proved to be triphenylmethane m.p. 92° (lit. m.p.^{106} 94°). I.r. was identical to that of an authentic specimen.

(iv) *With t-Butyl peroxide-Triphenyl arsine.*[137] *t*-Butyl peroxide (0.76g, 5m mol) was allowed to decompose under nitrogen at 120° in a stirred solution of triphenyl arsine (3.06g, 10m mol) in a dimethyl acetylenedicarbonylate (7.1g, 50m mol). After 12h the solid black mass was examined by t.l.c. and the presence of 1,2,3,4-tetramethoxycarbonylnaphthalene was confirmed. Work up as before gave the product (0.12g, 3%), m.p. and mixed m.p. 144-146°.

(v) *With t-Butyl hyponitrite-Triphenyl arsine.*[137] A mixture of *t*-butyl hyponitrite (1.04g, 10m mol) and triphenyl arsine (3.06g, 10m mol) in dimethyl acetylenedicarboxylate was stirred at 35° for 48h. Examination of the tarry reaction mixture by t.l.c. indicated total absence of any annelated product. The reaction mixture was dissolved in acetone and the solid thus precipitated was collected and recrystallised from methanol giving triphenylarsonium methoxycarbonylmethoxyoxallylmethylide (2.6g, 71%) as lustrous plates, m.p. 210-212° (lit. m.p.[138a] 214°). N.m.r. ($CDCl_3$): τ, 2.2-2.7 (m, 15H, aromatic); τ, 6.16 (s, 3H, CO_2Me); τ, 6.70 (s, 3H, CO_2Me). I.r. (nujol): $1740cm^{-1}$, $1675cm^{-1}$ and $1545cm^{-1}$ among others. This spectral data was identical to that published for an authentic sample of this compound.[138b]

(vi) With Dibenzoyl peroxide. Dibenzoyl peroxide (1.21g, 5m mol) was allowed to decompose at 80°, under nitrogen in dimethyl acetylenedicarboxlate (14.2g, 100m mol). Removal of excess solvent gave a yellow oil (8.7g) which was chromatographed on an alumina dry column (90 x 3.5cm), developed with benzene to give a brown tacky solid (2.0g). Recrystallisation from methanol gave 1,2,3,4-tetramethoxycarbonylnaphthalene (0.69g), m.p. 145°. Another 0.21g of the product, m.p. 144° was obtained by chromatography, as above, of the mother liquors (combined yield 0.90g, 50m/100 mol peroxide). I.r. (nujol): $1730cm^{-1}$, $1740cm^{-1}$. N.m.r. ($CDCl_3$): τ, 1.80-2.50 (m, 4H, aromatic); τ, 5.99 (s, 3H, CO_2Me); τ, 6.09 (s, 3H, CO_2Me). U.V. (methanol): λ_{max} 243nm, log ε 4.31. I.r. and n.m.r. were identical to that of an authentic sample. This reaction was carried out using benzene as solvent. Thus dibenzoyl peroxide (5.84g, 20m mol) was allowed to decompose in a solution of dimethyl acetylenedicarboxylate (8.5g, 60m mol) in benzene (200ml) at the b.p. Removal of the solvents gave an orange oil which was redissolved in chloroform and extracted with 10% sodium bicarbonate solution (3 x 20ml) to give benzoic acid (0.26g, 12m/100 mol peroxide). The residue (7.0g) was chromatographed on an alumina dry column (60 x 4cm), developed with benzene to give three main fractions. The first fraction was a yellow oil which on recrystallisation from methanol gave a solid, identified as biphenyl (1.25g, 40m/100 mol peroxide), m.p. and mixed m.p. 70°. The second fraction was a yellow oil (0.2g). G.l.c. examination (2% N.P.G.S., 180°) indicated a number of components; two of these components had retention times identical to those of authentic samples of cis and trans dimethyl 1,2-diphenylmaleates. Examination of the two components by mass spectrum/g.l.c. gave parent ions for both at $^{m}/e$ 296. The third fraction gave a yellow solid after recrystallisation from methanol and was shown to be 1,2,3,4-tetramethoxycarbonylnaphthalene (0.27g, 4m/100 mol peroxide), m.p. and mixed m.p. 145-146°.

The reaction was also carried out using t-butylbenzene as solvent. Dibenzoyl peroxide (1.21g, 5m mol) was allowed to decompose at 80° in a solution of t-butylbenzene (13.4g, 100m mol) containing dimethyl acetylenedicarboxylate (7.1g, 50m mol). After 12h the reaction mixture was allowed to cool. The solid which precipitated out was filtered off and identified as the naphthalene tetraester (0.17g, 9m/100 mol peroxide).

The residue (3.9g) remaining after removal of solvents was distilled to give a dark red gum (0.4g), b.p. 160-200° at 0.05mm Hg. Examination of this gum by mass spectrum/g.l.c. (2% CAR, 200°) indicated four major components all with parent ions at $^{m}/e$ 352. The mixture was boiled under reflux in t-butylbenzene containing a crystal of iodine for 24h. Examination of the reaction mixture by g.l.c. indicated that no change in the isomer distribution ratio had occurred.

b Reactions of diaroyl peroxides with dimethyl acetylenedicarboxylate (DMAD)

General Method: The peroxide (5m mol) was allowed to decompose at 80^{o} under nitrogen in dimethyl acetylenedicarboxylate (50m mol). After 12h, excess solvent was removed and the residue was examined by t.l.c. to determine the presence of any products and the best solvent system. The residue was absorbed on alumina (25g) and chromatographed on a dry column (60 x 3.5cm), developed with either benzene or dichloromethane. The products were detected as either intense, fluorescent blue bands or dark heavily masked bands which were separated from alumina with methanol. Evaporation of the extracts yielded the crude product which was recrystallised from methanol to give the substituted tetramethoxycarbonylnaphthalene as a white crystalline solid. These were characterised in the usual manner by analysis, n.m.r. etc.

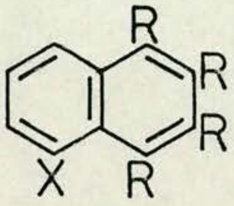
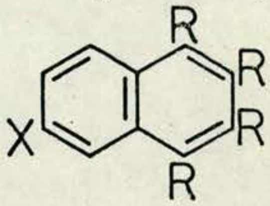
In the cases of 3-substituted peroxides where both the 5- and 6- substituted napthalenes were possible products, the ratio of isomers was determined by 'H n.m.r. spectroscopy. Thus for a mixture of 5- and 6-methyl-1,2,3,4-tetramethoxycarbonylnaphthalenes, direct comparison of the integral tracings for the respective methyl singlets gave the isomer ratio, the methyl singlet of the 5-isomer appearing downfield relative to that of the 6-isomer as in the case of 5-substituted tetraphenylnapthalenes. When substituents gave no signal e.g. Br, Cl, the signal due to the 5-proton of the 6-isomer was easily fixed as it appeared furthest downfield as a _meta_ coupled doublet. The integral tracing of this fixed signal was compared with that for other fixed signals and the ratio of isomers was determined by simple computation.

Pure samples of 5-isomer were obtained from mixtures of 5- and 6-isomers by chromatography, as described previously for substituted tetraphenylnaphthalenes. However a mixture of 5- and 6-methyl-1,2,3.4-tetramethoxycarbonylnaphthalene could not be separated by either chromatography or fractional crystallisation.

The results obtained are summarised in Table III.

TABLE III

Formation of 1,2,3,4-tetramethoxycarbonylnaphthalenes (T.M.N.) from (X - $PhCO_2$-$)_2$ - D.M.A.D.

	Radical Adduct	(m/100m peroxide)
		
X	5-X-T.M.N.	6-X-T.M.N.
H	50	-
2-NO_2	0	-
3-Cl	10.2	3.8
3-Br	14.5	5.5
3-Me	12.7⁺	6.3
4-Cl	-	22
4-Br	-	18
4-Me	-	16
4-CN	-	18

R = CO_2Me

All compounds listed in this table are new compounds.

⁺ This compound could not be separated from the 6-isomer.

The physical characteristics of these novel, substituted naphthalenes are summarised as follows:

5-Chloro-1,2,3,4-tetramethoxycarbonylnaphthalene, m.p. 165-168°. (Found: C, 55.0; H, 3.9; $^{m}/e$ 396/394. $C_{18}H_{15}ClO_8$ requires C, 54.8; H, 3.9%; $^{m}/e$ 396/394). N.m.r. ($CDCl_3$): τ, 2.00-2.10 (dd, 1H, aromatic); τ, 2.20-2.30 (dd, 1H, aromatic); τ, 2.40-2.56 (dd, 1H, aromatic); τ, 6.01 (s, 3H, CO_2Me); τ, 6.04 (s, 3H, CO_2Me); τ, 6.12 (s, 6H, $2CO_2Me$). I.r. (nujol): 1720cm^{-1} (C = 0).

6-Chloro-1,2,3,4-tetramethoxycarbonylnaphthalene, m.p. 143.5-144°. (Found: C, 54.9; H, 3.9; $^{m}/e$ 396/394. $C_{18}H_{15}ClO_8$ requires C, 54.8; H, 3.9%; $^{m}/e$ 396/394). N.m.r. ($CDCl_3$): τ, 1.90 (d, 1H, aromatic); τ, 1.90-2.20 (d, 1H, aromatic); τ, 2.32-2.45 (dd, 1H, aromatic); τ, 6.00 (s, 6H, $2CO_2Me$); τ, 6.11 (s, 6H, $2CO_2Me$). I.r. (nujol): 1730cm^{-1} (C = 0).

5-Bromo-1,2,3,4-tetramethoxycarbonylnaphthalene, m.p. 155-156°. (Found: C, 48.8; H, 3.5; $^{m}/e$ 440/438. $C_{18}H_{15}BrO_8$ requires C, 49.2; H , 3.4%; $^{m}/e$ 440/438). N.m.r. ($CDCl_3$): τ, 1.93 (s, 1H, aromatic); τ, 2.01 (s, 1H, aromatic); τ, 2.42-2.60 (dd, 1H, aromatic); τ, 5.97 (s, 3H, CO_2Me); τ, 6.00 (s, 3H, CO_2Me); τ, 6.17 (s, 6H, $2CO_2Me$). In the aromatic region of the n.m.r. spectrum, the expected A B C system has degenerated into a system closely resembling AB_2.[139]

6-*Bromo*-1,2,3,4-*tetramethoxycarbonylnapthalene*, m.p. 123.5-125°. (Found: C, 49.1; H, 3.4; ^{m}/e 440/438. $C_{18}H_{15}BrO_8$ requires C, 49.2; H, 3.4%; ^{m}/e 440/438). N.m.r. ($CDCl_3$): τ, 1.75 (d, 1H, aromatic); τ, 2.00-2.10 (d, 1H, aromatic); τ, 2.20-2.34 (dd, 1H, aromatic); τ, 6.00 br (s, 6H, $2CO_2Me$); τ, 6.10 br (s, 6H, $2CO_2Me$). I.r. (nujol): 1730cm^{-1} and 1720cm^{-1} (C = O).

6-*Methyl*-1,2,3,4-*tetramethoxycarbonylnaphthalene*, m.p. 141-143°. (Found: C, 60.9; H, 4.9; ^{m}/e 374. $C_{19}H_{18}O_8$ requires C, 61.0; H, 4.8%; ^{m}/e 374). N.m.r. ($CDCl_3$): τ, 2.00-2.10 (d, 1H, aromatic); τ, 2.18-2.20 (dd, 1H, aromatic); τ, 2.44-2.54 (dd, 1H, aromatic); τ, 5.99 (s, 6H, $2CO_2Me$); τ, 7.47 (s, 3H, CH_3). I.r. (nujol): 1715cm^{-1} (C = O).

6-*Cyano*-1,2,3,4-*tetramethoxycarbonylnaphthalene*, m.p. 203-204°. (Found: C, 59.0; H, 3.8; N, 3.6; ^{m}/e 385. $C_{19}H_{15}NO_8$ requires C, 59.2; H, 3.9; N, 3.6%; ^{m}/e 385). N.m.r. ($CDCl_3$): τ, 1.52 (d, 1H, aromatic); τ, 1.78-1.86 (d, 1H, aromatic); τ, 2.18-2.38 (dd, 1H, aromatic); τ, 5.97 (s, 3H, CO_2CH_3); τ, 5.99 (s, 3H, CO_2Me); τ, 6.09 (s, 6H, $2CO_2Me$). I.r. (nujol): 2225cm^{-1} ($C \equiv N$), 1740cm^{-1} and 1720cm^{-1} (C = O).

c *Reactions of other peroxides with dimethyl acetylenedicarboxylate*

(i) *Bis-2-naphthoyl peroxide*. Bis-2-naphthoyl peroxide (1.02g, 3m mol) was allowed to decompose at 80^o under nitrogen in dimethyl acetylenedicarboxylate (7.1g, 50m mol). Excess solvent was removed and the residue (2.1g) was chromatographed on an alumina dry column (50 x 2cm), developed with dichloromethane. A cream coloured solid (0.07g, 6m/100m) was the only product recovered from the column and was identified as a mixture of 1,2,3,4-*tetramethoxycarbonylanthracene* and 1,2,3,4-*tetramethoxycarbonylphenanthrene*. The mass spectrum showed the correct parent ion at $^m/e$ 410 ($C_{22}H_{18}O_8$ requires M^+, 410). N.m.r. ($CDCl_3$): τ, 1.70-1.80 (m, 1H, aromatic); τ, 2.02-2.24 (m, 3H, aromatic); τ, 2.26-2.48 (m, 2H, aromatic); τ, 5.98, 6.02, 6.07, 6.08 (4s, 12H, 4 x CO_2Me). The appearance at *ca* 6.0 τ in the n.m.r. spectrum of four singlets was compatible with the assignation of the product as a mixture of two, different carbocyclic tetraesters. From the ratio of the singlets at τ, 5.98 and τ, 6.02, the isomer ratio was determined as 3:2 respectively, and by analogy with 3-substituted benzoyl peroxides where the 5-substituted adduct predominated, the major isomer in this case was taken to be the 1,2,3,4-tetramethoxycarbonylphenanthrene. All attempts to separate either component from the mixture failed.

(ii) *Bis-2-phenylbenzoyl peroxide*. Bis-2-phenylbenzoyl (0.79g, 2m mol) was allowed to decompose at 100^o under nitrogen in dimethyl acetylenedicarboxylate (4.3g, 30m mol).

Excess solvent was removed; the residue (1.1g) was dissolved in chloroform (20ml), and the solution was extracted with 10% sodium bicarbonate solution (2 x 10ml). The aqueous layer was acidified with hydrochloric acid. No trace of 2-phenylbenzoic acid was found.

The organic layer was evaporated and the amber residue (1.0g) was chromatographed on an alumina dry column (20 x 3cm), developed with carbon tetrachloride, to give a crystalline solid (0.2g). Examination by mass spectrum/g.l.c. (5% N.P.G.S., 170°; 10% S.I.L., 190°) indicated one major component, $^{m}/e$ 196. Recrystallisation from petrol afforded material (0.15g) which was identified as 3,4-benzocoumarin (37m/100m peroxide), m.p. 90-92° (lit. m.p.[106] 92.5°). Mass spectrum showed a correct parent ion at $^{m}/e$ 196 ($C_{13}H_8O_2$ requires M^+ 196) and a minor fragment at ion $^{m}/e$ 168 i.e. (M^+-28), indicating loss of CO. I.r. (nujol): 1730cm^{-1} (C = O of lactone). No phenanthrene -9,10-dimethoxycarbonyl was detected using mass spectrum/g.l.c. either in the isolated solid or in the crude reaction mixture.

(iii) Bis-2-thenoyl peroxide. Bis-2-thenoyl peroxide (1.27g, 5m mol) was allowed to decompose at 80° under nitrogen in dimethyl acetylenedicarboxylate (7.1g, 50m mol). After 12h, excess solvent was removed and the black residue was distilled to give a bright yellow oil (1.0g) b.p. 120°/0.05mm Hg and a white crystalline solid which sublimed at the b.p. of the oil. T.l.c. analysis of the oil indicated two components one of which had the same Rf value as the white solid. The two products were combined and chromatographed on an alumina dry column (60 x 2cm), developed with dichloromethane, to give two fractions.

The first fraction, a dark brown oil, was redistilled to give a yellow oil b.p. 125°/0.05mm Hg which solidified on cooling. Recrystallisation from methanol gave a pale yellow solid (0.27g, 20m/100mol peroxide), identified as cis-<u>dimethylthenoylmaleate</u>, m.p. 75-76°. (Found: C, 49.1; H, 3.7. $C_{11}H_{10}O_6S$ requires C, 48.9; H, 3.7%). The mass spectrum showed the parent ion at $^m/e$ 270. (Found: M^+, 270.020054. $C_{11}H_{10}O_6S$ requires M^+, 270.019804). N.m.r. ($CDCl_3$): τ, 2.00-2.08 (dd, 1H, aromatic); τ, 2.24-2.33 (dd, 1H, aromatic); τ, 2.78-2.89 (dd, 1H, aromatic); τ, 3.22 (s, 1H, vinylic); τ, 6.25 (s, 3H, CO_2Me); τ, 6.29 (s, 3H, CO_2Me). I.r. (nujol): 1730cm^{-1} br (C = O); 1655cm^{-1} (C = C).

This compound was assigned the <u>cis</u> structure on the basis of a comparison with the known <u>cis</u> and <u>trans</u> dimethyl diphenylmaleates viz. COOMe (<u>trans</u>), τ, 6.51; COOMe (<u>cis</u>), τ, 6.20.

The second fraction, a sticky green solid (0.1g) was recrystallised from chloroform: petrol to give 2,3,4-trimethoxyfuran-5-methoxyfuran (0.07g, 5m/100m peroxide), m.p. 117-119° (lit. m.p.^{140} 117-118°). The mass spectrum showed the parent ion at $^m/e$ 272. (Found: M^+, 272.052698. $C_{11}H_{12}O_8$ requires M^+, 272.053208).

N.m.r. ($CDCl_3$): τ, 5.78 (s, 3H, OMe); τ, 6.07 (s, 3H, CO_2Me); τ, 6.16 (s, 3H, CO_2Me); τ, 6.22 (s, 3H, CO_2Me). I.r. (nujol): $1740cm^{-1}$, $1720cm^{-1}$ and $1705cm^{-1}$ (C = O). U.V. λ_{max} 273nm, log ε 3.92 (lit. U.V.[140] λ_{max} 276, log ε 4.18).

(iv) Bis-2-furoyl peroxide. Bis-2-furoyl peroxide (1.11g, 5m mol) was allowed to decompose at 80° under nitrogen in dimethyl acetylenedicarboxylate (7.1g, 50m mol). After 12h, excess solvent was removed and the residue was taken up in chloroform (50ml) and extracted with 10% sodium bicarbonate solution (3 x 10ml). The aqueous layer was acidified but no 2-furoic acid was obtained.

After removal of solvent from the organic layer the residue (2.2g) was chromatographed on silica (100g). Elution with chloroform gave a brown oil which had fluoresced on the column under U.V. light. T.l.c. and g.l.c. examination (2% CAR, 160°) of this oil indicated a multicomponent mixture. The oil was purified by distillation to give a yellow solid (0.12g), b.p. 50° at 0.05mm Hg which was shown however to be a mixture of several components. Further purification could not be achieved.

(v) Benzoyl-4-nitrobenzoyl peroxide. Benzoyl-4-nitrobenzoyl peroxide (1.44g, 5m mol) was allowed to decompose at 80° under nitrogen in dimethyl acetylenedicarboxylate (7.1g, 50m mol). The residue (3.5g), left after removal of excess solvent, was chromatographed on an alumina dry column, developed with benzene. The fluorescent band which was isolated from the column yielded a brown solid which was recrystallised from methanol to give a cream solid (0.24g) which was identified as a mixture of 1,2,3,4-tetramethoxycarbonylnaphthalene and 6-nitro-1,2,3,4-tetramethoxycarbonylnaphthalene in the ratio of 1:1 by direct comparison of the integral tracings for the aromatic respective aromatic protons. N.m.r. ($CDCl_3$): τ, 0.94-1.02 (m, 1H, aromatic 6-NO_2); τ, 1.60-1.76 (m, 2H, aromatic, 6-NO_2); τ, 1.80-2.50 (m, A_2B_2, 4H, aromatic); τ, 5.92-6.10 (5 overlapping singlets, 24H, 8 x CO_2Me).

Chromatography of the mother liquors as before gave a second fraction (0.12g) which was shown to be a pure sample of 1,2,3,4-tetramethoxycarbonylnaphthalene, m.p. and mixed m.p. 145-146°. By simple computation, the total yield of unsubstituted naphthalene was estimated as 0.23g, 13m/100mol peroxide. Similarly, the yield of substituted naphthalene was estimated as 0.13g, 6.5m/100mol peroxide. The overall ratio of unsubstituted to substituted naphthalene was thus 2:1.

d Reactions of phenyl radicals with some other acetylenes

(i) Phenylacetylene. Dibenzoyl peroxide (1.21g, 5m mol) was allowed to decompose at 80° under nitrogen in phenylacetylene (5.1g, 50m mol). The reaction mixture darkened very quickly and was completely black after 1h. After 8h, excess phenylacetylene was distilled off and the residue was examined by t.l.c. No characteristic, blue fluorescence of a substituted naphthalene was observed. This residue was chromatographed on alumina (100g).

Elution with the usual graded series of solvents and solvent mixtures gave only minute traces of unidentified compounds. A large black band remained on the column even after elution with methanol.

(ii) 1-Hexyne. Dibenzoyl peroxide (1.21g, 5m mol) was decomposed under nitrogen in 1-hexyne at the b.p. After 24h, excess of solvent was evaporated and the residue was taken up in benzene. After extraction with 0.5M NaOH (2 x 10ml), the aqueous layer was acidified to give benzoic acid (0.18g, 30m/100 mol peroxide).

Chromatography of the organic residue on alumina gave only intractable tars.

(iii and iv) Dibenzoyl peroxide was similarly decomposed in both 1-octyne and oct-4-yne. The reaction mixtures were worked up as described for 1-hexyne, giving benzoic acid (30m/100m peroxide) as the only recognisable product in either case.

(v) Ethyl propiolate. Dibenzoyl peroxide (1.21g, 5m mol) was allowed to decompose in ethyl propiolate (4.9g, 50m mol) at 80°. After 12h, excess solvent was distilled off and the residue (4.4g) was chromatographed on an alumina dry column (60 x 4cm), developed with benzene. The blue fluorescent segment was removed and washed with ether to give a brown oil (0.5g) which was purified by distillation to give a tacky solid (0.37g, 27m/100m, b.p. 90°/0.05mm Hg, which was identified as a mixture of at least two isomeric naphthalene diesters. G.l.c. analysis of the solid indicated two components. Mass spectrum/g.l.c. gave parent ions for each at $^{m}/e$ 272. H.s.l.c. (sperical alumina, 20μ-CH_2Cl_2) gave two major components. N.m.r. ($CDCl_3$): τ, 1.01-1.05 (dd, 1H, aromatic); τ, 1.27 (s, 2H, aromatic); τ, 1.94-2.74 (m, 4H, aromatic); τ, 5.40-5.65 (2 overlapping quartets, 4H, 2 x CO_2Et); τ, 8.45-8.66 (2 overlapping triplets, 6H, 2 x CO_2Et). I.r. (nujol): 1720cm^{-1} (C = O). The n.m.r. spectrum was compatible with a mixture of two naphthalene diesters; the low field double doublet indicated the presence of 1,3-diethoxycarbonylnaphthalene, however it was not possible to determine which of the remaining diesters was responsible for the low field singlet: at τ, 1.27.

8. REACTIONS OF RADICALS WITH AZO COMPOUNDS

a Reaction of aroyl radicals with diethyl azodiformate

(i) Dibenzoyl peroxide. Dibenzoyl peroxide (1.21g, 5m mol) was allowed to decompose at 80°, under nitrogen, in diethyl azodiformate (8.7g, 50m mol). After 12h, excess solvent was distilled off and the residue, an amorphous sticky solid (3.0g), was examined by t.l.c. (alumina/dichloromethane). Only one component was observed. The residue was dissolved in boiling methanol, and on cooling the product crystallised as lustrous plates (1.50g, 60m/100mol peroxide), m.p. 137.5-138°. (Found: C, 57.3; H, 5.8; N, 11.0. $C_{24}H_{30}N_4O_8$ requires C, 57.4; H, 6.0; N, 11.2%). This product was identified as 1,4-diphenyl-1,2,3,4-tetraethoxycarbonyl-tetrazane on the basis of the following evidence: the mass spectrum showed the parent ion at $^m/e$ 502. (Found: M^+, 502.207545. $C_{24}H_{30}N_4O_8$ requires M^+, 502.206370) and two important fragments at ion $^m/e$ 251 (mass abundance ratio 13%) and at ion $^m/e$ 179 (mass abundance ratio 100%). (Found: M^+, 179.082351. $C_9H_{11}N_2O_2$ requires M^+, 179.082037). N.m.r. ($CDCl_3$): τ, 2.20-2.60 br (m, 4H, aromatic); τ, 2.60-2.73 br (m, 6H, aromatic); τ, 5.60-6.50 (2 v. broad quartets, 8H, 4 x O_2CH_2); τ, 8.60-8.88 and , 9.20-9.42 (2 broad triplets, 12H, 4 x OCH_2CH_3). The integral tracings for the two ester triplets gave a ratio of 3:2 as did the tracings for the two ester quartets. No change in the spectrum was observed after shaking the deuterochloroform solution with a solution of sodium dithionite in D_2O. ^{13}C N.m.r. ($CDCl_3$): ppm, 154.9 (C = O); ppm, 153.0 (C = O); ppm, 140.3 (C - N, aromatic); ppm 128.3-128.0 (C-H, aromatic); ppm, 63.8, 63.3, 62.9 (3 x OCH_2); ppm, 14.5 (OCH_2CH_3); ppm, 13.5 (OCH_2CH_3). I.r. (nujol): 1730cm^{-1} (C = O). U.V. λ_{max} 207nm, log ε 3.98. H.s.l.c. (spherical alumina, 20μ-CH_2Cl_2) indicated a single product with a retention time of 4.6 min.

The reaction was repeated using benzene as solvent. Dibenzoyl peroxide (1.21g, 5m mol) was decomposed in a solution of diethyl azodiformate (5.22g, 30m mol) in benzene (7.8g, 100m mol) at the b.p. The reaction mixture was cooled and allowed to stand at 10° for 48h. The precipitate was filtered off and recrystallisation from methanol afforded a product (1.04g, 40m/100mol peroxide) identical in every respect to that obtained above. After removal of solvents, the filtrate (2.7g) was chromatographed on an alumina dry column to give biphenyl (0.15g, 20m/100m peroxide), m.p. and mixed m.p. 70°.

(ii) N-<u>Nitrosacetanilide</u>. <u>N</u> Nitrosoacetanilide (1.67g, 10m mol) was decomposed in diethyl azodiformate (6.6g, 37.5m mol), stirred under nitrogen in an ice bath. The solution was gradually allowed to room temperature and then stirred for 12. Excess solvent was distilled off, and the residue was dissolved in boiling methanol to give to give a cream coloured solid (0.08g, 2%) which was identical to the product obtained from dibenzoyl peroxide.

(iii) Bis-4-methylbenzoyl peroxide. Bis-4-methylbenzoyl peroxide (1.35g, 5m mol) was decomposed in diethyl azodiformate (8.7g 50m mol) at 80°. After 12h, excess solvnet was distilled off and the residue was examined by t.l.c. The residue was dissolved in hot methanol. Cooling the solution at -20° gave a yellow crystalline solid (0.09g) which was collected and dried. The filtrate was evaporated and the residue was dissolved in aqueous acetone and then cooled to give a yellow amorphous solid (0.07g). Examination by t.l.c. (alumina/dichloromethane) and g.l.c. (10% A.P.L. 170°) indicated that the two products were identical. The two fractions were combined and recrystallised from water to give a crystalline compound (0.15g, 17m/100m peroxide), m.p. 131-133° which was identified as diethyl hydrazodiformate (lit. m.p.[106] 130°). I.r. and n.m.r. were identical to that of an authentic sample.

(iv) Bis-4-bromobenzoyl peroxide. Bis-4-bromobenzoyl peroxide (0.87g, 2m mol) was decomposed at 80° in diethyl azodiformate (4.0g, 24m mol). After 12h, excess solvent was distilled off and the residue was dissolved in boiling methanol. The solid which separated out was purified by sublimation to give a white powder (0.2g, 50m/100mol peroxide) m.p. 251°, identified as 4-bromobenzoic acid (lit. m.p.[106] 254.5°). I.r. (nujol): $3100cm^{-1}$-$2500cm^{-1}$ br (O-H); $1675cm^{-1}$ (C = O). The mass spectrum showed the parent ion at $^{m}/e$ 202/200. N.m.r. ($CDCl_3$): τ, 2.08-2.17 (d, 2H, aromatic); τ, 2.29-2.38 (d, 2H, aromatic).

(v) Bis-2-thenoyl peroxide. Bis-2-thenoyl peroxide (1.27g, 5m mol) was decomposed at 80° in diethyl azodiformate (8.7g, 50m mol). After 12h, excess solvent was distilled off and the residue (4.4g) was examined by t.l.c., which indicated one product with the same Rf value as diethyl hydrazodiformate. Dry column chromatography gave after recrystallisation from water a crystalline solid (0.4g, 55m/100mol peroxide) identified as diethyl hydrazodiformate m.p. and mixed m.p. 131°.

b Reactions of some sources of phenyl radicals with dimethyl azodiformate

(i) Dibenzoyl peroxide. Dibenzoyl peroxide (1.21g, 5m mol) was allowed to decompose in dimethyl azodiformate (7.3g, 50m mol), stirred under nitrogen at 80°. After 12h, excess solvent was distilled off and the residue, a sticky orange gum (4.5g) was recrystallised from benzane: cyclohexane (1:3) to give a colourless solid (1.55g, 69m/100mol peroxide), m.p. 225° identified as described below as 1,4 diphenyl-1,2,3,4-tetramethoxycarbonyltetrazane. (Found: C, 53.6; H, 5.1; N, 12.6. $C_{20}H_{22}N_4O_8$ requires C, 53.8; H, 4.9; N, 12.6%). The mass spectrum showed the parent ion at $^m/e$ 282 (mass abundance ratio 10%), ion mass $^m/e$ 223 (mass abundance ratio 100%) and at ion mass $^m/e$ 179 (mass abundance ratio 15%). N.m.r. ($CDCl_3$): τ, 2.20-2.50 br (m, 4H, aromatic); τ, 2.50-2.75 br (m, 6H, aromatic); τ, 6.23 and 6.79 (2 broad singlets, 12H, 4 x CO_2CH_3). The integral tracings for the two methyl singlets gave a ratio of 2:1 ^{13}C.N.m.r. ($CDCl_3$ + 0.05M) chromium acetate): ppm, 155.4, 155.3, 155.2, 153.5 (4 x C = O); ppm, 140.1, 140.0 (2 x C-N, aromatic); ppm, 128.4-127.1 (C-H, aromatic); ppm, 54.6, 54.3, 53.8, 53.4, (4 x OCH_3). I.r. (nujol): 1730cm^{-1} (C = O). H.s.l.c. (spherical alumina, 20μ- CH_2Cl_2) indicated a single product with a retention time of 7min.

The reaction was repeated using benzene (7.8g, 100m mol) as solvent and also t-butylbenzene (13.4g, 100m mol) as solvent. In both cases the above product was obtained in yields of 56m/100mol peroxide and 27m/100mol peroxide respectively.

(ii) N-Nitrosoacetanilide. N-Nitrosoacetanilide (0.83g, 5m mol) was decomposed in dimethyl azodiformate (3.65g, 25m mol) stirred under nitrogen in an ice bath. The solution was gradually allowed to room temperature and then stirred for 12h. Excess solvent was distilled off and the black tarry residue was boiled with methanol. The hot solution was filtered and the brown powder obtained was recrystallised from benzene:cyclohexane (1:3) to give a cream coloured solid (0.12g, 11%), which was found to be identical with the product obtained from dibenzoyl peroxide.

(iii) Acetanilide-Amyl nitrite. To a solution of acetanilide (0.85g, 5m mol) in dimethyl azodiformate (3.7g, 25m mol) at 80° was added dropwise during ½h amyl nitrite (0.9g, 7.5m mol). After 12h, excess solvent was distilled off and the residue was dissolved in hot methanol. Only polymeric tars were obtained from this reaction.

(iv) Phenylazotriphenylmethane. Phenylazotriphenylmethane (3.48g, 10m mol) was decomposed in a solution of dimethyl azodiformate (5.84g, 40m mol) in benzene (7.8g, 100m mol) at the b.p. The dark residue obtained (5.6g) after removal of solvents was chromatographed on alumina (350g).

Elution with petrol gave a yellowish solid which on recrystallisation from ethanol yielded triphenylmethane (0.03g, 1%) m.p. and mixed m.p. 93° (lit. m.p.[106] 94°).

Elution with petrol/ether (1:1 v/v) gave a yellow solid which when recrystallised from benzene gave a white, amorphous powder (0.5g, 11%) which sublimed without melting and was subsequently identified as N'-triphenylmethyl-N,N'-dimethoxycarbonyl-N-phenylhydrazine. (Found: C, 74.8; H, 5.8; N, 5.9. $C_{29}H_{26}N_2O_4$ requires C, 74.7; H, 5.6; N, 6.0%). The mass spectrum showed the parent ion at $^m/e$ 466 ($C_{29}H_{26}N_2O_4$ requires M^+ 466) and a fragment at ion $^m/e$ 243 (mass abundance ratio 100%). I.r. (nujol): 1725cm^{-1} and 1710cm^{-1} (C = O). N.m.r. ($CDCl_3$): τ, 2.82 (s, 18H, aromatic); τ, 3.26-3.53 br (m, 2H, aromatic); τ, 6.23, 6.29 and 6.70 (2 broad singlets and a sharp singlet, 6H, 2 x CO_2CH_3). ^{13}C N.m.r. ($CDCl_3$): ppm, 157.4, 156.4, 156.0, 155.3 (4 x C = O); ppm, 143.1, 142.4, 141.9, 141.2 (4 x C-N, aromatic); ppm, 130.8-125.7 (C-H, aromatic); ppm, 53.5 and 52.5 (2 x OCH_3).

c Phenyl radicals with other azo compounds

(i) t-Butyl azodiformate. Dibenzoyl peroxide (1.21g, 5m mol) was decomposed under nitrogen in a solution of t-butyl azodiformate (3.45, 15m mol) in benzene (7.8g, 100m mol) at the b.p. After 12h, excess solvent was evaporated and the yellow oil was dissolved in boiling petrol. On cooling, unreacted t-butyl azodiformate (0.4g) crystallised out. The filtrate was evaporated and the yellow residue (3.0g) was chromatographed on silica (150g).

Elution with petrol/ether (4:1 v/v) gave an orange solid which on recrystallisation from methanol gave a white solid (0.15g, 20m/100m peroxide), m.p. 69° identified as biphenyl.

Elution with petrol/ether (2:1 v/v) gave a cream solid which on recrystallisation from benzene/petrol (1:1) gave t-butyl hydrazodiformate (0.16g, 14m/100m peroxide), m.p. and mixed m.p. 124-125°. I.r. was identical to that of an authentic specimen.

Elution with petrol/ether (1:1) gave an oily solid (0.34g). Recrystallisation twice from cyclohexane gave the product as colourless needles (0.18g, 6m/100mol peroxide), m.p. 127°. The compound was identified as 1,4-diphenyl-1,2,3,4-tetra-t-butoxycarbonyltetrazane. The mass spectrum showed the parent ion at $^{m}/e$ 614. (Found: M^+, 614.330839. $C_{32}H_{46}N_4O_8$ requires M^+, 614.331542). N.m.r. ($CDCl_3$): τ, 2.1-2.6, v broad (m, 4H, aromatic); τ, 2.6-2.9 br(m, 6H, aromatic); τ, 8.5 and 8.6, 2 broad singlets and τ, 8.95, broad singlet (36H, 4 x $CO_2C_4H_9$). The integral tracings for the two sets of broad singlets gave a ratio of 1.8:1. I.r. (nujol): 1740cm^{-1} and 1725cm^{-1} (C = O).

Continual elution with the usual graded series of solvent mixtures gave a series of yellow oils which seemed polymeric in nature and from which no identifiable products could be isolated.

(ii) Phenylazoethoxycarbonyl. Dibenzoyl peroxide (1.21g, 5m mol) was decomposed at 80° in phenylazoethoxycarbonyl (8.7g, 50m mol), stirred under nitrogen. After 12h, excess solvent was removed and the residue, a black oil was dissolved in boiling methanol. No precipitate was obtained. After evaporation of the methanol, the residue (4.5g) was chromatographed on silica (200g).

Elution with the usual solvents gave only trace quantities of various oils.

(iii) 4-Phenyl-1,2,4-triazoline-3,5-dione. A solution of dibenzoyl peroxide (1.21g, 5m mol) and 4-phenyl-1,2,4-triazoline-3,5-dione (5.25g, 30m mol) in benzene (7.8g, 100m mol) was boiled under reflux in the dark. After 12h, the benzene was evaporated and the pinkish white residue was broken up and washed with acetone to remove an oily contaminant. The solution was filtered and the white solid obtained was recrystallised from aqueous dimethyl sulphoxide to give a mass of opaque platelets, identified as 2,6-diphenyl-s-triazolo[1,2-a]-s-triazole-1,3,5,7(2H, 6H)-tetraone (3.2g, 66%), which sublimed without melting. (Found: C, 59.4; H, 3.2; N, 17.4. $C_{16}H_{10}N_4O_4$ requires C, 59.6; H, 3.2, N, 17.4%). The mass spectrum showed the parent ion at $^m/e$ 322. (Found: M^+ 322.069299. $C_{16}H_{10}N_4O_4$ requires M^+ 322.070198) and a fragment at ion $^m/e$ 119. (Found: M^+ 119.037157. C_7H_5NO requires M^+ 119.037111). N.m.r. (d.m.s.o. d^6): τ, 2.56 (s, aromatic). I.r. (nujol): 1780cm^{-1}, 1750cm^{-1} (C = O).

Removal of solvents from the filtrate gave a brown residue which was chromatographed on silica. No identifiable products were obtained.

(iv) To avoid the possibility of thermal decomposition of the triazoline, the experiment was repeated using a milder source of phenyl radicals. Thus N-Nitrosoacetanilide (0.29, 1.8m mol) was decomposed at room temperature in a solution of the triazoline (0.48g, 2.7m mol) in benzene (7.8g, 100m mol). After 12h, the solution was filtered to give a brown solid (0.38g) which resisted attempts at purification by sublimation. The mass spectrum indicated the solid was polymeric. Evaporation of the filtrate gave a brown residue which was boiled in methanol (40ml). The precipitate obtained was recrystallised from benzene/methanol to give an amorphous solid (0.16g, 37%) which was identical to the triazolotriazole derivative obtained above.

9. MISCELLANEOUS REACTIONS

a Attempted oxidation of N,N'-diethoxycarbonyl-N-phenylhydrazine

(i) With lead dioxide. The method used was an adaptation of that used by Goldschmidt and Euler[141] for the oxidation of monoacetyl hydrazobenzene.

A suspension of lead dioxide (4.7g, 20m mol) in benzene (40ml) containing N,N'-diethoxycarbonyl-N-phenylhydrazine (0.50g, 2m mol) and sodium sulphate (1g) was shaken for 24h. T.l.c. examination of the reaction mixture showed only starting material. The solution was then boiled under reflux with vigorous stirring. After 12h, the solution was filtered and the clear filtrate was evaporated to give quantitative recovery of unchanged starting material.

The above procedure was repeated using a variety of oxidising agents including mercuric oxide, activated manganese dioxide and silver oxide. In each case there was quantitative recovery of starting material.

(ii) With t-butyl peroxide. t-Butyl peroxide (0.2g, 1m mol) was decomposed at 120° in t-butyl benzene (5.4g, 40m mol) containing N,N'-diethoxycarbonyl-N-phenylhydrazine (0.50g, 2m mol). After 12h, excess solvent was distilled off and the brown residue was recrystallised from benzene/petrol (2:1) to give the starting material (80% recovery).

(iii) With lead tetraacetate. To a stirred solution of *N*,*N'*-diethoxycarbonyl-*N*-phenylhydrazine (0.5g, 2m mol) and potassium carbonate (1g) in benzene (20ml) at room temperature was added lead tetraacetate (0.9g, 2m mol). The solution, which turned orange immediately, was stirred for 1h, then filtered. Evaporation of the solvent gave a dark oil (0.5g) which was distilled to give a dark red viscious liquid (0.28g, 78%), b.p. 55°/ 0.05mm Hg (lit. b.p.[124] 130-132/24mm Hg), identified as phenylazoethoxycarbonyl by comparison of g.l.c. retention times with an authentic sample (10% A.P.L., 180°; 10% S.I.L. 160°). N.m.r. ($CDCl_3$): τ, 1.95-2.30 (m, 2H, aromatic); τ, 2.35-2.65 (m, 3H, aromatic); τ, 5.30-5.70 (q, 2H, $CO_2C_2H_5$); τ, 8.40-8.55 (t, 3H, $CO_2C_2H_5$).

b Reactions with 4-phenyl-1,2,4-triazoline-3,5-dione

A solution of methyl azodiformate (2.2g, 15m mol) and 4-phenyl-1,2,4 - triazoline-3,4-dione (0.87g, 5m mol) in benzene (3.9g, 50m mol) at the b.p. was stirred under nitrogen for 24h. The solution was filtered and the precipitate was washed with benzene and dried to give a white solid (0.13g, 16m/100mol dione) identified as the triazolo-triazole derivative obtained previously. The excess solvents were removed from the filtrate and the residue (1.7g) was chromatographed on silica.

Elution with ether gave a brown solid (0.04g) which could not be sublimed and did not melt below 350°.

Elution with ether/methanol (1:1 v/v) gave another brown solid (0.06g) which also did not melt or sublime. A mass spectrum of both these compounds indicated they were polymeric in nature.

DISCUSSION

DISCUSSION

An efficient and facile production of arynes from either arylamines or acetylarylamines had been recently developed in our laboratories which utilised the *in situ* formation and subsequent decomposition of acetylarylnitrosamines. As a result of the research described herein, the scope of this method of aryne generation has been delineated and some limitations in the synthetic utility of this reaction have been exposed.

In addition, it had been suggested that the decomposition of *N*-nitrosoacetanilide in the presence of dimethyl acetylenedicarboxylate led to the trapping of a pre-aryne intermediate, a betaine, formed by removal of an *ortho* proton from benzenediazonium cation. The mechanism of this reaction has been elucidated and this has led to the development of a general aromatic annelation reaction involving reaction of an aryl radical with two molecules of dimethyl acetylenedicarboxylate. An attempted extension of this reaction to azo compounds has revealed some new aspects of the chemistry of hydrazyl radicals.

1. THE CONVERSION OF ANILINES AND ACETANILIDES INTO ARYNES

a Studies on the scope of this reaction

Since the early work of Wittig and Roberts, the discovery of more facile routes to arynes has occupied the attentions of many workers. The in situ diazotisation of 2,5-di-t-butylaniline by butyl nitrite had been shown to lead to the corresponding aryne[102] and it became apparent that application of this diazotisation method to anilines in the presence of acetate ion might provide a superior route to arynes, since it fulfilled two basic requirements rarely met by existing methods, viz. mild reaction conditions and general availability of substrate.

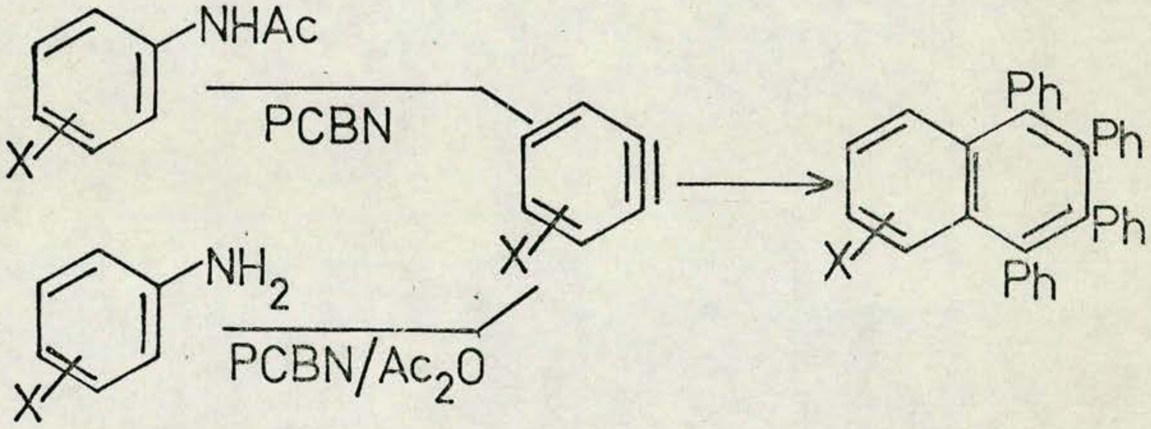
The reported failure of aniline to produce benzyne on diazotisation with pentyl nitrite in the presence of acetate ion was ascribed to the formation of water as a by-product in this reaction.[96,133] Steps taken to suppress this side effect proved successful[104] and a simple procedure for the direct conversion of aniline into benzyne, involving diazotisation of aniline with pentyl nitrite in the presence of acetic anhydride, was thereby effected (see Introduction, p. 40). Development of more powerful nitrosating agents in tandem with the use of acetanilide rather than aniline led to the highly efficient system, acetanilide-4-chlorobenzoyl nitrite (P.C.B.N.), which was capable of producing benzyne

TABLE IV

Formation of Arynes as measured by 1,2,3,4-tetraphenylnapthalenes (T.P.N.) from (a) P.C.B.N.-X-$C_6H_4NH_2$-Ac_2O and (b) P.C.B.N.-X-C_6H_4NHAc

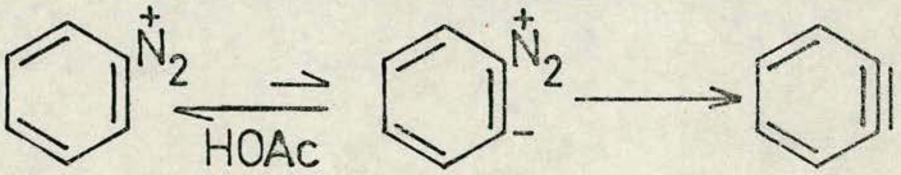
	Aryne Adduct			
X	5X-T.P.N.		6X-T.P.N.	
	a	b	a	b
H	46	72	-	-
3F		75		0
3Cl		78		0
3Br		77		0
3I		57		6
3CO_2Et	16	21.5	32	43
3MeO		59		0
3CF_3	48	69.5	8	11.5
4MeO		-		24
4-t-Bu		-		35
4-CO_2Et	-	-	48	46
4-CF_3	-	-	32	50
4-NO_2		-		0
2-Me		0		-
2-MeO		0		-
2-CO_2Et	5	23	-	-
2-CF_3	0	0	-	-
2-NH_2-C_5H_4N		0		-
3-NH_2-C_5H_4N	0	0	12	18
2,5-$(MeO)_2$		49		

adducts in yields up to 70%. The mildness and efficiency of this new route to benzyne compared favourably with that of standard methods e.g. anthranilic acid-pentyl nitrite[68] and 1-aminobenzotriazole-lead tetraacetate.[71,72] The expectation that this new method could be extended in a general production of arynes from readily available starting materials had yet to be realised. It was towards this goal that an examination of the scope of this reaction was undertaken.

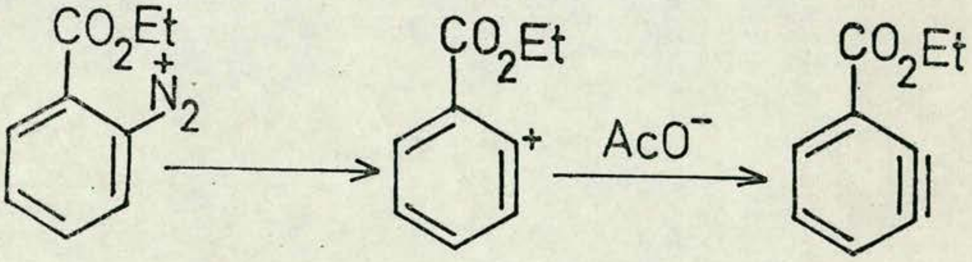


The efficiency of this reaction in converting substituted anilines and acetanilides into the corresponding arynes as indicated by the trapping reaction with tetracyclone, as shown above, is outlined in Table IV from which several points emerge. The yield of aryne adduct was higher when preformed acetanilide-P.C.B.N. rather than the aniline-acetic anhydride-P.C.B.N. system was used; both in turn gave higher yields of aryne than the aniline-acetic anhydride-pentyl nitrite system, examined previously by Robertson.[134] The overall efficiency of the systems using P.C.B.N. can be readily rationalised in terms of an extremely rapid nitrosation of the acetylarylamine. Kinetic studies on the reaction of P.C.B.N. and acetanilide at 80° have shown that the nitrosation step and subsequent decomposition of the nitrosamine is extremely rapid, 95% of the nitrogen being evolved within four minutes.[134] The greater efficiency of preformed acetanilide over anilide formed *in situ* from aniline and acetic anhydride is less readily explained since at 80° one might expect almost quantitative conversion to the anilide. It may be that the excess acetic acid produced from this reaction reverses the equilibrium sufficiently to affect the yield of aryne.

$$\mathrm{PhNH_2 + Ac_2O \longrightarrow PhNHAc + HOAc}$$

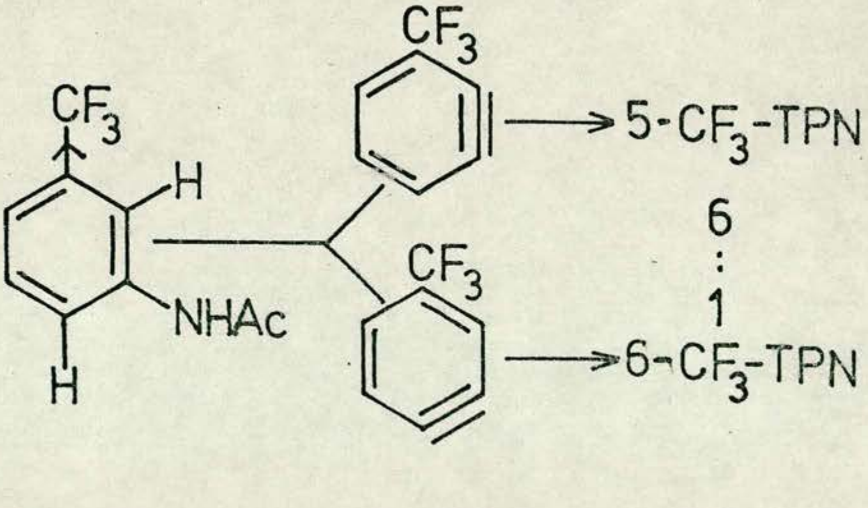


meta-Substituted anilides gave far higher yields of adduct than the corresponding *para*-isomers, which in turn were better than those from the *ortho*-derivatives, most of which gave no aryne adduct at all. The anomalous behaviour of *o*-substituted anilides remains difficult to rationalise. Although *o*-bromo-*N*-nitrosoacetanilide (which gives little or no aryne) rearranges seven times more slowly than the corresponding *meta*-isomer (which gave aryne in good yield), any explanation based on the premise that differences in the rates of decomposition of these acylarylnitrosamines are responsible for these anomalies appears porous in view of the fact that a few ortho-substituted anilides were found to give aryne adducts. Thus 2,5-dimethoxyacetanilide was found to give the corresponding adduct in a respectable yield of 49% although the effect of the meta-methoxy group may have been largely responsible for the high yield. When the substituent was o-ethoxycarbonyl, the aryne adduct was obtained in moderate yield. It may be that this is another example of the special case of steric acceleration of the loss of nitrogen leading to o-ethoxycarbonylbenzyne via the ethoxycarbonyl cation, a situation which also occurs when the t-butyl group is ortho to the diazonium function.[93]



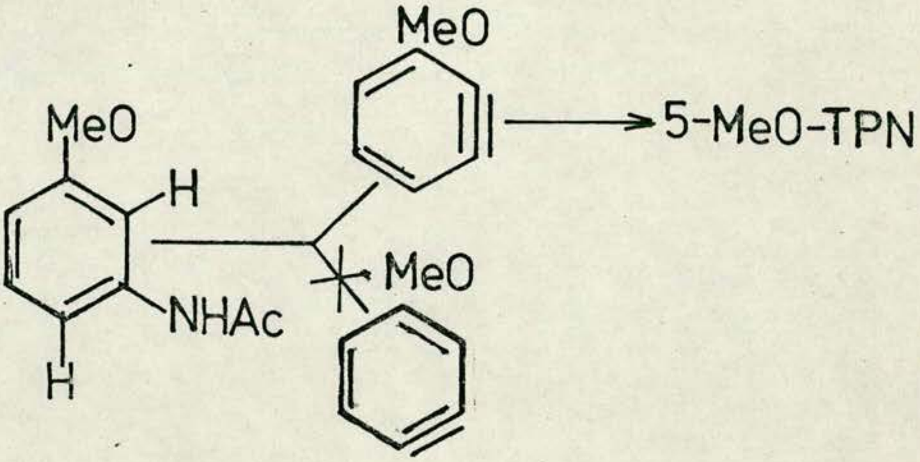
The failure of other anilides with bulky groups (Br, NO_2) in the ortho-position to give adducts is, however, puzzling.[134]

The differences in the isomer ratios of the substituted 1,2,3,4-tetraphenylnaphthalenes (T.P.N.), produced in the reactions of meta-substituted anilides with P.C.B.N. can be explained on consideration of the relative acidities of the hydrogens being lost to form the aryne or arynoid species brought about by the electronic influence of the substituent. Groups can exert mesomeric (M) and/or inductive (I) effects: the former are of second order importance since any charge in an arynoid species will reside in an sp^2 orbital which is orthogonal to the π-electron through which mesomeric influences are transmitted (see 10, page 13), hence inductive effects will predominate. With 3-acetamidobenzotrifluoride the hydrogen on carbon 2 is more acidic than that on carbon 4 since the inductive effect of the trifluoromethyl group (-I) decreases with increasing distance from the central carbon. One would predict, on this basis, that the 3-substituted benzyne be formed preferentially. This prediction was confirmed by experimental observations.

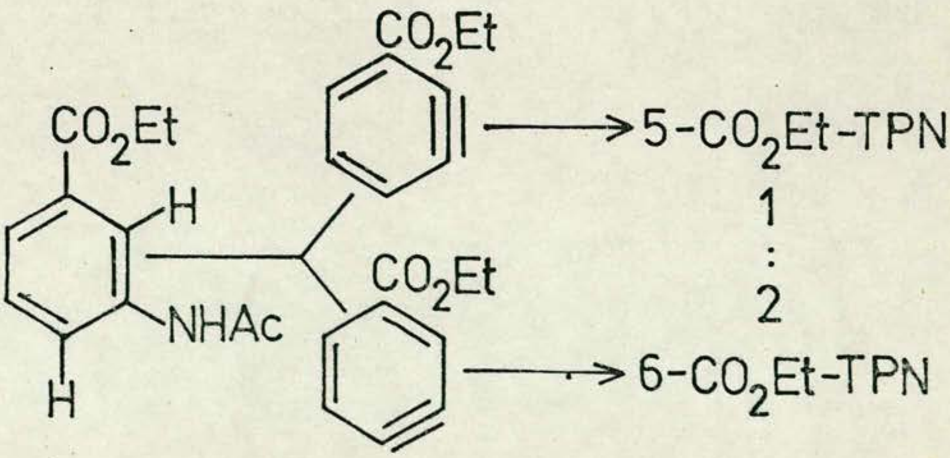


A similar effect occurs with 3-haloacetanilides although in these cases so great is the acidity of the hydrogen on carbon 2 that only the corresponding 5-substituted adduct was obtained.

With 3-methoxyacetanilide where both the inductive (-I) and mesomeric (+M) effects are in operation, although in opposing directions, the former effect was predominant to the extent that only the preferred 3-methoxybenzyne was produced.

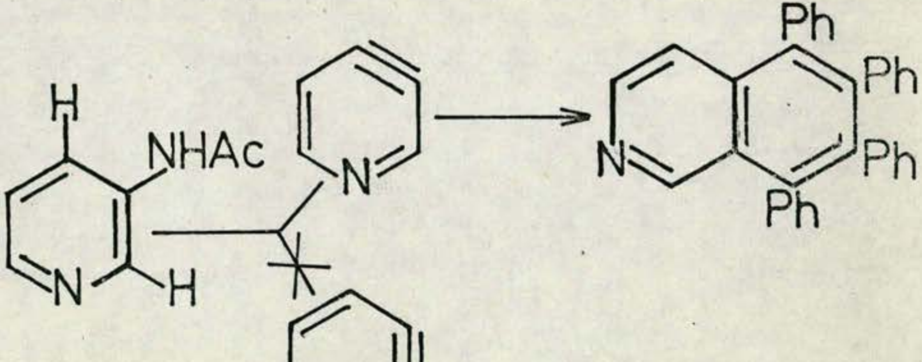


With 3-ethoxycarbonylacetanilide, the two isomers were produced in a ratio at variance with that expected from considerations of the inductive effect of the ethoxycarbonyl group (-I).



However if the rationale advanced for the formation of aryne adduct from o-ethoxycarbonylacetanilide is acceptable, then using similar argument, steric shielding of the hydrogen on carbon 2 from attack by acetate ion by the bulky ethoxycarbonyl group will lead to preferential formation of 4-ethoxycarbonylbenzyne thereby accounting for the observed ratio of isomers.

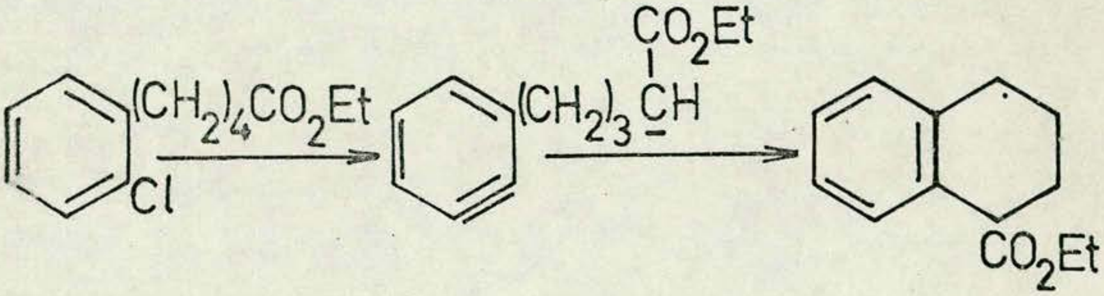
Analogous formation of pyridynes from acetamidopyridines occurred according to the precepts observed for aryne formation: 2-acetamidopyridine was found to give no adduct while 3-acetamidopyridine was found to give the expected 4,5,6,7-tetraphenylisoquinoline.



While isomer ratios can in most cases be satisfactorily rationalised the superior yields of aryne adduct observed with 3-substituted anilides cannot be adequately explained by consideration of only the electronic influences of the substituents, since this phenomenon occurred with both electron withdrawing and electron donating substituents; nor can they be readily explained in terms of faster decomposition of 3-substituted acylnitrosamines. The substituent effects appear to be subject to many complicating factors including the rate of formation, and hence concentration of the diazonium acetate ion pair, the nature of the subsequent deprotonation-protonation equilibrium, and the related question of interconversion of isomeric benzyne precursors in the meta-cases.

b Synthetic applications of this reaction

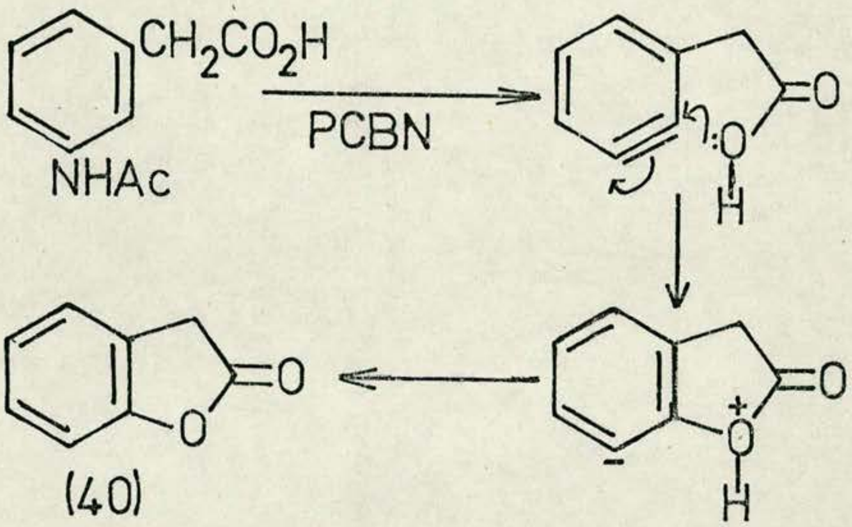
Being an electrophilic species, arynes exhibit a natural proclivity for reaction with nucleophiles of all kinds. A useful synthetic development of the nucleophilic addition reaction has been the generation of arynes containing nucleophiles in an adjacent side chain. The intramolecular nucleophilic addition results in ring closure as exemplified by the following reaction:



This principle was first discussed by Wittig[143] and has been synthetically exploited mainly by the groups of Huisgen and Bunnett.[64] The reactions were usually carried out with potassamide in liquid ammonia, the side chain nucleophile was a carbanion or nitrogen, oxygen, or sulphur anion which was usually produced in situ in the strongly basic medium. In order to effect ring closure, the side chain has to be of adequate length, since the tendency towards ring closure depends largely on achieving a favourable steric arrangement of the nucleophile and the aryne bond. Hence four-, five- and six-membered rings are readily formed but seven-membered rings are more difficult to close and satisfactory yields of larger rings can only be achieved by application of high dilution principles.

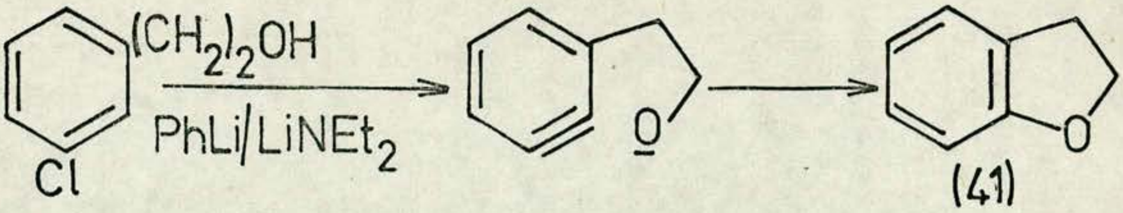
When the aryne is generated by the action of base on a halogeno-compound, the yield of product obtained by intramolecular nucleophilic addition can be depressed, often severely, by the competitive intermolecular addition of the base to the aryne. With the advent of milder routes to arynes which dispensed with the need for a strongly basic medium, this competitive reaction could be effectively circumvented. The development of these routes, outlined earlier in the text, has culminated in a neutral, mild and efficient method of producing arynes from acetanilides. It has been shown that this reaction is of general applicability encompassing a wide range of 3- or 4-substituted anilides with possible extensions to hetarynes. It was interesting therefore to discover if intramolecular nucleophilic addition could be effected to arynes generated by this new method which obviates the need for a strongly basic medium.

The system chosen for investigation was 3-acetamidophenylacetic acid: reaction of this anilide with P.C.B.N. in boiling benzene under conditions of high dilution was expected to give the corresponding aryne which would then undergo nucleophilic attack by the oxygen lone pair, followed by proton transfer.



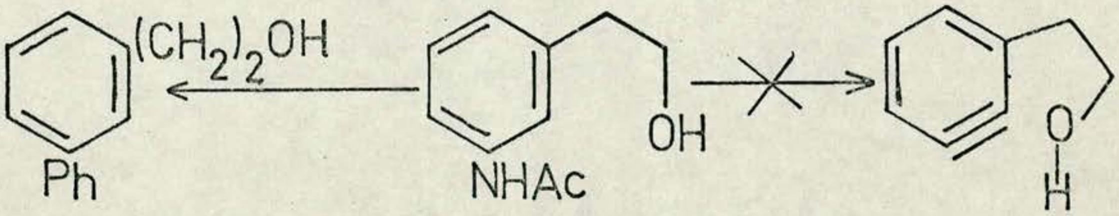
No trace of the cyclised product, 2-cumaranone (40) was observed but only the corresponding radical derived product, 3-phenyl-phenylacetic acid.

An alternative anilide, 3-acetamidophenethyl alcohol was chosen which had already been shown to cyclise under strongly basic conditions to give 2,3-dihydrobenzofuran (41).[144]



(41)

Reaction of this anilide with P.C.B.N. however was found to give only the radical substitution product 3-phenylphenethyl alcohol. No trace of the expected 2,3-dihydrobenzofuran was observed.



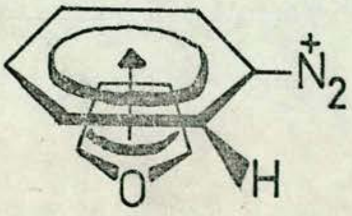
The failure of these methods to effect intramolecular nucleophilic addition can be ascribed simply to the inherent mildness of the reaction conditions employed and the low nucleophilicity of the side chain under these conditions. While these conditions minimised the side reaction of intermolecular nucleophilic addition, the absence of strong base prevented ionisation of either the carboalkoxy or alkoxy groups. Moreover it is known that alternative aryne reactions (e.g. 1,4-cycloaddition) can compete successfully with addition of poor nucleophiles such as carboxylic acids or even methanol or water. So feeble is the nucleophilicity of either the carboalkoxy or alkoxy side chains employed here, that the competing radical phenylation pathway is predominant.

2. THE REACTIONS OF RADICALS WITH ACETYLENES

Cadogan had demonstrated in a series of papers[93-96, 101] the existence of a competitive mode of decomposition open to acylarylnitrosamines, including N-nitrosoacetanilide itself, which involved the intermediacy of arynes. In those cases of nitrosoacylarylamines giving arynes, two classes of behaviour had been identified; a choice between them depending on the timing of the loss of nitrogen from the diazonium cation. One was the special case of a t-butyl group ortho to the diazonium function in which steric acceleration of the loss of nitrogen was predominant with production of an o-t-butylphenyl cation and hence o-t-butylbenzyne, by subsequent proton loss;[95,96] the other case involved prior loss of the proton ortho to the diazonium function (see scheme 15, page 39).

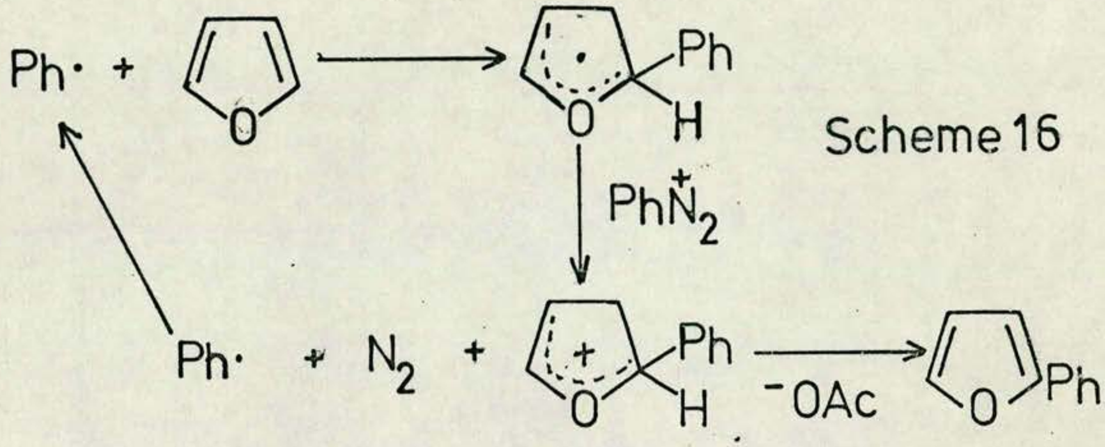
Major anomalies had been observed which disturbed the smooth functionality of scheme 15. It had been reported that decomposition of N-nitrosoacetanilide (NNA) in furan at room temperature gave 2-phenylfuran via radical phenylation of furan[103] and that decomposition of NNA in 2,5-dimethylfuran under similar conditions gave 2-benzyl-5-methylfuran instead of the respective aryne adducts.[96] In addition Cook[99] observed that when authentic benzyne (from anthranilic acid-pentyl nitrite) was generated in the presence of dimethyl acetylenedicarboxylate, the product obtained was 5,6,11,12-tetramethoxycarbonyl [a,e] cyclooctatetraene (37) whereas the product from the decomposition of NNA in dimethyl acetylenedicarboxylate was 1,2,3,4-tetramethoxycarbonyl naphthalene (38) (see also scheme 14). Before the generality of scheme 15 could be accepted it was necessary to resolve these anomalies.

Although the absence of a furan-benzyne adduct in reactions carried out at room temperature had been confirmed, Mitchell[97] later obtained a low yield (5%) of the adduct from the decomposition of NNA in boiling furan, a result which was in accord with the observations of Ruchardt et al.[98] Furthermore, it was known that the presence of furan suppressed the formation of benzyne adducts with other aryne traps[99] and that the rate ratio $K^{\text{furan}}_{\text{benzene}}$ for the phenylation of equimolar mixtures of furan and benzene was high for those radical sources incorporating the benzenediazonium cation as radical precursor. Mitchell therefore concluded that in the decomposition of NNA in furan either the benzene diazonium cation formed a π-complex with furan (42), thus decreasing the acidity of the proton ortho to the diazonium group and/or that a redox scheme (scheme 16),

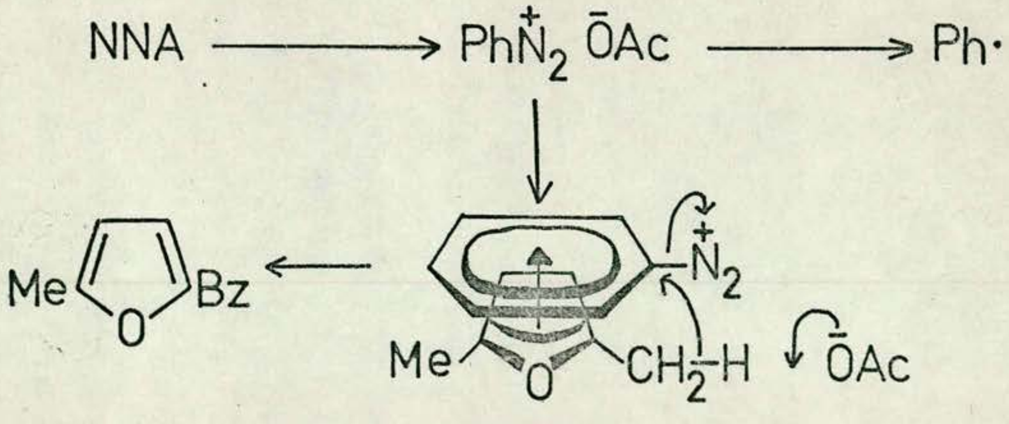


(42)

similar to that proposed for the decomposition of NNA in ether, applied here.[97]



Mitchell repeated the decomposition of NNA in 2,5-dimethylfuran, this time in boiling benzene, and was able to detect the presence of the aryne adduct 1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalene, albeit in small amounts. To account for the unexpected side chain phenylation product, 2-benzyl-5-methylfuran, Cadogan[145] suggested formation of a π-complex (43) between the electron-rich 2,5-dimethylfuran and the benzene diazonium cation.

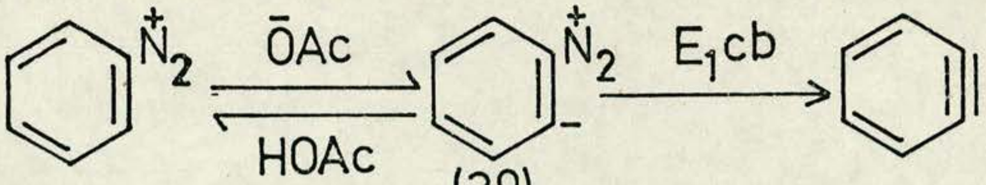


(43)

Formation of a π-complex enhanced the acidity of the methyl proton which was removed by the acetate ion. This led to the more strongly complexed 5-methylfurfuryl carbanion which then reacted with the adjacent benzene diazonium cation by nucleophilic displacement to give the observed 2-benzyl-5-methylfuran.

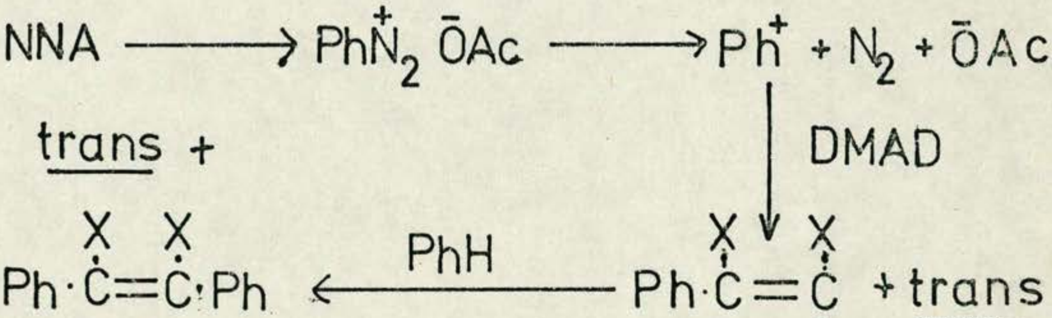
Thus the divergence from normalcy, experienced with furan and 2,5-dimethylfuran, had been successfully rationalised in terms harmonious with the decomposition mechanism in scheme 15.

The anomaly presented by the reaction of NNA with dimethyl acetylenedicarboxylate (DMAD) in benzene was rationalised[99,101] by invoking the reaction of the arynoid betaine (39) with two molecules of DMAD to give the substituted naphthalene (38) (see scheme 14, page 38). While this assumption was in keeping with the general scheme for the production of arynes from acylarylnitrosamines it had important ramifications concerning the mode of decomposition of benzenediazonium cation to benzyne. Thus while Ruchardt[100] favoured an E_2 mechanism involving concerted loss of the <u>ortho</u> proton and diazo function, Cook's assertion required that benzyne be formed from the benzenediazonium cation by an E_1cb mechanism:



(39)

In addition to the substituted naphthalene, Cook had also obtained biphenyl and a mixture of <u>cis</u>- and <u>trans</u>-dimethyl diphenylmaleates (44). Biphenyl had obviously been produced <u>via</u> radical arylation of benzene, but the failure to detect either the naphthalene tetraester or the <u>cis</u>- and <u>trans</u>-maleates in a similar reaction with phenylazotriphenylmethane led Cook to postulate formation of the maleates <u>via</u> an ionic rather than radical pathway (scheme 17).[99]

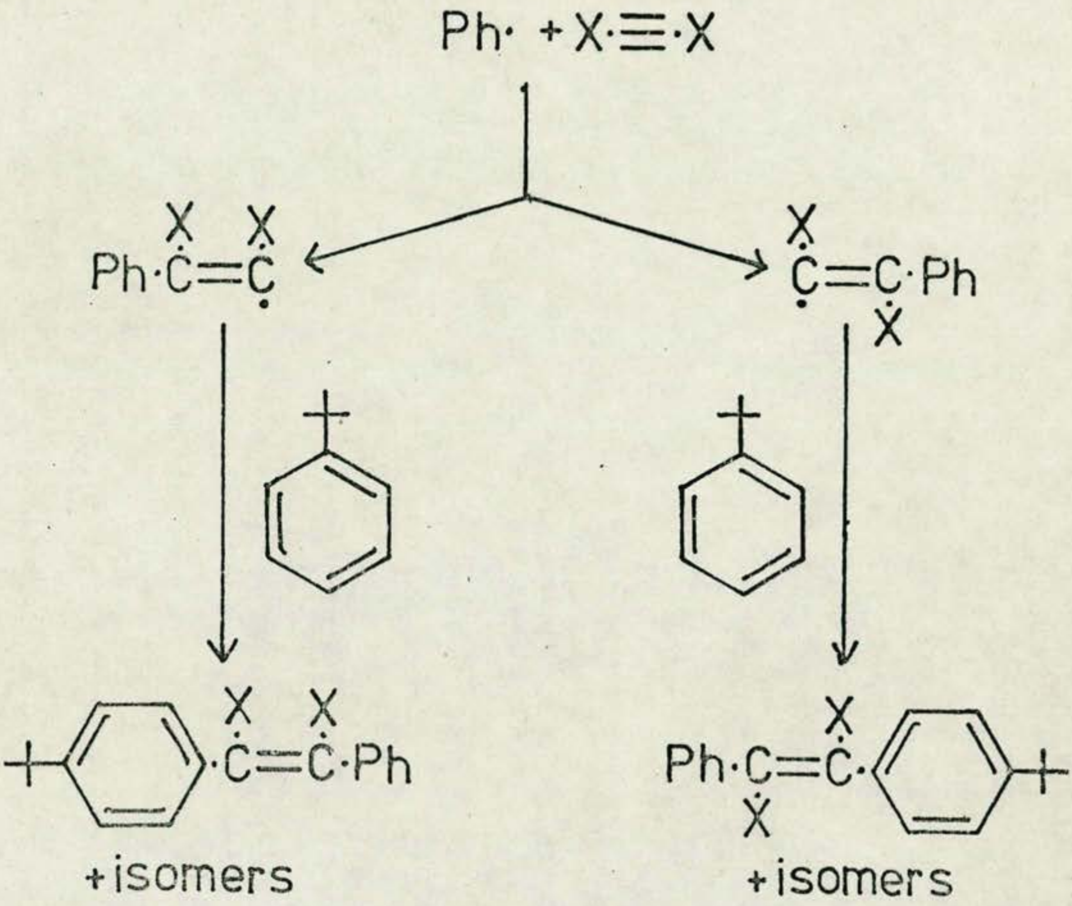


(44)

Scheme 17

Although providing a rationale for the experimental observations, the scheme suggested by Cook, whereby three different intermediates were responsible for the reaction products, was aesthetically unsatisfactory. A more cogent argument however, against the likelihood of scheme 17, was that the phenylcarbonium ion would not be expected to attack the electron deficient carbon of dimethyl acetylenedicarboxylate.

In an effort to elucidate the mechanism of this reaction, attention was focussed on the mode of formation of the cis and trans maleates. On the premise that these maleates might logically be formed *via* phenyl radicals, benzoyl peroxide was allowed to decompose in benzene containing the acetylene trap. This reaction was found to give a multicomponent mixture. Two of the products however were found to have g.l.c. retention times identical to those for authentic *cis* and *trans* maleates; in addition these two products both had the correct parent ion at $^m/e$ 296. Further proof as to the radical nature of this reaction was afforded when, from the decomposition of benzoyl peroxide in *t*-butylbenzene containing DMAD, a mixture of four products was isolated. Each had a parent ion at $^m/e$ 352 and thus corresponded to a mixture of isomeric *cis*- and *trans*-dimethyl-1-phenyl-2-(*t*-butylphenyl) maleates. An identical mixture was obtained on decomposition of NNA in *t*-butylbenzene containing DMAD.



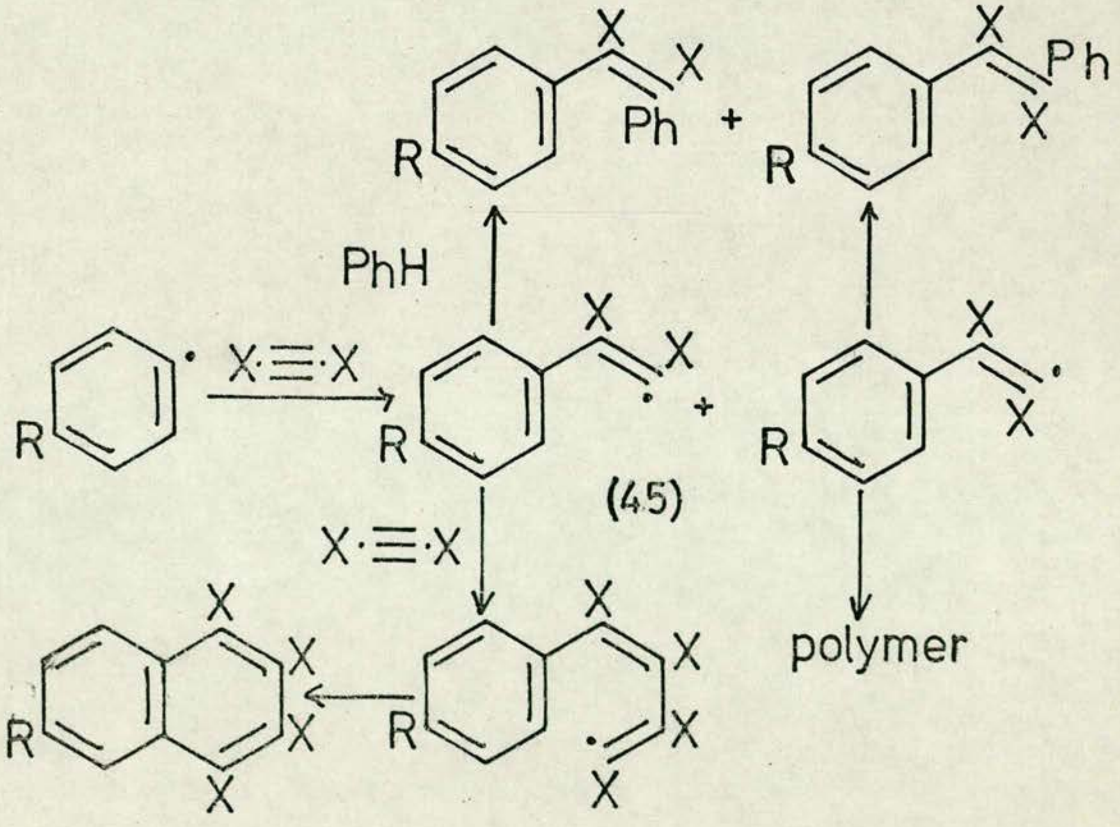
Congruent with these experiments, were others designed to confirm the intermediacy of the betaine (39) in the production of naphthalene tetraester. Kinetic studies on the reaction of P.C.B.N. with acetanilide had proved that nitrosation and decomposition of the nitrosamine were extremely rapid, while trapping experiments with tetracyclone had also shown that the reaction was a more efficient generator of benzyne than decomposition of NNA.[134] It seemed logical to assume that this reaction would then be more efficient in producing the betaine and would consequently lead to higher yields of the naphthalene tetraester.

It was puzzling therefore to find that reaction of P.C.B.N.-acetanilide in boiling benzene containing DMAD consistently gave very low yields of the naphthalene tetraester (maximum of 4% cf. 20% from NNA). The yield of maleates was also reduced by half. Since the conditions employed minimised the production of phenyl radicals, and yet were coincidental with a drastic reduction in the yield of tetraester it became apparent that formation of the tetraester might also involve phenyl radicals. In accord with this prediction reaction of benzoyl peroxide with DMAD at 80° was found to give 1,2,3,4-tetramethoxycarbonylnaphthalene (50m/100mol peroxide). Similarly, 4-methyl and 4-bromobenzoyl peroxides gave 6-methyl and 6-bromo-1,2,3,4-tetramethoxycarbonylnaphthalene respectively.

It has therefore been shown unequivocally that all the products from the decomposition of NNA in dimethyl acetylenedicarboxylate were formed through the intermediacy of phenyl radicals thereby ruling out the possibility, tentatively advanced previously,[99,101] of the intermediacy of a betaine (39) in this reaction (scheme 15).

Recent work on the mechanisms involved in the decomposition of arenediazonium ions by Buxton and Heaney[146] has suggested that benzenediazonium ion is in equilibrium with the betaine and that benzyne is formed from this cation by an E_1cb mechanism. However similar work in our laboratories[147] has refuted the claims of these workers and at present there is no firm experimental evidence which supports the existence of the betaine. Until more concrete evidence is available, the precise mode of decomposition of benzenediazonium ion to benzyne must remain in the realm of speculation.

As demonstrated above, recent investigations into the precise mode of decomposition of NNA have led to the discovery of a novel aromatic annelation reaction involving reaction of aryl radicals with two molecules of DMAD. It is suggested that the reaction proceeds as in scheme 18 <u>via</u> addition of an aryl radical to DMAD, followed by further addition of the first formed styryl radical (45) to another molecule of DMAD with subsequent cyclisation of the phenylbutadienyl radical.



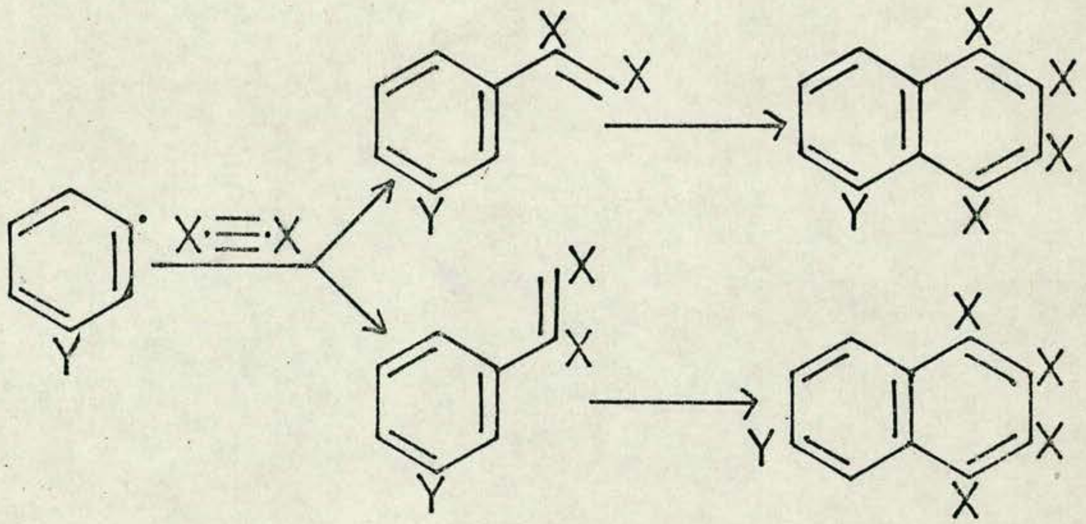
Scheme 18

It followed that aryl radicals were involved since different sources of radicals (NNA, acetanilide-P.C.B.N., t-butyl peroxide-triphenyl arsine) also gave the naphthalene tetraester albeit in lower yields but it is interesting at this juncture to note the failure of phenylazotriphenylmethane to give the adduct. This was presumably due to the combination of the intermediate 1,2-dimethoxycarbonylstyryl radical (45) with the long-lived triphenylmethyl radical. That this radical could be intercepted easily, was also demonstrated when dilution of the reaction mixture with benzene was found to give cis and trans dimethyl-1,2-diphenylmaleate (scheme 18) as discussed earlier (page 124).

Although the stereochemistry of radical addition to acetylenes can be said to be mainly trans, leading to cis vinyl radicals[148] stereospecificity is generally lower than with ionic additions and little is known about either the rate of equilibration of vinyl radicals or the activation energy of the radical inversion process.

In this connection it is noteworthy that the optimum yield of 1,2,3,4-tetramethoxycarbonylnaphthalene obtained was that theoretically possible, assuming equal chance of formation of cis and trans-styryl or phenylbutadienyl radicals and the absence of cis-trans isomerism in each step of the reaction.

The scope of this aromatic annelation reaction is outlined in Table III, from which the following points emerge (1). The yield of annelated product from benzoyl peroxide is much greater than that obtained from other aroyl peroxides. (ii) The yields of tetraesters obtained from meta- and para-substituted peroxides are comparable (ca 20m/100mol peroxide) and are independent of the electronic nature of the substuent. (iii) ortho-Substituted peroxides do not appear to give any adduct. (iv) With meta-substituted aroyl peroxides two isomers are possible, the 5- and 6-substituted tetramethoxycarbonylnaphthalenes (T.M.N.)



In all cases the 5-substituted isomer is formed preferentially (Table V).

TABLE V

Isomer ratios of 5- and 6-substituted T.M.N.'s obtained from reaction of meta-substituted aroyl peroxides with DMAD

Radical (3Y-$C_6H_4^{\cdot}$)	Ratio of Products
Y	5Y-TMN : 6Y-TMN
Cl	2.7
Br	2.7
Me	2.0

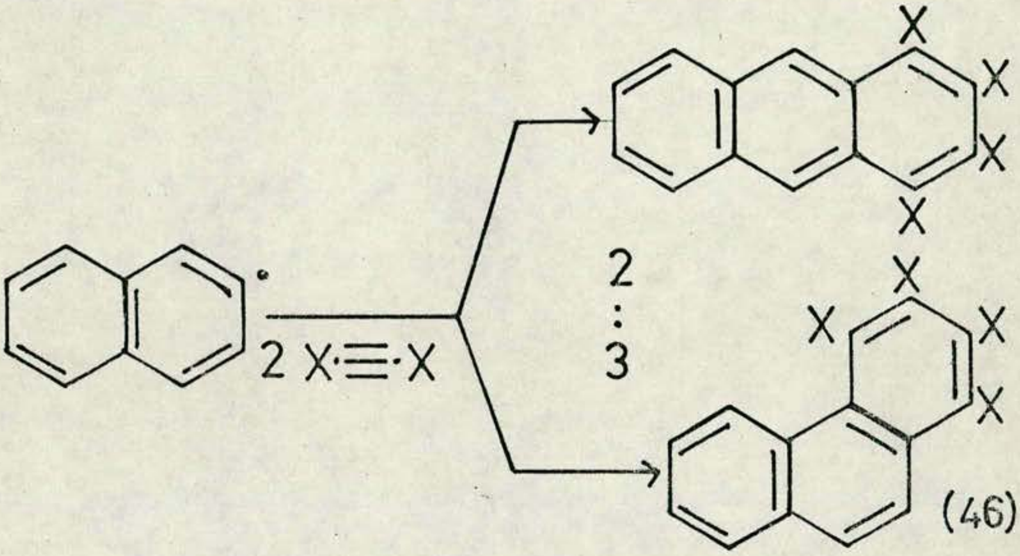
These observations indicate that intramolecular attack takes place more readily *ortho* rather than *para* to the substituent and thus support the concept of radical participation, it being well known that aromatic radical substitution follows this pattern.[149]

Although the overall selectivity of the reaction is small, this being in keeping with the radical nature of the reaction, it is puzzling to find such a large discrepancy between yields obtained with phenyl and substituted phenyl radicals. *A priori* one might expect the 4-tolyl radical to attack the electron-deficient triple bond system more readily than the phenyl radical. The fact that lower yields are recorded with all substituents and not with just electron withdrawing substituents remains to be explained. The discrepancy cannot be attributed to differences in the rate of decomposition of aroyl peroxides since, while electron withdrawing groups in the meta and para positions generally retard decomposition, the reverse is true for electron donating groups.[150] In any case the differences in decomposition rates seem to be too insignificant to be responsible for such a large effect. The failure of o-nitrobenzoyl peroxide to give any product may be related to the fact that it decomposes considerably faster than other aroyl peroxides,[151] although the reason for this connection is not immediately obvious.

When the mixed peroxide benzoyl-p-nitrobenzoyl peroxide was reacted with DMAD, a mixture of the respective annelated products 1,2,3,4-tetramethoxycarbonylnapthalene and 6-nitro-1,2,3,4-tetramethoxycarbonylnaphthalene was obtained. The product ratio was 2:1 respectively, again indicating that the phenyl radical reacts preferentially, however the overall yield of the reaction was only 20m/100mol peroxide. It seems, therefore, that substitution in the phenyl radical effectively deactivates it for this reaction a fact which is at variance with the accepted tenets of aromatic radical reactivity.

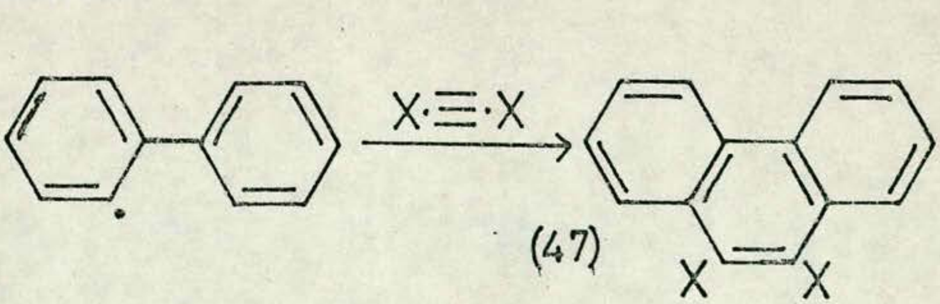
Extension of this reaction to polycyclic, heterocyclic and other aryl radicals met with varying success.

The 2-naphthoyl radical was found to react in similar fashion to give a mixture of the corresponding carbocyclic tetraesters, but in such low yield (6m/100m peroxide) as to vitiate its usefulness. The major isomer was taken to be 1,2,3,4-tetramethoxycarbonylphenanthrene (46), derived via intramolecular attack at the favoured ortho position.



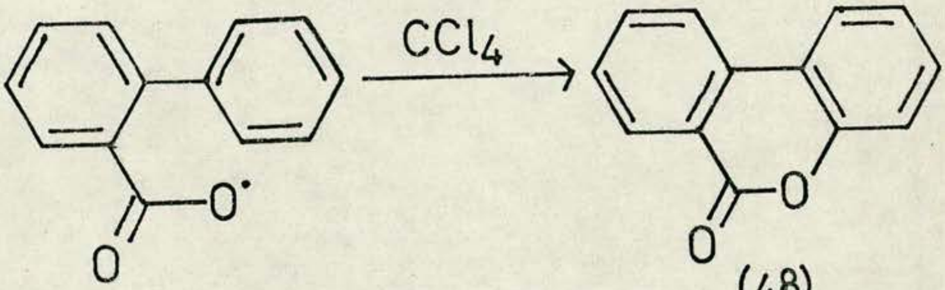
(46)

Bis-o-phenylbenzoyl peroxide was reacted with DMAD in an attempt to effect cyclization after the first addition and thus minimise the incidence of polymer formation.



(47)

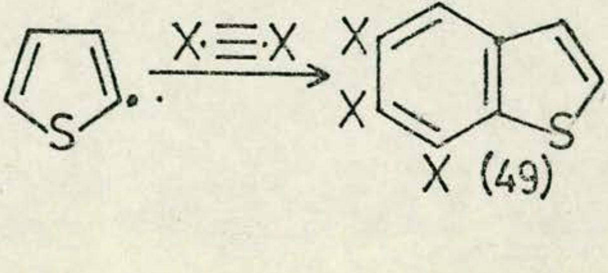
No trace of the expected 9,10-dimethoxycarbonylphenanthrene (47) was observed, instead the only recognisable product was 3,4-benzocoumarin (48) (37m/100mol peroxide). This product had been obtained from decomposition of the peroxide at 80° in acetic acid[152] or carbon tetrachloride.[152,153] Kenner et. al had shown that decarboxylation of the benzoyloxy radical occurred in only 26% extent but that intramolecular substitution occurred in 38% yield.



(48)

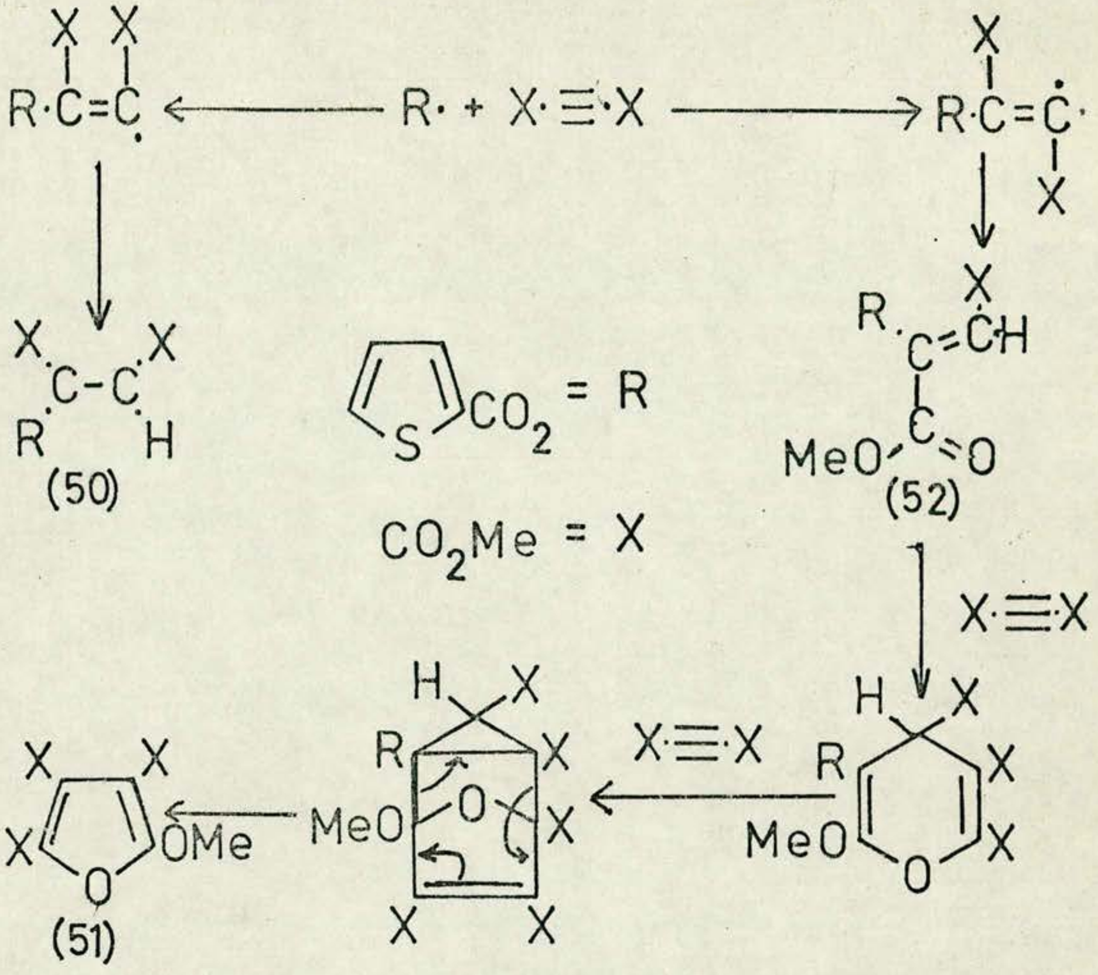
In view of the conformation of the o-phenylbenzoyloxy radical, the reason for the failure of this reaction becomes apparent.

As a continuation of this work on radical addition to acetylenes, the reactions of heterocyclic peroxides were next investigated. Thenoyl peroxide was allowed to decompose in DMAD, in anticipation of the thenyl radical undergoing an analogous annelation reaction leading to 49.



(49)

Two products, neither of which possessed structure 49, were isolated: the major product was a 1:1 adduct of the thenoyl rather than thenyl radical, identified as <u>cis</u>-dimethylthenoylmaleate (50) from the usual physical data. The <u>cis</u> structure was assigned from comparison of the n.m.r. spectrum with that of the known <u>cis</u>-dimethyl-1,2-diphenylmaleate. The minor product of the reaction was identified as 2,3,4-trimethoxycarbonyl-5-methoxyfuran (51) by comparison of physical characteristics with those published for the authenticated compound.[140] Previous workers had obtained this compound from copyrolysis of DMAD with methyl fumarate (although not from methyl maleate) and had outlined a possible mechanism for its formation.[140] While the origin of this unusual product in the reaction of thenoyl peroxide with DMAD is rather obscure, a possible mechanism for its formation is advanced (scheme 19).



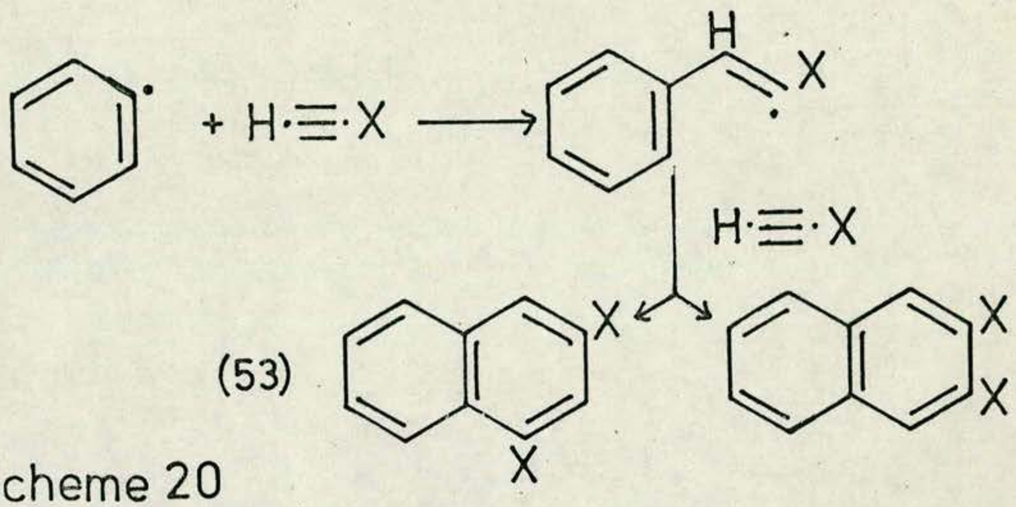
Scheme 19

As can be seen, this scheme accounts not only for product (51) but also for the hitherto puzzling lack of the *trans*-dimethyl-1,2-diphenylmaleate (52). It requires the reaction of (52) with DMAD in a Diels-Alder type reaction, followed by cycloaddition of a second molecule of DMAD to this product. The intermediate thus formed undergoes an electrocyclic ring opening with extrusion of the cyclopropene moiety to give (51).

That these products were derived from the thenoyl radical is in accord with the observations of several workers[117,154] who reported 2-thenoic acid as the major product from the decomposition of thenoyl peroxide in aromatic solvents, together with very low yields of carbon dioxide, suggesting little or no decarboxylation of the thenoyl radical.

Similar reaction with furoyl peroxide gave, in addition to much polymeric material, a low yield of a multicomponent mixture. The failure of this peroxide to give products analogous to those obtained with thenoyl peroxide may be ascribed to the greater instability and reactivity of furoyl peroxide.[118]

Experiments were designed to test if these reactions of radicals with DMAD were peculiar to that acetylene, or if they represented a general reaction of acetylenes. Reaction of benzoyl peroxide with ethyl propiolate under identical conditions was found to give a mixture of at least two disubstituted naphthalenes in reasonable yield (27m/100m peroxide). One of the products was identified as 1,3-diethoxycarbonylnaphthalene (53) on the basis of there being two meta-coupled doublets at τ, 1.01-1.05 in the n.m.r. spectrum. It was not possible to prove conclusively from the spectrum which of the other isomers were present. However, attack by the phenyl radical would be expected to occur at the carbon bearing the hydrogen, since the styryl radical thus formed could be effectively stabilised by the ethoxycarbonyl group (scheme 20). Addition of the styryl radical to a second molecule of DMAD would then give the expected 1,3 diester (53) and also the 2,3 diester



Scheme 20

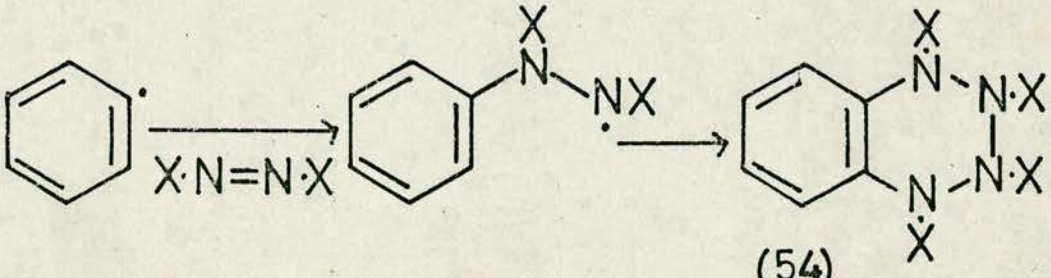
The appearance of a sharp singlet at τ, 1.27 is in accord with the aromatic hydrogens being on the α position of the naphthalene ring.

When benzoyl peroxide was reacted with phenylacetylene, polymerisation occurred very rapidly to the exclusion of the annelation reaction. Similarly, with acetylenes containing readily abstractable hydrogens <u>viz</u> 1-octyne, oct-4-yne, and 1-hexyne, large amounts of polymeric tars were obtained together with some benzoic acid (30m/100m peroxide) in each case. From these results it would seem that annelation occurs best when the acetylene contains strong electron withdrawing groups.

In conclusion, we can now present a correct mechanism for the formation of 1,2,3,4-tetramethoxycarbonylnaphthalene in the decomposition of NNA in dimethyl acetylenedicarboxylate and in doing so have described an easily effected aromatic annelation reaction involving reaction of an aryl radical with two molecules of dimethyl acetylenedicarboxylate. The scope of this reaction appears to be restricted by the reluctance of heterocyclic peroxides to undergo decarboxylation, by limitations in the choice of suitable acetylenes and by the propensity of this system to give polymeric byproducts.

3. THE REACTIONS OF RADICALS WITH AZO COMPOUNDS

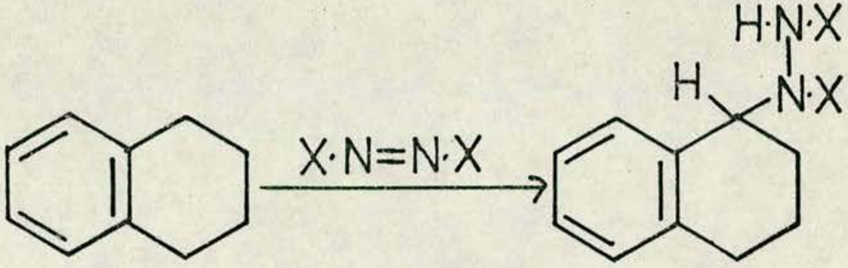
As we have seen, aryl radicals were shown to undergo an annelation reaction with dimethyl acetylenedicarboxylate. This electron deficient acetylene has found wide use in its role as a powerful dienophile, undergoing Diels-Alder reactions with consummate ease, even at low temperatures. The analogous nitrogen compound methyl azodiformate is also noted for its powerful dienophilic character, and many azo compounds containing electron withdrawing groups have proved useful in Diels-Alder syntheses of heterocyclic systems, in fact this famous reaction was discovered with these azo diesters.[155,156] It seemed logical to extend this reaction of radicals with acetylenes to azo compounds.



(54)

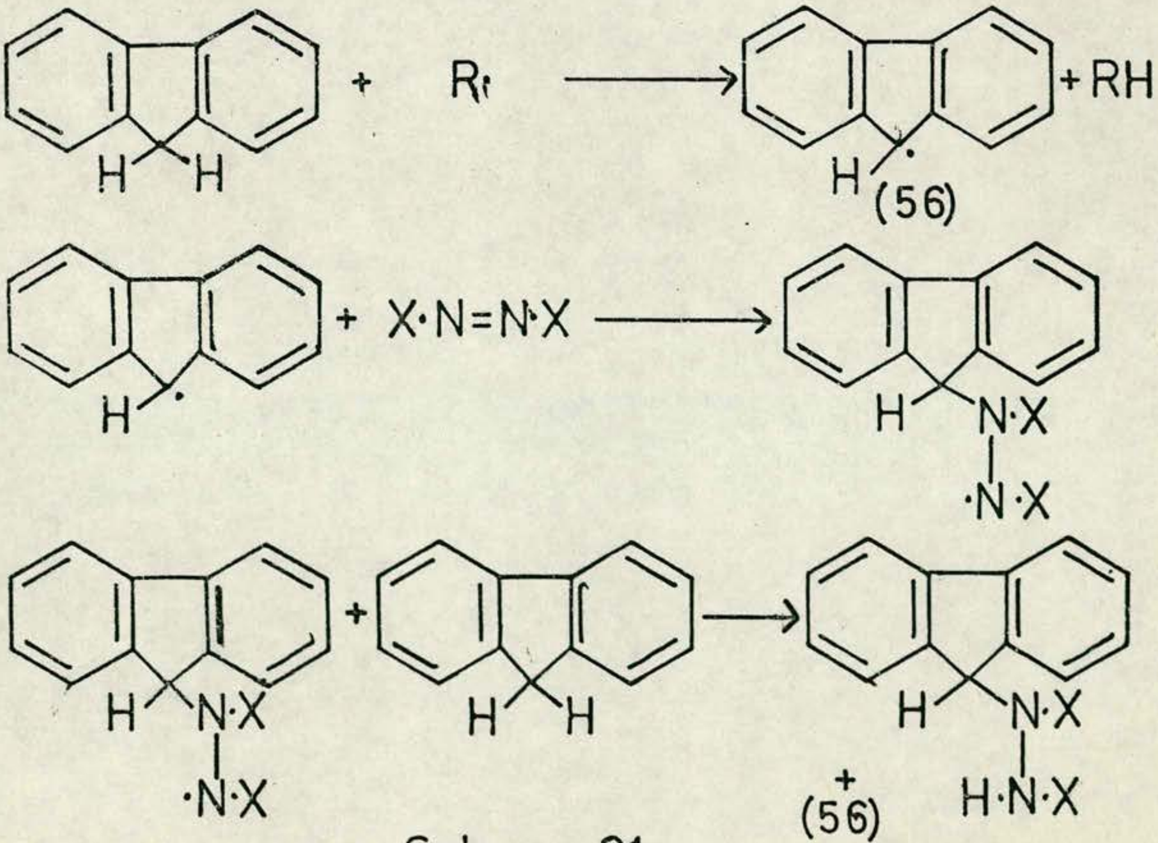
Analogous reaction of phenyl radicals with dimethyl azodiformate should lead to a substituted benzotetrazine, 1,2,3,4-tetramethoxycarbonyl-1,2,3,4-tetrahydrobenzotetrazine (54) an unknown member of the esoteric tetrahydrobenzotetrazine series.[157]

Although the dienophilic and electrophilic properties of esters of azodiformic acid have been known for some time and are well documented,[34a] little is known about the homolytic reactions of these compounds. Alder *et. al*[158] found that in the absence of acid and under thermal conditions, 1,2,3,4-tetrahydronaphthalene was attacked by the ester in the saturated ring with formation of the hydrazine (54).



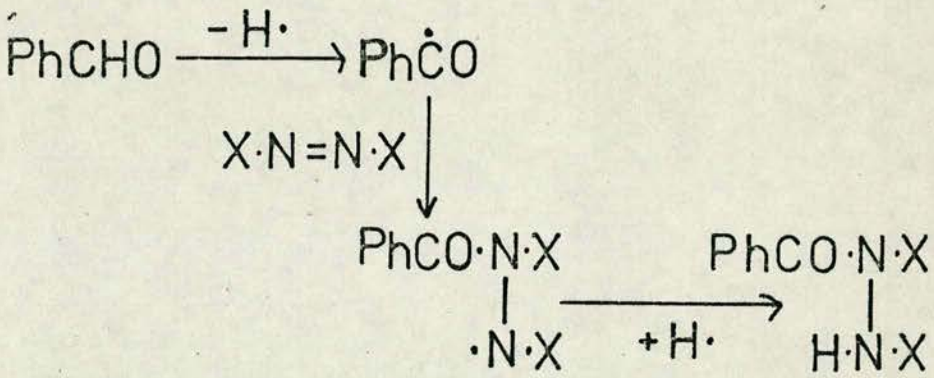
(55)

Experiments with initiators such as azobisisobutyronitrile among others, and inhibitors led Horner[159] to postulate a radical mechanism in this and similar reactions. Huisgen[100] also postulated a radical chain mechanism (scheme 21) to account for the observed products from the reaction of ethyl azodiformate with fluorene



Scheme 21

Furthermore, the thermal addition of ethyl azodiformate to cyclic olefins gave a 1:1 addition product and free radical mechanism was also suggested by Huisgen[161] to account for the effect of radical initiators and inhibitors on these reactions. More recently, work on the thermal and photochemical additions of azo esters to olefins and dienes has confirmed the radical nature of the addition.[162] The reaction of azo esters with aldehydes[163] and the substitution of olefins in the 'allyl position'[158] also proceed by radical routes.

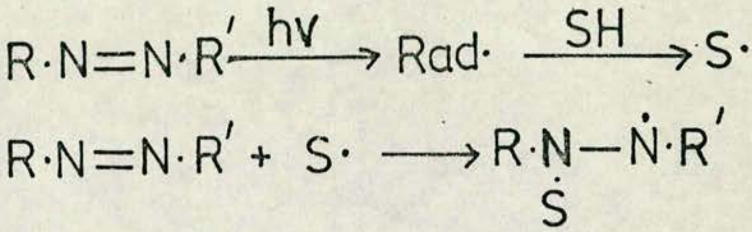


Further evidence for the radical reactivity of azodiformic esters comes from their ready acceptance of hydrogen, capable as they are of dehydrogenating hydriodic acid,[160] hydroquinone[164] and substituted hydrazines.[165]

In the past year there has been a renewed interest in the nature of the intermediates formed from radical additions to azo compounds and the nature of the radical species produced by photolysis of azodiformic esters has proved particularly controversial. Stilbs[166] suggested that the species produced from symmetric azodiformic esters were diazenyl radicals, formed by scission of the

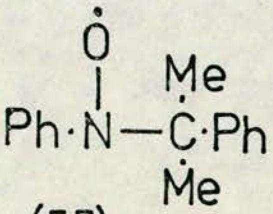
$$X\text{-}N{=}N\text{-}X \xrightarrow{h\nu} X\text{-}N{=}N\cdot + (R\cdot)$$

nitrogen-carbon bond. Marnett et. al.[167] rejected Stilb's diazenyl radical assignment and concluded from photolytic studies on symmetrical azo compounds that hydrazyl radicals were produced by addition of a solvent derived radical to the starting azo compound.



$$R\cdot N{=}N\cdot R' \xrightarrow{h\nu} Rad\cdot \xrightarrow{SH} S\cdot$$
$$R\cdot N{=}N\cdot R' + S\cdot \longrightarrow R\cdot \underset{\dot{S}}{N}{-}\dot{N}\cdot R'$$

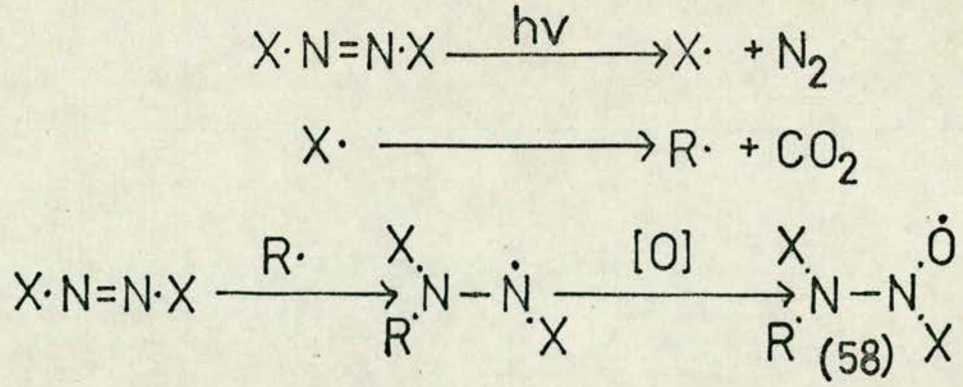
Unfortunately, Marnett used as an example of an authentic hydrazyl radical a species which Ingold[168a] showed to be phenyl cumyl nitroxide (57).



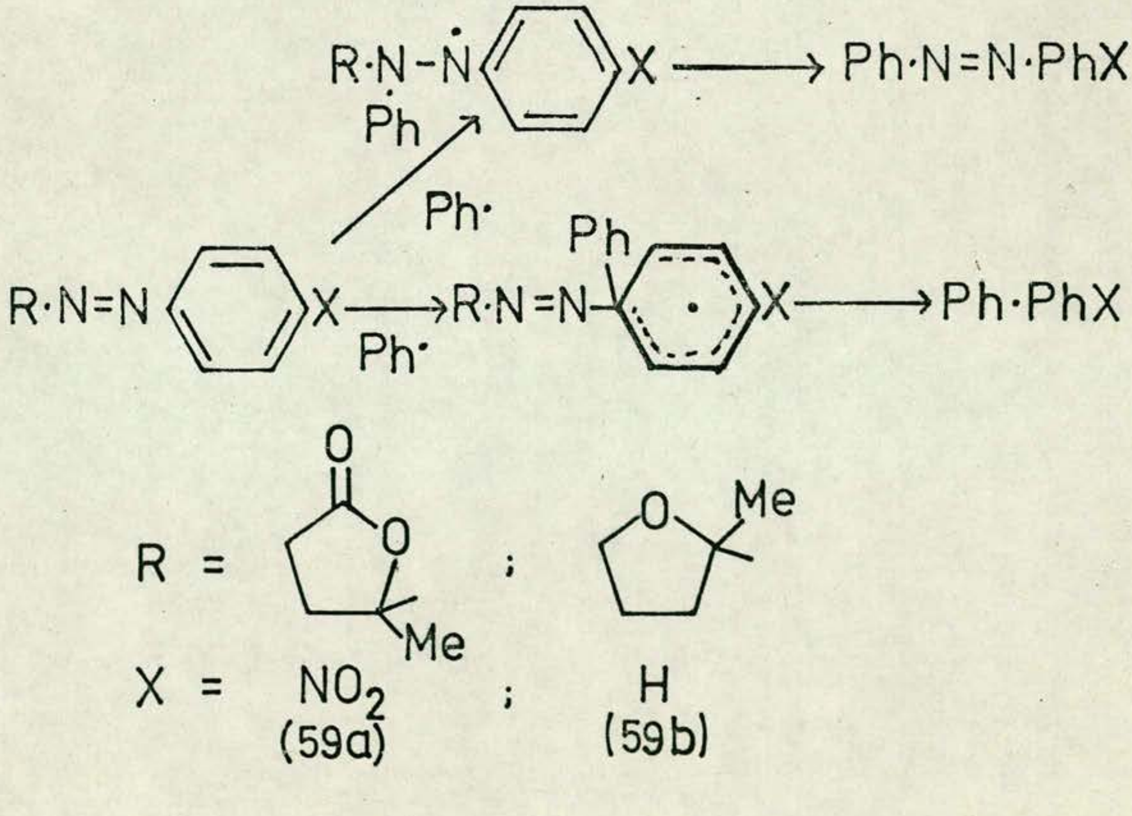
$$Ph\cdot \overset{\dot{O}}{N}{-}\underset{Me}{\overset{Me}{C}}\cdot Ph$$

(57)

Ingold[168b] presented further proof that the radicals obtained by both Stilbs and Marnett were, in fact, hydrazoxyl radicals (58) by comparison of the characteristics of these radicals with authentic hydrazoxyl radicals. He concluded that these radicals were formed by a process similar to that outlined below.



While radical additions to azo compounds were found to be commonplace, radical substitution reactions were unknown. The first example of such a reaction was reported recently by Lui and Warkentin[169] who found that treatment of γ-(4-nitrophenylazo)-γ-valerolactone (59a) with benzoyl peroxide in benzene at 85° gave 4-nitroazobenzene and 4-nitrobiphenyl. Similarly α-methyl-α-phenylazotetrahydrofuran (59b) was found to give azobenzene. Radical substitution at both azo nitrogen and at nitrogen-bearing benzeneoid carbons were the suggested mechanisms.



(59a) (59b)

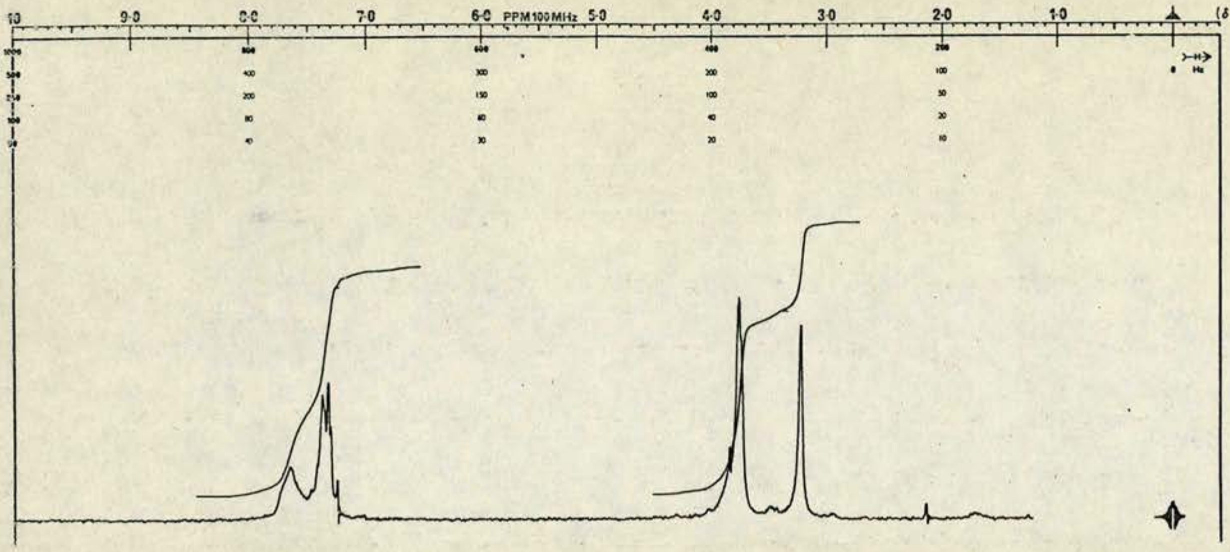


Fig. I. N.m.r. spectrum of 1,4 diphenyl-1,2,3,4-tetramethoxycarbonyltetrazane.

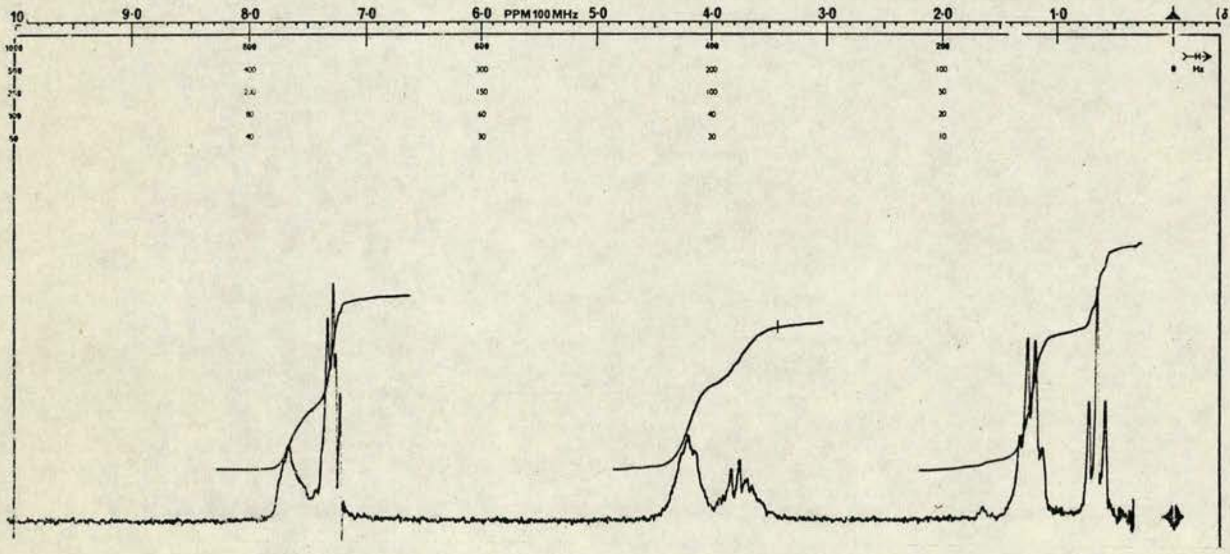


Fig. II. N.m.r. spectrum of 1,4 diphenyl-1,2,3,4-tetraethoxycarbonyltetrazane

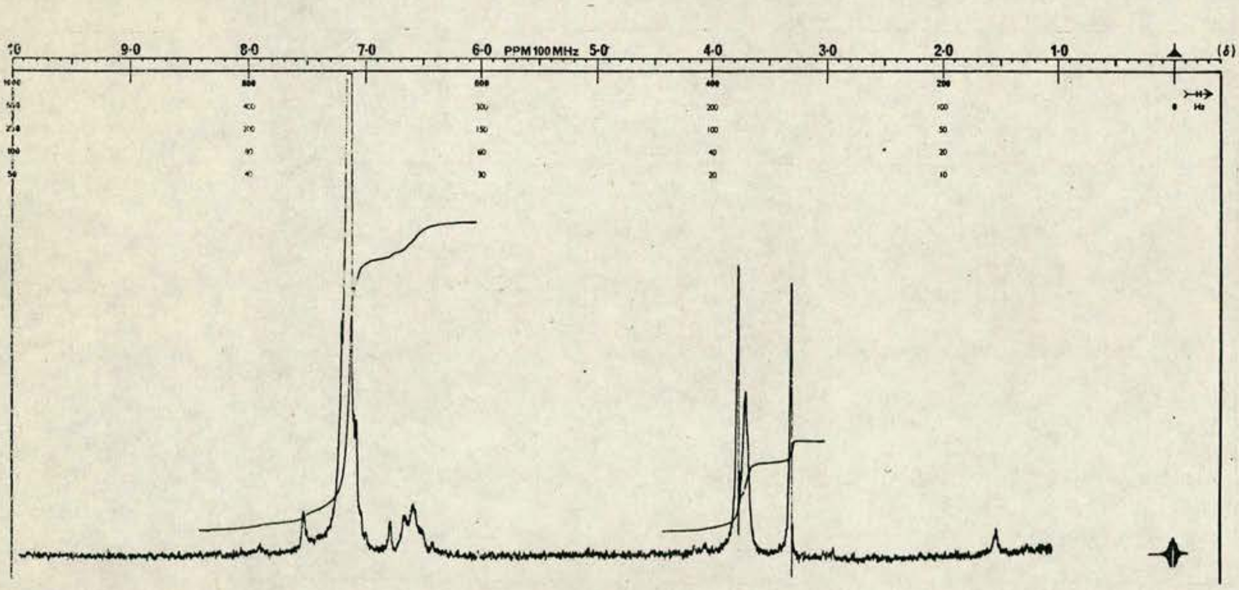
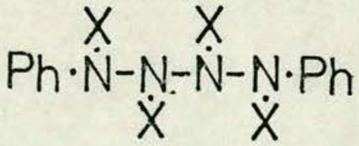


Fig. III. N.m.r. spectrum of N,N'-dimethoxycarbonyl-N'-triphenylmethyl-N-phenyl hydrazine.

The general pattern of reactivity which has emerged from radical additions to azo esters is addition by the radical to the azo bond to form an intermediate hydrazyl radical, followed by abstraction of a hydrogen atom to give a substituted hydrazine. In this work, to encourage addition of the first formed hydrazyl radical to a second molecule of the azo ester, it was decided to dispense with solvent, thereby optimising the probability of a second addition and minimising that of the abstraction step.

Accordingly benzoyl peroxide was decomposed in neat dimethyl azodiformate at 80°. Work up gave a crystalline solid, in good yield (69%) which was not the expected 1:2 adduct, 1,2,3,4-tetrahydromethoxycarbonyl-1,2,3,4-tetrahydrobenzotetrazine (54). The physical characteristics (analysis, exact mass, etc.) suggested a dimeric form of the 1:1 adduct, a fully substituted tetrazane, 1,4-diphenyl-1,2,3,4-tetramethoxycarbonyltetrazane (60).



$$Ph\cdot\overset{X}{N}-\underset{X}{N}-\overset{X}{N}-\underset{X}{N}\cdot Ph$$

$X = CO_2Me$ (60)
$X = CO_2Et$ (61)

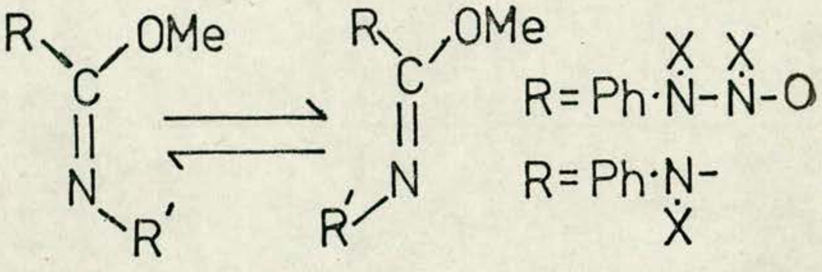
A complicating factor in the structure determination was the 'H n.m.r. spectrum of the product (Fig. I). As expected, there were two methyl singlets at τ, 6.2 and 6.8; both singlets were very broad, possibly indicating a number of almost equivalent absorptions under each signal. The integral tracings of the respective methyl signals gave a ratio of 2:1. A variable temperature study of the n.m.r. spectrum gave the maximum ratio as 2:1 at all temperatures between -60° and 80°; between 80-140° the ratio converged to unity, reaching a minimum of 1.2:1 at 140° and all temperatures up to 200° (Table VI). At no stage did the signals coalesce, although the separation between the signals had decreased by 24Hz, from 54Hz at 28° to 30Hz at 200°.

TABLE VI

Variation of the ratios of methyl absorptions in tetrazanes 60 and 61 with temperature

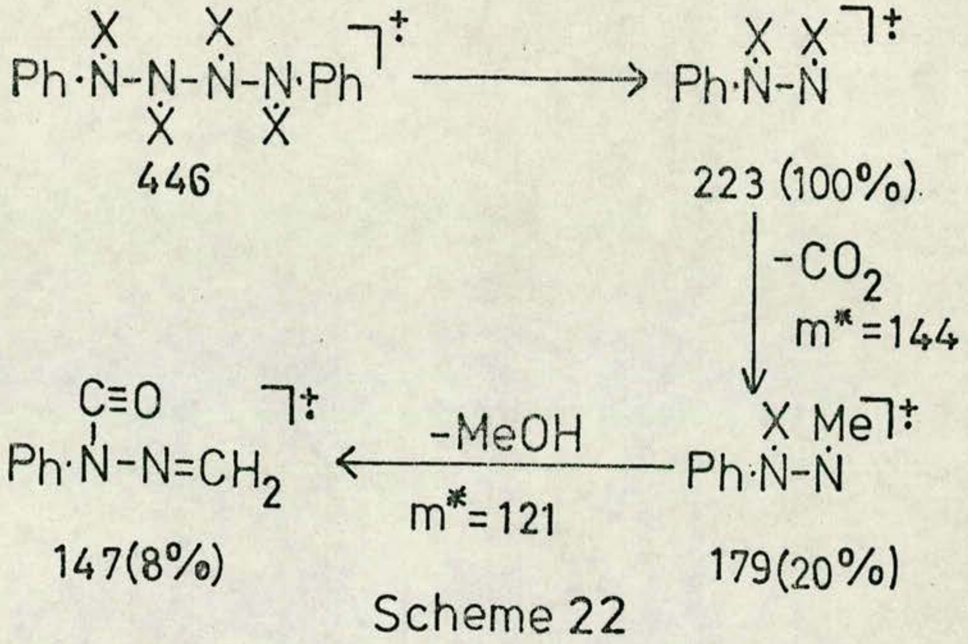
Temp. °C	Solvent	Ratio of Methyl Singlets in 60	Ratio of Methyl Triplets in 61
-60	$CDCl_3$	2:1	3:2
-20	$CDCl_3$	2:1	3:2
0	$CDCl_3$	2:1	3:2
28	$CDCl_3$	2:1	3:2
60	$CDCl_3$	12:7	4:3
80	Ph_2O	2:1	5:4
120	Ph_2O	3:2	1.1:1
140	Ph_2O	1.2:1	1.1:1
160	Ph_2O	1.2:1	1.1:1

The n.m.r. data suggested that the product was either a mixture of two isomers e.g.



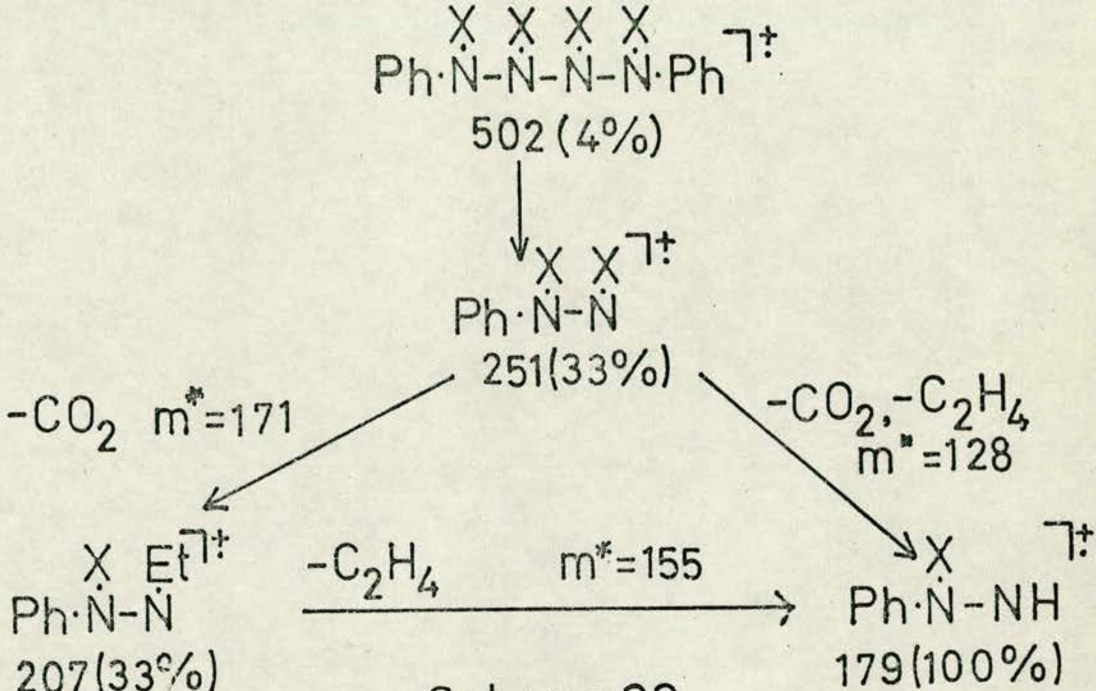
or that in solution the product existed as an equilibrium mixture of two preferred conformers. Examination of the compound by h.s.l.c. indicated a single product, suggesting that the latter of these options was the most feasible.

Data from ^{13}C n.m.r. spectroscopy also provided supporting evidence for this contention: four different carbonyl absorptions were observed at ppm 155.4, 155.3, 155.2 and 153.5, four different methyl absorptions were observed at ppm 54.6, 54.3 53.8, 53.3 while two distinct aromatic nitrogen bearing carbon atoms were also observed. Finally, detailed analysis of the mass spectrum confirmed that the compound had structure 60 (scheme 22). The product fragmented as expected to give a hydrazyl radical ion at $^m/e$ 223 (mass abundance 100%) which then underwent two common skeletal rearrangements as shown. The prediction of metastable peaks at $^m/e$ 144 and $^m/e$ 121 for the respective rearrangements was borne out.



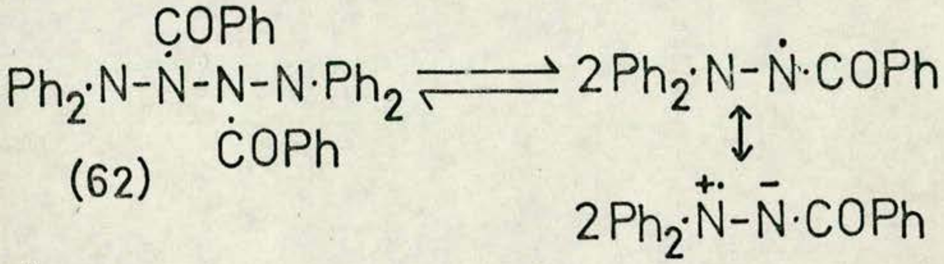
Scheme 22

When benzoyl peroxide was decomposed in diethyl azodiformate, the analogous 1,4-diphenyl-1,2,3,4-tetraethoxycarbonyltetrazane (61) was obtained also in good yield (60%). The ^{1}H n.m.r. spectrum (Fig. II) was similar to that for the methyl analogue (60), having 2 broad quartets between τ, 5.6 and 6.5 and 2 broad triplets at τ, 8.6-8.9 and τ, 9.2-9.4. The ratio of these triplets was 3:2 and variable temperature study indicated that with increasing temperature, the ratio converged to unity (Table VI). H.s.l.c. indicated a single component and ^{13}C n.m.r. data confirmed that there were two distinct ethoxycarbonyl groups. As with the methyl analogue, the mass spectrum proved a most useful tool in determining the structure (scheme 23). Fragmentation of the tetrazane gave rise to the hydrazyl radical ion which then fragmented as shown <u>via</u> the various skeletal rearrangements open to the ethoxycarbonyl group to give the base peak $C_9H_{11}N_2O_2$ at $^m/e$ 179. Exact mass measurement of this fragment gave the correct formula $C_9H_{11}N_2O_2$. Moreover the expectation of metastable peaks at $^m/e$ 128, 155 and 170.7 for the various skeletal rearrangements was fulfilled.



Scheme 23

There seems no doubt that these novel tetrazanes are formed by attack of the phenyl radical on the azo ester with subsequent dimerisation of the long-lived hydrazyl radical. That this dimerisation step was favoured was demonstrated when dilution of the respective reaction mixtures with benzene still gave the tetrazanes in comparable yields. It is well known that hydrazyl radicals including 1,2-diphenyl-1-acyl hydrazyl dimerise to give the corresponding tetrazane[170] although several including 1,1,4,4-tetraphenyl-2,3-dibenzoyltetrazane (62) are known to undergo reversible dissociation.[171] However tetrazanes 60 and 61 were found to be particularly stable as they showed no signs of dissociating in solution at temperatures up to 200°.

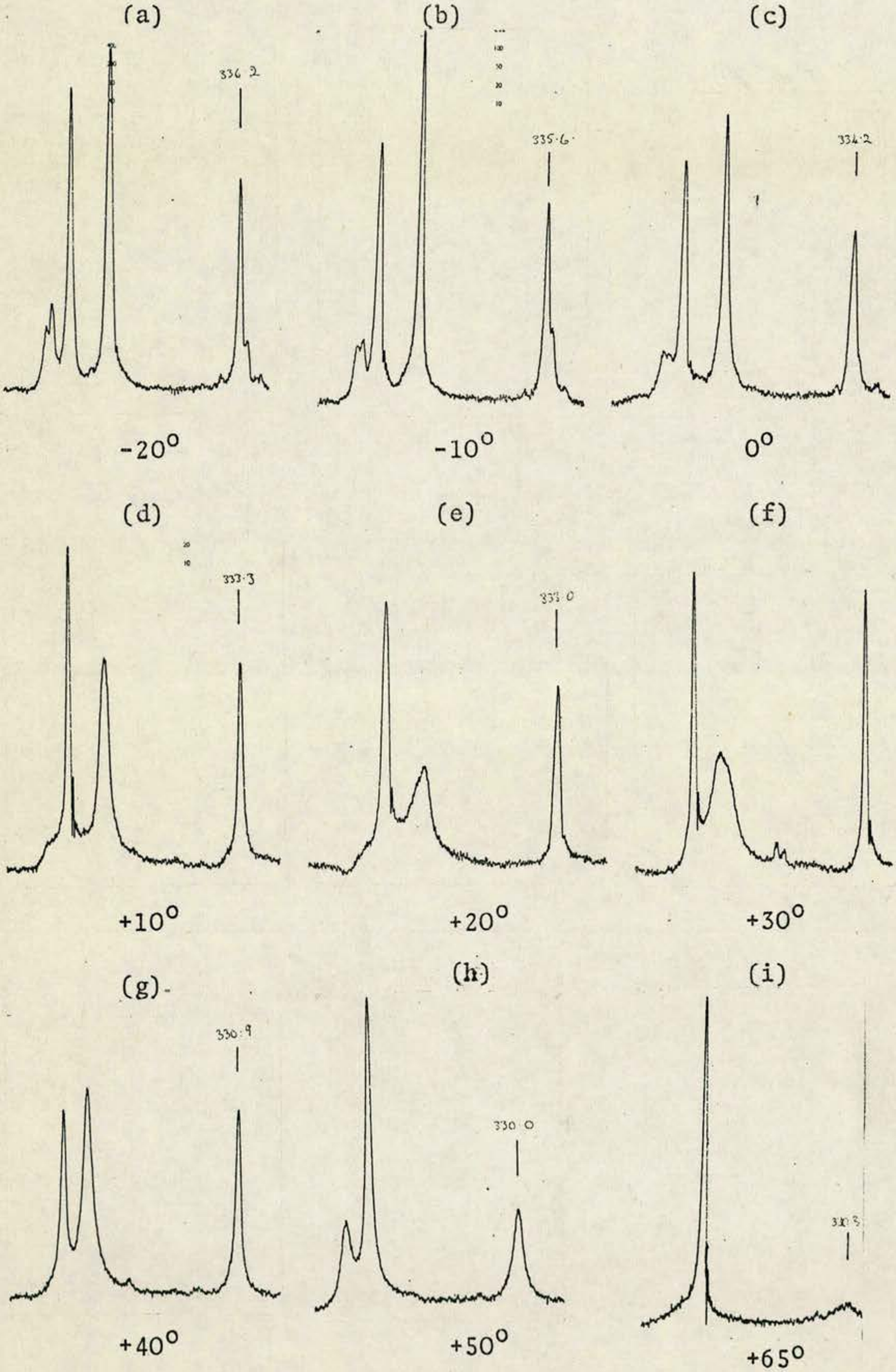


(62)

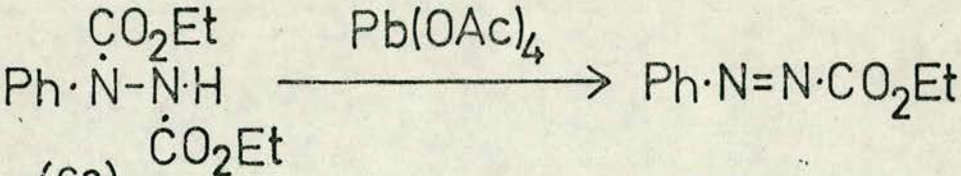
$$Ph_2\cdot N-\underset{}{\overset{COPh}{\dot{N}}}-\underset{\dot{C}OPh}{N}-N\cdot Ph_2 \rightleftharpoons 2Ph_2\cdot N-\dot{N}\cdot COPh \updownarrow 2Ph_2\cdot\overset{+\cdot}{N}-\overset{-}{N}\cdot COPh$$

An attempt was made to prepare the tetrazane 61 by the classical route of oxidation of the corresponding hydrazine,[141] thus proving conclusively, by direct comparison, that the tetrazane (61) was the product obtained from reaction of benzoyl peroxide with diethyl azodiformate. Attempted oxidation of N,N' diethoxycarbonyl-N-phenylhydrazine (63) with a variety of heavy metal oxides proved fruitless, yielding only starting material, as did further attempts using t-butyl peroxide or N-bromosuccinimide as oxidant. The inertness of some hydrazines to oxidation is well known;[170] e.g. 2-benzyl- and 2-cyclohexyl-2-phenylhydrazines do not give hydrazyl radicals on treatment with lead dioxide, hence an alternative route was sought. Oxidation of the hydrazine (63) was accomplished by use of the powerful oxidising agent, lead tetraacetate. The product obtained was not the desired tetrazane (61) but an azo

Fig. IV. Methyl signals from N,N-dimethoxycarbonyl-N'-triphenylmethyl-N-phenylhydrazine at various temperatures

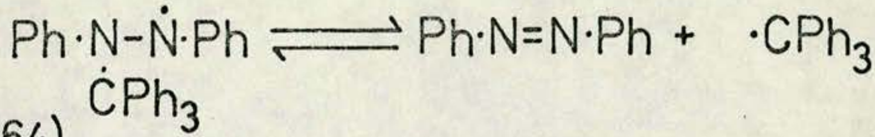


compound, phenylazoethoxycarbonyl. Not only had the hydrogen atom been oxidised off, but removal of the adjacent ethoxycarbonyl group had also been effected.



$$\mathrm{Ph\cdot\overset{CO_2Et}{N}-\underset{CO_2Et}{N}\cdot H \xrightarrow{Pb(OAc)_4} Ph\cdot N{=}N\cdot CO_2Et}$$

(63)

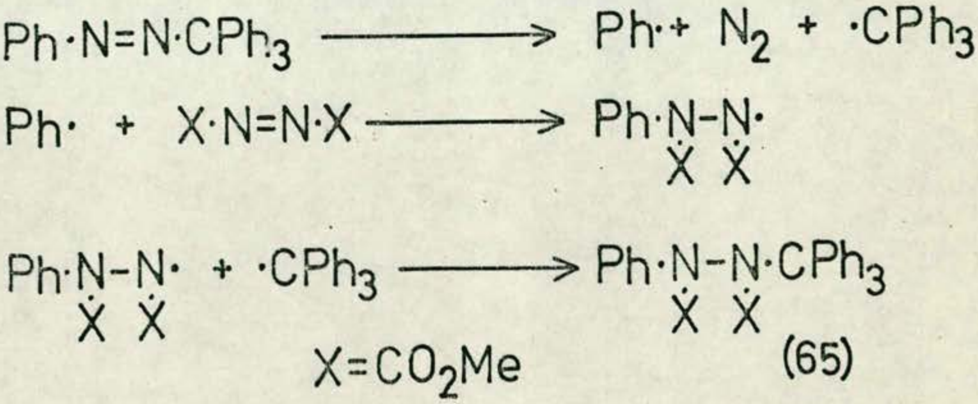


$$\mathrm{Ph\cdot\underset{CPh_3}{N}-\dot{N}\cdot Ph \rightleftharpoons Ph\cdot N{=}N\cdot Ph + \cdot CPh_3}$$

(64)

Although it is known that 1,2-diphenyl-2-triphenylmethylhydrazyl (64) is an unstable hydrazyl radical, decomposing readily to azobenzene and trityl carbinol,[172] it seems unlikely that oxidation of (63) with lead tetraacetate proceeds in analogous fashion. The precise mechanism of this reaction however remains a mystery.

In the absence of air, hydrazyl radicals are known to combine with triphenylmethyl radicals to give adducts.[141] If the proposed reaction scheme is correct then decomposition of phenylazotriphenylmethane in azodiformic esters should give a tetrasubstituted hydrazine.



$$\mathrm{Ph\cdot N{=}N\cdot CPh_3 \longrightarrow Ph\cdot + N_2 + \cdot CPh_3}$$

$$\mathrm{Ph\cdot + X\cdot N{=}N\cdot X \longrightarrow Ph\cdot\underset{X}{N}-\underset{X}{N}\cdot}$$

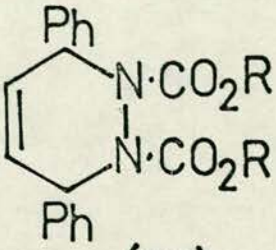
$$\mathrm{Ph\cdot\underset{X}{N}-\underset{X}{N}\cdot + \cdot CPh_3 \longrightarrow Ph\cdot\underset{X}{N}-\underset{X}{N}\cdot CPh_3}$$

$$\mathrm{X{=}CO_2Me}$$

(65)

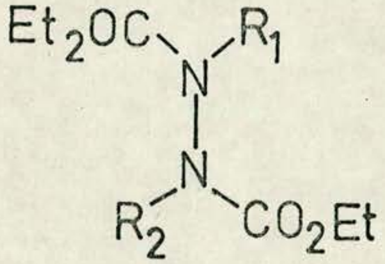
Isolation of the adduct *N*,*N*'-dimethoxycarbonyl-*N*'-triphenylmethyl-*N*-phenylhydrazine (65) in 11% yield from phenylazotriphenylmethane-methyl azodiformate confirmed the intermediacy of the hydrazyl radical in these reactions. In addition the 'H n.m.r. spectrum of the adduct (65) was essentially similar to that of the tetrazane (60) in that three distinct methyl singlets were observed at τ, 6.23 (sharp), τ, 6.29 (broad) and τ 6.70 (sharp) thus indicating a mixture of conformers (Fig. III). A variable temperature study on this compound was revealing since it confirmed that this compound existed as a mixture of different conformers which could be 'frozen' at low temperatures (Fig. IVa) but which equilibrated rapidly at higher temperatuers (IVh and IVi).

The apparent anomalies posed by the 'H n.m.r. spectra of compounds 60, 61, 65 can be successfully rationalised in terms of these compounds existing in solution as a mixture of conformers, this occurring as a result of hindered rotation about the N-CO_2R bonds. The first reported example of this phenomenon in the system N-CO_2R(R=Me, Et) was reported by Breliere[173] who studied the conformational rate process occurring in tetrahydropyridazines (66)



(66)

and reported conformational isomerism involving the $N\text{-}CO_2R$ group. Price[174] studied conformational changes in acyclic hydrazine system (67) in which only rotational isomerism about the $N\text{-}CO_2R$ bond was expected.



$R_1 = R_2 = Me$ (67)

$R_1 = R_2 = Ph \cdot N \cdot CO_2Et$ (61)

His observations from the low temperature 'H n.m.r. of (67) were compatible with equilibrium between some or all of the possible trans coplanar conformations of (67), involving rotation about the $N\text{-}CO_2Me$ bonds. If one considers the numerous possible conformations occurring in the above system when $R_1 = R_2 = Ph\text{-}N\text{-}CO_2Et$ (61) then the complex nature of the n.m.r. spectrum of these tetrazanes becomes obvious. In the simpler case of rotation about an amide bond the energy barrier is 105 k J mol^{-1} at 25° and in this case the energy barrier is both an enthalpy and entropy barrier.[175] The inability to obtain coalescence of the CO_2R signals in tetrazanes 60 and 61 may be due to an extremely large contribution from the entropy barrier in these systems.

Reaction of benzoyl peroxide with t-butyl azodiformate in benzene gave only a small amount of the corresponding tetrazane while reaction with the unsymmetrical azo compound, phenylazoethoxycarbonyl gave only polymeric material. It would seem that these reactions are dependent on the strength of the electron withdrawing groups on the azo linkage (Table VII), with highest yields being recorded for the more powerful electron withdrawing groups:

$$CO_2Me > CO_2Et > CO_2Bu^t \gg Ph.$$

TABLE VII

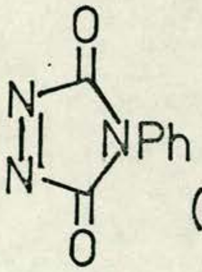
Reaction of benzoyl peroxide with azo compounds X-N=N-Y

X	Y	Solvent	Biphenyl (m/100m)	Tetrazane ^{m}/100m
CO_2Me	CO_2Me	-	-	69
CO_2Et	CO_2Et	-	-	60
CO_2Me	CO_2Me	Benzene	10	56
CO_2Et	CO_2Et	Benzene	20	40
CO_2Bu^t	CO_2Bu^t	Benzene	20	6
CO_2Me	CO_2Me	^{t}Bu. benzene	-	27
CO_2Et	Ph	-	-	0

In addition to this dependence on the nature of the azo diester, the reaction was found to be extremely susceptible to substitution in the phenyl radical. Thus while reaction of benzoyl peroxide with diethyl azodiformate gave the tetrazane (61) in good yield, 4-bromobenzoyl peroxide gave only 4-bromobenzoic acid and reaction of 4-tolyl peroxide gave diethyl hydrazodiformate. Since the relative indifference of aromatic radical reactions to the polar effects of substituents either in the substrate or in the attacking radical is well known,[149] the total refusal of these substituted aryl radicals to undergo this reaction is inexplicable.

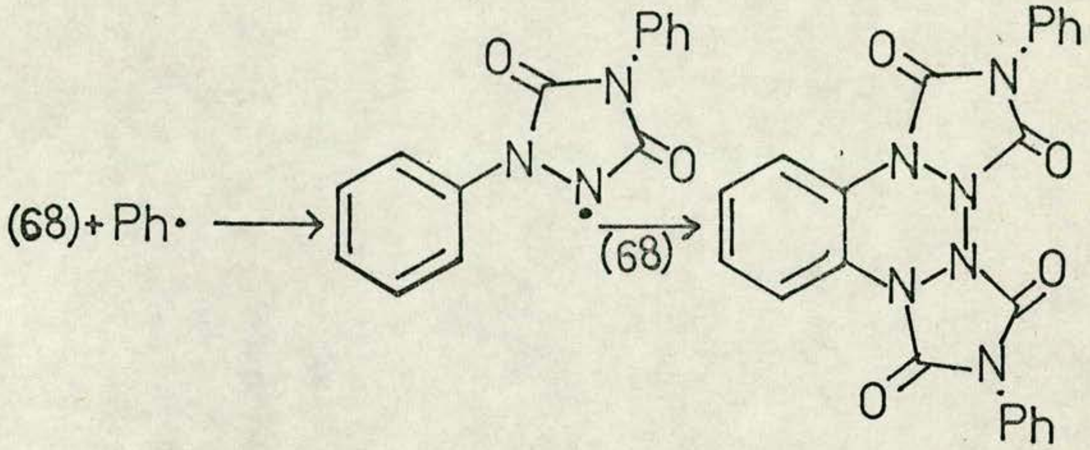
In view of these observations and in the light of results with dimethyl acetylendicarboxylate, it was not surprising to find that reaction of thenoyl peroxide gave only diethyl hydrazodiformate.

One reason for the failure of phenyl radicals to undergo an annelation reaction with azo esters may be the loss of the necessary cis stereochemistry required for cyclisation. To over come this deficiency, the powerful dienophile 4-phenyl-1,2,4-triazoline, 3,5-dione (68) was used as azo trap.

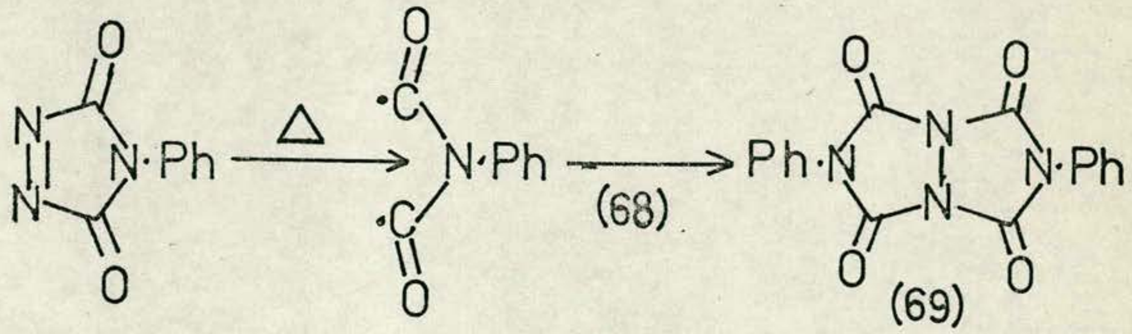


(68)

The reactivity of this compound as a dienophile is readily explained by the cisoid conformation which is maintained by incorporation of the azo group in a fivemembered ring. Attack by a phenyl radical would be expected to generate a <u>syn</u>-hydrazyl radical only, a necessary prerequisite if annelation is to be achieved.



Reaction of the triazoline (68) with benzoyl peroxide at 80° was found to give the triazolo triazole derivative (69). This product was thought to arise <u>via</u> thermal decomposition of the triazoline (68):



Attempts to trap out the intermediate diradical with methyl azodiformate and with DMAD were unsuccessful, moreover reaction of NNA with triazoline (68) at room temperature gave only the triazolo triazole (69) and polymeric by-products and so the precise mode of formation (69) remains obscure. It may well be that the extremely reactive nature of the azo compound precludes the formation of a hydrazyl radical capable of undergoing dimerisation but rather will favour polymerisation.

In summary, it appears that azodiformic esters do not undergo an aromatic annelation analogous to that described for acetylenic esters. The first formed hydrazyl radicals display a marked reluctance to undergo addition to a second molecule of azo ester, preferring instead to dimerise to give the corresponding substituted tetrazanes, in surprisingly good yields. The success of this reaction is dependent to a large degree on the nature of both the substrate and attacking radical species.

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