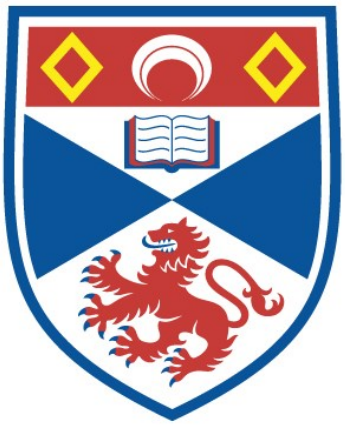
THE REACTION OF AROMATIC NITRO-COMPOUNDS WITH TERVALENT PHOSPHORUS REAGENTS

Michael James Todd

A Thesis Submitted for the Degree of PhD
at the
University of St Andrews



1967

THE REACTION OF AROMATIC NITRO-COMPOUNDS WITH TERVALENT PHOSPHORUS REAGENTS

A Thesis

presented for the degree of

Doctor of Philosophy

in the Faculty of Science of the

University of St. Andrews

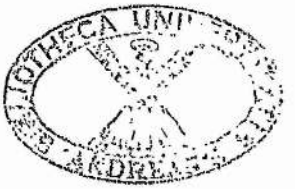
by

MICHAEL JAMES TODD, B.Sc.

September, 1967

St. Salvator's College,

St. Andrews.



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

The thesis describes the results of research carried out in the Chemistry Department, St. Salvator's College, University of St. Andrews under the supervision of Professor J.1.G. Cadogan since 1st October 1964, the date of my admission as a research student.

I hereby certify that Michael James Todd has spent twelve terms at research work under my supervision, has fulfilled the conditions of Ordinance No. 16 (St. Andrews) and is qualified to submit the accompanying thesis in application for the degree of Doctor of Philosophy.

Director of Research.

ACKNOWLEDGEMENTS

I should like to thank Professor J.I.G. Cadogan for suggesting this topic of research and for his constant advice and encouragement during the course of the work.

I should like to express my gratitude to Dr. R.K. Mackie for many helpful discussions and for the interest he has taken in this work. Thanks are also due to Dr. J. Feeney of Varian Associates for his assistance with one of the 100 Mc./sec. p.m.r. spectra described herein.

Finally, I should like to thank the Science Research Council for the award of a maintenance grant during the course of this work.

CONTENTS

INTRODUCTION

1. Oxidation of Tervalent Organophosphorus Compounds.-

Tervalent organophosphorus compounds (X_3P), of which the phosphines and phosphites are the most widely investigated classes, react with most oxygen containing compounds to yield the corresponding quinquevalent derivative (X_3PO).[4] Ethers, alcohols and most esters, however must be mentioned as exceptions, being resistant to reduction. The principal driving force behind these reactions is the high energy of the P=O bond formed in the product. Typical values[1] for P=O bond dissociation energies in phosphates and phosphine oxides lie in the range 120-150 kcal./mole compared with values[2] in the range 50-70 kcal./mole for the $\overset{+}{N}-\overline{O}$ bond in amine oxides. The large dissociation energies, small lengths, and high vibration frequencies of P=O bonds have been interpreted as evidence for some degree of $p_\pi-d_\pi$ bonding in contrast to the coordinate bonding in amine oxides. A considerable amount of physical evidence for participation of this type of bonding in phosphoryl compounds has been produced[3] and chemical evidence in favour of $p_\pi-d_\pi$ bonding stresses the high energies of P=O bonds when compared with the corresponding bonds of nitrogen. The stability of the phosphonate form of the dialkyl phosphites is a consequence of this tendency for P=O bond formation:

$$(RO)_2P(OH) \rightleftharpoons (RO)_2P\overset{O}{\underset{H}{<}}$$

and the driving force behind the second stage of the Arbusov reaction may be explained in the same way:

$$(RO)_3\overset{+}{P}-R' \quad X^- \longrightarrow RX + (RO)_2P\overset{O}{\underset{R'}{<}}$$

In general terms, the propensity of tervalent phosphorus compounds to become oxidised to the quinquevalent form is a phenomenon of great synthetical utility as is briefly illustrated by the following examples.

Direct oxidation of tervalent organophosphorus compounds with oxygen is not a thoroughly investigated field.[4] The majority of these compounds undergo at least partial oxidation but the mechanisms are not well understood and in some cases conflicting results have been published.

Triaryl phosphines,[5] triaryl phosphites,[6] and trialkyl phosphites[6] all react with ozone giving excellent yields of the corresponding P=O compound.

The reaction between diaroyl peroxides and aryl phosphines has been investigated[7a-d] and found to produce the appropriate anhydride and phosphine oxide. Since no attack on the solvent occurs in these reactions, the possibility of a homolytic mechanism has been dismissed.[7a] Denney and Greenbaum have further shown[8] by the use of oxygen-18 tracers that the phosphine displaces the more electropositive peroxidic oxygen in unsymmetrical peroxides, O' in the case shown:

$$\underline{p}\text{-}\ O_2N\text{--}\ C_6H_4\ \text{--CO.O'.O.CO--}\ Ph$$

In marked contrast, the reaction between trialkyl phosphites and dialkyl peroxides appears to be a homolytic process, Walling and Rabinowitz[9] having isolated bi-α-cumyl and triethyl phosphate from the reaction between triethyl phosphite and di-α-cumyl peroxide. They postulated a mechanism involving an intermediate phosphoranyl radical:

$$ROOR \rightarrow 2RO.$$

$$RO. + (EtO)_3P \rightarrow (EtO)_3\overset{\circ}{P}OR \rightarrow R. + (EtO)_3PO$$

$$R. + R. \rightarrow R\text{--}R \qquad \text{where } R. = Ph\overset{\circ}{C}Me_2$$

Peresters,[10] hydroperoxides,[11] and ozonides[12] are rapidly reduced to esters, alcohols, and carbonyl compounds respectively. In each case, heterolytic reaction mechanisms involving nucleophilic attack on oxygen have been proposed.

Oxides of nitrogen are, in general, reduced by phosphines and phosphites. Amine <u>N</u>-oxides are smoothly reduced[13] tothe corresponding amine and the order of the reactivities of the following phosphorus compounds with pyridine <u>N</u>-oxide suggests that in this reaction, the phosphorus is acting as an electrophile[14]: $PCl_3 > PhPCl_2 \gg (PhO)_3P > (EtO)_3P >>> Ph_3P > Bu_3P > Et_2PPh$. However, evidence has been advanced[15] to suggest that, at least in some solvents, the reaction proceeds by a radical mechanism in the case of triethyl phosphite. Azoxy compounds[16] are also reduced to the corresponding azo-compounds. Staudinger and Hauser[17] have reported the reduction

of nitrous oxide by triethyl phosphine, and dinitrogen tetroxide is reduced[18] by tervalent phosphorus compounds at low temperatures ($-78^{\circ}C$ in CH_2Cl_2) giving mixtures of nitrous oxide and nitrogen. At these temperatures, the nitrous oxide produced in the latter reaction reacts much more slowly than the N_2O_4 since it is, in effect, an amine oxide:

$$N{\equiv}N{\rightarrow}O + (RO)_3P \longrightarrow (RO)_3P{=}O + N_2$$

The reaction of phosphites with nitric oxide has been found[19] to be a convenient route to phosphates. The insensitivity of this reaction to the polarity and dielectric constant of the solvent has led to the postulation of a radical mechanism:

$$NO. + (EtO)_3P \xrightarrow{slow} (EtO)_3\overset{\bullet}{P}{-}N{=}O \xrightarrow[fast]{NO.} (EtO)_3PO + N_2O$$

Many other oxidation reactions of tervalent phosphorus compounds have been described,[4] quinones, aldehydes, ketones, lactones, and anhydrides being among the compounds which undergo attack. In nearly all these cases, however, the oxidised phosphorus entity is bonded to the substrate and as this is not, in general, typical of the reactions involved in the present investigation, they will not be dealt with here.

It is clear, however, that tervalent phosphorus compounds as exemplified by triethyl phosphite or triphenyl phosphine are among the most reactive deoxygenating substances available to the organic chemist, and it was the realisation of this that led Cadogan and his co-workers in 1960 to begin an investigation into the deoxygenation of aromatic nitroso-

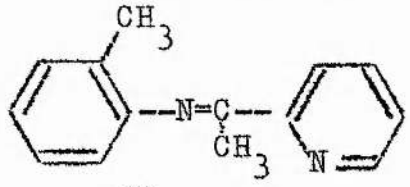
and nitro-compounds. This thesis is concerned with synthetical extension and mechanistic studies of the deoxygenation of nitro-compounds by tervalent organophosphorus compounds, a reaction which has found wide applicability since it was first reported five years ago.

2. Preparative Aspects of the Reaction between Tervalent Phosphorus Compounds and Aromatic Nitroso- and Nitro-compounds.- (a) Reactions of aromatic C-nitroso-compounds. Comparatively few studies of the reduction of nitroso-compounds have been reported, the principal reason presumably being the inaccessibility of the starting materials.

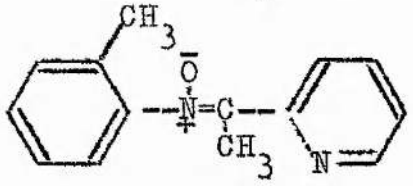
Bunyan and Cadogan[20] showed that nitrosobenzene and o-ethylnitrosobenzene afford the corresponding azoxy-compounds on reduction with triethyl phosphite or triphenyl phosphine. In an investigation of the reaction of NN-dimethyl-p-nitrosoaniline with triethyl phosphite they also found that, using equimolar quantities, triethyl N-p-dimethylaminophenylphosphorimidate (1)(13%) was formed in addition to 4,4'-bisdimethylaminoazoxybenzene (63%). When a ten-molar excess of phosphite was employed, the phosphorimidate (58%) and the azoxy-compound (23%) were obtained. Horner and Hoffmann[16] in a study of the reaction of this nitroso-compound with triphenyl phosphine found only the azoxy-compound.

$$p\text{-}Me_2N.C_6H_4.N{=}P(OEt)_3 \qquad (1)$$

Since the present work was commenced, Sundberg[21] has extended Bunyan and Cadogan's reaction in an investigation of the deoxygenation of o-methyl, o-propyl, and o-butylnitrosobenzenes with triethyl phosphite and has found a much wider spectrum of products. Thus, in addition to the corresponding phosphorimidate (9%), he found, taking o-nitrosotoluene as an example, o-toluidine (2.5%), N-(o-tolyl)-2-acetimidylpyridine (2)(20%) and N-(o-tolyl)-α-methyl-α-(2-pyridyl)nitrone (3)(15%).



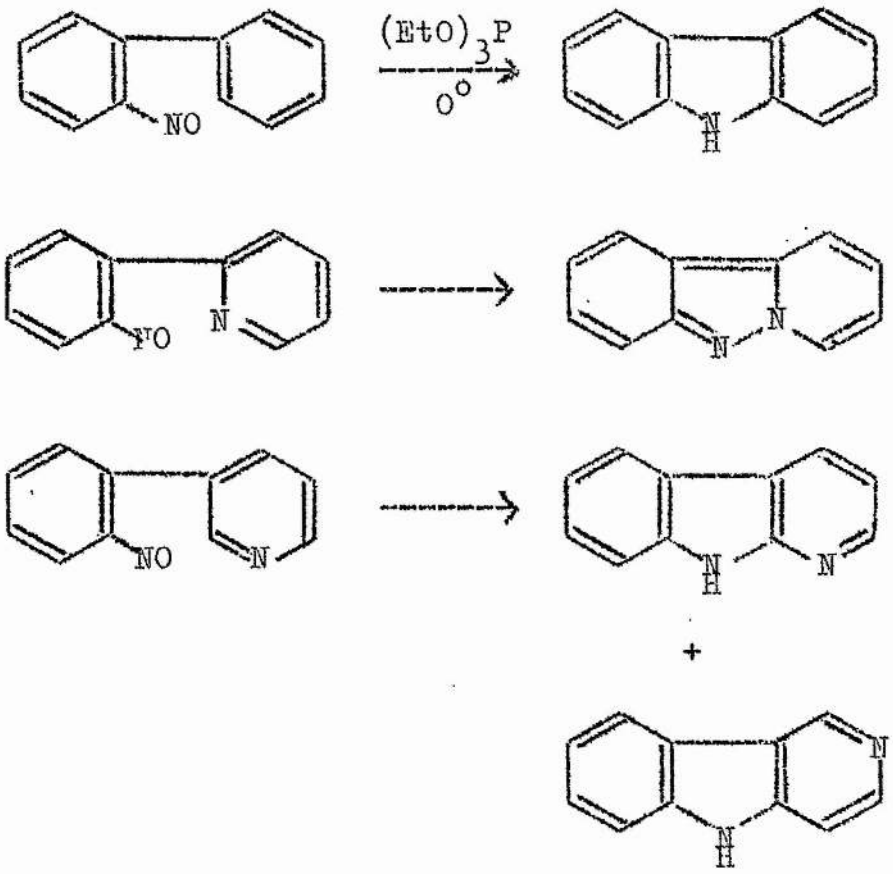
(2)



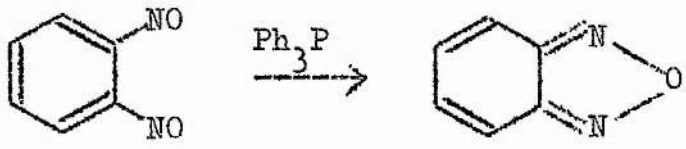
(3)

In addition he reported trace amounts of o-propenylanilines and 2-methylindoline in the deoxygenation of o-propylnitrosobenzene while analogous products were detected in the butyl case.

In their study,[20] Bunyam and Cadogan also developed a new cyclisation reaction. By taking suitably constituted nitro-compounds, they obtained good yields of heterocyclic compounds, all with five-membered nitrogen-containing rings. Thus, reaction of 2-nitrosobiphenyl, 2-o-nitrosophenylpyridine, and 3-o-nitrosophenylpyridine with triethyl phosphite led respectively to carbazole (4)(76%), pyrido [1,2-b]indazole (5)(98%), and a mixture (64%) of α-carboline (6)(81.5%) and γ-carboline (7)(18.5%).



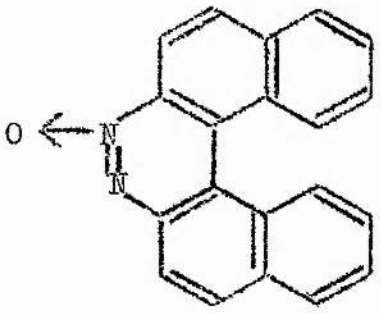
Another example of this type of reaction is Boyer and Ellzey's[22] report of the formation of benzofurazan (8) by deoxygenation of o-dinitrosobenzene with triphenyl phosphine.



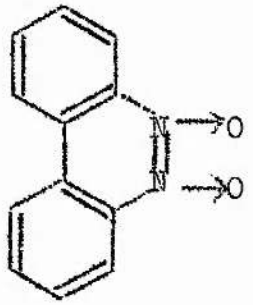
(b) Reactions of aromatic nitro-compounds. Before 1962, very little work had been published on the reaction between ter-valent phosphorus compounds and aromatic nitro-compounds. Such reports as existed[23] did not, in general, involve

reduction of the nitro-group.

Buckler and his co-workers[24] obtained good yields of azoxy-compounds by reduction of aromatic nitro-compounds with phosphine in alkaline media. This reaction has been extended by Bellaart[25] to include the formation of benzo[f]naphtho-[2,1-c]cinnoline-N-oxide (9) and benzo[c]cinnoline-N,N'-di-oxide (10) from 2-nitronaphthalene and 2,2'-dinitrobiphenyl respectively.

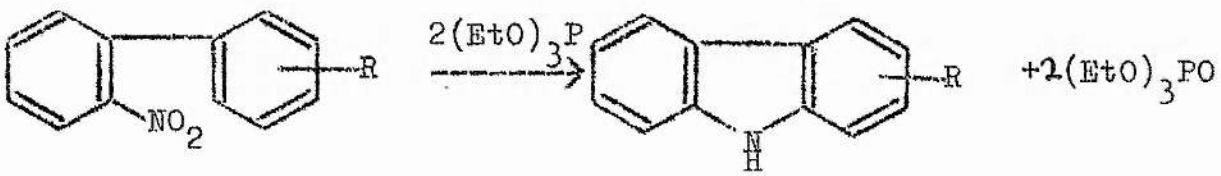


(9)

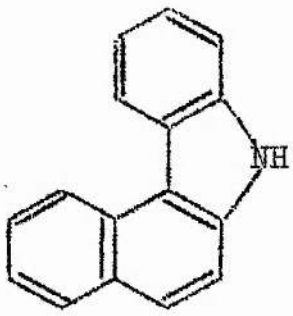


(10)

Cadogan and his co-workers[26] making good use of the more ready availability of the nitro-compounds, have extended the cyclisation of nitroso-compounds in a series of elegant heterocyclic syntheses. As with the corresponding nitroso-compounds, 2-nitrobiaryls were found to give good yields (75-85% in general and 35-45% for biphenyls substituted in one of the 2'-positions) of carbazoles on being heated with excess triethyl phosphite.

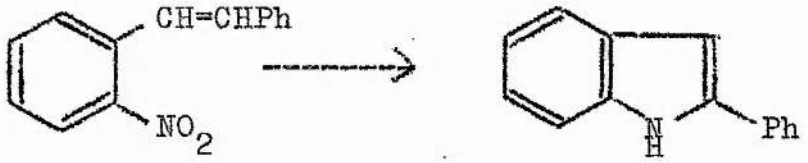


Similarly, 2-o-nitrophenylpyridine gave pyrido[1,2-b]indazole (5)(90%), while 1-o-nitrophenylnaphthalene underwent ring-closure to give 3,4-benzocarbazole (11)(64%).



(11)

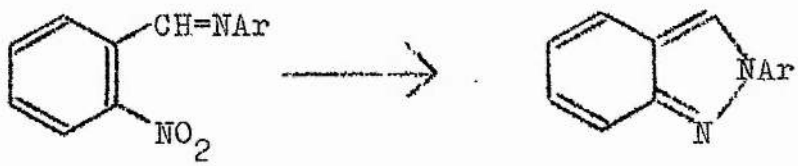
In extension of these reactions, cis- and trans-2-nitrostilbene were shown to yield 2-phenylindole (12), a higher yield being obtained from the former (85% cf. 58%).



(12)

o-Nitrostyrene, however, afforded only a trace of indole, suggesting in conjunction with the previous result, that the efficiency of the ring-closure is very sensitive to steric factors.

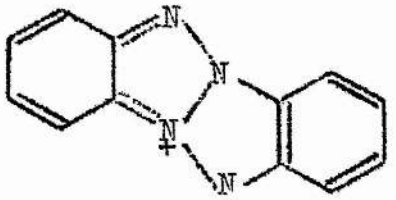
In the same way, series of 2-arylindazoles (yields varying between 35% and 60%)(13) and 2-aryl-2H-benzotriazoles (14) (30%-70%) have been prepared from o-nitroanils and 2-nitro-azobenzenes.



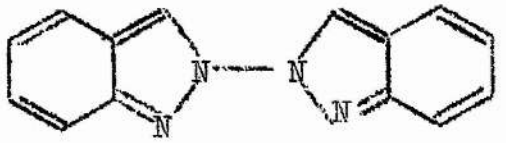
(13)

(14)

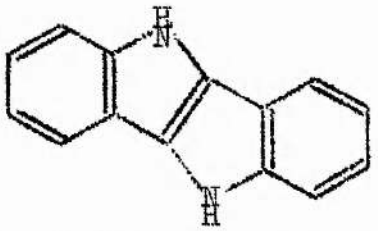
Reaction of triethyl phosphite with suitably constituted dinitro-compounds was found to lead to polycyclic compounds containing fused five-membered rings. Dibenzo[b,f]-1,3a,4,6a-tetra-azapentalene (15)(63%), 2,2'-bi-2H-indazolyl (16)(22%) and indolo [3,2-b]indole (17)(2%) were obtained by cyclisation of 2,2'-dinitroazobenzene, o-nitrobenzaldehyde azine, and 2,2'-dinitrostilbene respectively. This route to the tetra-azapentalene system has recently been the subject of considerable industrial interest[34].



(15)



(16)

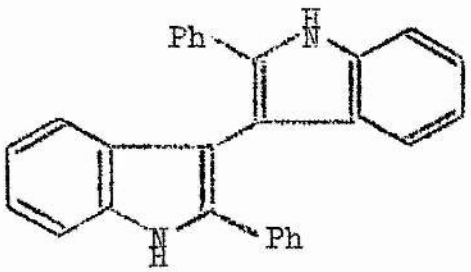


(17)

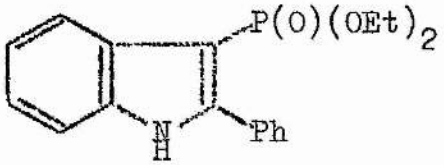
In the course of this investigation it was found that triphenyl phosphine produced results similar to those from triethyl phosphite, but greatly increased the difficulty of separating the products since the phosphorus compounds could not be distilled out of the reaction mixture. Phosphorus

trichloride apparently did not produce deoxygenation.

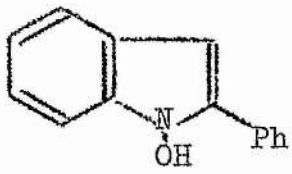
In a paper published during the course of the present work, Sundberg[27] described the reaction of β-alkyl- and β-acyl-o-nitrostyrenes with triethyl phosphite in rather greater detail. In all cases, he found the corresponding 2-substituted indole as the main product, the alkyl and phenyl indoles being formed in 50-70% yields and the acyl indoles being produced in 15-20% yields. In addition, taking trans-o-nitrostilbene as his most thoroughly investigated example, he discovered some most interesting minor products. As well as 2-phenylindole (12)(71%), he found 2,2'-biphenyl-3,3'-biindole (18)(7%) and diethyl 2-phenyl-3-indolylphosphonate (19) (1.6%). Postulating 1-hydroxy-2-phenylindole (20) as an intermediate, he proceeded to isolate this from a deoxygenation interrupted well before completion, and further demonstrated that on heating with triethyl phosphite, (20) gave a product distribution similar to that of the original nitro-compound.



(18)

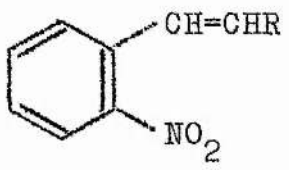


(19)

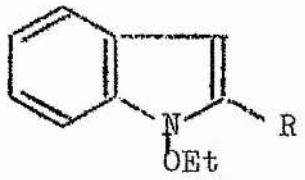


(20)

Bi-indoles analogous to (18) were also obtained from the deoxygenation of β-methyl- (21,R=Me) and β-propyl-o-nitrostyrene (21, R=n-C_3H_7).



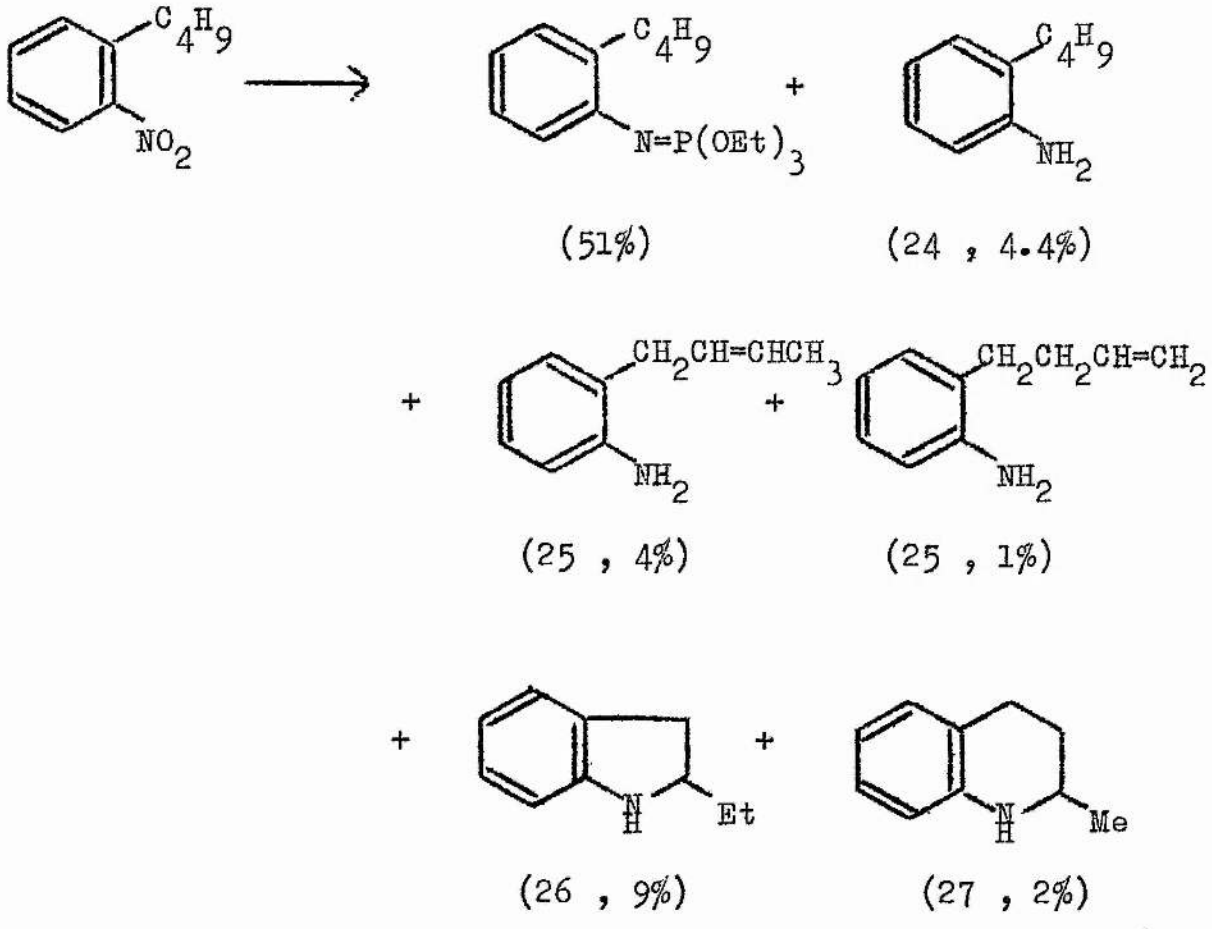
(21)

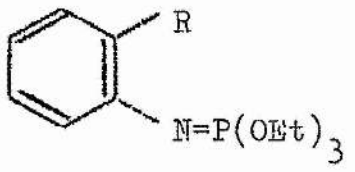


(22)

In a few cases, he also isolated 1-ethoxyindoles (22), obtaining a 3% yield when R=n-C_3H_7 and 4% when R=-CO.Ph. These compounds presumably arise from ethylation of the corresponding 1-hydroxyindole by triethyl phosphate. It is noteworthy that in his most thoroughly examined case (21, R=trans-Ph) he failed to find any ethoxyindole.

As an isolated experiment in this paper, Sundberg reported that deoxygenation of o-ethylnitrobenzene gave a compound which he isolated and identified as triethyl N-(o-ethylphenyl)phosphorimidate (23, R=-C_2H_5)(44%).

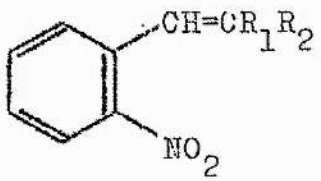

C4H9
NO2
C4H9
N=P(OEt)3
C4H9
NH2
(51%)
(24 , 4.4%)
CH2CH=CHCH3
NH2
CH2CH2CH=CH2
NH2
(25 , 4%)
(25 , 1%)
N
H
Et
N
H
Me
(26 , 9%)
(27 , 2%)



(23)

In two further publications,[21,28] the same author confirmed that the phosphorimidates (23) are, in general, the major products of deoxygenation of o-alkylnitrobenzenes. In addition, he detected and estimated by g.l.c. small amounts of o-alkylanilines (24), o-alkenylanilines (25), and heterocyclic indoline (26) and tetrahydroquinoline (27) derivatives. In the case of o-butylnitrobenzene the product distribution was as shown on the facing page. These figures which are quoted in the text of the paper unfortunately do not correspond with the details given in the experimental section of the paper, which describes the isolation of the phosphorimidate (40%) and an amine fraction containing compounds (24)-(27) which accounts for only 8.6% of the nitro-compound.

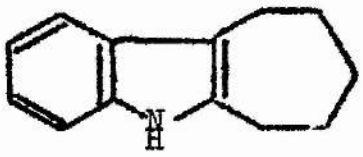
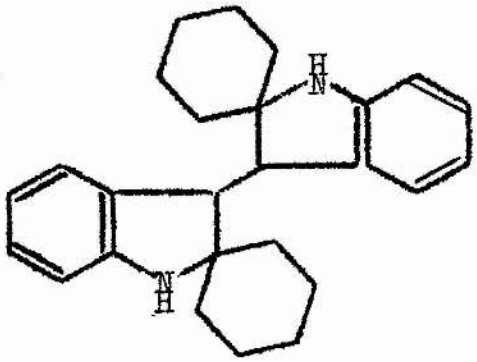
In his latest contribution[29] to this field, Sundberg has described rearrangements and ring expansions which take place on deoxygenation of four β,β-disubstituted o-nitrostyrenes (28)-(31).



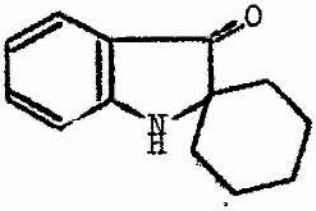
(28) $R_1,R_2=(CH_2)_5$

(29) $R_1,R_2=(CH_2)_4$

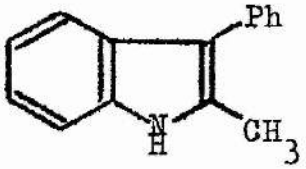
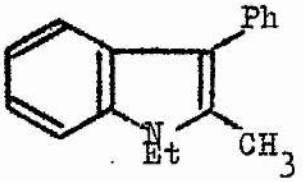
(30) $R_1=R_2=CH_3$

(28) $\xrightarrow{(EtO)_3P}$  + 

(32) (33)

+ 

(34)

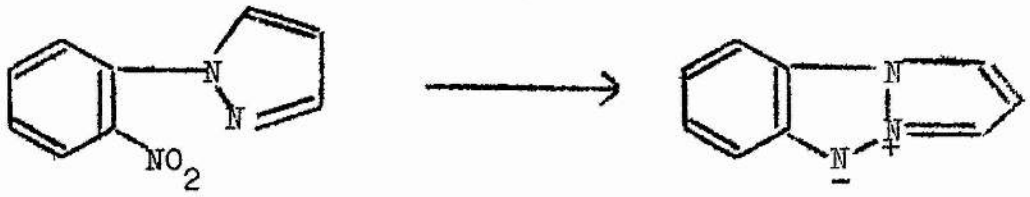
(31) $\longrightarrow$  + 

(35) (36)

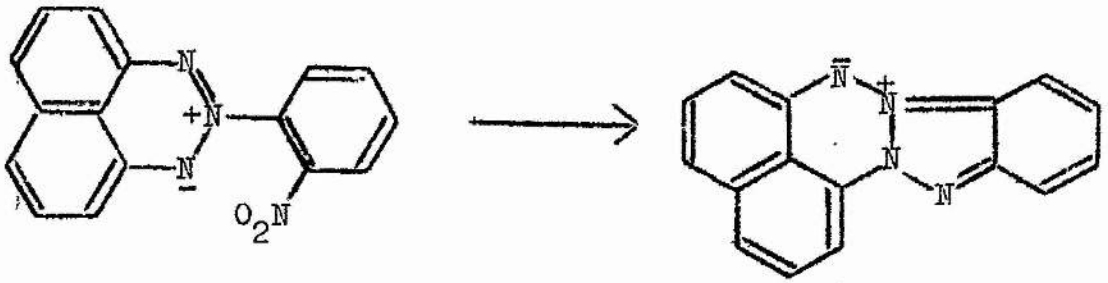
(31) R_1=Ph, R_2=CH_3

Cyclohexylidene(o-nitrophenyl)methane (28) gave as the major product 2,3-pentamethyleneindole (32)(35%). In addition, 3',3'''-bispiro[cyclohexane-1,2'-indoline](33)(24%) and spiro-[cyclohexane-1,2'-indolin-3'-one] (34)(8%) were isolated (see facing page). The cyclopentylidene compound (29) gave only a low yield (15%) of the rearranged indole, 1,2,3,4-tetrahydrocarbazole, analogous to (32) but β,β-dimethyl-o-nitrostyrene gave products corresponding to all those formed from (28). α-Methyl-2'-nitrostilbene (31), however, underwent deoxygenation with rearrangement in high yield (77%), no bi-indoline or indolinone being detected. In addition to the major product, 2-methyl-3-phenylindole (35), a 21% yield of 1-ethyl-2-methyl-3-phenylindole (36) was isolated, presumably formed by ethylation of (35) by triethyl phosphate. It was suggested that the high yield of rearranged product was a consequence of the known[30] effectiveness of the phenyl group in migration reactions. In the case of (28), (29) and (30) where only alkyl groups were available for migration, other reaction pathways could compete more successfully with the rearrangement-aromatisation which leads to the major products.

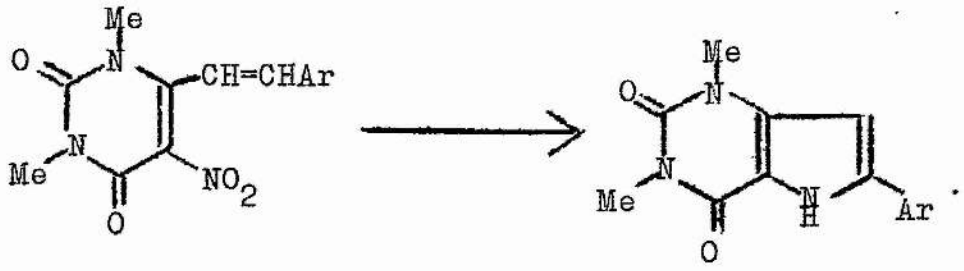
Several other workers have made use of reductive cyclisation of aromatic nitro-compounds by tervalent phosphorus compounds as a preparative procedure. Thus, Lynch and Hung[31] have prepared pyrazolo[1,2-a]benzotriazole (39)(18%) from 1-



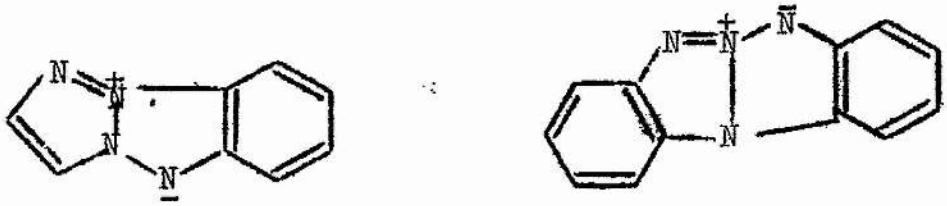
(38) (39)



(40) (41)



(42) (43)



(44) (45)

(o-nitrophenyl)pyrazole (38) and Sieper[32] has made the new benzotriazolonaphthotriazine (41)(46%) from 2H-2-(o-nitrophenyl) naphtho [1,8-de]-1,2,3-triazine (40).

Taylor and Garcia[33] have prepared two of the biologically interesting pyrrolo[3,2-d]pyrimidines (43) from the corresponding 5-nitro-6-styrylpyrimidine derivatives (42).

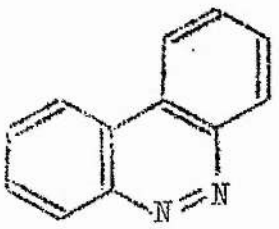
Finally, in a very recent publication, Carboni and Kauer[34] have described the synthesis of the dibenzotetra-azapentalene (15)(p. 11) from 2-(o-nitrophenyl)-2H-benzotriazole. They also reported the formation of the compounds benzo [b]-1,3a,4,6a-tetra-azapentalene (44) and dibenzo [b,f]-1,3a,6,6a-tetra-azapentalene (45) from 2-(o-nitrophenyl)-2H-triazole and 1-(o-nitrophenyl)-1H-benzotriazole respectively.

3. Cyclisation of Aromatic Nitro-Compounds not involving Tervalent Phosphorus Compounds.-

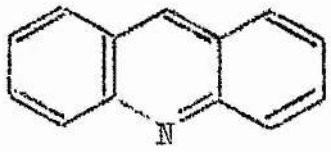
Many reductive cyclisations of nitro-compounds related to the examples described in the previous section can be effected by reagents other than tervalent phosphorus compounds.

The first report of deoxygenation of an aromatic nitro-compound leading to cyclisation seems to be that of Waterman and Vivian[35] who prepared phenazine in 46% yield from 2-nitro-diphenylamine by heating with lead shot or iron filings at about 300°. They later discovered that ferrous oxalate had

wider applicability as a deoxygenating agent, and by heating with this, they prepared carbazole (63%) from 2-nitrobiphenyl, benzo[c]cinnoline (46)(17%) from 2,2'-dinitrobiphenyl, and acridine (47)(yield not stated) from 2-nitrobenzophenone.

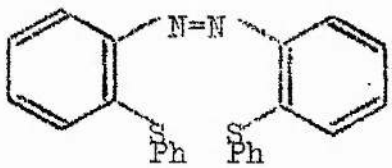


(46)



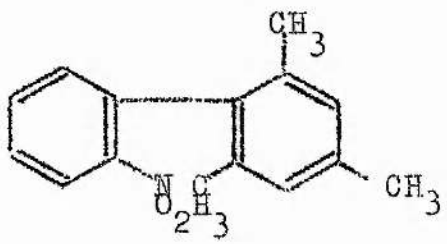
(47)

The removal of the carbonyl oxygen in the latter case is a feature of this reaction not shared by the reaction of the same starting material with triethyl phosphite, as will be shown later in this thesis. In a series of papers[36], Waterman and Vivian and their co-workers then extended the phenazine synthesis to a very wide range of substituted phenazines. An attempt by the same workers[37] to prepare phenothiazine from 2-nitrodiphenyl sulphide resulted in the formation of 2,2'-bis(phenylmercapto)azobenzene (48)(60%). 2-Nitrodiphenyl sulphone also failed to undergo ring closure to phenothiazine dioxide, giving instead a low yield of 2-aminodiphenyl sulphone.

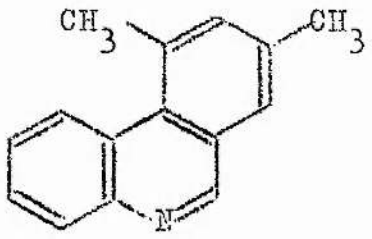


(48)

Pyrido [1,2-b]indazole (5)(p. 8) can be obtained from this type of reaction by taking 2-o-nitrophenylpyridine as starting material[38]. In a further communication[39], Abramovitch and his co-workers examined the deoxygenation of 2-nitro-2',4',6'-trimethylbiphenyl (49) with ferrous oxalate and found 8,10-dimethylphenanthridine (50)(22.5%) along with 2-amino-2',4',6'-trimethylbiphenyl (27%).



(49)

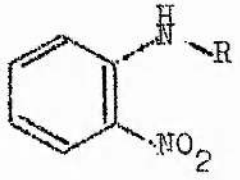


(50)

This reaction has important implications on the mechanism of the deoxygenation which will be discussed later. The same publication also describes the ring closure of o-nitrophenylcyclohexane to carbazole (40%), formation of the latter rather than its tetrahydro-derivative being ascribed to the severity of the reaction conditions (heating with ferrous oxalate at 300°). In a more recent paper[40], Abramovitch describes the preparation of β-carboline (52)(yield not stated) from 4-o-nitrophenylpyridine (51).

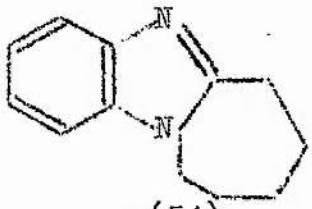
(51) (52)

Suschitzky[41] has prepared several benzimidazoles from N-substituted o-nitroanilines (53) by heating both alone and with ferrous oxalate.

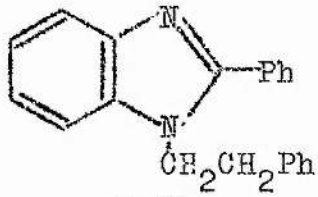


(53)

(53, R=cyclohexyl) gave hexahydroazepino-(1',2'-1,2)benzimidazole (54) in 20% yield on heating with ferrous oxalate. When R=benzyl, the product is the expected 2-phenylbenzimidazole (40%), but when R=$PhCH_2CH_2$-, a mixture of benzimidazole (6%) and 1-phenethyl-2-phenylbenzimidazole (55)(7%) results. Although unable to explain the formation of (54) and (55), Suschitzky does suggest a mechanism for the general ring closure and this will be discussed later.



(54)



(55)

In the course of a study of the reductive coupling of nitro-compounds to give azo-compounds, Kniecik[42] repeated two of the cyclisations already described, obtaining carbazole (37.5%) and benzo[c]cinnoline (46, p. 17)(15.5%) from 2-nitrobiphenyl and 2,2'-dinitrobiphenyl respectively. The reaction conditions employed, however, (ca. 200° in an atmosphere of CO at pressures of 2000-3000 p.s.i.g.) render this particular procedure of

little preparative value.

Photochemical cyclisation of nitro-compounds has been known for some time[43] and more recently, several groups of workers have been active in this field[44]. However, where mechanisms are proposed in these recent studies[44], cycloaddition by a nitro-group to a double bond, and not deoxygenation, is generally postulated as the initial step. One report which may be relevant to the present study is that of Taylor and Garcia[33] who obtained low yields of the pyrrolopyrimidine (43, Ar=C_6H_4(OMe)-p)(facing p. 16) from (42, Ar=C_6H_4(OMe)-p) by irradiating a solution in triethyl phosphite for 114 hours at 3500 Å. It is not clear though, if the reaction is photochemically initiated as they mention some warming of the reaction tube and the product might therefore be arising from the previously mentioned thermal process.

4. Mechanistic Aspects of the Deoxygenation of Nitro- and Nitroso-Compounds.-

Since so many discussions of the mechanism of the deoxygenation of nitro-compounds by tervalent phosphorus compounds postulate the intermediacy of species containing electron deficient nitrogen, Ar-$\dot{N}$:, a survey of the derivation and properties of these intermediates is necessary.

(a) The chemistry of monovalent nitrogen intermediates. There has

been a certain degree of controversy regarding the nomenclature of monovalent nitrogen fragments carrying six electrons in the outer valency shell. They have been referred to variously[45] as nitrenes, azenes, azylenes, imine radicals, imene(German), azacarbenes, and imidogens. Until recently, Chemical Abstracts employed the term imidogen, but nitrene now seems to be acceptable also, and, on euphonic grounds, if no other, will be used in this thesis. This discussion will be concerned principally with aromatic nitrenes.

Thermal or photolytic decomposition of azides has been the most widely investigated route to nitrene intermediates, and almost all the work done to justify their formation was on nitrenes from this source.

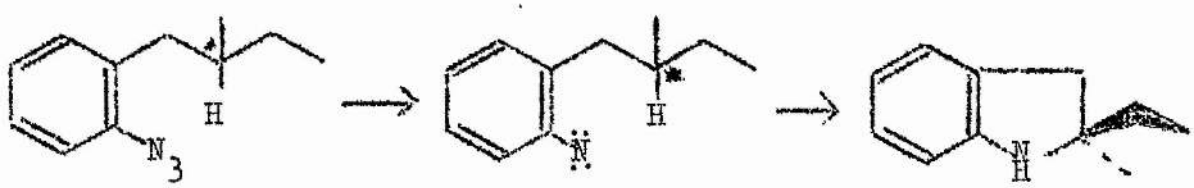
Since it is theoretically possible for a nitrene to exist as either a triplet diradical, R-$\dot{N}\cdot$, or a highly electrophilic singlet species, R-$\ddot{N}$, attempts were made to record e.s.r. spectra of the former state. Smolinsky[46] irradiated dilute solutions of several azides, R-N_3, frozen in a plastic matrix at 77°K. When R=Ph-, o-$CF_3.C_6H_4$-, $C_6H_5SO_2$-, and p-$CH_3.C_6H_4.SO_2$-, resonance signals were observed and assigned to a triplet ground state or a slightly higher excited state. When R=

cyclohexyl, $C_6H_5CH=CH-$, C_2H_5OCO- or C_6H_5OCO-, no signals were obtained and it was suggested that the nitrenes from these azides undergo further reaction too rapidly to permit the formation of a detectable stationary concentration. The signal from phenyl nitrene was stable for at least 18 hours at 77°K after the cessation of irradiation, suggesting that the resonance was in fact due to the ground state. This work has now been extended to include observation of e.s.r. signals from aromatic dinitrenes[47] and alkyl nitrenes[48].

Using a similar technique, Reiser and his co-workers[49] have recorded ultraviolet spectra of several aromatic nitrenes at 77°K. Flash photolysis[50] of 1-azidoanthracene at room temperature and observation of the spectrum produced 4μsec. after excitation showed a peak at 342mμ which was assigned to a triplet nitrene intermediate. The nitrene was estimated to have a half-life of 3-10μsec. at this temperature. The validity of this observation was confirmed by showing the presence of the same absorption band in the low temperature spectrum of photolysed 1-azidoanthracene.

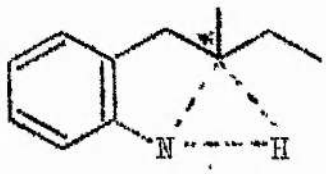
Since it is obviously not possible to generate nitrenes by thermal decomposition of azides under conditions which will permit physical observations to be made, any deductions on the electronic state of the intermediate must be based on its subsequent chemical reactions. Most authors now seem to

favour the view that photolytically generated nitrenes exist in a triplet ground state, whereas pyrolysis of an azide gives a nitrene in an excited singlet state. Provided a suitable substrate is present, the nitrene will react as a singlet species; otherwise, decay to the triplet ground state occurs. Smolinsky[51] examined the thermal decomposition of optically active 2-azido-(2'-methylbutyl)benzene (56) in the vapour phase and in diphenyl ether solution. In each case, the major product was optically active 2-ethyl-2-methylindoline (58)(50% and 43%) which he suggested was formed by direct insertion of a singlet nitrene (57) in the aliphatic C-H bond at the 2-position of the side-chain.

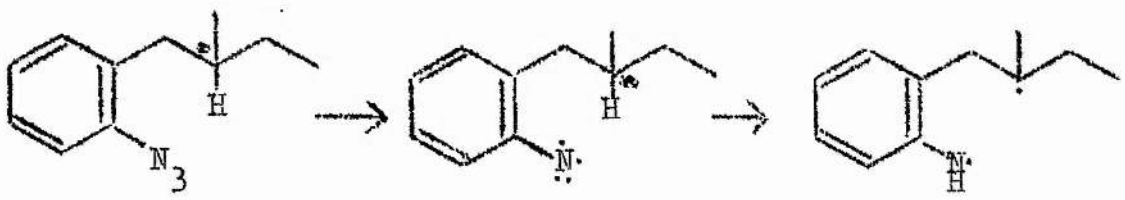


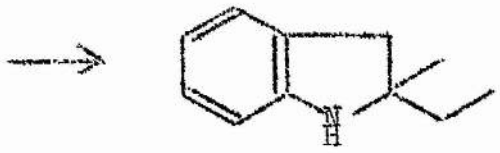
(56) (57) (58)

He felt that a transition state of the form



was involved and dismissed the alternative radical abstraction + recombination process as this would lead to extensive racemisation:





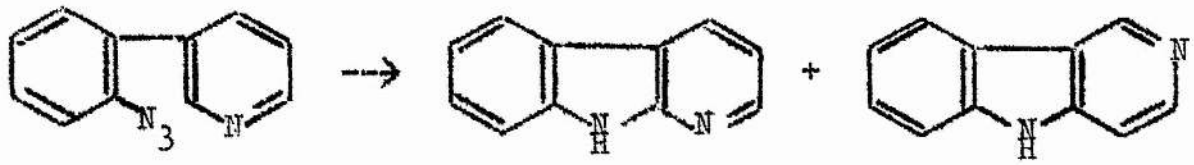
A significantly greater degree of retention of configuration was observed in the vapour phase reaction suggesting, as would be expected, that collisional deactivation of the singlet nitrene, possibly followed by reaction according to the second of the above schemes, takes place more readily in solution.

It seems, though, that even if pyrolysis of an azide does give rise to a singlet nitrene, this will only react as such in the presence of a suitably constituted side-chain since thermal decomposition of p-methoxyphenyl azide in cumene[52] produces substantial yields of bicumyl, a product which can only arise from interaction of the solvent with a radical species.

Similar conclusions have been reached regarding the electronic states of alkyl, acyl, and sulphonyl nitrenes[45,53].

The most characteristic reactions of aromatic nitrenes seem to be the abstraction and insertion processes referred to in the foregoing paragraphs. Addition of an aromatic nitrene to a double bond yielding an aziridine has not been observed directly for nitrenes derived from azide precursors since the azide itself undergoes 1,3-dipolar addition to give a triazoline[54]. However, photolysis or pyrolysis of the triazoline causes loss of nitrogen and formation of the expected aziridine.

(b) Deoxygenation of nitro- and nitroso-compounds. Several workers[20,21,26,39] have noted the striking similarity in products which often arises when corresponding azides are decomposed and nitro- or nitroso-compounds deoxygenated. This parallel led to the postulation of nitrene intermediates in the deoxygenation reaction since these were by then known to occur in azide decompositions. A series of carbazoles has been prepared by photolysis or pyrolysis of 2-azidobiphenyls[55]. 3-o-Azidophenylpyridine (59) on thermal decomposition[56] gave the same mixture of α- (6) and γ-carboline (7) obtained from the nitro- and nitroso-compounds.

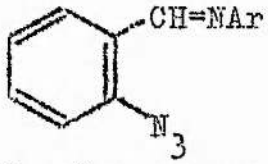


(59) (6) (7)

(60) (4)

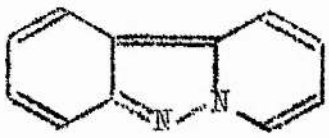
The 2-o-azido-compound (60) was said[56] to give none of the pyrido [1,2-b] indazole (4) found in the deoxygenation of the nitro- and nitroso-compounds, the only product isolated being 2-o-aminophenylpyridine (94%). A reinvestigation[38] of the reaction contradicted this result, however, (4) being obtained

in 57% yield. Thermal decomposition of o-azidoanils (61) has led[57] to high yields of 2-substituted indazoles (13, p.10) and dibenzo-1,3a,4,6a-tetra-azapentalene (15, p. 11) was prepared[58] from 2,2'-diazidoazobenzene before deoxygenation of the nitro-compound was accomplished.

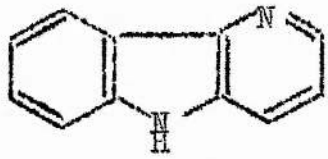


(61)

In his study of the ferrous oxalate deoxygenation of nitro-compounds, Abramovitch[38,39] decides in favour of a nitrene mechanism. He attributes the formation of pyrido[1,2-b] indazole (4) rather than the isomeric ɛ-carboline (62) from 2-o-nitrophenylpyridine to attack by a singlet nitrene on the electron rich pyridine N-atom.



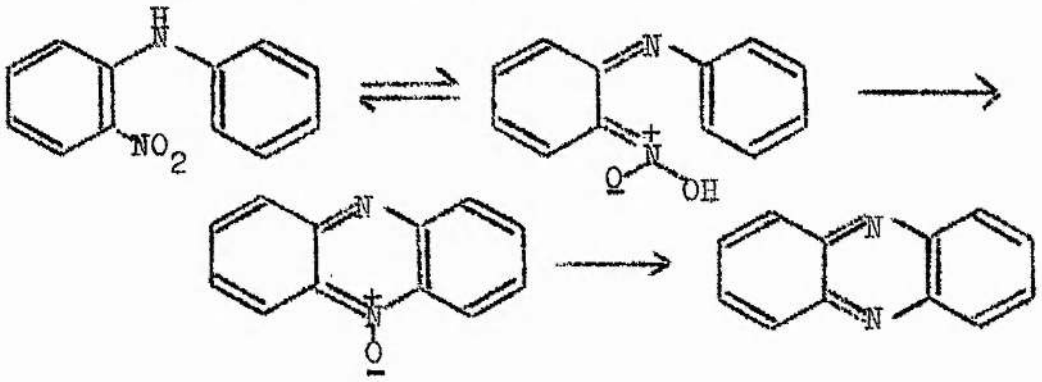
(4)



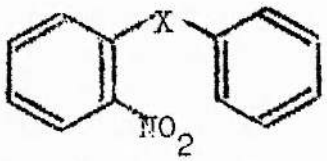
(62)

The isolation of 2-amino-2',4',6'-trimethylbiphenyl and 8,10-dimethylphenanthridine (50, p. 18) arising from the deoxygenation of 2-nitro-2',4',6'-trimethylbiphenyl (49) after being heated with ferrous oxalate was interpreted on the basis of hydrogen abstraction by a triplet nitrene from other molecules of (49) and insertion in an aliphatic C-H bond by a singlet nitrene. Abramovitch explained substantial yields of amino-compound obtained in other deoxygenations in the same way.

Suschitzky[41], however, in his paper on the synthesis of the benzimidazoles (54) and (55)(p. 19) suggests a plausible alternative mechanism based on loss of water from the aci-nitro form of the starting material. Taking the synthesis of phenazine as an example, he formulates this as follows:



He lends support to this mechanism by showing that low yields of phenazine and the benzimidazoles can be obtained by heating in the absence of ferrous oxalate, agreeing with the earlier observation[59] that amine N-oxides deoxygenate under the influence of heat alone. The failure[37] to obtain cyclised products from the compounds (63, X=S, SO_2 or O) is also consistent with this mechanism.

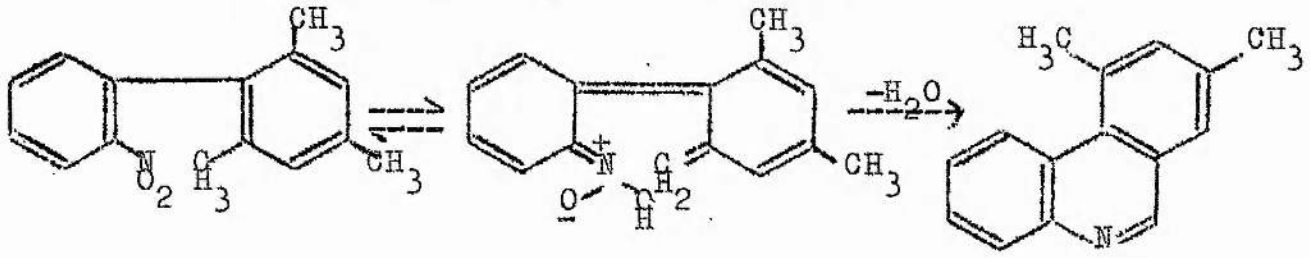


(63)

To explain the formation of carbazole, which would be impossible to accommodate in this mechanism, he postulates thermal cyclisation of the 2-aminobiphenyl (a known reaction[60]) which he found as a by-product in the reaction of 2-nitrobiphenyl with ferrous oxalate. In agreement with this theory, he shows that 2-nitrobiphenyl does not cyclise in the absence of a reducing

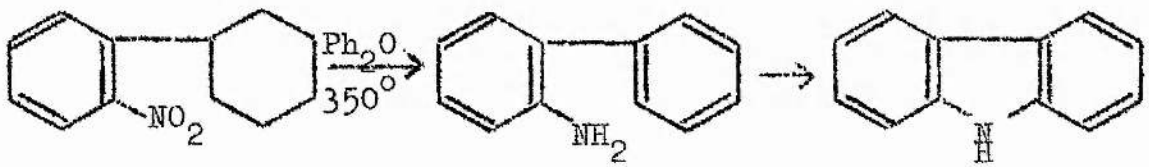
agent. However, there seems little reason why this route should not also be followed for the sulphide, sulphone and ether mentioned above, provided thermal cyclisation of the 2-amino-compounds could be achieved.

In a recent paper[61], Smolinsky has re-examined the reaction of 2-nitro-2',4',6'-trimethylbiphenyl (49) with ferrous oxalate and decided that the intervention of a nitrene is not necessary to justify formation of the phenanthridine (50). Like Suschitzky he visualizes reaction through the aci-nitro form:



(49) (50)

and shows that ferrous oxalate is unnecessary by obtaining (50)(32%) by heating (49) in diphenyl ether for 2 hours at 350°. He has also demonstrated that ferrous oxalate is unnecessary for the conversion of o-nitrophenylcyclohexane to carbazole previously described by Abramovitch[39]. Since an aci-nitro structure cannot be formed in this case, he suggests simultaneous oxidation of the cyclohexane ring and reduction of the nitro-group followed by thermal cyclisation of the 2-aminobiphenyl so formed:

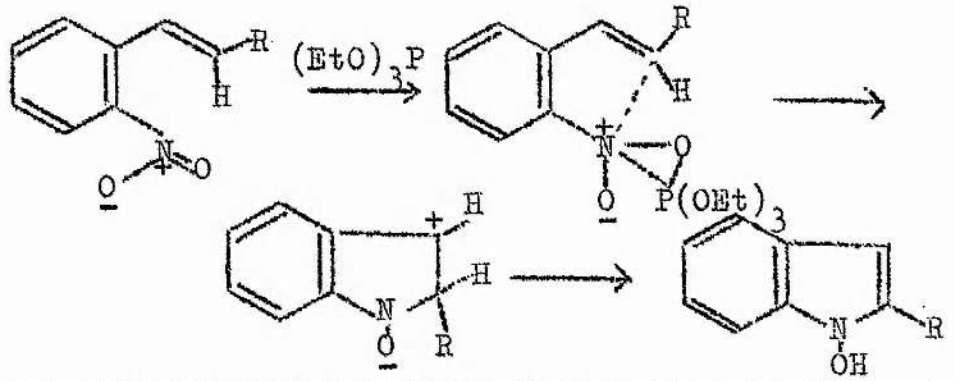


This route requires spontaneous reduction of the nitro- function which, even at 350°, seems a questionable process.

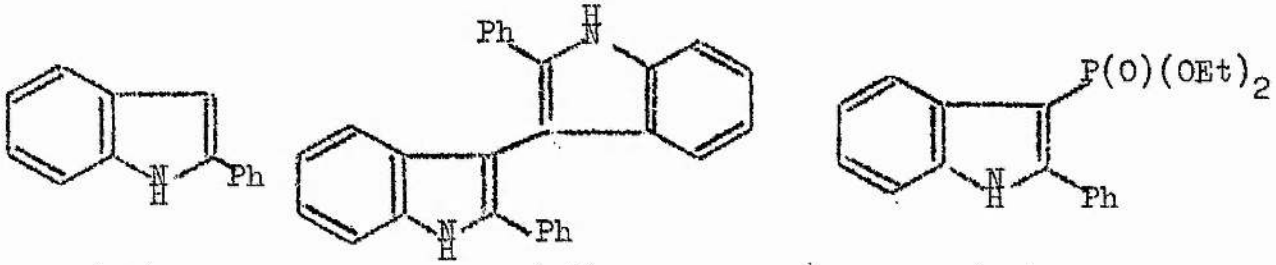
In their paper[20] on the deoxygenation of C-nitroso-compounds by triethyl phosphite, Bunyan and Cadogan attributed the formation of azoxy-compounds from o-nitrosoethylbenzene and p-dimethylaminonitrosobenzene to attack on unchanged nitroso-compound by a nitrene intermediate. In agreement with this hypothesis, increasing the relative amount of triethyl phosphite used in the latter case caused a decrease in the amount of azoxy-compound and an increase in the proportion of triethyl N-p-dimethylaminophenylphosphorimidate, $p\text{-}Me_2N.C_6H_4.N{=}P(OEt)_3$, (1), produced. This latter product could obviously arise from interaction of the nitrene with triethyl phosphite in a reaction similar to the formation of methylenephosphoranes[62] from triphenyl phosphine and carbenes. In his subsequent work[26] on deoxygenation and cyclisation of aromatic nitro-compounds, Cadogan suggested prior reduction of nitro- to nitroso-groups but was able to offer no further evidence for the participation of a nitrene. Proof of the formation of an intermediate nitroso-compound would be very difficult to obtain due to the very great difference in reactivity of nitro- and nitroso-compounds with triethyl phosphite (reaction times ca. 8 hours at 150° and a few minutes at 0° respectively).

As mentioned previously, Sundberg[27] considers that 2-

substituted 1-hydroxyindoles are intermediates in the formation of indoles from β-substituted o-nitrostyrenes. He envisages these as arising from ring closure prior to complete deoxygenation of the nitro-group:

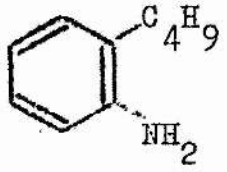


and showed that heating 1-hydroxy-2-phenylindole in a mixture of triethyl phosphite and phosphate gave the products (12, p.10), (18, p. 12) and (19) obtained from trans-o-nitrostilbene. He was unable to do more than speculate on the mechanism of formation of (18) and (19), drawing a somewhat obscure analogy between the formation of (19) and the reaction of triethyl phosphite with dibenzoyl peroxide to form trace amounts of diethyl phenylphosphonate[63] and on this basis postulating a radical mechanism.

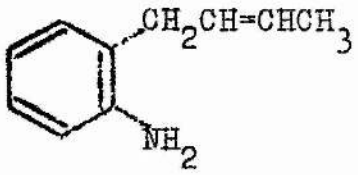


(12) (18) (19)

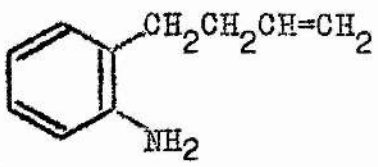
A more likely explanation would seem to be that (19) is in fact diethyl N-(o-styrylphenyl)phosphoramidate (64), a structure



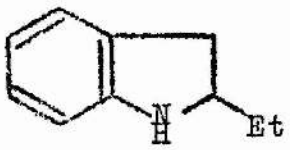
(24)



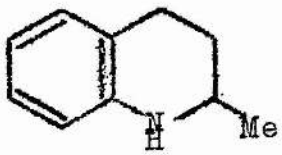
(25)



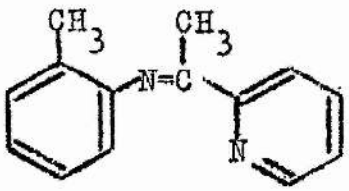
(25)



(26)

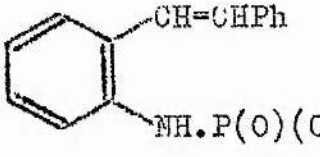


(27)



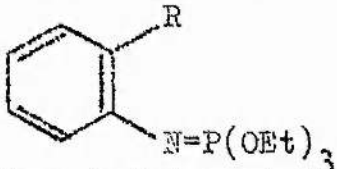
(2)

which appears equally probable from the data which Sundberg presents and which could arise from hydrolysis of the corresponding phosphorimidate.



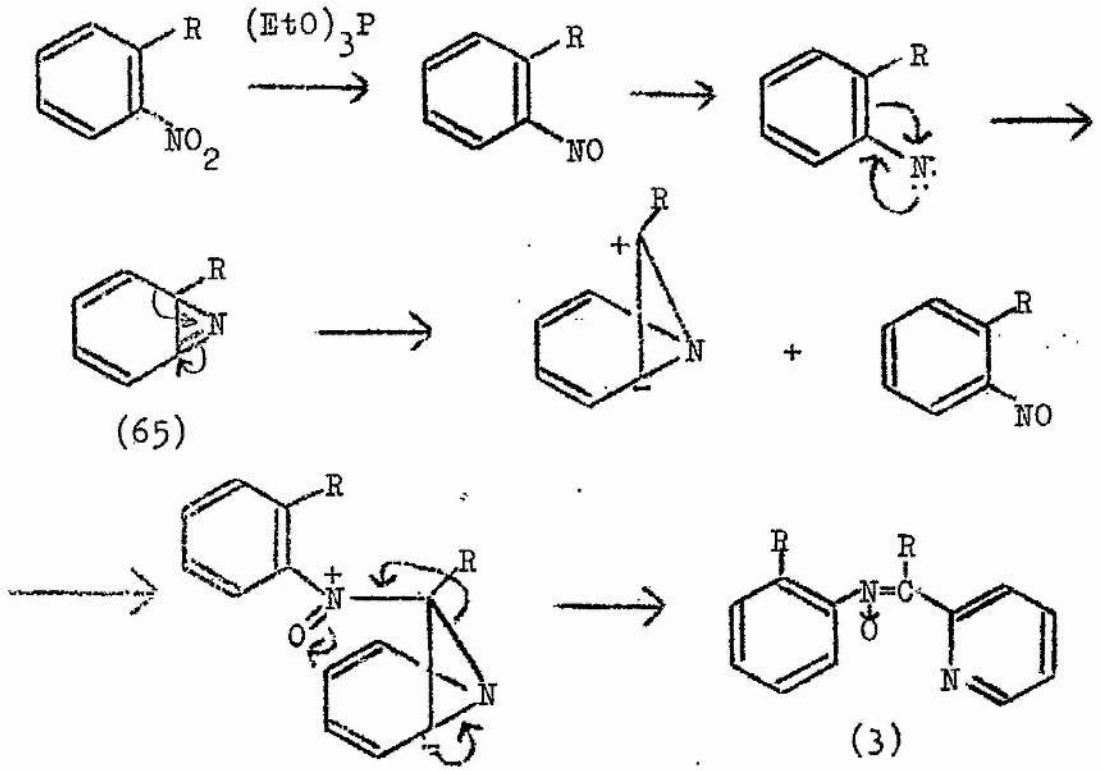
(64)

The products from the deoxygenation of o-alkylnitro- and nitrosobenzenes, however, lead Sundberg[21] to the view that in these reactions a nitrene intermediate is involved. He explains the phosphorimidates (23) which are the main products of deoxygenation of o-alkylnitrobenzenes in the same way as Cadogan[20] (i.e. nitrene attack on triethyl phosphite).

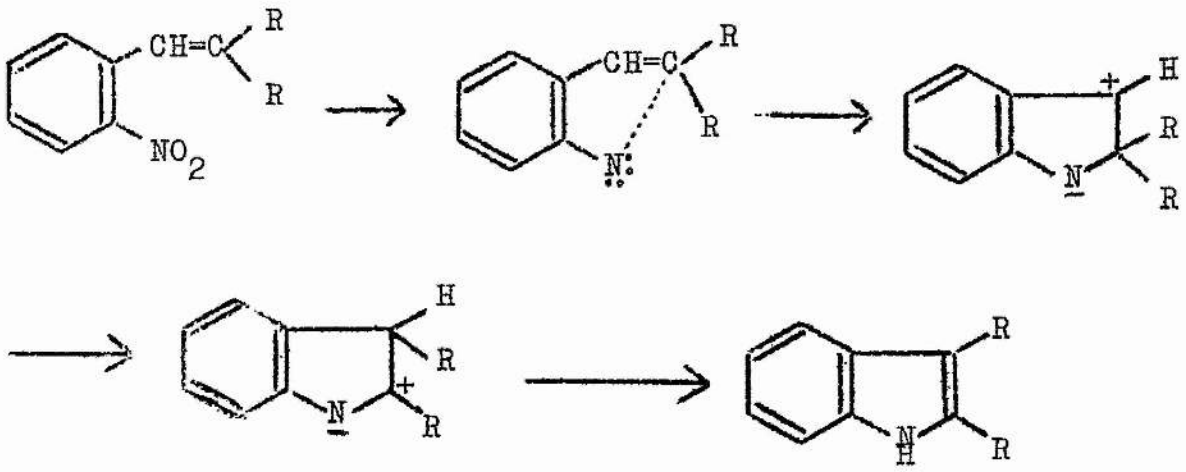


(23)

Attention is drawn to the striking similarity between the composition of the amine fraction and that obtained from pyrolysis of o-azidobutylbenzene which undoubtedly involves a nitrene. The amine (24, p. 14) could arise from extra-molecular hydrogen abstraction, the alkenyl anilines (25) by hydrogen abstraction from the side chain, and the cyclised products (26) and (27) by insertion in a C-H bond of the side chain (see facing page). The o-alkylnitrosobenzenes he examined gave much lower yields of phosphorimidate and products of insertion or abstraction processes, the major products being the acetimidyl-pyridines (2) and the nitrones (3). It is pointed out that this difference in product composition need not preclude the



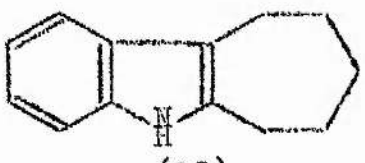
Scheme I



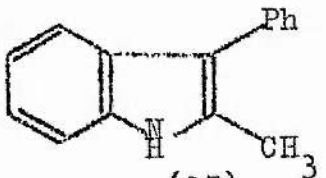
Scheme II

prior reduction of nitro- to nitroso-compounds since there would be a great difference in the environment of such an intermediate nitroso-molecule compared with one present as starting material. In the latter case, there will be a finite concentration of nitroso-compound present, and the products (2) and (3) are explained in terms of a reaction between unreacted nitroso-compound and an intermediate derived directly from a nitrene (see facing page, Scheme I). The azabicycloheptatriene structure (65) has been invoked by other workers[114] and will be discussed later in this thesis. In support of this mechanism, Sundberg observes that increasing the proportion of triethyl phosphite in the reaction mixture causes a progressive decrease in the yield of products (2) and (3).

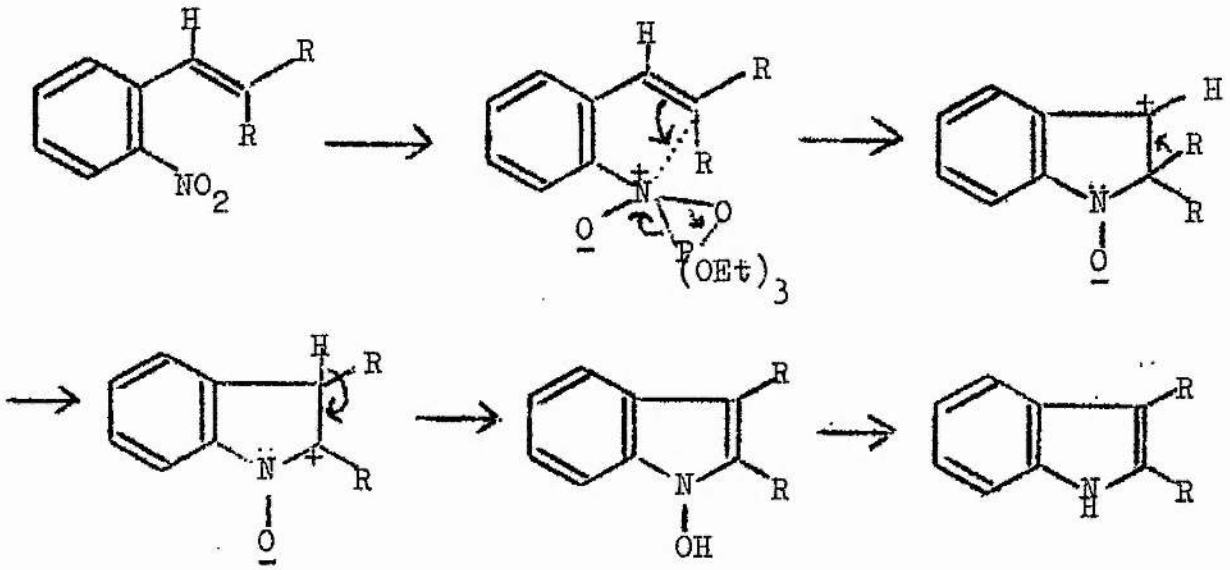
In his latest paper on deoxygenation of β,β-disubstituted o-nitrostyrenes[29], Sundberg points out that the rearranged indoles (32) and (35)(facing p. 15), which are the major products from cyclohexylidene(o-nitrophenyl)methane (28, p. 14) and α-methyl-2'-nitrostilbene (31, p. 15), could arise either by a nitrene mechanism (see facing page, Scheme II) or by a process involving an N-hydroxyindole such as he postulated in the case of β -monosubstituted o-nitrostyrenes (facing p. 33, Scheme III).



(32)

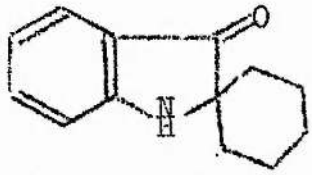


(35)



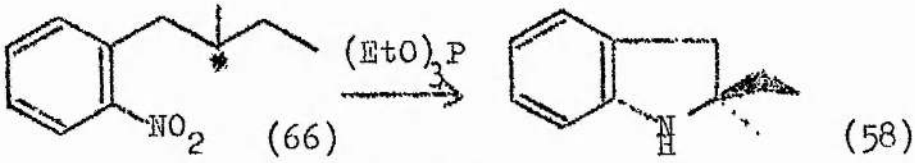
Scheme III

He demonstrates that the indolinone (34, p. 15) from cyclohexylidene(o-nitrophenyl)methane (28) and the corresponding product from β,β-dimethyl-o-nitrostyrene (30) do not arise from oxidation of the indoles, but is only able to make tentative suggestions regarding the mechanism of formation of (34) and the bi-indoline (33).



(34)

In a logical extension of his earlier work on 2-azido-(2'-methylbutyl)benzene (56, p. 23), Smolinsky[61] has studied the deoxygenation of optically active 2-nitro-(2'-methylbutyl)-benzene (66) with triethyl phosphite. He succeeded in isolating a 25% yield of partially (ca. 50%) active 2-ethyl-2-methyl-indoline (58) which compares reasonably with his previous finding that pyrolysis in solution of the azide gave (58)(60%) of 65% optical purity.



The same explanation (insertion in the C-H bond by a singlet nitrene) presumably holds.

When the present work was started, therefore, the deoxygenation of aromatic nitro-compounds by ferrous oxalate had been studied and though a nitrene intermediate had been suggested, a plausible alternative mechanism had been put

forward. Little was known about the mechanism of the apparently related deoxygenation by triethyl phosphite although since this research was started, several papers on this subject have been published and most seem to favour a nitrene intermediate.

EXPERIMENTAL

EXPERIMENTAL

All solvents were redistilled. Benzene, ether, and light petroleum were dried with sodium wire. Unless stated otherwise, starting materials used were commercially available samples and were not further purified.

Elution chromatography was performed on columns of alumina (Spence and Sons, Grade H, 100/120 mesh) or silica gel (Whatman Chromedia SG 31). Thin layer chromatography (t.l.c.) was done on 0.3mm. layers of alumina (Merk, Aluminium Oxide G) or silica gel (Macherey, Nagel and Co., Silica Gel G).

1. Instrumentation.- Melting points were determined using a Kofler hot stage microscope and are corrected. Infrared (i.r.) spectra were normally recorded on a Perkin-Elmer Model 237 Grating Spectrophotometer and, where stated, on a Perkin-Elmer Model 621 instrument. Solids were examined as Nujol mulls and liquids as thin films. Ultraviolet (u.v.) spectra were recorded on a Unicam SP 800 Spectrophotometer. Proton magnetic resonance (p.m.r.) spectra were, in general, recorded on a Perkin-Elmer Model R 10 Nuclear Magnetic Resonance Spectrometer operating at a frequency of 60 Mc./sec., and a probe temperature of 33.5°. A few spectra were run on a Varian HA-100 instrument operating at a frequency of 100 Mc./sec. and a probe temperature of 33°. Chemical shifts are recorded as tau (t) values in

parts per million employing tetramethylsilane as an internal reference (t=10.0). Spectra were determined on 15-20%w/v solutions unless solubility or availability of the sample imposed limitations.

Quantitative gas-liquid chromatography (g.l.c.) was carried out on a Griffin D6 Gas Density Balance Chromatograph using 2 metre $\frac{1}{4}$" o.d. columns. The carrier gas was nitrogen flowing at a rate of 60 ml./minute. Analytical g.l.c. work was done on Perkin-Elmer F 11 or Wilkens 1520B instruments. Both used 2 metre $\frac{1}{8}$" o.d. columns with nitrogen carrier gas and were fitted with flame ionisation detectors.

The use of the gas density balance detector[64] in quantitative work depends on the relationship which exists between the integral response of the detector (the peak area in this case) and the molecular weight of the compound passing through it. The relationship is stated as follows:-

$$n = \frac{kA}{M-m}$$

where n = number of moles injected,

m = molecular weight of carrier gas,

k = constant dependent on the characteristics of the instrument,

A = peak area,

M = molecular weight of compound.

Therefore, for a mixture of compounds and using nitrogen carrier

gas :-

$$\frac{n_1}{n_2} = \frac{A_1(M_2-28)}{A_2(M_1-28)}$$

If one of the compounds is an unreactive internal standard present in measured amount, then the number of moles of the other compound present in a reaction mixture can be calculated at any time by comparing the areas of the g.l.c. peaks of the two compounds. Peak areas were computed by taking the product of the height of the peak and its width at half this height.

Microanalyses were carried out by Bernhardt of Mulheim, Germany, and by Weiler and Strauss, Oxford.

2. Preparation of Materials.- Trimethyl and triethyl phosphite (Albright and Wilson) were allowed to stand over sodium wire for 24 hours and were then distilled in an atmosphere of nitrogen (b.p. 42°/50mm. and 53°/14mm. respectively).

Diethyl methylphosphonite of purity better than 95% was supplied by the Chemical Defence Experimental Establishment, Porton and was used without further treatment.

2-Nitrobiphenyl was purified by elution with light petroleum (b.p. 60-80°) from an alumina column followed by recrystallisation from light petroleum (b.p. 40-60°) and had m.p. 36-37° (lit.,[65] 37°).

2-Nitrodiphenyl ether was redistilled and had b.p. 122°/0.05mm.

0.05mm.

Nitrobenzene and o-ethylnitrobenzene were redistilled (b.p. 90°/14mm. and 110°/14mm. respectively) and their purity was confirmed by g.l.c.

Cumene was deperoxidised by elution from an alumina column immediately before use.

Ethyl N-tetraethylphosphorodiamidite. This compound was prepared according to the procedure described by Michaelis.[66] Ethanol (46 g., 1 mole) was added dropwise with stirring to phosphorus trichloride (137.5 g., 1 mole) cooled to -40°. The resulting ethyl phosphorodichloridite was distilled and the fraction with b.p. 23-25°/14 mm. was collected (56.2 g., 38%). The phosphorodichloridite (55 g., 0.375 mole) was then added dropwise to a solution of diethylamine (109.5 g., 1.5 mole) in light petroleum (b.p. 60-80°)(200 ml.). The mixture was boiled under reflux for 3 hours, cooled, and filtered to remove the amine hydrochloride formed. The solvent was removed on a rotary evaporator and the residual colourless oil distilled in an atmosphere of nitrogen. The material with b.p. 80-84°/14 mm. was collected (48 g., 58%). Michaelis[66] reported a 45% yield and b.p. 105-108°/28 mm. Examination of the product at this stage by g.l.c. (10% silicone oil/135°) showed the presence of several impurities so it was redistilled through a short vigreux column. Four fractions were collected, the last (23.4 g., b.p. 43-45°/0.5 mm.) of which showed only one minor impurity on

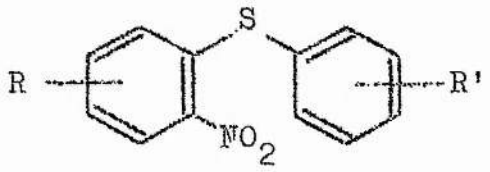
analysis by g.l.c. Microanalysis of a sample from this fraction gave unsatisfactory results, however, (Found: C, 52,6; H, 11.15 Calc. for $C_{10}H_{25}N_2OP$: C, 54.5; H, 11.35%).

Hexaethyl phosphorous triamide. The method described by Michaelis[66] was used. Phosphorus trichloride (30 g., 0.218 mole) in ether (100 ml.) was added dropwise with vigorous stirring to excess diethylamine (105 g., 1.44 mole) in ether (700 ml.). The amine hydrochloride formed was filtered off and the solvent removed on a rotary evaporator. The colourless oil which remained was dissolved in light petroleum (b.p. 40-60°) (200 ml.) causing a further small quantity of hydrochloride to precipitate. This was filtered off once more and the petrol evaporated. Distillation of the product yielded 46.7 g. (86.5%) with b.p. 73-75°/1.0 mm. (Found: C, 58.3; H, 11.75. Calc. for $C_{12}H_{30}N_3P$: C, 58.3; H, 12.15%).

2-Nitrophenyl phenyl sulphide. This compound was prepared by the general method of Galt and Loudon.[67] Sodium hydroxide solution (4.4 g., 0.11 mole, in 4 ml. of water) was added dropwise with shaking to a solution of o-chloronitrobenzene (15.8 g., 0.10 mole) and thiophenol (12.1 g., 0.11 mole) in ethanol (40 ml.). The yellow solution darkened while an exothermic reaction took place. After heating under reflux for 25 minutes, the mixture was cooled and the solid product filtered off and washed with hot water. Recrystallisation from ethanol gave yellow

2-nitrophenyl phenyl sulphide (12.8 g., 55%) with m.p. 80-81° (lit.,[68] 79°).

In this way, a series of 2-nitrodiaryl sulphides (67) was prepared from the appropriate thiophenols and o-chloronitrobenzenes.



(67)

R	R'	M.p.	Lit.	Found(%) C	Found(%) H	Required(%) C	Required(%) H
H	4-CH_3	89°	89-90[69]	-	-	-	-
4-CH_3	H	71-72	72[67]	-	-	-	-
H	4-Cl	93.5	94[70]	-	-	-	-
H	4-$C(CH_3)_3$	65-66	-	67.4	5.9	67.0	6.0
4-Cl	H	82.5-83.5	84[71]	-	-	-	-
6-Cl	H	72	-	53.9	3.05	54.3	3.05
4-NH_2	H	138-139	138[70]	-	-	-	-
H	4-$NHCOCH_3$	197-198	-	58.6	4.2	58.3	4.2
4-$COOC_2H_5$	H	90.5-92	-	59.8	4.05	59.5	4.3
4-$COOC_2H_5$	4-$C(CH_3)_3$	133-134	-	63.0	5.75	63.5	5.9
4-CF_3	H	78.5-79	-	52.65	2.85	52.2	2.7

4-Methyl-2'-nitrodiphenyl sulphoxide. This compound (m.p. 94-96°, 57%) was prepared by oxidation of 4-methyl-2'-nitrodiphenyl sulphide with one molar equivalent of hydrogen

peroxide solution (30% w/w) in glacial acetic acid as described by Gillespie and Passerini.[72]

4-Methyl-2'-nitrodiphenyl sulphone. 4-Methyl-2'-nitrodiphenyl sulphide (4 g., 0.016 mole) in glacial acetic acid (80 ml.) was oxidised by heating on a water-bath for two hours with excess (50 ml.) hydrogen peroxide solution (30% w/v). On cooling the product separated as colourless needles. Recrystallisation from light petroleum (b.p. 60-80°) yielded 3.73 g. (83%), m.p. 156-158° (Found: C, 56.0; H, 4.05. $C_{13}H_{11}NO_4S$ requires C, 56.3; H, 4.0%).

2-Nitrophenyl phenyl selenide. This was prepared by the method described for the corresponding sulphide, using selenophenol in place of thiophenol. The selenide had m.p. 91° (lit.,[73] 91°) on crystallisation from ethanol.

10-Ethyl-2-methylphenothiazine. This compound was prepared from 2-methylphenothiazine, ethanol and ethyl bromide according to the procedure of Gilman, Van Ess and Shirley.[74] The yield of crude product was 91% and elution of a sample from an alumina column with light petroleum (b.p. 40-60°) gave colourless crystals, m.p. 131-132°.

2'-Nitrochalcone. This compound (m.p. 126-128°, 58%) was prepared by condensation of o-nitroacetophenone with benzylidene diacetate in the presence of alkali as described by Davey and Gwilt,[75] who reported m.p. 124°. Other workers,[76] however,

have reported values as high as 129°.

3-Phenylanthranil. A modification of the procedure described by Kliegl[77] was used to prepare this compound. o-Nitrobenzaldehyde (5 g.), benzene (20 g.) and concentrated sulphuric acid (20 g.) were mixed together in a flask cooled in ice-water and stirred for 24 hours. The mixture was then treated with water (100 ml.) and extracted with ether (2 x 150 ml.). The ether solution was dried ($MgSO_4$) and sufficient alumina was added to adsorb the dissolved material. Elution from an alumina column with light petroleum (b.p. 40-60°)/20% benzene gave three fractions (2.1 g.) which were shown by g.l.c. (1.5% N.P.G.S./200°) (see Appendix for key to stationary phase abbreviations) to contain a major product and an impurity. These fractions were combined and rechromatographed. Light petroleum/10% benzene eluted a first fraction (0.63 g.) which was shown by g.l.c. to be pure, but subsequent fractions contained the impurity previously mentioned. The material from the first fraction (m.p. 48-49°, 9.8%) was recrystallised from light petroleum (b.p. 40-60°) to give m.p. 49.5-51.5° (lit.,[78] 52-53°)

2-Aminobenzophenone. Since 2-nitrobenzophenone was not available, an alternative route to this compound had to be found. Although it was by no means the most efficient method, the procedure described by Chattaway[79] was chosen on the grounds of simplicity. 2-Aminobenzophenone (m.p. 104-105°, <1%) was thus obtained (lit.,[80] 105-106°).

2'-Nitro-2-stilbazole. This compound (m.p. 99-100°, 45%) was prepared by condensation of o-nitrobenzaldehyde with 2-picoline in the presence of acetic anhydride as described by Horwitz[81] who reported m.p. 102-103°. Microanalysis was satisfactory, however, (Found: C, 68.9; H, 4.4. Calc. for $C_{13}H_{10}N_2O_2$: C, 69.0; H, 4.45%) and values as low as 95-96° have been reported[82] for the m.p.

α-(o-Nitrophenyl)-2-chlorocinnamic acid. This compound was prepared by condensation of o-nitrophenylacetic acid (1.0 mole) with o-chlorobenzaldehyde (1.0 mole) in warm acetic anhydride (1000 ml.) and triethylamine (1.1 mole) as described by Pailer and his co-workers.[83] The product so obtained (66%) had m.p. 220-222° (lit.,[83] 225°)(Found: C, 58.8; H, 3.2. Calc. for $C_{15}H_{10}ClNO_4$: C, 59.3; H, 3.3%).

3-(o-Nitrophenyl)coumarin. This compound (47%) was made in the same way using salicylaldehyde instead of o-chlorobenzaldehyde. The material so obtained was impure and even after recrystallisation from glacial acetic acid and then ethanol (twice), melting still commenced at 155° although most of the sample melted in the range 172-173°. Pailer[83] reported m.p. 176-177°.

2-Nitro-2',4',6'-trimethylbiphenyl. o-Nitroaniline (10.0 g., 0.0725 mole) was dissolved in hot (90°) mesitylene (70 ml.). This solution was added dropwise to a solution of pentyl nitrite

(11.9 g., 0.102 mole) in mesitylene (200 ml.) and the mixture heated with stirring on a water-bath for two hours. The stirrer and dropping funnel were then removed and the flask heated at 140° for a further two hours. After removal of the mesitylene by distillation (14 mm.), the residue was distilled under vacuum and the fraction with b.p. 118-124°/0.03 mm. collected (5.06 g., 29%)(Found: C, 74.3; H, 6.2. Calc. for $C_{15}H_{15}NO_2$: C, 74.65; H, 6.3%). Recrystallisation from aqueous ethanol gave orange crystals with m.p. 55-56° (lit.,[61] 42-43°). The p.m.r. spectrum in carbon tetrachloride solution was as expected for this structure: 3-H, quartet (1 proton) at t=2.03 ($J_{3,4}$= 6.5 c.p.s., $J_{3,5}$≑ 3.0 c.p.s.); 4'-CH_3, singlet (3 protons) at t= 7.7; 2'- and 6'-CH_3, singlet (6 protons) at t=8.07. The remaining aromatic protons gave a complex pattern in the range t=2.3-3.2.

2-Azido-2',4',6'-trimethylbiphenyl. This compound (87%) was prepared from the amine as described by Smolinsky.[84] The crude product was eluted from an alumina column with light petroleum (b.p. 40-60°) to yield a yellow oil which had a strong peak at 2110 $cm.^{-1}$ in its infrared spectrum due to the $-N_3$ group.

Triethyl N-phenylphosphorimidate. This compound (b.p. 92° /0.03 mm., 85%) was prepared from triethyl phosphite and phenyl azide according to the method of Kabachnik and Gilyarov.[85] The

product had an infrared peak at 1360 cm.$^{-1}$ which has been attributed[86] to the P=N bond in this type of compound. The p.m.r. spectrum showed signals due to the following protons: $POCH_2$, quintet (six protons) at t=6.0; $POCH_2CH_3$, triplet (nine protons) at t=8.76; and a complex absorption (five protons) in the aromatic region (t=2.8-3.5).

Triethyl N-(o-ethylphenyl)phosphorimidate. This compound (b.p. 90-100°/0.05 mm., 87%) was prepared by the preceding method and had an i.r. peak at 1360 cm.$^{-1}$ (P=N) and p.m.r. signals as follows: $POCH_2$, quintet (six protons) at t=5.93; $POCH_2CH_3$, triplet (nine protons) at t=8.70; o-CH_2-, quartet (two protons) at t=7.36; o-CH_2CH_3, triplet (three protons) at t=8.83; and the aromatic protons, complex pattern (four protons) at t=2.9-3.6.

Triethyl N-(2',4',6'-trimethylbiphenyl-2-yl)phosphorimidate. The same method was used to prepare this compound (b.p. 105-115°/0.01 mm., 86%)(Found: C, 67.0; H, 8.1; N, 3.95. $C_{21}H_{30}NO_3P$ requires C, 67.25; H, 8.1; N, 3.7%).

Diethyl N-ethyl-N-phenylphosphoramidate. This compound (b.p. 92-94°/0.03 mm., 92%) was obtained as a yellow oil by heating triethyl N-phenylphosphorimidate under reflux with ethyl iodide as described by Kabachnik and Gilyarov.[85] There was no i.r. peak due to P=N in the product and the p.m.r. spectrum showed the expected signals: $POCH_2$-, quintet (four protons) at t=6.02 ;

$POCH_2\underline{CH_3}$, triplet (six protons) at t=8.79; $-N\underline{CH_2}-$, overlapping quartets (two protons)($J_{PH}\doteqdot$10.4 c.p.s.) at t=6.3 and t=6.45; $-NCH_2\underline{CH_3}$, triplet (three protons) at t=8.9; aromatic protons, broad singlet (five protons) at t=2.8.

3. Deoxygenation of 2-Nitrobiaryl Sulphides.- Reaction of 4-methyl-2'-nitrodiphenyl sulphide with triethyl phosphite. 4-methyl-2'-nitrodiphenyl sulphide (2.45 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were boiled under reflux (156°) in an atmosphere of nitrogen for 12 hours. The mixture rapidly turned dark brown. The excess of triethyl phosphite and the triethyl phosphate formed in the reaction were removed by distillation at 0.05 mm. from a flask packed with glass wool. The products were leached from the glass wool with acetone which was then evaporated on a water-bath. The dark brown semi-solid residue was chromatographed on alumina. Elution with light petroleum (b.p. 40-60°) gave five fractions containing a total of 0.62 g. of a colourless crystalline solid. Small amounts of ether were now added to the eluting solvent and light petroleum/30% ether eluted a yellow powdery solid (0.76 g.). Ethanol eluted black tar (1.2 g.).

The colourless product had m.p. 131-133° on recrystallisation from light petroleum (b.p. 60-80°)(Found: C, 74.3; H, 6.3; S, 13.35. $C_{15}H_{15}NS$ requires C, 74.6; H, 6.3; S, 13.3%). Its

ultraviolet spectrum was very similar to that of the second product (λmax., 256 and 255 mμ; ε, 40050 and 44240 respectively). The p.m.r. spectrum showed signals which might be ascribed to a methyl group (singlet at t=7.8), an ethyl group attached to oxygen or nitrogen (quartet at t=6.17 and triplet at t=8.61 , J=7 c.p.s.), and seven aromatic protons (complex at t=2.15). On this basis, the structure 10-ethyl-2-methylphenothiazine (25%) was assigned to the product. The melting point was undepressed on mixing with a sample prepared by ethylation of the second product of this reaction.

The yellow product had the physical characteristics expected for 2-methylphenothiazine (36%), and the infrared spectrum had a sharp peak at 3290 cm.$^{-1}$ due to the N-H bond. However, the material obtained after vacuum sublimation (85°/ 0.1 mm.) and recrystallisation from carbon tetrachloride was unsatisfactory with respect to both m.p. (176-177°, lit.,[87] 187-188°) and analysis (Found: C, 71.8 ; H, 5.2 . Calc. for $C_{13}H_{11}NS$: C, 73.2 ; H, 5.2%).

The experiment was repeated using a fresh sample of the sulphide and heating for 12 hours at 140°. In this case, the products were 10-ethyl-2-methylphenothiazine (3%)(m.p. 132-133°) and 2-methylphenothiazine (50%)(m.p. 176-177°). Examination of the major product by t.l.c. (silica gel/benzene) showed a very faint spot behind that due to the phenothiazine.

Reaction of 2-methylphenothiazine with triethyl phosphate. 2-Methylphenothiazine (0.213 g., 0.001 mole) obtained from the previous experiment and triethyl phosphate (0.73 g., 0.004 mole) were heated at 169° in the apparatus illustrated facing page 78 . The course of the reaction was followed by g.l.c. (2% N.P.G.S./215°) and it was shown that after 15 hours, conversion to the 10-ethyl-2-methylphenothiazine formed in the previous reaction was almost complete.

Reaction of 2-nitrophenyl phenyl sulphide with triethyl phosphite. The sulphide (2.31 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were boiled under reflux in an atmosphere of nitrogen for 12 hours. Triethyl phosphate and the excess phosphite were removed by distillation under reduced pressure and the residue was chromatographed on alumina. Elution with light petroleum (b.p. 40-60°) gave discoloured oily crystals which on recrystallisation from light petroleum (b.p. 60-80°) yielded 10-ethylphenothiazine (0.054 g., 2.4%), m.p. 101.5-102.5° and mixed m.p. with an authentic[74] sample 101-102°. Light petroleum/30% ether eluted cream coloured powdery phenothiazine (1.07 g., 54%), m.p. and mixed m.p. 183-185° (lit.,[88] 185°).

Reaction of 2-nitro-4'-t-butyldiphenyl sulphide with triethyl phosphite. The sulphide (2.87 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were heated under reflux

for 10 hours in an atmosphere of nitrogen. After removal of triethyl phosphate and the excess phosphite, the residue was chromatographed on alumina. Light petroleum (b.p. 40-60°)/10% ether eluted an oily yellow solid (0.152 g.) which after rechromatography on a short column had m.p. 105-109° (0.13 g.). Recrystallisation from light petroleum (b.p. 60-80°) gave colourless crystals of 10-ethyl-2-(t-butyl)phenothiazine (4.6%), m.p. 120-121°, (Found: C, 77.05; H, 7.8. $C_{18}H_{21}NS$ requires C, 76.4; H, 7.5%). The p.m.r. spectrum in carbon tetrachloride was compatible with this structure, showing the following signals: $-NCH_2CH_3$, quartet (2 protons) at t=6.09 and triplet (3 protons) at t=8.59 ; $-CMe_3$, singlet (9 protons) at t=8.72 ; and the aromatic protons, complex pattern (7 protons) centred at t= 3.05.

Ether eluted cream coloured 2-(t-butyl)phenothiazine (1.38 g., 55%), m.p. 158-159° (lit.,[89] 166-167°)(Found: C, 75.4; H, 6.6 . Calc. for $C_{16}H_{17}NS$: C, 75.25 ; H, 6.7%). The infrared spectrum had an N-H stretching vibration at 3360 $cm.^{-1}$.

Reaction of 4-carbethoxy-2-nitro-4'-(t-butyl)diphenyl sulphide with triethyl phosphite. The sulphide (3.59 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were heated for 12 hours, with stirring, at 120° in an atmosphere of nitrogen. Triethyl phosphate and the excess phosphite were removed by distillation under reduced pressure and the residue was chrom-

atographed on alumina. Light petroleum/ether mixtures eluted traces of yellow oily material. Ether eluted a yellow crystalline solid (1.76 g.) which on recrystallisation from ethanol afforded 2-carbethoxy-8-(t-butyl)phenothiazine (54%), m.p. 181-183° (Found: C, 69.4 ; H, 6.3 . $C_{19}H_{21}NO_2S$ requires C, 69.75 ; H, 6.5%). The infrared spectrum showed an N-H stretching vibration at 3355 cm.$^{-1}$ and confirmed the absence of a nitro-group. The p.m.r. spectrum in deuterochloroform was compatible with the assigned structure, showing the following signals: $-OCH_2-$, quartet (2 protons) at t=5.65 ; $-OCH_2CH_3$, triplet (3 protons) at t=8.62 ; $-CMe_3$, singlet (9 protons) at t=8.74 ; aromatic protons and -NH- , complex pattern (7 protons) at t=2.6-3.6 .

Reaction of 4-methyl-2-nitrodiphenyl sulphide with triethyl phosphite. The sulphide (2.45 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were heated under nitrogen for 12 hours at 130°. The excess triethyl phosphite and triethyl phosphate formed were distilled off and the residue chromatographed on alumina. The following fractions were collected:

1. Colourless crystals (0.068 g.), eluted with light petroleum/5% ether.

2-3. A hard brown glass (0.29 g.) eluted with light petroleum/10% ether.

4-5. An impure brown solid (0.25 g.) eluted with light petroleum/50% ether.

6-9. Tars (0.65 g.) eluted with ether/50% methanol.

Fraction 1. was recrystallised from light petroleum (b.p. 60-80°) to give material with m.p. 149-150°. The p.m.r. spectrum in carbon tetrachloride solution was as would be expected for 10-ethyl-2-methylphenothiazine (2.8%), showing the following signals: $-NCH_2-$, quartet (2 protons) at t=6.14 ; $-NCH_2CH_3$, triplet (3 protons) at t=8.62 ; $2-CH_3$, singlet (3 protons) at t=7.77 ; and the aromatic protons, complex pattern (7 protons) centred at t=3.15. However, mixed m.p. with the analogous product from 4-methyl-2'-nitrodiphenyl sulphide was 112-116°. The p.m.r. spectrum was very similar to that of this other product (see p.48), but the signals due to the alkyl protons were all shifted downfield by approximately 0.06 p.p.m. In addition, the infrared spectra, while also very similar, showed differences of detail. In particular, peaks of medium intensity at 852 and 1490 $cm.^{-1}$ present in the spectrum of the previous compound were absent from that of the compound isolated from this reaction.

Fractions 4-5. were sublimed (90°/0.1 mm.) to give an impure powdery yellow solid (0.22 g.). Recrystallisation from carbon tetrachloride gave white powdery crystals of 2-methylphenothiazine (10.3%), m.p. 186-188° (lit.,[87] 187-188°). The

infrared spectrum was again not absolutely identical with that of the corresponding product from 4-methyl-2'-nitrodiphenyl sulphide. A low intensity peak in the spectrum of the phenothiazine from the earlier experiment (888 $cm.^{-1}$) was absent and a strong peak at 810 $cm.^{-1}$ was shifted to 797 $cm.^{-1}$ in the spectrum of the phenothiazine from this reaction.

Reaction of 4-chloro-2'-nitrodiphenyl sulphide with triethyl phosphite. The sulphide (2.65 g., 0.01 mole), t-butylbenzene (10 ml.) and triethyl phosphite (4.0 g., 0.03 mole) were stirred for 12 hours at 135° in an atmosphere of nitrogen. The solvent, triethyl phosphate and excess triethyl phosphite were removed by distillation and the residue chromatographed on alumina, the following fractions being collected:

1. A colourless oily film (0.017 g.) eluted with light petroleum (b.p. 40-60°).

2-4. White solids (0.021 g.) eluted with light petroleum /10% benzene.

5-6. Yellow crystals (0.86 g.) eluted with benzene.

7-8. Tars (0.034 g.)

9-11. Thick oils with solid suspended in them (0.044 g.) eluted with benzene/10% ether.

12-14. Tars (0.85 g.) eluted with methanol.

Fractions 2-4. had m.p. 99-114° and t.l.c. (silica gel/light petroleum) showed six spots.

Fractions 5-6. were recrystallised from ethanol to give m.p. 93-94°, undepressed on mixture with the starting material.

Fractions 9-11. were treated with carbon tetrachloride (2 ml.) which dissolved the oily material. The solid (0.0025 g.) was separated and sublimed (120°/0.1 mm.) to give 2-chlorophenothiazine (0.1%), m.p. 194-195° (lit.,[90] 196-198°).

Reaction of 4-chloro-2-nitrodiphenyl sulphide with triethyl phosphite. The sulphide (2.65 g., 0.01 mole) and phosphite (6.65 g., 0.04 mole) were heated in the usual way for 12 hours at 140°. After distillation of the phosphorus compounds, the residue was chromatographed on alumina and the following fractions collected:

1. A white solid (0.0037 g.) eluted with light petroleum.
2. A brown powder (0.14 g.) eluted with benzene.
3. A tarry film (0.03 g.) eluted with benzene/10% ether.
4. A yellow crystalline solid (0.068 g.) eluted with benzene/50% ether.

5-6. Brown solids (0.06 g.) eluted with benzene/75% ether.

7-12. Tars (1.9 g.) eluted with ethyl acetate and methanol.

T.l.c. examination of fraction 1. (silica gel/light petroleum) showed seven spots and no further work was done on it.

Fraction 2. could not be crystallised or sublimed. Its infrared spectrum showed only a few very broad peaks.

Fraction 3. was sublimed (115°/0.1 mm.) to give a pale yellow solid. It had peaks at 3390 and 3480 cm.$^{-1}$ in its infrared spectrum, indicating the presence of an NH_2 group and it was identified as 2-amino-4-chlorodiphenyl sulphide (2.9%), m.p. 60-61°(lit.,[91] 63-65°). The infrared spectrum was superimposable on that of an authentic sample prepared by reduction of starting material with tin and HCl.

Fractions 5-6. were sublimed (125°/0.1 mm.) and recrystallised from carbon tetrachloride to yield 2-chlorophenothiazine (2.5%), m.p. 202-203° (lit.,[90] 196-198°). The infrared spectrum showed an N-H stretching vibration at 3340 cm.$^{-1}$ and mixed m.p. with the phenothiazine from 4-chloro-2'-nitrodiphenyl sulphide was 194-196°.

Reaction of 2-nitro-4-trifluoromethyldiphenyl sulphide with triethyl phosphite. The sulphide (2.99 g., 0.01 mole) and phosphite (6.65 g., 0.04 mole) were heated under nitrogen for 12 hours at 140°. After distilling off the phosphorus compounds, the residue gave the following fractions after chromatography on alumina:

1-2. Brown oils (0.03 g.) eluted with light petroleum/10% benzene.

3-6. Brown solids (0.10 g.) eluted with benzene/20% ether.

7-9. Brown oils (0.084 g.) eluted with ether.

10. Tar (1.18 g.) eluted with methanol.

T.l.c. (silica gel/light petroleum) on fractions 1-2. showed seven spots.

Fractions 3-6. were sublimed (120°/0.1 mm.) to yield a compound believed to be 2-trifluoromethylphenothiazine (0.35%), m.p. 189°. The infrared spectrum had an N-H stretching vibration at 3380 cm.$^{-1}$, but the results of microanalysis were unsatisfactory (Found: C, 60.2 ; H, 3.0 . $C_{13}H_8F_3NS$ requires C, 58.5 ; H, 3.0%).

Reaction of 4-amino-2-nitrodiphenyl sulphide with triethyl phosphite. The sulphide (0.83 g., 0.0034 mole) and triethyl phosphite (3.32 g., 0.02 mole) were heated under nitrogen for 12 hours at 130°. Triethyl phosphite and phosphate were distilled off and the residue chromatographed on alumina, giving the following fractions:

1-2. Red solids (0.009 g.) eluted with benzene.

3. A red oil (0.029 g.) eluted with benzene.

4-9. Crimson solids (0.62 g.) eluted with benzene/20% ether.

10-13. Tars (0.73 g.) eluted with ether/methanol mixtures.

Fractions 1-2. had m.p. 91-93°. The infrared spectrum showed an N-H stretching vibration at 3300 cm.$^{-1}$ and the presence of strong absorptions at 1310 and 1525 cm.$^{-1}$ suggested that the nitro-group was still intact. On this basis, the structure 4-ethyl-

amino-2-nitrodiphenyl sulphide was tentatively suggested.

Fraction 3. was shown by t.l.c. (alumina/benzene) to be a mixture of the solids occurring in fractions 2. and 4.

Fractions 4-9. were starting material as shown by m.p. (134-136°), mixed m.p. (135-137°) and infrared spectrum.

Reaction of 4-acetamido-2'-nitrodiphenyl sulphide with triethyl phosphite. The sulphide (2.88 g., 0.01 mole) and phosphite (6.65 g., 0.04 mole) were heated under nitrogen for 11 hours at 140°. After distilling off the phosphorus esters, the residue was chromatographed on alumina. Light petroleum and benzene did not elute any product, and ether gave only a trace of a yellow oily film. Elution with ether/methanol mixtures gave a series of thick dark oils from which no solid product could be separated.

Reaction of 4-carbethoxy-2-nitrodiphenyl sulphide with triethyl phosphite. The sulphide (3.05 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were heated for 12 hours at 125° under nitrogen. The phosphate and phosphite were distilled off and the residue chromatographed as before. Ether eluted a series of brown oils (2.29 g.) which were shown by g.l.c. (10% P.E.G.A./150°) to contain triethyl phosphate. Ether/methanol mixtures gave tars (1.19 g.).

Reaction of 4-methyl-2'-nitrodiphenyl sulphide with triphenylphosphine. The sulphide (2.45 g., 0.01 mole) and

triphenylphosphine (10.48 g., 0.04 mole) were heated under nitrogen for 12 hours at 150°. The mixture rapidly turned dark brown, and at the end of this time, it set solid on cooling. An aliquot (2.9 g.) was removed, dissolved in a few ml. of benzene and chromatographed on alumina. Light petroleum/10% ether eluted colourless crystals of triphenylphosphine (0.38 g.), m.p. and mixed m.p. 77-79°. Elution with ether gave dark brown oils (0.53 g.) and methanol gave a solid black tar (1.21 g.). Triphenylphosphine oxide was not isolated although t.l.c. (silica gel/ether) had shown that this was formed.

Reaction of 4-methyl-2'-nitrodiphenyl sulphide with tributylphosphine. The sulphide (2.45 g., 0.01 mole) and tri-n-butylphosphine (8.08 g., 0.04 mole) were warmed gradually in an atmosphere of nitrogen. The mixture began to go brown at 60° and heating was continued at 65° for 18 hours. On cooling, a black semi-solid tar was obtained and examination of a sample by g.l.c. (2% N.P.G.S./225°) showed that no phenothiazine had been formed.

Attempted reaction of 2-nitrophenyl phenyl sulphide with phosphorus trichloride. The sulphide (2.31 g., 0.01 mole) and phosphorus trichloride (6.87 g., 0.05 mole) were boiled under reflux (76°) in an atmosphere of nitrogen for 15 hours. T.l.c. (silica gel/benzene) of the reaction mixture showed only starting material. The mixture was dissolved in ether (80 ml.), and water

(50 ml.) was added gradually. After shaking, the ether layer was separated, dried ($MgSO_4$), and evaporated. Starting material (2.21 g.), m.p. and mixed m.p. 80-81°, was recovered after recrystal-lisation from ethanol.

The reaction was then repeated with sulphide (1.15 g.) and chloride (3.4 g.) heated in a sealed tube at 170° for 36 hours. The mixture went black, but on opening the tube, t.l.c. showed that no phenothiazine was formed. Working up as described in the previous paragraph yielded starting material (0.64 g.), m.p. and mixed m.p. 79-81°.

Reaction of 2-nitrophenyl phenyl sulphide with hexaethyl phosphorous triamide. The sulphide (2.31 g., 0.01 mole) and hexaethyl phosphorous triamide were heated on a water-bath for 6 hours in an atmosphere of nitrogen. After removing the phosphorus compounds by vacuum distillation, the residue was dissolved in a few ml. of benzene and chromatographed on alumina. The following fractions were eluted:

1-2. Brown oils (0.22 g.) eluted with benzene.

3-5. Oily yellow-brown crystals (0.44 g.) eluted with benzene/15% ether.

6-8. Dark brown oils (0.15 g.) eluted with ether.

9-11. Tars (2.28 g.) eluted with methanol.

T.l.c. (silica gel/benzene) alongside an authentic sample showed that there was no phenothiazine present in any fraction.

Fractions 3-5. were dissolved in hot ethanol and on cooling, yellow crystals of starting material (0.28 g.) separated, m.p. 75-78° and mixed m.p. 74-78°.

Reaction of 2-nitrophenyl phenyl sulphide with diethyl methylphosphonite. The sulphide (2.31 g., 0.01 mole) and diethyl methylphosphonite (5.45 g., 0.04 mole) were heated on a water-bath under nitrogen for 2 hours. The mixture went very dark brown almost immediately. After distilling off the phosphonate and excess phosphonite, the residue was chromatographed as before:

1. A light brown powder (0.04 g.) eluted by light petroleum/10% ether.

2-3. Yellow oils (0.11 g.) eluted by light petroleum/20% ether.

4-9. Dark brown oils (0.27 g.) eluted with ether.

10-13. Tars (1.71 g.) eluted by methanol.

Fraction 1. melted over a wide range (92-113°) and t.l.c. (silica gel/benzene) showed the presence of three components, one of which had the same R_f value as an authentic sample of phenothiazine.

Fractions 2-3. were shown by t.l.c. to contain starting material and by g.l.c. (10% P.E.G.A./150°) to contain diethyl methylphosphonate.

Reaction of 2-nitrophenyl phenyl sulphide with diethyl methylphosphonite in hexadecane. The nitro-compound (2.31 g.,

0.01 mole) was dissolved in warm n-hexadecane (34 g., 0.15 mole) and heated to 140° under nitrogen. The phosphonite (4.08 g., 0.03 mole) was then added dropwise over one hour and after the final addition, heating was continued at 140° for 6 hours. On cooling, the hexadecane solidified and the mixture was made liquid by the addition of light petroleum (10 ml.). It was then chromatographed on a large (3x30 cm.) alumina column and the hexadecane rapidly eluted with light petroleum. The remaining material was eluted as a black tar with methanol, dissolved in benzene, and chromatographed in the usual way on another column. Benzene and benzene/ether mixtures containing up to 50% ether eluted only a series of oily films. Benzene/75% ether eluted an impure brown solid (0.185 g.) which, after sublimation (100°/0.04 mm.) and recrystallisation from carbon tetrachloride was shown to be phenothiazine (9.3%), m.p. and mixed m.p. 185-186°. Methanol eluted a dark brown tar (2.2 g.).

Control experiment: Reaction of phenothiazine with diethyl methylphosphonite in toluene. Phenothiazine (1.99 g., 0.01 mole), diethyl methylphosphonite (6.8 g., 0.05 mole) and toluene (20 ml.) were boiled under reflux in an atmosphere of nitrogen for 16 hours. G.l.c. analysis (3% QF-1/195°) at this stage showed trace amounts of a product, but this was neither carbazole or diphenylamine. The toluene was removed on a rotary evaporator and and the phosphorus esters then removed by vacuum distillation.

The solid residue was washed thoroughly with water and dried. The yield was 1.95 g. and both t.l.c. and infrared spectroscopy indicated that the product was pure phenothiazine.

Control experiment: Attempted reaction of diphenyl sulphide with diethyl methylphosphonite in toluene. The sulphide (3.72 g., 0.02 mole) and diethyl methylphosphonite (10.88 g., 0.08 mole) were boiled under reflux with toluene (20 ml.) for 12 hours in an atmosphere of nitrogen. The mixture did not change colour, and no new peaks or spots were found on g.l.c. or t.l.c.

Reaction of 4-methyl-2'-nitrodiphenyl sulphoxide with triethyl phosphite. The nitro-compound (1.5 g., 0.0057 mole) and triethyl phosphite (3.8 g., 0.023 mole) were heated in an atmosphere of nitrogen for 12 hours at 150°. The phosphite and phosphate were distilled off and the residue, dissolved in benzene, was chromatographed on alumina:

1. A white solid (0.105 g.) eluted with light petroleum.
2. A yellow gum (0.012 g.) eluted with light petroleum/10% benzene.
3. Yellow crystals (0.016 g.) eluted with light petroleum/50% benzene.

4-5. Gums (0.019 g.) eluted with light petroleum/10% ether.

6-7. An impure grey solid (0.06 g.) eluted with ether.

8-13. Tars (1.45 g.) eluted with ether/methanol mixtures.

Fraction 1. had m.p. 110-120° and mixed m.p. with 10-ethyl-2-methylphenothiazine, 116-120° (7.7%).

Fraction 3. gave m.p. 74-76°, mixed m.p. with starting material 57-60°, and mixed m.p. with 4-methyl-2'-nitrodiphenyl sulphide 76-79° (1.15%).

Fractions 6-7. had m.p. 147-155° after vacuum sublimation (100°/0.1 mm.) and mixed m.p. with 2-methylphenothiazine 153-163° (5%).

Reaction of 4-methyl-2'-nitrodiphenyl sulphone with triethyl phosphite. The sulphone (2.77 g., 0.01 mole) and phosphite (6.65 g., 0.04 mole) were heated under nitrogen for 12 hours at 150°. On cooling, the mixture set to a solid black tar which was insoluble in all solvents except dimethyl formamide. A small sample was dissolved in this solvent and examined by t.l.c. (silica gel/ether), but no well defined spots were observed.

Reaction of 2-nitrophenyl phenyl selenide with triethyl phosphite. The nitro-compound (2.78 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were heated for 22 hours at 135° in an atmosphere of nitrogen. After distilling off the phosphorus esters, the residue was chromatographed on alumina, the following fractions being collected:

1. A foul smelling red liquid (0.075 g.) eluted with light petroleum.

2-3. Yellow oily films (0.023 g.) eluted with light

petroleum/20% benzene.

4-5. Yellow oils (0.071 g.) eluted with light petroleum/ 50% benzene.

6-7. Impure brown crystals (0.25 g.) eluted with benzene.

8-16. Dark brown oils (4.125 g.) eluted with benzene/ ether mixtures.

17-18. Tars (0.78 g.) eluted with methanol.

T.l.c. (silica gel/light petroleum) of fraction 1. showed only one spot. The p.m.r. spectrum in carbon tetrachloride solution showed signals which might be ascribed to either an ethyl group attached to nitrogen (quartet at t=7.16 , triplet at t=8.60) and five aromatic protons (complex pattern at t=2.75) or two identical ethyl groups and nine or ten aromatic protons. On the basis of the second assignment, it might be tentatively suggested that the compound was 2-diethylaminophenyl phenyl selenide.

Fractions 2-3. each showed five spots on t.l.c. (silica gel/ benzene), one of which had the same R_f value as the product in fraction 1. and one of which stained the same characteristic dark green colour as phenothiazines on development in iodine vapour.

Fractions 4-5. also gave several spots on t.l.c.

Fractions 6-7. were distilled (110-120°/0.1 mm.) to yield 2-aminophenyl phenyl selenide (0.207 g., 8.4%), m.p. and mixed m.p. with a sample prepared by reduction of the starting material

33-34° (lit.,[92] 34°). The p.m.r. spectrum in carbon tetrachloride solution was compatible with this assignment showing signals in the aromatic region (complex pattern centred at t=2.95) and at t=5.95 (broad singlet) of relative area 9:2 .

Reaction of 2-nitrophenyl phenyl ether with triethyl phosphite. The nitro-compound (10.75 g., 0.05 mole) and triethyl phosphite (33 g., 0.2 mole) were heated under nitrogen for 19 hours at 100°. On working up in the usual manner, the only compound isolated was residual starting material (2.43 g.). Examination of the reaction mixture by g.l.c. (2% N.P.G.S./ 205°) demonstrated the absence of any product with the same retention time as an authentic sample of phenoxazine.

4. Deoxygenation of o-Nitrophenyl Ketones.- Reaction of o-nitrobenzophenone with triethyl phosphite. o-Nitrobenzophenone (0.83 g., 0.0036 mole) and triethyl phosphite (2.67 g., 0.016 mole) were heated together under nitrogen for 12 hours at 100° and then for 4 hours at 120°. The phosphate and the excess phosphite were distilled off and the residue chromatographed on alumina. Light petroleum/20% benzene eluted yellow crystals which on recrystallisation from light petroleum (b.p. 40-60°) gave 3-phenylanthranil (56%), m.p. 50.5-52° and mixed m.p. 49-51° (lit.,[78] 52-53°)(Found: C, 79.8 ; H, 4.6 . Calc. for $C_{13}H_9NO$: C, 80.0 ; H, 4.6%). Benzene eluted another crystalline

yellow solid (0.14 g.) which on recrystallisation from light petroleum (b.p. 60-80°) gave 2-aminobenzophenone (19.5%), m.p. 99.5-100.5° and mixed m.p. 102-105° (lit.,[80] 105-106°)(Found: C, 78.8 ; H, 5.6 . Calc. for $C_{13}H_{11}NO$: C, 79.2 ; H, 5.7%).

Reaction of 2'-nitrochalcone with triethyl phosphite. The chalcone (2.53 g., 0.01 mole) and triethyl phosphite (9.6 g., 0.058 mole) were heated at 100° for 16 hours under nitrogen. After distilling off the phosphorus esters, the residue was dissolved in a few ml. of benzene and chromatographed on alumina. Light petroleum/20% ether eluted yellow crystals which had m.p. 117.5-119° after recrystallisation from ethanol (Found: C, 81.8 ; H, 4.9 . $C_{15}H_{11}NO$ requires C, 81.45 ; H, 5.0%). The product was shown to be pure by t.l.c. and its infrared spectrum confirmed that there was no longer a nitro-group present. The p.m.r. showed only a complex pattern in the aromatic region. On this basis, and by analogy with the previous reaction, the compound was assumed to be 3-styrylanthranil (52%).

Reaction of 5-chloro-2-nitroacetophenone with triethyl phosphite. The nitro-compound (2.00 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were heated in an atmosphere of nitrogen for 1 hour at 115° and then for 11 hours at 100°. The phosphorus esters were then distilled off and the residue chromatographed on alumina, the following fractions being collected:

1-2. Colourless crystals (0.067 g.) eluted with light petroleum/20% benzene.

3-6. Yellow crystals (0.81 g.) eluted with light petroleum/50% benzene.

7-12. Thick yellow oils (2.16 g.) eluted with benzene/ether mixtures.

13-14. Tars (1.36 g.) eluted with ether/20% methanol.

Fractions 1-6. were shown by g.l.c. (2% N.P.G.S./190°) to contain several impurities and were, therefore, combined and rechromatographed on silica gel. Light petroleum/50% benzene eluted colourless crystals of 5-chloro-3-methylanthranil (0.62 g., 37%), m.p. 97.5° (lit.,[93] 97-98°)(Found: C, 57.1 ; H, 3.4 . Calc. for C_8H_6ClNO: C, 57.35 ; H, 3.6%). The p.m.r. spectrum in carbon tetrachloride solution was consistent with this structure showing only a complex pattern in the aromatic region and a singlet of equal area at t=7.25.

Fractions 7-12. were shown by g.l.c. to contain some of the anthranil, but were mainly composed of triethyl phosphate and diethyl ethylphosphonate.

Reaction of o-nitroacetophenone with triethyl phosphite. The nitro-compound (3.3 g., 0.02 mole) and phosphite (13.3 g., 0.08 mole) were heated under nitrogen for 14 hours at 125°. After distilling off the phosphite and phosphate, the residue was chromatographed on alumina:

1-2. Yellow oils (0.238 g.) eluted with benzene/20% ether.

3-7. Yellow oils (1.025 g.) eluted with ether.

8-10. Yellow oily solids (1.42 g.) eluted with ether/50% ethyl acetate.

11-14. Tars (0.65 g.) eluted with ethyl acetate/methanol mixtures.

Fractions 1-2. showed two closely spaced spots on t.l.c. (silica gel/ether). The p.m.r. spectrum was not consistent with any of the expected products, showing signals due to a methyl group and 8 or 9 aromatic protons.

Fractions 3-7. were shown by g.l.c. (3% QF-1/135°) to be mainly triethyl phosphate and diethyl ethylphosphonate.

Fractions 8-10. were shown by g.l.c. (2% N.P.G.S./195°) to contain a little triethyl phosphate in addition to a much less volatile product. Distillation gave the latter (1.04 g., b.p. 110-120/0.05 mm.). On standing, this gave a pale yellow solid which after recrystallisation from light petroleum (b.p. 60-80°) yielded diethyl N-(2-acetylphenyl)phosphoramidate (19%), m.p. 52-53° (Found: C, 53.9 ; H, 7.0 . $C_{12}H_{18}NO_4P$ requires C, 53.2 ; H, 6.7%). The p.m.r. spectrum in deuterochloroform solution was consistent with this stucture, showing the following signals: $-CH_3$, singlet (three protons) at t=7.38 ; $POCH_2-$, quintet (four protons) at t=5.85 ; $POCH_2CH_3$, triplet (six protons) at t=8.6 ; NH, broad

singlet (one proton) at t=-0.16 ; and the aromatic protons, complex pattern (four protons) at t=2.0-3.2 .

5. Miscellaneous Deoxygenation Reactions.- Reaction of 2-nitrobiphenyl with diethyl methylphosphonite. 2-Nitrobiphenyl (1.99 g., 0.01 mole) and diethyl methylphosphonite (5.44 g., 0.04 mole) were heated together on a water-bath in an atmosphere of nitrogen for two hours. The phosphorus esters were removed by vacuum distillation and the residue, dissolved in a few ml. of benzene, was chromatographed on alumina. Carbazole (1.42 g., 85%) was eluted by light petroleum/10% ether as colourless crystals, m.p. and mixed m.p. 243-246°.

Reaction of 2-nitrobiphenyl with hexaethyl phosphorous triamide. The nitro-compound (1.99 g., 0.01 mole) and hexaethyl phosphorous triamide (9.88 g., 0.04 mole) were heated under nitrogen for six hours on a boiling water-bath. Working up as described in the previous experiment gave carbazole (0.92 g., 55%) with m.p. and mixed m.p. 241-242°.

Reaction of 2-nitrobiphenyl with tri-n-butylphosphine. The nitro-compound (1.99 g., 0.01 mole) and the phosphine (8.08 g., 0.04 mole) were warmed together in an atmosphere of nitrogen. The mixture began to go black at 90° and after heating for 5 hours at 110°, g.l.c. (3% QF-1/200°) showed that all the nitrobiphenyl had reacted. The excess phosphine was distilled off under

vacuum and the residue was chromatographed on alumina. Benzene/20% ether eluted carbazole (1.15 g., 58%) which after recrystallisation from benzene, had m.p. and mixed m.p. 242-244°.

Reaction of ethyl 2-nitrobenzoate with triethyl phosphite.

The nitro-compound (1.95 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were heated under nitrogen for 16 hours at 128°. After distilling off the phosphorus esters, chromatography on alumina gave the following fractions:

1. A yellow solid (0.0068 g.) eluted with light petroleum/20% benzene.

2-6. Yellow oils (0.23 g.) eluted with benzene.

7-10. Yellow oils (0.55 g.) eluted with ether.

11-13. Yellow oils (0.69 g.) eluted with ether/20% ethyl acetate.

14-15. Tars eluted with methanol.

The infrared spectrum of fraction 1. was superimposable on that of the starting material.

The infrared spectrum of fractions 2-6. showed NH_2 stretching vibrations at 3380 and 3490 $cm.^{-1}$ and a carbonyl stretching vibration at 1690 $cm.^{-1}$. The p.m.r. spectrum in carbon tetrachloride solution showed signals which were assigned as follows: ester ethyl group, quartet (two protons) at t=5.75 and triplet (three protons) at t=8.65 ; amino-group, broad singlet (two protons) at t=4.3 ; proton o- to the carbonyl group, quartet at

t=2.2 ; and the remaining aromatic protons, two complex patterns (one proton and two protons) at t=2.87 and t=3.5 . On this basis, the compound was identified as ethyl anthranilate (14%).

Fractions 7-13. were shown by t.l.c. (silica gel/ether) to contain several components and were combined and rechromatographed on silica gel:

1-2. Yellow oils (0.023 g.) eluted with benzene.

3. A yellow oil (0.048 g.) eluted with benzene/10% ether.

4-6. Yellow oils (0.33 g.) eluted with benzene/50% ether.

7-9. Yellow oils (0.49 g.) eluted with ether.

Fractions 1-2. were shown by g.l.c. (3% QF-1/160°) to be the amine previously described.

Fraction 3. was shown by g.l.c. (3% QF-1/200°) to contain one major component which also occurs in fractions 4-6. and several minor ones.

Fractions 4-6. were distilled to yield a compound identified as diethyl N-(2-carbethoxyphenyl)phosphoramidate (0.30 g., 10%), b.p. 100-110°/0.1 mm. (Found: C, 51.7 ; H, 6.5 . $C_{13}H_{20}NO_5P$ requires C, 51.85 ; H, 6.7%). The infrared spectrum showed peaks at 3260 cm.$^{-1}$ (NH), 1695 cm.$^{-1}$ (C=O), 1260 cm.$^{-1}$ (P=O), and 1040 and 980 cm.$^{-1}$ (POEt). The p.m.r. spectrum in carbon tetrachloride solution showed the following signals: ester ethyl group,

quartet (two protons) at t=6.6 and triplet (three protons) at t=8.61 ; $POCH_2$-, quintet (four protons) at t=5.91 ; $POCH_2CH_3$, triplet (six protons) at t=8.69 ; NH, doublet (one proton) at t=0.65 (J_{PH} =9.5 c.p.s.); proton o- to the carbonyl group, doublet (one proton) at t=2.06 (J=8.5 c.p.s.); and the remaining aromatic protons, complex patterns (two protons and one proton) at t=2.58 and t=3.16.

Fractions 7-9. showed only one spot on t.l.c. (silica gel/ether) and were identified as diethyl N-ethyl-N-(2-carbethoxyphenyl)phosphoramidate (15.5%), b.p. 125-130°/0.1 mm. (Found: C, 55.7 ; H, 7.45 . $C_{14}H_{24}NO_5P$ requires C, 54.8 ; H, 7.35%). The infrared spectrum showed no NH stretching vibration, but had peaks for C=O, P=O, and POEt similar to those described for the previous compound. The p.m.r. in deuterochloroform solution showed signals which were assigned as follows: ester ethyl group, quartet (two protons) at t=5.66 and triplet (three protons) at t=8.6 ; $POCH_2$-, quintet (four protons) at t=5.95 ; $POCH_2CH_3$, triplet (six protons) at t=8.72 ; NCH_2-, overlapping quartets (two protons) at t=6.37 and t=6.55 ($J_{PH}\doteq 10$ c.p.s.); NCH_2CH_3, triplet (three protons) at t=8.73 .

Reaction of 2-nitrochalcone with triethyl phosphite. The chalcone (2.53 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were heated together in an atmosphere of nitrogen for 15 hours at 100°. Distillation of the phosphorus esters and

chromatography as previously described yielded an impure solid (0.21 g.) which after recrystallisation from light petroleum (b.p. 60-80°) had m.p. and mixed m.p. with starting material 108-113°. The only other products obtained were dark coloured oils and tars eluted with ether/methanol mixtures.

Reaction of 2-nitrostilbazole with triethyl phosphite. The nitro-compound (2.26 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were heated under nitrogen for 12 hours at 130°. After distilling off the phosphorus esters, the residue was chromatographed on alumina. Benzene/50% ether eluted pale yellow crystals (0.71 g.) which on recrystallisation from benzene gave 2-(2'-pyridyl)indole (37%), m.p. 156-158° (lit.,[94] 154°) as a colourless solid. The ultraviolet spectrum agreed with a published spectrum (λmax., 325.5 mμ in methanol solution; logε, 4.42 . Lit.,[95] 325 mμ ; 4.42 .). The p.m.r. spectrum in deuterochloroform solution showed the α-pyridyl proton as a doublet at t=1.35 and the remaining protons as a complex pattern between t=2.1 and t=3.1 .

Reaction of α-(o-nitrophenyl)-2-chlorocinnamic acid with triethyl phosphite. The nitro-compound (2.67 g., 0.0088 mole) and triethyl phosphite (6.65 g., 0.04 mole) were stirred under nitrogen for 18 hours at 110°. After removing the phosphite and phosphate, the residue was chromatographed on alumina and the following fractions collected:

1-3. Oily solids (0.62 g.) eluted with light petroleum/20% benzene.

4. A yellow solid (0.132 g.) eluted with light petroleum/60% benzene.

5. A cream coloured solid (0.04 g.) eluted with benzene.

6-9. White solids (1.093 g.) eluted with benzene/30% ether.

10-12. Oily films (0.04 g.) eluted with ether.

13-14. Tars (1.7 g.) eluted with ether/methanol mixtures.

Fractions 1-3. were each shown by g.l.c. (2% N.P.G.S./225°) to contain several components. They were combined and rechromatographed on silica gel, but separation of the components was still not achieved.

Fraction 4. showed only one g.l.c. peak. Recrystallisation from ethanol gave a compound identified as ethyl α-(o-nitrophenyl)-2-chlorocinnamate (4.5%), m.p. 126-127° (Found: C, 61.3 ; H, 4.3 . $C_{17}H_{14}ClNO_4$ requires C, 61.5 ; H, 4.25%). The infrared spectrum showed peaks characteristic of a nitro-group (1360 and 1530 $cm.^{-1}$) and an α,β-unsaturated ester carbonyl group (1710 $cm.^{-1}$). The p.m.r. spectrum in deuterochloroform solution showed the following signals: ester ethyl group, quartet (two protons) at t=5.78, and triplet (three protons) at t=8.77 ; and the aromatic protons, complex pattern (ca. nine protons) from t=1.95 to t=3.25 .

Fraction 5. showed two g.l.c. peaks and was not further investigated.

Fractions 6-9. were shown to be pure by t.l.c. (silica gel/benzene). Recrystallisation from ethanol gave a compound which was assigned the stucture 2-(o-chlorophenyl)-3-carbethoxyindole (46%), m.p. 146-147° (Found: C, 67.9 ; H, 4.7 . $C_{17}H_{14}ClNO_2$ requires C, 68.1 ; H, 4.7%). The infrared spectrum showed an NH stretching vibration at 3290 cm.$^{-1}$. The p.m.r. spectrum in deuterochloroform solution showed signals which were assigned as follows: ester ethyl group, quartet (two protons) at t=5.86, and triplet (three protons) at t=8.89 ; indole NH, broad singlet at t=1.02 ; and the aromatic protons, two complex patterns (ca. eight protons) at t=1.98 and t=2.90 .

Reaction of 3-(o-nitrophenyl)coumarin with triethyl phosphite. The impure nitro-compound (2.67 g., 0.01 mole) and triethyl phosphite (6.65 g., 0.04 mole) were heated under nitrogen for 12 hours at 130°. On cooling, the mixture set almost solid due to the formation of an insoluble product. This was filtered off and washed with ether to give pink flakes (1.48 g., 63% based on $C_{15}H_9NO_2$)(Found: C, 76.0 ; H, 4.0 . $C_{15}H_9NO_2$ requires C, 76.6 ; H, 3.9%). The product was insoluble in all common solvents and had m.p. $>400°$. The p.m.r. spectrum in dimethyl sulphoxide solution showed only a complex pattern in the aromatic region. The infrared spectrum confirmed that the nitro-group had reacted

and showed no peaks attributable to an NH group or an α,β-unsaturated δ-lactone carbonyl group.

Control experiment: Attempted reaction of coumarin with triethyl phosphite. Coumarin (2.92 g., 0.02 mole) and triethyl phosphite (6.65 g., 0.04 mole) were stirred under nitrogen for 36 hours at 135°. The reaction was followed by g.l.c. (1% A.P.L./180°) which showed that coumarin was not being attacked. There was no evidence for formation of any product. On cooling, a white solid separated; a further crop was obtained by treating the phosphite with light petroleum (b.p. 60-80°) giving a total recovery of 2.6 g. It had m.p. and mixed m.p. with starting material 65-67°.

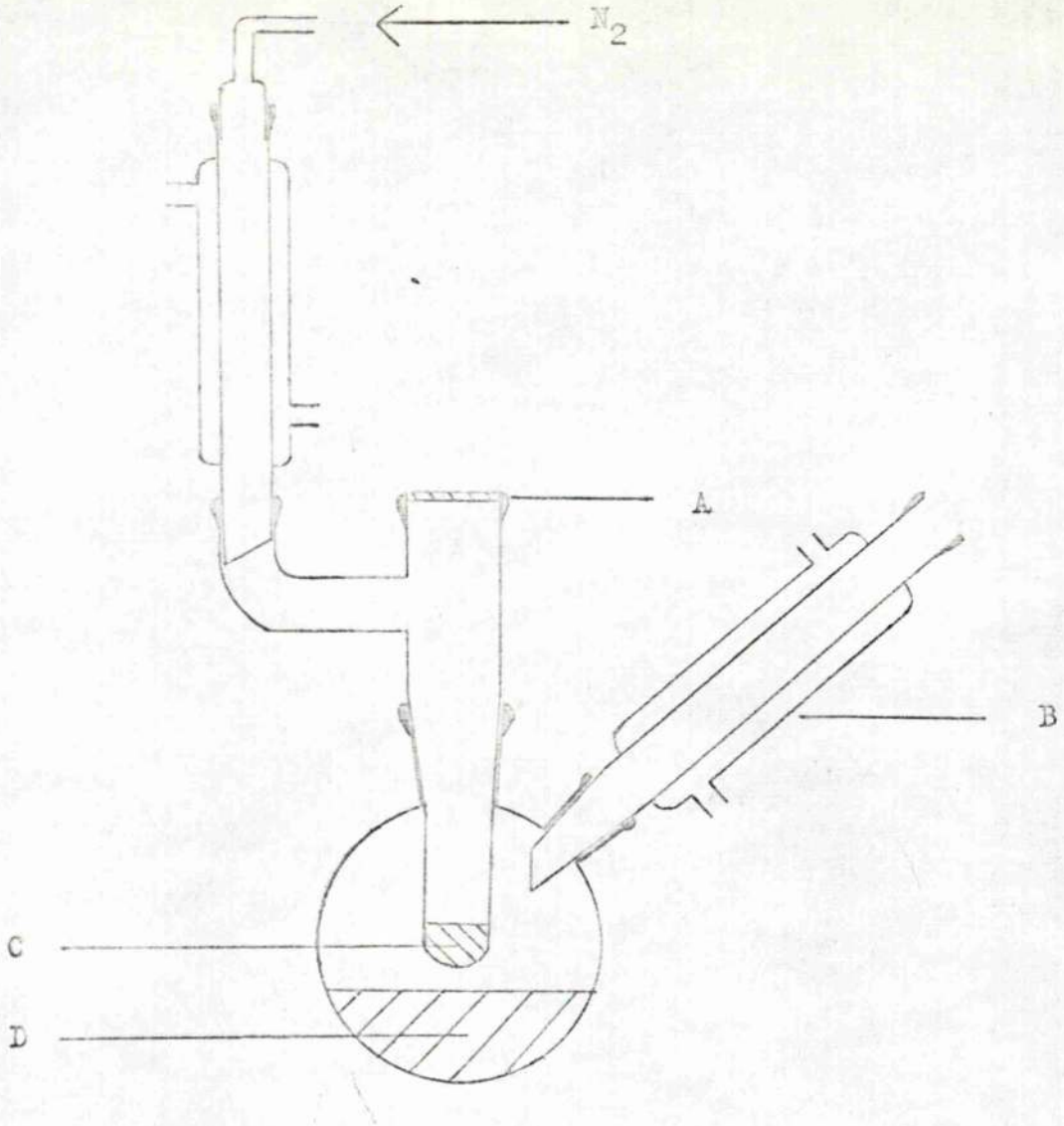
6. Studies of the Rate of Deoxygenation of Nitro-Compounds.-

Determination of the method of analysis. It was decided that quantitative g.l.c. would provide the most rapid and convenient means of analysis for conducting a kinetic survey of the reaction between 2-nitrobiphenyl and a series of tervalent phosphorus compounds. A column-temperature combination therefore had to be found which would separate 2-nitrobiphenyl, carbazole and some inert marker-compound into sharp well-resolved peaks. Test solutions of 2-nitrobiphenyl and carbazole (0.05 g.) in acetone (1 ml.) were prepared and injected in turn onto the columns under test. It was immediately evident that carbazole

would not pass through columns containing more than 5% of the stationary phase without heating the oven to unacceptable levels. Of the low percentage columns, 2% N.P.G.S. (see Appendix for key to stationary phase abbreviations) absorbed on celite and operating at 200° was found to be the most suitable. Under these conditions, trans-stilbene was a suitable internal standard being well resolved from the other two compounds. When a mixture of triethyl phosphite, triethyl phosphate, 2-nitrobiphenyl, trans-stilbene, and carbazole in molar ratio 20:2:1:1:1 was injected, the latter three compounds gave sharp, well separated peaks.

Accuracy of the analytical method. As 2-nitrobiphenyl reacts, the area of its g.l.c. peak diminishes, and consequently the accuracy of its measurement also decreases. A calibration mixture of trans-stilbene and 2-nitrobiphenyl in approximately 2:1 molar ratio was prepared, these being the relative amounts present at the half-life time in the kinetic determinations. Using the formula given on page 38, six determinations of the number of moles of 2-nitrobiphenyl were made and compared with the actual value.

Weight of 2-nitrobiphenyl	= 0.0344 g. (0.000173 mole)
Weight of trans-stilbene	= 0.0668 g. (0.000371 mole)
Calculated values of (moles nitrobiphenyl)	= 0.000173 , 0.000171 ,
	0.000163 , 0.000169 ,
	0.000172 , 0.000180 .



A – Rubber serum cap

B – Reaction temperature measured by thermometer passed through this condenser

C – Reaction mixture

D – Refluxing solvent providing constant temperature

The maximum error in any of these determinations is 5.8% and since in the subsequent kinetic work, the average of at least two concordant results was taken to represent (moles nitrobiphenyl) at any given time, the accuracy on individual values was assumed to be about 5% .

After the bulk of this kinetic work was completed, an electronic integrator became available and in a few of the later kinetic runs, peak areas were computed using this. These runs are indicated and a separate investigation of the accuracy of the instrument was performed.

Weight of nitrobiphenyl = 0.0959 g. (0.000482 mole)

Weight of trans-stilbene = 0.0915 g. (0.000508 mole)

Calculated values of (moles nitrobiphenyl) = 0.000482 , 0.000493 ,
0.000486 , 0.000492 ,
0.000483 .

The maximum deviation in any one calculation is only 2.3%, but in this case the ideal ratio (1:1) of nitrobiphenyl to marker was used and the overall accuracy is probably similar to that of the previous method.

Apparatus and general method. The apparatus used is illustrated on the opposite page. All reactions were studied under pseudo-unimolecular conditions using roughly equimolar amounts of nitro-compound and trans-stilbene in a 15-20 molar excess of the phosphorus compound. The rate of reaction was determined by

following the loss of nitro-compound. Samples (ca. 20 µl.) were withdrawn through the serum cap using a gas-tight syringe, transferred to a small test-tube, and immediately frozen at -80°. When convenient, they were warmed to room temperature, diluted with ether (ca. 50 µl.) and analysed.

Reaction of 2-nitrobiphenyl with triethyl phosphite.

Temperature = 145°

Wt. of nitrobiphenyl = 0.2662 g. (0.00134 mole)

Wt. of trans-stilbene = 0.2275 g. (0.00126 mole)

Time (T min.) :	0	4	23	46
Moles nitrobiphenyl:	0.00134	0.00109	0.00091	0.000715

65	82.5
0.00058	0.00048

Half-life ($t_{\frac{1}{2}}$) = 51 min. (see fig. iii, p. 138)

Plots of log(moles nitrobiphenyl) against (time) are shown in the Discussion (fig. iii, facing p. 138).

In a second run the following results were obtained.

Temperature = 144.5°

Wt. of nitrobiphenyl = 0.250 g. (0.00125 mole)

Wt. of trans-stilbene = 0.226 g. (0.001255 mole)

Time (T min.) :	0	4	21	37
Moles nitrobiphenyl:	0.00125	0.001245	0.000935	0.000713

80	100	126	190
0.00039	0.000265	0.000198	0.000085

$t_{\frac{1}{2}}$ = 47 min. (see fig. iii, p. 138)

Nitrobiphenyl and ethyl N-tetraethylphosphorodiamidite.

Temperature = 121°

Wt. of nitrobiphenyl = 0.2533 g. (0.001272 mole)

Time (T min.) : 0 , 3 , 8 , 35 ,

Moles of nitrobiphenyl: 0.001272 , 0.000649 , 0.000532 , 0.000228 ,

40 .

0.000202 .

$t_{\frac{1}{2}}$ ≒ 5 min.

Nitrobiphenyl and hexaethyl phosphorous triamide.

Temperature = 111°

Wt. of nitrobiphenyl = 0.2607 g. (0.00131 mole)

Time (T min.) : 0 , $5\frac{1}{4}$, 18 , $34\frac{1}{2}$,

Moles nitrobiphenyl: 0.00131 , 0.00108 , 0.000845 , 0.000691 ,

$51\frac{1}{2}$, $58\frac{1}{2}$, $69\frac{1}{2}$.

0.000575 , 0.000554 , 0.00045 .

$t_{\frac{1}{2}}$ = 41 min. (see fig. v, p. 138)

Plots of the log and the reciprocal of (moles nitrobiphenyl) are reproduced in the Discussion (fig. v , p. 138.

Nitrobiphenyl and diethyl methylphosphonite.

Temperature = 61°

Wt. of nitrobiphenyl = 0.1251 g. (0.00063 mole)

Time (T min.) : 0 , $19\frac{1}{2}$, $31\frac{3}{4}$, 82 ,

Moles nitrobiphenyl: 0.00063 , 0.00056 , 0.000533 , 0.000406 ,

Time (T min.) : $141\frac{1}{2}$, $214\frac{1}{2}$.

Moles nitrobiphenyl: 0.000331 , 0.000261 .

$t_{\frac{1}{2}}$ = 154 min.

Log and reciprocal plots are reproduced in the Discussion (fig. vi, p. 138).

Nitrobiphenyl and tri-isopropyl phosphite.

Temperature = 143.5°

Wt. of nitrobiphenyl = 0.1314 g. (0.00066 mole)

Time (T min.) : 0 , $7\frac{1}{4}$, 15 , $31\frac{1}{4}$,

Moles nitrobiphenyl: 0.00066 , 0.000642 , 0.00056 , 0.00044 ,

50 , $65\frac{1}{2}$, 100 , 175 .

0.00037 , 0.00031 , 0.00023 , 0.000105 .

$t_{\frac{1}{2}}$ = 63 min.

The peak areas in this run were obtained by electronic integration of the recorder signal. A plot of log(moles nitrobiphenyl) against (T) is shown in the Discussion (fig. iv , p.138).

Nitrobiphenyl and triethyl phosphite.

Temperature = 135°

Wt. of nitrobiphenyl = 0.1548 g. (0.000778 mole)

Time (T min.) : 0 , $8\frac{1}{2}$, $17\frac{1}{2}$, 45 ,

Moles nitrobiphenyl: 0.00078 , 0.00076 , 0.00069 , 0.00054 ,

$79\frac{1}{2}$, 140 , 208 .

0.00037 , 0.00026 , 0.000155 .

$t_{\frac{1}{2}}$ = 83 min. (see fig. vii, p. 138)

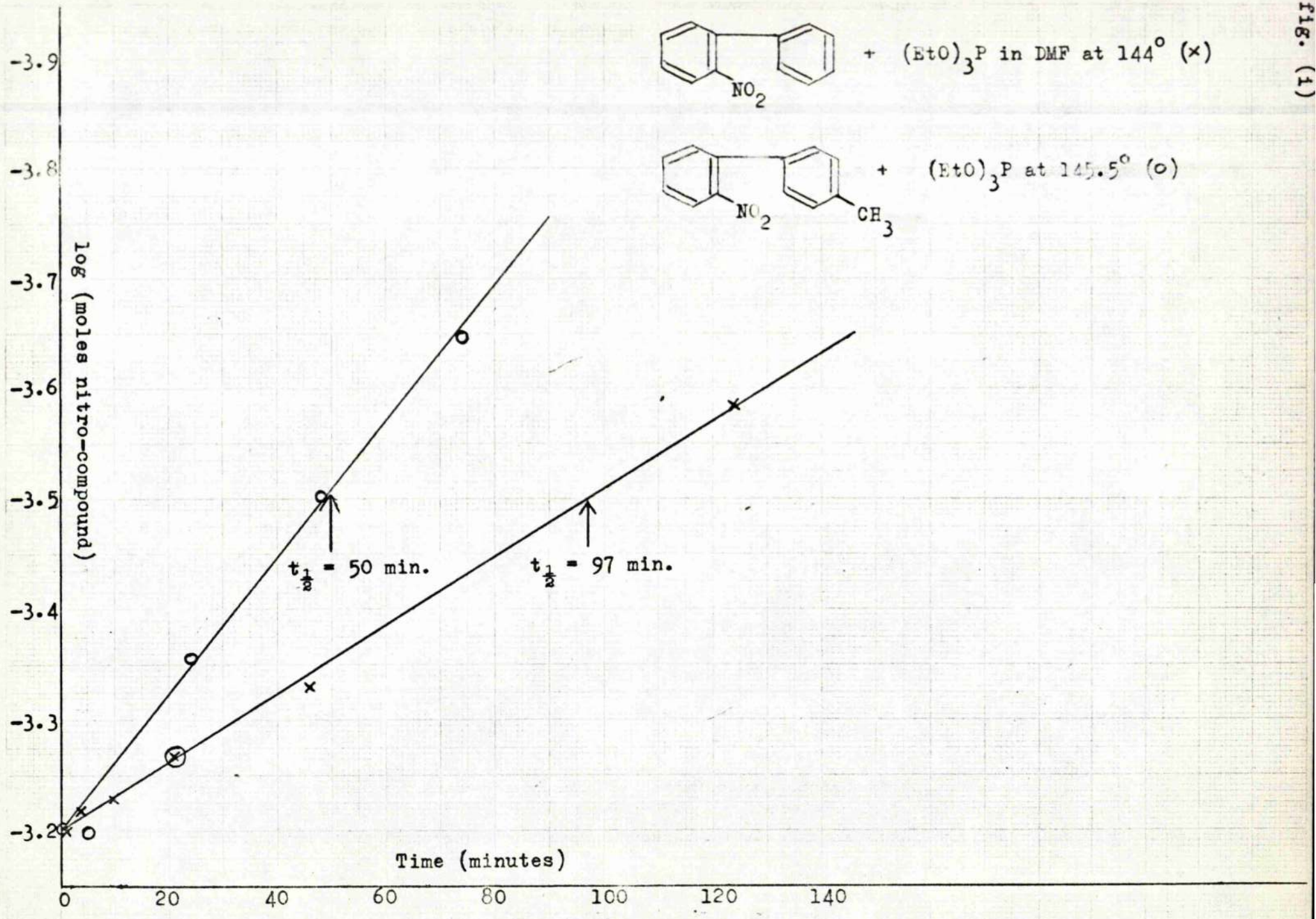

+ (EtO)3P in DMF at 144° (×)
NO2
+ (EtO)3P at 145.5° (o)
NO2
CH3
-3.9
-3.8
-3.7
-3.6
-3.5
-3.4
-3.3
-3.2
log (moles nitro-compound)
t½ = 50 min.
t½ = 97 min.
Time (minutes)
0
20
40
60
80
100
120
140

fig. (1)

Nitrobiphenyl and triethyl phosphite.

Temperature = 155°

Wt. of nitrobiphenyl = 0.1623 g. (0.000815 mole)

Time (T min.) : 0 , $3\frac{1}{4}$, $6\frac{1}{4}$, 12 ,

Moles nitrobiphenyl: 0.000815 , 0.00076 , 0.000725 , 0.00063 ,

25 , $48\frac{1}{2}$, $76\frac{3}{4}$.

0.00045 , 0.00025 , 0.000135 .

$t_{\frac{1}{2}}$ = 32 min. (see fig. vii, p.138)

Peak areas in this run were determined by the electronic integrator.

Nitrobiphenyl and triethyl phosphite in dimethyl formamide.

Temperature = 144°

Wt. of nitrobiphenyl = 0.1256 g. (0.000631 mole)

Wt. of triethyl phosphite = 1.703 g. (0.01025 mole)

Wt. of D.M.F. = 0.965 g. (0.0132 mole)

Time (T min.) : 0 , 4 , 10 , 21 ,

Moles nitrobiphenyl: 0.000631 , 0.000607 , 0.000592 , 0.000544 ,

46 , 124 , 250 .

0.000471 , 0.000262 , 0.000113 .

$t_{\frac{1}{2}}$ = 97 min. (see fig. i , opposite)

In addition to this study of the reaction of 2-nitrobiphenyl with a series of organophosphorus compounds, the reactions of a few other nitro-compounds with triethyl phosphite were similarly investigated. Only those nitro-compounds which gave sharp g.l.c.

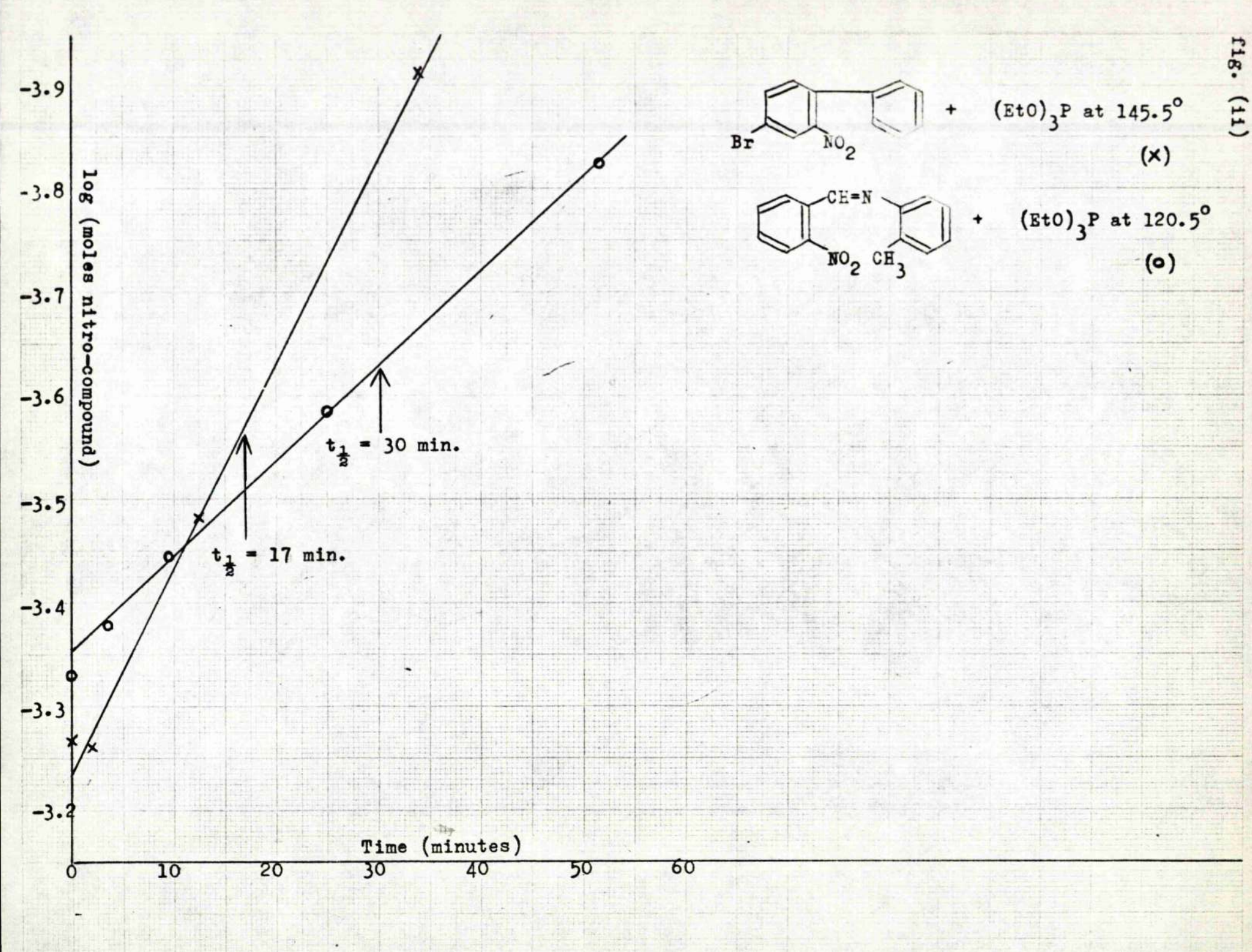

-3.9
-3.8
-3.7
-3.6
-3.5
-3.4
-3.3
-3.2
log (moles nitro-compound)
0
10
20
30
40
50
60
Time (minutes)
$t_{\frac{1}{2}}$ = 30 min.
$t_{\frac{1}{2}}$ = 17 min.
Br
NO_2
+ $(EtO)_3P$ at 145.5°
(x)
CH=N
NO_2
CH_3
+ $(EtO)_3P$ at 120.5°
(o)

fig. (ii)

peaks could be considered.

4-Methyl-2'-nitrobiphenyl and triethyl phosphite.

Temperature = 145.5°

Wt. of nitro-compound = 0.1324 g. (0.000622 mole)

Time (T min.) : 0 , 5 , 11 , 24 ,

Moles nitro-compound: 0.000622 , 0.000636 , 0.000592 , 0.000441 ,

48 , 74 , 160 .

0.000315 , 0.000226 , 0.000084 .

$t_{\frac{1}{2}}$ = 50 min. (see fig. i, facing p. 82)

4-Bromo-2-nitrobiphenyl and triethyl phosphite.

Temperature = 145.5°

Wt. of nitro-compound = 0.1498 g. (0.00054 mole)

Time (T min.) : 0 , 2 , $12\frac{1}{2}$, 34 ,

Moles nitro-compound: 0.00054 , 0.00055 , 0.00033 , 0.000123 ,

$59\frac{1}{2}$.

0.000106 .

$t_{\frac{1}{2}}$ = 17 min. (see fig. ii, opposite)

o-Nitrobenzylidene-o-toluidine and triethyl phosphite.

Temperature = 120.5°

Wt. of nitro-compound = 0.1136 g. (0.00047 mole)

Time (T min.) : 0 , $3\frac{1}{2}$, $9\frac{1}{2}$, 25 ,

Moles nitro-compound: 0.00047 , 0.00042 , 0.00036 , 0.00026 ,

$51\frac{1}{2}$, 88 .

0.00015 , 0.000075 .

$t_{\frac{1}{2}}$ = 30 min. (see fig. ii, facing p. 83)

7. Experiments Designed to Investigate the Mechanism of the Deoxygenation Reaction.- Reaction of nitrosobenzene with triethyl phosphite in norbornene. Nitrosobenzene (2.14 g., 0.02 mole) and norbornene (18.8 g., 0.2 mole) were mixed with just enough light petroleum (ca. 5 ml.) to give a homogeneous mixture. To this, triethyl phosphite (6.65 g., 0.04 mole) was added dropwise with stirring in an atmosphere of nitrogen. The mixture rapidly turned dark brown and stirring was continued for 3 hours. The contents of the flask were then chromatographed on alumina. Norbornene was eluted with light petroleum (b.p. 40-60°), and the following fractions were then collected:

1-4. Traces of oily material eluted with light petroleum/30% benzene.

5. An orange coloured oil (0.45 g.) eluted with light petroleum/50% benzene.

6. Oily yellow crystals (0.063 g.) eluted with benzene.

7. A yellow oil (0.004 g.) eluted with benzene/10% ether.

8-14. Traces of oily films eluted with benzene/ether mixtures.

15-16. Dark brown oils (5.3 g.) eluted with ether.

17-18. Tars (3.05 g.) eluted with ether/methanol mixtures.

Fraction 5. was shown by g.l.c. (10% A.P.L./65°) to be

mainly benzene.

The infrared spectrum of fraction 6. was superimposable on that of an authentic sample of azoxybenzene (3%).

Fractions 15-16. were identified as triethyl phosphate on the basis of their infrared spectra.

A sample of 3-phenyl-3-azatricyclo[3,2,1,$0^{2,4}$]octane was prepared from norbornene and phenyl azide as described by Huisgen[54] and fractions 4-7. were then examined by g.l.c. (10% A.P.L./250°) for a product of identical retention time, but none was found.

Reaction of 2-nitro-2',4',6'-trimethylbiphenyl with triethyl phosphite. The nitro-compound (6.1 g., 0.0253 mole) and triethyl phosphite (16.6 g., 0.1 mole) were stirred under nitrogen for 12 hours at 156°. Distillation of the phosphorus esters followed by chromatography on alumina yielded the following fractions:

1-6. Brown oils setting to tars (0.19 g.), eluted with light petroleum/ether mixtures.

7. A brown oily solid (0.13 g.), eluted with ether.

8-10. Brown crystals (0.21 g.), eluted with ether.

11-13. Impure oily solids (0.44 g.), eluted with ether/5% methanol.

14-16. Tars (5.08 g.), eluted with methanol.

Fractions 8-9. on sublimation, gave colourless crystals of 2-amino-2',4',6'-trimethylbiphenyl, m.p. 97-98.5°, (lit.,[84] 98-99°)

(Found: C, 84.95 ; H, 7.85 . Calc. for $C_{15}H_{17}N$: C, 85.3 ; H, 8.1 %). The infrared spectrum was superimposable on that of an authentic sample. The p.m.r spectrum in deuterochloroform solution was compatible with this structure, showing the following signals: 4'-CH_3, singlet (three protons) at t=7.67 ; 2'- and 6'-CH_3, singlet (six protons) at t=7.99 ; NH_2, singlet (two protons) at t=6.59 ; and the aromatic protons, complex pattern (six protons) at t=2.8-3.4 . Sublimation of the material in fractions 7, 10, 11, and 12 gave a further quantity (0.14 g.) (total yield 0.70 g., 13%).

Examination of the reaction mixture by g.l.c. (3% A.P.L./ 225°) confirmed the absence of 8,10-dimethylphenanthridine and 2,4,9-trimethylcarbazole, authentic samples having been obtained by thermal decomposition of 2-azido-2',4',6'-trimethylbiphenyl as described by Smolinsky.[84]

G.l.c. (1% A.P.L./225° and 1.5% N.P.G.S./225°), however, indicated the presence of one other product which was tentatively identified as triethyl N-(2',4',6'-trimethylbiphenyl-2-yl)phosphorimidate by comparison of its retention times with those of an authentic sample. Assuming that the detector responds equally to the phosphorimidate and the amine, the yield was estimated as 15% by comparison of the peak areas.

Reaction of 2-nitro-2',4',6'-trimethylbiphenyl with triethyl phosphite in cumene. The phosphite (5.0 g., 0.03 mole),

in cumene (15 ml.), was added dropwise in an atmosphere of nitrogen to a solution of the nitro-compound (2.41 g., 0.01 mole) in cumene (60 ml.) at 150°, and the mixture was stirred at 150° for 5 days. Cumene was removed on a rotary evaporator (15 mm.), and the residue dissolved in benzene (5 ml.) and chromatographed on alumina to give the following fractions:

1-2. Colourless crystals (0.218 g.) eluted with light petroleum (b.p. 40-60°).

3-6. Orange oils (0.386 g.) eluted with light petroleum/75% benzene. Fraction 5. eventually gave oily crystals.

7-11. Colourless crystals (0.56 g.) eluted with benzene/50% ether.

12-14. Brown solids (0.307 g.) eluted with ether.

15-17. Brown oils (1.155 g.) eluted with ether/5% methanol.

18-19. Tars eluted with methanol.

Fractions 3-6. were shown by g.l.c. (1.5% N.P.G.S./225°) to be almost pure starting material and the infrared spectrum was superimposable on that of the starting material. Yields were therefore based on the amount of nitro-compound consumed (2.03 g.).

Fractions 1-2. were identified as bi-α-cumyl (11%), m.p. 118.5-119.5° (lit.,[96] 119°). The infrared spectrum was super-

imposable on that of an authentic sample, and the p.m.r. spectrum in carbon tetrachloride solution showed only two singlets of relative area 6:5 at t=8.7 and t=2.9, due to the methyl and aromatic protons respectively.

Fractions 7-11. were shown to be 2-amino-2',4',6'-trimethylbiphenyl (31.5%) by comparison of the g.l.c. retention time with that of an authentic sample. Sublimation (85°/0.02 mm.) gave colourless crystals, m.p. and mixed m.p. 96.5-97.5° (lit.,[84] 98-99°).

Fractions 12-14. were combined and rechromatographed, elution with benzene/75% ether giving 8,10-dimethylphenanthridine (0.234 g., 13.4%), m.p. and mixed m.p. 148-149° (lit.,[84] 149-150°). The infrared spectrum was superimposable on that of an authentic sample.

Fractions 15-17. were shown by g.l.c. (1% A.P.L./225°) to contain an involatile product in addition to triethyl phosphate. They were combined and rechromatographed on silica gel, elution with benzene/25% ether giving fractions which on standing deposited colourless crystals of diethyl N-(2',4',6'-trimethylbiphenyl-2-yl)phosphoramidate (0.168 g., 5.5%). Recrystallisation from light petroleum (b.p. 60-80°) at -80° gave material with m.p. 54-56°, undepressed on mixing with an authentic sample prepared by hydrolysis of triethyl N-(2',4',6'-trimethylbiphenyl-2-yl)phosphorimidate as described on p. 89 .

The infrared and p.m.r. spectra were identical with those of the authentic sample.

Reaction of 2-nitro-2',4',6'-trimethylbiphenyl with triethyl phosphite in t-butylbenzene. The reaction was carried out in the same manner and using the same quantities as in the previous experiment. The products from the chromatography were characterised in the same way and were as follows:

Starting material (0.44 g.).

2-Amino-2',4',6'-trimethylbiphenyl (0.325 g., 19%).

8,10-Dimethylphenanthridine (0.205 g., 12%).

Diethyl N-(2',4',6'-trimethylbiphenyl-2-yl)phosphoramidate (0.14 g., 5%).

Control experiment: Attempted reaction of cumene with triethyl phosphite. Cumene (80 ml.) and triethyl phosphite (5 g., 0.03 mole) were heated at 150° in an atmosphere of nitrogen for 5 days. The mixture was cooled and the cumene then removed on a rotary evaporator (15 mm.). The residue was dissolved in benzene (2 ml.) and examined by g.l.c. (1% A.P.L./225°) which confirmed the absence of bi-α-cumyl.

Hydrolysis of triethyl N-(2',4',6'-trimethylbiphenyl-2-yl)-phosphorimidate. The phosphorimidate (0.6 g., 0.0016 mole) was shaken with dilute (2$\bar{N}$) hydrochloric acid for 10 minutes. The aqueous mixture was then extracted with light petroleum (b.p. 60-80°)(2x15 ml.), and the extract dried ($MgSO_4$) overnight.

Evaporation of the solvent gave colourless, crystalline, diethyl N-(2',4',6'-trimethylbiphenyl-2-yl)phosphoramidate (0.53 g., 95%). Recrystallisation from light petroleum (b.p. 60-80°) at -80° gave crystals, m.p. 56.5-57° (Found: C, 65.2 ; H, 7.4 . $C_{19}H_{26}NO_3P$ requires C, 65.65 ; H, 7.5%). The infrared spectrum had peaks due to the following groups: NH (3380 $cm.^{-1}$), P=O (1250 $cm.^{-1}$) and POEt (1025 and 970 $cm.^{-1}$). The p.m.r. spectrum in carbon tetrachloride solution showed the expected signals: 4'-CH_3, singlet (three protons) at t=7.7 ; 2'- and 6'-CH_3, singlet (six protons) at t=8.04 ; NH, doublet (one proton) at t=5.5 (J_{PH} ≒9 c.p.s.); and the aromatic protons, complex pattern (six protons) at t=2.6-3.2 .

Reaction of 2-nitro-4'-t-butyldiphenyl sulphide with triethyl phosphite in cumene. The nitro-compound (2.2 g., 0.0076 mole), triethyl phosphite (5.0 g., 0.03 mole), and cumene (75 ml.) were boiled under reflux (151°) for 52 hours in an atmosphere of nitrogen. At the end of this time, the starting material was not detectable by t.l.c. (silica gel/benzene). The cumene was removed on a rotary evaporator and the residual brown oil, dissolved in light petroleum (b.p. 60-80°), was chromatographed on alumina, the following fractions being collected:

1-4. Colourless oils (0.059 g.), eluted with light petroleum (b.p. 40-60°). Fraction 2. (0.008 g.) contained bi-α-cumyl as a minor component as shown

by g.l.c. (3% QF-1/160°).

5-7. 10-Ethyl-2-t-butylphenothiazine (0.054 g., 2.5%), m.p. and mixed m.p. 120-121°.

8-12. 2-t-butylphenothiazine (1.45 g., 74%), m.p. and mixed m.p. 158-159° with the product described on p.50.

Reaction of 2-nitrophenyl phenyl sulphide with triethyl phosphite in trans-stilbene. The sulphide (2.31 g., 0.01 mole), triethyl phosphite (5.0 g., 0.03 mole), and trans-stilbene (45 g., 0.25 mole) were heated under nitrogen for 24 hours at 145°. Most (43 g.) of the trans-stilbene was removed from the reaction mixture by crystallisation from benzene, each crop of crystals being washed with benzene and ethanol and the washings collected. The mother liquors and the combined washings were then chromatographed on alumina. Further trans-stilbene (1.16 g.), starting material (0.47 g.), and phenothiazine (0.76 g., 38%) were collected. No other product was found.

Reaction of nitrobenzene with diethyl methylphosphonite in diethylamine. Nitrobenzene (2.5 g., 0.02 mole), diethyl methylphosphonite (18.5 g., 0.136 mole), and diethylamine (80 ml.) were heated at the boiling point (55°) under nitrogen for 5 days. At the end of this time, g.l.c. (capillary column, Carbowax 20M/200°) showed only a trace of nitrobenzene remaining. Diethylamine and excess phosphonite were removed on a rotary evaporator and the residue chromatographed on alumina. Benzene/ether (9:1)

eluted eight fractions (2.73 g.) which showed a single g.l.c. peak. Distillation gave a yellow oil (2.185 g.), b.p. 50-60°/0.05 mm., n_D^{25} 1.5509 (lit.,[97] 1.5500), which was identified as 2-diethylamino-3H-azepine (83%) on the basis of its p.m.r. spectrum in carbon tetrachloride solution which was identical with a published[97] spectrum.

Reaction of 2-nitrobiphenyl with diethyl methylphosphonite in diethylamine. 2-Nitrobiphenyl (20 g., 0.1 mole), diethyl methylphosphonite (111 g., 0.81 mole), and diethylamine (800 ml.) were boiled under reflux in an atmosphere of nitrogen for 2 days. At the end of this time, g.l.c. (3% A.P.L./225°) confirmed that no nitrobiphenyl remained. The diethylamine was removed on a rotary evaporator and the phosphorus esters were distilled off at 15 mm. The remaining oily orange solid was leached with ether and the undissolved carbazole filtered off (4.7 g.). The residue was chromatographed on alumina and the following fractions collected:

1. Brown oil (0.063 g.), eluted with light petroleum/30% benzene.

2-4. Brown oils (2.51 g.), eluted with light petroleum/50% benzene.

5-12. Solids (6.35 g.), eluted with benzene.

Fraction 1. had the same g.l.c. retention time as 2-nitrobiphenyl.

Fractions 2-4. were practically pure as shown by g.l.c. (3% A.P.L./220°). Distillation gave 2-diethylamino-3H-3-phenylazepine (10.5%) as a yellow oil, b.p. 110-112°/0.1 mm., n_D^{25} 1.5904, (Found: C, 79.8 ; H, 8.3 . $C_{16}H_{20}N_2$ requires C, 80.0 ; H, 8.4%). The infrared spectrum confirmed the absence of an NH-group and phosphonite and phosphonate ester sructures. The ultraviolet spectrum was similar to that of 2-diethylamino-3H-azepine[97] (λ max., 301 and 297 mμ; log ε, 3.9 and 3.86 respectively). The stuctural assignment rests principally on the p.m.r. spectrum, however, and will be justified in the following chapter.

Fractions 5-11. were carbazole, m.p. and mixed m.p. 243-245°(total yield, 66%).

Reaction of 2-nitro-4'-t-butyldiphenyl sulphide with diethyl methylphosphonite in diethylamine. The nitro-compound (5.74 g., 0.02 mole), diethyl methylphosphonite (8.16 g., 0.06 mole) and diethylamine (200 ml.) were heated under reflux in an atmosphere of nitrogen for 5 days. The initial work-up was as described in the previous experiment and chromatography on alumina yielded the following fractions:

1-9. Oils and solids (3.81 g.), eluted with light petroleum/benzene mixtures.

10-11. Thick oils, setting to a black tar (0.209 g.), eluted with benzene/30% ether. T.l.c. (silica gel/benzene) showed traces of 2-t-butylphenothia-

zine running ahead of the tar.

12-14. Tars (4.5 g.), eluted with ether/methanol mixtures.

Fractions 1-9. were all shown by t.l.c. (silica gel/benzene) to contain several components. They were combined and rechromatographed on alumina, yielding the following fractions:

1-2. Colourless solids (0.28 g.), eluted with light petroleum.

3-4. Traces of colourless solid.

5-11. Impure yellow solids (3.34 g.), eluted with light petroleum/20% benzene.

T.l.c. (silica gel/light petroleum) showed the presence of an impurity in fractions 1-2., so they were rechromatographed on silica gel to give di-(p-t-butylphenyl)disulphide (0.21 g., 11.7% based on starting material consumed), m.p. 89-90° (lit.,[98] 88.5-89°) (Found: C, 72.7 ; H, 7.9 . Calc. for $C_{20}H_{26}S_2$: C, 72.7 ; H, 7.9%). The p.m.r. spectrum in carbon tetrachloride solution showed two singlets of relative area 4:9 at t=2.7 (aromatic protons) and t=8.7 (t-butyl protons).

Fractions 5-11. appeared to be mainly starting material, but t.l.c. (silica gel/benzene) showed the presence of two other compounds, so they too were combined and rechromatographed on silica gel to give the following fractions:

1. A white solid (0.031 g.), eluted with light petroleum.

2-3. Yellow crystals (2.32 g.), eluted with light

petroleum/30% benzene.

4. A trace of oily material eluted with light petroleum/ 50% benzene.

5-6. Brown oils (0.23 g.), eluted with benzene.

7-9. Light brown tars (0.31 g.), eluted with benzene/ 50% ether.

10. A brown solid (0.31 g.), eluted with ether.

The infrared spectrum of fraction 1. was superimposable on that of the di-t-butylphenyl disulphide previously isolated.

The infrared spectrum of fractions 2-3. was superimposable on that of the starting material.

Fractions 5-6. were shown by t.l.c. (silica gel/benzene) to contain two compounds. The infrared spectrum showed similarities to those of the azepines previously described (see Appendix). The p.m.r. spectrum showed signals which can be attributed (see following chapter) to 2-diethylamino-3H-7-(4'-t-butyl)thiophenyl-azepine. In addition, the signals due to the aromatic protons and the t-butyl group were enhanced, suggesting that the second t.l.c. spot was caused by an impurity containing the t-butylphenyl group. No other signals appeared, suggesting that the impurity was possibly a polysulphide. The p.m.r. integral indicated the presence of the azepine (ca. 66%) corresponding to 0.15 g., (2.3% yield). Distillation, however, caused extensive decomposition and gave only a very small sample (1.6 mg.) of purified material,

b.p. 130-140°/0.02 mm. (Found: C, 72,9 ; H, 7.9 . $C_{20}H_{28}N_2S$ requires C, 73.15 ; H, 8.6%).

Fractions 7-9. had very diffuse infrared spectra and the p.m.r. spectrum showed only aromatic and t-butyl signals which suggested that these fractions were polymeric sulphides.

The infrared spectrum of fraction 10. was superimposable on that of the 2-t-butylphenothiazine obtained by reaction of 2-nitro-4'-t-butyldiphenyl sulphide with triethyl phosphite.

Reaction of 2-ethylnitrobenzene with triethyl phosphite.

The nitro-compound (3.02 g., 0.02 mole) and triethyl phosphite (13.3 g., 0.08 mole) were boiled under reflux in an atmosphere of nitrogen for 14 hours. After removing the phosphite and phosphate, the distillation residue was diluted with ether (30 ml.) and extracted with 2$\bar{N}$ HCl (2x20 ml.) and then with 1% NaOH (2x20 ml.). The acid extract was made alkaline with solid NaOH, when a dark oil separated. This was extracted with ether, dried ($CaCl_2$) and distilled to give a yellow oil (1.68 g.), b.p. 90-105°/0.05 mm., which was chromatographed on silica gel to give the following fractions:

1-4. Colourless crystals (0.185 g.), eluted with ether.

5-6. Yellow oils (0.59 g.), eluted with ether/50% methanol.

7. A tar (0.083 g.), eluted with methanol.

Fractions 1-4. were recrystallised from light petroleum

(b.p. 60-80°) to give diethyl N-(2-ethylphenyl)phosphoramidate, m.p. 103-105° (lit.,[27] 103-104°). The infrared spectrum showed peaks due to NH (3240 cm.$^{-1}$), P=O (1240 cm.$^{-1}$), and POEt (1030 and 980 cm.$^{-1}$) and was superimposable on that of an authentic sample prepared by hydrolysis of triethyl N-(2-ethylphenyl)phosphorimidate. The p.m.r. spectrum in deuterochloroform solution was compatible with this structure and also agreed with a published spectrum[27]: $ArCH_2$-, quartet (two protons) at t=7.37 ; $ArCH_2CH_3$, triplet (three protons) at t=8.7 ; $POCH_2$-, quintet (four protons) at t=5.87 ; $POCH_2CH_3$, triplet (six protons) at t=8.76 ; NH, broad doublet (one proton) at t=4.8 (J_{PH}≒8.5 c.p.s.); and four aromatic protons, complex pattern at t=2.87 .

Fractions 5-6. were shown by g.l.c. (3% QF-1/190°) to be almost pure and were identified as diethyl (2-ethyl-3H-azepine-7-yl)phosphonate (11.5%), b.p. 120-130°/0.03 mm., (Found: C, 55.7 ; H, 7.9 . $C_{12}H_{20}NO_3P$ requires C, 56.0 ; H, 7.8%). The infrared spectrum showed peaks due to the P=O (1250 cm.$^{-1}$) and POEt (1035 and 970 cm.$^{-1}$) groups and also the peak at 1140 cm.$^{-1}$ which occurs in the spectra of the azepines previously isolated. The structural assignment rests principally on the p.m.r. spectrum, however, and this is interpreted in the following chapter.

Extraction of the drying agent with benzene gave a further quantity (0.49 g.) of yellow oil which was shown by g.l.c. (3%

QF-1/205°) to be mainly the azepinylphosphonate, making the total yield 21%.

The ether extract from the initial work-up was now evaporated to give an oily black solid. G.l.c. (3% QF-1/195°) showed this to be a mixture of the amidate, triethyl phosphate and one other component. Chromatography on silica gel gave the following fractions:

1. A brown oil (0.017 g.), eluted with benzene/50% ether.

2-4. Colourless solids (1.14 g.) contaminated with oily material, eluted with ether.

5-6. Tars (0.197 g.) eluted with methanol

Fraction 1. was shown by g.l.c. to be a mixture of the amidate and the unknown compound in approximately 1:2 molar ratio. The p.m.r. spectrum in carbon tetrachloride was compatible with a mixture of diethyl N-(2-ethylphenyl)phosphoramidate and diethyl N-ethyl-N-(2-ethylphenyl)phosphoramidate showing the following signals in addition to those already described for the former compound: $ArCH_2-$, quartet (two protons) at t=7.22 ; NCH_2-, overlapping quartets (two protons) at t=6.5 and t=6.65 , ($J_{PH} \doteqdot 9.5$ c.p.s.). The five different types of methyl group present appeared as a complex pattern from t=8.5 to t=9.1 .

The solid material (0.65 g.) was removed from fractions 2-4., washed with light petroleum (b.p. 60-80°) and recrystallised from the same solvent to give further diethyl N-(2-ethylphenyl)-

phosphoramidate, m.p. and mixed m.p. 104-105°. The total yield was 0.83 g. (16%). The remaining oil was a mixture of the two phosphoramidates.

Reaction of triethyl N-(2-ethylphenyl)phosphorimidate with triethyl phosphite. The phosphorimidate (0.85 g., 0.003 mole) and triethyl phosphite (3.32 g., 0.02 mole) were heated under nitrogen for 12 hours at 145°. G.l.c. (3% QF-1/185°) of the reaction mixture showed mainly the imidate along with a small amount of diethyl N-(2-ethylphenyl)phosphoramidate. No azepinyl-phosphonate was detected. Triethyl phosphite was then distilled off and the residual oil, dissolved in ether (30 ml.), was extracted with 2$\bar{N}$ HCl (2x20 ml.). The acid extract was made alkaline with solid NaOH and the colourless oil which separated was extracted with ether. This ether extract was then dried ($MgSO_4$) and evaporated to yield a colourless oily solid (0.61 g.) which was shown by g.l.c. to be mainly amidate along with a little (ca. 5%) of the imidate. Recrystallisation from light petroleum (b.p. 60-80°) gave the amidate (0.61 g., 79%), m.p. and mixed m.p. 104-105°.

Attempted reaction of diethyl N-(2-ethylphenyl)phosphoramidate with triethyl phosphate. The amidate (0.5 g., 0.002 mole) and triethyl phosphate (10 ml.) were stirred under nitrogen for 13 hours at 140°. G.l.c. (3% QF-1/185°) showed that diethyl N-ethyl-N-(2-ethylphenyl)phosphoramidate was not formed.

Formation of ethylene in the reaction of 2-ethylnitrobenzene with triethyl phosphite.- (i) Isolation. The nitrocompound (9.0 g., 0.06 mole) and triethyl phosphite were stirred under nitrogen for 8 hours at 140° in apparatus connected to a cold trap (liquid air). Small amounts of a white solid condensed in the trap which was then attached to a vacuum line. The contents were warmed and allowed to expand into an infrared gas-sample cell to a pressure of ca. 25 mm. The spectrum obtained (Perkin-Elmer 621 Spectrophotometer) was superimposable on that of an authentic sample of ethylene.

(ii) Estimation. 2-ethylnitrobenzene (1.51 g., 0.01 mole) and triethyl phosphite (30 ml.) were boiled under reflux in an atmosphere of nitrogen. The apparatus was connected to a gas-burette filled with water and the following measurements of volume against time were made (760.3 mm. at 17°)

Time (min.): 0 , 1 , 2 , 3 , 5 , 8 , 14 , 18 ,
Volume (ml.): 0.1 , 6.1 , 9.2 , 12.0 , 16.8 , 21.0 , 27.3 , 29.2 ,
23 , 28 , 35 , 40 , 63 , 90 , 105 , 130 ,
30.0 , 32.1 , 32.9 , 32.7 , 32.4 , 31.8 , 32.1 , 32.3 ,
192 , 360 .
32.0 , 32.1 .

In a second run using the same apparatus containing only triethyl phosphite (31.5 ml.), the following readings were taken:

Time (min.) : 0 , 1 , 4 , 7 , 12 , 15 , 60 , 106 ,

Volume (ml.): 0.1 , 2.2 , 8.8 , 12.1 , 14.9 , 16.1 , 21.2 , 15.5 ,

270 , 390 .

10.0 , 9.9 .

∴ Volume of ethylene (measured at S.T.P.) = (32.1-9.9)

$$\times \frac{760.3}{760.0} \times \frac{273}{290}$$

= 20.7 ml.

∴ 0.01 mole of nitro-compound produces $\frac{20.7}{22400}$

= 0.000924 mole

= 9.24% .

Reaction of 2-ethylnitrobenzene with triethyl phosphite in cumene. The nitro-compound (1.51 g., 0.01 mole), triethyl phosphite (5.0 g., 0.03 mole) and cumene (60 ml.) were boiled under reflux in an atmosphere of nitrogen for 5 days. Cumene was removed on the rotary evaporator and the remaining material chromatographed on alumina. Light petroleum (b.p. 40-60°) eluted bi-α-cumyl (0.23 g., 9.7%), m.p. and mixed m.p. 117.5-118°. The remaining fractions of the chromatography were examined by g.l.c. (3% QF-1/90°) for 2-ethylaniline, but none was found. Small amounts were detected in the cumene distillate, but an attempt to extract it with acid was unsuccessful.

Reaction of nitrobenzene with triethyl phosphite. Nitrobenzene (2.46 g., 0.02 mole) and triethyl phosphite (30 ml.) were

boiled under reflux in an atmosphere of nitrogen for 8 hours, after which time, g.l.c. (3% QF-1/115°) showed the absence of nitrobenzene. Four product peaks were observed with retention times very similar to those of the products from 2-ethylnitrobenzene and it was confirmed that one of these had the same retention time as an authentic sample of triethyl N-phenylphosphorimidate. After removal of the phosphate and the excess phosphite, the residue was distilled under vacuum (0.03 mm.) from a flask packed with glass wool; four fractions were collected:

1. 0.37 g., b.p. 50-65°
2. 0.24 g., b.p. 65-75°
3. 0.91 g., b.p. 80-115°
4. 0.62 g., b.p. 120-140°

The residue (0.22 g.) was a black tar.

Fractions 1-2. were mainly triethyl phosphate, as shown by g.l.c. (5% SE-30/105°).

Fractions 3-4. were shown (3% QF-1/185°) to contain the four products mentioned above, and were combined and chromatographed on alumina:

1-3. Brown oils (0.49 g.), eluted with ether/20% ethyl acetate.

4-5. Brown solids (0.28 g.), eluted with ethyl acetate.

6. Brown crystals (0.33 g.), eluted with ethyl acetate/

10% methanol.

7-9. Tars (0.22 g.), eluted with methanol.

Fractions 1-3. were shown by g.l.c. (3% QF-1/180°) to contain considerable amounts of impurity, but distillation gave a yellow oil (0.39 g.), b.p. 120-130°/0.1 mm., which was identified as diethyl N-ethyl-N-phenylphosphoramidate (7.6%) (Found: C, 55.1 ; H, 8.2 . Calc. for $C_{12}H_{20}NO_3P$: C, 56.0 ; H, 7.85%). The infrared and p.m.r. spectra were identical with those of an authentic sample prepared as described on p. 46 .

Fractions 4-5. were mainly diethyl N-phenylphosphoramidate, but g.l.c. showed another peak which, by analogy with the reaction of 2-ethylnitrobenzene, and the respective retention times, could be diethyl 3H-azepine-7-ylphosphonate. The p.m.r. spectrum in carbon tetrachloride showed the signals expected for the phosphoramidate: $POCH_2$-, quintet (four protons) at t=5.91 ; $POCH_2CH_3$, triplet (six protons) at t=8.7 ; NH, doublet (one proton) at t=1.78 , (J_{PH}=9.5 c.p.s.); and the aromatic protons, complex pattern (five protons) at t=2.95 . In addition, weak signals were observed which might be ascribed to the 3-protons and the 4-proton of the azepinylphosphonate (ca. 12% of the fraction, <1% yield)(see following chapter).

The solids from fractions 4-6. were rechromatographed on alumina to give diethyl N-phenylphosphoramidate (0.48 g., 10.5%). Recrystallisation from light petroleum (b.p. 60-80°) gave

material with m.p. and mixed m.p. 95-96° (lit.,[99] 96-97°).

Isolation of ethylene from the reaction of nitrobenzene with triethyl phosphite. The procedure was as described for 2-ethylnitrobenzene and, as before, a spectrum superimposable on that of an authentic sample was obtained.

Reaction of triethyl N-phenylphosphorimidate with triethyl phosphate. The phosphorimidate (2.57 g., 0.01 mole) and triethyl phosphate (18.2 g., 0.1 mole) were stirred in a nitrogen atmosphere for 15 hours at 140°. G.l.c. (3% QF-1/175°) of the reaction mixture showed the presence of peaks with the same retention times as authentic samples of triethyl N-phenylphosphorimidate, diethyl N-ethyl-N-phenylphosphoramidate and diethyl N-phenylphosphoramidate. The reaction mixture was then distilled, giving the following fractions (0.05 mm.):

1. A colourless oil, 17.5 g., b.p. 55°.
2. A colourless oil, 0.29 g., b.p. 110-120°.
3. A colourless oil, 0.41 g., b.p. 130-145°.
4. A colourless solid, 0.33 g., b.p. 145-150°.

Fraction 1. was identified as triethyl phosphate on the basis of its infrared spectrum.

Fraction 2. gave g.l.c. peaks (3% QF-1/175°) shown to be triethyl N-phenylphosphorimidate, diethyl N-ethyl-N-phenylphosphoramidate, and diethyl N-phenylphosphoramidate by comparison with the retention times of authentic samples. The relative

areas of the peaks were respectively 1.3:1.69:1.0 , corresponding approximately to 0.094 g., 0.123 g., and 0.073 g. The p.m.r. spectrum in carbon tetrachloride solution showed the signals to be expected of such a mixture. In particular, the overlapping quartets at t=6.33 and t=6.49 , and the sharp peak at t=2.8 in the aromatic region which occur in the spectrum of diethyl N-ethyl-N-phenylphosphoramidate were both observed.

Fraction 3. showed g.l.c. peaks which suggested that it was a mixture of diethyl N-ethyl-N-phenylphosphoramidate and diethyl N-phenylphosphoramidate in the ratio 1:3.8 corresponding to 0.085 g. and 0.315 g. The estimated overall yield of the former compound was therefore 0.208 g. (8.1%).

Fraction 4. and the distillation residue (1.22 g.) were diethyl N-phenylphosphoramidate, m.p. and mixed m.p. 95.5-97°. The overall yield of this compound was 1.94 g. (85%).

Examination of triethyl phosphite for the presence of diethyl phosphite. G.l.c. (3% QF-1/105°) analysis of the triethyl phosphite used in these experiments showed only a trace (≤1%) of diethyl phosphite present as an impurity. The amount of diethyl phosphite was not increased on heating the triethyl phosphite under nitrogen for 12 hours at 140° either alone or in the presence of a tertiary base (pyridine).

Reaction of nitrobenzene with triethyl phosphite in an excess of diethyl phosphite. Nitrobenzene (2.46 g., 0.02 mole),

triethyl phosphite (10 ml.) and diethyl phosphite (75 ml.) were heated under nitrogen for 6 days at 140°. Examination of the mixture by g.l.c. (3% QF-1/180°) showed that no azepinylphosphonate was formed.

Reaction of o-nitrotoluene with with triethyl phosphite. o-Nitrotoluene (4.11 g., 0.03 mole) and triethyl phosphite (40 ml.) were heated under nitrogen for 14 hours at 140°. The phosphate and the excess of phosphite were distilled off and the residue, dissolved in benzene (5 ml.), was chromatographed on alumina to give the following fractions:

1-3. Oils (0.085 g.), eluted with ether.

4-6. Oils (0.167 g.), eluted with ether/20% ethyl acetate.

7-9. Brown oils (0.69 g.), eluted with ether/50% ethyl acetate.

10-11. Brown solid (3.04 g.), eluted with ether/5% methanol.

12. Tar (0.178 g.), eluted with methanol.

Fractions 1-6. were all complex mixtures of minor products and were not proceeded with.

Fractions 7-9. were shown by g.l.c. (3% QF-1/180°) to be a mixture of triethyl phosphate and a compound which, by comparison with the g.l.c. traces from the corresponding reactions of nitrobenzene and 2-ethylnitrobenzene, could have been diethyl N-ethyl-N-(o-tolyl)phosphoramidate. Distillation separated the

phosphate and afforded the suspected N-ethylphosphoramidate (0.41 g., 5%), b.p. 120-130°/0.03 mm. (Found: C, 57.1 ; H, 8.15 . $C_{13}H_{22}NO_3P$ requires C, 57.6 ; H, 8.2%). The p.m.r. spectrum in carbon tetrachloride solution was compatible with this structure, showing the following signals: $ArCH_3$, singlet (three protons) at t=7.7 ; NCH_2-, overlapping quartets (two protons) at t=6.56 and 6.74, (J_{PH}=9.6 c.p.s.); NCH_2CH_3, triplet (three protons) at t= 9.0 ; $POCH_2$-, quintet (four protons) at t=6.03 ; $POCH_2CH_3$, triplet (six protons) at t=8.76 ; and the aromatic protons, singlet (four protons) at t=2.9 .

Fractions 10-11. were shown by g.l.c. to be a mixture of two components with retention times which suggested, by analogy with the previous cases, that they might be diethyl N-(o-tolyl)-phosphoramidate and diethyl 2-methyl-3H-azepine-7-ylphosphonate. They were combined and chromatographed on silica gel to give the following fractions:

1-2. A tar (0.16 g.), which failed to adsorb on the column.

3-16. White solids (1.63 g.), eluted with ether.

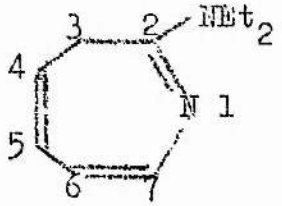
17-20. Brown oils (0.78 g.), eluted with ether/20% methanol.

Fractions 3-16. were recrystallised from light petroleum (b.p. 60-80°) to yield diethyl N-(o-tolyl)phosphoramidate (22.5%), m.p. 93-94° (lit.,[100] 95°). The p.m.r. spectrum in deutero-

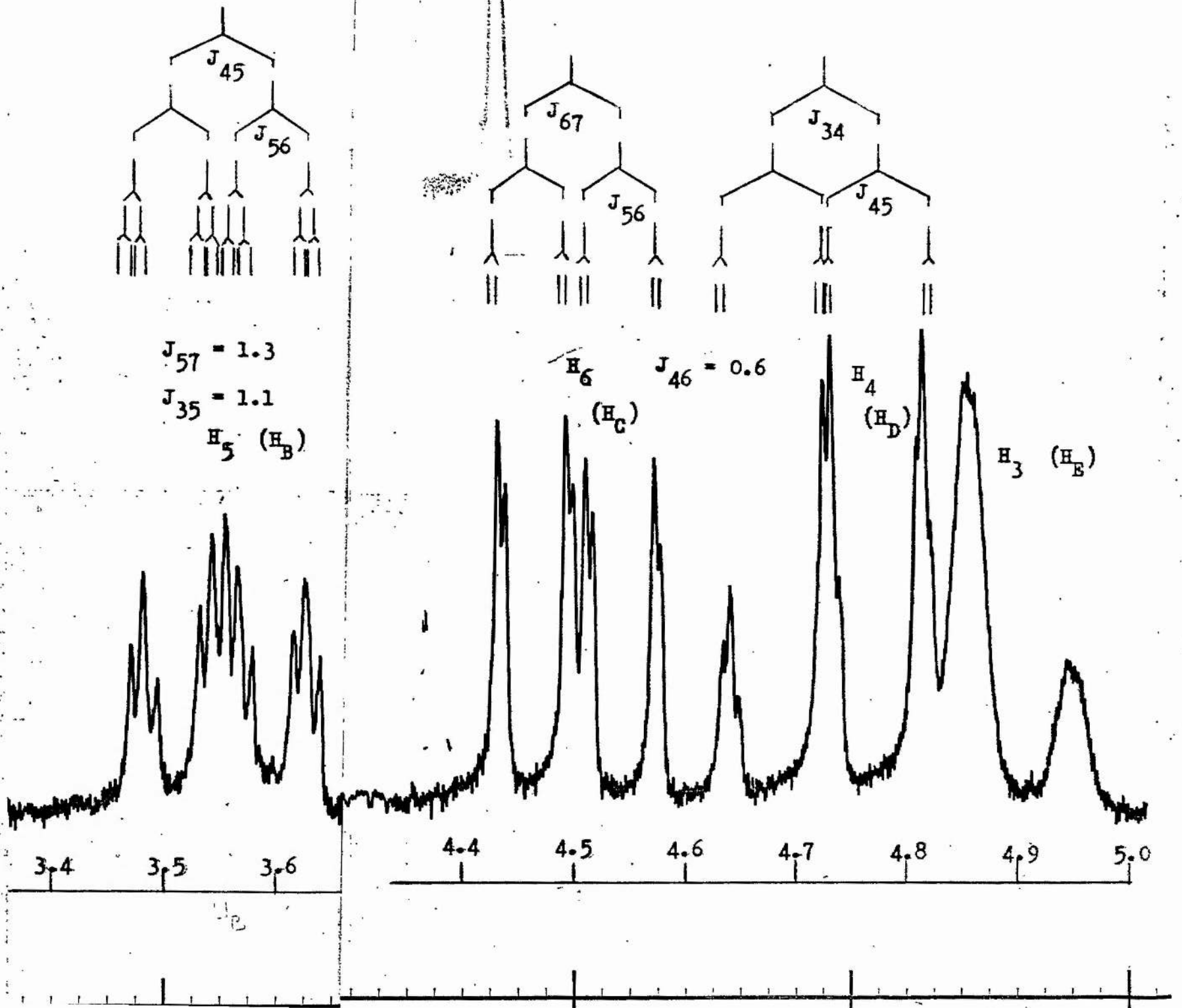
chloroform solution gave the expected signals: $ArCH_3$, singlet (three protons) at t=7.75 ; $POCH_2$-, quintet (four protons) at t=5.89 ; $POCH_2CH_3$, triplet (six protons) at t=8.7 ; NH, broad doublet (one proton) at t=4.72 , (J_{PH}=8.5 c.p.s.); and the aromatic protons, complex pattern (four protons) from t=2.6 to t=3.2 .

Fractions 17-20. were distilled to yield almost pure diethyl 2-methyl-3H-azepine-7-ylphosphonate (0.59 g., 8.1%), b.p. 125-130°/0.03 mm. (Found: C, 52.3 ; H, 7.4 . $C_{11}H_{18}NO_3P$ requires C, 54.35 ; H, 7.5%). Despite this analysis, the infrared spectrum (see Appendix) and the p.m.r. spectrum (see following chapter) were fully compatible with the assigned structure.

8. P.M.R. Spectra of Products containing the Azepine Ring System.- Unknown compound from the reaction of 2-nitrobiphenyl with diethyl methylphosphonite in diethylamine. In view of the isolation of 2-diethylamino-3H-azepine (68) from the reaction of nitrobenzene with diethyl methylphosphonite in diethylamine, an analogous structure was suspected for this unidentified product.



(68)


J_{45}
J_{56}
$J_{57} = 1.3$
$J_{35} = 1.1$
H_5 (H_B)
3.4
3.5
3.6
J_{67}
J_{56}
J_{34}
J_{45}
H_6 (H_C)
$J_{46} = 0.6$
H_4 (H_D)
H_3 (H_E)
4.4
4.5
4.6
4.7
4.8
4.9
5.0

(68) was identified by comparison of its p.m.r. spectrum in carbon tetrachloride solution with that published by Doering and Odum.[97] In addition to the signals from the ethyl protons, the spectrum of (68) showed four separate absorptions (each one proton) in the region t=2.9-5.2 which were ascribed to the olefinic protons, and a doublet (two protons) at t=7.44 ascribed to the methylene group at the 3-position.

In addition to a complex pattern (five protons) in the aromatic region and signals which were attributed to two identical ethyl groups attached to nitrogen (quartet (four protons) at t=6.65 and triplet (six protons) at t=8.86), the 100 Mc. p.m.r. spectrum in carbon tetrachloride solution of the unknown compound showed a doublet (one proton) at t=3.42 , a triplet (one proton) at t=3.65 and a complex pattern (three protons) centred at t=4.73 .

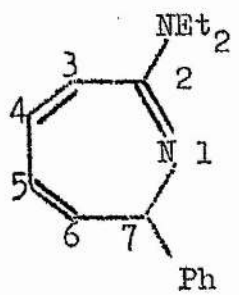
Dissolving the sample in deuterobenzene brought about a considerable improvement in the resolution of the complex pattern centred at t=4.76 in carbon tetrachloride solution. The spectrum now showed a complex pattern (six protons) from t=2.65 to t=3.15 ; a triplet (one proton), H_B, at t=3.55 ; a doublet of doublets (one proton), H_C, at t=4.50 ; a triplet (one proton), H_D, at t=4.725 ; and a broad doublet (one proton), H_E, at t=4.88 . A scale expansion of the regions of the spectrum containing H_B-H_E is shown on the facing page.

Decoupling experiments showed that the doublet, H_A, which had been centred at t=3.45 in carbon tetrachloride was now shifted to about t=3.0 in the aromatic region. Irradiation at this frequency caused the doublet of doublets at t=4.48 to collapse to a doublet. Irradiation of the triplet at t=3.55 also caused almost complete collapse of the doublet of doublets to a doublet and, in addition, caused the triplet at t=4.72 to collapse to a doublet. Finally, irradiation in the aromatic region (t= 2.78) caused the broad doublet at t=4.88 to sharpen and show a small superposition of doublet structure on each of the peaks.

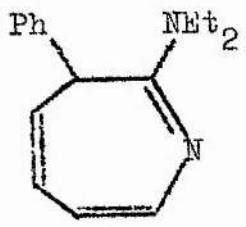
Scale expansion of the spectrum in conjunction with the decoupling experiments allowed the following coupling constants (c.p.s.) to be evaluated:

J_{AC}	= 8.2	J_{AB}	= 1.3
J_{BC}	= 6.5	J_{BE}	= 1.1
J_{BD}	= 9.1	J_{CD}	= 0.6
J_{DE}	= 9.6		

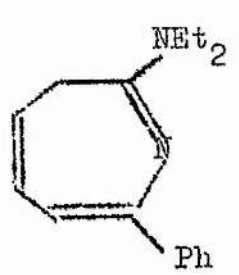
By analogy with the structure of 2-diethylamino-3H-azepine (68), the following structures might be possible:



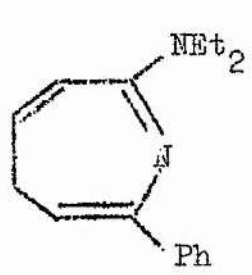
(69)



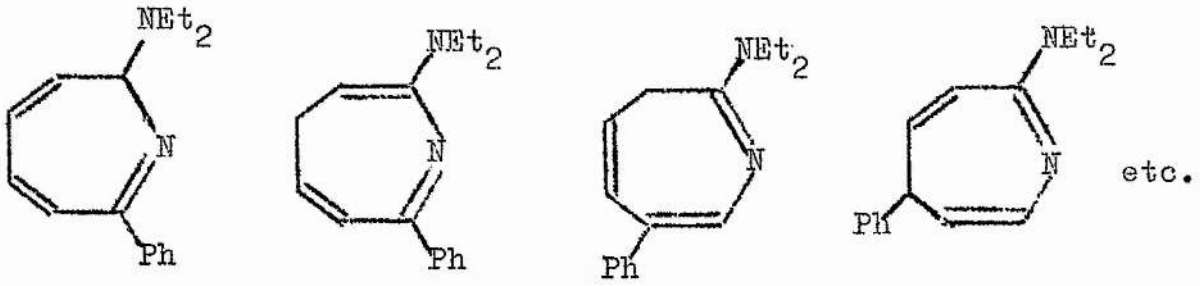
(70)



(71)



(72)



(73) (74) (75) (76)

Only structures (69) and (70) are compatible with the features of the spectrum described so far. Since there were four large (6.5-9.6 c.p.s.) couplings between the five protons A-E, any structures not having these protons on consecutive carbon atoms can be eliminated. The final decoupling experiment showed that one proton (H_E) is attached to the same carbon atom as the phenyl group, eliminating structure (73). H_E has only one large (9.6 c.p.s.) coupling constant, thus excluding structure (76). The absence of a ring-methylene signal from the spectrum is further evidence against many of these structures.

Assuming structure (69) to be correct, since H_E is coupled to the phenyl group, it must be H_7. The following assignments can then be made (chemical shifts in carbon tetrachloride solution):

Proton	Assignment	Chemical shift (t)	Coupling constant
H_E	H_7	ca. 4.78	$J_{67} = 9.6$
H_D	H_6	ca. 4.68	$J_{56} = 9.1$
H_B	H_5	3.65	$J_{45} = 6.5$
H_C	H_4	ca. 4.65	$J_{34} = 8.2$
H_A	H_3	3.42	

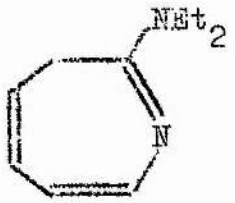
The corresponding parameters for structure (70) would be:

Proton	Assignment	Chemical shift	Coupling constant
H_E	H_3	ca. 4.78	$J_{34} = 9.6$
H_D	H_4	ca. 4.68	$J_{45} = 9.1$
H_B	H_5	3.65	$J_{56} = 6.5$
H_C	H_6	ca. 4.65	$J_{67} = 8.2$
H_A	H_7	3.42	

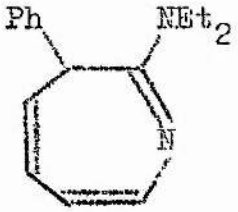
Arguments put forward by Doering[97] in his analysis of the p.m.r. spectrum of 2-diethylamino-3H-azepine (68) permit a distinction to be drawn between (69) and (70). If structure (69) were correct, then H_3 would be α- to the amidine carbon atom, and H_4 would be β-. In α,β-unsaturated carbonyl compounds and nitriles, the signal due to the β-proton is always found at lower field. Assuming the electronic similarity of the amidine function, H_4 would then be expected to appear at lower field than H_3 when, in fact, the reverse is found. In addition to this argument against structure (69), another argument based on expected chemical shifts can be advanced in favour of structure (70). It is known that in double bonds attached to atoms with unshared electrons, the α-hydrogen is found at lower field than the β-, the α- and β-protons in pyridine providing a well known example of this effect (t=1.50 and 3.02 respectively). In agreement with this, the doublet assigned to H_7 in structure (70) appears at lower field (t=3.42) than the signal assigned to H_6

(t=4.65).

The unknown compound was therefore given the structure 2-diethylamino-3H-3-phenylazepine (70).



(68)



(70)

Further confirmation of the correctness of this structure is given by the similarity of the chemical shifts and coupling constants for H_4-H_7 with the corresponding protons of 2-diethylamino-3H-azepine (68):

Proton	Chemical shift	Coupling constant
H_4	4.98	J_{45} = 8.7
H_5	3.73	J_{56} = 5.5
H_6	4.36	J_{67} = 7.8
H_7	2.97	

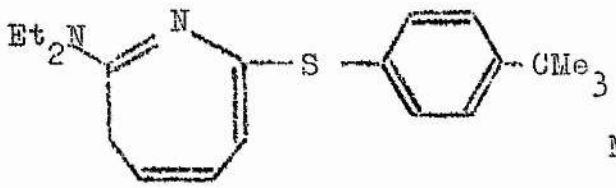
A theoretical pattern for the signals due to H_4-H_6 was built up from the observed coupling constants and is reproduced in the figure facing page 109 .

Suspected azepine from the reaction of 2-nitro-4'-t-butyldiphenyl sulphide with diethyl methylphosphonite. The p.m.r. spectrum in carbon tetrachloride of this compound showed a singlet (six protons) at t=2.71 , a quartet (four protons) at

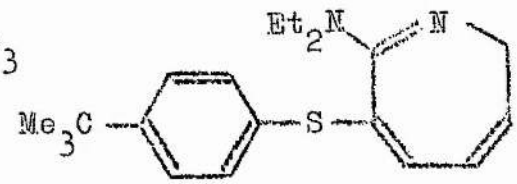
t=6.76 , a singlet (fourteen protons) at t=8.71 , and a triplet (six protons) at t=9.0 . These were attributed to aromatic protons, an N-ethyl group and a t-butyl group. Signals reminiscent of those produced by the ring protons in the two azepines previously discussed were also observed: a quartet (one proton), H_A, at t=3.90 ; a doublet (one proton), H_B, at t=4.35 ; a broad quartet (one proton), H_C, at t=5.15 ; and a doublet (two protons), H_D, at t=7.36 . Coupling constants (c.p.s.) were found as follows:

$$J_{AB} = 5.9 \ , \ J_{AC} = 8.3 \ , \ J_{CD} = 7.0 \ .$$

By analogy with the chemical shift of the protons at the 3-position in 2-diethylamino-3H-azepine (t=7.44), the two proton doublet at t=7.36 was thought to be due to a ring methylene group. Since there are three large coupling constants between five protons, two of which are attached to the same carbon atom, the four carbon atoms concerned must be adjacent. Since the signal due to the methylene group appears as a doublet, it can be further asserted that it comes at one end of this group of four carbon atoms. These considerations eliminate all but two of the possible 2-diethylaminoazepine structures:



(77)



(78)

As mentioned previously, the chemical shift of the methylene protons (t=7.36) is very similar to that observed for the protons at the 3-position in 2-diethylamino-3H-azepine. If structure (78) were correct, the methylene doublet would appear at much lower field (cf. the methylene protons in the diethylamino group, t=6.76).

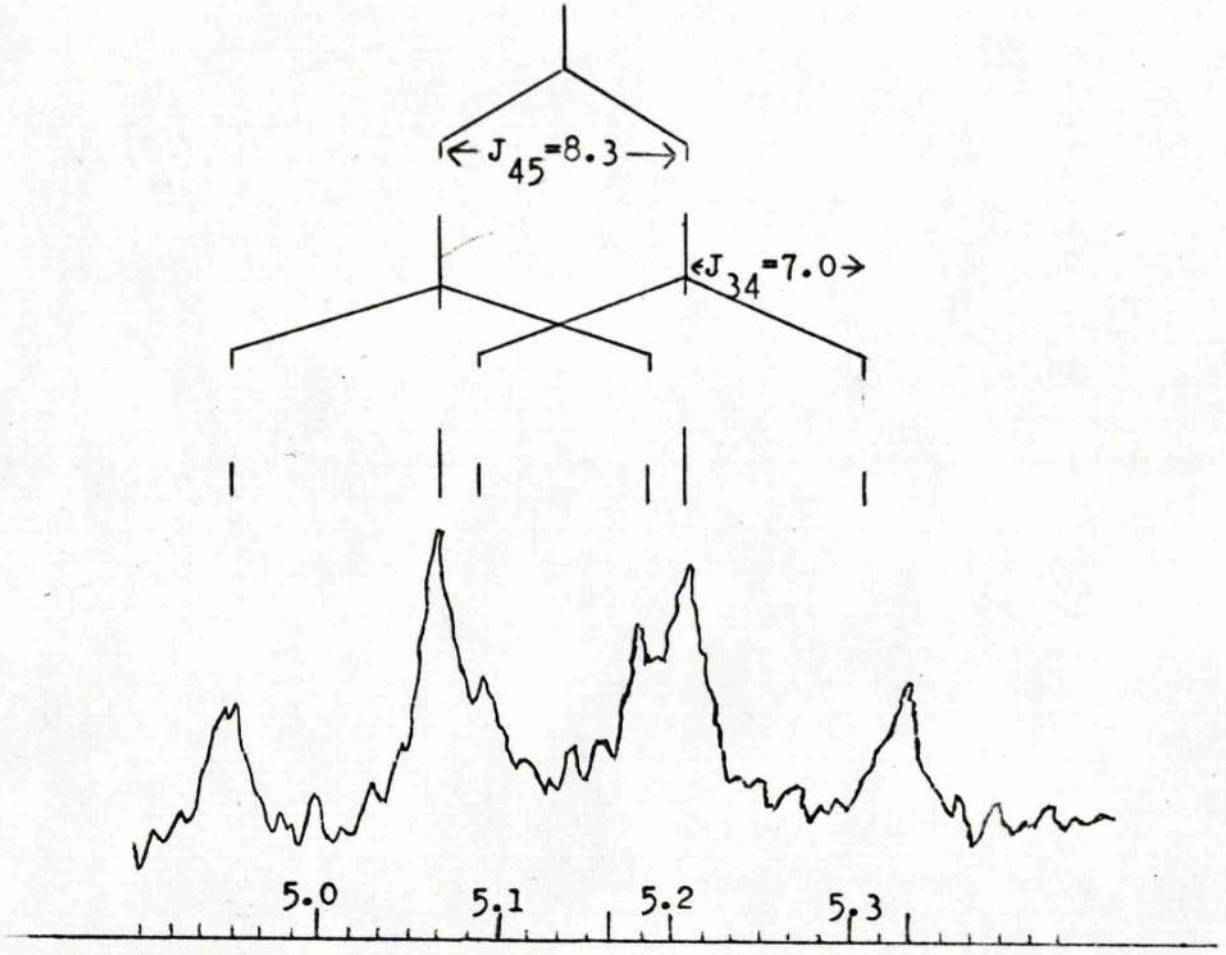
The compound was therefore given the structure 2-diethylamino-3H-7-(p-t-butyl)thiophenylazepine (77). It was shown in the Experimental Section that this product was not absolutely pure and since the only irregularities observed in the p.m.r. spectrum were enhancements of the aromatic and t-butyl signals, it was suggested that the impurity might be poly(p-t-butylphenyl) sulphide.

The doublet at t=4.35 must be H_6 and starting from this point, the azepine protons can now be assigned to the observed resonances.

Proton	Assignment	Chemical shift	Coupling constant
H_B	H_6	4.35	$J_{56} = 5.9$
H_A	H_5	3.90	$J_{45} = 8.3$
H_C	H_4	5.15	$J_{34} = 7.0$
$H_D(2)$	$H_3(2)$	7.36	

These chemical shifts and coupling constants are in excellent agreement with those obtained from the corresponding protons in 2-diethylamino-3H-azepine (see p.113).

H_4 signal in 2-diethylamino-3H-7-(p-t-butyl)thiophenylazepine.



A scale expansion of the broad quartet assigned to H_4 and a theoretical pattern constructed from the coupling constants is shown on the facing page.

Suspected azepine from the reaction of o-nitrotoluene with triethyl phosphite. The spectrum in carbon tetrachloride showed a singlet (three protons) at t=7.84 , a quintet (four protons) at t=5.93 , and a triplet (six protons) at t=8.69 which were respectively assigned to the tolyl methyl group and to two ethoxy groups attached to phosphorus. The ring protons appeared as a quartet (one proton), H_A, at t=3.07 ; a quintet (one proton), H_B, at t=3.61 ; a quartet (one proton), H_C, at t=4.54 ; and a doublet (two protons), H_D, at t=7.48 . A broad similarity to the spectrum of the 2-diethylamino-3H-7-thiophenylazepine discussed in the previous section suggested that in this case, the azepine ring might be similarly substituted.

Scale expansion of the region from t=2.5 to t=5.0 revealed that each of the protons H_A-H_C was coupled to some other nucleus in addition to the adjacent protons. The additional coupling could only be with phosphorus, and examination of the expanded spectrum produced the following coupling constants:

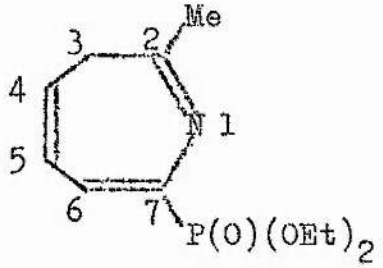
$$J_{AB} = 6.0 \ , \ J_{BC} = 8.9 \ , \ J_{CD} = 6.8 \ .$$

$$J_{PH_A} = 14.5 \ , \ J_{PH_B} = 4.4 \ , \ J_{PH_C} = 1.8 \ .$$

Since there are three large proton coupling constants between the protons H_A-H_D, the carbon atoms to which they are

attached must be adjacent. The chemical shift of the ring methylene protons is incompatible with their being situated at the 7-position. The coupling constant between P and H_A can only be accommodated by a stucture PC-CH (cf. $P{>}C{=}C{<}_{H}$ in dimethyl cis-3-pent-2-enylphosphonate,[118] J_{PH} = 23.5 c.p.s.).

In view of these considerations, the structure (79) was proposed.



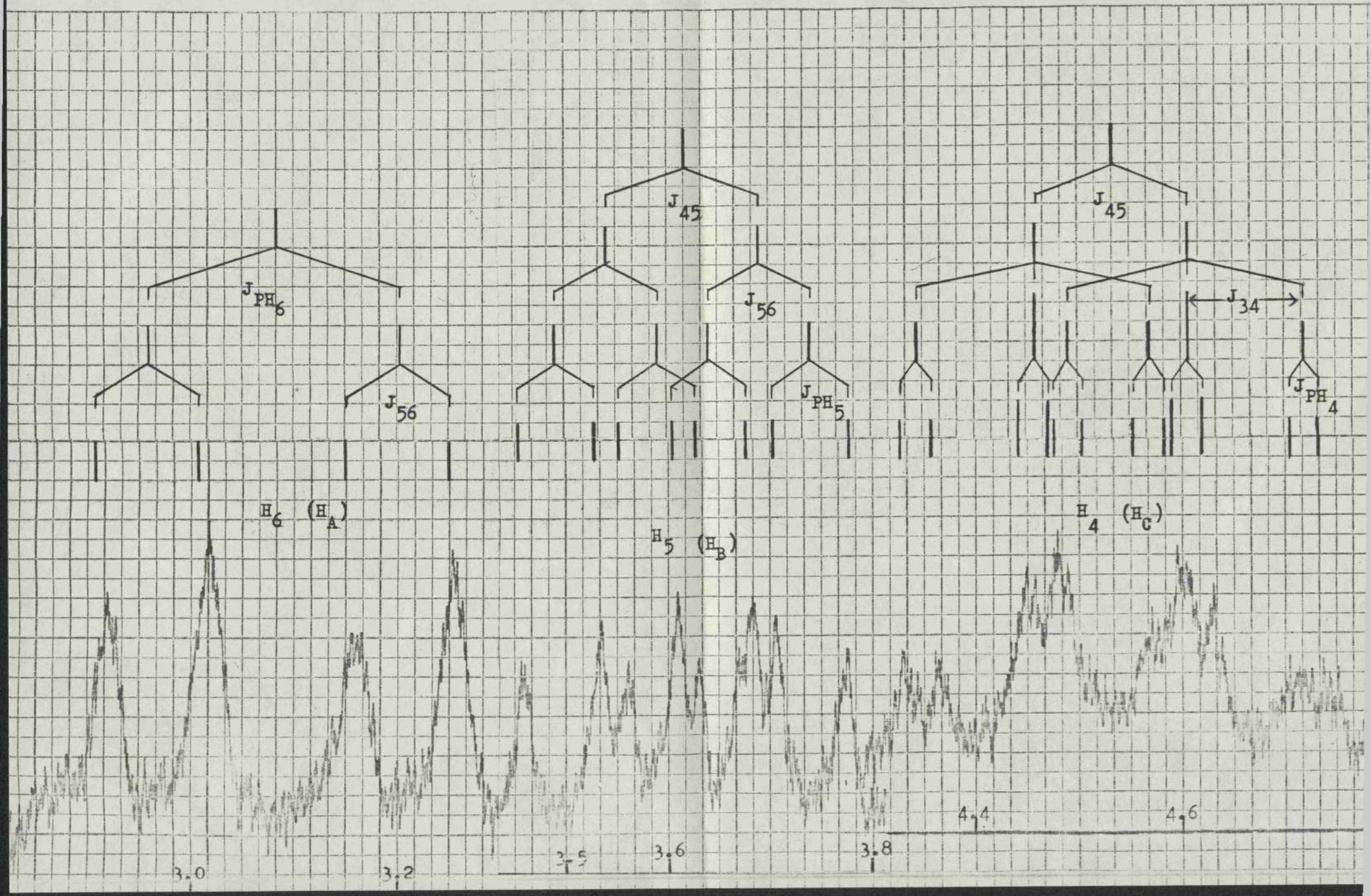
(79)

Decoupling experiments confirmed that H_C was coupled to the protons H_D, since irradiation at t=4.55 caused the doublet at t= 7.48 to collapse to a broad singlet. Since the proton with the large PH coupling constant must be H_6, the following assignments can be made on the basis of structure (79):

Proton	Assignment	Chemical shift	J_{HH}	J_{PH}
H_A	H_6	3.07	J_{56}=6.0	J_{PH_6}=14.5
H_B	H_5	3.61	J_{45}=8.9	J_{PH_5}=4.4
H_C	H_4	4.54	J_{34}=6.8	J_{PH_4}=1.8
$H_D(2)$	$H_3(2)$	7.48		

Again, the chemical shifts and proton coupling constants of those protons which can be reasonably compared (H_3-H_5 in this

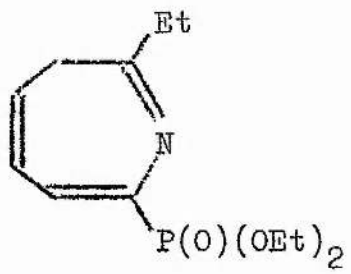
EC. SHIFT	REF. STD.	R.F. FIELD	R.F. GAIN	RE	SENSITIVITY NORM: ____ INT: ____	SWEEP RATE ____ UNITS ____ PER MIN	TIME CONST. ____ SECS 0.15 M. SECS.	SCAL



case) are very similar to those observed for the corresponding protons in 2-diethylamino-3H-azepine (68 , p.113). The compound was therefore assumed to be diethyl 2-methyl-3H-azepine-7-yl-phosphonate (79).

An expansion of the region t=2.5-5.0 and a theoretical spectrum built up from the coupling constants are shown on the facing page.

The suspected azepine from the reaction of 2-ethylnitrobenzene with triethyl phosphite. The p.m.r. spectrum in carbon tetrachloride of the product isolated from this experiment was identical in all but two respects with that of the product (79). There was an additional triplet (three protons) at t=8.87 and the doublet at t=7.48 in (79) now appeared as part of a complex pattern (four protons) centred at t=7.50 . These differences are compatible with the substitution of an ethyl group for the ring methyl group in (79). The product was therefore given the structure diethyl 2-ethyl-3H-azepine-7-ylphosphonate (80).

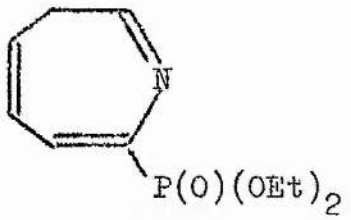


(80)

The chemical shifts and coupling constants obtained from the spectrum are tabulated below.

Proton	Chemical shift	Proton coupling	Phosphorus coupling
H_6	3.08	$J_{56} = 6.0$	$J_{PH_6} = 14.3$
H_5	3.61	$J_{45} = 8.9$	$J_{PH_5} = 4.5$
H_4	4.59	$J_{34} = 7.0$	$J_{PH_4} = 1.8$
$H_3(2)$	ca.7.50		

The suspected azepine from the reaction of nitrobenzene with triethyl phosphite. No product corresponding to the azepines in the previous two sections was isolated from this experiment. The p.m.r. spectrum in carbon tetrachloride of a mixture of diethyl N-phenylphosphoramidate with a small amount of another compound showed signals which suggested that the second component of the mixture might be diethyl 3H-azepine-7-ylphosphonate (81).



(81)

The ring methylene protons in this compound would be expected to appear as a quartet due to the additional coupling with the proton at the 2-position. The spectrum shows such a quartet at t=7.59 with couplings of ca. 7 c.p.s. and ca. 5 c.p.s. A weak quartet was also observed at t=4.65 which by analogy with (79) and (80) should be due to H_4. Any other signals were obscured by a complex pattern in the aromatic region.

DISCUSSION

A. Synthetic Aspects.

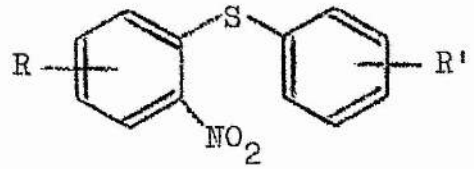
1. Reaction of 2-Nitrodiphenyl Sulphides with Tervalent Organophosphorus Compounds.- Although not embraced by this heading, the reactions of 4-methyl-2'-nitrodiphenyl sulphoxide, 4-methyl-2'-nitrodiphenyl sulphone, 2-nitrophenyl phenyl ether, and 2-nitrophenyl phenyl selenide with triethyl phosphite will be considered in this section.

General considerations. Before the present work was commenced, the preparative value of the deoxygenation of nitro-compounds by tervalent organophosphorus compounds was limited to the synthesis of heterocyclic compounds with 5-membered rings containing from one to three nitrogen atoms. Synthesis of 6-membered rings and cyclisation onto an atom other than carbon had not been achieved.

Earlier workers had met with some success in their efforts to prepare 6-membered ring compounds by the other methods of cyclisation referred to in the Introduction. The synthesis of phenazine from 2-nitrodiphenylamine on heating with ferrous oxalate[35] has been dealt with elsewhere (p. 15). Smith and his co-workers[101] synthesised phenothiazine (32%) and phenothiazine dioxide (16%) by thermal decomposition of 2-azidophenyl phenyl sulphide and 2-azidophenyl phenyl sulphone, but were unsuccessful in their attempts to prepare phenazine and phenoxazine from

2-azidodiphenylamine and 2-azidophenyl phenyl sulphide.

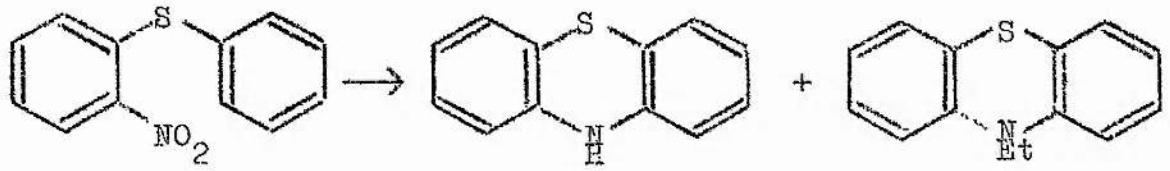
Summary of results. A range of 2-nitrobiaryl sulphides (67) was allowed to react with triethyl phosphite to give the products tabulated below:



(67)

R	R'	Products isolated
H	H	Phenothiazine (54%) and 10-ethylphenothiazine (2.4%)
H	4-Me	2-Methylphenothiazine (36%) and 10-ethyl-2-methylphenothiazine (25%)
H	4-t-Bu	2-t-Butylphenothiazine (55%) and 10-ethyl-2-t-butylphenothiazine (4.6%)
4-COOEt	4-t-Bu	8-Carbethoxy-2-t-butylphenothiazine (54%)
4-Me	H	2-Methylphenothiazine (10.3%) and 10-ethyl-2-methylphenothiazine (2.8%)
H	4-Cl	2-Chlorophenothiazine (0.1%) and starting material (32%)
4-Cl	H	2-Chlorophenothiazine (2.5%) and 2-amino-4-chlorodiphenyl sulphide (2.9%)
4-CF_3	H	2-Trifluoromethylphenothiazine (0.35%)
4-NH_2	H	Starting material (75%)
H	4-NHCOMe	Tar
4-COOEt	H	Tar

In the successful ring closures, the general process seems to be as follows (taking 2-nitrophenyl phenyl sulphide as an example):



It was demonstrated that the N-ethylphenothiazines could arise from ethylation of the unsubstituted phenothiazines by triethyl phosphate. The conditions required to effect this ethylation were relatively severe (ca. 15 hours at 169° for complete conversion) and consequently, repetition of the deoxygenation of 4-methyl-2'-nitrodiphenyl sulphide under milder conditions (12 hours at 140° cf. 12 hours at 156°) led to the formation of 2-methylphenothiazine (50%) and 10-ethyl-2-methylphenothiazine (3%)(cf. 36% and 25%).

The situation with regard to the two methylnitrodiphenyl sulphides cannot be claimed to be satisfactory. Although there was t.l.c. evidence to suggest that the 2-methylphenothiazine from 4-methyl-2'-nitrodiphenyl sulphide was impure, which would account for the low m.p. observed, no such evidence could be obtained to explain the disparity in the melting points of the N-ethyl derivatives. Although the p.m.r. spectra (see Experimental) showed that both compounds were methyl-N-ethylphenothiazines, the differences in the infrared spectra suggested that either one product was very impure or they were two

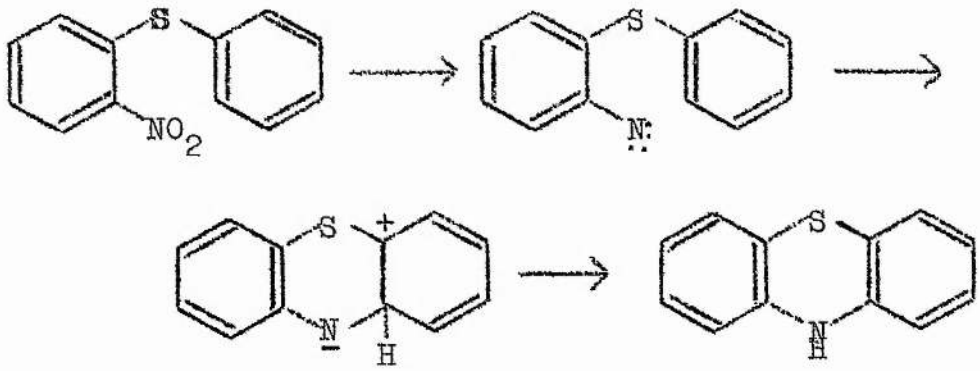
different isomers. The nitrodiphenyl sulphides both had literature m.p. and an examination by p.m.r. of the thiols and 2-chloronitrobenzenes from which they were prepared failed to reveal any inconsistencies.

The reactions of 4-methyl-2'-nitrodiphenyl sulphide with triphenylphosphine and tri-n-butylphosphine gave tars, but no isolable products. Reaction of 2-nitrophenyl phenyl sulphide with hexaethyl phosphorous triamide and diethyl methylphosphonite met with a similar lack of success, although t.l.c. indicated that a trace of phenothiazine was formed in the latter case. Repetition of this experiment in a large excess of hexadecane resulted in the formation of phenothiazine in 9.3% yield. 2-Nitrophenyl phenyl sulphide was recovered unchanged after heating at 76° in phosphorus trichloride and reaction in a sealed tube at 170° produced a black tar in which phenothiazine could not be detected, along with recovered starting material (55%).

Possible mechanisms for the cyclisation of 2-nitrodiphenyl sulphides. The results given above show that this reaction, which was initially regarded as most promising in view of the early synthetic successes, is of limited applicability. Apart from those sulphides with a p-alkyl group in the ring not containing the nitro-group, the reaction was more or less unsuccessful regardless of whether the substituents were electron donating or withdrawing. This feature was irreconcilable with

either of the postulated mechanisms (see below). Equally puzzling was the failure of those cyclisations in which reagents other than triethyl phosphite were used to effect deoxygenation. The nitro-group undoubtedly reacts in these cases, as shown by the large amounts of tar formed and it was shown for diethyl methylphosphonite that reaction with the sulphur in diphenyl sulphide or phenothiazine does not occur.

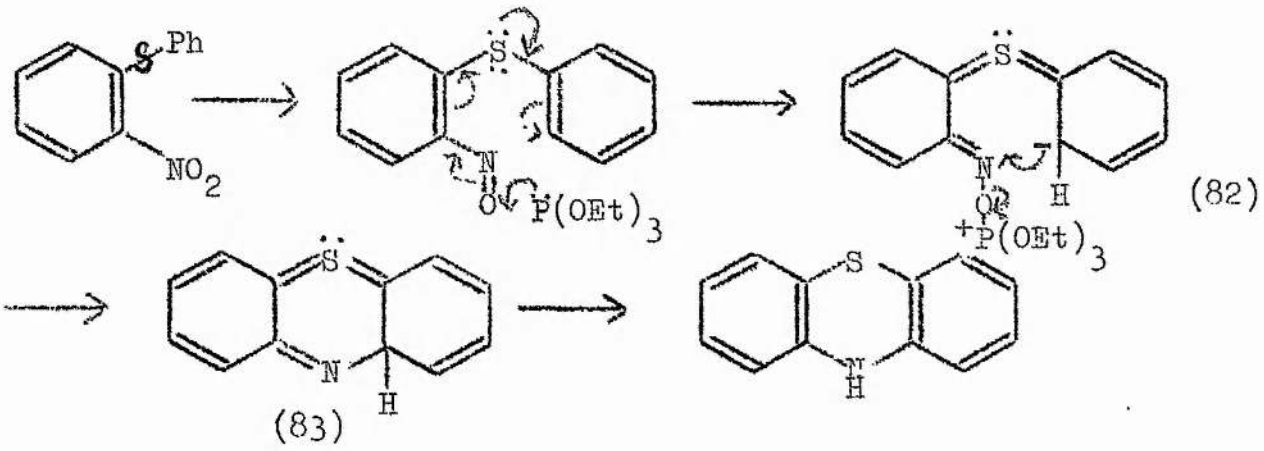
It is felt that the most likely mechanism for the successful cyclisations involves attack by a nitrene intermediate, produced by deoxygenation of the nitro-group, at the 2-position in the adjacent ring.



It is difficult to explain the failure of 2-nitrophenyl phenyl ether and 2-nitrodiphenylamine[26] to produce phenoxazine and phenazine if this mechanism is correct. However, thermal decomposition of the corresponding azides,[101] which almost certainly involves a nitrene intermediate, gave analogous results in these three cases. The isolation of 2-diethylamino-3H-7-(p-t-butyl)thiophenylazepine (77 , p.114) from the reaction in

diethylamine of 2-nitro-4'-t-butyldiphenyl sulphide with diethyl methylphosphonite can be explained in terms of a nitrene mechanism as discussed below (p. 155).

At first sight, a mechanism not involving a nitrene, similar to those discussed in the two following sections, appears to be impossible due to loss of the conjugation between the nitrogen and the point of ring closure. If utilisation of the vacant sulphur 3d-orbitals is permitted, however, such a mechanism can be visualised:

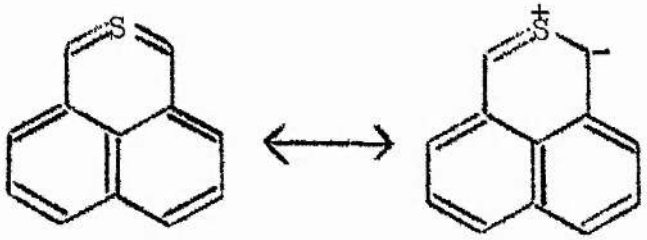


Nearly all the available evidence (see below), however, argues against the possibility of intermediate structures such as (82) and (83).

Expansion of the sulphur valence shell has been a controversial subject for some years. In a review of the subject,[102] Cilento concludes that the evidence for decet structures of sulphur flanked by two double bonds is scanty. A considerable amount of evidence, mainly spectral, is presented against this type of structure. Of particular relevance is the work of Mangini and

Passerini[103] who concluded on the basis of electronic absorption spectra that conjugation of the type Ar ⇄ S ⇄ Ar' was not operative in diaryl sulphides. It was shown that this process was spectrally unimportant in the compound, 4-dimethylamino-4'-nitrodiphenyl sulphide which would provide it with maximum opportunity. In a similar study of the ultraviolet spectra of some aryl alkyl and aryl alkenyl sulphides Montanari[104] has come to the same conclusion. More recently, Bendazolli and Zauli[105] have predicted, by means of refined theoretical calculations, that participation of the d-orbitals in aromatic sulphides was not likely to be significant.

Very recently, two groups of workers[106] have synthesised a compound formulated as 2-thiaphenalene (84), but it is not clear whether the tetracovalent structure makes as important a contribution to the resonance hybrid as dipolar forms such as (85).

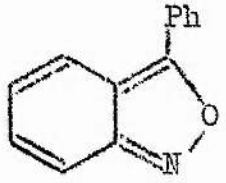


(84) (85)

If d-orbital expansion were operative, 2-nitrophenyl phenyl selenide would be expected to lead to phenoselenazine on deoxygenation. The reaction of the selenide with triethyl phosphite, however, afforded only 2-aminophenyl phenyl selenide.

4-Methyl-2'-nitrodiphenyl sulphoxide reacted with triethyl phosphite giving low yields of 4-methyl-2'-nitrodiphenyl sulphide, 2-methylphenothiazine and 10-ethyl-2-methylphenothiazine, suggesting that deoxygenation takes place at sulphur before nitrogen. The reaction of 4-methyl-2'-nitrodiphenyl sulphone with triethyl phosphite gave only an intractable black tar, in contrast to the thermal decomposition of 2-azidophenyl phenyl sulphone[101] which yielded phenothiazine dioxide (16%). In a reinvestigation of this reaction, Cadogan and Sears[107] detected a low yield of diethyl o-nitrophenylphosphonate, arising from replacement of the SO_2Ph-group.

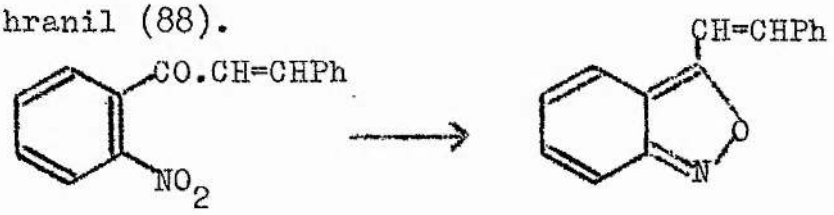
2. Reactions of 2-Nitrophenylketones with Triethyl Phosphite.- The reaction of 2-nitrobenzophenone with triethyl phosphite yielded two products which were identified as 3-phenylanthranil (86 , 56%) and 2-aminobenzophenone (19.5%). Only the former product had been isolated from the thermal decomposition of 2-azidobenzophenone.[101] Waterman and Vivian[35] reported a low yield of a product which they tentatively identified as acridine (47 , p. 17) from the ferrous oxalate deoxygenation of 2-nitrobenzophenone.



(86)

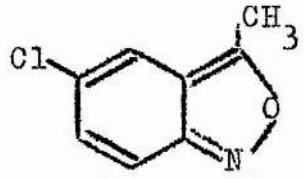
Anthranils had not previously been synthesised by this route and the cyclised product (86) differs from all those previously obtained in that cyclisation has taken place onto an oxygen atom rather than a carbon or nitrogen. In view of the success of this reaction, the deoxygenation of several 2-nitrophenylketones with triethyl phosphite was studied.

The reaction of 2'-nitrochalcone (87) with triethyl phosphite gave one product which was assigned the structure 3-styrylanthranil (88).



(87) (88)

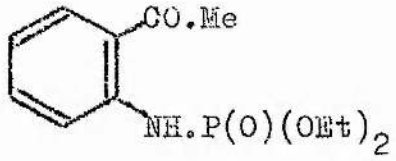
Similarly the only product derived from 5-chloro-2-nitroacetophenone was the anticipated 3-methyl-5-chloroanthranil (89 , 37%).



(89)

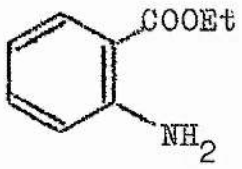
In the reaction of 2-nitroacetophenone with triethyl phosphite, no cyclised product was obtained, the only product isolated being diethyl N-(2-acetylphenyl)phosphoramidate (90 , 19%). However, the first fraction from the chromatography (ca. 9%) contained two components and although these could not be separated, the p.m.r. spectrum of the mixture showed only aromatic and methyl

protons which is consistent with one of the components being 3-methylanthranil.

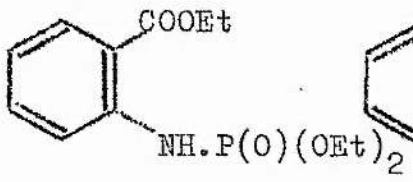


(90)

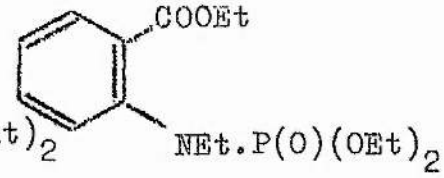
Although not strictly a nitrophenylketone, the reaction of ethyl 2-nitrobenzoate with triethyl phosphite was also examined. No cyclised product was observed, but ethyl anthranilate (91, 14%), diethyl N-(2-carbethoxyphenyl)phosphoramidate (92 , 11%), and diethyl N-ethyl-N-(2-carbethoxyphenyl)phosphoramidate (93 , 15.5%) were isolated.



(91)



(92)

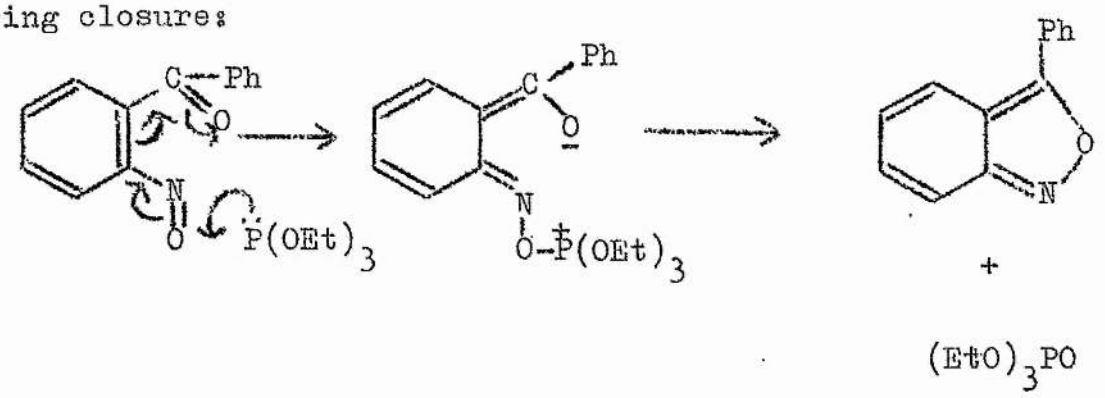


(93)

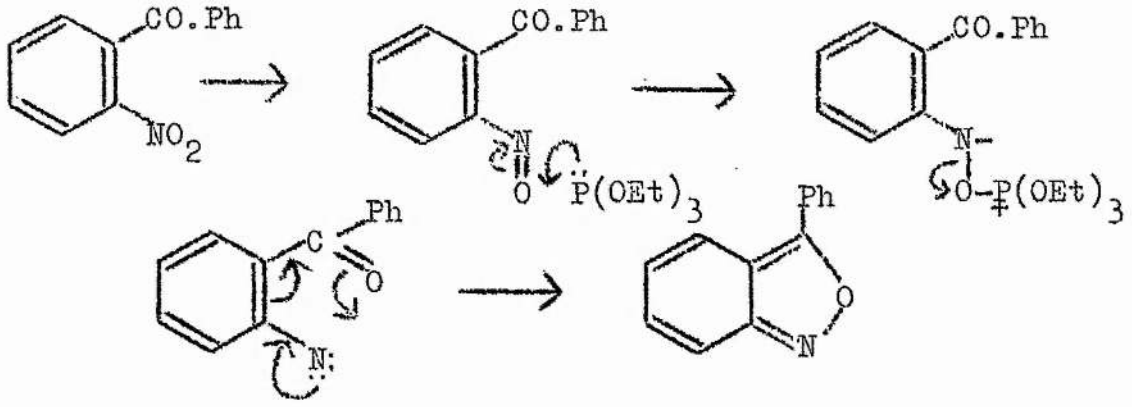
The deoxygenations described in this chapter do not in themselves constitute evidence for the mechanism of the reaction, but as with the sulphides described in the previous chapter, two possible routes to the observed products can be postulated at this stage.

All the cyclisations described in the Introduction and in this chapter can be explained on the basis of a mechanism involving nucleophilic attack on an intermediate nitroso-compound by triethyl phosphite, followed by conjugation to the point of

ring closure:



The other possibility involves deoxygenation of the nitro-group, probably again by way of an intermediate nitroso structure, to give an electron deficient nitrene which attacks at the position of ring closure:



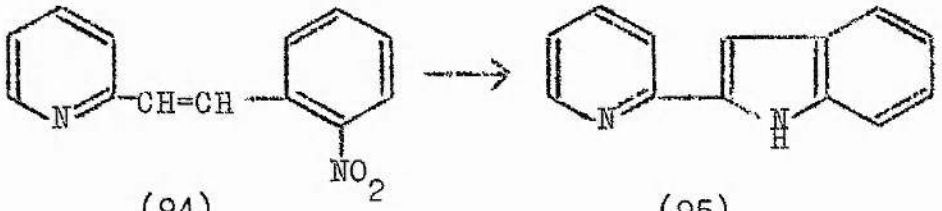
This mechanism has the advantage of being able to explain the products arising from the reactions of 2-nitroacetophenone and ethyl 2-nitrobenzoate with triethyl phosphite. Coupling of a nitrene with triethyl phosphite would lead initially to a triethyl N-arylphosphorimidate ($(EtO)_3P{=}NAr$). These compounds are known[85] to undergo rapid hydrolysis to the corresponding diethyl N-arylphosphoramidate ($(EtO)_2(O)P.NHAr$), thus accounting

for the formation of (90) and (92). The triethyl N-arylphosphorimidates have also been shown[85] to undergo ethylation leading to diethyl N-ethyl-N-phenylphosphoramidates on reaction with ethyl iodide. The N-ethylphosphoramidate (93) obtained in the reaction of ethyl 2-nitrobenzoate could arise in a similar way, triethyl phosphate acting as the ethylating agent. Hydrogen abstraction from triethyl phosphite by 2-carbethoxyphenyl nitrene would explain the formation of ethyl anthranilate (91) in the same experiment.

3. Miscellaneous Deoxygenation Reactions.- Reaction of 2-nitrobiphenyl with tervalent phosphorus compounds other than triethyl phosphite. The reactions of 2-nitrobiphenyl with diethyl methylphosphonite, hexaethyl phosphorous triamide and tri-n-butylphosphine were studied as part of an investigation of the scope of the deoxygenation. The yields of carbazole were 85% (2 hours/100°), 55% (6 hours/100°) and 58% (5 hours/110°) respectively. The reaction conditions in the first two cases were estimated prior to performing the reaction, on the basis of the kinetic results described in the following chapter. It is clear, therefore, that diethyl methylphosphonite is a convenient reagent for deoxygenation, an observation that proved to be useful in mechanistic studies of the deoxygenation reaction described below.

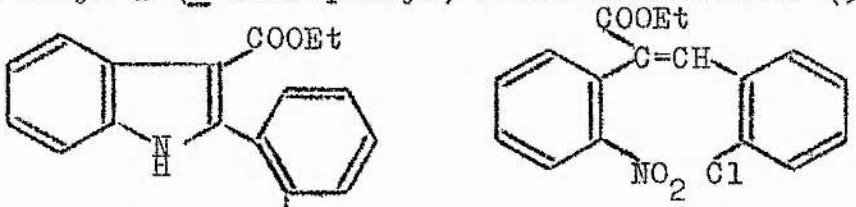
Further cyclisation reactions. The reaction of 2-nitro-

stilbazole (94) with triethyl phosphite was studied as it was hoped that cyclisation might take place onto the electron rich pyridine nitrogen atom, thus yielding a diazepine derivative. The only product found, however, was 2-(2'-pyridyl)indole (95 , 37%).



(94) (95)

The reaction of α-(o-nitrophenyl)-2-chlorocinnamic acid with triethyl phosphite gave rise to a cyclised product, 2-(o-chlorophenyl)-3-carbethoxyindole (96 , 46%), and a low yield of ethyl α-(o-nitrophenyl)-2-chlorocinnamate (97 , 4.5%).

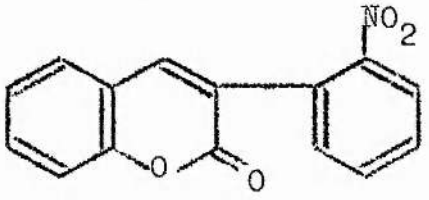


(96) (97)

Ethylation of the carboxyl group is presumably brought about by triethyl phosphate formed in the reaction. The starting material in this reaction was prepared in error for 3-(o-nitrophenyl)coumarin (see next section) on account of an incorrect entry in Chemical Abstracts.[108] The last two reactions are, of course, only extensions of the general synthesis of 2-aryl-indoles described in the Introduction.

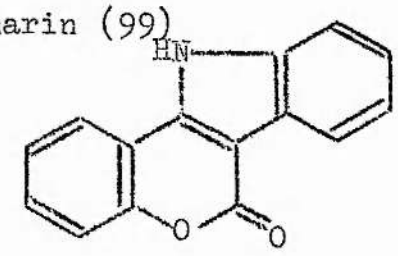
The reaction of 3-(o-nitrophenyl)coumarin (98) was

investigated because there was a possibility of ring closure taking place either at the carbonyl oxygen or at the carbon atom in the 4-position.



(98)

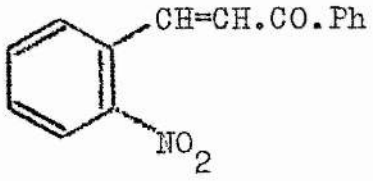
Although the starting material was impure, (see Experimental, p. 44) reaction with triethyl phosphite gave a pink crystalline product (63% based on $C_{15}H_9NO_2$) which could not be identified. Ring closure onto the 4-carbon of the coumarin structure would give rise to indolo [3,2-c]coumarin (99)



(99)

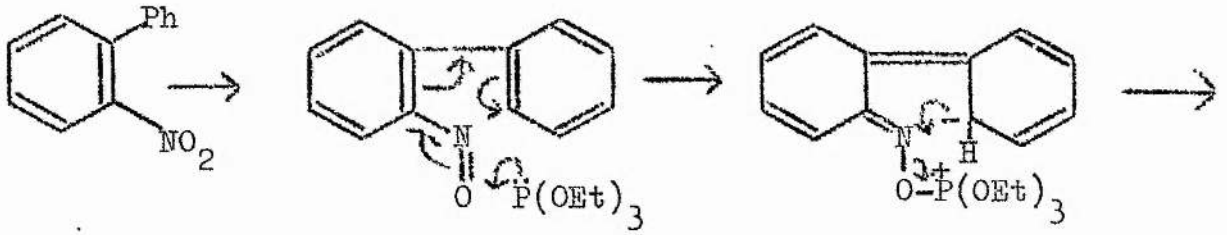
Intermolecular hydrogen bonding between the indole 1-hydrogen and the carbonyl group can be visualised, leading to dimeric structures. Such hydrogen bonding would certainly account for the physical properties of the product (see p. 75). It was verified in a control experiment that triethyl phosphite does not react with coumarin itself.

In a further attempt to prepare a product containing a seven membered ring system, 2-nitrochalcone (100) was reacted with triethyl phosphite, but only tars and a small amount of starting material were obtained.

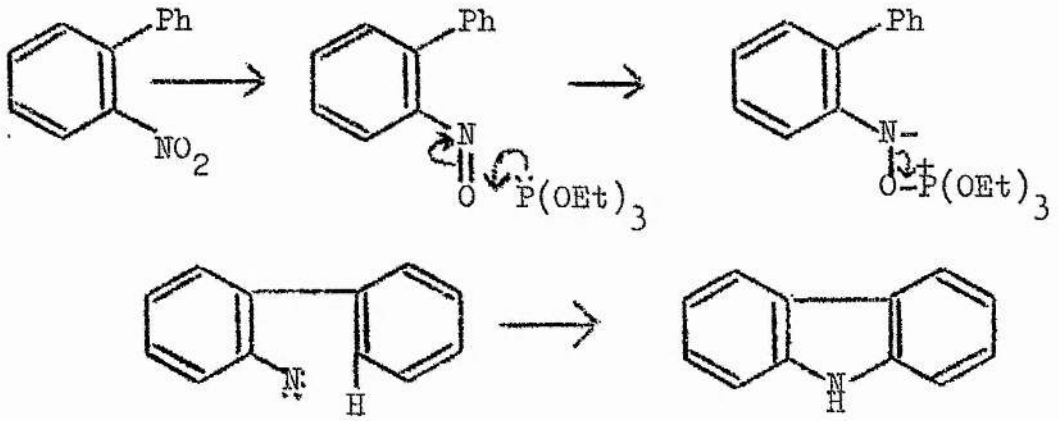


(100)

The products of the reactions described in this section could arise by mechanisms analogous to either of those shown on p.131 as further illustrated below for 2-nitrobiphenyl[8]



or



B. Mechanistic Aspects.

1. Investigation of the Rate of Deoxygenation of Aromatic Nitro-compounds.- In order to cast light on the nature of the rate

determining step in the deoxygenation of aromatic nitro-compounds, the rate of reaction of 2-nitrobiphenyl with a series of tervalent organophosphorus compounds was studied. In each case, the loss of nitro-compound from a mixture containing 15-20 moles excess of phosphorus compound was followed, the value of the half-life time found and in some cases, the order of the reaction with respect to the nitro-compound determined. The results obtained for 2-nitrobiphenyl are summarised below:

Phosphorus compound	Reaction temperature	Half-life(min.)
$(EtO)_3P$	145°	51
$(EtO)_3P$ (repeat)	144.5	47
$(EtO)P(NEt_2)_2$	121	ca. 5
$(Et_2N)_3P$	111	41
$(EtO)_2PMe$	61	154
$(Pr^iO)_3P$	143.5	63
$(EtO)_3P$ + DMF (equimolar)	144	97
$(EtO)_3P$	135	32
$(EtO)_3P$	155	83
PCl_3	130	No reaction after 9 hours.[26]

The increase in rate observed on passing from triethyl phosphite to ethyl N-tetraethylphosphorodiamidite and hexaethyl phosphorous triamide, which both have electron donating groups attached to the phosphorus, suggests that the rate determining step involves

a nucleophilic attack by phosphorus leading to deoxygenation. The possibility that deoxygenation of the nitro-group leads to formation of an intermediate nitroso-structure is discussed in the next chapter. The failure of phosphorus trichloride to produce deoxygenation is in agreement with this postulated nucleophilic attack by phosphorus.

The extremely rapid reaction of diethyl methylphosphonite cannot be explained on this basis, however. An explanation based on relief of steric crowding in the intermediate by substitution of a methyl for an ethoxy group is also unlikely. If the deoxygenation were as sensitive to steric factors as this would suggest, then the reaction of tri-isopropyl phosphite would be expected to be appreciably slower than that of triethyl phosphite; this was not found to be the case.

The only effect of carrying out the deoxygenation in an equimolar mixture of triethyl phosphite and a dipolar aprotic solvent (dimethyl formamide) was to decrease the half-life in the same ratio as the dilution of the triethyl phosphite. This suggests that the transition complex does not arise from a step involving anion attack. This finding is in accordance with a mechanism involving nucleophilic attack by triethyl phosphite in the slowest step. It should be borne in mind, however, that the reactions in triethyl phosphite are taking place in a medium of continuously changing polarity due to the formation of triethyl

fig. (iii)

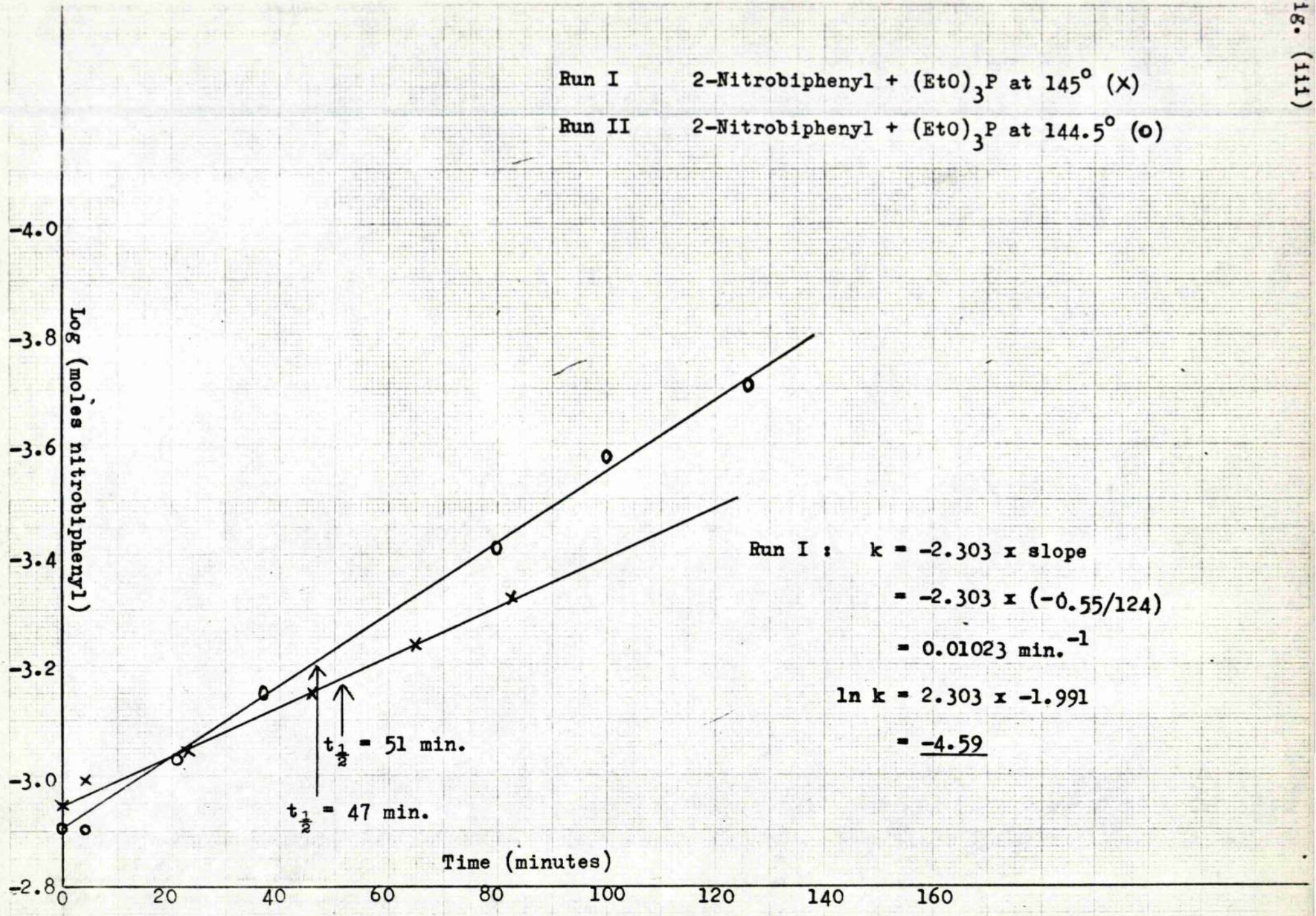
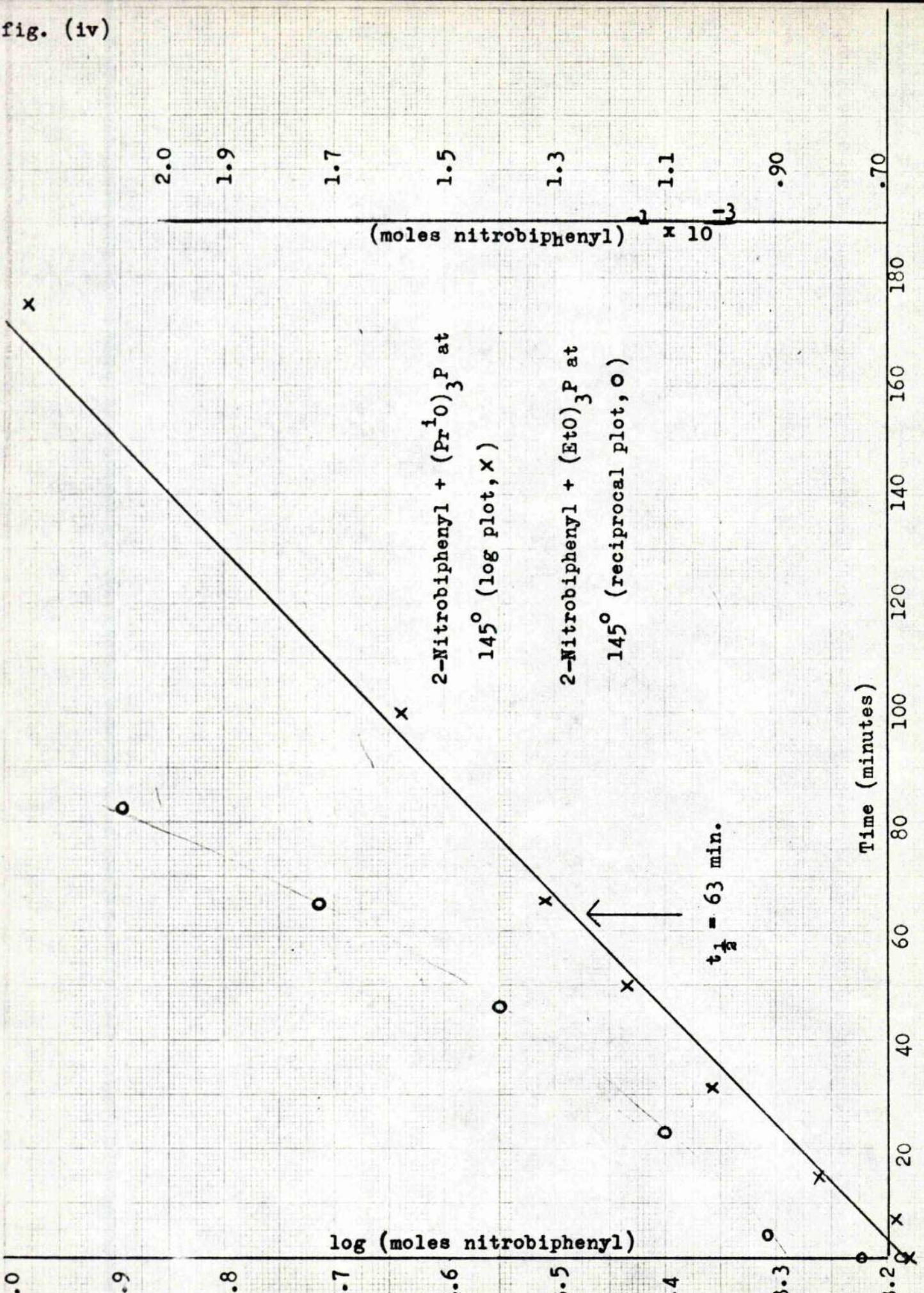

Run I 2-Nitrobiphenyl + $(EtO)_3P$ at 145° (X)
Run II 2-Nitrobiphenyl + $(EtO)_3P$ at 144.5° (o)
Log (moles nitrobiphenyl)
-4.0
-3.8
-3.6
-3.4
-3.2
-3.0
-2.8
0
20
40
60
80
100
120
140
160
Time (minutes)
$t_{\frac{1}{2}}$ = 51 min.
$t_{\frac{1}{2}}$ = 47 min.
Run I : k = -2.303 x slope
= -2.303 x (-0.55/124)
= 0.01023 min.$^{-1}$
ln k = 2.303 x -1.991
= -4.59

fig. (iv)


2-Nitrobiphenyl + $(Pr^{i}O)_3P$ at
145° (log plot, x)
2-Nitrobiphenyl + $(EtO)_3P$ at
145° (reciprocal plot, o)
$t_{\frac{1}{2}}$ = 63 min.
log (moles nitrobiphenyl)
(moles nitrobiphenyl) x 10^{-3}
Time (minutes)

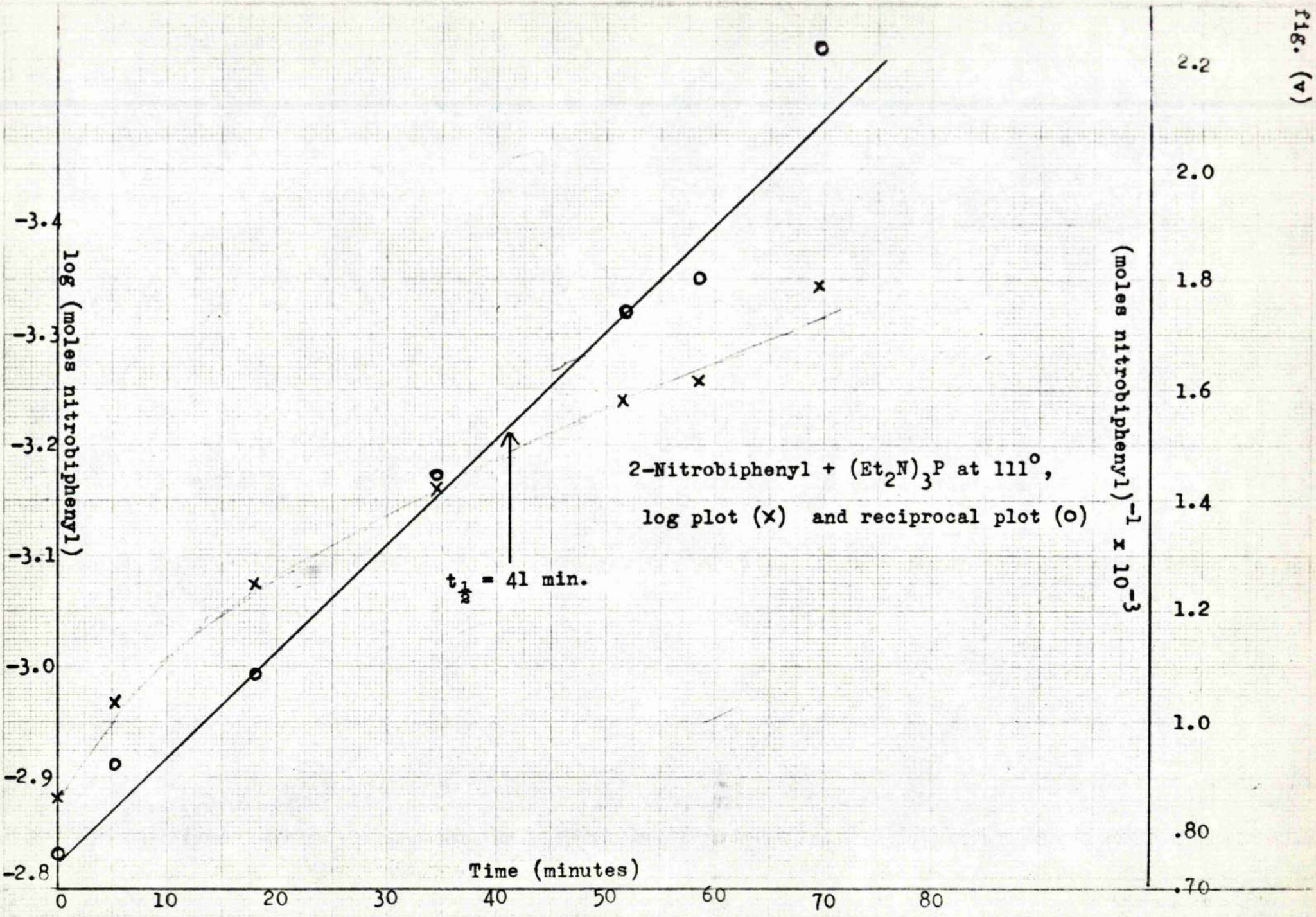

log (moles nitrobiphenyl)
-3.4
-3.3
-3.2
-3.1
-3.0
-2.9
-2.8
Time (minutes)
0
10
20
30
40
50
60
70
80
(moles nitrobiphenyl)$^{-1}$ x 10^{-3}
2.2
2.0
1.8
1.6
1.4
1.2
1.0
.80
.70
2-Nitrobiphenyl + $(Et_2N)_3P$ at 111°,
log plot (X) and reciprocal plot (O)
$t_{\frac{1}{2}}$ = 41 min.

fig. (v)

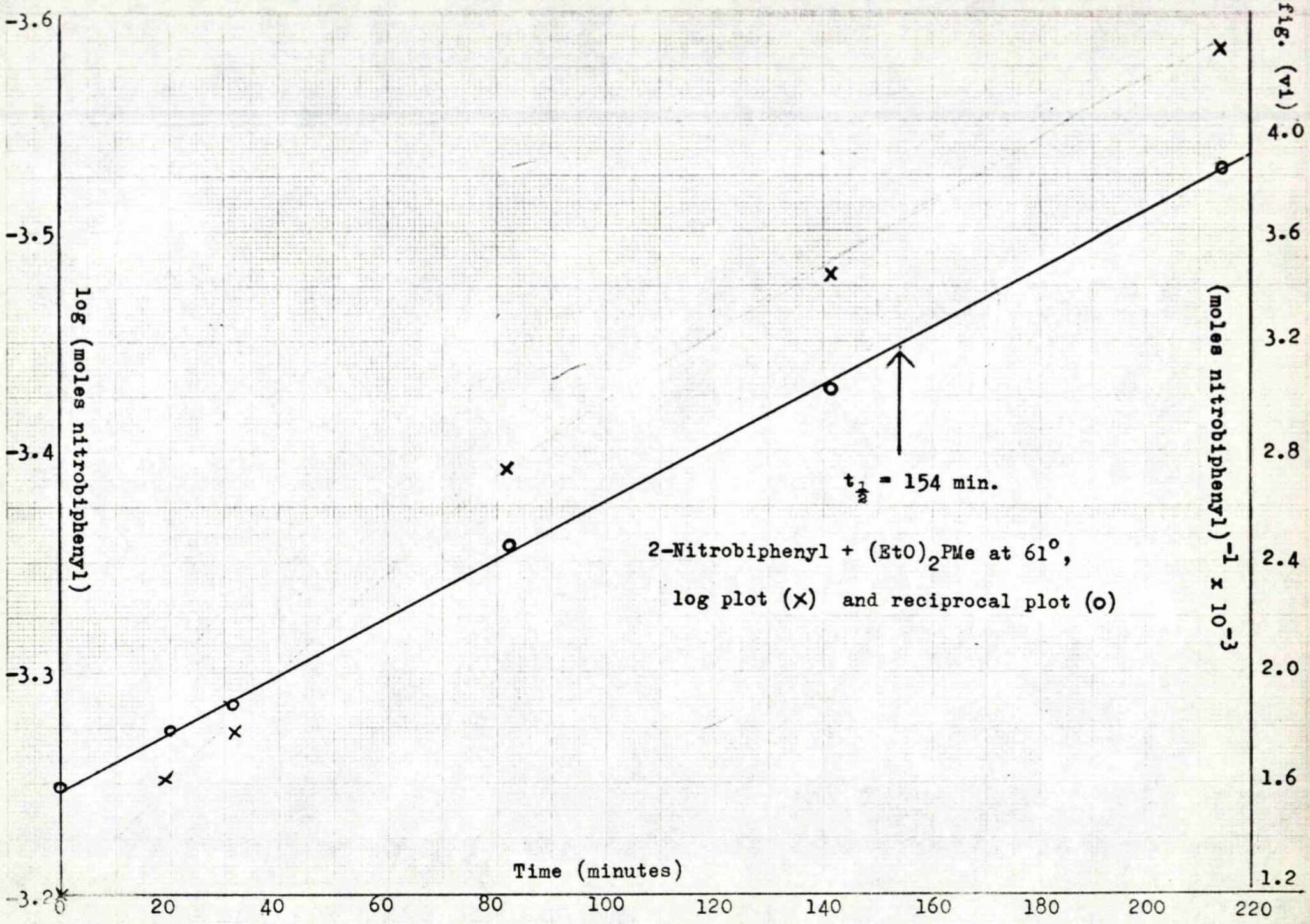
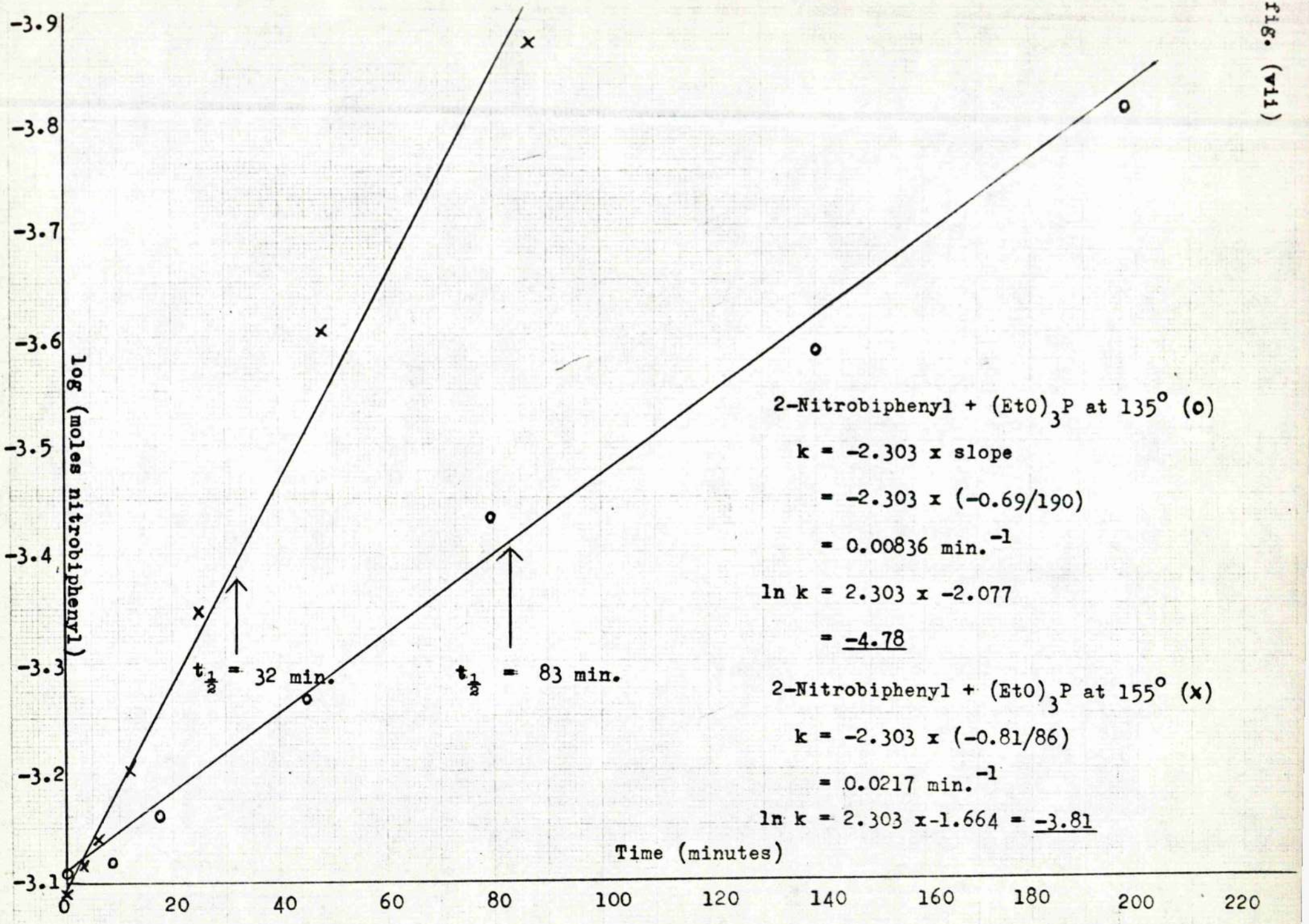


fig. (vi)
-3.6
-3.5
-3.4
-3.3
-3.2
log (moles nitrobiphenyl)
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
(moles nitrobiphenyl)$^{-1}$ x 10^{-3}
0
20
40
60
80
100
120
140
160
180
200
220
Time (minutes)
$t_{\frac{1}{2}}$ = 154 min.
2-Nitrobiphenyl + $(EtO)_2PMe$ at 61°,
log plot (×) and reciprocal plot (o)



2-Nitrobiphenyl + $(EtO)_3P$ at 135° (o)

k = -2.303 x slope

= -2.303 x (-0.69/190)

= 0.00836 $min.^{-1}$

ln k = 2.303 x -2.077

= <u>-4.78</u>

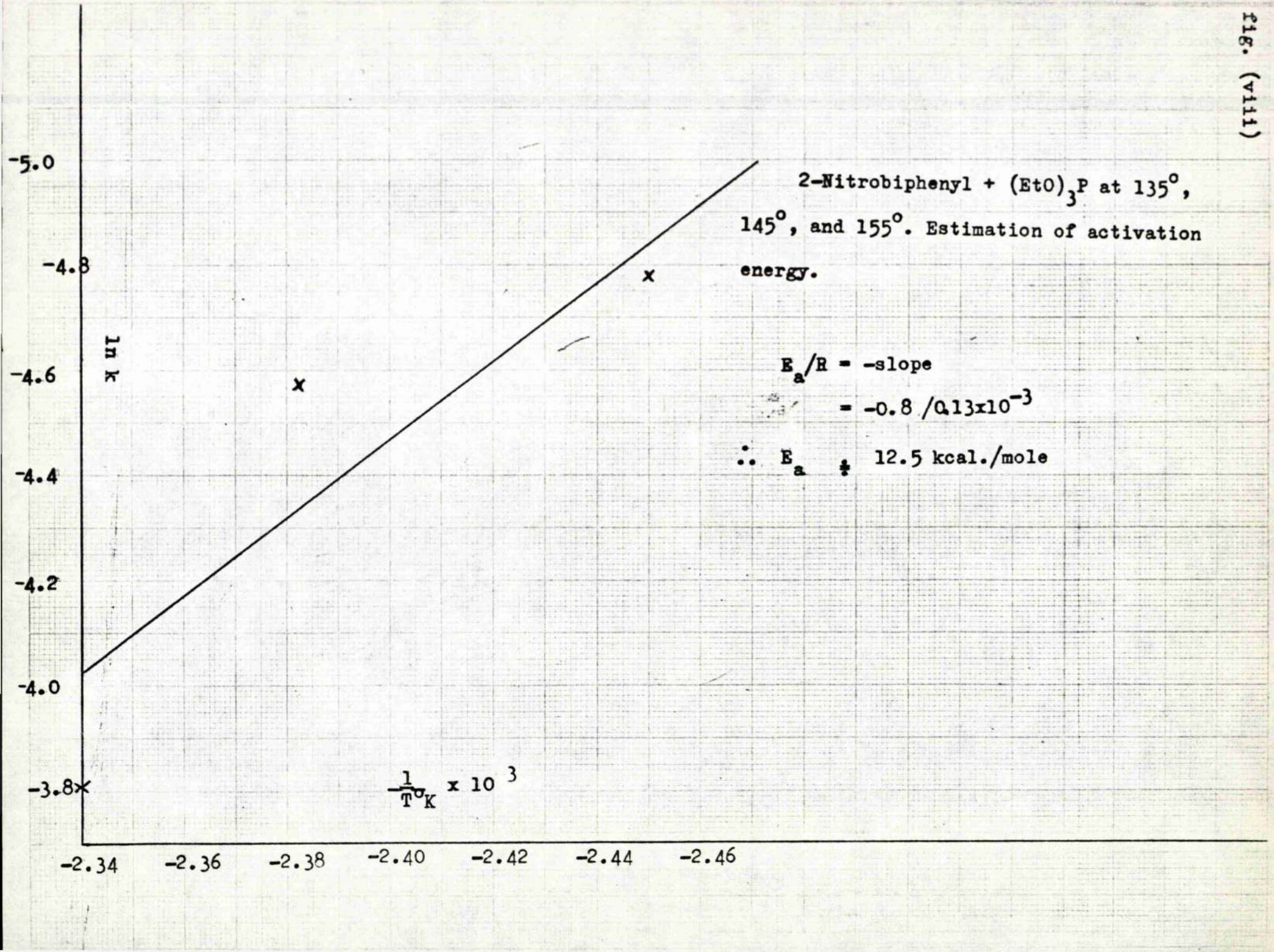
2-Nitrobiphenyl + $(EtO)_3P$ at 155° (x)

k = -2.303 x (-0.81/86)

= 0.0217 $min.^{-1}$

ln k = 2.303 x-1.664 = <u>-3.81</u>

fig. (viii)



2-Nitrobiphenyl + $(EtO)_3P$ at 135°, 145°, and 155°. Estimation of activation energy.

E_a/R = -slope

= $-0.8 / 0.13 \times 10^{-3}$

$\therefore$ E_a ≠ 12.5 kcal./mole

phosphate.

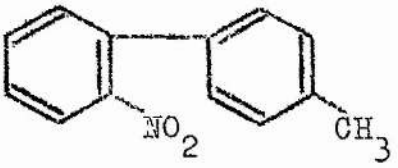
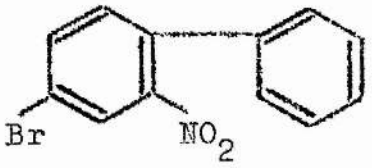
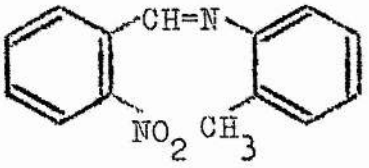
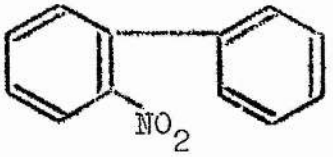
From the values of the rate constants for reaction of 2-nitrobiphenyl with triethyl phosphite at 135°, 145° and 155°, the activation energy was estimated as 12.5 kcal. /mole which is a reasonable value for a rate determining step of this nature (see figs. iii, vii and viii).

Determination of the order of the deoxygenation reaction for triethyl phosphite, tri-isopropyl phosphite, hexaethyl phosphorous triamide and diethyl methylphosphonite produced some interesting results. In the first two cases, the data corresponded to 1st order kinetics, plots of log(moles nitrobiphenyl) against (time) being almost linear (see fig. iii). A reciprocal (2nd order) plot of (moles nitrobiphenyl) against (time) is included for comparison (fig. iv). The reactions of the latter two compounds appeared to be 2nd order with respect to nitrobiphenyl, however. Plots of the reciprocal of (moles nitrobiphenyl) against (time) were nearly linear (see fig. v) and a plot of log(moles nitrobiphenyl) is included for comparison (fig. vi). This change in order is certainly consistent with the observed increase in rate, but there is no obvious reason for a fundamental change in the nature of the rate determining step with these phosphorus compounds.

A much more sophisticated kinetic investigation would be necessary to confirm this observation before any attempt at its

rationalisation is made.

The rate of the reaction of three other nitro-compounds with triethyl phosphite was also determined:

Nitro-compound	Reaction temperature	Half-life (min.)
	145.5	50
	145.5	17
	120.5	30
	145	51

As would be expected for a mechanism postulating deoxygenation rather than ring closure as the rate determining step, the methyl group in 4-methyl-2'-nitrobiphenyl causes no change in the rate relative to 2-nitrobiphenyl. The increase in rate observed with 4-bromo-2-nitrobiphenyl lends support to the possibility of nucleophilic attack at the nitro-group since a m-bromo-group will activate the nitro-group towards this type of attack.

The large increase in rate observed for o-nitrobenzylidene-

o-toluidine is less easy to explain. Possibly the longer conjugated chain (compared with 2-nitrobiphenyl) in the o-position provides improved delocalisation of negative charge in an intermediate structure. Another possibility is that ring closure onto nitrogen (the product in this reaction is 2-(o-tolyl)-indole) is more facile than onto carbon, but this suggestion is difficult to reconcile with the concept of an initial slow deoxygenation step.

The reaction of further nitro-compounds with triethyl phosphite was not attempted because none could be found with sufficiently sharp g.l.c. peaks to permit accurate measurement.

2. Investigation of the Mechanism of Deoxygenation by Product Analyses.- There are two important questions which ought to be answered in this connection. Does deoxygenation of a nitro-group involve the formation of an intermediate nitroso-structure? Does the deoxygenation result in the formation of a discrete nitrene intermediate, or can the products be explained without invoking this type of intermediate? The bulk of this chapter is devoted to the second question and a brief discussion of the first is given in the following section.

Attempted trapping of a nitroso-compound in the deoxygenation of 2-nitrophenyl phenyl sulphide. The formation of a nitroso-compound as the primary product of reduction of the corresponding

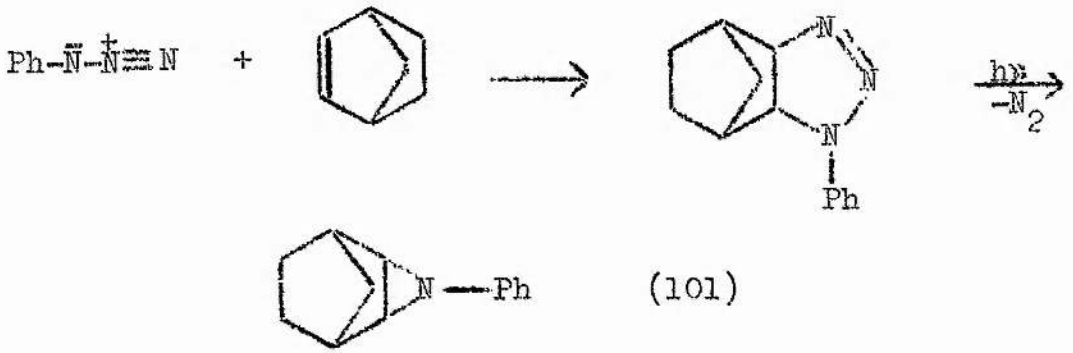
nitro-compound was postulated as long ago as 1898.[109] In almost all cases, it is impossible to isolate the nitroso-compound during the reduction of the nitro-compound on account of the rapidity with which it is further reduced. As a result of their extremely facile reduction, nitroso-compounds are generally prepared by oxidation of the corresponding amine or hydroxylamine.

The relative conditions required to effect deoxygenation of nitro- and nitroso-compounds (8-10 hours/140° and ca. 30 minutes /0° respectively) with triethyl phosphite suggest that interception of an intermediate nitroso-compound in the former case would be extremely difficult to achieve. Prior reduction of a nitro- to a nitroso-group during deoxygenation has been postulated by other workers[21, 26] and Allen refers tentatively to a trace of blue-green colouration observed during the deoxygenation of large excesses of α-halonitro-compounds with triethyl phosphite.[110]

Hamer and Macaluso[111] have reported that nitrosobenzene derivatives react with many alkenes to yield the corresponding azoxy-compound. The list of olefins which gave this reaction included trans-stilbene and it was therefore decided to attempt the interception of a nitroso-intermediate by carrying out a deoxygenation reaction in a large excess of this olefin. No 2,2'-diphenylthioazoxybenzene was detected in the deoxygenation of 2-nitrophenyl phenyl sulphide by triethyl phosphite in excess

(25 molar) trans-stilbene. The only compounds isolated were starting material and phenothiazine (38%). Further work on this aspect of the deoxygenation reaction was not attempted.

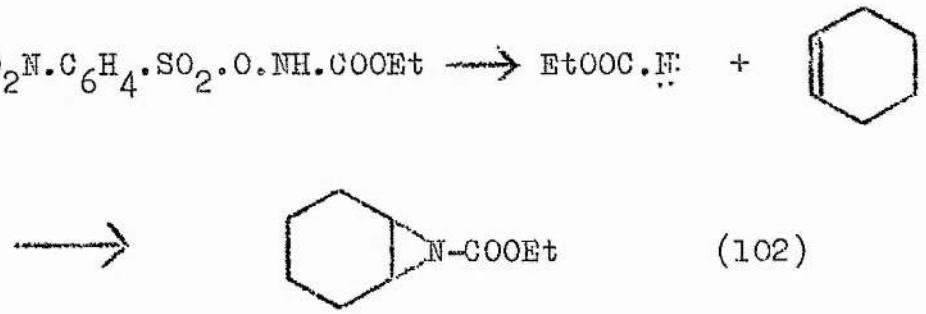
Attempted trapping of a nitrene intermediate with norbornene. Addition to a suitably constituted double bond yielding an aziridine seemed to be an obvious means of trapping a nitrene intermediate. Such a process has a well established analogy in the formation of cyclopropanes by addition of the isoelectronic carbenes to double bonds. Most attempts to produce this addition were frustrated, however, by the readiness with which azides (the normal nitrene precursors in early work) themselves added to the double bond to form a triazoline which could subsequently be decomposed to yield the aziridine. Huisgen[54] for instance, obtained this initial 1,3-dipolar addition when he decomposed phenyl azide in norbornene:



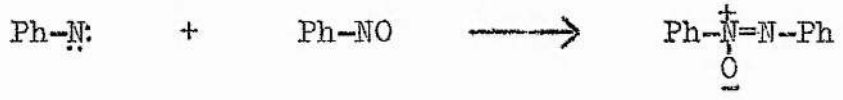
(101)

The feasibility of direct addition was demonstrated by Lwowski and his co-workers[112] who generated carbethoxynitrene in the presence of cyclohexene by α-elimination from the N-hydroxyurethane

ester of p-nitrobenzenesulphonic acid and obtained 7-carbethoxy-7-azabicyclo[4,1,0]heptane (102) as the major product:

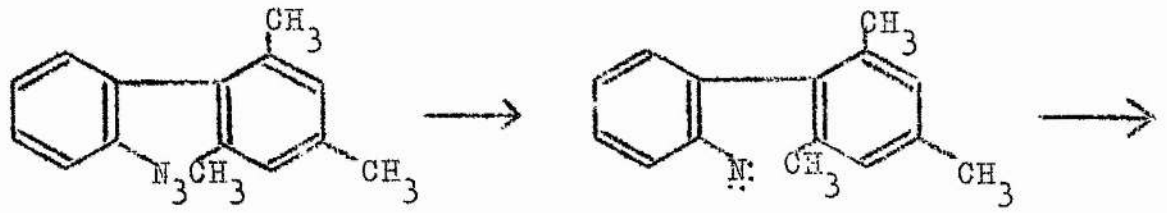


An attempt was therefore made to trap a possible nitrene intermediate in the triethyl phosphite deoxygenation of nitrosobenzene by carrying out the reaction in the presence of the highly strained olefin, norbornene. A sample of the relevant aziridine, 3-phenyl-3-azatricyclo[3,2,1,$0^{2,4}$]octane (101) was prepared as indicated above and the reaction products examined by g.l.c. for a compound of similar retention time. The aziridine (101) was thus shown to be absent. The only product identified was azoxybenzene (3%) which could arise from coupling of a nitrene intermediate with unreacted nitrosobenzene:

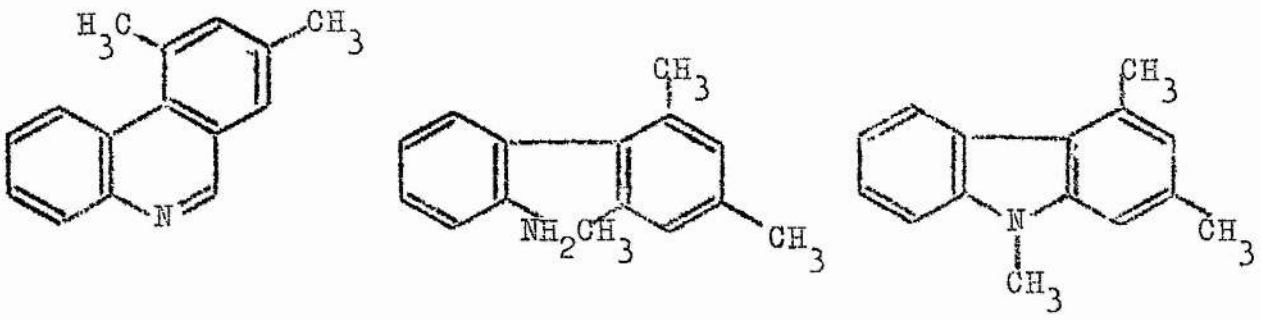


The reaction of 2-nitro-2',4',6'-trimethylbiphenyl with triethyl phosphite. As shown in the Introduction, hydrogen abstraction from the solvent and insertion in aliphatic C-H bonds appear to be the most characteristic reactions of nitrene intermediates. Smolinsky observed both these processes in his

study[84] of the thermal decomposition of 2-azido-2',4',6'-trimethylbiphenyl (103) which gave the following product distribution:



(103)

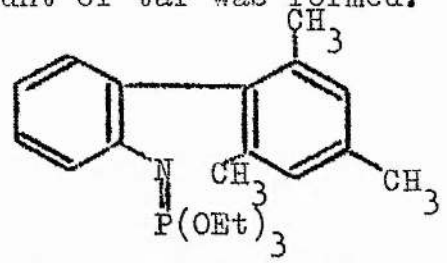


(50) (104) (105)

8,10-Dimethylphenanthridine (50 , 50%) was explained on the basis of insertion by the nitrene intermediate in a C-H bond of the 2'-methyl group, and 2-amino-2',4',6'-trimethylbiphenyl (104 , 30%) by hydrogen abstraction from the solvent or other molecules of substrate. The minor product, 2,4,9-trimethylcarbazole (105 , 5%) presumably arises from insertion in a C-C bond.

The products (50) and(104) had previously been observed[39] in the ferrous oxalate deoxygenation of 2-nitro-2',4',6'-trimethylbiphenyl and the deoxygenation of this compound with triethyl phosphite was studied with the intention of obtaining evidence for a nitrene intermediate. When the deoxygenation was carried out in triethyl phosphite, (104 , 13%) was isolated and evidence for the formation of triethyl N-(2',4',6'-trimethylbi-

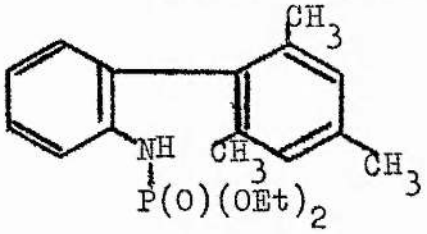
phenyl-2-yl)phosphorimidate (106 , ca. 15%) was obtained by g.l.c. A large amount of tar was formed.



(106)

A reasonable mode of formation of (106) is by coupling of a nitrene with triethyl phosphite.

In an effort to reduce the amount of tar formed and to inhibit interception of the postulated nitrene by triethyl phosphite, the reaction was repeated in a large excess of cumene when the following products were isolated: 2-amino-2',4',6'-trimethylbiphenyl (104 , 31.5%), 8,10-dimethylphenanthridine (50 , 13.4%), diethyl N-(2',4',6'-trimethylbiphenyl-2-yl)phosphoramidate (107 , 5.5%) and bi-α-cumyl (108 , 11%).



(107)

$PhCMe_2.Me_2CPh$

(108)

Thus when the possibility of coupling with triethyl phosphite is reduced, the presumably less energetically favourable abstraction and insertion processes occur to a considerable extent. The phosphoramidate (107) probably arises from hydrolysis of initially formed phosphorimidate (106) during the work-up. In accord with this suggestion, it was shown during the preparation of authentic amidate that this hydrolysis takes place very

readily. Bi-α-cumyl can only arise by dimerisation of α-cumyl radicals produced by abstraction of α-hydrogen from the solvent by a triplet species, presumably a nitrene. A control experiment confirmed that bi-α-cumyl is not formed in the absence of nitro-compound. Since Smolinsky's work[51] on optically active 2-azido-(2-methylbutyl)benzene (see Introduction, p. 23) suggests that insertion in an aliphatic C-H bond is a reaction of the nitrene in its singlet configuration, the present experiment therefore seems to involve a nitrene reacting in both its singlet and triplet forms, a possibility which has been discussed in the Introduction (pp. 23-24).

Repetition of the experiment in t-butylbenzene gave similar results, amine (19%), phenanthridine (12%) and phosphoramidate (5%) being isolated. The difference in the yields of the amine in these two experiments accounts almost exactly for the amount of bi-α-cumyl formed in the reaction in cumene. t-Butylbenzene, of course, has no hydrogen atom which can be readily abstracted to yield a resonance stabilised radical.

Reaction of 2-nitro-4'-t-butyldiphenyl sulphide with triethyl phosphite in cumene. This experiment was undertaken in the hope of isolating bi-α-cumyl and 2-amino-4'-t-butyldiphenyl sulphide as evidence for participation of a nitrene in the sulphide ring closures. Only a trace of bi-α-cumyl (ca. 0.01%) was found, but the yield of 4-t-butylphenothiazine increased

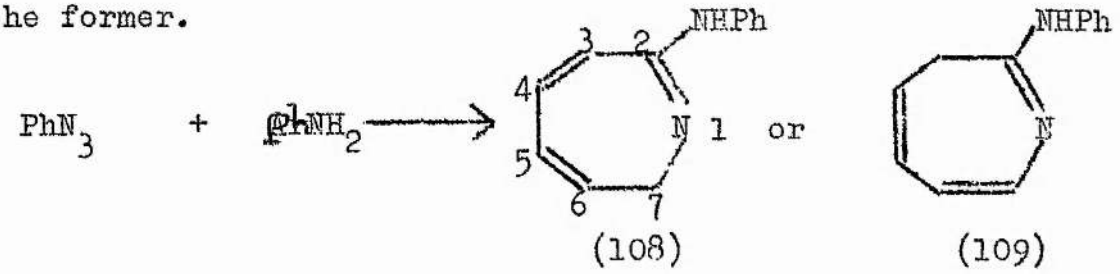
relative to that from the reaction in triethyl phosphite (74% cf. 55%).

Of the three reactions investigated in cumene, this is the only one which under normal circumstances (i.e. reaction in triethyl phosphite) gives a good yield of cyclised product. It is possible that, as suggested in the Introduction, a nitrene is being generated in an excited singlet state, and a reaction of this form takes place leading to cyclisation before deactivation to the triplet ground state occurs. If the alternative mechanism previously discussed (see pp. 126 and 131)were valid, then, equally, no products of radical abstraction would be expected in these cases where conjugation to the point of ring closure could occur.

Reaction of 2-ethylnitrobenzene with triethyl phosphite in cumene. In this case, bi-α-cumyl (9.7%) was isolated in similar yield to that obtained from the same reaction of 2-nitro-2',4',6'-trimethylbiphenyl. o-Ethylaniline (yield not determined) was detected by g.l.c. in the distillate obtained on removing the cumene from the reaction mixture, but attempts to isolate it were unsuccessful.

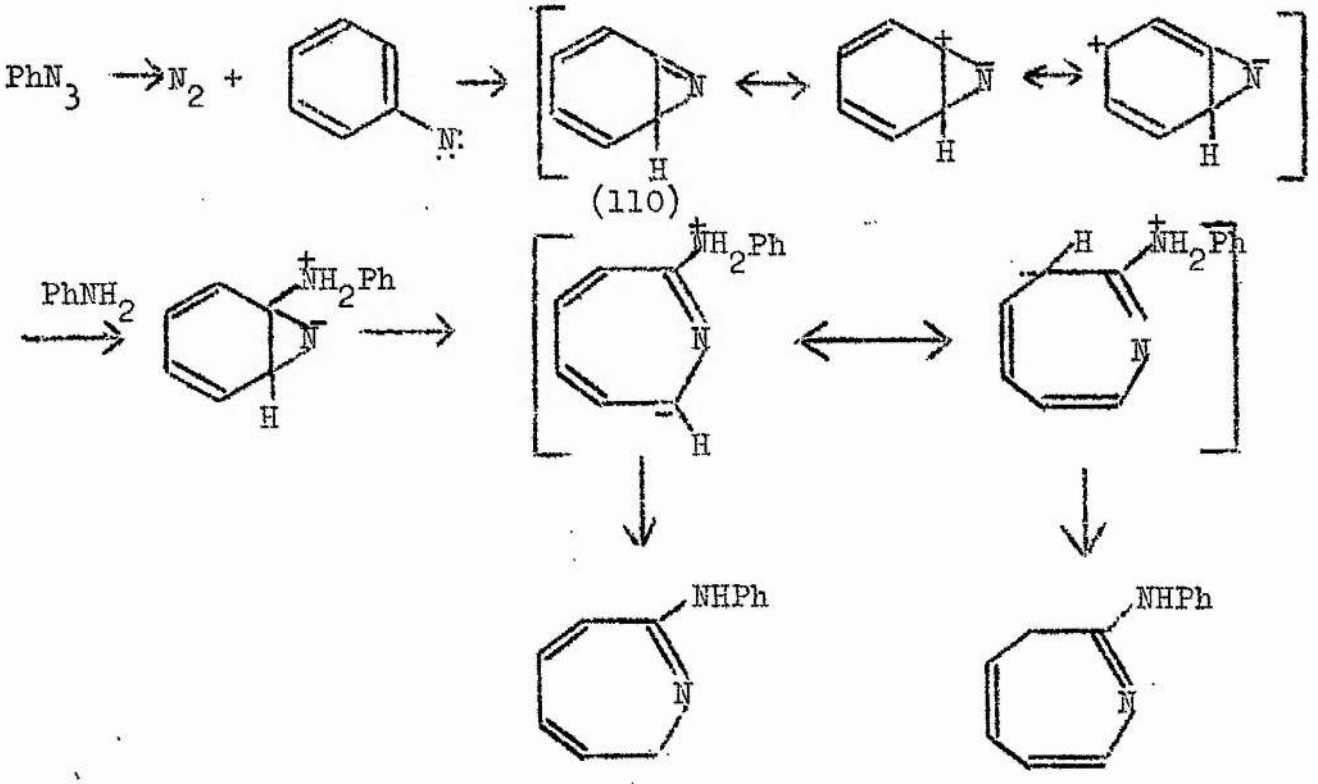
Reaction of nitrobenzene and 2-nitrobiphenyl with diethyl methylphosphonite in diethylamine. The thermal decomposition of phenyl azide in aniline has been investigated by Huisgen and his co-workers[113,114,115] who assigned a seven membered ring

amidine structure to the product. They were unable to distinguish conclusively between the structures 2-anilino-7H-azepine (108) and 2-anilino-3H-azepine (109), but seem to have preferred the former.



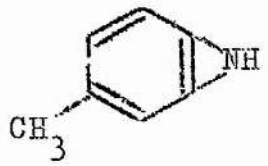
(108) (109)

They suggested a mechanism involving attack on the o-position of the benzene ring by a nitrene intermediate giving 7-aza-bicyclo [4,1,0]hepta-2,4,6-triene (110), followed by nucleophilic attack by the amine and ring expansion:



The formation of only one product from p-tolyl azide was quoted

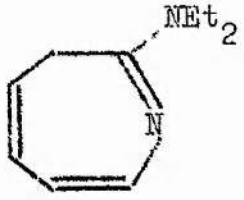
as evidence in favour of this mechanism since an intermediate such as (111) would have been expected to give rise to two products.



(111)

The absence of any substituent effect on the rate of decomposition of a series of m-substituted phenyl azides suggested[115] that formation of the azirine ring was not concerted with loss of nitrogen.

Recently, the same ring expansion has been reported by Doering and Odum[97] in the photolysis of phenyl azide in a series of nucleophiles. Taking the photolysis in diethylamine as their most detailed example, they assigned the structure 2-diethylamino-3H-azepine (68) to the product.



(68)

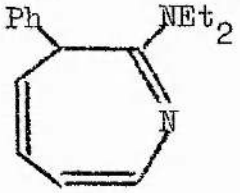
The gross structure was determined by chemical methods and by analogy with Huisgen's product from the thermal decomposition of the same azide, while the position of the double bonds was decided from a consideration of the p.m.r. spectrum. On the basis of the p.m.r. spectrum, they decided that Huisgen's product was the 3H-compound also, and not the 7H-isomer as

thought originally. Doering and Odum made no further contribution to the mechanism of the reaction, stating that they regarded Huisgen's suggestions as adequate.

Odum and Brenner[116] have made use of this ring expansion to provide evidence for the formation of a nitrene in the deoxygenation of nitrosobenzene by triphenylphosphine in aliphatic amines. They obtained 2-diethylamino-3H-azepine (68) in 62% yield on carrying out the deoxygenation in excess of diethylamine. Similar results were obtained using dimethylamine and n-butylamine. Once more, Huisgen's mechanism was thought to be satisfactory.

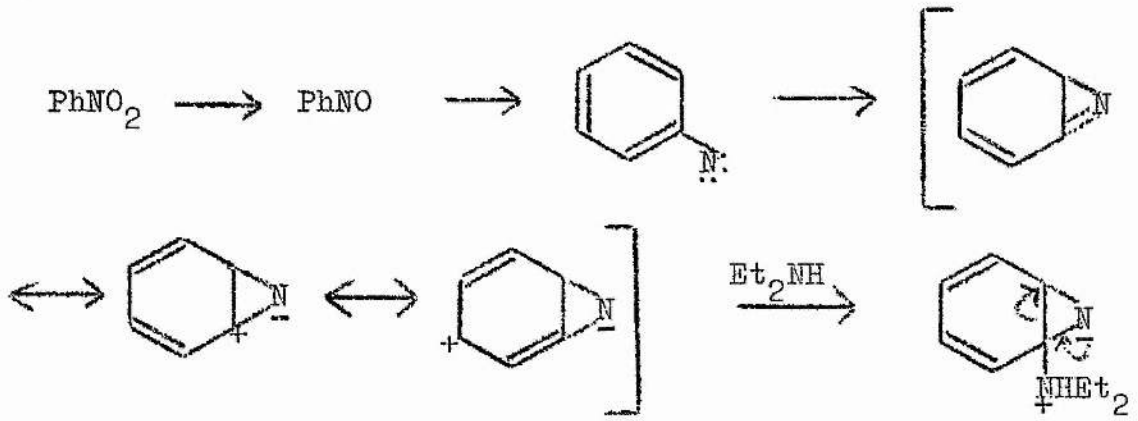
In view of the work described above, it was decided to attempt to effect this ring expansion during the deoxygenation of nitro-compounds in the presence of large amounts of amine. Reaction of a nitro-compound with triethyl phosphite in diethylamine would have necessitated the use of a sealed tube to attain the required temperature. The results of the kinetic study of the deoxygenation using a series of tervalent phosphorus compounds (see p. 136) suggested, however, that deoxygenation could be achieved in a few days at the temperature of boiling diethylamine by using the much more reactive diethyl methylphosphonite. Deoxygenation of nitrobenzene under these conditions gave 2-diethylamino-3H-azepine (68 , 83%) whose p.m.r. spectrum was identical with that reported by Doering.[97]

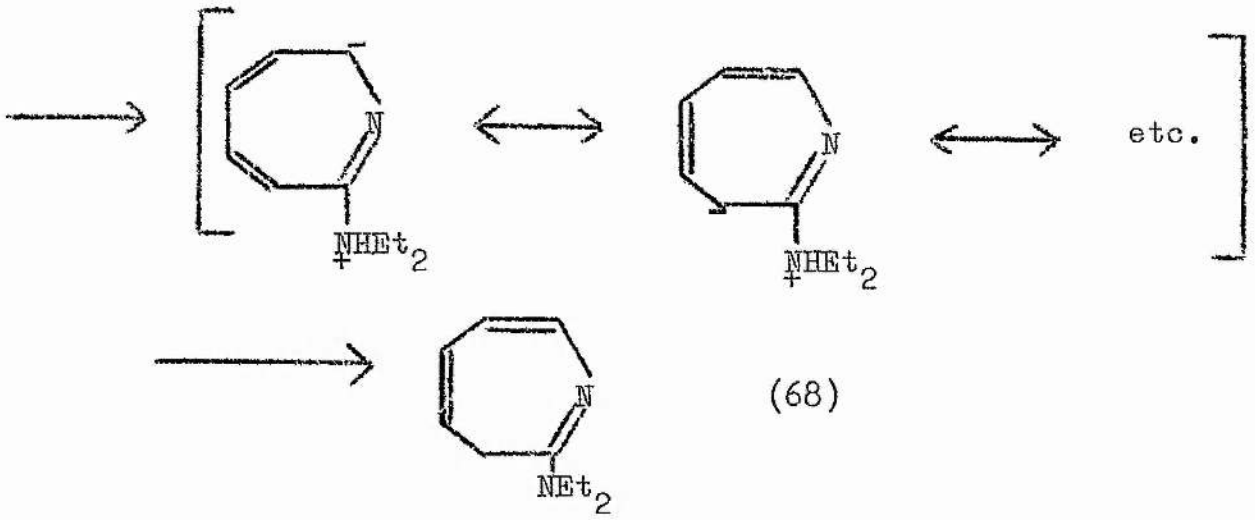
Extension of the reaction to a substrate which could also achieve ring closure was expected to present difficulties, and the reaction of 2-nitrobiphenyl with diethyl methylphosphonite in diethylamine did, in fact, yield carbazole (67%) as the major product. However, another product which was characterised as 2-diethylamino-3H-3-phenylazepine (70 , 10.5%) was isolated. The p.m.r. spectrum on which this assignment was principally based has been discussed on pp.108-113.The similarity of the ultraviolet spectrum to that of 2-diethylamino-3H-azepine[97] was also evidence for this structure as it can be seen that in the other possible structures, the phenyl group is often conjugated with the azepine ring (see pp. 110-111).



(70)

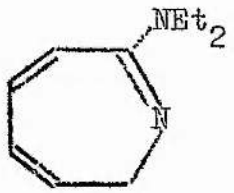
A mechanism very similar to that suggested by Huisgen would explain the formation of 2-diethylamino-3H-azepine from nitrobenzene:





(68)

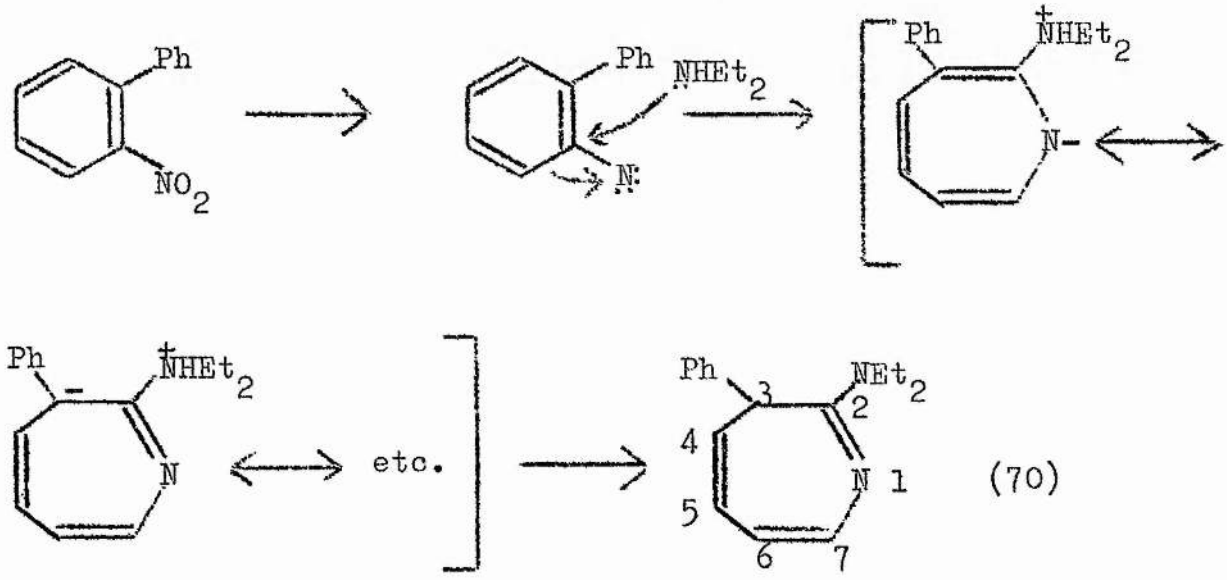
The formation of the 3H-isomer rather than the 7H-isomer (112) may be due to the presence of the longer continuous chain of conjugation in the former structure.



(112)

The formation of 2-diethylamino-3H-3-phenylazepine (70) from 2-nitrobiphenyl might be explained in the same way, but several new considerations make a more detailed examination of the possibilities necessary. The most plausible explanation for the formation of carbazole depends on attack by a nitrene intermediate at the 2'-position of the biphenyl structure. This could take the form of either radical abstraction of hydrogen followed by recombination or direct insertion in the C-H bond. Since it is difficult to visualise the formation of carbazole arising from Huisgen's postulated azabicycloheptatriene intermediate (p. 148), it would be preferable to construct

a mechanism for azepine formation by some direct or concerted process involving a nitrene intermediate alone. The three membered ring intermediate can also be criticised on energetic grounds, since its formation (with or without the intermediacy of a nitrene) involves loss of aromaticity in the benzene ring, and on steric grounds, owing to the high degree of strain which must exist in such a structure. A concerted mechanism such as that shown below might be more satisfactory since it does not involve the formation of the bicyclic intermediates

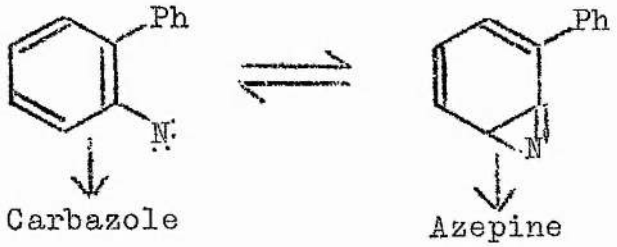


(70)

Once again, the existence of a longer continuous chain of conjugation can be advanced as reason for the formation of the 3H-3-phenyl- isomer rather than the 5H-3-phenyl- or 7H-3-phenyl- compounds.

While it seems attractive to postulate the formation of both products from the same intermediate, the preceding arguments do not preclude the possibility that the formation of the

azabicycloheptatriene from a nitrene intermediate is a reversible process, carbazole arising from the nitrene and the azepine from the bicyclic intermediate.

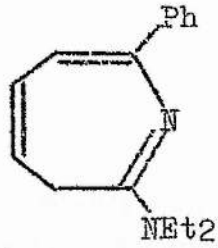


Abramovitch and Davis[45] also make this suggestion in the course of a discussion of Huisgen's work. To summarize, the isolation of both carbazole and the azepine in this experiment indicates the following possibilities:

1. That carbazole and the azepine (70) arise from the same intermediate, either the nitrene or the azabicycloheptatriene.
2. That both intermediates are formed, carbazole arising from the nitrene and the azepine from the azabicycloheptatriene.
3. That the two intermediates are in equilibrium, the products arising as indicated in 2.

So far, it has been assumed that the postulated nitrene attacks the benzene ring in the position m- to the phenyl group; indeed, the observed product can only be explained in this way. Attack at the carbon to which the phenyl group is attached would give rise to 2-diethylamino-3H-7-phenylazepine (113) or a

tautomeric structure.

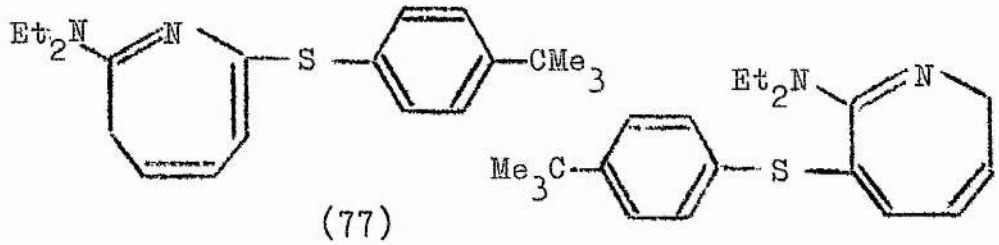


(113)

Attack at this position presumably does not take place on account of the steric barrier imposed by the coplanarity of the benzene rings.

Reaction of 2-nitro-4'-t-butyldiphenyl sulphide with diethyl methylphosphonite in diethylamine. In addition to 2-t-butylphenothiazine (10%), this reaction yielded di-(p-t-butylphenyl) disulphide (6.4%), a trace of material whose p.m.r. spectrum showed signals characteristic of an azepine ring, and several tarry fractions which were tentatively identified as polysulphides on the basis of their p.m.r. spectrum.

The p.m.r. spectrum of the azepine fraction (see pp. 113-115) did not permit conclusive distinction between the structures 2-diethylamino-3H-7-(4'-t-butyl)thiophenylazepine (77) and 2-diethylamino-7H-3-(4'-t-butyl)thiophenylazepine (78), but the chemical shift of the ring methylene protons strongly suggested that (77) was the correct structure.



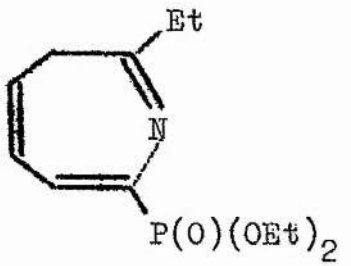
(77) (78)

These structures would arise from attack by a nitrene at the 1'-

or 3'-carbons respectively of the diphenyl sulphide according to the mechanism described above (p. 153). It is possible that the steric objection to attack at the 1'-position is not so great as in the case of 2-nitrobiphenyl since the condition of coplanarity of the rings, necessary in the latter case to maintain conjugation, is probably no longer essential. For this reason, and on account of the longer continuous chain of conjugation which it contains, structure (77) seems preferable. The electron donating properties of the S-Ar group will also tend to facilitate attack by a nitrene at the 1'-position.

The formation of disulphide and polysulphide is possibly due to cleavage of the bond between sulphur and the azepine ring, it have being shown that the azepine (77) is unstable, extensive decomposition having occurred during distillation.

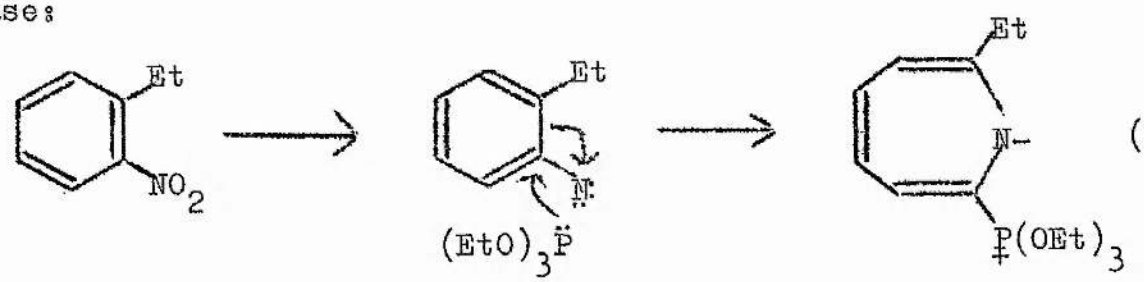
Reaction of 2-ethylnitrobenzene with triethyl phosphite. The major product of this reaction was identified, mainly on the basis of its p.m.r. spectrum (see pp. 116-118), as diethyl 2-ethyl-3H-azepine-7-ylphosphonate (80, 21%).



(80)

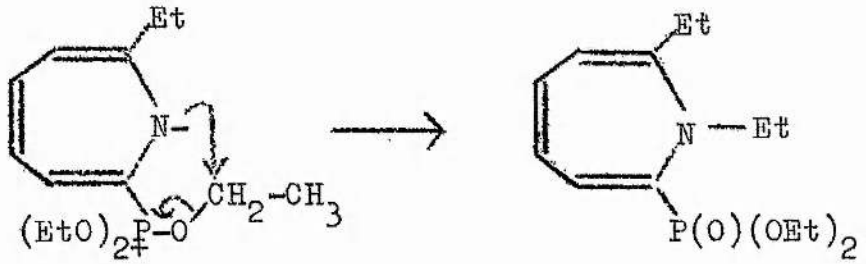
This most interesting product presumably arises by a mechanism similar to that previously suggested for the diethylaminoazepines,

with the triethyl phosphite acting as the nucleophile in this case:



(114)

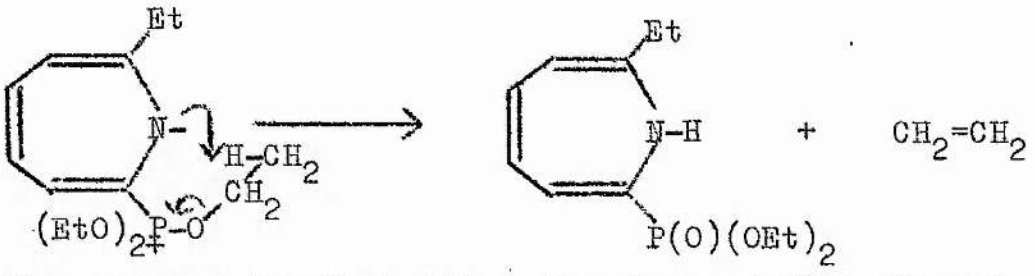
The most obvious step at this stage in the mechanism would be an intramolecular process similar to the Arbusov reaction, but this would lead to an N-ethylated product such as (115) which does not fit the analysis or the p.m.r. spectrum of the product.



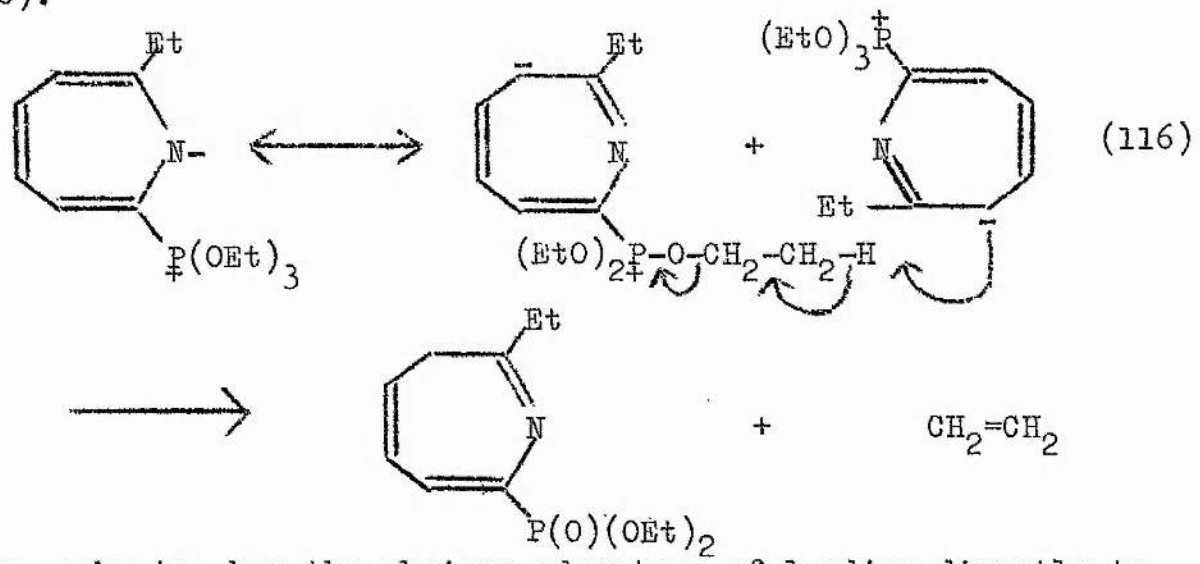
(115)

In view of this absence of N-ethylazepine, it was possible that the phosphonium structure (114) might be breaking down by elimination of ethylene. This theory was confirmed by the isolation and spectral identification of ethylene on repetition of the reaction. An approximate determination of the amount produced found ethylene corresponding to 44% of the azepinyl-phosphonate formed. Two ways of eliminating ethylene can be visualised. The first, by attack of the negatively charged nitrogen atom on a methyl proton of the phosphonium intermediate, would give rise, possibly via a seven membered cyclic inter-

mediate, to the 1H-azepine which could then tautomerise, possibly:



The alternative process involves intermolecular reaction through the canonical form bearing a negative charge on the 3-carbon (116):

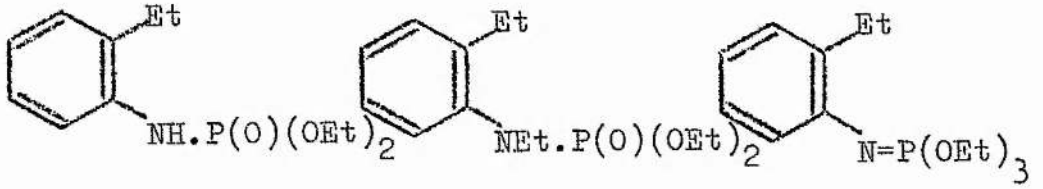


(116)

This mechanism has the obvious advantage of leading directly to the observed product. Since interaction of a nucleophilic reagent with an alkoxy quasi-phosphonium intermediate in all reported cases leads to dealkylation, as in the Arbusov reaction, rather than to deprotonation, this elimination of ethylene is a most unusual reaction. In this case,however, the nucleophile is probably a carbanion, and carbanion interaction with phosphonium salts has not been studied. The carbanion site in the intermediate (116) might be expected to have a greater affinity for hydrogen

than carbon on account of its highly basic character.

The other products of this reaction were diethyl N-(2-ethylphenyl)phosphoramidate (117 , 16%) and diethyl N-ethyl-N-(2-ethylphenyl)phosphoramidate (118 , not isolated, but detected by p.m.r. spectroscopy as a mixture with (117)).



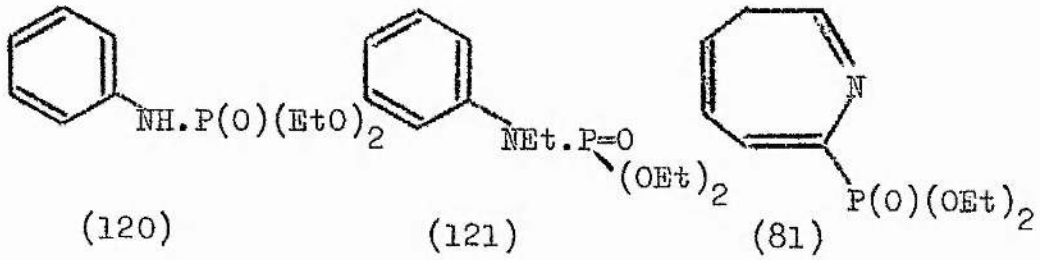
(117) (118) (119)

Triethyl N-(2-ethylphenyl)phosphorimidate (119) was detected in the reaction mixture by g.l.c. As stated previously, this type of compound is regarded as the result of coupling between 2-ethylphenylnitrene and triethyl phosphite, and its hydrolysis during the work-up will give rise to (117). It was shown by g.l.c. that the N-ethylphosphoramidate (118) was not being formed by ethylation of (117) by triethyl phosphate. This is in agreement with the expected reduction in basicity of the NH-group due to the adjacent P=O group. Later work (see p. 161) has thrown light on the mode of formation of (118).

The study of this reaction was undertaken to investigate apparent inconsistencies in another author's work. Sundberg[27] reported that the reaction of 2-ethylnitrobenzene with triethyl phosphite yielded only diethyl N-(2-ethylphenyl)phosphoramidate (117 , 2.5%) and triethyl N-(2-ethylphenyl)phosphorimidate (119 ,

44%). In view of the ease of hydrolysis of the phosphorimidates under the conditions of Sundberg's work-up, which included aqueous acidic and alkaline extraction steps, the validity of these observations was doubted. Preparation of an authentic sample of (119) and its subjection to the series of operations described by Sundberg confirmed that hydrolysis to (117 , ca. 95%) took place. As the reaction conditions were the same as those employed in the deoxygenation of 2-ethylnitrobenzene, the failure to detect any of the azepinylphosphonate (80 , p. 156) in this experiment proved, incidentally, that this compound was not formed by reaction of the phosphorimidate with triethyl phosphite. In addition, the p.m.r. spectrum reported by Sundberg for the alleged phosphorimidate is not consistent with that structure. Sundberg described an irregular quintet at t=7.37 containing a quartet which he attributed to the benzyl CH_2. Triethyl N-(2-ethylphenyl)phosphorimidate would be expected to show only a regular quartet in this region, and, indeed, the authentic sample prepared in this investigation showed such a quartet at t=7.36 . Sundberg also found a quintet for the $POCH_2$ protons centred at t=5.80 whereas the authentic sample of the phosphorimidate shows the pattern in question at t=5.93 in the same solvent. It seems likely, therefore, that Sundberg has made an error of structure assignment, although there is no doubt that some of the phosphorimidate (119) is formed.

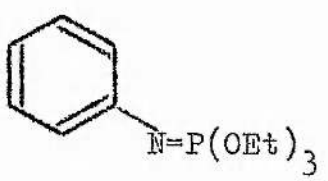
Reaction of nitrobenzene with triethyl phosphite. This reaction followed a course very similar to that of 2-ethylnitrobenzene. In this case, diethyl N-phenylphosphoramidate (120 , 10.5%), diethyl N-ethyl-N-phenylphosphoramidate (121 , 7.6%) and ethylene (yield not determined) were isolated and diethyl 3H-azepine-7-ylphosphonate (81) was detected, mixed with (120), by g.l.c. and p.m.r. spectroscopy (see p. 119).



(120) (121) (81)

The isolation of ethylene in this reaction confirmed that it had not arisen in any way from the ethyl side chain in the previous experiment.

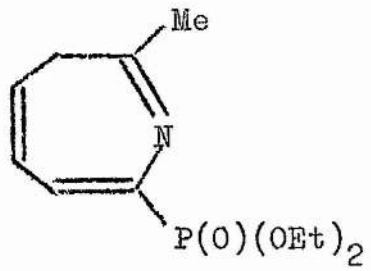
Reaction of triethyl N-phenylphosphorimidate with triethyl phosphate. In view of the work of Kabachnik and Gilyarov[85] who obtained diethyl N-ethyl-N-phenylphosphoramidate (121) from triethyl N-phenylphosphorimidate (122) by refluxing with ethyl iodide, it was considered that this product might be arising in the deoxygenation of nitrobenzene by reaction of the phosphorimidate with triethyl phosphate, a known[117] ethylating agent.



(122)

It was shown by g.l.c. and p.m.r. spectroscopy that the reaction between these two compounds did, in fact, give rise to a mixture of the phosphoramidate (120 , ca. 85%) and the N-ethylphosphoramidate (121 , ca. 8.5 %). None of the azepine (81) was detected.

Reaction of o-nitrotoluene with triethyl phosphite. The reaction of this nitro-compound followed the same course as those of nitrobenzene and 2-ethylnitrobenzene, and the products isolated were diethyl N-o-tolylphosphoramidate (22.5%), diethyl N-ethyl-N-o-tolylphosphoramidate (5%) and diethyl 2-methyl-3H-azepine-7-ylphosphonate (79) which was again identified by its p.m.r. spectrum.



(79)

SUMMARY

As a synthetic procedure, the deoxygenation of aromatic nitro-compounds by tervalent organophosphorus compounds has been extended to include new routes to the anthranil and phenothiazine nuclei. Synthesis of anthranils from 2-nitrophenyl ketones has been exemplified by the preparation of 3-phenylanthranil, 3-styrylanthranil and 5-chloro-3-methylanthranil from 2-nitrobenzophenone, 2'-nitrochalcone and 5-chloro-2-nitroacetophenone respectively. The preparation of phenothiazines from 2-nitrobiaryl sulphides has been studied more extensively. It was found that when successful, this ring closure gave the cyclised product in about 55% yield. Rather more than half the sulphides used, however, gave no products or only a very low yield, and no rational means of predicting the success of a given ring closure could be found. Triethyl phosphite was the only phosphorus compound found to be capable of effecting this cyclisation. The use of several other phosphorus compounds was investigated, but although deoxygenation of the nitro-group undoubtedly took place, as evidenced by the large amounts of tar formed, no cyclised products could be isolated. Although a comprehensive investigation was not undertaken, the results of two experiments suggested that a considerable improvement in the yields of the phenothiazines could be achieved by carrying out the deoxygenations in a

solvent (as opposed to pure phosphorus compound) and thus, reducing the extent of tar-forming side reactions. In addition, an unidentified product has been obtained from the reaction of 3-(o-nitrophenyl)coumarin with triethyl phosphite. Several unsuccessful attempts were made to synthesise a seven membered ring system.

As part of an examination of the mechanism of the deoxygenation, the rate of reaction of a series of phosphorus compounds with 2-nitrobiphenyl was studied. It was found that phosphorus compounds with electron donating groups attached to the phosphorus atom reacted more rapidly, suggesting that the rate determining step involved a nucleophilic attack by phosphorus. No adequate explanation could be advanced for the finding that of all the phosphorus compounds studied, diethyl methylphosphonite reacted most rapidly. While the reactions of triethyl and triisopropyl phosphites were first order with respect to nitrobiphenyl, the reactions of hexaethyl phosphorous triamide and diethyl methylphosphonite appeared to be second order. A detailed kinetic study would be necessary to confirm this observation and investigate the fundamental change in mechanism which it implies.

The possibility of the formation of nitroso-compounds as intermediates in the deoxygenation of the nitro-compounds has been discussed, and an unsuccessful attempt to trap such an intermediate has been made. Further attempts ought to be made

in this direction and should be concentrated on finding a compound which will react more rapidly with the nitro-compound than does triethyl phosphite. Such a trapping agent must also be capable of operating in the presence of an excess of nitro-compound.

Much of the work in this thesis has been directed towards establishing whether an electron deficient nitrene intermediate is formed during the course of the deoxygenation of an aromatic nitro-compound. Although no one experiment could be regarded as conclusive, the overall weight of evidence argued convincingly in favour of this type of intermediate. There was a general parallel between the syntheses achieved by deoxygenation of aromatic nitro-compounds and by photolysis or thermal decomposition of the corresponding azides. The occurrence of abstraction and insertion reactions in the thermal decomposition of 2-azido-2',4',6'-trimethylbiphenyl has been attributed to the participation of a nitrene intermediate, and the isolation of the same products from the deoxygenation of the nitro-compound can be most plausibly explained in terms of the same intermediate. Deoxygenation of this nitro-compound in cumene led to the formation of bi-α-cumyl which can only arise by interaction of the solvent with a radical species, presumably a nitrene in its triplet configuration. Photolysis or thermal decomposition of phenyl azide in the presence of large amounts of amines has been found to cause ring expansion leading to the formation of

azepines. It was thought that these ring expansions involved a nitrene intermediate which attacked the aromatic ring to form a bicyclic structure which underwent further attack by the amine leading to ring expansion. Similar ring expansions have now been observed in the deoxygenation of nitrobenzene and 2-nitrobiphenyl by diethyl methylphosphonite in diethylamine, and a mechanism has been proposed in which the products arise directly from a nitrene rather than via a second bicyclic intermediate. It was subsequently discovered that in the deoxygenation of o-alkylnitrobenzenes, triethyl phosphite could act as the nucleophile in addition to deoxygenating the nitro-group, thus leading to a series of diethyl azepinylphosphonates. In view of these considerations, it can be concluded that the chemical evidence for the participation of nitrene intermediates in the deoxygenation of nitro-compounds is at least as good as that advanced in the case of photolysis and thermal decomposition of azides.

Areas which might be profitably further investigated include the kinetics of the deoxygenation and the problem of the ring expansion mentioned above. The first has already been touched on. Investigation of the ring expansion reaction might include attempts to increase the yield of ring expanded product by altering the reaction conditions and a survey of the nucleophilic reagents capable of bringing about ring expansion. It is

unfortunate that there seems to be very little prospect of obtaining physical evidence for a nitrene intermediate as has been achieved in the photolysis of azides.

In addition to the products mentioned in the preceding paragraphs, most of the reaction designed to investigate the mechanism of the deoxygenation also gave substantial yields of phosphoramidates, $(RO)_2(O)PNHAr$, which were thought to arise from hydrolysis of initially formed phosphorimidates, $(RO)_3P{=}NAr$. In many cases, the amine corresponding to the initial nitro-compound was also isolated or detected. It is clear, therefore, from the wide variety of possible products that a rather delicate balance of factors is involved in these reactions and this in turn may play some part in the formation of the tars which have frequently frustrated these investigations.

APPENDIX I

Infrared Spectra of Azepines.- 2-Diethylamino-3H-azepine. 1610 (m.), 1570 (s.), 1515 (s.), 1430 (s.), 1360 (s.), 1320 (m.), 1270 (s.), 1225 (m.), 1140 (m.), 1080 (m.), 1030 (m.).

2-Diethylamino-3H-3-phenylazepine. 1610 (m.), 1565 (s.), 1510 (s.), 1425 (s.), 1350 (s.), 1310 (m.), 1260 (s.), 1240 (m.), 1205 (w.), 1140 (m.), 1090 (w.), 1075 (m.), 1030 (w.).

2-Diethylamino-3H-7-(p-t-butyl)thiophenylazepine. 1600 (w.), 1500 (s.), 1505 (m.), 1470 (m.), 1380 (w.), 1365 (m.), 1355 (m.), 1345 (m.), 1270 (m.), 1225 (m.), 1140 (m.), 1105 (m.), 1020 (m.).

Diethyl 2-ethyl-3H-azepine-7-ylphosphonate. 1610 (s.), 1445 (m.), 1395 (m.), 1290 (w.), 1255 (s.), 1170 (m.), 1142 (m.), 1118 (m.), 1045 (s.), 970 (s.).

Diethyl 2-methyl-3H-azepine-7-ylphosphonate. 1615 (s.), 1440 (m.), 1395 (m.), 1370 (w.), 1285 (w.), 1250 (s.), 1170 (m.), 1115 (m.), 1045 (s.), 970 (s.).

w. = weak

m. = medium

s. = strong

APPENDIX II

Abbreviations employed to designate g.l.c. stationary phases.-

N.P.G.S. ---- Neopentyl glycol succinate.

QF-1 ------ Fluorosilicone oil FS-1265.

P.E.G.A. --- Polyethylene glycol adipate.

SE-30 ----- Silicone gum rubber.

REFERENCES

1. S.B. Hartley, W.S. Holmes, J.K. Jacques, M.F. Mole and J.C. McCoubrey, Quart. Rev., 1963, 17, 217.
2. T.L. Cottrell, "The Strengths of Chemical Bonds", Butterworth (1958).
3. R.F. Hudson, "Structure and Mechanism in Organo-phosphorus Chemistry", Academic Press (1965), Chapter 3 .
4. J.I.G. Cadogan, Quart. Rev., 1962, 16, 208.
5. L. Horner, W. Ludwig and H. Schaefer, Chem. Ber., 1958, 91, 75.
6. Q.E. Thomson, J. Amer. Chem. Soc., 1961, 83, 845.
7. (a) F. Challenger and V.K. Wilson, J., 1927, 213.
   (b) L. Horner and W. Jurgeleit, Annalen, 1955, 591, 138.
   (c) L. Horner and H. Brüggemann, Annalen, 1960, 635, 27.
   (d) N.B. Desai, R.B. Mitra and F. Ramirez, J. Amer. Chem. Soc., 1961, 83, 492.
8. D.B. Denney and M.A. Greenbaum, J. Amer. Chem. Soc., 1957, 79, 979.
9. R. Rabinowitz and C. Walling, J. Amer. Chem. Soc., 1959, 81, 1243.
10. D.B. Denney, B. Goldstein and W.F. Goodyear, J. Amer. Chem. Soc., 1961, 83, 1727.
11. D.B. Denney, B. Goldstein and W.F. Goodyear, J. Amer. Chem. Soc., 1960, 82, 1393.

12. R. Criegee, Annalen, 1953, 583, 1.

13. E. Ochai, J. Org. Chem., 1953, 18, 534.

14. A.M. Aguiar and F. Ramirez, Amer. Chem. Soc., Abs. 134th Meeting, 1958, 42N.

A.M. Aguiar, Diss. Abs., 1960, 21, 457.

15. T.R. Emerson and C.W. Rees, Proc. Chem. Soc., 1960, 418.

T.R. Emerson and C.W. Rees, J., 1962, 1917.

16. H. Hoffmann and L. Horner, Angew. Chem., 1956, 68, 473.

17. E. Hauser and H. Staudinger, Helv. Chim. Acta, 1921, 4, 861.

18. C.C. Addison and J.C. Sheldon, J., 1956, 2705.

19. J.O. Doali, L.P. Kuhn and C. Wellman, J. Amer. Chem. Soc., 1960, 82, 4792.

20. P.J. Bunyan and J.I.G. Cadogan, J., 1963, 42.

21. R.J. Sundberg, J. Amer. Chem. Soc., 1966, 88, 3781.

22. J.H. Boyer and S.E. Ellzey, J. Org. Chem., 1961, 26, 4684.

23. L. Horner and K. Klupfel, Annalen, 1955, 591, 69.

V.A. Kukhtin and K.M. Kirillova, J. Gen. Chem. (U.S.S.R.), 1961, 31, 2078. (Chem. Abs., 1962, 56, 3507.)

24. S.A. Buckler, M. Epstein, L. Doll and F.K. Lind, J. Org. Chem., 1962, 27, 794.

25. A.G. Bellaart, Tetrahedron, 1965, 21, 3285.

26. J.I.G. Cadogan, M. Cameron-Wood, R.K. Mackie and R.J.G. Searle, J., 1965, 4381.

27. R.J. Sundberg, J. Org. Chem., 1965, 30, 3604.

28. R.J. Sundberg, Tetrahedron Letters, 1966, 477.

29. R.J. Sundberg and T. Yamazaki, J. Org. Chem., 1967, 32, 290.

30. W.F. Gannon, E.J. Grubbs, and H.O. House, J. Amer. Chem. Soc., 1960, 82, 4099.

31. Y.Y. Hung and B.M. Lynch, J. Heterocyclic Chem., 1965, 2, 218.

32. H. Sieper, Tetrahedron Letters, 1967, 1987.

33. E.E. Garcia and E.C. Taylor, J. Org. Chem., 1965, 30, 655.

34. R.A. Carboni and J.C. Kauer, J. Amer. Chem. Soc., 1967, 89, 2633.

35. D.L. Vivian and H.C. Waterman, J. Org. Chem., 1949, 14, 289.

36. G.Y. Greenberg, J.L. Hartwell and D.L. Vivian, J. Org. Chem., 1951, 16, 1.

J.L. Hartwell and D.L. Vivian, J. Org. Chem., 1953, 18, 1065.

J.L. Hartwell, D.L. Vivian and H.C. Waterman, J. Org. Chem., 1954, 19, 1136 and 1955, 20, 797.

37. D.L. Vivian and H.C. Waterman, J. Org. Chem., 1956, 21, 914.

38. R.A. Abramovitch and K.A.H. Adams, Canad. J. Chem., 1961, 39, 2516.

39. R.A. Abramovitch, Y. Ahmad and D. Newman, Tetrahedron Letters, 1961, 752.

40. R.A. Abramovitch and J.G. Saha, J., 1964, 2175.

41. R.H. Smith and H. Suschitzky, Tetrahedron, 1961, 16, 80.

42. J.E. Kmiecik, J. Org. Chem., 1965, 30, 2014.

43. P. Pfeiffer, Annalen, 1916, 411, 72.

I. Tanasesca, Bull. Soc. chim. France, 1927, 41, 1074.

44. M. Calvin and J.S. Splitter, J. Org. Chem., 1955, 20, 1086.

B. Furth, M. Pfau and E.C. Taylor, J. Amer. Chem. Soc., 1965, 87, 1400.

45. R.A. Abramovitch and B.A. Davis, Chem. Rev., 1964, 64, 149.

46. G. Smolinsky, E. Wasserman and Y.A. Yager, J. Amer. Chem. Soc., 1962, 84, 3220.

47. R.W. Murray, G. Smolinsky, A.M. Trozzolo, E. Wasserman and W.A. Yager, J. Amer. Chem. Soc., 1963, 85, 2526.

48. G. Smolinsky, E. Wasserman and W.A. Yager, J. Amer. Chem. Soc., 1964, 86, 3166.

49. V. Frazer and A. Reiser, Nature, 1965, 208, 682.

G. Bowes, A. Reiser and H. Wagner, Tetrahedron Letters, 1966, 2635.

50. A. Reiser, G.C. Terry and W. Willets, Nature, 1966, 211, 410.

51. B.I. Feuer and G. Smolinsky, J. Amer. Chem. Soc., 1964, 86, 3085.

52. P. Walker and W.A. Waters, J., 1962, 1632.

53. F.P. Woerner and W. Lwowski, J. Amer. Chem. Soc., 1965, 87, 5491.

J.S. McConaghy and W. Lwowski, J. Amer. Chem. Soc., 1967, 89, 2357.

54. R. Huisgen, L. Möbius, G. Müller, H. Stangl, G. Szeimies

and J.M. Vernon, Chem. Ber., 1965, 98, 3992.

55. B.B. Brown and P.A.S. Smith, J. Amer. Chem. Soc., 1951, 73, 2435.

56. J.H. Boyer and P.A.S. Smith, J. Amer. Chem. Soc., 1951, 73, 2626.

57. L. Krbechek and H. Takimoto, J. Org. Chem., 1964, 29, 1150.

58. R.A. Carboni and J.E. Castle, J. Amer. Chem. Soc., 1962, 84, 2453.

59. C.C.J. Culvenor, Rev. Pure Appl. Chem. (Australia), 1953, 3, 83.

60. A. Blank, Chem. Ber., 1891, 24, 306.

61. B.I. Feuer and G. Smolinsky, J. Org. Chem., 1966, 31, 3882.

62. S.O. Grim, T.O. Read and D. Seyferth, J. Amer. Chem. Soc., 1960, 82, 1510.

63. P.J. Bunyan, A.J. Burn and J.I.G. Cadogan, J., 1963, 1527.

64. A.T. James and A.J.P. Martin, Biochem. J., 1956, 63, 138.

65. H. Hubner, Annalen, 1881, 209, 341.

66. A. Michaelis, Annalen, 1903, 326, 161.

67. R.H.B. Galt and J.D. Loudon, J., 1959, 885.

68. E. Roberts and E.E. Turner, J., 1926, 1208.

69. H.S. Broadbent and H. Gilman, J. Amer. Chem. Soc., 1947, 69, 2053.

70. R. Passerini, Boll. sci. Fac. Chim. ind. Bologna, 1950, 8, 122.

71. J.D. Loudon and N. Shulman, J., 1938, 1618.

72. R.J. Gillespie and R.C. Passerini, J., 1956, 3850.

73. O. Behaghel and K. Hofmann, Chem. Ber., 1939, 72, 582.

74. H. Gilman, D.A. Shirley and P.R. Van Ess, J. Amer. Chem. Soc., 1944, 66, 1214.

75. W. Davey and J.R. Gwilt, J., 1957, 1008.

76. F. Schacher and C. Weygand, Chem. Ber., 1935, 68, 227.

77. A. Kliegl, Chem. Ber., 1908, 41, 1845.

78. E. Bamberger and S. Lindberg, Chem. Ber., 1909, 42, 1723.

79. F.D. Chattaway, J., 1904, 394.

80. D.F. De Tar and H.J. Scheifele, Org. Synth., 1952, 32, 8.

81. L. Horwitz, J. Org. Chem., 1956, 21, 1639.

82. K. Feist, Chem. Ber., 1901, 34, 465.

83. A. Meller, M. Pailer and A. Schleppnik, Monatsh., 1958, 89, 211.

84. G. Smolinsky, J. Amer. Chem. Soc., 1960, 82, 4717.

85. V.A. Gilyarov and M.I. Kabachnik, Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk, 1956, 790.

86. G.I. Derkach and E.S. Gubnitskaya, Zhur. obshchei Khim., 1964, 34, 604.

87. P. Charpentier, P. Gailliot, J. Gaudechon and R. Jacob, Compt. Rend., 1952, 235, 59.

88. O.A. Nelson and L.E. Smith, J. Amer. Chem. Soc., 1942, 64, 461.

89. U.S.P. 2931810. Chem. Abs., 1960, 54, 19724.

90. B.P. 716205. Chem. Abs., 1956, 50, 1929.

91. A. Burger and J. Stanmeyer, J. Org. Chem., 1956, 21, 1382.

92. L. Chierici and R. Passerini, Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat., 1953, 15, 69.

93. A.J. Boulton and A. Rahman, Tetrahedron, 1966, Supplement No. 7, 49.

94. Y. Kanaoka, S. Sugasawa and M. Terashima, Pharm. Bull. (Japan), 1956, 4, 16.

95. K.B. Prasad and G.A. Swan, J., 1958, 2024.

96. D.H. Hey, B.W. Pengilly and G.H. Williams, J., 1956, 1463.

97. W. von E. Doering and R.A. Odum, Tetrahedron, 1966, 22, 87.

98. H.J. Backer and E. Westerhuis, Rec. Trav. chim., 1952, 71, 1071.

99. H. McCombie, B.C. Saunders and G.J. Stacey, J., 1945, 380.

100. A. Michaelis and G. Schulze, Chem. Ber., 1894, 27, 2578.

101. B.B. Brown, R.K. Putney, R.F. Reinisch and P.A.S. Smith, J. Amer. Chem. Soc., 1953, 75, 6335.

102. G. Cilento, Chem. Rev., 1960, 60, 147.

103. A. Mangini and R. Passerini, J., 1956, 4954.

104. F. Montanari, Boll. sci. Fac. Chim. ind. Bologna, 1956, 14, 55. Chem. Abs., 1957, 51, 5723.

105. G.L. Bendazolli and C. Zauli, J., 1965, 6827.

106. M.P. Cava, N.M. Pollack and D.A. Repella, J. Amer. Chem.

Soc., 1967, 89, 3640.

I.S. Ponticello and R.H. Schlessinger, J. Amer. Chem. Soc., 1967, 89, 3641.

107. J.I.G. Cadogan and D.J. Sears, unpublished work.

108. Ref. 83. Chem. Abs., 1959, 53, 9129.

109. F. Haber, Z. Elektrochem., 1898, 5, 77.

110. J.F. Allen, J. Amer. Chem. Soc., 1957, 79, 3071.

111. J. Hamer and A. Macaluso, Tetrahedron Letters, 1963, 387.

112. T.J. Maricich, T.W. Mattingly and W. Lwowski, J. Amer. Chem. Soc., 1963, 85, 1200.

113. M. Appl, R. Huisgen and D. Vossius, Chem. Ber., 1958, 91, 1.

114. M. Appl and R. Huisgen, Chem. Ber., 1958, 91, 12.

115. M. Appl and R. Huisgen, Chem. Ber., 1959, 92, 2961.

116. M. Brenner and R.A. Odum, J. Amer. Chem. Soc., 1966, 88, 2074.

117. J.H. Billman, B.W. Mundy and A. Radike, J. Amer. Chem. Soc., 1942, 64, 2977.

J.H. Billman, C.E. Davis and D.G. Thomas, J. Amer. Chem. Soc, 1946, 68, 895.

118. C. Benezra, S. Nseic and G. Ourisson, Bull. Soc. chim. France., 1967, 1140.