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SOME ASPECTS OF THE CHEMISTRY
OF CATIONIC INTERMEDIATES

by

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A Doctoral Thesis

Submitted in partial fulfilment of the requirements

for the award of

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Department of Chemistry

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SUMMARY

A review of the chemistry of the reactions between trivalent phosphorous derivatives and sources of positive halogen is presented.

The alkylation of various nucleophilic substrates has been achieved using alkoxy-tris(dimethylamino)phosphonium hexafluorophosphates. In particular a new method for the preparation of alkyl aryl ethers and alkyl aryl sulphides has been developed which is both stereospecific and proceeds without rearrangement. The alkoxy-tris(dimethylamino)phosphonium hexafluorophosphates are stable, highly crystalline solids, which can be stored for long periods of time with no sign of decomposition.

Ligand exchange involving a phosphorane intermediate has been proposed to explain the formation of p-nitro-N,N-dimethylaniline in the reaction of potassium p-nitrophenate with neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate. Similar reactions involving ligand exchange were also observed in the reactions of potassium p-nitrophenate with other tris(dimethylamino)phosphonium salts.

A careful investigation of the reactions of benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with aromatic amines revealed that formylation of nitrogen occurred as well as the expected alkylation. N-formylation of N-methylaniline was also achieved using other tris(dimethylamino)phosphonium salts in dimethylformamide. The formylation reactions implicate the intermediacy of phosphoranyl cations.

A brief review of the preparation and synthetic utility of alkyloxonium and alkylhalonium salts is presented as an introduction to Part 2.

The methylation of a wide variety of weak nucleophiles has been achieved using O-methyldibenzofuranium fluoroborate. The methylating agent is generated in the presence of the nucleophile in methylene dichloride from the decomposition of 2'-methoxybiphenyl-2-ylidiazonium fluoroborate.

The ability of O-methyldibenzofuranium fluoroborate to act as a hydride ion acceptor has also been demonstrated.

O-Ethyldibenzofuranium fluoroborate has also been generated and its use as an alkylating agent has been shown.

A series of precursors to potential alkylating agents has also been prepared from 2-hydroxy-2'-nitrobiphenyl

ACKNOWLEDGEMENTS

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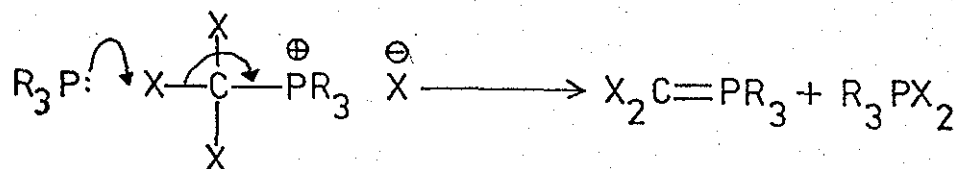
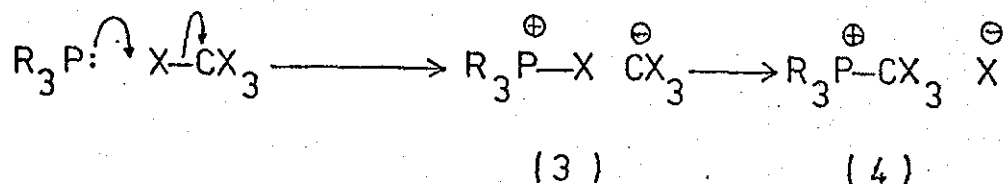
PART 1

Some Reactions of Phosponium Salts derived
from Chloro-tris(dimethylamino)phosponium
trichloromethylide.

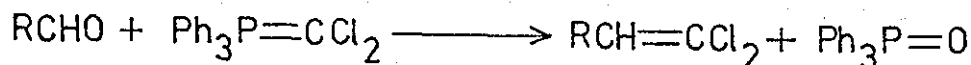
INTRODUCTION

The Chemistry of the Reactions between
Trivalent Phosphorous derivatives and
Sources of Positive Halogen

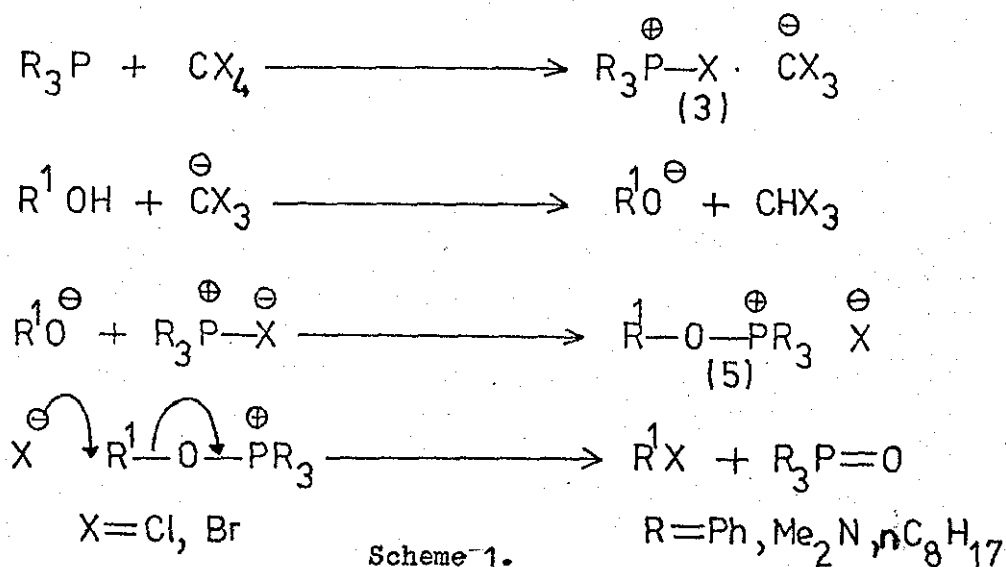
Miller¹ invoked an ionic mechanism involving nucleophilic displacement on halogen to account for the reaction products



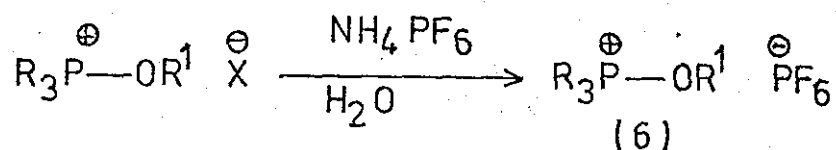
Ylides of structure (1) possess considerable synthetic potential. For example, they provide a route to 1,1-dihaloalkenes by reaction with carbonyl compounds.^{2,3,4}



Halophosphonium salts of structure (3) have also proved to be both versatile and valuable intermediates for general organic synthesis. These salts are unstable and anionic exchange rapidly takes place to yield the trihalomethylphosphonium halides (4). However, the reactive species (3) can be trapped by alcohols to form alkoxyphosphonium salts (5), which collapse to give alkyl halides and tertiary phosphine oxide.^{5a,b,c} It is generally accepted that these reactions also proceed via an ionic mechanism as shown below in Scheme 1.⁶ The initial reaction step is the removal of the hydroxylic proton by the trihalomethyl anion to furnish the alcoholate anion and a haloform, the alkoxyphosphonium salt is formed by subsequent attack of the alcoholate anion on the halophosphonium salt (3).

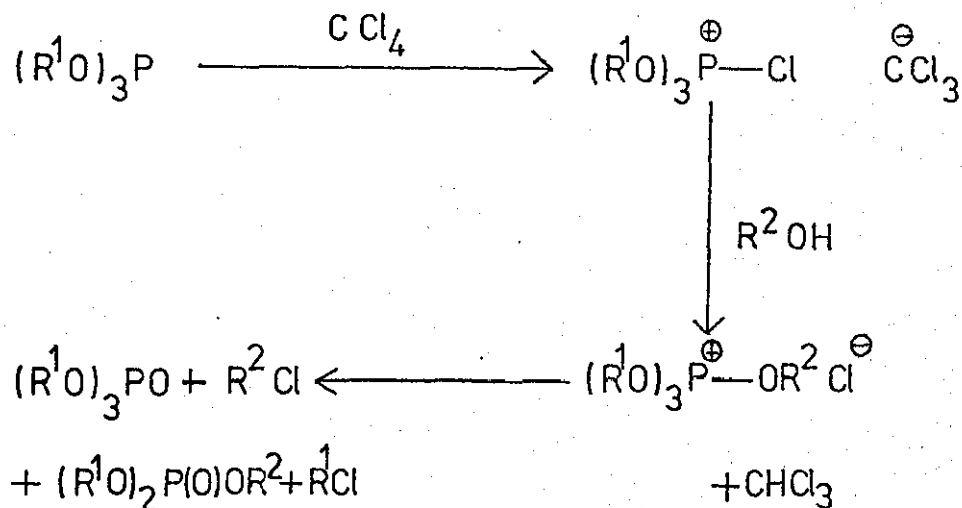


The intermediacy of (5) has been conclusively proved by the isolation and characterisation of the alkoxyphosphonium salt as the stable hexafluorophosphate (6, $R=Me_2N$, $R^1 = (CH_3)_3C-CH_2$).⁷



This method of converting primary and secondary hydroxyl groups into halides by reaction with a carbon tetrahalide and a phosphine has been synthetically very useful since the conditions are so mild that "sensitive" alcohols, such as carbohydrates,^{8a,b} have been converted into halides. The reaction is a simple modification of earlier work which involved the addition of trialkylphosphites, $(R^1O)_3P$, to carbon tetrachloride in the presence of an alcohol, (R^2OH) ,⁹ the resulting products were a mixture of phosphates, alkyl chlorides, R^1Cl and R^2Cl and chloroform. The reaction is outlined in Scheme 2.

It was soon realised that substitution of the phosphite by a tertiary phosphine would produce an intermediate (5) for which only one mode of breakdown was possible and hence the problem of mixed halide formation has been obviated.



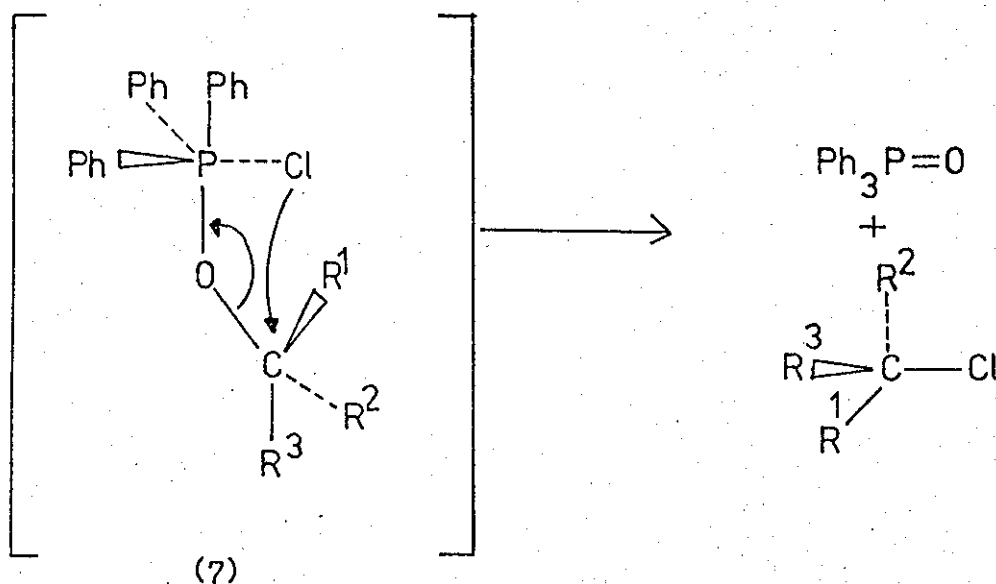
Scheme 2

The literature reveals that the majority of the work on this reaction utilises triphenylphosphine. The report¹⁰ that trioctylphosphine is more reactive has apparently been ignored. Also the use of tris(dimethylamino)phosphine allows particular ease of isolation of the alkyl halide since the resulting phosphine oxide, hexamethylphosphoric triamide, is water soluble.⁷

The reaction shows a remarkable propensity to give products of inversion. Even when solvolysis of the corresponding esters was assisted the reaction gave overall retention of configuration.¹¹ Weiss and Snyder have demonstrated that the reaction gave chlorides with predominant, if not exclusive, inversion in acyclic primary and secondary alcohols,¹¹ a primary thiol,¹¹ 7-norbornanol,¹² and also proceeded with significant if not predominant, inversion in such systems as anti-7-norbornenol and exo-2-norbornanol.¹¹ However there was considerable racemisation in the products obtained from the analogous reactions with carbon

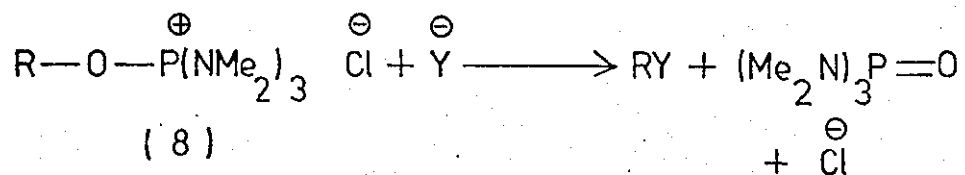
tetrabromide.¹³

The stereochemical path for chlorination is typical of S_N2 reactions, however the reaction products can be derived from either a pentacovalent haloalkoxyphosphorane (7) or from a tight ion pair in which ionic chloride wanders around the periphery of a tetrahedral phosphorus cation. Weiss and Snyder^{12,13} have favoured the former suggestion and proposed that the reaction proceeds via an intramolecular, fairly concerted decomposition of (7).



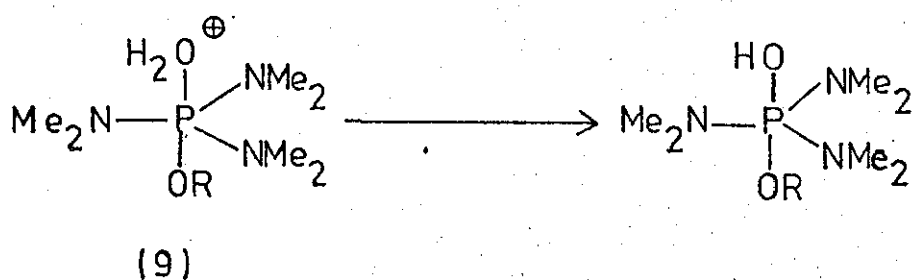
This rationale, however, is incompatible with the report¹⁴ that nitriles are formed in high yields when primary and secondary alcohols are treated with triphenylphosphine, carbon tetrachloride and sodium cyanide in dimethyl sulphoxide. This reaction presumably involves competitive attack of the cyanide ion on the intermediate quasi-phosphonium species, (Ph₃P⁺-OR). Furthermore, Castro and Selve¹⁵ have shown that, at low temperatures in tetrahydrofuran, the alkoxyphosphonium chlorides (8) are stable and that nucleophiles can

compete favourably with chloride ions in the decomposition of the salts.



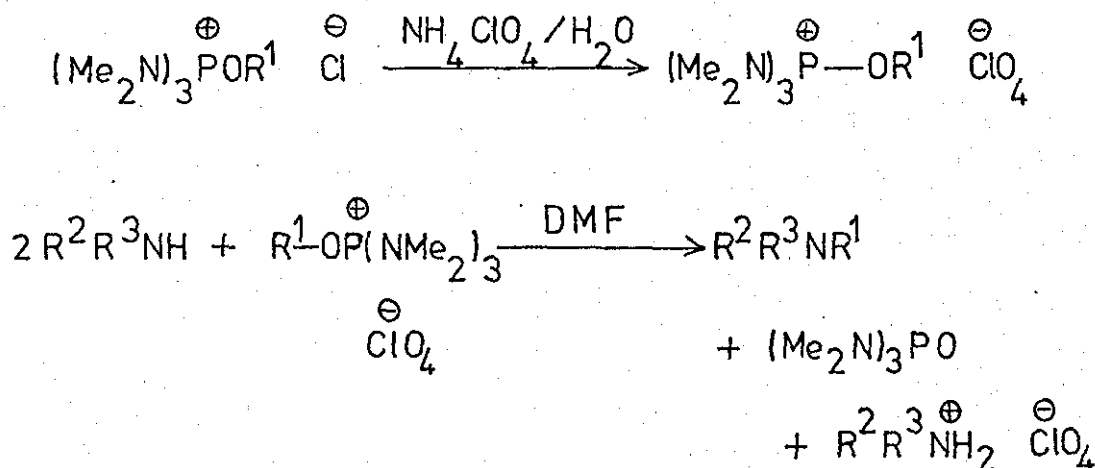
Y = N₃, SCN, PhS, CN, and I.

These authors also observed that the alkoxyphosphonium chlorides are stable in water, with no sign of decomposition to the alkyl chloride. Presumably this effect is due to co-ordination of water molecules both to the chloride anion and the phosphorus cation. The phosphonium salt would give a phosphorane (9) bearing two oxygen ligands, thus increasing the stability of the system, particularly if deprotonation occurred.



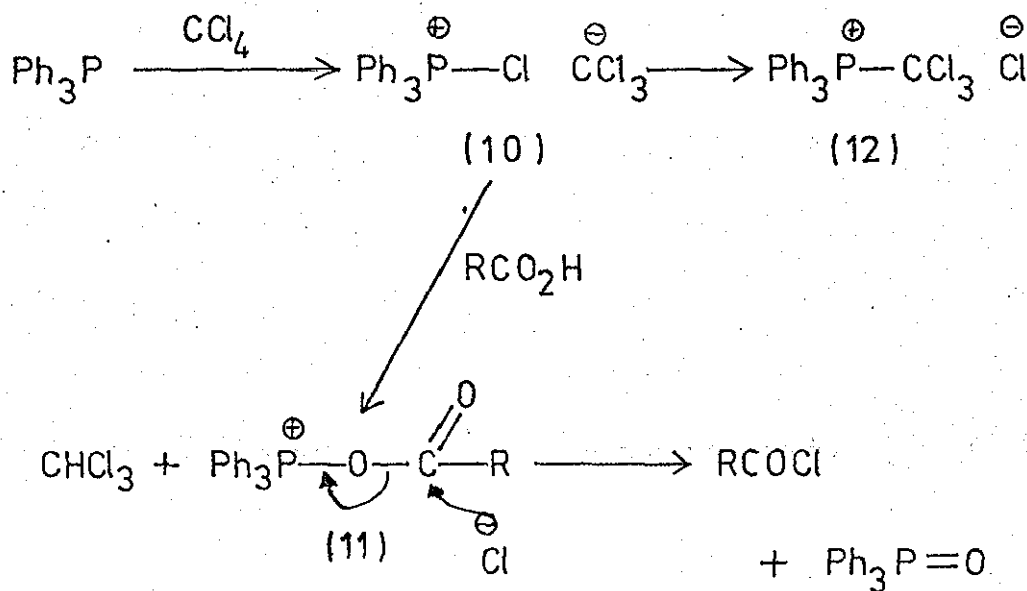
The problem of less powerful nucleophiles being unable to compete satisfactorily with chloride ions has been circumvented by conversion of the alkoxyphosphonium chloride into the perchlorate prior to reaction with the weak nucleophile.¹⁶ This method has been utilised to give

good yields of monoalkylated amines from primary and secondary amines as shown in Scheme 3.



Scheme 3.

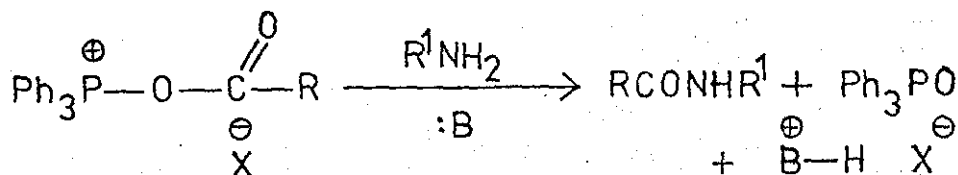
Carboxylic acids react in a similar manner to alcohols on treatment with the triphenylphosphine-carbon tetrachloride product (10) to afford triphenylacyloxyphosphonium chlorides (11), which readily decompose to yield the corresponding acyl halide and triphenylphosphine oxide,¹⁷ as illustrated in Scheme 4.



Scheme 4.

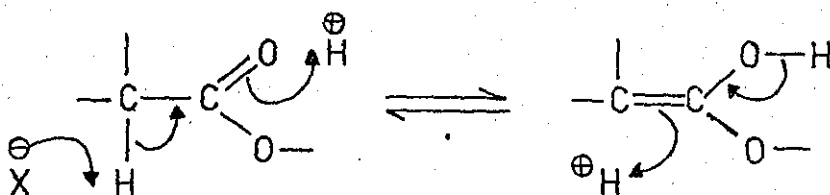
A modification of this reaction involving the addition of an

amine to the reaction mixture in tetrahydrofuran resulted in the reaction of the amine with the acyloxyphosphonium chloride and thus provided a new method for the preparation of amides.^{18,19}

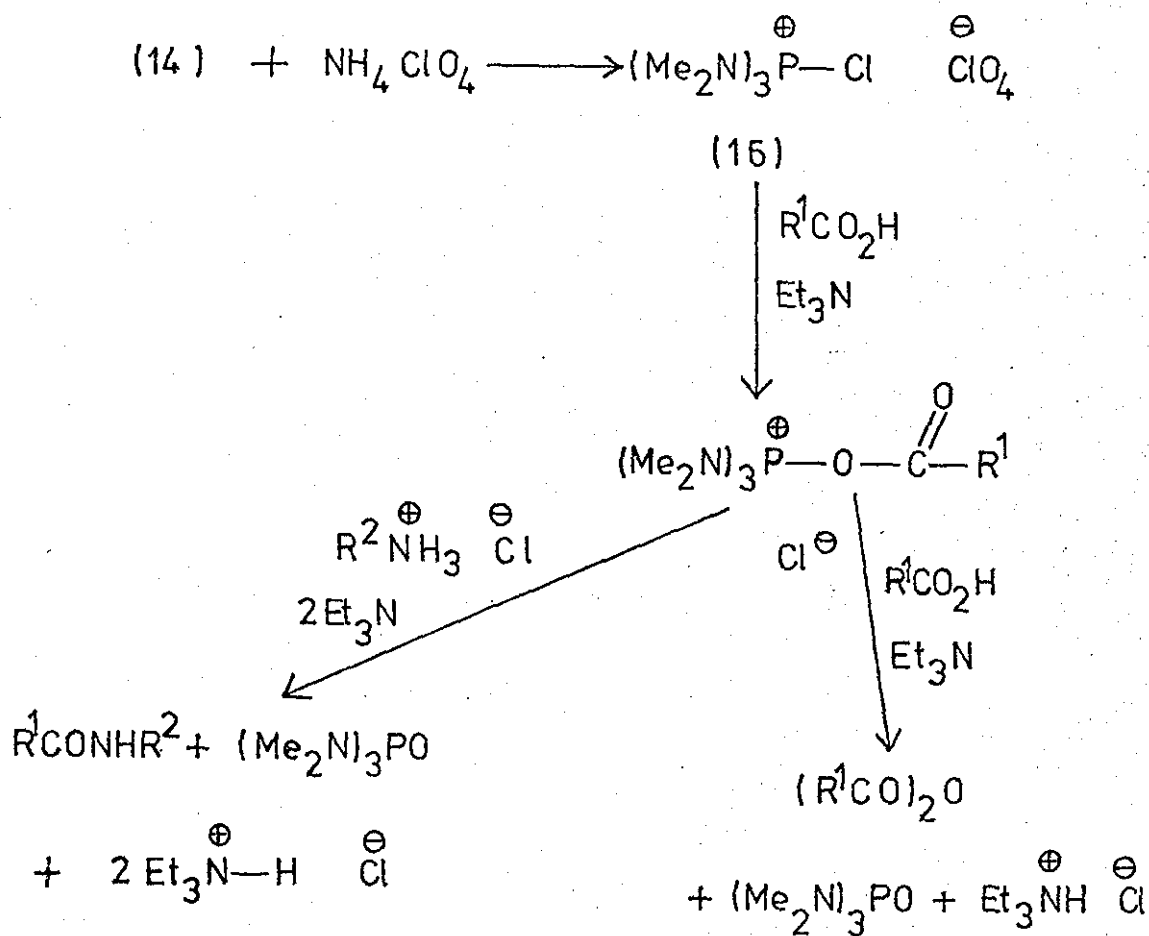


X = Br and Cl

This method has been applied to peptide synthesis. Thus condensation of N-benzyloxycarbonyl-L-phenylalanine and ethyl glycinate hydrochloride gave an 85% yield of the purified peptide.¹⁸ Yamada²⁰ reported that substituting aminophosphines for triphenylphosphine improved both the yield and optical purity of peptide product, though appreciable racemisation had still occurred. The loss of optical purity in this reaction could have resulted from enolisation of the acyl carbonyl function, catalysed by the by-product HCl; or more



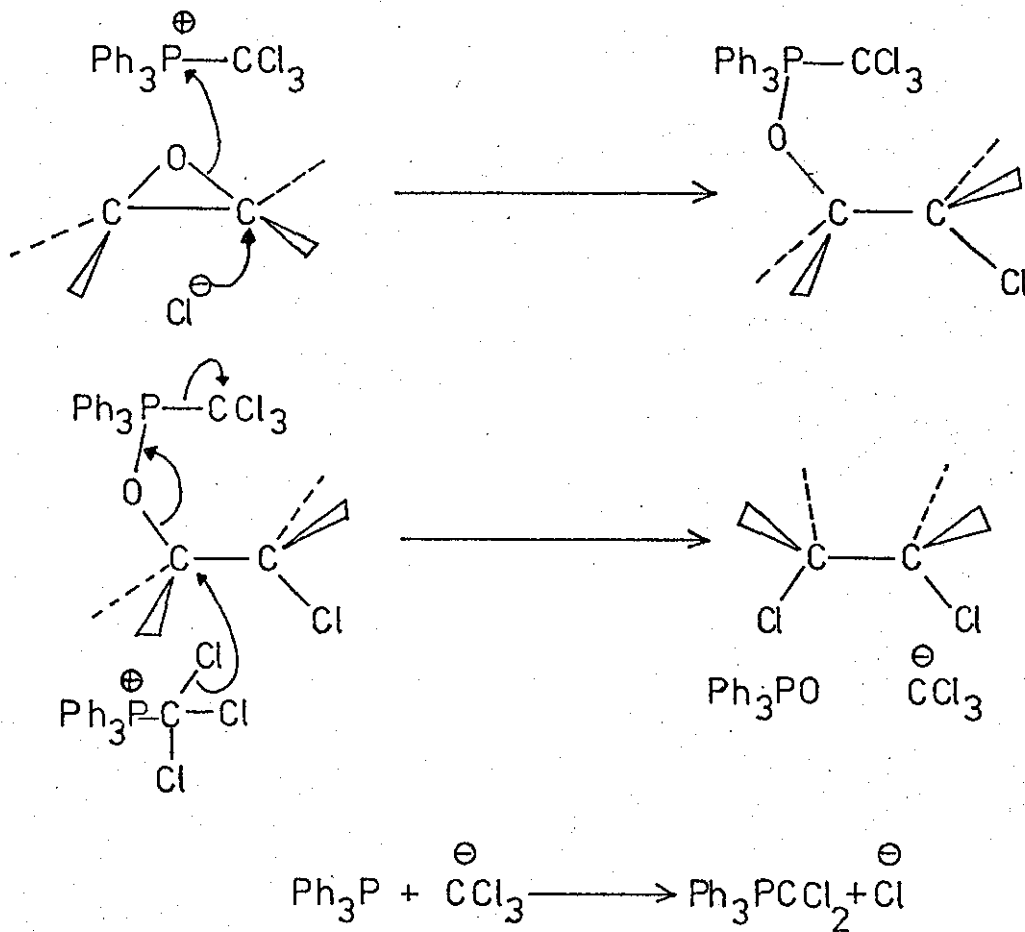
probably, the presence of chloride ion could have resulted in some diversion of the intermediate acyloxyphosphonium salt to acyl halide prior to reaction with the amine derivative. The use of a non-nucleophilic anion in the peptide synthesis would therefore produce an improvement in the optical purity of the product and this has been established by Kenner and his co-workers, who have used the



Scheme 5.

Use of the triphenylphosphine-carbon tetrachloride reagent as a specific reagent for the replacement of oxygenated functions by chlorine has been extended to include chlorination of epoxides.²⁴ The epoxides were converted into the corresponding 1,2-dichloroalkanes in a highly stereo-specific reaction. Only cis-1,2-dichloro-cycloalkanes were obtained from 1,2-epoxycycloalkanes. Reaction with dextrorotatory propylene oxide gave 1,2-dichloropropane which was found to be laevorotatory. From the known relative configurations of these compounds it was clear that inversion had occurred at C-2 and, since in the cyclic cases a cis-product was obtained, the authors reasoned that inversion

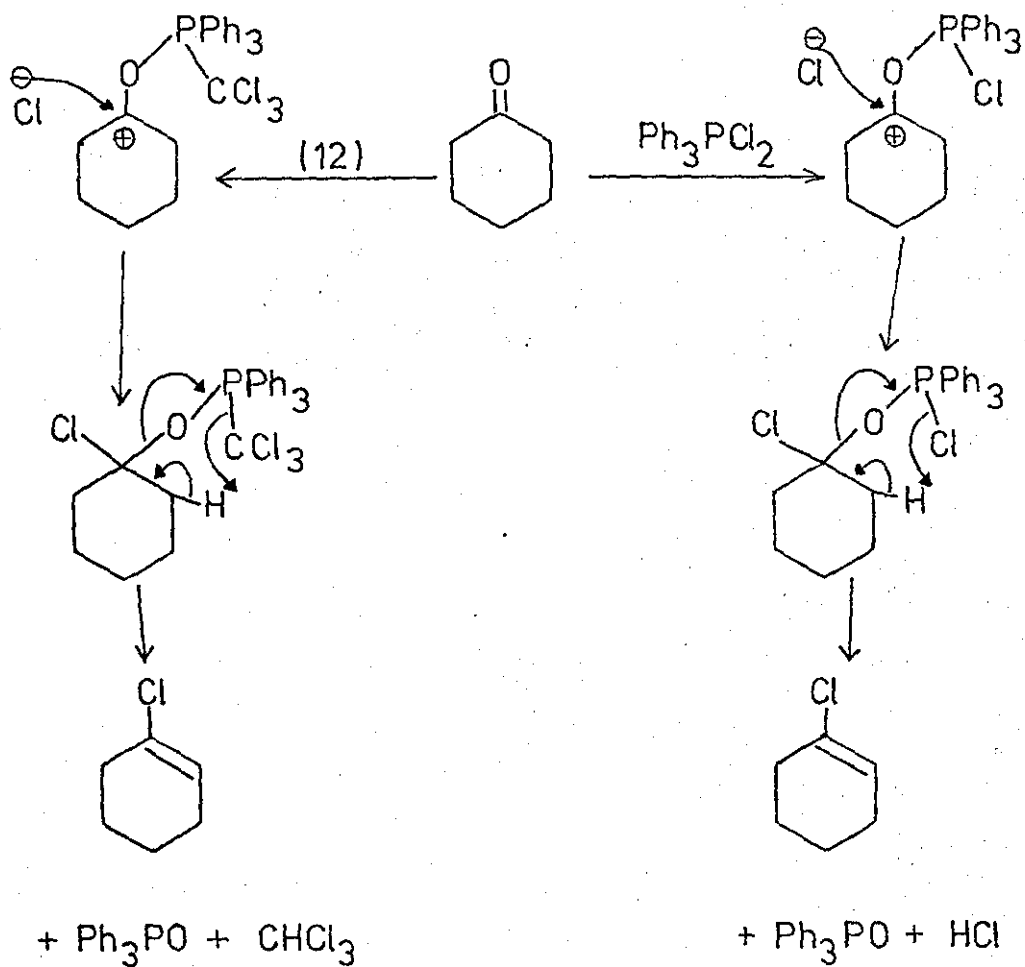
had taken place at each carbon. The following reaction mechanism was proposed (Scheme 6). However, this proposal is clearly incorrect.



Scheme 6.

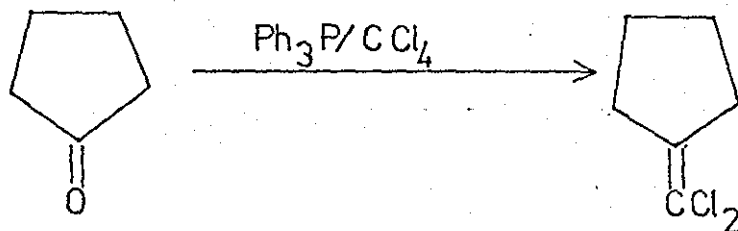
Bromination using carbon tetrabromide was also successful, but was much less stereospecific.

The same system as a chlorinating agent has been applied to the reaction with enolisable ketones;²⁵ acyclic and 6-membered cyclic ketones gave predominantly enyl chlorides. The presence of both HCl and chloroform among the reaction products implied that the enyl chlorides were derived from attack by the ketone on either the intermediate (12) or triphenyldichlorophosphorane (2, R=Ph, X=Cl), as illustrated in Scheme 7.



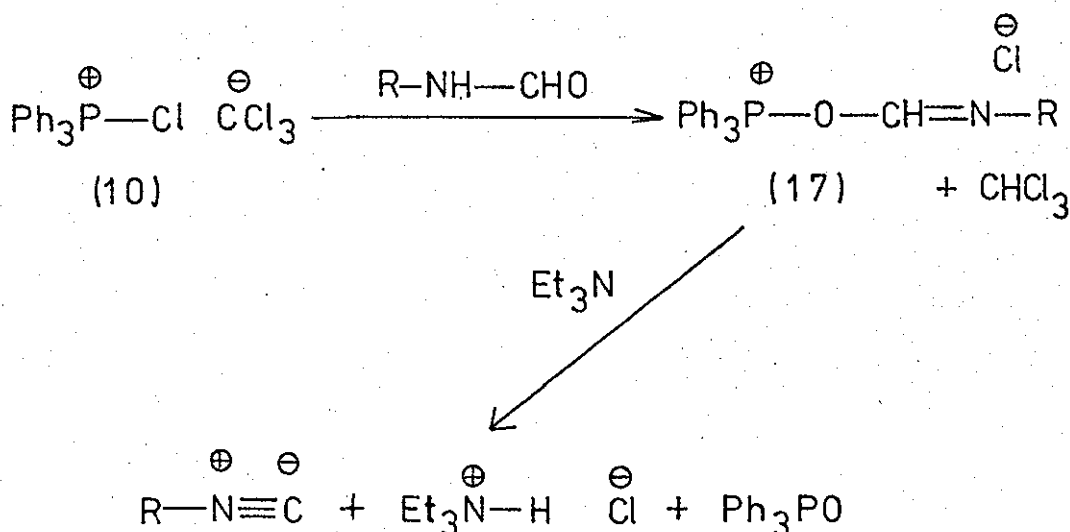
Scheme 7.

However, 5- and 4- membered ring cyclic ketones reacted to give exocyclic dichloromethylene compounds, presumably derived from reaction of the carbonyl function with the ylide 1 (R=Ph, X=Cl).



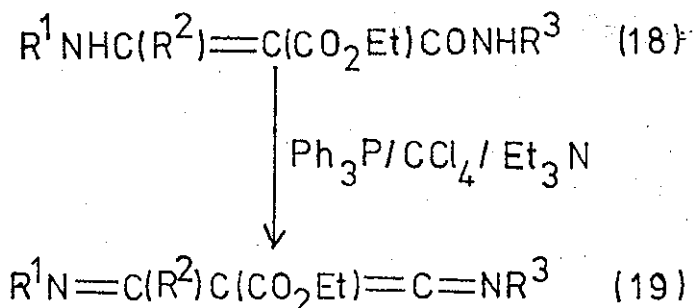
The ability of the triphenyl-phosphine-carbon tetrachloride adduct (10) to behave as a dehydrating system has been utilised by Appel and his co-workers in designing new methods for the preparation of nitriles from both carboxylic amides²⁶ and oximes,²⁷ carbodi-imides

from ureas,²⁸ and isocyanides from monosubstituted aliphatic and aromatic formamides.²⁹ The reaction involves the simultaneous addition of triphenylphosphine, carbon tetrachloride, and triethylamine to the compound being dehydrated. Scheme 8 outlines the reaction sequence for the formation of isocyanides.

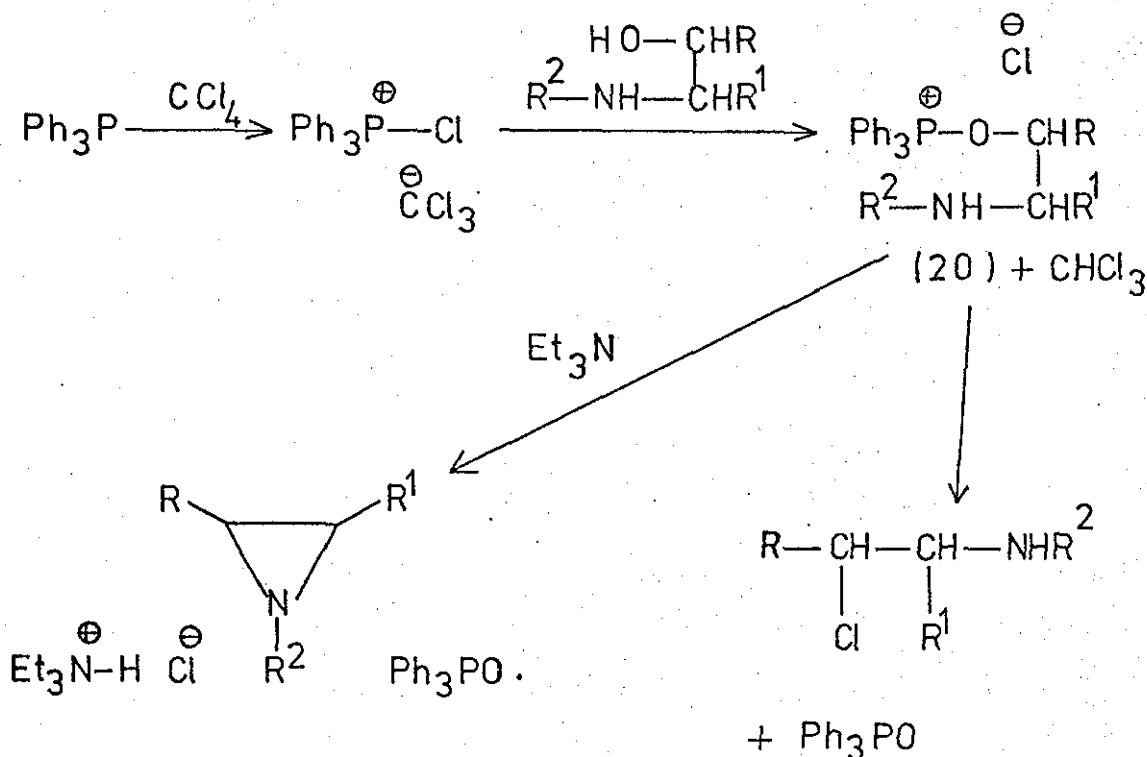


Scheme 8.

The elimination of the elements of water occurs in a stepwise process as shown by deuteration experiments. Thus it was demonstrated that the proton in the chloroform came exclusively from the N-H bond by performing experiments with formamides deuteriated at the nitrogen. An adduct (17) is initially formed with the liberation of chloroform, the intermediate then decomposes to produce hydrogen chloride and the dehydrated product. The procedure has also been effective in converting the amides (18) to the substituted ketenimines (19).³⁰



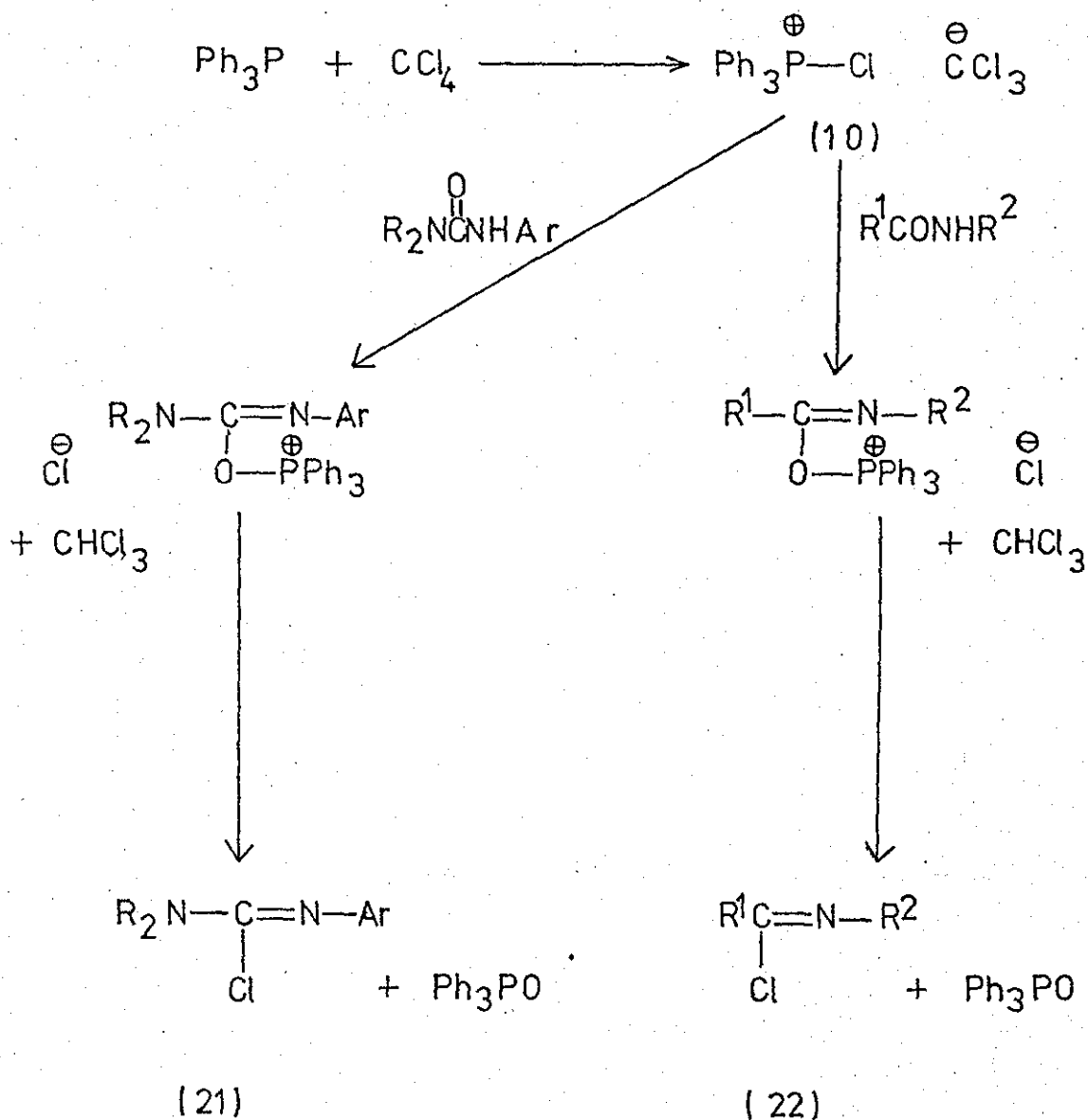
The dehydrating system has been used to convert N-substituted α -amino alcohols into aziridines.³¹ The alcohols react with triphenylphosphine and carbon tetrachloride in the normal manner to afford the alkoxyphosphonium chlorides (20) and chloroform. The phosphonium salt subsequently decomposes by an intramolecular reaction, involving the elimination of triphenylphosphine oxide, to yield the aziridine. Competitive attack by the chloride ion on the intermediate (20) leads to the formation of α -chloramines, albeit in extremely low yields. The reaction sequence is outlined in Scheme 9.



Scheme 9.

The synthetic importance of the reaction of phosphines together with carbon tetrachloride using various ammonia derivatives has been demonstrated by Appel and his co-workers. These authors have developed a procedure for the conversion of trisubstituted ureas into chloroformamidines (21)^{32a,b} and also for the preparation of imidoyl halides (22)³³ from monosubstituted amides. The reaction steps are

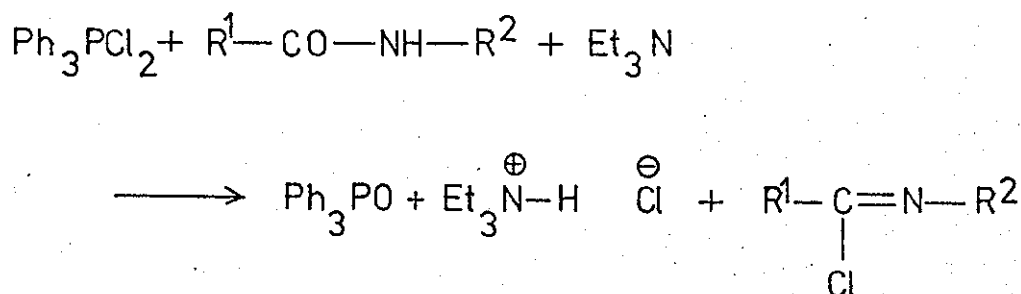
illustrated in Scheme 10. A phosphonium chloride intermediate is formed after the proton of the N-H bond has been removed by the CCl_3^- anion of the adduct (10) and subsequent phosphorylation at the oxygen has occurred. The intermediate phosphonium salt then collapses to give the required product and triphenylphosphine oxide.



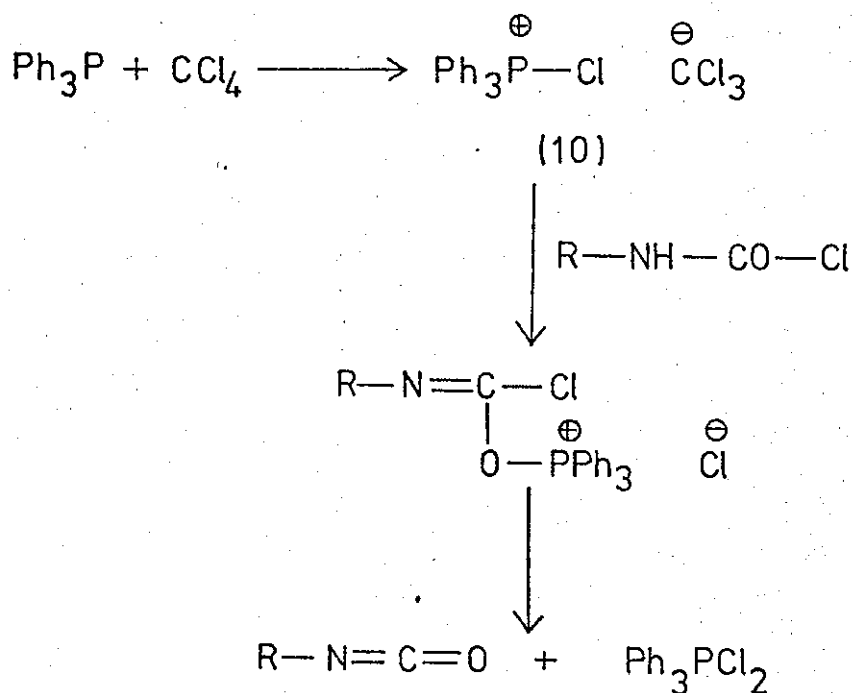
Scheme 10.

An alternative procedure for the above transformations has also been established by the same authors. This essentially similar method involves the use of triphenyldichlorophosphorane in the presence of triethylamine (to remove hydrogen chloride formed in the reaction).

e.g.

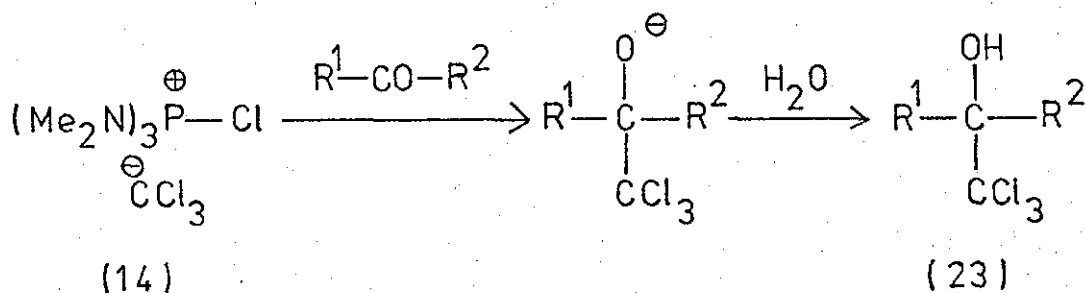


Isocyanates³⁴ have been prepared by reaction of the triphenylphosphine-carbon tetrachloride adduct with carbamoyl chlorides, the by-product of this reaction is triphenyldichlorophosphorane (Scheme 11).

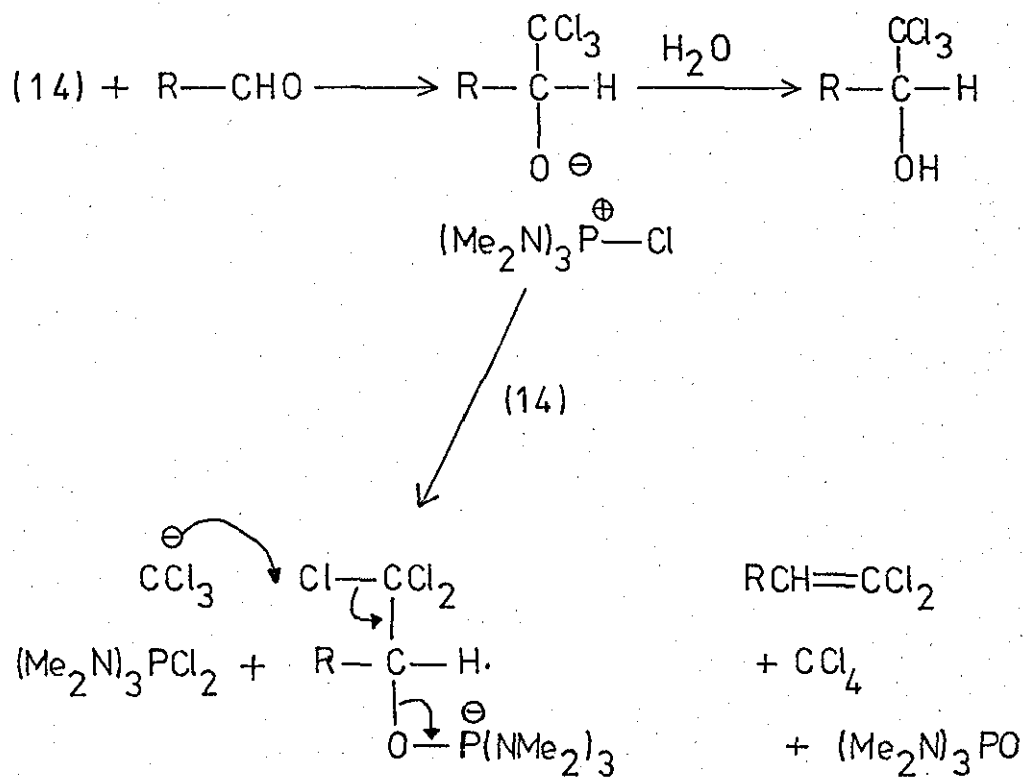


Scheme 11.

In some instances the reactivity of the trichloromethyl anion, formed from carbon tetrachloride and tris(dimethylamino) phosphine, has been exploited. The anion has been trapped by addition to carbonyl compounds to give the alcohols (23).^{35a.b} Aldehydes react with greater efficiency than ketones, presumably this is due to the higher electrophilic nature of the carbonyl group in aldehydes.

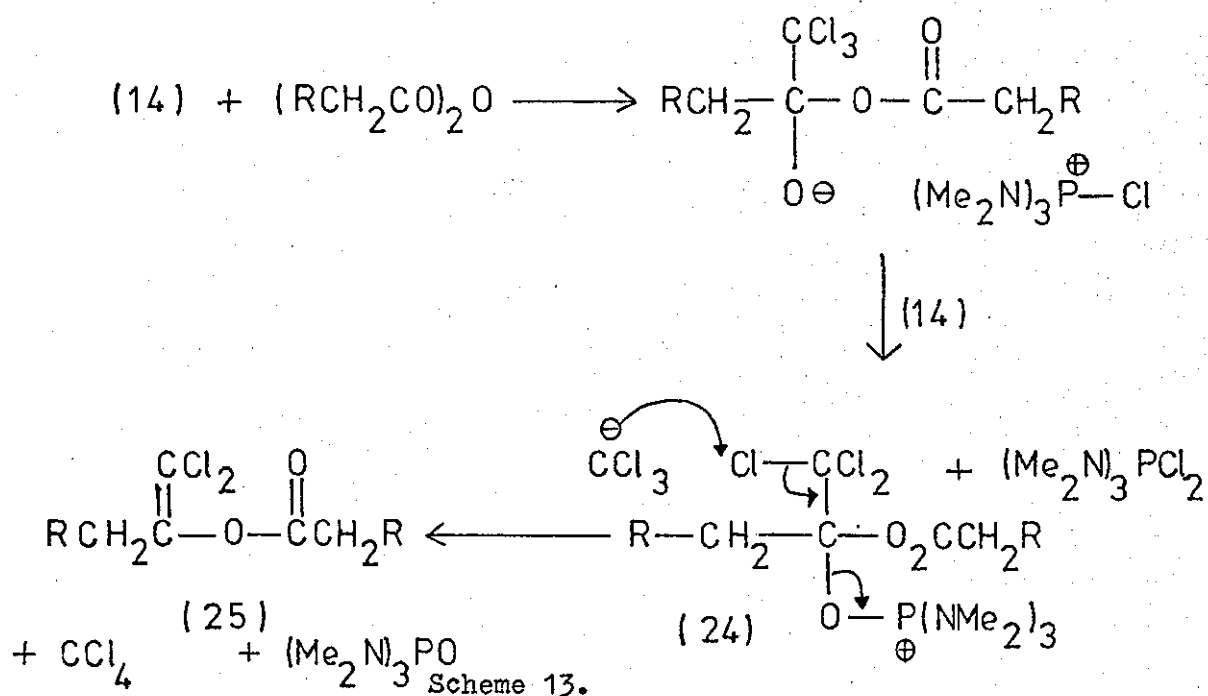


By using excess carbon tetrachloride-tris(dimethylamino)phosphine reagent, this reaction has been modified to provide a new route for the conversion of aldehydes into 1,1-dihalo-olefins.³⁶ The mechanism of the reaction is outlined in Scheme 12.



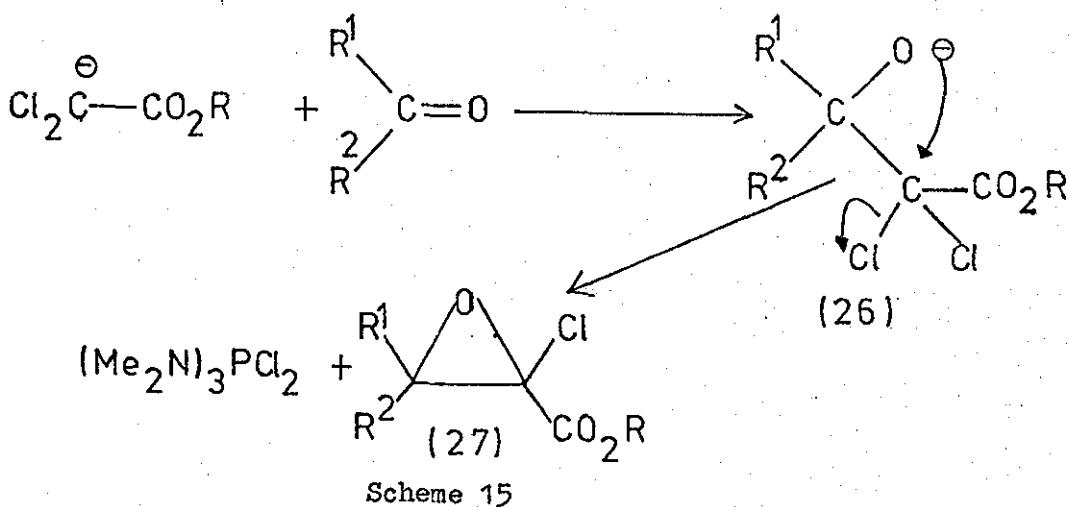
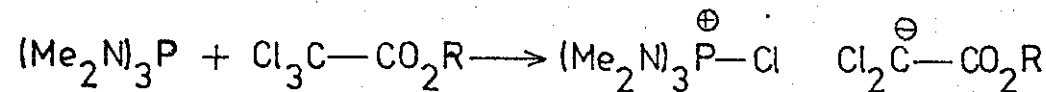
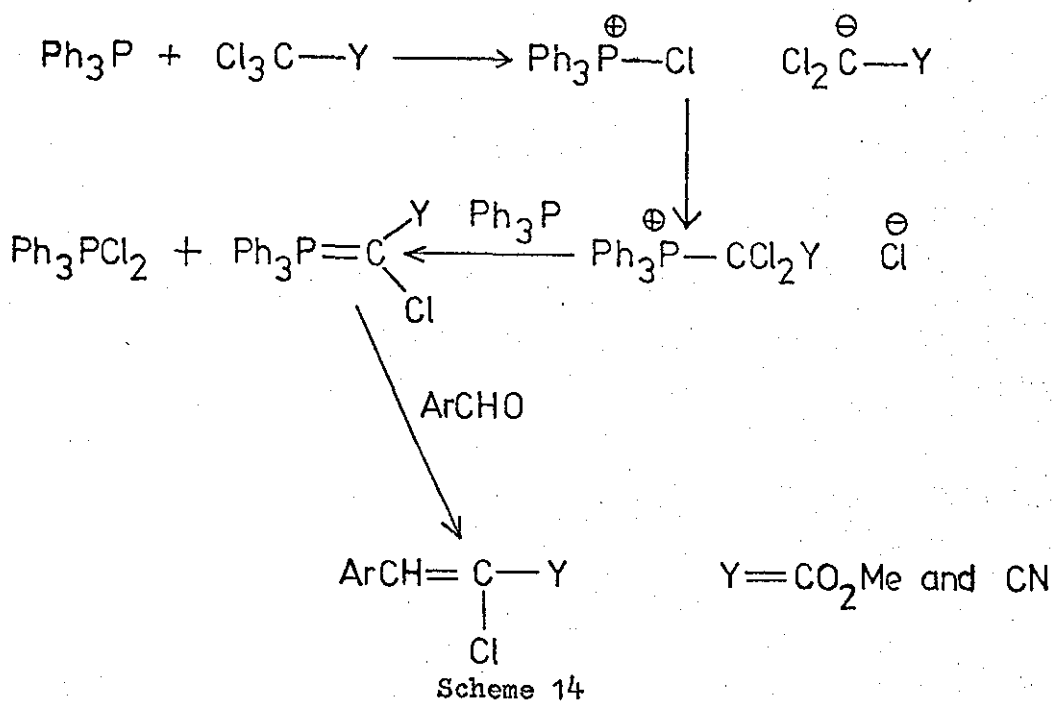
Scheme 12.

The trichloromethyl anion has been used in the preparation of the enol esters (25) from acid anhydrides.³⁷ The enol esters are derived from a β -elimination of hexamethylphosphoric triamide from the phosphonium salt (24) as shown in Scheme 13.

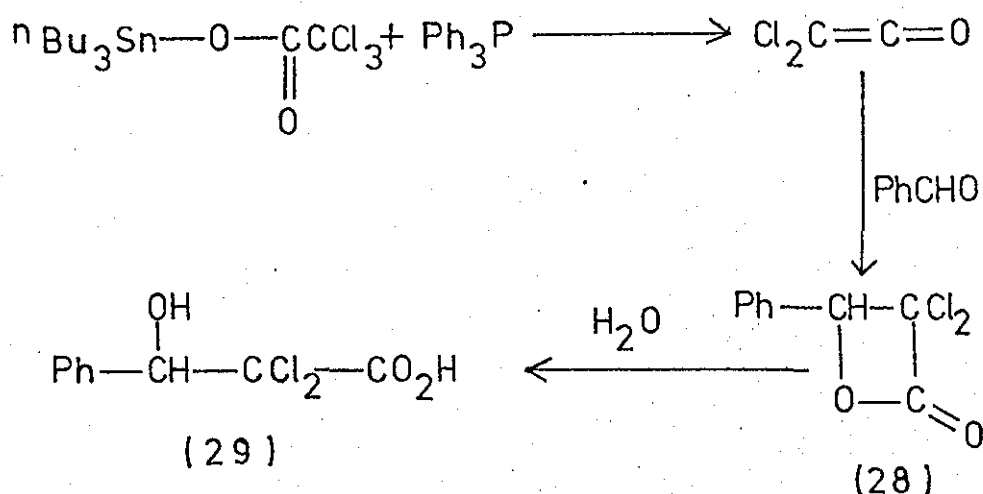


Many extensions of these reactions have been reported in which other highly chlorinated anions have been employed. Thus the complex formed by the reaction of triphenylphosphine with a trihaloacid derivative has been utilised in a convenient preparation of α -halovinylesters and nitriles from aromatic aldehydes.³⁸ (Scheme 14).

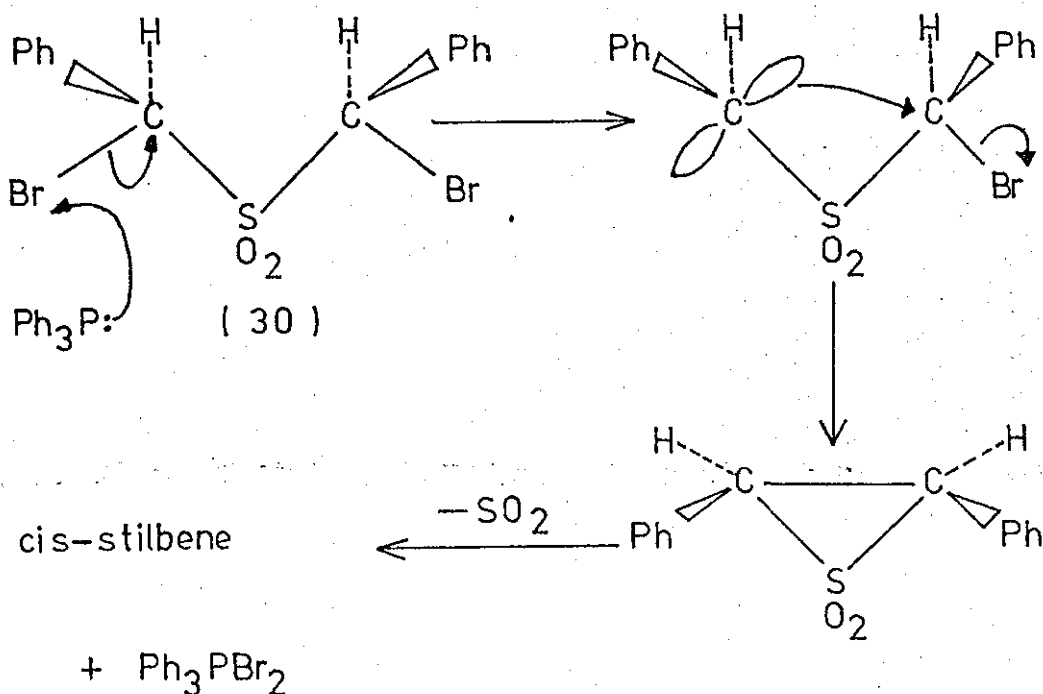
The anions obtained by reaction of tris(dimethylamino)phosphine with esters or amides of trichloroacetic acid have been trapped by addition to carbonyl compounds to give the glycidic esters or amides (27).³⁹⁻⁴¹ The reaction is thought to proceed via initial nucleophilic attack on the carbonyl function to produce an alcoholate ion (26), which then undergoes an intramolecular reaction to yield the glycidic ester or amide by elimination of chloride ion (Scheme 15). Although aldehydes react readily to give high yields of product, the only ketones that have been reported to undergo the reaction are cyclohexanone and acetone.



The dichloroacid (29) has been prepared in a similar reaction involving the addition of tributyl tin trichloroacetate to triphenylphosphine in the presence of benzaldehyde.⁴² Spectral evidence has indicated that dichloroketen and the β -lactone (28) are reaction intermediates.

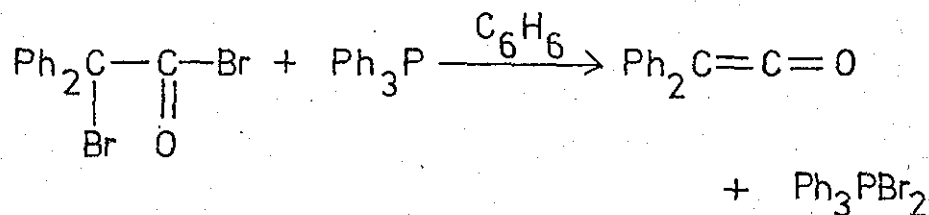


Dehalogenation reactions using tertiary phosphorus compounds have featured regularly in the recent literature. Debromination of α, α' -dibromodibenzyl sulphone (30) with triphenylphosphine was shown to be stereospecific⁴³ involving inversion at both centres. Thus the meso form gave cis-stilbene and the (\pm) form, trans-stilbene. The mechanism is illustrated for the former case (Scheme 16).

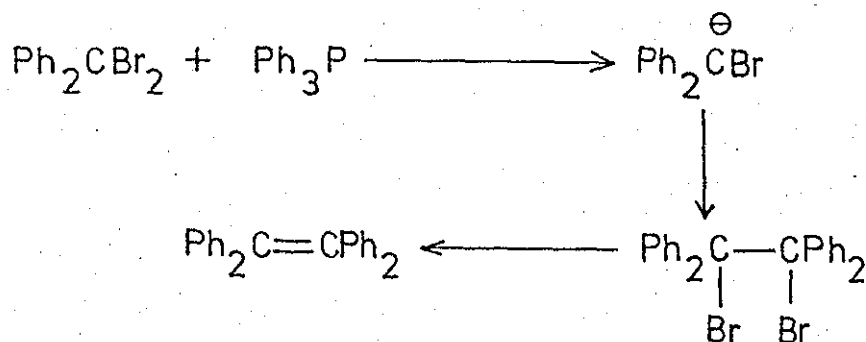


Scheme 16.

The debromination of α -bromodiphenylacetyl bromide has been used as a convenient method for the preparation of diphenylketen.⁴⁴ The dibromotriphenylphosphorane is insoluble in the reaction mixture.



Stilbene dibromides and other vicinal dibromides have been debrominated stereospecifically in an anti-elimination.⁴⁵ 9,9-dibromofluorene and dibromodiphenylmethane have been converted into the corresponding olefins.⁴⁶



It is clear from this brief review that reactions of tertiary phosphines with sources of formal positive halogen has provided a number of synthetically useful methods. However, it is equally clear that this field still contains considerable potential.

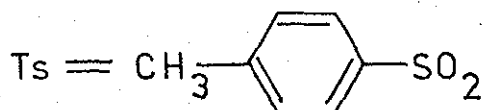
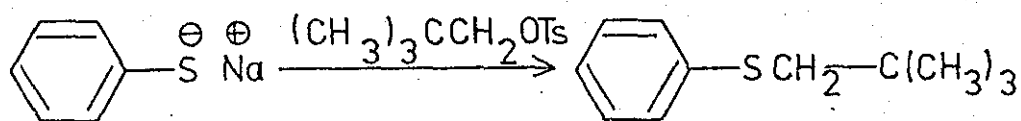
Discussion

As part of an interest in the preparation of O-alkyldibenzo-furanium salts (see Part 2), a method was required for the conversion of 2-hydroxy-2'-nitrobiphenyl into 2-alkoxy-2'-nitrobiphenyls. The method should be both stereospecific and also not lead to any rearrangement. In particular, it was necessary to prepare chiral aryl-(1-methylheptyl)ethers, and aryl neopentyl ethers which were free from other isomers.

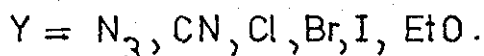
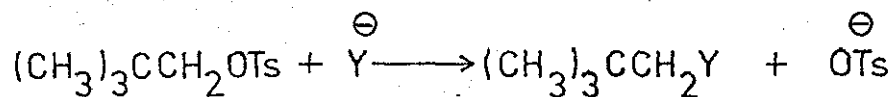
The reaction of the potassium salt of 2-hydroxy-2'-nitrobiphenyl with neopentyl chloride in dimethylsulphoxide resulted only in recovery of the starting material. Similar results were observed using neopentyl bromide and 1-methylheptyl chloride as the alkylating agents. This apparent lack of reaction with the neopentyl halides is due to the presence of the bulky tert-butyl group which interferes sterically with the approaching nucleophile. Reactions in the neopentyl system are frequently very slow particularly those proceeding by an S_N2 mechanism. Rearrangement via the neopentyl cation to the tert-amyl group frequently predominates and indicates an S_N1 process. However, substitutions without rearrangement have been reported.

Whitmore and his co-workers⁴⁷ obtained a 70% yield of neopentyl acetate by the reaction of neopentyl iodide with potassium acetate in ethanol (sealed tube, 200°, 20hr.). Similarly ethyl neopentyl ether has been prepared by the treatment of neopentyl bromide with sodium ethoxide in ethanol (sealed tube, 125°, 760hr.).⁴⁸ Bordwell and his co-workers⁴⁹ obtained good yields of unrearranged products by using the more reactive p-toluenesulphonate as the leaving group and stronger nucleophiles such as the iodide and thiophenoxide anions. For example, the

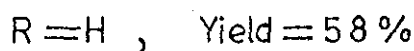
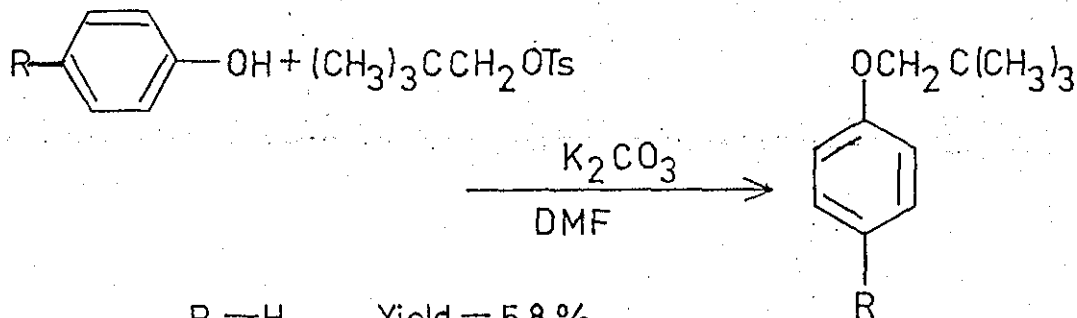
reaction of sodium thiophenoxide with neopentyl *p*-toluenesulphonate in 2-methoxyethanol gave neopentyl phenyl sulphide in 56% yield.



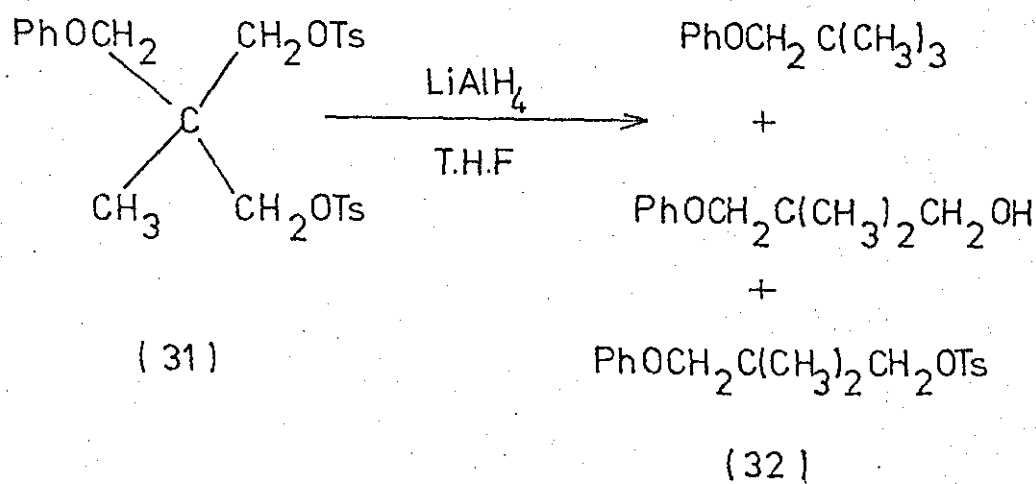
Mosher and his co-workers⁵⁰ have also reported recently that neopentyl *p*-toluenesulphonate undergoes nucleophilic displacement without rearrangement with a variety of nucleophiles in hexamethylphosphoric triamide.



The preparation of aryl neopentyl ethers has also been achieved recently by the reaction of potassium aryloxides with neopentyl *p*-toluenesulphonate in dimethylformamide.⁵¹



This relatively simple procedure is a considerable improvement on the first reported synthesis of aryl neopentyl ethers, which involved the reduction of the bis-*p*-toluenesulphonates of 2-aryloxy-2-methyl-1,3-propane diol using lithium aluminium hydride in tetrahydrofuran.^{52,53} This method gives a mixture of products which are separated by fractional distillation. For example the reduction of the phenyl derivative (31) gave neopentyl phenyl ether (60%), 2,2-dimethyl-1-hydroxy-3-phenoxypropane (8%), and the *p*-toluenesulphonate (32) in 13% yield.



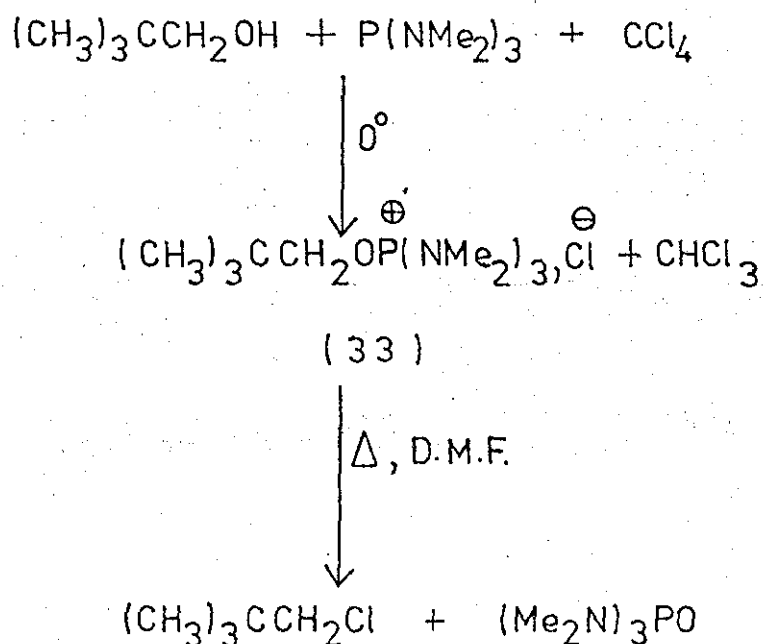
Thus neopentyl *p*-toluenesulphonate has been established as a reagent for the introduction of the neopentyl group without leading to any rearrangement. However its synthetic utility is considerably reduced by the fact that the reagent decomposes on storage and hence it has to be freshly prepared for each reaction.

The preparation of chiral 1-methylheptyl phenyl ether has been achieved⁵⁴ by treatment of potassium phenoxide with optically active 1-methylheptyl *p*-toluenesulphonate. However this reagent is an oily product which cannot be purified readily

and once again decomposes on storage.

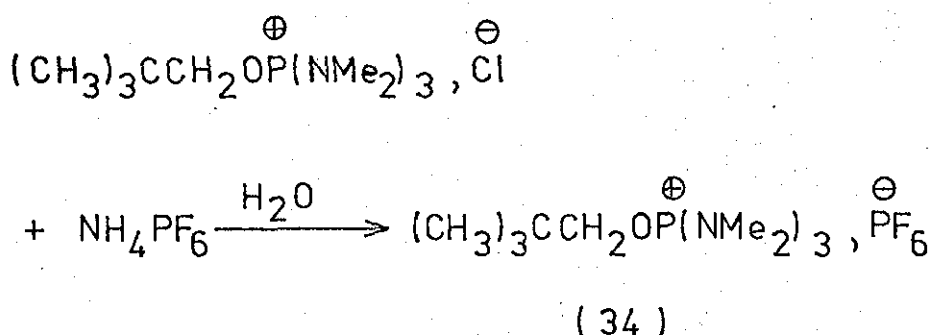
The previous isolation⁷ of a stable alkoxy-tris(dimethylamino) phosphonium hexafluorophosphate suggested the use of this type of reagent as an alkylating agent.

Neopentyl chloride was prepared according to the method developed by Downie⁷ for the conversion of alcohols to alkyl chlorides. The first step of the reaction involved the addition of phosphorous trisdimethylamide in dry ether to an ice-cold solution of carbon tetrachloride and neopentyl alcohol in dry ether to give the quasi-phosphonium species (33) as a yellow oil. This salt was then dealkylated by heating under reflux in dimethylformamide to afford neopentyl chloride and hexamethylphosphoric triamide (Scheme 17). In general, dealkylation of alkoxy-tris(dimethylamino)phosphonium chlorides can readily be achieved by heating under reflux in ether.



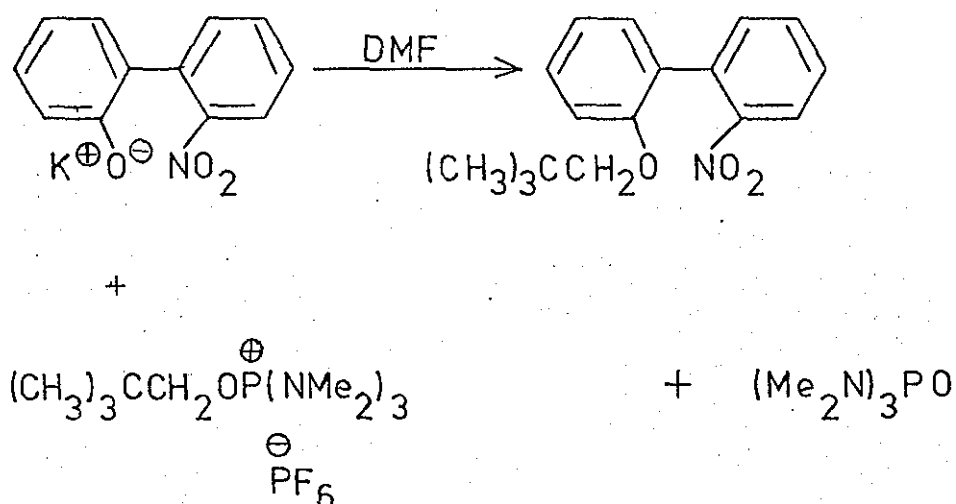
Scheme 17.

Since the chloride anion had dealkylated the quasi-phosphonium salt it seemed reasonable to assume that aryloxy anion would also be capable of displacing the neopentyl group. The quasi-phosphonium salt was isolated as the stable hexafluorophosphate in a 70% yield by the addition of a saturated aqueous solution of ammonium hexafluorophosphate to an aqueous solution of the chloride salt.

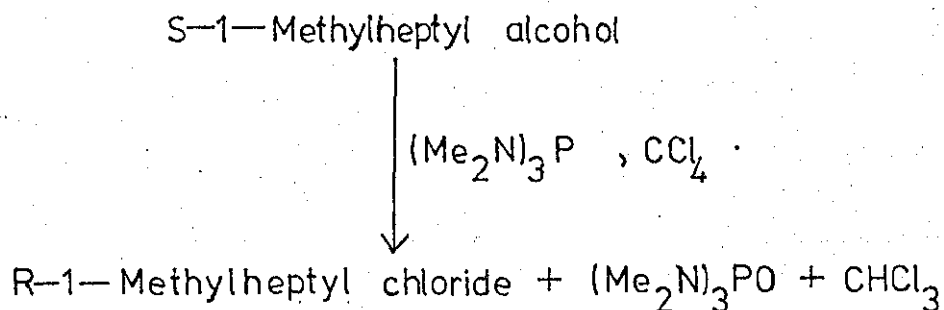


Neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate(34) is a non-hygroscopic, crystalline solid which may be purified easily by recrystallisation from ethanol. Conversion of the phosphonium chloride to the hexafluorophosphate salt effectively removes the possibility of competitive attack by the chloride ion in subsequent displacement reactions with other nucleophiles. Accordingly, the reaction of the potassium salt of 2-hydroxy-2'-nitrobiphenyl with neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate in dimethylformamide gave 2-neopentyloxy-2'-nitrobiphenyl in 90% yield.

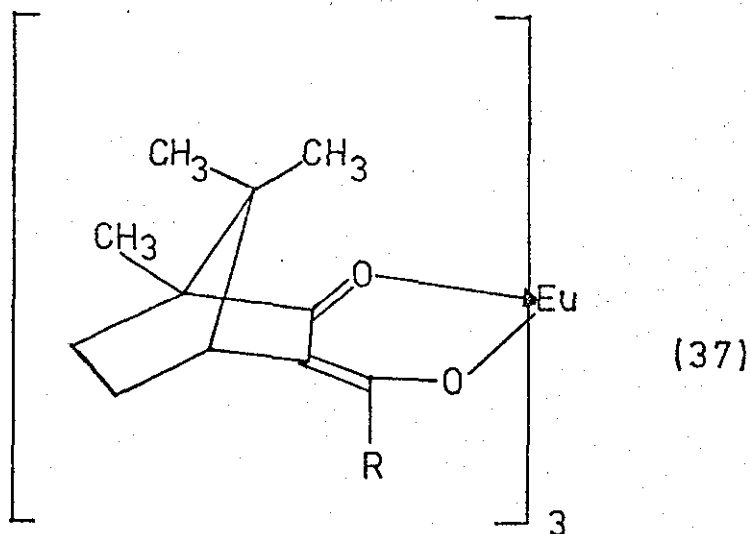
There was no evidence for the formation of rearranged products.



The formation of 1-methylheptyl chloride from chiral 1-methylheptyl alcohol with complete inversion of configuration has also been achieved using phosphorous trisdimethylamide and carbon tetrachloride.⁵⁵



When this reaction was repeated at -20° the present author obtained a precipitate of trichloromethyl-tris(dimethylamino) phosphonium chloride, which was filtered off and subsequently characterised as its stable perchlorate²² (5% yield) which was already known. Addition of an aqueous solution of ammonium hexafluorophosphate to the filtrate afforded 1-methylheptyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (35) in 46% yield; a small amount of 1-methylheptyl chloride was



from the (R) and (S) enantiomers in each case, thus providing a simple method for determining optical purity of partially separated enantiomeric mixtures. However the utility of this chiral reagent appears to be limited to strong donors since although large downfield shifts were observed with weaker Lewis bases, the magnitudes of the differential downfield shift were generally too small to be useful. The trifluoromethyl derivative (37, R = CF₃)⁵⁸ and the heptafluoropropyl derivative (37, R = C₃F₇)⁵⁹ have been prepared recently and these chiral n.m.r. shift reagents have been effective in differentiating between signals for a much wider variety of enantiomeric mixtures. The n.m.r. spectra of chiral alcohols, amines, esters, ketones, sulphoxides, and epoxides observed in the presence of either the trifluoromethyl or the heptafluoropropyl derivative generally show large chemical shift differences for the enantiotopic nuclei and thus the proportions of enantiomers can be measured directly by integration. This improvement in both the size of the downfield

shift and the resolving ability of the trifluoromethyl and the heptafluoropropyl compounds over the t-butyl derivative has been attributed to the increase in the Lewis acid character.

In order to assess the purity of the commercially available sample of the heptafluoropropyl derivative, some earlier work of Fraser, Petit, and Saunders⁵⁹ was repeated by studying the n.m.r. spectrum of (\pm) 1-phenylethanol in the presence of the chiral shift reagent. The above authors obtained the following results using 0.4 equivalents of the shift reagent (Table 1).

TABLE 1.

<u>Proton</u>	<u>Effect of Eu(hfc)₃</u>	
	<u>A</u>	<u>B</u>
Me	2.65	0.05
CH	4.64	0.07
H ortho	2.27	0.02

A-the average downfield shift in p.p.m. of the protons in the two enantiomers.

B-Difference in chemical shift for structurally identical protons in the two enantiomers.

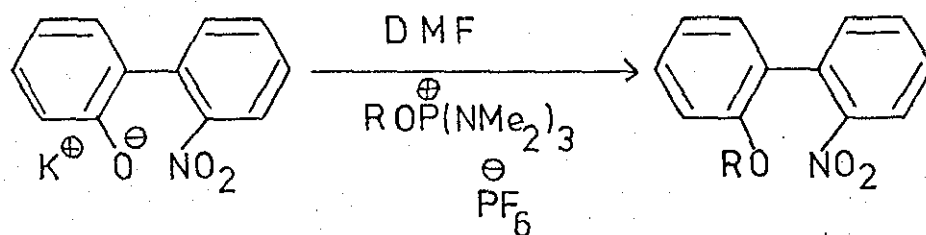
In our experiment a considerable improvement on these results was observed even when only 0.33 equivalents of the shift reagent was used (Table 2).

TABLE 2.

<u>Proton</u>	<u>Effect of Eu(hfc)₃</u>	
	<u>A</u>	<u>B</u>
Me	4.20	0.07
CH	7.60	0.19
H ortho	3.45	0.07

Unfortunately the addition of $\text{Eu}(\text{hfc})_3$ to (\pm)-1-methylheptyl phenyl ether did not produce any significant downfield shift in the $^1\text{H.n.m.r.}$ signals of the ether. Also the $^{13}\text{C.n.m.r.}$ spectrum of the ether was superimposable with that of the ether in the presence of the chiral shift reagent and hence the optical purity of the ether could not be established using this technique. This failure is presumably due to a lack of co-ordination between the oxygen lone pair and the Lewis acid.

The reaction of 1-methylheptyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with the potassium salt of 2-hydroxy-2'-nitrobiphenyl in dimethylformamide gave 2-(1-methylheptyloxy)-2'-nitrobiphenyl in 81% yield.



$\text{R}=1\text{-methylheptyl}$

Thus a method for the preparation of aryl 1-methylheptyl ethers and aryl neopentyl ethers has been developed which is both stereospecific and proceeds without rearrangement. The major advantage of this method over the alternative method involving the use of *p*-toluenesulphonates results from the high stability of the crystalline phosphonium hexafluorophosphates.

The generality of the method was established and is exemplified by the following results (Tables 3 - 5).

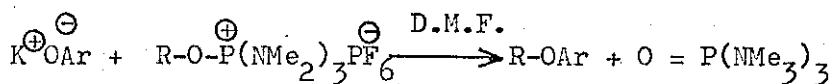
TABLE 3

Preparation of Phosphonium Salts, $R-O-P(NMe_2)_3^{\oplus}, PF_6^{\ominus}$.

<u>R</u>	<u>Temperature of Formation(°)</u>	<u>Yield(%)</u>
Neopentyl	0	70
1-Methylheptyl	-20	46
<u>n</u> -Propyl	-78	52
Benzyl	-78	68
Allyl	-78	86
Phenyl	0	67

TABLE 4

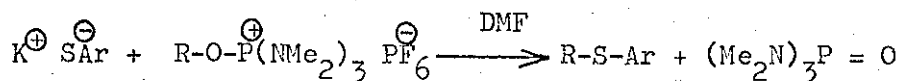
Preparation of alkyl aryl ethers from the reaction of alkoxy-tris(dimethylamino)phosphonium hexafluorophosphates with potassium aryloxides.



<u>Potassium Salt of</u>	<u>R in $(Me_2N)_3P^{\oplus}-O-R, PF_6^{\ominus}$</u>	<u>Yield of Ether(%)</u>
2-Hydroxy-2'-nitro-biphenyl	Neopentyl	90
<u>p</u> -Nitrophenol	Neopentyl	42
<u>p</u> -Methoxyphenol	Neopentyl	66
Phenol	Neopentyl	75
2-Hydroxy-2'-nitro-biphenyl	1-Methylheptyl	81
<u>p</u> -Methoxyphenol	1-Methylheptyl	68
<u>p</u> -Nitrophenol	1-Methylheptyl	80
Phenol	1-Methylheptyl	99
Phenol	Allyl	79
Phenol	<u>n</u> -Propyl	86

TABLE 5

Preparation of alkyl aryl sulphides from the reaction of alkoxy-tris(dimethylamino)phosponium hexafluorophosphates with potassium arylthioides.

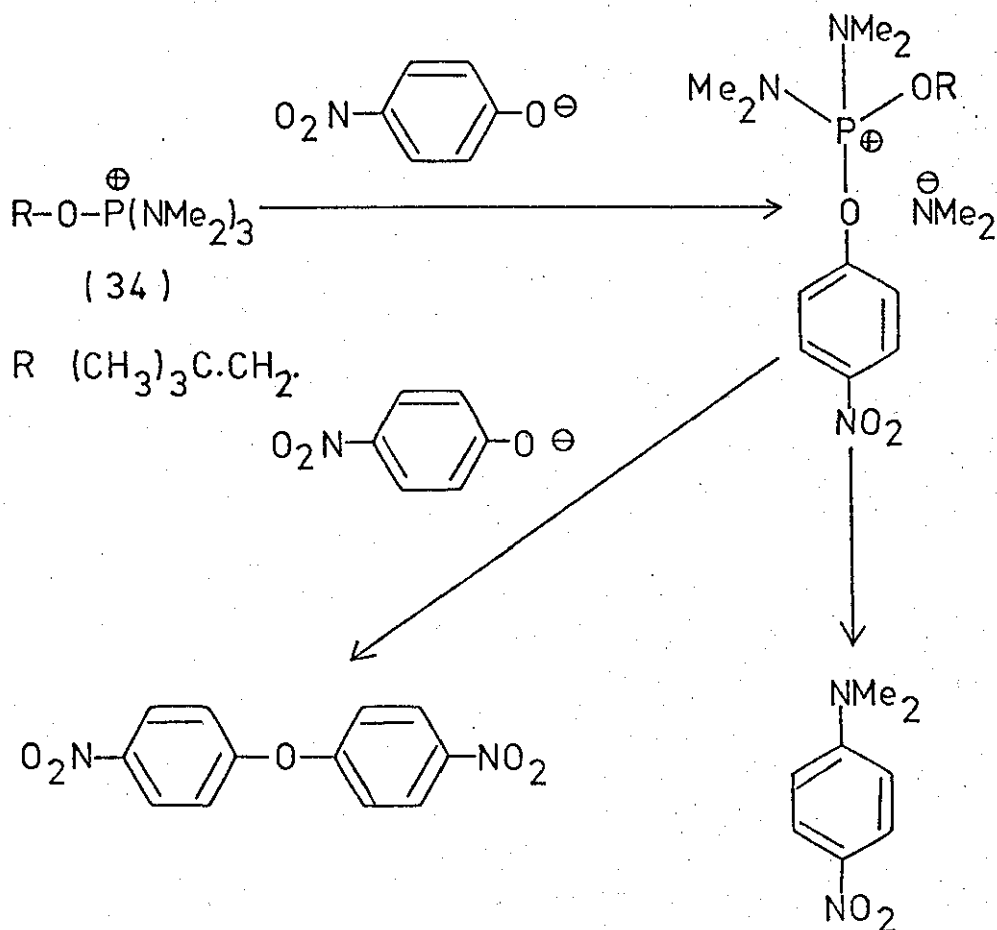


<u>Potassium Salt of</u>	<u>R in</u> <u>$(Me_2N)_3P^{\oplus}OR, PF_6^{\ominus}$</u>	<u>Yield of</u> <u>Sulphide (%)</u>
Thiophenol	1-Methylheptyl	61
<u>p</u> -Methylthiophenol	1-Methylheptyl	68
Thiophenol	Benzyl	83
<u>p</u> -Methylthiophenol	Benzyl	98
<u>p</u> -Methylthiophenol	Allyl	97
Thiophenol	Allyl	90

There was no evidence for the formation of products derived from Claisen or thio-Claisen rearrangements in the allyl aryl ether and allyl aryl sulphide preparations.

The relatively low yield (42%) of neopentyl p-nitrophenyl ether from the reaction of potassium p-nitrophenoxide with neopentyloxy-tris(dimethylamino)phosponium hexafluorophosphate was surprising. However, a re-investigation of the reaction, employing a longer reaction time, revealed that another important product, p-nitro-N,N-dimethylaniline, was also formed and this was isolated in 29% yield. The observation of the same products using tetrahydrofuran as the solvent established that the dimethylamino residue was derived from the phosponium salt and not from the dimethylformamide. The reaction mixtures were analysed by gas chromatography (Column D at 244°) since it was

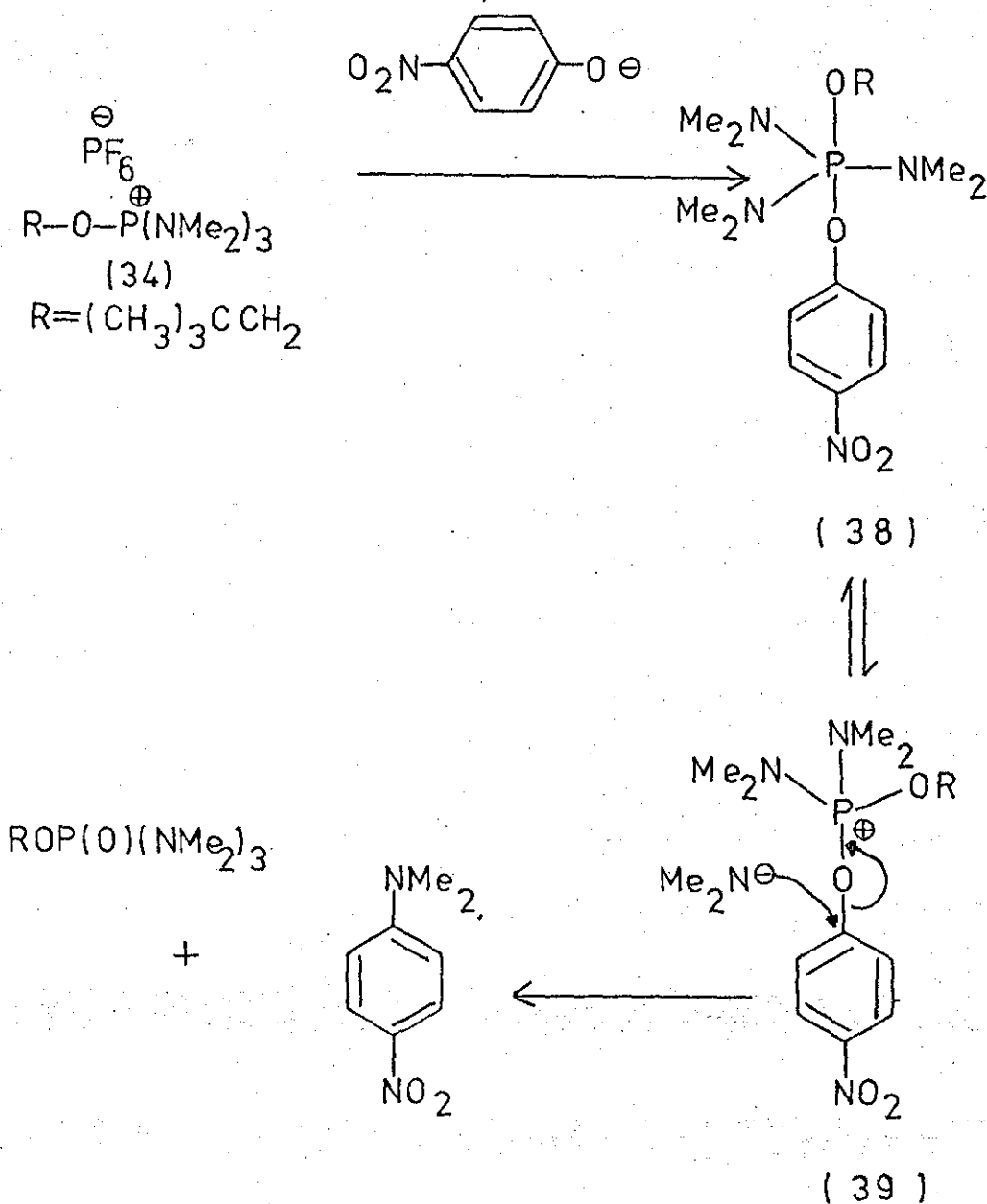
of particular interest to find out whether 4,4'-dinitrodiphenyl ether was formed in these reactions. This product would be expected to be formed in significant amounts if the reaction proceeded via ligand exchange involving a direct displacement of the dimethylamide ion (or the neopentyloxy anion) from the phosphonium salt (34) by the *p*-nitrophenoxide anion (Scheme 19).



Scheme 19

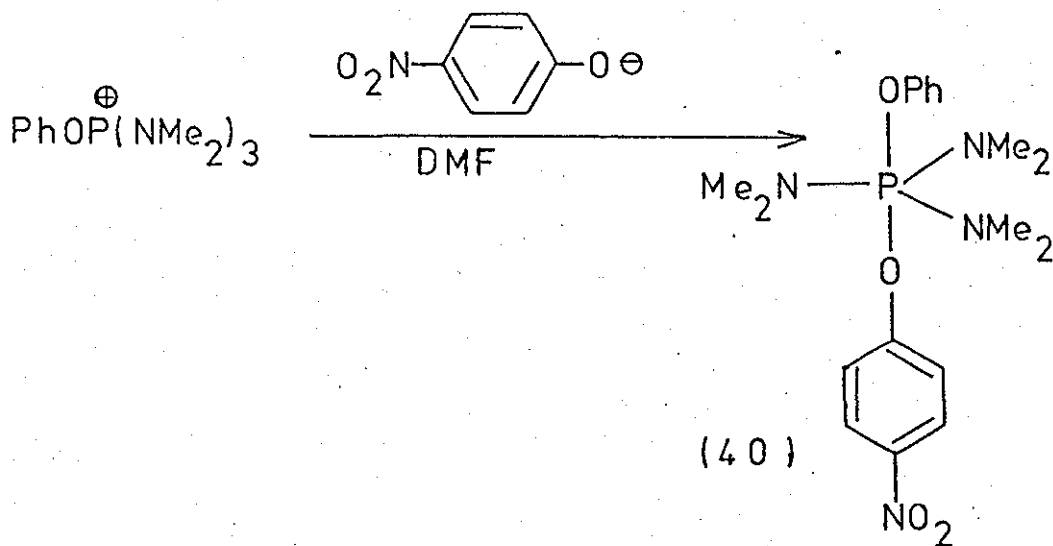
The complete absence of 4,4'-dinitrodiphenyl ether invalidates this mechanism. However, the results can be rationalised in terms of a long-lived phosphorane intermediate. Thus, in this mechanism, the *p*-nitrophenoxide anion not only displaces

hexamethylphosphoric triamide from the phosphonium salt (34) but also attacks on phosphorus to give a relatively stable phosphorane (38). Loss of the dimethylamide anion then generates a new phosphonium salt (39) which can then form the p-nitro-N,N-dimethylaniline by an S_NAr reaction (Scheme 20).

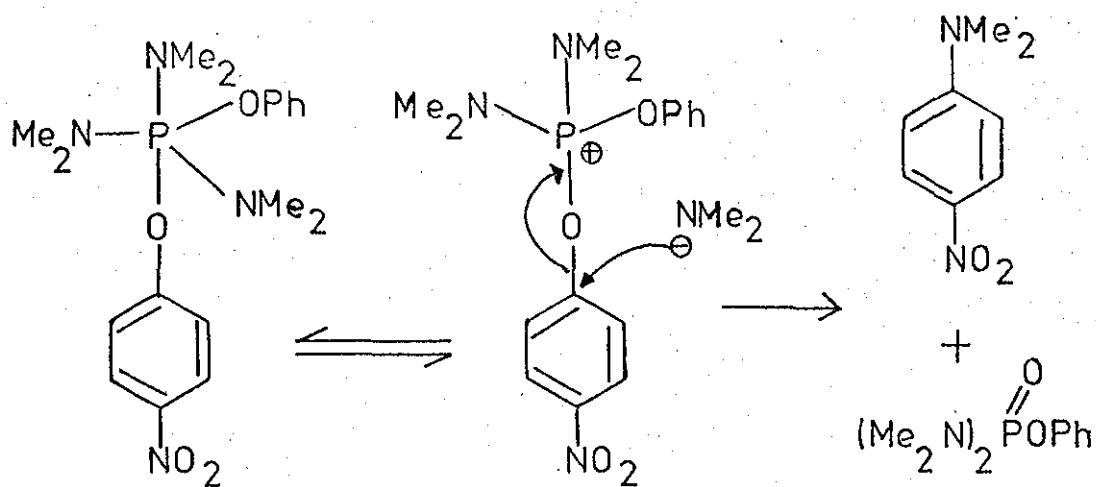


Scheme 20

A similar reaction involving ligand exchange was also observed in a reaction of potassium p-nitrophenoxide with phenoxy-tris(dimethylamino)phosphonium hexafluorophosphate in dimethylformamide. In this reaction p-nitro-N,N-dimethylaniline (15%) and 4-nitrodiphenyl ether (10%) were isolated. Once again the absence of 4,4'-dinitrodiphenyl ether indicates that the reaction proceeds via a phosphorane intermediate (40) which results from attack of p-nitrophenoxide anion on phosphorus.

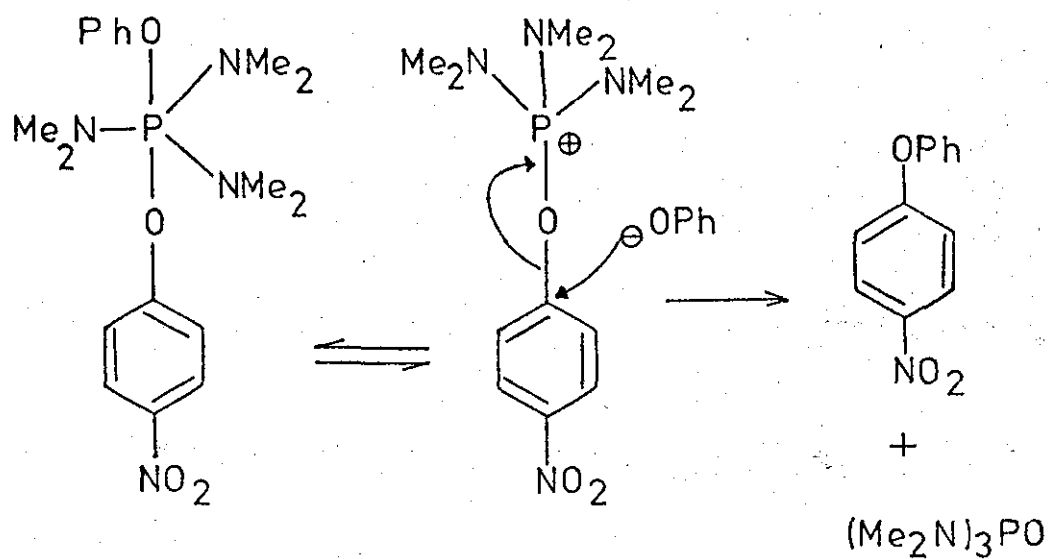


The phosphorane then loses a dimethylamide ion to give a new phosphonium salt (41) which can undergo an $\text{S}_{\text{N}}\text{Ar}$ reaction to afford p-nitro-N,N-dimethylaniline (Scheme 21).



Scheme 21 (41)

The formation of 4-nitrodiphenyl ether can be rationalised in an analogous manner (Scheme 22).

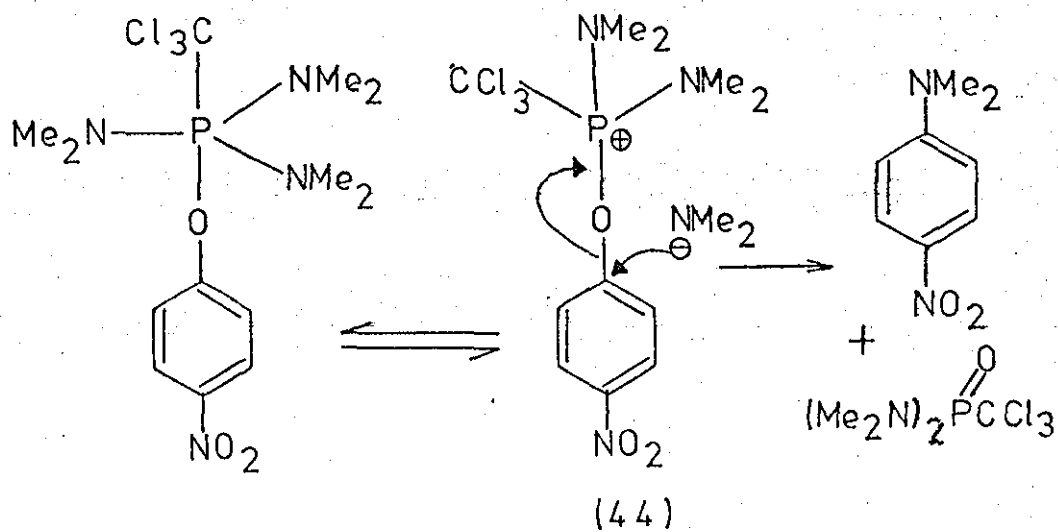
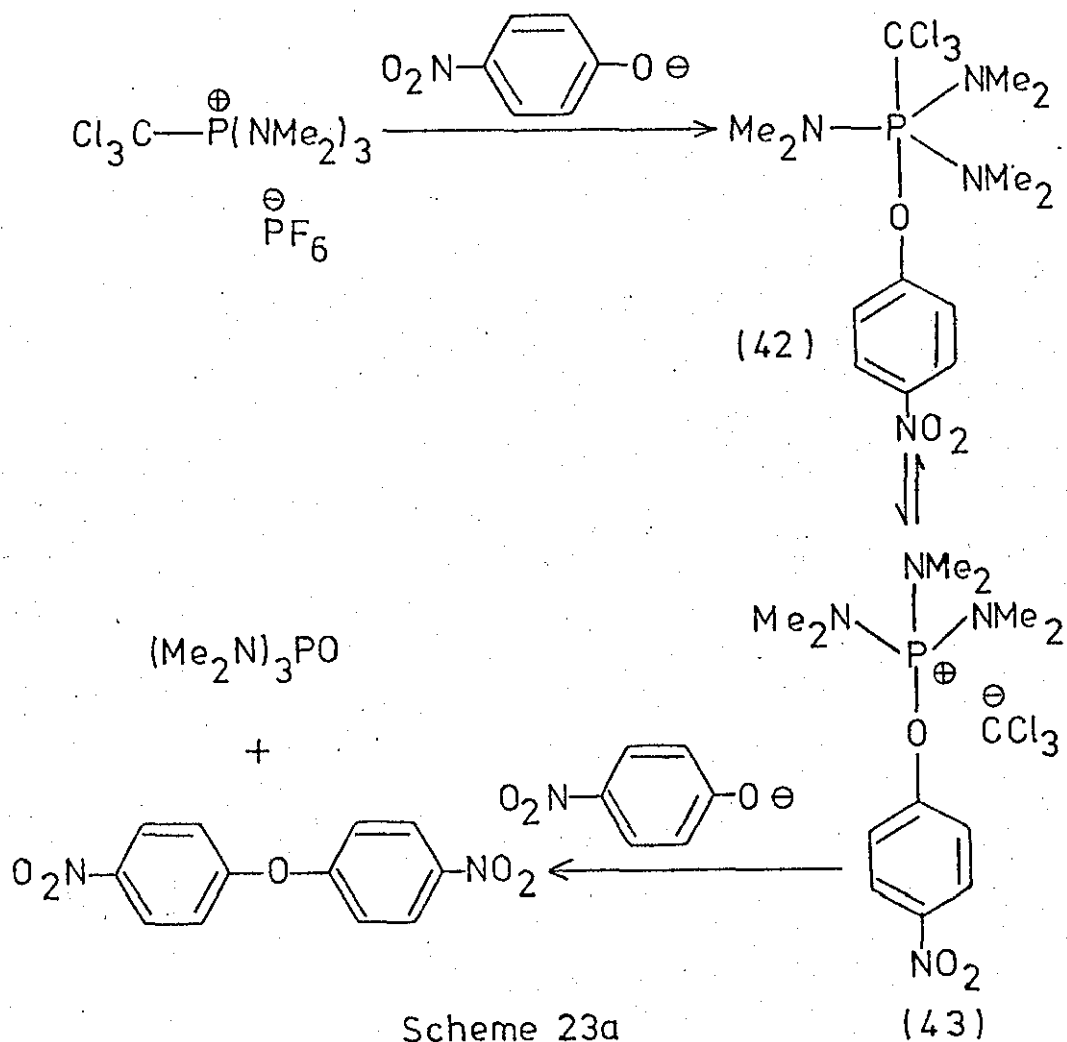


Scheme 22

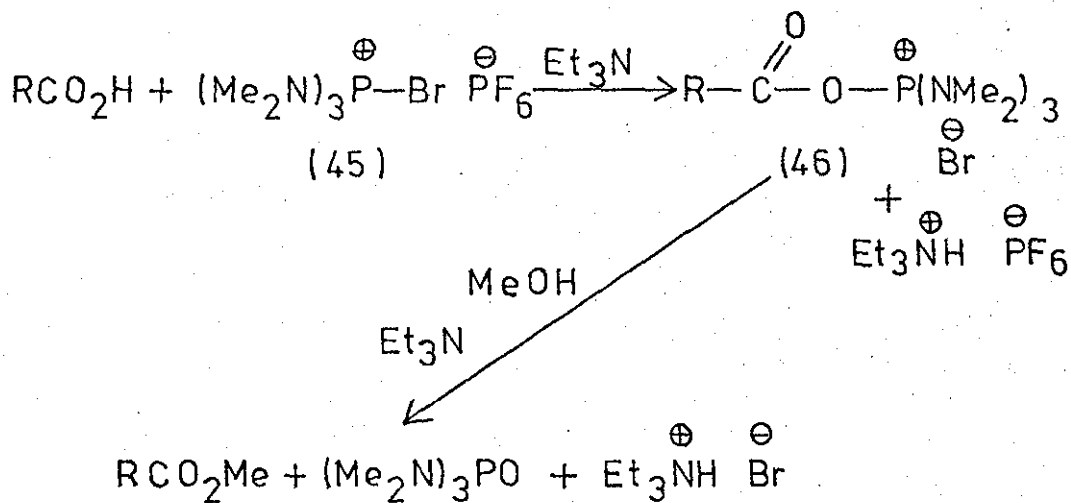
On the other hand the reaction of potassium p-nitrophenoxide with trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate⁶⁰ in dimethylformamide gave p-nitro-N,N-dimethylaniline (23%) and 4,4'-dinitrodiphenyl ether (14%), while chloroform and hexamethylphosphoric triamide were also detected by gas chromatography. This reaction can also be envisaged as occurring via a phosphorane intermediate. It is possible that the p-nitrophenoxide ion attacks on phosphorus to afford a comparatively unstable phosphorane (42), which rapidly eliminates either the dimethylamide anion or the trichloromethyl anion. If this elimination occurred more rapidly than the addition reaction of the p-nitrophenoxide ion to phosphorus then there would be some unreacted p-nitrophenoxide available for reaction with the newly-formed phosphonium salt. Hence the formation of 4,4'-dinitrodiphenyl ether can be attributed to the reaction of the p-nitrophenoxide anion on the phosphonium salt (43) derived from the phosphorane (42) (Scheme 23 a).

Similarly p-nitro-N,N-dimethylaniline can be formed by an S_NAr reaction of the dimethylamide anion on the phosphonium salt (44) (Scheme 23b).

Phosphorane intermediates have also been invoked by Castro and Dormoy⁶¹ recently to account for the formation of substituted amides from the decomposition of acyloxy-tris(dimethylamino)phosphonium salts. These authors have shown that the reaction of a carboxylic acid with the phosphonium salt (45) in the presence of 2 equivalents of triethylamine at 0-10° using methanol as the solvent resulted in the formation of the corresponding methyl ester in high yield. The esterification

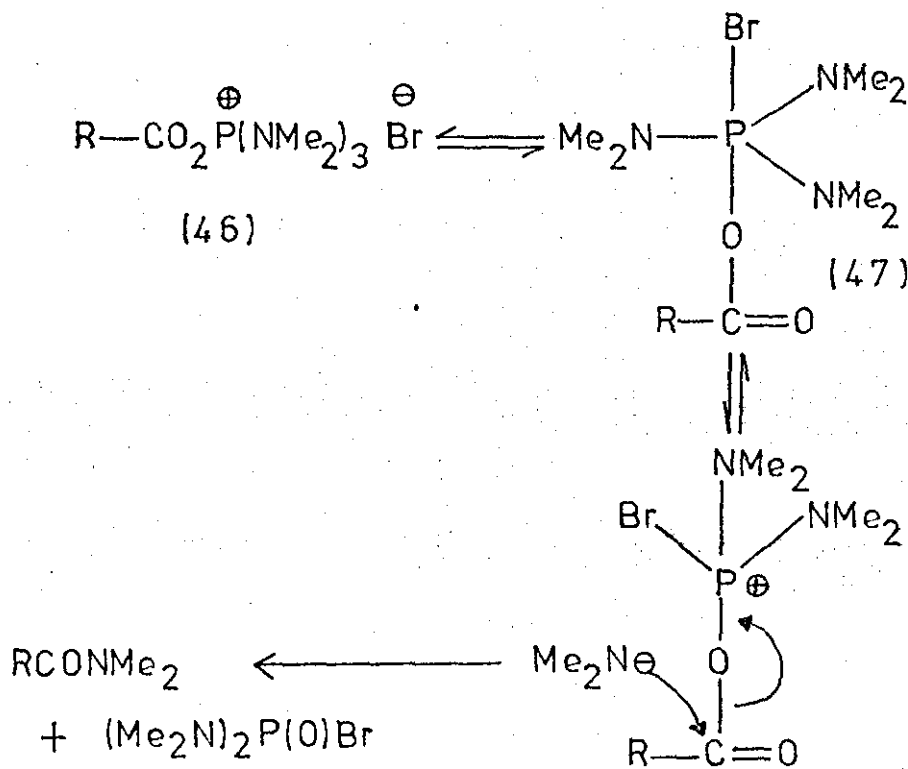


reaction proceeds via an intermediate acyloxy phosphonium salt (46) which readily collapses by attack of the methoxide anion to give the methyl ester and hexamethylphosphoric triamide (Scheme 24).



Scheme 24

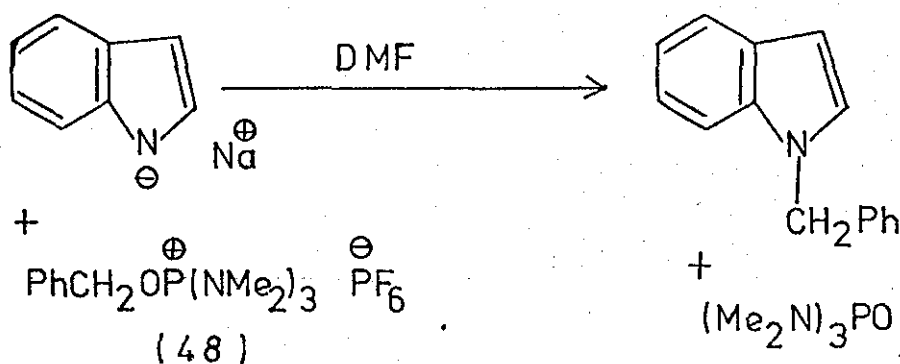
However, when the conversion was performed at a higher temperature, a second product, the dimethylamide of the acid, was also formed. The formation of this product was rationalised in terms of a phosphorane intermediate (47) (Scheme 25).



Scheme 25

Castro and his co-workers^{62,63} have reported dealkylation reactions of phosphonium salts of the type, $R-O-P^{\oplus}(NMe_2)_3X^{\ominus}$, with a variety of nucleophiles using dimethylformamide as the solvent. These reactions have also been shown to proceed efficiently in non-polar solvents such as methylene dichloride, ether, and tetrahydrofuran.^{15,56}

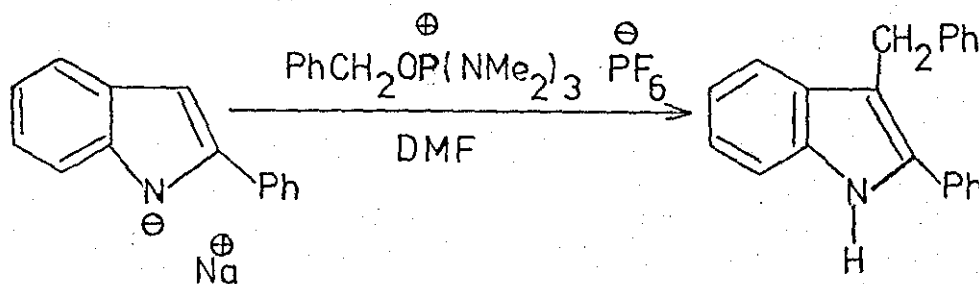
The reaction of benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate(48) with various nitrogen bases was also investigated as part of our interest in the reactivity of phosphonium salts derived from phosphorous trisdimethylamide. For example, the phosphonium salt (48) reacted with the sodium salt of indole in dimethylformamide to afford N-benzylindole in 74% yield.



The presence of a substituent at position-2 of indole has been reported by Garner and his co-workers⁶⁴ to impart a considerable influence on the course of alkylation. These authors observed that the alkylation of the potassium salts of 2-substituted indoles occurred predominantly at the nitrogen to afford the N-alkyl product. They also claim that higher proportions of the 3-alkyl and 1,3-dialkyl derivatives are obtained as the S_N1 character

of the alkylating agent increases. This effect was particularly pronounced with 2-phenylindole and hence the authors infer that this compound could be used to determine the S_N1 or S_N2 character of alkylating agents.

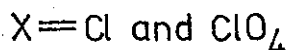
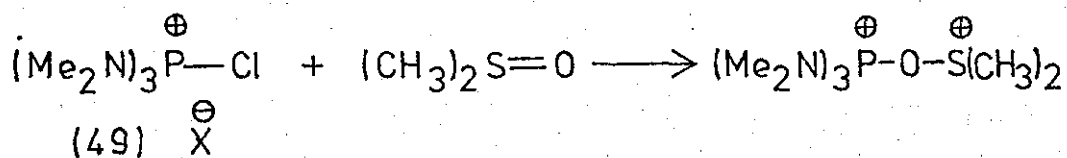
All of the evidence currently available suggests that the dealkylation of alkoxy-tris(dimethylamino)phosphonium salts proceed by an S_N2 mechanism. It was therefore of interest to study the reaction of benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with the sodium salt of 2-phenylindole in dimethylformamide. The only product detected was shown to be 3-benzyl-2-phenylindole which was isolated in 53% yield.



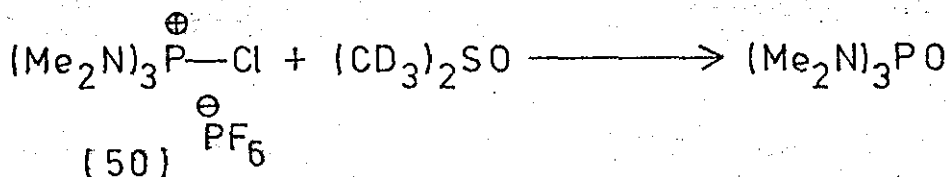
It is unfortunate that this reaction was not found to be amenable to kinetic investigation because of the lack of suitable apparatus. However, it would be very surprising if this reaction in fact involved the fragmentation of the phosphonium salt to generate the benzyl cation and hexamethylphosphoric triamide. In this author's opinion the 2-phenylindolyl anion should not be used as a diagnostic test for S_N1 alkylations.

Reactions of nucleophiles at phosphorus suggests that care should be taken to avoid the use of nucleophilic solvents

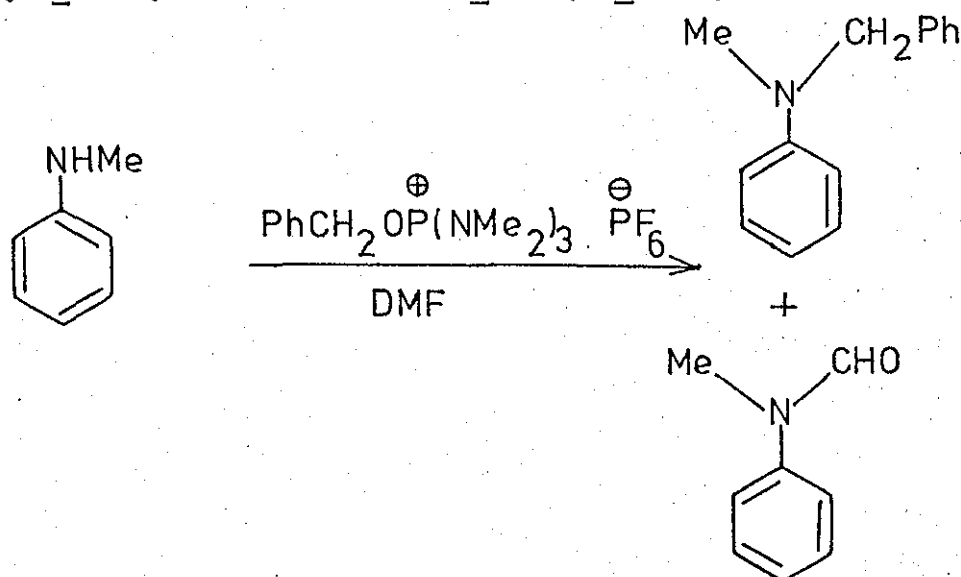
particularly when carrying out alkylations of weak nucleophiles. Albright⁶⁵ has suggested, for example that dimethylsulphoxide may interact with the chlorophosphonium salt (49) to produce an oxidising system similar to that described originally by Pfitzner and Moffatt.^{66a,b}



We have not attempted to carry out nucleophilic displacements using alkoxyphosphonium salts in dimethylsulphoxide because of our experience when attempting to characterise certain phosphonium salts by ¹H.n.m.r. spectroscopy in the presence of hexadeuteriodimethylsulphoxide. For example, the ¹H.n.m.r. spectrum of the chlorophosphonium salt (50) in CDCl₃/DMSO-d₆ changed rapidly from a doublet at 7.15 τ to a doublet at 7.42 τ which suggested that the following conversion was taking place.



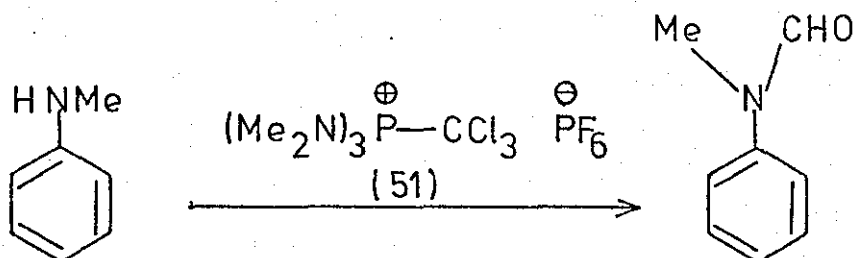
The reaction of dimethylformamide with phosphoryl chloride in Vilsmeier formylation reactions is well known.⁶⁷ These reactions involve, as the first step, the displacement of chloride ion by the dimethylformamide. It would therefore not be surprising if attempted alkylations of free amines by alkoxyphosphonium salts in dimethylformamide resulted in some formylation. Although these reactions have been carried out by Castro and his collaborators,¹⁶ formylation was not reported. However the reaction between N-methylaniline and benzyloxy-tris(dimethylamino) phosphonium hexafluorophosphate in dimethylformamide gave N-benzyl-N-methylaniline (74%) and N-formyl-N-methylaniline (9%).



When this reaction was repeated using tetrahydrofuran as the solvent, the only product was N-benzyl-N-methylaniline, which was isolated in 79% yield. It was therefore decided to repeat Castro's¹⁶ work on the alkylation of aniline. In our hands, the reaction of benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with aniline in dimethylformamide gave not only N-benzylaniline but also two other products which mass spectrometry and ¹H.n.m.r. evidence indicated to be N-formylaniline and N-benzyl-N-formylaniline.

Similarly a reaction of trichloromethyl-tris(dimethylamino) phosphonium hexafluorophosphate (51) with N-methylaniline gave N-formyl-N-methylaniline in 31% yield, while using the chlorophosphonium salt (50), a quantitative yield of the N-formylated product was obtained.

e.g.

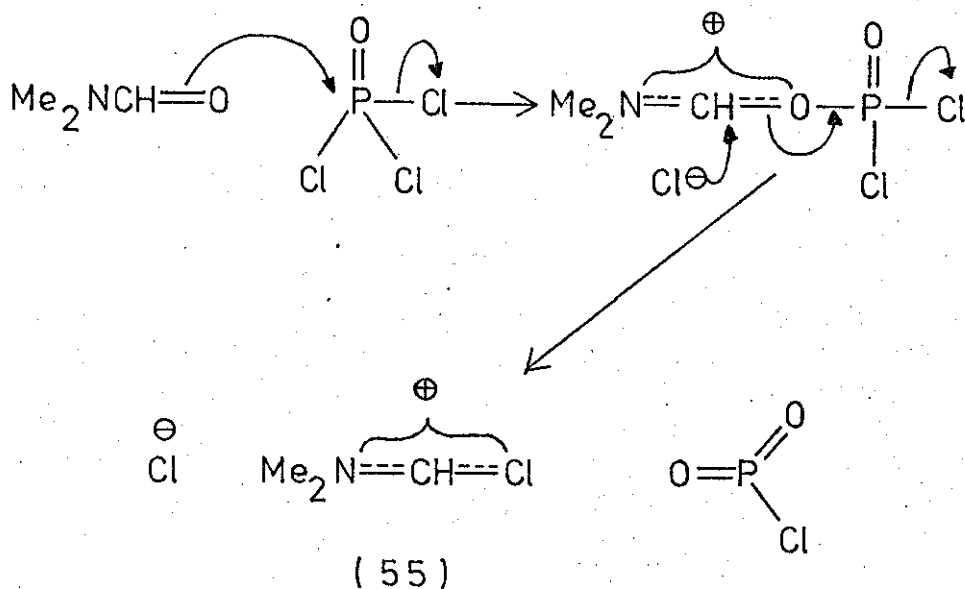


The formylation reactions implicate the intermediacy of phosphoranyl cations such as (52), (53), and (54).

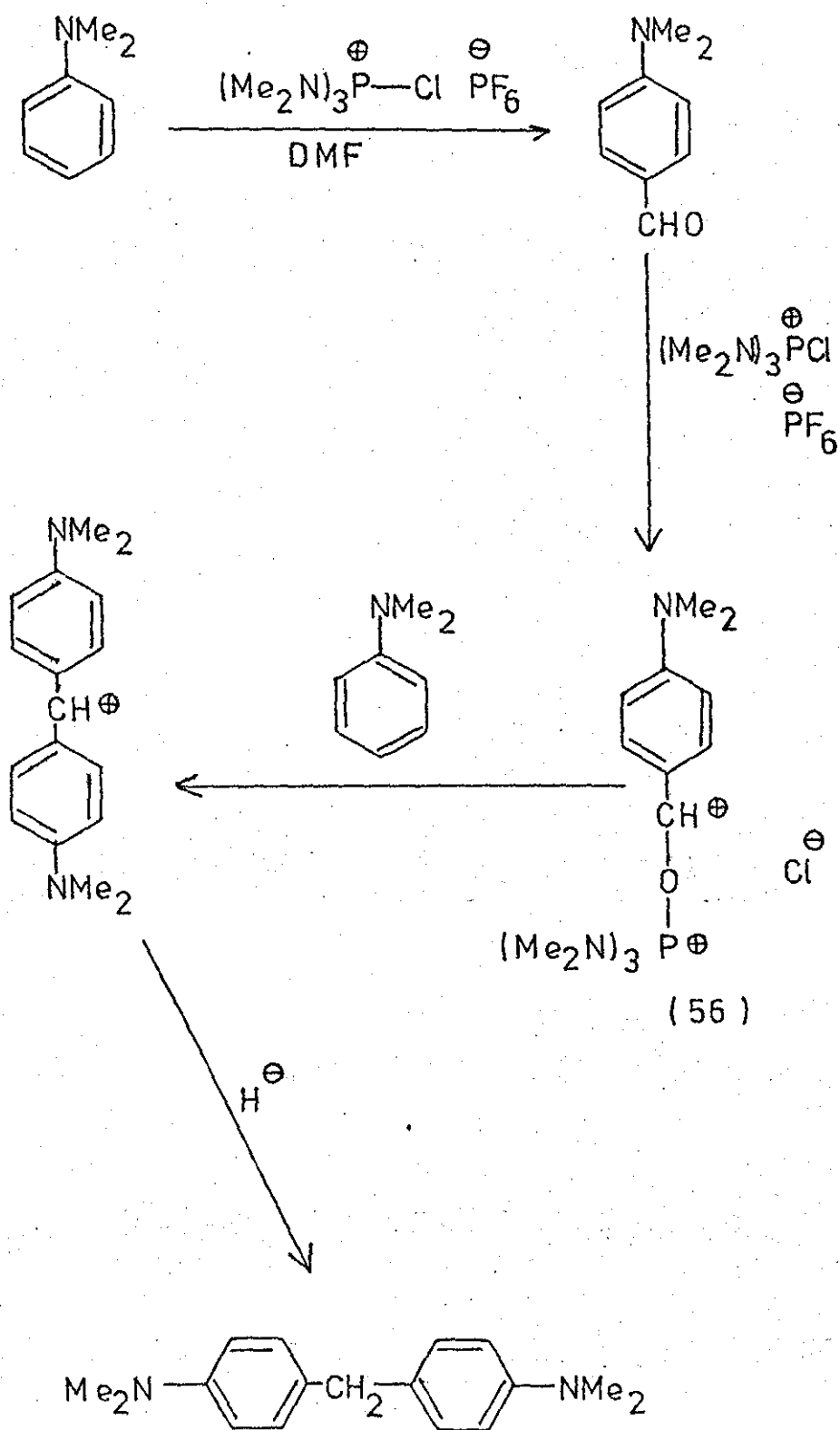


A possible mechanistic pathway is outlined in Scheme 26.

The available evidence suggests that Vilsmeier formylation reactions involve the formation of a phosphorus free electrophile. This has been detected, in the absence of nucleophilic aromatic substrates such as indole, pyrrole, and N,N-dimethylaniline and identified by spectroscopic methods as the ion (55), and is presumably formed as shown:

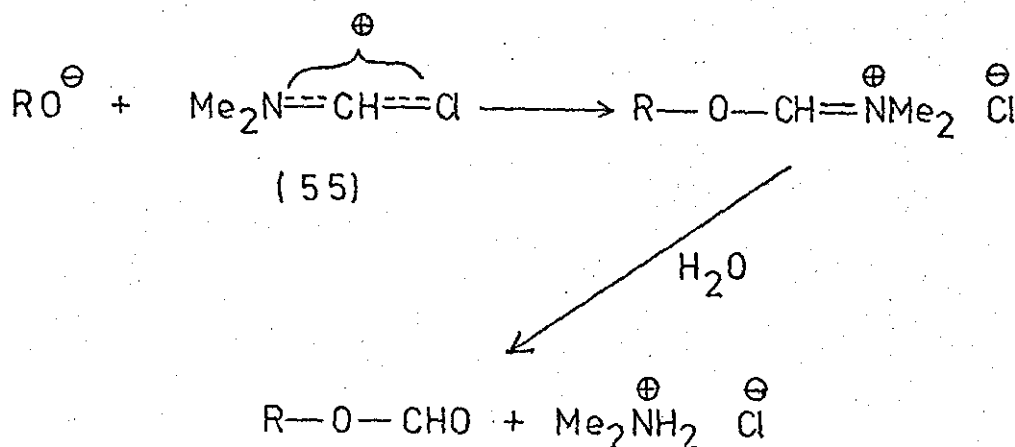


Since the ion (54) would be expected to collapse readily to give hexamethylphosphoric triamide and the cation (55), it seemed reasonable to assume that the reaction of the chlorophosphonium salt (50) with nucleophilic aromatic substrates in dimethylformamide would lead to the formation of C-formylated products in high yields. However when these reactions were performed only trace amounts of C-formylated products were observed. Although the reaction of the chlorophosphonium salt (50) with N,N-dimethylaniline gave a 7% yield of bis-(p-dimethylaminophenyl)methane. The formation of this product can be envisaged as occurring by initial formylation to afford p-dimethylaminobenzaldehyde, which then reacts with the chlorophosphonium salt to give the dication (56). This salt can then combine with N,N-dimethylaniline to yield the diarylmethane (Scheme 27).



Scheme 27

Czernecki and Georgoulis⁶⁸ have reported recently that the reaction of certain sterically hindered secondary alcohols with phosphorous trisdimethylamide and carbon tetrachloride in dimethylformamide gave the corresponding O-formyl esters in excellent yields and not the expected chlorinated derivatives. The authors consider that the formylation reaction involves the cation (55), the presumed intermediate in Vilsmeier formylations (Scheme 28).



Scheme 28

Thus N- and O-formylation reactions, but significantly not C-formylation, have been achieved using the chlorophosphonium cation $(\text{Me}_2\text{N})_3\text{P}^{\oplus}\text{-Cl}$ in dimethylformamide. These results suggest that the reactive intermediate necessary for heteroatom formylation is different from that required to effect C-formylation. Also the absence of C-formylated products argues strongly against the cation (55) being the intermediate in Vilsmeier formylations. Evidently more experimental results should be sought in connection with these various formylation reactions. The use of ³¹P.n.m.r. spectroscopy is one obvious tool which could be invaluable. It may well be, for example, that the ion (55) would not be formed

in the presence of substrates which do undergo Vilsmeier formylation reactions.

Experimental

General:-

All solvents were distilled and dried by conventional methods prior to usage.

Analytical thin layer chromatography was carried out using silica gel (GF₂₅₄ according to Stahl), for layers 0.25mm. thick. Column chromatography was carried out with silica gel (ex. Fisons), and 'CAMAG' alumina (Brockmann activity I).

Analytical gas chromatography was carried out using a Pye 104 series gas chromatograph using a hydrogen flame ionisation detector. The 5ft. columns used were:

- A. 10% APIEZON L on chromosorb W.
- B. 15% S.E. 30 on firebrick.
- C. 20% S.E. 30 on chromosorb W.
- D. 10% S.E. 30 on celite.
- E. 10% Polyethylene glycol adipate on chromosorb W.

Infra-red spectra were determined for potassium bromide discs in the case of solids or thin films in the case of liquids unless otherwise stated, on a Perkin-Elmer 257 spectrometer. Ultra violet spectra were determined for solutions in ethanol, unless otherwise stated, with a Pye-Unicam SP 8000 spectrophotometer. ¹H Nuclear magnetic resonance spectra were determined at 90 MHz. for approximately 20% w/v solutions using tetramethylsilane as an internal standard, with a Perkin-Elmer R 32 spectrometer. Mass spectra were recorded on an A.E.I. M.S. 12 spectrometer. High resolution mass spectrometry was carried out

on an A.E.I. M.S. 9. at P.C.M.U. by courtesy of the S.R.C.

Melting points were determined on a Kofler block and are uncorrected. All compounds were colourless solids unless otherwise stated. All dilute acids were 2N.

1. Preparation of Neopentyl chloride.

A solution of phosphorous trisdimethylamide (16.3g., 0.1 mole) in ether (15ml.) was added dropwise to a stirred ice-cold solution of neopentyl alcohol (2.8g., 0.1 mole) and carbon tetrachloride (15.4g., 0.1 mole) in ether (50ml.). A yellow oil separated out which was dissolved in dimethylformamide (100ml.). The solution was heated under reflux for 1 hour and then poured into water (100ml.). The mixture was extracted with ether (2 x 75ml.) and each extract was washed with water (2 x 50ml.). The combined ether layers were then dried over anhydrous magnesium sulphate. The ethereal solution was carefully distilled at atmospheric pressure to give, after removal of solvent (b.p. 35°), neopentyl chloride (6.02g., 61%); b.p. $84-5^{\circ}$ (lit. ⁶⁹ b.p. 84.4°).

2. Preparation of Crotyl bromide.

Phosphorous trisdimethylamide (24.4g., 0.15 mole) in ether (100 ml.) was added dropwise to a stirred solution of crotyl alcohol (10.8g., 0.15 mole) and carbon tetrabromide (49.8g., 0.15 mole) in ether (100 ml.) at -40° .

After the addition was completed, the reaction mixture was allowed to come to room temperature and the stirring was continued at this temperature for 1 hour. The ethereal solution was washed with water (2 x 100 ml.) and then dried over anhydrous magnesium sulphate. Careful distillation of the solution at atmospheric pressure gave, after removal of solvent (b.p. 35°), crotyl bromide (13.1g., 67%); b.p. $102-106^{\circ}$ (lit., ⁷⁰ b.p. $103-6^{\circ}$).

3. Preparation of Neopentyl bromide.

A mixture of neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (8.0g., 0.02 mole) and potassium bromide (7.20g., 0.06 mole) in dimethylformamide (100ml.) was heated under reflux for 15 hours. After cooling to room temperature, the reaction mixture was poured into water (100 ml.) and extracted with ether (2 x 50ml.). Each extract was washed with water (2 x 30 ml.) and the combined ether layers were then dried over anhydrous magnesium sulphate. The ethereal solution was distilled at atmospheric pressure to give, after removal of solvent (b.p. 35°), neopentyl bromide (0.67g., 22%); b.p. $104-6^{\circ}$ (lit.,⁴⁸ b.p. 105°).

4. Preparation of Neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate.

A solution of phosphorous trisdimethylamide (32.6g., 0.2 mole) in ether (100ml.) at 0° was added to a stirred solution of neopentyl alcohol (18g., 0.2 mole) and carbon tetrachloride (38.5g., 0.25 mole) in ether (100ml.), also at 0° .

When the addition was completed the cold mixture was poured into an ice-chilled saturated aqueous solution of ammonium hexafluorophosphate (34g., 0.2 mole) with the immediate formation of a white solid. The precipitate was collected, washed with ice-cold water (75ml.) and ether (75ml.), and then dried over calcium chloride. Recrystallisation from ethanol gave neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (58g., 70%) as colourless plates; m.p. $202-4^{\circ}$ (lit.,⁷¹ m.p. $202-4^{\circ}$).

$^1\text{H.n.m.r.}$ τ (CDCl_3) 6.18(d., 2H, $J_{\text{PH}} = 4\text{Hz.}$); 7.18
(d., 18H, $J_{\text{PH}} = 11\text{ Hz.}$); and 8.95(s., 9H).

V_{max} 2960, 1460, 1310, 1170, 1065, 995, 825, 765,
and 750cm^{-1} .

5. Preparation of Phenoxy-tris(dimethylamino)phosphonium hexafluorophosphate.

Using the procedure described for experiment 4, phosphorous trisdimethylamide (8.15g., 0.05 mole), phenol (4.7g., 0.05mole), carbon tetrachloride (10.0g., 0.065 mole) and ammonium hexafluorophosphate (8.5g., 0.05 mole) reacted to give phenoxy-tris(dimethylamino)phosphonium hexafluorophosphate (13.4g., 67%) as white plates; m.p. $93-4^\circ$ (from ethanol) (lit., 72 m.p. 92°).

$^1\text{H.n.m.r.}$ τ (CDCl_3) 2.35-2.9 (m., 5H) and 7.20 (d., 18H,
 $J_{\text{PH}} = 10\text{Hz.}$).

V_{max} 2970, 1600, 1495, 1465, 1320, 1210, 1180, 1170,
1010, 955, 840(broad), 785, 775, 760, and 690 cm^{-1} .

6. Preparation of n-Propoxy-tris(dimethylamino)phosphonium hexafluorophosphate.

Phosphorous trisdimethylamide (16.3g., 0.1mole) in ether (50 ml.) at -78° was added dropwise to a stirred solution of n-propyl alcohol (6.0g., 0.1 mole) and carbon tetrachloride (23g., 0.15 mole) in ether (100ml.) also at -78° .

When the addition was completed the cold mixture was poured into an ice-chilled saturated aqueous solution of ammonium hexafluorophosphate (16.3g., 0.1 mole) with the immediate formation of a white solid. The precipitate was filtered off, washed with ice-cold water (30ml) and ether (30ml.), and then dried over calcium chloride. Recrystallisation from ethanol gave n-propoxy-tris(dimethylamino)phosphonium hexafluorophosphate (19.1g., 52%) as a white crystalline solid, m.p. 226-8°.

¹H.n.m.r. τ (CDCl₃) 5.82 (t., 2H, J = 6Hz); 7.18(d., 18H, J_{PH} = 11Hz.); 8.15(sextet, 2H, J = 6Hz); and 8.96(t., 3H, J = 6Hz).

V_{max} 2950, 1500, 1470, 1320, 1180, 1075, 1060, 1010, 880, 850, 780, 770, 740, and 665 cm⁻¹.

7. Preparation of Allyloxy-tris(dimethylamino)phosphonium hexafluorophosphate.

Reaction as in experiment 6 using phosphorous trisdimethylamide (16.3g., 0.1 mole), allyl alcohol (5.8g., 0.1 mole), carbon tetrachloride (23g., 0.15mole) and ammonium hexafluorophosphate (16.3g., 0.1 mole) gave allyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (32g., 86%); m.p. 208-9° (from ethanol).

¹H.n.m.r. τ (CDCl₃) 4.0(m., 1H); 4.55(m., 2H); 5.25(m., 2H); and 7.15(d., 18H, J_{PH} = 10Hz.).

V_{max} 2940, 1500, 1470, 1430, 1320, 1180, 1040, 950, 830, 775, 760, and 670cm⁻¹.

8. Preparation of Benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate.

Phosphorous trisdimethylamide (16.3g., 0.1 mole) in ether (30ml.) at -78° was added dropwise to a stirred solution of benzyl alcohol (10.8g., 0.1 mole) and carbon tetrachloride (23.0g., 0.15 mole) in ether (100ml.), also at -78° . When the addition was completed the reaction mixture was poured into an ice-chilled saturated aqueous solution of ammonium hexafluorophosphate (16.3g., 0.1 mole) with immediate formation of a white solid. This solid was filtered off, washed with ice-cold water (50ml.) and ether (50ml.), and then dried over calcium chloride.

The solid was then washed with chloroform (3 x 50ml.) to remove the insoluble chloro-tris(dimethylamino)phosphonium hexafluorophosphate (3.27g., 9%), m.p. $198-200^{\circ}$, from the crude product. Removal of the solvent gave a white solid which recrystallised from ethanol to afford benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (28.1g., 68%) as colourless plates, m.p. $130-2^{\circ}$.

$^1\text{H.n.m.r.}$ τ (CDCl_3) 2.55(s., 5H); 4.78(d., 2H, $J_{\text{PH}} = 8\text{Hz.}$);
and 7.2(d., 18H, $J_{\text{PH}} = 10\text{Hz.}$);

ν_{max} 2940, 1495, 1470, 1460, 1320, 1180, 1170, 1075,
1010, 840, 780, 770, 750, 705, and 670 cm^{-1} .

9. Preparation of 1-Methylheptyloxy-tris(dimethylamino)phosphonium hexafluorophosphate.

A solution of phosphorous trisdimethylamide (32.6g., 0.2 mole) in ether (100ml.) at -20° was added dropwise over a period of 2 hours to a stirred solution of 1-methylheptyl alcohol (26g.,

0.2 mole) and carbon tetrachloride (38.5g., 0.25mole) in ether (150ml.), also at -20° .

A white precipitate of trichloromethyl-tris(dimethylamino) phosphonium chloride was formed, which was filtered off and subsequently characterised as its stable perchlorate (3.8g., 5%) m.p. $280-5^{\circ}$ (with decomposition)(from water), (lit., ²² m.p. $> 290^{\circ}$).

The addition of an ice-chilled saturated aqueous solution of ammonium hexafluorophosphate (32.6g., 0.2 mole) to the filtrate afforded a white solid which was filtered off and washed with ether (75 ml.), and then dried over calcium chloride. Recrystallisation from ethanol gave 1-methylheptyloxy-tris(dimethyl amino)phosphonium hexafluorophosphate (40g., 46%) as a white crystalline solid, m.p. $113-4^{\circ}$.

¹H.n.m.r. τ (CDCl_3) 5.4(m., 1H); 7.18(d., 18H, $J_{\text{PH}} = 11\text{Hz.}$); and 8.2-9.3(m., 16H).

V_{max} 2970, 2940, 1490, 1470, 1390, 1315, 1190, 1075, 1020, 1000, 840(broad), 770, and 665cm^{-1} .

Preparation of Alkyl aryl ethers and sulphides.

A series of alkyl aryl ethers and alkyl aryl sulphides were prepared by a procedure identical to that employed for the preparation of neopentyl phenyl ether which is described in detail.

10. Preparation of Neopentyl phenyl ether.

Dimethylformamide (50ml.) was added with stirring to powdered potassium hydroxide (1.12g., 0.02mole). Phenol (0.94g., 0.01mole) was then added and the mixture was stirred for 30 minutes. Neopentylloxy-tris(dimethylamino)phosphonium hexafluorophosphate (8.2g., 0.02mole) was added, and the mixture was heated under reflux for 15 hours. After cooling to room temperature the reaction mixture was poured into water (100ml.) and extracted with ether (3 x 50ml.) and each extract was washed with water (3 x 30ml.). The combined ether layers were twice washed with an aqueous solution of sodium hydroxide, to remove unreacted phenol, and then dried over anhydrous magnesium sulphate. The solvent was removed and the residue was placed on a column of alumina, elution with 10% ether-light petroleum gave a colourless liquid which on distillation gave neopentyl phenyl ether (1.24g., 75%); b.p. 55-8° at 1.5mm. (lit., 51 b.p. 82-3° at 12mm.).

¹H.n.m.r. τ (CDCl₃) 2.6 - 3.2(m., 5H); 6.4(s., 2H); and 9.0(s., 9H),

V_{\max} 2960, 2910, 2880, 1610, 1595, 1500, 1480, 1370, 1300,
1245, 1055, 1020, 755, and 690 cm⁻¹.

Mass Spectrometry: M^+ = 164.

11. Preparation of 2-Neopentylloxy-2'-nitrobiphenyl.

The reaction of 2-hydroxy-2'-nitrobiphenyl (0.7g.) with potassium hydroxide (0.8g.) and neopentylloxy-tris(dimethylamino) phosphonium hexafluorophosphate (2.76g.) in dimethylformamide (35ml.) gave 2-neopentylloxy-2'-nitrobiphenyl (0.68g., 70%); m.p.

90-1° (from light petroleum b.p. 60-80°).

(Found: C, 72.0; H, 6.6; N, 5.2%; M, (mass spectrometry) 285,

$C_{17}H_{19}NO_3$ requires C, 71.55; H, 6.7; N, 4.9%; M, 285);

1H .n.m.r. τ ($CDCl_3$) 1.9 - 3.2(m., 8H); 6.45(s., 2H); and 9.22(s., 9H).

V_{max} 2960, 2940, 2880, 1615, 1530, 1505, 1470, 1370, 1360,
1250, 1125, 1020, 750, and 740 cm^{-1} .

λ_{max} 215(log ϵ , 4.32); 240(3.93); and 274(3.73)n.m..

12. Preparation of p-Methoxyphenyl neopentyl ether.

The reaction of p-methoxyphenol (0.62g., 0.005 mole) with potassium hydroxide (0.56g., 0.01 mole) and neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (3.95g., 0.01mole) in dimethylformamide (25ml.) gave p-methoxyphenyl neopentyl ether (0.22g., 66%*) as a white solid; m.p. 59-60° (from light petroleum b.p. 60-80°), (lit.,⁵¹ m.p. 60°).

1H .n.m.r. τ ($CDCl_3$) 3.30(s., 4H); 6.32(s., 3H); 6.5(s., 2H);
and 9.0(s., 9H),

Mass spectrometry: M^+ = 194.

*yield based on reacted p-methoxyphenol.

13. Preparation of 2-(1-Methylheptyloxy)-2'-nitrobiphenyl.

The reaction of 2-hydroxy-2'-nitrobiphenyl (0.1g.) with potassium hydroxide (0.13g.) and 1-methylheptyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (0.36g.) in dimethylformamide (25ml.) gave 2-(1-methylheptyloxy)-2'-nitrobiphenyl (0.14g., 81%) as a yellow oil b.p. 186-196° at 1mm.

$^1\text{H.n.m.r. } \tau(\text{CDCl}_3)$ 2.0-3.2(m., 8H); 5.72 (sextet, 1H, $J=6\text{Hz.}$);
and 8.30-9.2(m., 16H),

V_{max} 2940, 2860, 1620, 1530, 1500, 1455, 1360, 1250, 1130,
855, 755, and 740cm.^{-1} ,

Mass Spectrometry: $M^+ = 327$.

14. Preparation of 1-Methylheptyl phenyl sulphide.

The reaction of thiophenol (0.6g) with potassium hydroxide (0.6g) and 1-methylheptyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (4.4g.) in dimethylformamide (25ml.) gave 1-methylheptyl phenyl sulphide (0.73g., 61%), b.p. 107° at 0.7mm. (lit.,⁷³ b.p. 197° at 13mm.).

$^1\text{H.n.m.r. } \tau(\text{CDCl}_3)$ 2.4 - 2.85(m., 5H); 6.8(sextet, 1H, $J = 6\text{Hz.}$);
and 8.30 - 9.25 (m., 16H),

Molecular weight by high resolution mass spectrometry:-

Measured mass: $M^+ = 222.1440$

Expected formula, $\text{C}_{14}\text{H}_{22}\text{S}$.

Calculated mass: $M^+ = 222.1442$.

15. Preparation of 1-Methylheptyl p-tolyl sulphide.

The reaction of p-toluenethiol (0.6g.) with potassium hydroxide (0.6g.) and 1-methylheptyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (4.37g.) in dimethylformamide (25ml.) gave 1-methylheptyl p-tolyl sulphide (0.78g., 68%)
b.p. 124° at 0.7mm. .

$^1\text{H.n.m.r. } \tau(\text{CDCl}_3)$ 2.78 (q., 4H, $J = 12\text{Hz.}$); 6.8(sextet, 1H, $J = 6\text{Hz.}$); 7.65(s., 3H); and 8.2 - 9.3(m., 16H).

V_{\max} 2940, 2860, 1495, 1460, 1380, 1265, 1095, 1020, and
810 cm^{-1} .,

Molecular Weight by high resolution mass spectrometry:-

Measured mass: $M^+ = 236.1595$

Expected formula, $\text{C}_{15}\text{H}_{24}\text{S}$.

Calculated mass: $M^+ = 236.1599$.

16. Preparation of p-Methoxyphenyl 1-methylheptyl ether.

The reaction of p-methoxyphenol (0.5g.) with potassium hydroxide (0.5g.) and 1-methylheptyloxy-tris(dimethylamino) phosphonium hexafluorophosphate (3.5g.) in dimethylformamide (25ml.) gave p-methoxyphenyl 1-methylheptyl ether (0.55g., 68%), b.p. 119° at 1.5mm.

$^1\text{H.n.m.r.}$ τ (CDCl_3) 3.2(s., 4H); 5.78(sextet, 1H, $J = 6\text{Hz.}$);
6.25(s., 3H); and 8.25 - 9.25(m., 16H),

V_{\max} 2940, 2860, 1510, 1470, 1445, 1380, 1290, 1235, 1180,
1135, 1125, 1105, 1045, and 825 cm^{-1} .,

Molecular Weight by high resolution mass spectrometry:-

Measured mass: $M^+ = 236.1772$

Expected formula, $\text{C}_{15}\text{H}_{24}\text{O}_2$.

Calculated mass: $M^+ = 236.1776$

17. Preparation of 1-Methylheptyl p-nitrophenyl ether.

The reaction of p-nitrophenol (0.7g., 0.005 mole) with potassium hydroxide (0.56g., 0.01 mole) and 1-methylheptyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (4.37g., 0.01 mole) in dimethylformamide (30ml) gave 1-methylheptyl p-nitrophenyl ether (1.20g., 80%); b.p. 154° at 1.5mm.

(Found: C, 66.8; H, 8.3; N, 5.2%; M, (mass spectrometry) 251,

$C_{14}H_{21}NO_3$ requires C, 66.9; H, 8.4; N, 5.6%; M, 251);

1H .n.m.r. τ ($CDCl_3$) 1.80(ABd., 2H, $J_{AB} = 9Hz.$); 3.10(ABd., 2H, $J_{AB} = 9Hz.$); 5.52(sextet, 1H, $J = 6Hz.$); and 8.2 - 9.3(m., 16H).

V_{max} 2960, 2940, 2860, 1615, 1600, 1520, 1500, 1470, 1385, 1345, 1300, 1266, 1175, 1115, 940, 845, 755, and $690cm^{-1}$.

18a. Preparation of 1-Methylheptyl phenyl ether.

The reaction of phenol (0.94g., 0.01 mole) with potassium hydroxide (1.12g., 0.02mole) and 1-methylheptyloxy-tris(dimethyl amino)phosphonium hexafluorophosphate (8.74g., 0.02mole) in dimethylformamide (60ml) gave 1-methylheptyl phenyl ether (2.02g., 99%); b.p. 104° at 1.5mm. (lit., ⁵⁴ b.p. 144° at 20mm.).

1H .n.m.r. τ ($CDCl_3$) 2.6-3.2(m., 5H); 5.6(sextet, 1H, $J = 6Hz.$); and 8.2-9.3(m., 16H),

V_{max} 2960, 2940, 2870, 1605, 1595, 1500, 1380, 1300, 1245, 1175, 1120, 755, and $690 cm^{-1}$.

Mass spectrometry: $M^+ = 206.$

18b. Preparation of (+)(S) -1-Methylheptyl phenyl ether.

The reaction of phenol (0.94g., 0.01mole) with potassium hydroxide (1.12g., 0.02mole) and the tris(dimethylamino)phosphonium hexafluorophosphate (8.74g., 0.02mole) derived from (-) (R)-1-methylheptyl alcohol in dimethylformamide (60ml.) gave (+)(S)-1-methylheptyl phenyl ether (1.94g., 93%); b.p. 99° at 1mm.;

$[\alpha]_D^{26} = + 15.5$ (c.5.0 in ethanol). (-)(R)-1-Methylheptyl phenyl ether,

²⁶
 $[\alpha]_D^{20} -15.0$ (c.5.0 in ethanol).⁵⁴

19. Preparation of Benzyl phenyl sulphide.

The reaction of thiophenol (0.6g.) with potassium hydroxide (0.6g.) and benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (4.75g.) in dimethylformamide (30ml.) gave benzyl phenyl sulphide (0.84g., 83%); m.p. 40-41° (from light petroleum b.p. 60-80°), (lit.,⁷⁴ m.p. 39-40°).

¹H.n.m.r. τ (CDCl₃) 2.45-2.85(m., 10H) and 5.90(s., 2H),
Mass spectrometry: $M^+ = 200$.

20. Preparation of Benzyl p-tolyl sulphide.

The reaction of p-toluenethiol (0.62g., 0.005mole) with potassium hydroxide (0.56g., 0.01 mole) and benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (4.15g., 0.01mole) in dimethylformamide (30ml) gave benzyl p-tolyl sulphide (1.01g., 98%); m.p. 45-6° (from light petroleum b.p. 60-80°), (lit.,⁷⁵ m.p. 40-41°).

¹H.n.m.r. τ (CDCl₃) 2.45-3.05(m., 9H); 5.93(s., 2H); and 7.7
(s., 3H),

Mass Spectrometry: $M^+ = 214$.

21. Preparation of Allyl p-tolyl sulphide.

The reaction of p-toluenethiol (1.24g., 0.01 mole) with potassium hydroxide (1.12g., 0.02mole) and allyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (7.30g., 0.02mole) in dimethylformamide (50ml.) gave allyl p-tolyl sulphide (1.53g., 97%) b.p. 70° at 0.2mm. (lit.,⁷⁶ b.p. 99-100.5° at 7.5mm.).

¹H.n.m.r. τ (CDCl₃) 2.8(q., 4H, J = 9Hz.); 3.8 - 4.4(m., 1H);
4.75 - 5.05(m., 2H); 6.40-6.60(m., 2H); and
7.68(s., 3H),

Mass Spectrometry: M⁺ = 164.

22. Preparation of Allyl phenyl sulphide.

The reaction of thiophenol (1.10g., 0.01 mole) with potassium hydroxide (1.12g., 0.02mole) and allyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (7.30g., 0.02mole) in dimethylformamide (50ml) gave allyl phenyl sulphide (1.36g., 90%); b.p. 75° at 2mm. (lit.,⁷⁷ b.p. 84-6° at 5mm.).

¹H.n.m.r. τ (CDCl₃) 2.5-2.9(m., 5H); 3.85-4.4 (m., 1H);
4.7 - 5.05(m., 2H); and 6.4-6.6(d., 2H),

ν_{\max} 1650, 1590, 1490, 1445, 1230, 1090, 1030, 990,
925, 745, and 695cm.⁻¹,

Mass Spectrometry: M⁺ = 150.

23. Preparation of Allyl phenyl ether.

The reaction of phenol(0.47g., 0.005 mole) with potassium hydroxide (0.56g., 0.01 mole) and allyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (3.65g., 0.01mole) in dimethylformamide (30ml) gave allyl phenyl ether (0.47g., 79%); b.p. 40° at 2mm. (lit.,⁷⁸ b.p. 191-2° at 760mm.).

¹H.n.m.r. τ (CDCl₃) 2.45-3.2 (m., 5H); 3.7-4.15(m., 1H);
4.4-4.8(m., 2H); and 5.4-5.6(d., 2H).

24. Preparation of Phenyl n-propyl ether.

The reaction of phenol (0.47g., 0.005mole) with potassium hydroxide (0.56g., 0.01 mole) and n-propoxy-tris(dimethylamino) phosphonium hexafluorophosphate (3.67g., 0.01mole) in dimethylformamide (50ml.) gave phenyl n-propyl ether (0.58g., 86%); b.p. 56° at 4.5mm, (lit.,⁷⁹ b.p. 69° at 14mm.).

¹H.n.m.r. τ (CDCl₃) 2.5 - 3.2(m., 5H); 6.1(t., 2H, J = 8Hz.);
8.2(sextet, 2H, J = 6Hz.); and 8.95(t., 3H, J = 8Hz.),
V_{max} 2980, 2960, 2900, 1615, 1595, 1505, 1480, 1400,
1310, 1250, 1180, 980, 755, and 695cm.⁻¹,

Mass Spectrometry: M⁺ = 136.

25. Reaction of Benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with the sodium salt of Indole.

Dimethylformamide (100ml.) was added to sodium hydride (0.6g., 0.025mole) and the mixture was stirred for 5 minutes. Indole (2.9g., 0.025 mole) was then added and the mixture was stirred for 1 hour. Benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (20.8g., 0.05mole) was added and the mixture was heated under reflux for 15 hours. After cooling to room temperature, the reaction mixture was poured into water (250 ml.) and extracted with ether (3 x 100ml.). Each extract was washed with water (3 x 50ml) and the combined ether layers were dried over anhydrous magnesium sulphate. Removal of the solvent gave a red oil which on distillation under reduced pressure afforded N-benzyl indole (3.68g., 74%); b.p. 148-50° at 2mm., m.p. 42-3° (from ethanol) (lit.,⁸⁰ m.p. 45°).

¹H.n.m.r. τ (CDCl₃) 2.25 - 2.45 (m., 1H); 2.6-3.1(m., 9H);
3.45(d., 1H, J = 3Hz.); and 4.78(s., 2H).

26. Reaction of Benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with the sodium salt of 2-phenylindole.

Reaction as in experiment 25 using 2-phenylindole (1.45g., 0.0075 mole), sodium hydride (0.18g., 0.0075 mole), and benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (6.22g., 0.015 mole) in dimethylformamide (100ml.) gave a red oil (1.93g.) which was placed on a column of silica gel (100g.). Elution with 3% ether-light petroleum gave 3-benzyl-2-phenylindole (1.13g., 53%) as yellow crystals, m.p. 118-9° (from light petroleum b.p. 60-80°) (lit.,⁸¹ m.p. 118-9°).

¹H.n.m.r. τ (CDCl₃) 2.0 - 3.1(m., 15H) and 5.72(s., 2H);
Mass Spectrometry: M⁺ = 283.

27. Reaction of Benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with N-methylaniline in dimethylformamide.

A solution of N-methylaniline (0.54g., 0.005mole) and benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (1.04g., 0.0025 mole) in dimethylformamide (50ml.) was heated under reflux for 15 hours. After cooling to room temperature the reaction mixture was poured into a saturated aqueous solution of sodium bicarbonate (100ml.) and then extracted with ether (2 x 50 ml.). Each extract was washed with water (2 x 30ml.) and the combined ether layers were dried over anhydrous magnesium sulphate. Removal of the solvent afforded an orange liquid which was distilled under reduced pressure and gave, after removal of excess of N-methylaniline (0.26g.) b.p. 45-50° at 2.5mm.
a) N-formyl-N-methylaniline (0.03g., 9%) b.p. 86-8° at 25mm. (lit.,⁸² b.p. 95° at 4mm.), and

b) N-benzyl-N-methylaniline (0.37g., 74%) b.p. 108-10° at 2.5mm.,
(lit.,⁸³ b.p. 187-8° at 26mm.).

¹H.n.m.r. τ (CDCl₃) 2.6-3.4(m., 10H); 5.6(s., 2H); and 7.12(s., 3H)

Mass Spectrometry: M⁺ = 197.

28. Reaction of Benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with N-methylaniline in tetrahydrofuran.

Reaction as in experiment 27 using N-methylaniline (0.53g., 0.005 mole) and benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (2.08g., 0.005 mole) in tetrahydrofuran (40ml.) gave N-benzyl-N-methylaniline (0.81g., 79%); b.p. 96-100° at 1.5mm..

29. Reaction of Benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with aniline.

Reaction as in experiment 27 using aniline (0.30g., 0.0033 mole) and benzyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (0.68g., 0.0016 mole) in dimethylformamide (50ml.) gave a red liquid (0.47g.). The product was analysed by gas chromatography (column D at 202°), mass spectrometry, and ¹H.n.m.r. spectroscopy and shown to be a mixture of N-benzylaniline (major component), N-benzyl-N-formylaniline, and N-formylaniline.

30. Reaction of Phosphorous trisdimethylamide with N-chloro-di-isopropylamine.

Phosphorous trisdimethylamide (0.46g., 0.028 mole) in ether (10ml.) was slowly added to stirred solution of N-chloro-di-isopropylamine (0.76g., 0.056mole) in ether(10ml.) at 0°. When the addition was completed, the cold reaction mixture was poured into a solution of ammonium hexafluorophosphate

(0.46g., 0.028 mole) in water (5ml.) with immediate formation of a white solid. This solid was filtered off, washed with ice-cold water (10ml.) and ether (10ml.), and then dried over calcium chloride. Recrystallisation from water gave chloro-tris(dimethylamino)phosphonium hexafluorophosphate (0.56g., 61%); m.p. 198-200°;

¹H.n.m.r. τ (DMSO-d₆) 7.10(d., J_{PH} = 14Hz).

31. Preparation of Chloro-tris(dimethylamino)phosphonium hexafluorophosphate.

A solution of ammonium hexafluorophosphate (8.2g., 0.05mole) in water (15ml.) was added to a stirred solution of carbon tetrachloride (8.0g., 0.052mole) in ether (25ml.) at 0°. The dropwise addition of phosphorous trisdimethylamide (8.2g., 0.05mole) to the ice-cold emulsion resulted in the immediate formation of a white solid. When the addition was completed, the solid was removed by filtration and washed with ether (25ml.), and ice-cold water (25ml.). After drying over calcium chloride the solid was recrystallised from water and gave chloro-tris(dimethylamino)phosphonium hexafluorophosphate (9.9g., 60%); m.p. 198-199°.

32. Preparation of Trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate.

Phosphorous trisdimethylamide (16.3g., 0.1mole) in ether (40ml.) was added dropwise to a stirred solution of carbon tetrachloride (30.8g., 0.2 mole) in ether (60ml.) at 0°. When the addition was completed the reaction mixture was poured into an ice-chilled saturated aqueous solution of ammonium hexafluorophosphate (16.3g., 0.1 mole) with the immediate formation of a white solid. The precipitate was collected, washed

with water (50ml.) and ether (50ml.) and then dried over calcium chloride. This crude product was washed with chloroform (3 x 50ml.) and gave an insoluble residue of chloro-tris(dimethylamino)phosphonium hexafluorophosphate (5.5g., 16%) m.p. 198-200°.

The chloroform extracts were combined and solvent removed to give trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate (30.8g., 72%) as white plates; m.p. 290-3° (from aqueous acetone).

¹H.n.m.r. τ (CDCl₃) 6.95(d., J_{PH} = 10Hz.).

33. Reaction of Chloro-tris(dimethylamino)phosphonium hexafluorophosphate with N,N-Dimethylformamide in the presence of N-methylaniline.

Chloro-tris(dimethylamino)phosphonium hexafluorophosphate (1.8g., 0.005mole) was added to a stirred solution of N-methylaniline (2.7g., 0.025 mole) in dimethylformamide (25ml.). The solution was heated under reflux for 12 hours and then poured into water (50ml.). After stirring at room temperature for 30 mins., the reaction mixture was extracted with ether (3 x 50ml.) and each extract was washed with water (3 x 30ml.). The combined ether layers were dried over anhydrous magnesium sulphate. Removal of the solvent gave a red liquid which was distilled under reduced pressure to afford, after removal of excess of N-methylaniline (1.33g.); b.p. 48-50 at 2.5mm., N-formyl-N-methylaniline (0.71g., 99%); b.p. 86-8° at 2mm. (lit.,⁸² b.p. 95° at 4mm.).

¹H.n.m.r. τ (CDCl₃) 1.52(s., 1H); 2.45-2.95(m., 5H); and 6.78(s., 3H).

Mass Spectrometry: M⁺ = 135.

34. Reaction of Trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate with N,N-dimethylformamide in the presence of N-methylaniline.

Using the procedure described above trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate (2.2g., 0.005mole) was reacted with N-methylaniline (2.7g., 0.025 mole) in dimethylformamide (25ml.) and gave N-formyl-N-methylaniline (0.21g., 31%); b.p. 78-80° at 1mm. (lit.,⁸² b.p. 95° at 4mm.).

35. Reaction of Neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with potassium p-nitrophenate.

a) p-Nitrophenol (0.7g., 0.005mole) was added with stirring to a mixture of powdered potassium hydroxide (0.56g., 0.01mole) in dimethylformamide (30ml.). The mixture was stirred for 30 minutes and neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (3.95g., 0.01mole) was added. After stirring at room temperature for a further 2 hours, the mixture was heated under reflux for 1 hour. After cooling, the reaction mixture was poured into water (100ml.) and extracted with ether (3 x 50ml.) and each extract was washed with water. The combined ether layers were washed with an aqueous solution of sodium hydroxide. Acidification of the aqueous phase and standard work-up gave p-nitrophenol (0.38g., 54% recovery).

The organic phase was dried over anhydrous magnesium sulphate and the solvent removed to give a yellow oil, which was placed on a column of alumina. Elution with 10% ether-light petroleum gave neopentyl p-nitrophenyl ether (0.42g., 42%^{*}) as a yellow solid; m.p. 34-5° (from aqueous ethanol) (lit.,⁵¹ m.p. 34°).

¹H.n.m.r. τ (CDCl₃) 1.85(ABd., 2H, J_{AB} = 9Hz.); 3.05(ABd., 2H, J_{AB} = 9Hz.); 6.3(s., 2H); and 8.95(s., 9H).

V_{\max} 1600, 1500, 1330, 1250, 1170, 1110, 1040, 1010,
850, and 750cm.^{-1} ,

Mass Spectrometry: $M^+ = 209$.

* 85% yield based on reacted p-nitrophenol.

b) The reaction was repeated using the procedure described above with the exception that the reaction mixture was heated under reflux for 48 hours. Chromatography on alumina gave:

a) neopentyl p-nitrophenyl ether (0.23g., 24 %) m.p. 35° .

and b) p-nitro-N,N-dimethylaniline (0.24g., 29%*) as a yellow solid; m.p. $163-4^\circ$, (from light petroleum b.p. $60-80^\circ$) (lit.,⁸⁴ m.p. 165°).

¹H.n.m.r. τ (CDCl_3) 1.9(ABd., 2H, $J_{AB} = 9\text{Hz.}$); 3.4(ABd., 2H, $J_{AB} = 9\text{Hz.}$); and 6.88(s., 6H);

V_{\max} 1610, 1490, 1250, 1205, 1120, 825 and 755cm.^{-1} ,

Mass Spectrometry: $M^+ = 166$.

* 67% yield based on reacted p-nitrophenol.

36. Reaction of Neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate with potassium p-nitrophenate using tetrahydrofuran as the solvent.

a) Reaction as in experiment 35a using p-nitrophenol (0.7g., 0.005 mole), potassium hydroxide (0.56g., 0.01mole) and neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (3.95g., 0.01 mole) in tetrahydrofuran (30ml.) gave neopentyl p-nitrophenyl ether (0.28g., 26%) as a yellow solid; m.p. 35° (from aqueous ethanol).

b) Reaction as in experiment 35b using p-nitrophenol (0.7g., 0.005 mole), potassium hydroxide (0.56g., 0.01 mole) and neopentyloxy-tris(dimethylamino)phosphonium hexafluorophosphate (3.95g., 0.01 mole) in tetrahydrofuran (30ml.) gave:

a) neopentyl p-nitrophenyl ether (0.13g., 12%), and

b) p-nitro-N,N-dimethylaniline (0.19g., 23%) as a yellow solid m.p. 163-4°.

37. Reaction of Trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate with potassium p-nitrophenate in dimethylformamide.

p-Nitrophenol (1.39g., 0.01 mole) was added with stirring to a mixture of powdered potassium hydroxide (0.56g., 0.01 mole) in dimethylformamide (50ml.). The mixture was stirred for 2 hours and trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate (4.28g., 0.01mole) was added. After stirring at room temperature for a further 1 hour, the mixture was heated under reflux for 15 hours. After cooling to room temperature, the reaction mixture was poured into water (150ml.) and extracted with ether (3 x 50ml.) and each extract was washed with water. The combined ether layers were washed with an aqueous solution of sodium hydroxide (2N, 2 x 50ml.). Acidification of the aqueous phase and standard work-up gave p-nitrophenol (1.01g., 73% recovery).

The organic phase was then washed with conc. hydrochloric acid (2 x 25ml.). Basification of the combined aqueous layers and standard work-up gave p-nitro-N,N-dimethylaniline (0.11g., 23%); m.p. 163-4° (from light petroleum b.p. 60-80°).

After drying the organic phase over anhydrous magnesium sulphate, the solvent was removed to give a pale yellow solid. Recrystallisation from ethanol afforded 4,4'-dinitrodiphenyl ether (0.13g., 14%) as yellow needles m.p. 141-2° (lit.,⁸⁵ m.p. 144.5°).

38. Reaction of Trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate with potassium p-nitrophenate in tetrahydrofuran.

Reaction as in experiment 37 using p-nitrophenol (1.39g., 0.01 mole), potassium hydroxide (0.56g., 0.01 mole), and trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate (4.28g., 0.01 mole) in tetrahydrofuran (50ml.) gave:

- a) p-nitrophenol (0.85g., 61% recovery),
- b) p-nitro-N,N-dimethylaniline (0.09g., 10%) m.p. 163-4°, and
- c) 4,4'-dinitrodiphenyl ether (0.07g., 7%) m.p. 141-3°.

39. Reaction of Phenoxy-tris(dimethylamino)phosphonium hexafluorophosphate with potassium p-nitrophenate in dimethylformamide.

Reaction as in experiment 37 using p-nitrophenol (0.7g., 0.005 mole), potassium hydroxide (0.28g., 0.005 mole); and phenoxy tris(dimethylamino)phosphonium hexafluorophosphate (2.05g., 0.005 mole) in dimethylformamide (30ml.) gave:

- a) p-nitrophenol (0.60g., 86% recovery).
- b) p-nitro-N,N-dimethylaniline (0.12g., 15%) m.p. 163-4°, and
- c) 4-nitrodiphenyl ether (0.10g., 10%) as yellow plates; m.p. 60-1° (from methanol) (lit.,⁸⁶ m.p. 61°).

40. Reaction of Trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate with N,N-dimethylaniline.

A solution of N,N-dimethylaniline (6.05g., 0.05mole) and trichloromethyl-tris(dimethylamino)phosphonium hexafluorophosphate (4.28g., 0.01 mole) in dimethylformamide (50ml.) was heated under reflux for 18 hours. After cooling to room temperature, water (100ml.) was added and the reaction mixture was stirred for 1 hour, and then extracted with ether (3 x 50ml.). Each extract was washed with water (3 x 30ml.) and the combined ether layers were dried over anhydrous magnesium sulphate. Removal of the solvent gave a blue liquid which was distilled under reduced pressure to remove excess of N,N-dimethylaniline (3.7g.,) b.p. 60° at 2mm. The oily residue solidified on standing and recrystallisation from ethanol afforded bis-(p-dimethylaminophenyl) methane (0.16g., 7%) m.p. 91-3° (lit.,⁸⁷ m.p. 90°).

¹H.n.m.r. τ (CDCl₃) 2.95(m., 4H); 3.35(m., 4H); 6.2(s., 2H);
and 7.15(s., 12H).

V_{\max} 2890, 2810, 1625, 1530, 1450, 1360, 1350, 1235,
1195, 1170, 955, 830, and 800cm.⁻¹,

Mass Spectrometry: M^+ = 254.

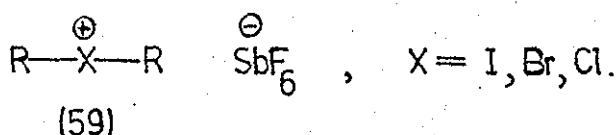
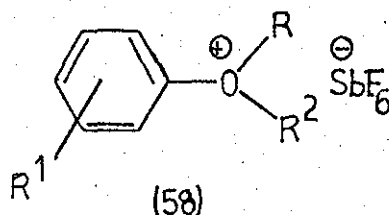
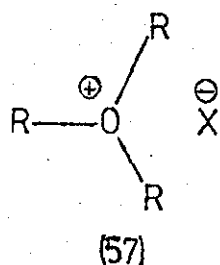
PART 2

The Generation and Reactions of
O-Alkyldibenzofuranium Salts.

INTRODUCTION

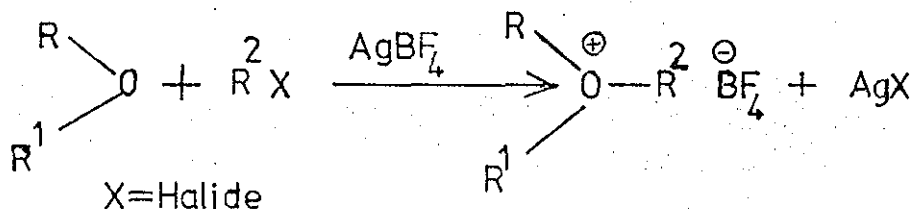
Oxonium and Halonium Salts:
Their use as Alkylating Agents

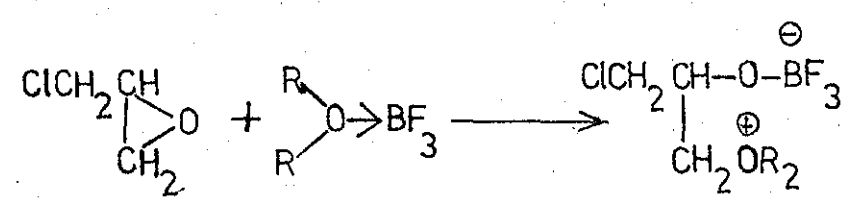
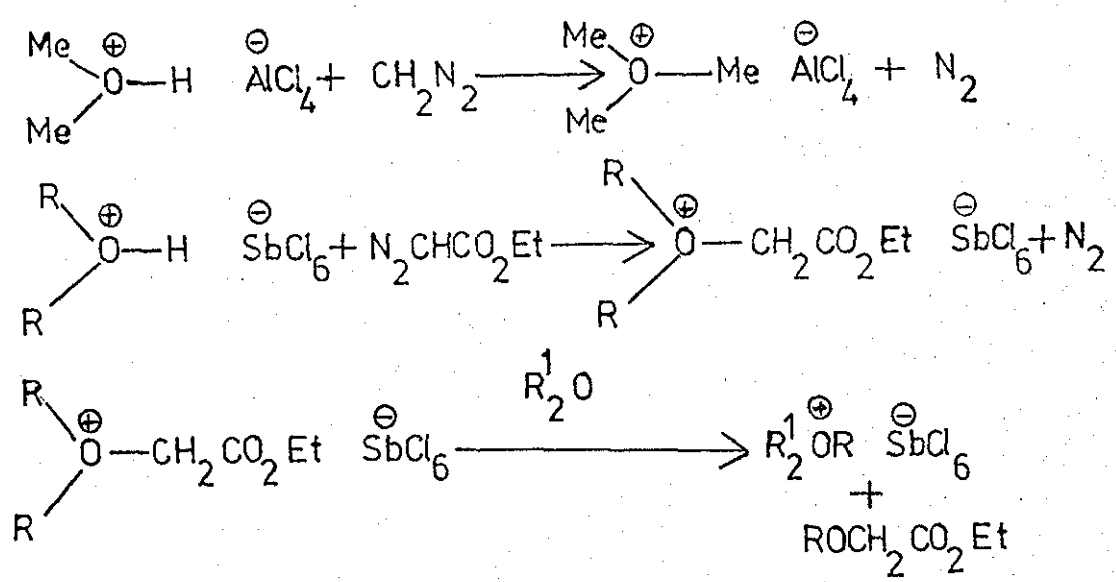
Trialkyloxonium salts (57) were first prepared by Meerwein and his co-workers in 1937,⁸⁸ and their use as highly reactive alkylating agents has been known since that time. However, it is only recently that other saturated onium ion reagents have been prepared and their synthetic application as alkylating agents established. In particular, dialkylaryloxonium ions (58)⁸⁹ and dialkylhalonium ions (59)⁹⁰ have proved to be extremely powerful reagents in alkylation reactions.



Several methods have been developed for the preparation of trialkyloxonium salts. The most widely used method for the formation of trialkyloxonium fluoroborates (57, X = BF₄) is based on the reaction between epichlorohydrin and the appropriate ether complex of boron trifluoride in excess of the ether.^{88,91} This convenient synthesis is outlined in Scheme 29.

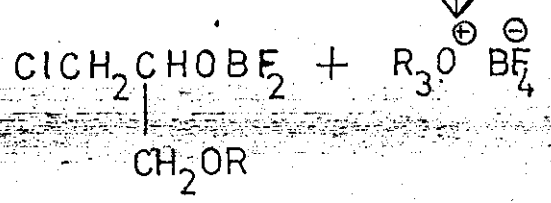
Unsymmetrical oxonium fluoroborates have been prepared by the reaction of alkyl halides with dialkyl ethers in the presence of silver fluoroborate.⁹¹ Other methods of preparation have included the reaction of dialkyl oxonium salts with diazomethane⁹² or diazoacetic acid esters.⁹³





R = Me, Et, ⁿPr, and ⁿBu.

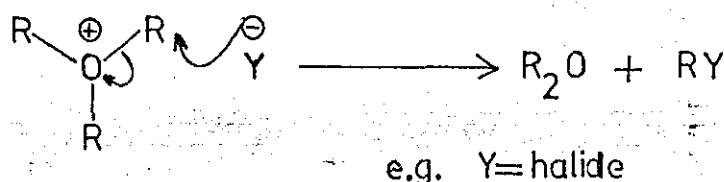
R₂O → BF₃



Scheme 29.

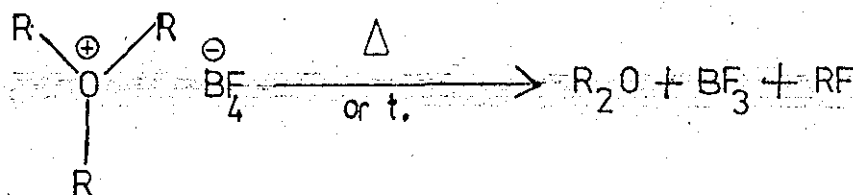
Irrespective of the mode of preparation, the yields of oxonium salts decrease with increasing size of the alkyl groups. The only symmetrical trialkyloxonium cations (57) that have been prepared so far are the trimethyl,⁹⁴ triethyl,⁹⁴ tri-n-propyl,⁹⁴ and tri-n-butyloxonium salts;⁹⁵ all attempts at the synthesis of tri-isopropyloxonium or tri-tert-butyloxonium salts have been unsuccessful.

The original trialkyloxonium ion complexes prepared by Meerwein were the fluoroborate and hexachloroantimonate salts,^{88,94} non-nucleophilic anions of this type have to be employed in order to form stable oxonium salts, since the complex would decompose in the presence of strongly nucleophilic anions by dealkylation (Scheme 30).



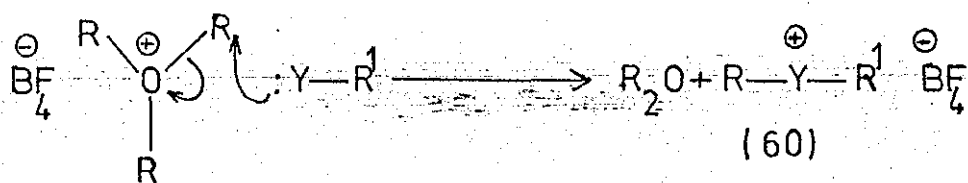
Scheme 30.

However, even the fluoroborate salts have limited stability and decomposition occurs fairly readily to yield the dialkyl ether, alkyl fluoride, and boron trifluoride.⁹⁶



An improvement in both the stability and solubility of trialkyloxonium salts has been reported recently by utilising the hexafluorophosphate anion (57, X = PF₆).⁹⁷

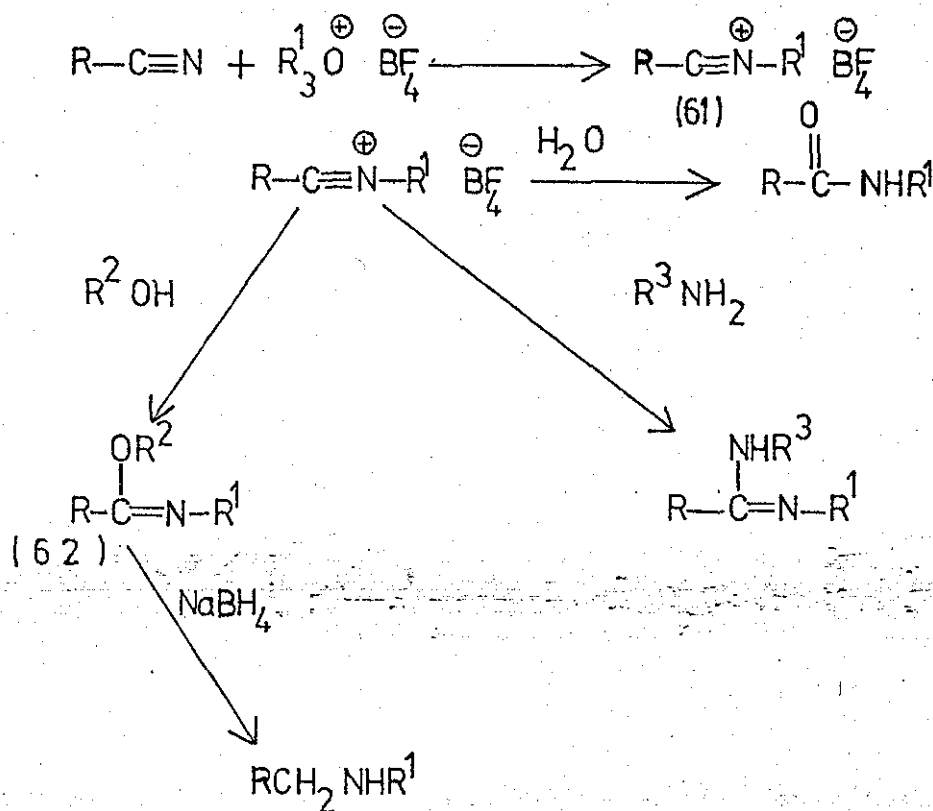
Trialkyloxonium salts are characterized by their ability to eliminate alkyl groups readily and hence have acquired considerable synthetic importance as powerful alkylating agents. The salts have therefore been used extensively for the alkylation of weakly nucleophilic functional groups, e.g. ethers, which are too unreactive to be alkylated by more conventional reagents such as methyl iodide or dimethyl sulphate. The salts have also been used for the alkylation of compounds containing a functional group which is normally readily alkylated (e.g. an amine), but whose reactivity is unusually low due to some steric or electronic effect. Thus a wide variety of hetero-organic compounds have been alkylated by trialkyloxonium salts (Scheme 31), the nucleophilic centre, Y, includes functional groups with oxygen, sulphur, nitrogen and phosphorus.^{94,98}



Scheme 31.

The cations (60) which are formed as the primary products of the reaction between trialkyloxonium ions and neutral molecules have generally been isolated, often in the form of well-crystallised fluoroborate or hexachloroantimonate salts.⁹⁴ The high reactivity of these onium ions has been advantageously applied in synthetic chemistry. For example, N-alkylnitrilium salts (61) have been prepared by reaction of nitriles with trialkyloxonium fluoroborates and the high electrophilic character of these salts has been demonstrated by their instantaneous conversion to amides upon treatment

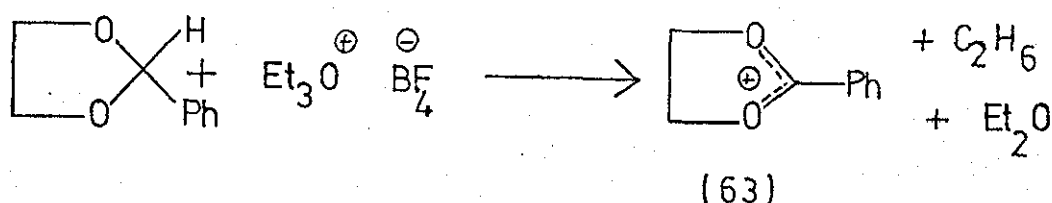
with water.⁹⁹ The nitrilium salts have also been converted to amidines by treatment with ammonia or primary amines,⁹⁹ while reduction of the salts with sodium borohydride in alcohol gave secondary amines.^{100a,b} The latter reaction has been shown to proceed via an imidic ester (62) intermediate. The various possibilities for the convenient transformations of the nitrile function via N-alkylnitrilium salts are outlined in Scheme 32,



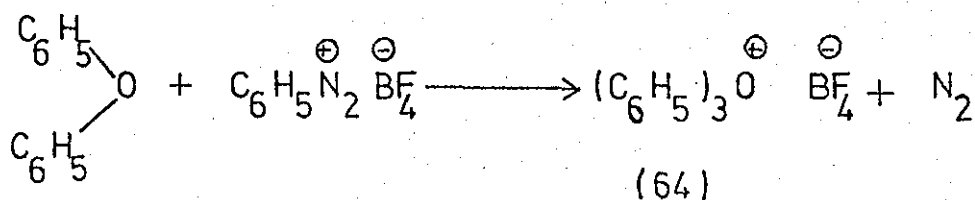
Scheme 32.

Trialkyloxonium salts have also been effective in the selective alkylation of ambifunctional compounds, in these conversions the reagents have usually displayed a preference for oxygen-containing functional groups.^{94,98} In addition, the ability of trialkyloxonium ions to behave as hydride-ion acceptors has been demonstrated by the formation of ethane and the carbonium ion (63) from the reaction of 2-phenyl-1,3-dioxolan and triethyloxonium

fluoroborate.^{96,101}

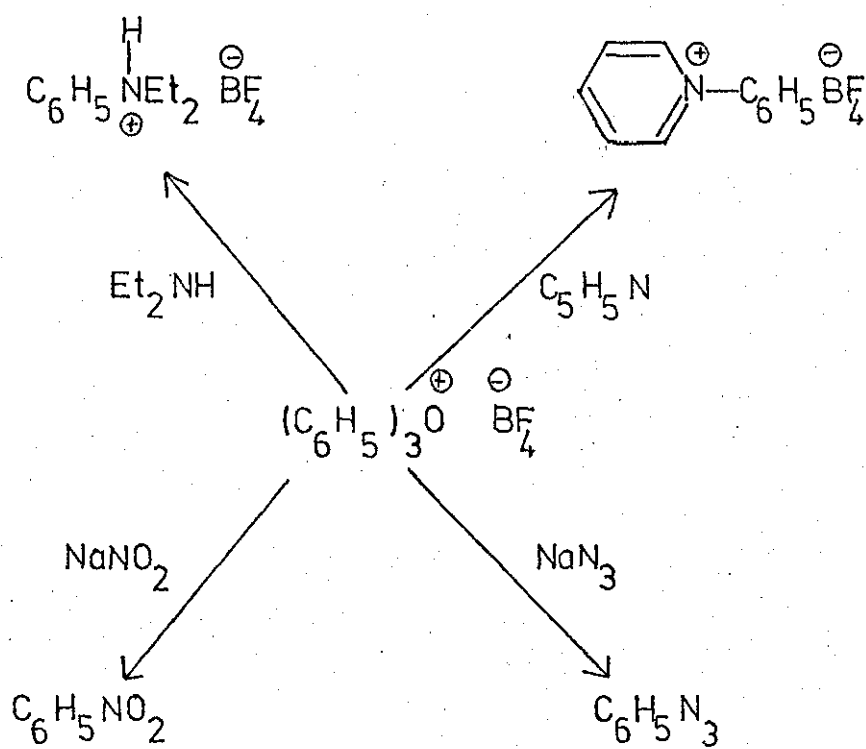


The preparation of triphenyloxonium salts (64) has been achieved, though only in low yields, by the reaction of phenyl diazonium salts with diphenyl ether.¹⁰²

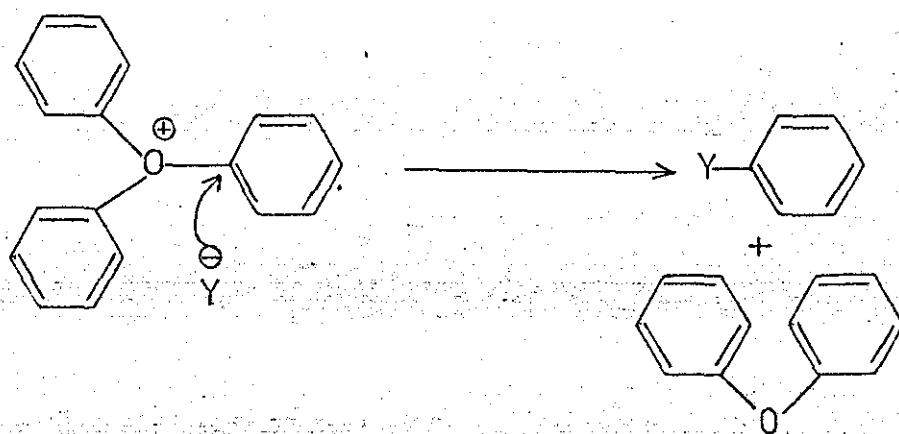


These salts are extremely unreactive toward nucleophiles in comparison with trialkyloxonium salts and this property has been demonstrated by the isolation of stable triphenyloxonium halides.¹⁰² The synthetic use of these compounds as arylating agents is thus very limited in view of the long reaction times and severe conditions that have been required for reaction with nucleophiles to occur. However, the following reactions have been described (Scheme 33), diphenyl ether being the co-product in each reaction.¹⁰³

The observation that the tris(*p*-nitro-phenyloxonium)ion is more reactive towards nucleophiles than the unsubstituted triphenyloxonium ion indicates that the arylation reactions proceed via a bimolecular mechanism.¹⁰⁴ The general lack of reactivity of these ions is probably due to the steric hinderance in the approach of the nucleophile to the site of substitution (Scheme 34)

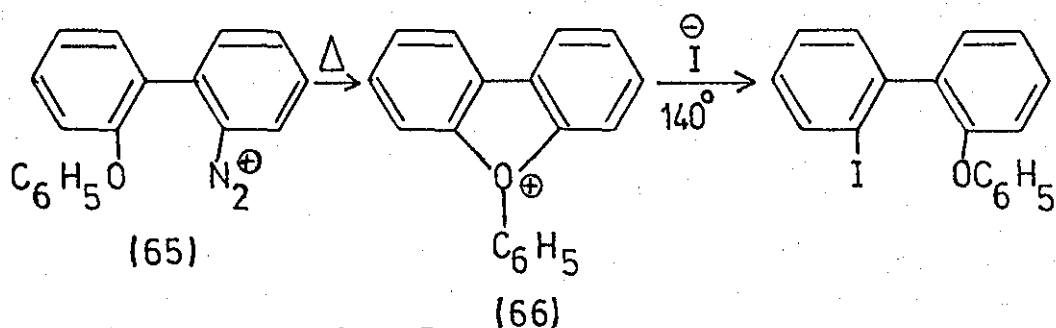


Scheme 33



Scheme 34

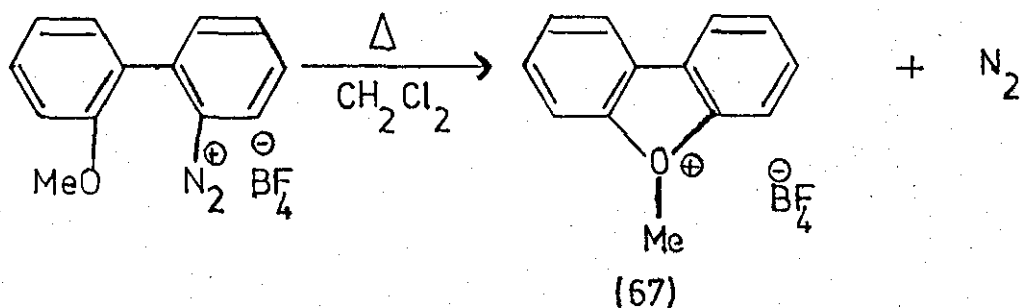
The O-phenyldibenzofuranium ion (66) is a cyclic representative of triaryloxonium salts. The preparation of this ion has been achieved by an intramolecular cyclisation of the diazonium salt (65), here again, the stable iodide has been isolated. However, the thermal decomposition of this particular salt was reported to result in the opening of the ring with the formation of 2-iodo-2'-phenoxybiphenyl (Scheme 35).¹⁰³



Scheme 35

This unexpected result warrants further investigation.

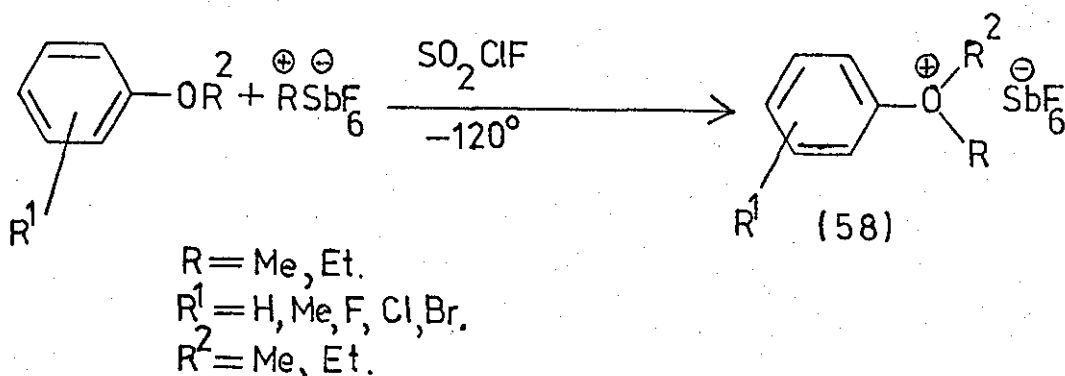
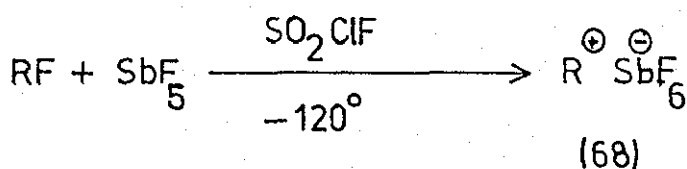
The preparation of O-methyldibenzofuranium fluoroborate (67) has been reported¹⁰⁵ recently by the cyclisation of 2'-methoxybiphenyl-2-yl diazonium fluoroborate.



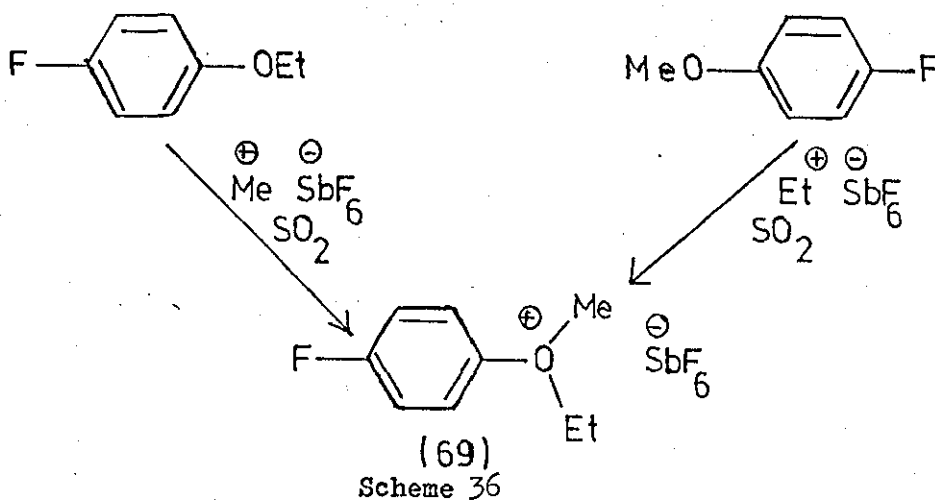
The application of this oxonium salt and other O-alkyldibenzofuranium ions as powerful alkylating agents will be discussed in detail later.

Alkylcarbonium fluoroantimonates (68) are the strongest alkylating agents available at present,^{106a,b} they are generated in

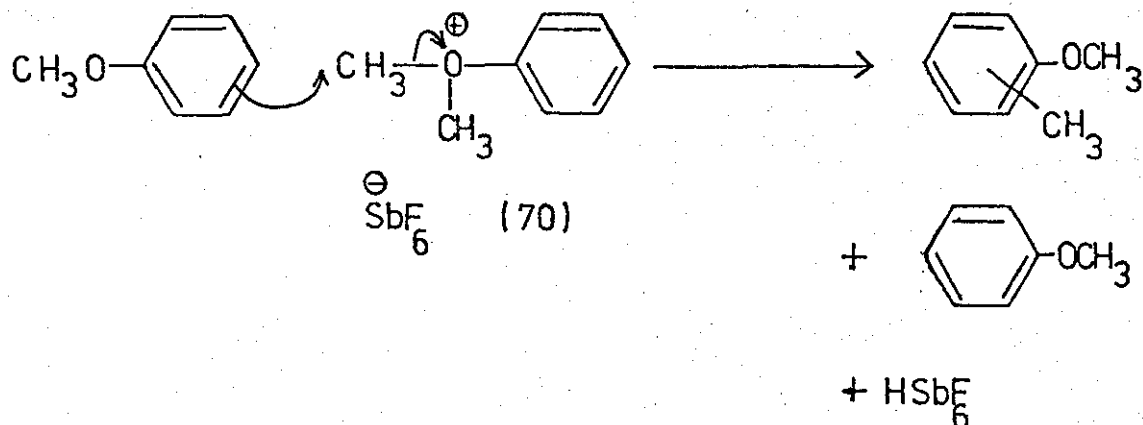
situ from the corresponding alkyl fluoride and antimony pentafluoride at low temperatures in completely non-nucleophilic solvents, such as sulphur dioxide or sulphuryl chloride (SO_2ClF). These salts have been used recently in the preparation of other classes of onium ions, thus dialkylaryloxonium ions have been prepared by the alkylation of alkyl aryl ethers.⁸⁹



The assignment of dialkylaryloxonium ions to the reaction products was based initially on n.m.r. data alone, however further proof of the structure has been obtained by the formation of the ethylmethyl-4-fluorophenyloxonium ion (69) from two pathways (Scheme 36).

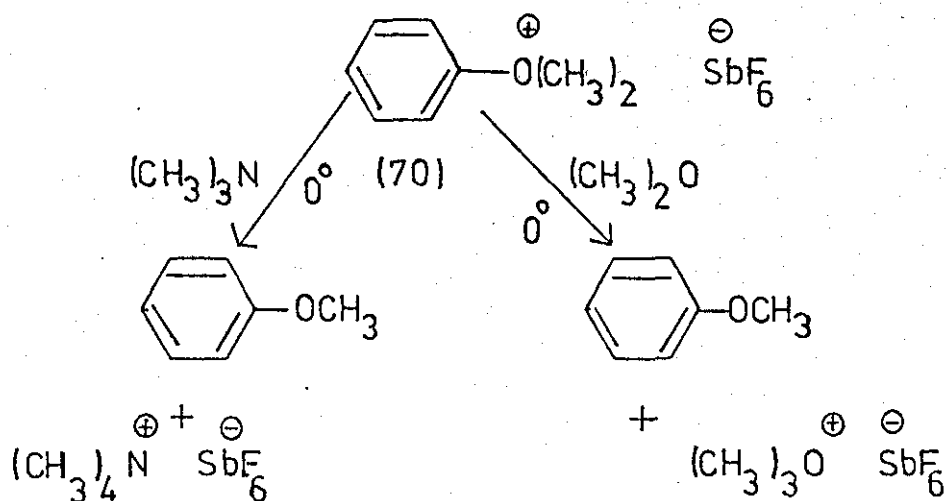


Dialkylaryloxonium ions are very strong alkylating agents. For example, the dimethylphenyloxonium ion (70) has been used to methylate the aromatic π system of anisole (Scheme 37). The ring alkylated products are derived from an intermolecular nucleophilic displacement by the π system on the oxonium ion.



Scheme 37

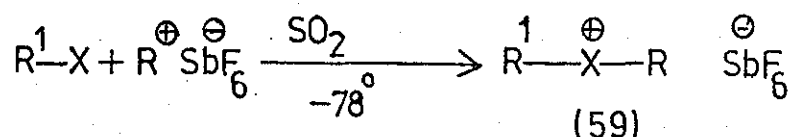
The same ion has also been used to alkylate lone-pair donor bases. Thus, dimethyl ether has been converted to the trimethyloxonium ion by reaction with a solution of (70) in sulphuryl chlorofluoride, similarly trimethylamine reacted to give the tetramethylammonium ion (Scheme 38).



Scheme 38

The fact that trimethyloxonium hexafluorophosphate was unable to methylate anisole under the same experimental conditions established that dimethylphenyloxonium ion was the stronger alkylating agent. Although the dialkylaryloxonium ions are reasonably stable in sulphuryl chlorofluoride solution at low temperatures, they rearrange on warming to room temperature to give ring alkylated alkoxybenzenes via nucleophilic displacement on the oxonium ion by uncomplexed anisole. The salt (70) has been isolated as a dark, hygroscopic solid which hydrolysed immediately on exposure to atmospheric moisture.

The recent preparation in quantitative yields of dialkylhalonium fluoroantimonates (59)¹⁰⁷ by the reaction of alkyl halides with alkylcarbonium fluoroantimonates has made available another new class of powerful alkylating agents.

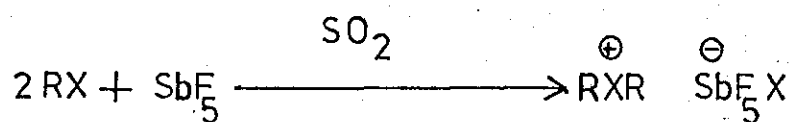


R = Me, Et.

R¹ = Me, Et, ⁿPr.

X = Br, Cl, I.

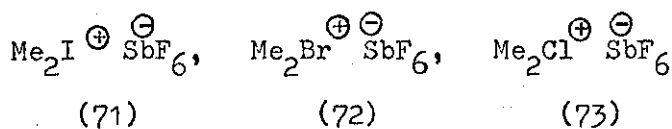
Symmetrical dialkylhalonium ions have also been prepared by the addition of an excess of alkyl halide in sulphur dioxide to a solution of antimony pentafluoride in sulphur dioxide at -78^o.¹⁰⁷



R = Me, Et, ⁱPr

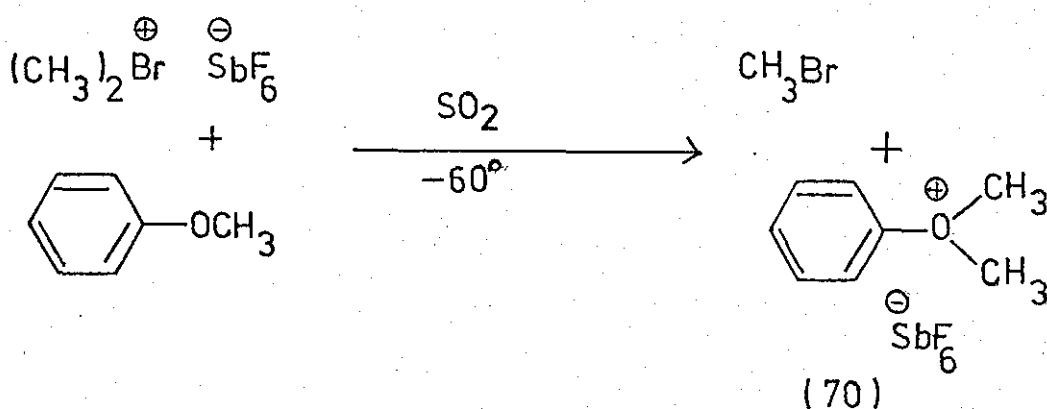
X = Br, Cl, I.

The halonium ions (71-73) have been isolated as white crystalline solids, however the salts are very hygroscopic and are stable only in a dry nitrogen atmosphere at room temperature.

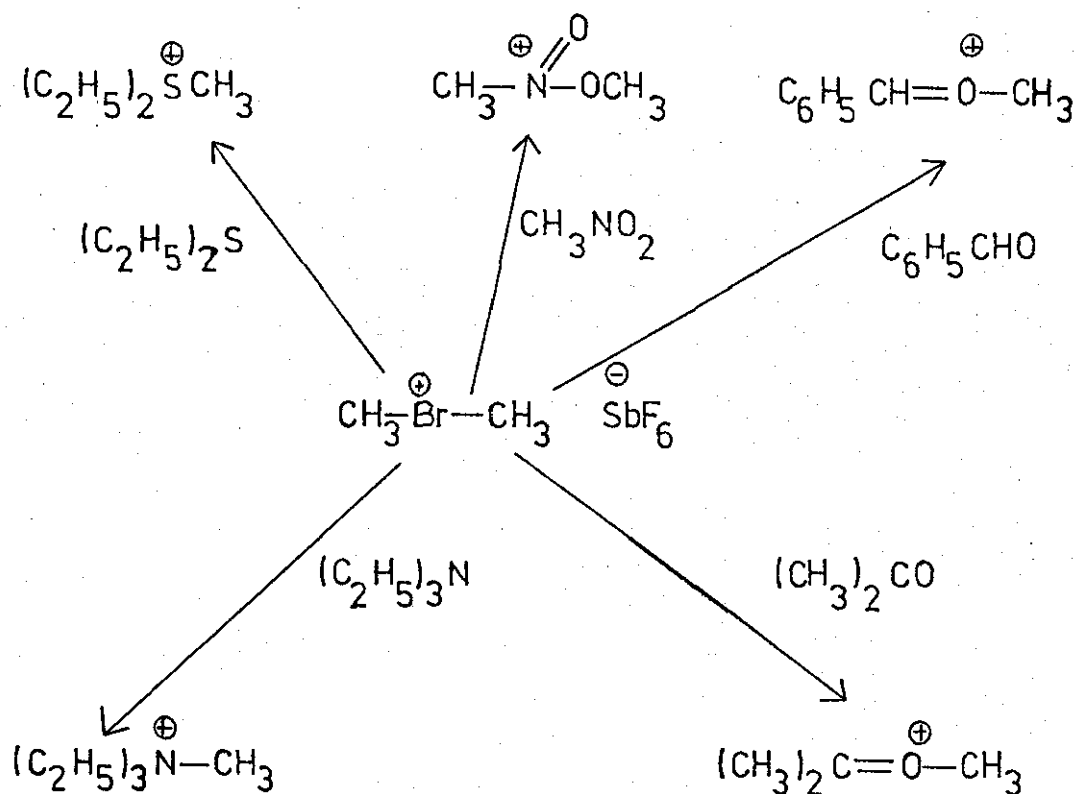


The alkylation of alkyl fluorides on the fluorine atom by alkyl fluoroantimonates is precluded by the high electronegativity of fluorine, thus dialkylfluoronium ions have not been observed. In general the relative stability of dialkylhalonium ions follows the order $\text{R}_2\text{I}^+ > \text{R}_2\text{Br}^+ > \text{R}_2\text{Cl}^+$, indicating that the larger halogen atom is more capable of accomodating the positive charge. As expected, these ions are excellent alkylating agents and even the weakest nucleophiles are capable of displacing alkyl halide from these compounds.^{90,108} For example, anisole has been alkylated by the dimethylbromonium and dimethylchloronium ions at low temperatures to give the dimethylphenyloxonium ion (70).

e.g.

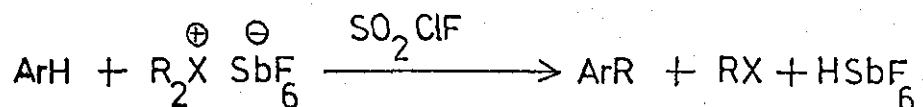


The irreversibility of this reaction established that dialkylhalonium ions are more powerful than dialkylaryloxonium ions as alkylating agents. Some examples of the methylation reactions that have been achieved using dimethylbromonium fluoroantimonate are illustrated in Scheme 39. The reactions were performed by the addition of the halonium ion in sulphur dioxide at -60° to the lone-pair base at -78° , the yield of onium ion was quantitative for each reaction.



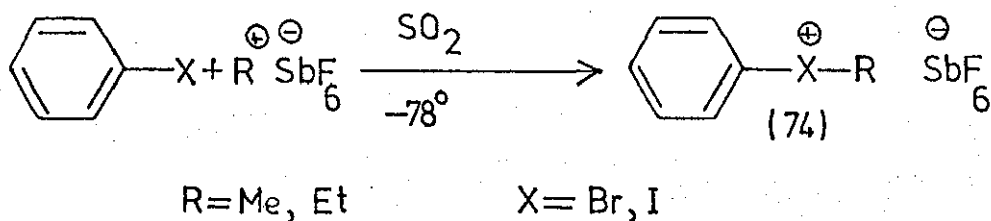
Scheme 39

Alkylation of aromatic hydrocarbons has also been achieved using halonium ions in sulphuryl chlorofluoride.

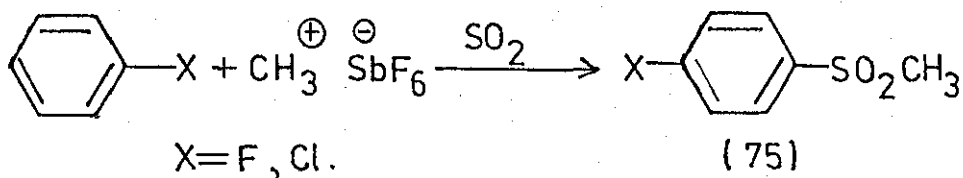


The synthetic advantage of dialkylhalonium ions over other alkylating agents lies not only in their very powerful alkylating ability but also in their selectivity, which results from the possibility of changing the nature of the halogen onium centre from the more stable and therefore less reactive iodonium ion to the highly reactive bromonium and chloronium ions.

Alkylarylhalonium salts (74) have also been prepared recently by the alkylation of halobenzenes with alkyl fluoroantimonates in sulphur dioxide. 109



Sulphonylation occurred at the para position in the corresponding reactions of methyl fluoroantimonate with chlorobenzene and fluorobenzene to afford the methyl sulphonylates (75).

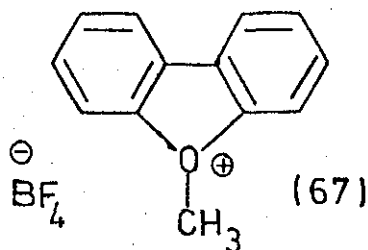


Like dialkylaryloxonium ions, the alkylarylhalonium ions are only stable in solution at low temperatures. Thus decomposition of the phenylmethylbromonium ion occurred readily at 0° to give a mixture of bromoxylenes, a similar rearrangement with the more stable phenylmethyliodonium ion was only accomplished after 15 hr. at room temperature. The strong alkylating ability of these ions has been established by their reactions with both aromatic π systems and lone-pair bases. The results of some methylation reactions involving the use of the phenylmethylbromonium ion (74, X = Br, R = Me) are outlined in Scheme 40.

Thus, the evidence available at present indicates that these new oxonium and halonium ion reagents, along with alkylcarbonium fluoroantimonates are the most powerful alkylating agents known. However, their synthetic utility is currently restricted by the

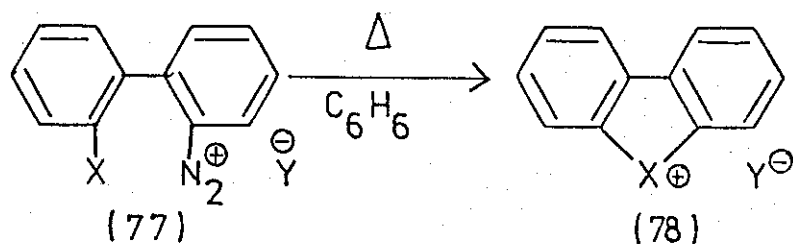
Discussion

Since trialkyloxonium salts and dialkylaryloxonium ions are characterised by their ability to act as powerful alkylating agents, it was thought that the methyldiaryloxonium salt, O-methyldibenzofuranium fluoroborate (67) would display enhanced capabilities as a powerful electrophile.

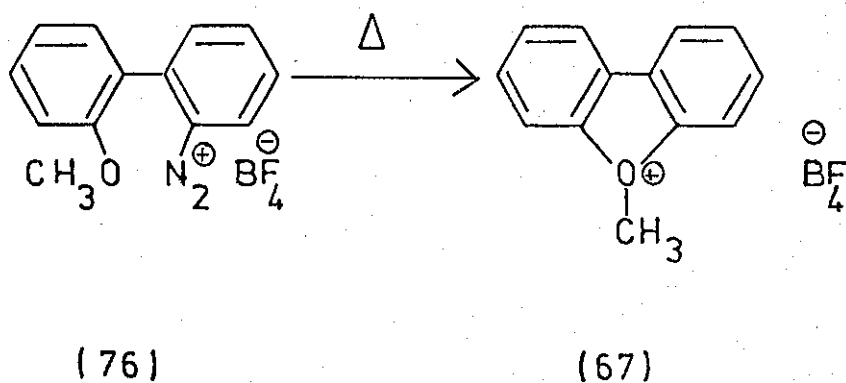


It was reasoned that the highly stable aromatic compound, dibenzofuran, would be an excellent leaving group in nucleophilic substitution reactions and therefore the salt (67) would readily eliminate the alkyl residue. The low basicity of dibenzofuran compared with that of dimethyl ether suggests that O-methyldibenzofuranium fluoroborate will be a stronger methylating agent than trimethyloxonium fluoroborate, since the strength of an alkylating agent varies inversely with the basicity of the leaving group.

The highly reactive dibenzofuranium salt (67) has not been isolated in a pure form. It is normally generated, in the presence of nucleophiles, from 2'-methoxybiphenyl-2-yl diazonium fluoroborate (76). The observation¹¹⁰ that 2'-halogenobiphenyl-2-yl diazonium fluoroborates (77, Y = BF₄) and hexafluorophosphates (77, Y = PF₆) decomposed readily on heating to give bridged halonium ions (78) in high yield via intramolecular cyclisation suggested that the diazonium salt (76) should cyclise in a similar manner to afford O-methyldibenzofuranium fluoroborate.

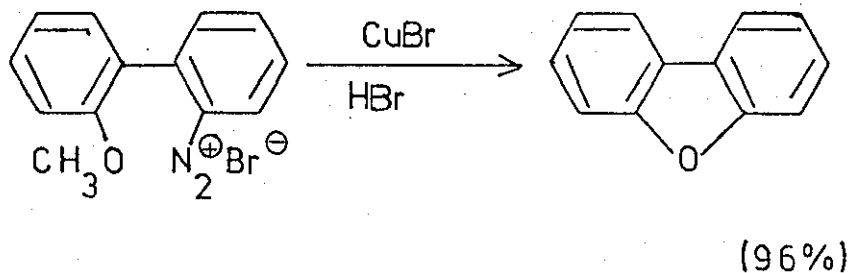


X = I, Br, Cl.

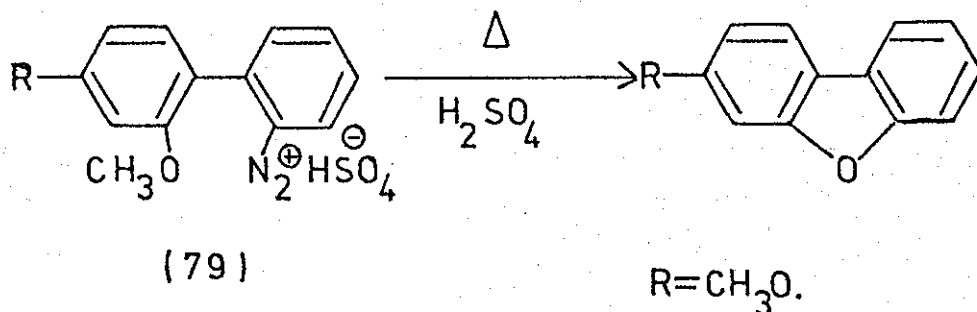


Precedent for the cyclisation exists. For example the diazotisation of 2-amino-2'-methoxybiphenyl in aqueous solution in the presence of either bromide or iodide ions has been reported¹¹¹ to give dibenzofuran in high yields (> 90%) and not the desired 2-halogeno-2'-methoxybiphenyl.

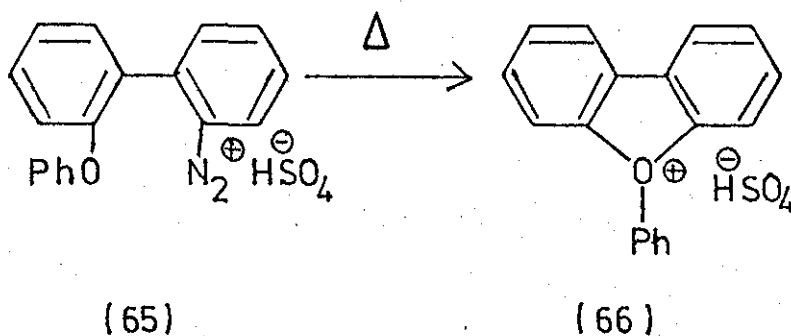
e.g.



Similarly the diazonium salt (79) derived from 2-amino-2'4'-dimethoxybiphenyl gave 3-methoxydibenzofuran in 86% yield, when heated in sulphuric acid.¹¹²



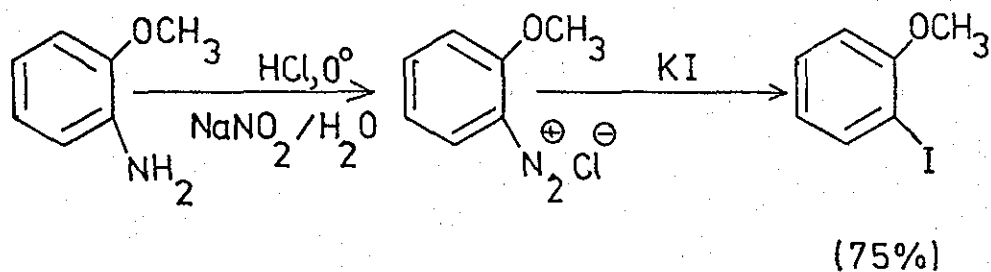
Also, the formation of the O-phenyldibenzofuranium salt (66) from the decomposition of the diazonium salt (65) is further evidence for the occurrence of this type of intramolecular cyclisation.¹⁰³



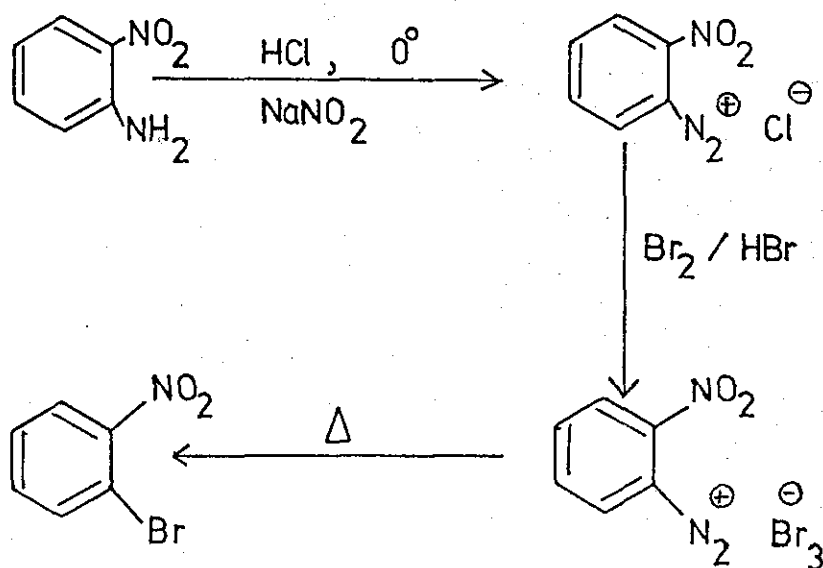
Some aspects of this project have already been briefly examined in these laboratories and the results have been published in a preliminary form.¹⁰⁵ However this work has been reinvestigated here on a more quantitative basis.

The initial step of the reaction sequence leading to the preparation of 2'-methoxybiphenyl-2-yl diazonium fluoroborate was the formation of o-iodoanisole from o-anisidine. This was achieved

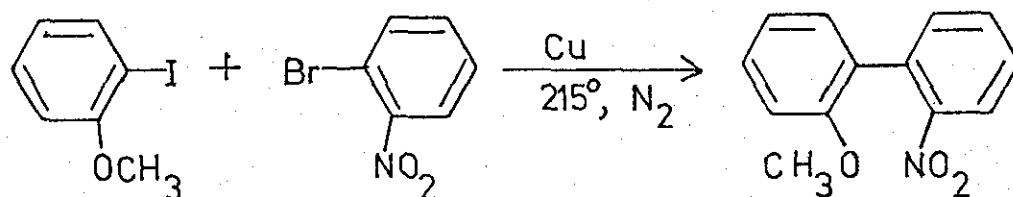
by adding an aqueous solution of potassium iodide to the solution of the diazonium salt obtained by diazotising o-anisidine in dilute hydrochloric acid.



Similarly, o-bromonitrobenzene was prepared by adding a solution of bromine in hydrobromic acid to the diazonium salt solution obtained by diazotising o-nitroaniline in dilute hydrochloric acid. Decomposition of the diazonium perbromide in acetic acid gave o-bromonitrobenzene.

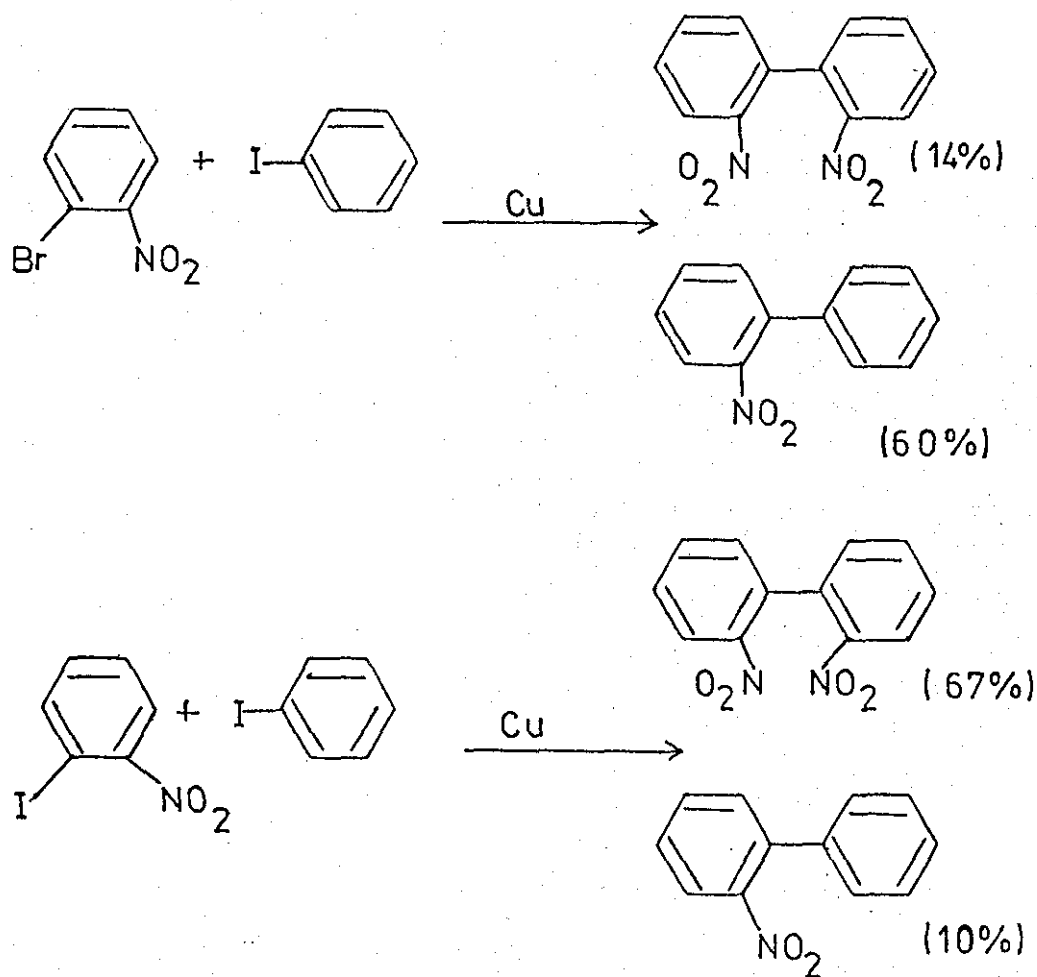


The next step in the sequence involved a mixed Ullmann reaction in which *o*-iodoanisole and *o*-bromonitrobenzene were condensed in the presence of an excess of finely divided copper to give 2-methoxy-2'-nitrobiphenyl, with the elimination of copper halides. ¹¹³



Forrest ¹¹⁴ has shown that in the synthesis of unsymmetrical biaryls, an optimum yield is usually obtained when one of the aryl halides is activated and the other is relatively unreactive. An aryl halogen is strongly activated by the presence of an electronegative group such as a nitro or a methoxycarbonyl group in the ortho position. However, Forrest has also observed that the success of a synthesis depends largely on the choice of the halogen atom, bromo compounds, and to a lesser extent chloro compounds, have been the most useful for the activated components. The corresponding iodo derivatives undergo predominantly self condensation (i.e. formation of symmetrical biaryls), (Scheme 41). However iodo compounds have found general application as the other component, these unreactive components should also lack electronegative groups in the ortho position to obtain the best yields.

In view of this evidence it was surprising that 2-methoxy-2'-nitrobiphenyl was only obtained in low yields from this particular

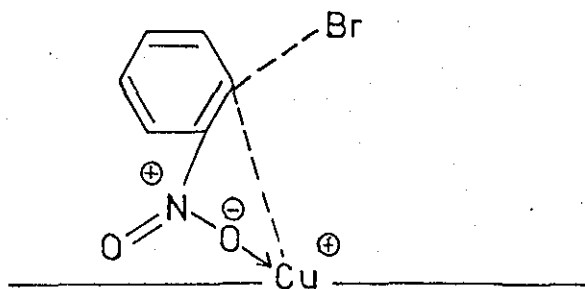


Scheme 4

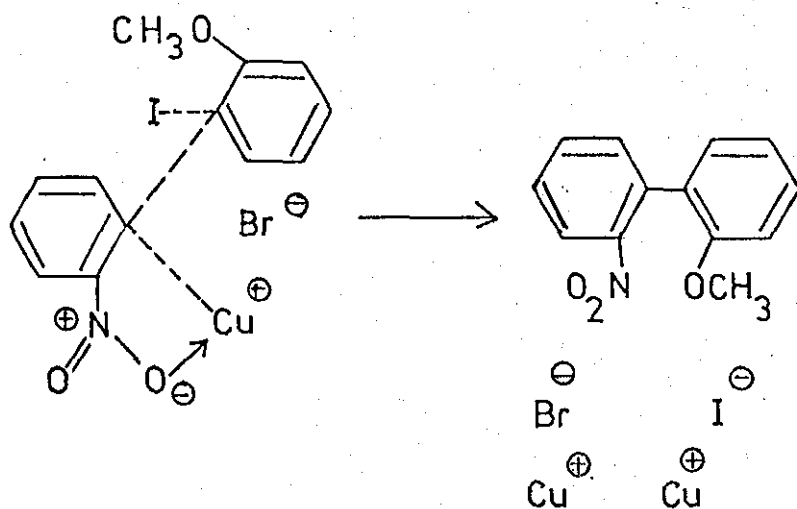
Ullmann reaction. Several attempts were then made to improve the efficiency of the reaction.

The use of activated copper in Ullmann reactions has been reported by Kleiderer and Adams ¹¹⁵ to give improved yields of the biaryl products. The activation is achieved by treating the copper powder with iodine in acetone and subsequently washing with a mixture of acetone and hydrochloric acid, and finally with pure acetone. However, this purification step gave only a slight increase in the yield of 2-methoxy-2'-nitrobiphenyl. Also, the biaryl was obtained in low yields when the reaction was performed

using either dimethylformamide or nitrobenzene as a solvent. The formation of 2-methoxy-2'-nitrobiphenyl was finally achieved in high yield by increasing the efficiency of the stirring of the reaction mixture which after complete addition of the copper powder is a heavy sludge. A copper stirrer, which was designed to fit exactly the geometry of the large reaction vessel, was used to ensure that intimate mixing of the reagents occurred during the long reaction time. This simple expedient enabled us to obtain the biaryl in a reproducible yield of ca. 80%, which is amongst the highest reported for the synthesis of unsymmetrical biaryls.^{116,117} Although a free radical mechanism has been postulated for the Ullmann reaction,^{118a, b} the vast amount of experimental evidence available tends to support an ionic mechanism.^{113,115,119} The reaction is believed to proceed in two stages, the first of which involves nucleophilic attack of metallic copper on the activated carbon-halogen bond to give an aryl-copper complex on the surface of the metal. The particular role of an ortho electronegative group in promoting the reaction may be due to the possibility of chelation as well as electron withdrawal from the aromatic nucleus, which facilitates nucleophilic attack by copper.

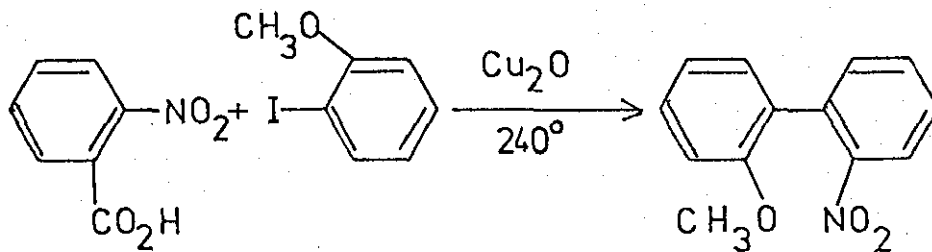


The second stage of the reaction is thought to involve nucleophilic attack of the aryl-copper complex on the second molecule of aryl halide to form the biaryl and copper halide (Scheme 42).

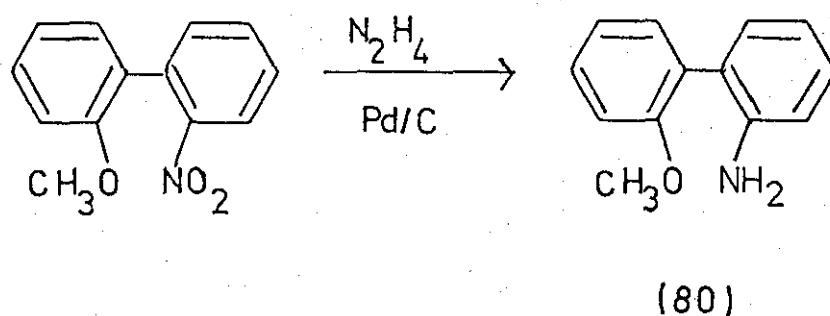


Scheme 42

2-Methoxy-2'-nitrobiphenyl has also been prepared in moderate yields by the decarboxylative coupling of *o*-nitrobenzoic acid and *o*-iodoanisole with copper(I) oxide in quinoline.¹²⁰



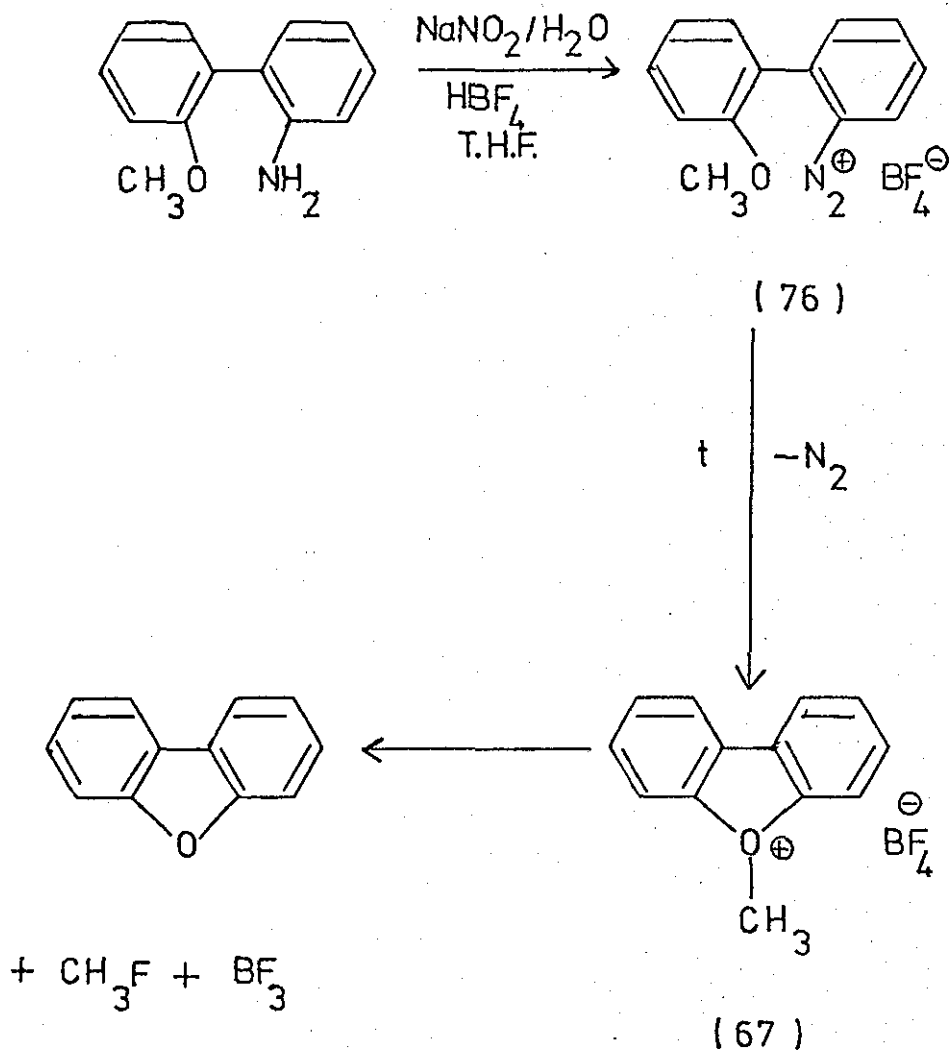
2-Methoxy-2'-nitrobiphenyl was reduced using hydrazine hydrate in the presence of a catalytic quantity of palladium on charcoal to afford 2-amino-2'-methoxybiphenyl (80) in almost quantitative yield. This method,¹²¹ although not widely used, deserves more attention. The only potential disadvantage involves the fact that aromatic halogen is also removed. This property later proved to be beneficial.



In general, the Ullmann reaction is either greatly inhibited or prevented by the presence of substituents, such as amino and hydroxy groups, which provide an alternative path for the reaction of the aryl halide. Thus the direct formation of 2-amino-2'-methoxybiphenyl is not possible by an Ullmann synthesis.

The diazonium salt (76) was obtained in quantitative yield by the diazotisation of 2-amino-2'-methoxybiphenyl in the presence of aqueous fluoroboric acid. The diazonium salt was fairly stable at room temperature and could be stored in vacuo for several days over phosphoric anhydride. However, the salt slowly decomposed when stored for a longer period of time. The identification of the decomposition product as dibenzofuran confirmed that the diazonium salt had collapsed by an intramolecular cyclisation via the intermediate oxonium salt (67), the volatile

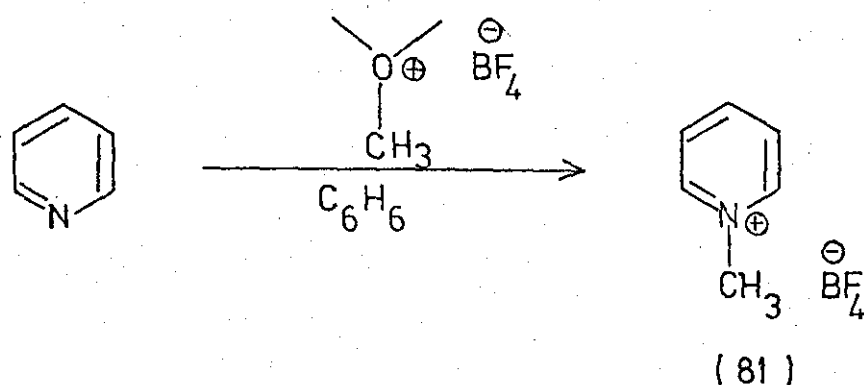
products from the decomposition are presumably nitrogen, boron trifluoride, and methyl fluoride (Scheme 43).



Scheme 43

When the diazonium salt was heated in anhydrous benzene an off-white solid was obtained, which was presumed to be the oxonium salt (67). The ability of this salt to behave as a methylating agent was then established by performing a series of reactions with various lone-pair bases.

The addition of excess of pyridine to the oxonium salt in anhydrous benzene resulted in the formation of N-methylpyridinium fluoroborate in 28% yield.

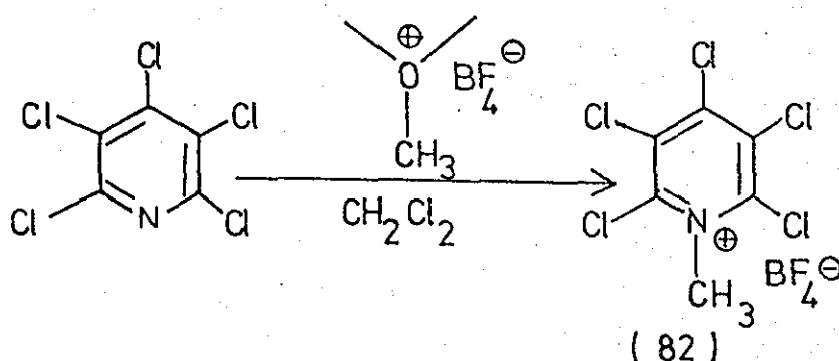


The fluoroborate salt (81) was characterised by conversion to the double picrate salt;¹²² this was simply achieved by the addition of a saturated solution of sodium picrate to an aqueous solution of the pyridinium fluoroborate. However, an improvement in the yield of alkylated product was observed by generating the methylating agent in situ in dry methylene dichloride. Thus a quantitative yield of N-methylpyridinium fluoroborate was obtained when the diazonium salt (76) was decomposed in the presence of pyridine with methylene dichloride as the solvent.

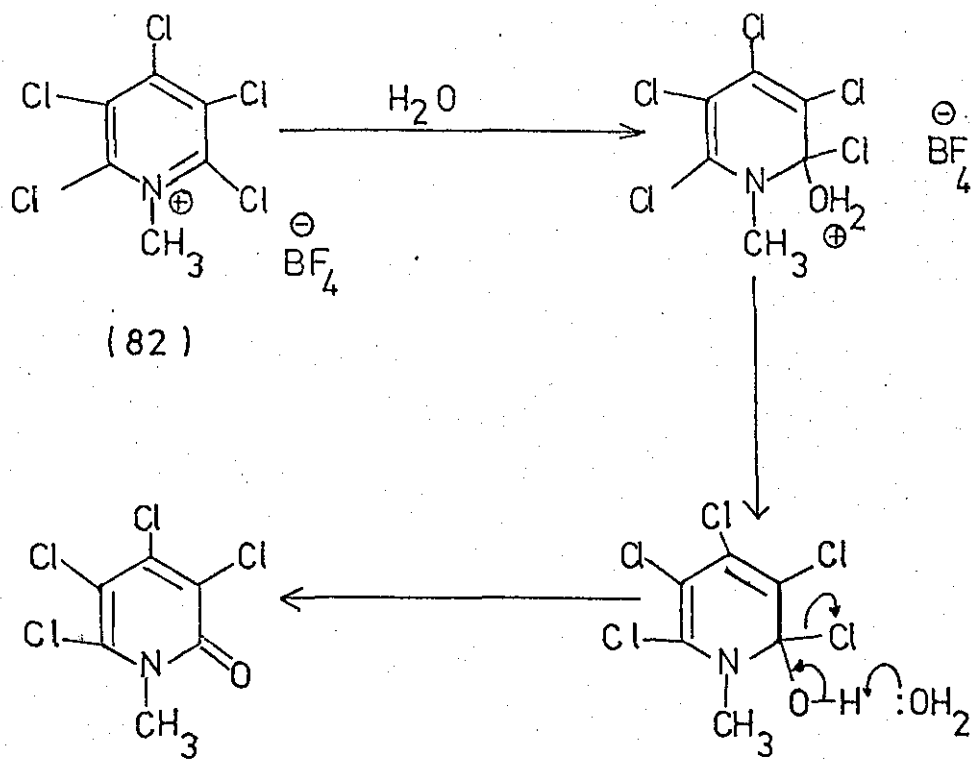
Although pyridine is readily alkylated by conventional reagents, the introduction of halogen atoms on the ring gives rise to a strong inductive effect which considerably reduces the nucleophilicity of

the nitrogen lone pair. Hence the N-alkylation of polyhalogenopyridines is extremely difficult. For example, the reaction of pentachloropyridine with triethyloxonium fluoroborate has been reported¹²³ to give the N-ethylpyridinium fluoroborate in a yield of only 12%.

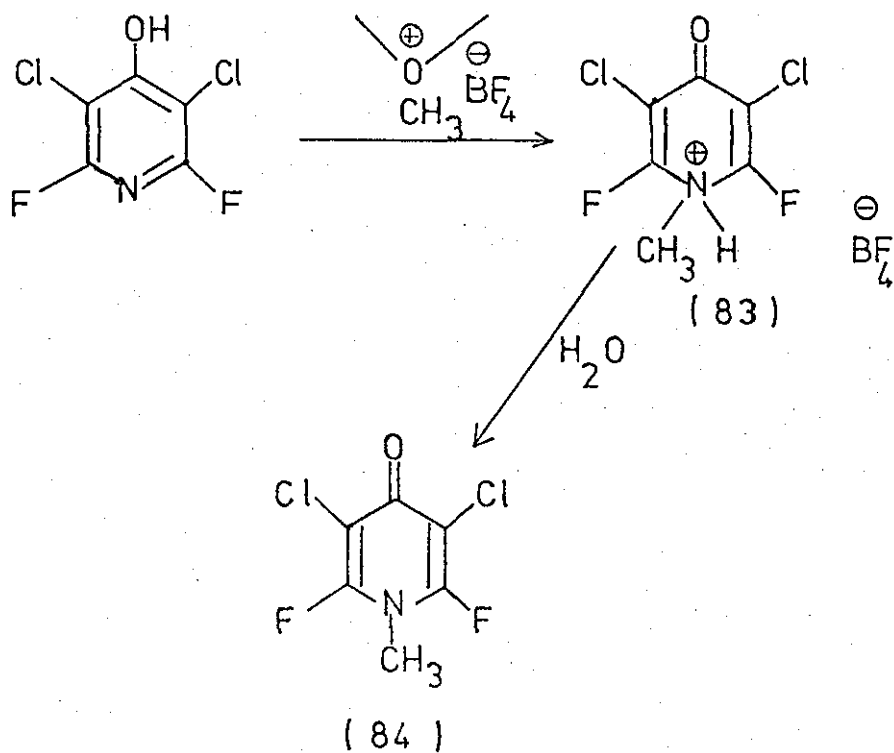
However decomposition of the diazonium salt (76) in methylene dichloride in the presence of an equimolar amount of pentachloropyridine gave N-methylpentachloropyridinium fluoroborate (82) in 30% yield. When the reaction was repeated using a slight excess of the diazonium salt, the yield of alkylated product was improved to 41%.



This reaction is synthetically very useful since the strong inductive effect of the positively charged nitrogen atom activates the 2(6) position to nucleophilic substitution. Thus hydrolysis of the highly reactive pyridinium salt (82) gave N-methyltetrachloro-2-pyridone in high yield. The reaction probably proceeds by the mechanism outlined in Scheme 44 involving the elimination of the elements of hydrogen chloride. Similarly 3,5-dichloro-2,6-difluoro-4-hydroxypyridine was methylated to afford the N-methyl fluoroborate salt (83) in 60% yield. Hydrolysis of this salt gave 3,5-dichloro-2,6-difluoro-N-methyl-4-pyridone (84).

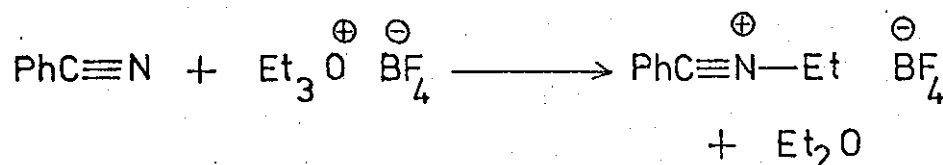


Scheme 44

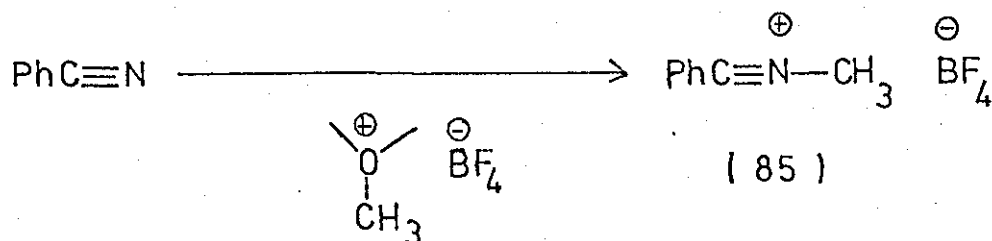


The formation of N-methylpolyhalogenopyridinium salts has been achieved recently in excellent yields by Suschitzky and Ager using the reaction of polyhalogenopyridines with a large excess of methyl fluorosulphate at 90°. ^{123,124} However, a comparison of these results with those obtained using O-methyl dibenzofuranium fluoroborate as the alkylating agent is extremely difficult since no attempt was made to optimise the yield of alkylated products by employing a large excess of the diazonium salt (76).. Suschitzky and Ager, on the other hand, used the alkylating agent as solvent!

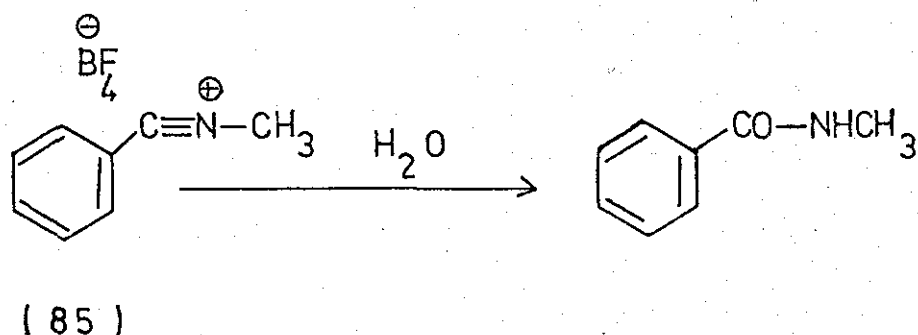
The alkylation of nitriles was achieved initially by Meerwein and his co-workers ⁹⁹ using trialkyloxonium salts. Thus the reaction of benzonitrile with triethyloxonium fluoroborate gave N-ethylbenzotrilium fluoroborate in 64% yield.



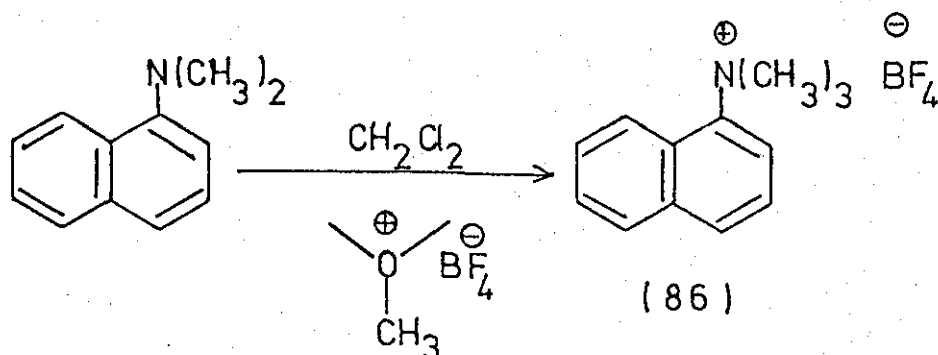
The weakly basic nitrile group is, of course, too unreactive to be alkylated by conventional reagents. The methylation of benzonitrile to N-methylbenzotrilium fluoroborate (85) was achieved in almost quantitative yield using O-methyl dibenzofuranium fluoroborate in methylene dichloride.



The carbon atom of the nitrilium salt is highly activated towards nucleophilic attack and hence hydrolysis of the salt (85) occurred rapidly with the formation of N-methylbenzamide.

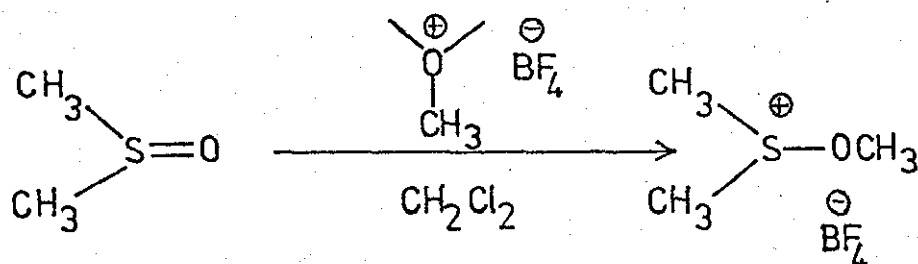


The quaternisation of a sterically hindered amine has also been achieved using O-methyldibenzofuranium fluoroborate. Thus N,N-1-dimethyl-1-naphthylamine was methylated to give a quantitative yield of N,N,N-trimethyl-1-naphthylammonium fluoroborate (86).

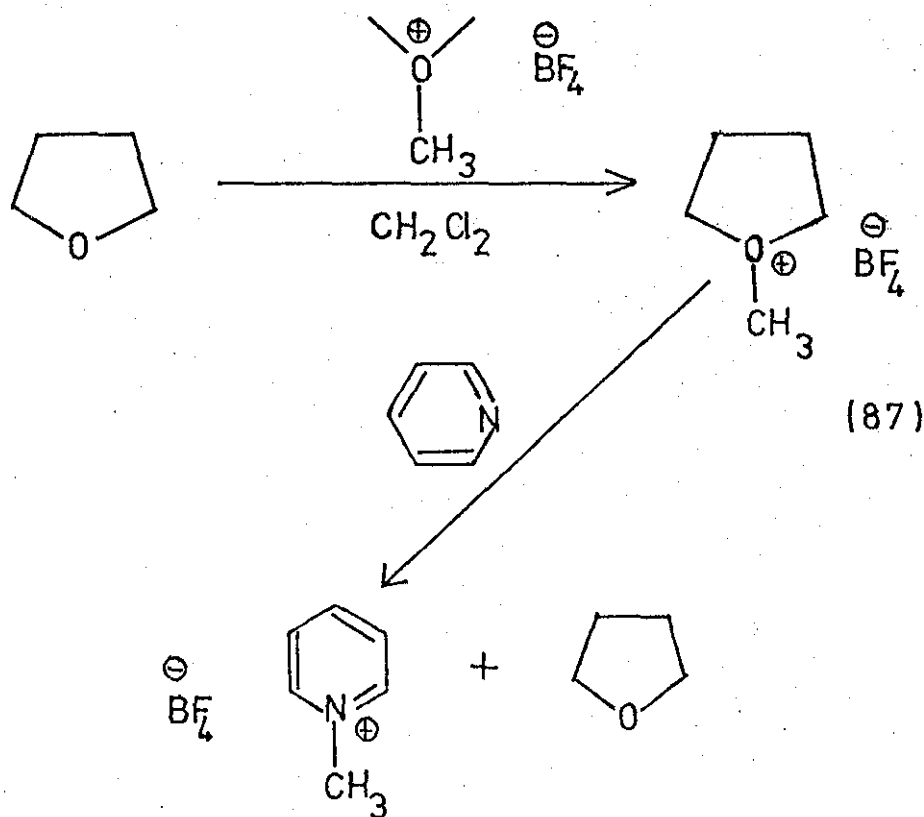


Another important class of functional groups which are not readily alkylated by methyl iodide or dimethyl sulphate, are those containing oxygen atoms with lone pair of electrons. However O-methyldibenzofuranium fluoroborate has been used to methylate several of these weak nucleophiles.

Dimethylsulphoxide was converted to O-methyl dimethylsulphoxonium fluoroborate¹²⁵ in excellent yield.

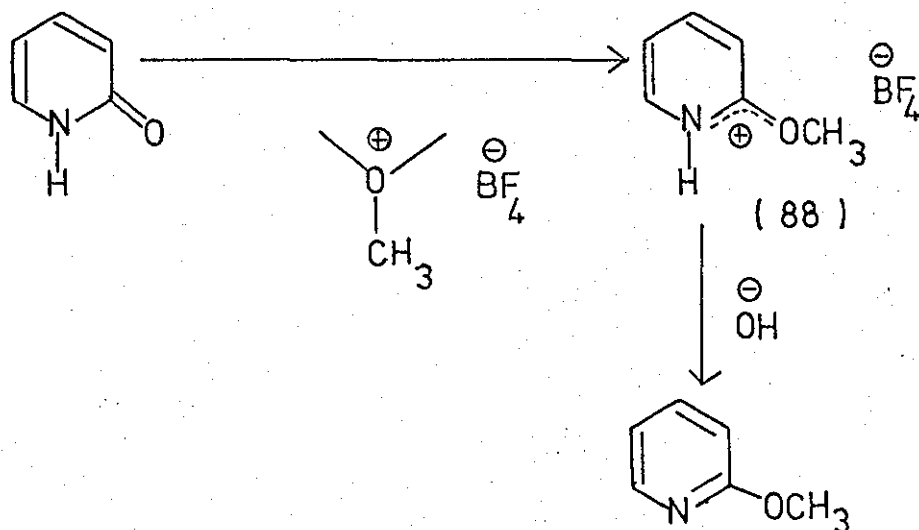


Also, the conversion of tetrahydrofuran into methyltetrahydrofuranium fluoroborate (87) was achieved in 70% yield. The methyltetrahydrofuranium salt is, not unexpectedly, also a powerful methylating agent. The addition of excess of pyridine to the salt in methylene dichloride at room temperature resulted in the immediate formation of N-methylpyridinium fluoroborate in a quantitative yield (Scheme 45).



Scheme 45

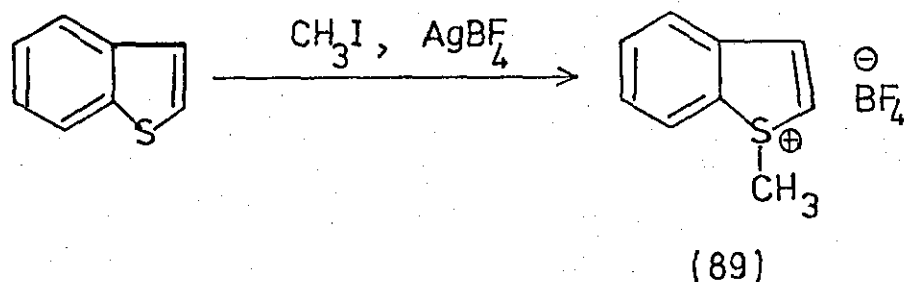
Similarly decomposition of the diazonium salt (76) in the presence of α -pyridone resulted in the formation of the fluoroborate salt (88) which on alkaline hydrolysis gave 2-methoxypyridine (Scheme 46).



Scheme 46

Treatment of α -pyridone with conventional alkylating agents results in the formation of N-alkylated derivatives. For example Rath¹²⁶ obtained yields of 30-85% of N-alkylated products by reacting the potassium salt with ethyl, n-propyl, isopropyl, n-butyl, n-octyl, and benzyl halides. Similarly N-methylation has been effected in good yield with dimethyl sulphate. However the reaction of α -pyridone with diazomethane has been reported¹²⁷ to give 2-methoxypyridine exclusively. These results suggest that the position of alkylation varies with the strength of the leaving group of the alkylating agent. Alkylating agents containing relatively poor leaving groups such as halide anions give N-alkylation, whereas O-alkylation predominates when better leaving groups are employed.

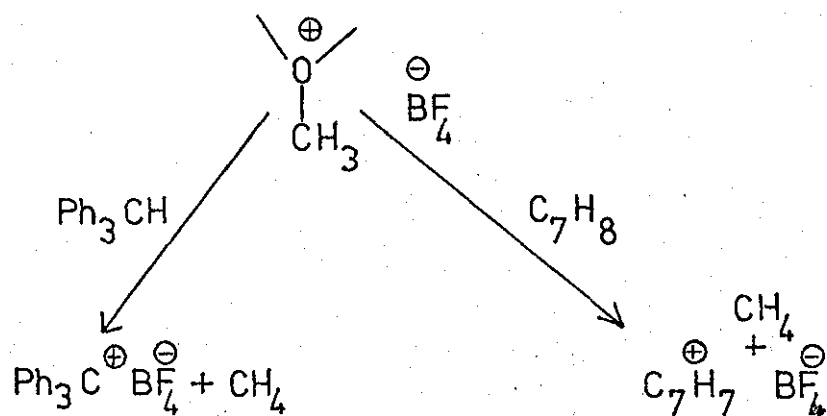
The lone pair electrons of the sulphur atom in benzod**[b]**thiophen forms part of an aromatic sextet and are therefore relatively unavailable for reaction. Hence S-alkylation has only been observed with the more powerful alkylating agents. The S-alkylation of benzo thiophen was first achieved by Acheson and Harrison¹²⁸ using the reaction of an alkyl iodide with benzod**[b]**thiophen in the presence of silver fluoroborate. For example the S-methylated salt, 1-methylbenzod**[b]**thiophenium fluoroborate (89) was isolated in 73% yield.



This salt has also been prepared in 40% yield by the alkylation of benzod**[b]**thiophen with trimethyloxonium fluoroborate.¹²⁸

The reaction of O-methyldibenzofuranium with benzod**[b]**thiophen gave a 77% yield of the S-methylated product (89).

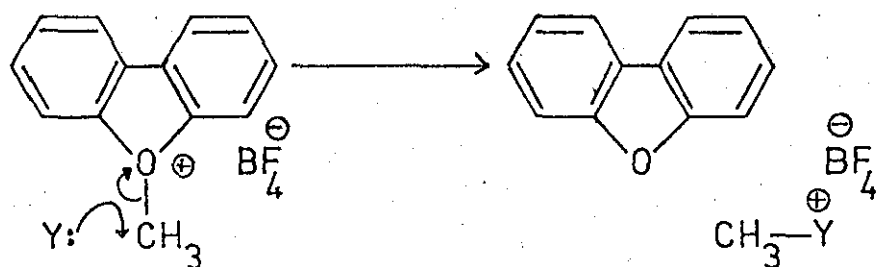
The ability of O-methyldibenzofuranium fluoroborate to act as a hydride-ion acceptor has also been established. The isolation of triphenylmethyl fluoroborate (21%) and tropylium fluoroborate (54%) from the decomposition of the diazonium salt (76) in the presence of triphenylmethane and cycloheptatriene respectively exemplified this property. (Scheme 47).



Scheme 47

Dibenzofuran was obtained in almost quantitative yield from each alkylation reaction.

The methylation reactions can be envisaged as occurring via a nucleophilic displacement by the weak nucleophile on the O-methyldibenzofuranium ion to give the alkylated product and dibenzofuran. Since primary methyl cations are highly unlikely to be formed in any "free" state, the alkylations most probably proceed through an S_N2 displacement (Scheme 48).



Scheme 48

However, an S_N1 ion-pair mechanism may be possible with the more stable secondary or tertiary systems.

Since the diazonium fluoroborate salt (76) could only be stored for 3 or 4 days before decomposition occurred, it was decided to prepare other diazonium salts derived from 2-amino-2'-methoxybiphenyl in an attempt to obtain a more stable precursor to the methylating agent. Thus a series of diazonium salts was prepared using the following non-nucleophilic anions; hexafluorophosphate, hexafluoroantimonate, hexafluoroarsenate, and 2,4,6-tri-nitrobenzenesulphonate. The salts were isolated in high yields (Table 6) by the addition of an aqueous solution of the requisite anion to an aqueous solution of 2'-methoxybiphenyl-2-ylidiazonium chloride.

e.g.

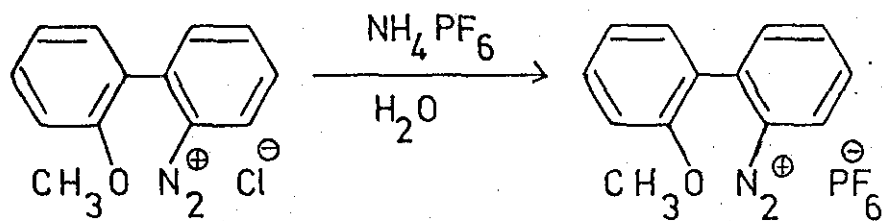


TABLE 6

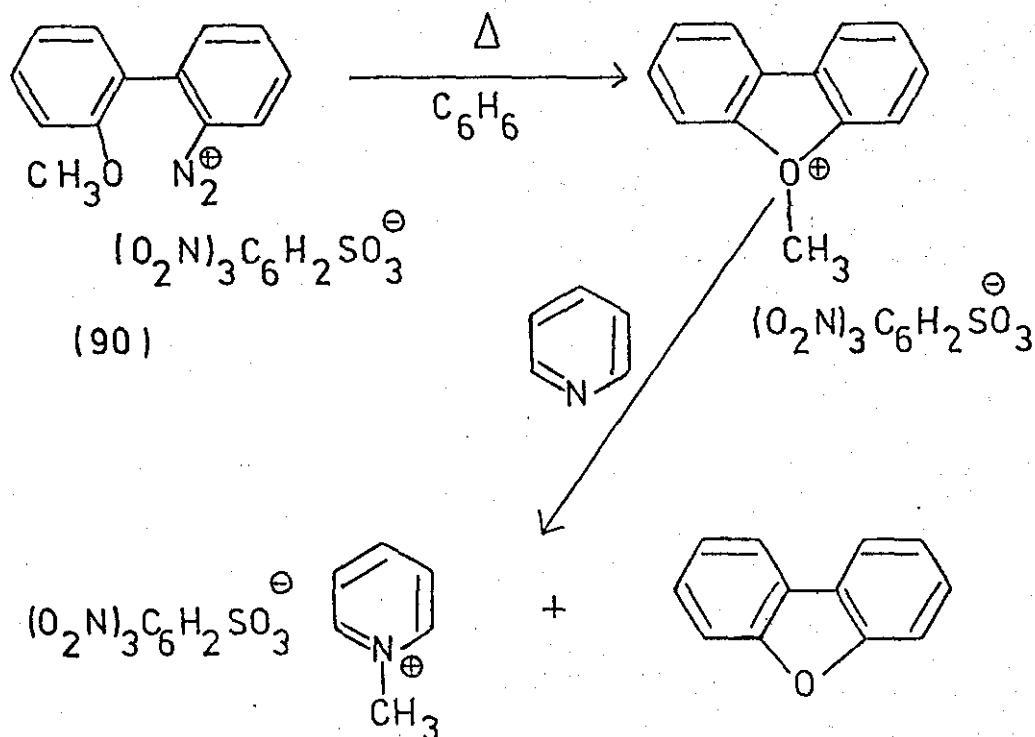
Preparation of 2'-Methoxybiphenyl-2-yl diazonium Salts

<u>Anion</u>	<u>Yield of Diazonium Salt(%)</u>
PF_6^\ominus	75
SbF_6^\ominus	80
AsF_6^\ominus	90
$(\text{O}_2\text{N})_3\text{C}_6\text{H}_2\text{SO}_3^\ominus$	68

However the only diazonium salt to show an improvement in stability over the fluoroborate salt was the 2,4,6-tri-nitrobenzenesulphonate derivative (90). This salt could be stored in vacuo over phosphoric anhydride for 10-12 days. The stability of the various diazonium salts was qualitatively estimated by observing the disappearance of the bond occurring at ca. 2270cm⁻¹ in the infra-red spectrum of each salt, which corresponded to the $\text{N}\equiv\text{N}$ stretch. The ability of the diazonium salts to act as precursors to a methylating agent was established by the formation, in quantitative yield, of the corresponding N-methylpyridinium salts when each diazonium salt was decomposed in the presence of pyridine.

Since the diazonium 2,4,6-tri-nitrobenzenesulphonate was more stable than the corresponding fluoroborate derivative it was possible that the oxonium salt derived from this diazonium salt (90) would also be relatively stable. When the diazonium salt was

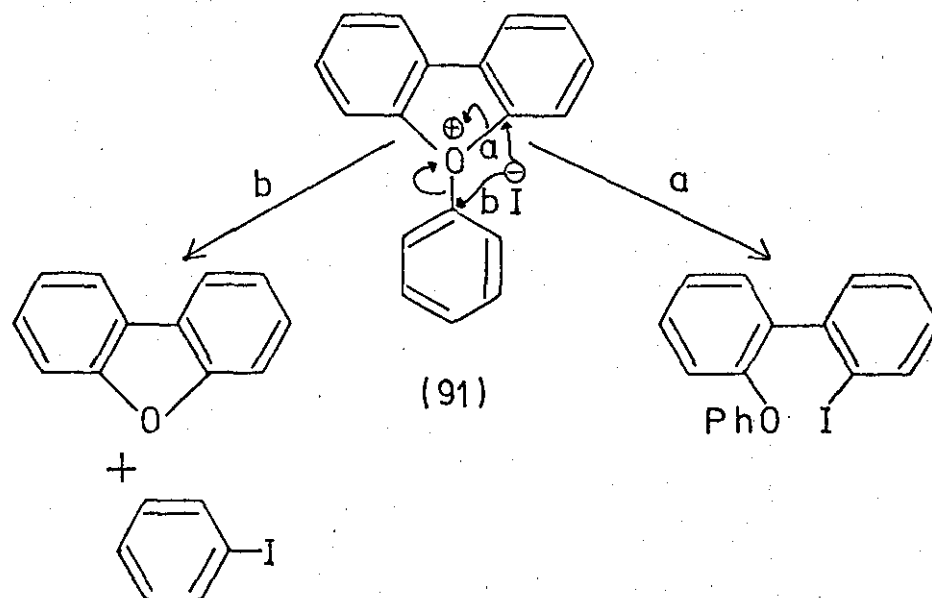
decomposed in anhydrous benzene an off-white solid was obtained whose infra-red spectrum was similar to that of sodium 2,4,6-tri-nitrobenzenesulphonate. The fact that this isolated product was capable of alkylating was established by the formation of N-methylpyridinium 2,4,6-tri-nitrobenzenesulphonate in 44% yield when the salt was added to an excess of pyridine in methylene dichloride.



Also the high melting point ($> 300^\circ$ with decomposition) of the isolated salt indicated that the product was not methyl 2,4,6-tri-nitrobenzenesulphonate (m.p. $180-1^\circ$). However, the off-white solid could not be fully characterised due to its complete insolubility in the available $^1\text{H.n.m.r.}$ solvents.

In view of the results obtained on the decomposition of O-methyldibenzofuranium fluoroborate it was decided to reinvestigate the work of Nesmeyanov¹⁰³ on the thermal decomposition of

O-phenyldibenzofuranium iodide (91). Nesmeyanov¹⁰³ claimed that the pyrolysis of this salt resulted in the formation of only 2-phenoxy-2'-iodobiphenyl, via nucleophilic attack of the iodide ion on the dibenzofuran moiety of the compound (Scheme 49, route a). O-Phenyldibenzofuranium iodide was prepared by essentially the same reaction sequence as that described by Nesmeyanov, however, subsequent pyrolysis of the salt at 150°C in a tube sealed under vacuum gave a mixture of three products. The major component, isolated in 64% yield, was 2-phenoxy-2'-iodobiphenyl. The other products were dibenzofuran (15%) and iodobenzene (18%), both derived from attack of the iodide ion on the phenyl group (Scheme 49, route b).



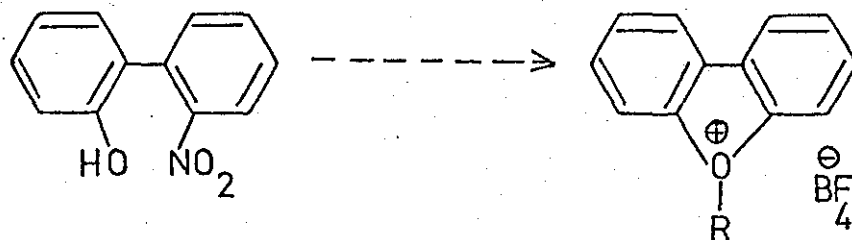
Scheme 49.

The opening of the dibenzofuran in preference to the loss of the phenyl group is surprising in view of the fact that presumably more

resonance energy is lost in going to the biaryl. However, the fact that severe reaction conditions are necessary in order to bring about this reaction may result in the almost statistical breaking of the aryl-oxygen bonds.

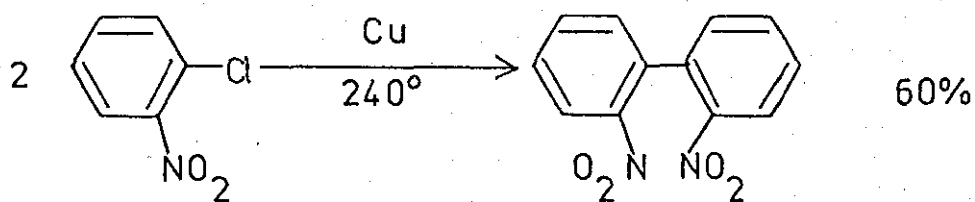
The strong electrophilic character of O-methyldibenzofuranium fluoroborate suggested that O-alkyldibenzofuranium salts should generally behave as powerful alkylating agents. The preparation of such alkylating agents is synthetically very desirable since there are few reagents available for the introduction of the higher alkyl groups.

Thus by using the same reaction sequence as that described for the preparation of the methylating agent, a series of alkylating agents could be envisaged using 2-alkoxy-2'-nitrobiphenyls as starting materials. The synthetic utility of this scheme would be further enhanced by the fact that all of these ethers can be prepared from 2-hydroxy-2'-nitrobiphenyl. Hence a wide variety of powerful alkylating agents should be preparable from the same compound.

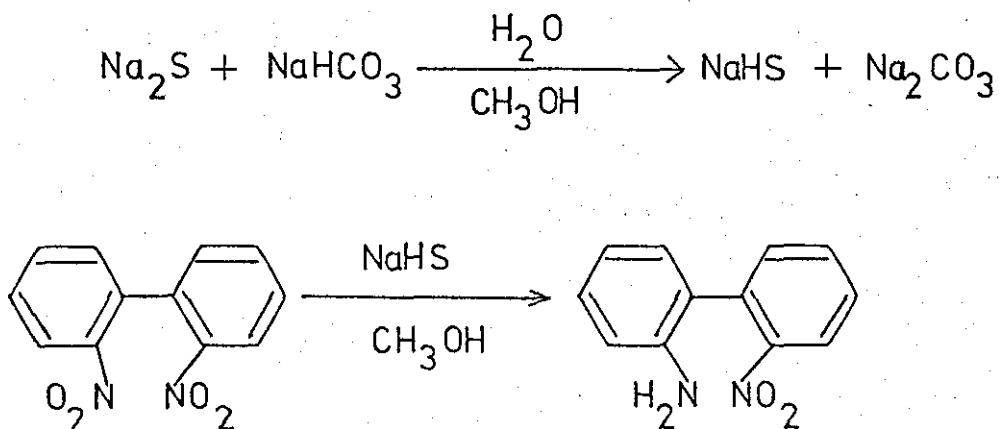


A number of possible routes to the key intermediate were considered.

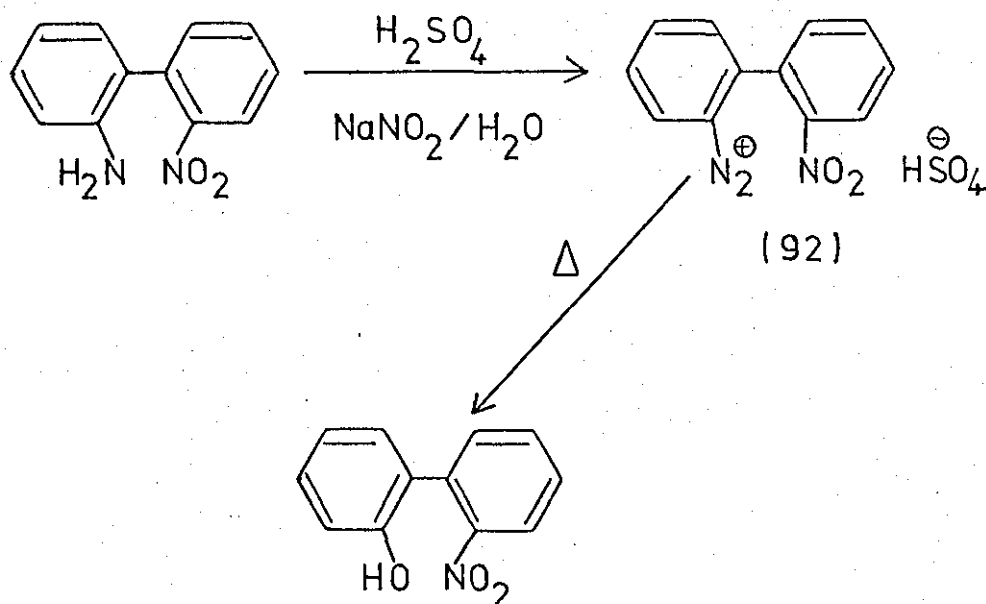
One approach involved the formation of 2,2'-dinitrobiphenyl by the self-condensation of *o*-chloronitrobenzene in the presence of an excess of copper powder.¹²⁹



Selective reduction of one of the nitro groups of 2,2'-dinitrobiphenyl was achieved using freshly prepared sodium hydrogen sulphide¹³⁰ to afford 2-amino-2'-nitrobiphenyl¹³¹ in 83% yield.



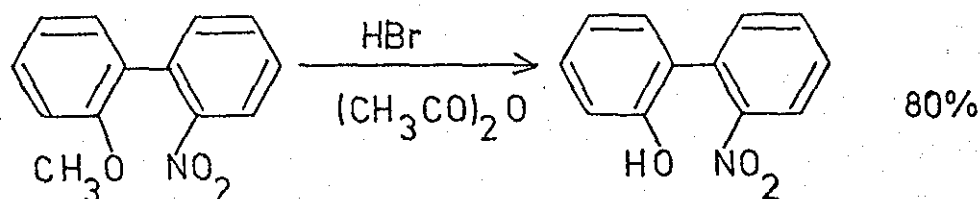
Diazotisation of 2-amino-2'-nitrobiphenyl in the presence of sulphuric acid gave the diazonium salt (92), which decomposed when heated in sulphuric acid to afford 2-hydroxy-2'-nitrobiphenyl (Scheme 50).



Scheme 50.

However, although several variations in the experimental conditions were employed, the yield of this reaction was always very low (<10%) and hence this approach was abandoned. These results confirm a previous report.¹³²

The preparation of 2-hydroxy-2'-nitrobiphenyl has also been reported by the demethylation of 2-methoxy-2'-nitrobiphenyl using hydrobromic acid in acetic anhydride.¹³²

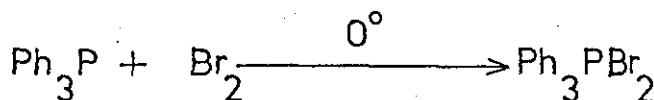


However, in our hands, this reaction gave not only 2-hydroxy-2'-nitrobiphenyl but also a second product which was assigned on the basis of mass spectrometry and n.m.r. evidence as 3-bromo-2-hydroxy-2'-nitrobiphenyl. The formation of the bromophenol is perhaps not surprising in view of the fact that it is extremely difficult to obtain constant boiling hydrobromic acid which is free from bromine. The mass spectrum of the phenol obtained indicated the presence of one bromine atom. Conversion of the phenol into 2-ethoxy-2'-nitrobiphenyl gave a product whose ¹H.n.m.r. spectrum showed two quartets at 6.05 τ and 6.08 τ . The deshielding of the methylene resonance from its normal position (6.08 τ) was evidently due to the presence of the ortho-bromine atom in the impurity. The reaction sequence leading to the formation of the alkylating agent may be continued using this mixture of 2-hydroxy-2'-nitrobiphenyl and the brominated derivative, since the potency of the alkylating agent should not be diminished by having 4-bromodibenzofuran as the leaving group. In addition the reduction of the nitro-group using hydrazine hydrate and palladium on charcoal effectively removes the unwanted bromine atom. On the other hand a route to pure 2-hydroxy-2'-nitrobiphenyl was necessary, if only to obtain pure samples of the new 2-alkoxy-2'-nitrobiphenyls. A number of alternative methods of

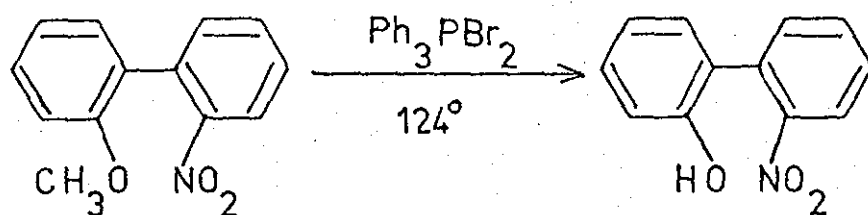
dealkylating 2-methoxy-2'-nitrobiphenyl were therefore investigated. Alkaline hydrolysis of the biphenyl with potassium hydroxide in digol gave only polymeric material and an attempted cleavage of the alkyl aryl ether using aluminium chloride resulted only in the recovery of the starting material. No dealkylation was observed using hydroiodic acid as the demethylating agent in acetic anhydride.

The formation, in high yields, of alkyl bromides in the reaction of dialkyl and phenyl ethyl ethers with triphenyldibromophosphorane has been reported recently by Anderson and Freenor.¹³³ These results implicated the use of this compound as a possible demethylating agent for 2-methoxy-2'-nitrobiphenyl. It was reasoned that triphenyldibromophosphorane would not give rise to the bromonium ion and hence the dealkylated product in this reaction should be free from the brominated impurity noted previously.

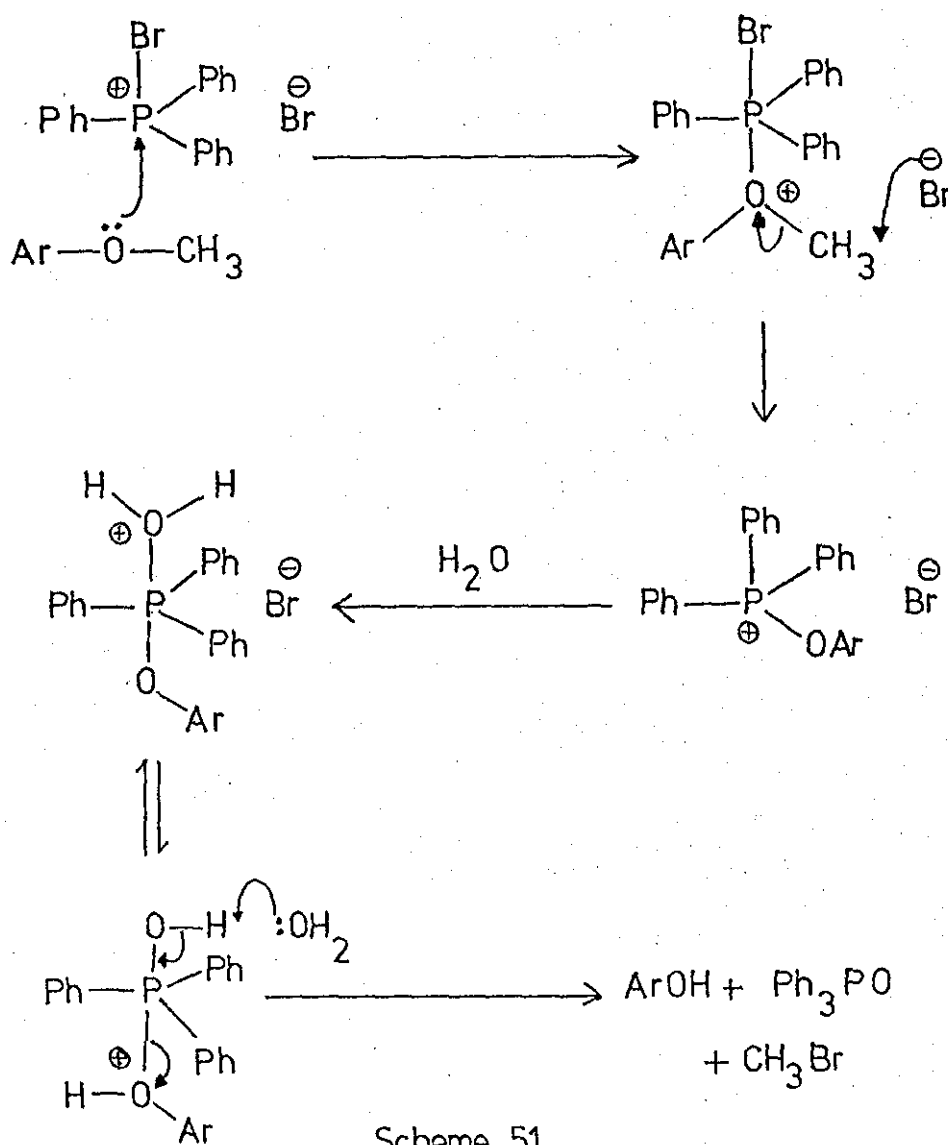
Triphenyldibromophosphorane was generated using the method of Schaefer and Higgins¹³⁴ by the addition of bromine to a slight excess of triphenylphosphine in benzonitrile.



Subsequent addition of the ether to the preheated reaction mixture gave after an aqueous work-up a 55% yield of pure 2-hydroxy-2'-nitrobiphenyl.

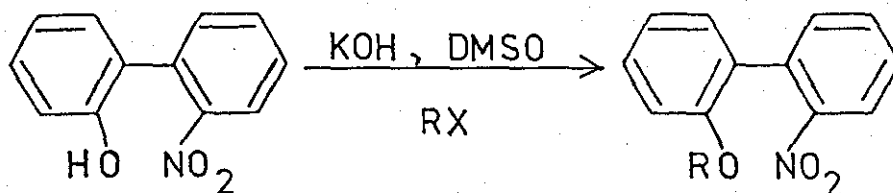


The formation of the phenolic compound can be envisaged as occurring in the following way (Scheme 51).



Scheme 51

The conversion of 2-hydroxy-2'-nitrobiphenyl into various 2-alkoxy-2'-nitrobiphenyls was then achieved by the addition of the appropriate alkyl halide to the phenol in dimethyl sulphoxide containing freshly powdered potassium hydroxide.¹³⁵



The following results were obtained (Table 7).

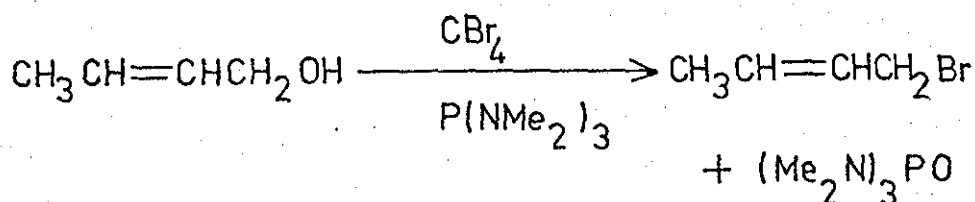
TABLE 7.

The Preparation of 2-Alkoxy-2'-nitrobiphenyls

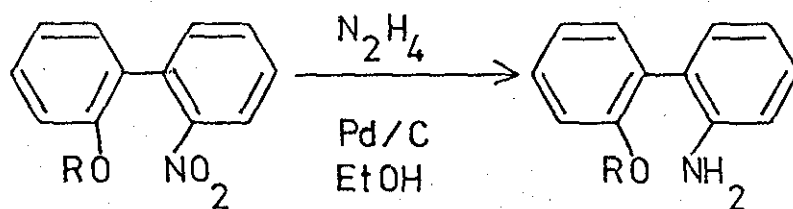
<u>Alkyl Group, R.</u>	<u>Halide, X</u>	<u>Yield of Alkyl Aryl Ether(%)</u>
Methyl	Iodide	81
Trideuteriomethyl	Iodide	96
Ethyl	Iodide	97
<u>n</u> -Propyl	Bromide	94
Isopropyl	Bromide	94
<u>n</u> -Butyl	Bromide	79
Allyl	Bromide	93
Crotyl	Bromide	94
Benzyl	Bromide	68
* Neopentyl	Bromide	0
* 1-Methylheptyl	Chloride	0

* These compounds were prepared by the dealkylation of the corresponding alkoxy-tris(dimethylamino)phosphonium hexafluorophosphates (See Part 1).

Crotyl bromide was prepared according to the method of Downie⁷ by the addition of an ethereal solution of phosphorous trisdimethylamide to a solution of crotyl alcohol and carbon tetrabromide in ether at low temperature.



The 2-alkoxy-2'-nitrobiphenyls were subsequently reduced with hydrazine hydrate in the presence of palladium on charcoal catalyst to afford a series of 2-alkoxy-2'-aminobiphenyls (Table 8).



Thus a series of precursors to alkylating agents has been prepared from 2-hydroxy-2'-nitrobiphenyl. The O-trideuteriomethyl-dibenzofuranium salt is synthetically very useful. For example, trideuteriomethylation using deuteriated trimethyloxonium fluoroborate would be very expensive since a compound containing nine deuterium atoms would have to be prepared. Similarly trideuteriomethyl fluorosulphate would be prepared from bis(trideuteriomethyl)sulphate.

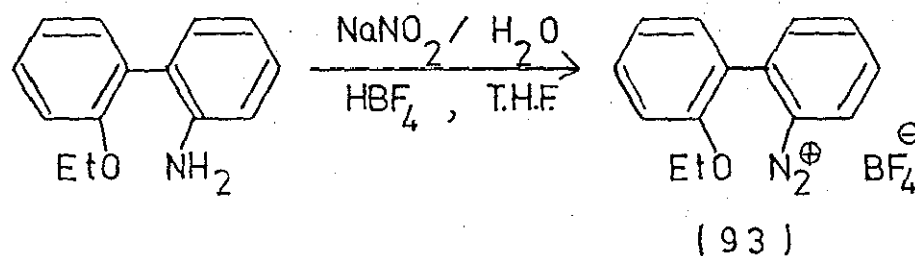
TABLE 8

Preparation of 2-Alkoxy-2'-aminobiphenyls

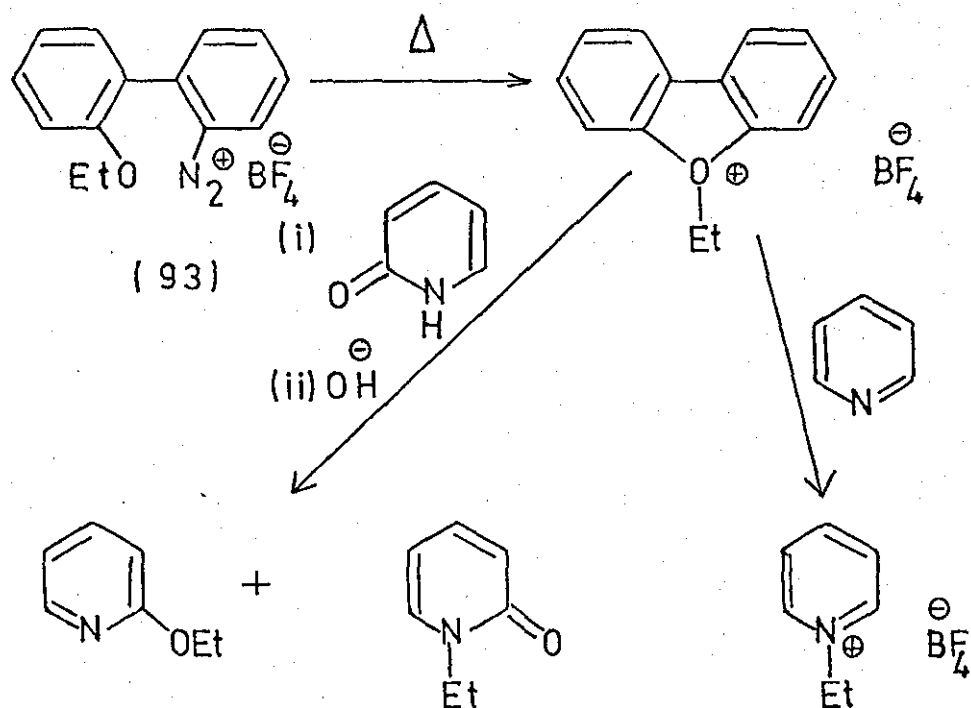
<u>Alkyl Group, R</u>	<u>Yield of 2-alkoxy-2'-aminobiphenyl</u> (%)
Methyl	80
Trideuteriomethyl	78
Ethyl	80
<u>n</u> -Propyl	55
Isopropyl	87
<u>n</u> -Butyl	90
Neopentyl	83
1-Methylheptyl	87
Benzyl	95

The sequence was continued for the ethyl and isopropyl derivatives.

Diazotisation of 2-amino-2'-ethoxybiphenyl in the presence of fluoroboric acid gave the diazonium salt (93) in 90% yield.

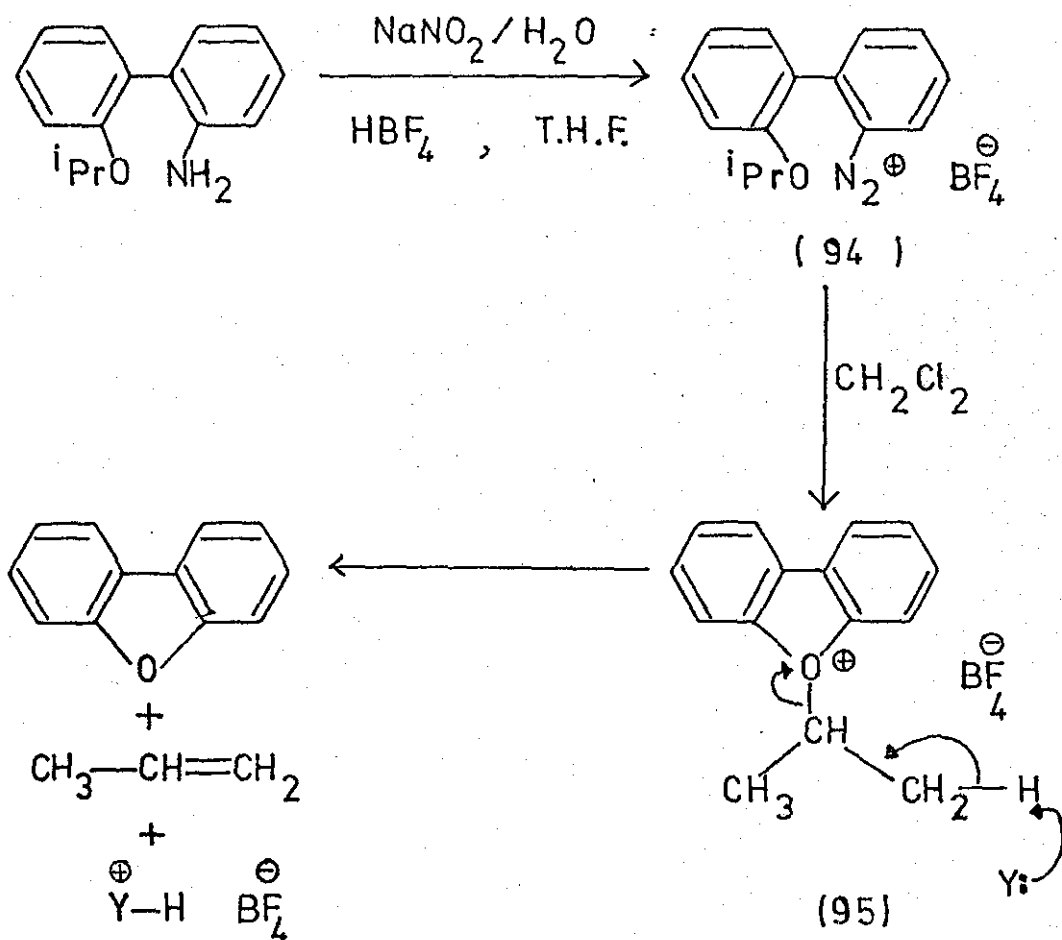


Decomposition of this salt in the presence of pyridine in methylene dichloride gave a quantitative yield of N-ethylpyridinium fluoroborate. Similarly the reaction of the diazonium salt with α -pyridone resulted in the formation of 2-ethoxypyridine (27%) and N-ethyl-2-pyridone (7%) (Scheme 52).



Scheme 52

The preparation of the diazonium salt (94) from 2-amino-2'-isopropoxybiphenyl was achieved in 82% yield. However, attempts at the alkylation of both pyridine and α -pyridone with the diazonium salt (94) were unsuccessful and starting material was recovered on each occasion. The isolation of dibenzofuran from the reactions confirmed that the diazonium salt had decomposed by an intramolecular cyclisation to form the O-isopropylidibenzofuranium fluoroborate (95). The apparent failure of this salt to alkylate the substrate used could be due to the salt collapsing to give dibenzofuran by loss of a proton and propene (Scheme 53).



Scheme 53

Alternatively the salt (95) could decompose to give dibenzofuran by an $\text{S}_{\text{N}}1$ mechanism involving the loss of the isopropyl cation, which subsequently loses a proton to afford propene. The possibility that decomposition of the salt is occurring via a tight ion-pair must also be considered. For example, Vowinkel¹³⁶ has recently reported that the alkylation of phenol and acetic acid using O-(1-methylheptyl)-N,N-dicyclohexylisourea involved a tight ion-pair. No choice between these explanations can be made at this stage. Clearly an investigation of the reactions of the 2-neopentyloxybiphenyl-2'-yldiazonium salts and of the 2-(1-methylheptyloxy)-analogue should provide useful evidence on this point.

Experimental

General The general details were as described in Part 1. All diazonium salts were handled with wooden applicator sticks. All alkylation reactions using O-alkyldibenzofuranium salts were carried out in glassware dried overnight at 120°. Methylene dichloride was kept over molecular sieve (4A) and distilled from phosphoric anhydride. Dimethylsulphoxide was kept over molecular sieve (4A) and distilled from calcium hydride.

1. Preparation of o-Iodoanisole.

o-Anisidine (186g) was dissolved in a mixture of conc. hydrochloric acid (360ml) and water (360ml). The hydrochloride solution, so formed, was cooled to 0° by means of an ice-salt mixture, and a solution of sodium nitrite (129g) in water (300ml) added with stirring, maintaining the temperature below 5°. After a further 15 minutes a solution of potassium iodide (375g) in water (600ml) was slowly added to the cold diazonium salt solution, the stirring was continued at room temperature for another 1 hour to ensure that the diazonium salt had completely decomposed.

The solution was made alkaline by the addition of sodium hydroxide solution (1300ml, 10%). A black oil separated out which was extracted into ether (3 x 250ml), the combined ether layers were successively washed with saturated aqueous solutions of sodium bicarbonate, sodium thiosulphate, and sodium metabisulphite, and then dried over anhydrous magnesium sulphate. Removal of solvent gave a black oil which on distillation gave o-iodoanisole (242-277g, 70-82%); b.p. 86° at 1.5mm (lit.¹³⁷ b.p. 237-8° at 760mm).

V_{\max} 2940, 2840, 1585, 1475, 1435, 1295, 1280,
 1250, 1055, 1020, and 750cm⁻¹.

2. Preparation of o-Bromonitrobenzene.

o-Nitroaniline (114g) was dissolved in concentrated hydrochloric acid (240ml) and crushed ice (201g) was added. The hydrochloride solution was cooled to 0° and a solution of sodium nitrite (69g) in water (120ml) added with stirring, maintaining the temperature below 5°. The orange solution was filtered to remove any insoluble material.

A solution of bromine (195g) in hydrobromic acid (405ml, 48% aqueous solution) was slowly added to the diazonium salt solution at 0°, the simultaneous addition of crushed ice helped to maintain the low temperature. The orange precipitate, the diazonium perbromide, was filtered off and carefully added in small portions to glacial acetic acid (180ml) at 100°. The hot solution was poured into water (4l) and a pale yellow solid was liberated, which was filtered off and recrystallised from ethanol to give o-bromonitrobenzene (135g., 80%) m.p. 42-3° (lit., ¹³⁸ m.p. 42°) ν max. 3100, 1590, 1530, 1470, 1350, 1040, 850, 780, 730, 700 and 640cm⁻¹.

3. Preparation of 2-Methoxy-2'-nitrobiphenyl.

Copper powder (100g) was added in portions over a period of about 1 hour to a well-stirred solution of o-iodoanisole (82.6g, 0.35mole) and o-bromonitrobenzene (83g, 0.413mole) maintained at 200° in a nitrogen atmosphere. The stirring and heating of the reaction mixture was continued for an additional 2½ hours after the addition of copper was completed. The copper powder lost its shiny appearance as the reaction proceeded and the mixture became quite viscous. After cooling,

the reaction mixture was exhaustively extracted with ether. The solvent was removed and gave an orange oil which was placed on a column of alumina. Elution with 5% ether-light petroleum gave 2-methoxy-2'-nitrobiphenyl (58g-64.2g., 70-77%) as a yellow solid; m.p. 81-2° (from methanol) (lit., ¹¹³m.p. 83°); ¹H.n.m.r. τ (CDCl₃) 2.0 - 3.3(m., 8H) and 6.34(s., 3H).

V_{\max} 2940, 2840, 1615, 1530, 1500, 1360, 1250, 1125, 1025, 760, and 745cm⁻¹.,

Mass Spectrometry: M^+ = 229.

4. Demethylation of 2-Methoxy-2'-nitrobiphenyl .

Hydrobromic acid (25ml, 48% aqueous solution) was slowly added to a solution of 2-methoxy-2'-nitrobiphenyl (20g., 0.09mole) in acetic anhydride (25ml) at 0°. The solution was heated under reflux for 48 hours and gave a dark brown viscous solution which was diluted by the addition of water (250ml). The reaction mixture was extracted with ether (3 x 250ml) and the combined ether layers were washed with 10% sodium hydroxide solution. The aqueous phase was acidified with concentrated hydrochloric acid and extracted with ether. Removal of the solvent, after drying with anhydrous magnesium sulphate, gave a brown oil which slowly solidified on standing. This solid (16.3g, 91%) m.p. 132-8° was shown to be a mixture of 2-hydroxy-2'-nitrobiphenyl and 3-bromo-2-hydroxy-2'-nitrobiphenyl by mass spectrometry and ¹H.n.m.r. spectroscopy.

5. Reaction of Triphenyldibromophosphorane with 2-methoxy-2'-nitrobiphenyl.

Bromine (4.3g) was slowly added to a stirred solution of

triphenylphosphine (8.6g) in benzonitrile (100ml, dry) at 0° under a nitrogen atmosphere. When the addition of bromine was ca. one-half complete, a colourless crystalline precipitate of triphenyldibromophosphorane formed. After the complete addition of bromine, the reaction mixture was heated to 110° and 2-methoxy-2'-nitrobiphenyl (5g) was added in one portion. The solution was heated to 125° and maintained at that temperature for 12 hours with stirring. After cooling to room temperature, an aqueous solution of acetone (100ml, 50%) was added and the resulting two-phase system was well stirred for 4 hours at ca. 60°. The reaction mixture was then made alkaline with 10% sodium hydroxide solution. The aqueous layer was separated from the organic phase and acidified with concentrated hydrochloric acid before being extracted with ether. Removal of the solvent, after drying over anhydrous magnesium sulphate gave 2-hydroxy-2'-nitrobiphenyl (2.52g, 55%) m.p. 139-140° (from benzene) (lit.,¹³² m.p. 140°).

ν_{\max} 3430, 1620, 1530, 1510, 1460, 1370, 1340, 1310, 1265, 1200, 1115, 860, 835, 790, 775, and 735 cm.^{-1}

Mass spectrometry: $M^+ = 215$.

Preparation of 2-Alkoxy-2'-nitrobiphenyls .

A series of 2-alkoxy-2'-nitrobiphenyls were prepared from 2-hydroxy-2'-nitrobiphenyl by a procedure identical to that employed for the preparation of 2-ethoxy-2'-nitrobiphenyl which is described in detail.

6. Preparation of 2-Ethoxy-2'-nitrobiphenyl.

Dimethylsulphoxide (100ml, dry) was added to powdered potassium hydroxide (2.24g, 0.04mole) and the mixture was stirred for 30 minutes. 2-Hydroxy-2'-nitrobiphenyl (2.15g, 0.01 mole) was then added and the mixture was stirred for another 30 minutes and gave a green solution. Ethyl iodide (3.12g, 0.02mole) was added and the mixture was stirred for a further 2 hours before water (100ml) was added. The mixture was extracted with ether (2 x 100ml) and each extract was washed with water (100ml). The combined ether layers were dried over $MgSO_4$. Removal of solvent gave a colourless oil which was placed on a column of alumina (100g), elution with 10% ether-light petroleum gave 2-ethoxy-2'-nitrobiphenyl (2.26g., 97%); m.p. $84-5^\circ$ (from light petroleum b.p. $60-80^\circ$) (lit., $^{139}m.p.82-3^\circ$);

$^1H.n.m.r.$ $\tau(CDCl_3)$ 2.0-3.25 (m., 8H); 6.08 (q., 2H); and 8.8(t., 3H).

ν_{max} 2980, 2940, 2880, 1615, 1590, 1530, 1500, 1475, 1360, 1250, and $760cm^{-1}$.

λ_{max} 214(log ϵ , 4.37); 240 (4.11); and 272 (3.79)n.m.,

Mass spectrometry: $M^+ = 243$.

7. Preparation of 2-Nitro-2'-n-propoxybiphenyl.

Reaction as in experiment 6 using 2-hydroxy-2'-nitrobiphenyl (2.15g., 0.01mole), potassium hydroxide (2.24g., 0.04mole) and n-propyl bromide (2.4g., 0.02mole) in dimethylsulphoxide (100ml) gave 2-nitro-2'-n-propoxybiphenyl (2.42g. 94%); m.p. $71-2^\circ$ (from light petroleum b.p. $60-80^\circ$).

(Found: C, 70.2; H, 5.9; N, 5.3%, M, (mass spectrometry)257

$C_{15}H_{15}NO_3$ requires C, 70.05; H, 5.85; N, 5.45%; M,257):

$^1H.n.m.r.$ τ ($CDCl_3$) 2.0-3.2(m., 8H); 6.15 (t., 2H, $J = 6Hz$);
8.37 (sextet, 2H, $J = 8Hz$); and 9.2 (t., 3H, $J = 6Hz$).

V_{max} 2970, 2940, 2880, 1615, 1530, 1500, 1470, 1360,
1250, 975, and $755cm^{-1}$.

λ_{max} 214 ($\log \epsilon$ 4.43); 240(4.08); and 272(3.77)n.m. .

8. Preparation of 2-Isopropoxy-2'-nitrophenyl .

Reaction as in experiment 6 using 2-hydroxy-2'-nitrophenyl
(2.15g., 0.01 mole), potassium hydroxide (2.24g., 0.04mole)
and isopropyl bromide (2.44g., 0.02 mole) in dimethylsulphoxide
(100ml) gave 2-isopropoxy-2'-nitrophenyl (2.44g., 94%);
m.p. $91-2^\circ$ (from light petroleum b.p. $60-80^\circ$).

(Found: C, 70.2; H,5.9; N, 5.5%; M, (mass spectrometry) 257.

$C_{15}H_{15}NO_3$ requires C, 70.05; H, 5.85; N, 5.45%; M, 257);

$^1H.n.m.r.$ τ ($CDCl_3$) 2.0-3.2(m., 8H); 5.55 (septet, 1H, $J = 6Hz$);
and 8.82 (d, 6H, $J = 6Hz$).

V_{max} 2980, 2930, 2870, 1615, 1530, 1500, 1480, 1360,
1250, 1135, 950, 855, and $755cm^{-1}$.,

λ_{max} 214($\log \epsilon$ 4.45); 238(4.13); and 273(3.79)n.m. .

9. Preparation of 2-n-Butoxy-2'-nitrobiphenyl.

Reaction as in experiment 6 using 2-hydroxy-2'-nitrobiphenyl (4.3g., 0.02 mole), potassium hydroxide (4.48g., 0.08mole), and n-butyl bromide (5.44g, 0.04mole) in dimethylsulphoxide (125ml) gave 2-n-butoxy-2'-nitrobiphenyl (4.28g., 79%); m.p. 72-3° (from light petroleum b.p. 60-80°).

(Found: C, 70.4; H, 6.1; N, 5.2%; M, (mass spectrometry) 271, $C_{16}H_{17}NO_3$ requires C, 70.85; H, 6.3; N, 5.15%; M, 271);

1H .n.m.r. τ ($CDCl_3$) 2-3.2(m., 8H); 6.12(t., 2H, $J = 7Hz$); 8.2-9.0(m., 4H) and 9.18(t., 3H, $J = 7Hz$).

V_{max} 2940, 2870, 1610, 1530, 1500, 1470, 1365, 1250, 1130, 850, 780, and $755cm^{-1}$.

λ_{max} 214(log ϵ 4.36); 240(4.07); and 272(3.76)n.m.

10. Preparation of 2-Allyloxy-2'-nitrobiphenyl.

Reaction as in experiment 6 using 2-hydroxy-2'-nitrobiphenyl (2.15g., 0.01 mole), potassium hydroxide (2.24g., 0.04mole) and allyl bromide (3.63g., 0.03 mole) in dimethylsulphoxide (100ml) gave 2-allyloxy-2'-nitrobiphenyl (2.37g., 93%); m.p. 43-4° (from light petroleum b.p. 60-80°).

(Found: C, 70.6; H, 5.1; N, 5.25%; M, (mass spectrometry) 255,

$C_{15}H_{13}NO_3$ requires C, 70.6; H, 5.1; N, 5.5%; M, 255);

1H .n.m.r. τ ($CDCl_3$) 2.0-3.2(m, 8H); 3.8-4.35(m., 1H); 4.65-4.95(m., 2H); and 5.5-5.7(m., 2H).

V_{max} 3080, 2930, 2860, 1615, 1590, 1530, 1505, 1455, 1360, 1250, 1225, 755, and $735cm^{-1}$.

λ_{max} 216(log ϵ , 4.33); 241(4.15); and 271 (4.01)n.m.

11. Preparation of 2-Crotyloxy-2'-nitrobiphenyl .

Reaction as in experiment 6 using 2-hydroxy-2'-nitrobiphenyl (1.5g), potassium hydroxide (1.5g) and crotyl bromide (2.7g) in dimethylsulphoxide (40ml), gave 2-crotyloxy-2'-nitrobiphenyl (1.82g., 94%); m.p. 81-2° (from light petroleum b.p. 60-80°).

¹H.n.m.r. τ (CDCl₃) 2.0-3.2(m., 8H); 4.2-4.6(m., 2H);
5.5-5.7(m., 2H); and 8.2-8.45 (d.d., 3H).

ν_{\max} 3040, 2930, 2880, 1615, 1585, 1530, 1500, 1450,
1360, 1250, 1225, 1125, 995, 860, 760, and 735cm⁻¹.

λ_{\max} 214 (log ϵ , 440); 244(4.26); and 272(4.30)n.m.,

Mass Spectrometry: M⁺ = 269

12. Preparation of 2-Benzyloxy-2'-nitrobiphenyl .

Reaction as in experiment 6 using 2-hydroxy-2'-nitrobiphenyl (1.08g., 0.005mole), potassium hydroxide (1.12g, 0.02mole) and benzyl bromide (2.55g., 0.015mole) in dimethylsulphoxide (50ml) gave 2-benzyloxy-2'-nitrobiphenyl (1.02g., 67%); m.p. 84-5° (from light petroleum b.p. 60-80°).

(Found: C, 74.6; H, 4.8; N, 5.0%; M, (Mass Spectrometry) 305,

C₁₉H₁₅NO₃ requires C, 74.75; H, 4.95; N, 4.6%; M, 305);

¹H.n.m.r. τ (CDCl₃) 2.0-3.2(m., 13H); 5.02(s., 2H).

ν_{\max} 3080, 2880, 1620, 1590, 1535, 1505, 1455, 1360,
1130, 860, and 755 cm⁻¹.

λ_{\max} 213(log ϵ 4.46); 240(4.08); and 272 (3.75)n.m. .

13. Preparation of 2-Nitro-2'-trideuteriomethoxybiphenyl .

Reaction as 6 using 2-hydroxy-2'-nitrobiphenyl (4.3g., 0.02 mole), potassium hydroxide (4.48g., 0.08 mole), and trideuteriomethyl iodide (10.0g., 0.07 mole) in dimethylsulphoxide (50ml) gave 2-nitro-2'-trideuteriomethoxybiphenyl (4.3g., 96%) as a yellow solid m.p. 83-4° (from methanol);

¹H.n.m.r. τ (CDCl₃) 1.95 - 3.25(m.).

V_{max} 3070, 2930, 2230, 2080, 1615, 1590, 1530,
1500, 1360, 1290, 1250, 1125, 1105, 990,
755, and 740 cm⁻¹.

Mass Spectrometry: M⁺ = 232.

14. Preparation of 2-Amino-2'-methoxybiphenyl .

Hydrazine hydrate (31ml, 64%) was slowly added to 2-methoxy-2'-nitrobiphenyl (22.9g, 0.1mole) and palladium on charcoal (300mg, 5.0%) in ethanol (250ml) at 50°. After complete addition (30 minutes), a further quantity of catalyst (100mg, 5%) was added and the mixture was heated under reflux for 6 hours. Removal of the catalyst by filtration and the solvents by evaporation under reduced pressure gave a colourless oil, which crystallised from methanol to give 2-amino-2'-methoxybiphenyl (16.1g., 80%); m.p. 78-9° (lit., ¹¹³ m.p. 80°);

¹H.n.m.r. τ (CDCl₃) 2.55 - 3.4(m., 8H); 6.25(s., 3H);
and 6.42 (broad s., 2H, exchangeable with D₂O).

V_{max} 3420, 3290, 3180, 2840, 1635, 1575, 1505,
1480, 1450, 1435, 1270, 1230, and 755cm⁻¹.

Mass Spectrometry: M⁺ = 199.

Preparation of 2-Alkoxy-2'-aminobiphenyls

A series of 2-alkoxy-2'-aminobiphenyls were prepared from 2-alkoxy-2'-nitrobiphenyls using an identical procedure to that described for the preparation of 2-amino-2'-methoxybiphenyl.

15. Preparation of 2-Amino-2'-ethoxybiphenyl.

The reaction of 2-ethoxy-2'-nitrobiphenyl (7.29g., 0.03mole) in ethanol (100ml.) with hydrazine hydrate (12ml., 64%) in the presence of palladium on charcoal (100mg., 5%) gave 2-amino-2'-ethoxybiphenyl (5.11g., 80%); m.p. 75-6° (from light petroleum b.p. 60-80°).

(Found: C, 79.3; H, 7.1; N, 6.4%; M, (mass spectrometry) 213,

$C_{14}H_{15}NO$ requires C, 78.9; H, 7.1; N, 6.6%; M, 213);

1H .n.m.r. τ ($CDCl_3$) 2.55-3.4(m., 8H); 6.0(q., 2H, $J = 8Hz$); 6.4(Broad s., 2H exchangeable with D_2O); and 8.75 (t., 3H, $J = 9Hz$).

ν_{max} 3480, 3390, 2990, 2940, 2890, 1625, 1505, 1490, 1475, 1450, 1245, 1230, 1045, and $750cm^{-1}$,

λ_{max} 210(log ϵ 4.43); 226(4.30) and 282(3.65)n.m. .

16. Preparation of 2-Amino-2'-n-propoxybiphenyl .

The reaction of 2-nitro-2'-n-propoxybiphenyl (1.8g., 0.007 mole) with hydrazine hydrate (4ml., 64%) in ethanol (30ml) using palladium on charcoal (100mg., 5%) catalyst gave 2-amino-2'-n-propoxybiphenyl (0.77g., 55%) as a colourless oil.

(Found: C, 79.8; H, 7.2; N, 5.6% M, (mass spectrometry) 227,

$C_{15}H_{17}NO$ requires C, 79.3; H, 7.5; N, 6.1%; M. 227);

$^1\text{H.n.m.r.}$ τ (CDCl_3) 2.55-3.4(m., 8H); 6.12 (t., 2H, $J = 7\text{Hz}$);
 6.4(broad s., 2H, exchangeable with D_2O);
 8.35(sextet, 2H, $J = 7\text{Hz}$); and 9.15 (t., 3H,
 $J = 7\text{Hz}$).

V_{max} 3480, 3395, 2980, 2950, 2890, 1625, 1510, 1495,
 1450, 1275, 1235, and 755cm^{-1} .

λ_{max} 210(log ϵ , 4.41); 226(4.28); and 283(3.71)n.m..

17. Preparation of 2-Amino-2'-isopropoxybiphenyl.

The reaction of 2-isopropoxy-2'-nitrobiphenyl (3.6g.,
 0.014 mole) with hydrazine hydrate (10ml., 64%) in ethanol
 (60ml) using palladium on charcoal (200mg., 5%) catalyst
 gave 2-amino-2'-isopropoxybiphenyl (2.80g., 87%); m.p. $51-2^\circ$
 (from light petroleum b.p. $60-80^\circ$)

(Found: C, 79.7; H, 7.0; N, 6.0%; M, (mass spectrometry) 227,
 $\text{C}_{15}\text{H}_{17}\text{NO}$ requires C, 79.3; H, 7.5; N, 6.1%; M, 227);

$^1\text{H.n.m.r.}$ τ (CDCl_3) 2.6-3.4(m., 8H); 5.72(m., 1H); 6.32(broad
 s., 2H, exchangeable with D_2O); and 8.88 (d.,
 6H, $J = 9\text{Hz}$).

V_{max} 3470, 3390, 2980, 2940, 2880, 1630, 1505, 1480,
 1440, 1270, 1230, 1130, 1105, and 750cm^{-1} .

λ_{max} 212(log ϵ 4.43); 226(4.3); and 284(3.6)n.m..

18. Preparation of 2-Amino-2'-n-butoxybiphenyl.

The reaction of 2-n-butoxy-2'-nitrobiphenyl (0.75g.,
 0.0028 mole) with hydrazine hydrate (2ml., 64%) in ethanol (30ml)
 using palladium on charcoal (100mg., 5%) catalyst gave

2-amino-2'-n-butoxybiphenyl (0.67g., 90%) as a colourless oil.

(Found: C, 80.0; H, 8.0; N, 5.5%; M (mass spectrometry) 241,

$C_{16}H_{19}NO$ requires C, 79.65; H, 7.95; N, 5.8%; M, 241);

$^1H.n.m.r.$ τ ($CDCl_3$) 2.55-3.4(m., 8H); 6.10(t., 2H, $J = 6Hz$);
6.35(broad s., 2H, exchangeable with D_2O);
8.25-8.9(m., 4H); and 9.15 (t., 3H, $J = 6Hz$).

V_{max} 3490, 3400, 2980, 2950, 2890, 1625, 1510, 1495,
1450, 1275, 1250, 1130, 1010, and 755 cm^{-1} .

λ_{max} 208(log ϵ 4.45); 226(4.31); and 284(3.58)n.m..

19. Preparation of 2-Amino-2'-neopentyloxybiphenyl .

The reaction of 2-neopentyloxy-2'-nitrobiphenyl (5.5g;
0.02mole) with hydrazine hydrate (14ml, 64%) in ethanol (100ml)
in the presence of palladium on charcoal (300mg., 5%) gave
2-amino-2'-neopentyloxybiphenyl(4.25g., 83%) as a yellow oil.

$^1H.n.m.r.$ τ ($CDCl_3$) 2.45-3.4(m., 8H); 6.42(broad s., 4H, 2
protons exchangeable with D_2O); and 9.15(s., 9H);

V_{max} 3470, 3380, 2960, 2870, 1620, 1505, 1490, 1475,
1445, 1240, 1195, 1120, 1020, 750, and 720 cm^{-1} .

λ_{max} 208(log ϵ 4.41); 226(4.22); and 282(3.61)n.m.

Mass Spectrometry: M^+ = 255.

20. Preparation of 2-Amino-2'-(1-methylheptyloxy)biphenyl.

The reaction of 2-(1-methylheptyloxy)-2'-nitrobiphenyl
(5.85g., 0.018 mole) with hydrazine hydrate (13ml., 64%) in
ethanol (100ml) using palladium on charcoal (200mg., 5%) catalyst
gave 2-amino-2'-(1-methylheptyloxy)biphenyl (4.66g., 87%) as a
yellow oil (b.p. $186-196^\circ$ at 1mm).

¹H.n.m.r. τ (CDCl₃) 2.5-3.45(m., 8H); 5.8(sextet, 1H,
 $J = 6\text{Hz}$); 6.4 (broad s., 2H, exchangeable with
D₂O); and 8.22-9.15 (m., 16H),
 ν_{max} 3470, 3380, 2960, 2940, 2860, 1620, 1505,
1485, 1445, 1230, 1120, and 750cm⁻¹,
 λ_{max} 210(log ϵ 4.39); 227(4.28); and 281(3.72)n.m.,
Mass Spectrometry: $M^+ = 297$.

21. Preparation of 2-Amino-2'-benzyloxybiphenyl.

The reaction of 2-benzyloxy-2'-nitrobiphenyl (0.2g., 0.00066
mole) with hydrazine hydrate (1.5ml., 64%) in the presence of
palladium on charcoal (50mg., 5%) gave 2-amino-2'-benzyloxybiphenyl
(0.18g., 95%); m.p. 96-7° (from light petroleum b.p. 60-80°).

¹H.n.m.r. τ (CDCl₃) 2.35-3.45(m., 8H); 5.05 (s., 2H); and
5.55 (broad s., 2H, exchangeable with D₂O),
 ν_{max} 3470, 3380, 2960, 2940, 2870, 1625, 1510,
1490, 1455, 1280, 1230, 1115, and 755cm⁻¹,
 λ_{max} 212(log ϵ 4.60); 245(4.04); and 284(3.90)n.m.,
Mass Spectrometry: $M^+ = 275$.

22. Preparation of 2-Amino-2'-trideuteriomethoxybiphenyl.

The reaction of 2-nitro-2'-trideuteriomethoxybiphenyl (4.31g)
with hydrazine hydrate (15ml., 64%) in ethanol (150ml) using
palladium on charcoal (300mg, 5%) catalyst gave 2-amino-2'-
trideuteriomethoxybiphenyl (2.87g., 78%); m.p. 71-2° (from methanol).

¹H.n.m.r. τ (CDCl₃) 2.50-3.4(m., 8H) and 6.55(broad s., 2H,
exchangeable with D₂O),
 ν_{max} 3450, 3380, 2220, 2080, 1625, 1600, 1505, 1485,
1445, 1275, 1250, 1125, 1110, and 755 cm⁻¹,
Mass Spectrometry: $M^+ = 202$.

23. Preparation of 2'-Methoxybiphenyl-2-ylidiazonium fluoroborate.

2-Amino-2'-methoxybiphenyl (7.8g., 0.04mole) was dissolved in tetrahydrofuran (30ml) and fluoroboric acid (75ml, 40% aqueous solution), and water (20ml) added. The solution was cooled to 0° and a solution of sodium nitrite (2.8g) in water (30ml) added dropwise with stirring, maintaining the temperature at 0°. After stirring for 30 minutes, the yellow diazonium salt was filtered off, washed with fluoroboric acid and cold tetrahydrofuran and dried overnight in vacuo over phosphoric anhydride. The yield of 2'-methoxybiphenyl-2-ylidiazonium fluoroborate was 11.61g (98%).

V_{\max} 3070, 2980, 2950, 2260, 1600, 1590, 1550, 1480,
1420, 1290, 1260, 1170, 1060(broad), 1010,
760, and 750 cm^{-1} .

24. Preparation of 2'-Ethoxybiphenyl-2-ylidiazonium fluoroborate.

By an identical procedure to that described for the methoxy analogue using 2-amino-2'-ethoxybiphenyl (2.4g., 0.011mole), tetrahydrofuran (20ml), fluoroboric acid (25ml., 40% aqueous solution), and sodium nitrite (1.0g) in water (10ml) to give 2'-ethoxybiphenyl-2-ylidiazonium fluoroborate (3.24g., 90%) as a yellow solid.

$V_{\max}(\text{CH}_2\text{Cl}_2)$ 2960, 2870, 2270, 1610, 1560, 1500,
1475, 1455, 1425, 1165, 1065(broad) and 895 cm^{-1} .

25. Preparation of 2'-Isopropoxybiphenyl-2-ylidiazonium fluoroborate.

By an identical procedure to that described for the methoxy analogue using 2-amino-2'-isopropoxybiphenyl (1.55g), tetrahydrofuran (5ml), fluoroboric acid (12.5, 40%) and sodium nitrite (0.5g) in

water (5ml) gave 2'-isopropoxybiphenyl-2-ylidiazonium fluoroborate (1.82g, 82%) as a yellow solid.

$V_{\max}(\text{CH}_2\text{Cl}_2)$ 3080, 2980, 2940, 2280, 1605, 1590,
1550, 1480, 1390, and 1060 (broad) cm^{-1} .

26. Preparation of 2'-Methoxybiphenyl-2-ylidiazonium hexafluorophosphate.

2-Amino-2'-methoxybiphenyl (1.99g., 0.01 mole) in concentrated hydrochloric acid (6ml) was diazotised at 0° by the slow addition of a solution of sodium nitrite (0.7g) in water (4ml). After stirring the diazonium salt solution for 15 minutes, ammonium hexafluorophosphate (1.6g) in water (3ml) was rapidly added. Ether (10ml) was added and the cold suspension was stirred for a further 30 minutes. The yellow precipitate was filtered off, washed with cold methanol and ether and dried overnight in vacuo over phosphoric anhydride. The yield of 2'-methoxybiphenyl-2-ylidiazonium hexafluorophosphate was 2.7g (75%).

V_{\max} 3090, 2990, 2940, 2270, 1610, 1595, 1560,
1485, 1430, 1295, 1270, 1260, 1120, 1070,
1060, 1015, 830(broad), 775, and 730 cm^{-1} .

27. Preparation of 2'-Methoxybiphenyl-2-ylidiazonium hexafluoroantimonate.

2-Amino-2'-methoxybiphenyl (1.99g., 0.01 mole) in concentrated hydrochloric acid (6ml) was diazotised at 0° by the slow addition of sodium nitrite (0.7g) in water (4ml). After stirring for 15 minutes, sodium hexafluoroantimonate (2.6g) in water (10ml) and ether (10ml) were added to the cold solution, which was subsequently stirred for another 30 minutes. The precipitated diazonium salt was filtered off, washed with cold methanol and ether and

dried overnight in vacuo over phosphoric anhydride and gave
2'-methoxybiphenyl-2-ylidiazonium hexafluoroantimonate (3.4g 80%)

V_{\max} (Nujol) 2280, 1610, 1595, 1490, 1260, 1200, 1125,
1020, 775, 755 and 725 cm^{-1} .

28. Preparation of 2'-Methoxybiphenyl-2-ylidiazonium hexafluoroarsenate.

2-Amino-2'-methoxybiphenyl (0.95g., 0.005 mole) in concentrated hydrochloric acid (4ml) was diazotised at 0° by the slow addition of sodium nitrite (0.4g) in water (3ml). After stirring for 15 minutes, potassium hexafluoroarsenate (2.3g) in water (10ml) was rapidly added. Ether (5ml) was added and the stirring continued for a further 30 minutes. The precipitated diazonium salt was collected, washed with cold methanol and ether and dried overnight in vacuo over phosphoric anhydride. The yield of 2'-methoxybiphenyl-2-ylidiazonium hexafluoroarsenate was 1.8g(90%)

V_{\max} (Nujol) 2290, 1610, 1500, 1485, 1295, 1260, 1240,
1170, 1125, 1055, 1020, 780, 760, and
700(broad) cm^{-1} .

29. Preparation of 2'-Methoxybiphenyl-2-ylidiazonium 2,4,6-trinitrobenzenesulphonate.

2-Amino-2'-methoxybiphenyl(0.95g., 0.005mole) in concentrated hydrochloric acid (4ml) was diazotised at 0° by the slow addition of sodium nitrite (0.35g) in water (5ml). After stirring the diazonium salt solution for 15 minutes, sodium 2,4,6-trinitrobenzenesulphonate (1.6g) in water (20ml) was rapidly added. Ether (10ml) was added and the cold suspension was stirred for a further 30 minutes. The yellow precipitate was filtered off, washed with cold methanol and ether and dried overnight in vacuo over phosphoric anhydride to give 2'-methoxybiphenyl-2-ylidiazonium

2,4,6-trinitrobenzene sulphonate (1.7g., 68%).

V_{\max} (Nujol) 3100, 2270, 1610, 1595, 1560, 1485, 1360,
1295, 1270, 1250, 1130, 1075, 1040, 1020,
765, 755, 740, and 725cm^{-1} .

Alkylation Reactions using O-Alkyldibenzofuranium salts

The alkylation of various weakly-nucleophilic compounds using O-alkyldibenzofuranium salts was achieved by a procedure identical to that employed for the methylation of dimethylsulphoxide which is described in detail.

In several instances the structures of the primary reaction products have followed from their reactions since the high reactivity of these salts prevented the acquirement of good spectroscopic data.

30. Reaction of O-Methyldibenzofuranium fluoroborate with dimethylsulphoxide.

2'-Methoxybiphenyl-2-yl diazonium fluoroborate (1.0g., 0.0033mole) was decomposed in a solution of dimethylsulphoxide (dry, 1.30g., 0.0166mole) in methylene dichloride (dry, 25ml) at room temperature. After 2 hours at this temperature, the suspension was slowly warmed and the reaction was completed by heating under reflux for 4 hours. The solvent was removed by distillation and gave a tan solid residue, which was washed with ether (dry, 3 x 15ml). The insoluble material was a white solid, which on recrystallisation from methylene dichloride - diethyl ether gave O-methyldimethylsulphoxonium fluoroborate (0.48g., 79%) m.p. $107-9^{\circ}$ (lit.,¹²⁵ m.p. $106-8^{\circ}$);

¹H.n.m.r. τ (DMSO- d_6) 6.0 (s., 3H); and 6.72 (s., 6H).

The combined ether layers were washed with water (2 x 25ml) to remove unreacted dimethylsulphoxide, and then dried over anhydrous magnesium sulphate. Recrystallisation of the residue after removal of solvent afforded dibenzofuran (0.49g., 87%); m.p. 87-8° (from light petroleum b.p. 60-80°) (lit.,¹⁴⁰ m.p. 86-7°).

V_{\max} 3050, 1600, 1475, 1455, 1450, 1325, 1240, 1200,
1155, 1100, 930, 850, 840, 755, 745 and 725cm⁻¹.

31. Reaction of O-Methyldibenzofuranium fluoroborate with benzo(b)thiophen

The decomposition of 2'-methoxybiphenyl-2-yldiazonium fluoroborate (3.0g., 0.01mole) in the presence of benzo(b)thiophen (2.8g., 0.02mole) in methylene dichloride (40ml) gave 1-methylbenzo(b)thiophenium fluoroborate (1.81g. 77%); m.p. 70-3° (from methylene dichloride-ether) (lit.,¹²⁸ m.p. 72-3°);

¹H.n.m.r. τ (DMSO-d₆) 2.0-2.92(m., 6H) and 6.7(s., 3H);

λ_{\max} 224, 227(sh), 266, and 294n.m.

32. Reaction of O-Methyldibenzofuranium fluoroborate with pentachloropyridine

The decomposition of 2'-methoxybiphenyl-2-yldiazonium fluoroborate (2.3g., 0.0077 mole) in a solution of pentachloropyridine (0.64g, 0.0026mole) in methylene dichloride (40ml) gave N-methylpentachloropyridinium fluoroborate (0.37g., 41%) as white needles m.p. 269-271° (from methylene dichloride);

¹H.n.m.r. τ (DMSO-d₆) 6.32(s.);

V_{\max} (Nujol) 1570, 1550, 1350, 1245, 1185, 1060(broad),
950, and 705cm⁻¹.

33. Reaction of N-Methylpentachloropyridinium fluoroborate with water.

A mixture of N-methylpentachloropyridinium fluoroborate (0.11g) and water (25ml) was stirred at ca.60° for 1 hour to give a precipitate of N-methyltetrachloro-2-pyridone (0.044g., 5%); m.p. 150-151° (from methanol) (lit., ¹⁴¹ m.p. 148.5-149.5°);

¹H.n.m.r. τ (CDCl₃) 6.22(s.).

V_{\max} 1690, 1660, 1570, 1480, 1300, 1160, 930, and 740 cm⁻¹,

λ_{\max} 223(log ϵ , 4.45); and 338(3.84)n.m. .

34. Reaction of O-Methyldibenzofuranium fluoroborate with benzonitrile

The decomposition of 2'-methoxybiphenyl-2-ylidiazonium fluoroborate (1.5g., 0.005mole) in a solution of benzonitrile (2.5g., 0.025mole) in methylene dichloride gave N-methylbenzotrilium fluoroborate (0.95g., 87%) as a brown hygroscopic solid m.p. 108-118°.

A sample of the nitrilium salt (0.63g) was stirred for 2 hours in water (30ml) at ca.60°. The aqueous solution was extracted with ether (2 x 20ml) and the combined ether layers were dried over anhydrous magnesium sulphate. Removal of solvent gave N-methylbenzamide (0.24g. 57%); m.p. 81-2° (from ethanol) lit., ¹⁴² m.p. 82°);

¹H.n.m.r. τ (CDCl₃) 2.05-2.80(m., 5H); 2.90 (Broad s., 1H, exchangeable with D₂O); and 7.08(d., 3H, J=6Hz.)

V_{\max} 3340, 1640, 1580, 1495, 1410, 1310, 1170, 1040, and 725cm⁻¹.

35. Reaction of O-Methyldibenzofuranium fluoroborate with
3,5-dichloro-2,6-difluoro-4-hydroxypyridine

2'-Methoxybiphenyl-2-yl diazonium fluoroborate (1.0g., 0.0033mole) was allowed to decompose in the presence of 3,5-dichloro-2,6-difluoro-4-hydroxypyridine (1.31g., 0.0066mole) in methylene dichloride (30ml) and gave a colourless viscous liquid (0.6g).

The reaction product was hydrolysed in the usual manner to give N-methyl-3,5-dichloro-2,6-difluoro-4-pyridone (0.29g., 43%); m.p. 173-5° (from carbon tetrachloride);

ν_{\max} 2920, 1670, 1620, 1565, 1505, 1220, 790,
and 745 cm^{-1} ;

λ_{\max} 261 (log ϵ , 4.13) n.m.,

Molecular Weight by high resolution mass spectrometry:-

Measured mass: $M^+ = 212.9549$

Expected formula: $\text{C}_6\text{H}_3\text{Cl}_2\text{F}_2\text{NO}$

Calculated mass: $M^+ = 212.9559$

36. Reaction of O-Methyldibenzofuranium fluoroborate with
cycloheptatriene

2'-Methoxybiphenyl-2-yl diazonium fluoroborate (4.0g., 0.0133 mole) was decomposed in the presence of cycloheptatriene (0.92g., 0.01mole) in methylene dichloride (60ml) to give tropylium fluoroborate (1.30g., 54%) m.p. 200-60° (lit., ¹⁴³ m.p. 210-270°).

λ_{\max} (CH_2Cl_2) 278 and 283 (sh.) n.m.

37. Reaction of O-Methyldibenzofuranium fluoroborate with triphenylmethane

2'-Methoxybiphenyl-2-ylidiazonium fluoroborate (4.0g., 0.0133mole) was decomposed in the presence of triphenylmethane (2.1g., 0.009mole) in methylene dichloride (35ml) and gave triphenylmethyl fluoroborate (0.94g., 21%) m.p. (decomposition) 190-235° (lit., ¹⁴⁴ m.p. ca.200° with decomposition).

V_{\max} (Nujol) 1587, 1490, 1450, 1365, 1095, 1060, 1040, 810, and 705 cm^{-1} .

38. Reaction of O-Methyldibenzofuranium fluoroborate with N,N-dimethyl-1-naphthylamine

2'-Methoxybiphenyl-2-ylidiazonium fluoroborate (1.0g., 0.0033mole) was allowed to decompose in a solution of N,N-1-dimethyl-1-naphthylamine (1.2g., 0.0065mole) in methylene dichloride (25ml) to give N,N,N-trimethyl-1-naphthylammonium fluoroborate (0.93g., 98%) as a blue oil.

¹H.n.m.r. τ (DMSO- d_6) 1.70-2.60(m., 7H) and 6.72 (s., 9H).

39. Reaction of O-Methyldibenzofuranium fluoroborate with pyridine.

The decomposition of 2'-methoxybiphenyl-2-ylidiazonium fluoroborate (1.0g., 0.0033mole) in a solution of pyridine (0.8g., 0.01mole) in methylene dichloride (25ml) gave N-methylpyridinium fluoroborate (0.61g., 99%) as a colourless oil (lit., ¹⁴⁵ m.p. 10-11.5°).

An excess of a saturated aqueous solution of sodium picrate was added to the pyridinium salt in water (5ml) to give a yellow precipitate which was filtered off and washed with ether. Recrystallisation from ethanol gave N-methylpyridinium picrate-sodium picrate (1.5g., 75%); m.p. 217-8° (lit.,¹²² m.p. 216-9°),

V_{\max} 3080, 1640, 1565, 1520, 1375, 1350, 1285,
790, and 745 cm^{-1} .

40. Preparation of O-Methyldibenzofuranium fluoroborate and its subsequent reaction with pyridine.

A mixture of 2'-methoxybiphenyl-2-ylidiazonium fluoroborate (1.0g., 0.0033mole) in anhydrous benzene (25ml) was heated at ca. 50° for 1 hour and then heated under reflux for a further 1 hour. The solid rapidly changed colour from yellow to off-white and the colour of the solution was also discharged.

Pyridine (0.78g., 0.01mole) was added and the mixture was heated under reflux for 6 hours. The solvent was removed by distillation and a yellow oily residue was obtained, which after washing with ether (dry, 3 x 25ml) gave N-methylpyridinium fluoroborate (0.17g, 28%) as a colourless oil. Addition of an excess of a saturated aqueous solution of sodium picrate to the pyridinium salt in water (5ml) gave N-methylpyridinium picrate-sodium picrate (0.37g., 70%); m.p. 217-8°, infra-red spectrum identical with that of an authentic sample.

41. Reaction of O-Methyldibenzofuranium fluoroborate with tetrahydrofuran.

2'-Methoxybiphenyl-2-ylidiazonium fluoroborate (1.0g., 0.0033mole) was decomposed in a solution of tetrahydrofuran (10ml) in methylene dichloride (15ml) and gave O-methyltetrahydrofuranium fluoroborate (0.41g., 70%) as a colourless oil.

An exothermic reaction occurred when an excess of pyridine (1.0g) was added dropwise to the tetrahydrofuranium salt in methylene dichloride at room temperature. Removal of the solvent by distillation gave a residue which after washing with ether (dry, 3 x 25ml) gave N-methylpyridinium fluoroborate (0.42g, 98%) as a colourless oil. The pyridinium salt was characterised as N-methylpyridinium picrate-sodium picrate (0.82g, 63%) using the procedure described above.

The ether solution was shown by g.l.c. to contain tetrahydrofuran and pyridine.

42. Reaction of O-Methyldibenzofuranium fluoroborate with α -pyridone

2'-Methoxybiphenyl-2-ylidiazonium fluoroborate (4.5g., 0.015mole) was decomposed in a solution of α -pyridone (2.25g., 0.023mole) in methylene dichloride (60ml). The solvent was removed by careful distillation and gave an oily residue, which was washed with ether (2 x 50ml). The insoluble material was dissolved in aqueous sodium hydroxide (50ml, 2N) and after stirring at room temperature for 2 hours, the aqueous solution was extracted with ether (2 x 40ml). The combined ether layers were then dried over anhydrous magnesium sulphate. The ethereal solution was distilled at atmospheric pressure to give, after

removal of solvent (b.p. 35°), 2-methoxypyridine (1.24g., 81%)
b.p. $138-41^{\circ}$ (lit., ¹⁴⁶ b.p. $142-3^{\circ}$);

¹H.n.m.r. τ (CDCl₃) 1.8 - 3.25(m., 4H) and 6.08(s., 3H),

V_{\max} 1605, 1575, 1480, 1420, 1290, 1040, 1020,
810, and 775cm^{-1} .

Mass Spectrometry: $M^+ = 109$.

43. Reaction of O-Methyldibenzofuranium hexafluorophosphate with pyridine.

The decomposition of 2'-methoxybiphenyl-2-yl diazonium hexafluorophosphate (1.0g., 0.003mole) in a solution of pyridine (0.8g., 0.009mole) in methylene dichloride gave N-methylpyridinium hexafluorophosphate (0.70g., 98%) as a tan solid. The pyridinium salt was dissolved in methylene dichloride (5ml) and an excess of a saturated solution of sodium picrate added. The yellow precipitate was collected and washed with ether, recrystallisation from ethanol gave N-methylpyridinium picrate-sodium picrate (1.51g., 79%) m.p. $216-9^{\circ}$, infra-red spectrum identical with that of an authentic sample.

44. Reaction of O-Methyldibenzofuranium hexafluoroantimonate with pyridine.

Using an identical procedure as in the hexafluorophosphate analogue and the same molar scale, N-methylpyridinium hexafluoroantimonate (0.76g., 100%) was obtained which was subsequently characterised as N-methylpyridinium picrate-sodium picrate (0.87g., 68%) m.p. $217-219^{\circ}$, infra-red spectrum identical with that of an authentic sample.

45. Reaction of *O*-Methyldibenzofuranium hexafluoroarsenate with pyridine.

Using an identical procedure as in the hexafluorophosphate analogue and the same molar scale, *N*-methylpyridinium hexafluoroarsenate (0.70g., 99%) was obtained which was subsequently characterised as *N*-methylpyridinium picrate-sodium picrate (0.93g., 66%) m.p. 217-219°, infra-red spectrum identical with that of an authentic sample.

46. Reaction of *O*-Methyldibenzofuranium 2,4,6-trinitrobenzenesulphonate with pyridine.

Using an identical procedure as in the hexafluorophosphate analogue and the same molar scale, *N*-methylpyridinium 2,4,6-trinitrobenzenesulphonate (0.77g., 99%) was obtained as a yellow solid m.p. 236-40° (from ethanol);

V_{\max} 3120, 1640, 1615, 1550, 1360, 1250, 1125,
1070, 1035, 910, 770, 755, 735, 725, and
680cm⁻¹.

47. Preparation of *O*-Methyldibenzofuranium 2,4,6-trinitrobenzenesulphonate and its subsequent reaction with pyridine.

2'-Methoxybiphenyl-2-ylidiazonium 2,4,6-trinitrobenzenesulphonate (0.6g) was heated under reflux in anhydrous benzene (25ml) for 1 hour. After cooling to room temperature, the grey solid (0.51g) m.p. > 300° with decomposition, was filtered off under an atmosphere of nitrogen.

V_{\max} 3600, 3510, 3100, 2910, 1610, 1550, 1390,
1360, 1275, 1260, 1250, 1130, 1080, 1040,
925, 755, 725, and 640cm⁻¹.

The solid was then added to a solution of an excess of pyridine

which was shown by $^1\text{H.n.m.r.}$ to be an isomeric mixture of 2-ethoxypyridine and N-ethyl-2-pyridone (4:1) in 28% and 7% yields respectively.

50. Preparation of 2-Amino-2'-nitrobiphenyl.

2,2'-Dinitrobiphenyl (50g., 0.20mole) in methanol (650ml) was heated under reflux and a solution of sodium hydrogen sulphide (20.6g., 0.37mole) in aqueous methanol (4.40ml, 50%) was slowly added. The orange solution was heated under reflux for 4 hours and then water (220ml) was added. After removal of the organic solvent by distillation, the reaction mixture was extracted with ether. The ethereal solution was repeatedly washed with hydrochloric acid and the combined aqueous extracts were then basified with sodium hydroxide solution to liberate the amino compound. The product was re-extracted with ether and the combined ether layers were dried over anhydrous magnesium sulphate. Removal of the solvent gave a residue which was dissolved in the minimum volume of benzene and placed on a column of alumina. Elution with 10% benzene-ether gave after recrystallisation from ethanol, 2-amino-2'-nitrobiphenyl (35g., 83%) m.p. 69-70° (lit., ¹³¹ m.p. 64-64.5°) as a yellow solid,

V_{max} 3470, 3390, 3070, 1625, 1530, 1355, 855, and 750 cm^{-1} .

The ethereal solution remaining after the acid extraction was dried over anhydrous magnesium sulphate. Removal of the solvent gave a solid residue which was placed on a column of alumina. Elution with ether gave 3,4-benzocinnoline-N-oxide (4.2g, 11%) m.p. 138-9° (lit., ¹⁴⁷ m.p. 137-137.5°), infra-red spectrum identical with authentic sample.

51. Preparation of 2-Iodo-2'-nitrobiphenyl.

2-Amino-2'-nitrobiphenyl (29g., 0.14mole) in hydrochloric acid (180ml) and water (1500ml) was diazotised at 0° by the slow addition of sodium nitrite (11.4g) in water (150ml). After stirring for 10 minutes, a solution of potassium iodide (90g) in water (300ml) was rapidly added to the cold diazonium salt solution. Nitrogen was evolved and the reaction mixture was heated for 1 hour at ca.80°. The black organic oil was separated from the aqueous layer and washed with hot aqueous sodium hydroxide (2 x 600ml, 5%) and water (5 x 100ml) before being extracted with ether. Removal of solvent, after drying with anhydrous magnesium sulphate, gave a red oil which was placed on a column of alumina. Elution with 50% ether-light petroleum afforded 2-iodo-2'-nitrobiphenyl (23.4g., 49%) m.p. 80-1° (from light petroleum b.p. 60-80°) (lit.,¹⁴⁸ m.p. 81-2°)

V_{\max} 3070, 1615, 1525, 1350, 855, 750, and 690 cm^{-1} .

52. Preparation of 2-Nitro-2'-phenoxybiphenyl.

An intimate mixture of 2-iodo-2'-nitrobiphenyl (16g., 0.05mole) and potassium phenolate (18.9g), phenol (24g) and copper powder (0.2g) was heated at 150° for 5 hours and then for an additional 1 hour at 200°. Aqueous sodium hydroxide (400ml, 20%) was added to the cooled reaction mixture and the alkaline solution was extracted with ether. After drying over anhydrous magnesium sulphate, the solvent was removed to give a dark brown oil.

2-nitrobiphenyl, (2.1g., 20%) m.p. 36-7° (from ethanol) (lit.¹⁴⁹ m.p. 35-37) was removed from the crude product by

distillation at reduced pressure (b.p. 124° at 1.5mm). The residual oil was placed on a column of alumina (300g) and elution with benzene gave 2-nitro-2'-phenoxybiphenyl (5.45g., 40%) m.p. $51-52.5^{\circ}$ (from ethanol) (lit., ¹⁰³ m.p. $51.5-52.5^{\circ}$).

V_{\max} 3060, 1580, 1530, 1490, 1350, 1245, 1220,
850, 745, 735, and 690cm^{-1} .

53. Preparation of 2-Amino-2'-phenoxybiphenyl.

Hydrazine hydrate (10ml, 64%) was slowly added to 2-nitro-2'-phenoxybiphenyl (5.4g) and palladium on charcoal (100mg, 10%) in ethanol (100ml) at 50°C . After the addition was completed, a further quantity of catalyst (ca.25mg) was added and the mixture was heated under reflux for 9 hours. Removal of the catalyst by filtration and the solvents by evaporation under reduced pressure gave a dark oil, which slowly crystallised on standing. Several recrystallisations from ethanol gave 2-amino-2'-phenoxybiphenyl (3.01g. 60%); m.p. $83-4^{\circ}$ (lit., ¹⁰³ m.p. $83.5-84.5^{\circ}$).

¹H.n.m.r. τ (CDCl_3) 2.4-3.6(m., 13H) and 6.4(broad s., 2H, exchangeable with D_2O),

V_{\max} 3470, 3380, 3060, 2960, 1620, 1470, 1435,

1220, 1010, 745, and 695cm^{-1} .
Mass Spectrometry: $M^+ = 261$.

54. Preparation of O-Phenyldibenzofuranium fluoroborate.

Sodium nitrite (0.89g) in water (9ml) was added dropwise to a solution of 2-amino-2'-phenoxybiphenyl (3.3g) in sulphuric acid (50ml, 10%) at 0° . The diazonium salt solution was slowly heated to ca. 60° and nitrogen was evolved to give a dark brown

aqueous solution of o-phenyldibenzofuranium sulphate.

The solution was decolourised by treatment with activated charcoal and a solution of sodium tetrafluoroborate (1.5g) in water (5ml) added. The white solid liberated was filtered off and recrystallised from ethanol to give o-phenyldibenzofuranium fluoroborate (2.03g, 49%) m.p. (decomposition) 170-5° (lit., ¹⁰³ m.p. (decomposition) 172.5-173°)

λ_{max} 245(sh), 276, and 284n.m. .

55. Preparation of o-Phenyldibenzofuranium iodide.

o-Phenyldibenzofuranium fluoroborate (0.18g) was dissolved in water (25ml) and an excess of a saturated solution of potassium iodide added. The white precipitate was collected and after recrystallisation from ethanol gave o-phenyldibenzofuranium iodide (0.22g, 91%) m.p. 137-8° (lit, ¹⁰³ m.p. 137.5-138°) as white shining leaflets, which slowly turned yellow in the light.

λ_{max} 246(sh) 254, 263(sh), 276, and 284 n.m. .

56. Pyrolysis of o-Phenyldibenzofuranium iodide.

o-Phenyldibenzofuranium iodide(200mg) was heated at 150° for 6 hours in a tube sealed under vacuum to give a red oil which slowly solidified. G.l.c. analysis (Column A at 202°) showed that the pyrolysate consisted of 2-iodo-2'-phenoxybiphenyl (64%), iodobenzene (17.5%), and dibenzofuran (14.5%).

Several recrystallisations of the solid product from ethanol gave 2-iodo-2'-phenoxybiphenyl(0.092g, 46%) m.p. 89-90° (lit. ¹⁰³ m.p. 88.5-89°).

57. Preparation of 2-Hydroxy-2'-nitrobiphenyl from 2-amino-2'-nitrobiphenyl.

2-Amino-2'-nitrobiphenyl (4.28g 0.02mole) was dissolved in a mixture of concentrated sulphuric acid (25ml) and water (25ml). The solution was cooled to 0° and a solution of sodium nitrite (1.4g) in water (3ml) added slowly with stirring. After the addition was completed, the cold diazonium salt solution was added dropwise to aqueous sulphuric acid (50ml, 1:1 v/v) at 100°. The reaction mixture was made alkaline with concentrated sodium hydroxide solution and extracted with ether to remove unreacted 2-amino-2'-nitrobiphenyl. The aqueous layer was acidified with concentrated hydrochloric acid and extracted with ether. Removal of solvent gave a tarry residue, which after several recrystallisations from benzene gave 2-hydroxy-2'-nitrobiphenyl (0.30g, 7%) m.p. 138-40° (lit ¹³² m.p. 140°) as pale yellow needles.

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