

ABSTRACT OF THESIS

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Title of Thesis Studies in the Chemistry of Heterocyclic Compounds of Nitrogen
and Phosphorus.

The first part of this study was devoted to the synthesis of various nitrogen heterocycles via nitrene-induced reactions.

Thus, decomposition of several aryl 2-azidophenyl ethers containing substituents in the relevant ortho positions led to the isolation of many new compounds. In this way the first successful synthesis of 5, 11-dihydro 4-methyldibenzo[b, e][1, 4]-oxazepine and its 2, 4-dimethyl homologue by a nitrene (or nitrenoid) reaction has been achieved. 4-Methoxyphenoxazine and 1, 2-dimethoxyphenoxazine were similarly obtained. This again is the first successful synthesis of a phenoxazine via a nitrene-induced cyclisation.

Deoxygenation of the corresponding aryl 2-nitrophenyl ethers by triethyl phosphite led to isolation of the hitherto unreported phosphoranylidene azepine in two instances. Thus 2, 6-dimethylphenyl- and 2, 4, 6-trimethylphenyl 2-nitrophenyl ether gave the novel 7-triethoxyphosphoranylidene 2-(2, 6-dimethylphenoxy)azepine and its 2, 4, 6-trimethylphenoxy homologue respectively. These azepines were observed to undergo a novel, rapid hydrolysis resulting in loss of the three ethoxy groups and leading to the corresponding azepinyl phosphonic acids.

In the thermal decomposition of aryl 2-azidophenyl sulphones it was established that the competing processes of rearrangement and direct insertion led to a mixture of phenothiazine 5, 5-dioxides.

In the thermal deoxygenation of 2, 4, 6-trimethylphenyl 2-nitrophenyl methane by triethyl phosphite a novel, nucleophilic attack by phosphorus on the methylene function of the substrate was observed. This reaction resulted in the formation of diethyl 2-N-(2, 4, 6-trimethylphenyl)amino benzyl phosphonate.

An attempt to prepare 3-methyl 6-oxo-anthra[1, 9-cd]isoxazole by reductive cyclisation of 2-methyl 1-nitro-anthraquinone resulted in the isolation of bis 9, 9'-(10-ethoxy 2-methyl 1-nitro)anthryl in addition to the primary amine and the phosphoramidate.

The second part of this study consisted of experiments directed towards the synthesis of 2, 6-disubstituted phosphorins via the 1, 2-dihydrophosphorins. The latter objective has been achieved by the reaction of phenyl phosphine with various diynols - a novel synthetic route to phosphorus heterocycles.

STUDIES IN THE CHEMISTRY OF HETEROCYCLIC
COMPOUNDS OF NITROGEN AND PHOSPHORUS

by

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Thus, decomposition of several aryl 2-azidophenyl ethers containing substituents in the relevant ortho positions led to the isolation of many new compounds. In this way the first successful synthesis of 5, 11-dihydro 4-methyldibenzo[b, e][1, 4]oxazepine and its 2, 4-dimethyl homologue by a nitrene (or nitrenoid) reaction has been achieved. 4-Methoxyphenoxazine and 1, 2-dimethoxyphenoxazine were similarly obtained. This again is the first successful synthesis of a phenoxazine via a nitrene-induced cyclisation.

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In the thermal decomposition of aryl 2-azidophenyl sulphones it was established that the competing processes of rearrangement and direct insertion led to a mixture of phenothiazine 5, 5-dioxides.

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I. 1. DEFINITION, NOMENCLATURE AND HISTORICAL DEVELOPMENT OF NITRENES

In many reactions, species containing a monovalent nitrogen atom are formed or have been postulated as reactive intermediates. Such species in which the electron-deficient nitrogen atom possesses six electrons in its outer shell, have been variously named: azenes, azacarbenes, azylenes, imine radicals, imidogens, nitrenes.¹ In recent years the term "nitrene" seems to have been generally accepted.

As early as 1891, Tiemann² postulated a carbonylnitrene, R-CO-N in his interpretation of the Lossen rearrangement. Curtius³ adopted the nitrene mechanism to account for the reactions of some carbonyl azides while Bertho⁴ in 1924 proposed phenylnitrene as an intermediate in the decomposition of phenyl azide in *p*-xylene.

The appearance of reviews in 1959,⁵ 1963⁶ and 1964⁷ indicated a revival of interest in the chemistry of nitrenes. However, it was only in 1962 that physical evidence for the existence of organic nitrenes was obtained. Smolinsky, Wasserman and Yager⁸ reported the E. S. R. signals of stable triplet species obtained by irradiating solid solutions of phenyl azide and related molecules in a plastic matrix at 77°K.

I. 2. ELECTRONIC STRUCTURE AND SPECTRA.

The nitrogen atom in a nitrene is bonded to a single carbon centre and is therefore sp-hybridised. Thus one of its five valence electrons is involved in the σ -bond to carbon; one pair occupies the non-bonding sp-orbital and the remaining two electrons are in the unhybridised orbitals p_x and p_y . Since the spin multiplicity is given by $2S + 1$ where S is the total spin, the nitrene is a singlet when the two electrons are spin-paired (i. e. $S = 0$; $2S + 1 = 1$). If the spins of the electrons are parallel, then the nitrene is a triplet (i. e. $S = \frac{1}{2} + \frac{1}{2} = 1$; $2S + 1 = 3$).

Nitrenes can therefore exhibit the properties either of triplet

diradicals, $R-\dot{N}$ or of electrophilic singlet species, $R-\ddot{N}$. Since the two p-orbitals are equivalent in energy and will contain one electron each, both electrons having the same spin, the ground state for nitrenes is expected to be the triplet state.

Spectroscopic data of the triplet state of nitrenes is quite well documented largely due to the electron paramagnetic resonance studies of Smolinsky and his co-workers⁸⁻¹¹ and to the optical spectroscopy of azide photolysis products achieved by Reiser and his group.¹²⁻¹⁵

By irradiating dilute solutions of phenyl azide and related molecules frozen in a plastic matrix at 77°K, Smolinsky and his co-workers⁸ observed E. S. R. signals which are characteristic of two strongly interacting unpaired spins localised essentially on a single atom. These were assigned to the triplet ground state of the nitrene. This work has been extended to aromatic dinitrenes⁹ and alkylnitrenes.¹⁰

Using a similar technique, Reiser and his group have been able to record ultra-violet spectra of several aromatic nitrenes and dinitrenes¹² and also to detect the nitrene intermediate in the photocyclisation of 2-azidobiphenyl.¹³ Direct observation of a nitrene at room temperature was first reported in the flash photolysis of 1-azidoanthracene.¹⁴ The peak at 342 nm. in the u. v. spectrum was assigned to the nitrene intermediate whose half-life was provisionally estimated to be between 3 and 10 μ sec. The absorption bands were identified by comparison with the spectra of 1-azidoanthracene when photolysed in a solid matrix at 77°K.

There is as yet no spectroscopic information on the first excited singlet state of a nitrene. This is because intersystem crossing of the excited singlet to the triplet state is possible, provided a low-lying singlet state exists. The intermediate may then react in either form. Thus if a singlet nitrene produced in the primary step finds no suitable substrate with which to react, decay to the triplet state occurs. This makes it difficult to predict the spin state of the nitrene intermediate generated in the primary step. Application of the Wigner spin conservation rule¹⁶ would suggest that thermolysis of azides should

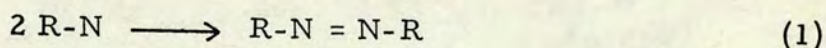
initially generate a singlet nitrene while photolysis should yield the triplet species. As it is not possible thus far to generate nitrenes by thermolysis of azides under conditions which will allow physical observations to be made, any conclusion on the state of the reactive intermediate will have to be based on the nature of the final products.

I. 3. GENERAL REACTIONS OF NITRENES

The most extensive work on nitrenes has been carried out with carbethoxynitrene, EtO-CO-N, mainly by Lwowski and his co-workers.¹⁷ In these reactions, the same products have been obtained from very different precursors. It thus seems reasonable to deduce that the nitrene is the common intermediate in the reactions. In the case of many other reactions of nitrene precursors, there is no rigorous proof that nitrenes are intermediates. Very often, the reaction products can be rationalised by alternative mechanisms that do not involve nitrenes. Some of the general reactions of nitrenes are discussed in the following sections.

(A) Recombination

The reaction of two nitrenes to form an azo compound is spin allowed for both the singlet and triplet species.

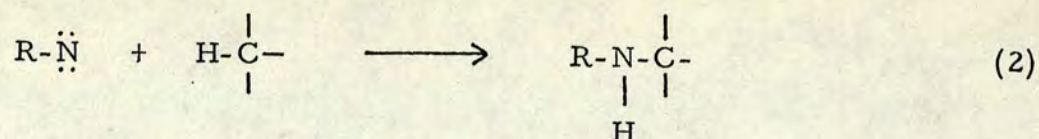


Such a process requires a high local nitrene concentration. Provided the solvent is inert, the preferred reaction pathway in flash photolysis is recombination.¹⁵

(B) Electrophilic Attack On Bonding Pairs

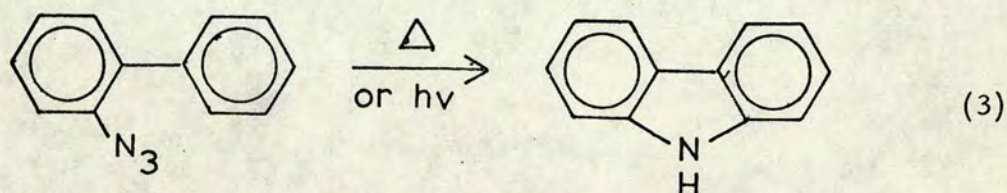
(i) Insertion into C-H bonds

Only singlet nitrenes undergo insertion into C-H bonds;

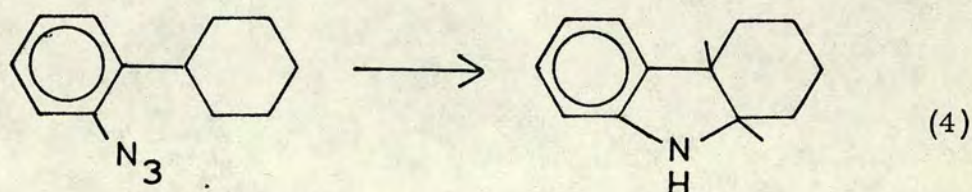


the yield of secondary amine depending on the substrate and on the rate of competing processes. It appears that in alkylnitrenes the insertion reaction is less favourable than the faster process of hydrogen migration which results in imine formation.^{18, 19} However when hydrogen migration and other rearrangements are inhibited, insertion becomes important: e.g. carbethoxynitrene inserts into cyclohexane with a yield of 50%.²⁰ The yields of insertion products of pivaloylnitrene (tert-butyl carbonylnitrene) into primary, secondary and tertiary C-H bonds are in the ratio of 1:19:160.²¹

Arylnitrenes are more selective in their insertion reactions than carbonylnitrenes. Phenylnitrene inserts into primary, secondary and tertiary C-H bonds in the ratio of 1:100:4000.²² The insertion of arylnitrenes into aromatic C-H bonds is as efficient as that into secondary C-H bonds of aliphatic hydrocarbons, e.g. photolysis and thermolysis of 2-azidobiphenyl yielded 78% of carbazole,^{23, 24}

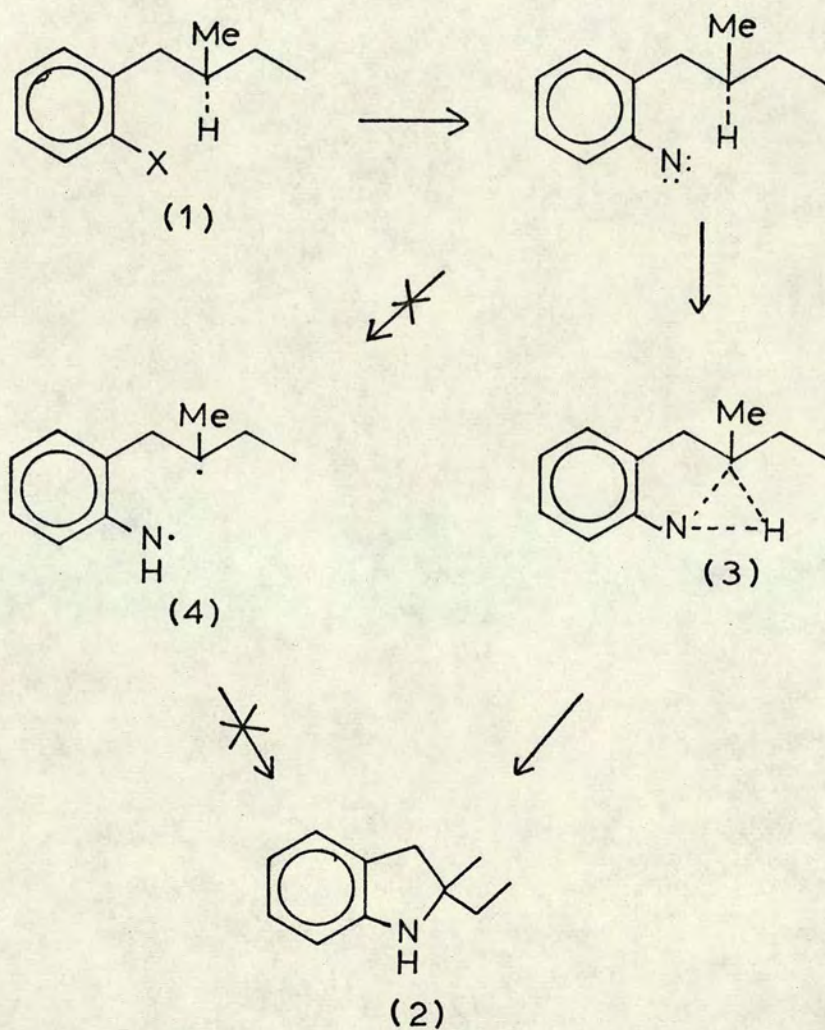


while the corresponding insertion into a cyclohexane ring gave the ring closure product in 86% yield.²⁵



The pyrolysis of optically active 1-azido-2-(2-methylbutyl)benzene (1), ($X = N_3$), in the vapour phase and in diphenyl ether solution gave

active 2-ethyl-2-methyl indoline (2), in yields of 50% and 43% respectively. Smolinsky and Feuer²⁶ interpreted these results as suggesting the direct insertion of a singlet nitrene into the C-H bond at the 2-position of the side chain via a transition state such as (3) (Scheme 1). The alternative process involving triplet nitrene via radical abstraction to give the intermediate (4) followed by recombination would have led to extensive racemisation.



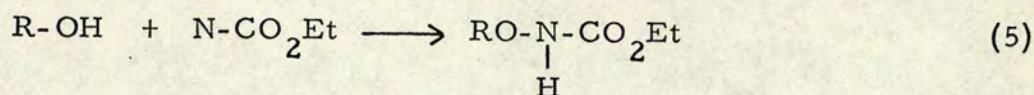
Scheme 1.

The degree of retention was greater in the vapour phase than in solution. This suggests, as would be expected, that collisional deactivation of the singlet to the triplet nitrene occurred more readily

in solution.

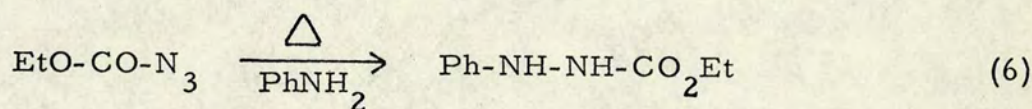
(ii) Insertion into O-H bonds.

Carbonylnitrenes insert into O-H bonds with the formation of hydroxylamine derivatives. The photolysis and thermolysis of ethyl azidoformate in *t*-butanol gave the insertion product in 55% yield.²⁷

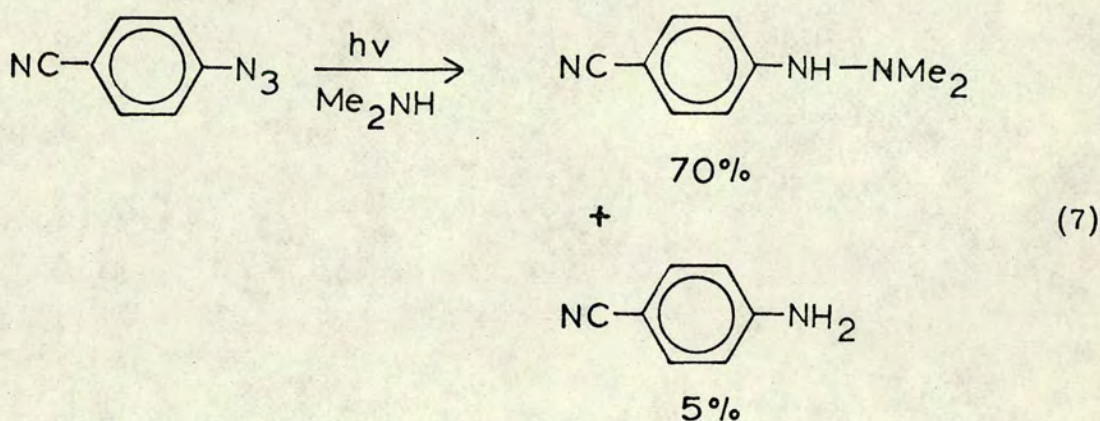


(iii) Insertion into N-H bonds.

Thermolysis of ethyl azidoformate in aniline gave a 52% yield of the hydrazine which can be formally accounted for by insertion of the nitrene into the N-H bond of the amine.²⁸



The photolysis of *p*-cyanophenyl azide in dimethylamine was reported by Odum and Aaronson²⁹ to yield 70% of 1,1-dimethyl 2-(4-cyanophenyl)hydrazine and 5% of *p*-cyanoaniline (eq. 7).



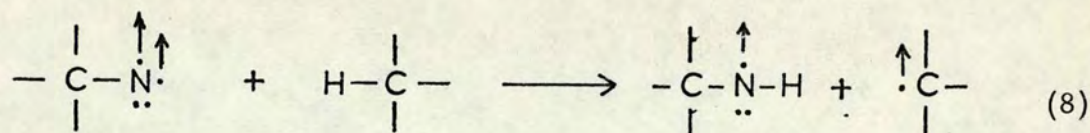
In the presence of a triplet sensitizer, the photolytic reaction gave a

reversal of product yields, 70% of *p*-cyanoaniline and 6% of hydrazine. By implication the large yield of hydrazine in the absence of sensitiser is due to the intermolecular insertion reaction of the singlet nitrene.

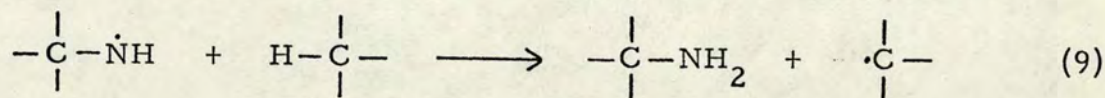
The synthetic applicability of the N-H insertion reaction with primary amines is limited by the dehydrogenation of the primary product $R-NH-NH-CO_2R'$ to the azo compound $R-N=N-CO_2R'$ by the nitrene.³⁰

(iv) Hydrogen abstraction.

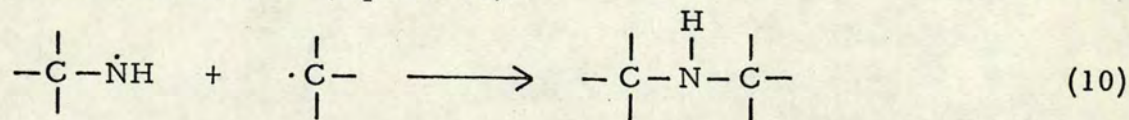
This is possibly the most general reaction of triplet nitrenes. Two separate abstraction steps are required to saturate the electron deficiency of the triplet. The nitrene is converted to an amino radical and the substrate into a carbon radical in the first step:

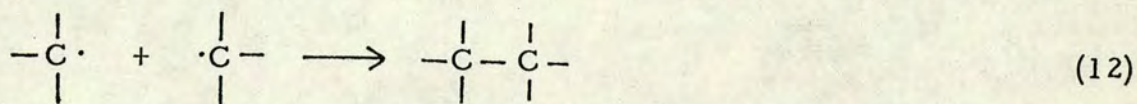
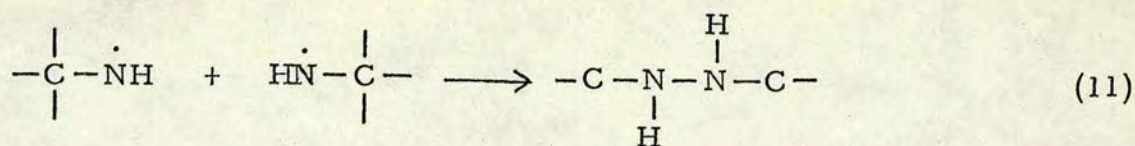


The two radicals have unpaired spins at this stage and cannot couple unless one of their spins is reversed. The time required for spin reversal is usually sufficient to allow the two radicals to diffuse away from each other.³¹ The amino radical will then abstract a second hydrogen to form the primary amine.



Other probable reactions include a series of radical recombinations resulting in secondary amines (pseudo insertion), hydrazines and hydrocarbon dimers (eq. 10-12).



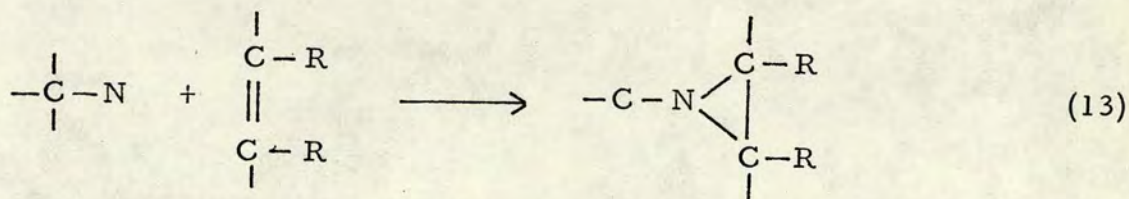


Sensitisation experiments have given proof for the triplet character of the hydrogen abstracting species e.g. photolysis of ethyl azidoformate in cyclohexene gave the hydrogen abstraction product (urethane, $\text{H}_2\text{N}-\text{CO}_2\text{Et}$) in 3% yield and a trace of bis-cyclohexene.²⁰ These yields are increased to 74% and 63% respectively in the sensitised photoreaction.

(C) Addition To Multiple Bonds.

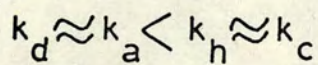
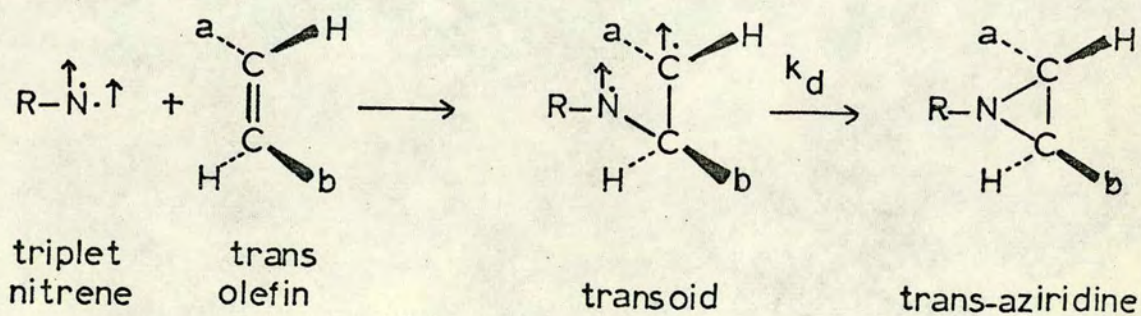
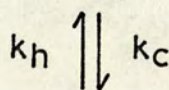
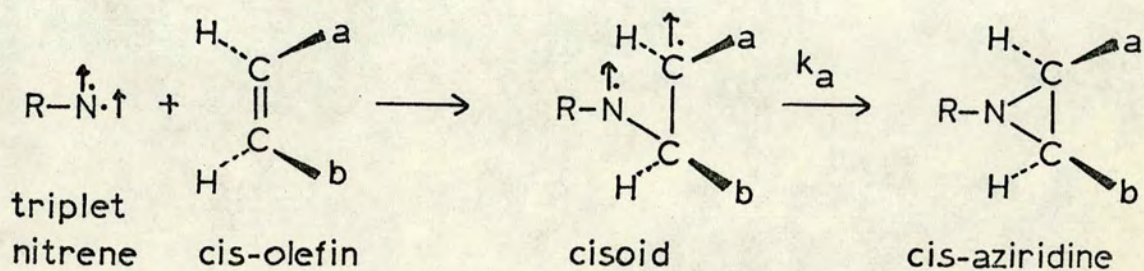
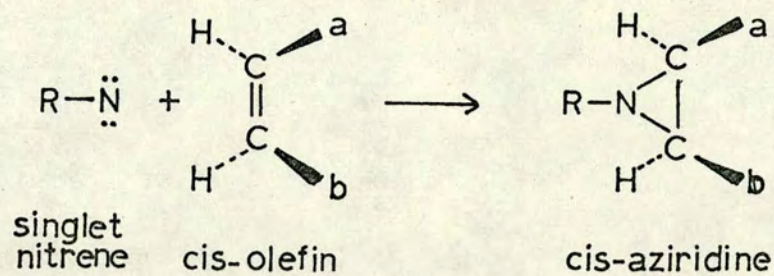
(i) Addition to carbon-carbon double bonds.

Addition of nitrenes to olefins is a reaction of both the singlet and triplet species. Such reactions, resulting in aziridine formation has been positively established only for some carbonylnitrenes like carbethoxynitrene.¹⁷



By adapting Skell's model³² for correlation of data in the carbene field, Lwowski¹⁷ has shown that in the addition of carbethoxynitrene to olefins, the singlet species adds stereospecifically while the triplet adds non-stereospecifically. (Scheme 2).

Lwowski assumed that the singlet nitrenes adds stereospecifically in one step to the $\text{C}=\text{C}$ bond while the triplet adds in two discrete steps via a triplet 1,3-diradical intermediate. The rate of ring closure of



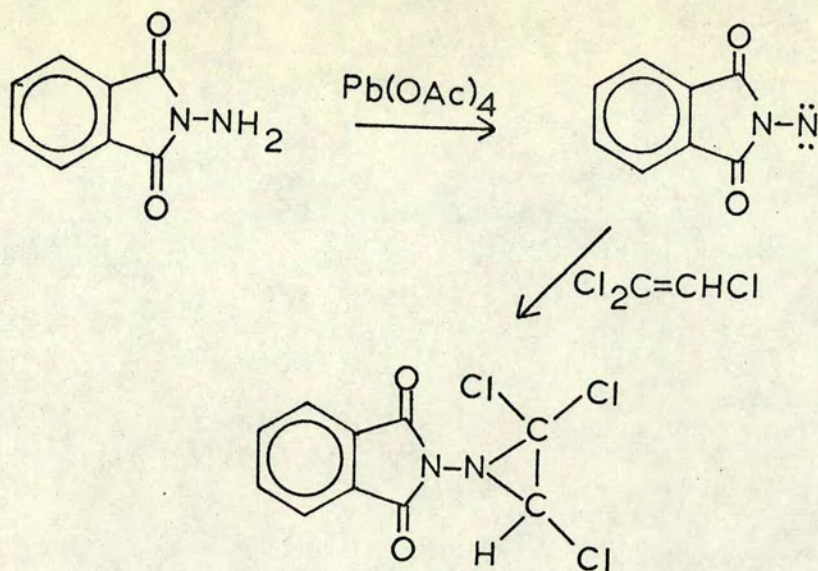
Scheme 2 - Skell's scheme for the addition of singlet and triplet species to olefin adapted for the addition of a nitrene.

the latter is supposed to be considerably smaller than that for rotation about the C-C bond between the two former olefin carbons. Consequently stereospecificity is lost and a mixture of cis- and trans-aziridines result.

Using cis- and trans-4-methylpent-2-ene as the olefin^{33, 34} and producing carbethoxynitrene in three independent ways:^{20, 35, 36} by thermolysis of ethyl azidoformate, by the alkali-induced decomposition of N-(*p*-nitrobenzenesulphonoxy)urethane (an α -elimination reaction) and by the direct photolysis of ethyl azidoformate, Lwowski obtained the same aziridine in good yield. In thermolysis and in α -elimination the addition of the nitrene to the double bond is almost completely stereospecific if conducted in neat olefin; trans-aziridine is formed from trans-pentene and cis-aziridine from the cis-isomer. In photolysis, a mixture of about 70% of the stereospecific and 30% of the non-stereospecific addition products was obtained.³⁷ Thus in direct photolysis the nitrene is generated as a mixture of 70% of the singlet and 30% of the triplet species. This conclusion is borne out by interception experiments in cyclohexane.³⁸

As a result of Lwowski's work the mechanism of the primary photolytic step is better understood. Since the singlet carbethoxynitrene is intercepted quantitatively in the neat olefin in thermolysis, the triplet nitrene observed in photolysis must originate from an excited triplet azide. Intersystem crossing from the singlet excited azide to the triplet state competes successfully with the dissociation of the excited singlet azide. Both the singlet and triplet states of the azide group must be capable of dissociation, a conclusion borne out by sensitisation experiments.

Rees and his co-workers³⁹ have also synthesised aziridines in good yields by oxidation of cyclic N-amino compounds with lead tetraacetate in the presence of a wide range of olefins e. g. oxidation of N-aminophthalimide in the presence of trichloroethylene gave 2, 2, 3-trichloro-1-phthalimidoaziridine, via an aminonitrene intermediate in 90% yield.

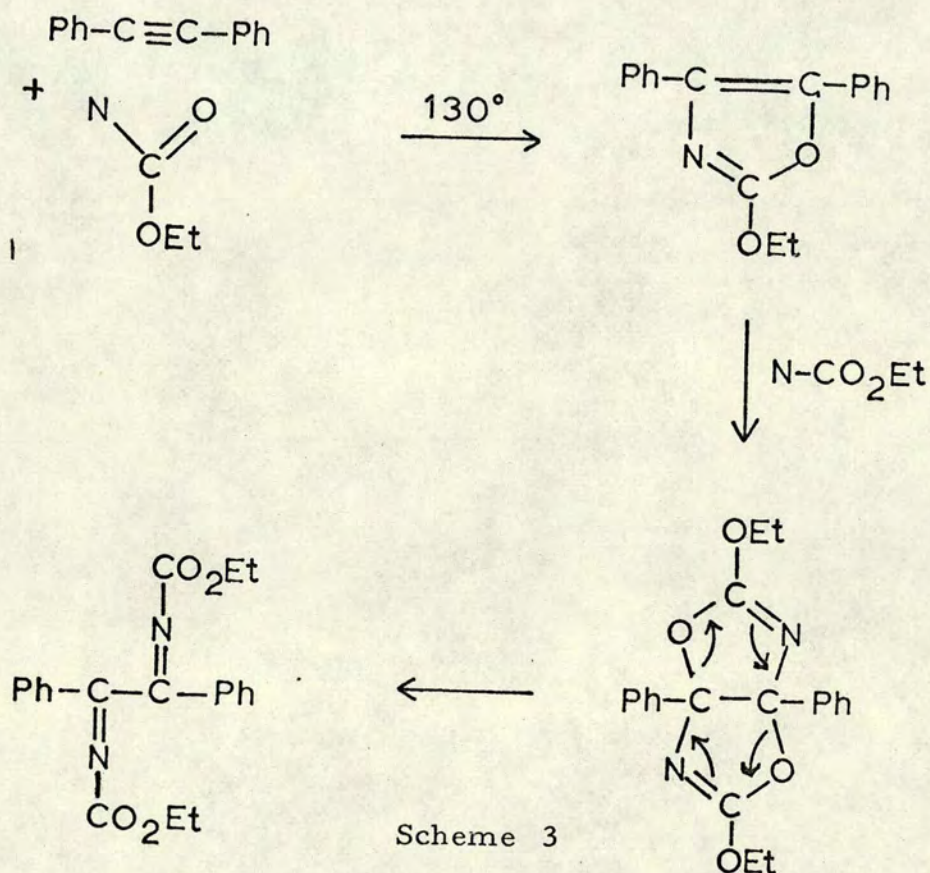


(14)

The additions to cis- and trans-but-2-ene are at least 95% stereoselective indicating the singlet nature of the aminonitrene.

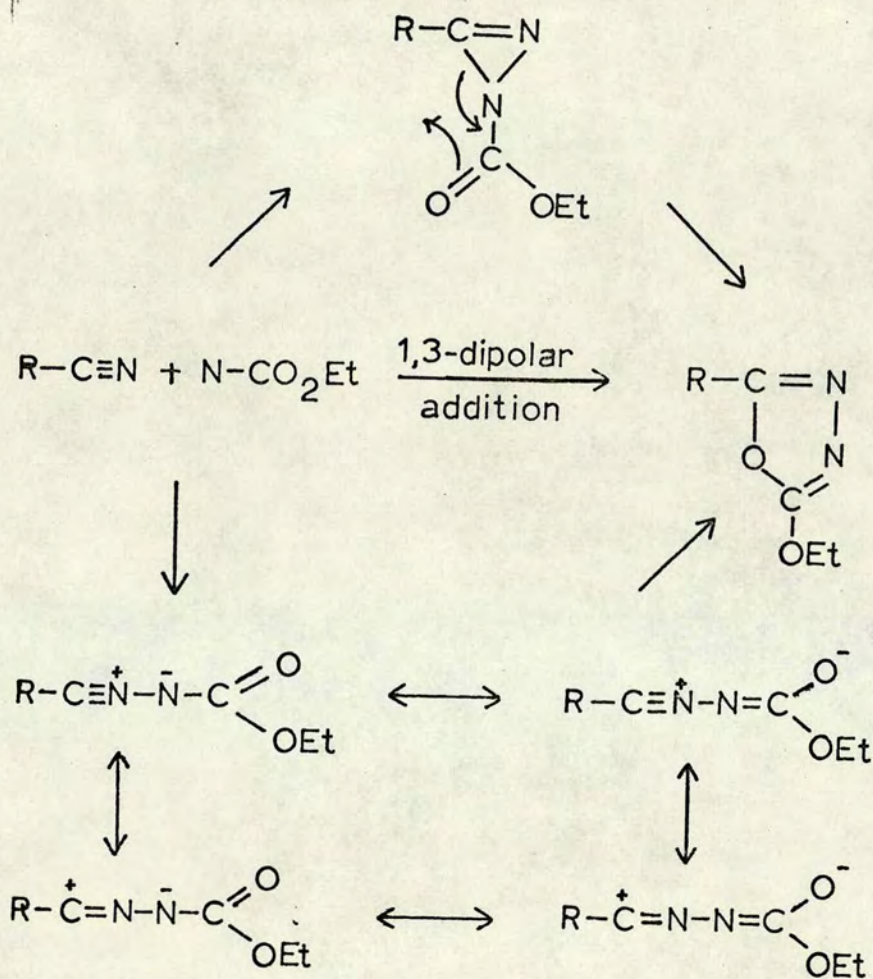
(ii) 1, 3 Cycloaddition.

Huisgen has reported^{40,41} 1, 3 cycloaddition of carbethoxy-nitrene to triple bonds (e.g. diphenylacetylene) to yield a mono-adduct and a diadduct. (Scheme 3)



Scheme 3

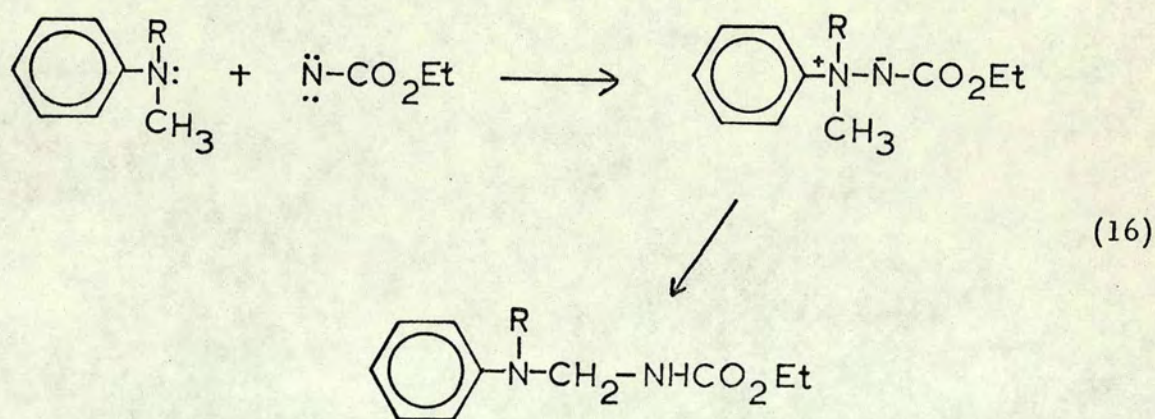
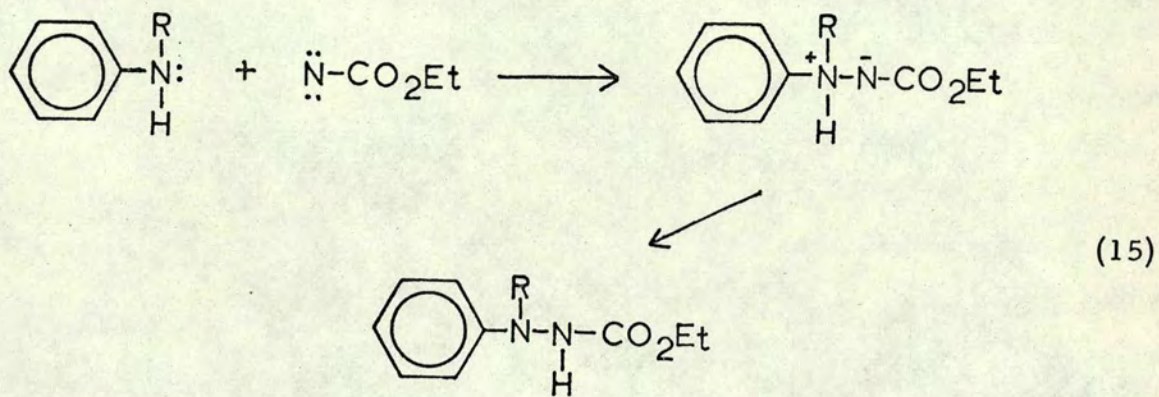
Carbethoxynitrene adds to nitrile groups to give 1,3,4-oxadiazoles in good yield e. g. irradiation of ethyl azidoformate with acetonitrile gave 2-ethoxy-5-methyl 1,3,4-oxadiazole in 55% yield.⁴² The mechanism is not known. A concerted 1,3-dipolar addition as well as a diazir-2-ene or a nitrilimine intermediate seems reasonable. (Scheme 4)



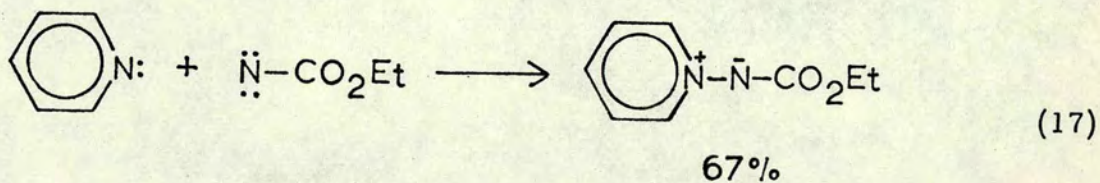
Scheme 4

(D) Electrophilic Attack On A Non-Bonding Pair.

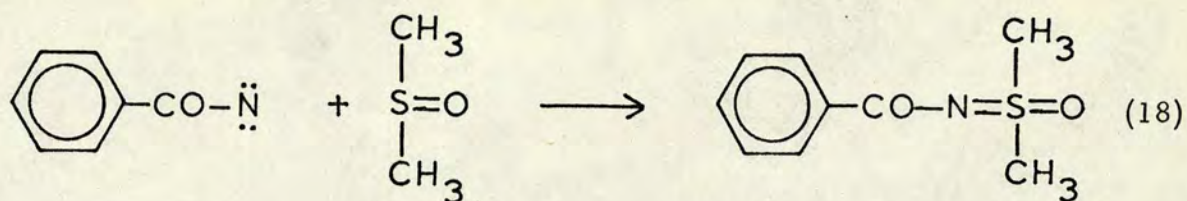
Being strongly electron-deficient nitrenes will react with non-bonding pairs. Thus carbethoxynitrene attacks the lone pair of amino groups²⁸ to form hydrazine derivatives and polyamines.



The intermediate zwitterion-betaine has actually been isolated in the case of pyridine.²⁸



Similarly, benzonitrene is trapped by strong nucleophile with lone pairs like dimethylsulphoxide.⁴³



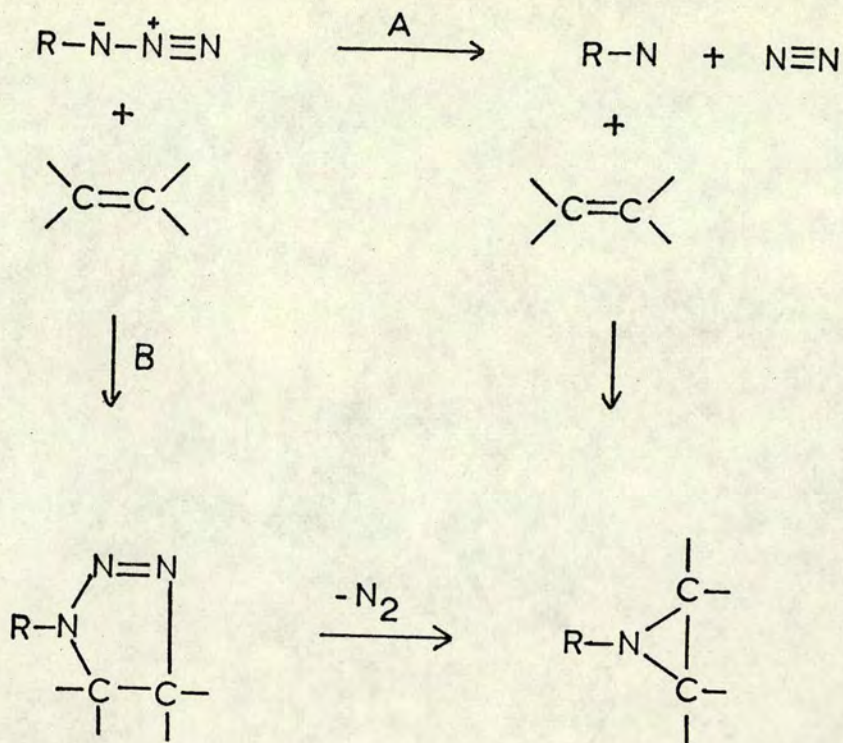
I. 4. METHODS OF GENERATION OF NITRENES

(A) The Question Of Nitrene Participation.

Being monovalent nitrogen species, nitrenes are usually generated from some derivative of tervalent nitrogen by some elimination, reduction or oxidation process, in the presence of the substrate with which the nitrene is supposed to react. In these circumstances, it is possible that the reactions observed are not those of the nitrene but those of the precursor, of an excited state or of a partially reduced form of the precursor, and so on.

In the case of azides as nitrene precursors, loss of nitrogen as the first, unassisted, reaction step leads to a nitrene. Reactions of excited azides with the substrate followed by loss of nitrogen are not nitrene reactions; neither are concerted cyclisation and loss of nitrogen nitrene reactions. For example, photolytic or thermal decomposition of an azide in the presence of olefins yield an aziridine and liberate nitrogen. A nitrene mechanism (route A, Scheme 5) requires loss of nitrogen as the first step. The azide mechanism involves formation of a triazoline and subsequent loss of nitrogen leading to an aziridine (route B, Scheme 5). This latter reaction is well documented.⁴⁴ A decision between the two mechanisms must be made for every reaction studied as long as the azide is used as a nitrene precursor. From the structure of the product alone the intermediacy of a nitrene species can neither be proved nor disproved.

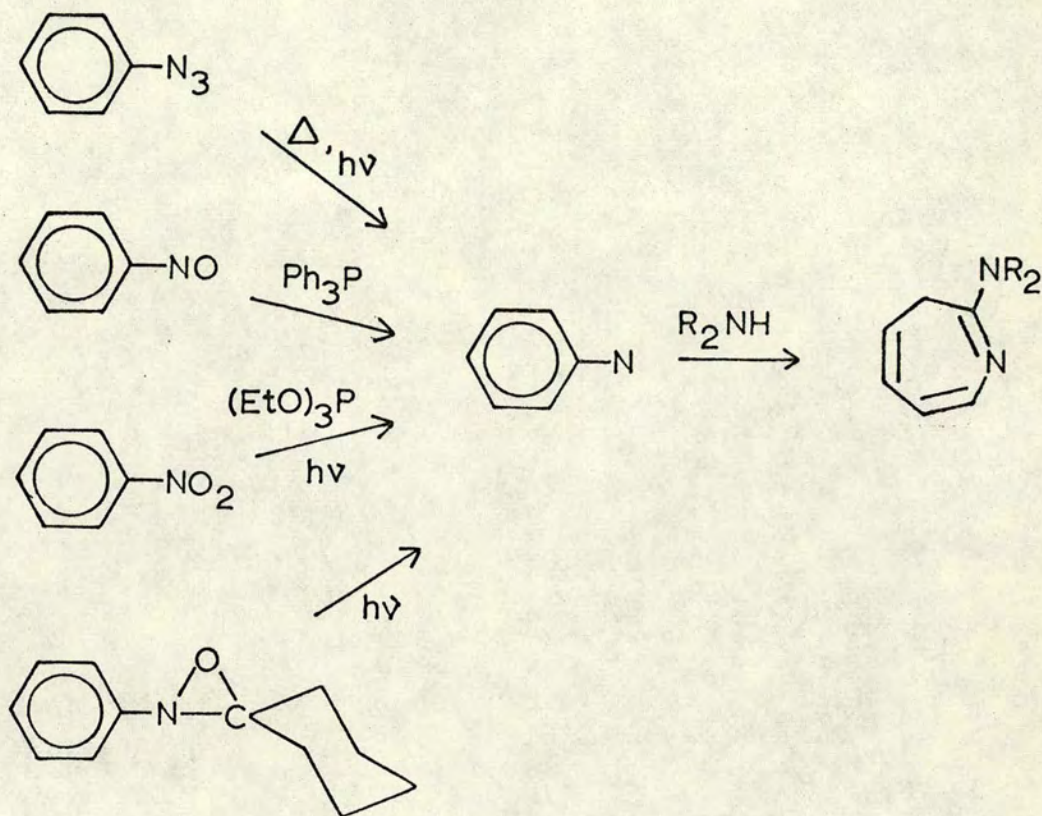
An interesting example which illustrates the necessity to



Scheme 5

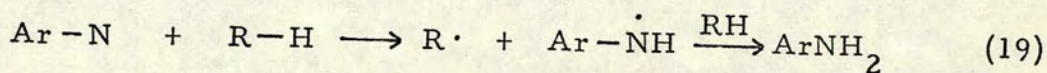
consider both the nitrene mechanism and the concerted reaction is the work of Boyer and Mikol⁴⁵ on the photolysis of 2-2'-diazidobiphenyl. These workers obtained 50% of 4-azidocarbazole (3) and trace amounts of benzo[*c*]cinnoline (2). The postulated reaction pathways are shown in Scheme 6. Since the formation of carbazole by either photolysis or pyrolysis of 2-azidobiphenyl proceeds from an intermediate nitrene,¹³ the formation of (3) from (1) may be construed as diagnostic evidence for the intermediacy of 2-azido-2'-nitrenobiphenyl (4). The formation of benzo[*c*]cinnoline could proceed either by a concerted mechanism not involving nitrenes (route B) or via the nitrene (4).

The intermediacy of a nitrene species has been shown to be highly probable in many reactions by generating the species by two or more independent routes and showing that the same products or product mixtures result. The example of the addition of carbethoxynitrene

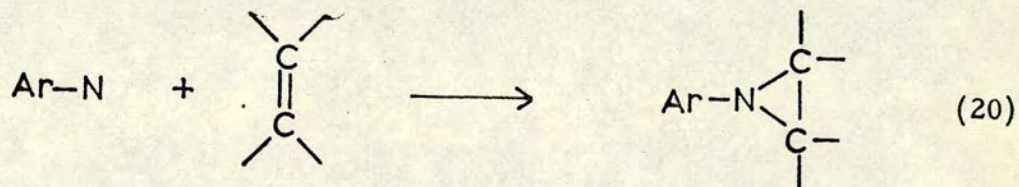


Scheme 7

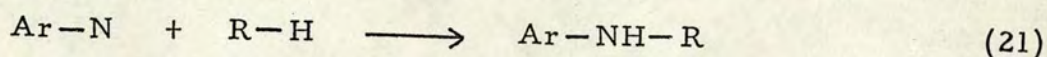
Each of these reactions is more or less difficult to explain without invoking a nitrene but none of them by itself constitutes absolute proof: abstraction of hydrogen,



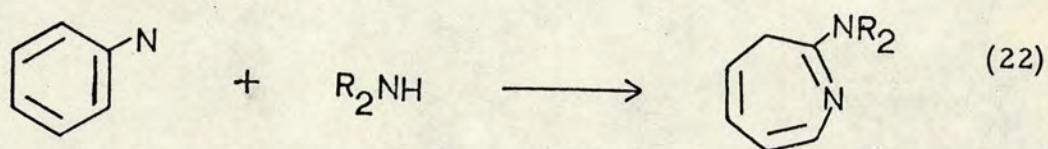
addition to a multiple bond,



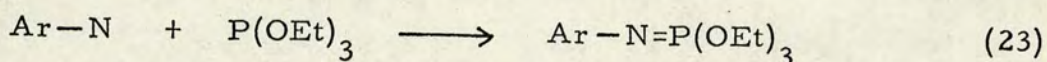
insertion into a single bond (usually C-H),



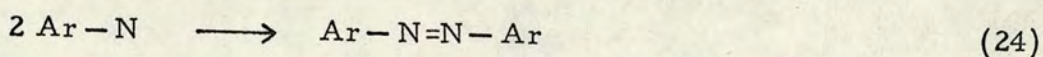
ring expansion accompanied by reaction with a suitable nucleophile,



bond formation at an unshared electron pair (usually on phosphorus),



and dimerisation.

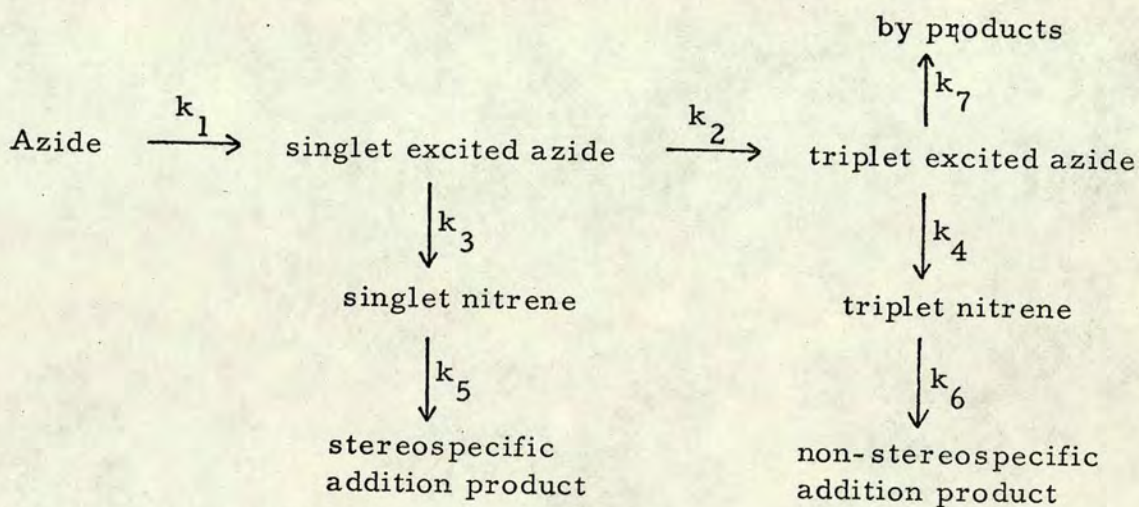


The isolation of a specific reaction product does not necessarily allow the unambiguous deduction of the reaction by which it arose. There are usually other possible routes to be considered some of which may not involve a nitrene. Interpretation may be further complicated by the fact that the initial products may be so labile that the final products actually isolated are the result of further transformation.

(B) Thermolysis and Photolysis of Azides

The extensive work of Lwowski and his group¹⁷ on the thermolysis and photolysis of ethyl azidoformate in olefins has been discussed in the section on the addition of nitrenes to C=C double bonds. Thermolysis of the azide yielded a completely stereospecific product, a result of the reaction of singlet nitrene with olefin. From photolysis

they obtained a mixture of stereospecific and racemised products, the latter being formed from the reaction of triplet nitrene which has its origin in an excited triplet state of the azide. There is thus a competition between dissociation of the singlet excited state and the intersystem crossing from the excited singlet azide to the triplet state. The decomposition can thus be summarised in Scheme 8.



Scheme 8

Sensitised decomposition provides a useful method of studying the triplet nitrene with minimum contamination by the singlet species. In a study of the photodecomposition of 2-azidobiphenyls, Swenton⁵² found that direct irradiation of 2-azidobiphenyl in various solvents produced carbazole (68-74%) and azo-2-biphenyl (8-12%). Acetophenone-sensitised photolysis yielded 40-49% of the azo compound and less than 5% of carbazole, thus establishing the intermediacy of the excited triplet state in the formation of the azo compound. Quenching studies using piperylene a known triplet quencher reduced the formation of azo compound to less than 3% while enhancing the yield of carbazole to 90%.

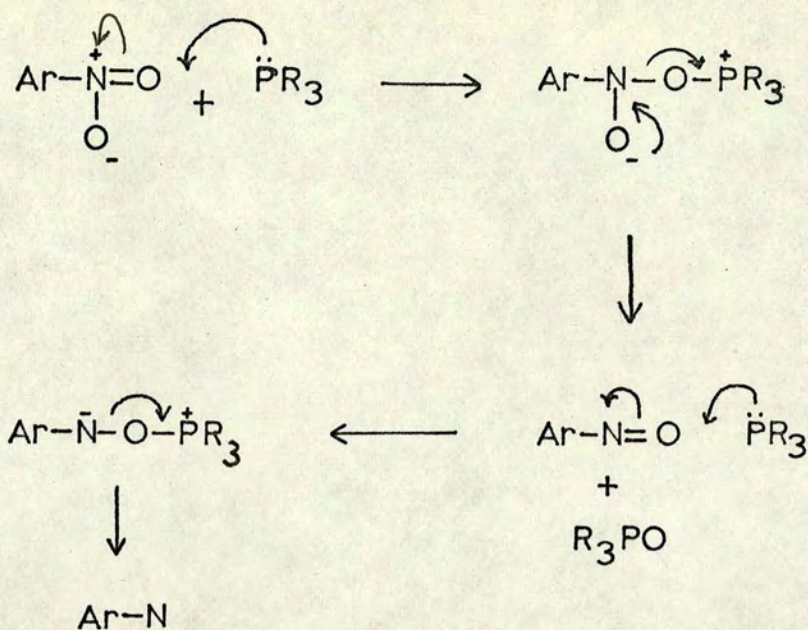
In practice, most azides decompose smoothly in solution or in the vapour phase at temperatures between 140-200°. Thermolysis of azides is usually accomplished in dilute solution in order to moderate

the exothermic reaction. Decomposition does not appear to depend on the nature of the solvent (as long as it is not acidic) although the final products may involve reaction with the solvent. Some examples of the solvents used are decalin, tetralin, hexadecane and resorcinol dimethyl ether.

(C) Deoxygenation Of Nitro And Nitroso Compounds By Tervalent Phosphorus Reagents.

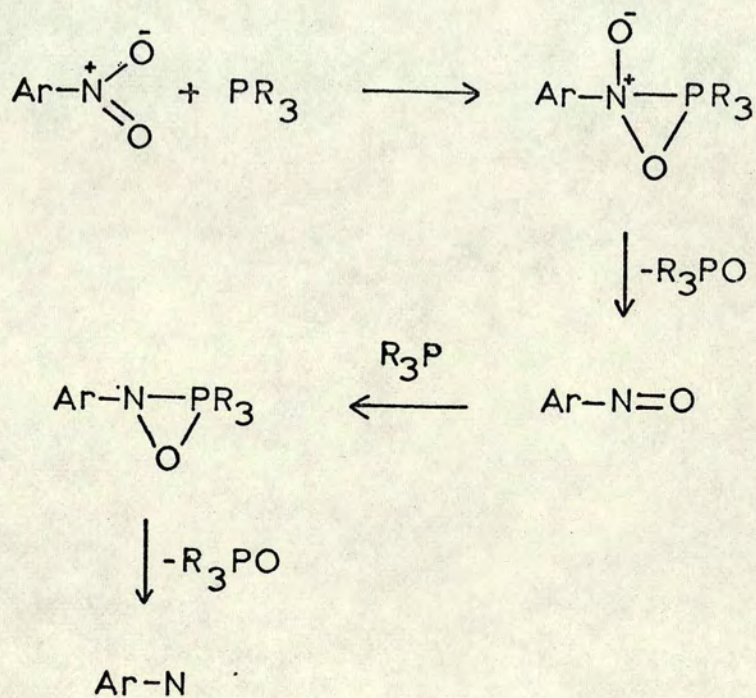
Tervalent phosphorus reagents (X_3P) such as trialkyl phosphites and triaryl phosphines react with a wide variety of oxygen-containing compounds to yield the corresponding pentavalent phosphorus compounds (X_3PO).⁵³ The great strength of the $P=O$ bond provides the major driving force for these reactions. Typical bond dissociation energies of the $P=O$ bond in phosphates and phosphine oxides lie in the range 500-630 kJ mole^{-1} (120-150 kcal. mole^{-1})⁵⁴ compared with values in the range 210-300 kJ mole^{-1} (50-70 kcal. mole^{-1}) for the $N^+ - \bar{O}$ bond in amine oxides.⁵⁵

The deoxygenation of nitro and nitroso compounds by tervalent phosphorus reagents has been the subject of recent reviews by Cadogan^{56, 57} and Boyer.⁵⁸ Recent evidence indicates nitrene intermediacy in many of these reactions since many cyclisations similar to those observed in azide decompositions have been achieved by such reactions. Aromatic nitro compounds react more slowly than the corresponding nitroso compounds and it has been proposed that stepwise deoxygenation first transforms the nitro compound into the nitroso group.⁵⁹⁻⁶¹ Cadogan⁶² proposed the following scheme



Scheme 9

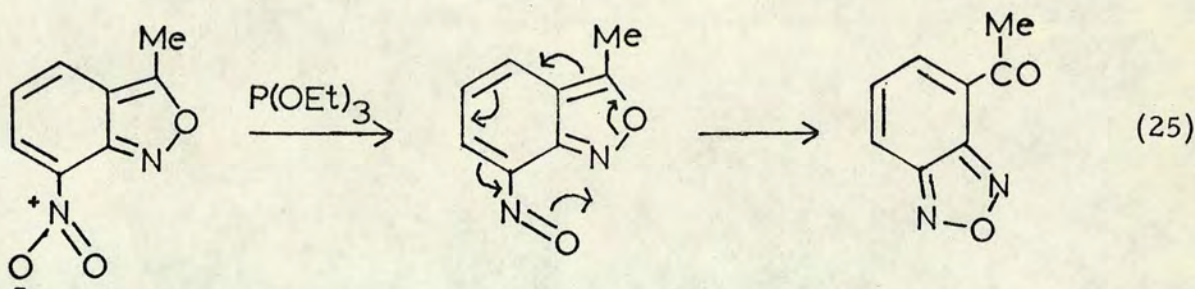
while Smolinsky⁵⁹ suggested a scheme involving a cyclic intermediate, thus:



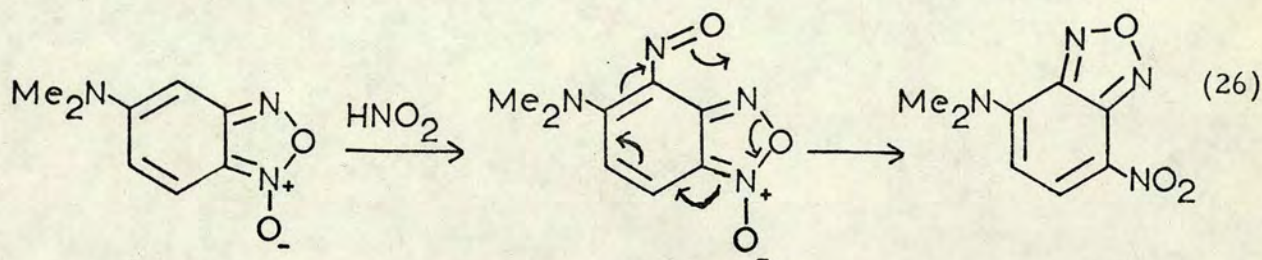
Scheme 10

The initial nucleophilic attack by the phosphorus reagent is substantiated by the fact that phosphorus trichloride PCl_3 will not deoxygenate 2-nitrobiphenyl.⁶¹

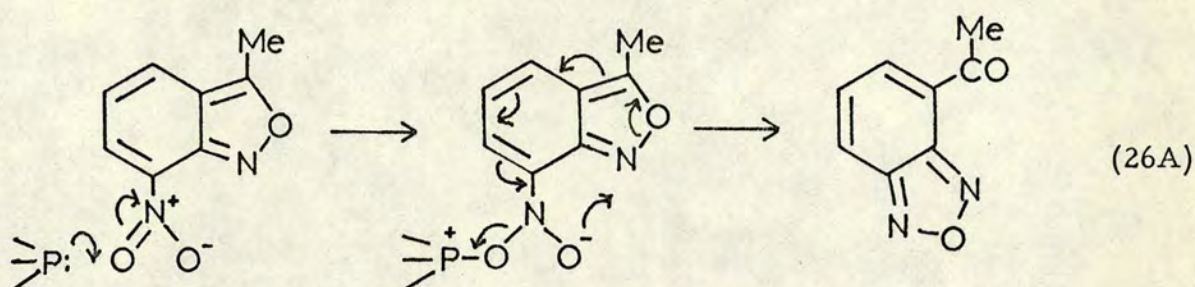
In practice it is difficult to establish that the nitro group is first reduced to the nitroso group because the latter is itself more easily reduced e. g. in the reduction of 2-nitro- and 2-nitrosobiphenyl by triethyl phosphite, the half-lives are 50 min. at 145° and 2 min. at 0° respectively.⁶¹ Katritzky et al.⁶³ have recently adduced indirect evidence that reduction of 3-methyl-7-nitroanthranil to 4-acetylbenzofurazan proceeds via the intermediacy of the corresponding nitroso compound,



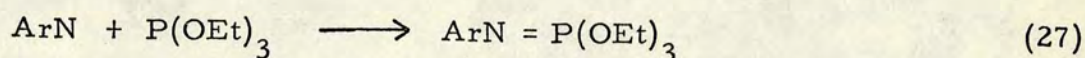
Earlier work⁶⁴ has shown that nitrosation of 5-dimethylaminobenzofuroxan gave 4-dimethylamino-7-nitrobenzofurazan via a similar rearrangement.



However it is not possible to rule out other routes to 4-acetylbenzofurazan (such as eq. 26A) which do not involve initial reduction of the nitro group to the nitroso.

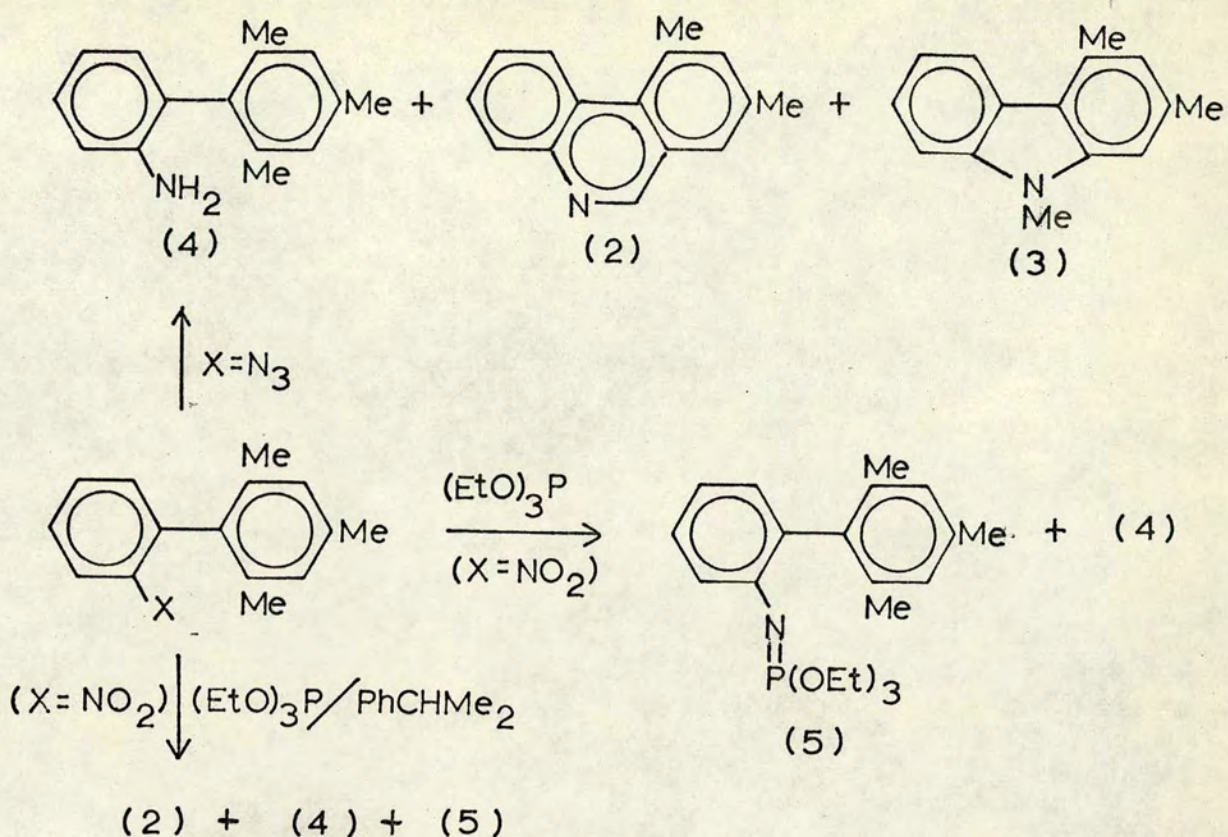


Pyrolysis of 2-azido-2',4',6'-trimethyl biphenyl was reported by Smolinsky⁶⁵ to yield 8,10-dimethylphenanthridine (2; 50%), 2,4,9-trimethylcarbazole (3; 5%) and 2-amino-2',4',6'-trimethylbiphenyl (4; 40%) (Scheme 11). These products were rationalised by a nitrene mechanism. Cadogan and Todd⁶¹ in a study of the triethyl phosphite-induced deoxygenation of 2,4,6-trimethyl-2'-nitrobiphenyl has given evidence in support of such a mechanism. Reaction of excess of phosphite with the nitro compound gave the amine (4; 13%) (suggesting hydrogen abstraction by an electron-deficient species, possibly a nitrene) and triethyl-N-(2',4',6-trimethylbiphenyl-2-yl)phosphorimidate (5; 15%) which could arise thus:



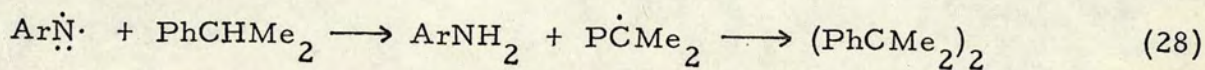
This interpretation was supported by the results of the deoxygenation in excess cumene as solvent. As expected the coupling reaction (eq. 27) was suppressed while insertion and hydrogen abstraction reactions were enhanced as indicated by the isolation of 32% amine (4) and 14% of the phenanthridine (2). (Scheme 11)

Furthermore 11% of 2,3-dimethyl 2,3-diphenylbutane was obtained. This product can arise only by dimerisation of α -cumenyl radicals produced by abstraction of hydrogen from cumene by a radical species

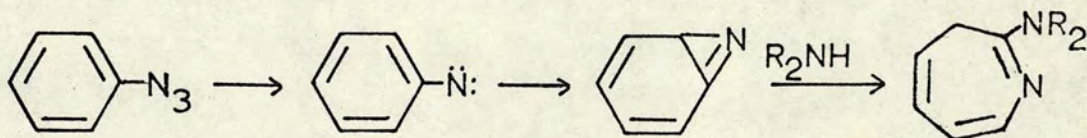


Scheme 11

presumably triplet nitrene.

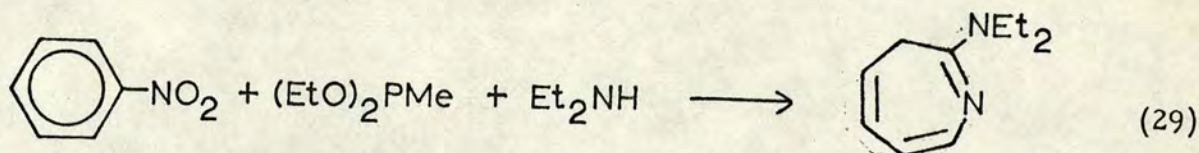


The decomposition of phenyl azide in amines to give azepines has been suggested to go via phenylnitrene and 7-azabicyclo[4, 1, 0]-hepta-2, 4, 6-triene.^{46, 47} (Scheme 12)

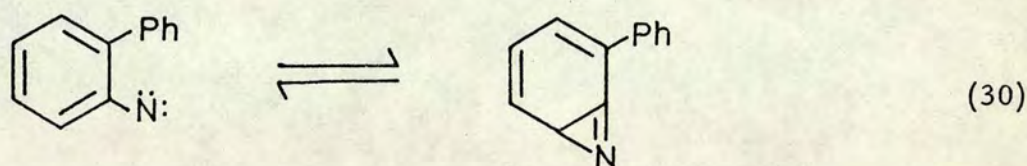


Scheme 12

This ring expansion has been used by Odum and Brenner⁴⁸ to support the suggestion⁶⁶ of nitrene participation in the triphenylphosphine-induced deoxygenation of nitrosobenzene. When nitrobenzene was deoxygenated by diethyl methyl phosphonite in a large excess of diethylamine, 2-diethylamino-3H-azepine was obtained in 83% yield.⁶¹

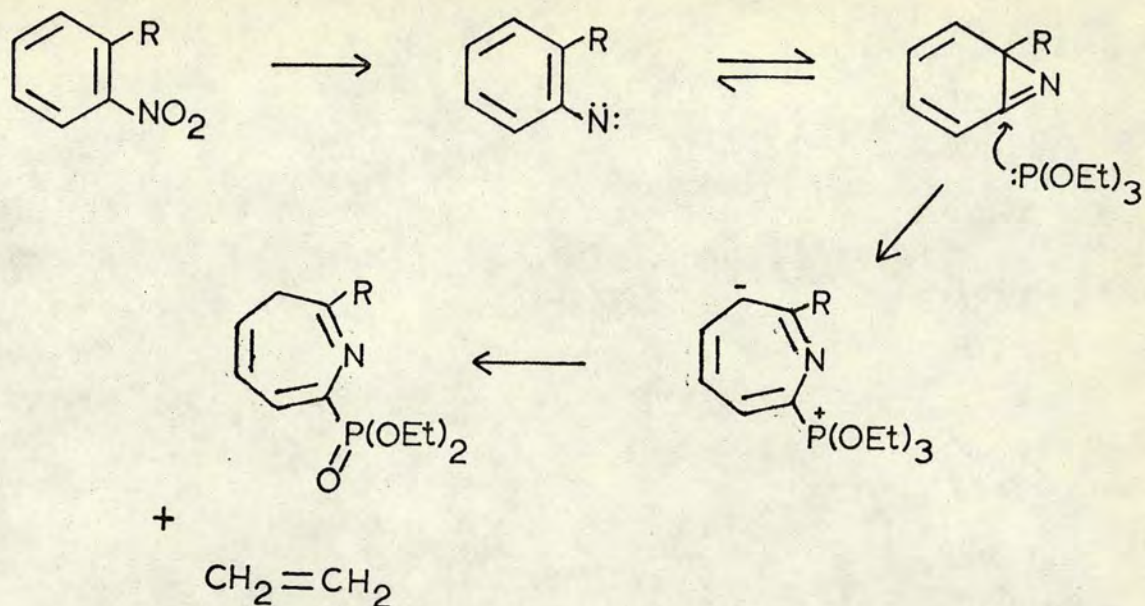


The corresponding reaction of 2-nitrobiphenyl gave 2-diethylamino-3-phenyl-3H-azepine (13%) in addition to carbazole (67%). Cadogan has suggested⁶¹ that the nitrene and azabicycloheptatriene are present in equilibrium (cf. Abramovitch and Davis' similar suggestion⁷),



carbazole arising from the nitrene and the azepine from the azabicycloheptatriene. That such a bond reorganisation is competitive with cyclisation has been established by Sundberg in a photolytic decomposition of 2-azidobiphenyl.⁶⁷

Cadogan et al.⁶⁸ have also established the intermediacy of nitrenes in the thermal reaction of nitrobenzene and substituted nitrobenzenes with trialkyl phosphites in the absence of amines. Low but significant yields (< 18%) of dialkyl 3H-azepin-7-ylphosphonates were formed (Scheme 13) in addition to dialkyl-N-arylphosphoramidates and dialkyl-N-alkyl-N-arylphosphoramidates.



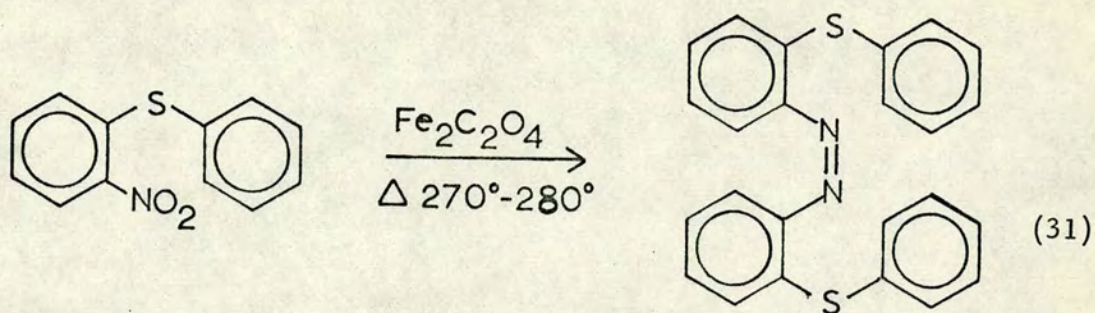
Scheme 13

Sundberg and his co-workers have also reported⁶⁹ the similar formation of diethyl 2,4,6-trimethyl-3H-azepin-7-yl phosphonate in the photochemical and thermal reaction of triethyl phosphite with 2-nitro mesitylene.

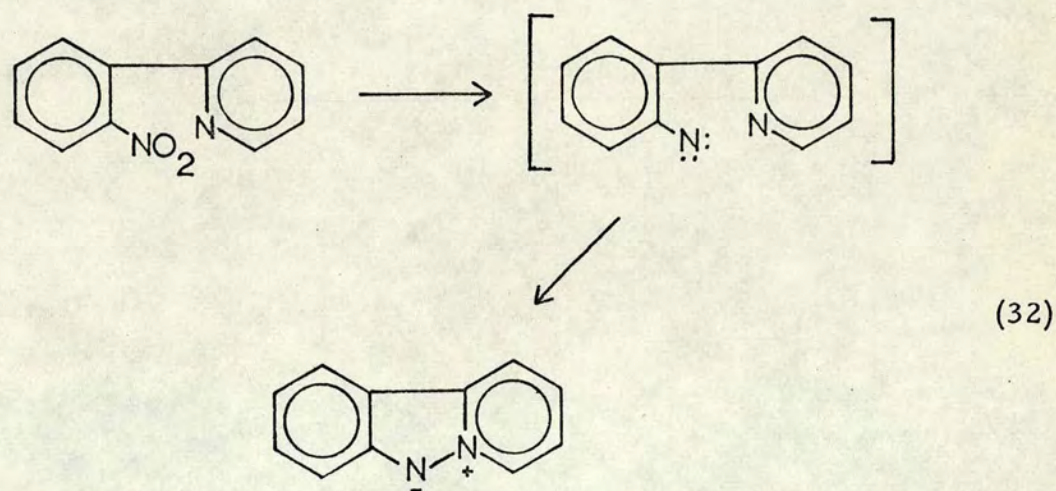
(D) Deoxygenation Of Nitro Compounds By Ferrous Oxalate

The cyclisation of nitro compounds using ferrous oxalate has long been known and constitutes the Waterman-Vivian synthesis of phenazine.⁷⁰ By heating a mixture of the nitro compound and ferrous oxalate to temperatures between 200-300^o, 2-methoxyphenazine was obtained from 4'-methoxy 2-nitrodiphenylamine in 49% yield; carbazole from 2-nitrobiphenyl in 63% yield; benzo[c]cinnoline from 2,2'-dinitrobiphenyl in 17% yield and acridine from 2-nitrobenzophenone. The phenazine synthesis has been extended to a wide range of phenazines.⁷¹⁻⁷³ However an attempt to prepare phenothiazine from 2-nitrodiphenyl sulphide gave only 2,2'-bis(phenylmercapto) azobenzene,⁷⁴ while 2-nitrodiphenyl sulphone gave only 2-aminodiphenyl sulphone.

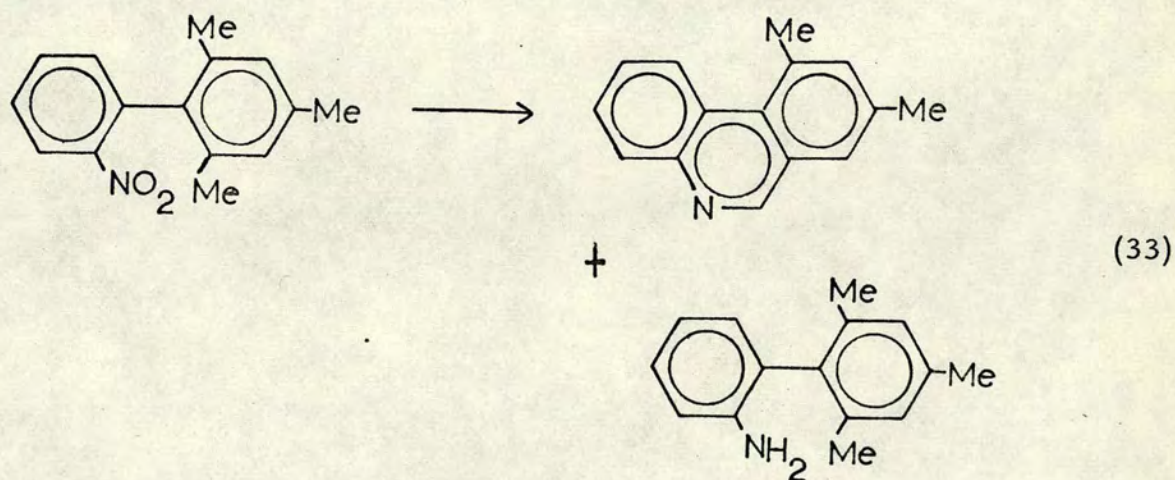
Abramovitch et al. have postulated a nitrene mechanism



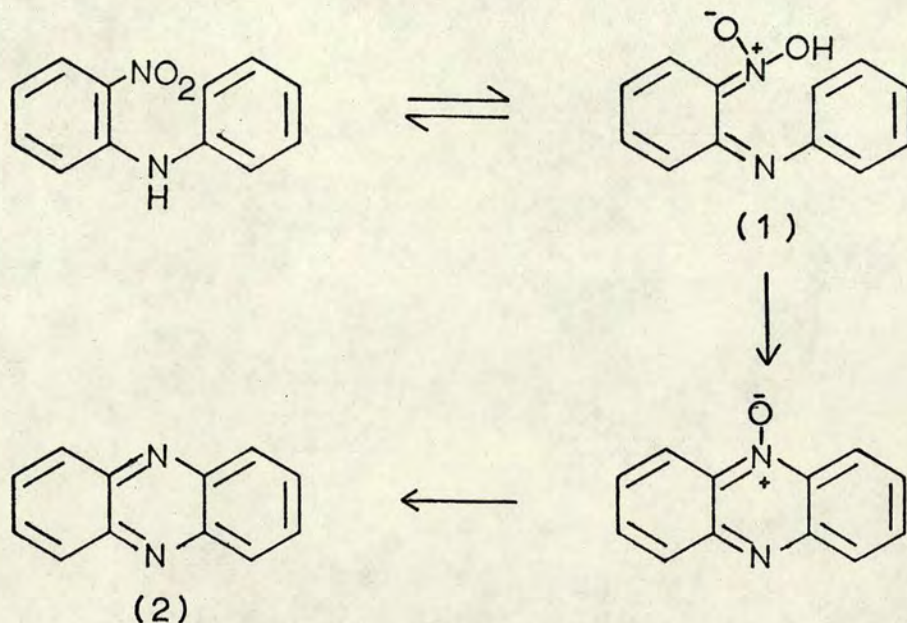
for the deoxygenation of nitro compounds by ferrous oxalate. They obtained pyrido[1,2-b]indazole from 2-o-nitrophenyl pyridine,⁷⁵



8,10-dimethylphenanthridine (22.6%) and 2-amino 2',4',6'-trimethylbiphenyl (27.4%) from 2-nitro 2',4',6'-trimethylbiphenyl.⁷⁶



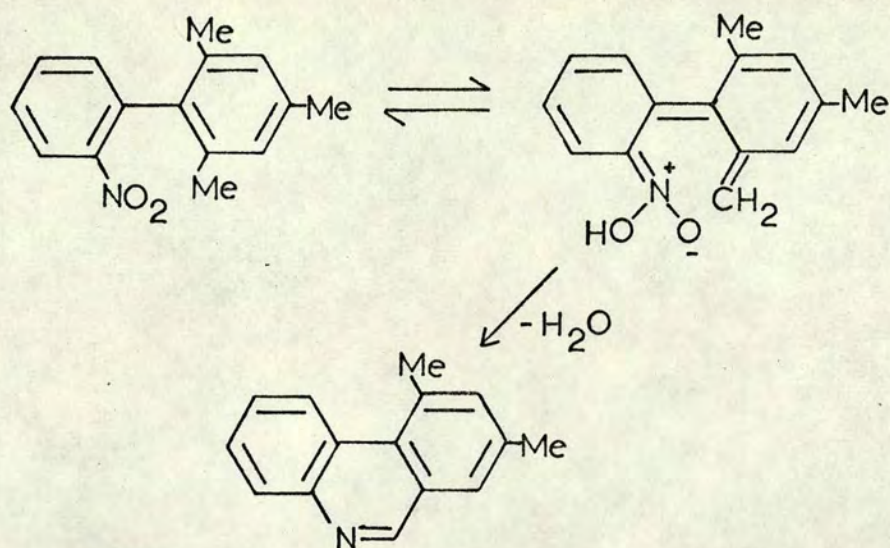
Suschitzky and Smith⁷⁷ have prepared phenazine (2) and several benzimidazoles from N-substituted o-nitroanilines and have suggested a plausible mechanism based on the loss of water from the aci-nitro form (1) thus:



Scheme 14

Likewise Smolinsky and Feuer⁵⁹ have obtained 8, 10-dimethylphenanthridine (32%) and carbazole (27%) by heating a diphenyl ether solution of 2-nitro 2', 4', 6'-trimethylbiphenyl at 350° without ferrous oxalate. They postulated that the nitro group was reacting through its aci form and concluded there was no need to invoke a nitrene intermediate in the ferrous oxalate reductions.

Abramovitch and Davis⁷⁸ in a further report reasoned that in cases where the aci-nitro compound can be formed the cyclisations proceed by two different mechanisms particularly if a suitable deoxygenating agent is absent. In the other cases he maintains that a mechanism involving complexed nitrene bound to the surface of the reagent and therefore not necessarily free, will account for all the products observed.



Scheme 15

I. 5. SYNTHETIC APPLICATIONS

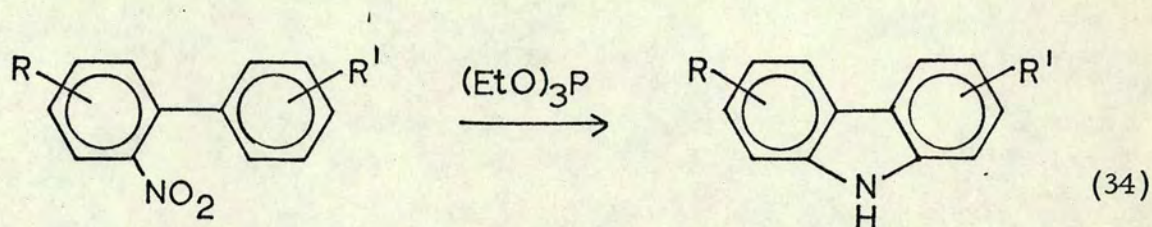
This section will be limited to a review of cyclisation reactions which occur on decomposition of aromatic azides and on reduction of aromatic nitro compounds by triethyl phosphite. In many cases they represent useful synthetic routes to heterocyclic compounds of nitrogen. Most of the examples cited proceed via a nitrene intermediate. Where a concerted cyclisation is the preferred pathway this will be mentioned specifically.

(A) Five-membered Heterocycles.

(i) Carbazoles, carbolines and benzocarbazoles.

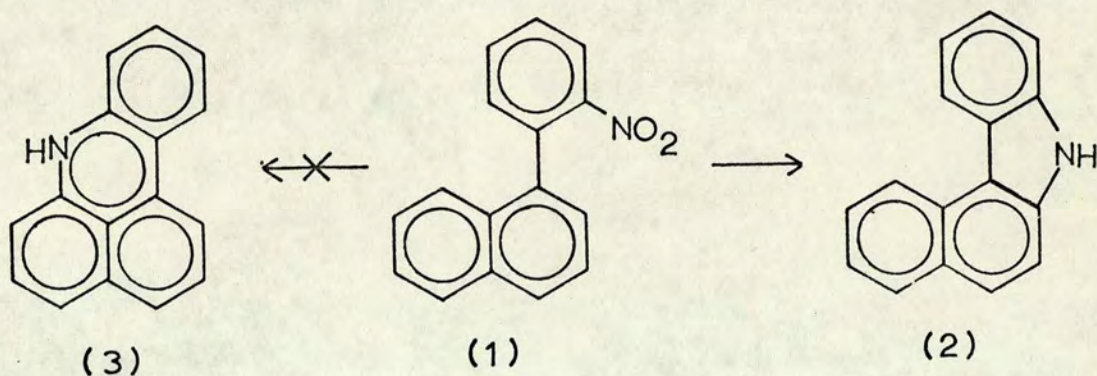
Smith et al.²³ synthesized carbazole in 77% yield by the thermal and photolytic decomposition of 2-azidobiphenyl. This work was extended to include halo-, methoxy- and nitro-substituted carbazoles. Cadogan et al.⁶² obtained carbazoles in good yield

(35-83%) by deoxygenation of the readily available 2-nitrobiaryls:



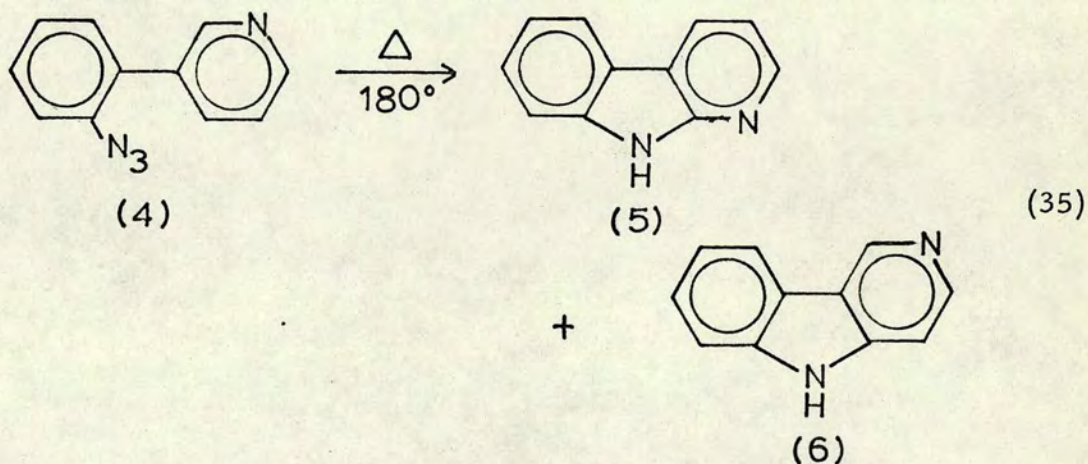
R, R' = H, Br, CH₃ or polymethyl.⁷⁹

The reduction of 1-(2-nitrophenyl)naphthalene (1) gave 7H-benzo[c]-carbazole (2; 64%) rather than the isomeric six-membered heterocycle (3) thus showing a preference for formation of five-membered rings.

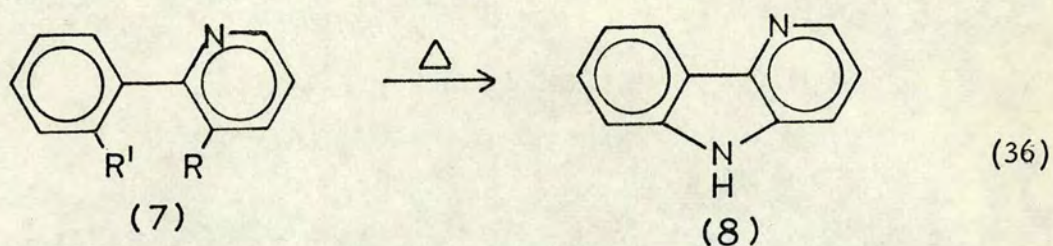


Scheme 16

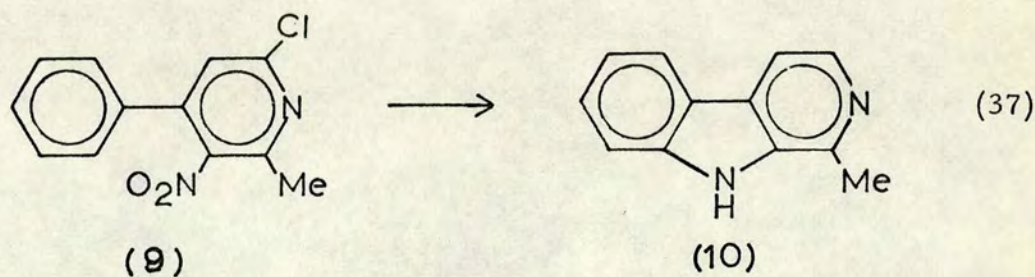
A mixture of α - and γ -carboline (5) and (6) respectively was obtained in high yield by thermolysis of 3-(2-azidophenyl)pyridine (4),⁸⁰



whereas thermolysis of 2-(2-azidophenyl)pyridine (7; R = H, R' = N₃) failed to yield the expected β -carboline (8) which has since been prepared in good yield by pyrolysis of the isomeric 3-azido-2-phenylpyridine (7; R = N₃, R' = H).⁸¹

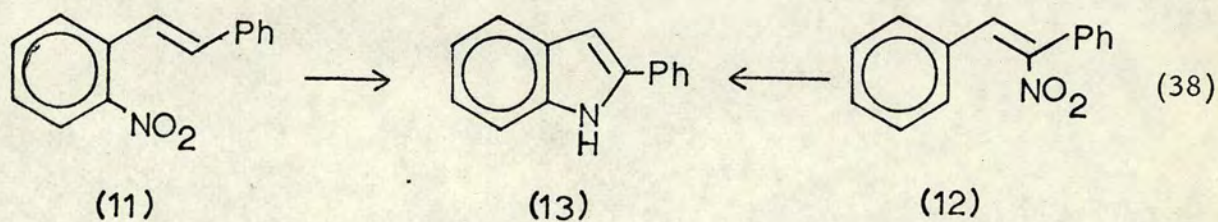


Harman, a β -carboline alkaloid (10) was synthesized by reductive cyclisation of 6-chloro 3-nitro 2-methyl 4-phenylpyridine (9) and subsequent dechlorination.⁸²



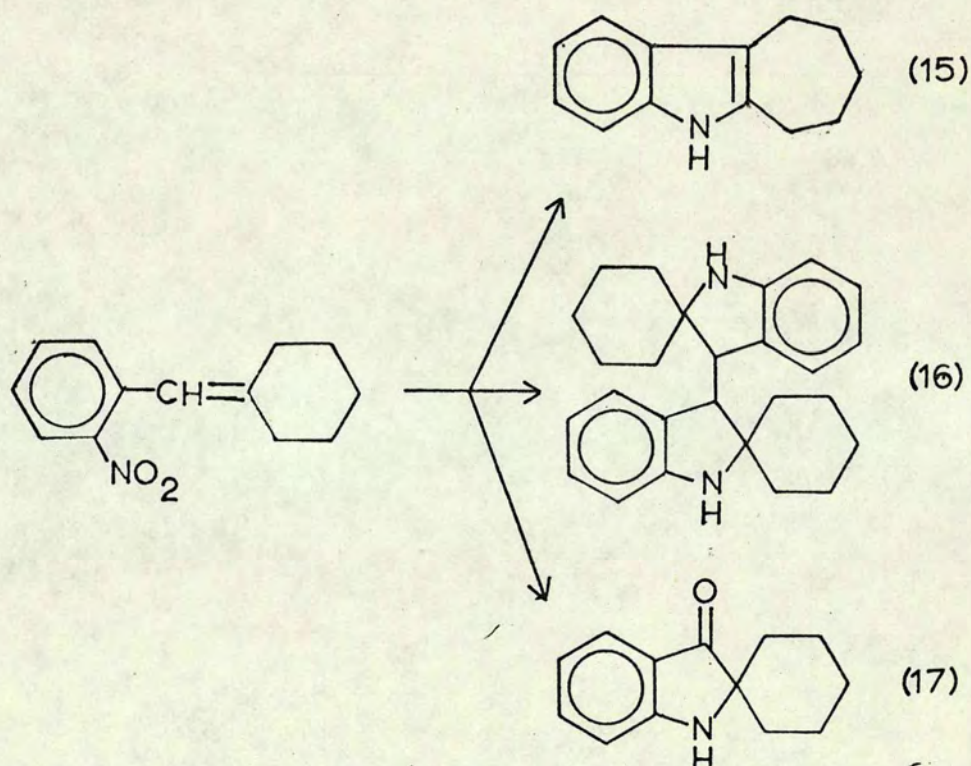
(ii) Indoles and related systems.

Tri ethyl phosphite-induced deoxygenation of cis- and trans-2-nitrostilbene (11) and α -nitrostilbene (12) gave 2-phenylindole (13) in 85, 58 and 16% yields respectively.⁶²



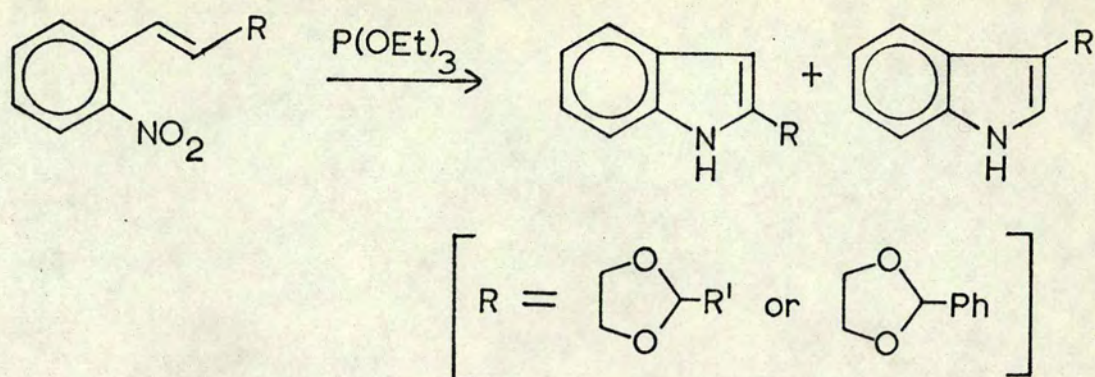
Sundberg⁸³ has extended the indole synthesis to include 2-alkyl (CH_3 , C_2H_5 , 50-60% yields) and 2-acyl (CH_3CO , $\text{C}_6\text{H}_5\text{CO}$; 16% yields) indoles. Minor by-products of mechanistic interest are also formed.

When β, β -disubstituted 2-nitrostyrenes⁸⁴ are reductively cyclised indoles again form the major products. Thus cyclohexylidene-(2-nitrophenyl)methane (14) undergoes ring closure with rearrangement to give 5,6,7,8,9,10-hexahydro-cyclohepta[b]indole (15; 35%) together with smaller yields of the bi-indolyl (16; 24%) and the spiro-indolinone (17; 8%) (Scheme 17)



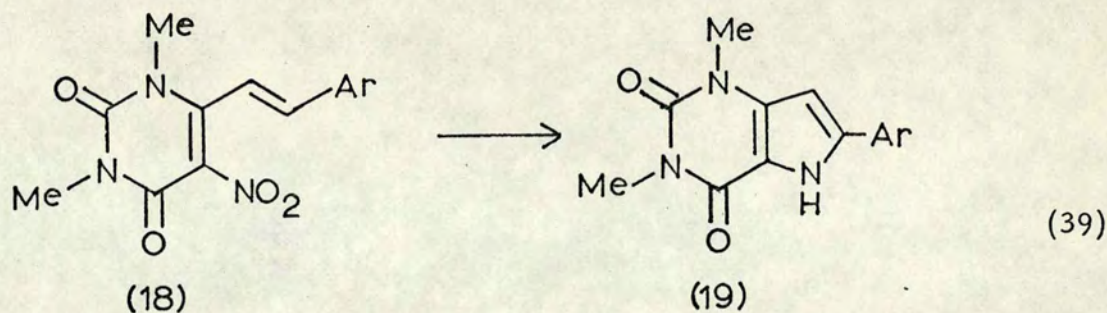
Scheme 17

Similarly, the reaction of 2-nitro β, β -dimethylstyrene gave 2,3-dimethylindole (33%). A further extension⁸⁵ to the indole synthesis involving migration of a β -substituent in a mono-substituted 2-nitro-styrene is outlined in Scheme 18.

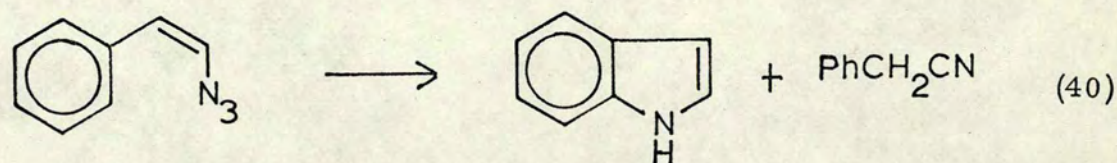


Scheme 18

Two biologically interesting pyrrolo[3, 2-d]pyrimidines (19) have resulted from the thermal and photolytic reaction of the corresponding 5-nitro-6-styrylpyrimidine derivative (18) in the presence of triethyl phosphite.⁸⁶



Pyrolysis of β -azidostyrenes has been reported to give indoles. Thus cis- and trans- β -azidostyrene in boiling n-hexadecane solution gave 85% of a 1:1 mixture of indole and phenylacetonitrile,⁸⁷

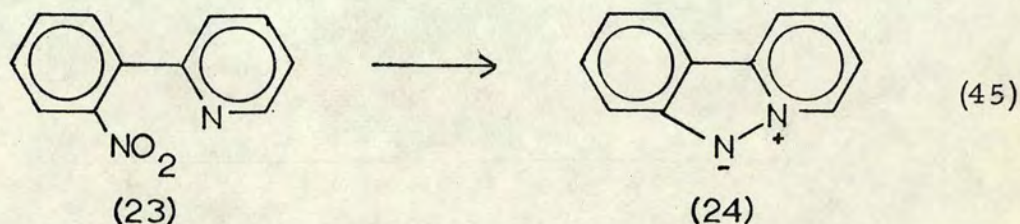


while the corresponding thermolysis of cis- and trans- β -azido- β -methylstyrene gave only 2-methylindole (86%).

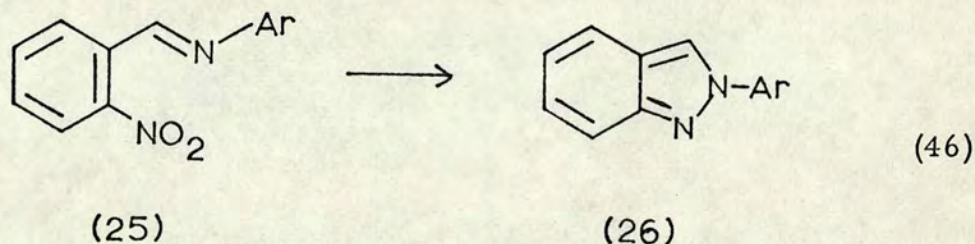
and by the pyrolysis of the corresponding azides (21; $R^1 = H$, $R^2 = N_3$).

(iii) Indazoles, imidazoles, triazoles and related systems.

Pyrido[1, 2-*b*]indazole (24) was obtained in almost quantitative yield when 2-(2-nitrophenyl)pyridine (23) was treated with triethyl phosphite and boiled under reflux.⁶²

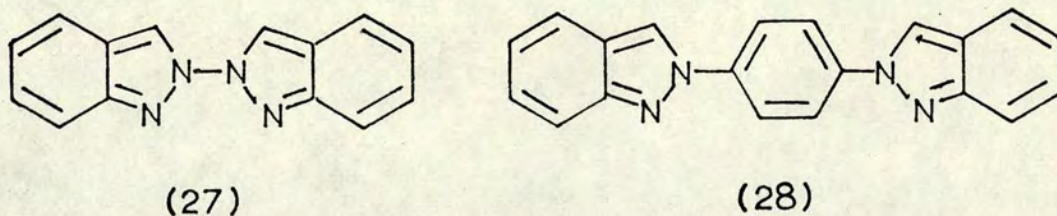


Similarly the successful cyclisations of *N*-(2-nitrobenzylidene)anilines (25) gave 2-arylidindazoles (26) in yields of 35-38%,⁶²

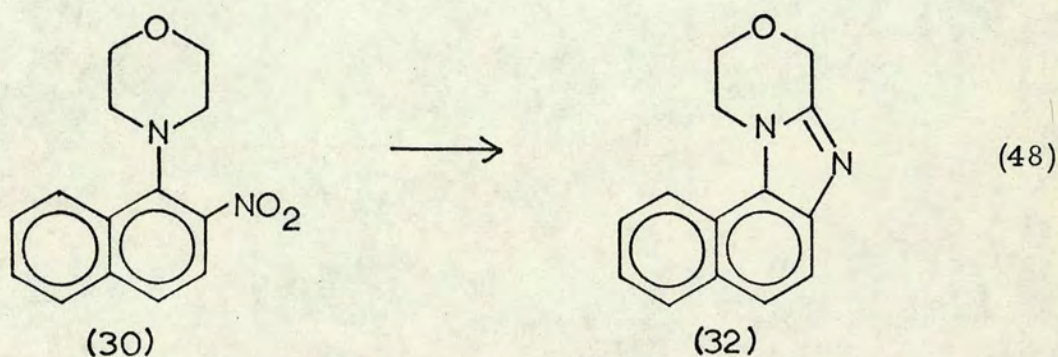
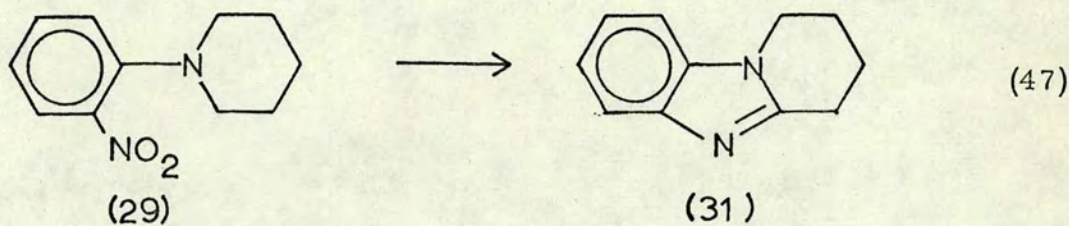


Ar = C_6H_5 , *o*-Br- C_6H_4 , *p*-MeO- C_6H_4 , *p*-CH₃- C_6H_4 , *o*-CH₃- C_6H_4 , 1-naphthyl.

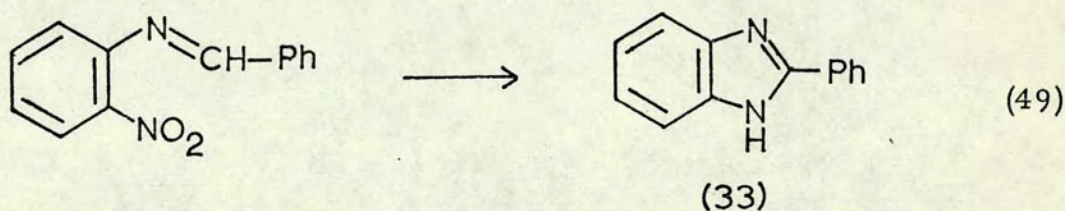
while 2-nitrobenzaldazine yielded 2-2'-bi-2*H*-indazolyl (27) and bis-(2-nitrobenzylidene)-*p*-phenylenediamine gave 1,4-bis(2*H*-indazolyl)-benzene (28).



The reductive cyclisation of the nitro compounds (29) and (30) gave the imidazoles (31), (32) in good yields.⁹⁰

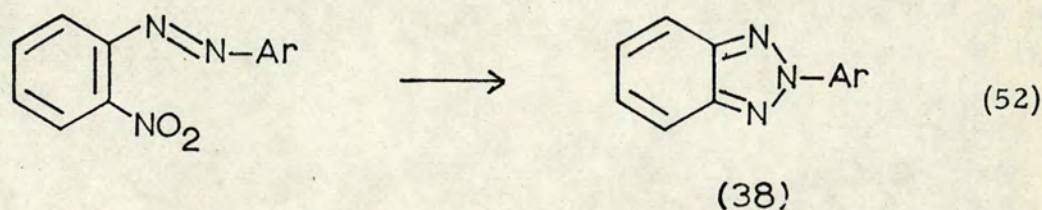
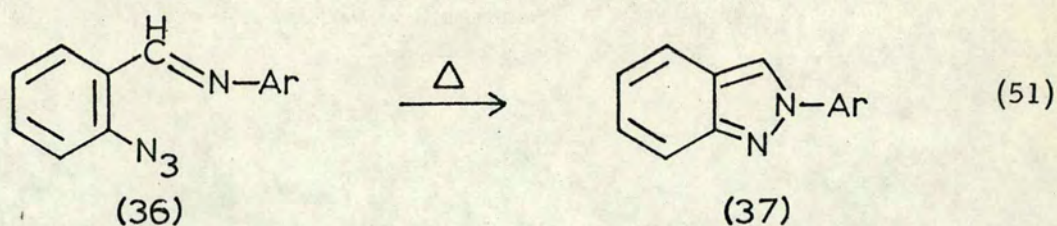
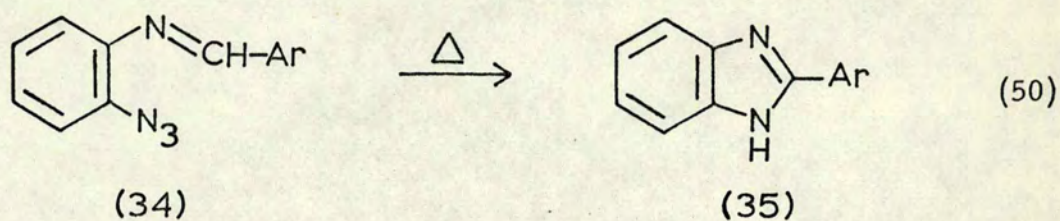


Similar treatment of N-benzylidene 2-nitroaniline resulted in the formation of 2-phenylbenzimidazole (33).⁹¹

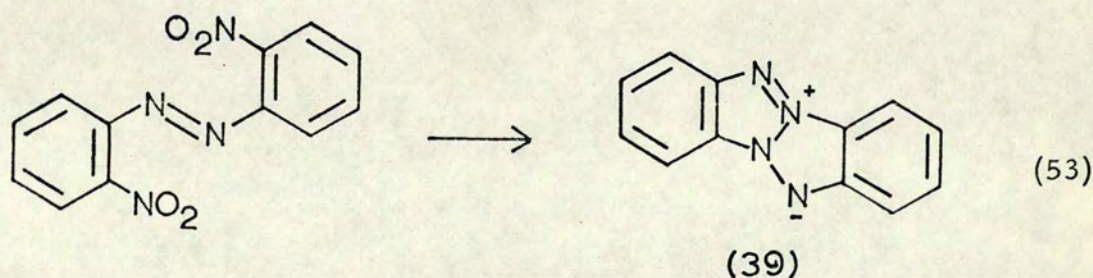


Benzimidazoles (35) have also been obtained in high yield by pyrolysis of the anils (34)⁹² while similar treatment of the isomeric anils (36) yielded the indazoles (37).⁹³

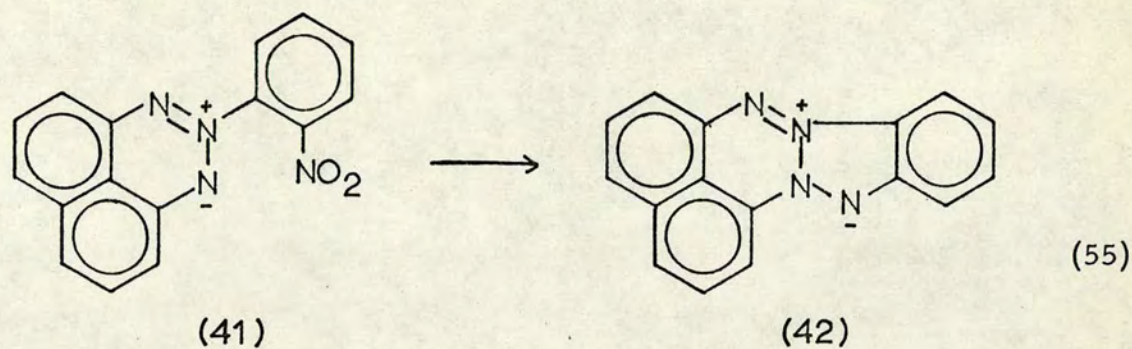
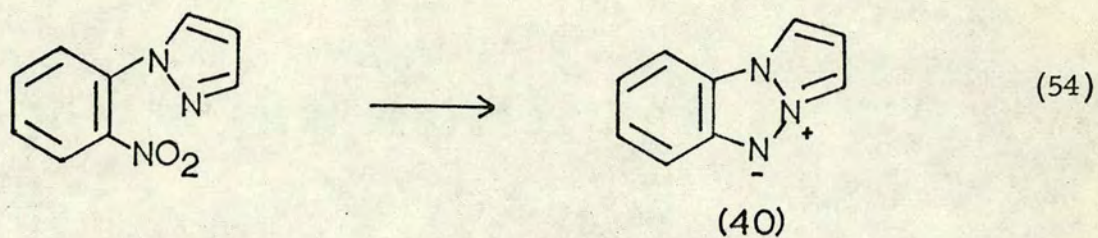
Bentotriazoles (38) are synthesized by the reductive cyclisation of 2-nitroazoarenes in yields of 30-37%.⁶²



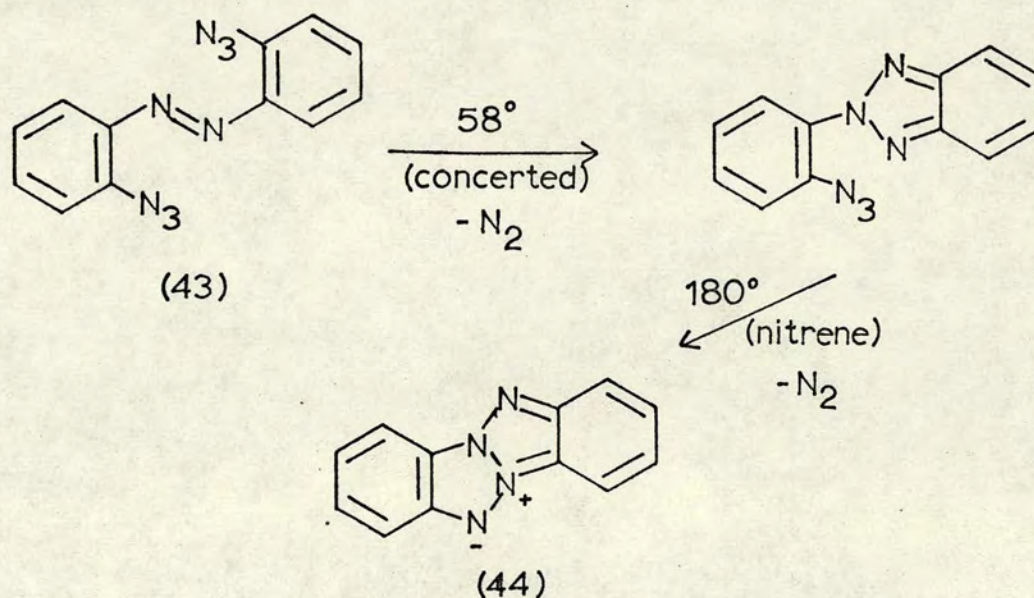
The interesting tetra-azapentalene ring system (39) has been successfully synthesized from 2-2'-dinitroazobenzene.⁶²



Extensions of these reactions include the formation of triazoles and triazines, two examples of which are given in eq. 54, 55. Pyrazolo[1,2-a]benzotriazole (40) from 1-(2-nitrophenyl)pyrazole,⁹⁴ and benzotriazolo[2,1-a]-naphtho[1,8-d,e]triazine (42) from the naphthotriazine (41).⁹⁵



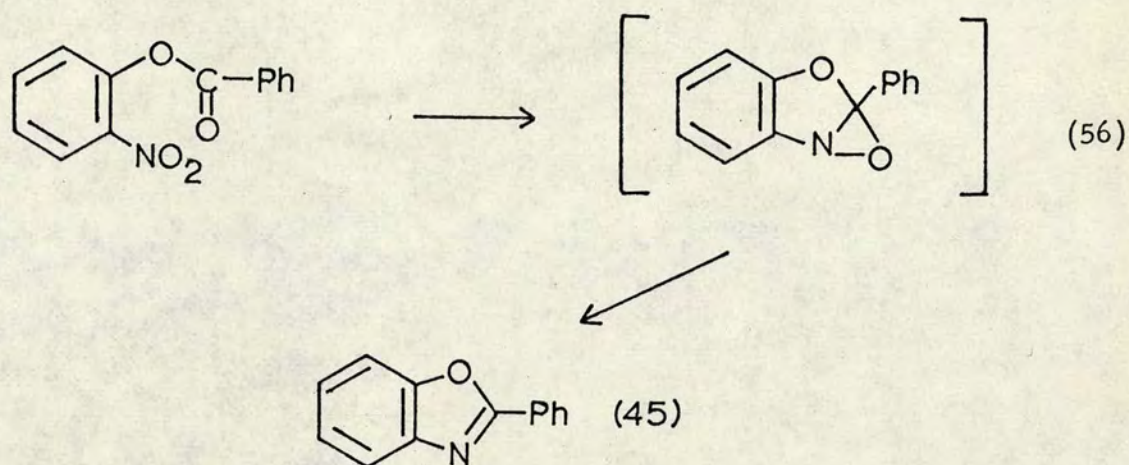
The ease of formation of benzotriazoles by low-temperature thermolysis of *o*-azido azo compounds has been interpreted as a concerted ring closure with loss of nitrogen.⁷ However the formation of the tetra-azapentalene system (44) from the diazine (43) proceeded in two distinct steps the latter of which definitely involved a nitrene intermediate.⁹⁶



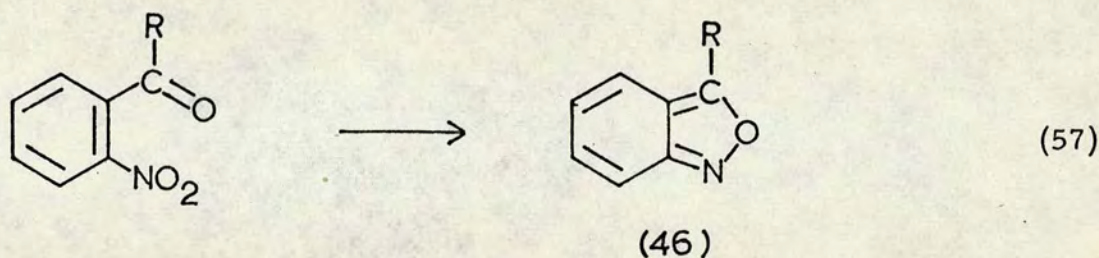
Scheme 19

(iv) Benzoxazoles, anthranils and furoxans.

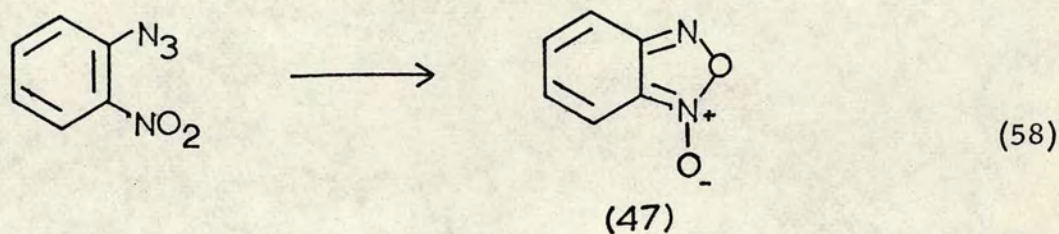
2-Phenyl-benzo 1,3-oxazole (45) is formed from the reaction of 2-nitrophenyl benzoate and excess phosphite,⁹⁷ presumably via nitrene insertion into the carbonyl function followed by deoxygenation:



2,1-Benzisoxazoles (anthranils) (46) are similarly prepared from 2-nitrophenyl ketones.⁹¹

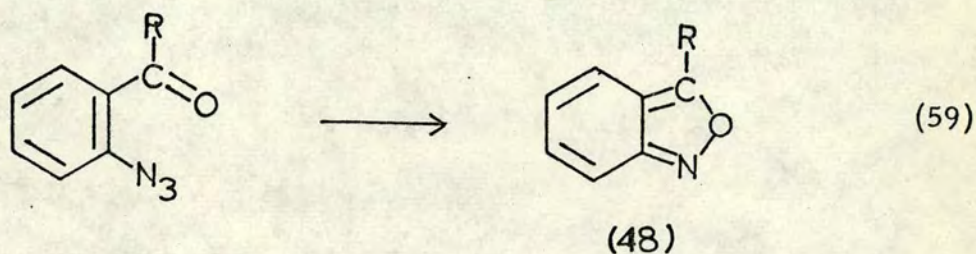


Pyrolysis or more usually photolysis of *o*-nitrophenyl azides is the most reliable method of preparing benzofuroxan (47).



This reaction has been used to prepare naphtho-, quinolino- and pyridofuroxans.⁹⁸ However kinetic evidence indicates a concerted ring

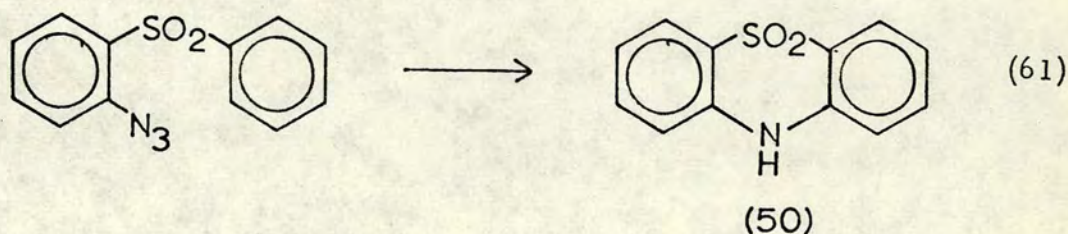
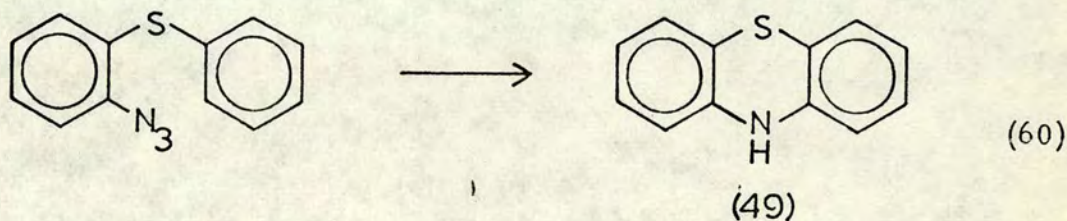
closure rather than a nitrene mechanism in these reactions. Likewise the formation of anthranils (48) is achieved by cyclisation of *o*-azido-aryl aldehydes or ketones.⁹⁹



(B) Six-membered Heterocycles.

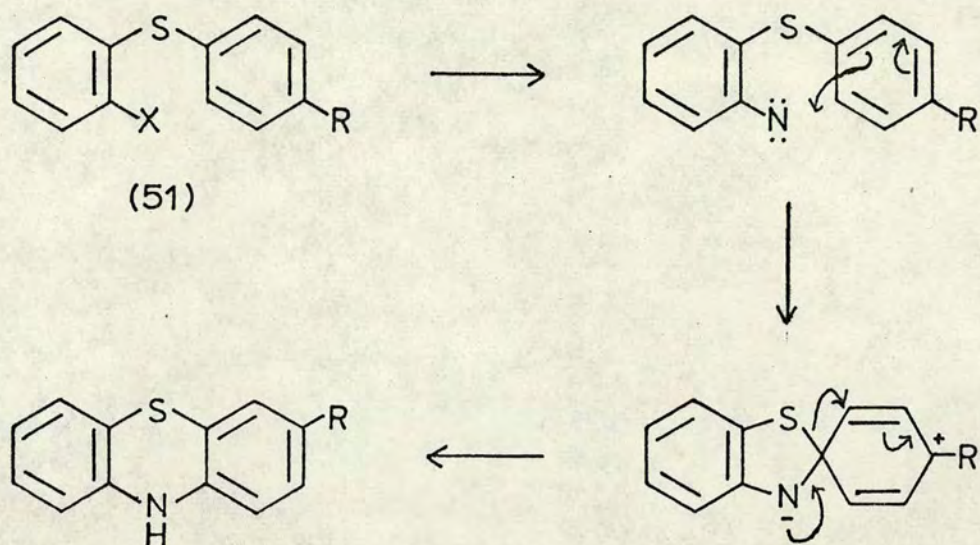
(i) Phenothiazines and related systems.

Six-membered ring heterocycles are not usually formed via nitrene intermediates. However the pyrolysis of 2-azidodiphenyl sulphide and sulphone has been reported¹⁰⁰ to give phenothiazine (49) and phenothiazine 5,5-dioxide (50) respectively. The reaction of the corresponding ether failed to cyclise.



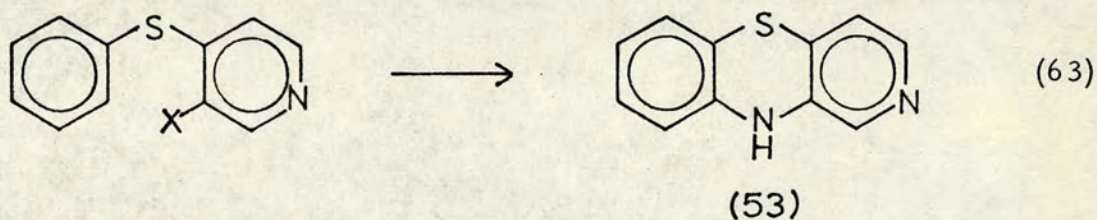
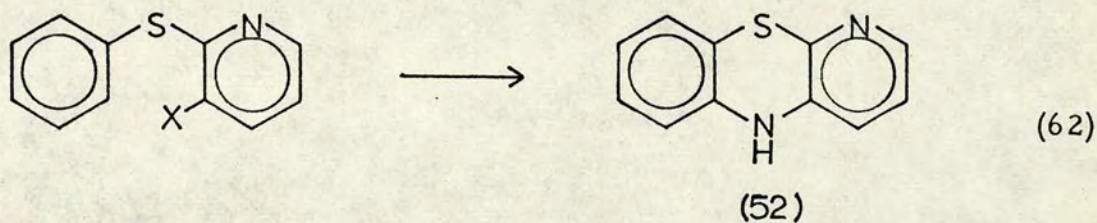
The formation of phenothiazine has been subsequently shown by Cadogan et al.¹⁰¹ to involve a five-membered spirodiene intermediate

which rearranges to the final product.



Scheme 20

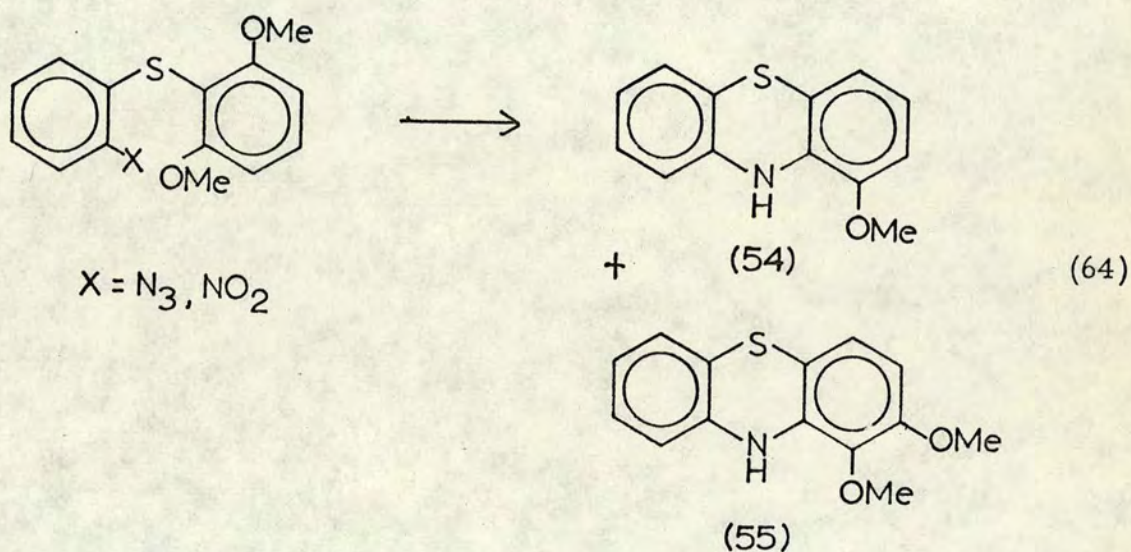
Thus, the thermolysis of aryl 2-azidoaryl sulphides (51; $X = N_3$) gave the phenothiazine in yields of 30% while the corresponding reductive cyclisation of aryl 2-nitroaryl sulphide (51; $X = NO_2$) with triethyl phosphite resulted in 50-85% yields of the phenothiazine. Similarly, 5H-pyrido[2,3-b][1,4]benzothiazine (52) and the isomeric 5H-pyrido[3,4-b][1,4]benzothiazine (53) were prepared from the corresponding azides and nitro compounds. ¹⁰²



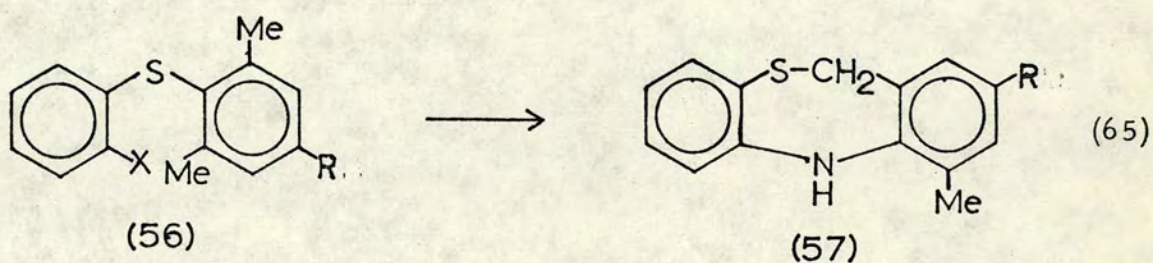
$X = N_3$ or NO_2

The rearrangement as outlined in Scheme 20 requires the aryl group $-C_6H_4-R$ to have a free ortho position. When both ortho positions are blocked, the reactions of the azides and nitro compounds have resulted in a new series of aromatic rearrangements leading to interesting phenothiazines and dibenzothiazepines thus:¹⁰³

1-Methoxy (54) and 1, 2-dimethoxyphenothiazines (55) from 2-azido- and 2-nitrophenyl 2, 6-dimethoxyphenyl sulphide:

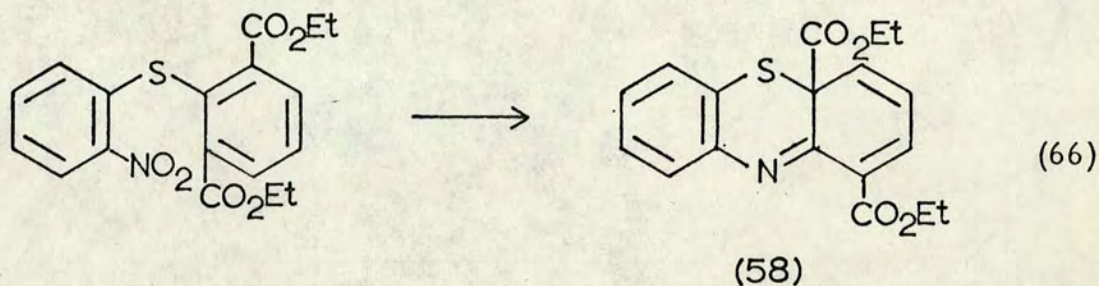


5, 11-dihydro-4-methyldibenzo[b, e][1, 4]thiazepine (57; R = H) and the 2, 4-dimethyl derivative (57; R = Me) from the azide (56; X = N_3) and nitro compound (56; X = NO_2),



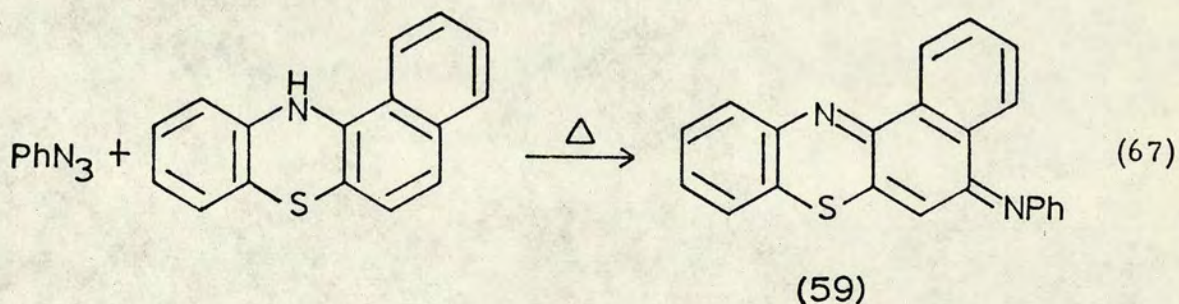
R = H, Me; X = N_3, NO_2

and diethyl-4aH-phenothiazine 1,4a-dicarboxylate (58) from 2,6-dicarbethoxyphenyl-2-nitrophenyl sulphide. This last compound (58) is specially interesting as it represents the isolation of one of the two key intermediates postulated in the rearrangement (Scheme 20), thus giving good evidence in support of the mechanism.



Details of these rearrangements will be discussed in the third chapter.

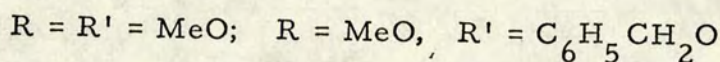
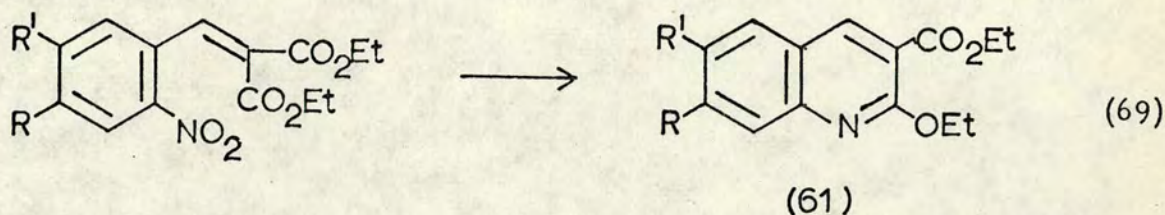
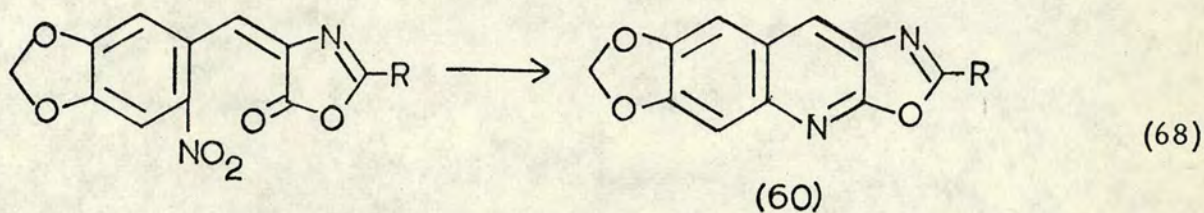
Recently azo-methine dyestuffs e. g. (59) have been prepared directly and in good yields (50-70%) by intermolecular insertion of phenyl nitrene into benzo[b]phenothiazine. ¹⁰⁴



(ii) Quinolines and derivatives.

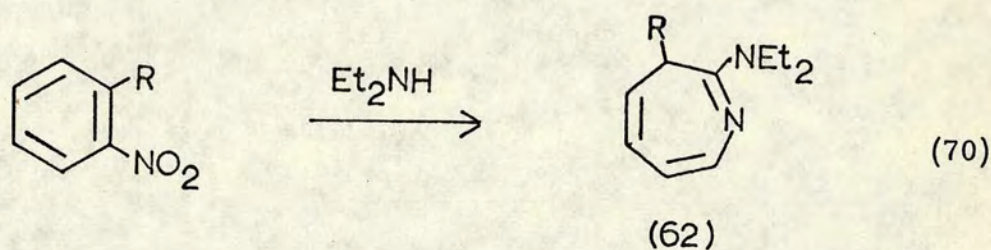
Reductive cyclisation with triethyl phosphite has been successfully used to prepare oxazolo[5,4-b]quinolines (60) and the

quinoline (61).¹⁰⁵



(C) Seven-membered Heterocycles.

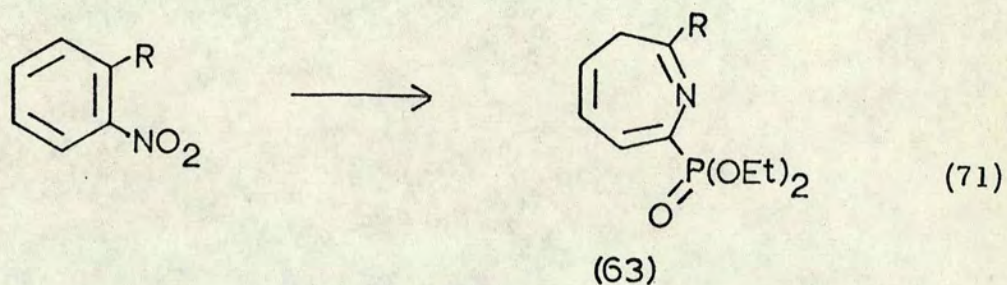
Two of the seven-membered azepines have been synthesized by reaction of diethyl methyl phosphonite in the presence of excess diethylamine with 2-nitrophenyl or nitrobenzene giving 2-diethylamino-3-phenyl-3H azepine (13%) (62; R = Ph) and 2-diethylamino 3H-azepine (83%) (62; R = H) respectively.⁶¹



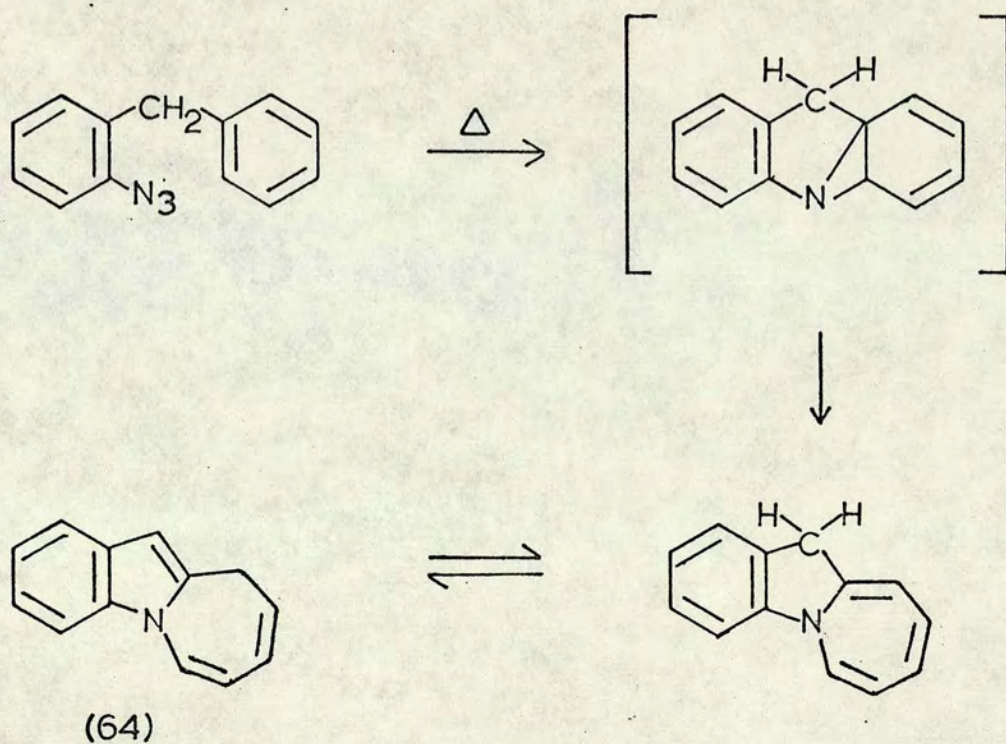
Photolysis of nitrobenzene, nitrotoluenes and nitromesitylene in triethyl phosphite with diethylamine have also resulted in the formation of 3H-azepines.⁶⁹

These azepines and others have been synthesized much earlier on by pyrolysis or photolysis of aryl azides in the presence of amines.^{46, 47}

When the thermal reaction of simple nitrobenzenes with triethyl phosphite was carried out in the absence of amines, phosphonylated 3H-azepines (63) in low yields (5-20%) result.⁶⁸



An indoloazepine (64) was obtained when 2-azidodiphenyl methane was pyrolysed, the product being formed by ring expansion of the initial aziridine.^{106, 107}



Scheme 21

I. 6. PROGRAMME OF RESEARCH.

The recent study by Cadogan and Kulik¹⁰³ on the 'blocked ortho effect' in the reactions of 2-azido- and 2-nitrophenyl 2,6-disubstituted-aryl sulphides has shown that many novel rearrangements occur in such reactions. It was considered to be worthwhile to investigate whether such an effect exists in the reactions of closely allied systems e. g. the corresponding ethers.

Only two reports^{100, 102} exist of attempts to synthesize phenoxazine or its derivatives by ring closure via nitrene or nitrenoid reactions. Both attempts resulted in failures. It was considered to be particularly interesting therefore to see if indeed the 'blocked ortho effect' will lead to successful cyclisations of these compounds.

Of interest too are the parallel reactions of the corresponding sulphones and methanes. Smith et al.¹⁰⁰ have isolated a cyclised product, phenothiazine 5,5-dioxide but no mechanism was postulated. Had Cadogan's 'phenothiazine rearrangement' occurred here too? The use of substituent groups in suitable positions should provide helpful clues in coming to some conclusions.

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Symbols and Abbreviations

b. p.	boiling point
m. p.	melting point
t. l. c.	thin-layer chromatography
R_f	ratio of distance moved by the substance to the distance moved by the solvent front
w/v	weight/volume ratio
v/v	volume/volume ratio
i. r.	infrared
u. v.	ultraviolet
p. m. r.	proton magnetic resonance
<u>s</u>	singlet
<u>bs</u>	broad singlet
<u>d</u>	doublet
<u>t</u>	triplet
<u>q</u>	quartet
<u>m</u>	multiplet
J	spin-spin coupling constant
M^+	mass of molecular ion
m/e	mass/charge ratio



II. 1. INSTRUMENTATION

Melting points were determined on a Kofler hot stage microscope and were corrected.

Infrared spectra were recorded on a Perkin-Elmer 337 Grating Spectrophotometer. Solids were examined as nujol mulls and liquids as thin films. Solution spectra were obtained using matched cells (path length 0.1 mm) with sodium chloride windows. Polystyrene, ν_{\max} 1603 and 1029 cm^{-1} was used as reference for calibration purposes.

Ultraviolet spectra were recorded on a Unicam SP 800 Ultraviolet and Visible Spectrophotometer using a matched pair of 1.0 cm quartz cells.

Nuclear magnetic resonance spectra were recorded on a Perkin-Elmer Model R10 Nuclear Magnetic Resonance Spectrometer operating at a frequency of 60MHz and a probe temperature of 33^o or on a Varian HA-100 instrument operating at 100MHz and a probe temperature of 28^o. Chemical shifts were recorded as tau (τ) values in parts per million using tetramethylsilane as internal reference ($\tau = 10.0$). Spectra were determined on 10-15% w/v solutions unless solubility or availability of the sample imposed limitations.

Mass spectra and exact mass measurements were recorded on an AEI MS 902 mass spectrometer.

Microanalyses were carried out on a Perkin-Elmer Elemental Analyser 240.

II. 2. PREPARATION OF MATERIALS

Benzene and light petroleum used in elution chromatography were redistilled and dried over sodium wire. Unless otherwise stated 'light petroleum' refers to light petroleum (b. p. 40-60^o). Elution chromatography was carried out on columns of alumina (Laporte Industries, Type H, 100/200's mesh, Brockmann activity 2) while thin layer chromatography was performed on 0.3 mm layers of alumina

(Merck, Aluminium oxide G type E) or of silica gel (Merck, silica gel G acc. to Stahl). Components in the developed chromatogram were detected by their fluorescence in ultraviolet light or by their reaction with iodine.

Except where stated, starting materials used were commercially available samples and were not further purified.

Triethyl phosphite was allowed to stand over sodium wire for 24 hr. and then distilled (b. p. $41-42^{\circ}/10$ mm) from fresh sodium wire in an atmosphere of dry nitrogen.

Cumene was dried and deperoxidised by storage over sodium wire. Decalin was purified by distillation from sodium wire in an atmosphere of dry nitrogen (b. p. $66-68^{\circ}/11$ mm) and stored over molecular sieve.

Ethyl diphenylphosphinite, Ph_2POEt , was prepared by the method of Rabinowitz and Pellon.¹⁰⁸ Diphenylphosphinous chloride (10.95 g; 0.05 mole) and dry ethanol (2.75 g; 0.06 mole) reacted in the presence of triethylamine (5.45 g; 0.05 mole) and benzene (30 ml) as solvent to give ethyl diphenylphosphinite (9.2 g; 80%), b. p. $96^{\circ}/0.05$ mm (lit.¹⁰⁸ $121^{\circ}/0.7$ mm).

4-Chlorophenyl-2-nitrophenyl sulphide was prepared by the method of Galt and Loudon¹⁰⁹ from *o*-chloronitrobenzene (50.3 g; 0.32 mole) and *p*-chlorothiophenol (50.8 g; 0.35 mole) in the presence of aqueous sodium hydroxide (14 g; 0.35 mole in 30 ml H_2O). The product crystallised from ethanol as yellow prisms (83 g; 98%) m. p. $94-95^{\circ}$ (lit.¹⁰⁹ 97°).

Bis-*o*-nitrophenyl disulphide was prepared from *o*-chloronitrobenzene, sodium sulphide and sulphur by Bogert and Stull's method¹¹⁰ in 60% yield.

o-Nitrophenyl sulphur chloride, was prepared by Hubacher's method¹¹¹ in 60% yield from bis-*o*-nitrophenyl disulphide.

Thanks are due to my colleagues Dr. S. Kulik and Miss E. M. Ramage for supplying samples of 4-*t*-butylphenyl 2-nitrophenyl sulphide, 2,4,6-trimethylphenyl-2-nitrophenyl sulphide, 3-*t*-butylphenothiazine,

and 2-chloro, 3-chlorophenothiazine-5, 5-dioxides respectively. I would also like to thank Dr. E. W. Greenhalgh, I. C. I. (Dyestuffs Division) who kindly supplied samples of 6-oxo-anthra[1, 9-cd]isoxazole, 1-aminoanthraquinone, 1-amino-2-methylantraquinone, 1-nitroanthraquinone and 2-methyl-1-nitroanthraquinone.

(A) Aryl 2-Nitrophenyl Ethers

These compounds were prepared by the method of Wright and Jorgensen¹¹² as described in the following example.

A mixture of 2, 6-dimethoxyphenol (27.7 g; 0.18 mole), o-chloronitrobenzene (23.7 g; 0.15 mole), potassium hydroxide pellets (8.4 g; 0.15 mole) and dimethyl sulphoxide (200 ml) was heated at 90° with stirring for 24 hours. The resultant dark-coloured solution was poured into 2N hydrochloric acid (300 ml) containing ice chips (100 g) and stirred thoroughly. After a few minutes the oil crystallised. This was collected and recrystallised from methanol to give 2, 6-dimethoxyphenyl 2-nitrophenyl ether as light yellow needles (30.0 g; 74%) m. p. 80-81°.

Found: C, 61.3; H, 4.7; N, 5.1;

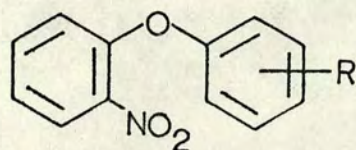
$C_{14}H_{13}NO_5$ requires C, 61.1; H, 4.7; N, 5.1%.

Table I shows a series of aryl-2-nitrophenyl ethers prepared by the same method from the appropriate phenols.

Attempts to prepare the following aryl-2-nitrophenyl ethers gave intractable tars which did not yield the expected product on subsequent work-up:

- 2, 6-dichlorophenyl 2-nitrophenyl ether,
- 2, 4, 6-trichlorophenyl 2-nitrophenyl ether,
- 2, 6-di-tert-butylphenyl 2-nitrophenyl ether,
- and 1-naphthyl 2-nitrophenyl ether.

Table I. Preparation of Aryl 2-Nitrophenyl Ethers



R	Yield		Analysis (%) [*]		
	(%)	M. p. (°C)	C	H	N
4-OMe	78	76-77 (lit. ¹¹³ 77)	63.2	4.4	5.6
			63.7	4.5	5.7
⁺ 2-Cl, 6-Me	31	89-90	59.4	3.8	5.3
			59.2	3.8	5.3
2, 6-DiMe	72	75-76 (lit. ¹¹⁴ 73-74)	69.0	5.2	5.4
			69.1	5.3	5.8
⁺ 2, 4, 6-TriMe	52	74-75	70.3	6.0	5.2
			70.3	5.8	5.4

* Upper row corresponds to 'Found' and lower row to 'calc'd' values. ⁺ New compounds.

(B) Aryl 2-Nitrophenyl Sulphones.

The method used involved the oxidation of the corresponding sulphides by hydrogen peroxide.

4-Chlorophenyl 2-nitrophenyl sulphide (42.5 g; 0.16 mole) was dissolved in warm glacial acetic acid (300 ml) and hydrogen peroxide (30% w/v, 80 ml) was added gradually to it with stirring at 100°. After the addition the mixture was stirred at 100° for 3 hours. Water was then added till crystals appeared. The rest of the product crystallised as colourless needles on standing. These were collected and recrystallised from ethanol to give 4-chlorophenyl 2-nitrophenyl sulphone as long colourless needles (45.3 g; 95%) m. p. 140-141°

(lit. ¹¹⁵ 137-8°).

Found: C, 48.2; H, 2.7; N, 4.6;

calc'd for $C_{12}H_8ClNO_4S$ C, 48.4; H, 2.7; N, 4.7%.

The following sulphones were prepared in the same manner from the corresponding sulphides:

4-t-butylphenyl 2-nitrophenyl sulphone (92%) m. p. 129-130° (EtOH)

Found: C, 60.4; H, 5.2; N, 4.3;

$C_{16}H_{17}NO_4S$ requires C, 60.2; H, 5.3; N, 4.4%.

2,4,6-trimethylphenyl 2-nitrophenyl sulphone (85%) m. p. 138-139°.

(Purified by column chromatography on alumina using ether/light petroleum (1:6 v/v) as eluent).

Found: C, 58.8; H, 4.8; N, 4.2;

$C_{15}H_{15}NO_4S$ requires C, 59.0; H, 4.9; N, 4.6%.

(C) Miscellaneous Aromatic Nitro Compounds.

(i) 4-Hydroxyphenyl 2-nitrophenyl sulphide.

This compound was prepared by the method of Levi and Smiles.¹¹⁶

A mixture of *o*-nitrophenyl sulphur chloride (28.5 g; 0.15 mole) and phenol (16.2 g; 0.17 mole) was heated to 100° while stirring. HCl gas was evolved. The mixture was kept at 100° for 12 hours. The product, a black tarry solid was stirred with a little benzene (10 ml) during which it solidified (28 g; 75%). Repeated attempts to recrystallise it failed to clean it up. It was finally sublimed at 120-140°/0.04 mm to give yellow crystals, m. p. 125-128° (lit.¹¹⁶ 132°)

Found: C, 58.5; H, 3.7; N, 6.3; M^+ 247;

calc'd for $C_{12}H_9NO_3S$, C, 58.3; H, 3.6; N, 5.7%; M, 247.

T. l. c. on alumina showed two spots with very close R_f values.

I. r. spectra (Nujol) showed two absorption maxima for the O-H stretching ν_{\max} 3400 and 3480 cm^{-1} . It would seem therefore that a mixture of the two isomers viz. 2-hydroxyphenyl and 4-hydroxyphenyl 2-nitrophenyl sulphide was obtained. Column chromatography on alumina failed to separate the isomers.

(ii) 2,4,6-Trimethoxyphenyl 2-nitrophenyl sulphide.

A solution of 1,3,5-trimethoxybenzene (14.3 g; 0.085 mole) in chloroform (25 ml) was added dropwise to a warm (40°) stirred solution of *o*-nitrophenyl sulphur chloride (15.15 g; 0.08 mole) in chloroform (50 ml). After a few minutes there was an evolution of acid fumes (HCl). An orange-yellow solid precipitated out after 30 min stirring at 40°. The mixture was stirred at 40° for a further hour to complete the reaction. The yellow solid was collected. Evaporation of the mother liquor yielded a further crop of crystals. Recrystallisation from benzene gave the product as bright yellow prisms (23 g; 90%) m. p. 188-189°.

Found: C, 56.6; H, 4.7; N, 4.7;

$C_{15}H_{15}NO_5S$ requires C, 56.1; H, 4.7; N, 4.4%.

(iii) 2,4,6-Trimethylphenyl 2-nitrophenyl methane.

This compound was prepared by a Friedel-Crafts reaction. To a chilled (ice-bath) solution of *o*-nitrobenzyl chloride (24.0 g; 0.14 mole) and mesitylene (dried and redistilled) (16.8; 0.14 mole) in dry benzene (20 ml) was added in small portions and with stirring, powdered anhydrous aluminium chloride (20.5 g; 0.19 mole) over 30 min. The dark reddish brown slurry was stirred at 0-5° for 1 hour and then at room temperature till no more HCl gas was evolved.

The paste was then poured into cold dil. HCl (400 ml) and stirred for 10 min. It was then extracted with ether and dried. Removal of ether gave a brownish oil which solidified on scratching. Recrystallisation from methanol gave the product as light yellow prisms, m. p. 90-91°.

Found: C, 75.0; H, 6.6; N, 5.4;

$C_{16}H_{17}NO_2$ requires, C, 75.3; H, 6.7; N, 5.7%.

An attempt to prepare 2,4,6-trimethoxyphenyl-2-nitrophenyl methane by the same method from *o*-nitrobenzyl chloride and 1,3,5-trimethoxybenzene gave only tarry products.

(D) 2-Aminophenyl Aryl Ethers, Sulphones and Sulphides.

These amines were prepared by the reduction of the corresponding nitro compounds using iron powder as described in the following example.

Hydrochloric acid (0.96 g; d 1.16) was added dropwise, to a stirred mixture of 2,6-dimethylphenyl 2-nitrophenyl ether (9.72 g; 0.04 mole), iron powder (8.96 g; 0.16 mole), ethanol (16 ml) and water (16 ml). The reaction mixture was stirred and boiled under reflux under nitrogen for 12 hours. When cool the product was neutralised by 2N sodium hydroxide, leached with hot ethanol and filtered through Celite. Removal of the ethanol gave a brown solid which was sublimed to yield 2-aminophenyl 2,6-dimethylphenyl ether as colourless needles, (6.0 g; 70%) m.p. 85-86°.

Found: C, 78.6; H, 7.1; N, 6.1;

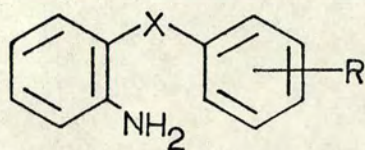
$C_{14}H_{15}NO$ requires C, 78.9; H, 7.0; N, 6.6%.

In the same manner a series of 2-aminophenyl aryl ethers, sulphones and sulphides were prepared from the corresponding nitro compounds, as listed in Table II. (Where the amine is a liquid, the alcoholic filtrate was extracted with ether, washed with water and dried. Removal of the ether and distillation in vacuo gave the product).

(E) Aryl 2-Azidophenyl Ethers, Sulphones and Sulphides.

These azides were prepared by diazotisation of the corresponding amines followed by treatment with sodium azide using the method of Smith et al.¹⁰⁰ as described in the following example. Water (5 ml) was added to a warm mixture of 2-aminophenyl 2,6-dimethoxyphenyl ether (4.9 g; 0.02 mole) and hydrochloric acid (5 ml; d 1.16) and the resultant mixture cooled to 0° in an ice-salt bath. While stirring this mixture, an aqueous solution of sodium nitrite (1.54 g; 0.022 mole in 3.5 ml water) was added dropwise to it, keeping the temperature between 0-3°. After the addition, the mixture was stirred at 0° for a further 2 hours to complete the reaction. An aqueous

Table II. Preparation of 2-Aminophenyl Aryl
Ethers, Sulphones and Sulphides.



R	Yield (%)	M. p. ($^{\circ}\text{C}$)		Analysis (%) [*]		
		b. p. ($^{\circ}\text{C}/\text{mmHg}$)		C	H	N
(i) X=O						
4-OMe	64	122-4 ^o /0.05		72.7	6.1	6.8
				72.6	6.1	6.5
2-Cl, 6-Me	96	66-67		67.0	4.9	5.7
				66.8	5.1	6.0
2, 6-DiOMe	91	103-104		69.1	6.0	5.9
				68.6	6.1	5.7
2, 4, 6-TriMe	77	63-64		79.2	7.3	5.9
				79.3	7.5	6.2
(ii) X=SO ₂						
4-Cl	84	134-135		54.1	3.8	5.5
				53.8	3.7	5.2
4-Bu ^t	86	107-108		66.8	6.5	5.2
				66.4	6.6	4.8
2, 4, 6-TriMe	84	153-154		66.0	6.1	5.2
				65.5	6.2	5.2
(iii) X=S						
⁺ 4-OH + 2-OH	74	-		66.7	5.2	6.2
				66.4	5.1	6.5

All the compounds listed in this table are new compounds.

* Upper row corresponds to 'Found' and lower row to 'calc'd' values.

⁺ Obtained as a mixture.

solution of sodium azide (3.15 g; 0.048 mole; in 40 ml water) was then added dropwise to the stirred mixture, keeping the temperature between 0-3°. It was then allowed to stand overnight at 0°. The solid which separated was collected, washed thoroughly with water and dried in vacuo over phosphorus pentoxide in the absence of light to give 2-azidophenyl 2,6-dimethoxyphenyl ether as a fine light brown powder (5.0 g; 93%) m.p. 67-68°.

Found: C, 61.8; H, 4.7; N, 15.6;

$C_{14}H_{13}N_3O_3$ requires C, 62.0; H, 4.8; N, 15.5%.

In the same way, a series of aryl 2-azidophenyl ethers, sulphones and sulphides were prepared from the corresponding amines as listed in Table III. (Where the azide separates as an oil, the mixture was extracted with ether, washed with sodium bicarbonate solution, then with water and dried over anhydrous magnesium sulphate in the dark. Removal of ether in vacuo gave the product as an oil).

In the same way, 2-methoxyaniline (7.38 g; 0.06 mole) was converted to 2-methoxyphenyl azide (8.3 g; 92%), obtained as a yellow-brown oil.

Found: C, 56.3; H, 4.7; N, 28.6;

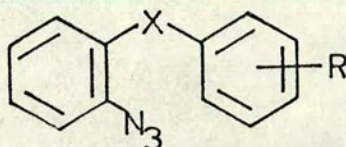
calc'd for $C_7H_7N_3O$, C, 56.4; H, 4.7; N, 28.2%.

(F) Triethyl-N-o-Anisyl Phosphorimidate and Triethyl-N-o-(4-Methoxyphenoxy) Phenyl Phosphorimidate.

These two phosphorimidates were prepared by the method of Kabachnik et al.¹¹⁷

To a stirred solution of triethyl phosphite (2.5 g; 0.015 mole) in benzene (30 ml) at 50° was added 2-methoxyphenyl azide (2.24 g; 0.015 mole) in benzene (5 ml) at such a rate that the temperature was maintained at 50-55°. The reaction was carried out in an atmosphere of nitrogen. After the addition the mixture was stirred at 50-55° for 30 min, then at 60° under reduced pressure (water pump) and finally kept at 70° at high vacuum (0.05 mmHg). The product was an orange

Table III. Preparation of Aryl 2-Azidophenyl Ethers,
Sulphones and Sulphides



R	Yield (%)	M. p. (°C)	Analysis (%) [*]		
			C	H	N
(i) X=O					
4-OMe	93	Liquid	64.6	4.4	17.7
			64.7	4.6	17.3
2-Cl, 6-Me	93	Liquid	60.2	3.8	16.3
			60.1	3.9	16.2
2, 6-DiMe	90	41-42	71.0	5.6	18.1
			71.0	5.4	17.6
2, 4, 6-TriMe	94	54-55	71.6	5.8	16.6
			71.1	5.9	16.6
(ii) X=SO ₂					
4-Cl	85	108-110	49.0	2.8	13.6
			49.1	2.7	14.3
4-Bu ^t	95	122-123	60.9	5.3	13.6
			61.0	5.4	13.3
2, 4, 6-TriMe	-	175-176	59.9	4.8	14.6
			59.8	5.0	14.0
(iii) X=S					
[†] 4-OH + 2-OH	97	Liquid	59.4	4.1	17.5
			59.3	3.7	17.3

All compounds listed in this table are new compounds.

* Upper row corresponds to 'Found' and lower row to 'calc'd' values.

[†] Obtained as a mixture.

liquid, triethyl-N-o-anisyl phosphorimidate (3.5 g; 82%).

P. m. r. spectrum (CCl_4): (τ) 8.75 (t, 9H, 3 x P-O-Et); 6.30 (s, 3H, OMe); 5.95 (overlapping quartet of doublets, 6H, 3 x P-O-Et); 3.2-3.5 (m, 4H, aromatic).

In the same way, triethyl phosphite (1.0 g; 0.006 mole) reacted with 2-azidophenyl 4-methoxyphenyl ether (1.2 g; 0.005 mole) to give triethyl-N-o-(4-methoxyphenoxy)phenyl phosphorimidate as an orange liquid (1.7 g; 90%).

P. m. r. spectrum (CCl_4): (τ) 8.85 (t, 9H, 3 x P-O-Et); 6.40 (s, 3H, OMe); 6.10 (overlapping quartet of doublets, 6H, 3 x P-O-Et); 3.0-3.5 (m, 8H, aromatic).

(G) 3-t-Butylphenothiazine 5,5-Dioxide.

This compound was prepared by the oxidation of the corresponding phenothiazine by hydrogen peroxide.

3-t-Butylphenothiazine (0.255 g; 0.001 mole) was stirred with glacial acetic acid (3 ml) at 100° and hydrogen peroxide (30% w/v, 0.5 ml) added dropwise to it. The dark coloured mixture was stirred at 100° for 24 hours to complete the reaction. Water was then added till a solid separated. This was collected and sublimed to give 3-t-butylphenothiazine 5,5-dioxide (0.17 g; 60%) m. p. $229-230^\circ$.

I. r. spectrum (nujol): ν_{max} 3300 (-NH); 1140 (SO_2) cm^{-1}

P. m. r. spectrum (CDCl_3): (τ) 8.70 (s, 9H, t-Bu); 3.2 (d, 2H, aromatic); 2.5-3.0 (m, 3H, aromatic); 2.20 (bs, 1H, NH);

1.95-2.05 (m, 2H, aromatic).

II. 3. THERMOLYSIS OF ARYL 2-AZIDOPHENYL ETHERS IN DECALIN.

General procedure: The azido-compound (0.01 mole) was added over 30 min to decalin (80 ml), stirred at $150-160^\circ$ under an atmosphere of nitrogen. After the mixture was boiled under reflux for a further 2 hr, the decalin was removed by distillation in vacuo. The dark-

coloured residue was chromatographed on activated alumina (23 x 420 mm column) and eluted with solvents.

(A) 2-Azidophenyl 4-Methoxyphenyl Ether.

Thermolysis of the azido compound (2.4 g; 0.01 mole) in decalin (80 ml) gave a black tar after removal of decalin. This tar was chromatographed on alumina and eluted with solvents. Trace amounts of a few coloured materials were obtained. Elution of the column with methanol gave a large quantity of an intractable tar.

(B) 2-Azidophenyl 2,6-Dimethylphenyl Ether.

Thermolysis of the azido compound (2.39 g; 0.01 mole) in decalin (80 ml) gave a dark-coloured residue which was chromatographed on alumina.

Elution with ether/light petroleum (1:12 v/v) gave a light brown solid which sublimed to yield 5,11-dihydro 4-methyldibenzo[b,e][1,4]-oxazepine (0.23 g; 11%). m. p. 120-121°.

Found: C, 79.6; H, 6.1; N, 6.2;

$C_{14}H_{13}NO$ requires C, 79.6; H, 6.2; N, 6.6%.

I. r. spectrum (nujol): ν_{\max} 3390 cm^{-1} (-NH). The mass spectrum showed the correct parent ion at m/e 211

Found: M^+ , 211.099437;

$C_{14}H_{13}NO$ requires M, 211.099708

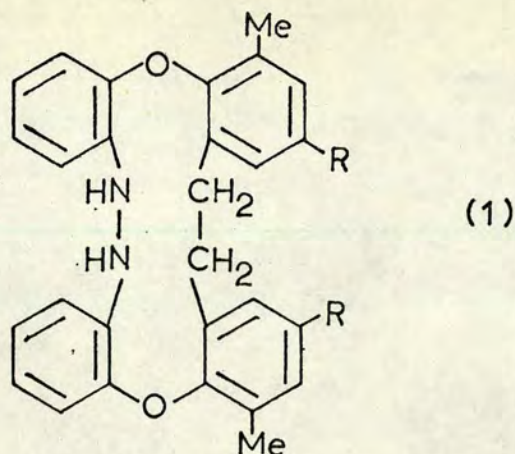
and an important fragment at ion m/e 182. Exact mass measurement of this fragment gave a value of 182.096761;

$C_{13}H_{12}N$ requires 182.096970.

P. m. r. spectrum ($CDCl_3$): (τ) 7.79 (s, 3H, Me); 5.11 (s, 2H, -O-CH₂-); 4.43 (bs, 1H, -NH) and 3.0-3.6 (complex band, 7H, aromatic).

Elution with ether/light petroleum (1:5 v/v) gave a white solid whose structure was assigned as the bis-ether (1; R=H) (0.02 g; 1%) m. p. 177-179°.

I. r. spectrum (nujol): ν_{\max} 3400 cm^{-1} (-NH).



The mass spectrum showed the parent ion at m/e 422

Found: M^+ , 422.199103

$C_{28}H_{26}N_2O_2$ requires M , 422.199417

and a major fragment at ion m/e 210 (mass abundance ratio 100%).

Found: M^+ , 210.091800;

$C_{14}H_{12}NO$ requires M , 210.091884

indicating a dimeric structure.

P.m.r. spectrum ($CDCl_3$): (τ) 8.00 (s, 3H, Me); 7.65 (s, 2H, $-CH_2-$); 4.05 (s, 1H, $-NH$); 2.6-3.4 (complex band, 7H, aromatic).

(C) 2-Azidophenyl 2,4,6-Trimethylphenyl Ether.

The dark-coloured residue from the thermolysis of the above azide (2.15 g; 0.0085 mole) was chromatographed on alumina.

Elution with ether/light petroleum (1:12 v/v) gave a light brown solid which sublimed to give 5,11-dihydro-2,4-dimethyldibenzo-[b,e][1,4]oxazepine (0.3 g; 15%) m.p. 119-120°

Found: C, 79.9; H, 6.6; N, 6.4; M^+ 225.115246;

$C_{15}H_{15}NO$ requires C, 80.0; H, 6.6; N, 6.15%; M , 225.115358.

I.r. spectrum (nujol): ν_{max} 3410 cm^{-1} ($-NH$).

The mass spectrum showed the half-mass ion at m/e 112.5 and an important fragment at m/e 196. Exact mass measurement of this latter ion gave a value of 196.111522;

$C_{14}H_{14}N$ requires 196.112619.

P.m.r. spectrum ($CDCl_3$): (τ) 8.03 (s, 6H, 2 x Me); 5.14 (s, 2H, $-CH_2-$); 4.54 (bs, 1H, $-NH$); 3.2-3.5 (m, 6H, aromatic).

Elution with ether (light petroleum (1:6 v/v) gave a brown

solid which on recrystallisation from ethanol/light petroleum (b. p. 60-80°) yielded the bis-ether (1; R=Me) as white needles (0.03 g; 1.5%) m. p. 169-170°.

I. r. spectrum (nujol): $\nu_{\max} 3440 \text{ cm}^{-1}$ (-NH). The mass spectrum showed the parent ion at m/e 450

Found: M^+ , 450.230114

$C_{30}H_{30}N_2O_2$ requires M, 450.230715.

and a major fragment (mass abundance ratio 100%) at m/e 224

Found: M^+ , 224.106708;

$C_{15}H_{14}NO$ requires M, 224.107533.

This was taken as strong evidence for a dimeric structure as assigned.

P. m. r. spectrum ($CDCl_3$): (τ) 8.04 (s, 3H, Me); 7.76 (s, 3H, Me); 7.70 (s, 2H, $-CH_2-$); 4.17 (bs, 1H, -NH); 2.7-3.3 (m, 6H, aromatic).

(D) 2-Azidophenyl 2,6-Dimethoxyphenyl Ether.

The azido compound (2.71 g; 0.01 mole) when decomposed in decalin gave a brown residue which was chromatographed on alumina.

Elution with ether/light petroleum (1:20 v/v) gave a colourless oil which turned purplish on prolonged exposure to light. This was sublimed to give light yellow crystals, identified as 4-methoxyphenoxazine, (0.64 g; 30%) m. p. 81-82°.

Found: C, 73.4; H, 5.1; N, 6.6; M^+ , 213.079522;

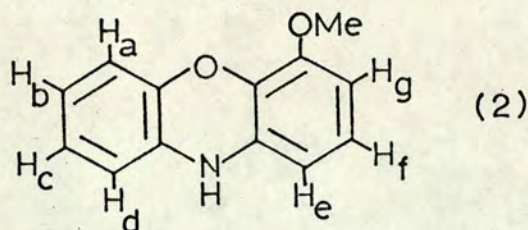
$C_{13}H_{11}NO_2$ requires C, 73.3; H, 5.2; N, 6.6%; M, 213.078973.

I. r. spectrum (nujol): $\nu_{\max} 3410 \text{ cm}^{-1}$ (-NH).

The mass spectrum showed an abundant fragment (mass abundance ratio 75%) at ion m/e 198, attributable to the loss of a methyl radical and formation of the quinoid ion. This is good evidence that the methoxy group is either o or p to the oxygen atom.

The p. m. r. spectrum ($CDCl_3$) showed the compound to be a monomethoxyphenoxazine: (τ) 6.24 (s, 3H, OMe); 4.62 (bs, 1H, -NH); 3.2-3.8 (complex band, 7H, aromatic). The aromatic region of the spectrum was fairly well resolved when hexadeuteriobenzene was

used as solvent and showed the following signals which are compatible with the assigned structure: (τ) 6.81 (s, 3H, OMe), 4.84 (bs, 1H, -NH); 4.10-4.20 (m, 1H, proton H_a) 3.93 (t, 1H, proton H_f ; J, 5Hz); 3.46-3.60 (m, 4H, protons H_b H_c , H_e H_g); 3.30-3.40 (m, 1H, proton H_d).



These couplings were confirmed by double irradiation.

Elution of the column with ether/light petroleum (1:2 v/v) gave a brown oil, identified as 1, 2-dimethoxyphenoxazine (0.29 g; 11%), which failed to crystallise.

The i. r. spectrum (thin film) showed the N-H stretching as a strong broad band at $\nu_{\max} 3340 \text{ cm.}^{-1}$

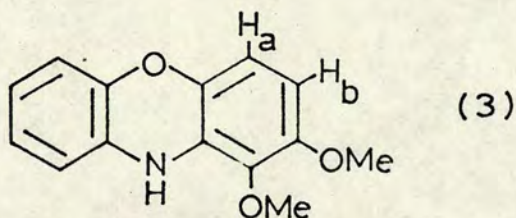
The mass spectrum showed the parent ion at m/e 243

Found: M^+ , 243.089137;

$C_{14}H_{13}NO_3$ requires M , 243.089537

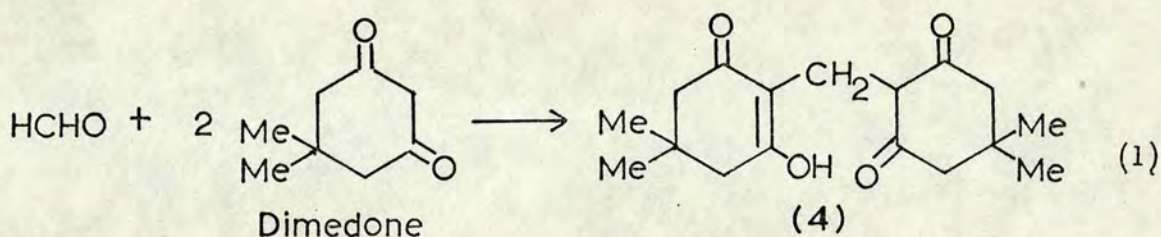
and a fairly abundant fragment (mass abundance ratio 30%) at ion m/e 228 corresponding to the loss of a methyl radical and formation of a quinoid ion. This again is good evidence for one of the methoxy groups to be o or p to the oxygen atom.

P. m. r. spectrum ($CDCl_3$): (τ) 6.25 (s, 3H, OMe); 6.19 (s, 3H, OMe); 4.42 (bs, 1H, -NH); 3.2-3.9 (m, 6H, aromatic). From the latter complex band, two doublets ($J = 9\text{Hz}$) are prominent, centred at 3.87 and 3.64 τ respectively. These are attributed to the protons H_a and H_b respectively.



Estimation of formaldehyde liberated during thermolysis of 2-azidophenyl 2,6-dimethoxyphenyl ether. The estimation was carried out by Yoe and Reid's method¹¹⁸ using dimedone (5,5-dimethyl cyclohexane 1,3-dione).

Nitrogen gas was bubbled through decalin (20 ml) stirred at 160°. The azido compound (0.27 g; 0.001 mole) in a small glass thimble was added to the decalin which was then boiled under reflux for 4 hr. The formaldehyde which was liberated was led through a condenser into two traps, each containing excess dimedone (0.11 g) dissolved in water (40 ml). The white precipitate (4), found only in the first trap was allowed to stand overnight. It was then collected in a weighed sintered glass crucible and dried to constant weight under high vacuum over phosphorus pentoxide in a vacuum desiccator. From the amount of the white solid obtained (0.043 g) and from eq.(1) the yield of formaldehyde was determined (0.0045 g; 14.7%).



The estimation was repeated once to give a comparable result (15.6%).

II.4. DEOXYGENATION OF ARYL 2-NITROPHENYL ETHERS BY TRIETHYL PHOSPHITE

General procedure: A mixture of the nitro compound (0.01 mole), purified cumene (80 ml) and triethyl phosphite (6.65 g; 0.04 mole) was boiled under reflux under dry nitrogen for 48 hr. After removal of the lower boiling fractions (cumene and phosphorus esters) by distillation in vacuo, the resulting residue was chromatographed on alumina (23 x 420 mm column) and eluted with various solvents.

(A) 4-Methoxyphenyl 2-Nitrophenyl Ether

The nitro compound (2.45 g; 0.01 mole) reacted with triethyl phosphite (6.65 g; 0.04 mole) in cumene (80 ml) to give a brown oil after removal of lower boiling fractions. This residue was chromatographed on alumina.

Elution with ether/light petroleum (1:20 v/v) gave a colourless oil (0.185 g; 7.5%), identified as 2-N-ethylaminophenyl 4-methoxyphenyl ether.

I. r. spectrum (thin film): ν_{\max} 3410 cm.^{-1}

The mass spectrum showed the parent ion at m/e 243

Found: M^+ , 243.126120;

$C_{15}H_{17}NO_2$ requires 243.125921

and a fragment at ion m/e 214 (mass abundance ratio 45%) corresponding to the loss of an ethyl group.

P. m. r. spectrum ($CDCl_3$): (τ) 8.60 (t, 3H, Et; J, 7.5 Hz); 6.33 (s, 3H, OMe); 6.00 (q, 2H, Et; J, 7.5 Hz); 4.20 (bs, 1H, -NH); 2.9-3.5 (m, 8H, aromatic).

Elution with ether/light petroleum (1:10 v/v) gave a yellow solid identified as the starting nitro compound (0.46 g; 19%) m. p. and mixed m. p. 76-77° (lit. ¹¹³ 77°).

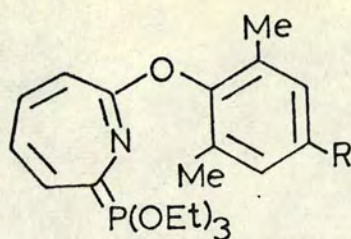
(B) 2,6-Dimethylphenyl 2-Nitrophenyl Ether.

Reaction of the nitro compound (2.43 g; 0.01 mole) with triethyl phosphite (6.65 g; 0.04 mole) in cumene (80 ml) gave a brown oil after removal of lower boiling fractions. The oil was chromatographed on alumina.

Elution with light petroleum gave a colourless oil which solidified on cooling. This was identified as 7-triethoxyphosphoranylidene 2-(2,6-dimethylphenoxy)azepine (5, R=H) (2.6 g; 70%) m. p. 36-38°.

I. r. spectrum (thin film): ν_{\max} 1260 (P=C) 1050 and 970 (P-O-Et) cm.^{-1}

The mass spectrum showed the correct parent ion at m/e 377.



(5)

Found: M^+ , 377.177548;

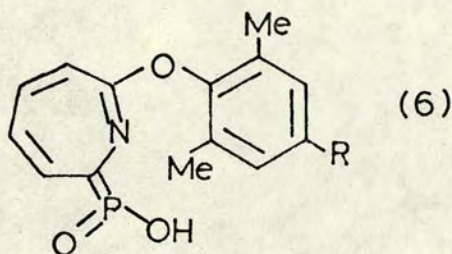
$C_{20}H_{28}NO_4P$ requires M , 377.185585.

P. m. r. spectrum (CCl_4): (τ) 9.0 (triplet of doublets, 9H, 3 x P-O-Et; $J_{H,H}$ 7Hz, $J_{P,H}$ 1.8Hz); 7.91 (s, 6H, 2 x Me); 6.12 (overlapping quartet of doublets, 6H, 3 x P-O-Et; $J_{H,H}$ 7Hz, $J_{P,H}$ 8.8Hz); 4.2 (m, 1H, azepine proton); 3.3-3.6 (m, 3H, azepine protons); 3.04 (s, 3H, aromatic).

Elution with ether/light petroleum (1:25 v/v) gave the starting nitro compound (0.05 g; 2%) m. p. and mixed m. p. 75-76° (lit. ¹¹⁴ 74°). Further elution of the column with ether/light petroleum (1:12 v/v) gave a light yellow solid identified as 5, 11-dihydro 4-methyldibenzo[b, e][1,4]oxazepine (0.01 g; 0.5%) m. p. and mixed m. p. 120-121°.

Total accountance of materials = 72.5%.

It was observed that when the phosphoranylidene azepine (5) was exposed to the air for an hour, a white solid, identified as 2-(2,6-dimethylphenoxy)azepin-7-ylidene phosphonic acid (6; R=H)



(6)

was obtained (m. p. $\sim 210^\circ$).

I. r. spectrum (nujol): ν_{\max} 2350 (P-OH) 1230 (P=C) and 1200

Fig.1 Before hydrolysis

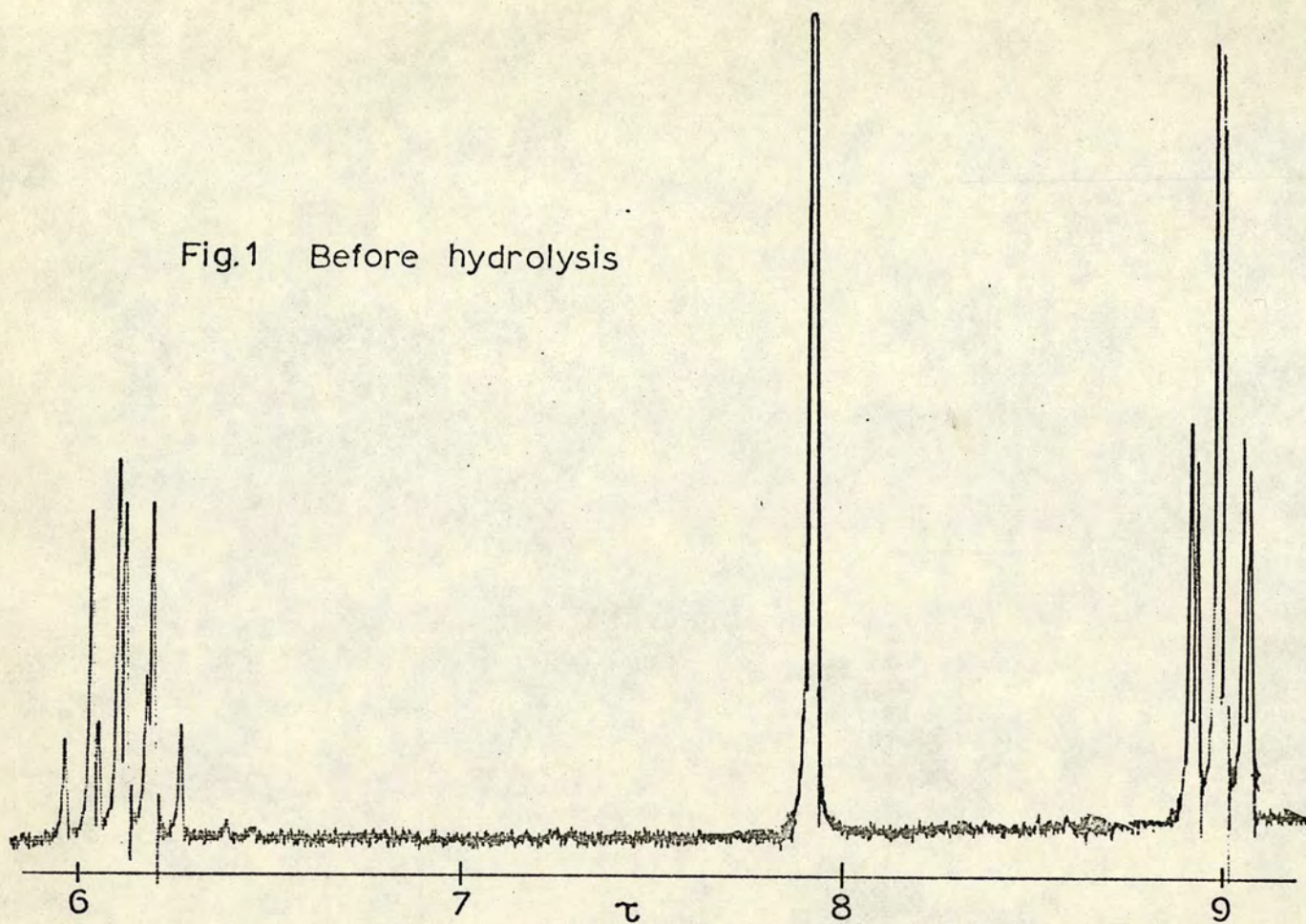
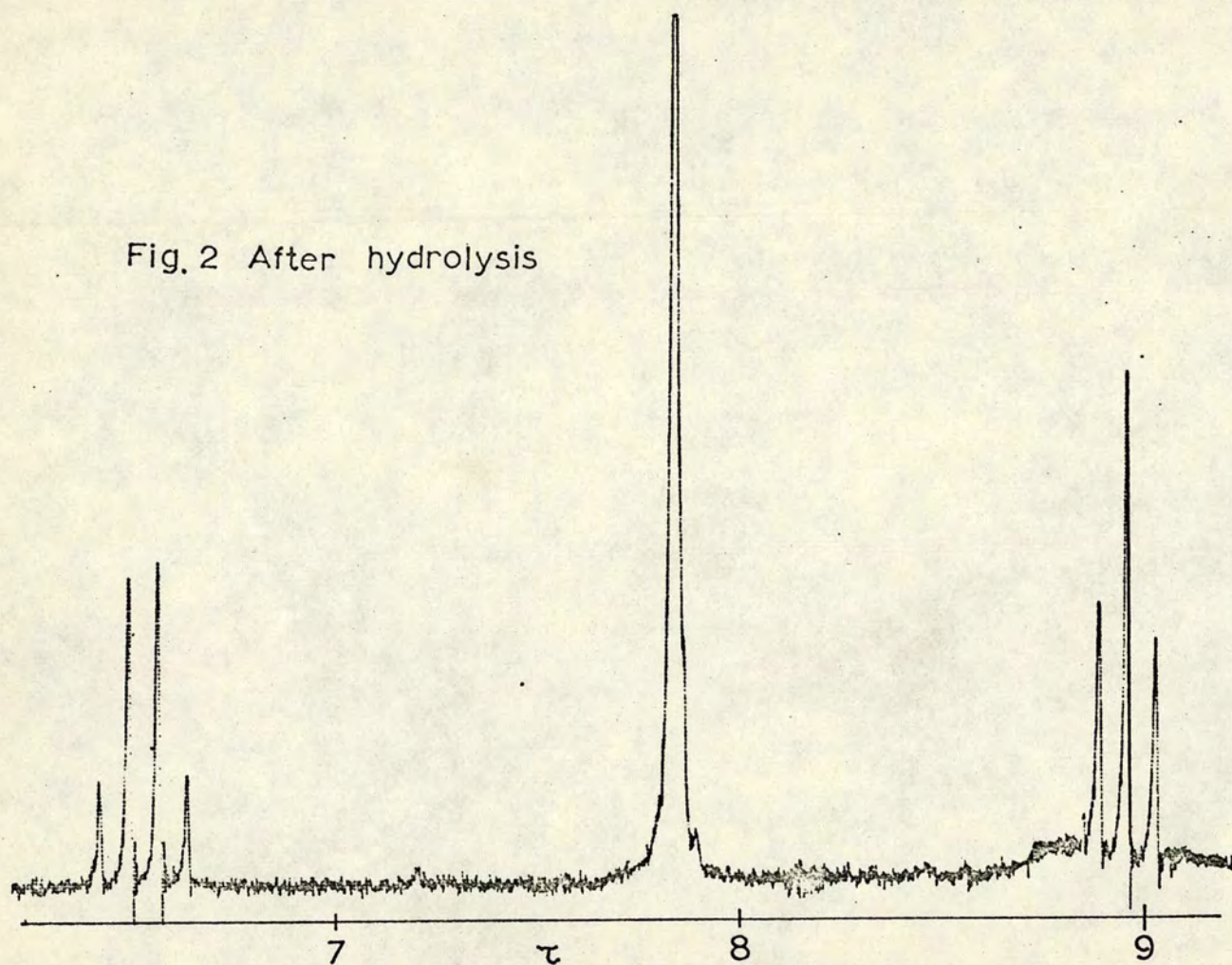


Fig.2 After hydrolysis



(P=O) cm.^{-1} The P-O-Et frequencies at 1060 and 970 cm^{-1} was absent.

The mass spectrum showed the parent ion at m/e 275

Found: M^+ , 275.069278;

$C_{14}H_{14}NO_3P$ requires M, 275.071125.

P. m. r. spectrum ($CDCl_3$): (τ) 7.80 (s, 6H, 2 x Me); 3.8-3.9 (m, 1H, azepine proton); 2.8-3.2 (complex band, 6H, azepine + aromatic protons).

When a solution of the phosphoranylidene azepine (5; R=H) in CCl_4 in an n. m. r. tube was shaken with a few drops of D_2O and allowed to stand for 1 hr, the signals assigned earlier to the P-O-Et groups were absent and the following were observed: (τ) 8.9 (t, 6H, 2 x Et) and 6.5 (q, 4H, 2 x Et). This was taken as good evidence for the hydrolysis of the phosphoranylidene azepine to the phosphenic acid (6; R=H) at a neutral pH. The relevant signals of the p. m. r. spectra of the azepine before and after hydrolysis are shown in fig. 1 and 2 respectively.

(C) 2,4,6-Trimethylphenyl 2-Nitrophenyl Ether.

The nitro compound (2.57 g; 0.01 mole) reacted with triethyl phosphite (6.65 g; 0.04 mole) in cumene (80 ml) to give a brown oil after removal of lower boiling fractions. This residue was chromatographed on alumina.

Elution with light petroleum gave a colourless oil which solidified on cooling. This was identified as 7-triethoxyphosphoranylidene 2-(2,4,6-trimethylphenoxy)azepine (5, R=Me) (2.4 g; 62%) m. p. 38-40°.

I. r. spectrum (thin film): ν_{max} 1250 (P=C), 1050 and 970 (P-O-Et) cm.^{-1}

The mass spectrum showed the correct parent ion at m/e 391

Found: M^+ , 391.191046,

$C_{21}H_{30}NO_4P$ requires M 391.191234.

P. m. r. spectrum (CCl_4): (τ) 9.0 (triplet of doublets, 9H, 3 x P-O-Et; $J_{\text{H,H}}$ 7Hz, $J_{\text{P,H}}$ 1.5Hz); 7.96 (s, 6H, 2 x Me); 7.74 (s, 3H, Me); 6.13 (overlapping quartet of doublets, 6H, 3 x P-O-Et; $J_{\text{H,H}}$ 7Hz, $J_{\text{P,H}}$ 8.5Hz); 4.19 (m, 1H, azepine proton); 3.3-3.6 (complex band, 3H, azepine protons); 3.2 (s, 2H, aromatic).

Elution with ether/light petroleum (1:20 v/v) gave the starting nitro compound (0.08 g; 3.5%) m. p. and mixed m. p. 74-75°.

Further elution of the column with ether/light petroleum (1:15 v/v) gave a light yellow solid, identified as 5, 11-dihydro 2, 4-dimethyl-dibenzo[b, e][1, 4]oxazepine (0.02 g; 1%) m. p. and mixed m. p. 119-120°. Total accountance of materials = 66.5%.

As with the case of the dimethyl analogue, this trimethyl phosphoranylidene azepine (5; R=Me) hydrolysed on exposure to the air to give 2-(2, 4, 6-trimethylphenoxy)azepin-7-ylidene phosphonic acid (6; R=Me) m. p. \sim 210°.

I. r. spectrum (nujol): ν_{max} 2400 (P-OH) 1260 (P=C) and 1200 (P=O) cm^{-1} P-O-Et frequencies were absent.

The mass spectrum showed the expected parent ion at m/e 289

Found: M^+ , 289.085937,

$\text{C}_{15}\text{H}_{16}\text{NO}_3\text{P}$ requires M, 289.086775.

P. m. r. spectrum (CDCl_3): (τ) 7.84 (s, 6H, 2 x Me); 7.72 (s, 3H, Me); 3.8-3.9 (m, 1H, azepine proton); 3.0-3.3 (m, 5H, azepine + aromatic); 0.5 (bs, 1H, P-OH).

A hydrolysis of this phosphoranylidene azepine (5; R=Me) by D_2O in an n. m. r. tube was observed in a manner similar to the dimethyl analogue as described in the previous section.

(D) 2-Chloro-6-Methylphenyl 2-Nitrophenyl Ether.

Reaction of the nitro compound (2.1 g; 0.008 mole) with triethyl phosphite (5.3 g; 0.032 mole) in cumene (60 ml) gave a brown oil after removal of lower boiling fractions. The oil was chromatographed on alumina.

Elution with ether/light petroleum (1:20 v/v) gave a colourless oil which solidified on cooling. This was identified as 2-N-ethyl-aminophenyl 2-chloro 6-methylphenyl ether (0.14 g; 6%).

I. r. spectrum (nujol): ν_{\max} 3390 cm^{-1} (N-H).

The mass spectrum showed the correct parent ion at m/e 261/263 ($\text{C}_{15}\text{H}_{16}\text{ClNO}$ requires M^+ , 261/263.)

P. m. r. spectrum (CDCl_3): (τ) 8.53 (t, 3H, Et); 7.78 (s, 3H, Me); 5.84 (q, 2H, Et); 2.6-3.9 (complex, 8H, aromatic + NH).

Elution with ether/light petroleum (1:15 v/v) gave the starting nitro compound (0.005 g; 2.5%) m. p. and mixed m. p. 89-90°.

Elution with ether/light petroleum (1:10 v/v) gave a purplish solid which sublimed to give white needles, identified as 1-methylphenoxazine (0.11 g; 7%) m. p. 82-83°.

I. r. spectrum (nujol): ν_{\max} 3300 cm^{-1} (N-H stretching).

The mass spectrum showed the parent ion at m/e 197.

Found: M^+ , 197.082599

$\text{C}_{13}\text{H}_{11}\text{NO}$ requires M 197.084059.

The p. m. r. spectrum (CDCl_3) was poorly resolved and showed the following signals: (τ) 7.87 (s, 3H, Me); 5.01 (bs, 1H, -NH); 3.6-3.9 (broad complex band, 2H, aromatic); 3.2-3.6 (broad complex band, 5H, aromatic). On shaking the CDCl_3 solution with a solution of sodium dithionite in D_2O , the spectrum was better resolved. The broad band at 3.2-3.6 τ resolved into two multiplets, each containing the $\underline{\delta}$ - $\underline{\delta}$ ' coupling quartet ($J_{\text{H,H}}$ 7.5Hz).

(E) 2,6-Dimethoxyphenyl 2-Nitrophenyl Ether.

The nitro compound (2.2 g; 0.008 mole) reacted with triethyl phosphite (5.3 g; 0.032 mole) in cumene (60 ml) to give a yellow oil after removal of lower boiling fractions. The yellow oil was chromatographed on alumina.

Elution with ether/light petroleum (1:15 v/v) gave a colourless oil which sublimed to give a yellow solid identified as 4-methoxyphenoxazine (0.09 g; 5%) m. p. and mixed m. p. 81°.

I. r. spectrum (nujol): ν_{\max} 3410 cm^{-1} (-NH).

Elution with ether/light petroleum (1:10 v/v) gave a white solid, identified as 2-N-ethylaminophenyl 2,6-dimethoxyphenyl ether (0.13 g; 6%) m. p. 137-8°.

I. r. spectrum (nujol): ν_{\max} 3390 cm^{-1} (-N-H stretching).

The mass spectrum showed the correct parent ion at m/e 273

Found: M^+ , 273.135573;

$\text{C}_{16}\text{H}_{19}\text{NO}_3$ requires M 273.136485.

P. m. r. spectrum (CDCl_3): (τ) 8.54 (t, 3H, Et); 6.22 (s, 6H, 2 x OMe); 5.88 (q, 2H, Et); 3.96 (bs, 1H, -NH) 3.56-3.7 (m, 1H, aromatic); 3.1-3.4 (m, 5H, aromatic); 2.9 (2d, 1H, aromatic; $J_{\text{H,H}}$ 8.5 Hz, $J_{\text{H,H}}$ 7.5 Hz).

Elution with ether/light petroleum (1:6 v/v) gave the starting nitro compound (0.28 g; 13%) m. p. and mixed m. p. 80-81°.

Elution with ether/light petroleum (1:5 v/v) gave a yellow oil, identified as 1,2-dimethoxyphenoxazine (0.04 g; 2%). The i. r. spectrum (thin film) showed the N-H stretching frequency at 3340 cm^{-1} and had an exactly identical fingerprint region as the compound identified as 1,2-dimethoxyphenoxazine in section II. 3 (D).

II. 5. THERMOLYSIS OF ARYL 2-AZIDOPHENYL SULPHONES AND SULPHIDES IN DECALIN.

(A) 2-Azidophenyl 4-Chlorophenyl Sulphone.

The azido compound (2.9 g; 0.01 mole) was added in small amounts over 30 min to decalin (80 ml) stirred at 160° under an atmosphere of dry nitrogen. After the mixture was boiled under reflux for 3 hr the decalin was removed by distillation in vacuo. The black residue was sublimed under high vacuum (0.05 mmHg) to give two fractions.

The first fraction, a white solid, was identified as 2-aminophenyl 4-chlorophenyl sulphone (0.27 g; 10%) m. p. and mixed m. p. 134°.

Fig. 3

2-Chloro Phenothiazine 5,5-Dioxide

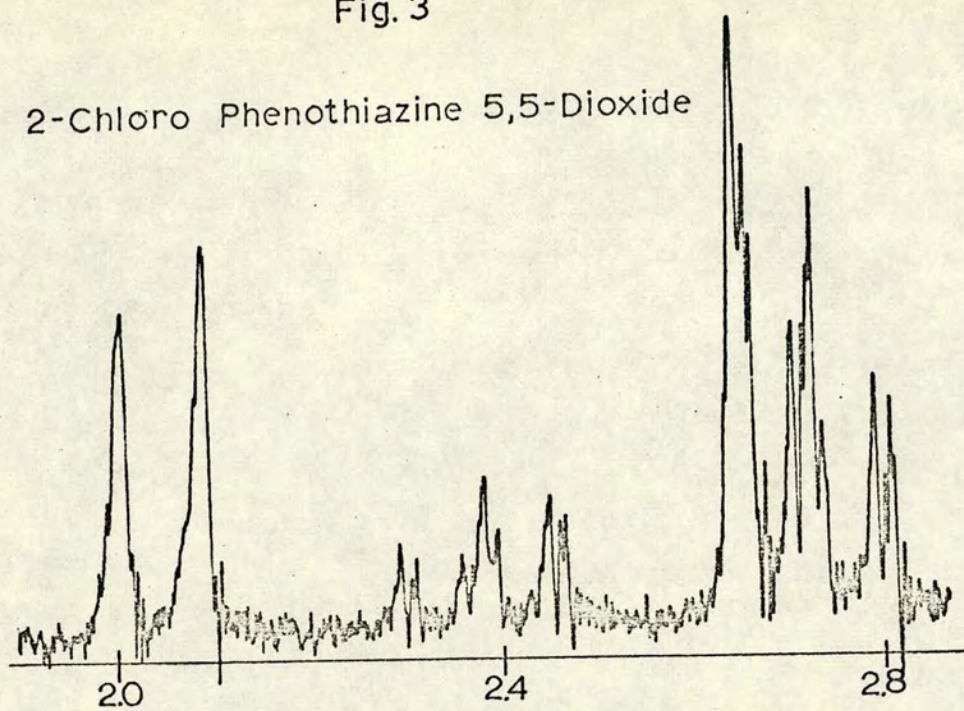


Fig. 4 3-Chloro Phenothiazine 5,5-Dioxide

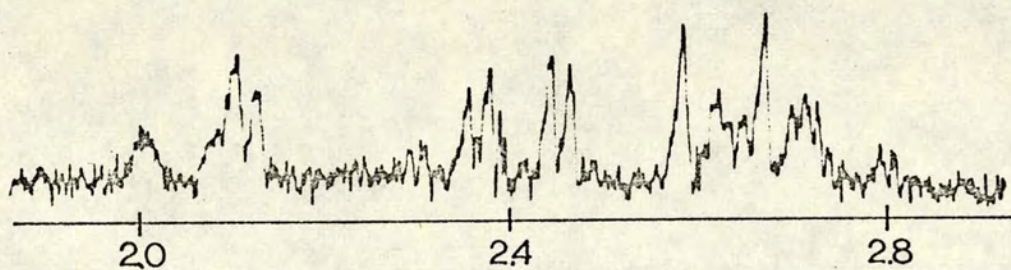
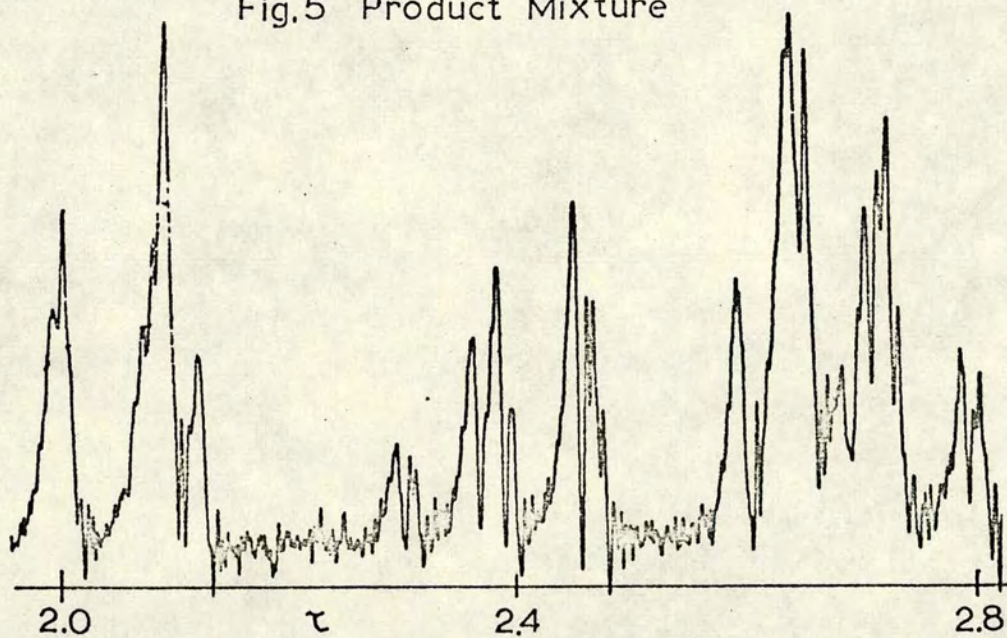


Fig. 5 Product Mixture



I. r. spectrum (nujol): ν_{\max} 3420 and 3350 (-N-H stretching, primary amine); 1140 ($-\text{SO}_2^-$) cm^{-1}

The second fraction, also a white solid was identified as a mixture of 2-chloro- and 3-chloro-phenothiazine 5, 5-dioxide (0.7 g; 26%) m. p. 248-254 $^{\circ}$.

I. r. spectrum (nujol): ν_{\max} 3300 (-NH) 1140 ($-\text{SO}_2^-$) cm^{-1}

Comparison of the fingerprint region of the spectrum of the mixture with that of authentic samples of 2-chloro and 3-chloro isomers indicated that the mixture contained mainly the 2-chloro isomer.

The p. m. r. spectra (CH_3COCH_3) gave further support to the evidence from i. r. spectra that the 2-chloro isomer was the main component of the mixture (see figs 3-5). The spectrum of these compounds had four bands: τ 2.58-2.82 (m, 4H, aromatic); 2.3-2.5 (m, 1H, aromatic); 2.0-2.1 (m, 2H, aromatic); 0.0 (bs, 1H, -NH).

The mass spectrum had the correct parent ion at m/e 265/267 $\text{C}_{12}\text{H}_8\text{ClNO}_2\text{S}$ requires M^+ , 265/267.

Attempts to separate the two isomers by fractional sublimation and crystallisation were not successful.

(B) 2-Azidophenyl 4-t-Butylphenyl Sulphone.

The azido compound (2.2 g; 0.007 mole) was decomposed in the usual way in decalin (60 ml). On removal of decalin, a black solid was obtained. This was chromatographed on alumina.

Elution with ether/light petroleum (1:1 v/v) gave a brown solid which sublimed to yield 2-aminophenyl 2-t-butylphenyl sulphone (0.29 g; 14%) m. p. and mixed m. p. 107 $^{\circ}$.

I. r. spectrum (nujol): ν_{\max} 3490 and 3390 (-NH stretching, primary amine) 1140 (SO_2) cm^{-1}

Elution with ether/methanol (25:1 v/v) gave a light brown solid which sublimed to yield a white solid, identified as a mixture of 2-t-butyl- and 3-t-butylphenothiazine 5, 5-dioxide (0.8 g; 40%) m. p. 223-5 $^{\circ}$. This was recrystallised from ethanol to give white needles m. p. 224-6 $^{\circ}$. T. l. c. showed two spots with very close R_f values.

The i. r. spectrum (nujol) showed the -NH stretching at 3320 cm^{-1} and a shoulder at 3300 cm^{-1} . The SO_2 frequency occurred at 1130 cm^{-1} . The mass spectrum showed the correct parent ion at m/e 287

Found: M^+ , 287.097059,

$\text{C}_{16}\text{H}_{17}\text{NO}_2\text{S}$ requires M 287.097994.

The p. m. r. spectrum (CDCl_3) was compatible with a mixture of two *t*-butylphenothiazine dioxides as assigned: (τ) 8.78 (\underline{s} , 9H, *t*-Bu); 8.72 (\underline{s} , 9H, *t*-Bu) 1.96-3.22 (complex band, aromatic + NH). The integral tracing for the two *t*-butyl singlets showed the ratio of the isomers i. e. 2-*t*-butyl to 3-*t*-butyl phenothiazine 5,5-dioxide to be approximately 4:3.

(C) 2-Azidophenyl 2,4,6-Trimethylphenyl Sulphone.

This azido compound (0.45 g; 0.0015 mole) was decomposed in decalin. Removal of decalin gave a bluish-black solid residue. A small portion of it was heated to 250° (0.02 mmHg) in a sublimation tube but no solid sublimed. The rest of the residue was chromatographed on alumina.

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 it was eluted with methanol.

(D) 2-Azidophenyl 2-Hydroxyphenyl- and 4-Hydroxyphenyl Sulphide.

A mixture of the two azido compounds (2.4 g; 0.01 mole) was decomposed in decalin (80 ml) in the usual way. Removal of decalin gave a dark-coloured tar as residue. This was chromatographed on alumina.

Elution with various solvents gave only trace quantities of several oils; elution with methanol gave a brown tar which did not sublime.

II. 6. MISCELLANEOUS DEOXYGENATION REACTIONS.

(A) 2-Hydroxy- and 4-Hydroxyphenyl 2-Nitrophenyl Sulphide.

A mixture of the above nitro compounds (1.85 g; 0.0075 mole) was boiled under reflux with triethyl phosphite (4.98 g; 0.03 mole) and cumene (60 ml) under nitrogen for 10 hours. Removal of lower boiling fractions yielded a black tar which was chromatographed on alumina.

Elution with ether/light petroleum (1:8 v/v) gave a yellow solid, identified as ethoxyphenyl 2-nitrophenyl sulphide (0.03 g) m. p. 111-112°.

I. r. spectrum (nujol): ν_{\max} 1520 and 1340 cm^{-1} ($-\text{NO}_2$).

The mass spectrum showed the correct parent ion at m/e 275

$\text{C}_{14}\text{H}_{13}\text{NO}_3\text{S}$ requires M^+ 275 and a minor fragment at ion m/e 246 i. e. ($\text{M}^+ - 29$), indicating loss of an ethyl group.

Elution with ether/light petroleum (1:1 v/v) gave a red oil which on addition of light petroleum gave a white solid (0.01 g), identified as mono-ethoxy phenothiazine.

I. r. spectrum (nujol): ν_{\max} 3350 cm^{-1} ($-\text{NH}$).

The mass spectrum gave the correct parent ion at m/e 243

$\text{C}_{14}\text{H}_{13}\text{NOS}$ requires M^+ 243 and a major fragment (mass abundance ratio 80%) at ion m/e 214 indicating loss of an ethyl group.

Elution with methanol gave an intractable tar.

(B) 2, 4, 6-Trimethoxyphenyl 2-Nitrophenyl Sulphide.

Reaction of this nitro compound (3.21 g; 0.01 mole) with triethyl phosphite (6.65 g; 0.04 mole) in cumene (80 ml) at the boiling point for 48 hr gave a brownish oil after removal of lower-boiling fractions. This residue was chromatographed on alumina.

Elution with ether/light petroleum (1:20 v/v) gave a white solid, identified as 2, 3-dimethyl 2, 3-diphenylbutane (0.01 g; 0.4%) m. p. and mixed m. p. 115°.

Elution with ether/light petroleum (1:15 v/v) gave a greyish solid which on recrystallisation from ethanol/light petroleum (b. p. 60-80°) yielded yellow prisms. This was identified as a mixture of 1, 3- and 2, 4-dimethoxyphenothiazine (0.86 g; 33%) m. p. 84-85° (lit. ¹⁰³ 1, 3-dimethoxyphenothiazine m. p. 80-81°).

I. r. spectrum (nujol): ν_{\max} 3380 cm^{-1} (-NH).

The mass spectrum showed the correct parent ion at m/e 259

Found: M^+ , 259.067372,

$\text{C}_{14}\text{H}_{13}\text{NO}_2\text{S}$ requires M 259.066696.

P. m. r. spectrum (CDCl_3): (τ) 6.32 (s, 3H, OMe); 6.28 (s, 3H, OMe); 6.23 (s, 3H, OMe); 6.21 (s, 3H, OMe); 2.6-3.9 (complex band 14H, aromatic + 2-NH).

T. l. c. on silica showed on 1 spot having a R_f value identical to that of the authentic sample.

Elution with ether/light petroleum (1:2 v/v) gave a yellow solid, identified as the starting nitro compound (0.24 g; 7%) m. p. and mixed m. p. 188-189°.

Elution with ether/methanol (15:1 v/v) gave a pinkish-white solid which yielded on sublimation white crystals of diethyl N-ethyl-N-[o-(2, 4, 6-trimethoxyphenylthio)phenyl]phosphoramidate (1.2 g; 26%) m. p. 99-100°.

Found: C, 55.3; H, 6.6; N, 3.3;

$\text{C}_{21}\text{H}_{30}\text{NO}_6\text{PS}$ requires C, 55.4; H, 6.6; N, 3.1%.

I. r. spectrum (nujol): ν_{\max} 1250 (P=O), 1040 and 960 (P-O-Et) cm^{-1}

The mass spectrum showed the parent ion at m/e 455

Found: M^+ 455.152837,

$\text{C}_{21}\text{H}_{30}\text{NO}_6\text{PS}$ requires M 455.153135.

P. m. r. spectrum (CDCl_3): (τ) 8.82 (t, 3H, Et; J, 7.5 Hz); 8.80 (triplet of doublets, 6H, 2 x P-O-Et; $J_{\text{H,H}}$ 7Hz, $J_{\text{P,H}}$ 1Hz); 7.22 (q, 2H, Et; J, 7.5 Hz); 6.28 (s, 9H, 3 x OMe); 5.82 (quintet, 4H, 2 x P-O-Et; J, 7 Hz); 3.94 (s, 2H, aromatic); 2.8-3.0 (m, 3H, aromatic); 2.0-2.2 (m, 1H, aromatic).

Total accountance of materials: 66%.

(C) 2,4,6-Trimethylphenyl 2-Nitrophenyl Methane.

A mixture of this nitro compound (2.55 g; 0.01 mole), triethyl phosphite (6.65 g; 0.04 mole) and cumene (80 ml) was boiled under reflux under nitrogen for 48 hr. The residue, after removal of lower boiling fractions, was chromatographed on alumina.

Elution with ether/light petroleum (1:20 v/v) gave a yellow oil which did not crystallise. This was probably an impure sample of 6,8,10-trimethyl 10H-azepino[1,2-a]indole (0.2 g; 10%).

The mass spectrum showed the correct parent ion at m/e 223

($C_{16}H_{17}N$ requires M, 223).

P.m.r. spectrum ($CDCl_3$): (τ) 8.66 (d, 3H, Me; J 8Hz); 8.16 (s, 3H, Me); 7.9 (s, 3H, Me); 4.8 (q, 1H, proton 10 in azepine ring); 4.1 (bs, 1H, proton 7) 3.35 (s, 1H, proton 11); 2.3-3.0 (complex band, 5H, aromatic + 1 azepine proton).

Elution with ether/light petroleum (1:5 v/v) gave a yellow solid which on sublimation gave white crystals, identified as 2-amino-phenyl 2,4,6-trimethylphenyl methane (0.21 g; 9%) m.p. and mixed m.p. 95-96°.

I.r. spectrum (nujol): ν_{max} 3480 and 3390 cm^{-1} ($-NH_2$).

The mass spectrum showed the correct parent ion at m/e 225

Found: M^+ 225,

($C_{16}H_{19}N$ requires M, 225).

P.m.r. spectrum ($CDCl_3$): (τ) 7.87 (s, 6H, 2 x Me); 7.72 (s, 3H, Me); 6.40 (bs, 2H, $-NH_2$); 6.32 (s, 2H, $-CH_2-$); 3.3-3.6 (m, 3H, aromatic); 3.1 (s, 2H, aromatic); 2.9-3.0 (m, 1H, aromatic).

Elution with ether/light petroleum (1:4 v/v) gave a brown oil (0.25 g; 7%).

I.r. spectrum (thin film): ν_{max} 3300 (NH) 1250 (P=O), 1050 and 960 (P-O-Et) cm^{-1}

The mass spectrum showed the parent ion at m/e 361.

P.m.r. spectrum ($CDCl_3$): (τ) 8.76 (t, 6H, 2 x P-O-Et; J 7Hz); 7.87 (s, 6H, 2 x Me); 7.72 (s, 3H, Me); 6.70 (d, 2H, J 20Hz); 5.96 (overlapping quintets, 4H, 2 x P-O-Et; J 7.5Hz); 3.72 (d, 1H,

aromatic; J 8Hz); 2.8-3.4 (complex band, 6H, aromatic + NH).

(D) 2-Methyl 1-Nitroanthraquinone

The nitroanthraquinone (3.2 g; 0.012 mole) was boiled under reflux with triethyl phosphite (4.0 g; 0.024 mole) under nitrogen for 5 hr. The dark mixture which resulted was chromatographed on alumina.

Elution with benzene/light petroleum (1:1 v/v) gave a yellow solid which on recrystallisation from ethanol yielded bis 9,9¹-(10-ethoxy 2-methyl 1-nitro)anthryl (0.25 g; 7.5%) m. p. 250-251^o.

Found: C, 72.2; H, 5.1; N, 5.1;

$C_{34}H_{28}N_2O_6$ requires C, 72.9; H, 5.0; N, 5.0%.

I. r. spectrum (nujol): ν_{\max} 1520 and 1320 cm^{-1} ($-NO_2$).

U. v. spectrum (EtOH): λ_{\max} 225, 262, 385, 408 nm. The spectrum had the same envelope as anthracene but a bathochromic shift of 5-10 nm was observed.

The mass spectrum showed the parent ion at m/e 560 ($C_{34}H_{28}N_2O_6$ requires M^+ 560) and two important fragments at ion m/e 504 (mass abundance ratio 70%) and at ion m/e 252 (mass abundance ratio 22%). The former fragment indicated loss of two molecules of ethylene and the latter fragment gave good evidence for the dimeric structure as assigned.

P. m. r. spectrum ($CDCl_3$): (τ) 8.36 (t, 3H, Et); 7.62 (s, 3H, Me); 5.72 (q, 2H, Et); 2.4-3.1 (complex band, 5H, aromatic); 1.65 (d, 1H, aromatic; J 8.5Hz).

Elution with benzene gave a dark purple solid which when recrystallised from ethanol yielded 1-ethylamino 2-methylantraquinone (0.16 g; 3.5%) m. p. 125-126^o (lit.¹¹⁹ 125^o).

Found: C, 76.4; H, 5.4; N, 5.9;

Calc'd for $C_{17}H_{15}NO_2$: C, 77.0; H, 5.7; N, 5.3%.

I. r. spectrum (nujol): ν_{\max} 1650 cm^{-1} (quinone).

U. v. spectrum (cyclohexane): λ_{\max} 235, 252, 267, 272, 315 nm (same envelope as anthraquinone).

The mass spectrum gave the correct parent ion at m/e 265.

P. m. r. spectrum (CDCl_3): (τ), 8.70 (t, 3H, Et); 7.56 (s, 3H, Me); 6.53 (q, 2H, Et); 2.7-2.8 (m, 1H, aromatic; 2.2-2.5 (m, 3H, aromatic); 1.7-1.9 (m, 2H, aromatic); 0.45 (bs, 1H, -NH).

Elution with benzene/ether (3:1 v/v) gave a brick-red solid, which yielded on recrystallisation from ethanol 1-amino 2-methyl-anthraquinone (0.70 g; 24.5%) m. p. 205-206° (lit.¹²⁰ 205°).

Found: C, 75.9; H, 4.8; N, 5.7;

calc'd for $\text{C}_{15}\text{H}_{11}\text{NO}_2$: C, 75.9; H, 4.6; N, 5.9%.

I. r. spectrum (nujol): ν_{max} 3420 and 3290 (NH_2), 1670 (Quinone) cm^{-1}

The mass spectrum showed the correct parent ion at m/e 237.

Elution with ether gave a brown solid which when recrystallised from acetone/light petroleum (b. p. 60-80°) yielded yellow needles, identified as diethyl N-1-(2-methylanthraquino)phosphoramidate (0.15 g; 3%) m. p. 150-151°.

Found: C, 61.3; H, 5.3; N, 4.1;

$\text{C}_{19}\text{H}_{20}\text{NO}_5\text{P}$ requires C, 61.1; H, 5.4; N, 3.8%.

I. r. spectrum (nujol): ν_{max} 1660 (quinone), 1260 (P=O), 1050 and 970 (P-O-Et) cm^{-1}

The mass spectrum showed the parent ion at m/e 373 ($\text{C}_{19}\text{H}_{20}\text{NO}_5\text{P}$ requires M, 373).

P. m. r. spectrum (CDCl_3): (τ) 8.60 (t, 6H, 2 x P-O-Et); 7.35 (s, 3H, Me); 5.80 (quintet, 4H, 2 x P-O-Et; J 8Hz); 1.6-2.7 (complex band, 7H, aromatic + NH).

Total accountance of material = 38.5%.

The reaction was repeated using cumene as a solvent. Thus triethyl phosphite (5.0 g; 0.03 mole) was boiled under reflux with a suspension of 2-methyl 1-nitroanthraquinone (2.0 g; 0.0075 mole) in cumene (60 ml) for 6 hr under nitrogen. A dark red solid residue was obtained when lower boiling fractions were removed. This residue was chromatographed on alumina.

Elution with benzene/light petroleum (1:1 v/v) gave a yellow solid, identified as bis 9,9^l-(10-ethoxy 2-methyl 1-nitro)anthryl

(0.09 g; 4%) m. p. and mixed m. p. 250-251°. Correct i. r. and mass spectra as described earlier.

Elution with benzene/ether (3:1 v/v) gave a red solid, identified as 1-amino 2-methylantraquinone (0.68 g; 38%), m. p. and mixed m. p. 205° (lit. ¹²⁰ 205°).

Elution with ether gave an orange yellow solid which on recrystallisation from acetone/light petroleum (b. p. 60-80°) yielded diethyl N-1-(2-methylantraquino)phosphoramidate (0.23 g; 8%), m. p. and mixed m. p. 150°.

Total accountance of materials = 50%.

(E) 1-Nitroanthraquinone.

Ethyl diphenylphosphinite (1.8 g; 0.08 mole) was added to a stirred mixture of 1-nitroanthraquinone (0.66 g; 0.003 mole) in benzene (25 ml). The mixture turned dark green immediately. It was then stirred at room temperature under nitrogen for 12 hr. The residue, after removal of benzene, was chromatographed on alumina.

Elution with benzene gave a brick-red solid, identified as 1-aminoanthraquinone (0.04 g; 69%), m. p. and mixed m. p. 252-253° (lit. ¹²¹ 253-254°).

I. r. spectrum (nujol): ν_{\max}^{-1} 3400 and 3290 (-NH₂), 1660 (Quinone) cm.⁻¹

The reaction was repeated using t-butylbenzene as solvent. 1-Nitroanthraquinone (0.9 g; 0.0035 mole) in t-butylbenzene (40 ml) was boiled under reflux with triethyl phosphite (2.4 g; 0.014 mole) under nitrogen for 6 hr. Removal of lower boiling fractions gave a black tar which was chromatographed on alumina.

Elution with benzene/ether (2:1 v/v) gave a red solid, identified as 1-aminoanthraquinone (0.1 g; 14%) m. p. and mixed m. p. 252-253° (lit. ¹²¹ 253-254°).

(F) 6-Oxo-Anthra[1,9-cd]Isoxazole.

A mixture of this isoxazole (0.11 g; 0.0005 mole), ethyl diphenylphosphinite (0.23 g; 0.001 mole) and benzene (10 ml) was stirred under

nitrogen at 50° for 20 hr. After removal of lower boiling fractions the residue was chromatographed on alumina.

Elution with benzene/ether (2:1 v/v) gave a red solid, identified as 1-aminoanthraquinone (0.55 g; 50%) m. p. and mixed m. p. 252-253° (lit. ¹²¹ 253-254°). Correct i. r. spectrum.

Elution with benzene ether (1:1 v/v) gave an orange solid identified as diphenyl-N-1-anthraquinophosphinamidate, (0.25 g; 12%) m. p. 244-245°.

I. r. spectrum (nujol): ν_{\max} 1660 (Quinone) 1250 (P=O) cm.^{-1}

The mass spectrum showed the correct parent ion at m/e 423

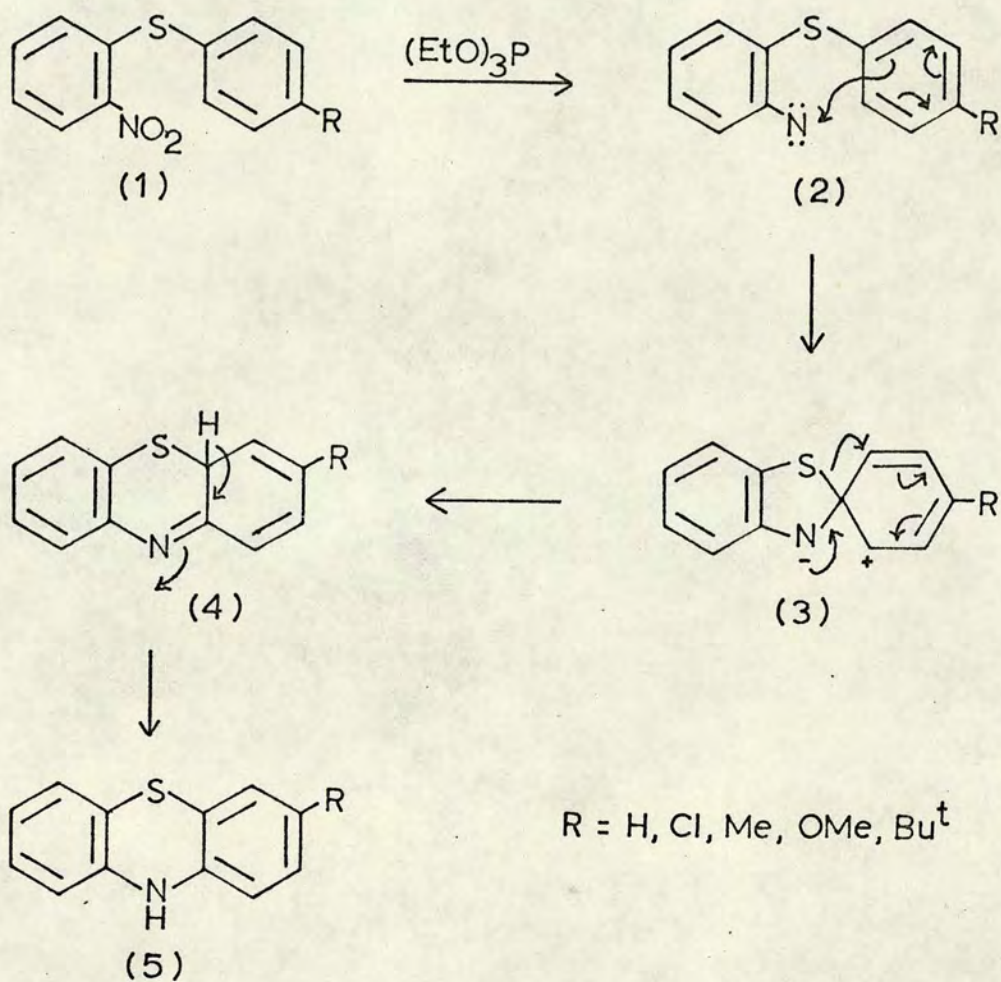
($\text{C}_{26}\text{H}_{18}\text{OP}$ requires M^+ 423) and two important fragments at m/e 346 (corresponding to loss of a phenyl group) and at m/e 201 (Ph_2PO).

III. DISCUSSION

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III. 1. REACTIONS OF ARYL 2-AZIDOPHENYL ETHERS

Cadogan et al.¹⁰¹ have successfully synthesized numerous phenothiazines (5) in good yields (50-85%) by the reductive cyclisation of aryl 2-nitrophenyl sulphides (1) by triethyl phosphite. The postulated mechanism (Scheme 1) involves an initial attack at the electron-rich 1' position to give a five-membered spirodiene intermediate (3). This then undergoes a 1, 2-sigmatropic rearrangement followed by a prototropic shift to give the phenothiazine (5).

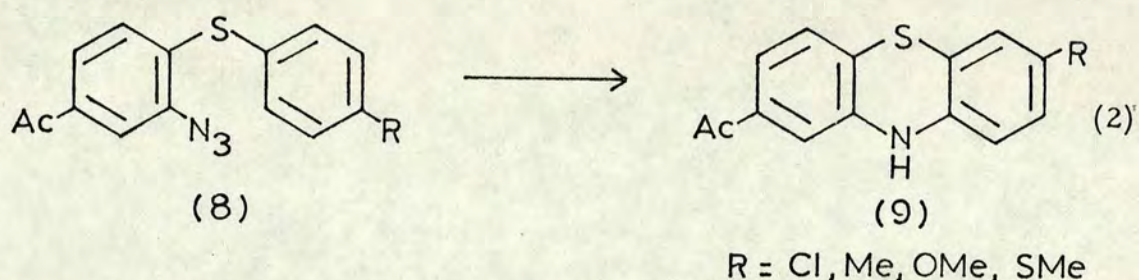
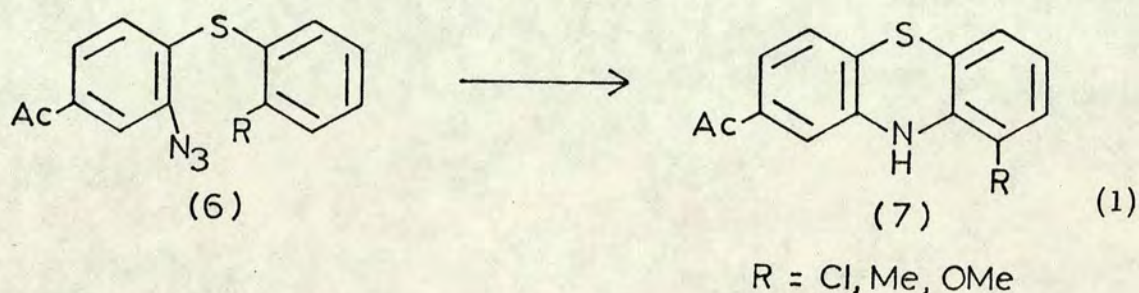


Scheme 1

This phenothiazine rearrangement was demonstrated to be a general one by the reductive cyclisation of [4-²H]phenyl 2-nitrophenyl sulphide (1; R = ²H). The product was shown to be [3-²H]phenothiazine by comparison of the e. s. r. spectrum of its cation radical with those computer-simulated for [2-²H]- and [3-²H]phenothiazine.

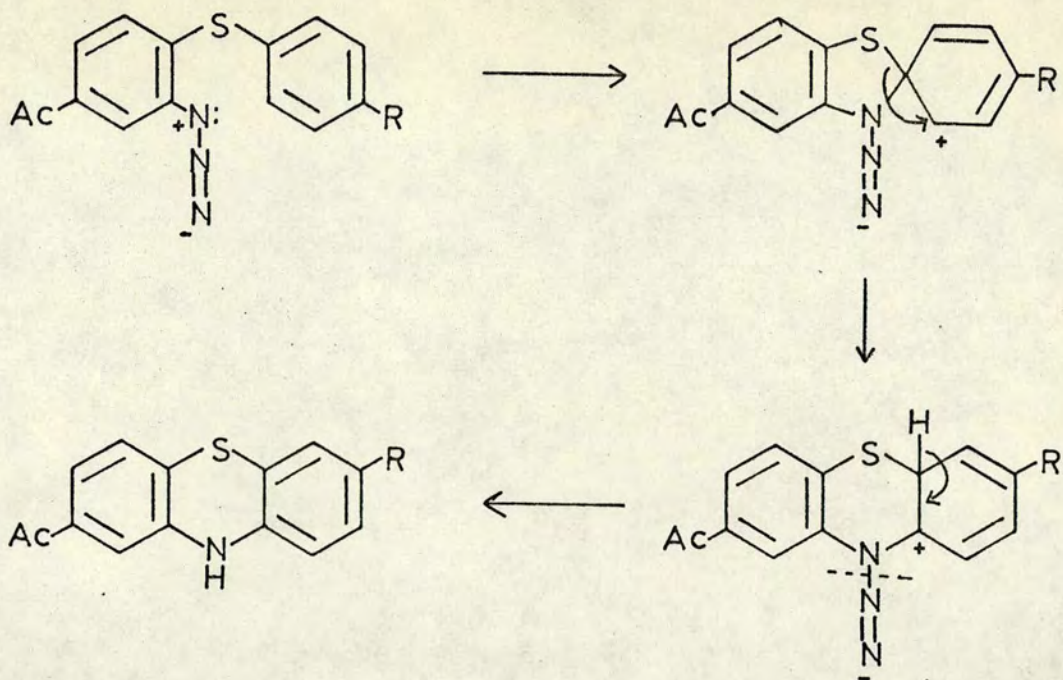
The same phenothiazines were obtained when the corresponding 2-azidophenyl aryl sulphides were decomposed in decalin. This would seem to be good evidence for the nitrene (2) as the common intermediate in these reactions.

After the preliminary communication of this work had been published, Messer and Farge¹²² also observed a similar rearrangement in the decomposition of 2-azido 4-acetylphenyl 2- and 4-substituted phenyl sulphides, (6) and (8) respectively.

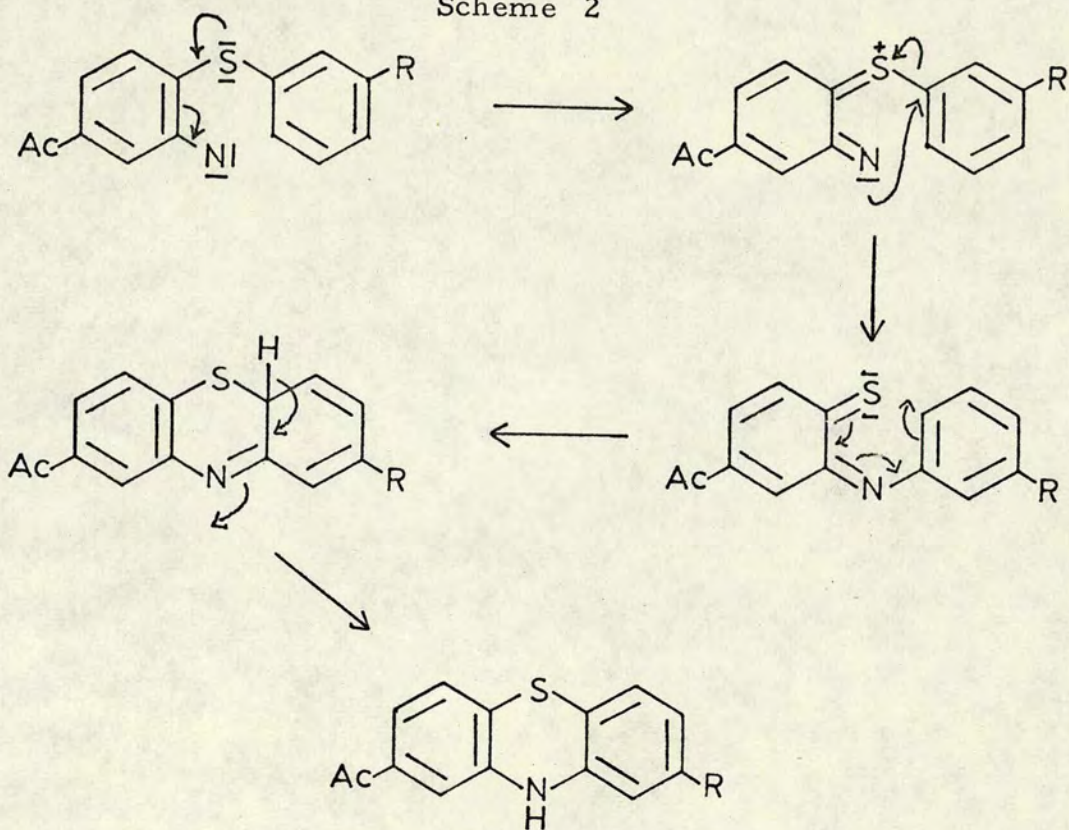


Two possible mechanisms were postulated. The first (Scheme 2) seems rather dubious as it has been established (see chapter I, Introduction) that thermal decomposition of aryl azides (especially in the absence of alkenes) yield aryl nitrenes with concomitant loss of nitrogen as the first reaction step.

The second mechanism (Scheme 3) is rather unlikely as it depends on a structure involving expansion of the sulphur valence shell. Considerable evidence, mainly spectral, has been presented against structures involving such a valence shell expansion in sulphur.¹²³ By means of refined theoretical calculations, Bendazolli and Zauli¹²⁴ have predicted that participation of d-orbitals in aromatic sulphides is likely to be negligible.

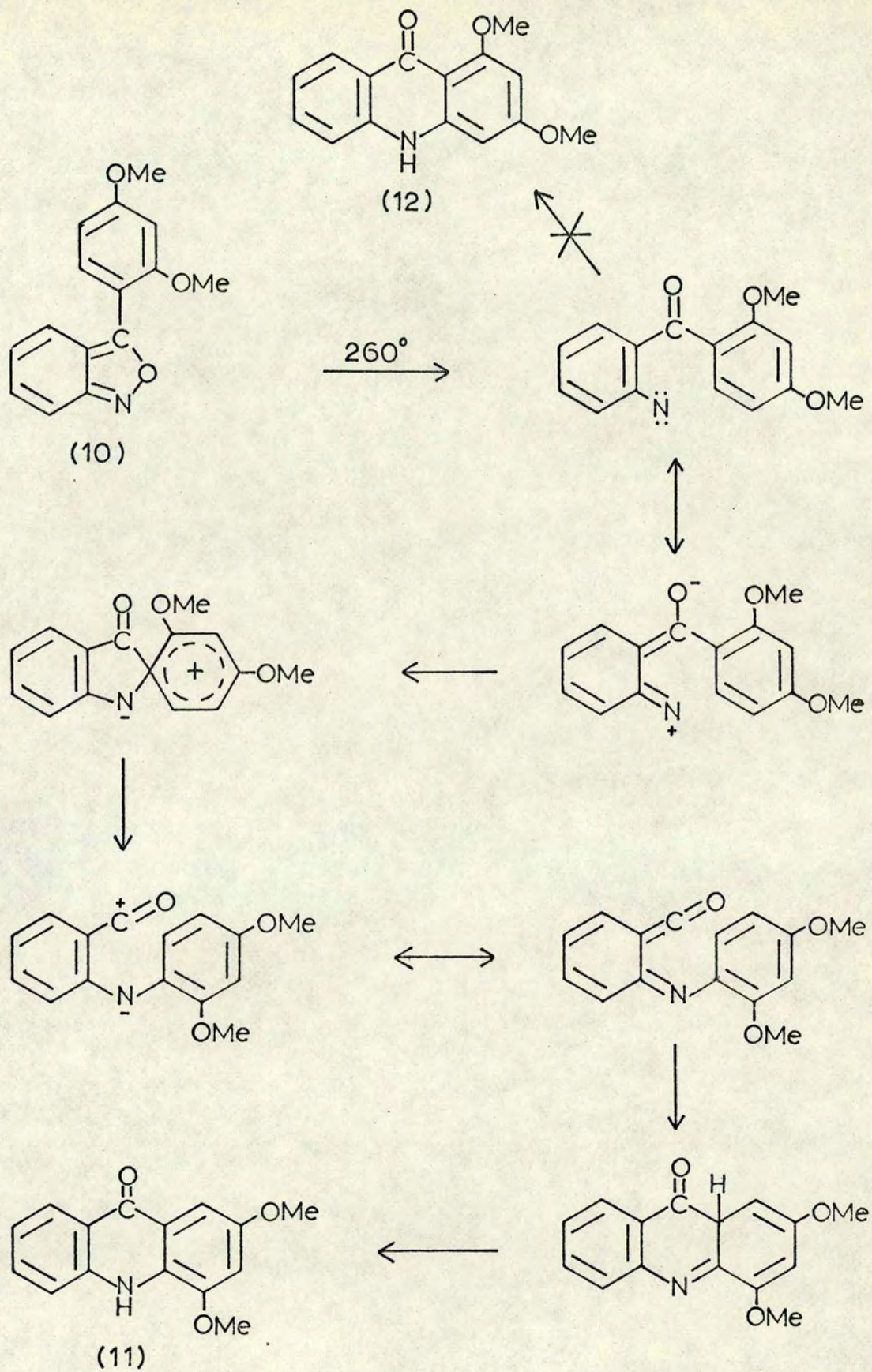


Scheme 2



Scheme 3

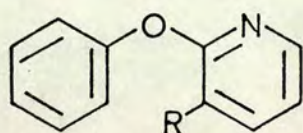
Kwok and Pranc¹²⁵ have also reported a similar type of rearrangement in a study of the formation of acridones from methoxylated phenylanthranils under pyrolytic conditions. Thus 2-(2,4-dimethoxyphenyl)anthranil (10) on heating to 260° gave 2,4-dimethoxyacridone (11) rather than the 1,3-dimethoxy isomer (12). The proposed mechanism is represented in Scheme 4.



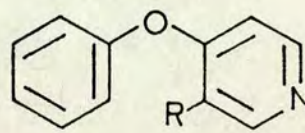
Scheme 4

It will be noted that one of the two key intermediates in Cadogan's phenothiazine rearrangement [(4), Scheme 1], requires an ortho hydrogen for aromatisation to the phenothiazine. By blocking both ortho positions (the so-called 'blocked ortho effect') in the ring not containing the nitrene Cadogan and Kulik¹⁰³ have shown that some very interesting and novel rearrangements result. Some of these reactions have been outlined in the Introduction and will be discussed in greater detail here in conjunction with the present investigations.

Only two reports exist of attempts to synthesize phenoxazine and its derivatives from nitrene or nitrene precursors by cyclisation reactions. Both attempts have resulted in failures. The first was by Smith et al.¹⁰⁰ Thermolysis of *o*-azidodiphenyl ether in inert solvents gave an intractable tar "from which was obtained only a small amount of an impure picrate resembling that reported from the expected phenoxazine." Smalley et al.¹⁰² in a very recent paper reported the failure of an attempt to cyclise nitropyridyl ethers (13, 14; R = NO₂) by reaction with triethyl phosphite.



(13)



(14)

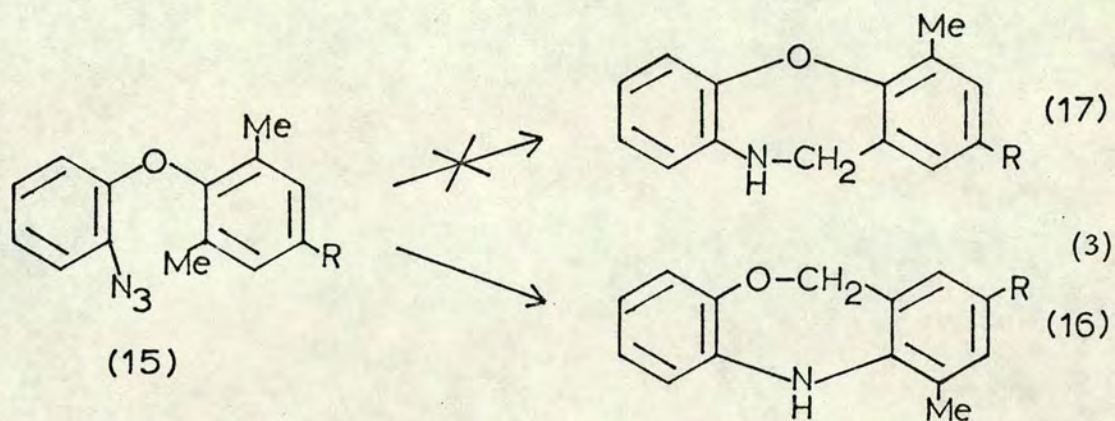
Decomposition of the corresponding azidopyridyl ethers (13, 14; R = N₃) in bromobenzene also failed to yield any cyclised products.

(A) 2-Azidophenyl 2,6-Dimethylphenyl- and 2,4,6-Trimethylphenyl Ether.

As expected the thermolysis of 2-azidophenyl 4-methoxyphenyl ether gave only minute traces of some unidentifiable compounds and a large amount of intractable tar.

However when both relevant ortho positions are blocked by methyl groups, the product (if formed) was expected to be either 10,11-dihydro 4-methyldibenzo[b,f][1,4]oxazepine (17; R = H) or the

5, 11-dihydro isomer (16; R = H). In the event, decomposition of 2-azidophenyl 2, 6-dimethylphenyl ether (15; R = H) gave 5, 11-dihydro 4-methyldibenzo[b, e][1, 4]oxazepine (16; R = H) (11%) rather than the isomer (17; R = H).



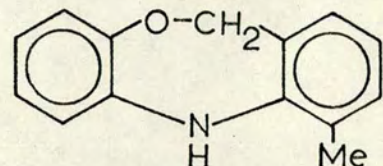
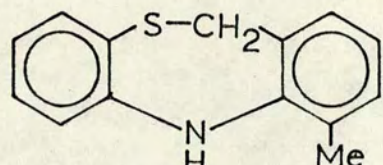
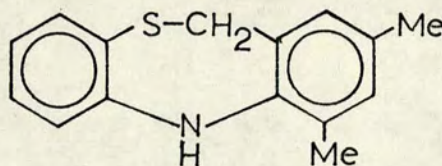
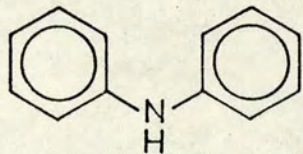
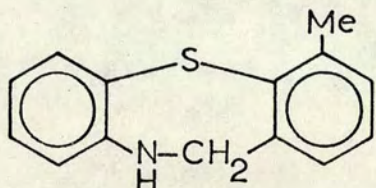
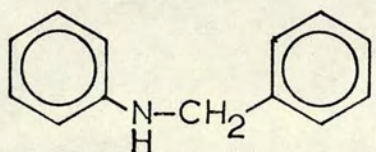
This represents the first successful synthesis of a dibenzo-oxazepine by cyclisation of a nitrene precursor. It parallels the reaction of the corresponding sulphide¹⁰³ which yielded the analogous thiazepine. The yield in the present study is however much lower.

The structure of this product was assigned as the 5, 11-dihydro (16; R = H) rather than the 10, 11-dihydro (17; R = H) isomer on the basis of p. m. r. and mass spectral data. In particular the chemical shifts of the N-H proton of several closely related compounds were compared (Table I). These values were all obtained from p. m. r. spectra of the compounds under identical conditions viz. as 10% w/v solutions in CDCl₃ as solvent.

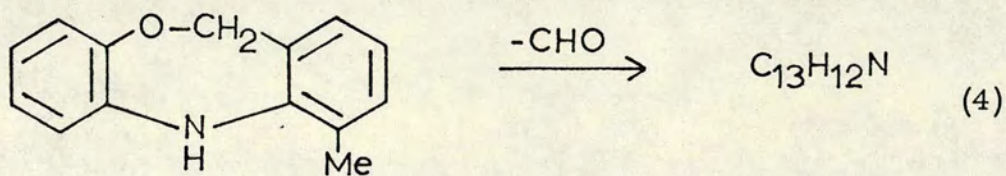
The chemical shifts of the methylene protons is also in agreement with the deshielding effect of the oxygen, nitrogen and sulphur atoms viz. O > N > S.

The mass spectrum of the 5, 11-dihydro-oxazepine (16; R = H) in addition to giving the correct parent ion at m/e 211 also showed a

Table I

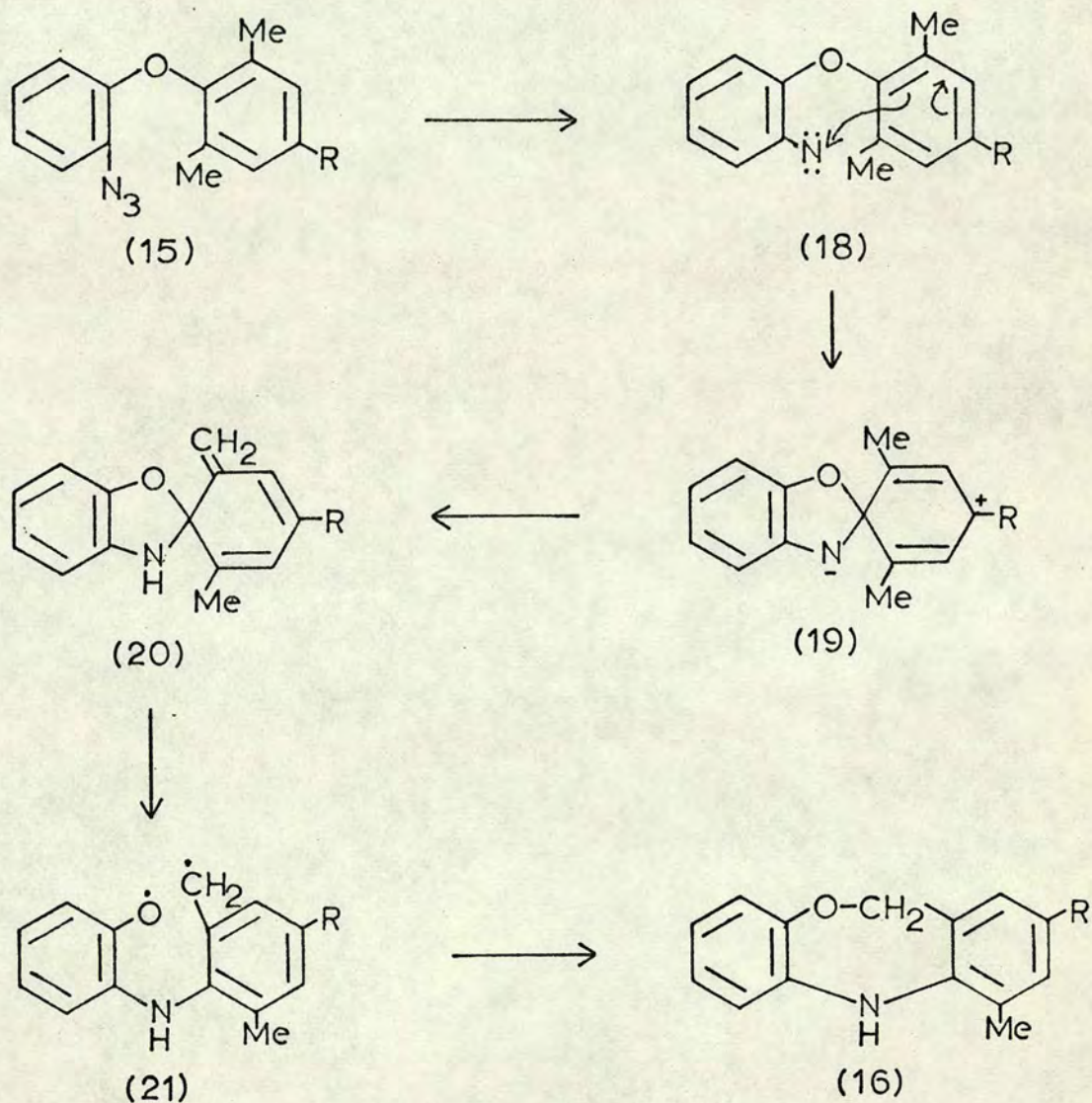
Compound	Chemical Shifts (τ)	
	NH	-CH ₂ -
	4.43	5.11
	4.34	6.10
	4.30	6.00
	4.60	←
	6.15	5.30
	6.25	5.80

fragment at m/e 182. This could arise by the process:



Exact mass measurement of the fragment showed it to be $C_{13}H_{12}N$.

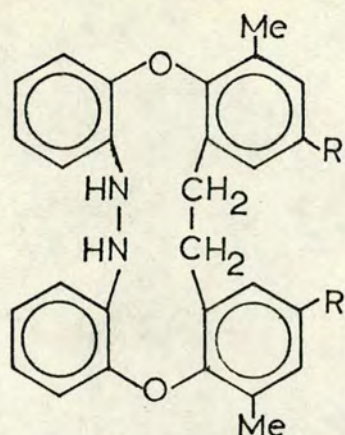
Thus the intermediate nitrene (or nitrenoid species) generated by thermolysis of the azide (15; R = H) prefers not to insert into the adjacent C-H bond but undergoes an aromatic rearrangement resulting in the oxygen atom being attached to one of the methyl carbon atoms. The mechanism is likely to be similar to that for the reaction of the analogous sulphur compound (see ref. 103), thus,



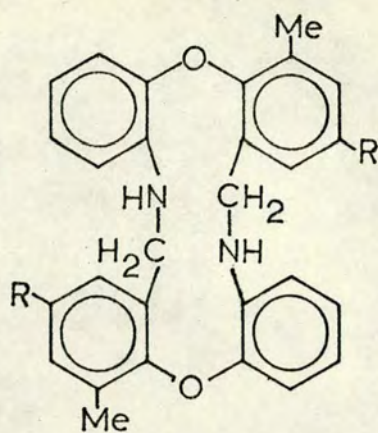
Scheme 5

As a 1, 3-sigmatropic shift is not symmetry allowed, it is more likely that a diradical species (21) is involved.

A minor reaction product (1%) is the bis-ether (22; R = H). Its mode of formation, however, is not easily rationalised.



(22)



(23)

The structure was assigned on the basis of evidence from spectral data to be (22) ($R = H$) rather than (23) ($R = H$). The chemical shift of the $-CH_2-$ group was found to be 7.65τ while that for compounds of the type $Ar-NH-CH_2-Ar$ are of the order of $5.0-6.0 \tau$ (see table I). Furthermore the signal of the N-H proton occurred at 4.05τ while that for compounds of the type $Ar-NH-CH_2-Ar$ are around $6.0-6.5 \tau$ (see table I).

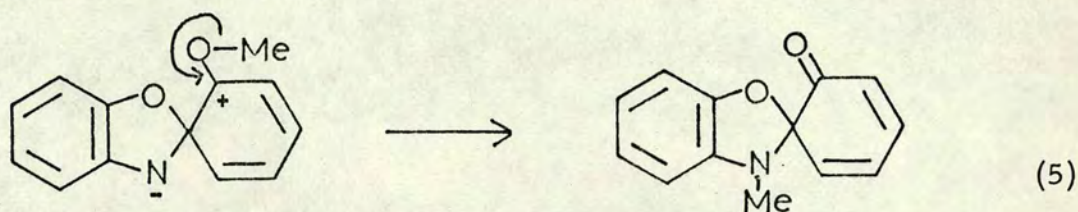
The dimeric nature of the product was established from the mass spectrum. It gave the correct parent ion at m/e 422 and the most abundant fragment (mass abundance ratio 100%) at m/e 210, corresponding to a molecular formula of $C_{14}H_{12}NO$ (from exact mass measurements).

Similarly the thermolysis of 2-azidophenyl 2,4,6-trimethylphenyl ether (15; $R = Me$) gave 5,11-dihydro 2,4-dimethyldibenzo-[b, e][1,4]oxazepine (16; $R = Me$) (15%) and the bis-ether (22; $R = Me$) (1.5%).

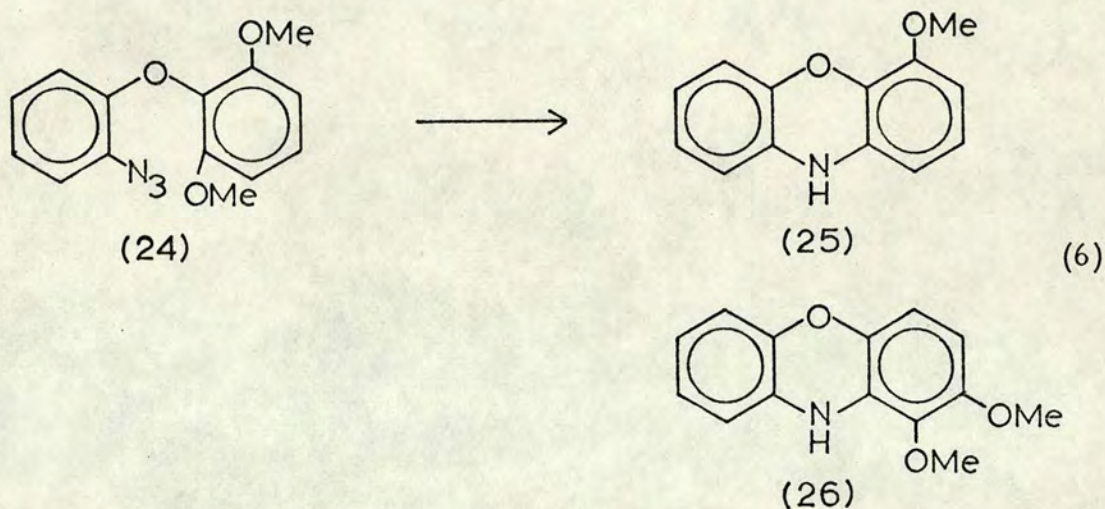
(B) 2-Azidophenyl 2,6-Dimethoxyphenyl Ether.

By analogy with the reaction of 2-azidophenyl 2,6-dimethoxyphenyl sulphide,¹⁰³ it was expected that the decomposition of this azido compound (24) would lead to 1-methoxyphenoxazine and 1,2-dimethoxyphenoxazine. Perhaps it might even lead to isolation of

the other key intermediate of Cadogan's phenothiazine rearrangement [cf. (3); Scheme 1] thus,



The products actually isolated from the thermolysis of 2-azidophenyl 2,6-dimethoxyphenyl ether (24) were 4-methoxyphenoxazine (25) (30%) and 1,2-dimethoxyphenoxazine (26) (11%) as shown by detailed p. m. r. and mass spectral investigations.



4-Methoxyphenoxazine.

The mass spectrum and exact mass measurements gave good evidence that the compound was a mono-methoxy phenoxazine. This conclusion was substantiated by the p. m. r. spectrum with CDCl_3 as solvent. When hexadeuteriobenzene was used as solvent the complex aromatic band resolved into four separate groups of signals. Scale expansion and double irradiation allowed the assignments of the signals due to protons H_a , H_d and H_f (see fig. 1)

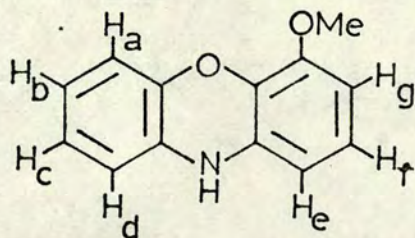


Fig.1

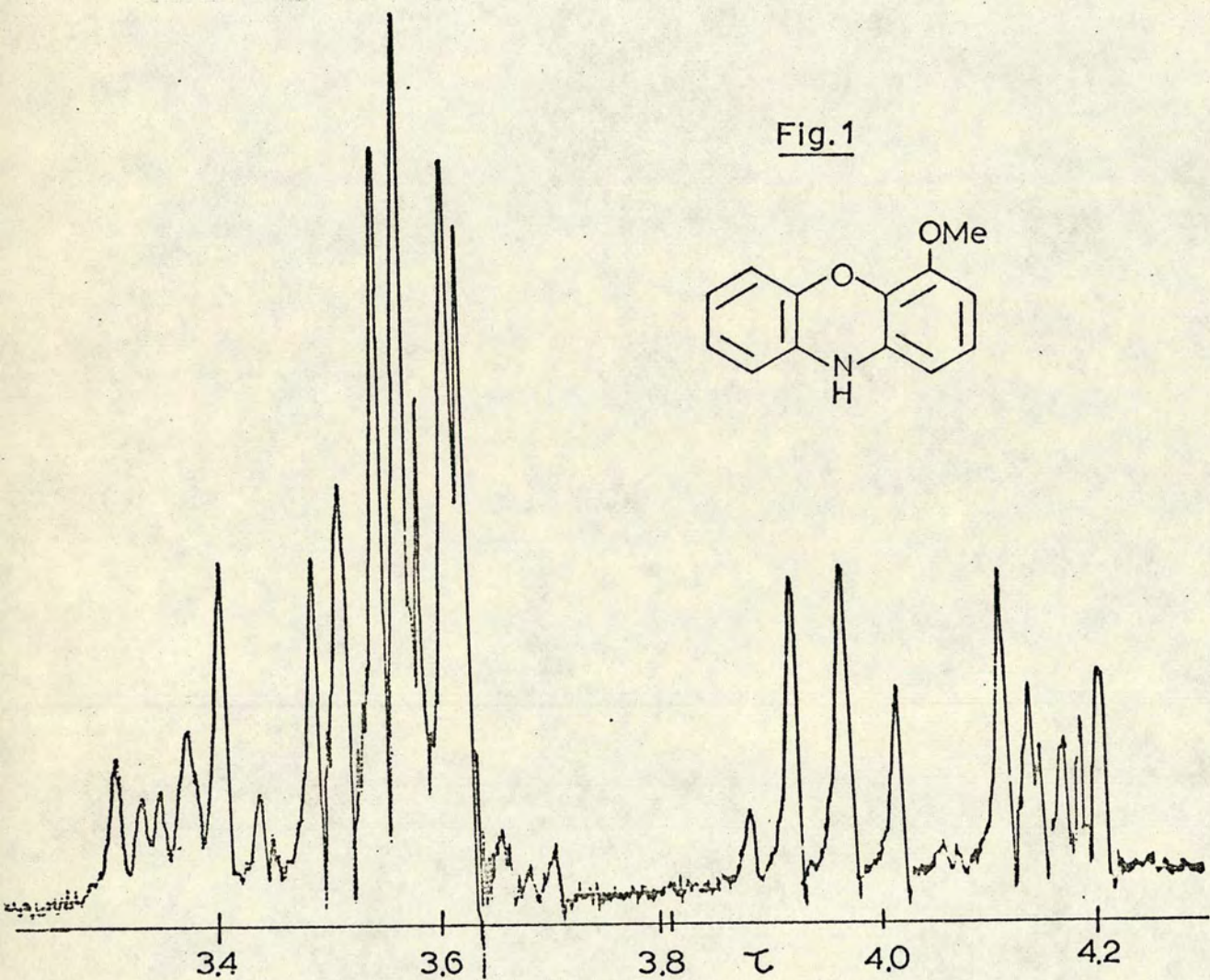
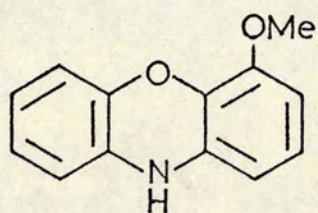


Table II summarises the results of the spin decoupling experiments.

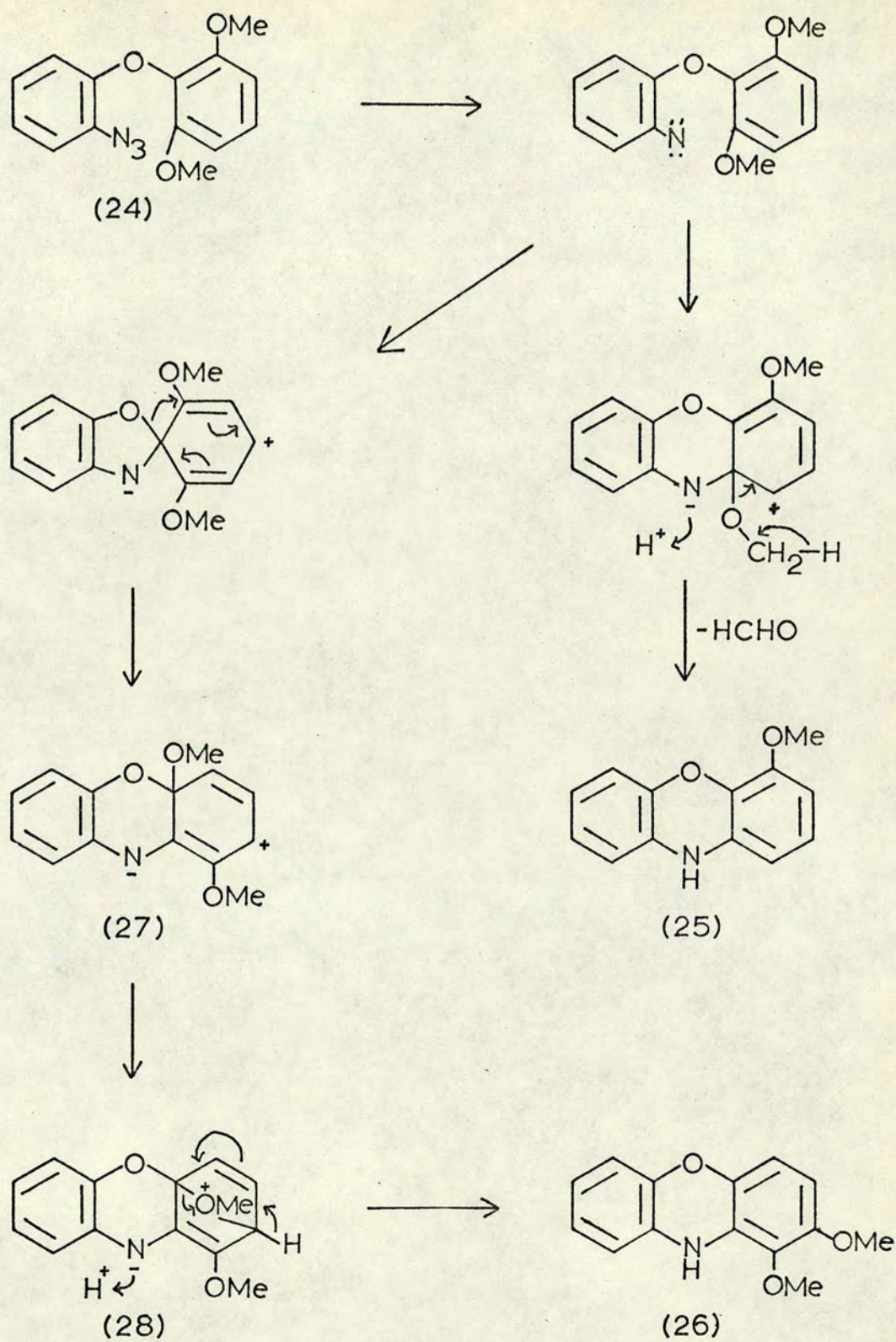
Irradiation frequency (equivalent chemical shift value, τ given)	Changes Observed on Irradiation
3.33	Multiplet at 4.15 τ \rightarrow Quartet ($J_{a,b}$ 6Hz; $J_{a,c}$ 3Hz)
3.58	Multiplet at 4.15 τ \rightarrow Singlet
3.62	Triplet at 3.97 τ \rightarrow Singlet

Thus the multiplet centred at 4.15 τ is the signal arising from H_a - this is the expected upfield signal for the proton ortho to the oxygen function. The triplet at 3.97 τ is due to the signal from H_f , the complex band at 3.48-3.62 τ due to H_b , H_c and H_e ; and the multiplet at 3.35 τ to H_d .

1, 2-Dimethoxyphenoxazine

The mass spectrum and exact mass measurements provided good evidence that the compound was a dimethoxy phenoxazine. The p.m.r. spectrum showed that the methoxy signals were not identical (viz. singlets at 6.19 and 6.25 τ). The two o-o coupled doublets (J 9 Hz) at 3.64 and 3.87 τ ruled out the 1,3, 2,3, and 2,4-dimethoxyphenoxazines. The 1,4-dimethoxy isomer is likewise unlikely as the methoxy signals for the analogous 1,4-dimethoxyphenothiazine¹⁰³ appear as a 6-proton singlet in the p.m.r. spectrum. This leaves only the 1,2 and 1,4 isomers to consider. As both o-o coupled doublets occur at higher field than the multiplet due to H_a , it indicates that the ortho position in the relevant ring must be unsubstituted. This indicates that the compound is 1,2-dimethoxy phenoxazine.

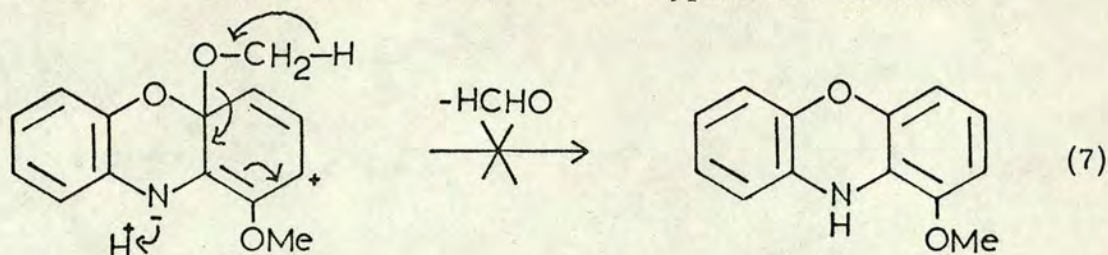
The formation of these products can be rationalised (Scheme 6) by assuming the formation of the spirodiene intermediate which undergoes a 1,2-sigmatropic shift to give the hydroaromatic intermediate (27).



Scheme 6

One of the two ways through which it can aromatise is by a 1,4 trans-methoxylation via the oxonium species (28) to give the observed 1,2-dimethoxyphenoxazine. The other way is through loss of formaldehyde

and concomitant formation of 1-methoxyphenoxazine thus:



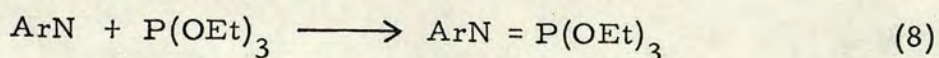
However, in contrast to the sulphur analogue, this product was not obtained in this investigation. A possible explanation is that its formation is by a higher energy pathway (as in the case of 1-methoxyphenothiazine¹²⁶) as compared to the 1, 2-dimethoxy compound. Otherwise it is difficult to explain this negative result.

In its place, 4-methoxyphenoxazine was obtained. Its formation is rationalised (Scheme 6) by an initial attack at the 2' position followed by aromatisation via loss of formaldehyde. However the quantity of formaldehyde trapped (by means of dimedone) is only about half the amount expected corresponding to the yield of 4-methoxyphenoxazine.

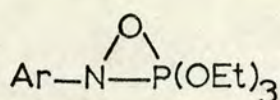
III. 2. REACTIONS OF ARYL 2-NITROPHENYL ETHERS

Cadogan et al.^{61, 62, 101, 103} have shown that reduction of aromatic nitro compounds by triethyl phosphite has led in many instances to formation of interesting heterocyclic compounds of nitrogen by the process of reductive cyclisation.

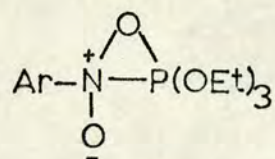
However, with many of these reactions a setback (against cyclisation) is the ready formation of phosphorimidates whose genesis is presumably by the reaction between an intermediate nitrene and the phosphite thus,



although it is not possible to rule out other non-nitrene pathways such as the deoxygenation of intermediates such as (29) and (30) by phosphite. The yields of these phosphorimidates have been reduced by carrying



(29)



(30)

out the reactions in solvents such as cumene and t-butyl benzene.

Thus used, this reaction has been put to great advantage as a synthetic route to nitrogen heterocycles.⁵⁷

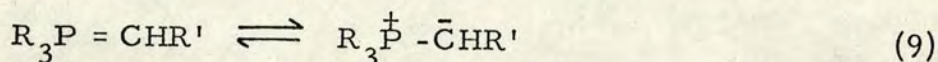
(A) 2, 6-Dimethylphenyl and 2, 4, 6-Trimethylphenyl 2-Nitrophenyl Ethers.

Reaction of 2, 6-dimethylphenyl 2-nitrophenyl ether with triethyl phosphite gave only a very small amount (0.5%) of the cyclised product, 5, 11-dihydro 4-methyldibenzo[b, e][1, 4]oxazepine (16; R=H) (Scheme 5). The major product (70%) was a colourless solid, initially assigned as triethyl N-o - (2, 6-dimethylphenoxy)phenyl phosphorimidate (33; R = H) (Scheme 7). This preliminary assignment was the obvious one in the light of existing results on such reactions. Thus Cadogan et al.^{61, 68} reported the isolation of phosphorimidates and phosphoramidates (being the products of hydrolysis of phosphorimidates) in the thermal deoxygenation of aromatic nitro compounds. Likewise Sundberg et al.⁶⁹ have obtained high yields (60-80%) of phosphorimidates in the photochemical deoxygenation of several aromatic nitro compounds.

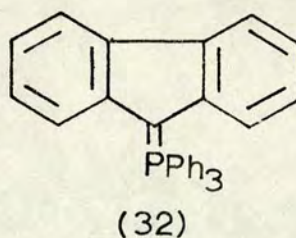
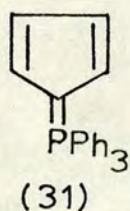
What is dubious about the present assignment is that the phosphorimidate and not the phosphoramidate should be isolated in view of the experimental method used viz. elution chromatography on alumina. Both Cadogan⁶¹ and Sundberg⁶⁹ have shown that phosphorimidates are converted by hydrolysis to the phosphoramidates by elution chromatography on silica or alumina. Furthermore Cadogan and Armour¹²⁷ have shown that hydrolysis of this product does not yield the expected phosphoramidate. Final proof that this product is not the phosphorimidate came by the preparation¹²⁷ of an authentic sample of triethyl-N-o - (2, 6-dimethylphenoxy)phenyl phosphorimidate by an unambiguous known

method¹¹⁷ viz. reaction of the azide with triethyl phosphite. The i. r. and p. m. r. spectra of this authentic is significantly different from those of the reaction product.

A closer study of the i. r. spectrum revealed a strong absorption band at 1260 cm^{-1} . This is too low for the usual P=N absorption band ($1415\text{-}1290\text{ cm}^{-1}$)¹²⁸. It fits however with values for P=C stretching frequencies. Data for P=C frequencies are limited since the majority of this type of compounds exist in the ylid rather than the ylene form.

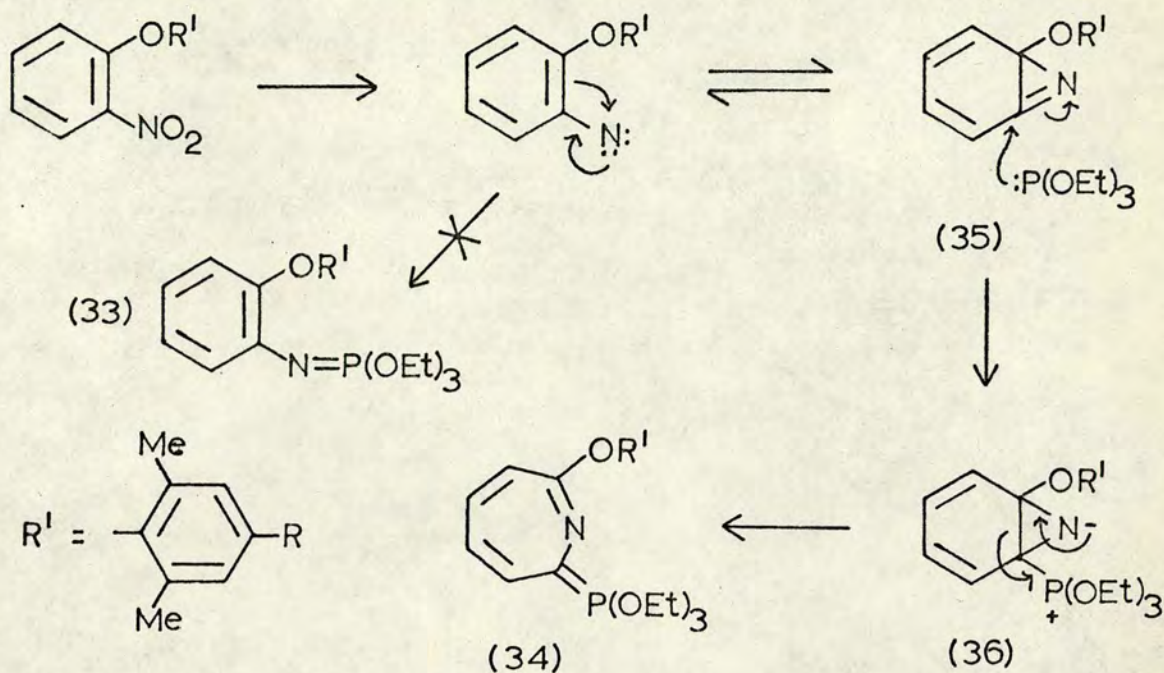


In cases where the ylene form is stabilised by conjugation [for e. g. (31) and (32)],^{129, 130} the characteristic absorption appears in the range $1180\text{-}1230\text{ cm}^{-1}$.



The p. m. r. spectrum showed the presence of three P-O-Et groups (overlapping quartet of doublets and triplet of doublets) and that the ring containing the methyl substituents remained intact (as indicated by the three-proton singlet in the aromatic region). The one-proton multiplet at $4.2\ \tau$ (probably non-aromatic) suggested that the other ring had undergone a change - probably a ring expansion.

From the spectral data the product isolated is assigned the structure of 7-triethoxyphosphoranylidene 2-(2,6-dimethylphenoxy)-azepine (34; R = H). The formation of this compound is rationalised (Scheme 7) by assuming deoxygenation of the nitro-group to give a nitrene which can be considered to be in equilibrium with a 7-azabicyclo[4, 1, 0]hepta-2, 4, 6-triene derivative (35) of the type postulated by Huisgen.⁴⁶



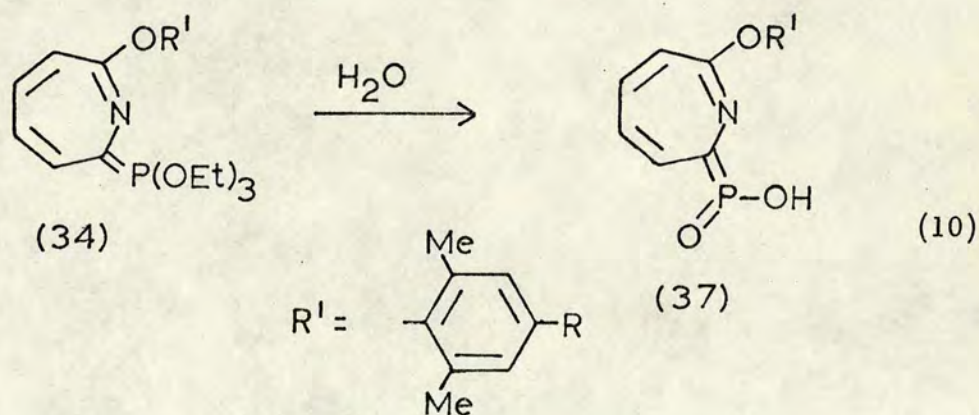
Scheme 7

Nucleophilic attack by the triethyl phosphite on the azabicyclo compound (35) gives rise to a phosphonium intermediate (36) which ring expands to the phosphoranylidene azepine (34). This is in accord with earlier work^{61, 68, 69} on the ring expansion of aryl nitrenes to $3H$ -azepinyl phosphonates consequent upon nucleophilic attack by triethyl phosphite.

It would seem that in the present case, ring expansion of the first-formed nitrene is more favourable than the alternative ring closure reaction to the dibenzo-oxazepine. There is some evidence supporting this conclusion from investigations currently in progress.¹³¹ A $3H$ -azepine was detected (mass spectrum) as a product of this reaction in the presence of an added nucleophile, diethylamine. The formation of $3H$ -azepines has been attributed to nucleophilic attack on the aza-bicyclo heptatriene by diethylamine. This reaction is well documented (see section I.4). The preference for ring expansion over ring closure could well account for the previous anomalous (by comparison with the sulphur analogues) results in the failure to obtain

any cyclised products. Such ring expansions could well be responsible for the tarry products previously obtained. Following on from this result, the next phase of investigation will obviously centre on the reasons for this preference for ring expansion over ring closure.

It was further observed that the phosphoranylidene azepine (34; R = H) hydrolysed within an hour on exposure to air. A similarly rapid hydrolysis in CCl_4 solution in an n.m.r. tube occurred on the addition of D_2O . The hydrolysed product was identified tentatively as 2-(2,6-dimethylphenoxy) azepin-7-ylidene phosphonic acid (37; R = H).

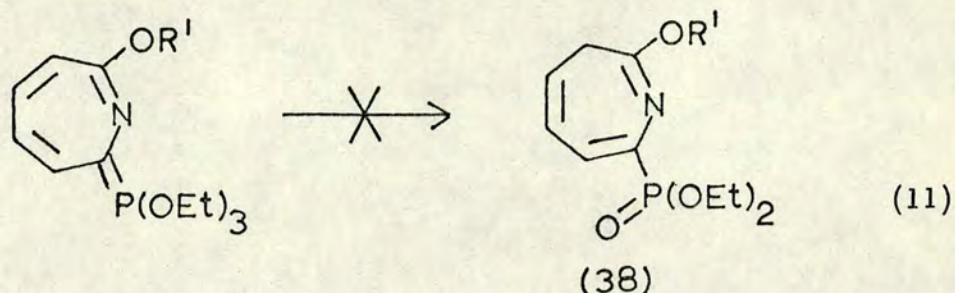


The structural assignment is based on spectral data. The i. r. spectrum showed a broad, shallow band at 2400 cm^{-1} typical of P-OH absorptions,¹²⁸ and the P=O frequency at 1200 cm^{-1} . When the hydrolysis was carried out in an n.m.r. tube the very striking replacement of the P-O-Et signals (overlapping quartet of doublets and the triplet of doublets) by the normal ethyl signals was observed (cf. fig. 1 and 2 on page facing page 70). The p.m.r. spectrum of the white solid obtained on aerial hydrolysis confirmed the complete disappearance of the P-O-Et signals. The molecular formula was confirmed by exact mass measurements.

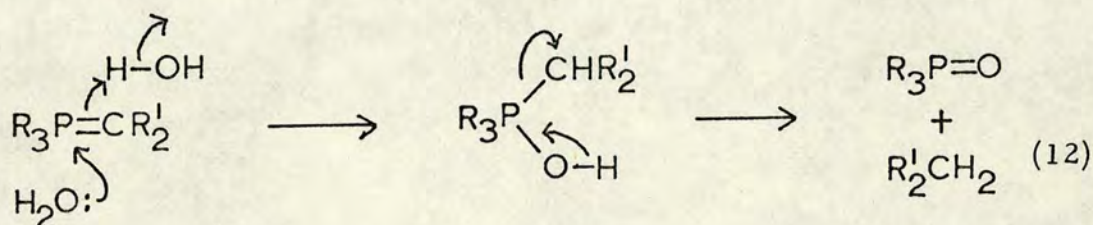
The half-life of this rapid hydrolysis, determined on an automatic radiometric titrator, was found to be 25 min at a pH 3.8 and 26° .¹²⁷

The isolation of the azepinylidene phosphonic acid (37) was most unexpected in view of earlier results^{68, 69} which would suggest the

3H-azepinyl phosphonate (38) as the product of hydrolysis.



Hydrolysis of phosphoranes usually lead to rupture of the P=C bond resulting in formation of the phosphine oxide¹³² (for example, eq. 12).

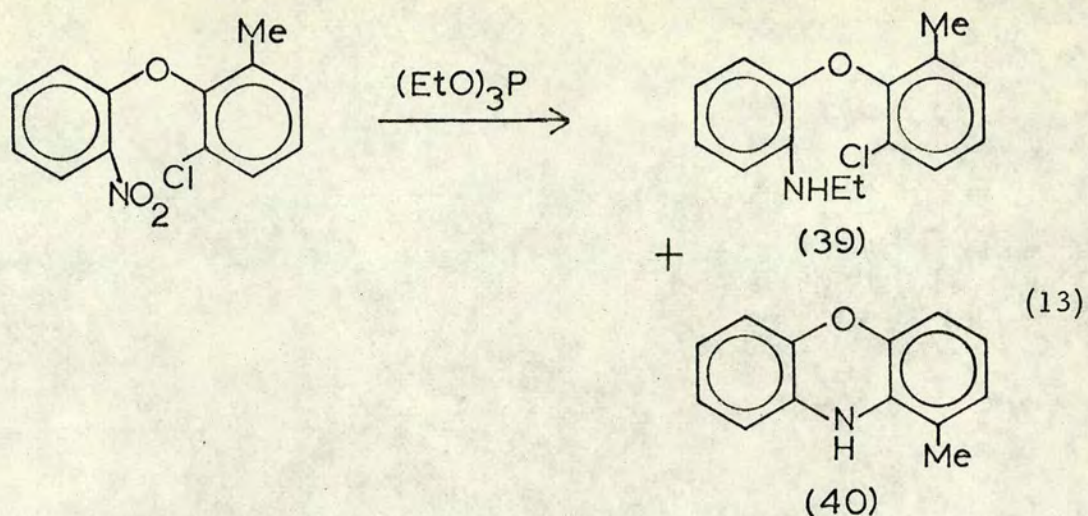


The loss of the three P-O-Et groups in the present hydrolysis reaction is most unusual. It has been further observed that a solution of the phosphenic acid in aqueous ethanol turned blue in colour when allowed to stand in air for a few days, thus suggesting further reactions. Further investigations are obviously necessary before a more definite conclusion on the structure of the hydrolysis product can be made.

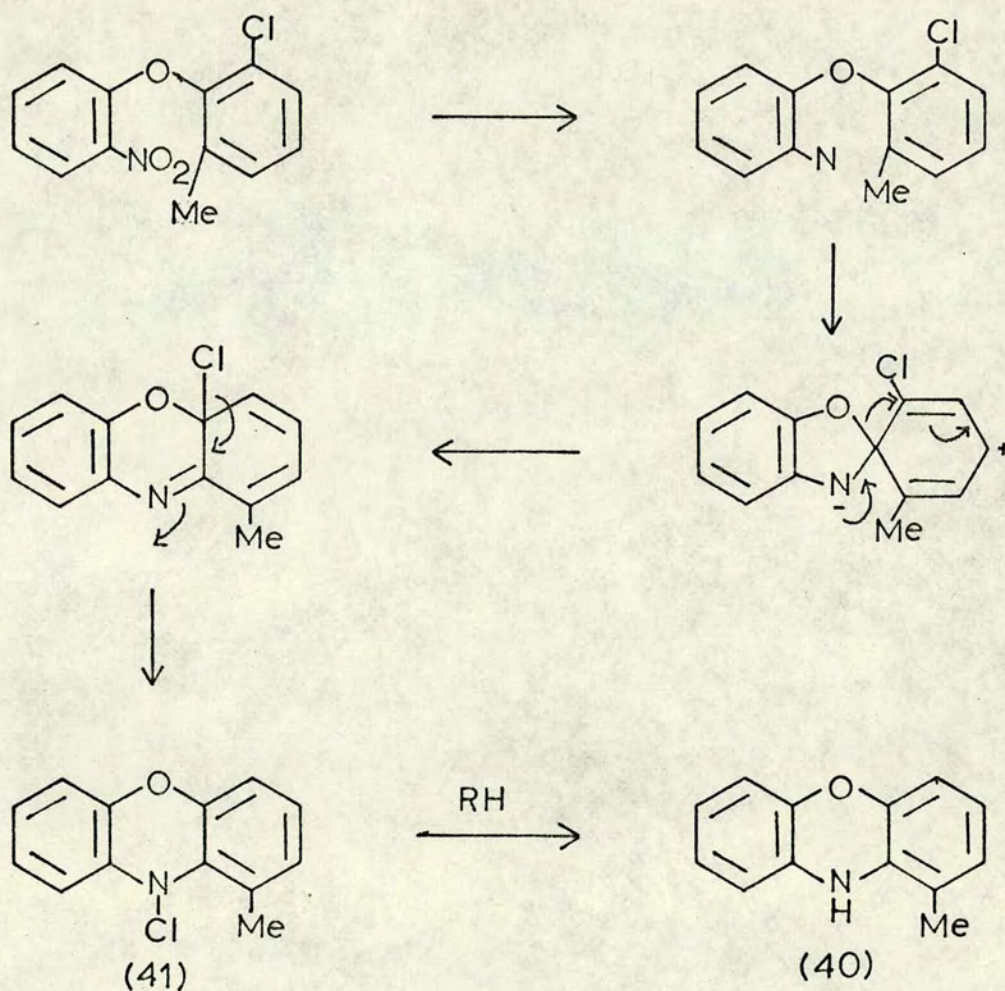
The reaction of 2,4,6-trimethylphenyl 2-nitrophenyl ether with triethyl phosphite gave similar products viz. the dibenzo-oxazepine (16; R = Me) (1%) and the phosphoranylidene azepine (34; R = Me) (62%). A similarly rapid hydrolysis of the phosphoranylidene azepine to the azepinylidene phosphenic acid (37; R = Me) was also observed.

(B) 2-Chloro 6-Methylphenyl 2-Nitrophenyl Ether.

The only products isolated from the deoxygenation of this compound by triethyl phosphite were 2-N-ethylaminophenyl 2-chloro 6-methylphenyl ether (39; 6%) and 1-methylphenoxazine (40; 7%). The N-ethylamino compound (39) is presumably produced as a result of ethylation of the first formed primary amine by triethyl phosphate¹³³



or phosphite.¹³⁴ By analogy with the case of the sulphur analogue¹⁰³ the formation of 1-methylphenoxazine is rationalised (Scheme 8) by the usual 'phenothiazine rearrangement' except that in this case, aromatisation is achieved probably by a loss of the chlorine atom.



Scheme 8

The postulated N-chloro intermediate (41) is converted to the phenox-

azine (40) by chlorination of decalin. The similar chlorination by N-chloro succinimide with decalin as reported by Cadogan and Kulik¹⁰³ is good evidence for this pathway.

Unlike the sulphur analogue, 4-methylphenoxazine was not isolated.

Trace amounts of the expected phosphoranylidene azepine was detected (by i. r. spectroscopy) but its very rapid hydrolysis prevented further spectral determinations. This would seem to indicate that the azepine produced was being hydrolysed on the column during elution.

(C) 2, 6-Dimethoxyphenyl 2-Nitrophenyl Ether.

The residue from the reaction of this compound with triethyl phosphite was unusually light in colour (indicating little tar formation). However the accountance of materials was very poor (26%). Not even trace amounts of the expected phosphoranylidene azepine was detected. It was considered that the azepine (assumed formed) hydrolysed on the column during elution chromatography to the very polar azepinylidene phosphenic acid. A faint yellow band remained at the top of the column even after elution with methanol.

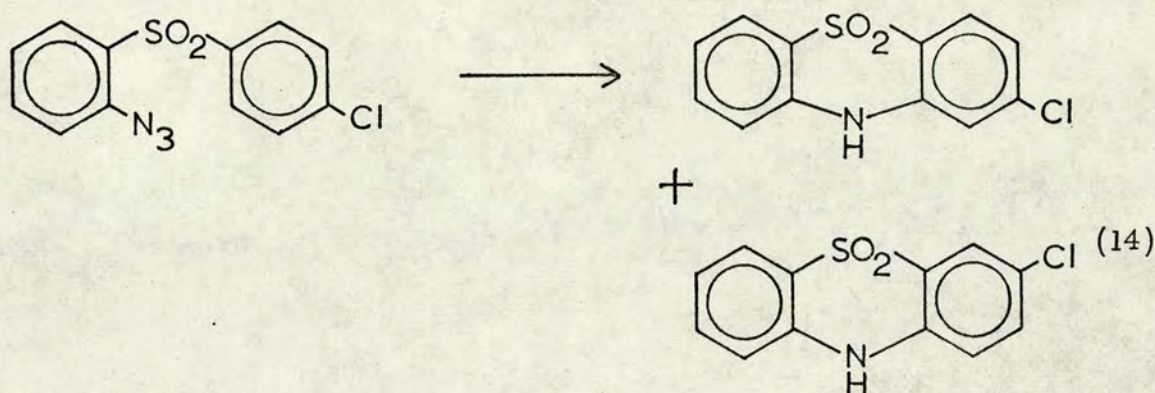
The products isolated from the reaction were 2-N-ethylaminophenyl 2, 6-dimethoxyphenyl ether (6%), 4-methoxyphenoxazine (5%) and 1, 2-dimethoxyphenoxazine (2%).

In the similar reaction of 4-methoxyphenyl 2-nitrophenyl ether only 2-N-ethylaminophenyl 4-methoxyphenyl ether was isolated (7.5%).

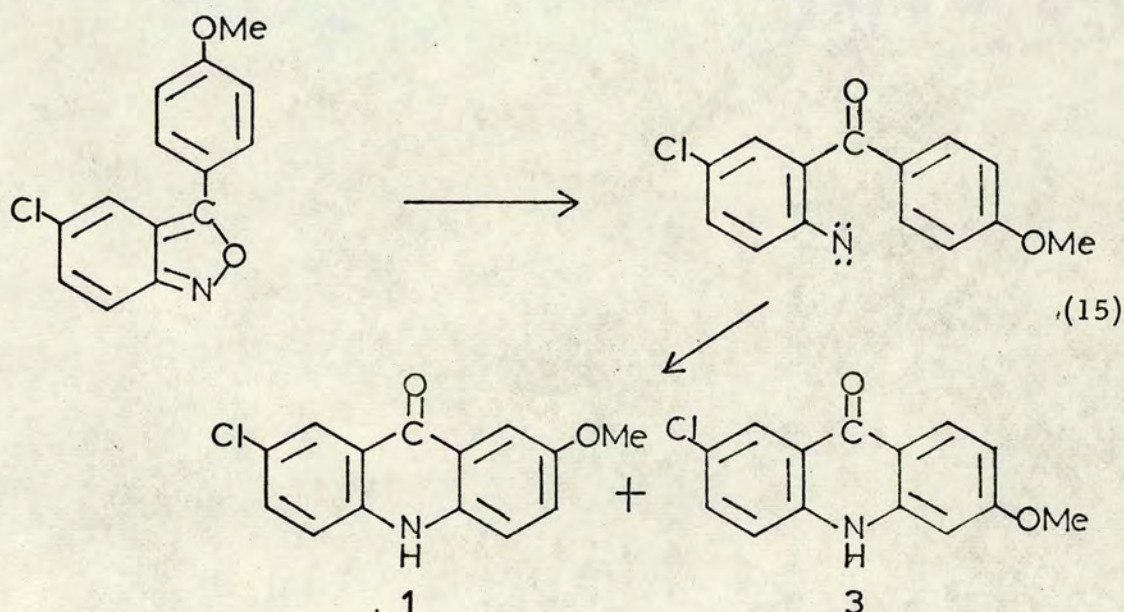
From these results it would seem rather fortuitous that the easily hydrolysed phosphoranylidene azepine was isolated at all in this series of reactions, but the isolation has opened up new avenues of investigation.

III. 3. REACTIONS OF ARYL 2-AZIDOPHENYL SULPHONES

Preliminary investigations by Cadogan and Ramage¹³⁵ on the thermolysis of 2-azidophenyl 4-chlorophenyl sulphones indicated the product to consist of a mixture of mono-chlorophenothiazine 5, 5-dioxides (probably the 2-chloro- and 3-chloro-isomers) thus,

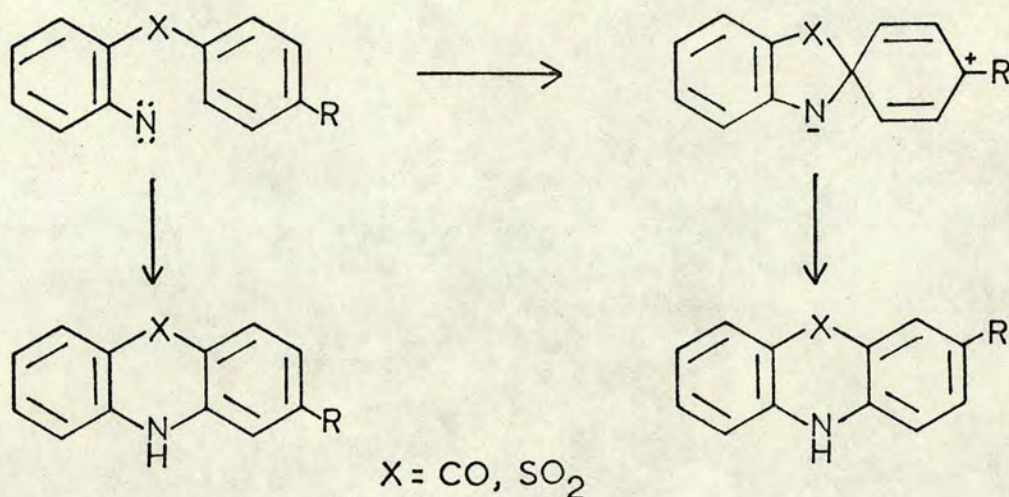


Kwok and Pranc¹²⁵ in their study of the pyrolysis of methoxylated phenylanthranils found that by heating 3-(p-methoxyphenyl) 5-chloroanthranil to 260°, a mixture of 2- and 3-methoxy 7-chloro acridones (identified as the corresponding 9-chloro acridines) in the ratio 1:3 was obtained.



An examination of these two sets of results in the light of Cadogan's phenothiazine rearrangement (Scheme 1) would seem to

indicate that the electron-withdrawing properties of both the carbonyl and sulphonyl functions have reduced the electron density at the 1' position to such an extent that the direct insertion by the intermediate nitrene into the 2' position becomes a competitive process.



Scheme 9

The present study of the thermolysis of 2-azidophenyl 4-chlorophenyl- and 4-t-butylphenyl sulphones is to show the validity of these suggestions. The former sulphone yielded on thermolysis a mixture of 2-chloro- and 3-chlorophenothiazine 5,5-dioxides in the ratio 3:1 (approx.) - the product ratio being estimated from p. m. r. spectra studies in conjunction with authentic samples.

A similar decomposition of 2-azidophenyl 4-t-butylphenyl sulphone led to a mixture of 2- and 3-t-butyl phenothiazine 5,5-dioxides in the ratio 4:3.

These results would appear to agree with the earlier suggestion that the electron-withdrawing sulphonyl group has reduced the electron density at the 1' position thus enabling the formation of the 2-substituted phenothiazine 5,5-dioxide by a direct insertion process. As the t-butyl group is fairly electron-releasing it would be expected to reduce the product ratio of the 2-isomer to the 3-isomer which is indeed the case (4:3 for the t-butyl compound compared with 3:1 for the chloro example).

Perhaps electron-releasing groups in the right positions viz. 2, 6 or 2, 4, 6 positions will allow the formation of only the rearranged product while electron-withdrawing groups in the same positions will lead to direct insertion products.

In this context it is difficult to explain why the thermolysis of 2-azidophenyl 2, 4, 6-trimethylphenyl sulphone should give only an intractable tar. It will be worthwhile to re-investigate this reaction and others involving sulphones with blocked ortho groups.

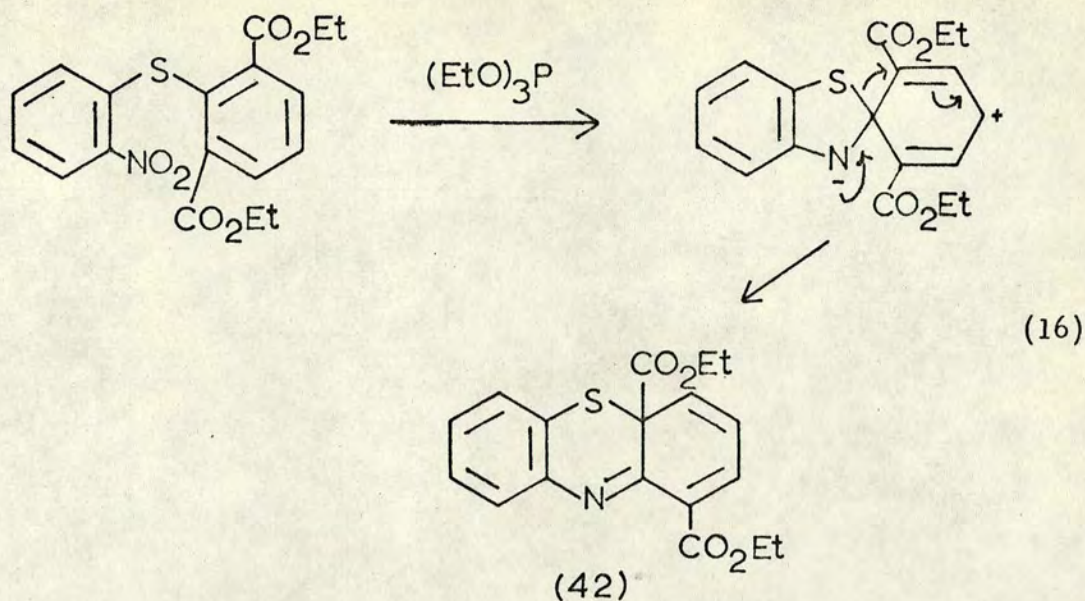
A practical difficulty in dealing with these sulphones is the question of polarity, involatility and insolubility of the expected products, the phenothiazine 5, 5-dioxides. This makes the standard techniques of separation of the isomers viz. column chromatography or fractional recrystallisation a difficult task. Their high involatility rules out the possibility of using gas-liquid chromatography as an experimental technique.

The other products in these reactions are the 2-aminophenyl aryl sulphones, formed presumably by hydrogen abstraction by the intermediate nitrene.

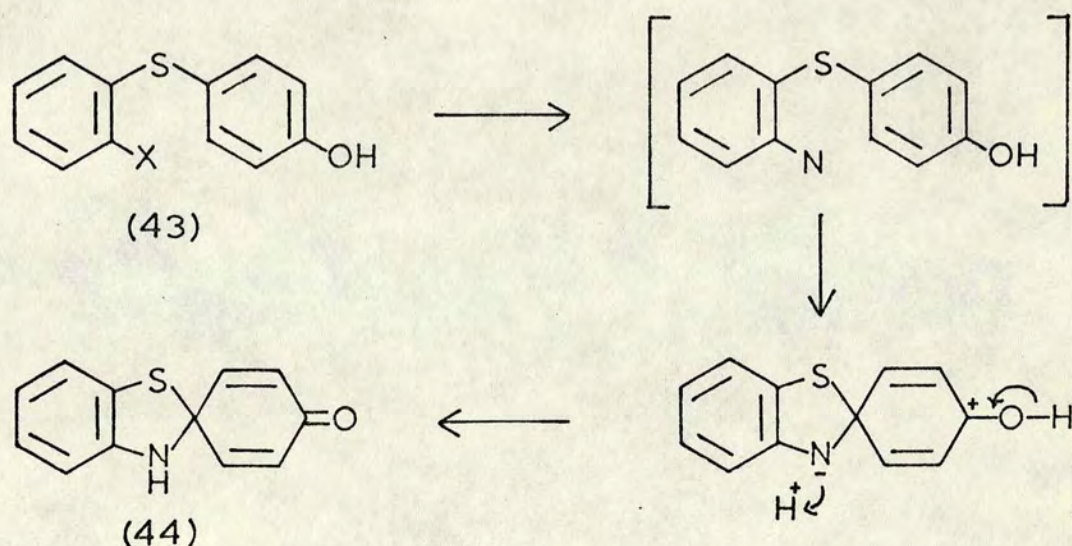
III. 4. MISCELLANEOUS REACTIONS.

(A) 4-Hydroxyphenyl 2-Azidophenyl- and 2-Nitrophenyl Sulphide.

In Cadogan's phenothiazine rearrangement (scheme 1) two key intermediates are postulated. These are the spirodiene (3) and the hydroaromatic species (4). The latter intermediate has been isolated¹⁰³ as diethyl 4aH-phenothiazine-1, 4a-dicarboxylate (42) thus,



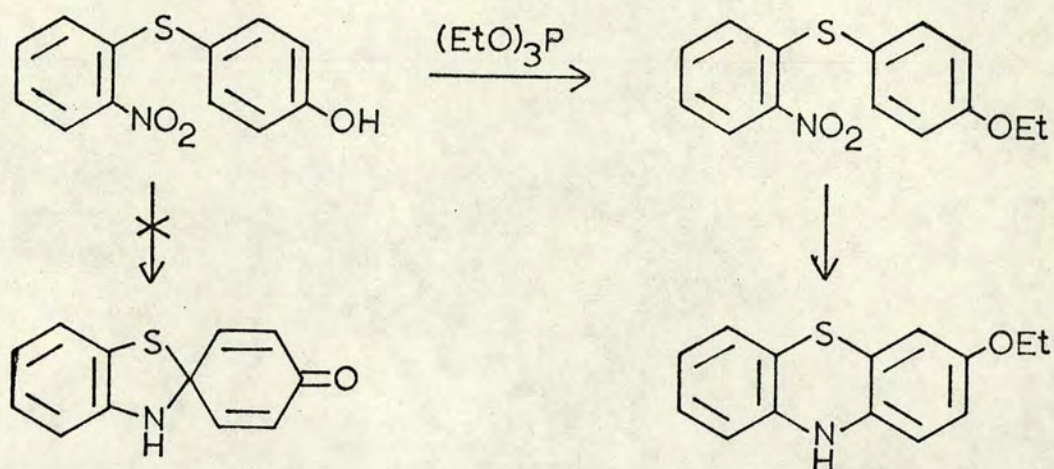
The rationale of the present study is the isolation of the other key intermediate as the spirodienone (44).



Scheme 10

As it turned out the attempt at reductive cyclisation of 4-hydroxy phenyl 2-nitrophenyl sulphide (43; X = NO₂) by triethyl phosphite gave only small amounts of a monoethoxy phenothiazine (probably 3-ethoxy). This was formed presumably by initial ethylation of the hydroxyl group by triethyl phosphate (or phosphite) followed by reductive cyclisation via the phenothiazine rearrangement. Isolation of trace amounts of ethoxyphenyl 2-nitrophenyl sulphide gives good support for this

conclusion (Scheme 11).



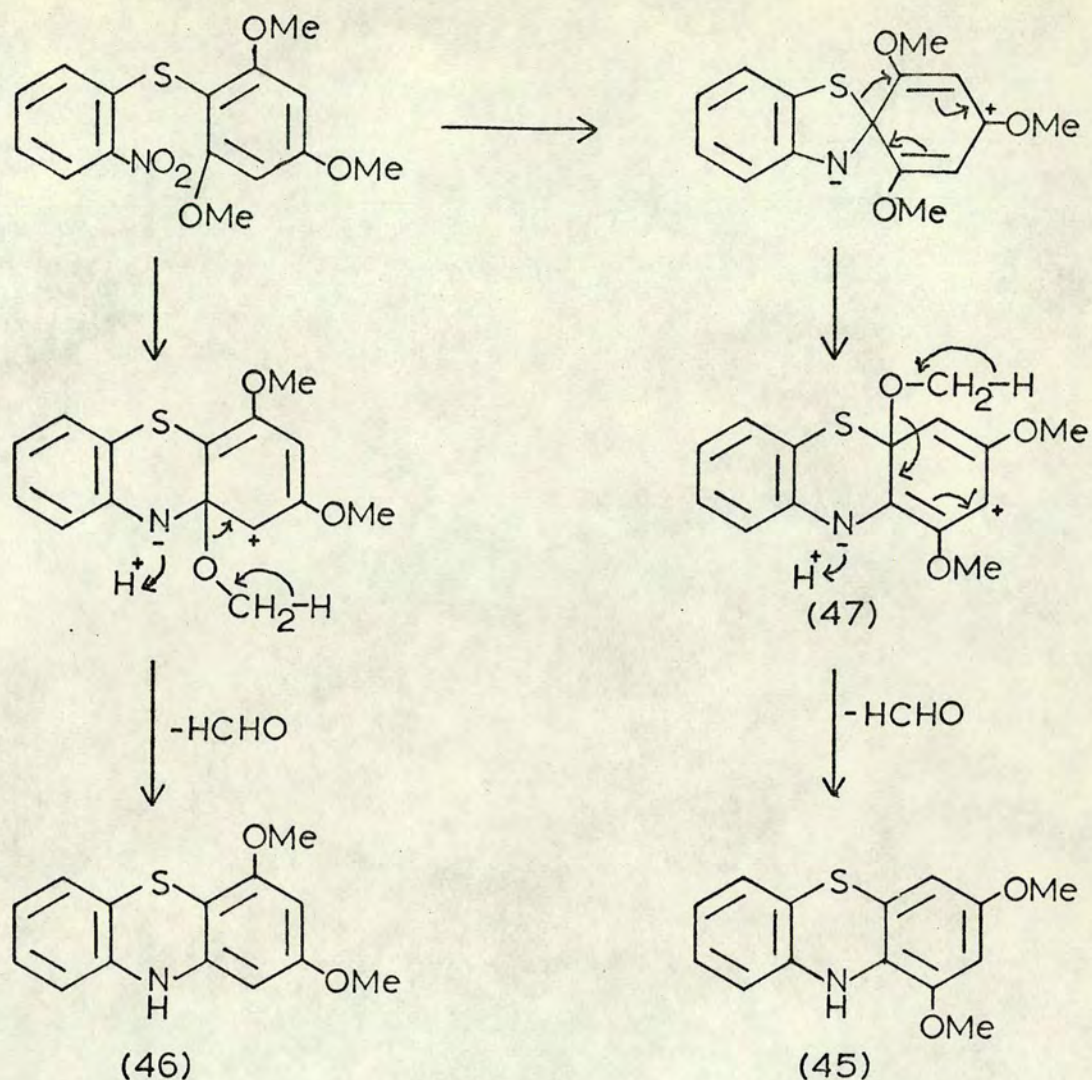
Scheme 11

It was hoped that by decomposing the azido compound (43; $\text{X} = \text{N}_3$) the spirodienone could be isolated. However only intractable tars were obtained. Perhaps by blocking the relevant ortho positions by suitable groups (like methoxy) it may be possible to isolate this elusive intermediate.

(B) 2, 4, 6-Trimethoxyphenyl 2-Nitrophenyl Sulphide.

Reductive cyclisation of this compound by triethyl phosphite led to a 1:1 mixture of 1, 3 and 2, 4-dimethoxyphenothiazine [(45), (46); 33%] and diethyl-N-ethyl-N-(2, 4, 6-trimethoxyphenylthio)phenyl phosphoramidate (26%).

The formation of 1, 3-dimethoxyphenothiazine can be rationalised (Scheme 12) by assuming that the first formed spirodiene undergoes a sigmatropic shift to give the hydroaromatic intermediate (47) which then aromatises by loss of formaldehyde. The other mode of aromatisation (as observed in the rearrangement of 2, 6-dimethoxyphenyl 2-nitrophenyl sulphide¹⁰³) by a transmethoxylation via the oxonium species is not likely here in view of unfavourable steric factors.



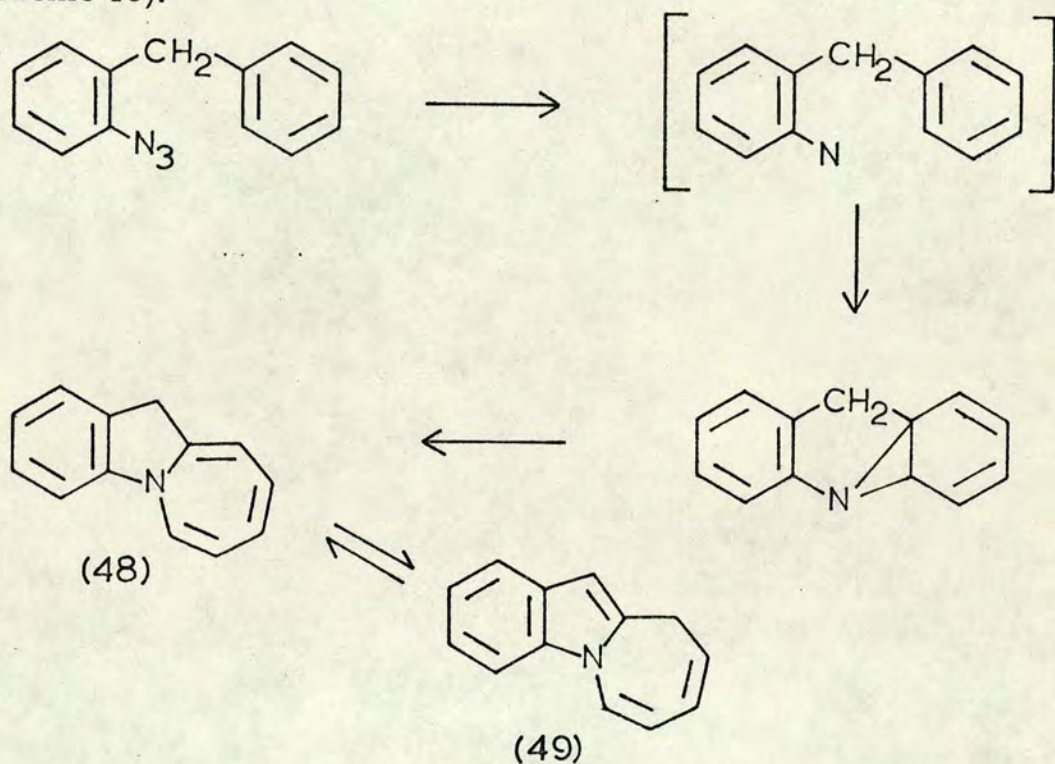
Scheme 12

The rather unexpected formation of 2,4-dimethoxyphenothiazine is rationalised by initial attack at the 2' position, followed by aromatisation by loss of formaldehyde. This sequence is similar to the formation of 4-methoxyphenoxazine (Scheme 6).

As noted earlier in section III. 2 the formation of phosphorimidates is a regular feature of reactions involving reduction of aromatic nitro compounds by triethyl phosphite. Where elution chromatography is used as the method of separation of the reaction products, the phosphorimidates are isolated as the phosphoramidates. In the present study, the N-ethyl phosphoramidate is isolated.

(C) 2, 4, 6-Trimethylphenyl 2-Nitrophenyl Methane

The preference for formation of five-membered rings is illustrated in a different way in the study of the thermolysis of *o*-azidodiphenyl methane. Krbecek and Takimoto¹⁰⁶ isolated a product to which they assigned the structure 11H-azepino[1, 2-a]indole (48) (Scheme 13).

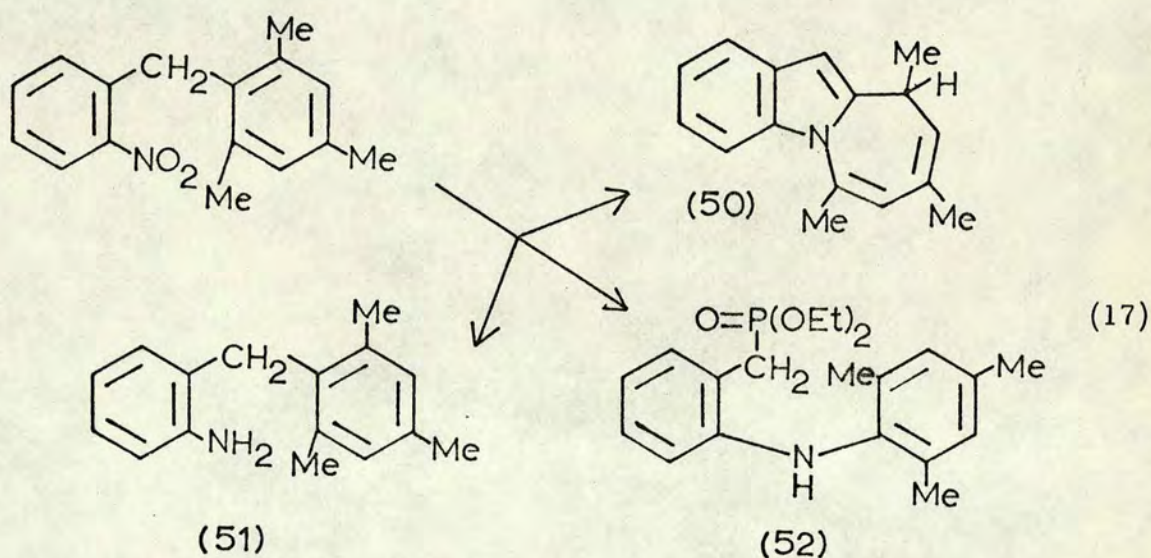


Scheme 13

As azepines show a marked preference to exist as the 3H tautomer Jones et al.¹⁰⁷ has re-assigned the structure of (48) as the tautomer 10H-azepino[1, 2-a]indole (49) on the basis of its ¹H n. m. r. spectrum. This re-assignment was confirmed by the isolation of 11-methyl 10H-azepino[1, 2-a]indole (rather than the 11H isomer) when *o*-(*o*-azidophenyl) *o*-methyltoluene was decomposed. A subsequent study by Cliff and Jones¹³⁵ on the thermolysis of 2-azidophenyl 2-methylphenyl and 2-methoxyphenyl methane revealed that the former reaction led to formation of only 10-methyl 10H-azepino[1, 2-a]indole while the latter reaction resulted in a host of products. By the use of gas-liquid chromatography, they have been able to trace the presence of methoxyazepinoindole, acridine, acridan and their methoxylated

derivatives. These products were attributed to new nitrene insertion reactions.

The present study is to investigate the effect (if any) of blocking both relevant ortho positions by methyl groups. The reduction of 2,4,6-trimethylphenyl 2-nitrophenyl methane by triethyl phosphite led to a complex mixture of numerous products (as indicated by t.l.c.). Among those isolated and identified were 6,8,10-trimethyl 10H-azepino[1,2-a]indole (50) (10%), 2-aminophenyl 2,4,6-trimethylphenyl methane (51) (9%) and diethyl 2-N-(2,4,6-trimethylphenyl)-amino-benzyl phosphonate (52).

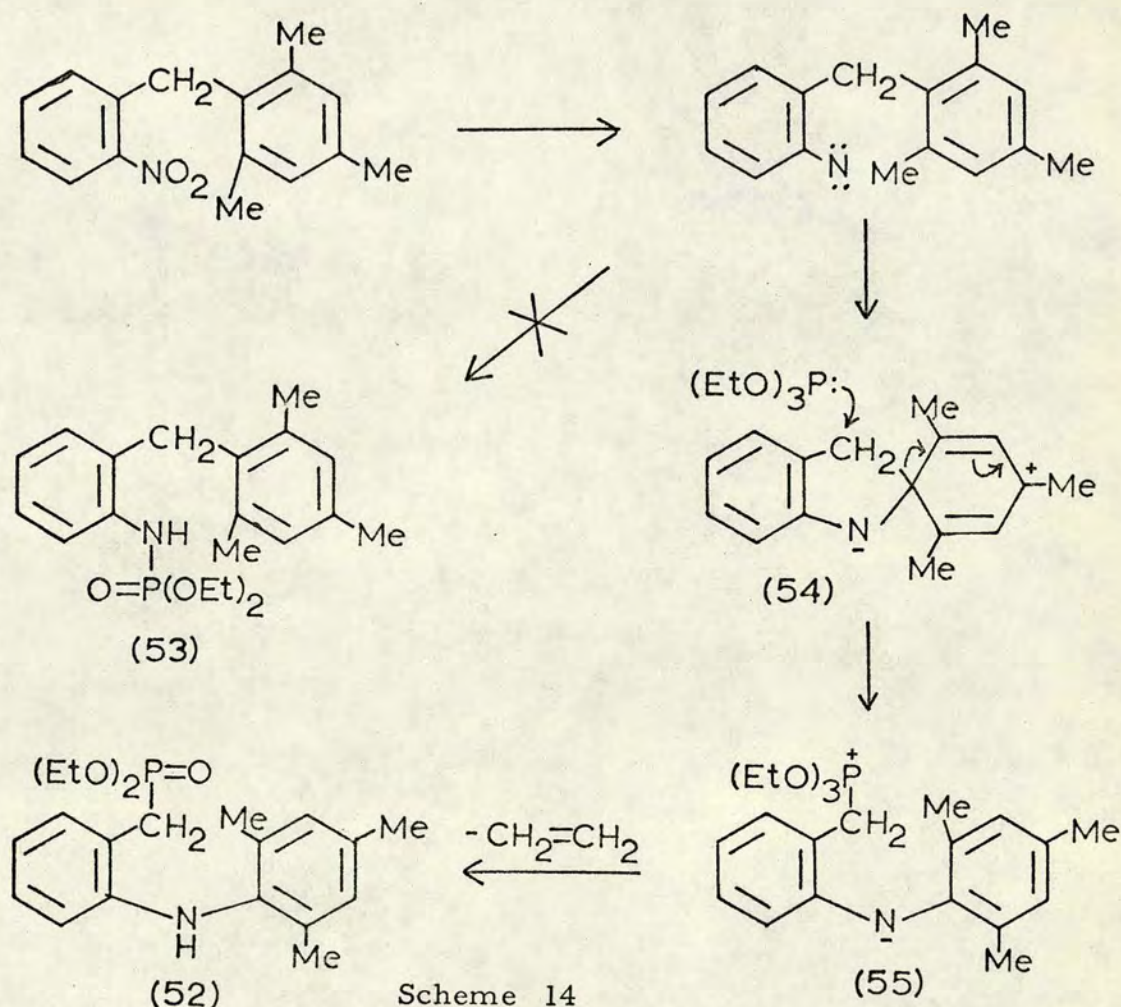


The azepino-indole (50) was presumably formed by a reaction sequence similar to that outlined in Scheme 13 while the amine (51) was produced by a hydrogen abstraction reaction of the intermediate nitrene.

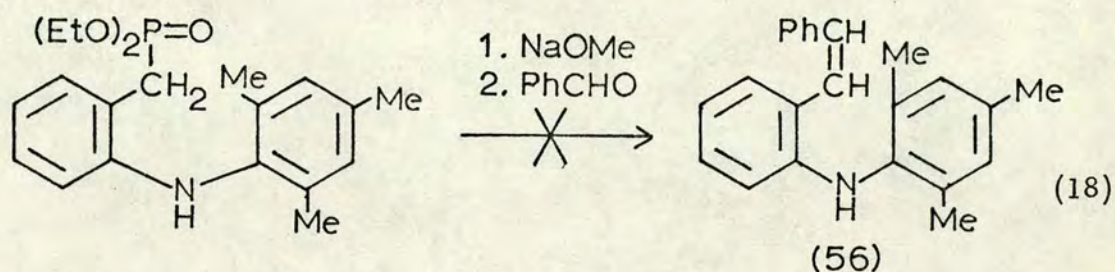
The structure of the phosphonate (52) was assigned from spectral data. I.r. spectrum showed the presence of an N-H group (3300 cm^{-1}) and the diethyl phosphonyl function ($1250, 1050\text{ and }960\text{ cm}^{-1}$). The p.m.r. spectrum ruled out the expected phosphoramidate (53) as a possible structure because the methylene protons appeared as a doublet ($J, 20\text{Hz}$). Heteronuclear spin decoupling indicated that the phosphonyl function was linked to the methylene group. The observed

phosphorus coupling compares favourably with that in diethyl benzyl phosphonate ($J_{P,H}$ 22Hz). The upfield doublet at 3.72 τ (J 8Hz) was assigned to the proton ortho to the amino group. Scale expansion showed this doublet to be unusually broad and could conceivably incorporate a small meta coupling of 1 Hz. The integral tracing showed a decrease of 1 proton in the aromatic region after shaking the $CDCl_3$ solution with D_2O , thus giving further evidence for the presence of the amino function.

The formation of the phosphonate was rationalised (Scheme 14) by a nucleophilic attack by triethyl phosphite on the strongly electrophilic methylene function of the first-formed spirodiene intermediate (54). Loss of ethylene (a process previously observed in formation of azepinyl phosphonates⁶⁸) by the phosphonium species (55) leads to the phosphonate.



As diethyl benzyl phosphonate underwent Horner's reaction with benzaldehyde under the influence of a strong base (e. g. NaOMe) to stilbene,¹³⁷ it was considered that the benzyl phosphonate (52) might likewise be converted to the corresponding alkene (56; eq. 18). However an attempt to achieve this conversion resulted in isolation of only unreacted starting materials.

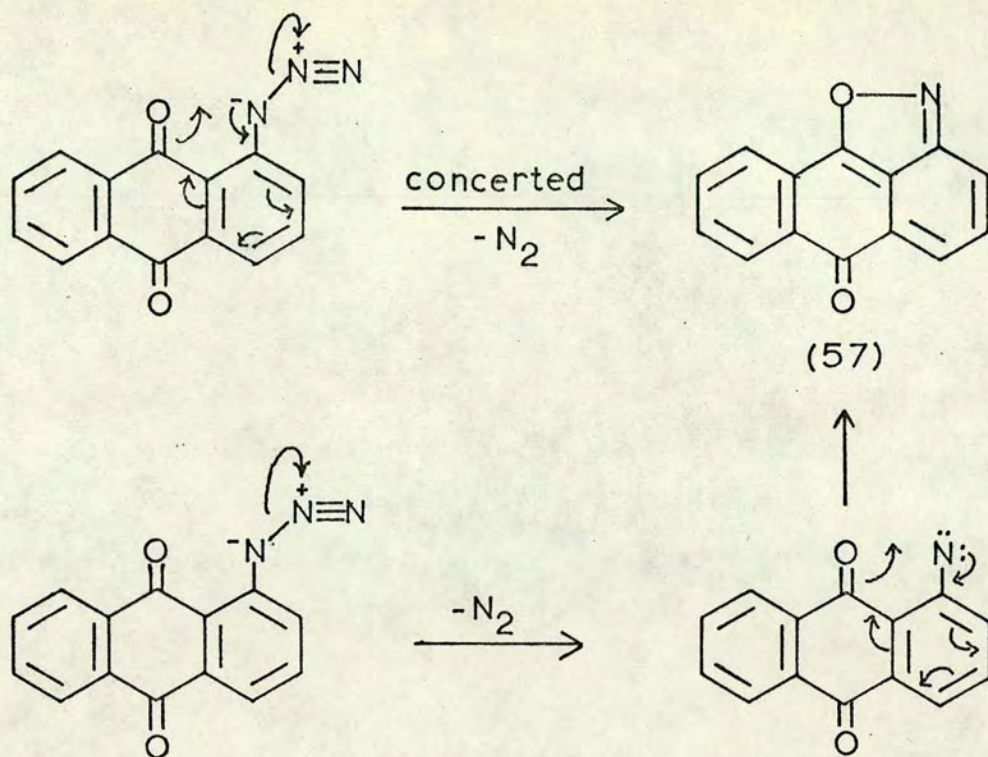


Steric hindrance by the mesityl function could well be responsible for this failure.

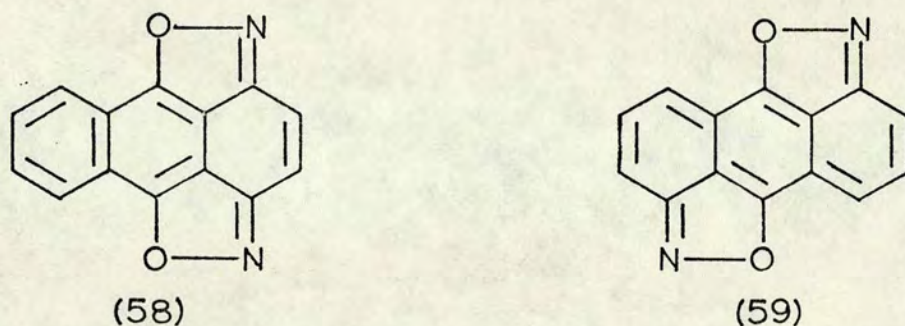
(D) 2-Methyl-1-Nitroanthraquinone.

Anthraquinone and its derivatives are of enormous importance to the dyestuff industry. Consequently there has been extensive investigations into the synthesis of various types of anthraquinoid structures, especially those with useful chromophores. Many of these attempts have resulted in interesting and useful products. For example as early as 1916 Schaarschmidt¹³⁸ prepared 6-oxo-anthra-[1,9-cd]isoxazole (57) by thermolysis of 1-azidoanthraquinone in water. As with all other azide decompositions one could write either a nitrene mechanism or a concerted non-nitrene pathway for the reaction (Scheme 15). In view of the low temperatures used (boiling water) it is likely that the concerted non-nitrene mechanism is in operation.

Among the many other similar products synthesized in this manner are the interesting anthra[1,9-cd: 4,10-c'd']diisoxazole (58) and anthra[1,9-cd: 5,10-c'd']diisoxazole (59).

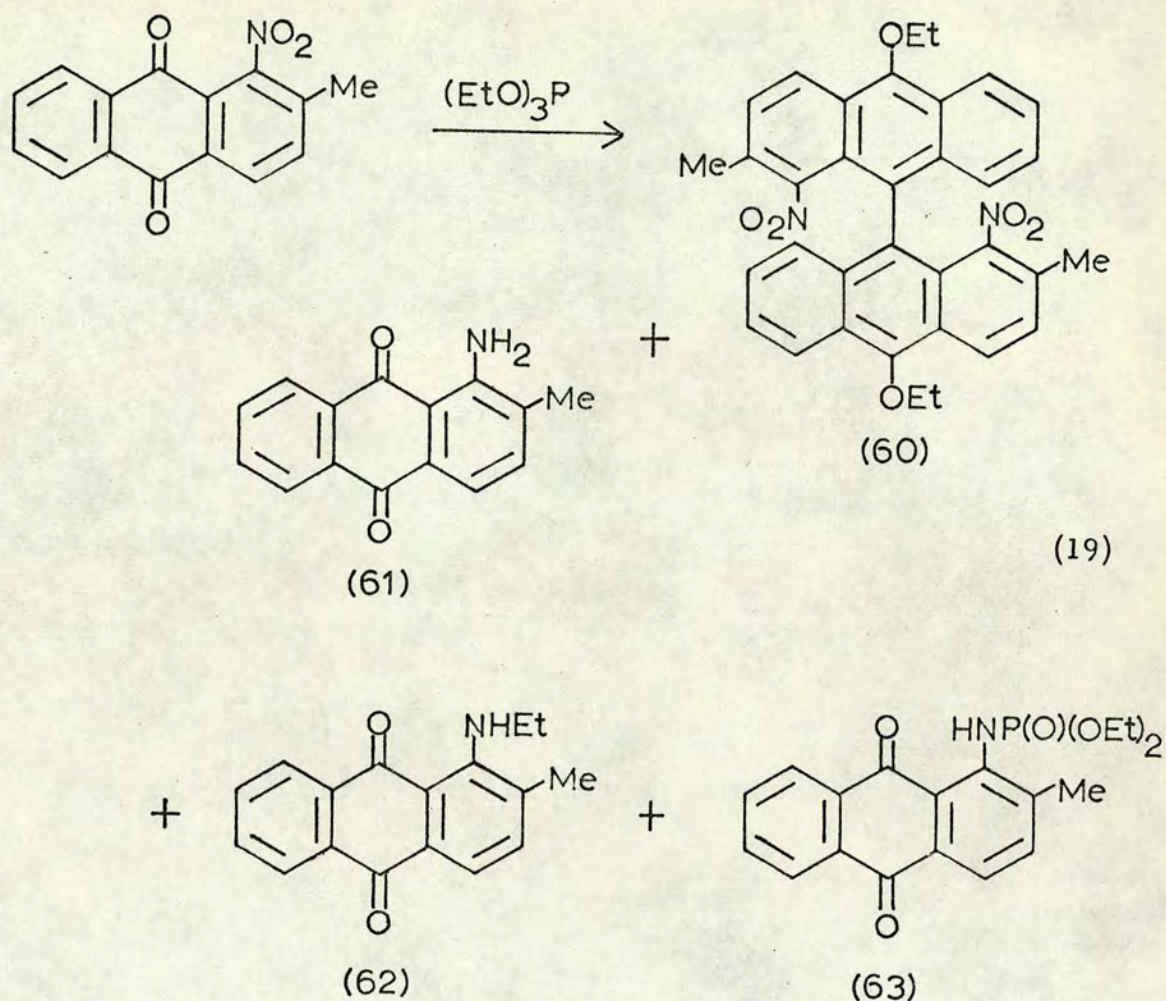


Scheme 15



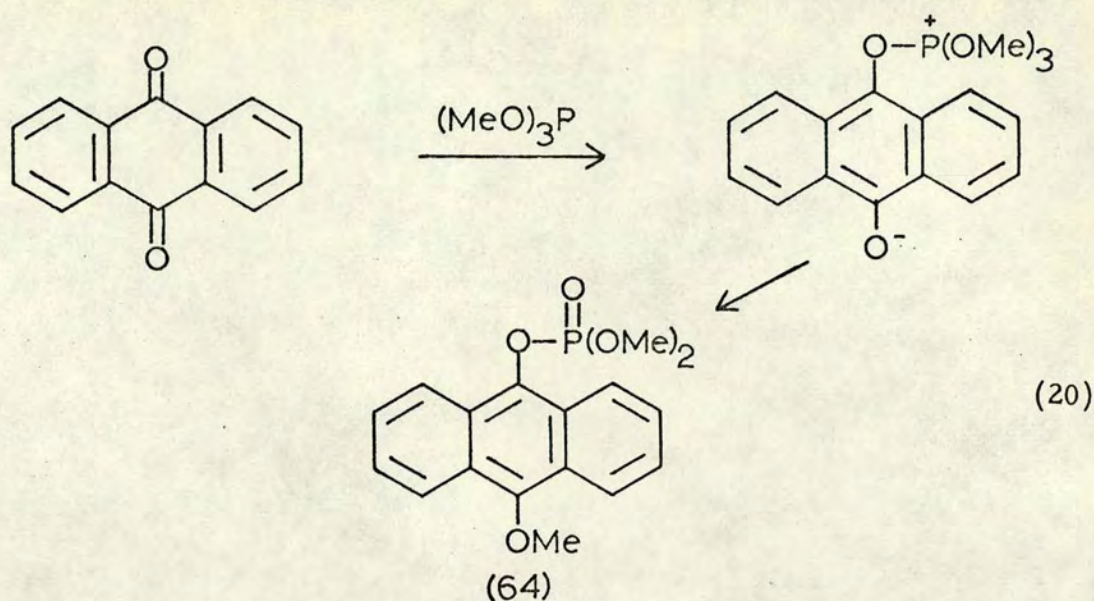
In the light of these results it was considered to be of interest to investigate whether reaction of the corresponding nitro compounds with triethyl phosphite would lead to the same products by reductive cyclisation. In the event, reaction of 2-methyl 1-nitroanthraquinone with triethyl phosphite yielded bis 9, 9' (10-ethoxy 2-methyl 1-nitro) anthryl (60) (7.5%), 1-amino 2-methylanthraquinone (61) (24.5%), 1-ethylamino 2-methyl anthraquinone (62) (3.5%) and diethyl N-1-(2-methylanthraquino)phosphoramidate (63) (3%).

It seems likely that the amine (61) was formed by hydrogen abstraction by the intermediate nitrene. Alkylation by triethyl phosphate



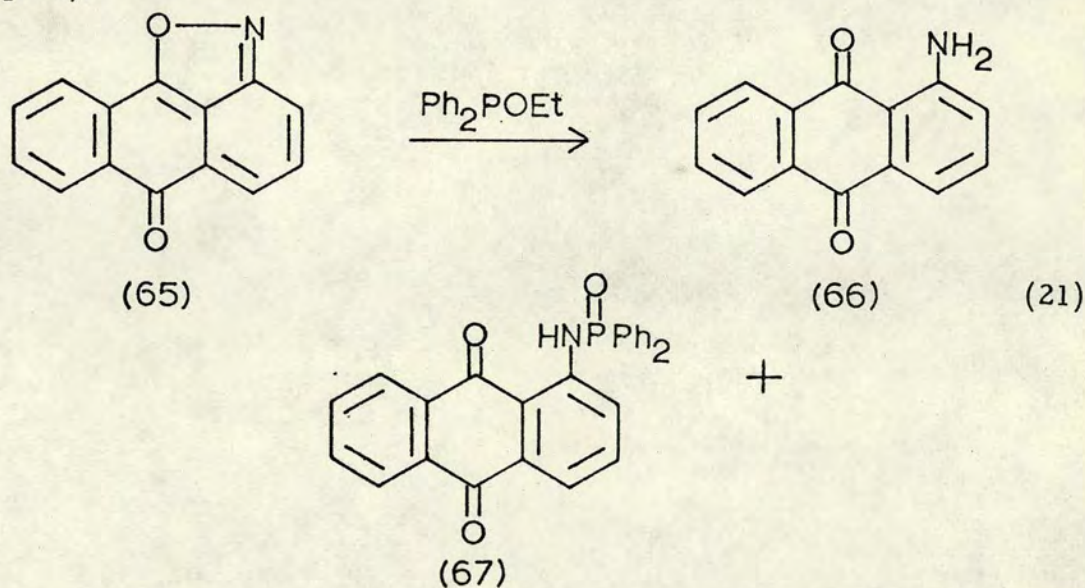
or phosphite of the amine accounts for the ethylamino compound. Formation of phosphoramidate has been attributed to hydrolysis of phosphorimidate (61) whose formation has in turn been rationalised (eq. 8) as a reaction of phosphite and nitrene. The formation of the bis-anthryl (60) is more difficult to rationalise. Ramirez et al.¹³⁹ have reported that reaction of trimethyl phosphite with anthraquinone led to formation of 10-methoxy 9-hydroxyanthracene 9-dimethyl phosphate (64).

It is obvious that the bis-anthryl was produced as a result of attack by the tervalent phosphorus reagent on the quinone function rather than on the nitro group, but the mechanism is unknown. A radical intermediate is likely to be involved in view of the dimeric structure.



When the reaction was repeated in the presence of a solvent, cumene, similar products (except the ethylamino compound, which was not isolated) but in different ratios were obtained. The yield of the bis-anthryl was reduced to 4% while that of the amine and phosphoramidate increased to 38 and 8% respectively.

The failure to isolate the anthra[1,9-cd]isoxazole from the reaction could be due to its subsequent reaction with the phosphorus reagent. To test the validity of this suggestion, 6-oxo-anthra[1,9-cd]isoxazole (65) was reacted with ethyl diphenyl phosphinite. The only products isolated were the amine (66) and the phosphinamidate (67) (eq. 21).



This is not totally unexpected as it is known⁹⁹ that the isoxazole ring is not stable towards attack by base. The nucleophilicity of the tervalent phosphorus reagent used could have been sufficient to cause rupture of the isoxazole ring. However little is known of the basicity of tervalent phosphorus reagents other than that of the primary phosphines.¹⁴⁰ The results of this reaction would seem to suggest that it is quite likely that the anthra[1,9-cd]isoxazole was formed. Subsequent ring rupture initiated by the reagent led to the amine.

III. 5. SYNTHETIC ASPECTS AND CONCLUSIONS

The unavailability of starting materials for this series of investigations was a great hindrance towards a more extensive study. Only a few of the aryl 2-nitrophenyl ethers with suitable substituents in the relevant ortho positions were successfully prepared. Likewise only one example of the aryl 2-nitro phenyl methane with ortho blocking groups was synthesized.

Another serious difficulty is the sensitivity of many of the products of the reactions (especially the phenoxazine and phenothiazine derivatives) towards light. This makes elution chromatography an onerous technique. However it still remains the most suitable, though time-consuming.

The successful synthesis of the phenoxazine derivatives and the isolation of the phosphoranylidene azepines has widened the scope of the two main reactions used in this study viz. thermolysis of azides and reduction of aromatic nitro compounds by triethyl phosphite. There remains much to be done. The isolation of the other key intermediate in Cadogan's phenothiazine rearrangement is of vital importance. In addition to the many other extensions already suggested, it should be extremely interesting to study the reaction of the aryl-2-nitrophenyl sulphide with t-butyl groups in the relevant ortho positions, and the reactions of benzophenones with ortho blocking groups.

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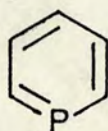
IV. 3. DISCUSSION

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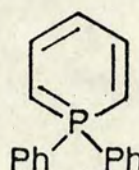
IV. 1. INTRODUCTION

(A) Methods of Synthesis of Phosphorins and Phosphabenzenes

The phosphorus analogue of benzene (1) named either phosphorin or phosphabenzene is not known.* But the corresponding compound with a pentavalent phosphorus atom has been synthesized with two phenyl groups saturating the lone pair of the phosphorus atom (2).¹



(1)



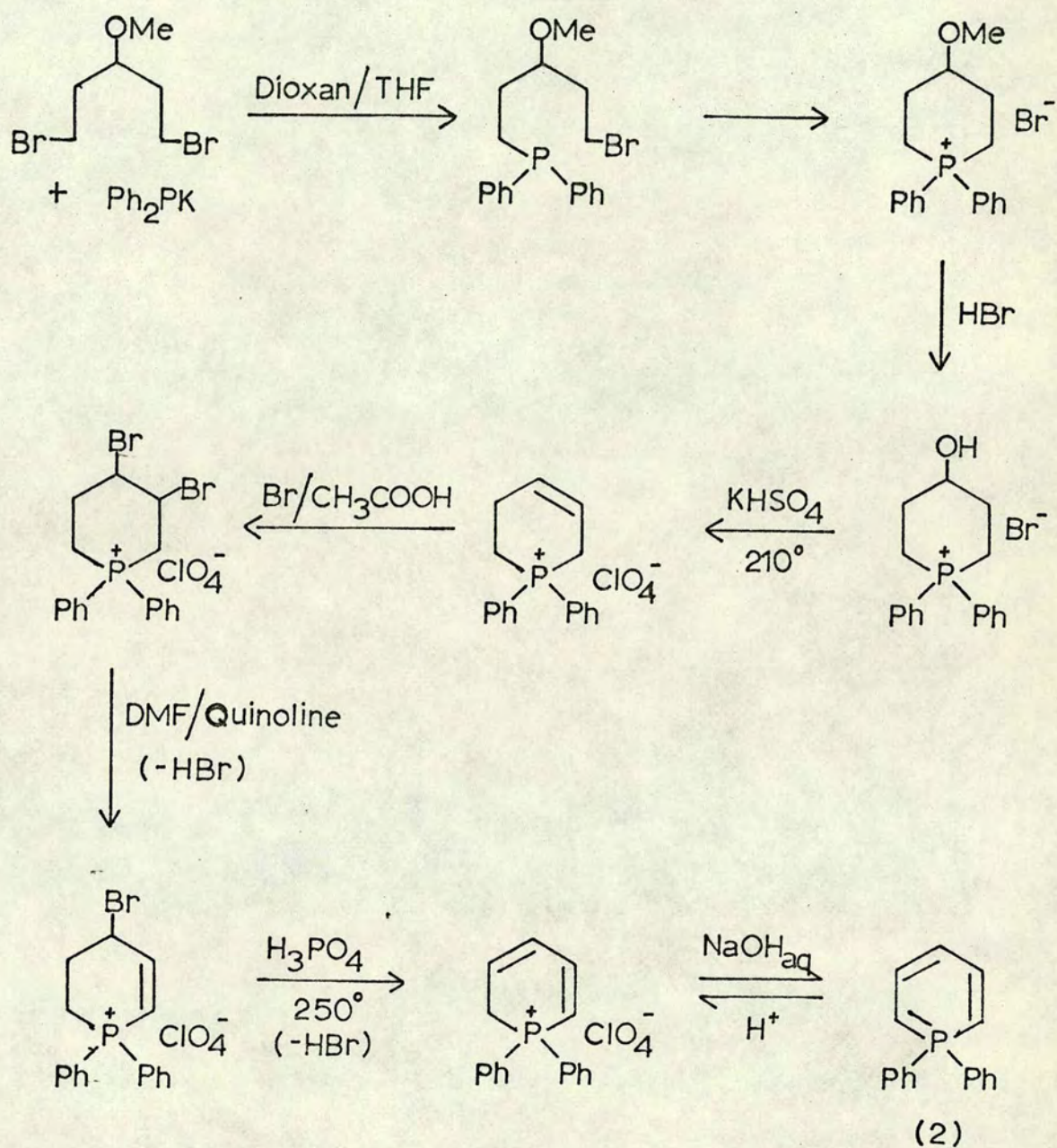
(2)

To date there has been a lack of agreement in the nomenclature of such compounds. They are referred to either as phosphorins or phosphabenzenes. For the sake of clarity and simplicity the ring system having a trivalent phosphorus atom will be named phosphorin, while that having a pentavalent phosphorus atom, phosphabenzene in this thesis.

Most of the knowledge of the chemistry of phosphorins and phosphabenzenes has been accrued from the investigations of G. Märkl and K. Dimroth and their respective co-workers.

The first compound of these six-membered phosphorus heterocycles to be synthesized is 1, 1-diphenylphosphabenzene (2) by Märkl.¹ This intriguing synthesis is outlined in Scheme 1.

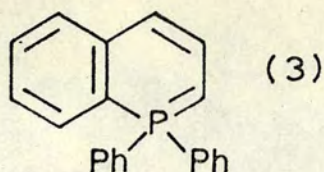
* But see appendix on a very recent report of the synthesis of phosphorin.



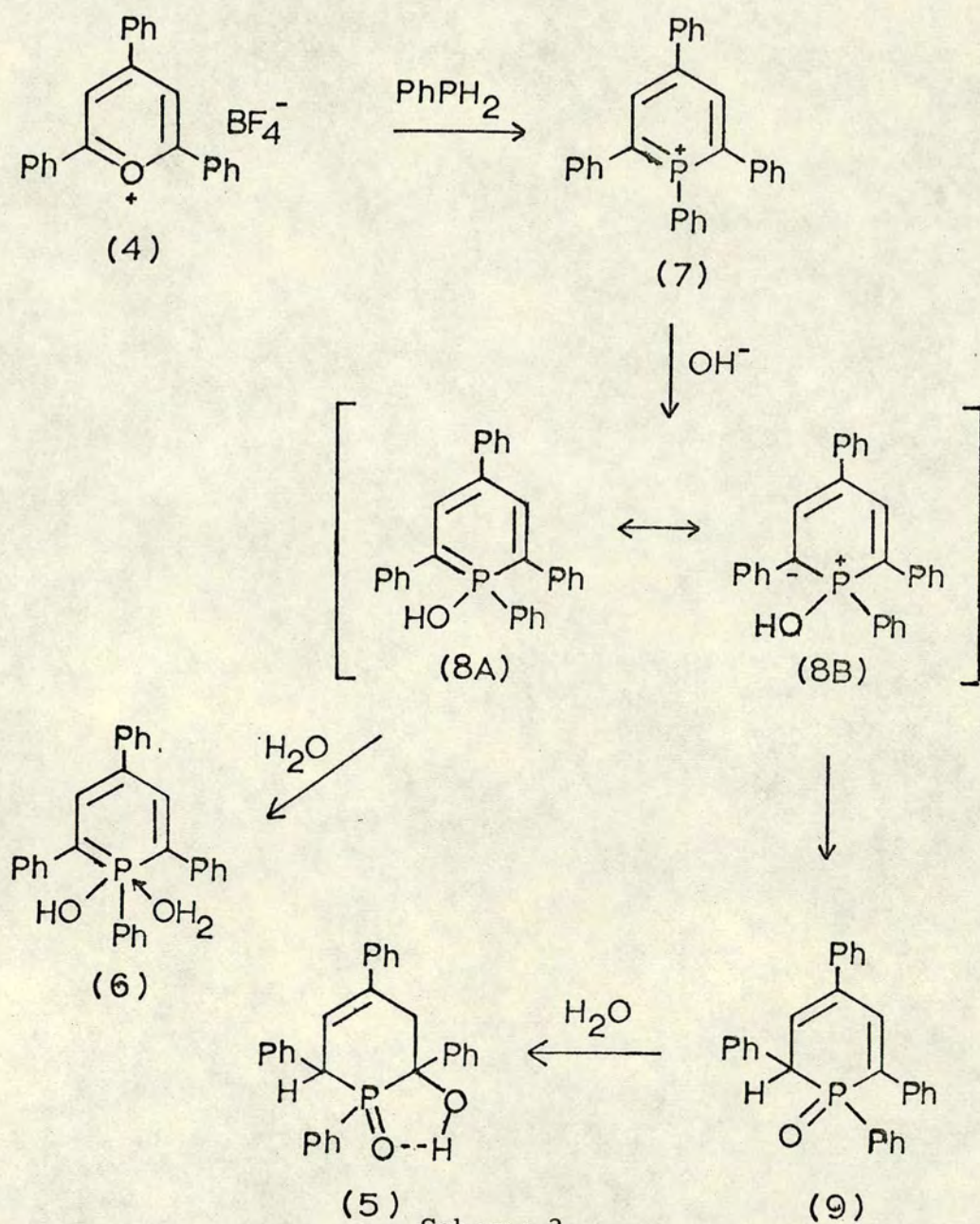
Scheme 1

The heterocycle (3) ("phosphanaphthalene") was prepared in a manner similar to that used in the synthesis of (2).²

Price et al.³ in an investigation designed towards a synthesis of the phosphorin system found that reaction of 2,4,6-triphenylpyrylium fluoroborate (4) with phenylphosphine in boiling pyridine produced a

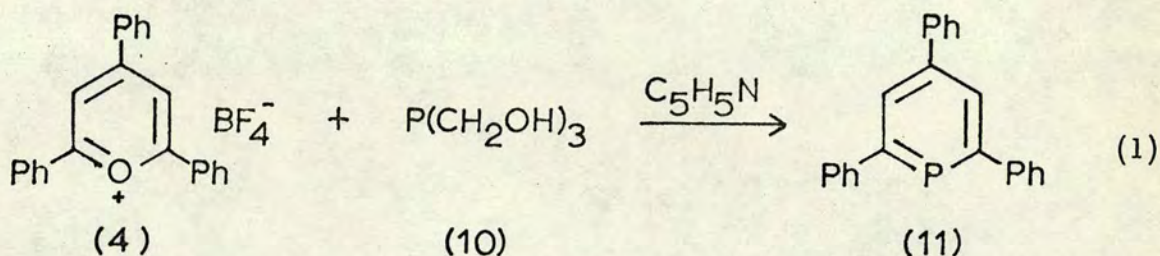


quantitative yield of two isomeric phosphorus heterocycles of composition $C_{29}H_{25}O_2P$. The evidence presented indicated the two isomers to be (5) and (6). It was postulated that the first transient intermediate (7) formed in the reaction coupled with hydroxyl ion to give a compound of which (8A) and (8B) are resonance forms. Prototropic rearrangement of (8B) followed by 1,4-addition of water would give (5) while direct addition of water to (8A) will yield (6). (Scheme 2).

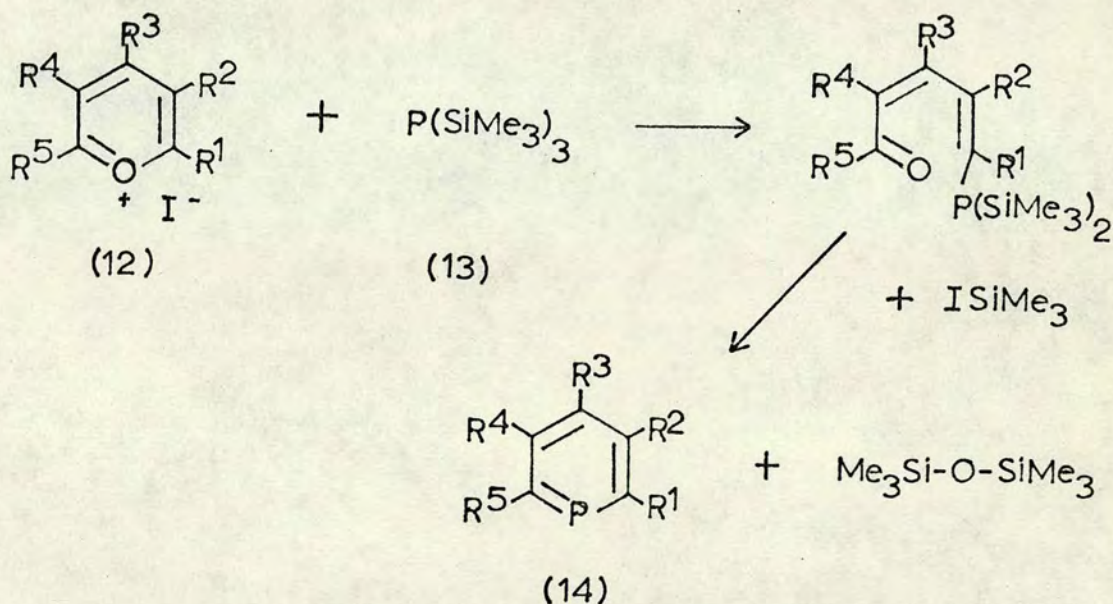


Scheme 2

The first phosphorin was prepared by Märkl in 1966,⁴ by reaction of the fluoroborate (4) and tris(hydroxymethyl)phosphine (10) in boiling pyridine. He obtained 2,4,6-triphenylphosphorin (11) as pale yellow needles in 24-30% yield.



In an improved synthesis Märkl and his co-workers⁵ have prepared a series of aryl-substituted phosphorins (14) by reaction of the corresponding pyrylium salts (12) and tris(trimethylsilyl) phosphine (13) in boiling acetonitrile (Scheme 3).



Scheme 3

The method is limited to examples where R¹, R³ and R⁵ are aryl groups and R² and R⁴ are phenyl groups or hydrogen but has the advantages that no basic solvent is required, no water is formed and gave higher yields.

Dimroth et al.⁶ have extended Märkl's original synthesis to include phosphorins with alkyl groups in the ring. By this method they have obtained 2,4,6-tri-t-butyl phosphorin the first known phosphorin containing only alkyl substituents.

A further improvement of his original method has enabled Märkl and his co-workers⁷ to prepare 2-alkyl 4,6-diaryl or 4-alkyl 2,6-diaryl phosphorins. This improvement required the reaction of phosphine (generated in situ from phosphonium iodide) with 2,4,6-trisubstituted pyrylium fluoroborate.

Another group of workers⁸ have modified Märkl's method by using 2,4,6-triaryl pyrylium perchlorate instead of the fluoroborate.

The 1,1-disubstituted phosphabenzenes have mostly been synthesized from the corresponding phosphorins and will be discussed in the next section.

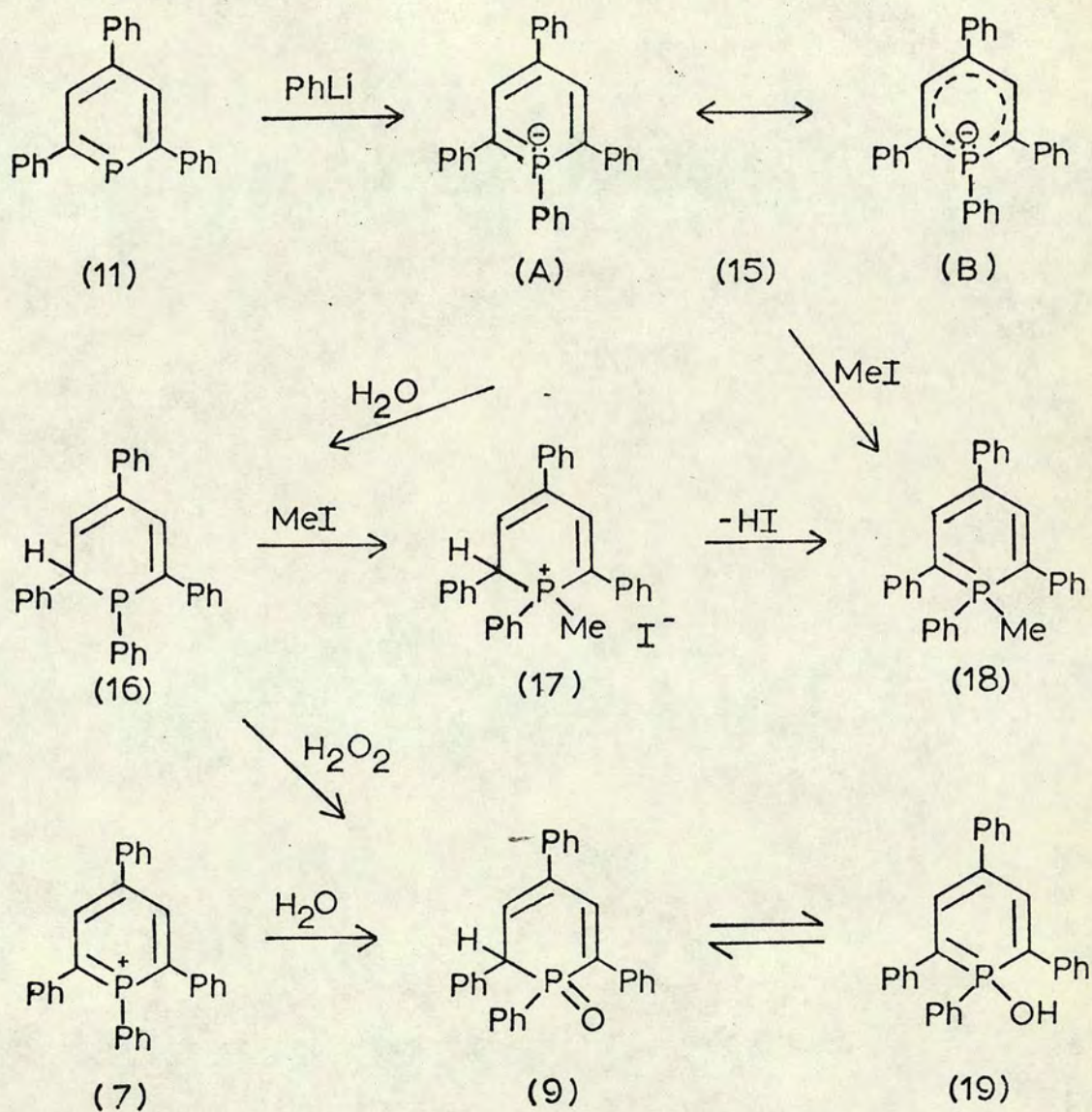
(B) Reactions, Spectra and Structure of Phosphorins and Phosphabenzenes.

(i) Electrophilic reactions.

2,4,6-Triphenylphosphorin (11) does not undergo alkylation with methyl iodide or even with triethyloxonium fluoroborate, $[(\text{CH}_3\text{CH}_2)_3\text{O}]\text{BF}_4$ but reacted readily with nucleophilic reagents such as alkyl or aryl lithiums.⁹ For example, phenyl lithium in benzene at room temperature added directly to phosphorus (whose valence shell apparently expands to a decet) giving a product, represented as the canonical forms (15A) and (15B), which formed a deep blue solution. Hydrolysis of (15) gave 1,2-dihydro 1,2,4,6-tetraphenyl phosphorin (16) which quarternised readily with methyl iodide to give the phosphonium iodide (17). Treatment of (17) with aqueous alkali gave the red, non-crystalline phosphabenzene (18) which was also obtained by the direct reaction of methyl iodide with (15).

Oxidation of the 1,2-dihydro phosphorin (16) with hydrogen

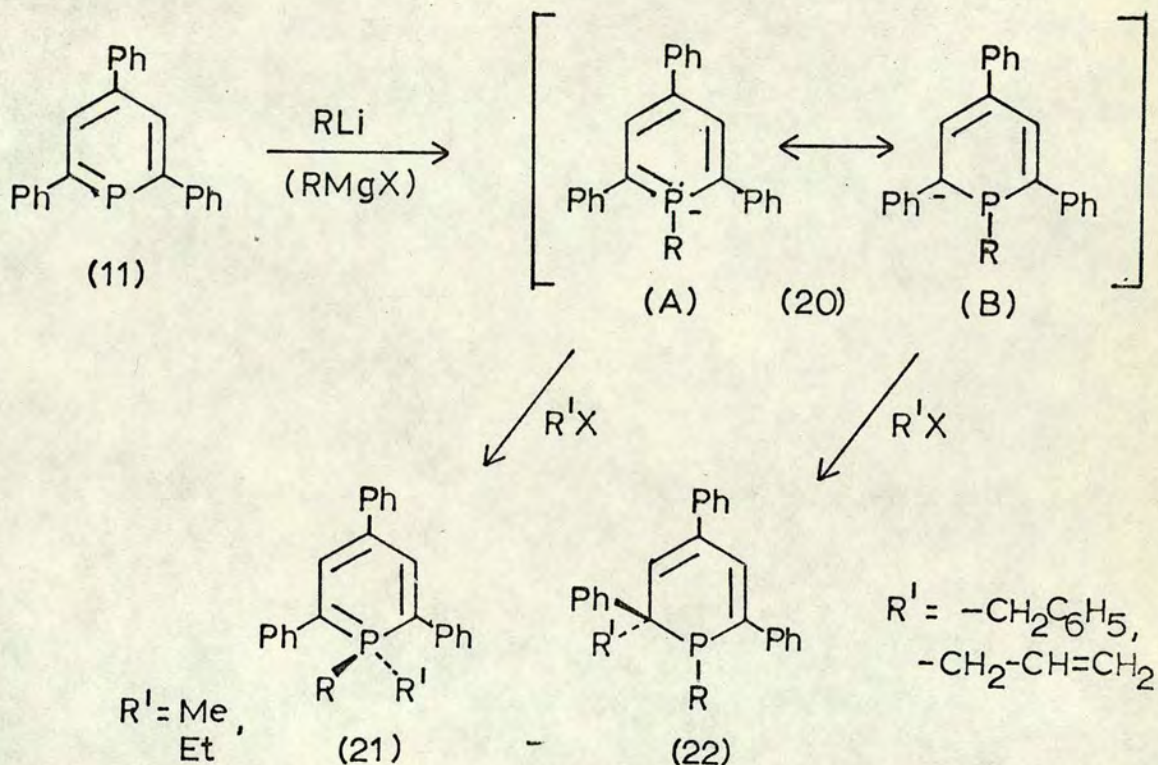
peroxide gave the phosphorin-1-oxide (9), the compound suggested as an intermediate in Price's work.³ (see Scheme 2) (9) was also obtained from phenylphosphine and the fluoroborate (4), being formed by the action of water on the cation (7).



Scheme 4

The ultraviolet spectra in methanol indicated that the phosphorin-1-oxide (9) is in tautomeric equilibrium with (19). Addition of weak bases to this tautomeric mixture produced a brilliant red resonance-stabilised anion.

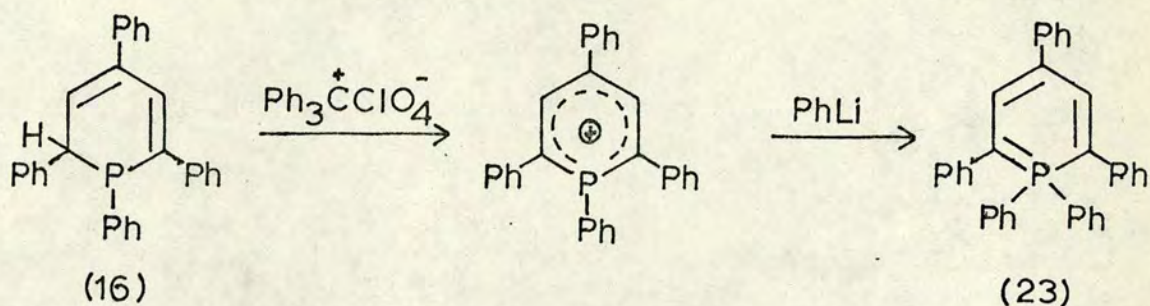
The marked electrophilic reactivity of 2,4,6-triphenylphosphorin (11) was further investigated in subsequent studies by Märkl et al.^{10, 11} Reaction with organolithium or Grignard compounds gave the 1-aryl and 1-alkyl phosphabenzene anions (20) whose contrasting dual electrophilic behaviour is indicated in Scheme 5.



Scheme 5

With S_N2 -reactive alkyl halides, the 1,1-disubstituted phosphabenzene (21) was obtained, but alkylation (as well as protonation) in the 2-position (which has the highest electron density) follow S_N1 mechanism to give (22). The orientation is directed by the leaving group in R'X. Methyl iodide alkylated (20), R = Ph to give (21), R' = Me while trimethyloxonium fluoroborate gave (22), R' = Me.

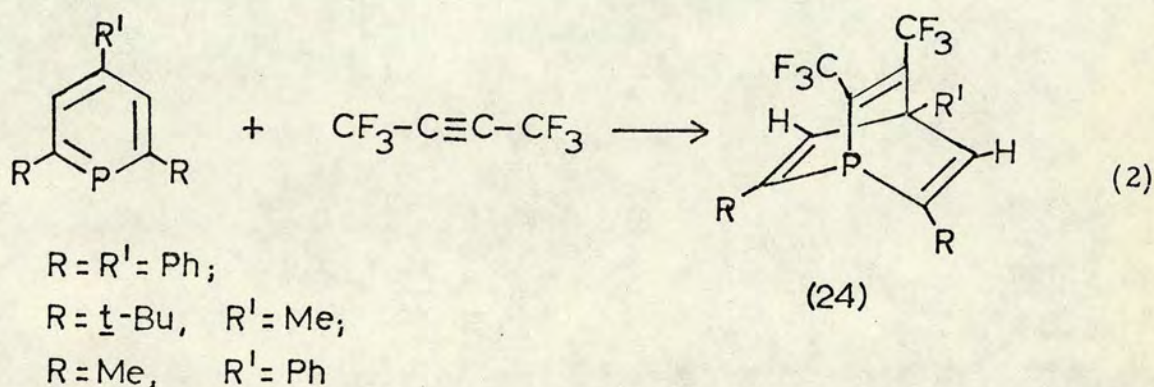
In another study, Märkl and Merz¹² achieved the conversion of the 1,2-dihydrophosphorin (16) to the phosphabenzene (23) by hydride transfer with trityl perchlorate followed by reaction with phenyl lithium as outlined in Scheme 6.



Scheme 6

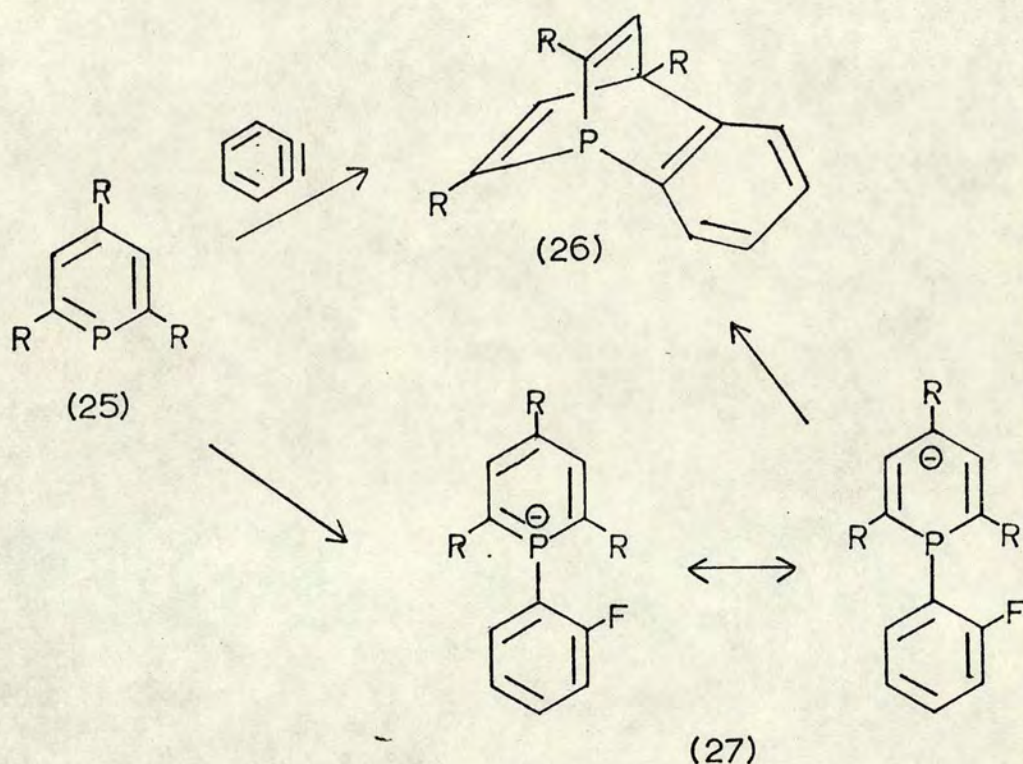
(ii) Cycloaddition reactions.

Markl has observed¹³ that 2, 4, 6-trisubstituted phosphorins have only slight diene reactivity. For example the triphenyl derivative did not react with diethyl acetylene dicarboxylate or with maleic anhydride. However it underwent cycloaddition with the highly reactive dienophile, hexafluoro-2-butyne, at 100°. The reaction occurred exclusively in the 1, 4-position yielding the substituted 1-phosphabarrelenes (24).



Following on from this result it was expected that phosphorins should react with arynes to form the cycloadduct, benzo-phosphabarrelene (26). However, no cycloadduct was obtained when 2, 4, 6-triphenyl phosphorin reacted with benzyne (generated from anthranilic acid and iso-amyl-nitrite). Likewise the reaction with benzene diazonium-*o*-carboxylate (a known benzyne precursor) failed.¹⁴ In view of the marked electrophilic character of the aryl-substituted phosphorins,¹¹ the reaction with

o-fluorophenyl magnesium bromide as aryne precursor was investigated. They obtained a cycloadduct (26; R = Ph, yield 15%; R = Bu^t, yield 69%).¹⁴ The cycloadduct was attributed to the reaction with benzyne while the route via the anion (27) was not ruled out in view of the failure to yield the cycloadduct with some other known aryne precursors. The cycloaddition was not limited to benzyne only as pentachlorophenyl lithium gave a similar adduct.

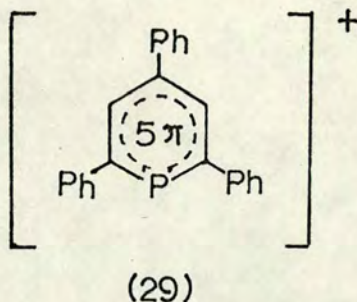
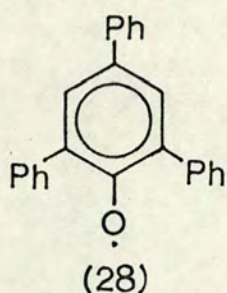


Scheme 7

(iii) Oxidation and reduction reactions.

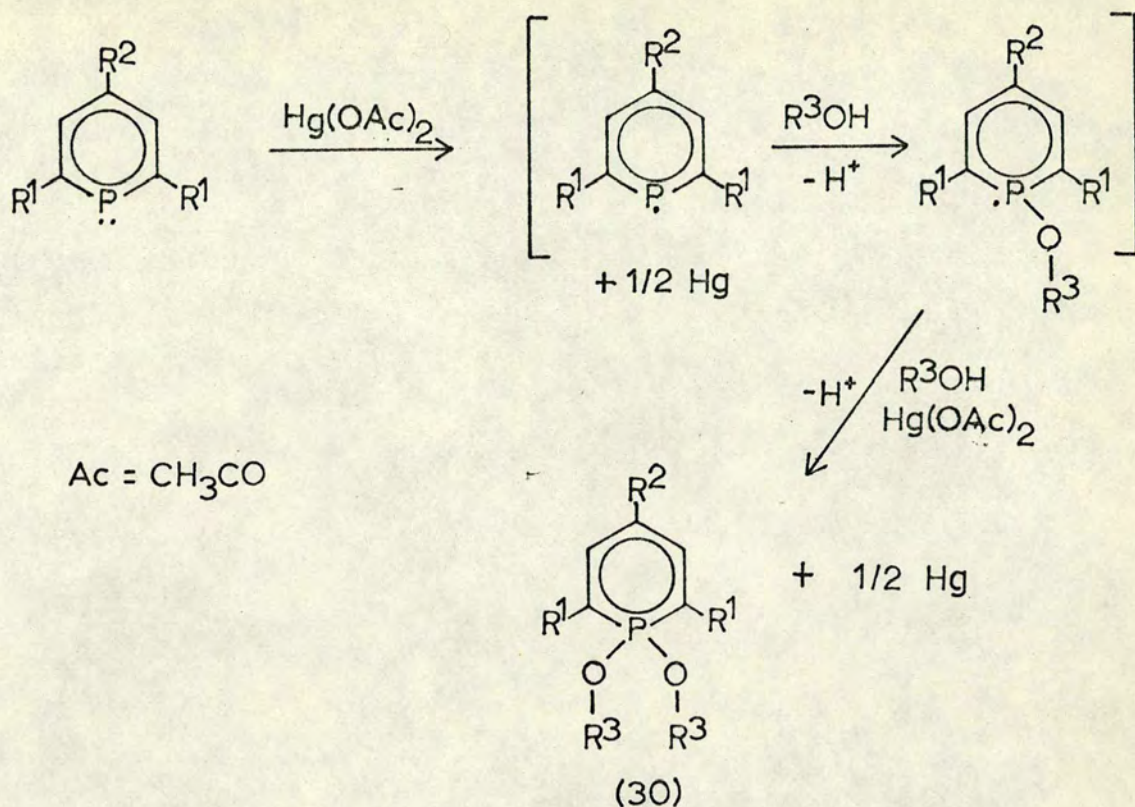
Dimroth and his co-workers have studied in some detail the oxidation and reduction of phosphorins. They found that when benzene solutions of 2, 4, 6-triphenylphosphorin (11) and the phenoxy radical (28) were mixed the deep red colour of the latter immediately faded to give a stable greenish yellow solution whose e. s. r. spectrum indicated a phosphorus radical. The same spectrum was obtained when (11) was

treated with various deuteriated-phenyl analogues of (28) or with the ^{17}O derivative of (28). This showed that the spectrum was independent of the oxidising phenoxy radical and must be due to the phosphorus radical cation shown in (29).¹⁵

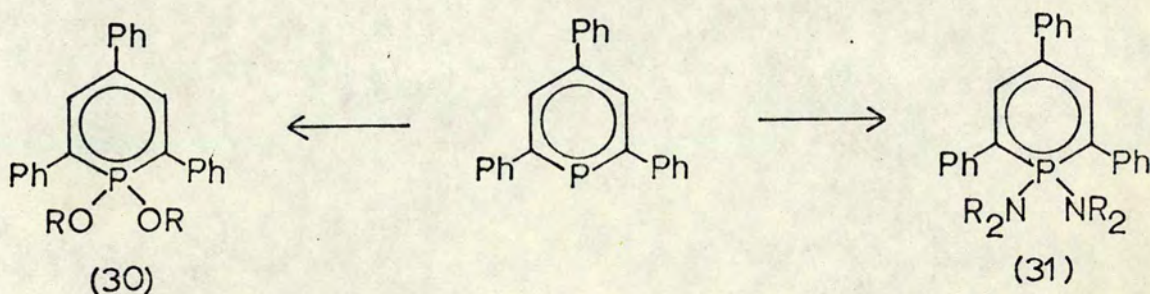


In a subsequent investigation,⁶ various 2,4,6-trisubstituted phosphorins were oxidised by 2,4,6-triarylphenoxy radicals, lead (IV) acetate or benzoate, or mercury (II) acetate. The e. s. r. spectra of all the radical cations so formed were very similar in type showing a doublet due to the interaction of the free electron with phosphorus. The phosphorus coupling constant a_p lies between 21.5 and 27 gauss.

A synthetic application of the oxidation of 2,4,6-trisubstituted phosphorins by various oxidising agents consisted in carrying out the reactions in the presence of alcohols and phenols.¹⁶ Using mercury (II) acetate the novel, strongly fluorescent, stable, crystalline 1,1-dialkoxy and 1,1-diaryloxyphosphabenzene were obtained. (Scheme 8). The reaction probably proceeded via the radical cation stage which can be detected by e. s. r. spectroscopy. Using 2,4,6-triphenylphenoxy as the oxidising agent and the phenoxide from the reaction as reaction partner, Dimroth et al.¹⁷ obtained 1,1-bis(2,4,6-triphenylphenoxy) 2,4,6-triphenylphosphorin (30; R = 2,4,6-triphenylphenoxy); with tetraphenylhydrazine the 1,1-bis(diphenyl amino)phosphorin (31) was obtained. (Scheme 9)



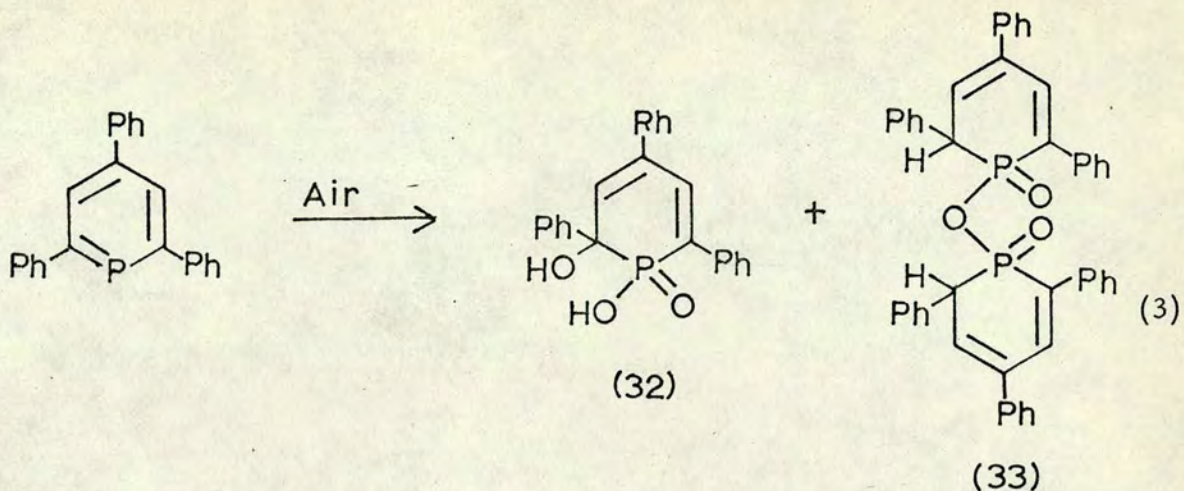
Scheme 8



Scheme 9

Aerial oxidation of benzene solutions of 2, 4, 6-triphenylphosphorin gave two products, a monomer (32) and a dimer (33).¹⁸ A product analogous to (33) was obtained when 2, 6-bis(4-methoxyphenyl) 4-phenylphosphorin was similarly oxidised. (eq. 3)

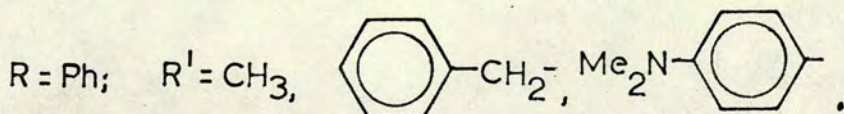
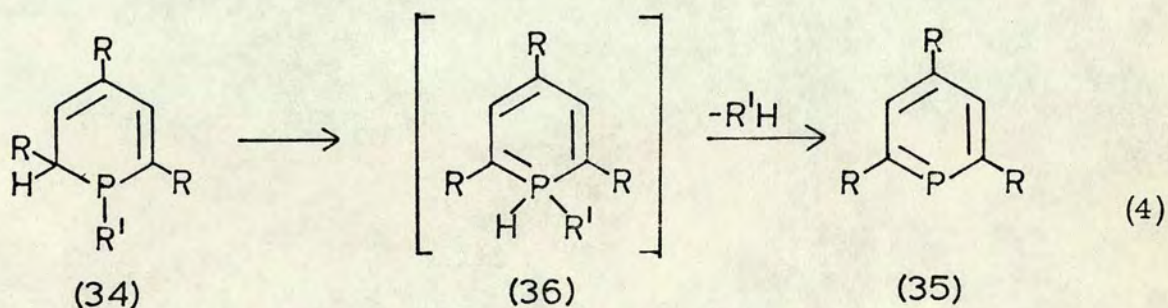
2, 4, 6-Triphenylphosphorin also gave stable radicals by reduction. Treatment of the phosphorin in tetrahydrofuran with potassium or potassium-sodium alloys gave three reduction stages,



considered by e. s. r. spectroscopy to indicate the stepwise addition of three electrons with the formation of a monoanion radical, a non-radical dianion and a trianion radical respectively.¹⁹

(iv) Miscellaneous reactions.

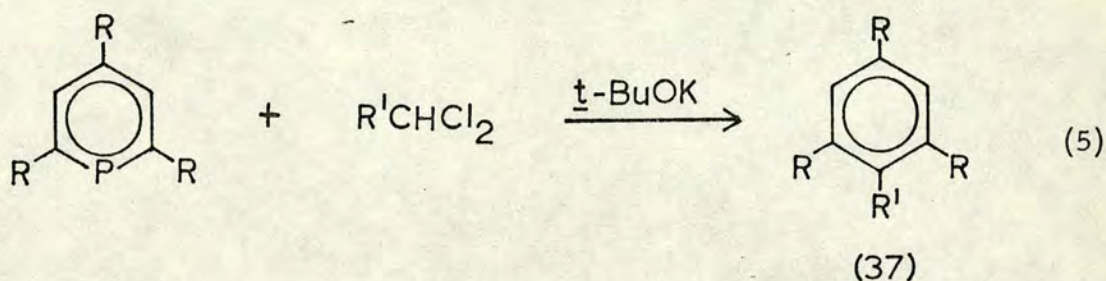
Märkl and Merz¹¹ found that thermolysis of 1, 2-dihydrophosphorins (34) at temperatures between 200-250° gave the corresponding phosphorins (35) thus:



The reaction probably proceeded via the intermediate (36) which underwent a synchronous 1, 1-elimination to give the phosphorin.

In another investigation, Märkl and Merz²⁰ found that 2, 4, 6-triphenylphosphorin did not react by thermolysis in the presence of known carbene precursors like CCl₃COONa or C₆H₅HgCCl₂Br. However they found that phosphorins reacted with halogeno-methanes

(CH_2Cl_2 , CHCl_3 and $\text{C}_6\text{H}_5\text{CHCl}_2$) in the presence of potassium t-butoxide thus



The postulated mechanism involved initial electrophilic reaction followed by ring expansion and extrusion of the phosphorus atom as the halide.

(v) Spectra and structure.

The u. v. spectrum of 2,4,6-triphenylphosphorin in methanol⁴ (λ_{max} 278 nm., $\epsilon = 41,000$) when compared with those of analogous compounds like 1,3,5-triphenylbenzene (λ_{max} 254 nm., $\epsilon = 56,000$) and 2,4,6-triphenylpyridine (λ_{max} 254 nm., $\epsilon = 49,500$) shows a bathochromic shift. U. v. spectra of other 2,4,6-trisubstituted phosphorins⁵ show similar trend.

The ¹H n. m. r. spectra of these compounds^{4,7} are also consistent with an aromatic phosphorin ring, the chemical shift of the ring protons ($\tau = 2.0$) indicating deshielding. The ³¹P n. m. r. spectrum⁴ showed a large chemical shift, $\delta = -178.2$ p. p. m. (in pyridine $\delta \text{H}_3\text{PO}_4 = 0$) indicating considerable deshielding of the phosphorus nucleus.

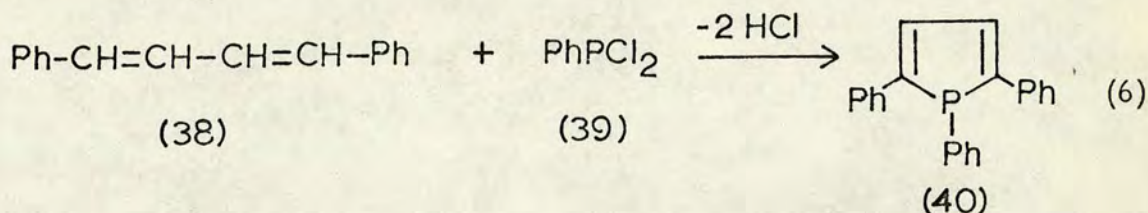
The e. s. r. spectra^{6,15} of the phosphorus radical cation has been discussed in the section on the oxidation reactions.

The crystal and molecular structure of a few 2,4,6-trisubstituted phosphorins and phosphabenzene have been determined by X-ray methods. Daly et al.²¹ found that in 2,6-dimethyl 4-phenylphosphorin, the two rings are planar, with the heterocyclic ring having two equal P-C bond lengths of 1.743 Å and four equal C-C bond lengths of 1.389 Å. For 1,1-dimethyl-2,4,6-triphenylphosphabenzene Daly and Märkl²² found an almost planar heterocyclic ring with a P-C bond length of 1.754 Å,

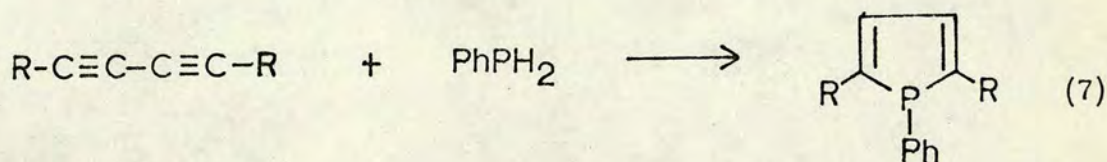
and C-C bond length of 1.399 Å. Thewalt²³ found similar values for 1,1-dimethoxy-2,4,6-triphenylphosphabenzene.

(C) Programme of Research.

One of the many varied reactions used in the synthesis of phosphorus heterocycles involves the reaction of phosphines and allied compounds with unsaturated hydrocarbons. For example, phenyl phosphonous dichloride (39) when heated with 1,4-diphenylbutadiene (38) at 230° for 10 hrs. gave the yellow, 1,2,5-triphenylphosphole (40) in 60% yield.²⁴



Märkl and Potthast²⁵ have developed a general synthesis of phospholes by reaction of phenylphosphine with butadiynes. This is analogous to the synthesis of pyrroles²⁶ and thiophenes.²⁷ They found that phenylphosphine added smoothly to butadiynes in benzene at room temperature in the presence of catalytic amounts of phenyl lithium to give 2,5-disubstituted-1-phenyl phospholes in yields of 50-90%.

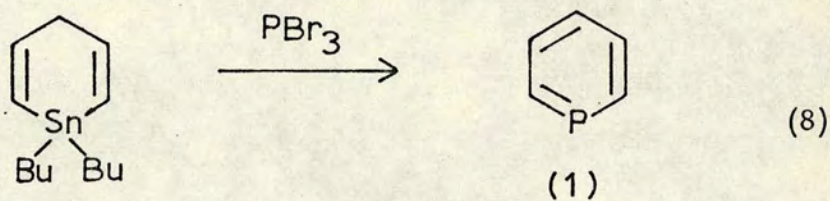


It would be useful therefore to investigate the reactions of 1,5-disubstituted-penta-1,4-diyne²⁸ and the penta 1,4-diyne-3-ols with phenyl phosphine as a route to six-membered phosphorus heterocycles. The products will have a useful, unsubstituted 4-position in the heterocyclic ring. Known methods of synthesis of phosphorins as developed by Märkl and Dimroth all gave 2,4,6-trisubstituted derivatives.

(D) Appendix.

Ashe²⁹ in a very recent communication has reported a one-step synthesis of the unsubstituted phosphorin (1). 1,4-dihydro 1,1-dibutyl stannabenzene was treated with phosphorus tribromide to give the hydrobromide of (1). Addition of 1,5-diazabicyclo[4.3.0]non-5-ene to the hydrobromide liberated the phosphorin which was isolated as a colourless volatile liquid by preparative g.l.c.

The ¹H n. m. r. of phosphorin indicated that the α -protons are shifted to lower field as compared with those of pyridine.



IV. 2. EXPERIMENTAL

(A) Instrumentation

See under Chapter II, section 1.

(B) Preparation of Materials.

(i) Hepta-2, 5-diyn-4-ol. This diynol was prepared by the reaction of propynyl magnesium bromide³⁰ and ethyl formate as described by Chauvelier.³¹

Propyne was generated by adding 1, 2-dibromopropane (340 g; 1.68 mole) dropwise to a stirred solution of potassium hydroxide (375 g) in *n*-butanol (750 ml) boiling under reflux. The gas thus formed was passed through water, dried over granular fused calcium chloride and bubbled into an ice-cooled and well-stirred solution of ethyl magnesium bromide (from Mg, 30 g; 1.25 mole; and EtBr, 144 g; 1.32 mole) in dry ether (700 ml) and kept under an atmosphere of dry, oxygen-free nitrogen. The propyne was generated over 6 hours. After all the dibromopropane had been added the butanol solution was refluxed until no more gas was liberated. The propynyl magnesium bromide thus prepared was allowed to stir overnight in a bath of cold water.

A solution of ethyl formate (39 g; 0.53 mole) in dry ether (100 ml) was then added dropwise to the stirred, ice-cooled solution of propynyl magnesium bromide over 1 hour. The resultant mixture was stirred at 0° for another hour and finally boiled under reflux for a further hour.

The dark-coloured solution was then poured into a mixture of ammonium chloride (200 g), water (100 ml) and crushed ice (200 g) and stirred for 15 min. The mixture was extracted with ether, and dried over anhydrous potassium carbonate. Removal of most of the ether gave colourless needles on standing. Recrystallisation from light petroleum (b. p. 60-80°) gave the product hepta-2, 5-diyn-4-ol, (16.0 g; 24% - yield based on Mg used), m. p. 102-103° (lit.³¹

105-107°).

I. r. spectrum (CHCl_3 sol'n): ν_{max} 3580 (OH) 2240 ($-\text{C}\equiv\text{C}-$) cm.^{-1}

(ii) Trideca-5,8-diyne-7-ol. This compound was prepared by a Grignard reaction of hex-1-ynyl magnesium bromide with hept-2-ynal.

Hept-2-ynal was first prepared by the method of Jones et al.³² An ethereal solution of hex-1-ynyl magnesium bromide was prepared from hex-1-yne³³ (41.0 g; 0.5 mole) and ethyl magnesium bromide (from Mg, 12 g; 0.5 mole and EtBr, 60 g; 0.55 mole). This was added to a stirred solution of dimethylformamide (110 g; 0.66 mole) in ether (250 ml). After decomposition in dil. H_2SO_4 and work-up in the usual way by extraction with ether, hept-2-ynal was obtained as a light yellow liquid (26.2 g; 48%) b. p. 60-61°/17-18 mm. (lit.³² 54-55°/16 mm).

A solution of hept-2-ynal (as prepared above) (26.0 g; 0.24 mole) in dry ether (50 ml) was added dropwise to a stirred solution of hex-1-ynyl magnesium bromide (as prepared above) (0.24 mole) in ether (150 ml) over 1 hour. This was decomposed by a mixture of ammonium chloride (100 g) water (100 ml) and crushed ice (300 g). Work-up by ether extraction etc. and distillation in vacuo gave trideca-5,8-diyne-7-ol as a light yellow liquid (34.3 g; 75%) b. p. 84-86°/0.04 mm (lit.³⁴ 155-156°/15 mm).

I. r. spectrum (thin film): ν_{max} 3300-3400 (broad, O-H), 2240 ($-\text{C}\equiv\text{C}-$) cm.^{-1}

(iii) 2,2,8,8-Tetramethyl-nona-3,6-diyne-5-ol. This was prepared by a method analogous to (ii) from 3,3-dimethylbut-1-ynyl magnesium bromide and 4,4-dimethylpent-2-ynal.

3,3-Dimethylbut-1-yne. Reaction of pinacolone (240 g; 2.4 mole) with phosphorus pentachloride (500 g; 2.4 moles) by the method of Bartlett and Rosen³⁵ gave 2,2-dichloro 3,3-dimethylbutane (197 g; 53%) and 2-chloro 3,3-dimethylbut-1-ene (40.0 g; 14%).

Dehydrochlorination of a mixture of 2,2-dichloro 3,3-dimethyl-

butane (166 g; 1.1 mole) and 2-chloro 3,3-dimethylbut-1-ene (40.0 g; 0.34 mole) by alcoholic potassium hydroxide (504 g in 65 ml ethanol) by the method of Puterbaugh and Newman³⁶ gave 3,3-dimethylbut-1-yne (64.7 g; 55%), b. p. 39-41°.

I. r. spectrum (CHCl₃ sol'n): ν_{\max} 3300 (CH stretching, -C≡CH), 2100 (-C≡C-) cm.⁻¹

4,4-Dimethylpent-2-ynal was prepared by the method of Bohlmann.³⁷ Reaction of 3,3-dimethylbut-1-ynyl magnesium bromide [from 3,3-dimethylbut-1-yne (49.5 g; 0.6 mole)] with triethyl orthoformate (95 g; 0.64 mole) gave the acetal (33.6 g; 30%) b. p. 74-80°/15 mm (lit.³⁷ 70-76°/12 mm). Hydrolysis of the acetal (33.6 g; 0.18 mole) by 10% oxalic acid solution (200 ml) gave on work-up 4,4-dimethylpent-2-ynal (13.1 g; 66%) b. p. 132° (lit.³⁷ 132°).

The required diynol was prepared from 4,4-dimethylpent-2-ynal (13.1 g; 0.12 mole) and 3,3-dimethylbut-1-ynyl magnesium bromide (0.12 mole) in a manner similar to that described in (ii). The product on recrystallisation from 80% ethanol gave colourless needles, 2,2,8,8-tetramethyl-nona-3,6-diyn-5-ol (10.8 g; 43%) m. p. 80-81° (lit.³⁸ no m. p. reported).

I. r. spectrum (CHCl₃ sol'n): ν_{\max} 3580 (-OH), 2240 (-C≡C-) cm.⁻¹

(iv) 1,5-Diphenyl-penta-1,4-diyn-3-ol. This was prepared by the reaction of phenylethynyl magnesium bromide with 3-phenylprop-2-ynal in a manner analogous to that described in (ii).

Phenyl acetylene was prepared from styrene dibromide (264 g; 1.0 mole) and sodamide by Vogel's method³⁹ in 65% yield, b. p. 73°/75 mm (lit.³⁹ 82°/80 mm).

3-Phenyl-prop-2-ynal. Reaction of phenyl acetylene (51.0 g; 0.5 mole) and triethyl orthoformate (74.0 g; 0.5 mole) by the method of Howk and Sauer⁴⁰ gave 3-phenylprop-2-ynal diethyl acetal (60.0 g; 59%), b. p. 105-107°/1.5 mm (lit.⁴⁰ 99-100°/2 mm). Acid hydrolysis of the acetal (59.0 g; 0.029 mole) gave 3-phenylprop-2-ynal (26.0 g; 70%) b. p. 104°/12 mm (lit.⁴¹ 114-117°/17 mm).

The required diynol was prepared from 3-phenylprop-2-ynal (13.4 g; 0.1 mole) and phenylethynyl magnesium bromide (0.1 mole) in a manner similar to that described in (ii). The product, 1,5-diphenylpenta-1,4-diyn-3-ol, crystallised as colourless needles from light petroleum (b. p. 60-80°) (11.8 g; 51%) m. p. 88-89° (lit.⁴² 88-89°).

I. r. spectrum (nujol): ν_{\max} 3220-3260 (broad, OH), 2230 (-C≡C-) cm.^{-1}

(v) Phenyl phosphine. The method used to prepare this compound was the original method of Michaelis-Köhler,⁴³ modified by Mann and Millar⁴⁴ for optimum conditions. Thus phenylphosphonous dichloride (330 g; 1.84 mole) was hydrolysed by ethanol (600 ml) to give phenylphosphonous acid which decomposed on heating to phenyl phosphine (35.0 g; 52%) b. p. 60-62°/23 mm (lit.⁴⁴ 157-159°).

(vi) Benzyl phosphine. Diethyl benzylphosphonate was first prepared by the Arbusov reaction from triethyl phosphite (127 g; 0.85 mole) and benzyl chloride (87 g; 0.69 mole) in 85% yield, b. p. 148-149°/7.5 mm (lit.⁴⁵ 169-171°/25 mm). The phosphonate (32 g; 0.14 mole) was then reduced by lithium aluminium hydride (6 g; 0.15 mole) using the method of Horner et al.⁴⁶ A very low yield of benzyl phosphine was obtained (0.7 g), b. p. 72°/25 mm (lit.⁴⁶ 180°).

(vii) Triphenylmethyl fluoroborate. This compound was prepared by the method of Dauben et al.⁴⁷ Triphenyl methanol (33.8 g; 0.12 mole) gave, on reaction with 48% fluoroboric acid (33.8 ml) in propionic anhydride as solvent (338 ml), orange crystals of triphenyl methyl fluoroborate (38 g; 95%).

(C) Reaction of Phenyl Phosphine with Various Diynols

(i) Trideca-5,8-diyn-7-ol. A mixture of trideca-5,8-diyn-7-ol (4.0 g; 0.021 mole) and phenyl phosphine (3.0 g; 0.027 mole) was stirred under an atmosphere of dry nitrogen and gradually heated to 180° in an oil bath. Reaction was evident at 150° when the colour of the mixture became brown. The mixture was stirred at 180° for 30 min. The viscous light-brown oil which resulted was distilled in vacuo

to give a yellow oil, probably 2,6-di-n-butyl-1-phenyl-1,2-dihydrophosphorin (1.3 g; 22%), b. p. 104-6°/0.05 mm.

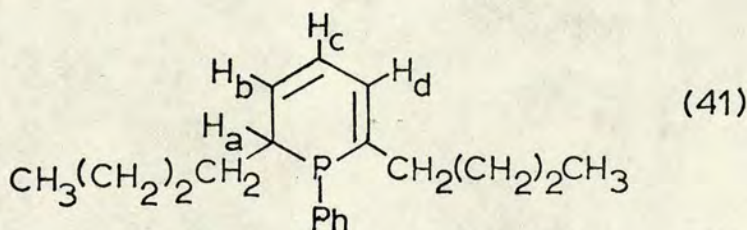
Found: C, 79.5; H, 9.5; M^+ 286.184191

$C_{19}H_{27}P$ requires C, 79.7; H, 9.4%; M , 286.185030.

I. r. spectrum (thin film): ν_{\max} 1440 cm^{-1} (P-Ph).

The mass spectrum showed the following fragmentation pattern:

m/e 286 (parent ion, M^+); 271 ($M - CH_3$); 255 ($M - C_2H_7$); 243 ($M - C_3H_7$); 230 ($M - C_4H_9$); 187 ($M - C_7H_{15}$). 1H n. m. r. spectrum ($CDCl_3$): (τ) 9.1-9.3 (2t, 6H, 2 x n-Bu; J 7Hz); 8.4-9.0 (m, 8H, 4 x $-CH_2-$); 7.9-8.1 (m, 1H, proton H_a); 7.5-7.75 (m, 4H, 2 x $-CH_2-$); 3.4-4.4 (m, 3H, ring protons); 2.6-2.8 (m, 5H, aromatic).



Scale expansion of the complex band at 3.4-4.4 τ showed it to consist of three groups of signals: (i) a doublet of doublets (broad), centred at 4.25 τ (proton H_b), (ii) three asymmetric peaks centred at 3.8 τ (proton H_c) and (iii) multiplet, centred at 3.5 τ (proton H_d). These assignments were supported by spin decoupling experiments which indicated that the proton at 4.25 τ (i. e. H_b) was coupled to proton H_a and to the proton at 3.8 τ (i. e. H_c). The ^{31}P n. m. r. showed two signals at $\delta = -21$ ppm and -77 ppm (in $CDCl_3$, $\delta H_3PO_4 = 0$).

The distillation residue, a viscous brown oil was chromatographed on silica. Elution with benzene gave a brown oil which when dissolved in benzene and added to light petroleum yielded a light brown solid, probably 2,6-di-n-butyl-1-phenyl 1,2-dihydrophosphorin-1-oxide (2.1 g; 17%) m. p. 103-6°.

I. r. spectrum (nujol): ν_{\max} 1180 cm^{-1} (P=O).

The 1H n. m. r. spectrum showed very broad signals from which no deductions could be made.

The mass spectrum was compatible with the assigned structure showing

the following fragmentation pattern: m/e 302 (parent ion M^+ ; $C_{19}H_{27}OP$ requires 302); 287 ($M - CH_3$) and 273 ($M - C_2H_5$).

A similar reaction using trideca-5,8-diyn-7-ol (0.77 g; 0.004 mole) and benzyl phosphine (0.6 g; 0.005 mole) gave a light brown oil (0.17 g) b. p. $146-148^\circ/0.05$ mm.

The mass spectrum showed the presence of two compounds with parent ions m/e 316 ($C_{20}H_{29}OP$ requires M , 316)

and 300 ($C_{20}H_{29}P$ requires M , 300).

The 1H n. m. r. (CCl_4) showed the following signals. τ 6.6-9.1 (m , 22H); 3.5-4.2 (m , 2H) and 2.8-3.0 (m , 5H, aromatic protons).

(ii) 2,2,8,8-Tetramethyl-nona-3,6-diyn-5-ol. A mixture of this diynol (2.87 g; 0.015 mole) and phenyl phosphine (2.45 g; 0.023 mole) was reacted in a manner similar to that used in (i). Distillation of the resultant mixture gave a light yellow-green oil which is probably a mixture of two isomers, viz. 2,6-di-t-butyl-1-phenyl 1,2-dihydro-phosphorin (42) and 2-t-butyl 5-(2,2-dimethylpropylidene) 1-phenyl-phosphol 2-ene (43) (1.02 g; 24%), b. p. $95-97^\circ/0.02$ mm.

I. r. spectrum (thin film): ν_{max} 1470 and 1430 cm^{-1} (P-Ph).

The mass spectrum showed the parent ion at m/e 286

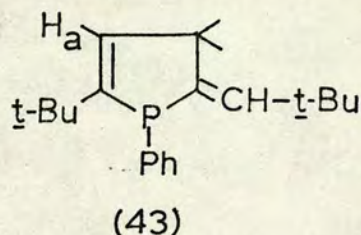
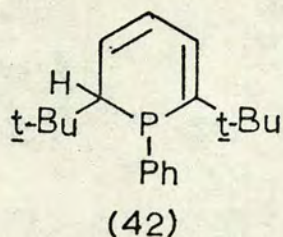
(Found: M^+ , 286.184550,

$C_{19}H_{27}P$ requires M , 286.185030) and a major fragment (mass abundance ratio 100%) at ion m/e 229, indicating a loss of a t-butyl group.

1H n. m. r. spectrum ($CDCl_3$): (τ) 9.1 (s , 18H, 2 x t-Bu); 8.90 (s , 18H, 2 x t-Bu); 7.9 (bs , 3H, $-CH_2-$ + CH); 3.8-4.2 (m , 1H, ring proton); 3.56 [m , 1H, proton H_a of compound (43)]; 3.44 [m , 2H, ring protons of compound (42)]; 3.3 (d , 1H, $=CH-$; $J_{P,H}$ 3Hz); 2.75 (m , 10H, aromatic).

Irradiation at 7.9 τ caused the multiplet at 3.56 τ to collapse to a doublet $J_{P,H}$ 3Hz.

The ^{31}P n. m. r. showed a major signal at $\delta = -70$ ppm and a minor one at $\delta = -111$ ppm (in $CDCl_3$, $\delta H_3PO_4 = 0$).



Further distillation of the residue gave a very viscous yellow-green liquid, probably a mixture of the oxides of compounds (42) and (43) (1.5 g; 33%), b. p. 130-140°/0.02 mm.

I. r. spectrum (thin film): ν_{\max} 1440 (P-Ph) 1180 (P=O) cm.^{-1}

The mass spectrum showed the correct parent ion at m/e 302

($\text{C}_{19}\text{H}_{27}\text{OP}$ requires M , 302).

^1H n. m. r. spectrum (CDCl_3): complex bands at 8.7-9.2 τ and 2.3-2.8 τ .

(iii) Hepta-2,5-diyne-4-ol. Phenyl phosphine (4.3 g; 0.04 mole) was added to a suspension of hepta-2,5-diyne-4-ol (3.25 g; 0.03 mole) in *t*-butylbenzene (15 ml). The mixture was stirred and heated to 160° in an oil bath. The temperature was kept at 160° for 2 hours. The resulting oil was distilled in vacuo to give two fractions of a yellow oil: (i) (0.35 g) b. p. 125-128°/0.02 mm (ii) (1.36 g) b. p. 130-132°/0.02 mm. Fraction (i) was identified as a mixture containing mainly 2-ethyl-5-methylphosphole.

I. r. spectrum (thin film): ν_{\max} 1430 cm.^{-1} (P-Ph).

The mass spectrum showed the parent ion at m/e 202 ($\text{C}_{13}\text{H}_{15}\text{P}$ requires M 202). A small peak at m/e 218 was also noted.

The ^1H n. m. r. (CDCl_3) was compatible with the assigned structure showing, among other signals, the following: (τ) 8.96 (t, 3H, Et; $J = 7.5$ Hz); 7.97 (d, 3H, Me; $J_{\text{P,H}} = 10.5$ Hz) and 3.52 (d, 2H, ring protons $J_{\text{P,H}} = 12.5$ Hz):

Fraction (ii) contained a mixture of a few compounds as indicated by a complicated ^1H n. m. r. spectrum.

The mass spectrum (m/e 218, 202; $C_{13}H_{15}P$ requires M , 202;
 $C_{13}H_{15}OP$ requires M , 218)
indicated that the mixture was isomeric with (i).

(iv) 1, 5-Diphenyl-penta-1, 4-diyn-3-ol. The diynol (1.0 g; 0.004 mole) was reacted in the usual way with phenyl phosphine (0.65 g; 0.005 mole) at 180° . An intractable viscous tar was obtained.

(D) Miscellaneous Reactions.

(i) Reaction of hepta-2, 5-diyn-4-ol with tetrakis(hydroxymethyl)phosphonium chloride (THPC). A mixture of the diynol (1.08 g; 0.01 mole) and THPC (5.7 g; 0.03 mole) in pyridine (50 ml) was boiled under reflux in an atmosphere of nitrogen for 4 hours. A white film of paraformaldehyde was coated on the walls of the condenser. The mixture was extracted by chloroform, washed with water, and dried over anhydrous $MgSO_4$. Removal of the chloroform gave a brown solid which was chromatographed on silica.

Elution with benzene/ether (4:1 v/v) gave a white solid identified as the starting diynol (0.8 g; 74%) m. p. and mixed m. p. 102° (lit.³¹ $105-107^{\circ}$). Elution with methanol gave a white polymeric material (0.1 g).

(ii) Reaction of 2, 6-di-n-butyl-1-phenyl-1, 2-dihydrophosphorin with triphenylmethyl fluoroborate. A solution of the fluoroborate (0.66 g; 0.002 mole) in redistilled acetonitrile (4 ml) was added dropwise to a stirred solution of the dihydrophosphorin (0.57 g; 0.002 moles) in acetonitrile (4 ml). The stirred mixture was then boiled under reflux in an atmosphere of dry nitrogen for 5 hr. Removal of the solvent yielded a brown oil which when triturated several times with ether gave a brownish yellow solid (0.6 g) m. p. $90-95^{\circ}$.

I. r. spectrum (KBr disc): ν_{max} 1435 (P-Ph) $1050 (BF_4^-)$ cm^{-1}
'H n. m. r. spectrum ($CDCl_3$): (very broad signals) (τ) 7.0-9.2 (m, 18H,); 2.2-2.8 (m, 8H).

The mass spectrum showed a peak at ion m/e 286.

The ethereal extracts yielded a mixture of two solids, separated by fractional recrystallisation and identified as triphenylmethane, m. p. and mixed m. p. 93° (lit.⁴⁸ 92.5°) and triphenylmethanol m. p. and mixed m. p. $160-162^{\circ}$ (lit.⁴⁹ $161-162^{\circ}$).

(iii) A mixture of methyl iodide (0.70 g; 0.005 mole) and 2,6-di-n-butyl-1-phenyl 1,2-dihydrophosphorin (0.143 g; 0.0005 mole) was boiled under reflux in an atmosphere of nitrogen for an hour. After this 2N NaOH (2 ml) was added and the mixture stirred for 24 hr. The organic layer was extracted with chloroform, dried over anhydrous MgSO_4 and distilled to give a yellow oil, identified as trideca-5,7-dien-5-yl methylphenyl-phosphine 1-oxide (0.04 g; 25%) b. p. $160-165^{\circ}/0.02$ mm.

I. r. spectrum (thin film): ν_{max} 1460 (P-Ph) 1180 (P=O) cm^{-1}

The mass spectrum gave the parent ion at m/e 318 ($\text{C}_{20}\text{H}_{31}\text{OP}$ requires M, 318).

^1H n. m. r. spectrum (CDCl_3): (τ) 9.1-9.2 (complex band, 6H, 2 x Me); 8.2-8.9 (complex band, 13H, Me + 5 x $-\text{CH}_2-$); 7.5-8.0 (broad band, 4H, 2 x $-\text{CH}_2-$); 3.7-4.2 (m, 2H, $-\text{CH}=\text{CH}-$); 2.3-2.8 (complex band, 6H, $-\text{CH}$ + aromatic). From the complex band at 8.2-8.9 τ , a doublet centred at 8.5 τ , $J_{\text{P,H}}$ 12Hz was very prominent. This was assigned to the methyl protons directly linked to the phosphorus atom.

(iv) 2,6-Di-n-butyl-1-phenyl 1,2-dihydrophosphorin (0.124 g; 0.0004 mole) was heated in an atmosphere of nitrogen at 240.250° for 2 hr. The product was a brown oil whose i. r. spectrum (thin film) showed a strong broad band at $1160-1170$ cm^{-1} (P=O).

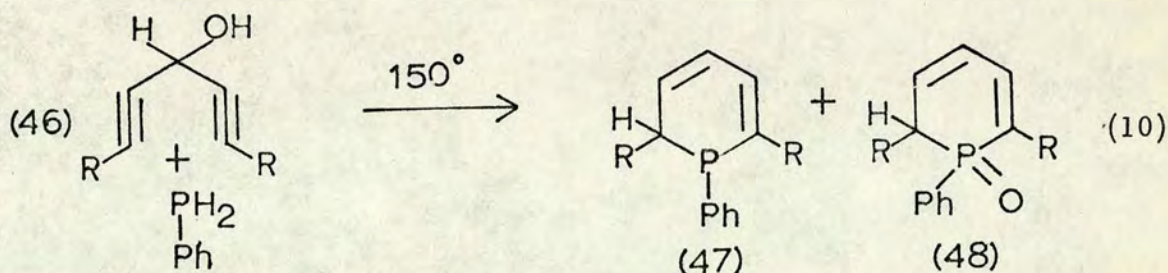
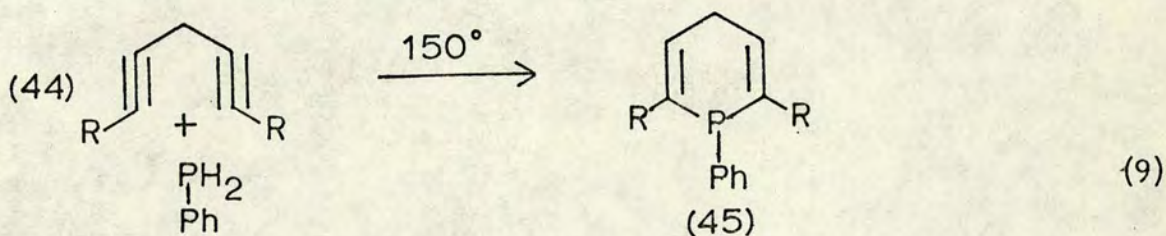
The mass spectrum gave an ion at m/e 304.

^1H n. m. r. spectrum (CDCl_3): (τ) 7.6-9.4 (complex broad band, 22H); 5.2 (bs, 1H); 2.3-2.8 (complex band, 6H).

IV. 3. DISCUSSION

(A) Reactions of Phenyl Phosphine with Various Diynols

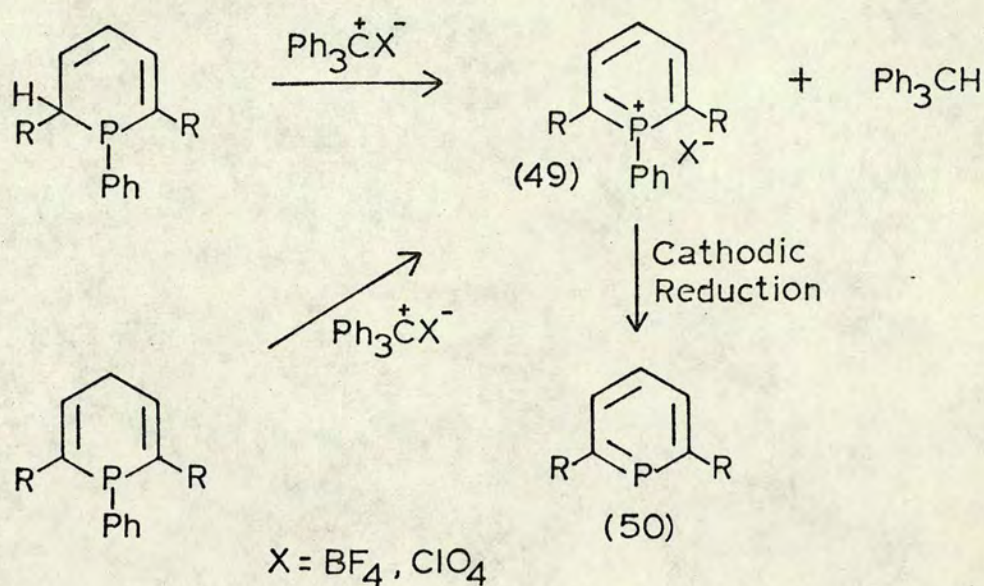
Preliminary investigations by Cadogan, Atkinson, and Gripper-Gray⁵⁰ on the reactions of phenyl phosphine with various diynes (44; R = *n*-Bu, Ph) and diynols (46; R = *n*-Bu, *t*-Bu) indicated that the products consisted of 1,4-dihydrophosphorins (45) in the first reaction series (eq. 9) and a mixture of 1,2-dihydrophosphorins (47) and the phosphorin-1-oxides (48) in the second series (eq. 10).



The isolation of these dihydrophosphorins led to the proposal of a reaction sequence (Scheme 10) as a possible route to the hitherto unknown 2,6-disubstituted phosphorins. This sequence envisages an initial hydride transfer reaction using trityl fluoroborate or perchlorate to give the phosphonium salt (49). Cathodic reduction by Horner's method⁵¹ should yield the desired phosphorin (50).

The present investigation was centred on the reaction sequence involving diynols while the reactions dealing with diynes were studied by a colleague.²⁸

The initial experiments were therefore designed towards the preparation of pure samples of the 1,2-dihydrophosphorins. Thus a mixture of phenyl phosphine and trideca 5,8-diyn-7-ol (46; R = *n*-Bu)



Scheme 10

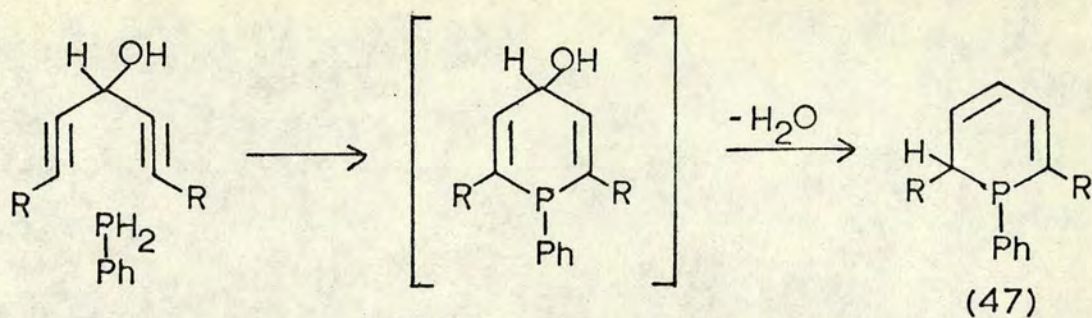
was allowed to react at 150° . Distillation yielded a fraction which consisted mainly of 2,6-di-*n*-butyl 1-phenyl 1,2-dihydrophosphorin (47; R = *n*-Bu). The ^{31}P n.m.r. spectrum showed two signals at $\delta = -20$ and -77 ppm, indicating a mixture of two phosphorus-containing compounds. The ^1H n.m.r. spectrum was not very well defined, especially for the signals assigned to the ring protons. However double irradiation technique enabled the proper assignments of these signals.

The residue of the reaction was a viscous oil, identified as the 1,2-dihydrophosphorin-1-oxide (48; R = *n*-Bu). Addition of light petroleum (b. p. $60-80^\circ$) precipitated out a brown solid which contained the oxide.

The 1,2-dihydrophosphorin is presumably formed (Scheme 11) by an initial addition reaction between phenyl phosphine and the diynol followed by dehydration and reduction.

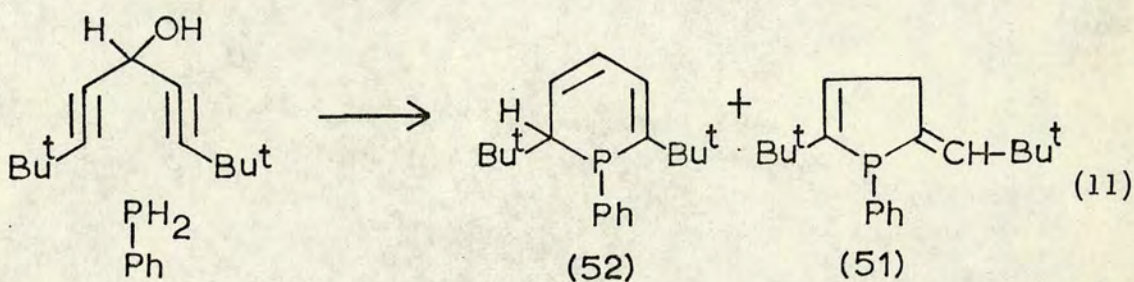
Oxidation of (47) leads to (48).

The reaction took a slightly different course when other alkyl-substituted diynols were used. For instance with *t*-butyl groups as



Scheme 11

substituents, the reaction led to the 1, 2-dihydrophosphorin (52) and the phospholene (51).



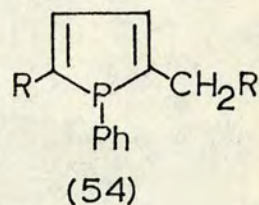
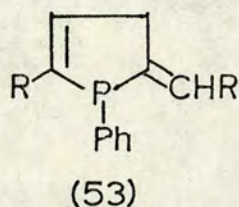
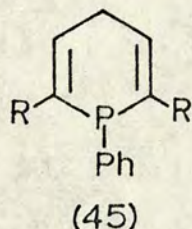
The mixture of (52) and (51) co-distilled. Their structures were assigned from ^1H n. m. r. and ^{31}P n. m. r. (the latter showed two signals - a major one at $\delta = -70$ ppm and a minor one at $\delta = -111$ ppm) and mass spectral data.

With methyl groups as substituents, the reaction between the diynol and phosphine led to an even more complex mixture. Mass spectral data indicated the mixture to consist of components whose masses were 202 and 218. From the ^1H n. m. r. spectrum the presence of 2-ethyl-5-methyl 1-phenyl phosphole as one of the components in the mixture was quite evident.

The main difficulty in dealing with these reaction mixtures lies in the inability to separate the components of the mixtures. These components all seem to co-distil. Attempts at preparative g. l. c.²⁸ as a means of separation led to ring opening reactions at the conditions required to achieve separation.

Cadogan and Gee²⁸ in their study of the reactions of phenyl

phosphine with various diynes (44; R = *n*-Bu; Ph) obtained similar mixtures of products. The products obtained in various ratios consisted of a mixture of three components viz. the 1,4-dihydrophosphorin (45), the phospholene (53) and the phosphole (54).



In trying to account for the formation of these products, the steric factors of the substituents could well play an important role. The five-membered heterocycles are presumably formed by addition at the end of the $-C\equiv C-$ bond not containing the substituent.

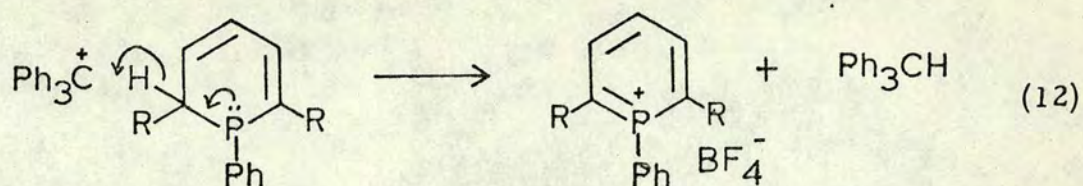
An attempt was also made to react hepta 2,5-diyn-4-ol with tris(hydroxymethyl) phosphine (generated *in situ* from tetrakis(hydroxymethyl) phosphonium chloride⁵²). Only a polymeric phosphorus-containing material was obtained.

(B) Miscellaneous Reactions

From the reactions of phenyl phosphine with various diynols, it appears that only in the case where *n*-butyl groups are the substituents, was a fairly pure product obtained. It was considered useful to carry out a few reactions to establish its structure as 2,6-di-*n*-butyl 1-phenyl 1,2-dihydrophosphorin.

(i) Hydride transfer

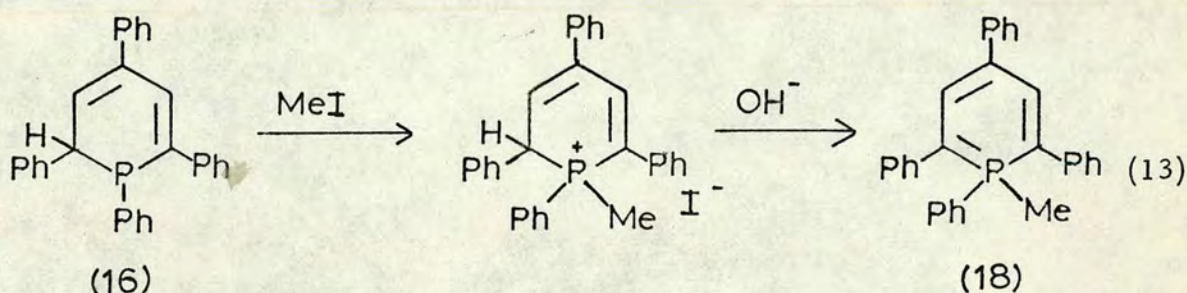
In accordance with the proposed plan (Scheme 10) of the synthesis leading to the 2,6-disubstituted phosphorin, a hydride transfer reaction was attempted using trityl fluoroborate as reagent. A brown solid, whose i. r. spectrum indicated the presence of the BF_4^- group was obtained. The mass and 1H n. m. r. spectral data were inconclusive. However the isolation of triphenylmethane was an indication that the



reagents had reacted. Subsequent to this attempt, Märkl and Merz¹² reported a one-step conversion of 1, 2, 4, 6-tetraphenyl 1, 2-dihydrophosphorin (16) to the phosphabenzene by hydride transfer (using trityl perchlorate) followed by reaction with phenyl lithium (see Scheme 6). It seems reasonable to assume that the intermediate phosphonium salt was not stable.

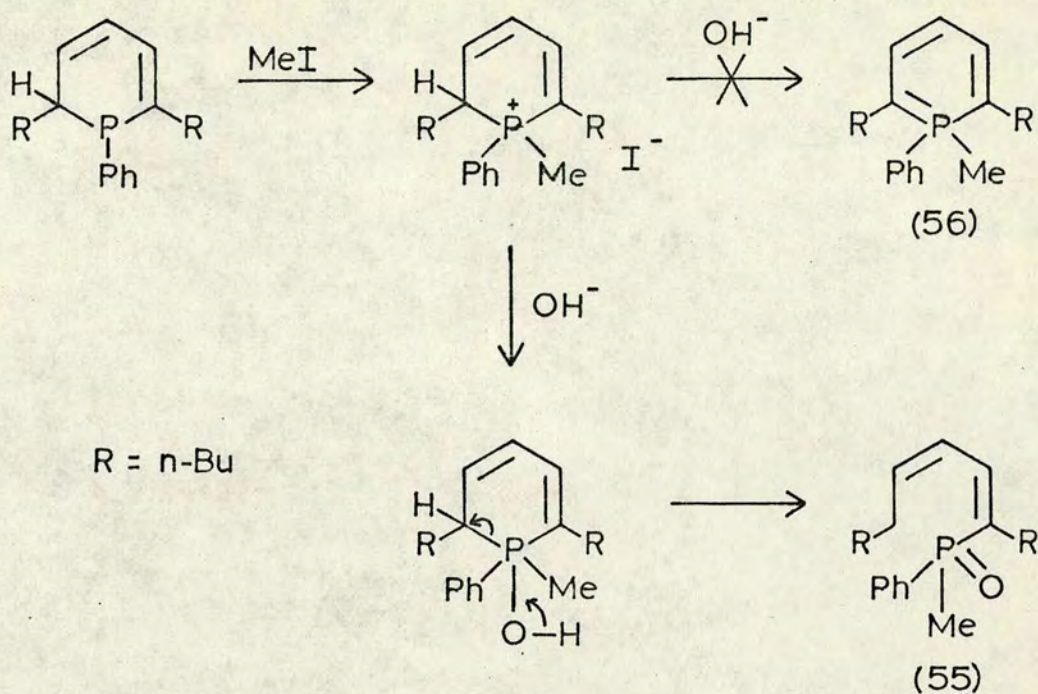
(ii) Conversion to the phosphabenzene.

Märkl et al.⁹ have achieved the conversion of the 1, 2-dihydrophosphorin (16) to the corresponding phosphabenzene (18) by quarter-nitisation followed by base hydrolysis.



A similar reaction sequence was attempted. The product isolated was however not the expected phosphabenzene (56) but a ring-opened phosphine oxide (55). The first step in this reaction is quarter-nitisation to the phosphonium salt. Alkaline hydrolysis afforded the phosphine-oxide.

It is very difficult to explain why the phosphabenzene (56) was not obtained by the expected proton abstraction by hydroxide ion.



Scheme 12

(iii) Pyrolysis

Märkl and Merz¹¹ in a very recent paper reported that pyrolysis of 1, 2-dihydrophosphorin afforded the phosphorin (see eq. 4). A similar pyrolysis at 200° of 2, 6-di-n-butyl 1-phenyl 1, 2-dihydrophosphorin gave a product of mass 304, which was not identified. The i. r. indicated the presence of the P=O group.

(C) Conclusions.

The reactions of phenyl phosphine with various diynols produced mixtures of products which proved very difficult to separate. These products are invariably the 1, 2-dihydrophosphorin, the phosphol-2-ene and the phosphole. The reactions of the 1, 2-dihydrophosphorin (46; R = n-Bu) seem to be different from those of 1, 2, 4, 6-tetraphenyl 1, 2-dihydrophosphorin. Apparently the presence of the phenyl groups as opposed to n-butyl groups must account for the differences. It would require further detailed investigations to account for these differences.

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