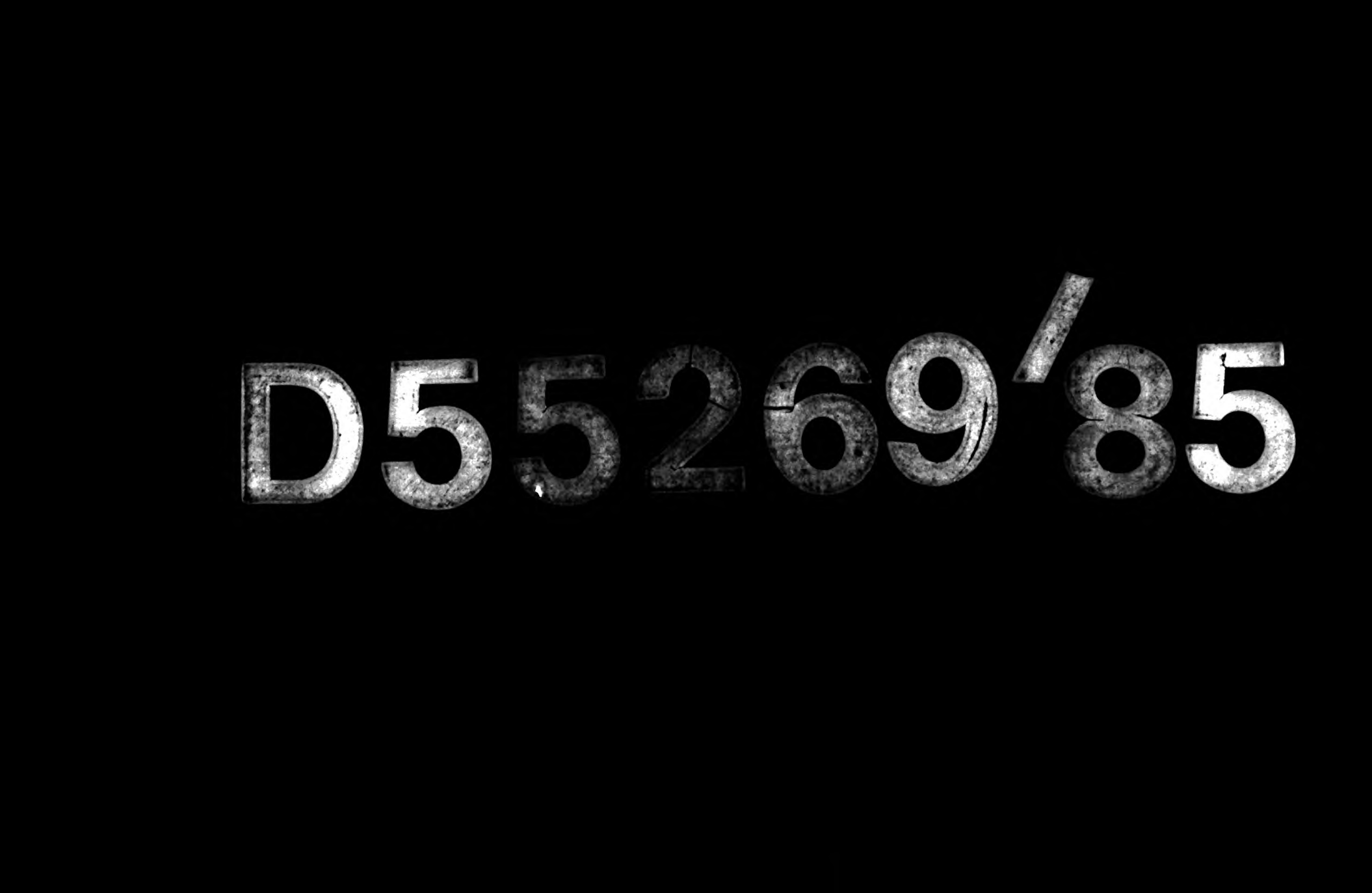

D552691/85

SOME INVESTIGATIONS OF PHOSPHORUS YLIDES

A Thesis Submitted to the Council for National Academic Awards in Partial Fulfilment of the Regulations for the Degree of Doctor of Philosophy

by

Anthony Francis Bradley, BSc, GRSC

Department of Chemistry
Sir John Cass Faculty of Science and Technology
City of London Polytechnic
Jewry Street
London EC3N

September 1984

To all those who helped and encouraged me during my formative years, with special mention of Dr. J. Borges-del-Castillo and Dr. F. Fariña.

ACKNOWLEDGEMENTS

I would like to express my most sincere gratitude to my supervisors Dr. G.W. Brown and Dr. E.M. Briggs for their expert advice and constant encouragement throughout the course of this work.

Thanks are also due to Mr. B. Saunderson for the micro-analytical work and mass spectra, and to Dr. B. Wood for the NMR spectra.

I am also grateful to the Inner London Education Authority for a Research Assistantship.

ABBREVIATIONS

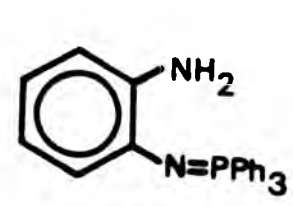
The following abbreviations are used in the text:

Ar	aryl
Et	ethyl
Me	methyl
Ph	phenyl
R	alkyl
X	halogen
AcOEt	ethyl acetate
DMA	dimethyl acetylenedicarboxylate
DMSO	dimethyl sulphoxide
Pet. ether	petroleum ether
Py	pyridine
TPPO	triphenylphosphine oxide
ITPP	iminotriphenylphosphorane
ITPPm	iminotriphenylphosphonium
ESCA	electron spectroscopy for chemical analysis
PES	photoelectron spectroscopy
IR	infrared
UV	ultraviolet
MS	mass spectra
DCI	direct or desorption chemical ionisation
CI	chemical ionisation
^{1}H NMR	proton nuclear magnetic resonance
^{13}C NMR	carbon-13 nuclear magnetic resonance
^{31}P NMR	phosphorus-31 nuclear magnetic resonance
br	broad
s	singlet

d	doublet
dd	double doublet
t	triplet
q	quartet
sext	sextet
m	multiplet

ABSTRACT

N-(o-aminophenyl)-iminotriphenylphosphorane (I) has been synthesised and its physical and chemical properties studied in depth, especially in its nucleophilic reactions.



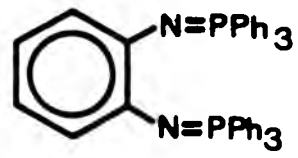
I

(I) can react through both the amino group or the nitrogen atom of the iminophosphorane group and this chemoselectivity is dependent on the reaction conditions and reagents used. Brønsted acids react exclusively with the imino group, alkyl halides react preferentially at the amino group but acyl halides, acid anhydrides and p-toluenesulphonyl chloride are less selective still. Overall, the nucleophilicity of the amino group was found to be greater than that of the imino group.

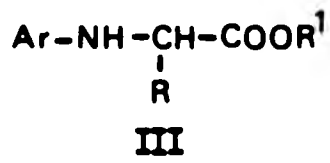
By blocking the reactivity of the latter group through the formation of the hydrochloride salt, greatly improved yields were obtained in the reactions with alkyl halides and acyl halides on the amino group.

The reactions of iminophosphoranes with acid chlorides were studied in detail and a mechanism for these reactions, which give imidoyl chlorides and triphenylphosphine oxide, is proposed involving an N-acyl-phosphonium salt and an O-phosphonium imidate salt.

Reactions of mono- and the bis-iminotriphenylphosphorane (II) with α-bromoesters have also been investigated as routes to α-anilinoesters (III) without notable success.



II



III

The mass spectra of o-, m- and p-substituted N-aryliminotriphenylphosphoranes were studied. These generally displayed strong molecular ion and (M-1) peaks. M- and p-substituted compounds show spectra dominated by the cleavage mode of the triphenylphosphorane group, while o-substituted compounds in addition show ready loss by fragmentation of the substituents. When the o-substituent carries a suitably positioned oxygen atom, rearrangement takes place with formation of triphenylphosphine oxide and a heterocyclic compound. These reactions have been reproduced under pyrolytic conditions and thus the rearrangement process observed in the mass spectra of these compounds can predict whether these reactions are likely to prove synthetically useful.

We have shown that pyrolysis of substituted N-aryliminotriphenylphosphoranes containing ester and amide groups proceeds readily via Wittig-type processes and in good yields, a novel synthetic approach to nitrogen heterocycles.

Intermolecular pyrolysis reactions have also been studied but no evidence was found for similar results.

CONTENTS

CHAPTER 1

INTRODUCTION

Ylides were named and defined by Wittig as compounds having charges of opposite sign on adjacent atoms in their ground state:

$$X^{+} - Y^{-}$$

It was not until Wittig[1] developed his reaction with the alkylidene-triphenylphosphoranes that this

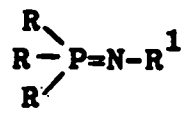
$$Ph_3P{=}CH{-}R \longleftrightarrow Ph_3\overset{+}{P}{-}C\bar{H}{-}R$$

type of compound attracted any considerable interest, but since then the number of papers and review articles devoted to this reaction has been enormous[2], reflecting the importance this reaction and this type of compound have in modern organic chemistry.

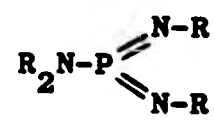
Although iminotriphenylphosphoranes (ITPPs) were first synthesised

$$Ph_3P{=}N{-}R \longleftrightarrow Ph_3\overset{+}{P}{-}\bar{N}{-}R$$

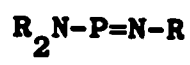
and described by Staudinger and Meyer in 1919[3], they attracted relatively little attention until Wittig published his results. General interest in and study of ITPPs was developing steadily during this time, but no systematic investigation of their properties and structure was undertaken, as pointed out by Johnson[2d]. The isolation of organometallic phosphinimines[4] led to a quick development of iminophosphorane chemistry which apart from classical 4-coordinate phosphorus (V) species[5,6,27] now includes 3-coordinate phosphorus (V)[5,6], 2-coordinate phosphorus (III)[5,6], cyclophosphazenes[6,7] and their use as ligands in coordination chemistry[5,6]. For example:



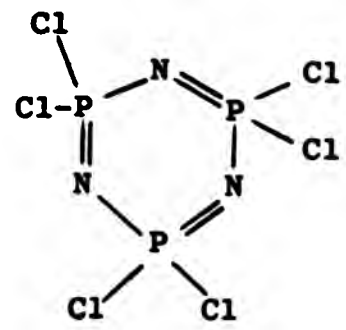
4-coordinate-
P(V)



3-coordinate-
P(V)



2-coordinate-
P(III)



Cyclophosphazene

These compounds have been named imidophosphoranes, iminophosphoranes, phosphazenes, phosphinimines and phosphinimides by different authors. Unfortunately no firm agreement appears to have been reached for their nomenclature, although the term phosphorane, derived from PH_5, has been proposed[2d,8] to name ylides in general, and therefore, the name iminophosphorane will be used in the present work.

Iminophosphoranes, and ylides in general, posed a significant challenge to our understanding of the chemical bond, reflected in the long-standing controversy over whether the phosphorus atom was capable of valence shell expansion with involvement of its d-orbitals in ($d\pi$-$p\pi$) bonding and to what extent this contribution was important. Much time and effort was dedicated to this subject and many physical and spectroscopic properties have been interpreted involving ($d\pi$-$p\pi$) bonding, and corroborated by theoretical calculations. The nature of the P=N bond is reflected in the chemical behaviour of these compounds, in particular the nucleophilicity of the nitrogen atom and the involvement of these molecules in Wittig reactions, although many other synthetic applications of these molecules are known.

Since Staudinger[3] reported the first synthesis of iminophosphoranes

a large number of different methods has been discovered and developed but few are generally applicable[5,27].

The Staudinger method involves reaction of a tertiary phosphine and an organic azide with formation of a sometimes isolable complex (1) (the Staudinger adduct) which decomposes into the iminophosphoranes with elimination of nitrogen.

$$R_3P + N_3R^1 \rightleftharpoons \underset{(1)}{[R_3P{=}N{-}N{=}N{-}R^1]} \xrightarrow{-N_2} R_3P{=}N{-}R^1$$

This reaction and its multiple applications have recently been reviewed[9]. Its mechanism is thought to involve nucleophilic attack of the phosphorus on the azide with formation of the adduct (1)[10] which on warming decomposes through a 4-membered ring transition state (2) with evolution of nitrogen, yielding the iminophosphorane[11].

$$\underset{(1)}{[R_3P{=}N{-}N{=}N{-}R^1]} \longrightarrow \underset{(2)}{\left[\begin{array}{c} R_3P \cdots N{-}R^1 \\ | \quad\quad | \\ N = N \end{array}\right]} \longrightarrow R_3P{=}NR^1{+}N_2$$

Over the years the reaction components used have included trialkyl, triaryl, and mixed phosphines, unsaturated phosphines, diphosphines; esters, thioesters, amides, halides, isocyanates and anhydrides of phosphorus (III) acids and a wide variety of organic, heteroorganic, and organometallic azides[9]. The only limitation of the reaction appears to be the explosive nature of the organic azides.

Another general method uses chloramine and substituted chloramines (3) instead of the azides, yielding after reaction with tertiary phosphines aminophosphonium salts (4)[12-14]. These are converted into the corresponding iminophosphoranes by a wide variety of bases, choice of which is usually dependent on the substituents on both phosphorus and nitrogen. The different bases used include ammonia[15],

$$\underset{(3)}{R_3P + X{-}NHR} \longrightarrow \underset{(4)}{[R_3\overset{+}{P}{-}NHR]\ X^-} \xrightarrow{:B} R_3P{=}NR$$

pyridine[28], triethylamine[28], sodamide[16,17], magnesium hydride[18] and lead acetate[19].

One of the earliest methods developed is essentially a variation of the one described previously, and involves the use of sodium salts of chloramines or dichloramines thus rendering unnecessary the use of a base for the dehydrohalogenation of the phosphonium salt[20]. For example

$$R_3P + Na^+(Cl\bar{N}SO_2C_6H_4Me(p)) \longrightarrow R_3P{=}NSO_2C_6H_4Me(p) + NaCl$$

(chloramine T)

Yet another modification due to Appel et al[15,21] involves reaction of triphenylphosphine with hydroxylamine-O-sulphonic acid. The amino-triphenylphosphonium hydrogen sulphate (5) obtained is said to yield the parent iminotriphenylphosphorane (6) in good yield upon deprotonation with sodamide in liquid ammonia.

$$Ph_3P + H_2NOSO_3H \longrightarrow Ph_3\overset{+}{P}NH_2\ HSO_4^- \xrightarrow[NH_3(\ell)]{NaNH_2} Ph_3P{=}NH$$

(5) (6)

A general and interesting method for the synthesis of iminophosphoranes with electron-withdrawing groups on the nitrogen atom was first described by Kirsanov et al.[22,23]. Reaction between an acid amide and phosphorus pentachloride affords an intermediate iminotrichlorophosphorane (7) which upon treatment with Grignard reagents, finally yields the iminophosphorane

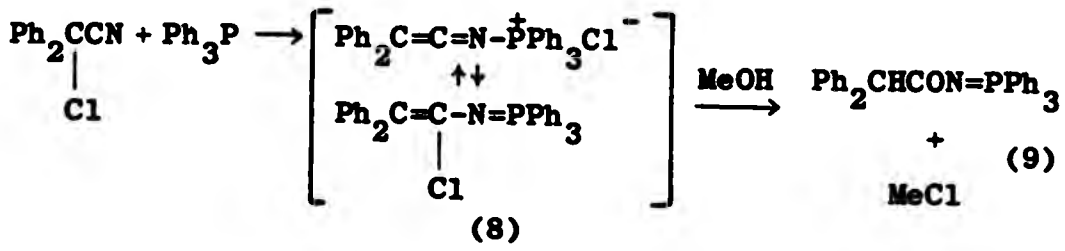
$$R\text{-}CONH_2 + PCl_5 \longrightarrow Cl_3P{=}N\,COR \xrightarrow{3R^1MgBr} R^1{}_3P{=}N\text{-}COR$$

(7)

Trichlorodiphenylphosphorane[24] and sulphonic acid amides have also been used as starting materials.

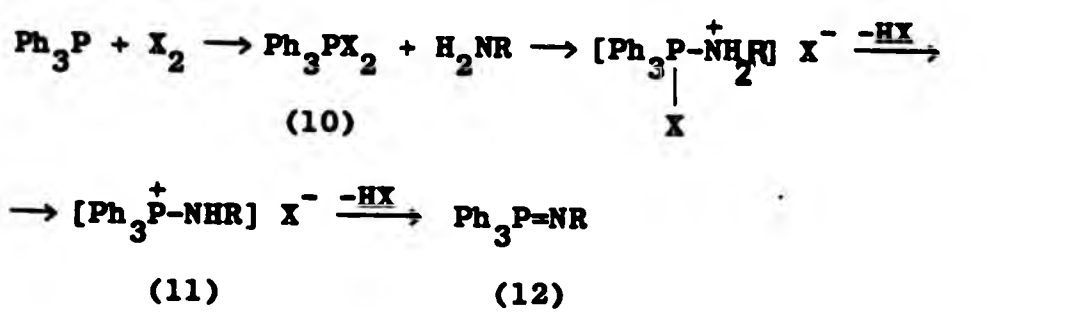
An interesting reaction which appears to have attracted very little attention is that between chlorodiphenylacetonitrile and triphenylphosphine[25]. The mixture afforded an intermediate (8) which on

treatment with methanol yielded (9)



(8)

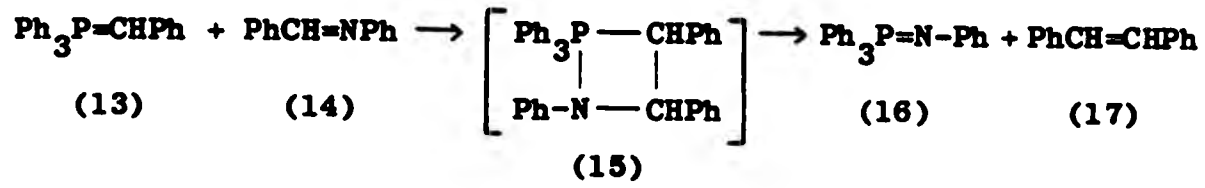
The method most widely used is that due to Horner and Oediger[28] because of the availability of starting materials and ease of procedure and isolation of products. Triphenylphosphine is mixed with elemental halogen (usually bromine) forming the dihalotriphenylphosphine (10) which in the presence of a mixture of a primary amine and triethylamine yields the iminotriphenylphosphorane (12). Presumably the reaction is initiated by attack of the amine on the phosphorus atom of (10),



(10) (11) (12)

followed by a removal of HX (repeated twice) by triethylamine. Interaction of alkylamines with (10) in the presence of triethylamine stops at the stage of the phosphonium salt (11), requiring a strong base, such as sodium amide in liquid ammonia, to liberate the iminotriphenylphosphorane (12). This synthetic route has also been frequently used for the synthesis of bis-ITPPs using aromatic bis-amines and hydrazine[26].

Alkylidenetriphenylphosphoranes which contain no CH_2 group β to phosphorus ($Ph_3P{=}CH{-}R$, R=aryl) and Schiff bases ($R^1N{=}CHR^2$) produce, in a Wittig type of olefination reaction, an iminophosphorane and an olefin[29]. Thus benzylidenetriphenylphosphorane (13) and benzylideneaniline (14) gave N-phenyl-ITPP (16) and stilbene (17)[29b] probably via a betaine intermediate (15) as in the Wittig reaction.

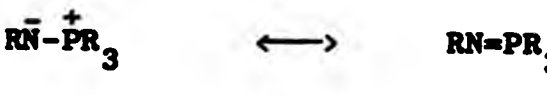


(13) (14) (15) (16) (17)

Iminophosphoranes (18) and alkylidenephosphoranes (19) are two typical examples of ylides. They are isoelectronic, display similar properties and have a phosphorus atom as the positive end of the dipole.

(18) (19)

Iminophosphoranes are generally monomeric and stable compounds, relatively easy to manipulate yet reactive enough to constitute useful reagents in organic synthesis. Reactivity is greatly influenced by the nature of the nitrogen substituent, N-aryl-substituted iminophosphoranes being generally stable under ordinary conditions while the N-alkyl substituted analogues usually hydrolyse spontaneously. This stability, together with that of most phosphorus ylides, has been interpreted in terms of electronic and structural factors which stabilise the adjacent anion by formation of a double bond. Thus, the structure of the iminophosphoranes can be represented as a resonance hybrid of two canonical forms:



The nature of this double bond is the most controversial aspect of their structure, which in turn, determines their chemical behaviour.

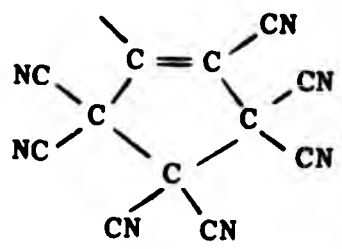
Before X-ray results were obtained hybridisation around the phosphorus atom was thought[2d] to resemble that in alkylidenephosphoranes, i.e. tetrahedral hybridisation with multiple bonding occurring by overlap of the 3d vacant orbitals on phosphorus with the appropriate filled nitrogen orbitals. However, the orbital picture around the nitrogen atom was very uncertain, involving possibly trigonal, tetrahedral or digonal hybridisations. Several iminophosphoranes'

crystallographic results have now been published and are listed in Table 1.

TABLE 1 Structures of iminophosphoranes

Compound	P=N(Å)	P=N-R(°)	Ref
$Ph_2FP{=}NMe$	1.641	119.1	30
$Ph_3P{=}NC_6H_4Br(p)$	1.567	124.2	31
$Ph_3P{=}N{-}SO_2C_6H_4Me(p)$	1.579	126.4	32
$Ph_3P{=}N{-}R^*$	1.615	130.0	33

*R =



The bond angles around phosphorus lie between 104±2° and 116±2° which correspond approximately to sp^3 hybridisation and are similar to those found for alkylidenephosphoranes[31]. The P=N bond length varies considerably from one structure to another but all fall closer to the covalent radii calculated[34] value of 1.64Å for a P=N bond than to the P-N bond length value of 1.78Å. The P=N-R bond angles are found to be close to the expected 120° for an sp^2-hybridised nitrogen atom with only the cyclopentene derivative's value of 130° deviating appreciably. (This has been interpreted in terms of steric effects.[33]) These results show the phosphorus-nitrogen bond in iminophosphoranes as being formed by an sp^3-hybridised phosphorus atom bonded to a nitrogen atom in a hybridisation state very close to sp^2. The double bond would therefore be formed by overlap of the filled $2p_z$ nitrogen orbital with the phosphorus $3d_{xz}$ vacant orbital giving rise to a (p-d)π back-bond (Figure 1). The experimental values for the P=N bond length seem to indicate a large contribution from this double bond and very little, if any, from the dipolar resonance

form (18). It would be difficult to estimate a $R_3\overset{+}{P}-\bar{N}R$ bond distance but it seems unlikely to be as short as 1.64Å [32]. These conclusions are supported by thermochemical data which show considerable resonance energy in iminophosphoranes[22].

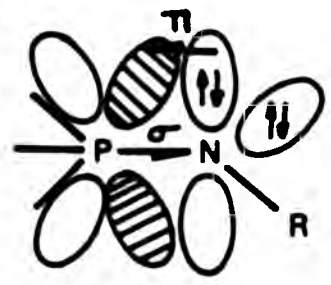


FIGURE 1

The photoelectron spectra of alkylidenephosphoranes[35a] and iminophosphoranes[35b] have recently been reported, and show the latter to be more stabilised (higher ionisation energies for the n_N^{π} electrons than the n_C- electrons). The parent iminotriphenylphosphorane displayed an energy gap of 1eV for the n_N^{π}/n_N^{σ} ionisations, with N-alkyl derivatives lowering the n_N^{π} and n_N^{σ} ionisations by different degrees and N-phenyl derivatives delocalising the negative charge. P-phenyl derivatives showed slightly reduced first ionisation energies with the phenyl groups delocalising the phosphorus positive charge. Parallel to the results obtained for alkylidenephosphoranes, N-trimethylsilyl substituents leave n_N^{π} ionisations practically unaffected but cause a degeneration of n_N^{π}/n_N^{σ} by lowering the ionisation energy of n_N^{σ} in the two iminophosphoranes studied. These results confirm an ylide type bond system for these compounds.

CNDO/2 model calculations[35b] predict for $(CH_3)_3P{=}NH$ a phosphorus-nitrogen bond distance of 1.66Å with n_N^{π} as the HOMO orbital and the nitrogen atom in an sp^2 hybridisation in close agreement with crystallographic experimental results. The conformation is predicted to have the N-H bond staggered in relation to the R_3P group with rotation taking place practically unhindered. Similar calculations for the $Me_3P{=}N{-}C_6H_5$ system predict the phenyl group to rotate relatively freely with some hindrance due to through-space interactions. The low temperature (-100°C) proton NMR spectrum of $Me_3P{=}NMe$ showed no changes from the room temperature

spectrum, implying a very low energy barrier to rotation. If rotation about the P=N double bond was slow on the NMR time scale, at low temperatures the methyl groups on phosphorus would become non-equivalent due to the non-linear P=N-C skeleton. If -100°C is taken as the upper limit, ΔG^* for the rotation process would be less than 33.5 kJ/mol[38], thus adding some experimental support to the above theoretical calculations. Charge distribution calculations agree well with ESCA results[36] showing iminophosphoranes to have a more positive phosphorus atom than the isoelectronic alkylidenephosphoranes. (Figure 2, π charges in parentheses).

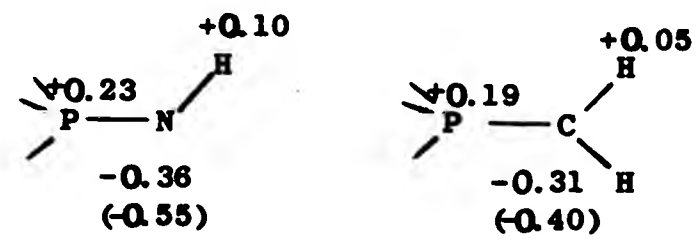
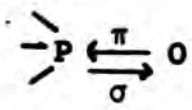


FIGURE 2

Dipole moments of iminophosphoranes have been measured by several groups[37] but comparison with those of alkylidenephosphoranes is not possible as the latter, except for stabilised ylides, seem not to have been measured. However, comparisons with the related phosphine oxides[35b] show the polarity of the P=N bond to be apparently greater than that of the P=O bond since they have comparable dipole moments in spite of oxygen's higher electronegativity:

Ph_3PO:4.5D Ph_3PNH:4.2D $Ph_3PNC_6H_5$:4.4 - 4.8D

The bond moment of the phosphoryl group is explained by the formation of a π-system over the donor σ-bond with the two non-bonding pairs of electrons on oxygen overlapping the vacant $3d_{xz}$ and $3d_{yz}$ orbitals on phosphorus[39]. In this way two π-bonds are established, transferring sufficient electron density back to phosphorus to counterbalance the σ-donor bond.



Therefore, the bond moment would be inversely proportional to the multi-

plicity of the bond and the greater the multiplicity the smaller the moment. On this basis (and in agreement with experiment[40]) the following order of relative polarity should be found:

$$\text{P=N} \;>\; \text{P=O} \;>\; \text{P=S}$$

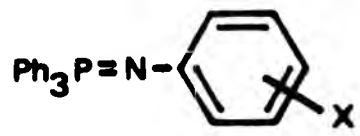
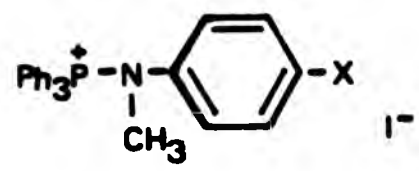
The UV spectra of N-aryliminotriphenylphosphoranes show little detail, and in contrast to analogous alkylidenephosphoranes, are of no great use in structure determination[2d,33]. However, they do point to a considerable π-electron delocalisation through the N-aryl group with a strong contribution from the mesomeric form (21)

(20) (21)

This transmission of substituent effects has been clearly demonstrated by ^{31}P NMR[41,42] and correlated by a Hammett relationship[43].

NMR spectroscopy provides probably the greatest wealth of structural information on phosphorus compounds. Proton NMR has proved exceptionally useful for the accurate measurement of J(^{31}P-^{1}H) coupling constants[44], ^{31}P NMR affords direct information on the phosphorus atom's environment and ^{13}C NMR spectra can provide complementary information on bonding properties where charge effects are dominant[35a].

The ^{31}P nucleus is particularly suited for NMR studies as it occurs in 100% natural abundance and with a spin quantum number (I) of ½. Table 2 lists some ^{31}P chemical shifts of N-aryl-ITPPs and their N-methyl salts. (In keeping with current convention, low field chemical shifts relative to 85% H_3PO_4 are reported as positive.)

TABLE 2  and 

Substituent	δ ^{31}P (ppm) o[43]	m[43]	p[42]	δ ^{31}P (ppm)[42]
OCH_3	3.62	3.11	2.65	45.7
CH_3	-0.55	2.61	2.93	45.2
H	3.29[42]	3.29[42]	3.29	45.4
F	4.56	3.67	3.05[43]	-
Cl	2.18	3.87	4.25	45.7
Br	2.02	3.75	4.35	45.5
I	2.71	3.87	4.50	45.5
CO_2Me	0.70*	-	-	-
CO_2Et	-	-	5.90	45.2
CN	-	-	7.20	45.5
$COCH_3$	4.00*	-	7.27	45.1
NO_2	4.60	5.46	7.73	45.5
CF_3	-	4.44	-	-
$\overset{+}{N}(CH_3)_3I^{\ominus}$	10.63*	-	5.70[43]	-

* This work

Anaylsis of Table 2 shows the phosphorus atom of the N-methyl-ITPPm salts to be deshielded by about 40 ppm from their corresponding N-aryl-ITPPs, thus providing additional evidence and confirming the ylide nature of the P=N bond with a strong contribution from resonance form (22), i.e. considerable back-donation to the phosphorus atom through the (p-d)π system.

$$Ph_3P{=}N\text{-}Ar \longleftrightarrow Ph_3\overset{+}{P}\text{-}\bar{N}\text{-}Ar$$

(22) (23)

A comprehensive study of the influence of substituents on the phosphorus and nitrogen atoms has not been published, with most of the

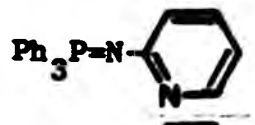
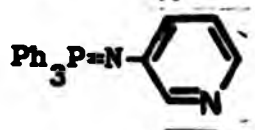
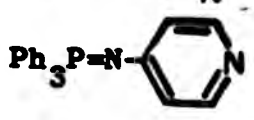
data available concentrating on triphenyl-P derivatives. However, Schweizer et al[45] reported some results on the influence of N-substituents, which are listed in Table 3. As expected, the deshielding of the phosphorus atom caused by electron-withdrawing substituents is very pronounced revealing extensive delocalisation of charge.

TABLE 3 ^{31}P NMR spectra of $Ph_3P{=}N{-}R$

Compound	Solvent	$\delta\ ^{31}P$ (ppm)
$Ph_3P{=}N{-}CPh_3$	$CDCl_3$	-10.3
$Ph_3P{=}N{-}SiMe_3$	$CDCl_3$	- 1.8
$Ph_3P{=}N{-}Ph$	$CDCl_3$	3.0
$Ph_3P{=}N{-}SO_2C_6H_4Me(p)$	$CDCl_3$	14.6
$Ph_3P{=}N{-}COPh$	$CDCl_3$	20.6
$Ph_3P{=}N{-}CN$	-	25.8[46]

The shielding of the phosphorus atom in the case of the N-trityl-triphenyliminophosphorane is attributed more to steric compressions between the two sets of phenyl rings than inductive effects.

A clear example where inductive and resonance effects could be separated was provided by Dawson[48] when studying the N-pyridyl-ITPPs:

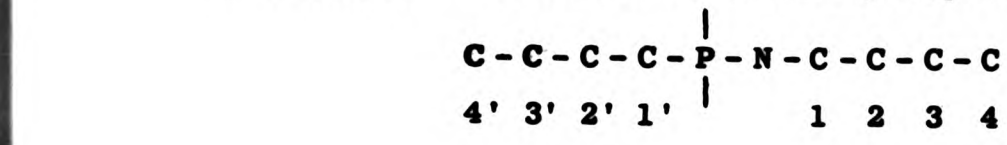
Compound	Type of electron withdrawal	$\delta\ ^{31}P$/ppm
$Ph_3P{=}N{-}$ 	inductive and resonance	14.8
$Ph_3P{=}N{-}$ 	inductive only	5.7
$Ph_3P{=}N{-}$ 	resonance only	8.6

ITPP hydrohalide salts are also deshielded with respect to the free ITPP but not to the same extent as the N-methyl-ITPP salts. A typical example is N-phenyl ITPP[41]:

$Ph_3P=N-Ph$	3.3 ppm
$Ph_3\overset{+}{P}-NH-Ph\ Br^-$	33.6 ppm
$Ph_3\overset{+}{P}-N(CH_3)Ph\ I^-$	45.4 ppm

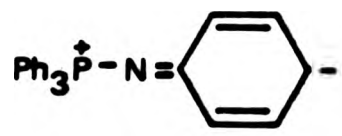
^{13}C NMR spectra results further corroborate the existence of wide delocalisation of charge through the entire molecule[5,35b,45,47].

TABLE 4 ^{13}C NMR data of iminophosphoranes and their hydrohalide salts



	δ(ppm) J(^{13}C-^{31}P)Hz							
Compound	1'	2'	3'	4'	1	2	3	4
Me_3PNH	20.0 (62)							
$Me_3\overset{+}{P}NH_2\ Cl^-$	13.6 (67)							
Me_3PNMe	14.9 (65)				31.8 (6)			
$Me_3\overset{+}{P}NHMe\ Cl^-$	11.2 (65)				26.9 (-)			
Me_3PNCMe_3	20.4 (65)				51.4 (5)	35.9 (12)		
$Me_3\overset{+}{P}NHCMe_3\ Cl^-$	14.7 (65)				54.4 (4)	31.9 (5)		
Ph_3PNCMe_3	135.4 (96)	132.6 (10)	128.0 (11)	130.5 (2)	51.7 (2)	35.4 (10)		
$Ph_3\overset{+}{P}NHCMe_3\ Cl^-$	123.3 (102)	134.5 (11)	130.6 (14)	135.6 (-)	56.2 (14)	31.9 (5)		
Me_3PNPh	15.3 (65)				152.3 (3)	122.2 (21)	128.6 (-)	116.3 (-)
$Me_3\overset{+}{P}NHPh\ Cl^-$	12.1 (65)				139.0 (-)	122.1 (-)	130.7 (-)	125.1 (-)
Ph_3PNPh	131.2 (99)	132.4 (10)	128.4 (12)	131.5 (3)	151.0 (2)	123.4 (18)	128.5 (-)	117.3 (-)
$Ph_3\overset{+}{P}NHPh\ Br^-$	119.8 (103)	135.5 (12)	130.0 (13)	135.2 (-)	137.8 (2)	123.5 (18)	129.2 (-)	121.8 (7)
$Ph_3PN-SiMe_3$	136.4 (102)	132.6 (10)	128.7 (12)	131.3 (3)	6.1 (3)			

Somewhat surprisingly the carbon atoms (C-1') directly linked to the phosphorus atom are seen to be shielded in the salts with respect to their corresponding ylides. This same result is observed for the resonances of the carbon atoms (C-1) bonded to the nitrogen atom except for the two t-butyl derivatives where the three methyl groups' inductive effect could help reverse this trend. This effect which is present for phosphorus-carbon ylides[49] and phosphine oxides may be due, in part, to an electric field effect of the P=X bond[50]. However, the chemical shifts of the ortho (C-2'), meta (C-3') and para (C-4') carbon atoms are shielded in the free ITPP and this may be taken as evidence of some charge being transferred from nitrogen to phosphorus. The N-phenyl ring carbon atoms show that the ortho position (C-2) remains essentially unaffected while the meta (C-3) and para (C-4) of the free iminophosphoranes are shielded, the latter to a greater degree, with respect to their respective ITPP hydrohalide salts. This situation seems to indicate a strong contribution from the mesomeric form (24), at the same time correlating well with UV and ^{31}P NMR results.



(24)

The $J(^{13}C-^{31}P)$ coupling constants are quite similar to those found for alkylidenephosphoranes[49].

IR spectroscopy has also proved very useful in the structure determinations of iminophosphoranes. The P=N stretching frequency gives rise to a strong absorption in the 1500-1147 cm^{-1} region[51]. Bock et al[52] have studied some ^{15}N-analogues' IR spectra confirming the above assignment. The ν(P=N) is very dependent on substituents (as shown by Table 5) but the range is considerably smaller for closely related compounds. For example, the N-aryl-ITPPs' ν(P=N) vibration spans the

TABLE 5 IR data of iminophosphoranes

Compound	ν(P=N)/cm^{-1}
Ph_3P=N-Ph	1344
Ph_3P=N-NHCOPh	1333
Ph_3P=N-COPh	1332
Ph_3P=N-$SiMe_3$	1315
Ph_3P=N-Me	1230
Ph_3P=N-$SO_2C_6H_4Me$(p)	1147
Cl_3P=N-$SO_2C_6H_4Me$(p)	1199

1390 cm^{-1} to 1300 cm^{-1} range[41,53]. This variation of the stretching frequency of the P=N bond has been attributed to polarisation of the bond, affected mostly by substituents on nitrogen[54].

It has recently been shown[55] that the ν(P=N) frequency increases with increasing electronegativity of the phosphorus substituents. In agreement with this, Egorov et al[56], using ^{31}P chemical shifts, have shown that in compounds of type $R^1R^2R^3P$=N-R, bond order increases with increasing electronegativity of substituents on phosphorus and decreases with increasing electronegativity of substituents on nitrogen.

The IR spectra of N-aryl-ITPP hydrohalides, as expected, show no absorption in the 1340 cm^{-1} region but a characteristic band at ca. 965 cm^{-1} while N-methyl-N-aryl-ITPPm halides show an absorption at ca. 910 cm^{-1}, assigned to $\nu(\overset{+}{P}$-N-H) and $\nu(\overset{+}{P}$-N-CH_3) respectively[41,57], correlations used widely in the present work to gain an insight into various reactions studied.

As was mentioned earlier, the order of basicity found for the iminophosphoranes and the isoelectronic phosphine oxides and sulphides is:

$$\text{>P=N-} \quad > \quad \text{>P=O} \quad > \quad \text{>P=S}$$

Iminophosphoranes are strong bases, comparable in many cases to tertiary

amines and guanidines, although the pKa values are affected by the nature of the substituents, both on phosphorus and nitrogen. Changes of substituents on phosphorus can alter the basicity by six orders of magnitude while the effect of nitrogen substituents is, as expected, even larger, being around nine orders of magnitude (see Tables 6, 7 and 8).

TABLE 6 pKa values of $R_3P=NPh$

Compound	pKa(CH_3NO_2)	Ref 40
$(MeO)_3P=N-Ph$	13.81	b
$(EtO)_3P=N-Ph$	14.71	a+b
$(EtO)Et_2P=N-Ph$	17.81	b
$Et_3P=N-Ph$	19.30	a
$(C_6H_5(Me)N)Et_2P=N-Ph$	19.32	a
$Ph_3P=N-Ph$	16.74	a+b
$(CF_3C_6H_4)_3P=N-Ph$	13.78	b
$(Me_2NC_6H_4)_3P=N-Ph$	20.77	b

TABLE 7 pKa values of $Ph_3P=NR$

Compound	pKa(CH_3NO_2)	Ref 40
$Ph_3P=NH$	20.65	a
$Ph_3P=NH$	13.37(H_2O)	a
$Ph_3P=N-Ph$	15.32(16.74)	a+b
$Ph_3P=N-COPh$	11.5	a

TABLE 8 pKa values of amines and imines

Compound	pKa(CH_3NO_2)	Ref 40
Et_3N	18.35	a
$PhNH_2$	9.07	b
$PhNMe_2$	11.00	b
$Ph_2C{=}NH$	6.82(H_2O)	a
$(PhNH)_2C{=}NH$	17.20	a

When compared with analogous phosphorus-carbon ylides, oxides and sulphides the basicity differences are found to be very large. The sulphides are by far the weakest and it is often difficult to measure their pKa values. Iminophosphoranes are intermediate between the methylenephosphoranes and the phosphine oxides: for example 16.40[40a] ($Ph_3P{=}CHCOPh$), 11.5 ($Ph_3P{=}NCOPh$, Table 7) and 5.5 ($Ph_3P{=}O$) and 8.18 ($Et_3P{=}O$).

Tables 6, 7 and 8 reveal the quantitative relationship between iminophosphoranes and aromatic amines, and Zhmurova et al[40b] have shown that when two centres of basicity are present on the same molecule, as with aryl-(triphenylphosphoranylidene)-anilines, N-benzylidene-N'-(triphenylphosphoranylidene)phenylenediamines and p-(arylazo)-N-(triphenylphosphoranylidene)anilines, it is the iminotriphenylphosphoranyl group which is exclusively or preferentially protonated. This behaviour is reflected in their electrophilic substitution reactions in weakly acidic media,which are unknown for iminophosphoranes in contrast to dimethylanilines. Only one example of this type of reaction is known (tricyanovinylation) and this proceeds in pyridine solution[58].

In contrast to its basic character, the iminophosphorane's electron-donating character with respect to an organic residue, -R, attached to the nitrogen atom is negligibly affected by the nature of the phosphorus

substituents because of the polar nature of the P=N bond[9,40b].

$R'_3P=N-R$

When -R is an aromatic ring, the electron-releasing effect of the iminophosphorane group approaches that of the dimethylamino radical, the main qualitative difference being the opposite sign of the Taft σ* constant and the inductive component of Hammett σ constants. The observed differences in the chemical properties of dimethylanilines and iminophosphoranes are due to the strong polarisation of the P=N bond, causing the iminophosphorane's nitrogen atom to possess a higher electron density than that in the dimethylamino group, thus explaining their different basicities.

Detailed investigations of substituent effects and their correlation with Hammett constants have been carried out[9,40].

Iminophosphoranes and alkylidenephosphoranes, as has already been said, are isoelectronic species and to a large extent this is reflected in their similar chemical behaviour.

Because of the polar nature of the P=N bond, iminophosphoranes are readily hydrolysed under both acid and basic conditions[5,27], and are good nucleophilic reagents as demonstrated by their reactions with alkyl halides[41,59], carbonyl compounds[5], activated alkynes[48,57,60] and their use as ligands in metal complexes[5,41,57]. The ease of hydrolysis is related to the basicity of the imine. Iminotriphenylphosphorane and N-alkyl-ITPPs are readily hydrolysed to triphenylphosphine oxide and ammonia or alkylamines respectively, either directly in moist air or under basic conditions depending on their basicities[3,16,18].

$$R_3P=N-R + H_2O \longrightarrow R_3PO + H_2N-R$$

The mechanism of the basic hydrolysis is thought to proceed by initial attack on phosphorus by the hydroxide ion (OH^-), followed by elimination of the amine and TPPO[5].

substituents because of the polar nature of the P=N bond[9,40b].

$R'_3P=N-R$

When -R is an aromatic ring, the electron-releasing effect of the iminophosphorane group approaches that of the dimethylamino radical, the main qualitative difference being the opposite sign of the Taft σ* constant and the inductive component of Hammett σ constants. The observed differences in the chemical properties of dimethylanilines and iminophosphoranes are due to the strong polarisation of the P=N bond, causing the iminophosphorane's nitrogen atom to possess a higher electron density than that in the dimethylamino group, thus explaining their different basicities.

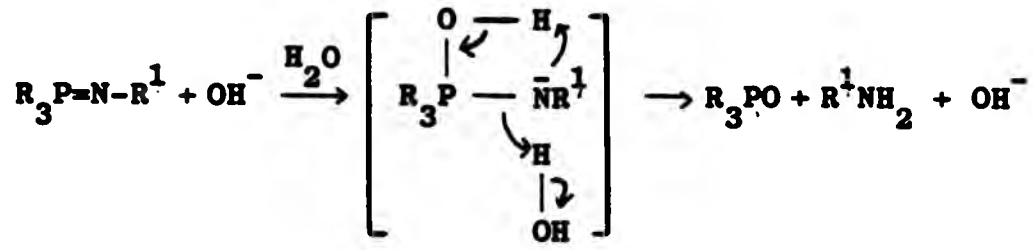
Detailed investigations of substituent effects and their correlation with Hammett constants have been carried out[9,40].

Iminophosphoranes and alkylidenephosphoranes, as has already been said, are isoelectronic species and to a large extent this is reflected in their similar chemical behaviour.

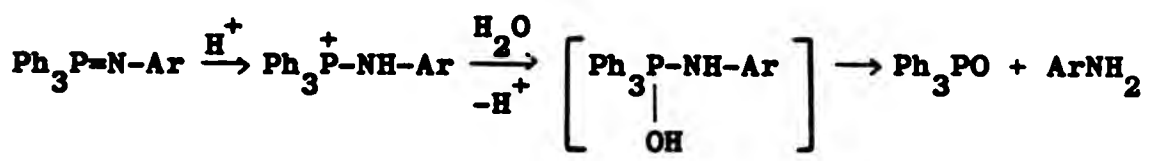
Because of the polar nature of the P=N bond, iminophosphoranes are readily hydrolysed under both acid and basic conditions[5,27], and are good nucleophilic reagents as demonstrated by their reactions with alkyl halides[41,59], carbonyl compounds[5], activated alkynes[48,57,60] and their use as ligands in metal complexes[5,41,57]. The ease of hydrolysis is related to the basicity of the imine. Iminotriphenylphosphorane and N-alkyl-ITPPs are readily hydrolysed to triphenylphosphine oxide and ammonia or alkylamines respectively, either directly in moist air or under basic conditions depending on their basicities[3,16,18].

$$R_3P=N-R + H_2O \longrightarrow R_3PO + H_2N-R$$

The mechanism of the basic hydrolysis is thought to proceed by initial attack on phosphorus by the hydroxide ion (OH^-), followed by elimination of the amine and TPPO[5].



The stabilised N-aryl-ITPPs are hydrolysed in dilute acid media[3], (or when heated with base,) to give TPPO and the corresponding arylamine. The mechanism of this acidic hydrolysis is depicted as taking place by initial protonation of the imine followed by formation of a pentavalent phosphorus intermediate (25) which collapses into the products. The hydrolysis



(25)

of the optically active imine (26)[61] gave predominantly inverted

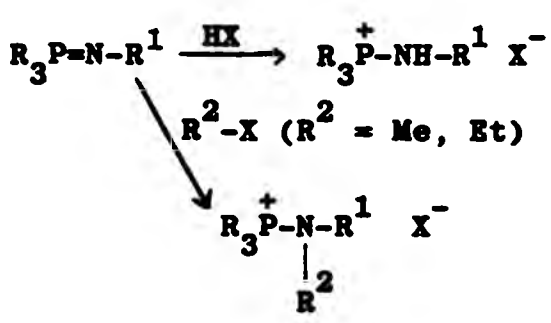
$PhMe(C_3H_7)P{=}N{-}C_6H_4NO_2(p)$

(26)

phosphine oxide, indicating that back-side attack by water occurred.

Iminophosphoranes are basic and nucleophilic compounds, and these two properties have been elegantly exploited in a synthesis of secondary amines[41,59,62] uncontaminated by bis-alkylation products.

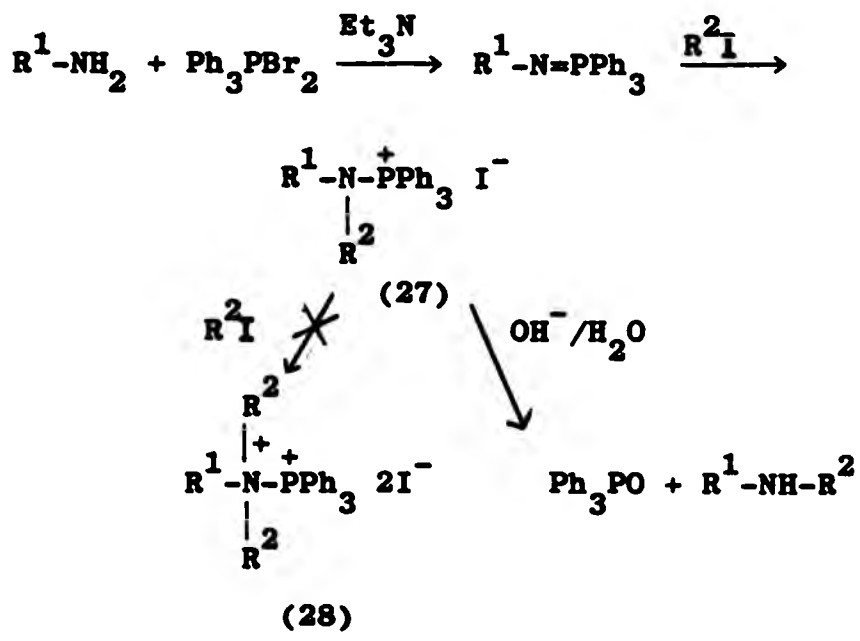
As nucleophiles, iminophosphoranes react with hydrogen halides and alkyl halides yielding the corresponding phosphonium salts[41,59,62].



However, this latter reaction is somewhat limited as the higher alkyl halides reacting with N-alkyl-ITPPs undergo hydrogen halide elimination with formation of an olefin and the corresponding aminophosphonium salt[62].

Meidine[41] found that N-phenyl-ITPP reacted with n-butyl and i-propyl iodides yielding the N-alkylated salts but with t-butyl bromide, 9-bromofluorene and bromodiphenylmethane only the N-phenylaminophosphonium bromide could be isolated, showing this reaction to be very dependent on the basicity of the iminophosphorane and on the ease of elimination of hydrogen halide from the alkyl halide, although steric effects cannot be ruled out.

Bearing in mind these limitations, the combination of these two reactions, alkylation followed by hydrolysis, nevertheless affords a general and very useful synthetic route to secondary amines[41,59,62].



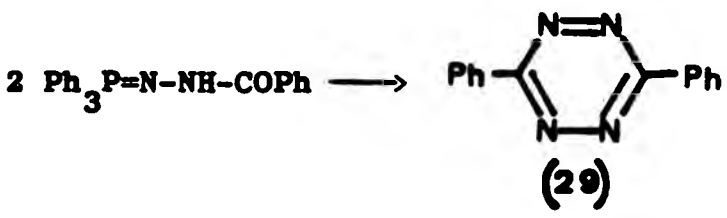
(28)

The elimination reaction problem can be conveniently avoided by choosing the initial primary amine to carry the required bulky group and, as (27) is unlikely to form (28) and its hydrolysis proceeds essentially without side reactions, a highly pure secondary amine is easily isolated.

As mentioned earlier, iminophosphoranes parallel phosphorus ylides in their chemical behaviour, and this is particularly true in their reactions with carbonyl compounds. Iminophosphoranes react with a variety of carbonyl compounds and thiocarbonyl compounds in Wittig-type reactions[2b,2d,3,6,27], forming, among other products, Schiff bases, ketenimines, isocyanates, isothiocyanates and N,N'-carbodiimides.

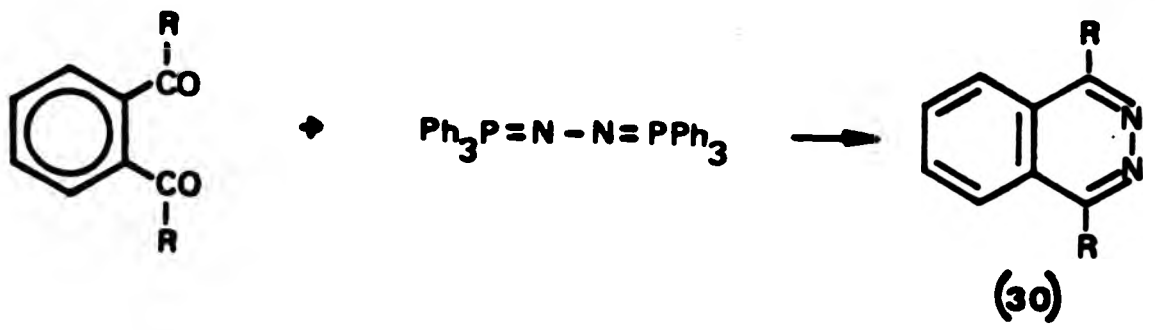
The reactions of iminophosphoranes with carbonyl compounds have been applied in the synthesis of a number of heterocyclic compounds.

N-acylamino-ITPP condenses intermolecularly to yield 1,2,4,5-tetrazines (29)[63], while bis-ITPPs



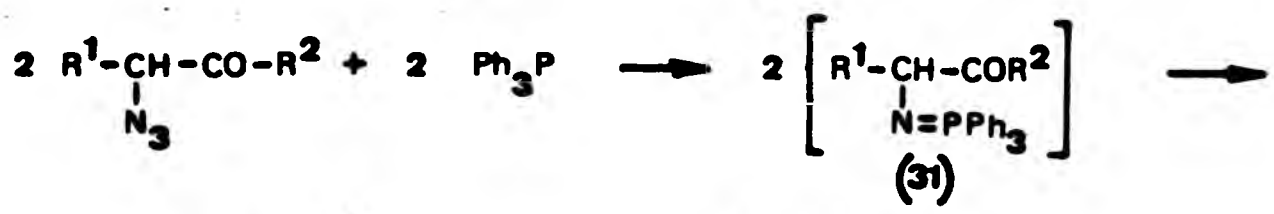
(29)

react with 1,4-carbonyl compounds yielding phthalazines (30)[64].

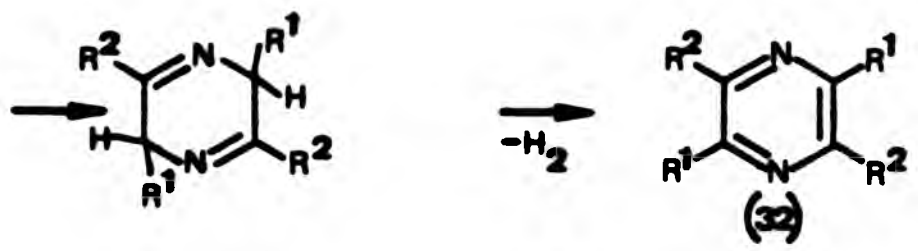


(30)

α-Azido-αH-ketones in the presence of triphenylphosphine afford 2,5-dihydropyrazine which finally oxidises to the pyrazine (32), probably through the formation of an intermediate N-(2-oxoalkyl)-iminophosphorane (31)[65]:

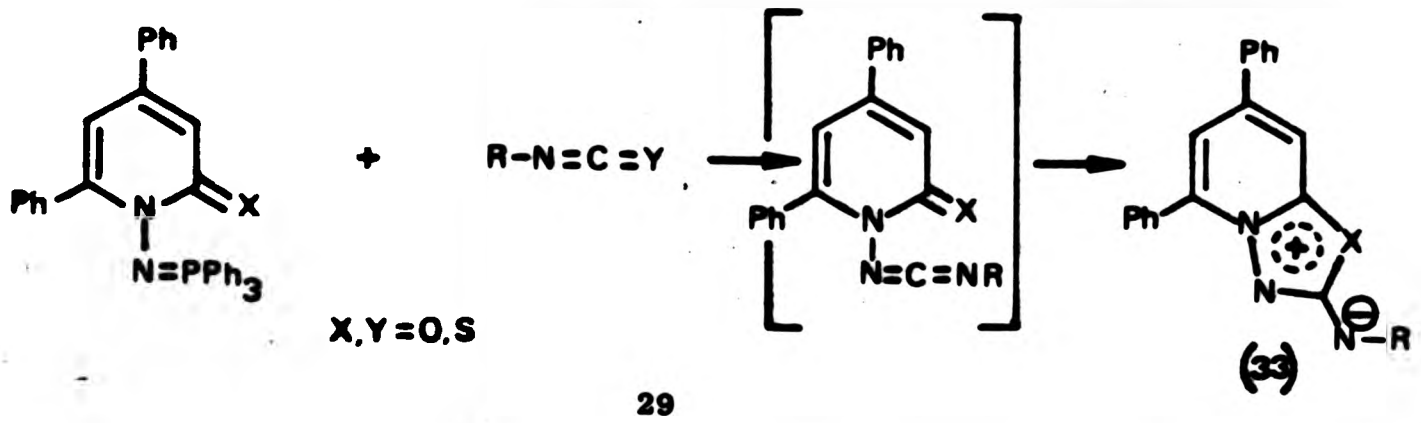


(31)



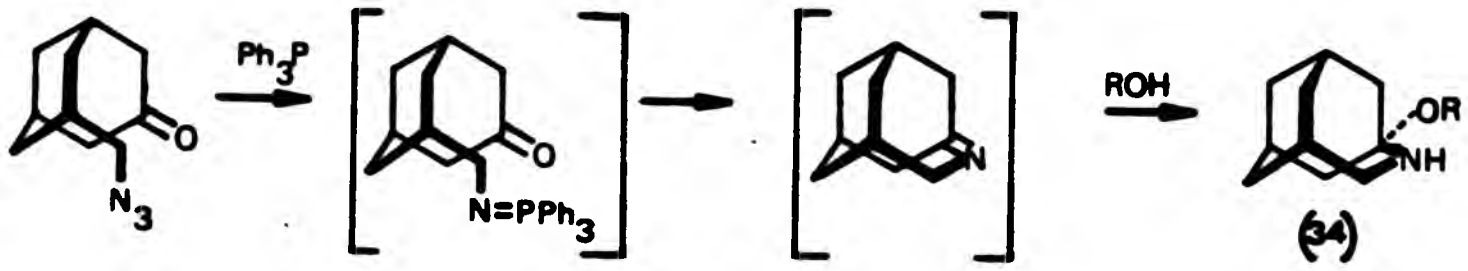
(32)

Fused mesoionic compounds (33) have been synthesised by reaction of iminophosphoranes with isocyanates and isothiocyanates[66]:



(33)

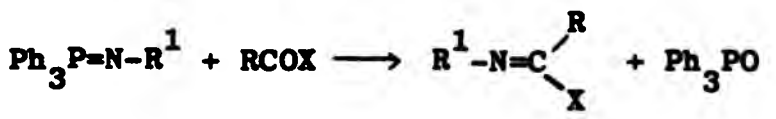
The isocyanates and isothiocyanates can be replaced with carbon dioxide and carbon disulphide[66]. Recently an intramolecular Wittig reaction has been used in the synthesis of azahomoadamantane derivatives (34)[67]



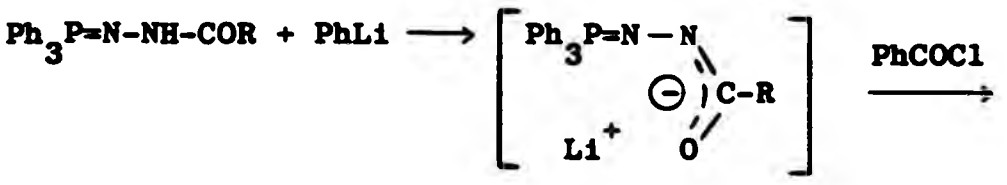
(34)

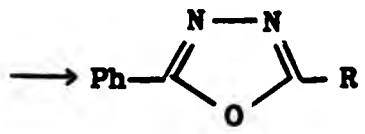
The use of acyl halides in reactions with iminophosphoranes has found widespread applications.

Iminophosphoranes and acyl halides in refluxing benzene yield imidoyl halides, including bromides and iodides, difficult to synthesise by other methods[68].



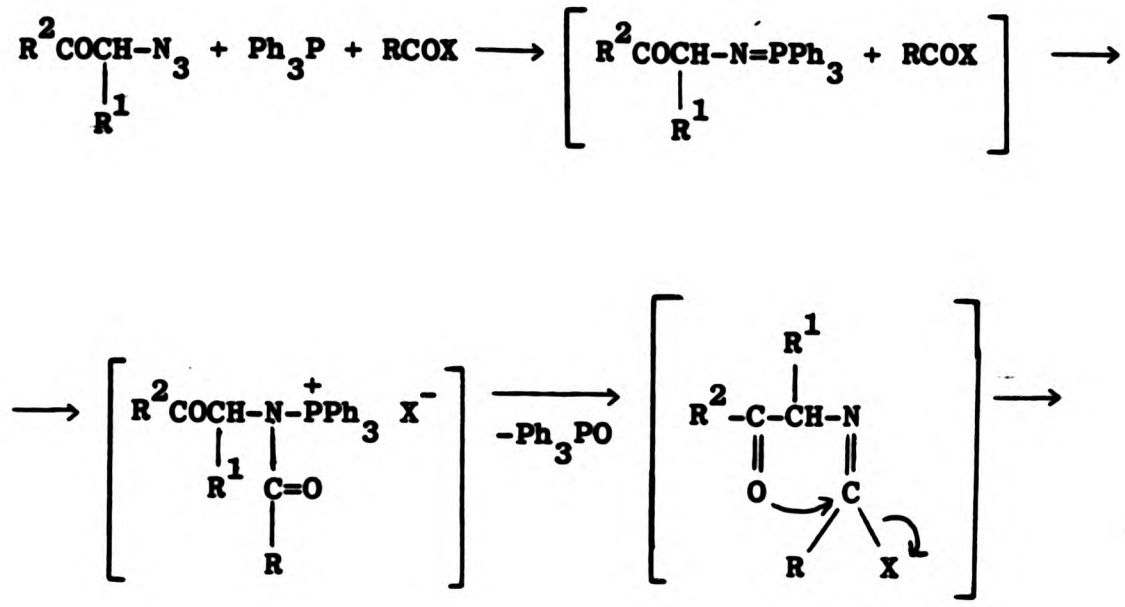
Phenyllithium proton abstraction from N-acylamino-ITPP and subsequent reaction with benzoyl chloride leads to the formation of 5-substituted-2-phenyl-1,3,4-oxadiazoles (35)[65]:

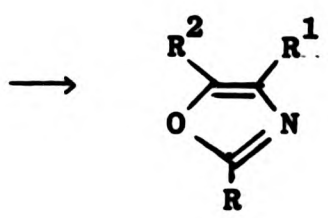




(35)

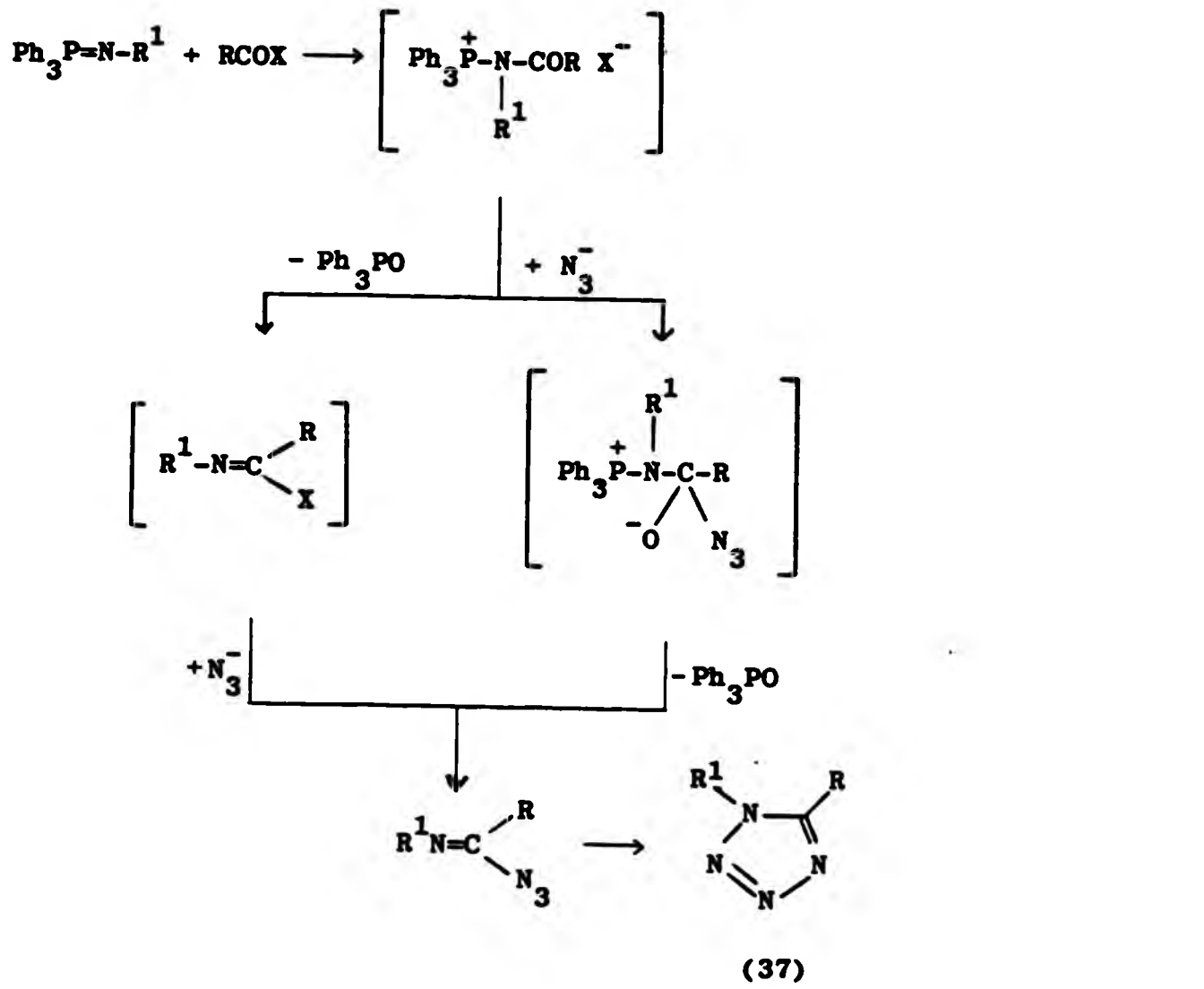
In a three component reaction between α-azido-αH-ketones, acyl halides and triphenylphosphine, 1,3-oxazoles (36) were isolated[68,69]





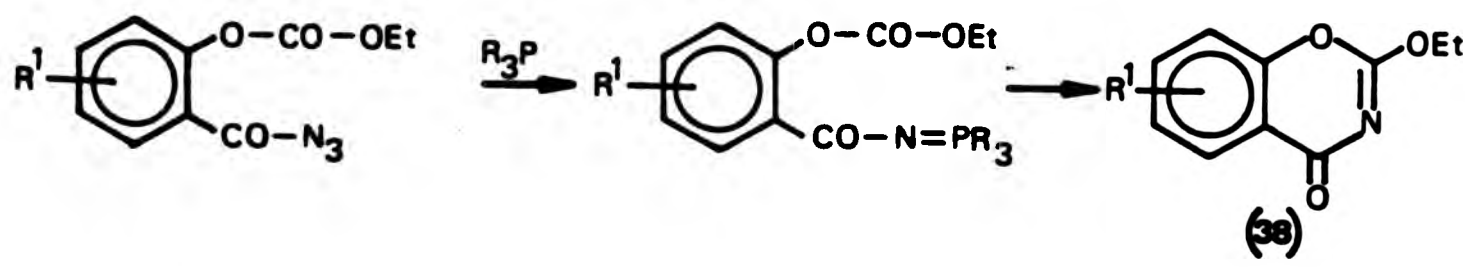
(36)

Another three component reaction yields tetrazoles (37) as final products. A mixture of an iminophosphorane, an acyl halide and sodium azide under very mild conditions affords (37)[70]

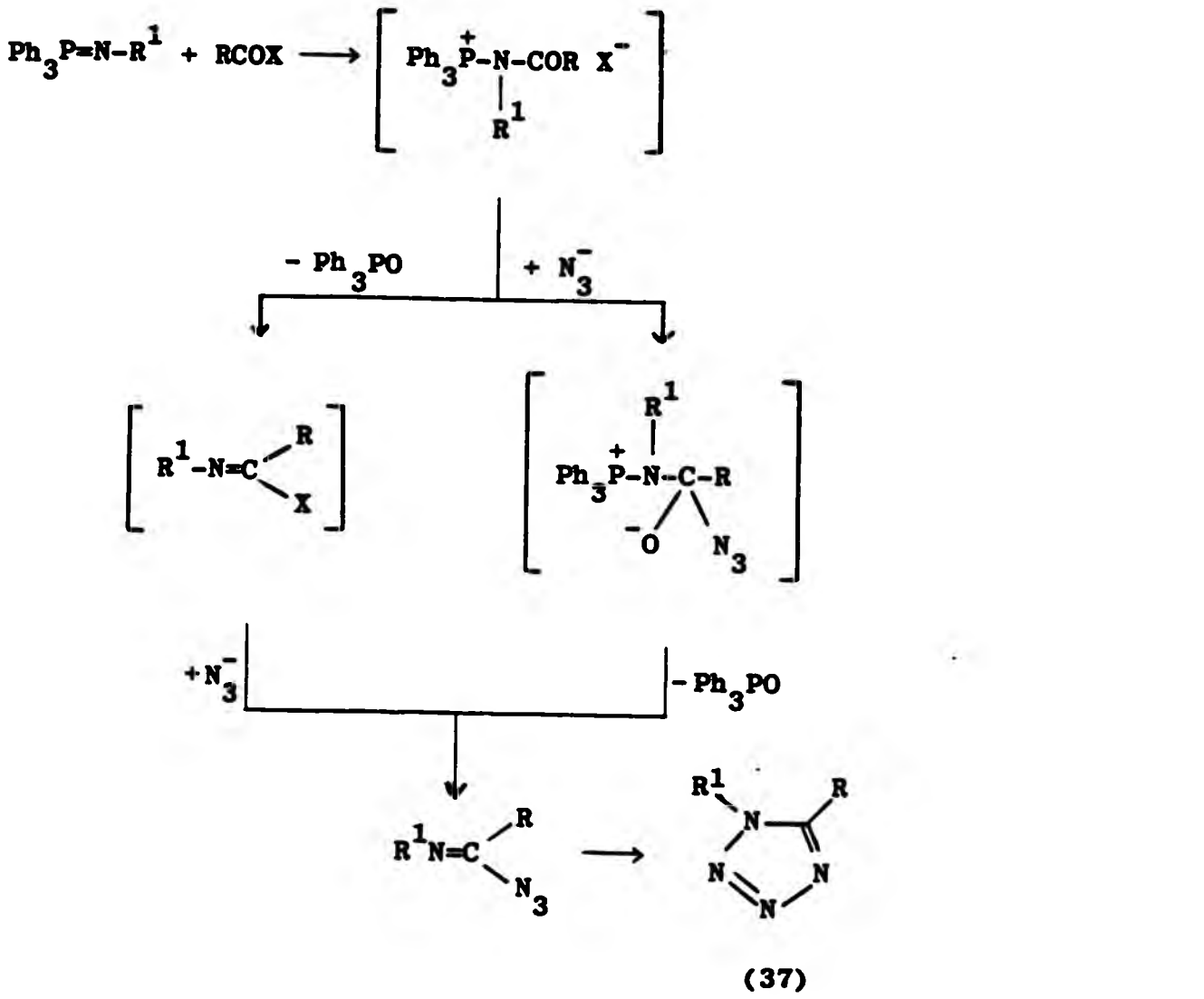


(37)

Iminophosphoranes also react with carbonates and thioureas to yield iminocarbonates[71] and guanidines[72] respectively. Especially interesting is the former reaction applied to the synthesis of a 1,3-benzoxazine (38)[71], where it involves a Wittig-like reaction on an ester carbonyl group.

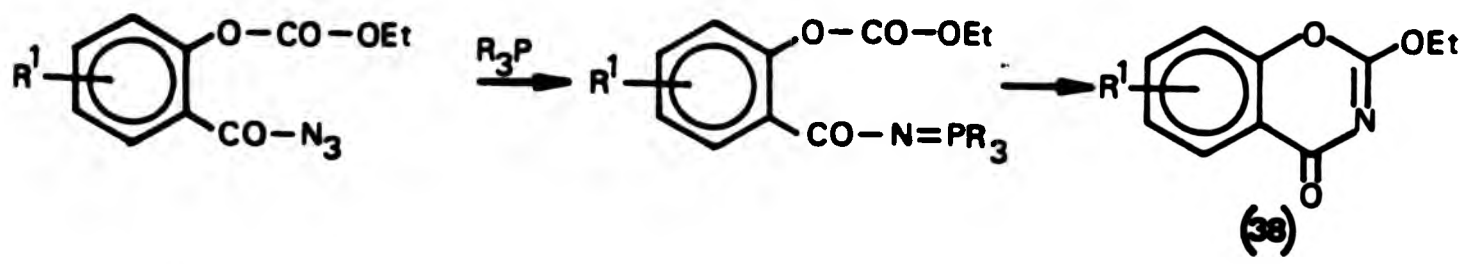


(38)



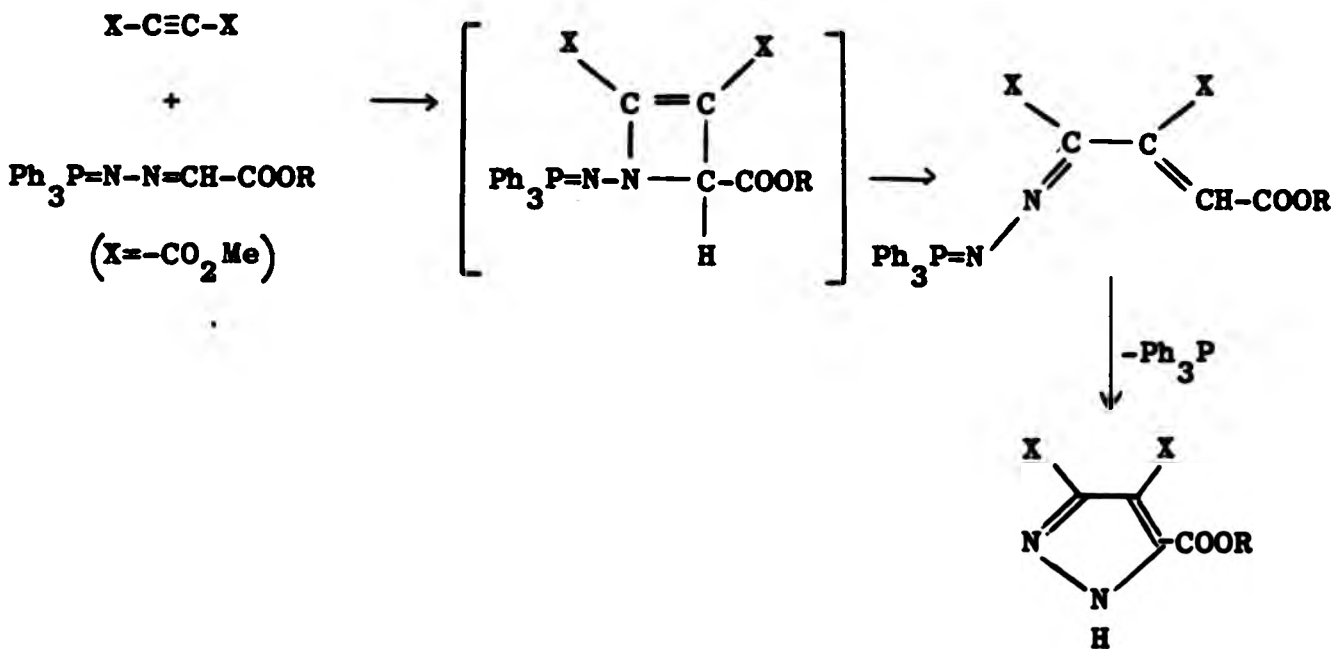
(37)

Iminophosphoranes also react with carbonates and thioureas to yield iminocarbonates[71] and guanidines[72] respectively. Especially interesting is the former reaction applied to the synthesis of a 1,3-benzoxazine (38)[71], where it involves a Wittig-like reaction on an ester carbonyl group.



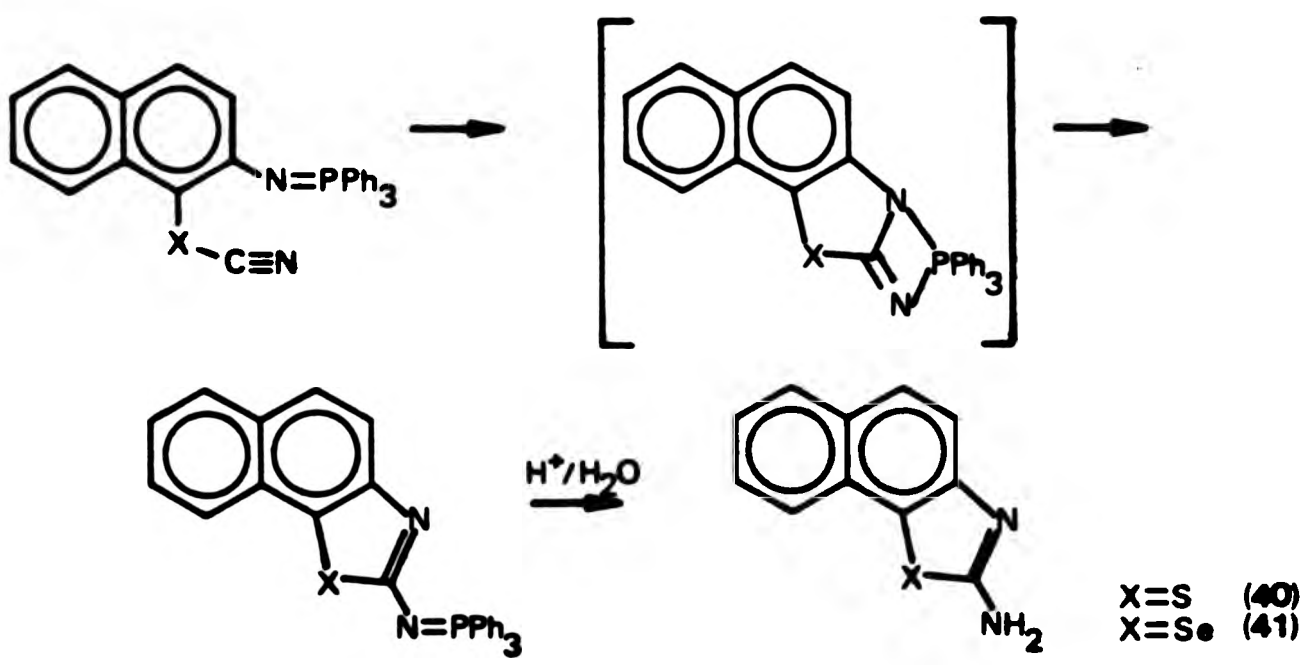
(38)

Iminophosphoranes react with activated acetylenes such as dimethyl acetylenedicarboxylate[60], thus providing another example of their nucleophilicity. A related reaction, although not involving the ITPP group directly, has been used in the synthesis of pyrazoles (39)[73]

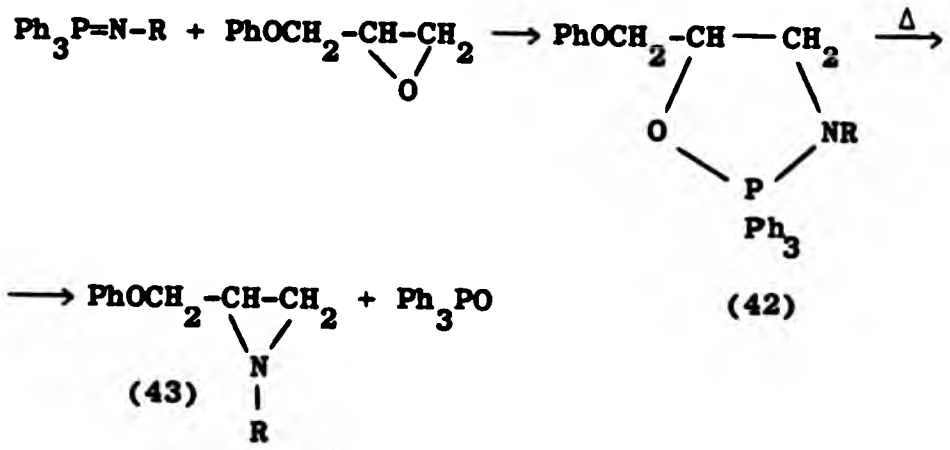


(39)

Iminophosphoranes also react with nitrile groups and this has provided a useful method for the synthesis of 1,3-thiazoles (40) and 1,3-selenazoles (41)[19] from thiocyanates and the selenium analogues.



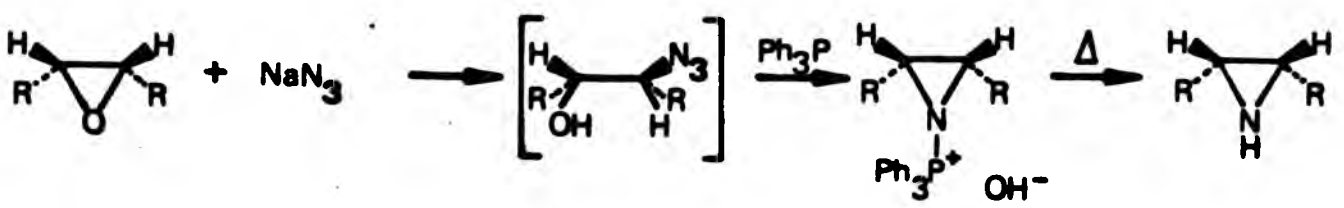
Three closely related aziridine syntheses have been recently developed. N-alkyl- and N-aryl-ITPP react with oxiranes forming an intermediate five-membered ring (42), which on heating eliminates TPPO yielding the N-substituted aziridine (43)[74]



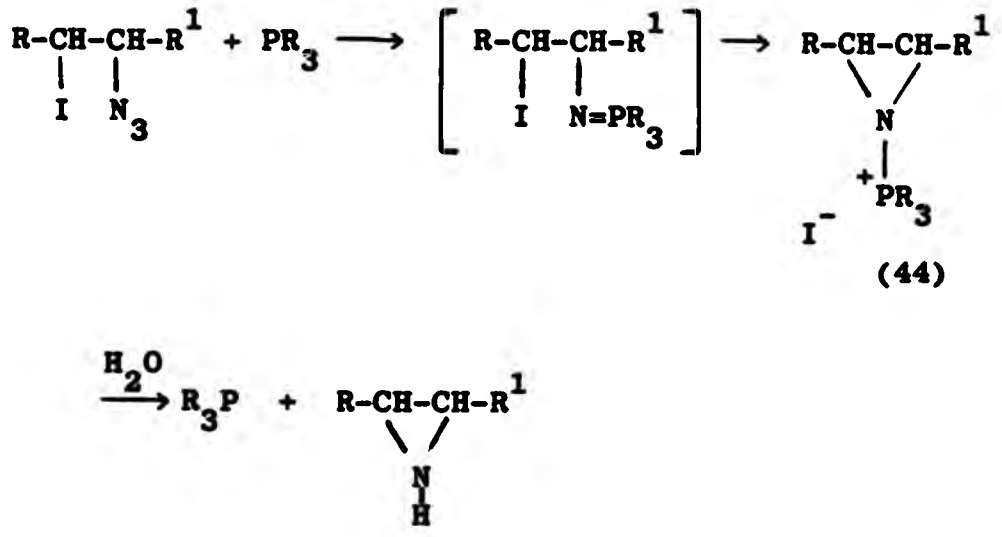
(42)

(43)

The second method involves reaction of an epoxide with sodium azide, followed by treatment with a tertiary phosphine[75], affording a stereospecific synthesis:



The last method[76] involves reaction of a tertiary phosphine with a vic-azidoiodoalkane followed by hydrolysis of the formed phosphonium salt (44):



(44)

Other applications of iminophosphoranes in synthesis include the preparation of primary enamines (45)[77]

$$Me_3SiN{=}PPh_3 + MeCOCH_2COX \xrightarrow{i\text{-}PrOH,TosOH} Me\text{-}C(NH_2){=}CH\text{-}COX$$

X=R,OR

(45)

the decomposition of N-acyl-iminophosphoranes to nitriles[27]:

$$R_3P{=}N\text{-}COR^1 \longrightarrow R_3PO + N{\equiv}C\text{-}R^1$$

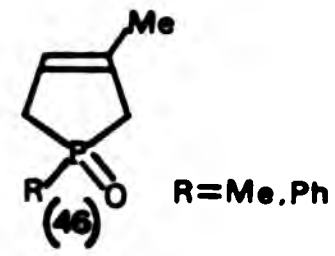
and the synthesis of pentaarylated phosphoranes[78]:

$$Ar_3P{=}NR + 2ArLi \longrightarrow Ar_5P + RNLi_2$$

Thus, as mentioned earlier, iminophosphoranes parallel phosphorus ylides in their chemical behaviour, particularly in their reactions with carbonyl compounds.

No mechanistic studies of this reaction were carried out until the mid-1960s although earlier[79] it had been suggested that iminophosphoranes were formed as intermediates in the following reaction:

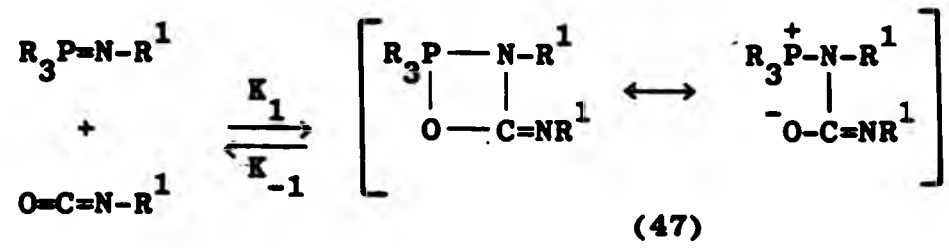
$$2PhN{=}C{=}O \xrightarrow{(46)} PhN{=}C{=}NPh + CO_2$$



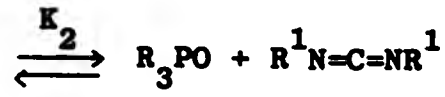
(46) R=Me,Ph

which took place only in the presence of the phospholene oxide (46). This was later extended to cover other tertiary phosphine oxides[80].

The mechanism of the reaction between iminophosphoranes and carbonyl compounds was thought to parallel that proposed for the analogous carbon ylides (Scheme 1):



(47)



Scheme 1

The carbonyl carbon atom undergoes attack by the imine nitrogen to give a betaine intermediate (47) followed by oxyanion attack on phosphorus to give the products, the second step being faster than the first, i.e. $K_2 > K_1$.

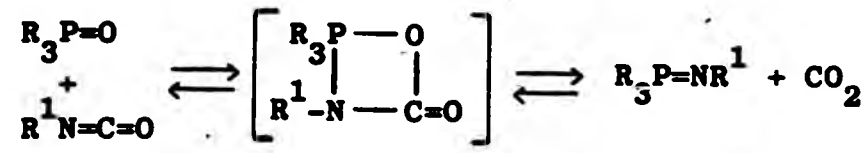
Kinetic studies of a large series of ITPPs with p-nitrobenzaldehyde[81] showed a substantial solvent effect, the reaction being 30 times as fast in ethanol as in benzene. This was consistent with a betaine intermediate (47) having a considerable degree of localised charge.

Electron-withdrawing substituents on the P-phenyl or on the N-phenyl group reduced the electron density on the P and N atoms, decreasing the nucleophilic character of the nitrogen, thus lowering K_1. At the same time the phosphorus atom became more susceptible to the oxyanion attack, increasing K_2. Therefore, K_1 remained the rate determining step and this was reflected in K_{obs}.

Electron-donating substituents produced opposite effects, making the nitrogen atom more nucleophilic, increasing K_1 and making the phosphorus atom less susceptible to the oxyanion attack lowering K_2. Hence K_2 became rate determining.

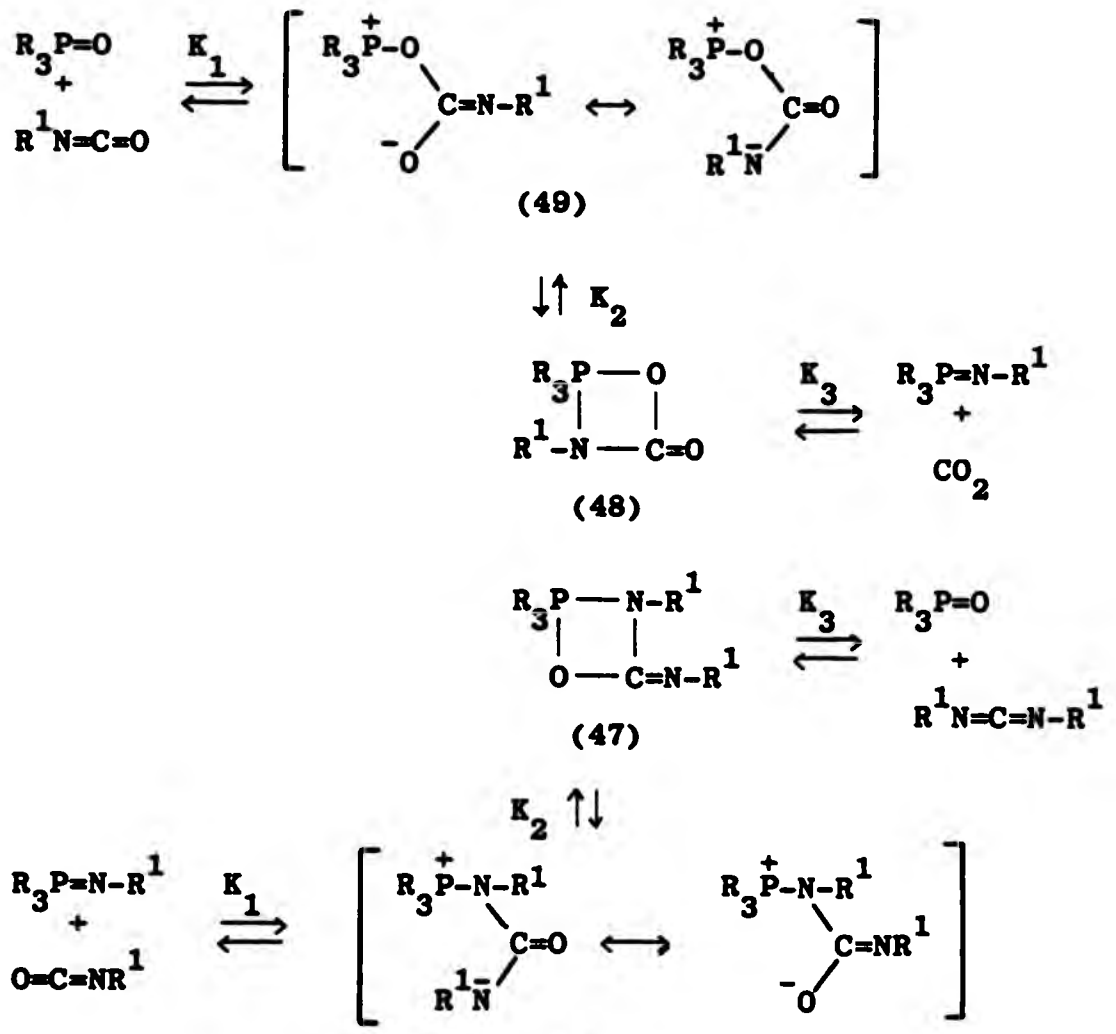
This change in rate determining step was later found to be general in the reaction of iminophosphoranes with aldehydes[82].

Aksnes and Frøyen[83] showed iminophosphoranes reacted 10^5-10^7 times faster with phenyl isocyanate than did the corresponding oxides:



(48)

In contrast to the phosphine oxide-phenyl isocyanate reactions, the activation energy for the iminophosphorane and phenyl isocyanate reactions was found to be independent of the substituents on phosphorus. This result was inconsistent with the proposed mechanism (Scheme 1) since two very similar intermediates (47) and (48) were postulated as rate determining. Therefore they proposed a modification of the mechanism for both reactions (Scheme 2)



(49)

(48)

(47)

(50)

Scheme 2

In this way, as phosphorus has a greater affinity for oxygen than nitrogen, in the first step (49) will revert to reactants faster than it will form (48) ($K_2 > K_3$) and similarly (50) will form (47) faster

than it will revert to the reactants ($K_2 < K_3$).

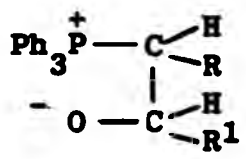
However, Frøyen[88] has recently pointed out some facts inconsistent with the proposed mechanism (Scheme 2). Electron donating substituents on the N-phenyl group increase the nucleophilicity of the iminophosphorane and slow the reaction by reducing K_2 and electron releasing substituents on phosphorus (such as Et) however do not slow down the reaction. These experimental results can be explained in terms of a concerted mechanism involving a pentacovalent 4-membered transition state without formation of a betaine[88]. However, no experimental proof for the existence of intermediates is yet available for these reactions.

It has also been shown[88] that the rate of reaction in benzene was similar to that in polar solvents (acetone, dimethylformamide), contrary to earlier results[82]. This has been attributed to a hydrogen bonding effect as the reaction was only accelerated by solvents capable of hydrogen bonding and the catalytic effect was approximately related to the hydrogen bonding ability of the solvent and not its acid strength. Previously[82], this faster rate of reaction in polar solvents was used as evidence to support the existence of intermediate betaines (47).

At the present time the precise mechanism of the reaction between iminophosphoranes and carbonyl compounds remains unresolved.

Some New Developments Regarding the Mechanism of the Wittig Reaction

Wittig reactions have been traditionally[2k] classified as taking place with either reactive or stabilised ylides, with borderline cases being referred to as moderate ylides. As the term implies, stabilised ylides are those capable of being isolated and not hydrolysed by atmospheric moisture, usually stabilised by an adjacent carbonyl group or other electron-withdrawing groups. The reactions have been explained by the assumption of polar key intermediates, named betaines (51), although no experimental evidence for the existence of true betaines has been provided[44]. Confusion prevails on this point as betaine-lithium halide adducts have been isolated as precipitates (and characterised) from ylides prepared in the presence of lithium halides. At the same time, several isolated betaine-hydrohalide adducts (β-hydroxy phosphonium halides) have also been presented as evidence for the formation of betaines as intermediates[2d]. Regret ably, the term betaine has been used in reference to both the unobserved salt-free species as well as the noncontroversial lithium halide and hydrohalide adducts. However, none of the mechanisms proposed satisfactorily

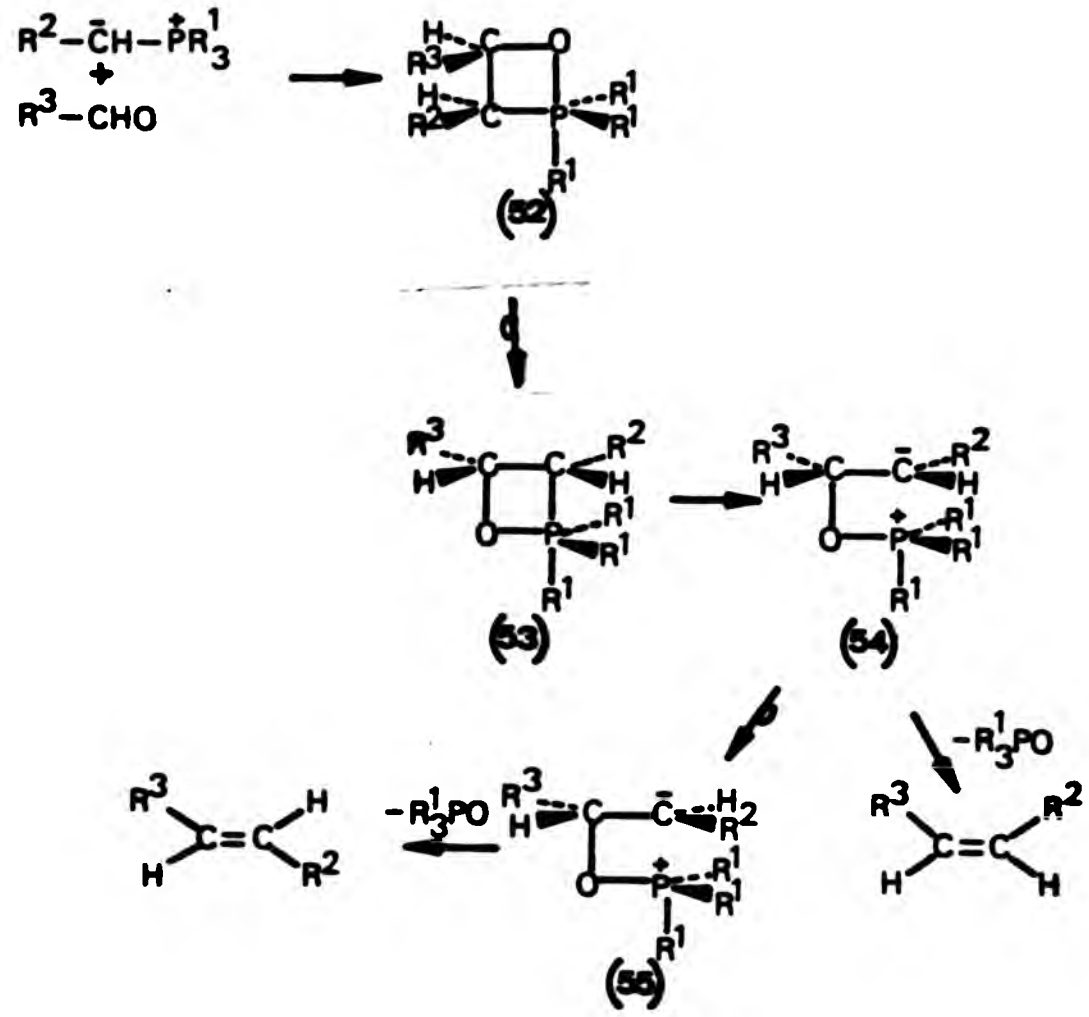


(51)

explained the stereoselectivity of the reaction and all its modifications[2k].

In recent years several papers have been published concerned with the salt-free Wittig reaction[44,89-93] of non-stabilised ylides. Suggestions to explain the remarkable cis-stereoselectivity observed for many of these reactions include coordination of carbonyl oxygen to phosphorus[94], (π2a + π2s) cycloaddition of ylide and carbonyl π-bonds [44,90], anti eliminations[89] and syn eliminations[90,92]. However, all these propositions, except that of Schneider[94], agree that cis-oxaphos-

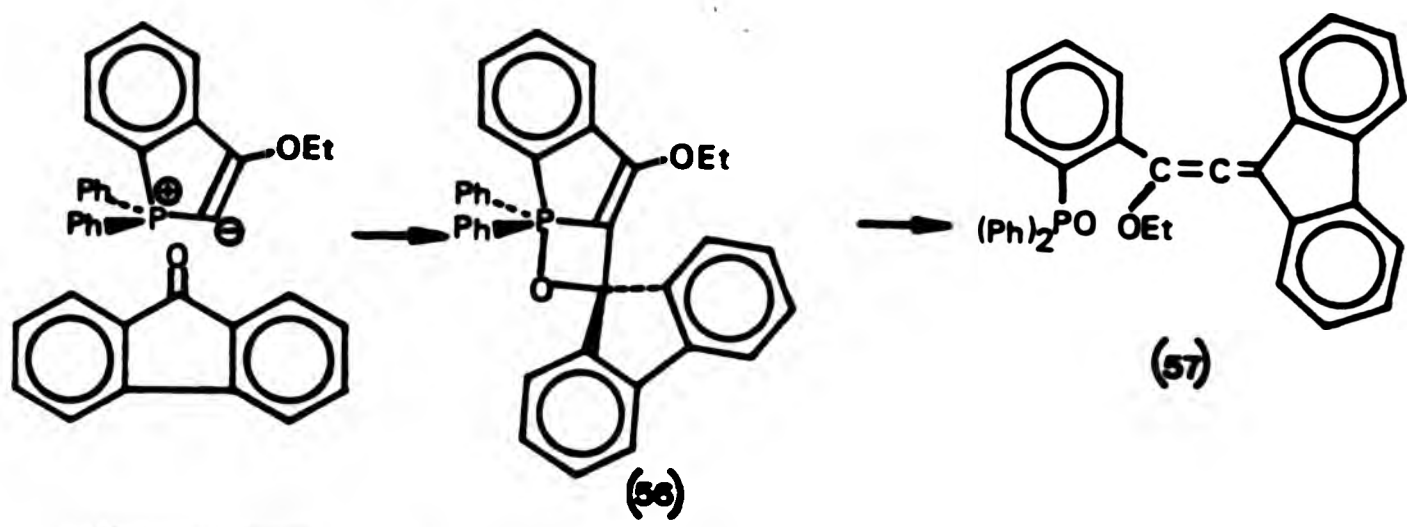
phosphetane formation is necessary as the first step. Bestmann[91,92] has recently proposed the following mechanism:



Ylide and aldehyde combine to give oxaphosphetane (52), in which the O-atom occupies an apical position on the pentavalent phosphorus and in which the substituents on the four-membered ring are Z to one another. Pseudorotation to oxaphosphetane (53) brings the C-P bond to an apical position necessary for C-P bond cleavage into (54). The electronic nature of substituents R^1 and R^2 in (54) determines the stereochemistry of the product olefin. When R^1 is a phenyl group and R^2 an electron-donating one, phosphine oxide elimination is very fast yielding Z-olefins. If R^2 is electron-withdrawing, the lifetime of (54) is extended enabling it to isomerise to the thermodynamically more stable (55), yielding E-olefins. If the R^1 ligands on phosphorus are electron-donating the rate of phosphine oxide elimination is also

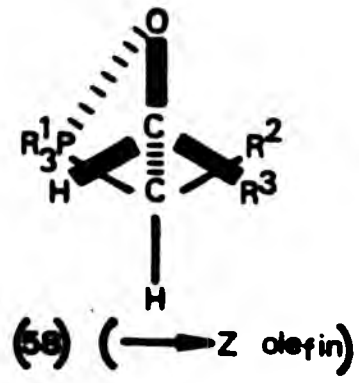
reduced and a large increase in E-olefin formation is observed.

As evidence for the ligand reorganisation around phosphorus (from (52) to (53)), Bestmann[92] has presented the X-ray structure of a primary adduct (56) which confirms the bipyramidal geometry around

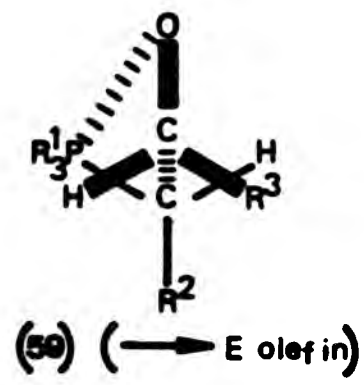


phosphorus and which decomposes only after several hours in boiling toluene or upon heating above its melting point. The products are partly starting materials and partly allene (57) due, it is thought, to a strong hindrance of the pseudorotation process by the rigidity of the system in (56).

The ylide-aldehyde approach is thought to proceed along the Dunitz trajectory[95] via a quasi-betaine transition state with the C-C bond more nearly formed than the P-O bond, leading to the oxaphosphetane (52). However, Vedejs et al[44] have pointed out that this quasi-betaine transition state could be analogous to a non-synchronous cycloaddition transition state and does not specify the difference from a transition state leading to a salt-free betaine. They also argue that the Dunitz trajectory does not explain why conformation (58) of the approaching complex should be strongly favoured over (59) or why selectivity should increase as R^3 in R^3-CHO becomes larger[96,97,100].



(58) (→ Z olefin)

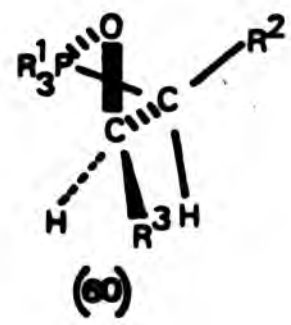


(59) (→ E olefin)

Vedejs and co-workers established cis-oxaphosphetanes[44,96] as intermediates in salt-free Wittig reactions of nonstabilised ylides, and recently cis and trans oxaphosphetanes have been detected by low-temperature ^{31}P NMR spectroscopy[93]. These studies have shown that cis oxaphosphetanes form preferentially and react faster than the trans diastereomers, and that oxaphosphetanes derived from hexanal (an aliphatic aldehyde) do not equilibrate while those from benzaldehyde (an aromatic aldehyde) undergo some form of equilibration at a rate competitive with the rate of decomposition (possibly through reversible interconversion of oxaphosphetanes and starting materials as shown earlier[44,97]). Therefore, some degree of thermodynamic control in aromatic aldehyde reactions appears to be present more as a result of oxaphosphetane interconversion than as a difference in the ylide-aldehyde condensation step. This is reflected in diminished alkene Z/E ratios compared to aliphatic aldehydes[2k,97].

Having established oxaphosphetanes as intermediates, that cis-oxaphosphetanes yield cis-olefins[44,93,98], that salt-free betaines were neither stable nor observable by available techniques and that absence of solvent effects on stereochemistry suggests a transition state with significant C-C and P-O bonding[99], Vedejs[44] proposed the following mechanism: a cycloaddition process having the plane of partially re-hybridised aldehyde tilted with respect to the ylide plane to minimise nonbonded interactions and also having the C=O and ylide C=P bonds

criss-crossed to maintain C ... C and P ... O bonding distance, the tilting of the aldehyde plane adopting any angle between that of parallel (58) and perpendicular (60) to the ylide.



(60)

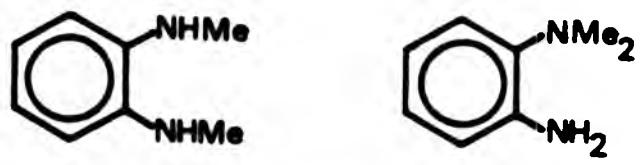
This approach would explain the high cis-stereoselectivity observed as well as the increase in Z-selectivity observed in going from R^3 = n-alkyl to R^3 = tert-alkyl[96,97,100]; the opposite effect expected if the transition state approach followed parallel plane arrangements such as (58) and (59), which would be expected to favour (59) relative to (58), thus increasing E-alkene proportions. Another important conclusion derived by this investigation[44] is that other mechanisms are involved when lithium halides are present and it must not be assumed that ylide-carbonyl reactions can be explained by one single scheme.

CHAPTER 2

SYNTHESIS AND REACTIONS OF N-(o-AMINOPHENYL)-ITPP (71) AND ITS HYDROCHLORIDE SALT (70)

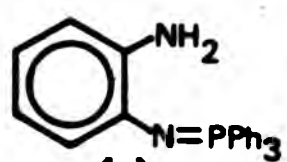
One of the challenges of classical organic synthesis is to bring about reaction at only one of two identical functional groups in a molecule, for example:

But when this reaction is carried out, mixtures result of the above product with unreacted o-phenylenediamine and the dialkylated products:



Many approaches to the general problem have been made, including the use of polymer-supported reagents[101], but it has been possible to convert o-phenylenediamine into the monoiminophosphorane as we shall show in this chapter, which by alkylation and hydrolysis should provide the monoalkylated-o-phenylenediamine[59].

N-(o-aminophenyl)-ITPP (71) had also been previously studied[48,57,102]

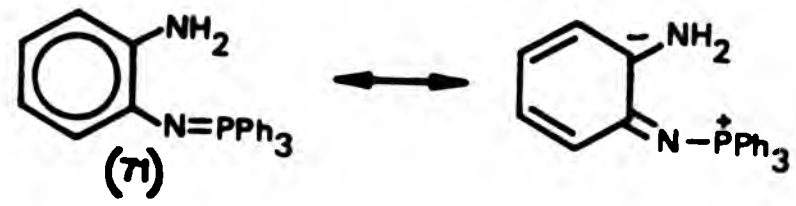


(71)

in its reactions with dimethyl acetylenedicarboxylate (DMA) which revealed a remarkable behaviour in that they involved the iminophosphorane group in Wittig-type reactions with ester carbonyl groups, a previously unrecognised pathway.

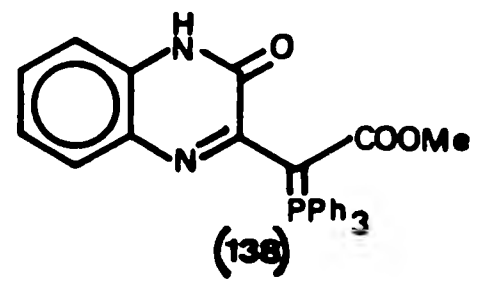
It was, therefore, decided to investigate further the chemistry of this system in its reactions with carbonyl groups (and also in its nucleophilic

reactivity with alkyl halides, and acid chlorides and anhydrides), in order to find out whether the amino group in the ortho position altered the reactivity of the molecule and to what extent, if any, resonance forms like the one illustrated participate in the structure of compound (71).

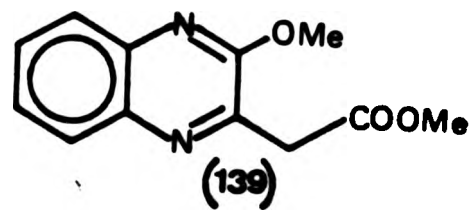


(71)

We have been able to prove that the Wittig-like reaction is a general one not only with ester carbonyl groups but also with amides, although reaction conditions need often to be more forcing than with aldehydes and ketones (see Chapter 4). N-(o-aminophenyl)-ITPP (71) reacts with DMA yielding two quinoxaline derivatives (138) and (139).

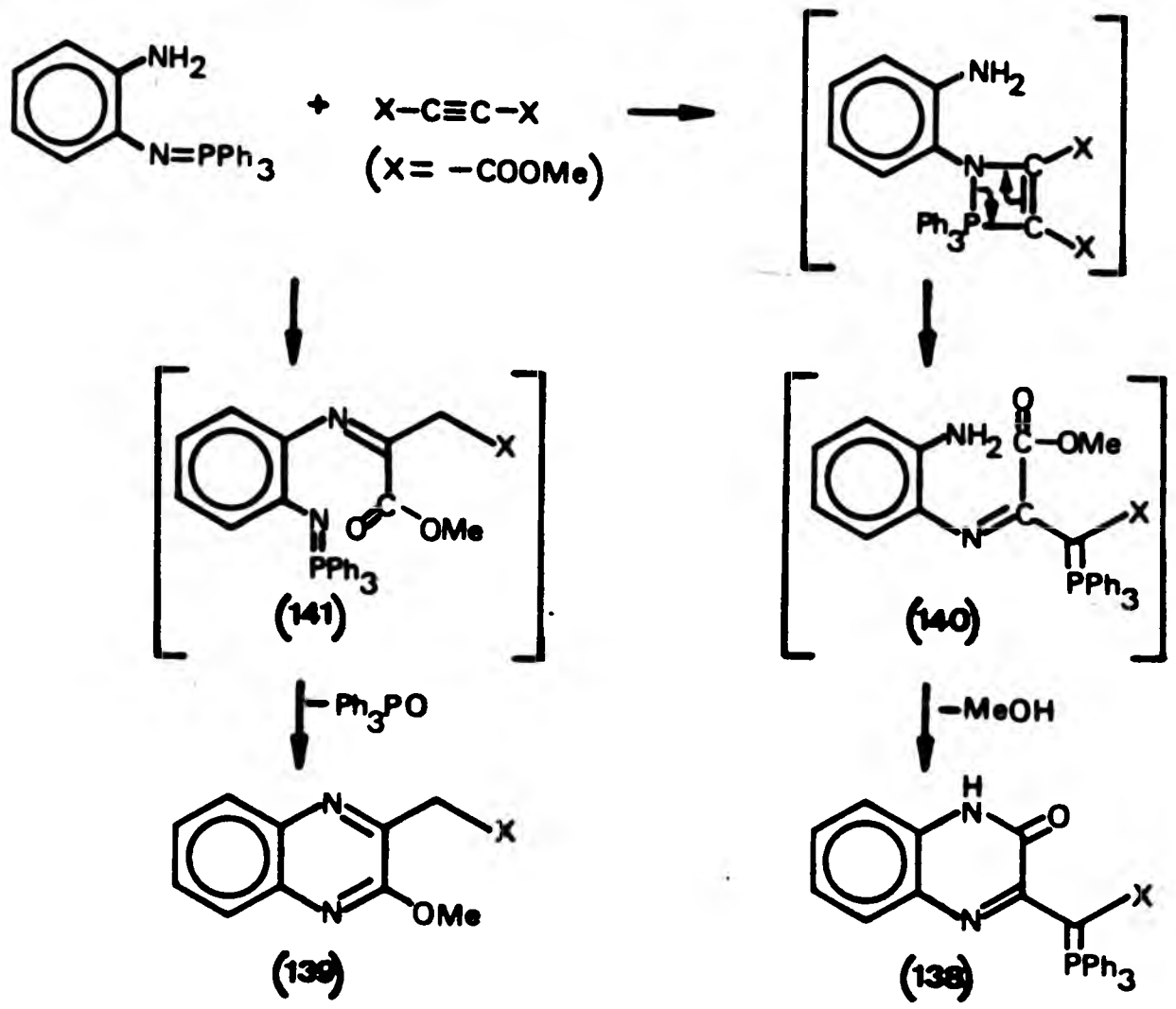


(138)



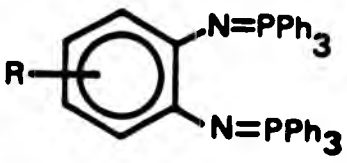
(139)

The former is thought to arise through the formation of an intermediate (140) via the phosphazacyclobutene[60] and subsequent cyclisation to form the amide (138) (although, as we shall suggest later, these two steps may be reversed), whilst the latter product (139) involves an initial nucleophilic addition of the amino group to the activated acetylene[102] (Michael addition) followed by the unprecedented intramolecular Wittig reaction with elimination of TPPO.



Attempts to synthesise N-(o-aminophenyl)-ITPP (71) following Horner and Oediger's[28] method with one equivalent of o-phenylenediamine and triphenylphosphine dibromide resulted in a mixture of unreacted diamine and o-bis-ITPP benzene (67). An identical result was reported by Meidine[41], confirming the difficulty alluded to in the opening to this chapter.

However, Dawson[48] and Jiricny[57] while trying to isolate and purify o-bis-ITPP benzene (67) in chloroform solution observed that it decomposed into N-(o-aminophenyl)-ITPP (71) and TPPO. Careful removal of ethanol, water and oxygen from chloroform proved that the bis-imine (67) reacted with the solvent to give an unstable intermediate which broke down to the observed products under chromatographic conditions. We have been able to confirm this result by following the decomposition process of o-bis-ITPP benzene (67) and its 4-methyl homologue (68) by ^{31}P NMR spectroscopy (Table 9).

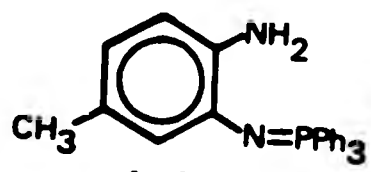
TABLE 9 Decomposition of  in $CDCl_3$

Compound	Time/h	$\delta^{31}P$ (ppm)
(67)	0	3.43
(67)	24	3.43(a), 20.12(b), 28.41(b)
(68)	4	8.1(a), 10.2(a)*
(68)	12	3.2(b), -12.1(a), 14.7(a), 28.6(b)
(68)	144	3.2(b), 18.4(b), 22.1(b), 28.6(b)

* This spectrum shows two negligible peaks at 3.3 and 28.8 ppm

a = strong, b = medium

The signal appearing at ≈28.6±2 ppm is assigned to one of the decomposition products, namely TPPO, while the up-field resonance at 3.2 ppm for compound (68) is tentatively assumed to correspond to the N-(5-methyl-3-aminophenyl)-ITPP derivative (142):



(142)

The relative position assigned to the methyl group with respect to the amino and -ITPP groups is based on the assumption that the iminophosphorane group para to the methyl substituent will be hydrolysed more rapidly than the other, just as compound (68) is decomposed more rapidly than (67) because of the electron-donating effect of the substituent. Noteworthy in this compound's decomposition is the gradual deshielding observed for the two initial signals and the increasing separation between them from 2.1 ppm, to 2.6 ppm and finally 3.7 ppm. The general deshielding effect could be at least partially explained by coordination or formation of a bond between the phosphorus atom and one or more chlorine atoms from the chloroform. Formation of triphenylphosphine

dichloride would be followed by its hydrolysis upon exposure to atmospheric water or oxygen into TPPO. Its ^{31}P NMR spectrum displays a strongly deshielded signal at +55.1 ppm[103] (in CH_2Cl_2).

In view of these results and the ready availability in large quantities of o-bis-ITPP benzene (67) we decided to exploit this decomposition process to synthesise N-(o-aminophenyl)-ITPP (71). After stirring a chloroform solution of (67) (48h at room temperature), decomposition was complete (tlc). The solvent was removed under reduced pressure and the solid material dissolved in sodium-dried benzene. From this solution a solid material precipitated, identified as the double hydrochloride salt of compound (67) by its IR spectrum, identical to that of an authentic sample. Final separation of the desired product (71) from TPPO was achieved by making its hydrochloride salt (70) which readily precipitated from the benzene solution in good yields.

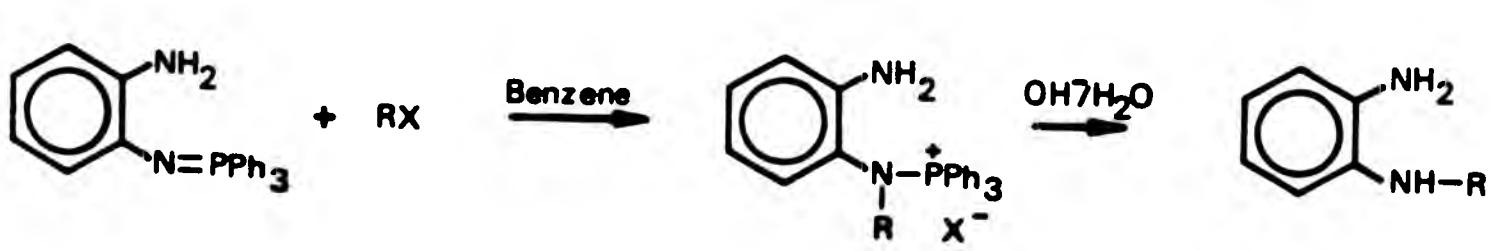
Its ^{31}P NMR spectrum gave one signal at 35.5 ppm typical of ITPP hydrohalide salts and its IR spectrum, as expected, showed no absorption band around 1350 cm^{-1} (ν(P=N)) but instead another band at 965 cm^{-1} assigned to the P^{+}-N-H system[57]. However, no $-NH_2$ bands were observed in this spectrum and the microanalytical results, although repeated several times, were poor. Final proof of its structure was achieved by its conversion into the free ITPP (71).

N-(o-Aminophenyl)-ITPP (71) was readily obtained as a bright yellow powder by stirring overnight a benzene suspension of the above salt with dry triethylamine, followed by recrystallisation from cyclohexane. It is advisable to store this product as its hydrochloride salt, as after several months an appreciable darkening, due to decomposition, takes place. The structural assignment was based mainly on its IR and ^{31}P NMR spectra: bands at 3460 and 3350 cm^{-1} for the $-NH_2$ group, one at 1360 cm^{-1} characteristic of N-ArITPP (see Table 5), and a single peak at +4.52 ppm in its ^{31}P NMR spectrum (Table 2).

Further corroboration was provided by its mass spectrum, with a molecular ion at m/e: 368, also being the base peak (see Chapter 3 for detailed analysis), and by its microanalytical data. The melting point (119-120°C) found for this sample did not correspond to the literature values of 147-8°C[57] and 143-4°C[48]. Repeated recrystallisations from cyclohexane failed to raise the melting point while attempts to recrystallise a small sample from AcOEt/Pet. Ether (60-80°C)[57] were also unsuccessful, yielding only tarry material. Other samples were obtained directly from the initial chloroform solution, and although their melting points after recrystallisation from cyclohexane were higher (136-8°C, 137-9°C), they were still nearly 10°C lower than the literature value. Another sample obtained from its hydroiodide salt (isolated as described later) still gave a low melting point (126-7°C).

One possible explanation for this difference in melting points could be ascribed to residual solvent in the sample, although careful drying in vacuo for several hours at 60°C had been carried out. The material isolated and subsequently used in all the experiments described in this work was undoubtedly (71), however.

The first of the major studies involved alkylation of compound (71) in an attempt to exploit the method developed for the synthesis of monoalkylated aromatic amines[41,59]. It was hoped that this approach would lead to high yields of monoalkylated o-phenylenediamine.



Scheme 3

However, all the reactions yielded complex mixtures and the recrystallisation of the solid materials isolated proved to be difficult and tedious and they had to be carried out with extreme care and over long

periods of time. Tlc of these solutions showed them to consist of a major product substantially contaminated with unidentified materials. Table 10 summarises the results obtained.

TABLE 10 Reactions of (71) with alkyl halides (R-X) in benzene

RX	Compound isolated	Reflux time/h	Yield/ %
ICH_3	(72)	2	16
ICH_3	(73)	2	2
$BrCH_2Ph$	(74)	7	9.5
$BrCH_2Ph$	(75)	7	7
9-Bromofluorene	(76)	5	4

All structures were determined mainly on the basis of ^{31}P and ^{1}H NMR spectra (Table 11) and were further confirmed by IR, MS (Table 11) and microanalytical data (see experimental section).

TABLE 11 IR, ^{31}P NMR, ^{1}H NMR and MS data

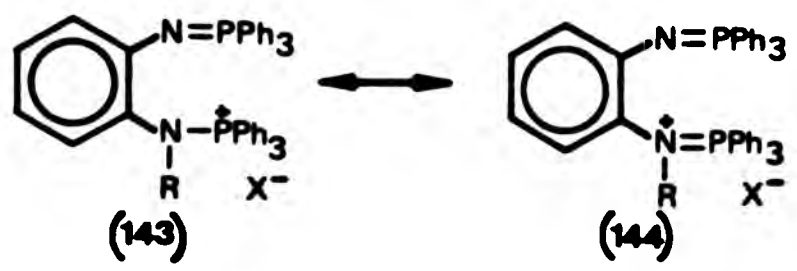
Compound	ν(P=N)	ν(P-NH)+	$^{31}P\delta$(ppm)	$^{1}H\delta$(ppm) R	MS M -X	MS M -RX
(72)	-	970	+36.51	-	369	368
(73)	1345	-	+10.63	4.01s	-	396
(74)	-	960	+36.75	4.02br s	-	-
(75)	-	970	+29.82(MeOH)	4.14br s	-	548
(76)	-	960	+36.0	-	369	368

[For more complete data see the experimental section 3].

Reaction yields were very poor, but the characterisation of these compounds provided an insight into these complex reactions.

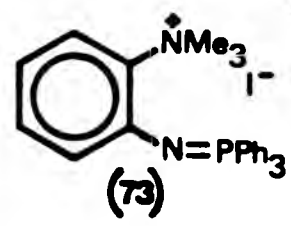
^{31}P NMR chemical shifts of N-aryl-ITPPs usually appear between 2.0 and 8.0 ppm, governed by the nature of any substituents on the N-aryl

ring, whilst N-alkyl-N-aryl-ITPP salts show a marked downfield shift to a practically constant value of 45 ppm and N-aryl-ITPP hydrohalide salts cover a range from 32 to 34 ppm[41,45]. Thus, inspection of Table 11 strongly suggests compounds (72), (74), (75) and (76) to be hydrohalide salts and compound (73) to possess a free ITPP group. This last value of δ: 10.63 ppm falls outside the usual range found for N-aryl-ITPPs but is typical of derivatives (143) with $\delta^{31}P$ values of 11.3 ppm to 11.7 ppm[41].



(143) (144)

The ^{1}H NMR spectrum of (73) shows a singlet at 4.01 ppm which integrates for nine protons, indicating the presence of three identical methyl groups in the molecule, all bonded to the same nitrogen atom forming a trimethylammonium group to appear as a singlet. They could not be linked to the imino nitrogen atom as these couple with the phosphorus atom to give doublets with $J(^{31}P\text{-}N\text{-}C\text{-}^{1}H)$ values between 7.0 and 10.0 Hz[110]. The most likely structure for compound (73) is therefore



(73)

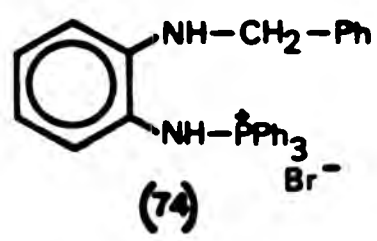
The trimethylammonium iodide substituent in the ortho position, although different in nature to that of compound (143), would be expected to exert a comparable deshielding effect (because of the positive charge) on the nitrogen atom of resonance form (144).

This structure was confirmed by its IR spectrum (displaying a prominent band at 1345 cm^{-1} due to the iminotriphenylphosphorane group) and by its microanalytical results. The halide ion's presence was

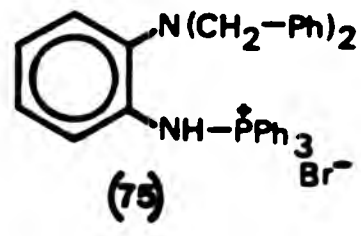
verified by a qualitative test and by a high resolution mass spectrum which gave a base peak corresponding to methyl iodide (m/e: 142) and the highest peak observed at m/e: 396 was assigned to a structure derived from (73) by loss of methyl iodide.

Quaternary ammonium salts cannot be volatilised unchanged but undergo an initial thermal decomposition into neutral molecules[111]. In our case it seems to follow the most prevalent dealkylation mechanism which results in superimposition of the mass spectra of the two neutral particles. Phosphonium salts are expected to behave analogously.

Similarly, the integrated proton NMR spectra of compounds (74) and (75) proved that benzyl bromide had reacted with the free amino group adding one and two benzyl radicals respectively. The absence of a free ITPP group was shown by their respective ^{31}P NMR spectra and by absorption bands at 960 cm^{-1} and 970 cm^{-1} respectively, all typical of an aminotriphenylphosphonium salt. Mass spectra and microanalytical data provided additional proof of the assignments made. Therefore, the structures of (74) and (75) would appear to be:

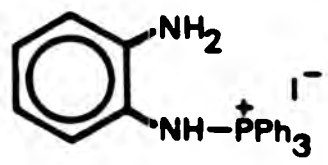


(74)

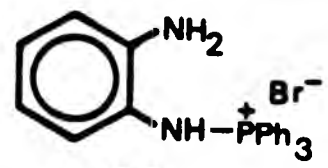


(75)

Finally, the IR spectra of compounds (72) and (76) were both very similar to that of compound (70). Additionally both gave bands in the 3460-3200 cm^{-1} region, indicating the presence of a free amino group. Their respective mass spectra were very similar, only showing differences in peak intensities apart from an ion at m/e: 128 assigned to HI in the spectrum of (72) and a doublet of ions at m/e: 80/82 assigned to HBr in the spectrum of (76). These data pointed to the following structures for these two compounds:



(72)

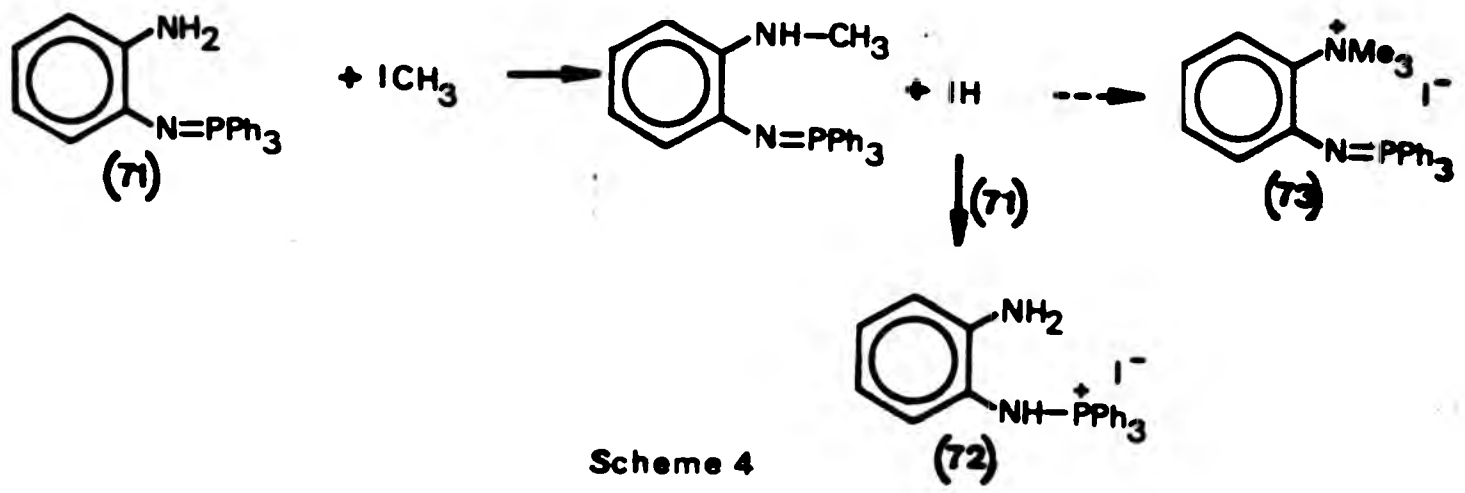


(76)

corroborated by their respective microanalyses. Further confirmation for structure (72) was obtained by its reaction with dry triethylamine which yielded N-(o-aminophenyl)-ITPP (71).

These unexpected results show conclusively that the amino group in (71) is the most nucleophilic site in the molecule, but the highest basicity is retained by the imino nitrogen atom. This conclusion agrees with Zhmurova's results[40b] who showed protonation preferentially occurred at the imino nitrogen atom. He was also able to show that the electron density around the imino nitrogen atom was higher than that found around the nitrogen atom in dimethylaniline and consequently even higher than that found around the nitrogen atom in aniline. This last result seems to contradict our conclusions above as a higher electron density on the imino nitrogen atom would favour this as the most likely reaction site with electrophiles. However, nucleophilicity is kinetically controlled while basicity is thermodynamically controlled, consequently factors slowing down the iminophosphorane's reaction rate would reduce this group's nucleophilicity. In the case of N-(o-aminophenyl)-ITPP (71), the imino nitrogen atom is attached to a phenyl ring on one side and to a phosphorus atom carrying three phenyl rings on the other. Thus, the steric hindrance and strain caused by an incoming electrophile would be expected to be very severe. At the same time, the presence of an ortho substituent would also contribute to a higher steric strain in the molecule. To reduce it as much as possible it would adopt a conformation that would locate the triphenylphosphorane moiety as far from the ortho substituent as the π(p-d) bond would allow,

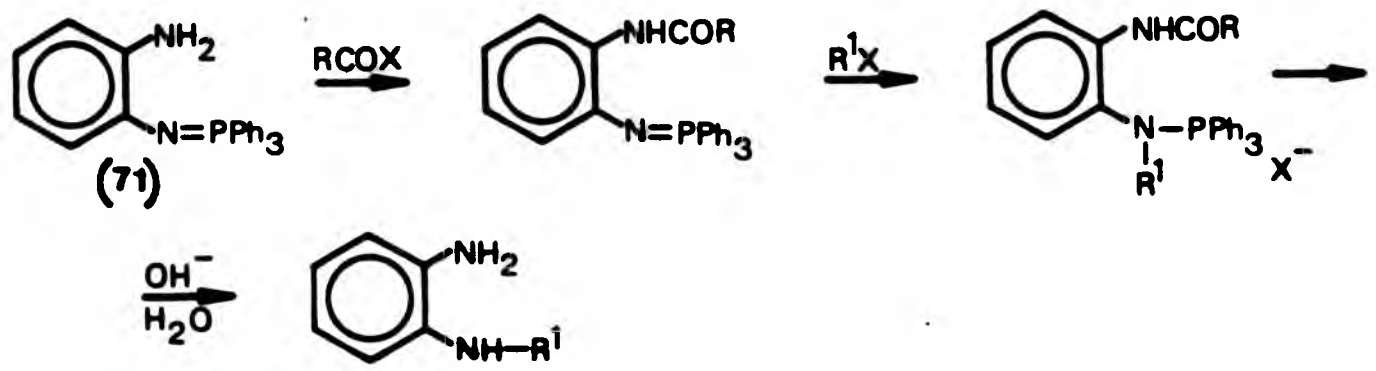
thus the approach of a reagent to a reactive ortho substituent would be favoured on kinetic grounds. The reaction with Brønsted acids is thermodynamically controlled and so it would be very difficult and, to a certain degree pointless, to establish the kinetic reaction site. The proton, due to its size, would not be affected by steric hindrance as much as, for example, methyl iodide and consequently it could react directly with the imino nitrogen atom. The extent of the control exerted by this steric hindrance is illustrated by the isolation of (73), in which three methyl groups react with the amino group to form the ammonium salt. These reactions are thought to follow the mechanism depicted in Scheme (4) with an initial S_N2 reaction between (71) and



Scheme 4

methyl iodide, with the iminophosphorane (71) acting as a base trapping the hydroiodic acid formed. Similar reaction schemes would explain the formation of all the other products isolated.

In view of the above results it was thought that reaction of (71) with an acyl halide would provide a way of blocking the reactivity of the o-amino group, thus enabling the introduction of an alkyl substituent on the imino nitrogen atom. At the same time, the introduction of this protecting group would only add an extra step to the overall synthesis (see Scheme 3) as the basic hydrolysis would be expected to remove this protecting group and the triphenylphosphorane moiety.



(A similar approach has been used[48,57] towards the protection of the pyridine nitrogen atom in pyridyliminotriphenylphosphoranes by complexing it with transition metals prior to attempting to bring about reaction on the imino nitrogen atom). Further, the acylation reaction scheme would also provide a simple synthesis of compounds with an amide carbonyl group in a specially favourable position to investigate the possible Wittig-type reactions of iminotriphenylphosphoranes.

N-(o-aminophenyl)-ITPP (71) was mixed with equimolar amounts of acetyl chloride, benzoyl chloride and p-toluenesulphonyl chloride under very mild reaction conditions yielding (77), (78) and (79) respectively. Crude yields varied from 63% to 84% but recrystallised yields showed a consistently uniform value of 53±2%. From the benzene filtrates TPPO was isolated.

TABLE 12 Reaction of (71) with RCOCl and RSO_2Cl

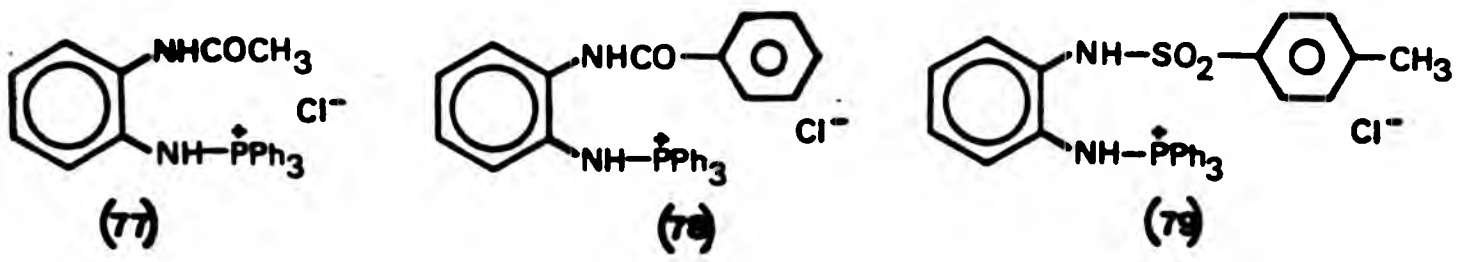
R-X	Compound isolated	Yield %	Crude Yield %
Acetyl chloride	(77)	53	84
Benzoyl chloride	(78)	51	63
p-Toluenesulphonyl chloride	(79)	55	68

The structure elucidation of these compounds was mainly based on their IR and ^{31}P NMR spectra (see Table 13). The chemical shifts observed in their ^{31}P NMR spectra and the stretching vibration band at

TABLE 13 Physical data of compounds (77), (78) and (79)

Compound	$\nu(\overset{+}{P}\text{-N-H})$ cm^{-1}	$\nu(C{=}O)$ cm^{-1}	$\nu(SO_2)$ cm^{-1}	$\delta^{31}P$ (ppm)
(77)	960	1665 1645	-	+35.8
(78)	960	1660 1645	-	+35.9
(79)	960	-	1335 1155	+33.7

960 cm^{-1} in their respective IR spectra clearly indicate these compounds are hydrochloride derivatives of compound (71). The observed carbonyl absorptions in the IR spectra of compounds (77) and (78), and the sulphonyl symmetric and asymmetric vibration bands at 1335 cm^{-1} and 1155 cm^{-1} respectively, conclusively showed that acylation or sulphonation had taken place, and the following structures were assigned to these compounds.



(The carbonyl amide stretching vibrations appear as doublets reflecting different degrees of hydrogen bonding and at slightly lower wave numbers than usual.)

In order to find out whether reaction conditions were important and yields could be improved, several alterations to the method outlined in the experimental section (3a) for acetyl chloride were made, but the same results were obtained with

(I) longer reaction time (48h) at room temperature;

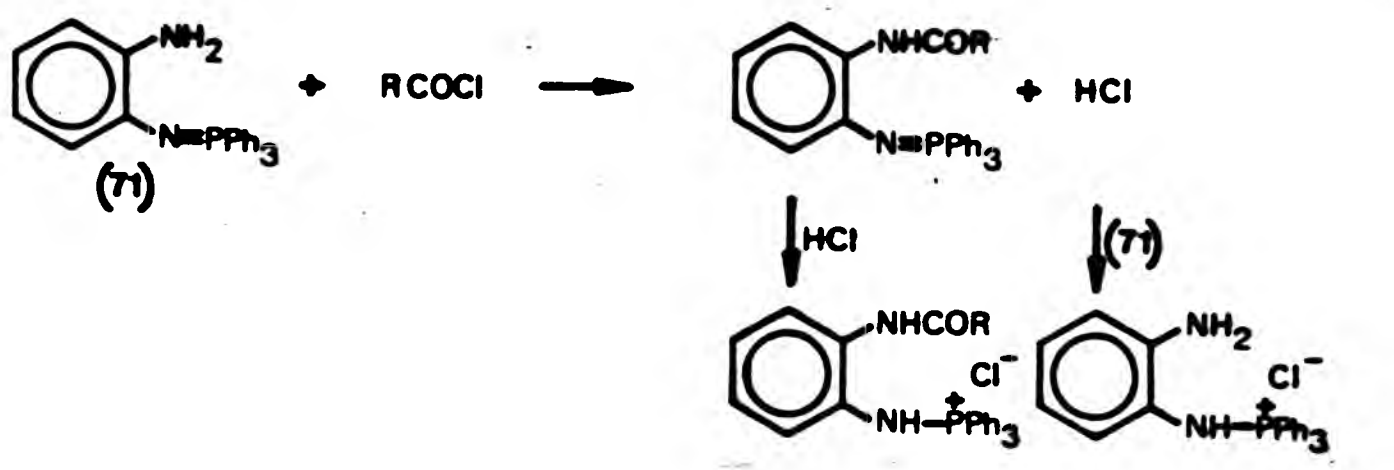
(II) addition of (71) to an ice-cold acetyl chloride solution;

(III) addition of acetyl chloride to a room temperature solution of (71);

(IV) addition of acetyl chloride to an ice/salt-cold solution of (71).

Yields of about 50% of acylated material strongly suggested that N-(o-aminophenyl)-ITPP (71) was acting, as in its reactions with alkyl halides, as a nucleophilic reagent and as a base.

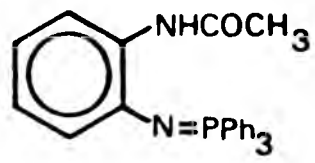
Evidently, (71) was reacting by some other mechanism also, as all the initial material disappeared after 24h. The crude yields indicated some other salt might have been formed which did not recrystallise from the solvents used (acetone, ethanol) either on concentration or/and prolonged cooling periods. The obvious choice would be N-(o-aminophenyl)-ITPP hydrochloride (70), which in turn would imply that (71) and the acyl chloride were reacting in such a way that hydrogen chloride was liberated and trapped by another molecule of N-(o-aminophenyl)-ITPP (71). Finally, such a reaction would have to account for the formation of TPPO.



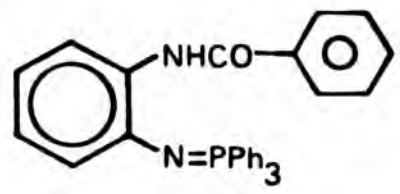
An alternative explanation for the formation of the TPPO could have been hydrolysis of compound (71) to o-phenylenediamine and subsequent reaction with the acyl chloride to yield its corresponding amide and hydrogen chloride. However, dry solvent, redistilled acyl chloride and dry N-(o-aminophenyl)-ITPP (71) had been used and the reaction carried out under a dry nitrogen atmosphere and very mild conditions, making this latter hypothesis less likely. A more detailed analysis of this reaction will be given later in this chapter.

Final proof of the structures of compounds (77), (78) and (79) was obtained by the synthesis of their respective free iminophosphorane

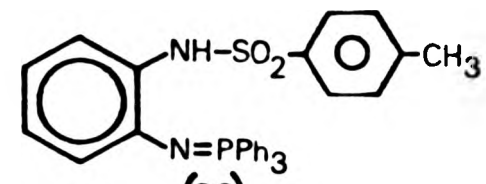
derivatives (80), (81) and (82) in high yields by stirring the salts with dry triethylamine.



(80)



(81)



(82)

The structure of these compounds was verified by the usual spectroscopic and analytical techniques (see Table 14). Their ^{31}P NMR spectra gave a single peak in the expected chemical shift range (see Table 2),

TABLE 14 Physical data of compounds (80), (81) and (82)

Compound	ν(P=N) cm^{-1}	ν(C=O) cm^{-1}	$\nu(SO_2)$ cm^{-1}	MS($M^{+\cdot}$)	δ^{31}P(ppm)
(80)	1350	1675	-	410 (19%)	7.20
(81)	1350	1655 1650	-	472 (87%)	7.78
(82)	1370	-	1340 1155	522 (16%)	8.14

supported by the strong bands at 1350 cm^{-1} for (80) and (81) and 1370 cm^{-1} for (82) in their respective IR spectra. The IR spectra also provided evidence for the presence of the amide and sulphonamide groups (see Table 14). High resolution mass spectra were recorded for compounds (80) and (81) giving the expected molecular formulae $C_{26}H_{23}N_2OP$ and $C_{31}H_{25}N_2OP$ respectively.

Further attempts to improve yields were made by using acid anhydrides instead of the acyl halides and catalysing these reactions with dry pyridine. A summary of the results obtained is given in Table 15.

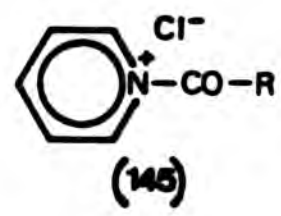
TABLE 15 Reactions of (71) with acid anhydrides, acid anhydride-pyridine and p-toluenesulphonyl chloride-pyridine

Reagents	Compound isolated	Yield (%)
$(MeCO)_2O$	(80)	57
$(PhCO)_2O$	(81)	28
$(MeCO)_2O$/Py	(80)	48
p-Toluenesulphonyl chloride/Py	(82)	30

[For experimental details see sections 3c and 3d]

All compounds were identified by their IR spectra, identical in all cases to those of the materials isolated in the earlier experiments.

The results show that the reactions proceeded with comparable results only when acetic anhydride was used, yields being greatly reduced in the two other reactions. The expected beneficial effect of pyridine was found to be absent and when used with p-toluenesulphonyl chloride appeared to hinder the reaction more than favour it. (The mode of action is thought to involve the formation of a quaternary salt (145) which then acylates the substrate[112].) By analogy, p-toluene-sulphonyl chloride would be expected to form a similar salt and the

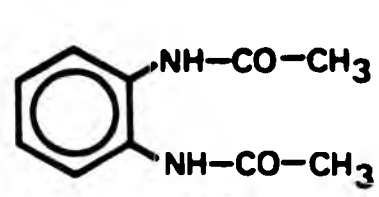


(145)

observed yield reduction could have been caused by an increase in steric hindrance due to the pyridinium nucleus. Similarly, steric strain would also explain the low yield with benzoic anhydride.

In order to avoid the separate triethylamine reaction and synthesise in one single step compounds (80), (81) and (82), N-(o-aminophenyl)-ITPP (71) was mixed with a slight excess of triethylamine before adding the acid halide to destroy the hydrochloride formed during the course of the reaction. Again, acetyl chloride was used and under a nitrogen

atmosphere, the course of the reaction followed by the disappearance of the original yellow colour of the solution during 2h at reflux. Filtration afforded a quantitative yield of triethylamine hydrochloride and from the filtrate (shown by tlc to contain a complex mixture of products) a nearly quantitative yield of TPPO was isolated. Also isolated and characterised were traces of N,N'-diacetyl-o-phenylene-diamine (83) which suggested that the original reaction mixture possibly

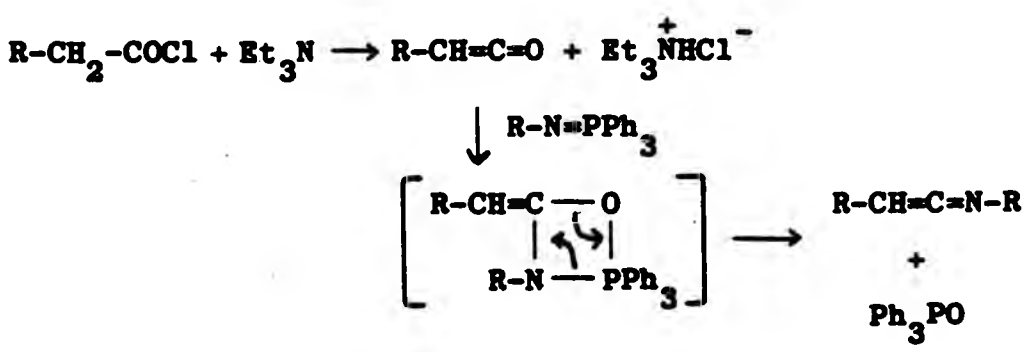


(83)

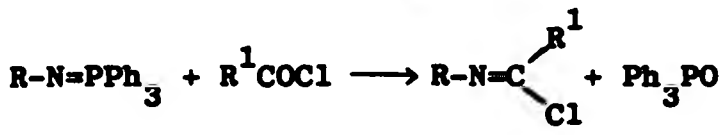
contained N,N'-diacetyl, N-acetyl and free o-phenylenediamine as only one equivalent of acetyl chloride had been used.

The nearly quantitative yields of triethylamine hydrochloride and TPPO obtained clearly indicated total reaction of the acetyl chloride and practically total cleavage of the P=N double bond. To check that simple hydrolysis of the N-(o-aminophenyl)-ITPP (71) had not taken place, the reaction was repeated twice under totally anhydrous conditions. Apart from the (routine) use of dry triethylamine and (71), dry solvent and redistilled acetyl chloride, the reaction chamber was evacuated and flushed alternately with nitrogen three times. However, both experiments yielded identical results, ruling out the simple hydrolysis hypothesis.

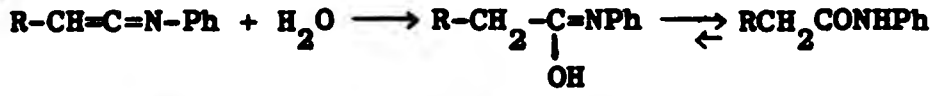
Acyl halides react with tertiary aliphatic amines forming ketenes[116], which in turn are known to react with iminophosphoranes yielding N-phenyl-ketenimines and TPPO[2d, 138].

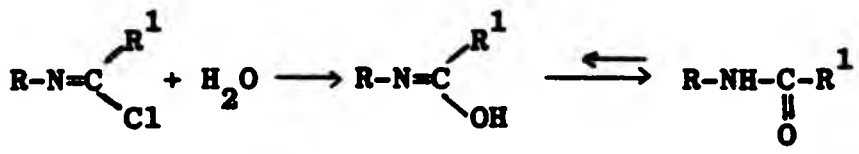


Acyl halides also react with iminotriphenylphosphoranes yielding imidoyl halides and TPPO[68].

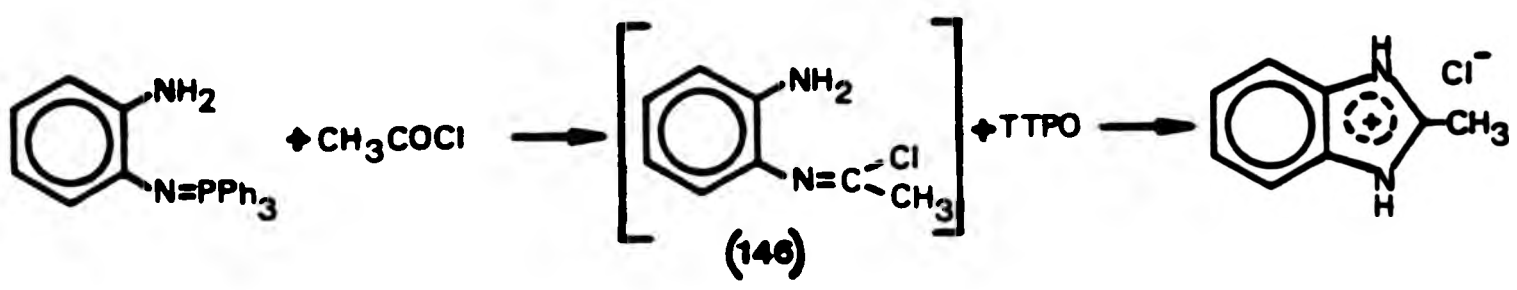


Under column chromatography conditions, both the ketenimines[138] and the imidoyl halides[146] would be expected to undergo hydrolysis to their corresponding amides:





It was shown above that N-(o-aminophenyl)-ITPP (71) reacts preferentially at the amino group with alkyl halides, acyl chlorides, acid anhydrides and p-toluenesulphonyl chloride, and in general these reactions are relatively complex. Indirect evidence for a second mechanism operating in its reactions with acyl halides which had to account for the formation of TPPO was provided earlier. This second mechanism could have been the formation of the imidoyl chloride (146), (which we have shown for (61) to be formed under the conditions used, see Chapter 5)



(146)

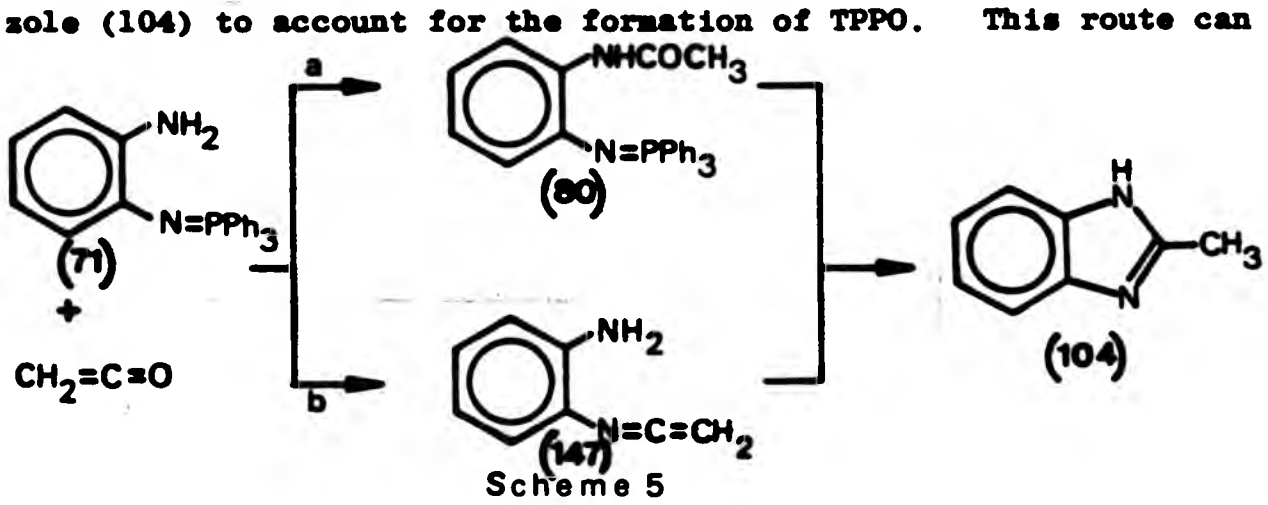
which is expected to react with the amino group[146] yielding 2-methyl-benzimidazole hydrochloride. This mechanism would account for the formation of TPPO and the salt formed would not have been the proposed N(o-aminophenyl)-ITPP hydrochloride (70). However, it has been conclusively shown that the most reactive site of N-(o-aminophenyl)-ITPP (71)

is the amino group and therefore until all the by-products of the reaction have been isolated and characterised the mechanism of this reaction should remain an open question.

The alternative mechanistic schemes found in the literature appeared to offer a plausible explanation for the Et_3N-acyl halide reaction once we had shown hydrolysis to be an unlikely possibility. But a closer study of these alternatives failed to account for all the observations made. If we assume ketenes are formed prior to reaction

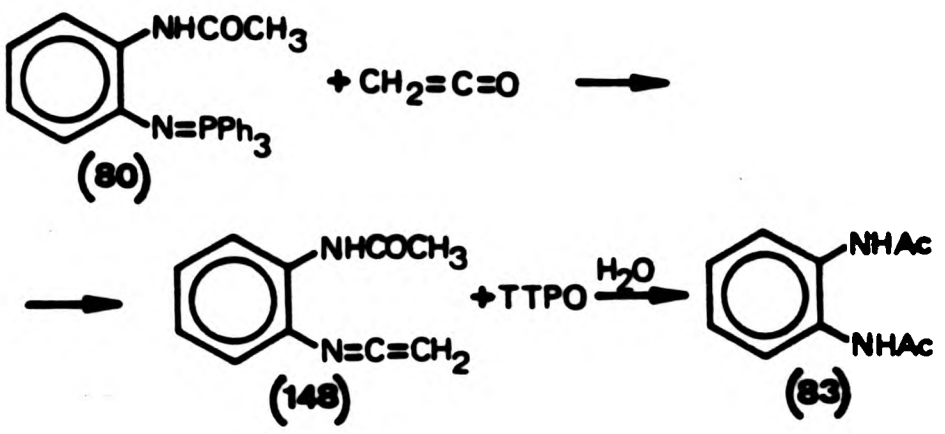
$$CH_3COCl + Et_3N \longrightarrow CH_2{=}C{=}O + Et_3\overset{+}{N}H\ Cl^-$$

with N-(o-aminophenyl)-ITPP (71), formation of triethylamine hydrochloride would be accounted for. The following step would then be the expected acylation of (71) by reaction of ketene with the free amino group (Scheme 5, route a), which would have to yield 2-methyl-benzimidazole (104) to account for the formation of TPPO. This route can be



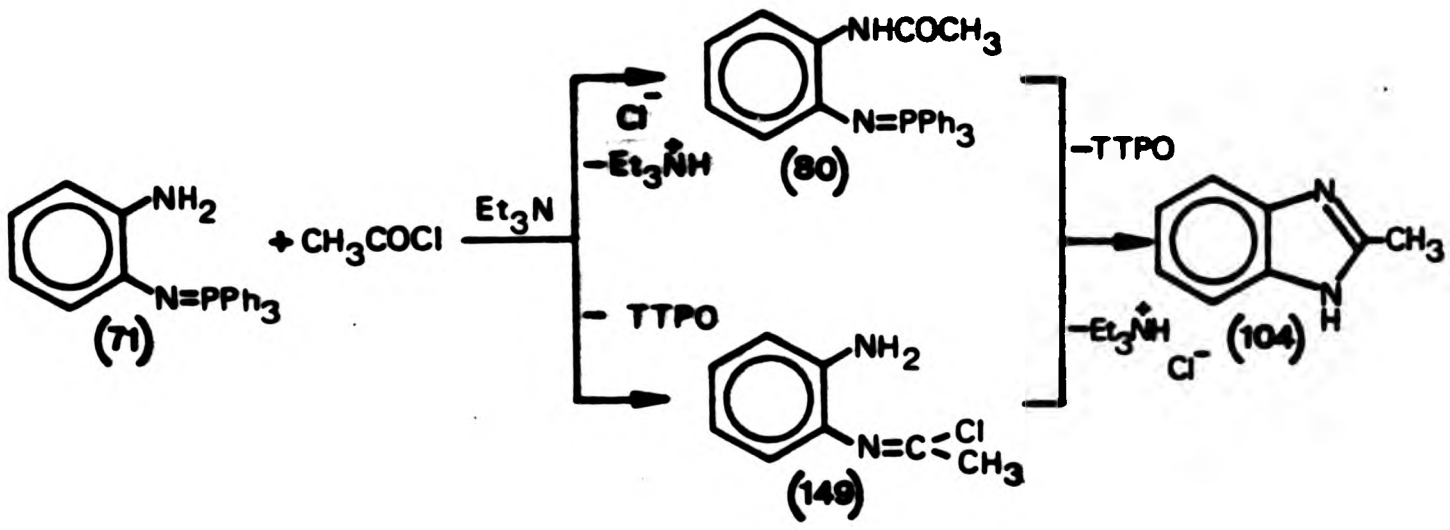
Scheme 5

eliminated as after 2h reflux, (80) is recovered unchanged. The next possibility (Scheme 5, route b) would involve reaction of ketene with the iminotriphenylphosphorane group yielding the intermediate ketenimine (147), which would also be expected to cyclise to (104). This last route seems unlikely as reaction would take place at the less reactive site of (71) and a good yield of (104) would have been found. A third possibility is reaction of (80) with ketene yielding the corresponding ketenimine (148) and hence compound (83) after hydrolysis.



However, this scheme would require two molecules of ketene per molecule of (71), and thus is not able to account for the nearly quantitative yield of TPPO as only one equivalent of acetyl chloride was used.

A similar discussion for the acetyl chloride-triethylamine reaction, if we assume reaction proceeds according to the imidoyl chloride mechanism, would provide analogous conclusions (Scheme 6).



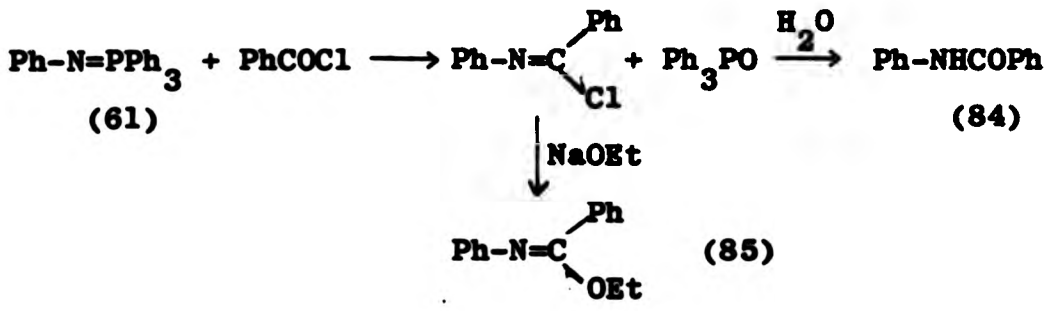
Scheme 6

To confirm our assumption that imidoyl halides hydrolyse during chromatography, N-phenyl-ITPP (61) was refluxed with benzoyl chloride and the resulting reaction mixture, after an attempted vacuum distillation, was finally separated by column chromatography yielding TPPO and benzanilide (84).

Once more, it could be argued that the formation of benzanilide (84) had occurred by hydrolysis of the N-phenyl-ITPP (61) to aniline, followed by its acylation to (84):

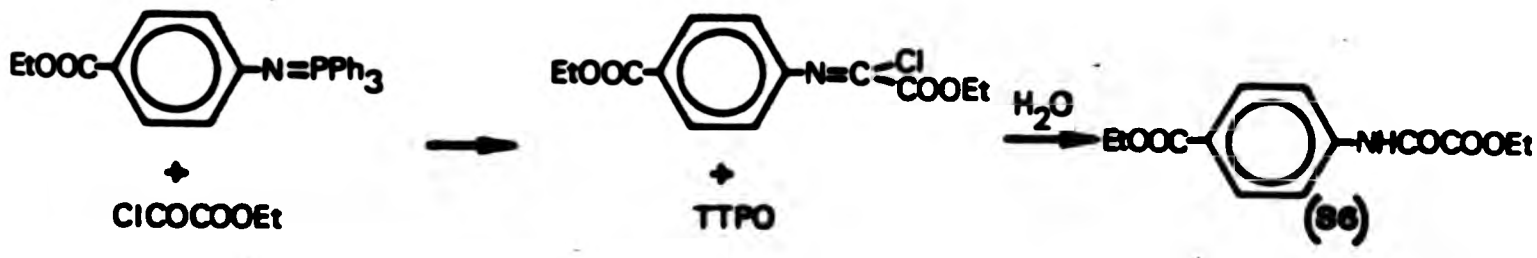
$$\underset{(61)}{Ph\text{-}N{=}PPh_3} \xrightarrow{H_2O} PhNH_2 + Ph_3PO \xrightarrow{PhCOCl} \underset{(84)}{PhCONHPh} + HCl$$

However, this hydrolysis mechanism seems unlikely as it would be expected that some aniline hydrochloride salt would form during the reaction and precipitate from the benzene solution. None was observed, and the intermediate formation of the imidoyl chloride was established by the synthesis of ethyl N-phenyl-benzimino ether (85), by reaction of the imidoyl chloride with sodium ethoxide, identified by comparison with reported data[139-141].



To check further the reaction of other N-ArITPPs (not containing an o-amino group) with acid halides, N-[(p-ethoxycarbonyl)-phenyl]-ITPP was stirred in sodium-dried ether in an ice-bath and ethyl oxalyl chloride was added dropwise. After the mixture had reached room temperature, sodium hydrogen carbonate work-up afforded a mixture of TPPO and ethyl (p-ethoxycarbonyl)-oxanilate (86) in low yields. The oxanilate (86) structure was confirmed by its IR spectrum, which showed ester carbonyl absorption bands at 1730 cm^{-1} and 1710 cm^{-1} and an amide carbonyl stretching vibration at 1695 cm^{-1}, its mass spectrum and its microanalysis.

We have shown therefore that iminophosphoranes react with acid halides even at room temperature, presumably through the formation of the intermediate imidoyl chloride which hydrolyses to the amide upon treatment with dilute sodium hydrogen carbonate[121].



These reactions of iminotriphenylphosphoranes with acid halides have received surprisingly little attention, as imidoyl chlorides are very useful synthetic intermediates[146,147]. Apart from offering a very simple, general and convenient synthesis of imidoyl chlorides from acid chlorides, this reaction could be developed into a very useful reduction of acid halides to aldehydes and hence, an overall synthetic reduction of carboxylic acids to aldehydes. Reduction of imidoyl chlorides was last studied in 1919[148] and 1934[148] and reviewed in 1954[149]. Two reagents were used, stannous chloride and chromous chloride, and with today's very wide range of reducing agents this approach merits a full investigation.

Finally, it was decided to block the ITPP group's reactivity by using N-(o-aminophenyl)-ITPP hydrochloride (70) as the starting material. Table 16 summarises the results obtained.

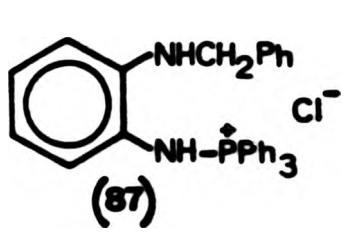
TABLE 16 Reactions of (70) with alkylation and acylation reagents

Reagents	Compound Isolated	Yield (%)
$(MeCO)_2O$/Py	(77)	57
PhCOCl/Py	(78)	71
p-Toluenesulphonyl chloride/Py	(79)	96
$PhCH_2Br$/Py	(87)	78
$EtO_2C-CH_2-CH_2-COCl$/Py	(88)	41
EtO_2C-Cl/Py	(89)	82

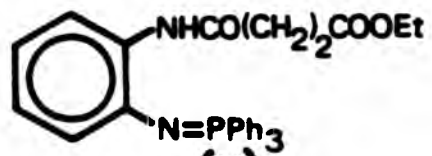
[For full experimental details see section 3g]

All the reactions were carried out in dry acetonitrile as this was the only suitable solvent in which N-(o-aminophenyl)-ITPP hydrochloride (70) dissolved appreciably. Dry pyridine was used as the base to remove the acid formed during the course of the reaction, while not converting the starting salts into their free bases.

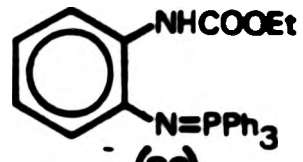
Compounds (77), (78) and (79) were identified by their mixed melting points with authentic samples, which were undepressed in all three cases. A microanalysis of this sample of compound (77) was performed which produced more accurate results than those obtained on the original sample. Chloride (87), an analogue of bromide (74), had very similar physical data, and the position of the benzyl radical was



(87)



(88)



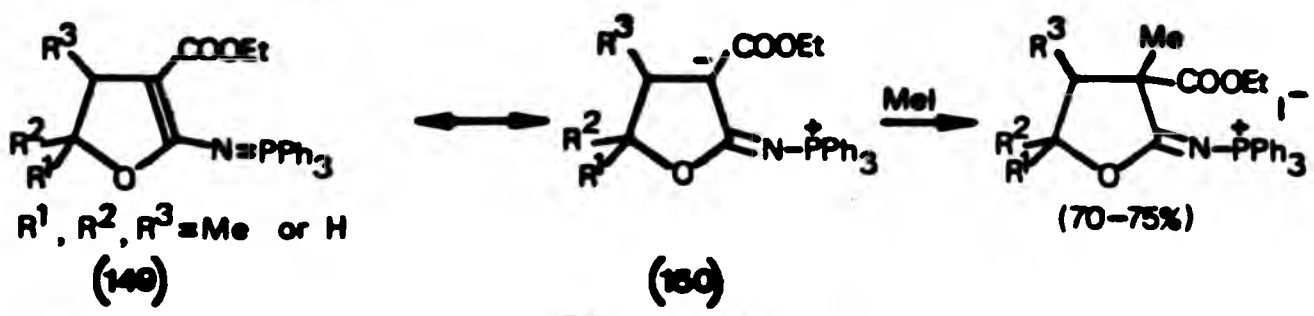
(89)

once more confirmed by the appearance of the methylene group as a singlet in the proton NMR spectrum, showing no coupling with the phosphorus atom.

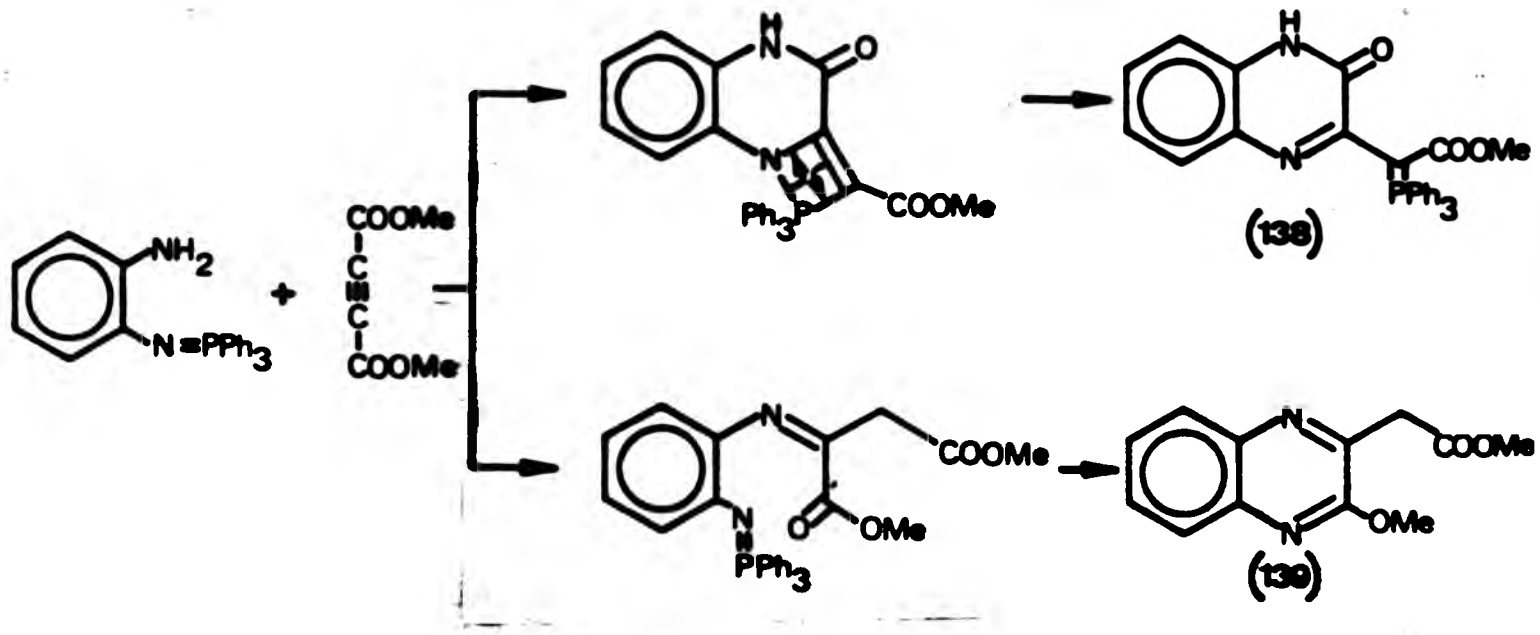
The corresponding hydrochloride salts of compounds (88) and (89) were not isolated and characterised. The crude reaction mixture, after the original solvent and reagents had been removed, was suspended in dry benzene and stirred at room temperature with excess dry triethylamine. After work-up, (88) was finally purified by column chromatography. Both ^{31}P NMR spectra gave single peaks at 7.1 ppm and 6.5 ppm for (88) and (89) respectively, and their integrated proton NMR spectra confirmed the presence of the ethoxycarbonyl groups, while the two succinyl methylene groups of compound's (88) ortho substituent appeared unexpectedly as a singlet at 2.75 ppm. Their respective IR spectra showed all the expected absorption bands with the P=N group's stretching vibration at 1345 cm^{-1} for both compounds and the ester carbonyl's absorption bands of compounds (88) and (89) respectively at 1730 cm^{-1} and 1715 cm^{-1}, compound's (88) spectrum showing an additional band at 1680 cm^{-1} for the amide group. Their respective mass spectra and microanalysis results fully corroborated these assignments.

Although it is difficult to compare these results with those

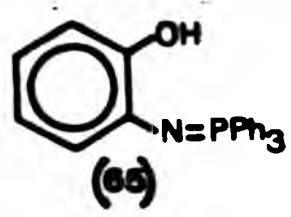
discussed earlier because of the change of solvent, some conclusions can be drawn. Except for the reactions of ethyl oxalyl chloride and acetic anhydride, yields were high, suggesting that low yields in previous reactions may have been caused by the great reactivity of the imino-triphenylphosphorane group which led to side reactions. Apparently N-(o-aminophenyl)-ITPP (71) can react both at the amino group or at the ITPP group and that selectivity is dependent on conditions and reagents used. While Brønsted acids react exclusively with the ITPP group, alkyl halides react preferentially at the amino group and acylation agents lie somewhere in between. Another example where the nucleophilicity of an ITPP group is shifted is the reaction of the imino-triphenylphosphorane (149) with methyl iodide[150], in which a 1,4 type



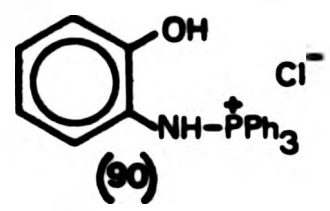
addition to the conjugated system takes place in preference to the typical formation of the N-alkyl-ITPPm salt, probably due to the stabilisation provided by the ethoxycarbonyl group shown in resonance form (150). As in the case of the N-(o-aminophenyl)-ITPP (71), the most nucleophilic site of the molecule is shifted, but in a more pronounced way. Similar considerations could also apply to the reaction of (71) with DMA[102]: it has been thought that product (138) results from initial azaphosphetane formation, followed by amide formation, but amide formation in (138) could be taking place through prior reaction of the ITPP moiety and thus both products (138) and (139) would arise from initial attack of the amino group at either the methoxycarbonyl group or at one of the acetylenic carbon atoms, possibly a more straightforward process.



To test these ideas further, we decided to study the analogous system N-(o-hydroxyphenyl)-ITPP (65), and to avoid side reactions its

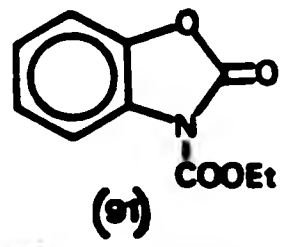


(65)



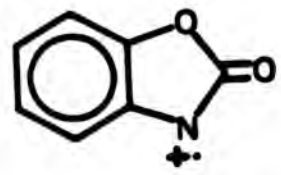
(90)

hydrochloride salt (90) was chosen as the starting material. Compound (90) was synthesised following the method previously described for N-(o-aminophenyl)-ITPP hydrochloride (70) (see section 3h), and all its reactions were carried out under the same conditions as those of (70). After 4h stirring at room temperature a mixture of N-(o-hydroxyphenyl)-ITPP hydrochloride (90), pyridine and ethyl chloroformate gave an oily residue, which after treatment with dry triethylamine and work-up yielded TPPO and a small amount of N-carbethoxy-2-oxo-1,3-benzo[d]oxazole (91), identified through its mass spectrum (a molecular ion at m/e: 207,



(91)

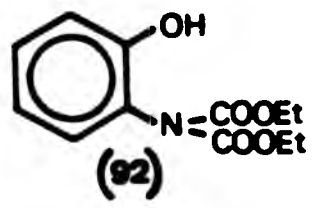
with a base peak at m/e: 135 assigned to an ion (151) originating by loss of the N-carbethoxy group), its mp (76-8°C, very close to the literature



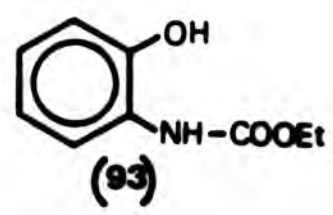
(151)

value of 78-9°C) and by its IR spectrum which exhibited a complex carbonyl pattern with bands at 1860, 1830, 1815 and 1750 cm^{-1}, but no bands between 3500 cm^{-1} and 3000 cm^{-1} due to -OH or NH groups.

The reaction was repeated but with the reaction time extended to 90h. The resulting mixture was triturated with dry diethyl ether affording pyridine hydrochloride and the filtrate was treated with dry triethylamine. Usual work-up yielded an oily residue from which were separated TPPO in a 54% yield and a red oil identified as N,N-dicarbethoxy-2-aminophenol (92) in a 31% yield.



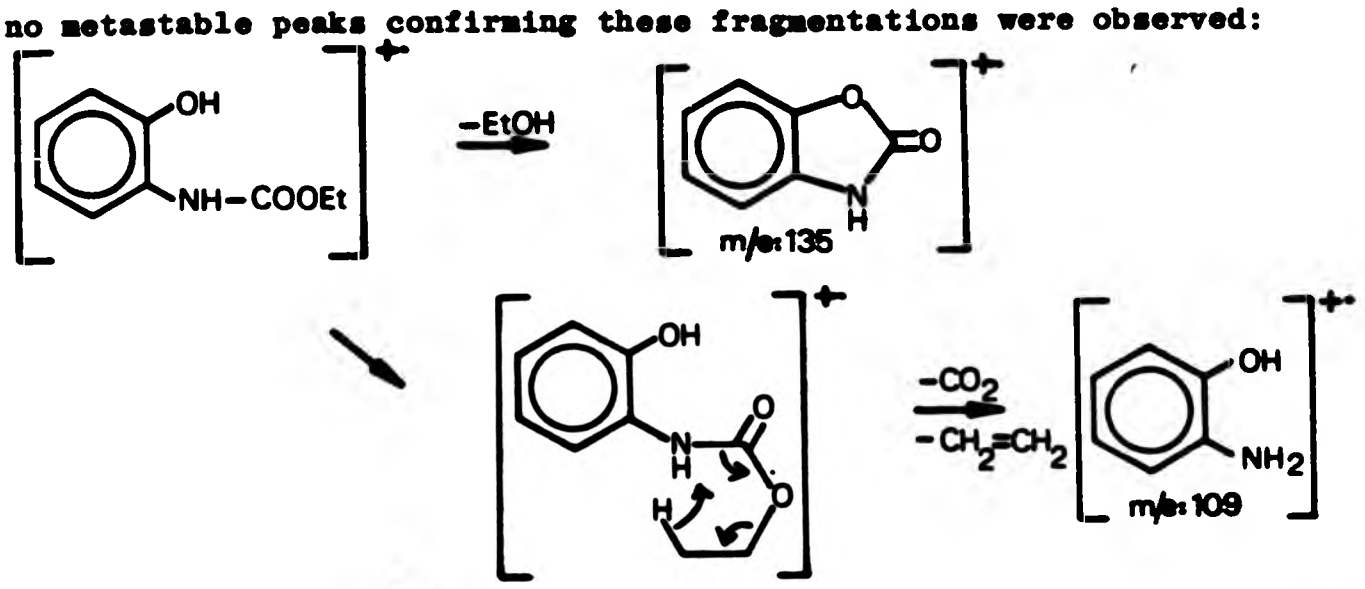
(92)



(93)

The characterisation of this compound was exclusively based on its mass and IR spectra as it decomposed to (93) during 24h: the molecular ion at m/e: 253 was confirmed by chemical ionisation, accurate mass measurements gave a molecular formula $C_{12}H_{15}NO_5$, and its IR spectrum showed a strong band at 3310 cm^{-1} typical of a hydroxyl group and carbonyl groups at 1830, 1765, 1735 and 1700 cm^{-1}. On standing at room temperature, the red colour of the oil gradually faded and finally totally disappeared as the oil crystallised. Recrystallisation yielded (93), as shown by its mass and proton NMR spectra. The former showed a molecular ion at m/e: 181, confirmed by chemical ionisation determination, and two strong peaks at m/e: 135 and 109 assigned to ions probably resulting from loss

of ethanol and a favourable rearrangement process respectively although no metastable peaks confirming these fragmentations were observed:



The integrated ^{1}H NMR spectrum confirmed the presence of only one carbethoxy group and the IR spectra showed bands at 3390 and 3250 cm^{-1} (assigned to -OH stretching vibrations) and carbonyl absorption bands at 1725 and 1670 cm^{-1}.

At this point, without full knowledge of all the products formed in these reactions, any attempt to account for the formation of these three compounds would be difficult.

Returning to our main synthetic aim, that of the synthesis of the monoalkylated o-phenylenediamine, outlined in Scheme 3, we attempted to alkylate substrates (80), (81) and (82) following the general method described in section 4 in the experimental part. Table 17 summarises the results obtained.

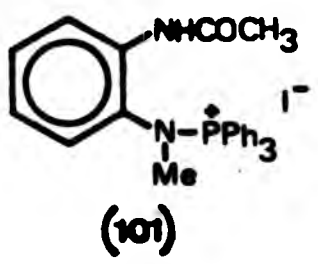
TABLE 17 Alkylation of compounds (80), (81) and (82)

Compound	Reagent	Reflux/h	Compound isolated	Yield (%)
(80)	MeI	24	(101)	61
(81)	MeI	43	(102)	31
(82)	MeI	24	(103)	26

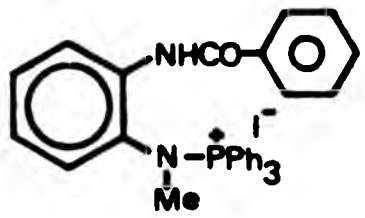
The identification of these products (101-103) was mainly based on

TABLE 18 Physical data of compounds (101), (102) and (103)

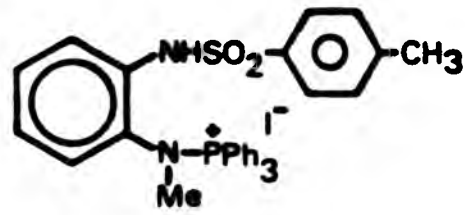
Compound	$\delta^{31}P$ (ppm)	$\nu(\overset{+}{P}\text{-N-C})$ cm^{-1}	$\nu(C{=}O)$ cm^{-1}	$\nu(SO_2)$ cm^{-1}
(101)	44.3	915	1690 1680	-
(102)	44.5	915	1655 1645	-
(103)	45.4	925	-	1340 1160



(101)



(102)

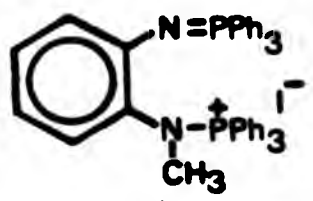


(103)

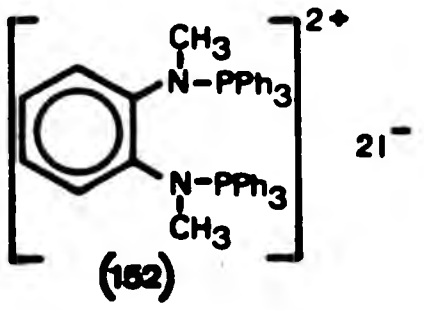
their ^{31}P NMR spectra which showed practically constant values for all three compounds, their IR spectra with typical absorption bands at 915 cm^{-1} and 925 cm^{-1} assigned to the stretching vibrations of the $\overset{+}{P}$-N-C structure, and by their respective microanalyses.

The yields obtained for these reactions show a marked reduction in going from (101) with the acetyl substituent to the other two compounds with bulkier substituents, so that steric hindrance is probably the main reason for these poorer yields. Under these conditions Scheme 3 would no longer be such a useful synthetic route and no further investigations were undertaken.

During the course of our studies we had attempted to synthesise the double salt (152) but only compound (100) was isolated. Characterisation

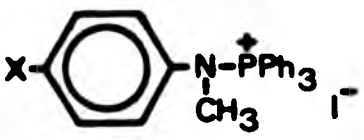


(100)



(152)

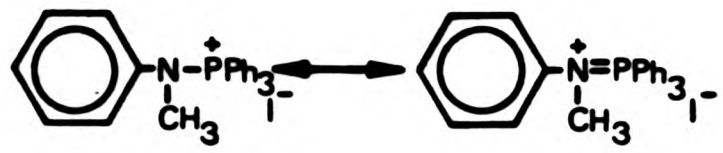
was carried out by comparison of its spectral properties and melting point with those reported in the literature[41]. No proton NMR data of this compound were available so N-methyl-N(p-bromophenyl)-ITPPm iodide (97) was synthesised as a reference. Both compounds exhibited a doublet corresponding to the N-methyl groups with the same coupling constant J(^{1}H-C-N-^{31}P) of 9.0 Hz. However, in compound (97) the N-aryl aromatic protons appeared as a singlet, and to investigate this unexpected result further compounds (95-98) were all synthesised, and characterised, according to the literature[41,59,144]. Table 19 summarises the results obtained, from which it is apparent that this

TABLE 19 ^{1}H NMR data of 

Compound	X	P-Ph(ppm)	N-aryl/(ppm)	$-CH_3$(ppm)(J, Hz)
(95)	F	7.8 m	(7.4; 6.9) m	3.54 (9.0)
(96)	Cl	7.8 m	7.25 m	3.53 (9.0)
(97)	Br	7.45 m	7.0 s	3.40 (9.0)
(98)	I	7.55 m	7.3; 6.9dd(8.0 Hz)	3.40 (9.0)

[For full experimental and spectral data see section 4]

effect only applies to the bromine atom and shows that the electronic environments of the protons ortho to bromine and to the $-N(CH_3)\overset{+}{P}Ph_3I^-$ group are identical. Consequently, the electron-withdrawing effects of the groups must be identical and therefore, perhaps, the effect of the $-N(CH_3)\overset{+}{P}Ph_3I^-$ group on electrophilic aromatic substitution of the N-aryl ring might be the same as that of the bromine atom, directing incoming substituents ortho and para, yet deactivating the ring. It must be kept in mind that an analogous mesomeric effect to that of bromine would seem unlikely as the corresponding resonance forms would locate the positive charge alternately on the phosphorus and nitrogen atoms, in



a manner not possible for the bromine compound. However, it would be interesting to see which effect predominates, although the steric effects of both groups would be different, making such a comparison difficult.

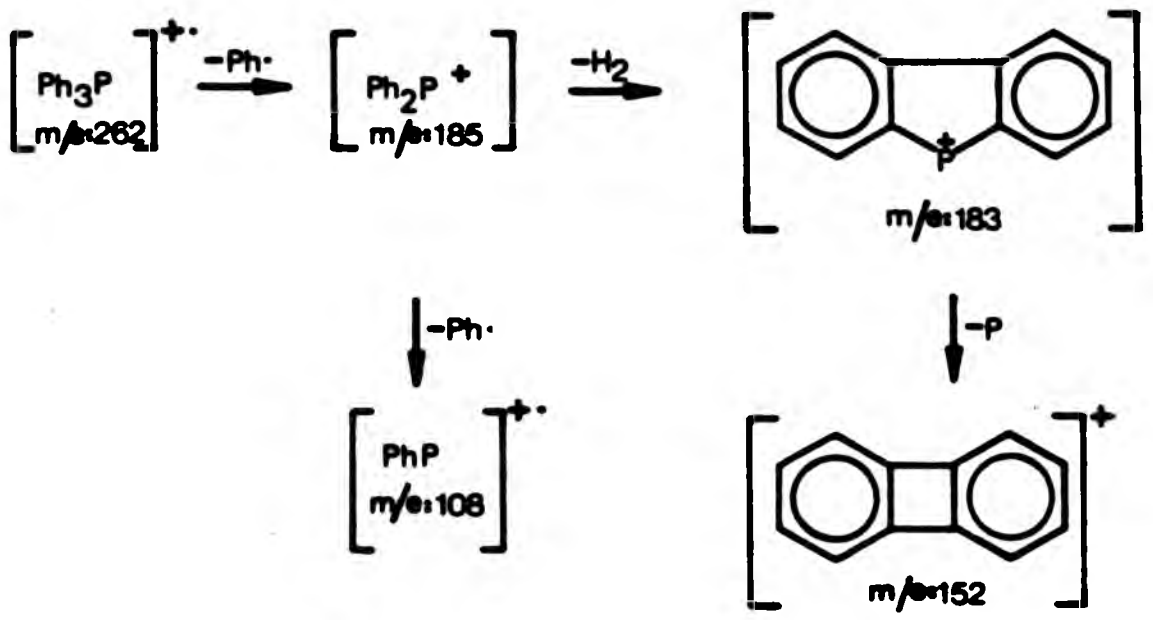
CHAPTER 3

MASS SPECTRA OF N-ArITPPs

In view of the importance of phosphorus ylides synthetically, it was surprising to find that very little work has been reported on the mass spectra of these compounds, with only the parent N-phenyl-ITPP (61) studied as a representative of the iminophosphoranes[151]. As a result of discovering this omission from the list of data which should be routinely available to assist in structure determinations we undertook a systematic survey during which it became clear that even N-aryl substituted iminophosphoranes decompose slowly on storage in the solid state, many needing to be recrystallised before the spectra could be run.

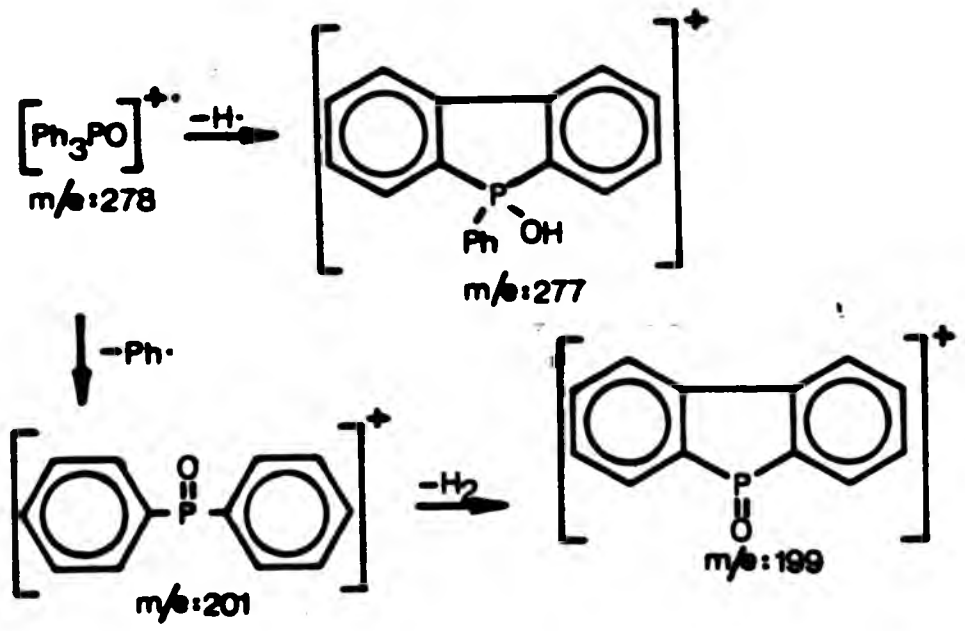
The mass spectra of these compounds show a strong molecular ion peak, often the base peak, and almost always a prominent (M-1) peak, as would be expected from aromatic compounds. The fragmentation pattern of these compounds can be divided into two distinct sets of ions: those arising from the triphenylphosphorane moiety and those from the N-aryl group (although interaction between the two groups can be detected in some cases), the former usually giving rise to the stronger signals.

The mass spectra of triphenylphosphine[111,152] and its oxide[152] have been studied in detail. Triphenylphosphine loses a phenyl radical and a hydrogen molecule successively to give as the most important ion of its spectrum that appearing at m/e: 183:



Further decomposition of this fragment by elimination of the phosphorus atom yields the biphenylene ion (or its equivalent) appearing at m/e: 152. The phenylphosphinidene ion at m/e: 108 is present in most spectra of phenyl-substituted phosphorus compounds, such as phenyl and diphenyl phosphines, phosphine oxides, phosphonium salts and ylides[152].

Triphenylphosphine oxide[152] behaves similarly, although the relative importance of the analogous ions is altered, favouring loss of a hydrogen radical:



It must be stressed however that all the proposed fragmentation pathways in the present work are suggested on the basis of analogy with other similar reactions. No metastable peaks were observed through which it would have been possible, using the formula $m^* = (m_2)^2/m_1$ where

m_2 is derived from m_1 by loss of a neutral fragment, to prove that a peak m_2 originated from m_1 generating a metastable peak m* in the process. (The mass spectrum computer print-out did not show the metastable peaks, and the required instrumentation was, unfortunately, unavailable.)

Para- and meta-substituted N-aryl-ITPP spectra are clearly dominated by the cleavage mode of the triphenylphosphorane moiety as shown by the strong intensities of its characteristic ions (see Tables 20 and 21). A minor and relatively unimportant fragmentation pattern arises from sequential loss of phenyl groups from the molecular ion peak. The importance of this series is greatly affected by the nature of the substituent present on the N-phenyl ring. When the substituent (R) gives rise to simple fissions, eliminates neutral molecules or is easily cleaved, the intensities of the former ions are greatly reduced and in many cases disappear completely.

TABLE 20 Mass spectra of p-substituted N-Ar-ITPPs

					m/e (% abundance)		(M-R)		
R	M	M-1	262	183	152	108	352	Other ions	
-H	353	352						M-155	M-231
	(100)	(95)	(2)	(70)	(10)	(9)	(95)	(20)	(26)
$-CH_3$	367	366							
	(100)	(80)	(2)	(56)	(7)	(11)	(-)		
$-CO_2Et$	425	424						M-29	M-45
	(100)	(60)	(17)	(54)	(5)	(16)	(6)	(23)	(11)
-CN	378	377							
	(100)	(98)	(2)	(79)	(9)	(11)	(-)		
$-NO_2$	398	397	-					M-30	
	(100)	(81)	(18)	(67)	(8)	(20)	(18)	(12)	
-Cl	387	386							
	(100)	(85)	(6)	(70)	(9)	(8)	(-)		
-Br	431	430							
	(71)	(47)	(15)	(100)	(11)	(22)	(4)		
-I	479	478							
	(100)	(54)	(24)	(83)	(8)	(23)	(10)		

TABLE 21 Mass spectra of m-substituted N-Ar-ITPPs

R	M	M-1	262	183	m/e (% abundance) 152	108	(M-R) 352	Other ions
$-CH_3$	367 (100)	366 (86)	(3)	(66)	(8)	(10)	(-)	
$-CO_2Et$	425 (100)	424 (56)	(16)	(83)	(8)	(22)	(6)	M-29 (27) M-45 (4)
$-COCH_3$	395 (100)	394 (90)	(8)	(74)	(8)	(18)	(5)	
$-NO_2$	398 (87)	397 (54)	(22)	(100)	(11)	(39)	(10)	M-(R+H) (30
-Cl	387 (100)	386 (93)	(6)	(98)	(13)	(15)	(2)	
-Br	431 (62)	430 (51)	(13)	(100)	(12)	(24)	(4)	

Para- and meta-substituted compounds show a low tendency to release their substituent (R), whilst o-substituted compounds cleave α to the N-phenyl ring more readily (see Table 22), this ortho effect being very probably due to steric hindrance.

When the R radical of these o-substituted ITPPs contains a suitably positioned oxygen atom, an interesting rearrangement takes place with elimination of TPPO as shown by the increased intensities of its derived ions of m/e: 277, 201 and 199 (see table 23). (The presence of small amounts of TPPO shown in the spectra of the ortho substituted -CN, -Cl and -Br could be due to slightly impure samples or to partial decomposition of the samples in the ionisation chamber.) This rearrangement process accounts for the formation of the base peak in the case of the N-[(o-benzamido)phenyl]-ITPP (81):

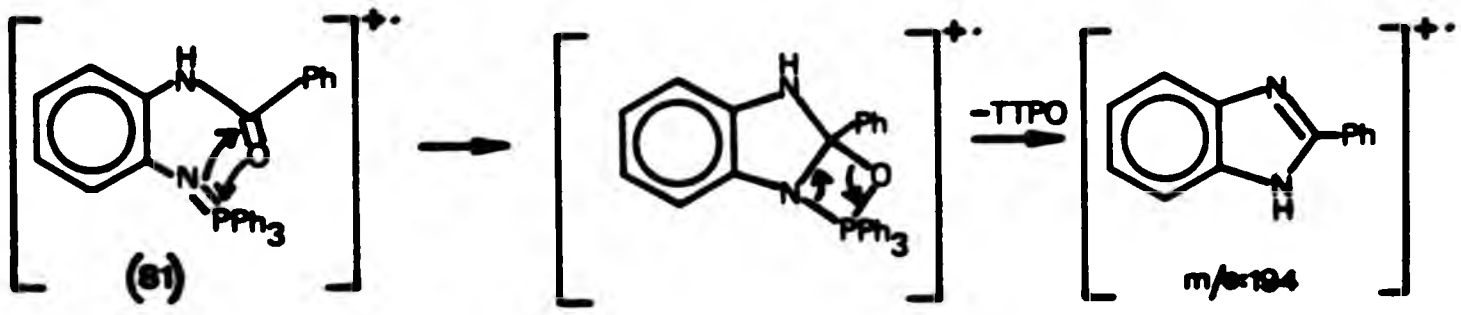


TABLE 22 Mass spectra of o-substituted N-Ar-ITPPs

R	m/e (% abundance) M	M-1	262	183	152	108	(M-R) 352	Other ions (m/e)		
$-NH_2$	368	367								
	(100)	(15)	(15)	(88)	(5)	(24)	(4)			
$-OCH_3$	383	382						M-15	M-43	M-91
	(67)	(18)	(66)	(100)	(12)	(56)	(24)	(3)	(19)	14
$-CN$	378	377						M-260		
	(93)	(100)	(8)	(56)	(8)	(11)	(10)	(14)		
$-NO_2$	398	397						M-30		
	(100)	(31)	(18)	(72)	(11)	(24)	(36)	(8)		
$-F$	371	370						M-21	51	
	(100)	(68)	(3)	(66)	(10)	(8)	(6)	(12)	(36)	
$-Cl$	387	386								
	(100)	(73)	(6)	(72)	(9)	(9)	(55)			
$-Br$	431	430						176	56	
	(87)	(60)	(13)	(100)	(13)	(18)	(67)	(19)	(60)	
$-I$	479	478						274		
	(100)	(38)	(10)	(63)	(8)	(15)	(40)	(18)		
$-CH_2-CO_2CH_3$	425	424						M-15	M-59	208
	(85)	(14)	(39)	(100)	(12)	(35)	(12)	(10)	(25)	(62)
$-NHCOCH_3$	410	409						M-15	M-43	213
	(19)	(-)	(14)	(100)	(23)	(35)	(-)	(33)	(12)	(17)
$-NHCOPh$	472	471						M-105	M-193	213
	(87)	(6)	(32)	(77)	(11)	(30)	(2)	(16)	(36)	(21)
$-NHSO_2C_6H_4CH_3(p)$	522	521						M-155	M-341	91
	(16)	(-)	(9)	(38)	(4)	(12)	(-)	(100)	(28)	(58)
$-CO_2CH_3$	411	410						M-15	M-31	M-33
	(100)	(22)	(9)	(94)	(16)	(22)	(73)	(12)	(14)	(42)
$-NHCO_2Et$	440	439						M-45	M-72	278
	(91)	(7)	(28)	(83)	(14)	(29)	(17)	(27)	(29)	(52)
$-COCH_3$	395	394						M-15		
	(96)	(32)	(100)	(76)	(18)	(29)	(17)	(17)		
$-NHCO(CH_2)_2CO_2Et$*	496	495						M-45	M-46	395
	(10)	(-)	(17)	(33)	(12)	(13)	(6)	(7)	(19)	(15)
$-NHC(CH_3)=CHCO_2Et$	480	479						M-45	M-73	M-87
	(100)	(23)	(46)	(84)	(14)	(41)	(3)	(2)	(12)	(40)
$-OH$	369	368						M-17		
	(89)	(22)	(80)	(86)	(16)	(39)	(4)	(4)		

* DCI mass spectrum

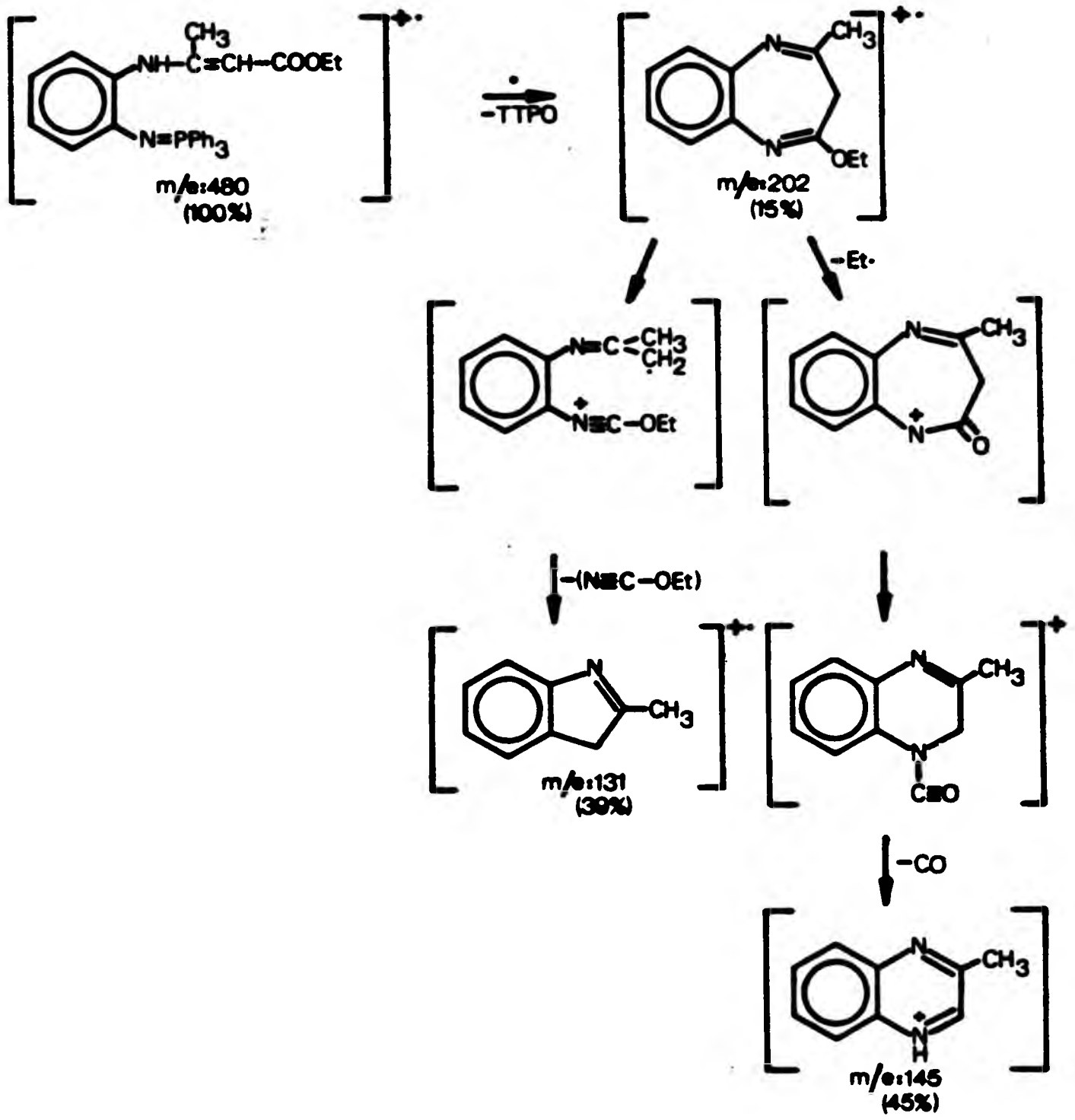
TABLE 23 Mass spectra of o-substituted N-Ar-ITPPs (cont)

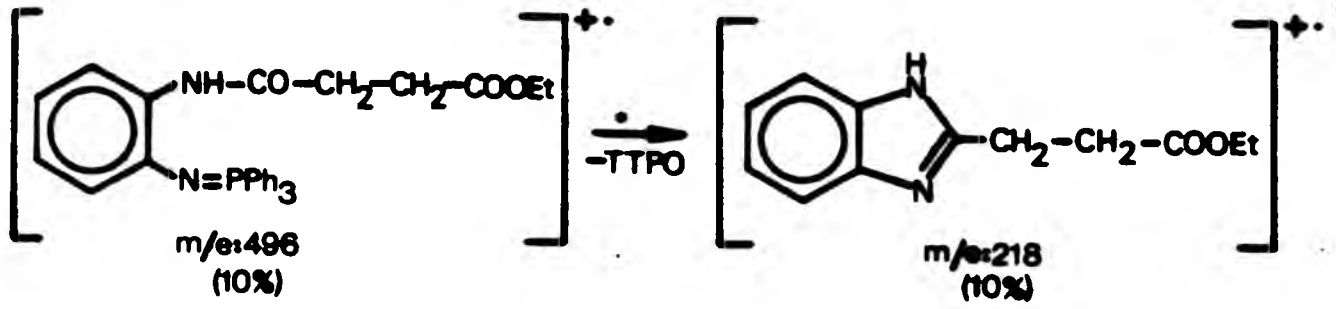
R	m/e (% abundance) 277	201	199	M-278				
$-NH_2$	(-)	(-)	(-)	(-)				
$-OCH_3$	(-)	(3)	(3)	(-)				
-CN	(11)	(1)	(3)	(-)				
$-NO_2$	(45)	(32)	(12)	(-)				
-F	(-)	(-)	(-)	(-)				
-Cl	(14)	(1)	(3)	(-)				
-Br	(10)	(2)	(3)	(-)				
-I	(3)	(-)	(-)	(-)				
$-CH_2CO_2CH_3$	(26)	(42)	(5)	147 (7)	132 (7)			
$-NHCOCH_3$	(29)	(15)	(12)	132 (21)				
-NHCOPh	(70)	(17)	(12)	194 (100)				
$-NHSO_2C_6H_4CH_3(p)$	(21)	(2)	(3)	244 (-)				
$-CO_2CH_3$	(1)	(51)	(14)	133 (6)				
$-NHCO_2Et$	(100)	(25)	(18)	162 (6)	134 (71)			
$-COCH_3$	(80)	(49)	(20)	117 (3)				
$-NHCO(CH_2)_2CO_2Et$*	(100)	(19)	(20)	218 (10)	173 (11)	172 (17)	145 (53)	118 (7)
$-NHC(CH_3)=CHCO_2Et$	(96)	(21)	(16)	202 (15)	278 (49)	145 (45)	131 (39)	
-OH	(100)	(21)	(18)	91 (2)				

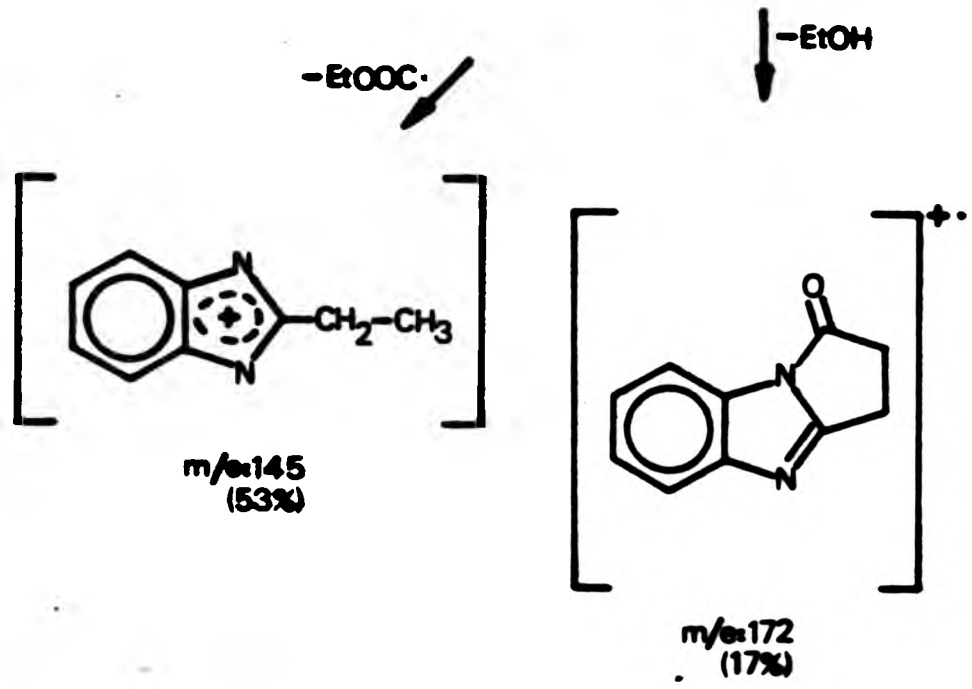
* DCI mass spectrum

A high resolution MS confirmed the molecular formula of the m/e: 194 ion.

The majority of the spectra where this elimination is seen to take place give rise to rearranged ions which are only barely detectable, probably as a consequence of the intermediates being unstable under these conditions and/or the positive charge being retained by the oxygen atom of Ph_3PO. The former possibility is illustrated by the following examples:







* These assignments are based on the results of pyrolysis experiments (see Chapter 4).

That the other products arising from N-(2-acetylphenyl)-ITPP (62) and N-(2-methoxycarbonylphenyl)-ITPP (63) are almost undetectable is not surprising as both structures, if formed, would be expected to have very short lifetimes under these conditions.

This rearrangement process, although unknown hitherto for ITPPs, has been observed for β-oxoalkylidenetriphenylphosphoranes and it was confirmed that the ion corresponding to TPPO did not arise from oxide impurity[153].

As we have already mentioned in the previous chapter and will demonstrate in the following, this rearrangement also occurs during pyrolysis, and thus mass spectral studies of these compounds could provide a useful and simple analytical test of whether these reactions would be likely to succeed in the laboratory, subject to the formation of a stable product. For example, N-[o-(p-toluenesulphonamido)-phenyl]-ITPP (82) gives rise to only weak ion signals corresponding to TPPO (see Table 23) and under laboratory conditions we were unable to carry out this reaction, whereas from R = $-CH_2COOCH_3$ to R = $-NHC(CH_3)=CHCO_2Et$ inclusive, the rearrangement process takes place relatively easily.

Noteworthy are the spectra of the amides and the sulphonamide studied (see Table 22). Their molecular ion ($M^{+\cdot}$) peaks are all relatively small, and the (M-1) ions are altogether absent, with the exception of the o-benzamide derivative. The low intensities of these ions could be partly explained taking into account the favourable benzylic cleavage which gives rise to a common ion at m/e: 367 and which accounts for the base peak in the case of the o-(p-toluenesulphonamide) derivative (see Table 24). These compounds also have in common the

TABLE 24 Mass spectra of amides and sulphonamides

R	(% abundance) m/e: 367	m/e: 213
$-NHCOCH_3$	12	17
-NHCOPh	16	21
$-NHSO_2C_6H_4CH_3(p)$	100	20
$-NHCO(CH_2)_2CO_2Et$	15	≈1
	82	

This rearrangement process, although unknown hitherto for ITPPs, has been observed for β-oxoalkylidenetriphenylphosphoranes and it was confirmed that the ion corresponding to TPPO did not arise from oxide impurity[153].

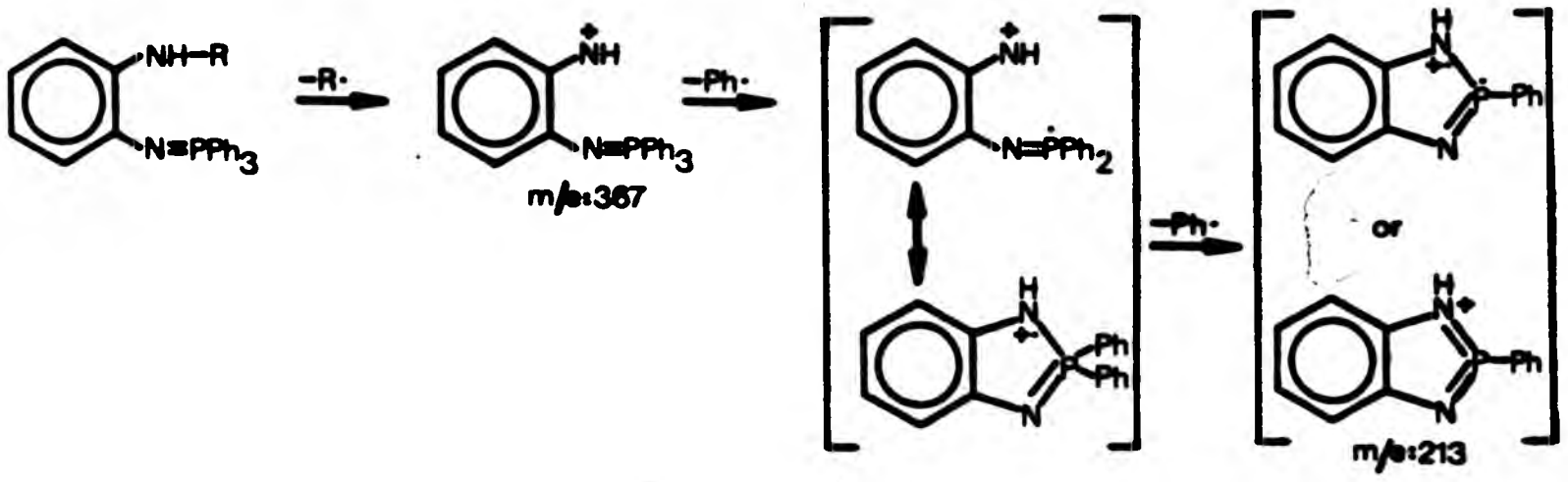
As we have already mentioned in the previous chapter and will demonstrate in the following, this rearrangement also occurs during pyrolysis, and thus mass spectral studies of these compounds could provide a useful and simple analytical test of whether these reactions would be likely to succeed in the laboratory, subject to the formation of a stable product. For example, N-[o-(p-toluenesulphonamido)-phenyl]-ITPP (82) gives rise to only weak ion signals corresponding to TPPO (see Table 23) and under laboratory conditions we were unable to carry out this reaction, whereas from R = $-CH_2COOCH_3$ to R = $-NHC(CH_3)=CHCO_2Et$ inclusive, the rearrangement process takes place relatively easily.

Noteworthy are the spectra of the amides and the sulphonamide studied (see Table 22). Their molecular ion ($M^{+\cdot}$) peaks are all relatively small, and the (M-1) ions are altogether absent, with the exception of the o-benzamide derivative. The low intensities of these ions could be partly explained taking into account the favourable benzylic cleavage which gives rise to a common ion at m/e: 367 and which accounts for the base peak in the case of the o-(p-toluenesulphonamide) derivative (see Table 24). These compounds also have in common the

TABLE 24 Mass spectra of amides and sulphonamides

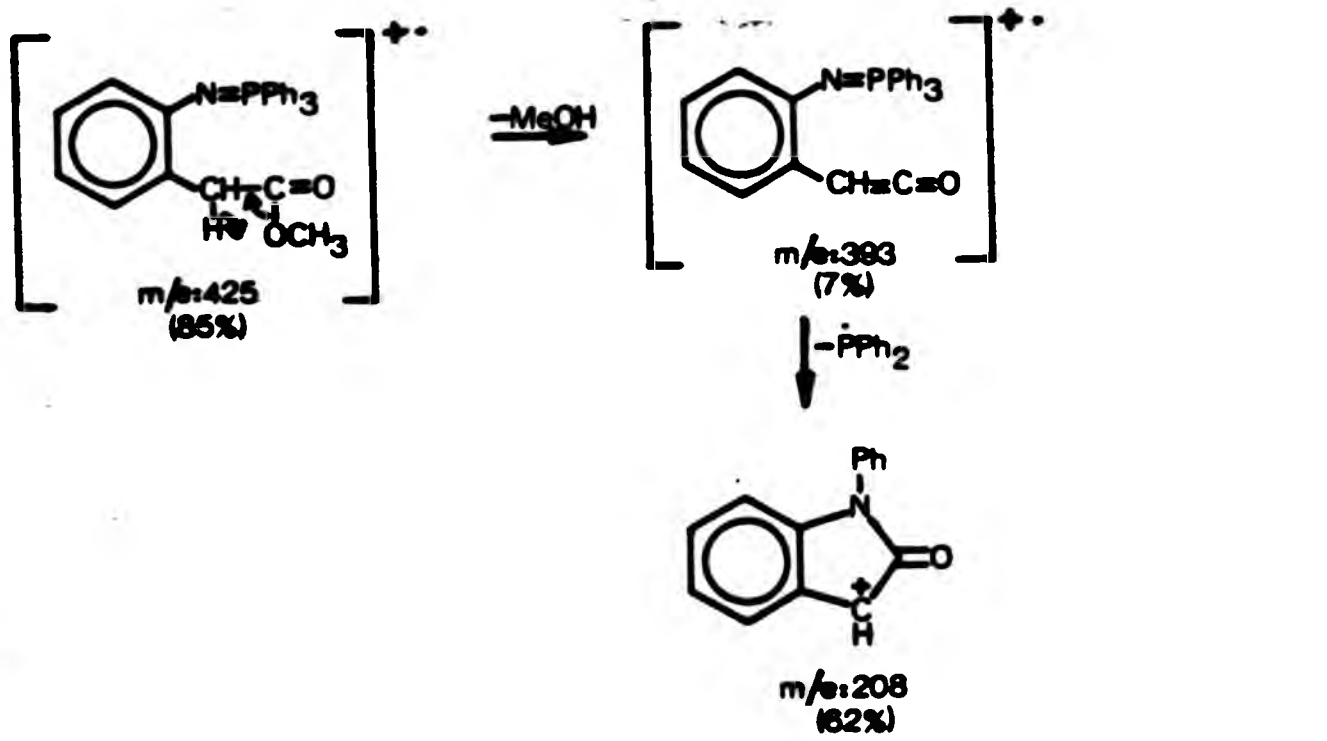
R	(% abundance) m/e: 367	m/e: 213
$-NHCOCH_3$	12	17
-NHCOPh	16	21
$-NHSO_2C_6H_4CH_3(p)$	100	20
$-NHCO(CH_2)_2CO_2Et$	15	≈1
	82	

ion appearing at m/e: 213 which could have its origin from ion m/e: 367 as shown:



These two ions m/e: 367 (M -73) and m/e: 213 are also detected in the mass spectra of the closely related N-[o-(carbethoxyamino)phenyl]-ITPP (89), both appearing with a 14% relative abundance.

Further comment is necessary on the spectrum of N-[2-(α methyl acetate)phenyl]-ITPP (64) which apart from showing the expected fragmentation pattern giving rise to ions at M-15, M-31, M-59, and M-73, shows a very prominent ion at m/e: 208 which cannot be accounted for on the basis of simple fissions. A plausible formation scheme could be:



Therefore, in summary, the mass spectra of N-Ar-ITPPs give rise to strong molecular ions and are dominated by the fragmentation pattern of the triphenylphosphorane group. N-aryl ortho-substituted derivatives which contain a carbonyl group give Wittig-type reactions (whereas the corresponding m- and p-substituted compounds, in which intermolecular elimination of TPPO would be necessary, do not), and evidence of such a reaction can be used to prove the orientation of the substituent and to suggest whether pyrolysis of the compound might be synthetically useful.

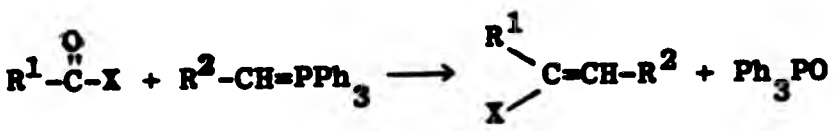
No threshold voltages were investigated for the iminophosphoranes although if the most easily removed electron, as expected and as shown by PES, is on the nitrogen atom, a correlation might be expected between appearance potential and N-aryl substituents.

CHAPTER 4

PYROLYSIS REACTIONS OF ORTHO SUBSTITUTED N-Ar-ITPPs AND SOME ALKOXY BENZIMIDAZOLES

As was mentioned earlier one of the main aims of this work was to investigate the possibility of performing Wittig-type reactions involving the iminotriphenylphosphorane group with ester and amide carbonyl groups. (Intramolecular reactions of this type would provide new routes to heterocyclic molecules.) The only two known examples of this type of reaction with an ester group[102] and a carbonate[71] have already been referred to.

During the last few years several reports on the reactions of alkylidenetriphenylphosphoranes with esters[154], thioesters[155], acid anhydrides[156], monothioimides[157] and amides[158] have appeared, all following the general mechanism outlined in Scheme 7.



X = OR, SR, OCOR, NHCSR, NR_2

Scheme 7

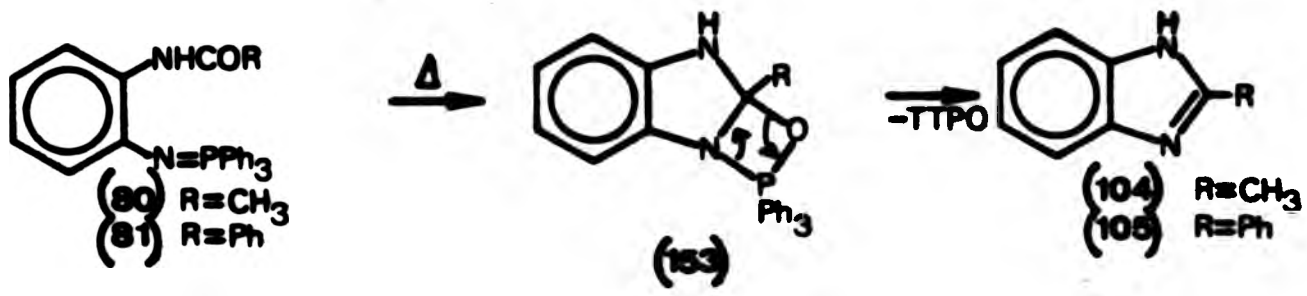
In general, these reactions may be carried out both in nonpolar solvents (for example toluene) and dipolar solvents (for example DMSO) and conditions are relatively mild.

In contrast, we have found that iminophosphoranes need more severe conditions, namely pyrolysis, to undergo these reactions, which nevertheless proceed with excellent yields. Several intermolecular reactions have been attempted, but these yielded complex reaction mixtures when reactions took place at all and, therefore, at the present moment

successful reactions of this type appear to be limited to intramolecular cyclisations.

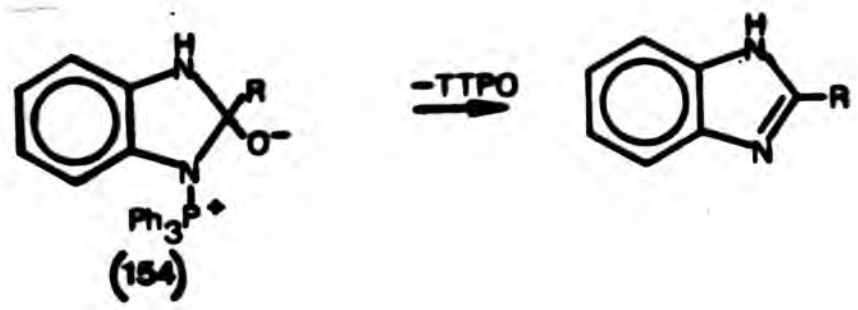
This difference in reactivity between alkylidene and iminotriphenylphosphoranes is not surprising as the former generally show a greater reactivity.

Table 25 summarises the results obtained from these pyrolysis reactions (see experimental, section 5): compounds (80) and (81) reacted readily, and, as shown by the triphenylphosphine oxide isolated, almost



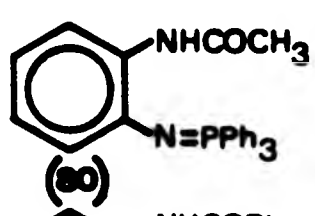
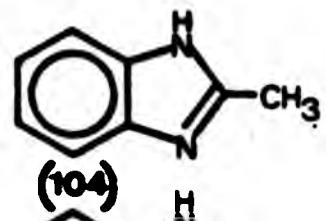
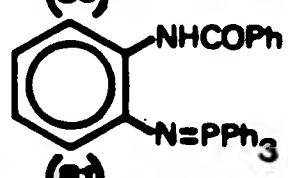
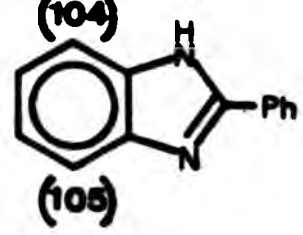
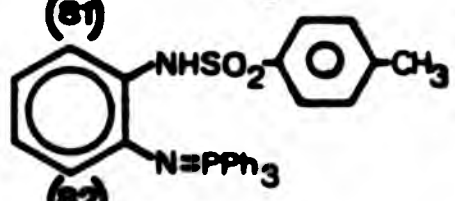
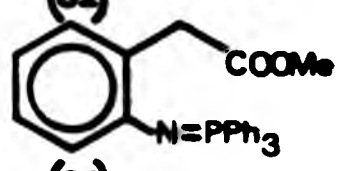
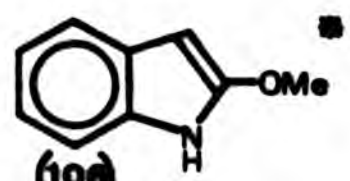
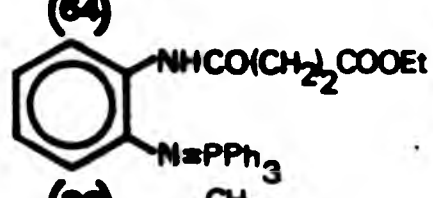
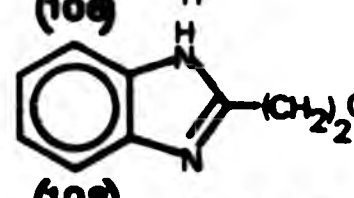
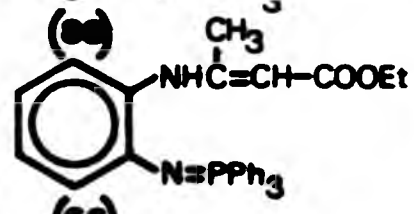
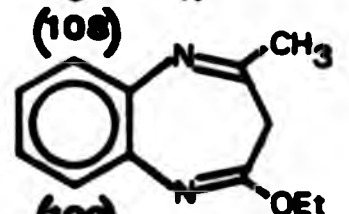
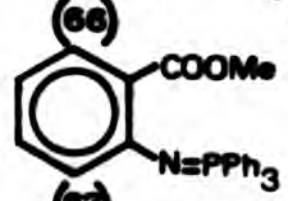
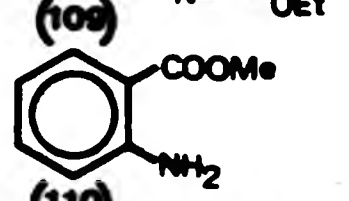
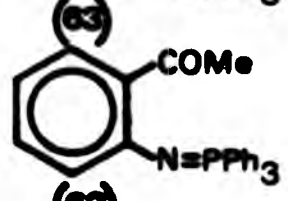
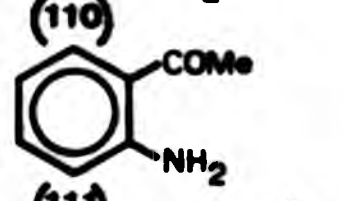
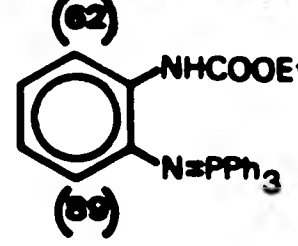
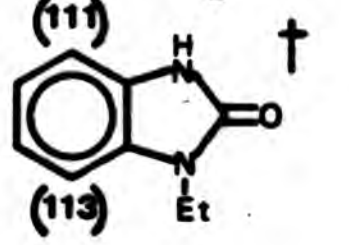
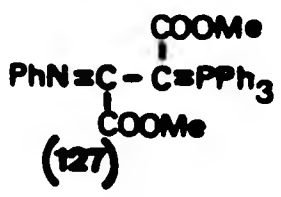
Scheme 8

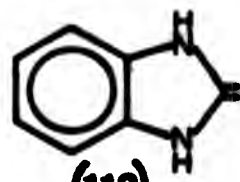
quantitatively. These reactions are thought to follow the mechanism depicted in Scheme 8, with the intermediate (153) formed by a cycloaddition process similar to that proposed by Vedejs for alkylidenetriphenylphosphoranes (see introduction). The formation of both benzimidazoles (104) and (105) could be accounted for on the basis of a betaine-like intermediate (154), but under the conditions used (total



absence of solvents), the opposite charges of the betaine structure would attract each other, collapsing or nearly collapsing to intermediate (153), to stabilise the system. It could be argued that these charges might be stabilised by other surrounding molecules, but steric considerations reflected in the absence of intermolecular products make

TABLE 25 Pyrolysis of ortho substituted N-Ar-ITPPs

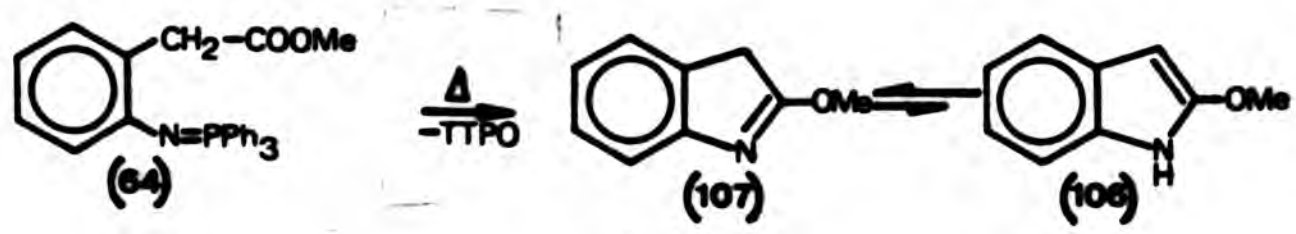
Compound	Product	Reaction Time (°C)	Yield %	TPPO %
 (80)	 (104)	3h (210)	86	96
 (81)	 (105)	3h (210)	86	90
 (82)	No reaction	4h (240)	-	-
 (84)	 (106)*	3h (150)	98	97
 (86)	 (108)	5h (170)	46	86
 (88)	 (109)	7h (170)	75	89
 (83)	 (110)	10h (210)	31	42
 (85)	 (111)†	7h (220)	undetermined	
 (89)	 (113)	8.5h (160)	36	85
 (127)	no reaction	8h (180)	-	-

* And its tautomer (107) † And  (112) =O (25%) and mixture (114)

this proposition unlikely. These conclusions apply to all the other pyrolysis reactions studied.

The characterisation of both benzimidazoles was carried out by comparing their physical and spectral data with those available in the literature.

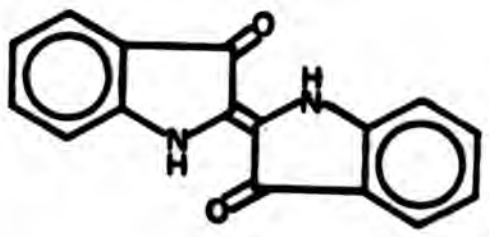
The pyrolysis of N-[2-(α methyl acetate)phenyl]-ITPP (64) yielded an almost quantitative yield of 2-methoxyindole (106), which was found by ^1H NMR to be in equilibrium with its tautomeric form (107) in solution.



(64) (107) (106)

The integrated proton NMR spectra showed a ratio of 6:4 for (107):(106) in exact agreement with the results found for the ethyl homologue by Harley-Mason[127], who demonstrated the existence of this tautomeric equilibrium by the isolation of both forms through sublimation, followed by recording their proton NMR spectra, which were identical.

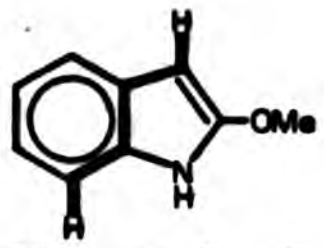
A few hours after isolation of our indole derivative we observed the emergence of a red colouration, which has been shown[128] to be due to the air oxidation of this compound to indirubin. Attempts to sublime the



oxidised mixture under vacuum led to contaminated sublimate.

Prior to this oxidation of the indole, we had managed to record, as mentioned above, its ^1H NMR and IR spectra, which correlated well with those of the reported ethyl analogue. The only noteworthy difference was the long range coupling of the -CH= proton of tautomeric form (106)

with H-7 on the aromatic ring. This coupling has been observed in

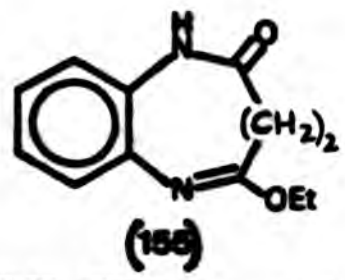


in similar indole systems[129], and is thought to arise from the coplanarity of the structure. For this reason the comparable coupling is absent from the tautomeric form (107).

Pyrolysis of N-[o-(ethoxysuccinylamido)phenyl]-ITPP (88) provided a chance to study a possible competition reaction between an amide and an ester. Although yields for TPPO and ethyl β-(2-benzimidazolyl)-propionate (108) shown in Table 25 are very far apart, the reaction yielded only these two products in an overall conversion of 98%. However, separation of these two products by column chromatography proved to be very difficult, and even after doubling the proportion of silica gel, a substantial amount of product was eluted still as a mixture.

The IR spectrum of the compound isolated clearly established structure (108) over that of (155) (see below) by the absence of the amide carbonyl and ν(NH) stretching vibrations when compared to that of the starting material (88). All other physical and spectral data were in accordance with this assignment.

The results say little however about any general comparison of reactivity between amide and ester groups, or about the formation of aromatic benzimidazole rings compared with non-aromatic benzodiazocines because of the usually overriding possibility in these reactions of forming a five-membered, rather than an eight-membered ring..

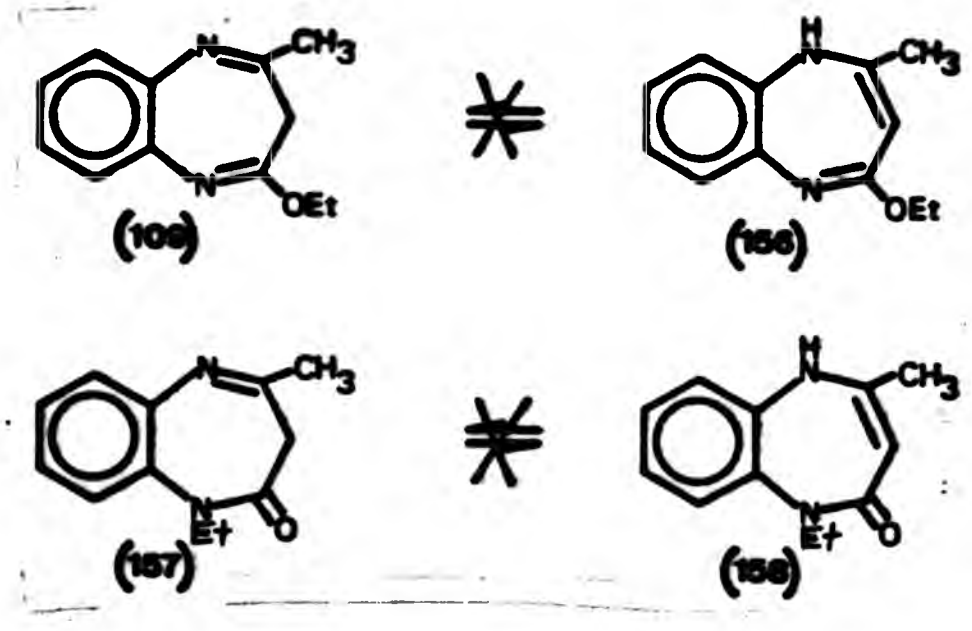


(156)

Nevertheless, larger rings are formed, as shown by the reaction of N-[2-(β ethyl crotonate)anilino]-ITPP (66), and in good yields (see Table 25).

(66) (109)

The structure elucidation of this product posed some difficulties, as there were four possible structures: (109), (156), (157) and (158), the former two and latter two tautomeric pairs:



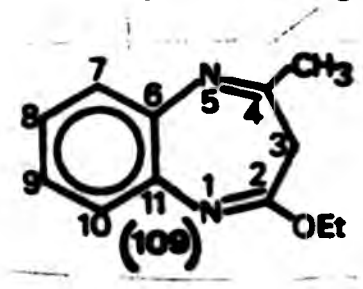
(109) (156)

(157) (158)

The consideration of structures (157) and (158) arose because imidates are known to rearrange under thermal conditions in an analogous process to the Chapmann rearrangement[147]. However, these alkyl rearrangements proceed by an intermolecular free radical mechanism and usually give poor yields, thus on these grounds, structures (157) and (158) looked less likely.

Proton NMR spectroscopy eliminated the possibility of a tautomeric equilibrium as neither a broad singlet for the NH proton nor any signal corresponding to an olefinic proton could be observed, and instead a singlet appeared at 2.88 ppm, integrating for two protons, at a value close to that of cyclic imidates[147]. Therefore, structures (156) and (158) could be discarded as, in addition, compound (66) showed the olefinic proton signal at 4.66 ppm.

The confirmation of the structure of the product as (109) was mainly based on its ^{13}C NMR spectrum. Amide carbonyl groups appear between 165.5 and 180.9 ppm[53], whilst that of the ethoxy imidate carbon atom of 2-ethoxybenzimidazole (119) appears at 158.6 ppm (see experimental section 6). Although this five-membered ring compound is not a very good model due to the aromatic nature of the imidazole ring, it offered tentative support for structure (109). In addition, the two values of 159.2 ppm and 154.2 ppm being very close together suggested similar



structures for both carbon atoms (C2 and C4). Further evidence for the structure (109) was obtained by comparing the chemical shift values of the ethyl group with those of O-ethyl and N-ethyl groups respectively (see Table 26). From these data it becomes clear that the ethyl group in structure (109) is linked to the oxygen atom and not to the nitrogen atom.

TABLE 26 ^{13}C NMR data of ethyl groups

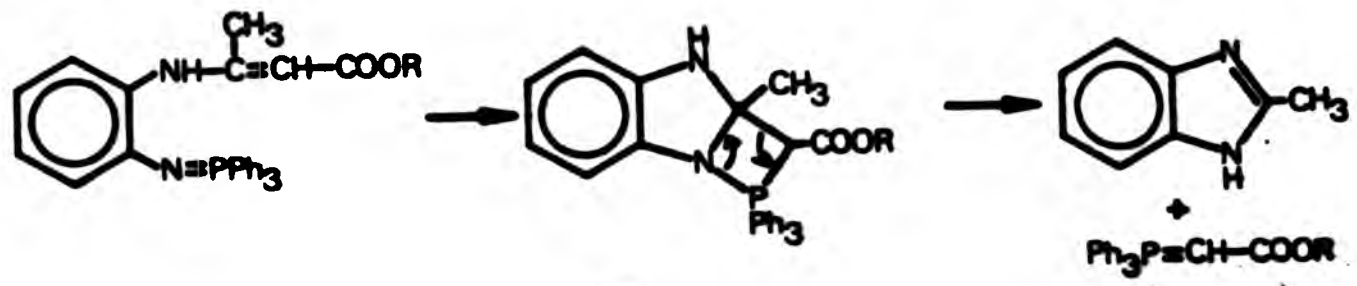
	$\delta^{13}C$ (ppm)			
Compound	$-O-CH_2-$	$-N-CH_2-$	$-O-CH_2-CH_3$	$-N-CH_2-CH_3$
(109)	63.3	-	14.2	-
(119)	66.0	-	14.6	-
(123)	71.7	43.6	11.4	10.3

In order to obtain further reference data the synthesis of 4-methyl-2-oxo-1H-1,5-benzo[f]diazepin (the tautomer of compound (126)) was attempted following Sexton's method[109,133]. ^{1}H NMR spectroscopy

(126)

conclusively showed that our material was solely tautomer (126) and its mp (142°C compared to a literature value of 148-9°C[133]) and UV spectrum[133] confirmed that we had reproduced the original work. (See experimental section 5). The methylene group at 3.14 ppm in the ^{1}H NMR spectrum was slightly deshielded (by the presence of the α-carbonyl group) from the 2.88 ppm value obtained for (109), further corroborating our assignment. Both compounds (109) and (126) showed an IR band at 1645 cm^{-1} (N=C-CH$_3$), while the band appearing at 1660 cm^{-1} in (109) showed the imidate group and that at 1690 cm^{-1} in (126) the amide carbonyl group. Pyrolysis of compound (*66*) offered the possibility of investigating whether the iminotriphenylphosphorane would react with a double bond, as this was suitably placed in the molecule and was activated by the ethoxycarbonyl group:

However, no evidence of such a reaction was found, the ITPP group showing a high kinetic preference towards reaction with the carbonyl ester group through the ylide's normal four-membered transition state, and no tendency either towards the ene reaction involving the standard four-membered ring:

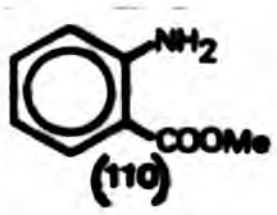


Pyrolyses of N-[2-(methoxycarbonyl)phenyl]-ITPP (63) and N-(2-acetylphenyl)-ITPP (62) were less successful. Neither the possible reaction products (159) and (160) nor starting materials were isolated from their respective reactions, only TPPO (in both reactions) and methyl

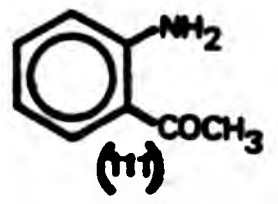
(159)

(160)

anthranilate (110) and 2-aminoacetophenone (111) respectively. (See Table 25).



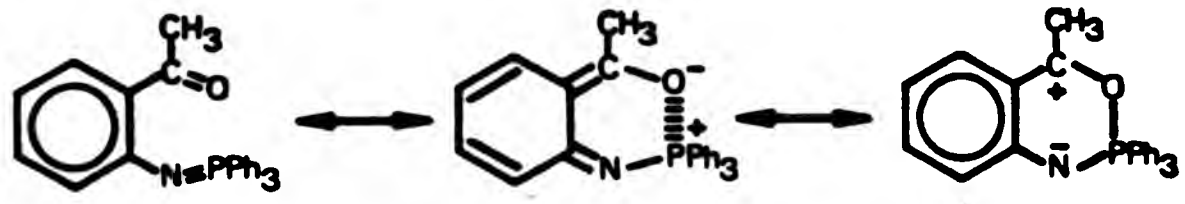
(110)



(111)

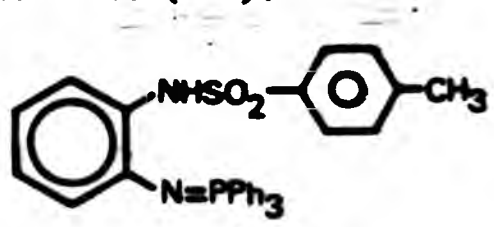
These results could be explained assuming that hydrolysis had either taken place prior to pyrolysis or it had taken place once (159) and (160) had been formed, during chromatographic work-up. In an attempt to distinguish between these two possibilities, the reaction of N-[2-(methoxycarbonyl)phenyl]-ITPP (63) was repeated ensuring totally anhydrous conditions, as outlined in the experimental section 5, and isolation of

the yellow oil formed was attempted via vacuum distillation. However, we were unable to separate the oil from the TPPO formed and chromatographic separation reproduced the above results. These results indicate that simple hydrolysis of the starting materials was unlikely. Both pyrolyses gave poor yields suggesting that perhaps highly reactive intermediates were involved, which taking into account structures (159) and (160), is not unreasonable. No intermolecular products were detected in either reaction possibly as a consequence of steric hindrance, or, as suggested by the stability of compound (62) in refluxing toluene[142], due to the ascribed formation of a resonance-stabilised chelate ring:

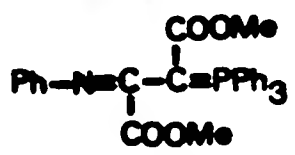


In either case, under forcing conditions, it appears that extensive decomposition takes place, but the transient formation of compounds (159) and (160) is uncertain.

No reaction of any type, apart from a little charring of material, was observed during the pyrolysis reactions of N-[o-(p-toluenesulphonamido)phenyl]-ITPP (82) and dimethyl (phenylimino-triphenylphosphoranylidene) succinate (127).



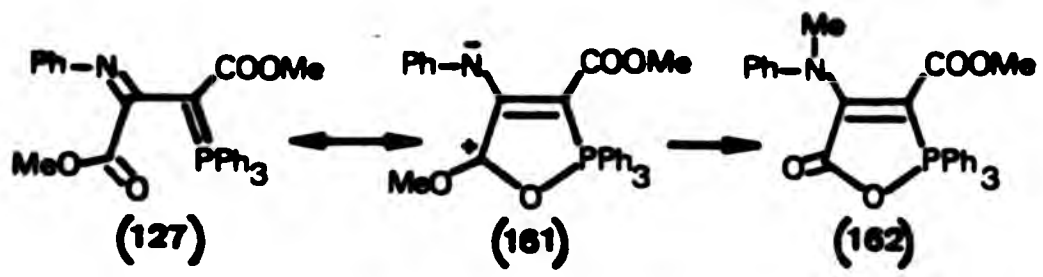
(82)



(127)

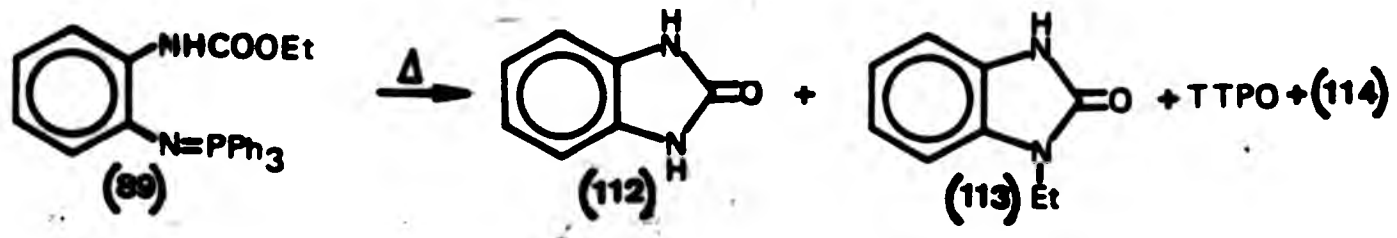
Although compound (127) is known to yield N-methylaniline[60] when pyrolysed in air at 220°C, under our conditions (180°C, 8h, under nitrogen), no reaction was observed. This failure of compound (127) to react via a Wittig-type reaction was predictable from the near absence of ions m/e: 278 and 277 and the low intensities of those at

m/e: 201 and 199 in its mass spectrum. Although potentially three sites for reaction are present in the molecule, none of them is favourable. It appears that the β-ethoxycarbonyl group is in a very good location to stabilise the system through resonance, thus preventing reaction with the two other sites (the α-ethoxycarbonyl group, and the phenyl-imino substituent which would regenerate its synthetic precursors DMA and N-phenyl-ITPP (61)).

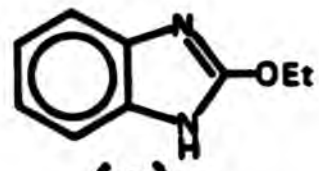


A methyl group migration from resonance form (161) to yield an intermediate like (162), could be thought to take place, and thus provide an explanation for the observed formation of N-methylaniline[60] if (162) decomposes further.

Pyrolysis of N-[o-(carbethoxyamino)phenyl]-ITPP (89) afforded a complex reaction mixture from which it was possible to isolate some unreacted material (8%), TPPO and four other products: 2-benzimidazolone (112), 1-ethyl-2-benzimidazolone (113) and a mixture of two compounds (114) in trace amounts. As usual in these reactions, the yield of TPPO was very good.

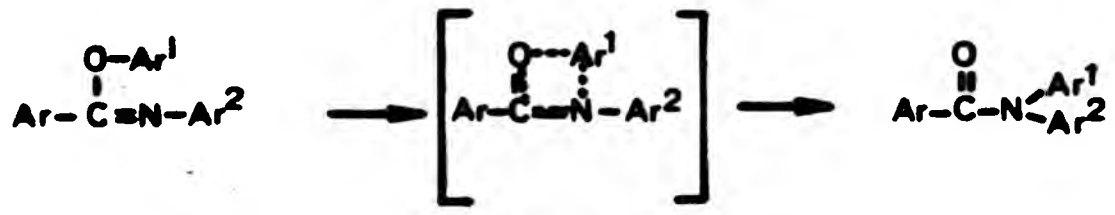


2-Ethoxybenzimidazole (119), an imidate of sorts, was the expected product from this pyrolysis reaction, if it involves a Wittig-like elimination, but imidates are known to rearrange thermally to give



(119)

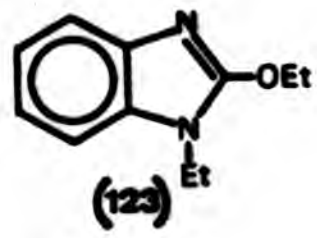
amides[147] (O-aryl systems especially give good yields) in the Chapman rearrangement.



When the migrating group is an alkyl radical, the reaction no longer proceeds as shown above however because an alkyl group cannot undergo a front side S_N2 attack.

The reaction mechanism becomes intermolecular involving free radicals and generally gives poor yields[147]. It has also been observed that when the O-alkyl group has a β-hydrogen, olefin formation seems to be a common result[159].

Formation of compounds (112) and (113) and not (119) seems to indicate that such a rearrangement is taking place in our reaction, i.e. formation of (119) is followed by the migration process. Further evidence was provided by the proton NMR of the mixture (114) (see experimental section 6b - mixture (114)) which appears to be a mixture of unknown proportions of 2-ethoxybenzimidazole (119) and 1-ethyl-2-ethoxybenzimidazole (123):



(123)

Identification of 2-ethoxybenzimidazole (119) would support our assumption that it is the first product formed and the isolation of (112) and (113),

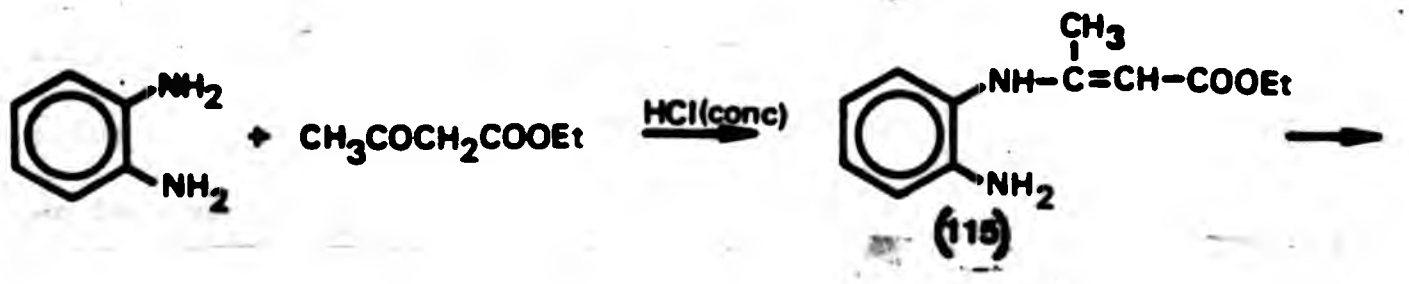
and identification of (123) would make more likely the intermolecular free radical mechanism.

Since most of the reactants are accounted for in the product mixture, it is possible to gain more information about the mechanism by determining the fate of the ethyl group initially present in (89). Some seems to have been lost (possible as ethene) and some rearranged. The extent of this elimination cannot be accurately calculated as we do not know the proportions in the mixture (114), but we can obtain an upper and lower limit. If we assume that the "mixture" (114) is entirely (123) we find by difference that a 40% elimination has taken place, and if we assume it is totally compound (119) we arrive at a figure of 47%. Even if the error made in these calculations is relatively large, nevertheless it does show elimination is taking place, in accordance with the assumed mechanism.

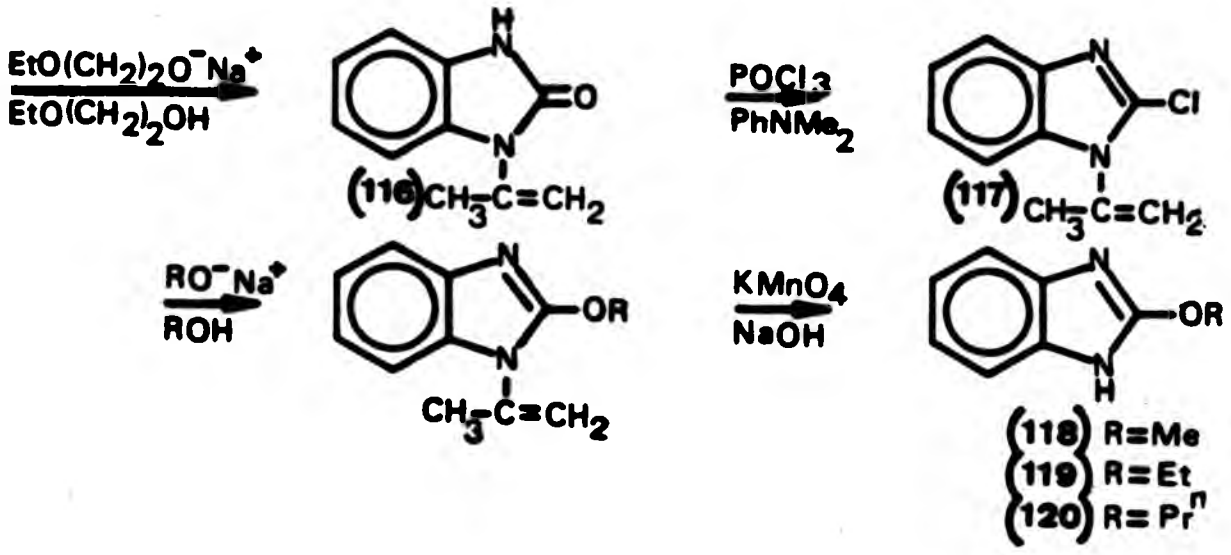
To check whether 2-benzimidazolone (112) partially or totally originated by a prior hydrolysis of the iminophosphorane (89), the reaction was repeated under strictly anhydrous conditions. After chromatographic work-up, a 21% yield of 2-benzimidazolone (112) was obtained, a result which correlated well with the original reaction (see Table 25) and suggested that accidental hydrolysis of (89) was not the source of (112).

To confirm all the above possibilities and assumptions it was decided to synthesise three representative 2-alkoxy-benzimidazoles, and pyrolyse them.

The following synthetic scheme was followed:



(115)



The results obtained are summarised in Table 26.

TABLE 26 Synthesis of 2-alkoxybenzimidazoles

R	2-alkoxybenzimidazole	Overall yield (%)
Me-	(118)	3
Et-	(119)	7
n-Pr-	(120)	10

[For experimental details see section 6a]

Pyrolysis of these three benzimidazole derivatives gave the following results (see Table 27):

TABLE 27 Pyrolysis of 2-alkoxybenzimidazoles

			Products (%)		
Compound pyrolysed	Unreacted material	(112)	1 alkyl-benzimidazole	1 alkyl-2 alkoxy-benzimidazole	1,3 dialkyl-benzimidazolone
(118)	15	23	38	-	8
(119)	51	15	-	18	-
(120)	60	8	3	19	-

[For full experimental details see section 6b]

All structures were determined by mixed mp with authentic materials or comparison of their spectral and physical data with relevant published data, except for the 1-n-propyl-2-n-propoxybenzimidazole (125), for which full spectral data and microanalytical results are given.

Sublimation of the 2-alkoxybenzimidazoles was the main cause for the poor yields obtained in the pyrolysis of the 2-ethoxy- and 2-propoxy-benzimidazoles (119) and (120) respectively, even after the reactions were repeated in a nitrogen atmosphere, instead of a high vacuum, to reduce sublimation to a minimum.

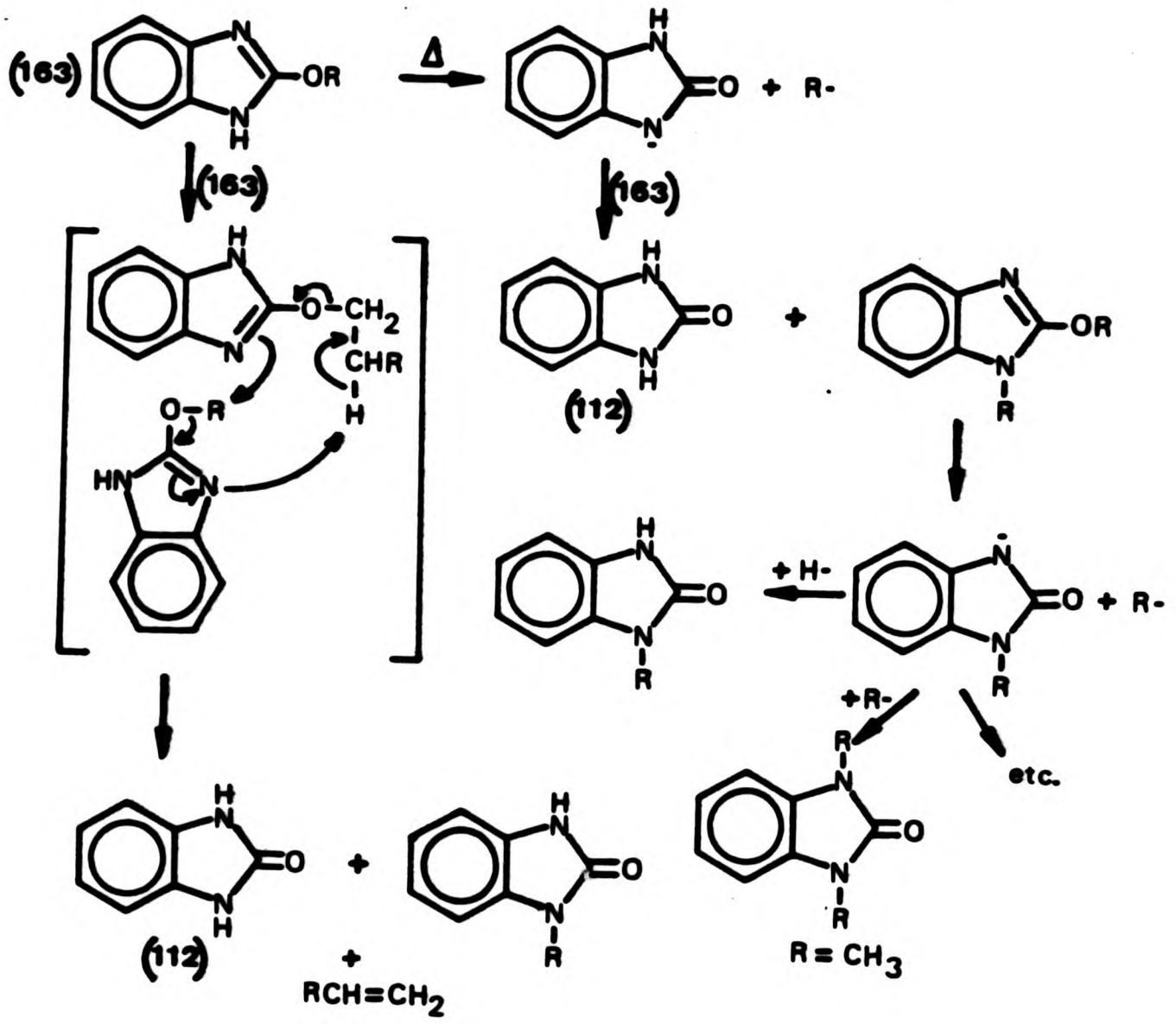
All three reactions confirm that the rearrangement process takes place, but the results obtained from the pyrolysis of 2-ethoxybenzi-midazole (119) cannot be correlated with those obtained from the pyrolysis of the ITPP (89). The major product isolated, apart from TPPO, from the latter reaction was 1-ethyl-2-benzimidazolone (113) which was not even detected in the former. This different behaviour could be explained if we assume that 1-ethyl-2-ethoxybenzimidazole (123) is an intermediate of the reaction leading to the benzimidazolone derivative (113), which was unable to rearrange, perhaps because of sublimation of 2-ethoxybenzi-midazole (119) or because the reaction was stopped too soon.

This latter hypothesis seems unlikely as the reaction was kept at 180°C during 3h, conditions which were found to furnish a 93% yield in the pyrolysis of the ITPP (89). The likelihood that 1-ethyl-2-ethoxy-benzimidazole (123) is an intermediate in the rearrangement process is supported by its tentative identification in mixture (114). Sublimation of compound (119), therefore seems to be the main cause of the observed different behaviour: during the pyrolysis of the ITPP (89), it did not take place, or was very limited, because of its very gradual formation in the molten lattice of the iminotriphenylphosphorane (89), which prevented its sublimation and favoured its rearrangement.

Results from the pyrolysis of 2-ethoxy- and 2-propoxybenzimidazoles are very similar and indicate that rearrangement follows the same mechanism. However, the results quoted for the 2-propoxy derivative (120) show that no elimination took place, probably also, as a consequence of the sublimation process.

The yield of 2-benzimidazolone (112) obtained from compound (118) (see Table 27) conclusively shows that this compound is not exclusively formed by the elimination mechanism and that the reaction follows an intermolecular pathway, as the 2-methoxybenzimidazole (118) cannot undergo elimination and, were the mechanism intramolecular, the only product isolated would have been the 1-methyl-2-benzimidazolone (121). This conclusion is further supported by the isolation of the 1,3-dimethyl-2-benzimidazolone (122).

Therefore, sublimation of these compounds is regarded as the main cause of their poor rearrangement, and two competing mechanisms are operating during the course of this reaction:



Several attempts were subsequently made to carry out the following intermolecular Wittig reactions using the conditions listed here, but either the reaction did not take place or it yielded very complex reaction mixtures.

$Ph_3P{=}N\text{-}Ph + CH_3CONH_2 \xrightarrow{\Delta}$ No reaction (164)

$Ph_3P{=}N\text{-}Ph + NH_2\text{-}CO_2Et \xrightarrow{\Delta}$ No reaction (165)

$Ph_3P{=}N\text{-}Ph + Ph\text{-}NH\text{-}CO_2Et \xrightarrow[\text{Reflux}]{48h}$ No reaction (166)

$Ph_3P{=}N\text{-}Ph + Ph\text{-}NH\text{-}CO_2Et \xrightarrow{\Delta}$ Complex mixture (167)

$Ph_3P{=}N\text{-}Ph + (CH_3)_2C{=}CH\text{-}CO\text{-}CH_3 \xrightarrow{\Delta}$ Complex mixture (168)

Reaction of N-phenyl-ITPP (61) with acetamide (164) and ethyl carbamate (165) failed mainly as a consequence of the sublimation of the carbonyl compound. Reaction was then attempted with ethyl N-phenyl-carbamate in refluxing toluene during 48h (166), no reaction taking place, whilst after pyrolysis of the two reagents, reaction (167), a complex mixture of unreacted reagents, TPPO and unidentified products resulted. Similarly, reaction (168) yielded a complex mixture of unreacted starting materials, TPPO and other products as indicated by tlc.

We have to conclude therefore that pyrolytic Wittig-type reactions of ITPPs, although at present limited to intramolecular processes, take place readily and in good yields, both with esters and amides, thus constituting a novel synthetic approach to nitrogen heterocyclic compounds. Where competing reaction sites are present, the most stable heterocyclic ring is favoured.

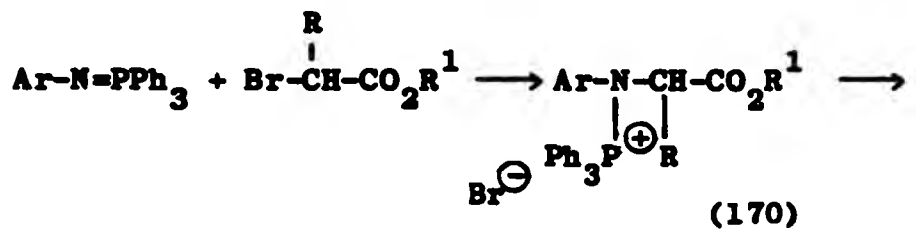
CHAPTER 5

FURTHER REACTIONS OF N-Ar ITPPs AND

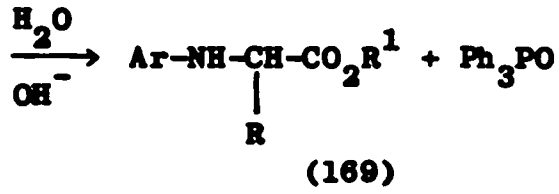
o-bis-ITPP BENZENE.

Reactions with α-bromoesters

Trying to broaden the scope and applications of the synthesis of monoalkylated aromatic amines[41,59], it was thought that the use of α-bromoesters would give access to a wide variety of α-anilinoesters (169) according to the following scheme.



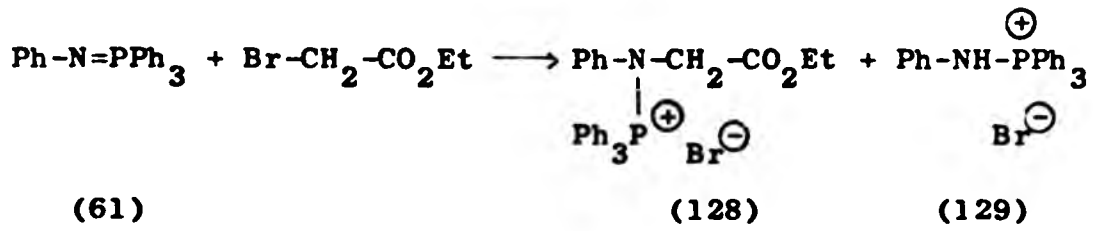
(170)



(169)

However, these reactions, carried out as described in experimental section 7a, led to mixtures from which the salts (170) could not be isolated in pure form, except for the mono-salt of o-bis-ITPP benzene (67) with ethyl α-bromoacetate.

The parent N-phenyl-ITPP (61) reacted rapidly and efficiently with ethyl α-bromoacetate and its methyl homologue yielding an oily mixture of the expected product (128) and N-phenyl-ITPPm hydrobromide (129) which we were unable to separate. After 2h reflux with excess dry triethylamine the original salt mixture was transformed into another mixture, of (128) and triethylamine hydrobromide, which we were, similarly, unable to separate by fractional crystallisation.

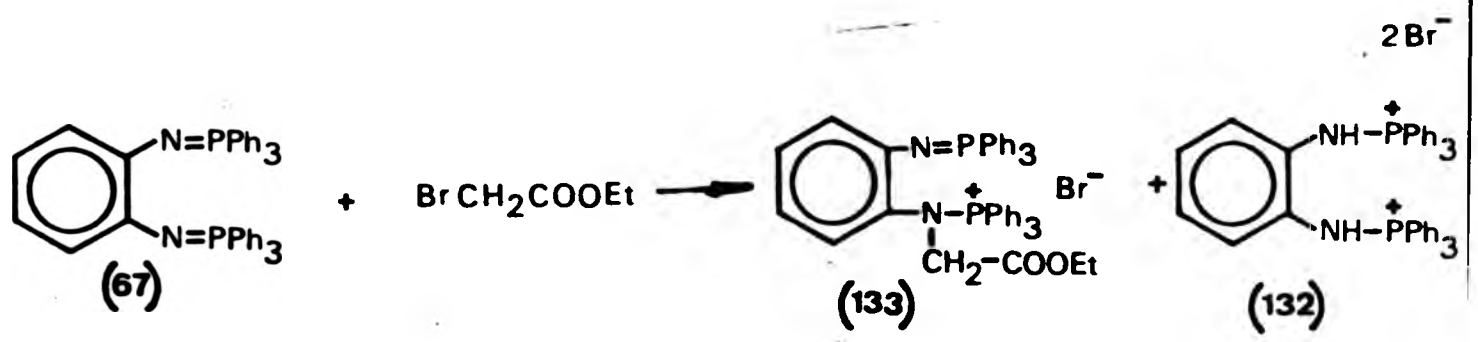


(61) (128) (129)

Attempts to separate the original salt mixture by column chromatography only resulted in the recovery of the salts.

Reactions of N-(p-methoxyphenyl)-ITPP with ethyl α-bromoacetate followed the same pattern, ^{31}P NMR and IR spectra showing that the mixture isolated was probably composed of N-(ethyl α-acetate)-N-(p-methoxyphenyl)-ITPPm bromide (130) and N-(p-methoxyphenyl)-ITPP hydrobromide (131).

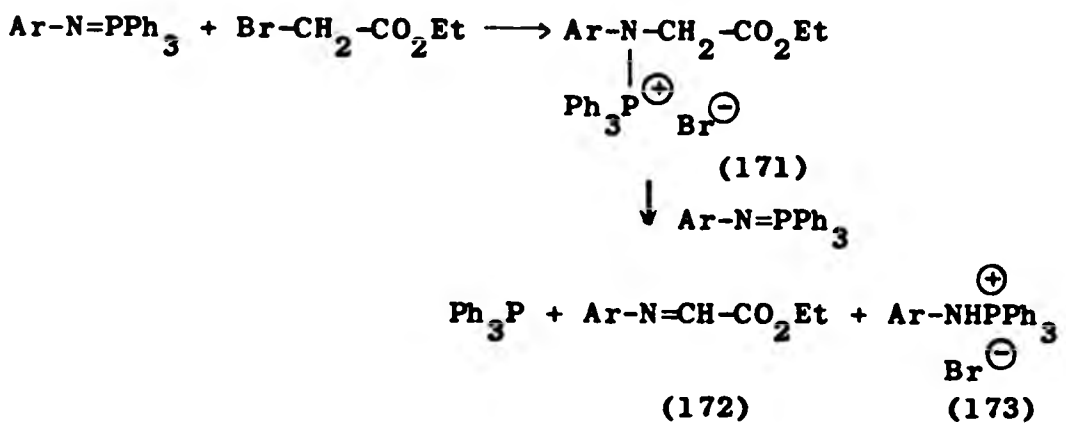
Finally, an elaborate isolation method provided a pure sample of o-bis-ITPP benzene mono N-(ethyl α-acetate) bromide (133) from the reaction of o-bis-ITPP benzene (67) with ethyl α-bromoacetate.



(67) (133) (132)

This reaction had previously been run in dry acetonitrile when only o-bis-ITPP benzene bis-hydrobromide (132) was isolated. When the reaction was rerun in dry benzene a 1:4 mixture of (132) and (133) was formed according to the integrated proton NMR spectrum. After stirring the mixture with dry triethylamine and washing the resultant mixture with distilled water, a pure sample of (133) was obtained in moderate yield.

These results suggest the iminotriphenylphosphorane is once more acting as a nucleophile and as a base:

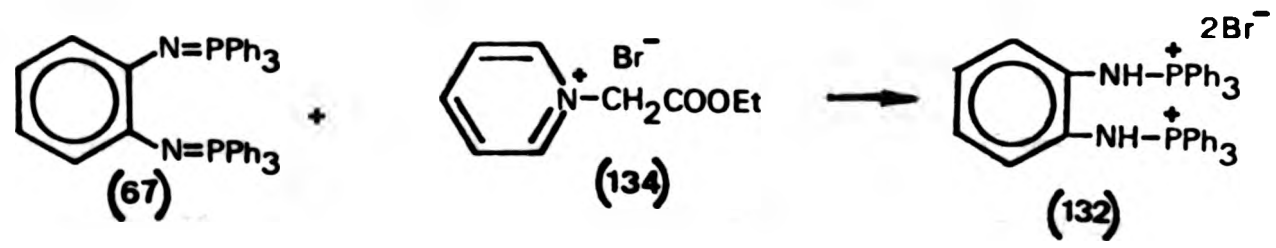


This preliminary idea is based on the isolation of salts (171) and (173), but no further experiments, trying to detect either compound (172) or triphenylphosphine were carried out. More work is therefore needed in the study of these reactions before a soundly based mechanism can be proposed.

Our main aim remained the synthesis of salts of type (171) and thus another attempt based on literature methods was carried out.

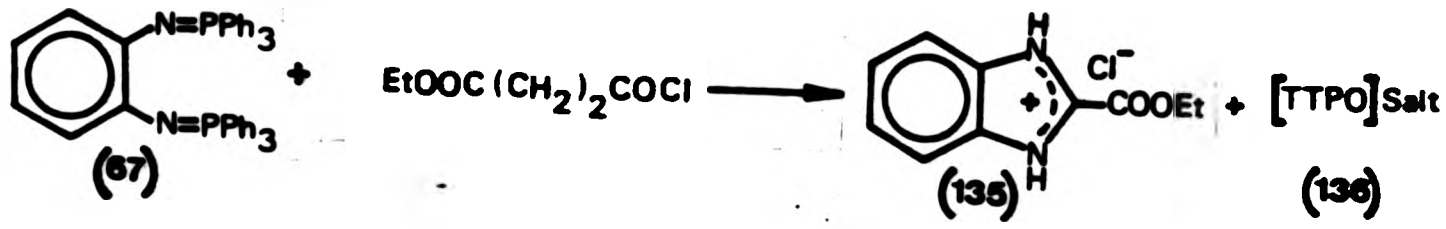
N-phenyl-ITPP (61) was added to a dry benzene solution of ethyl diazoacetate at room temperature under a nitrogen atmosphere. After stirring the solution during 64h (as no reaction had taken place), trimethyloxonium tetrafluoroborate was added as a catalyst[86]. Sodium hydrogencarbonate work-up afforded a white crystalline salt, tentatively identified as the hydrogen carbonate salt of N-phenyl-ITPP (61), after the same results were obtained when N-phenyl-ITPP (61) and trimetyl-oxonium tetrafluoroborate were mixed together. (This salt melts at 100°C with vigorous gas evolution.)

Similarly unsuccessful was the reaction of o-bis-ITPP benzene (67) with ethyl α-pyridinium acetate bromide (134)[145] which yielded o-bis-ITPP benzene bis-hydrobromide (132) contaminated with a small amount of unreacted (134).



So, returning to our studies of the reactions of iminotriphenylphosphoranes with acid chlorides in trying to gain a better understanding of the mechanisms, several reactions were carried out, some of them followed by low temperature ^{31}P NMR spectroscopy.

o-Bis-ITPP benzene (67) reacted with ethyl oxalyl chloride at room temperature under a nitrogen atmosphere to yield 2-ethoxycarbonylbenzimidazole hydrochloride (135) and a TPPO-salt (136) of uncertain structure (see experimental section 7b).



The structure of 2-ethoxycarbonylbenzimidazole hydrochloride (135) was established by its transformation into 2-ethoxycarbonylbenzimidazole (137).

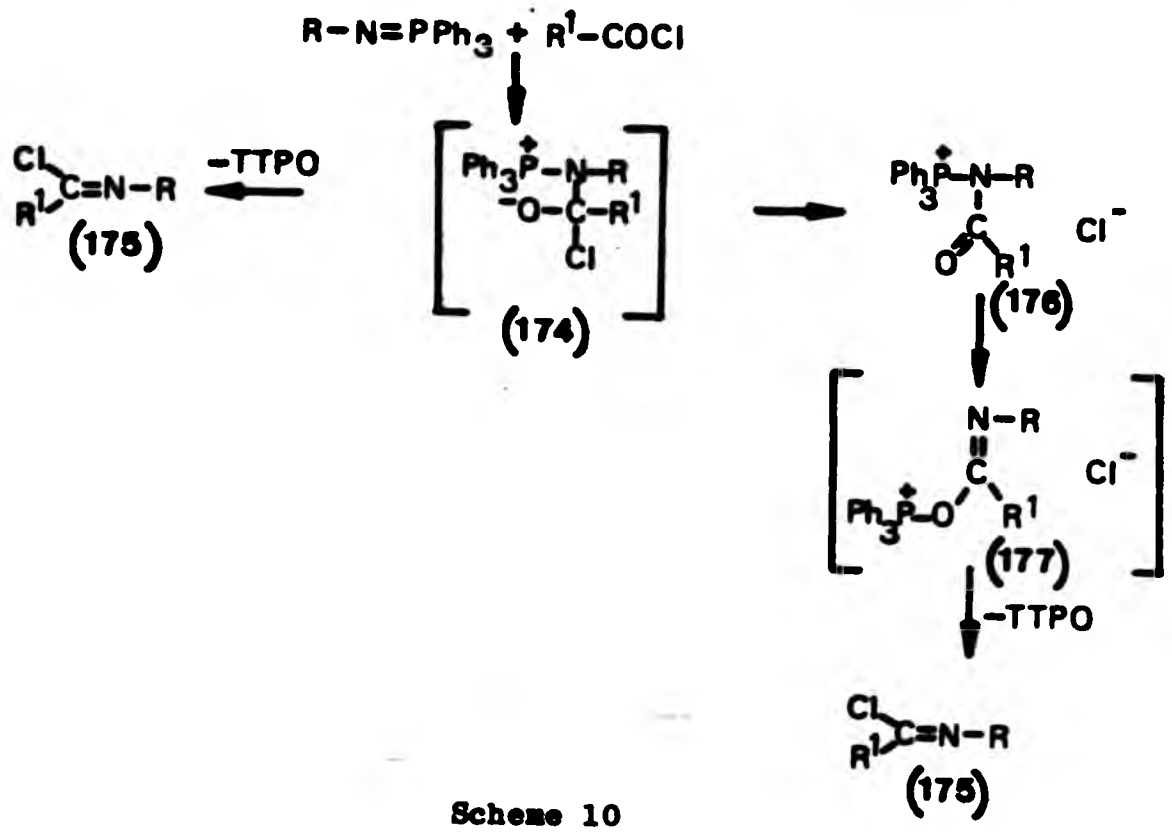
The absence of halogen atoms from the TPPO-salt (136) structure was established by the silver nitrate test after dissolving the salt in water containing dilute nitric acid and after a sodium fusion test on a small sample. The mass spectrum of (136) clearly shows that this compound fragments into TPPO and an ion at m/e: 44, which suggests that the salt also contains the CO_2 moiety. The ^{31}P NMR spectrum of (136) shows a single peak at +32.1 ppm and its ^{13}C NMR spectrum a signal at 160.1 ppm (typical of a carbonyl group) and a pattern of aromatic carbon atom resonances almost identical to those of TPPO[50]. Its proton NMR spectrum shows a very deshielded signal and its IR spectrum shows two broad absorption bands (at 2340 and 1925 cm^{-1}) which could be assigned either to a P-H[53] or $\overset{+}{P}$-OH[85a,b] stretching vibration, (similar to that observed for pyridine oxide hydrochlorides and hydrobromides[85b]). However, $\overset{+}{P}$-OH groups give rise to a broad absorption around 1100 cm^{-1} [85b] which is either obscured by other bands in the spectrum of (136) or is absent. Therefore, possible structures for this compound could be:

Before any explanation can be offered for this reaction, leading to the formation of (135) and (136), the structure of the TPPO-salt (136) must be definitely established.

TPPO is known to form 1:1 (TPPO HBr) and 2:1 [$(TPPO)_2$ HBr] adducts with hydrogen bromide[85b], and this possibility, in the case of (136), should be considered. However, tlc was not very helpful as the salt decomposed to TPPO cleanly, nor was its mp (131-5°C), as the salt also decomposed with vigorous gas evolution, similar to the TPPO-hydrogen peroxide salt[85c]. But, both ^{13}C and ^{1}H NMR seem to indicate this salt to be a 1:1 adduct. Microanalysis gives better agreement with the empirical formula $C_{19}H_{16}PO_3$, than with the required $C_{19}H_{17}PO_3$.

Returning to the reactions of iminotriphenylphosphoranes with acid halides, it was shown earlier in Chapter 2 that iminotriphenylphosphoranes react with acyl chlorides to yield imidoyl chlorides under reflux conditions,[68] although by mixing the reagents at 0°C and allowing the reaction mixture to reach room temperature (followed by sodium hydrogencarbonate work-up), an amide can be isolated which, according to the literature, is formed via an intermediate imidoyl chloride.[121b]

Zbiral[68] postulated the formation of an intermediate betaine structure (174) which could either collapse directly to the imidoyl chloride (175) or could form an acyl phosphonium salt (176) which by rearrangement would yield the imidoyl chloride (175) (Scheme 10):



Scheme 10

However, the possibility of a cycloaddition mechanism was not taken into account, and following Vedejs'[44] work for alkylidenetriphenylphosphoranes and the fact that these reactions were carried out in aprotic non-polar solvents, such as benzene, which would not favour the formation of the intermediate betaine (174), we carried out several experiments in an attempt at clarifying the mechanism.

N-phenyl-ITPP (61) was dissolved in sodium-dry toluene and the mixture kept at -78°C before the addition of ethyl oxalyl chloride. As soon as the acid chloride was added a white precipitate was formed, which on filtration in air and at room temperature, quickly decomposed. The reaction was repeated, and once the precipitate had formed, the acetone/dry ice bath was removed and the reaction stirred at room temperature. 36h later all the precipitate had disappeared leaving a clear light yellow solution, from which TPPO was identified by its ^{31}P NMR spectrum (peak at 25.7 ppm, ^{31}P NMR spectrum of pure TPPO in toluene has a peak at +25.4 ppm).

As the white precipitate could not be isolated we decided to follow the reaction by low temperature ^{31}P NMR spectroscopy.

It was repeated a third time in an NMR tube using $CDCl_3$ as solvent, and was monitored at -64°C and room temperature.

TABLE 28 ^{31}P NMR results ($CDCl_3$) of (61) with ethyloxalyl chloride

Time	δ (ppm)	relative height (cm)
≈0.5h (-64°C)	+5.6	4.6
	+31.6	5.4
	+46.0	4.4
≈1h (-64°C)	+31.0	1.0
	+31.6	2.6
	+46.0	10.1
≈24h (25°C)	+28.3	9.0
	+45.8	4.2
	+64.0	4.9
≈144h (25°C)	+28.4	5.4
	+63.9	2.7

This experiment was complicated by the use of $CDCl_3$ as solvent, as indicated by the signals at 64.0 and 63.9 ppm which could correspond to dichlorotriphenylphosphine[103]. However, when triphenylphosphine and N-phenyl-ITPP (61) were dissolved in $CDCl_3$ and their ^{31}P NMR spectra recorded 24h later (all operations conducted at room temperature), no peaks appeared in the +64 ppm region. These results show that dichlorotriphenylphosphine, if at all formed, does not originate from interaction of the solvent with either compound but could originate from any of the two intermediates (176) or (177), thought to be formed. The signal at 5.6 ppm was assigned to unreacted N-phenyl-ITPP (61), while those appearing at 31.0, 28.3 and 28.4 ppm were assigned to TPPO. A temperature effect might be the cause of the down-field shift observed for the signals of (61) and TPPO at -64°C which usually appear at 3.3 and 28.6 ppm respectively, as the magnitude of the shift is practically the same (+2.3 ppm) in both cases. The signal appearing at 31.6 ppm, which is absent after 24h at 25°C, probably arises from the phosphorus atom

bonded to oxygen which would be a rather unstable intermediate, thus fitting quite well with a structure of type (177) (see Scheme 10). Finally, the signal appearing at 45.9±1 ppm could be assigned to the N-acyl-ITPPm salt (176), as this chemical shift is similar to that found for N-alkyl-ITPPm salts. These results and assignments seem to confirm the formation of the N-acyl-ITPPm salt (176) and the rearrangement mechanism via (177), however it would be hard to explain the fact that (177) is consumed faster than the N-acyl-ITPPm salt (176) and on this basis it must be assumed that both mechanisms might be operating in a competitive manner.

When the experiment was repeated in dry acetonitrile and the reagents mixed at room temperature, the ^{31}P NMR spectrum showed a signal at 25.2 ppm for TPPO and two additional signals at 43.4 ppm and 45.2 ppm which were tentatively assigned to structures (177) and (176) respectively. This experiment suggests a solvent effect is probably the cause of the apparent stability of both structures, although after the original solvent had been removed and the solid obtained kept 5 min in dry diethyl ether, no appreciable decomposition took place (see experimental section 7b).

In order to find out whether oxazaphosphetane intermediates (typical ^{31}P NMR chemical shifts are: -55.4 ppm to -34.9 ppm in $CDCl_3$[87]) were actually formed during these reactions, the reaction between N-phenyl-ITPP (61) and a slight excess of acetyl chloride was followed by low temperature ^{31}P NMR spectroscopy. Table 29 summarises the results obtained.

TABLE 29 ^{31}P NMR results of (61) with acetyl chloride in toluene

Time	(°C)	δ (ppm)	relative heights (cm)
≈1 min	-60°C	-0.9	3.4
		+24.2	≈0.04
		+40.7	traces
≈3 min	-30°C	-1.6	4.8
		+23.8	0.1
		+31.2	0.06
		+41.1	0.06
≈10 min	-30°C	-1.8	4.5
		+23.8	0.13
		+31.2	0.16
		+41.2	0.20
≈10 min	0°C	-2.3	3.5
		+23.6	0.5
		+31.4	2.5
		+41.2	5.0
≈20 min	0°C	-2.4	1.1
		+23.6	not detected
		+31.4	2.1
		+41.2	4.0
≈25 min	25°C	+23.4	small shoulder
		+24.2	4.4
		+31.4	2.0
		+41.7	0.9
≈5 min	50°C	+23.8	6.0
		+31.2	1.2
≈10 min	50°C	+24.0	4.4
		+31.4	0.4
≈25 min	50°C	+24.0	6.0
		+31.4	0.2
≈67 h	25°C and 25 min at 100°C	+25.4	5.5
		+31.3	0.1

No signals between -30 ppm and -200 ppm were detected.but although no signals corresponding to oxazaphosphetanes were detected, these cannot be ruled out as transient intermediates. It should also be remembered that during the course of the reaction precipitation takes place, and therefore the observed intensities of the different signals probably do not reflect true proportions.

These results give support to our previous assignment of the peak

TABLE 29 ^{31}P NMR results of (61) with acetyl chloride in toluene

Time	(°C)	δ (ppm)	relative heights (cm)
≈1 min	-60°C	-0.9	3.4
		+24.2	≈0.04
		+40.7	traces
≈3 min	-30°C	-1.6	4.8
		+23.8	0.1
		+31.2	0.06
		+41.1	0.06
≈10 min	-30°C	-1.8	4.5
		+23.8	0.13
		+31.2	0.16
		+41.2	0.20
≈10 min	0°C	-2.3	3.5
		+23.6	0.5
		+31.4	2.5
		+41.2	5.0
≈20 min	0°C	-2.4	1.1
		+23.6	not detected
		+31.4	2.1
		+41.2	4.0
≈25 min	25°C	+23.4	small shoulder
		+24.2	4.4
		+31.4	2.0
		+41.7	0.9
≈5 min	50°C	+23.8	6.0
		+31.2	1.2
≈10 min	50°C	+24.0	4.4
		+31.4	0.4
≈25 min	50°C	+24.0	6.0
		+31.4	0.2
≈67 h	25°C and 25 min at 100°C	+25.4	5.5
		+31.3	0.1

No signals between -30 ppm and -200 ppm were detected but although no signals corresponding to oxazaphosphetanes were detected, these cannot be ruled out as transient intermediates. It should also be remembered that during the course of the reaction precipitation takes place, and therefore the observed intensities of the different signals probably do not reflect true proportions.

These results give support to our previous assignment of the peak

appearing at +63.95 ± 0.5 ppm in the ^{31}P NMR spectrum run in $CDCl_3$, and the same assignments are made for all the other signals observed.

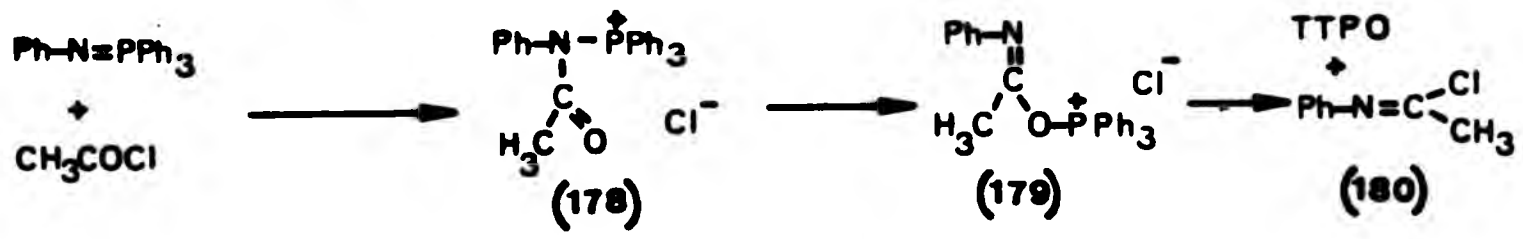
The most interesting results of this study are the up-field shift observed for the N-phenyl-ITPP (61) signal as the reaction proceeds, and the fact that no appreciable reaction takes place before 0°C temperature is reached.

The most reliable result is the spectrum recorded after the sample had been standing during 67h at room temperature and refluxed during 25 min, as all the material had dissolved when the spectrum was run. Although reaction had practically gone to completion, trace amounts of the signal assigned to a structure of type (177) still remained, thus supporting the rearrangement mechanism.

$CDCl_3$ is not an inert solvent in these reactions and so the corresponding results should be treated carefully and not given too much weight.

The most important conclusions from this study are the confirmation of N-acetyl-N-phenyl-ITPPm chloride (178) as an intermediate which rearranges to an O-triphenylphosphonium imidate structure (179) before yielding the imidoyl chloride (180), and that these reactions can be satisfactorily explained via this pathway, there being no need to assume other intermediates such as betaines or oxazaphosphetanes are formed.

Therefore the following mechanism seems to be the most likely:



CHAPTER 6: EXPERIMENTAL

General Notes

Benzene, toluene and diethyl ether were dried over sodium wire. Acetonitrile was refluxed 2h over phosphorus pentoxide, followed by distillation. All other solvents were dried by standard methods.

All starting materials were obtained commercially or prepared by literature methods to which reference is made.

Tlc was performed on silica gel plates, using Kieselgel HF 254 type 60.

Column chromatography was carried out using Kieselgel 60 (0.063-0.20 mm) (70-230) mesh ASTM on a proportion of 30 g silica gel to 1 g mixture. Flash column chromatography was performed under the same conditions using either Kieselgel 60G or Kieselgel 60H.

Gas liquid chromatograms were obtained on a Pye Unicam 304 chromatograph on a 25 m capillary column coated with SE 30 stationary phase.

Reported reaction yields refer to recrystallised products, unless otherwise indicated.

Melting points (uncorrected) were determined using an Electrothermal melting point apparatus.

Infrared spectra were recorded on a Perkin Elmer 298 spectrophotometer calibrated with a polystyrene film. Solid samples were run as nujol mulls unless stated and those of liquids as thin films held between sodium chloride plates.

Ultraviolet spectra were obtained on a Varian DMS 100 UV-Visible spectrophotometer linked to an Epson FX-80 plotter. Samples were run as solutions in 95% ethanol using 1 cm silica cells.

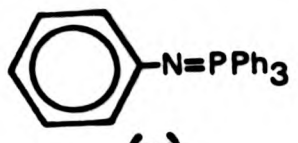
^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a JEOL FX 90Q or JEOL JNM-FX 60 fourier transform NMR instrument, using TMS as an internal

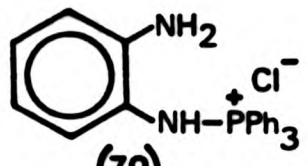
reference for ^{1}H and ^{13}C NMR spectra and 85% H_3PO_4 as an external reference for ^{31}P NMR spectra; positive chemical shifts correspond to downfield values.

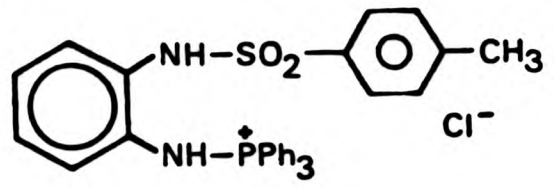
Mass spectra were recorded on a JEOL DX-300 instrument.

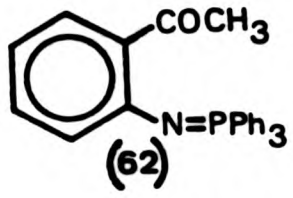
Microanalyses were performed by Mr. B. Saunderson in the Department of Chemistry, City of London Polytechnic.

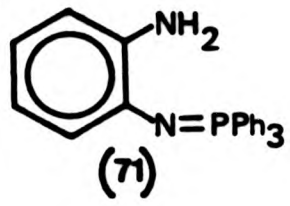
Compounds and structures referred to in the text

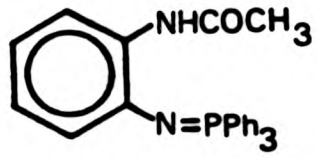

(61)

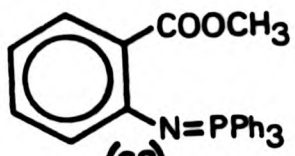

(70)

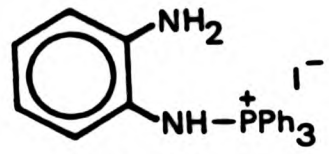

(79)

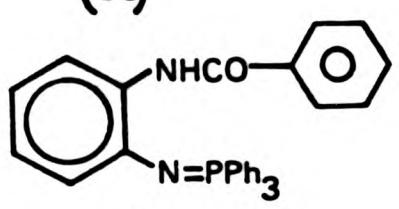

(62)

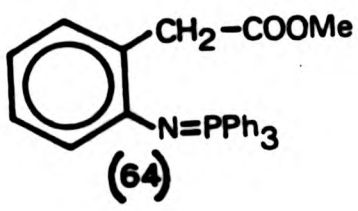

(71)

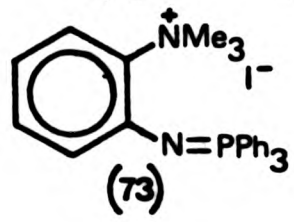

(80)

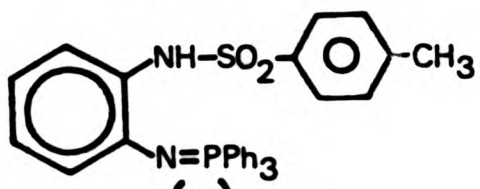

(63)

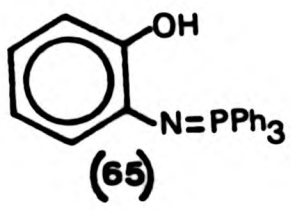

(72)

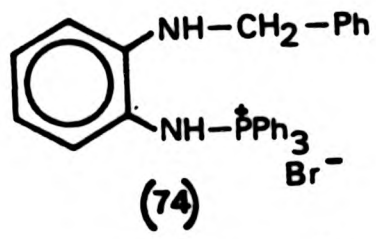

(81)

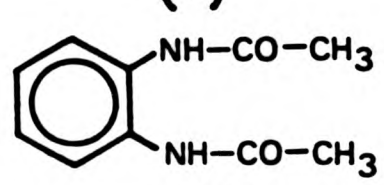

(64)

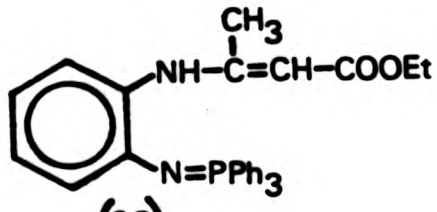

(73)

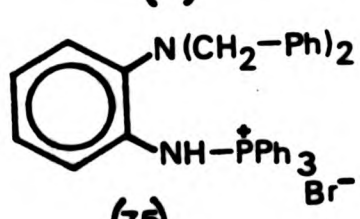

(82)

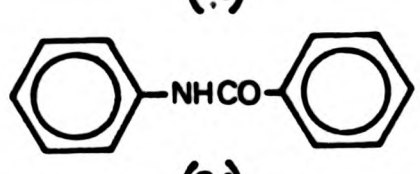

(65)

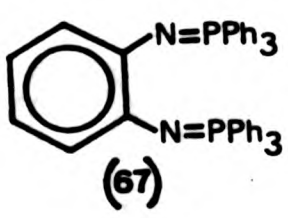

(74)

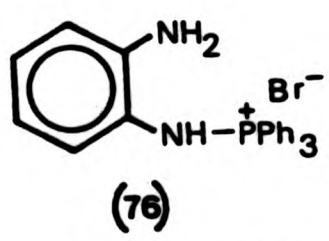

(83)

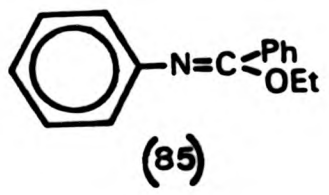

(66)

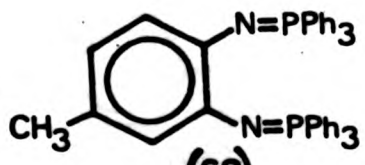

(75)

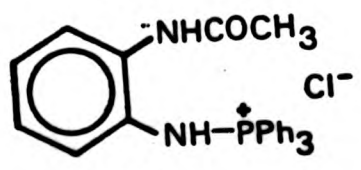

(84)

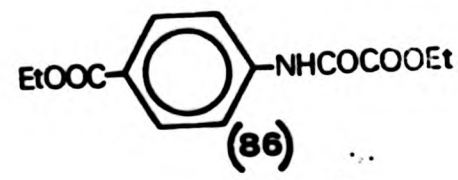

(67)

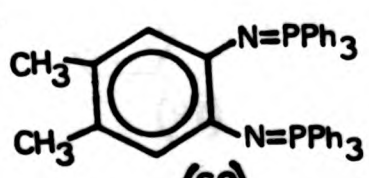

(76)

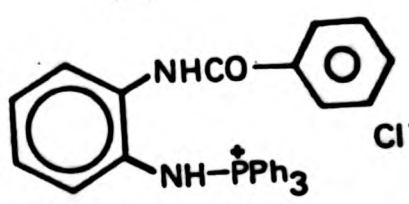

(85)

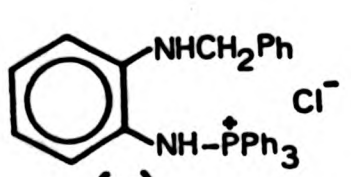

(68)

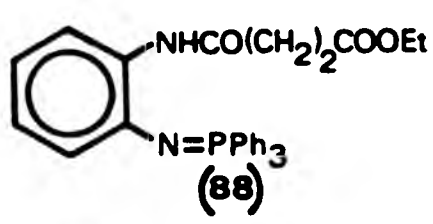

(77)


(86)

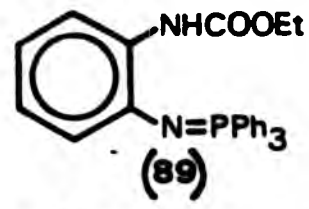

(69)


(78)

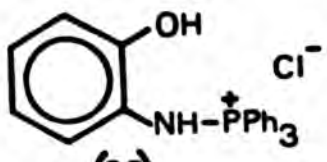

(87)



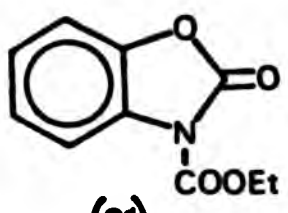
(88)



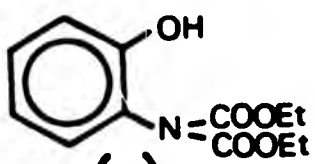
(89)



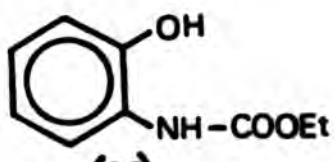
(90)



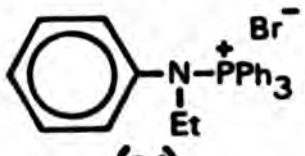
(91)



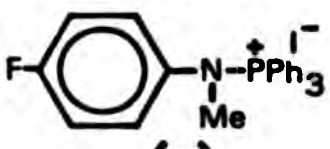
(92)



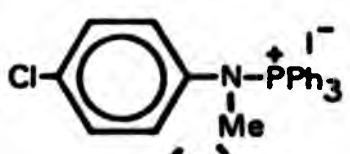
(93)



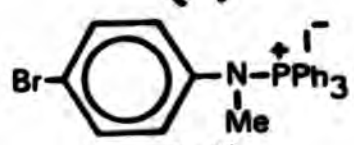
(94)



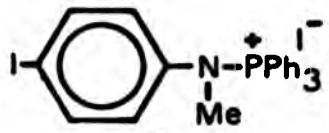
(95)



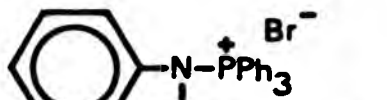
(96)



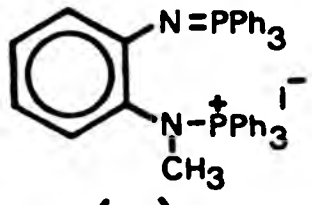
(97)



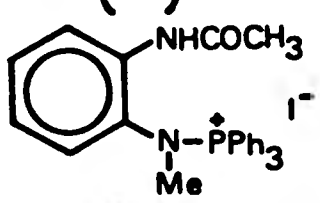
(98)



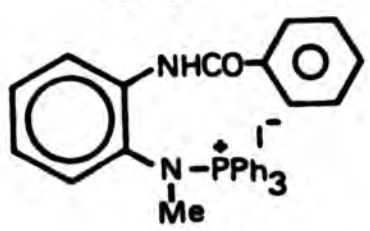
(99)



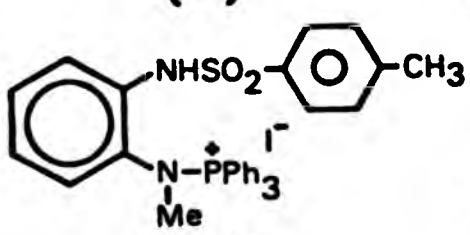
(100)



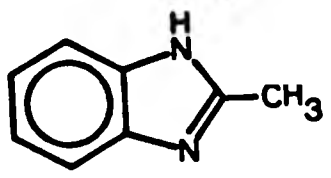
(101)



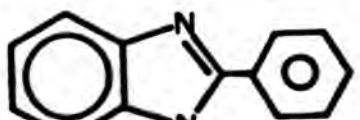
(102)



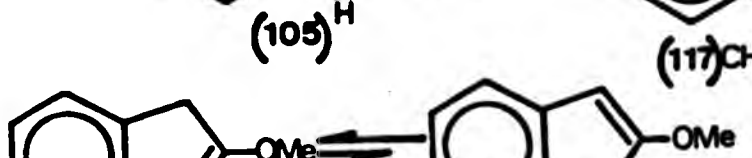
(103)



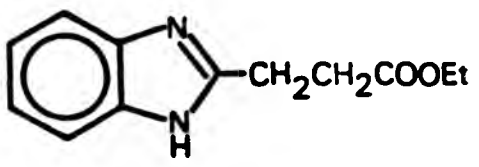
(104)



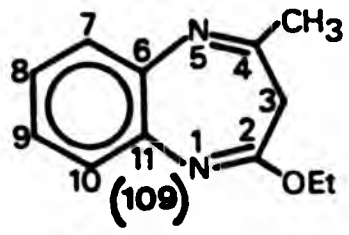
(105)



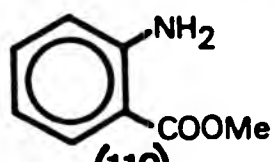
(107) (106)



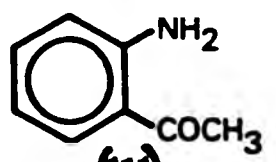
(108)



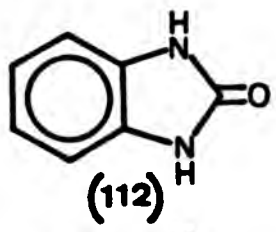
(109)



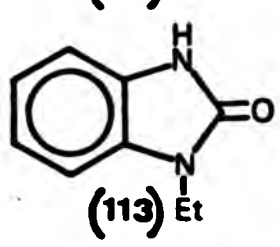
(110)



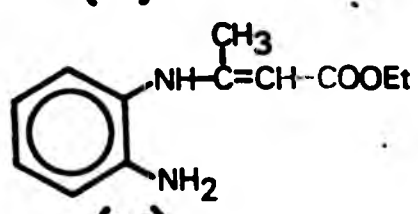
(111)



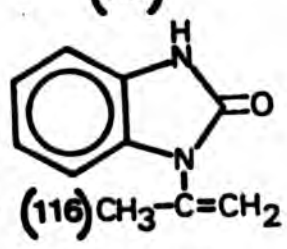
(112)



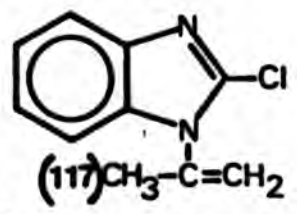
(113)



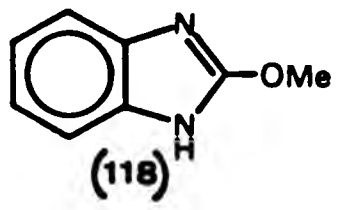
(115)



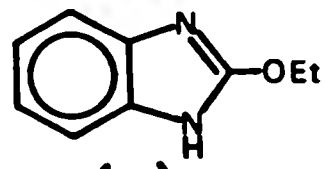
(116)



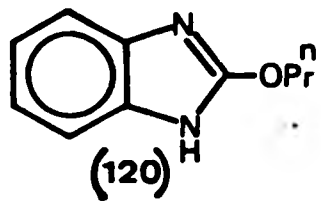
(117)



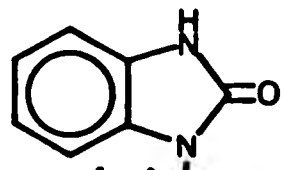
(118)



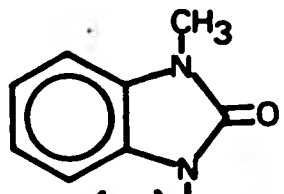
(119)



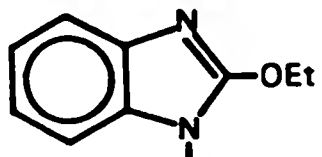
(120)



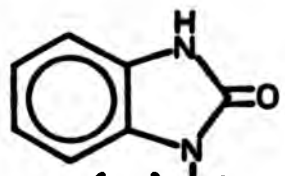
(121)



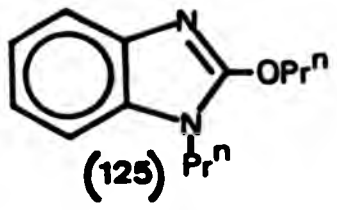
(122)



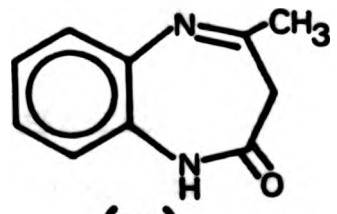
(123)



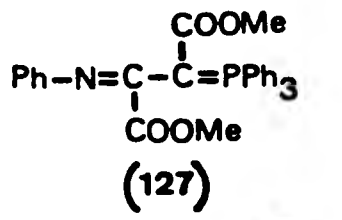
(124)



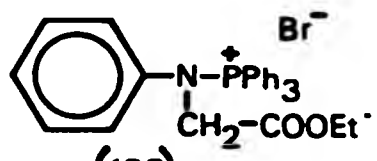
(125)



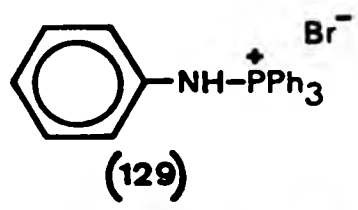
(126)



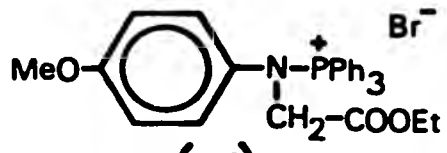
(127)



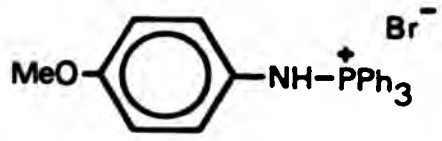
(128)



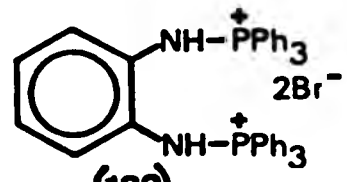
(129)



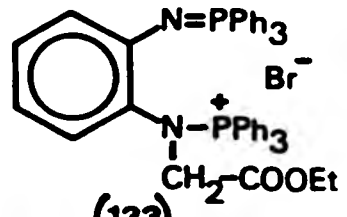
(130)



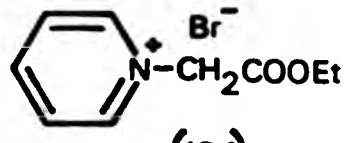
(131)



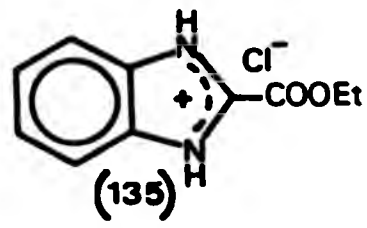
(132)



(133)



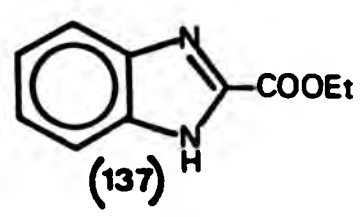
(134)



(135)

[TTPO] Salt

(136)



(137)

EXPERIMENTAL

1. Synthesis of N-ArITPPs

General Procedure

N-ArITPPs were synthesised according to the method developed by Horner and Oediger[28].

To a mechanically stirred solution of dried and recrystallised triphenylphosphine (13.1 g; 0.05 mol) in deaerated sodium-dried benzene (250 cm^3) at 0-5° (ice-water bath) was added dropwise a solution of bromine (8.0 g, 0.05 mol, 2.6 cm^3) in sodium-dried benzene (50 cm^3) under an atmosphere of nitrogen. When all the bromine had been consumed and the slurry had become off-white, KOH-dried triethylamine (10.1 g, 0.1 mol, 13.8 cm^3) was added to the mixture followed by a solution or slurry of the primary arylamine (0.05 mol) in sodium-dried benzene (50 cm^3) with constant stirring. The ice-water bath was next removed and the resultant mixture refluxed for varying periods of time. The triethylamine hydrobromide which had precipitated by this time was filtered off and the benzene was removed under reduced pressure from the filtrate. The resultant oil was triturated with petroleum ether (60-80°) until the solid ITPP emerged. This was filtered and was washed well with petroleum ether (60-80°) and dried in a vacuum oven. Recrystallisation of these compounds afforded analytically pure samples. The following N-ArITPPs were prepared.

N-Phenyl-ITPP (61)[27,28,41]

After 3h reflux was obtained (61) (28.54 g, 0.08 mol, 81%); mp (EtOH): 129-130°C (lit. mp 131-2°C[27]); IR: 1440, 1110 (P-Ph), 1350 (P=N) cm^{-1}; UV λmax (nm) (logε): 211 (4.59); ^{31}P NMR ($CDCl_3$): +3.3 ppm;

MS m/e: 353 ($M^{+\cdot}$) (100%), 352 (95%), 198 (20%), 183 (70%), 122 (26%).

N-[(2-Acetyl)-phenyl]-ITPP (62)[142]

5h reflux yielded (62) (4.31 g, 0.01 mol, 55%) (crude yield: 98%, decomposes on recrystallisation), mp (EtOH): 117-118.5°C (decomp) IR: 1650 (C=O), 1440, 1110 (P-Ph), 1350 (P=N) cm^{-1}; UV λmax (nm) logε): 208 (4.48); ^{31}P NMR ($CDCl_3$): +4.0 ppm (recorded immediately after being dissolved). ^{1}H NMR ($CDCl_3$): 7.49 (m, 15H, P-Ph), 6.69 (m, 4H, Ar), 2.81 (s, 3H, CH_3) ppm; MS m/e: 395 ($M^{+\cdot}$) (96%), 380 (17%), 352 (17%), 278 (41%), 277 (80%), 262 (100%), 201 (49%), 183 (76%), 108 (29%), 77 (27%), MS: (CI): 396 ($M^{+\cdot}$) (100%); anal: calcd. for $C_{26}H_{22}NOP$: C: 78.97, H: 5.61, N: 3.54, P: 7.83. Found C: 78.61, H: 5.62, N: 3.37, P: 7.79.

N-[(2-Methoxycarbonyl)-phenyl]-ITPP (63)[104]

The starting material, methyl anthranilate, was synthesised[105] and refluxed during 7h, yielding (63) (8.5 g, 0.02 mol, 76%); mp (AcOEt): 168-9°C (lit. mp 167-8°C[104]); IR: 1720 (C=O), 1440, 1110 (P-Ph), 1370 (P=N), 1290, 1130 (C-O) cm^{-1}; UV λmax (nm) (logε): 208 (4.61), 194 (3.97); ^{31}P NMR ($CDCl_3$): +0.7 ppm, J(^{13}C-^{31}P): 100.0 Hz; MS m/e: 411 ($M^{+\cdot}$) (100%), 410 (22%), 396 (12%); 380 (14%), 378 (42%), 352 (73%), 201 (51%), 183 (94%), 152 (16%), 108 (22%); anal: calcd. for $C_{26}H_{22}NO_2P$: C: 75.90, H: 5.39, N: 3.40, P: 7.53. Found: C: 75.60, H: 5.20, N: 3.12, P: 7.50.

N-[2-(α Methyl acetate) phenyl]-ITPP[106] (64)

1.014 g (5.2 mmol) methyl o-nitro phenylacetate was dissolved in methanol (15 cm^3) and 50 mg 10% palladium on carbon added. The mixture was shaken under hydrogen until absorption was quantitative (381 cm^3) (30 min), filtered to remove the catalyst and the solvent evaporated under reduced pressure leaving 0.86 g (5.2 mmol), methyl o-aminophenyl-acetate as an oil. This oil was dissolved in sodium-dried benzene and

used immediately. After 5h reflux following the general procedure was isolated (64)(0.73 g, 1.7 mmol, 33%) (crude yield: 70%, decomposes on recrystallisation); mp (EtOH): 118-9°C (lit. mp 117.5-118.5°C[106]). Mix mp: undepressed. UV λmax (nm) (iogε): 208 (4.70); MS m/e: 425 ($M^{+\cdot}$) (85%), 424 (14%), 410 (10%), 394 (9%), 366 (25%), 352 (12%), 277 (26%), 262 (39%), 208 (62%), 201 (42%), 183 (100%), 152 (12%), 108 (35%).

N-[(2-Hydroxy)-phenyl]-ITPP[107,108] (65)

Recrystallised o-aminophenol was refluxed 6h yielding (65) (2.53 g, 6.8 mmol, 69%); mp (AcOEt): 179-181°C (lit. mp 179°C[107]); IR: 3250 (OH), 1440, 1110 (P-Ph), 1320 (P=N) 1250 (C-O) cm^{-1}; UV λmax (nm) (logε): 209 (2.60); ^{31}P NMR[107,108] ($CDCl_3$)(Room temperature): +8.95 ppm (broad band γ1/2 ≈55 Hz); (room temperature +20°C): +8.20 ppm (broad band γ1/2 ≈90 Hz); (pyridine): +7.5 ppm and -44.4 ppm. All spectra were recorded immediately after dissolving the samples. MS m/e: 369 ($M^{+\cdot}$) (89%), 368 (22%), 352 (4%), 278 (49%), 277 (100%), 262 (80%), 201 (21%), 199 (18%), 183 (86%), 152 (16%), 108 (39%), 77 (26%); anal: calcd. for $C_{24}H_{20}NOP$: C: 78.03, H: 5.46, N: 3.79, P: 8.38. Found: C: 78.11, H: 5.44, N: 3.75, P: 8.35.

N-[2-(β Ethyl crotonate)anilino]-ITPP (66)

The required ethyl β-2-aminoanilinocrotonate was synthesised under acid conditions according to Sexton's method[109] yielding after recrystallisation from petroleum ether (60-80°) 29.95 g (0.13 mol, 68%); mp: 58-9°C (lit. mp: 59-62°C[109]). The amine was dissolved in sodium-dry benzene and used immediately. 2.5h reflux under standard conditions yielded (66) (3.87 g, 8 mmol, 27%); mp (AcOEt): 143-4°C (decomp.); IR: 3240(NH), 1650 (C=O), 1580, 1565 (C=C), 1440, 1110 (P-Ph), 1320 (P=N), 1165 (C-O) cm^{-1}; UV λmax (nm) (logε): 298 (3.71), 208 (4.58); ^{31}P NMR ($CDCl_3$): +3.7 ppm; ^{1}H NMR ($CDCl_3$): 10.75 (br s; 1H, -NH-), 7.81, 7.46 (m, 15H, P-Ph), 7.00 (m, 1H, Ar), 6.62 (m, 3H, Ar), 4.66 (s, 1H,

C=CH), 4.20 (q, J_{HH}: 7.1 Hz, 2H, O-CH_2), 2.05 (s, 3H, CH_3-C=C), 1.30 (t, J_{HH}: 7.1 Hz, 3H, -CH_2-CH_3) ppm. MS m/e: 480 ($M^{+\cdot}$) (100%), 407 (12%), 479 (23%), 393 (40%), 304 (17%), 278 (49%), 277 (96%), 262 (46%), 201 (21%), 183 (84%), 152 (14%), 145 (45%), 131 (39%), 108 (41%), 77 (31%); accurate mass calcd.[53] for $C_{30}H_{29}N_2O_2P$: 480.1960. Found: 480.1973; anal: calcd. for $C_{30}H_{29}N_2O_2P$: C: 74.98, H: 6.08, N: 5.83, P: 6.44. Found: C: 75.11, H; 6.06, N: 5.79, P: 6.64.

2. Synthesis of Aryl-o-bis-ITPPs

General Procedure:

To a suspension of triphenylphosphine dibromide (0.05 mol - see synthesis of N-ArITPP) in sodium-dried deaerated benzene (200 cm^3) at 0-5°C was added KOH-dried triethylamine (0.1 mol) in deaerated sodium-dried benzene (10 cm^3) followed by a slurry of the finely powdered bisamine (0.1 mol) (purified by sublimation) in deaerated sodium-dried benzene (40 cm^3) with constant mechanical stirring. The resultant mixture was refluxed 6h[41]. The bisphosphinimine and the triethylamine hydrobromide mixture were removed by filtration and washed well with cold benzene and sucked dry in a vacuum oven. The dried mixture was warmed with 2M sodium hydroxide (100 cm^3) for 5 min. at 40-50° to decompose the triethylamine salt. This gave a strong yellow colour to the product, which was filtered and washed well with distilled water, sucked dry and finally thoroughly dried in a vacuum oven. A satisfactory recrystallisation solvent could not be found for these compounds.

Synthesis of o-bis-ITPP-benzene[28,41] (67)

(14.91 g, 23.7 mmol, 95%); mp: 242-5°C (lit. mp: 206°C[28], 229-34°C[41]); IR: 1440, 1105 (P-Ph), 1320 (P=N) cm^{-1}; UV λmax (nm) (logε): 208 (4.68); ^{31}P NMR ($CDCl_3$): +3.43 ppm (recorded immediately after being dissolved); anal: calcd. for $C_{42}H_{34}N_2P_2$: C: 80.24, H: 5.45, N: 4.45, P: 9.85. Found: C: 79.09, H: 5.39, N: 4.25, P: 9.83.

Synthesis of 4-Methyl-o-bis-ITPP-benzene[41] (68)

(13.30 g, 20.7 mmol, 83%); mp: 173-6°C (lit. mp: 178-80°C[41]); IR: 1440, 1105 (P-Ph), 1345 (P=N) cm^{-1}; UV λmax (nm) (logε): 207 (4.70); ^{31}P NMR ($CDCl_3$): +8.1 ppm, +10.2 ppm. (Recorded 4h after being dissolved); (lit. ^{31}P NMR: +2.1, +3.0 ppm[41]). MS m/e 642 ($M^{+\cdot}$) (100%), 382 (30%), 381 (16%), 380 (10%), 379 (18%), 321 (23%), 277 (12%), 262 (63%), 197 (21%), 183 (55%), 108 (44%); anal: calcd. for $C_{43}H_{36}N_2P_2$:

C: 80.36, H: 5.64, N: 4.36, P: 9.64. Found: C: 76.18, H: 5.38, N: 4.15, P: 8.88.

Synthesis of 4,5-Dimethyl-o-bis-ITPP benzene[41] (69)

(7.17 g, 10.9 mmol, 44%); mp: 196-8°C (lit. mp: 210-2°C[41]); IR: 1440, 1105 (P-Ph), 1345 (P=N) cm^{-1}; UV λmax (nm) (logε): 292 (3.89), 208 (4.80); ^{31}P NMR ($CDCl_3$): -1.1 ppm (recorded immediately after being dissolved); MS m/e: 656 ($M^{+\cdot}$) (100%), 395 (11%), 393 (10%), 325 (25%), 317 (11%), 262 (30%), 183 (57%), 152 (4%), 108 (37%); anal: calcd. for $C_{44}H_{38}N_2P_2$: C: 80.47, H: 5.83, N: 4.26, P: 9.43. Found: C: 79.52, H: 5.78, N: 4.27, P: 9.58.

3. Synthesis of N-(o-aminophenyl)-ITPP and derivatives.

Synthesis of N-(o-aminophenyl)-ITPP hydrochloride (70)

Into a 500 cm^3 round bottom flask was placed 44.81 g (7.1 mol) o-bis-ITPP benzene (67) followed by 250 cm^3 chloroform. The mixture was stirred 48h at room temperature exposed to the atmosphere, the solvent removed under vacuum and the resulting slurry finally dried in a vacuum oven. Once dry, it was dissolved in sodium-dried benzene, filtered to remove undissolved material and excess dry hydrogen chloride[113] was bubbled through the solution. The solid formed was immediately filtered and the mother liquor again subjected to a stream of dry hydrogen chloride. The formed solids were collected together and washed thoroughly with sodium-dried benzene. After recrystallisation from methanol (ca 15 cm^3/g) was obtained (70) (23.69 g, 58.5 mmol, 82%); mp (MeOH): 230°C (decomp.); IR: 1440, 1115 (P-Ph), 965 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 295 (3.32), 275 (3.4), 268 (3.44), 225 (4.20), 213 (4.21); ^{31}P NMR (MeOH): +35.5 ppm; anal: calcd. for $C_{24}H_{22}ClN_2P$: C: 71.20, H: 5.48, N: 6.92, P: 7.65. Found: C: 65.06, H: 5.33, N: 6.35, P: 7.02.

Synthesis of N-(o-aminophenyl)-ITPP[41,48,57] (71)

0.49 g (1.2 mmol) (70) was suspended in sodium-dried benzene (15 cm^3), excess KOH-dried triethylamine added and the reaction protected with a calcium chloride tube. The mixture was stirred overnight at room temperature, filtered to remove the triethylamine hydrochloride formed and excess triethylamine and solvent evaporated under vacuum. The resulting yellow oil was triturated and recrystallised from cyclohexane yielding (71) (0.41 g, 1.1 mmol, 92%); mp (cyclohexane): 119-120°C (decomp.) (lit. mp: 147-8°C[57], 143-4°C[48]); IR: 3460, 3350 (NH_2), 1435, 1105 (P-Ph), 1360 (P=N) cm^{-1}; UV λmax (nm) (logε): 304 (3.67), 256 (3.83); ^{31}P NMR ($CDCl_3$): +4.52 ppm J(^{13}C-^{31}P): 99.5 Hz; MS m/e: 368 ($M^{+\cdot}$)

(100%), 367 (15%) 352 (4%), 262 (15%), 183 (88%), 152 (5%), 137 (12%), 108 (24%); anal: calcd. for $C_{24}H_{21}N_2P$: C: 78.22, H: 5.75, N: 7.60, P: 8.42. Found: C: 78.01, H: 5.71, N: 7.52, P: 8.38.

N-(o-aminophenyl)-ITPP hydroiodide (72)

N-(o-aminophenyl)-ITPP (71) (3.68 g, 0.01 mol) was dissolved in sodium-dried benzene (60 cm^3) and a slight excess of methyl iodide (2.28 g, 0.016 mol, 1.0 cm^3) added. The mixture was refluxed 2h under a nitrogen atmosphere, allowed to cool, the insoluble material formed separated by filtration and thoroughly washed with sodium-dried benzene. The isolated solid was extracted with boiling ethyl acetate three times, filtered and finally recrystallised from methanol benzeneyielding (72) (0.81 g, 1.63 mmol, 16%); mp (MeOH/benzene): 215-7°C (decomp.); IR: 3460, 3320, 3200 (NH), 1440, 1115 (P-Ph), 970 (P^+N) cm^{-1}; UV λmax (nm)(logε): 298 (3.62), 213 (4.62); ^{31}P NMR ($CHCl_3$): +36.51 ppm; MS m/e: 496 ($M^{+\cdot}$) (0%), 369 (26%), 368 (100%), 262 (24%), 183 (100%), 152 (12%), 128 (30%), 108 (24%); anal: calcd. for $C_{24}H_{22}IN_2P$: C: 58.06, H: 4.44, N: 5.64, P: 6.25. Found: C: 58.08, H: 4.45, N: 5.74, P: 6.35.

N-[o-Trimethylammonium-phenyl]-ITPP iodide (73)

Concentration under vacuum of the ethyl acetate extract obtained as described under compound (72) and recrystallisation yielded (73) (0.1 g, 0.19 mmol, 2%); mp (AcOEt): 164-5°C; IR: 1440, 1110 (P-Ph), 1345 (P=N) cm^{-1}; UV λmax (nm) (logε): 351 (3.0 4), 295 (3.82), 252 (4.09), 209 (4.59); ^{31}P NMR ($CHCl_3$): +10.63 ppm; ^1H NMR ($CDCl_3$): 7.25 (m, 15H, P-Ph), 6.45 (m, 4H, Ar), 4.01 (s, 9H, $-\overset{+}{N}(CH_3)_3$) ppm; MS m/e (high resolution): 538 ($M^{+\cdot}$) (0%), 396 (34%) ($C_{26}H_{25}N_2P$), 262 (70%) ($C_{18}H_{15}P$), 211 (56%) ($C_{14}H_{15}N_2$), 183 (74%) ($C_{12}H_8P$), 152 (10%) (-), 142 (100%) (CH_3I), 133 (62%) ($C_8H_9N_2$), 119 (62%) ($C_7H_7N_2$), 108 (38%) (C_6H_5P); anal: calcd. for $C_{27}H_{28}IN_2P$: C: 60.22, H: 5.20, N: 5.20, P: 5.77. Found: C: 59.72, H: 5.07, N: 5.26, P: 5.89. Qualitative halogen test confirmed iodide ion was present.

N-[(o-aminobenzyl)-phenyl]-ITPP hydrobromide (74)

N-(o-aminophenyl)-ITPP (71) (1.0 g, 2.7 mmol) was dissolved in sodium-dried benzene (30 cm^3) and a slight excess of benzyl bromide (0.47 g, 2.75 mmol, 0.33 cm^3) added. The mixture was refluxed 7h under a nitrogen atmosphere, allowed to cool, filtered and the solid thoroughly washed with sodium-dried benzene. Recrystallisation provided (74) (0.14 g, 0.26 mmol, 9.5%); mp (EtOH): 210-14°C (decomp.); IR: 3360, 3320 (NH), 1440, 1120 (P-Ph), 960 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 303 (3.60), 210 (4.57); ^{31}P NMR ($CHCl_3$): +36.75 ppm; ^1H NMR ($CDCl_3$): 7.35 (m, 15H, P-Ph), 6.88 (br s, 5H, $-CH_2-Ph$), 6.3 (m, 4H, Ar), 4.02 (br s, 2H, $-CH_2-Ph$) ppm; anal: calcd. for $C_{31}H_{28}BrN_2P$: C: 69.02, H: 5.20, N: 5.20, P: 5.75. Found: C: 68.04, H: 5.30, N: 5.20, P: 5.85.

N-[(o-aminodibenzyl)-phenyl]-ITPP hydrobromide (75)

Compound's (74) recrystallisation mother liquors (0.58 g) were chromatographed on a silica gel (20 g) packed column and eluted with ethyl acetate and ethyl acetate-methanol mixtures. Solvent removal from the collected fractions left a viscous oil which on trituration with acetone yielded (75) (0.12 g, 0.19 mmol, 7%); mp ($EtOH/Et_2O$): 188-190°C (decomp.); IR: 3190 (NH), 1435, 1105 (P-Ph), 970 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 211 (4.66); ^{31}P NMR (MeOH): +29.82 ppm; ^1H NMR (DMSO-d_6): 7.50 (m, 15H, P-Ph), 7.02 (s, 10H, $-CH_2-Ph$), 6.29 (m, 4H, Ar), 4.41 (br s, 4H, $-CH_2-Ph$) ppm; MS m/e (high resolution): 629 ($M^{+\cdot}$) (0%), 548 (1%) ($C_{38}H_{33}N_2P$), 457 (100%) ($C_{31}H_{26}N_2P$), 262 (36%) ($C_{18}H_{15}P$), 195 (65%) ($C_{13}H_{11}N_2$), 183 (45%) ($C_{12}H_8P$), 152 (2%) ($C_{12}H_8$), 108 (21%) (C_6H_5P), 92 (46%) (C_7H_8); anal: calcd. for $C_{38}H_{34}BrN_2P$: C: 72.50, H: 5.40, N: 4.45, P: 4.93. Found: C: 72.01, H: 5.42, N: 4.16, P: 4.88. Qualitative halogen test confirmed presence of bromide ion.

N-(o-aminophenyl)-ITPP hydrobromide (76)

N-(o-aminophenyl)-ITPP (71) (0.92 g, 2.5 mmol) was dissolved in sodium-dried benzene (30 cm^3) and a slight excess of 9-bromofluorene (0.62 g, 2.53 mmol) added. The mixture was refluxed 5h under a nitrogen atmosphere, allowed to cool, the solid material formed filtered and thoroughly washed with sodium-dried benzene. Recrystallisation afforded (76) (0.063 g, 0.14 mmol, 4%); mp ($EtOH/Et_2O$): 196-7°C (decomp.); IR: 3340, 3300, 3200 (NH), 1440, 1115 (P-Ph), 960 (P^+-N) cm^{-1}; ^{31}P NMR ($CHCl_3$): +36.0 ppm; MS m/e: 449 ($M^{+\cdot}$) (0%), 369 (20%), 368 (78%), 262 (20%), 183 (100%): 152 (8%), 108 (24%), 80/82 (18%/15%); anal: calcd. for $C_{24}H_{22}BrN_2P$: C: 64.15, H: 4.93, N: 6.23, P: 6.89. Found: C: 64.10, H: 4.93, N: 6.46, P: 6.73.

(a) Reactions of (71) with acyl halides and p-toluenesulphonyl chloride, General procedure:

N-(o-aminophenyl)-ITPP (71) (0.01 mol) was dissolved in sodium-dried benzene (50 cm^3) and the solution cooled in an ice bath. The acyl halide dissolved in benzene (5 cm^3) (slightly in molar excess) was added dropwise to the cooled, magnetically stirred mixture, keeping the reaction chamber under a nitrogen atmosphere. When the addition was complete, the ice bath was removed and the mixture stirred overnight at room temperature. The insoluble material formed was filtered under vacuum, thoroughly washed with sodium-dried benzene and recrystallised.

N-[(o-acetamido)-phenyl]-ITPP hydrochloride (77)

Freshly distilled acetyl chloride was used, which after work-up as indicated above furnished (77) (2.17 g, 5.3 mmol, 53%); mp (acetone): 199-200°C (decomp.); IR: 3480, 3430, 3210, 3170 (NH), 1665, 1645 (C=O), 1520, 1505 (N-C=O), 1435, 1110 (P-Ph), 960 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 209 (4.62); ^{31}P NMR ($CHCl_3$): +35.8 ppm, J(^{13}C-^{31}P: 102-8 Hz; anal: calcd. for $C_{26}H_{24}ClN_2OP$: C: 69.87, H: 5.41, N: 6.27, P: 6.93. Found: C: 68.91, H: 5.37, N: 6.06, P: 6.93.

N-[(o-benzamido)-phenyl]-ITPP hydrochloride (78)

Freshly distilled benzoyl chloride was used, which after work-up as outlined above yielded (78) (2.59 g, 5.1 mmol, 51%); mp (EtOH): 243-5°C (decomp.); IR: 3580, 3160 (NH), 1660, 1645, (C=O), 1530, 1500 (N-C=O), 1430, 1110 (P-Ph), 960 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 325 (3.82), 209 (4.69); ^{31}P NMR ($CDCl_3$): +35.9 ppm, J(^{13}C-^{31}P): 103.0 Hz; anal: calcd. for $C_{31}H_{26}ClN_2OP$: C: 73.15, H: 5.15, N: 5.50, P: 6.08. Found: C: 73.06, H: 5.16, N: 5.69, P: 6.07.

N-[o-(p-toluenesulphonamido)-phenyl]-ITPP hydrochloride (79)

Recrystallised p-toluenesulphonyl chloride (pet. ether 60-80°) was used, which after standard work-up provided (79) (3.07 g, 5.5 mmol, 55%);

mp (EtOH): 218-220°C (decomp.); IR: 1435, 1110 (P-Ph), 1335, 1155 (N-SO_2), 960 (P^+-N), 690 (S-N) cm^{-1}; UV λmax (nm) (logε): 302 (3.68), 209 (4.55); ^{31}P NMR (MeOH): +33.7 ppm; (DMSO-d_6): +33.0 ppm J(^{13}C-^{31}P): 100.9 Hz; anal: calcd. for $C_{31}H_{28}ClN_2O_2PS$: C: 66.60, H: 5.05, N: 5.01, P: 5.54. Found: C: 66.52, H: 5.59, N: 5.80, P: 5.32.

(b) <u>Synthesis of free N-ArITPPs from the hydrohalides (77),(78) and (79)</u>

<u>General procedure</u>:

The N-ArITPP hydrohalide salt (0.01 mol) was suspended in sodium-dried benzene (50 cm^3) and stirred 24 h at room temperature under a nitrogen atmosphere with excess KOH-dried triethylamine (0.015 mol). The resulting slurry was filtered to remove triethylamine hydrohalide salt formed, the filtrate concentrated in vacuo and allowed to crystallise.

<u>N-[o-(acetamido)-phenyl]-ITPP (80)</u>

Recrystallisation from toluene yielded (80) (3.57 g, 8.7 mmol, 87%); mp (toluene): 173-4°C (decomp.) IR: 3330 (NH), 1675 (C=O), 1510, 1505 (N-C=O), 1430, 1110 (P-Ph), 1350 (P=N) cm^{-1}; UV λmax (nm) (logε): 303 (3.68), 265 (3.87); ^{31}P NMR ($CDCl_3$): +7.20 ppm, J(^{13}C-^{31}P): 99.6 Hz; MS m/e: 410 ($M^{+\cdot}$) (19%), 395 (33%), 367 (12%), 277 (29%), 262 (14%), 213 (17%), 201 (15%), 183 (100%), 152 (23%), 132 (21%), 108 (35%); high resolution: 410 ($C_{26}H_{23}N_2OP$), 395 ($C_{25}H_{20}N_2OP$), 277 ($C_{18}H_{14}OP$), 262 ($C_{18}H_{15}P$), 213 ($C_{12}H_{10}N_2P$), 201 ($C_{12}H_{10}OP$), 183 ($C_{12}H_8P$), 152 ($C_{12}H_8$); anal: calcd. for $C_{26}H_{23}N_2OP$: C: 76.08, H: 5.65, N: 6.82, P: 7.55. Found: C: 75.87, H: 5.63, N: 6.82, P: 7.58.

<u>N-[o-(benzamido)-phenyl]-ITPP (81)</u>

After recrystallisation from benzene was isolated (81) (4.67 g, 9.9 mmol, 99%); mp (benzene): 188-190°C (decomp.); IR: 3290, 3270 (NH), 1655, 1650 (C=O), 1530, 1515 (N-C=O), 1430, 1100 (P-Ph), 1350

(P=N) cm^{-1}; UV λmax (nm) (logε): 327 (3.83), 248 (4.15), 209 (4.46); ^{31}P NMR ($CDCl_3$): +7.78 ppm, J(^{13}C-^{31}P): 100.1 Hz; MS m/e: 472 ($M^{+\cdot}$) (87%), 471 (6%), 395 (35%), 367 (16%), 279 (36%), 277 (70%), 262 (32%), 213 (21%), 201 (17%), 194 (100%), 183 (77%), 152 (11%), 108 (30%); high resolution: 472 ($C_{31}H_{25}N_2OP$); anal: calcd. for $C_{31}H_{25}N_2OP$: C: 78.80, H: 5.33, N: 5.93, P: 6.55. Found: C: 78.83, H: 5.28, N: 5.92, P: 6.54.

N-[o-(p-toluenesulphonamido)-phenyl]-ITPP (82)

Recrystallisation from toluene provided (82) (4.85 g, 9.3 mmol, 93%); mp (toluene: 208-9°C (decomp.) IR: 3160 (NH), 1435, 1105 (P-Ph), 1370 (P=N) (under nujol band), 1340, 1155 (N-SO_2), 695 (S-N) cm^{-1}; IR (C_4Cl_6): 3170 (NH), 1440, 1110 (P-Ph), 1375 (P=N), 1345, 1160 (N-SO_2), 700 (S-N) cm^{-1}; UV λmax (nm) (logε): 302 (3.80), 209 (4.68); ^{31}P NMR ($CDCl_3$): +8.14 ppm, J(^{13}C-^{31}P): 100.0 Hz; MS m/e: 522 ($M^{+\cdot}$) (16%), 367 (100%), 277 (21%), 262 (9%), 213 (20%), 183 (38%), 181 (28%), 152 (4%), 108 (12%), 91 (58%); anal: calcd. for $C_{31}H_{27}N_2O_2PS$: C: 71.25, H: 5.21, N: 5.36, P: 5.93. Found: C: 71.23, H: 5.12, N: 5.29, P: 5.83.

(c) Reactions of (71) with acid anhydrides

N-[o-(acetamido)phenyl]-ITPP (80)

N-(o-aminophenyl)-ITPP (71) (1.5 g, 4.08 mmol) in sodium-dried toluene (20 cm^3) was added dropwise to an ice-cooled solution of acetic anhydride (0.42 g, 4.1 mmol, 0.39 cm^3) in sodium-dried toluene (20 cm^3) under a nitrogen atmosphere. After the addition had been completed, the reaction was stirred 0,5h in the ice-bath, then further stirred for another 2h at room temperature. The resulting solution was extracted with dilute aqueous sodium hydrogen carbonate, washed with distilled water, dried over anhydrous magnesium sulphate and evaporated to dryness

under reduced pressure at room temperature. The solid material obtained was dissolved in warm sodium-dried toluene and allowed to crystallise. (80) (0.95 g, 2.3 mmol, 57%); mp (toluene): 174.5-175.5°C (decomp.); IR identical to that of authentic material. (See section 3b).

N-[o-(benzamido)phenyl]-ITPP (81)

N-(o-aminophenyl)-ITPP (71) (1.61 g, 4.37 mmol) in sodium-dried toluene (20 cm^3) was added dropwise to an ice cooled solution of benzoic anhydride (1.0 g, 4.42 mmol) in sodium-dried toluene (10 cm^3) under a nitrogen atmosphere. After the addition was completed, the reaction was stirred 0.5h, in the ice-bath, then further stirred for another hour at room temperature. The resulting solution was concentrated under vacuum and purified by flash column chromatography. The column was packed with silica gel (30 g) and the 1.94 g mixture eluted with a pet. ether (60-80)-AcOEt (7-3) mixture. Recrystallisation from toluene afforded (81) (0.58 g, 1.23 mmol, 28%); mp (toluene): 188-190°C (decomp.); IR identical to that of authentic material (see section 3b).

(d) Reactions of (71) with acetic anhydride and p-toluenesulphonyl chloride, catalysed by pyridine

N-[o-(acetamido)phenyl]-ITPP (80)

N-(o-aminophenyl)-ITPP (71) (1.5 g, 4.08 mmol) in sodium-dried toluene (20 cm^3) was added dropwise to an ice cooled mixture of acetic anhydride (0.42 g, 4.1 mmol, 0.39 cm^3) and KOH-dried pyridine (0.33 g, 4.1 mmol, 0.33 cm^3) in sodium-dried toluene (10 cm^3) under a nitrogen atmosphere. When the addition was completed the ice-bath was removed and the reaction stirred 2h at room temperature. The resulting solution was concentrated under vacuum and upon trituration with acetone the product crystallised. Recrystallisation from toluene furnished (80) (0.81 g, 1.97 mmol, 48%); mp (toluene): 174.5-175.5°C (decomp.) IR: identical to that of authentic material (see section 3b).

N-[o-(p-toluenesulphonamido)phenyl]-ITPP (82)

Following the method outlined above and using recrystallised (pet. ether 60-80°C) p-toluenesulphonyl chloride (0.78 g, 4.1 mmol) was obtained (82) (0.63 g, 1.2 mmol, 30%); mp (toluene): 206-8°C (decomp.); IR: identical to that of authentic material (see section 3b).

(e) Reactions of (71) with acetyl chloride and triethylamine

N,N'-Diacetyl-o-phenylenediamine (83)

N-(o-aminophenyl)-ITPP (71) (10.0 g, 0.027 mol) was dissolved in sodium-dried toluene (50 cm^3) followed by KOH-dried triethylamine (2.88 g, 0.028 mol, 4.0 cm^3) and the mixture stirred under a nitrogen atmosphere. Redistilled acetyl chloride (2.13 g, 0.027 mol, 1.94 cm^3) was added very cautiously, dropwise, and the mixture stirred overnight at room temperature followed by 2h reflux. After filtration to remove triethylamine hydrochloride the filtrate was concentrated under vacuum and the residue separated by column chromatography. The column was packed with silica gel (210 g) and eluted successively with mixtures of benzene-AcOEt in proportions of (3-7) and (1-9) and finally with pure AcOEt. Two compounds were isolated: triphenylphosphine oxide and N,N'-diacetyl-o-phenylenediamine (83).

Results:

Compound	Yield	mp (°C)	Lit. mp
$Et_3NH^+Cl^-$	100%	257°C (EtOH) (sub: 241-9°C)	260°C[114] (sub: 245°C)
Ph_3PO	94%	152-3°C (Cyclohexane)	156-7°C[114]
N,N'-DPDA	3%	182-84°C (H_2O)	185-6°C[115]

(sub: sublimes

N,N'-DPDA: N,N'-diacetyl-o-phenylenediamine (83))

Physical data of N,N'-DPDA (83): IR: 3230, 3190, 3130 (NH), 1665 (C=O), 1530 (N-C=O) cm^{-1}; UV λmax (nm) (logε): 214 (4.35); ^1H NMR

($CDCl_3$): 9.20 (br s, 1H, NH), 7.73 (m, 2H, Ar), 7.30 (m, 2H, Ar), 2.24 (s, 3H, CH_3) ppm; MS m/e: 192 ($M^{+\cdot}$) (30%), 174 (20%), 150 (8%), 132 (100%), 108 (84%), 42 (34%); mmp with synthesised[113] sample: undepressed. Synthetic material gave identical IR, UV and ^1H NMR results.

(f) Reactions of N-ArITPP with acid halides

Reaction with benzoyl chloride[68]

N-phenyl-ITPP (61) (3.53 g, 10 mmol) in sodium-dried benzene (70 cm^3) was refluxed 45 min with benzoyl chloride (1.405 g, 10 mmol, 1.16 cm^3) under a nitrogen atmosphere. The resulting solution was concentrated under reduced pressure and triturated with sodium-dried Et_2O. Removal of the solid formed yielded triphenylphosphine oxide (0.83 g, 3 mmol) and a clear filtrate which was again concentrated to dryness under reduced pressure. Attempts to vacuum-distil the pale yellow oil obtained failed and the product was finally purified by flash column chromatography. To a silica gel (100 g) packed column was carefully added the reaction mixture (3.31 g), eluted with a pet. ether (60-80°)-AcOEt (1:1) solvent system. After standard work-up triphenyl phosphine oxide (1.54 g, 5.54 mmol) and benzanilide (84) (1.66 g, 8.4 mmol) were isolated, representing an overall reaction yield of 85% and 84% respectively. Benzanilide (84) physical data: mp (EtOH): 160-2°C Lit. mp: 163°C[115], IR: 3350 (NH), 1660 (C=O), 1530 (N-C=O) cm^{-1}; UV λmax (nm)(logε): 265 (3.96), 206 (4.08); MS m/e: 197 ($M^{+\cdot}$) (40%), 105 (100%), 77 (51%). IR identical to the literature reference[117].

Synthesis of ethyl N-phenylbenzimino ether[118] (85)

N-phenyl-ITPP (61) (1.76 g, 5 mmol) in sodium-dried benzene (35 cm^3) was refluxed 45 min with benzoyl chloride (0.70 g, 5 mmol, 0.58 cm^3) under a nitrogen atmosphere. The resulting solution was cooled in an

ice-bath and a solution of sodium ethoxide in ethanol (0.34 g, 5 mmol) was slowly added dropwise. After 15 min stirring the solution was filtered to remove the sodium-chloride formed and the filtrate concentrated in vacuo. Trituration of the residue with sodium-dried Et_2O yielded triphenylphosphine oxide (1.33 g, 4.78 mmol, 95%) after filtration. The concentrated filtrate (1.05 g) was purified by flash chromatography on a silica gel (35 g) packed column and eluted with a pet. ether (60-80°)- AcOEt (9:1) solvent mixture. Traces of benzanilide (84) (0.046 g, 0.23 mmol, 4%) (mp and mmp 162°) were isolated and short path distillation finally afforded (85) (0.94 g, 4.2 mmol), 83%); bp (5 mmHg): 140-150°C; lit. bp (16 mmHg): 175-7°C[118]; IR[139]: 1665 (C=N), 1275, 1120 (O-C=N) cm^{-1}; UV λmax (nm) (log ε)[140]: 272 (3.36), 228 (4.15), 208 (4.12); ^1H NMR ($CDCl_3$)[141]: 8.03 (dd, J_{HH}: 1.47, 7.08 Hz, 1H, Ph), 7.17 (m, 9H, Ph), 4.37 (q, J_{HH}: 7.0 Hz 2H, $-O-CH_2-$), 1.38 (t, J_{HH}: 7.0 Hz, 3H, $-CH_2-CH_3$) ppm; MS m/e: 225 ($M^{+\cdot}$) (7%), 197 (4%), 180 (15%), 150 (13%), 122 (20%), 120 (11%), 105 (100%), 77 (57%), 51 (21%); accurate mass calcd.[53] for $C_{15}H_{15}NO$: 225.115. Found: 225.116.

Reaction with ethyl oxalyl chloride

N-[(p-ethoxycarbonyl)-phenyl]-IPP (1.5 g, 3.9 mmol) in sodium-dried ether (30 cm^3) was stirred in an ice-bath and ethyl oxalyl chloride (0.54 g, 3.95 mmol, 0.44 cm^3) added dropwise. The reaction mixture was stirred 2h until it reached room temperature, extracted with dilute sodium hydrogen carbonate, washed with distilled water and dried over anhydrous magnesium sulphate. Finally, column chromatography (silica gel) and recrystallisation furnished ethyl (p-ethoxycarbonyl)-oxanilate (86) (0.14 g, 0.53 mmol, 14%); mp (CCl_4): 128-130°C; lit. mp: 130-1°C[119]; IR: 3360 (NH), 1730, 1710 (C=O, ester) 1695 (C=O, amide), 1545 (N-C=O), 1300, 1280, 1120, 1110 (C-O) cm^{-1}; UV λmax (nm) (log ε): 283 (4.29), 206 (4.07); MS m/e: 265 ($M^{+\cdot}$) (65%), 220 (21%), 192 (100%),

164 (39%), 146 (45%); anal: calcd. for $C_{13}H_{15}NO_5$: C: 58.86, H: 5.70, N: 5.28. Found: C: 58.47, H: 5.62, N: 5.03.

(g) Reactions of N-(o-aminophenyl)-ITPP hydrochloride (70)

Reaction with acetic anhydride catalysed by pyridine

N-(o-aminophenyl)-ITPP hydrochloride (70) (1.01 g, 2.5 mmol) was suspended in phosphorus pentoxide-dried acetonitrile (20 cm^3) and KOH-dried pyridine (0.20 g, 2.53 mmol, 0.21 cm^3) added, followed by acetic anhydride (0.26 g, 2.54 mmol, 0.24 cm^3) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature 48h by which time all the starting material (70) had dissolved. The solution was evaporated to dryness under vacuum, toluene (20 cm^3) added and then removed in vacuo and the residue finally triturated with acetone. The precipitate was collected by filtration yielding pure N-[(o-acetamido)phenyl]-ITPP hydrochloride (77) (0.64 g, 1.43 mmol, 57%); mp (acetone): 200-201.5°C (decomp.); mmp undepressed; anal: calcd. for $C_{26}H_{24}ClN_2OP$: C: 69.87, H: 5.41, N: 6.27, P: 6.93. Found: C: 69.68, H: 5.48, N: 6.22, P: 7.14 (physical data: see section 3a).

Reaction with benzoyl chloride catalysed by pyridine

N-[o-aminophenyl)-ITPP hydrochloride (70) (1.01 g, 2.5 mmol) was suspended in phosphorus pentoxide-dried acetonitrile (20 cm^3) and treated with KOH-dried pyridine (0.20 g, 2.53 mmol, 0.21 cm^3), the mixture being cooled in an ice-bath under a nitrogen atmosphere. To the above stirred solution was added dropwise a slight excess of redistilled benzoyl chloride (0.36 g, 2.56 mmol, 0.30 cm^3). 5 min later the ice-bath was removed and the reaction mixture was stirred during 48h at room temperature. The white precipitate formed was filtered, washed with sodium-dried benzene and Et_2O successively yielding N-[o-benzamido)phenyl]-ITPP hydrochloride

(78) (0.91 g, 1.8 mmol, 71%); mp (EtOH): 248-50°C (decomp.); mmp: undepressed. (Physical data: see section 3a).

Reaction with p-toluenesulphonyl chloride catalysed by pyridine

Following the method outlined above with a slight excess of recrystallised p-toluenesulphonyl chloride (0.48 g, 2.52 mmol) was isolated N-[o-(p-toluenesulphonamido)phenyl]-ITPP hydrochloride (79) (1.35 g, 2.4 mmol, 96%); mp (EtOH): 208-210°C (decomp.): mmp: undepressed; UV λmax (nm) (logε): 209 (4.63); (Physical data: see section 3a).

Reaction with benzyl bromide catalysed by pyridine

N-(o-aminophenyl)-ITPP hydrochloride (70) (2.02 g, 5 mmol) was suspended in methanol under a nitrogen atmosphere and a slight excess of KOH-dried pyridine (0.40 g, 5.1 mmol, 0.41 cm^3) added, followed by benzyl bromide (0.86 g, 5 mmol, 0.60 cm^3). The reaction mixture was refluxed 25h, concentrated under reduced pressure and the oily residue triturated with acetone, also removed in vacuo to eliminate traces of unreacted benzyl bromide. Trituration with ethanol yielded N-[(o-aminobenzyl)phenyl]-ITPP hydrochloride (87) (1.94 g, 3.9 mmol, 78%); mp (EtOH): 242°C (decomp.); IR: 3360, 3320 (NH), 1440, 1115 (P-Ph), 960 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 299 (3.81), 209 (4.82); ^{31}P NMR ($CDCl_3$): +35.7 ppm; ^1H NMR ($CDCl_3$): 7.67 (m, 15H, P-Ph), 7.19 (br s, 5H, $-CH_2$-Ph), 6.45 (m, 4H, Ar), 4.26 (s, 2H, $-CH_2$-Ph) ppm; MS m/e: 494 ($M^{+\cdot}$) (0%), 459 (15%), 458 (45%), 450 (17%), 368 (97%), 277 (29%), 262 (27%), 183 (100%), 152 (8%), 108 (25%), 77 (12%) (Physical data very similar to compound (74), see section 3).

Reaction with ethyl succinyl chloride catalysed by pyridine

Synthesis of N-[o-(Ethoxysuccinylamido)phenyl]-ITPP (88)

N-(o-aminophenyl)-ITPP hydrochloride (70) (1.01 g, 2.5 mmol) was suspended in dry $CHCl_3$ (30 cm^3) with KOH-dried pyridine (0.2 g, 2.53 mmol, 0.2 cm^3) and ethyl succinyl chloride (0.41 g, 2.53 mmol, 0.36 cm^3) under

a nitrogen atmosphere. After 5.5h stirring at room temperature the solvent was removed in vacuo. The viscous oily residue was dissolved in sodium-dried benzene, over two equivalents KOH-dried triethylamine (0.51 g, 5.1 mmol, 0.72 cm^3) added and the mixture, protected by a calcium chloride tube, stirred overnight at room temperature. Filtration to remove triethylamine hydrochloride, was followed by evaporation of the solvent and repeated toluene additions (three times) also removed under reduced pressure. Finally flash chromatography of the oily residue (1.2 g) on a silica gel (36 g) packed column eluted with a pet. ether (40 - 60°C)-AcOEt (1:1) solvent mixture yielded after trituration with Et_2O (88) (0.51 g, 1.0 mmol, 41%); mp (Et_2O): 100-2°C (decomp.); IR: 3320 (NH), 1730 (C=O, ester), 1680 (C=O amide), 1520 (N-C=O), 1440, 1115 (P-Ph), 1345 (P=N), 1200, 1115 (C-O) cm^{-1}; UV λmax (nm) (logε): 259 (4.13), 208 (4.58); ^{31}P NMR ($CDCl_3$): +7.1 ppm; ^{1}H NMR ($CDCl_3$): 9.42 (br s, 1H, -NH-), 7.52 (m, 15H, p-Ph), 6.50 (m, 4H, Ar), 4.14 (q, J_{HH}: 7.1 Hz, 2H, $-O-CH_2-$), 2.75 (s, 4H, $-CO-CH_2-CH_2-CO-$), 1.23 (t, J_{HH}: 7.1 Hz, 3H, $-CH_3$) ppm; MS m/e: 496 ($M^{+\cdot}$) (0.3%); 450 (20%), 278 (100%), 277 (100%), 218 (15%), 201 (67%), 199 (72%), 185 (35%), 183 (61%), 173 (25%), 172 (63%), 152 (41%), 145 (100%), 144 (87%), 142 (48%), 118 (23%); MS (DCI) m/e: 496 ($M^{+\cdot}$) (10%), 450 (19%), 395 (15%), 352 (6%), 278 (41%), 277 (100%), 262 (17%), 218 (10%), 201 (19%), 199 (20%), 183 (33%), 172 (17%), 152 (12%), 145 (53%), 144 (17%), 118 (7%), 108 (13%), 77 (23%); Accurate mass calcd. for $C_{30}H_{29}N_2O_3P$: 496.1909. Found: 496.1911; anal: calcd. for $C_{30}H_{29}N_2O_3P$: C: 72.56, H: 5.88, N: 5.64, P: 6.24. Found: C: 72.35, H: 5.73, N: 5.34, P: 6.26.

Reaction with ethyl chloroformate catalysed by pyridine

Synthesis of N-[o-(carbethoxyamino)phenyl]-ITPP (89)

N-(o-aminophenyl)-ITPP hydrochloride (70) (1.5 g, 3.7 mmol) was suspended in phosphorus pentoxide-dried acetonitrile (30 cm^3) and KOH-

dried pyridine (0.3 g, 3.8 mmol, 0.31 cm^3) added to the above suspension under a nitrogen atmosphere. A slight excess of ethyl chloroformate (0.41 g, 3.8 mmol, 0.35 cm^3) was added cautiously and the mixture stirred at room temperature during 5h. Addition of sodium-dried Et_2O (100 cm^3) to the concentrated reaction mixture (ca 5 cm^3) precipitated compound's (89) hydrochloride salt, which was filtered and washed with sodium-dried Et_2O. Overnight stirring at room temperature of the above solid in sodium-dried benzene with excess KOH-dried triethylamine (0.76 g, 7.5 mmol, 1.1 cm^3) protected by a calcium chloride tube yielded (89). Isolation was achieved after filtration to remove the triethylamine hydrochloride formed, concentration under reduced pressure ensuring no benzene remained and trituration with ethanol. Recrystallisation finally afforded (89) (1.34 g, 3.0 mmol, 82%); mp (EtOH): 152°C (decomp.); IR: 3320 (NH), 1715 (C=O), 1440, 1105 (P-Ph), 1345 (P=N), 1230 (C-N), 1120 (C-O) cm^{-1}; UV λmax (nm) (logε): 296 (3.73), 210 (4.54); ^{31}P NMR ($CDCl_3$): +6.5 ppm; ^1H NMR ($CDCl_3$): 8.83 (br s, 1H, -NH-), 7.70 (m, 15H, P-Ph), 6.74 (m, 4H, Ar), 4.42 (q, J_{HH}: 7.1 Hz, 2H, CO-CH_2-), 1.51 (t, J_{HH}: 7.1 Hz, 3H, -CH_3) ppm; MS m/e: 440 ($M^{+\cdot}$) (91%), 395 (27%), 394 (32%), 393 (18%), 368 (29%), 352 (17%), 278 (52%), 277 (100%), 262 (28%), 201 (25%), 199 (18%), 185 (20%), 183 (83%), 162 (6%), 134 (71%), 108 (29%), 106 (21%), 77 (26%); anal: calcd. for $C_{27}H_{25}N_2O_2P$: C: 73.62, H: 5.72, N: 6.36, P: 7.03. Found: C: 73.78, H: 5.79, N: 6.20, P: 7.01

(h) Synthesis and reactions of N-[(o-hydroxy)phenyl]-ITPP hydrochloride (90)

Synthesis

N-[(o-hydroxy)-phenyl]-ITPP (65)(11.45 g, 31 mmol) was dissolved in sodium-dried benzene (150 cm^3) and excess dry hydrogen chloride[113] was bubbled through the solution. An oily product was deposited which on cooling

and being scratched crystallised. Recrystallisation furnished pure (90) (9.76 g, 24 mmol, 78%); mp (EtOH/Et_2O): 188-190°C (decomp); IR: 1440, 1110 (P-Ph), 970 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 275 (3.74), 207 (4.56); ^{31}P NMR ($CDCl_3$): +35.0 ppm; MS m/e: 405 ($M^{+\cdot}$) (0%),370 (17%), 369 (63%), 368 (15%), 352 (4%), 292 (12%), 278 (49%), 277 (100%), 262 (61%), 201 (21%), 199 (19%), 183 (78%), 152 (16%), 108 (37%), 77 (27%). Note this MS is practically identical to that of compound (65). Anal: calcd. for $C_{24}H_{21}ClNOP$: C: 71.02, H: 5.21, N: 3.45, P: 7.63. Found: C: 70.61, H, 5.12, N: 3.55, P:.7.72.

Reaction with ethyl chloroformate catalysed by pyridine

N-[(o-hydroxy)phenyl]-ITPP hydrochloride (90) (0.92 g, 2.27 mmol) was suspended in phosphorus pentoxide-dried acetonitrile (30cm^3) with KOH-dried pyridine (0.19 g, 2.4 mmol, 0.2 cm^3) under a nitrogen atmosphere. Addition of ethyl chloroformate (0.25 g, 2.3 mmol, 0.22 cm^3 followed and the reaction mixture was stirred during 4h at room temperature. Solvent evaporation in vacuo yielded an oily residue, washed with sodium-dried benzene and finally stirred overnight in sodium-dried benzene with over two equivalents of KOH-dried triethylamine (0.46 g, 4.55 mmol, 0.64 cm^3). Filtration to remove triethylamine hydrochloride, reduced pressure elimination of solvent and trituration with pet. ether (60-80°) yielded an oil from which were isolated by fractional recrystallisation tri-phenylphosphine oxide and N-carbethoxy-2-oxo-1,3-benzo[d]oxazole (91) (0.05 g, 0.24 mmol, 10%); mp (MeOH/H_2O): 76-8°C; lit mp: 78.5-9°C;[143] IR: 1860, 1830, 1815, 1750 (C=O), 1250, 1155 (C-O, C-N) cm^{-1}; UV λmax (nm) (logε): 275 (3.54), 268 (3.58), 223 (4.03), 207 (4.17); MS m/e: 207 ($M^{+\cdot}$) (16%), 162 (2%), 135 (100%), 106 (6%), 91 (16%), 90 (6%), 79 (31%), 78 (8%), 52 (10%), 51 (11%).

Ethyl (2-hydroxyphenyl)-carbamate (93)

The above reaction was repeated stirring 90h instead of four.

Trituration of the reaction mixture with sodium-dried Et_2O and filtration into a Schlenk tube afforded a very hygroscopic white solid identified as pyridine hydrochloride. Concentration of the filtrate to ca 5 cm^3 and saturation with sodium-dried Et_2O precipitated a white crystalline solid which was stirred 7h at room temperature in a mixture of sodium-dried benzene and excess KOH-dried triethylamine. After standard work-up the oily product obtained (0.72 g) was purified by flash chromatography on a silica gel (22 g) packed column and eluted with a pet. ether (40-60°)-AcOEt (7:3) solvent mixture. Work-up yielded triphenylphosphine oxide (0.34 g, 1.22 mmol, 54%) and a red oil identified as N,N-dicarbethoxy-2-aminophenol (92) (0.35 g, 1.41 mmol, 31%); IR: 3310 (-OH), 1830, 1765, 1735, 1700 (C=O) cm^{-1}; MS m/e: 253 ($M^{+\cdot}$) (3%), 209 (4%), 207 (4%)), 181 (20%), 135 (100%), 109 (80%), 108 (61%), 91 (25%), 80 (55%), 79 (49%), 52 (39%); MS (CI) m/e: 254 ($M^{+\cdot}$+H); Accurate mass calcd.[53] for $C_{12}H_{15}NO_5$: 253.0946, Found: 253.0921. Upon standing for 24 h this oil crystallised. Recrystallisation from benzene and analysis showed this product to be ethyl (2-hydroxyphenyl)-carbamate (93) (0.19 g, 1.05 mmol, 46%); mp (benzene): 76-8°C; lit. mp (EtOH/Et_2O): 86.5°C[115]; IR: 3390, 3250 (OH), 1725, 1670 (C=O) cm^{-1}; UV λmax (nm) (logε): 281 (3.63), 234 (4.10), 208 (4.38); ^1H NMR ($CDCl_3$): 7.71 (br s, 1H, -O<u>H</u> or -N<u>H</u>), 7.35 (s, 1H, -O<u>H</u> or -N<u>H</u>), 7.30 (dd, J_{HH}: 8.5 Hz and 2.8 Hz, 1H, <u>Ph</u>) 6.95 (m, 3H, <u>Ph</u>), 4.25 (q, J_{HH}: 7.1 Hz, 2H,-O-C<u>H</u>$_2$-), 1.31 (t, J_{HH}: 7.1 Hz, 3H, -C<u>H</u>$_3$) ppm; MS m/e: 181 ($M^{+\cdot}$) (57%), 135 (96%), 109 (100%), 108 (74%), 91 (21%), 80 (55%), 79 (44%), 52 (39%); MS (CI) m/e: 199 ($M^{+\cdot}$+NH_4) (67%), 182 ($M^{+\cdot}$+H) (100%) 181 ($M^{+\cdot}$) (88%); anal: calcd. for $C_9H_{11}NO_3$: C: 59.66, H: 6.12, N: 7.73. Found: C: 59.67, H: 6.00, N: 7.70.

4. Synthesis of N-Alkyl-N-ArITPPm halides

General Procedure

A solution of the N-Ar-ITPP (0.01 mol) and alkyl halide (0.011 mol) in sodium-dried benzene (25 cm^3) was refluxed for 24h under a nitrogen atmosphere. The mixture was allowed to cool, the crystalline salt filtered off and washed well with sodium-dried benzene.

N-Ethyl-N-phenyl-ITPPm bromide (94)

Yield: 11%; mp (EtOH/Et_2O): 245°C (decomp.); lit. mp ($CHCl_3$/AcOEt): 242-242.5°C[120]; IR: 1435, 1105 (P-Ph), 905 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 275 (3.98), 268 (4.08), 262 (4.04), 225 (4.79); ^{31}P NMR ($CDCl_3$): +45.0 ppm; J(^{13}C-^{31}P): 102.6 Hz; anal: calcd. for $C_{26}H_{25}BrNP$: C: 67.54, H: 5.45, N: 3.03, P: 6.70. Found: C: 67.50, H: 5.44, N: 2.97, P: 6.75.

N-Methyl-N-(p-fluorophenyl)-ITPPm iodide (95)[144]

Yield: 21%; mp (EtOH): 232-4°C (decomp); IR: 1440, 1110 (P-Ph), 915 (P^+-N) cm^{-1}; ^1H NMR ($CDCl_3$): 7.8 (m, 15H, P-Ph), 7.4, 6.9 (m, 4H, Ar-), 3.54 (d, J(^1H-C-N-^{31}P): 9.0 Hz, 3H, -CH_3) ppm.

N-Methyl-N-(p-chlorophenyl)-ITPPm iodide (96)

Yield: 76%; mp (EtOH): 217-8°C; (decomp); lit. mp (EtOH): 117-8°C[41,59]; IR: 1435, 1110 (P-Ph), 915 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 211 (4.66); ^1H NMR ($CDCl_3$): 7.8 (m, 15H, P-Ph), 7.25 (m, 4H, Ar-), 3.53 (d, J(^1H-C-N-^{31}P): 9.0 Hz, 3H, -CH_3) ppm.

N-Methyl-N-(p-bromophenyl)-ITPPm iodide (97)

Yield: 57%; mp (EtOH/Et_2O): 215-6°C (decomp); lit. mp (EtOH): 218-9°C[41,59]; IR: 1430, 1110 (P-Ph), 915 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 208 (4.61): ^1H NMR ($CDCl_3$): 7.45 (m, 15H, P-Ph), 7.0 (s, 4H, Ar-), 3.4 (d, J(^1H-C-N-^{31}P): 9.0 Hz, 3H, -CH_3) ppm.

N-Methyl-N-(p-iodophenyl)-ITPPm iodide (98)

Yield: 85%; mp (EtOH/Et_2O): 223-5°C (decomp); lit. mp (EtOH): 228-9°C[41,59]; IR: 1435, 1105 (P-Ph), 910 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 213 (4.69); ^1H NMR ($CDCl_3$): 7.55 (m, 15H, P-Ph), 7.3, 6.9 [d,d(AA'BB'), J_{HH}: 8.0, J_{HH}: 8.0 Hz, 4H, Ar-), 3.4 (d, J(^1H-C-N-^{31}P): 9.0 Hz, 3H, $-CH_3$) ppm.

N-Allyl-N-phenyl-ITPPm bromide (99)

Yield: 25%; mp (acetone/Et_2O): 204-5°C (decomp); IR: 1440, 1110 (P-Ph), 930 (P^+-N), 995, 895 ($-CH=CH_2$) cm^{-1}; UV λmax (nm) (logε): 268 (3.63), 208 (4.52); ^{31}P NMR ($CDCl_3$): +45.8 ppm; ^1H NMR ($CDCl_3$): 7.78 (m, 15H, P-Ph), 7.22 (s, 5H, Ph-N), 5.78 (m, 1H, $-CH=CH_2$), 5.11 (m, 2H, $-CH=CH_2$), 4.46 (m, 2H, $N-CH_2$) ppm; anal: calcd. for $C_{27}H_{25}BrNP$: C: 68.36, H: 5.31, N: 2.95, P: 6.53. Found: C: 68.25, H: 5.31, N: 2.61, P: 6.72.

o-bis-ITPP-benzene mono N-methyl iodide salt (100)

Yield: 73%; mp (EtOH): 240-3°C; lit. mp (EtOH): 242-5°C[41]; IR: 1435, 1115 (P-Ph), 1335 (P=N), 930 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 211 (4.88); ^{31}P NMR ($CDCl_3$): +10.97, +43.82 ppm; ^1H NMR ($CDCl_3$): 7.25 (m, 30H, P-Ph), 6.4 (m, 4H, Ar-), 3.3 (d, J(^1H-C-N-^{31}P): 9.0 Hz, 3H, CH_3) ppm.

N-Methyl-N-[o-(acetamido)-phenyl]-ITPPm iodide (101)

Yield: 61%; mp (EtOH): 221-3°C; IR: 3180, 3160 (NH), 1690, 1680 (C=O), 1505, 1495 (N-C=O), 1430, 1110 (P-Ph), 915 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 268 (3.77), 209 (4.59); ^{31}P NMR ($CDCl_3$): +44.3 ppm, J(^{13}C-^{31}P): 102.5 Hz; anal: calcd. for $C_{27}H_{26}IN_2OP$: C: 58.71, H: 4.74, N: 5.07, P: 5.61. Found: C: 58.48, H: 4.72, N: 4.95, P: 5.63.

N-Methyl-N-[o-(benzamido)-phenyl]-ITPPm iodide (102)

Yield: 31% (43h, reflux); mp (EtOH): 207.5-209°C; IR: 1655, 1645, (C=O), 1510 (N-C=O), 1430, 1110 (P-Ph), 915 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 211 (4.73; ^{31}P NMR ($CDCl_3$): +44.5 ppm, J(^{13}C-^{31}P): 102.5 Hz; anal: calcd. for $C_{32}H_{28}IN_2OP$: C: 62.55, H: 4.59, N: 4.56, P: 5.04, Found: C: 62.49, H: 4.58, N: 4.88, P: 5.05.

N-Methyl-N-[o-(p-toluenesulphonamido)-phenyl]-ITPPm iodide (103)

Yield: 26%, mp (MeOH): 244-7°C; IR: 1440, 1120 (P-Ph), 1340, 1160 (N-SO_2), 925 (P^+-N), 690 (S-N) cm^{-1}; UV λmax (nm) (logε): 212 (4.68); ^{31}P NMR ($CDCl_3$): + 45.4 ppm; anal: calcd. for $C_{32}H_{30}IN_2O_2PS$: C: 57.84, H: 4.55, N: 4.22, P: 4.66. Found: C: 58.17, H: 4.74, N: 4.48, P: 4.50.

5. Pyrolysis reactions of ortho-substituted N-ArITPPs

General Procedure

The solid iminotriphenylphosphorane (1.0 g) was placed in a round-bottom flask (50 cm^3) fitted with a cold finger, and the system provided with a side-arm. The system was evacuated and flushed with nitrogen successively at least three times using an oil pump. The evacuated reaction chamber was then heated in an oil bath during varying periods of time at temperatures exceeding by 30-70°C the melting point of the starting material. Separation and isolation of reaction products was accomplished through standard flash column chromatography work-up.

Pyrolysis of N-[o-(acetamido)phenyl-ITPP (80)

After 3h at 210°C and elution with acetone-pet. ether (60-80°) (1-1) were isolated triphenylphosphine oxide (96%) and 2-methyl-benzimidazole (104) (86%); mp (H_2O): 172-3°C; lit. mp (H_2O): 175-6°C[115,122]; mp (EtOH/Et_2O) hydrochloride derivative: 284-7°C, lit. mp: 293°C[115] mp (EtOH) picrate derivative: 206-7°C, lit. mp (EtOH): 207-8°C[123]; IR: 3000 (br band) (NH), 1620, 1550 (C=N) cm^{-1}[117]; UV λmax (nm) (logε): 280 (3.85), 273 (3.80), 242 (3.78), 208 (4.28); ^1H NMR (Acetone-d_6)[124]: 7.63 (m, 2H, 4-H and 7-H), 7.26 (m, 2H, 5-H and 6-H), 2.69 (s, 3H, $-CH_3$) ppm; ^{31}C NMR (DMSO-d_6)[53,125]: 115.6 (C-5 and C-6), 122.6 (C-6 and C-7), 140.7 (C-4 and C-9), 152.5 (C-2), 15.3 ($-CH_3$) ppm. MS m/e: 132 ($M^{+\cdot}$) (100%), 131 (69%), 77 (4%), 65 (9%); anal. calcd. for $C_8H_8N_2$: C: 72.70, H: 6.10, N: 21.19. Found: C: 72.50, H: 6.07, N: 21.30.

Pyrolysis of N-[o-(benzamido)phenyl]-ITPP (81)

After 3h at 210°C and elution with acetone-Pet. ether (60-80°C) (1:1) were isolated triphenylphosphine oxide (90%) and 2-phenyl-benzimidazole (105) (80%); mp (acetone): 283-5°C, mp (acetic acid): 289-290.5°C; lit. mp: 291°C[115] and 290°C[126]; IR: 3000 (br band) (NH), 1625, 1540 (C=N) cm^{-1}[117]; UV λmax (nm) (logε): 302 (4.45), 241 (4.17)

210 (4.36); MS m/e: 194 (100%), 193 (25%), 77 (6%); anal: calcd. for $C_{13}H_{10}N_2$: C: 80.39, H: 5.19, N: 14.42. Found: C: 80.32, H: 4.97, N: 14.38.

Pyrolysis of N-[o-(p-toluenesulphonamido)phenyl]-ITPP (82)

After 4h at 240°C only unreacted material was recovered (97%) showing no reaction had taken place, although a little charring of material was observed.

Pyrolysis of N-[2-(α-methyl acetate)phenyl]-ITPP (64)

After 3h at 150°C and elution with pet. ether (60-80°)-AcOEt (1:1) mixture were isolated TPPO (97%) and 2-methoxy-indole (106) (98%, unrecrystallised). This indole derivative exists in two tautomeric forms in solution[127]:

This compound is oxidised in air to indirubin[128]. Attempts to sublime the oxidised mixture under vacuum led to contaminated sublimate.

Physical data for (106) and (107): IR (recorded immediately after isolation): 3350 (NH), 1630, 1595, 1580, 1575 (C=N, C=C) cm^{-1}; ^1H NMR ($CDCl_3$): ratio was established by measurement of -CH= and $-CH_2-$ signals' integrals.

	Ratio	-NH-	Ar-	-CH=	$-CH_2-$	$-OCH_3$
(106)	4	8.64 br s	7.15m	5.51d (1.9 Hz)*	-	3.85s
(107)	6	-	7.15m	-	3.51s	4.01s

* Long range coupling with H-7 on aromatic ring[129].

Pyrolysis of N-[o-(Ethoxysuccinylamido)phenyl]-ITPP (88)

After 5h at 170°C and elution with pet. ether (60-80°C)-AcOEt (1:1) were isolated TPPO (86%) and ethyl β-(2-benzimidazolyl)-propionate (108) (46%); mp (EtOH): 134-5°C; lit. mp (EtOH/H_2O): 137°C[130]; IR: 1730 (C=O) cm^{-1}; UV λmax (nm) (logε): 280 (3.93), 273 (3.89), 239 (3.91), 208 (4.40); ^1H NMR ($CDCl_3$): 7.54 (m, 3H, NH and Ar-), 7.21 (m, 2H, Ar), 4.17 (q, J_{HH}: 7.1 Hz, 2H, O-CH_2-), 3.23 (t, J_{HH}: 6.8 Hz, 2H, =C-CH_2-CH_2-), 2.94 (t, J_{HH}: 6.8 Hz, 2H, =C-CH_2-CH_2-), 1.25 (t, J_{HH}: 7.1 Hz, 3H, -CH_3) ppm; MS m/e: 218 ($M^{+\cdot}$) (39%), 173 (31%), 145 (100%), 131 (20%), 118 (17%), 92 (20%), 77 (13%); accurate mass calcd.[53] for $C_{12}H_{14}N_2O_2$: 218.1052. Found: 218.1050. Anal: calcd. for $C_{12}H_{14}N_2O_2$: C: 66.04, H: 6.46, N: 12.83. Found: C: 66.06, H: 6.51, N: 12.80.

Pyrolysis of N-[2-(β-ethyl crotonate)anilino]-ITPP (66)

After 7h at 170°C and elution with pet. ether (40-60°)-AcOEt (8:2) were isolated TPPO (89%) and 2-ethoxy-4-methyl-3H-1,5-benzo[f]diazepin (109) (75%) as an oil. IR: 1660, 1645 (C=N), 1275, 1130, (O-C=N) cm^{-1}; UV λmax (nm) (logε): 214 (4.30); ^1H NMR ($CDCl_3$): 7.20 (m, 4H, Ar-), 4.29 (q, J_{HH}: 7.1 Hz, 2H, O-CH_2-), 2.88 (s, 2H, C-CH_2-C), 2.35 (s, 3H, =C-CH_3), 1.34 (t, J_{HH}: 7.1 Hz, 3H, -CH_2-CH_3) ppm; ^{13}C NMR ($CDCl_3$): 159.2 (N=C-OEt), 154.2 (N=C-CH_3), 139.8, 138.2 (C-6 and C-11), 127.5, 127.2 (C-8 and C-9), 125.4, 123.6 (C-7 and C-10), 63.3 (O-CH_2-CH_3), 39.3 (=C-CH_2-C=), 27.6 (N=C-CH_3), 14.2 (O-CH_2-CH_3) ppm; MS m/e: 202 ($M^{+\cdot}$) (59%), 197 (15%), 174 (17%), 159 (13%), 158 (26%), 157 (10%), 147 (15%), 132 (100%), 131 (48%), 107 (16%), 90 (15%), 77 (13%), 71 (9%), 57 (13%); accurate mass calcd.[53] for $C_{12}H_{14}N_2O$: 202.1103. Found: 202.1098; MS (CI) m/e: 203 ($M^{+\cdot}$+H)(100%). Anal: calcd. for $C_{12}H_{14}N_2O$: C: 71.26, H: 6.97, N: 13.85. Found: C: 70.71, H: 7.15, N: 12.51

Synthesis of 4-methyl-2-oxo-3H-1,5-benzo[f]diazepin (126)

The synthesis of 4-methyl-2-oxo-1H-1,5-benzo[f]diazepin (compound's (126) tautomer) was attempted following Sexton's alcoholic potash method[109,133]. ^{1}H NMR conclusively showed our material was the tautomer and was further corroborated by its mp: 142°C (lit. mp[133]: 148-9°C) and by its UV spectrum[133]. (Lit. UV λmax (nm) (logε): 213 (4.51), 280 (3.53), 289 (3.53)).

4-Methyl-2-oxo-3H-1.5-benzo[f]diazepin (126)

mp(EtOH): 142; IR: 3200, 3140, 3090, 3060 (NH), 1690 (C=O) 1645 (C=N) cm^{-1}; UV λmax (nm) (logε); 391 (2.75), 268 (3.64), 213 (4.45); ^{1}H NMR ($CDCl_3$): 9.88 (br s, 1H, -NH-), 7.13 (m, 4H, Ar-), 3.14 (s, 2H, $-CH_2-$), 2.39 (s, 3H, $-CH_3$) ppm; MS m/e: 174 ($M^{+\cdot}$) (28%), 159 (2%), 145 (3%), 144 (3%), 132 (100%), 131 (32%), 104 (6%), 92 (5%), 90 (5%), 77 (6%), 65 (7%), 51 (7%), 40 (11%).

Pyrolysis of N-[2-(Methoxycarbonyl)phenyl]-ITPP (63)

After 10h at 210°C and elution with hexane-Et_2O (7:3) were isolated TPPO (42%) and methyl anthranilate (110) (31%) both of which gave identical IR spectra to authentic materials. During the course of the reaction a yellow oil was formed and substantial charring took place. The reaction was repeated ensuring totally anhydrous conditions: the equipment was thoroughly dried, the inert gas, changed to argon, in turn dried through sodium hydroxide pellets, bubbled through sulphuric acid and passed through self-indicating silica gel, and starting material re-dried in vacuum. The reaction was heated at 270°C during 7h, allowed to cool and the residual yellow oil vacuum distilled, but was observed to co-distil with TPPO. Flash column chromatography using pet. ether (60-80°)-AcOEt (9:1) as solvent mixture again afforded TPPO and methyl anthranilate (110). No unreacted starting material was

detected in either of the two reactions.

Pyrolysis of N-[2-(acetyl)phenyl]-ITPP (62)

After 7h at 150°C and elution with pet. ether (40-60°) - AcOEt (3:7) the major product isolated was unreacted N-[2-(acetyl)phenyl]ITPP (62) and small amounts of TPPO and another compound identified as 2-aminoacetophenone (111) by its infrared spectrum. Identical to that of authentic material). Repetition of the reaction at 220°C during 7h produced a very complex reaction mixture from which unreacted N-[2-(acetyl)phenyl]-ITPP (62) TPPO and 2-aminoacetophenone (111) were identified showing decomposition had taken place although the reaction had not been completed.

Pyrolysis of N-[o-(carbethoxyamino)phenyl]-ITPP (89)

After 8.5h at160°C the reaction mixture was dissolved in AcOEt, from which was isolated by filtration 2-benzimidazolone (112)[115](25%). Flash column chromatography using a pet. ether (60-80°)-AcOEt solvent mixture in (7:3) and (3:7) proportions successively, furnished starting material (89) (8%), TPPO (85%), 1-ethyl-2-benzimidazolone (113)(36%) and a mixture of two compounds (114)(0.04 g). (See section 6b).

2-Benzimidazolone (112): mp (EtOH/H_2O): 309-310°C (decomp); lit. mp: 311°C (decomp)[115]; IR: 3000 (br. band) (NH), 1760, 1740 (C=O) cm^{-1}[117]; UV λmax (nm) (logε): 280 (3.74), 226 (3.89), 208 (4.27); MS m/e: 134 ($M^{+\cdot}$) (100%), 106 (41%), 105 (22%), 79 (34%), 78 (12%), 52 (19%), 51 (15%); anal: calcd. for $C_7H_6N_2O$: C: 62.68, H: 4.51, N: 20.88. Found: C: 62.42, H: 4.60, N: 20.80.

1-Ethyl-2-benzimidazolone (113): mp (Et_2O/pet. ether (60-80°)): 116-8°C; lit. mp: 117-8°C[131] and 118-120°C[132] IR: 3100 (br band) (NH), 1700, 1670 (C=O) cm^{-1}; UV λmax (nm) (logε): 282 (3.83), 228 (3.89), 212 (4.18); ^1H NMR ($CDCl_3$): 10.73 (br s, 1H, NH), 7.07 (m, 4H, Ar-),

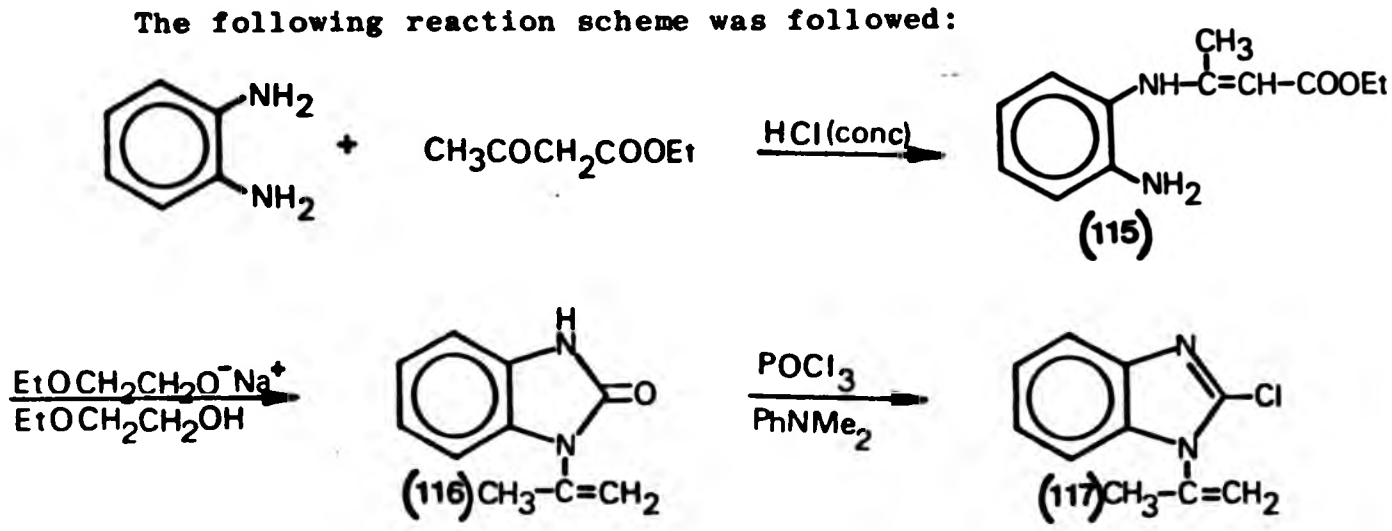
3.97 (q, J_{HH}: 7.20 Hz, 2H, N-CH_2-CH_3), 1.37 (t, J_{HH}: 7.20 Hz, 3H, -CH_2-CH_3) ppm; MS m/e: 162 ($M^{+\cdot}$) (100%), 147 (78%), 134 (48%), 119 (44%), 106 (28%), 92 (10%), 78 (11%), 65 (9%), 51 (13%); accurate mass calcd. for $C_9H_{10}N_2O$:[53] 162.0791. Found: 162.0775; anal: calcd. for $C_9H_{10}N_2O$: C: 66.65, H: 6.21, N: 17.27. Found: C: 66.55, H: 6.08, N: 17.01.

Reaction was repeated 175°C during 3h ensuring totally anhydrous conditions as described previously and flushing the reaction chamber with argon instead of nitrogen. After column chromatography separation were isolated 2-benzimidazolone (112)(21%), 1-ethyl-2-benzimidazolone (113)(46%), TPPO (93%) and starting material (89) (7%).

6. Synthesis and pyrolysis of 2-alkoxybenzimidazoles

(a) Synthesis

The following reaction scheme was followed:



Ethyl β-2-aminoanilinocrotonate (115) was synthesised following Sexton's method[109]. Sublimed o-phenylenediamine (21.6 g, 0.2 mol) and redistilled ethyl acetoacetate (27.3 g, 0.21 mol, 26.8 cm^3) were mixed together and five drops of concentrated hydrochloric acid added. After 2 min swirling the mixture warmed up and rapidly solidified. The solid was then thoroughly crushed during 20 min. breaking all the lumps formed, dissolved in warm pet. ether (60-80°C) (250 cm^3), filtered and allowed to crystallise. Vacuum filtration afforded pure ethyl β-2-aminoanilino-crotonate (115) (68%); mp (pet. ether 60-80°C): 58-9°C; lit. mp: 59-62°C and 85°C[109] (compound has two different forms) (lit. yield: 24%)[109]. Reaction was repeated under the same conditions yielding (115) (77%), mp (pet. ether (60-80°C)): 85-6°C; IR: 3480, 3380, 3300 (NH, NH_2), 1650 (C=O), 1625 (C=C), 1170 (C-O) cm^{-1}; ^1H NMR ($CDCl_3$): 9.70 (br s, 1H, -NH-), 6.84 (m, 4H, Ar-), 4.72 (q, J(H-C=C-CH_3): 0.6 Hz, 1H, -C=CH-), 4.14 (q, J_{HH}: 7.1 Hz, 2H, -O-CH_2), 3.82 (br s, 2H, -NH_2), 1.79 (d, J(H-C=C-CH_3): 0.6 Hz, 3H, -CH=C-CH_3), 1.28 (t, J_{HH}: 7.1 Hz, 3H, -CH_2-CH_3) ppm.

Synthesis of 1-isopropenyl-2-benzimidazolone (116) was carried out according to Davoll's method[133] increasing reflux time from 2h to 7h. After work-up was isolated (116) (91%) (lit. yield: 89%); mp: 118-120°C; lit. mp: 120-1°C[133], 121-2°C[109]. Finally, 1-isopropenyl-2-

chlorobenzimidazole (117) was obtained as an oil after (116) was refluxed for 7h in the presence of excess redistilled phosphoryl chloride and dimethylaniline in 60% yield (lit. yield: 100%[133]).

Synthesis of the respective 1-alkoxy-2-benzimidazoles was achieved following the method described by Harrison and Jones[134]. A solution of sodium (6.0 g) in dry alcohol (130 cm^3) was added to 1-isopropenyl-2-chloro benzimidazole (117) (5.0 g, 26 mmol) and the mixture refluxed 1h. The solution was filtered to remove sodium chloride, washed with a small volume of alcohol and the combined filtrates evaporated under reduced pressure. The residue was dissolved in water (25 cm^3), extracted with Et_2O (3 x 50 cm^3) dried ($MgSO_4$) and concentrated, furnishing a dark oil. Oxidation of the above oil (0.02 mol) with a solution of potassium permanganate (19.2 g, 0.12 mol) in 0.1M sodium hydroxide (500 cm^3), avoiding a rapid rise in temperature, and Et_2O extraction afforded after the usual work-up the 2-alkoxybenzimidazole. This last reaction was carried out rapidly to reduce excessive oxidation to a minimum.

2-Methoxybenzimidazole (118)

Overall yield: 0.833 g, 3%; mp (toluene): 194-7°C; lit. mp (Toluene): 198-200°C[134]; IR: 3000 (br band)(NH), 1630 (C=N), 1270, 1070 (O-C=N) cm^{-1}; (identical literature data[134]; UV λmax (nm) (logε): 280 (3.76), 274 (3.78), 229 (3.92), 209 (4.28); ^1H NMR ($CDCl_3$): 7.26 (m, 4H, Ar-), 4.18 (s, 3H, -O-CH_3) ppm; MS m/e: 148 ($M^{+\cdot}$) (100%), 147 (42%), 134 (6%), 133 (52%), 119 (22%), 118 (11%), 106 (45%), 91 (6%), 78 (19%), 77 (9%), 52 (8%), 51 (16%). Anal: calcd. for $C_8H_8N_2O$: C: 64.85, H: 5.44, N: 18.91. Found: C: 64.97, H: 5.41, N: 18.79.

2-Ethoxybenzimidazole (119)[134,135,137]

Overall yield: 2.10 g, 7%; mp (toluene): 157-8°C; lit. mp (toluene): 161-2°C[134]; IR: 3000 (br band)(NH), 1635 (C=N), 1270, 1065

(O-C=N) cm^{-1}; (identical literature data[134]); UV λmax (nm) (logε): 281 (3.73), 275 (3.76), 235 (3.85), 230 (3.85), 210 (4.19); ^{1}H NMR ($CDCl_3$)[135]: 10.6 (br s,1H, -NH), 7.23 (m, 4H, Ar-), 4.62 (q, J_{HH}: 7.1 Hz, 2H, -O-CH_2-), 1.44 (t, J_{HH}: 7.1 Hz, 3H, -CH_3) ppm; MS m/e: 162 ($M^{+\cdot}$) (43%), 147 (10%), 135 (10%), 134 (100%), 133 (9%), 106 (46%), 105 (8%), 79 (13%), 78 (11%), 52 (8%), 51 (11%); ^{13}C (NMR) ($CDCl_3$): 158.6 (C-2), 136.7 (C-4 and C-9), 121.5 (C-6 and C-7), 113.6 (C-5 and C-8), 66.0 (O-CH_2-), 14.6 (-CH_3) ppm; anal: calcd. for $C_9H_{10}N_2O$: C: 66.65, H: 6.21, N: 17.27. Found: C: 66.73, H: 6.10, N: 16.98.

2- n- Propoxybenzimidazole (120)

Overall yield: 3.41 g, 10%; mp (toluene): 159-161°C; lit. mp: 164-5°C[135] IR: 3000 (br band)(NH), 1630 (C=N), 1265, 1065 (O-C=N) cm^{-1}; UV λmax (nm) (logε): 281 (3.81), 275 (3.84), 235 (3.92), 209 (4.27); ^{1}H NMR ($CDCl_3$)[135]: 9.88 (br s, 1H, NH), 7.25 (m, 4H, Ar-), 4.50 (t, J_{HH}: 6.6 Hz, 2H, -O-CH_2-), 1.84 (sext., J_{HH}: 6.6 Hz, 2H, O-CH_2-CH_2-), 1.01 (t, J_{HH}: 6.6 Hz, 3H, -CH_3) ppm; MS m/e: 176 ($M^{+\cdot}$) (23%), 135 (10%), 134 (100%), 106 (29%), 105 (6%), 79 (9%), 78 (7%), 51 (6%), 41 (8%); anal: calcd. for $C_{10}H_{12}N_2O$: C: 68.16, H: 6.86, N: 15.90. Found: C: 68.16, H: 6.90, N: 15.82.

(b) Pyrolysis

All pyrolysis reactions were carried out following the method outlined in section 5.

Pyrolysis of 2-methoxybenzimidazole (118)

After 3h at 200-220°C the reaction mixture was dissolved in AcOEt and filtered to remove 2-benzimidazolone (112)[115] (23%), mp: 312-3°C (decomp), lit. mp: 311°C (decomp[115]), mmp: undepressed. The filtrate was separated by flash column chromatography affording two fractions after elution with a Pet. ether (60-80°)-AcOEt (1:1) solvent mixture.

The first one was shown to be a mixture of two components and the second yielded pure 1-methyl-2-benzimidazolone (121)(38%). The solid mixture from fraction one was extracted with boiling heptane, was filtered to remove insoluble material and allowed to cool, yielding 1,3-dimethyl-2-benzimidazolone (122). Toluene recrystallisation of the insoluble material gave pure 2-methoxybenzimidazole (118). The relative proportion of each compound in the mixture was calculated by gas chromatographic analysis using an AcOEt solution of known weight. Analysis was carried out at an oven temperature of 200°C on a 25m capillary column coated with SE-30 stationary phase.

Compound	t_R(min)	Rel.prop.(cm)	Weight	Prop.(mg)
(118)	1.3			
(121)	2.25			
(122)	1.8			
(118)+(122)	1.3,1.8	7.0, 2.2	54.8 mg	41.7, 13.1

1-Methyl-2-benzimidazolone (121)

Yield: 38%, mp 186-8°C; lit. mp (MeOH): 188-190°C[136]; IR: 3100 (br band)(NH), 1725, 1710, 1685 (C=O) cm^{-1}; UV λmax (nm) (logε): 281 (3.75), 228 (3.91), 209 (4.36); ^1H NMR ($CDCl_3$): 10.57 (br s, 1H, -NH-), 7.08 (m, 4H, Ar-), 3.43 (s, 3H, $-CH_3$) ppm; anal: calcd. for: $C_8H_8N_2O$: C: 64.85, H: 5.44, N: 18.91. Found: C: 64.72, H: 5.45, N: 18.70.

1,3-Dimethyl-2-benzimidazolone (122)

Yield: 8%; mp (heptane): 105-6°C, Lit. mp (benzene/pet. ether): 111-2°C[131]; mmp: undepressed; IR: 1725, 1700, 1660 (C=O) cm^{-1}; UV λmax (nm) (logε): 282 (3.86), 230 (3.89), 214 (4.17); ^1H NMR ($CDCl_3$): 7.02 (m, 4H, Ar-), 3.40 (s, 6H, $-CH_3$) ppm; MS m/e: 162 ($M^{+\cdot}$) (100%), 161 (46%), 147 (9%), 133 (9%), 119 (12%), 92 (9%), 81 (8%), 77 (7%), 65 (6%), 51 (7%), 42 (13%); accurate mass calcd.[53] for $C_9H_{10}N_2O$: 162.0791.

Found: 162.0778; anal: calcd. for $C_9H_{10}N_2O$: C: 66.65, H: 6.21, N: 17.27. Found: C: 66.67, H: 6.25, N: 17.30. Authentic sample for mmp. was synthesised[131], mp: 107-9°C, IR: identical to that of compound(122).

2-Methoxybenzimidazole (118)

Yield: 15%; mp: 202-4°C, lit. mp: 198-200°C[134], mmp: undepressed. IR: identical to that of an authentic sample.

Pyrolysis of 2-ethoxybenzimidazole (119)

After 3h at 180°C the reaction mixture was dissolved in AcOEt and 2-benzimidazolone (112) (15%) (IR: identical to that of authentic material isolated by filtration. Flash column chromatography of the filtrate (0.92 g) on a silica gel (50 g) packed column and elution with pet. ether (60-80°C)-AcOEt (7-3) afforded 2-ethoxy-benzimidazole (119) (51%) (mp: 156-7°C, mmp: undepressed) and a viscous yellow oil identified as 1-ethyl-2-ethoxy benzimidazole (123) (18%). The high yield of compound (119) obtained was due to its sublimation on to the cold finger during the course of the reaction.

1-Ethyl-2-ethoxybenzimidazole (123)[137]

IR: 1620 (C=N), 1280, 1040 (O-C=N) cm^{-1}; UV λmax (nm) (logε): 282 (3.83), 276 (3.84), 239 (3.84), 212, (4.32); ^1H NMR ($CDCl_3$): 7.55 (m, 1H, Ar-), 7.12 (m, 3H, Ar-), 4.58 (q, J_{HH}: 7.1 Hz, 2H, -O-CH_2-), 3.91 (q, J_{HH}: 7.2 Hz, 2H, -N-CH_2-), 1.44 (t, J_{HH}: 7.1 Hz, 3H, -O-CH_2-CH_3), 1.27 (t, J_{HH}: 7.2 Hz, 3H, -N-CH_2-CH_3) ppm; ^{13}C NMR ($CDCl_3$): 157.6 (C-2), 140.1 (C-9), 133.7 (C-4), 121.2, 120.6 (C-6 and C-7), 117.6 (C-5), 108.2 (C-8), 71.7 (O-CH_2-), 43.6 (N-CH_2-), 11.4 (O-CH_2-CH_3), 10.3 (N-CH_2-CH_3) ppm; MS m/e: 190 ($M^{+\cdot}$) (74%), 175 (19%), 162 (73%), 161 (10%), 148 (10%), 147 (100%), 134 (50%), 119 (35%), 118 (9%), 106 (14%), 92 (10%), 91 (13%), 77 (8%), 65 (7%), 51 (8%); accurate mass calcd.[53] for $C_{11}H_{14}N_2O$: C: 190.1103. Found: 190.1120; anal: calcd. for

$C_{11}H_{14}N_2O$: C: 69.45, H: 7.42, N: 14.72. Found: C: 69.65, H: 7.52, N: 14.70.

Mixture (114) (see section 5, pyrolysis of compound (89))

The ^1H NMR spectrum of this mixture, taking into account its origin and the ^1H NMR results obtained for compounds (119) and (123) can be tentatively assigned to a mixture of these two products although their relative proportions could not be calculated

	δ(ppm) (J_{HH}, Hz)					
Compound	-NH-	Ar	$N-CH_2$	$-O-CH_2$	$-CH_2-CH_3$	$N-CH_2-CH_3$
(119)	10.6	7.34 7.12	-	4.62(7.1)	1.44(7.1)	-
(123)	-	7.55 7.12	3.91(7.2)	4.58(7.1)	1.44(7.1)	1.27(7.2)
(114)	10.3	7.81 7.48 7.14	3.93(7.3)	4.26(7.3) 4.02(7.1)	1.43(7.1) 1.40(7.3)	1.26(7.3)

Pyrolysis of 2-n-propoxybenzimidazole (120)

After 3.5h at 180°C under a nitrogen atmosphere, and normal pressure to minimise sublimation, the reaction mixture was dissolved in acetone and separated by flash chromatography using pet. ether (60-80°C)-AcOEt (3:7) as solvent system. Three fractions were obtained, the first was a two component mixture, followed by a solid identified as 1-n-propyl-2-benzimidazolone (124) (3%) and finally 2-benzimidazolone (112) (8%) (mp: 307-10°C (decomp); lit. mp: 311°C (decomp)[115]; mmp: undepressed; IR: identical to that of an authentic sample). The two component mixture was again separated by flash column chromatography using the same solvent mixture but increasing the silica gel to substrate ratio to (60 g: 1 g). Elution yielded an oil identified as 1-n-propyl-2-n-propoxy-benzimidazole (125) (19%), followed by starting material (120) (60%) (mp: 162-4°C, lit. mp: 164-5°C[135], mmp: undepressed, IR: identical to that of authentic material).

1-n-propyl-2-benzimidazolone (124)

mp (pet. ether (60-80)): 101-2°C; lit. mp: 104°C[132]; IR: 3100 (br band)(NH), 1730, 1700, 1675 (C=O), cm^{-1}; UV λmax (nm) (logε): 282 (3.86), 228 (3.96), 211 (4.33); ^1H NMR ($CDCl_3$): 10.62 (br s, 1H, -NH-), 7.06 (m, 4H, Ar-), 3.87 (t, J_{HH}: 7.1 Hz, 2H, N-CH_2-), 1.81 (sext, J_{HH}: 7.1 Hz, 2H, -C-CH_2-C-), 0.99 (t, J_{HH}: 7.1 Hz, 3H, -CH_3) ppm; MS m/e: 176 ($M^{+\cdot}$) (90%), 161 (3%), 159 (6%), 148 (19%), 147 (100%), 134 (94%), 119 (38%), 107 (20%), 92 (11%), 78 (8%), 77 (7%), 65 (11%), 51 (11%); accurate mass calcd[53] for $C_{10}H_{12}N_2O$: 176.0947. Found: 176.0946; anal. calcd. for $C_{10}H_{12}N_2O$: C: 68.16, H: 6.86, N: 15.90. Found: C: 67.69, H: 6.86, N: 15.92.

1-n-propyl-2-n-propoxybenzimidazole (125)

IR: 1625 (C=N), 1260, 1065 (O-C=N) cm^{-1}; UV λmax (nm) (logε): 282 (4.02), 276 (4.03), 231 (4.12), 212 (4.55); ^1H NMR ($CDCl_3$): 7.54 (m, 1H, Ar-), 7.14 (m, 3H, Ar-), 4.50 (t, J_{HH}: 7.1 Hz, 2H, O-CH_2-), 3.91 (t, J_{HH}: 7.1 Hz, 2H, N-CH_2-), 1.83 (apparent hept., J_{HH}: 7.1 Hz, 4H, -C-CH_2-), 1.05 (t, J_{HH}: 7.1 Hz, 3H, O-$(CH_2)_2$-CH_3), 0.92 (t, J_{HH}: 7.1 Hz, 3H, N-$(CH_2)_2$-CH_3) ppm; MS m/e: 218 ($M^{+\cdot}$) (38%), 203 (3%), 199 (7%), 176 (79%), 159 (8%), 148 (18%), 147 (100%), 134 (87%), 119 (25%), 106 (12%), 92 (7%), 91 (5%), 90 (8%), 77 (7%), 65 (5%), 51 (5%), 43 (15%), 41 (29%), 39 (13%); accurate mass calcd[53] for $C_{13}H_{18}N_2O$: 218.1415; Found: 218.1410, anal: calcd. for $C_{13}H_{18}N_2O$: C: 71.53, H: 8.31, N: 12.83. Found: C: 69.97, H: 8.30, N: 12.21.

Synthesis and pyrolysis of dimethyl (phenylimino-triphenylphosphoranylidene) succinate (127)

Synthesis of (127) was carried out according to the literature method[60]. After 15h reflux in sodium-dried Et_2O (40 cm^3) upon cooling was collected (127) (2.62 g, 5.3 mmol, 93%); mp (Et_2O): 190-2°C (decomp); lit. mp (AcOEt): 170°C (decomp)[60]; IR: 1735, 1645 (C=O),

1570 (C=N), 1430, 1105 (P-Ph), 1215 (C=P), 1160 (C-O) cm^{-1}; UV λmax (nm) (logε): 274 (4.15), 209 (4.68); ^{31}P NMR ($CDCl_3$): +16.6 ppm; ^{1}H NMR ($CDCl_3$): 7.98 (m, 6H, ortho P-Ph), 7.50 (m, 9H, meta and para P-Ph), 6.93 (m, 3H, meta and para =N-Ph), 6.26 (m, 2H, ortho =N-Ph), 3.55 (s, 3H, O-CH_3), 3.26 (s, 3H, O-CH_3) ppm; MS m/e: 495 ($M^{+\cdot}$) (25%), 494 (10%), 480 (11%), 467 (16%), 466 (15%), 448 (27%), 437 (33%), 436 (100%), 301 (9%), 262 (14%), 220 (11%), 204 (15%), 201 (9%), 183 (33%), 158 (17%), 152 (6%), 143 (13%), 119 (19%), 108 (11%), 77 (22%), 51 (9%); MS (CI) m/e: 496 ($M^{+\cdot}$+H) (100%).

Pyrolysis

The reaction was carried out at 180°C during 8h and the brown oil obtained, separated by flash column chromatography [pet. ether. (60°-80°)-AcOEt (3:7)] yielded only starting material (127) (83%) [mp(AcOEt): 192°C]. During the course of the reaction some decomposition and charring took place.

7. Further reactions of N-ArITPP and o-bis-ITPP benzene

(a) Reactions with α-bromo-esters

General procedure

The solid N-ArITPP (4.25 mmol) was dissolved in sodium-dried benzene (30 cm^3) and excess α-bromo-ester (4.3 mmol) added to the solution. The mixture was then refluxed during varying periods of time under a nitrogen atmosphere and constant stirring. The reaction was allowed to cool, decanted and the oily product obtained thoroughly washed with fresh sodium-dried benzene three times. Upon trituration with sodium-dried Et_2O a crystalline product was obtained after filtration.

Reaction of N-phenyl-ITPP (61) with ethyl α-bromoacetate

After 5h reflux and work-up as described, a 95% crude yield was obtained. Both IR and ^{31}P NMR spectra showed the product was a mixture of two substances: N-(ethyl α-acetate)-N-phenyl-ITPPm bromide (128) and N-phenyl-ITPP hydrobromide (129). The structure of compound (129) was definitively established after a small amount was isolated by fractional recrystallisation from ethanol/Et_2O, mp: 198-9°C; lit. mp: 198-9[28]; IR: 3400 (NH), 1435, 1105 (P-Ph), 960 (P^+-N) cm^{-1}; ^{31}P NMR ($CDCl_3$): +32.8 ppm, J(^{13}C-^{31}P): 103.0 Hz (lit. ^{31}P NMR: +33.6 ppm[41]. Anal: calcd for $C_{24}H_{21}BrNP$: C: 66.37, H: 4.87, N: 3.22. Found: C: 66.02, H: 4.82, N: 2.88.

Having established the structure of (129), the reaction mixture was refluxed with excess KOH-dried triethylamine in sodium-dried benzene during 2h under a nitrogen atmosphere. Filtration afforded a mixture of (128) and triethylamine hydrochloride. All attempts to separate them by fractional crystallisation failed, resulting in contaminated product. The mixture was dissolved and a ^{31}P NMR recorded showing once again the product was impure with two peaks at +46.3 ppm and

+30.8 ppm, the latter tentatively assigned to TPPO.

From the original reaction mixture the following spectral data regarding (128) were extracted: ^{31}P NMR ($CDCl_3$): +46.5 ppm, IR: 1740 (C=O), 1440, 1110 (P-Ph), 1125 (C-O), 905 (P^+-N) cm^{-1}.

Reaction was repeated using methyl α-bromoacetate instead of its ethyl analogue with parallel results. A change of solvent from benzene to dried THF (15h reflux) proved equally unsuccessful.

Reaction of N-[p-methoxyphenyl]-ITPP[41] with ethyl α-bromoacetate

After 6h reflux a crude yield of 90% was obtained. ^{31}P NMR ($CDCl_3$): +47.2 ppm and +34.6 ppm and IR: 3670, 3380 (NH), 1745 (C=O), 1440, 1110 (P-Ph), 1205, 1030 (Ar-O-CH_3), 1140 (C-O), 995 (P^+-NH), 905 (P^+-N-C) cm^{-1} show the product isolated to be a mixture of probably N-(ethyl α-acetate)-N-[p-methoxyphenyl]-ITPPm bromide (130) and N-[p-methoxyphenyl]-ITPP hydrobromide (131) The solid sample was dissolved in benzene and stirred overnight with triethylamine at room temperature. Filtration and recrystallisation from acetone gave unchanged IR. Attempts to separate the mixture by dissolution in distilled water also failed as both compounds dissolve very readily.

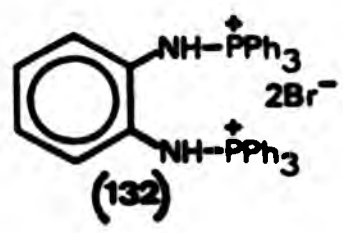
Reaction of o-bis-ITPP-benzene (67) with ethyl α-bromoacetate

o-bis-ITPP-benzene (67) (3.2 mmol) was suspended in phosphorus pentoxide-dried acetonitrile (10 cm^3) and a slight excess of ethyl α-bromoacetate (3.3 mmol) added. The suspension was stirred 20h at room temperature under a nitrogen atmosphere, filtered and the solid isolated (recrystallised from ethanol/Et_2O,) identified as o-bis-ITPP-benzene bis-hydrobromide (132): (0.45 mmol, 14%); mp: 210-1°C; lit. mp: 210-1°C[41]; IR: 1440, 1115, 1105 (P-Ph), 980 (P^+-N) cm^{-1}; ^{31}P NMR ($CDCl_3$): +21.9 ppm, lit. ^{31}P NMR: +36.9 ppm[41]; ^1H NMR ($CDCl_3$): 7.7 (m, 15H, P-Ph), 6.5 (s, 4H, Ar-) ppm. Final confirmation was obtained when stirring (132) with KOH-dried triethylamine at room temperature during 24h

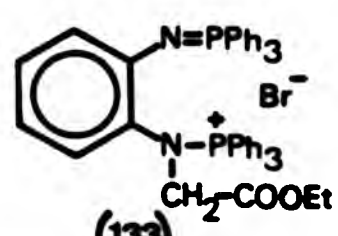
regenerated o-bis-ITPP benzene (67).

The acetonitrile filtrate was stirred with KOH-dried triethylamine but only triethylamine hydrobromide was isolated.

The reaction was repeated in sodium-dried benzene under the same conditions. A brown oil precipitated, which was separated by decantation and thoroughly washed with sodium-dried benzene. Crystallisation from ethanol/Et_2O afforded a brown solid. A ^{31}P NMR spectrum showed the product was a mixture of the two following structures:



(132)



(133)

with signals at +21.9 ppm, and +11.8 and +45.8 ppm respectively. These assignments were corroborated by the ^1H NMR spectrum, from which a ratio 1 to 4 (132):(133) was calculated.

			δ(ppm) (J, Hz)		
Ratio	Ph_3P-	Ar-	$N-CH_2$-	$O-CH_2$-	$-CH_3$
(132) 1	7.56m	6.5s	-	-	-
(133) 4		6.52m	4.57d	4.15q	1.20t
			[$J^1H-^{31}P$):8.5]	(J_{HH}:7.3)	(J_{HH}:7.3)

The solid was suspended in sodium-dried benzene and stirred 48h at room temperature with a slight excess of KOH-dried triethylamine protected with a calcium chloride tube. Filtration yielded a mixture of (133) and triethylamine hydrobromide, and from the benzene filtrate TPPO and N-(o-aminophenyl)-ITPP (71) were identified. Finally, (133) was isolated

by washing the above mixture with distilled water. No adequate recrystallisation solvent was found.

<u>o-bis-ITPP-benzene mono-N-(ethyl α-acetate) bromide (133)</u>

Yield: (0.87 g, 1.1 mmol, 35%); mp: 202-5°C; IR: 1745 (C=O), 1440, 1115 (P-Ph), 1315 (P=N), 910 (P^+-N) cm^{-1}; UV λmax (nm) (logε): 206 (4.38); ^{31}P (NMR) ($CDCl_3$): +45.8, +11.8 ppm; ^1H NMR ($CDCl_3$): 7.53 (m, 15H, P-<u>Ph</u>), 6.50 (m, 4H, <u>Ar</u>-), 4.52 (d, $J(^1H\text{-}C\text{-}N\text{-}^{31}P)$: 8.8 Hz, 2H, N-$C\underline{H}_2$-), 4.14 (q, J_{HH}: 7.1 Hz, 2H, O-$C\underline{H}_2$-), 1.19 (t, J_{HH}: 7.1 Hz, 3H, -$C\underline{H}_3$) ppm.

<u>Reaction of o-bis-ITPP-benzene (67) with ethyl α-pyridinium acetate bromide (134)</u>

Ethyl α-pyridinium acetate bromide[145] was synthesised by mixing KOH-dried pyridine (0.01 mol) with excess ethyl α-bromoacetate (0.011 mol) in sodium-dried benzene (30 cm^3) and stirring the solution overnight at room temperature protected by a calcium chloride tube. Filtration afforded pure (134) (9 mmol, 91%).

o-bis-ITPP-benzene (67) (3.2 mmol) was suspended in phosphorus-pentoxide-dried acetonitrile (30 cm^3) with (134) (3.3 mmol) and refluxed during 16h under a nitrogen atmosphere. The solvent was removed under reduced pressure and the residue triturated with acetone. Filtration and recrystallisation from ethanol/Et_2O afforded o-bis-ITPP-benzene bis-hydrobromide (132) (1.23 mmol, 38%) identified by its ^{31}P and ^1H NMR spectra. The ^1H NMR spectra showed a small impurity tentatively assigned to unreacted pyridinium salt (134): ^1H NMR ($CDCl_3$): 9.92 (d, J_{HH}: 7.1 Hz, o-<u>H</u>), 4.2 (d, J_{HH}: 5.8 Hz, p-<u>H</u>), 8.19 (t, J_{HH}: 7.1 Hz, m-<u>H</u>), 4.27 (q, J_{HH}: 7.1 Hz, O-$C\underline{H}_2$-), 2.17 (s, N^+-$C\underline{H}_2$-), 1.29 (t, J_{HH}: 7.1 Hz, -$C\underline{H}_3$) ppm. All coupling constant values are very approximate and measurement of integrals was not possible.

From the acetone filtrate TPPO and N-(o-aminophenyl)-ITPP (71) were identified.

(b) Reactions with acid chlorides

Reaction of o-bis-ITPP-benzene (67) with ethyl oxalyl chloride

o-bis-ITPP-benzene (67) (1.6 mmol) was suspended in sodium-dried benzene and a slight excess ethyl oxalyl chloride (1.7 mmol) added to the stirred mixture. Reaction was carried out during 5.5h at room temperature under a nitrogen atmosphere and strictly anhydrous conditions. The reaction mixture was filtered and the benzene filtrate left standing overnight. A white precipitate formed, was separated, recrystallised from EtOH/ Et_2O and identified as 2-ethoxycarbonyl-benzimidazole hydrochloride (135) (1.06 mmol, 66%). The benzene solution was concentrated in vacuo, and the resulting residue recrystallised from acetone yielded (136) (1.9 mmol, 60%).

TPPO-salt (136)

mp (acetone): 131-5°C. IR: 2340 (br band), 1925 (br band), 1715 (C=O), 1440, 1120 (P-Ph), 1130, 1085, 1075, 995 cm^{-1}; UV λmax (nm) (logε): 272 (2.99), 265 (3.11), 222 (4.22), 210 (4.26); ^{31}P NMR ($CDCl_3$): +32.1 ppm; ^{1}H NMR ($CDCl_3$): 12.41 (s, 1H), 7.59 (m, 15H, P-Ph) ppm; ^{13}C NMR ($CDCl_3$): 160.1 (C=O), 132.14 (d, $J(^{13}C-^{31}P)$: 9.8 Hz, o-C), 132.29 (d, $J(^{13}C-^{31}P)$: 3.05 Hz, p-C), 128.59 (d, $J(^{13}C-^{31}P)$: 12.2 Hz, m-C), 131.6 (d, $J(^{13}C-^{31}P)$: 105.5 Hz, ipso-C) ppm; MS m/e: 323 ($M^{+\cdot}$) (0%), 278 (47%), 277 (100%), 201 (17%), 199 (19%), 185 (11%), 183 (15%), 152 (11%), 77 (22%), 51 (15%), 44 (31%); anal: calcd for $C_{19}H_{16}PO_3$: C: 70.58, H: 4.99, P: 9.58. Found: C: 70.66, H: 4.93, P: 9.67. Qualitative halogen test shows no presence of halogen ions.

2-Ethoxycarbonyl-benzimidazole hydrochloride (135)

mp (EtOH/Et_2O): 176-7°C (decomp); IR: 3570, 3340 (NH), 2460 (br band)(N^{+}-H), 1740 (C=O), 1260 (C-O) cm^{-1}; UV λmax (nm) (logε): 291 (4.09), 229 (3.80), 210 (3.79).

Compound (135) was stirred with excess KOH-dried triethylamine in sodium-dried benzene, filtered, concentrated under vacuum and recrystallised yielding 2-ethoxycarbonyl-benzimidazole (137)[84]: mp (AcOEt): 215-6°C; lit. mp: 212°C[84]; IR: 2800 (br band) (NH), 1755 (C=O), 1245 (C-O) cm^{-1}; ($CDCl_3$): 3460 (NH), 1725 (C=O), 1250 (C-O) cm^{-1}; UV λmax (nm) (logε): 290 (4.16), 229 (4.17), 207 (4.25); ^1H NMR ($CDCl_3$): 10.7 (br s, 1H, N<u>H</u>), 7.55 (m, 4H, <u>Ar</u>-), 4.52 (q, J_{HH}: 7.1 Hz, 2H, O-C<u>H</u>$_2$-), 1.45 (t, J_{HH}: 7.1 Hz, 3H, -C<u>H</u>$_3$) ppm; MS m/e: 190 ($M^{+\cdot}$) (24%), 145 (13%), 144 (24%), 118 (100%), 91 (10%), 90 (15%), 64 (7%), 65 (8%); accurate mass calcd[53] for $C_{10}H_{10}N_2O_2$: 190.0740. Found: 190.0742, anal: calcd. for $C_{10}H_{10}N_2O_2$: C: 63.15, H: 5.30, N: 14.73. Found: C: 62.92, H: 5.30, N: 14.68.

<u>Reaction of N-phenyl-ITPP (61) with ethyl oxalyl chloride</u>

N-phenyl-ITPP (61) (2.83 mmol) was dissolved in sodium-dried toluene (10 cm^3) under a nitrogen atmosphere and strictly anhydrous conditions and a slight excess of ethyl oxalyl chloride (2.9 mmol, 0.132 cm^3) was added after the above solution had been stirred 10 min. in an acetone/dry ice bath (-78°C). Reaction was practically instantaneous, the reaction mixture becoming a solid cake with the white precipitate formed. A further 10 cm^3 sodium-dried toluene were added and the product filtered. The product immediately decomposed either through hydrolysis and/or thermally, being unstable at room temperature. The oily resulting product was left overnight in a vacuum desiccator containing self-indicating silica gel, but no change was observed.

The reaction was repeated as described above. Once the white precipitate had formed the acetone/dry ice bath was removed and the mixture allowed to reach room temperature always under strictly anhydrous conditions. After 36h all the precipitate had disappeared showing the initially formed solid to be unstable at this temperature. A ^{31}P NMR

spectrum of the decomposed reaction mixture was recorded showing one signal at +25.7 ppm (toluene) assigned to TPPO.

The reaction was repeated a third time in an NMR tube using $CDCl_3$ as solvent and monitoring the reaction at -64°C and room temperature. (See Chapter 5)

The experiment was repeated once more changing the solvent to phosphorus pentoxide-dried acetonitrile and mixing the reagents at room temperature. A major signal at +45.2 ppm with two other medium signals at +43.4 ppm and +25.2 ppm were observed in the ^{31}P NMR spectrum. The reaction was rerun on a bigger scale (2.83 mmol) in an attempt to isolate the reaction product. The acetonitrile was finally removed under vacuum and the remaining white solid triturated with Et_2O without exposing it to the surrounding atmosphere. After 5 min, it was quickly filtered at the pump, decomposing immediately it came in contact with the atmosphere, showing how extremely sensitive to hydrolysis it is. From the resulting mixture TPPO was identified.

REFERENCES

1. G. Wittig and G. Geissler, Ann. Chem., 1953, 44, 580.

2. (a) G. Wittig, Pure Appl. Chem., 1964, 9, 243.
   (b) S. Trippett, Quart. Rev., 1963, 17, 406.
   (c) A. Maercker, Org. React., 1965, 14, 270.
   (d) A.W. Johnson, in 'Ylid Chemistry', Academic Press, New York, 1966.
   (e) A.J. Kirby and S.G. Warren, in 'The Organic Chemistry of Phosphorus', Elsevier, Amsterdam, 1967.
   (f) H.J. Bestmann, Newer Methods Prep. Org. Chem., 1968, 5, 1.
   (g) H.J. Bestmann, Bull. Soc. Chim. Fr., 1971, 1619.
   (h) H.J. Bestmann and R. Zimmermann, in reference 27.
   (i) M. Schlosser, Methodicum Chimicum (Ed. F. Korte), 1978, 7(B), 506.
   (j) K.R. Becker, Tetrahedron, 1980, 36, 1717.
   (k) 'Organophosphorus Reagents in Organic Synthesis', Ed. J.I.G. Cadogan, Academic Press, London, 1979.

3. H. Staudinger and J. Meyer, Helv. Chim. Acta, 1919, 2, 635.

4. H. Schmidbaur, Adv. Organometal. Chem., 1970, 9, 259.

5. E.W. Abel and S.A. Mucklejohn, Phosphorus and Sulfur, 1981, 9, 235.

6. (a) M. Grayson and E.J. Griffith Eds., 'Top. Phosphorus Chem.', all issues.
   (b) 'Organophosphorus Chemistry', Specialist Periodical Reports, Chem. Soc., all issues.

7. R.A. Shaw, B.W. Fitzsimmons and B.C. Smith, Chem. Rev., 1962, 62, 247.
   R.A. Shaw, Int. J. Phosphorus and Sulfur, 1978, 4, 101.
   S.S. Krishnamurthy and A.C. Sau, Adv. Inorg. Chem. Radiochem., 1978, 21, 41.

8. Editorial Report on Phosphorus Nomenclature, J. Chem. Soc. 1952, 5122.

9. Yu. G. Gololobov, I.N. Zhmurova and L.F. Kasukhin, Tetrahedron, 1981, 37, 437.

10. (a) H. Bock and M. Schmöller, Chem. Ber., 1969, 102, 38.
    (b) G. Wittig and K. Schwarzenback, Ann. Chem., 1961, 650, 1.

11. J.E. Leffler and R.D. Temple, J. Am. Chem. Soc., 1967, 89. 5235.

12. H.H. Sisler, A. Sarkis, H.S. Ahuja, R.J. Drago and N.L. Smith, J. Am. Chem. Soc., 1959, 81, 2982.

13 R. Appel and A. Hauss, Angew. Chem., 1959, 71, 628.

14. Ibid, Chem. Ber., 1960, 93, 405.

15. R. Appel and E. Gutch, Z. Naturforsch, 1960, 15b, 57.

16. R. Appel and A. Hauss, Angew. Chem., 1959, 71, 626.

17. R. Appel, G. Köhnlein and R. Schölhorn, Chem. Ber., 1965, 98, 1355.

18. H.H. Sisler, H.S. Ahuja and N.L. Smith, J. Org. Chem., 1961, 26, 1819.

19. E. Zbiral, Tetrahedron Lett., 1966, 2005.

20. F.G. Mann and E.J. Chaplin, J. Chem. Soc., 1937, 527.

A.F. Kirsanov, A.S. Shtepaneek and V.I. Schevchenko, Dopovidi Akad. Nauk. Ukr. RSR., 1962, 1, 63. [C.A. 57: 11229a].

V.I. Shevshenko, A.M. Pinchuk and A.V. Kirsanov, Zh. Obsch. Khim., 1965, 35, 1488. [C.A. 63: 14899g].

21. R. Appel. W. Büchner and E. Guth, Ann. Chem., 1958, 618, 53.

22. A.P. Claydon, P.A. Fowell and C.T. Mortimer, J. Chem. Soc., 1960, 3284.

23. A.V. Kirsanov and Z.D. Nekrasova, J. Gen. Chem. USSR., 1956, 26, 903. [C.A. 50: 14631].

24. V.I. Shevchenko, A.S. Shtepanek and A.M. Pinchuk, J. Gen. Chem. USSR., 1960, 30, 1566. [C.A. 55: 1490g].

H. Bock and W. WiegrÄbe, Angew. Chem., 1962, 74, 327.

25. R.D. Partos and A.J. Speziale, J. Am. Chem. Soc., 1965, 87, 5068.

26. R. Appel and R. Schöllhorn, Angew. Chem., 1964, 76, 991.

M. Zimmer and G. Singh, J. Org. Chem., 1964, 29, 1579.

27. H.J. Bestmann and R. Zimmermann, 'Organic Phosphorus Compounds', Vol.3, Ch .5A, Ed. G.M. Kosolapoff and L. Meyer, Wiley Interscience, 1972, and references cited therein.

28. L. Horner and H. Oediger, Ann. Chem., 1956, 627, 142.

29. (a) H.J. Bestmann, Angew. Chem., 1965, 77, 651.

(b) H.J. Bestmann and F. Seng, Angew. Chem., 1963, 75, 475.

(c) Ibid, Tetrahedron, 1965, 21, 1373.

30. G.W. Adamson and J.C.T. Bart, J. Chem. Soc. Chem. Commun., 1969, 1036.

G.W. Adamson and J.C.J. Bart, J. Chem. Soc.(A), 1970, 1452.

31. M.J.E. Hewlins, J. Chem. Soc.(B), 1971, 942.

32. A.F. Cameron, N.S. Hair and D.G. Norris, Acta Cryst. 1974, 30B, 221.

33. P.J. Butterfield, J.C. Tebby and T.J. King, J. Chem. Soc. Perkin I, 1978, 1237.

34. L. Pauling, 'The Nature of the Chemical Bond', 3rd Ed, Cornell Univ. Press, Ithaca, NY 1960.

35. (a) K.A. Ostoja Starzewski and H. Bock, J. Am. Chem. Soc., 1976, 98, 8486.

(b) K.A. Ostoja Starzewski and H. Tom Dieck, Inorg. Chem., 1979, 18, 3307.

36. W.B. Perry, T.F. Schaaf and W.L. Jolly, J. Am. Chem. Soc., 1975, 97, 4899.

37. (a) H. Lumbroso, D.M. Bertin and P. Frøyen, Bull. Soc. Chim. Fr., 1974, 5-6, 819.

(b) A.E. Lutskii, L.I. Samarai, L.A. Kochergina, A.V. Shepel, Z.A. Shevchenko, G.I. Derkach, E.S. Kozlov and B.S. Drach, Zh. Obshch. Khim, 1967, 37, 2042. [C.A. 68, 34387a].

(c) Y.Y. Borovikov, Y.P. Egorov, I.N. Zhmurova, V. Kukhar, A.A. Tukhar and R.I. Yurchenko, Teor. Eksp. Khim., 1974, 10, 207.

38. J.E. Anderson and J.M. Lehn, Tetrahedron, 1968, 24, 123.

39. R.F. Hudson, 'Structure and Mechanism in Organo-Phosphorus Chemistry', Ed. A.T. Blomquist, Academic Press, 1965.

40. (a) M.I. Kabatschnik, Phosphorus, 1971, 1, 117.

(b) I.N. Zhmurova, R.I. Yurchenko, A.A. Tukhar', V.G. Yurchenko and O.M. Voitsekhovskaya, J. Gen. Chem. USSR., 1979, 49, 2119.

(c) R.A. Shaw, Phosphorus and Sulfur, 1979, 5, 363.

41. M.F. Meidine, PhD Thesis, CNAA 1982, and references cited therein.

42. E.M. Briggs, G.W. Brown, P.M. Cairns, J. Jiricny and M.F. Meidine, Org. Mag. Res., 1980, 13, 306.

43. J. Bödeker, P. Köckritz, H. Köppel and R. Radeglia, J. Prakt. Chem., 1980, 322, 735.

44. E. Vedejs, G.P. Meier and K.A.J. Snoble, J. Am. Chem. Soc., 1981, 103, 2823, and references cited therein.

45. T.A. Albright, W.J. Freeman and E.E. Schweizer, J. Org. Chem., 1976, 41, 2716.

46. H. Koehler and B. Kottle, Z. Chem., 1973, 13, 350.

47. T.A. Albright, W.J. Freeman and E.E. Schweizer, J. Am. Chem. Soc., 1975, 97, 940.

48. W.T. Dawson, PhD Thesis, University of London, 1975.

49. T.A. Albright, W.J. Freeman and E.E. Schweizer, J. Am. Chem. Soc., 1976, 98, 6249.

50. Ibid, J. Org. Chem., 1975, 40, 3437.

51. L.C. Thomas and R.A. Chittenden, Spectrochim. Acta., 1965, 21, 1905. [C.A., 64: 168f].

52. W. Wiegräbe, H. Bock and W. Lüttke, Chem. Ber., 1966, 99 3737.

53. E. Pretsch, T. Clerc, J. Seibl and W. Simon, in 'Tabellen Zur Strukturaufklärung Organischer Verbindungen mit Spektroskopischen Metoden', Springer Verlag - Berlin - Heidelberg - New York, 1976.

54. W. Wiegräbe and H. Bock, Chem. Ber., 1968, 101, 1414.

55. H.W. Roesky and L.F. Grimm, Angew. Chem. Int. Ed., 1970, 9, 244.

56. A.S. Tarasevich and Y.P. Egorov, Teor. Eksp. Khim., 1971, 7,828.

57. J. Jiricny, PhD Thesis, University of London, 1977.

58. I.N. Zhmurova and R.I. Yurchenko, J. Gen. Chem. USSR, 1968, 38, 613.

59. E.M. Briggs, G.W. Brown, J. Jiricny, M.F. Meidine, Synthesis, 1980, (4), 295.

60. G.W. Brown, J. Chem. Soc. (C), 1967, 2018.

61. L. Horner and H. Winkler, Tetrahedron Lett., 1964, 175.

62. H. Zimmer and G. Singh, J. Org. Chem., 1963 28,483. Ibid, J. Org. Chem., 1970, 35, 2826.

63. C.C. Walker and H. Shechter, J. Am. Chem. Soc., 1968, 90, 5626.

64. R. Appel and G. Siegmund, Z. Anorg. Chem., 1968, 363, 183.

65. E. Zbiral and J. Stroth, Ann. Chem., 1969, 727, 231.

66. P. Molina, M. Alajarin, A. Arques and R. Benzal, J. Chem. Soc. Perkin I, 1982, 351.

67. T. Sasaki, S. Eguchi and T. Okano, J. Am. Chem. Soc., 1983, 105, 5912.

68. E. Zbiral and E. Bauer, Phosphorus, 1972, 2, 35.

69. E. Zbiral, E. Bauer and J. Stroth, Monatsh. Chem., 1971. 102, 168.

70. E. Zbiral and J. Stroth, Ann. Chem., 1969, 725, 29.

71. H.B. Stegmann, F. Stöcker and G. Wax, Synthesis, 1981, 816.

72. P, Molina, M. Alajarin and J. Saez, Synth. Commun., 1983, 13, 67.

73. G.W. Brown, R.C. Cookson and I.D.R. Stevens., Tetrahedron Lett., 1964, 1263.

74. R. Appel and M. Halstenberg, Chem. Ber., 1976, 109, 814.

75. Y. Ittah, Y. Sasson, I. Shahak, S. Tsaroom and J. Blum, J. Org. Chem., 1978, 43, 4271.

76. A. Hassner and J.E. Galle, J. Am. Chem. Soc., 1970, 92, 3733.

77. J.A. Kloek and K.L. Leschinsky, J. Org. Chem., 1978, 43, 1460.

78. G. Wittig and A. Maercker, Chem. Ber., 1964, 97, 747.

79. T.W. Campbell, J.J. Monagle and V.S. Foldi, J. Am. Chem. Soc., 1962, 84, 3673.

J.J. Monagle, T.W. Campbell and H.F. McShane, .J. Am. Chem. Soc., 1962, 84, 4288.

80. J.J. Monagle, J. Org. Chem., 1962, 27, 3851.

81. A.W. Johnson and S.C.K. Wong, Can. J. Chem., 1966, 44, 2793.

82. Ibid, J. Org. Chem., 1972, 37, 1850.

83. G. Asknes and P. Frøyen, Acta Chem. Scand., 1969, 23, 2697.

84. R.A.B. Copland and A.R. Day, J. Am. Chem. Soc., 1943, 65, 1027.

85. (a) G.V. Howell and R.L. Williams, J. Chem. Soc.(A), 1968, 117.

(b) D. Hadzi, J. Chem. Soc., 1962, 5128.

(c) R.D. Temple, Y. Tsuno and J.E. Leffler, J. Org. Chem., 1963, 28, 2495.

86. W.L. Mock and M.E. Hartman, J. Am. Chem. Soc., 1970, 92, 5767.

87. A. Schmidpeter and T. von Criegern, Angew. Chem. Int. Ed., 1978, 17, 55.

88. P. Frøyen, Acta Chem. Scand., 1972, 26, 1777.

89. J.D. Thacker, M.H. Whangbo and J. Bordner, J. Chem. Soc. Chem. Commun. 1979, 1072.

90. D.W. Allen and H. Ward, Tetrahedron Lett., 1979, 2707.

91. H.J. Bestmann, Pure Appl. Chem., 1979, 51, 515.

92. Ibid, 1980, 52, 771.

93. A.B. Reitz, M.S. Mutter and B.E. Maryanoff, J. Am. Chem. Soc., 1984, 106, 1873.

94. W.P. Schneider, J. Chem. Soc. Chem. Commun., 1969, 785.

95. H.B. Bürgi, J.G. Dunitz, J.M. Lehn and G. Wipf, Tetrahedron, 1974, 30 1563.

96. E. Vedejs and K.A.J. Snoble, J. Am. Chem. Soc., 1973, 95, 5778.

97. M. Schlosser, Top. Stereochem., 1970, 5, 1.

98. E.J. Dewitt, C.T. Lester and G.A. Ropp, J. Am. Chem. Soc., 1956, 78, 2101.

D.N. Matthews and E.I. Becker, J. Org. Chem., 1966, 31, 1135.

R. Sustmann, Tetrahedron Lett., 1974, 963.

99. P. Frøyen, Acta Chem. Scand., 1972, 26, 2163.
G. Aksnes, F.Y. Khalil, Phosphorus, 1972, 2, 105 and 1973, 3, 79.
N.A. Nesmeyanov, E.V. Vishtok and U.A. Reutov, Dokl. Akad. Nauk. SSSR., 1973, 210, 1102.

100. E.J. Corey and G.T. Kwiatkowski, J. Am. Chem. Soc., 1966, 88, 5653.

101. C.C. Leznoff, Chem. Soc. Rev., 1974, 3, 65.

102. E.M. Briggs, G.W. Brown, W.T. Dawson and J. Jiricny, J. Chem. Soc. Chem. Commun., 1975, 641.

103. R. Appel, F. Knoll, W. Michel, W. Morbach, H. Wihler and H. Veltmann, Chem. Ber., 1976, 109, 58.

104. N.I. Gusar, M.P. Chaus and Yu. G. Gololobov, Zh. Obshch. Khim., 1979, 49, 21. [C.A. 90: 187041n].

105. C.M. Dougherty, R.L. Baumgarten, A. Sweeney Jr. and E. Concepcion, J. Chem. Educ., 1977, 54, 643.

106. P.M. Cairns, Private communication.

107. H.B. Stegmann, K. Scheffler, G. Bauer, R. Grimm, S. Hieke and D. Stürner, Phosphorus, 1974, 4, 165.

108. H.B. Stegmann, G. Bauer, E. Breitmaier, E. Herrmann and K. Scheffler, Phosphorus, 1975, 5, 207.

109. W.A. Sexton, J. Chem. Soc., 1942, 303. For revised compound assignments see J. Davoll, J. Chem. Soc., 1960, 308.

110. F. Kaplan, G. Singh and H. Zimmer, J. Phys. Chem., 1963, 67, 2509.

111. H. Budzikiewicz, C. Djerassi and D.H. Williams, in 'Mass Spectrometry of Organic Compounds', Holden-Day Inc., 1967, San Francisco.

112. See for example, J. March in 'Advanced Organic Chemistry', 2nd Ed., McGraw-Hill Kogakusha Ltd., 1977.

113. A.I. Vogel, in 'A Textbook of Practical Organic Chemistry', 3rd Ed., Longman, London, 1972.

114. Handbook of Chemistry and Physics, 55th Ed., CRC Press, Ohio, USA, 1974-5.

115. Dictionary of Organic Compounds, 4th Ed., Eyre and Spottiswoode (Publishers) Ltd., London, 1965.

116. W.E. Hanford and J.C. Sauer, Org. React., 1946, 3, 124.

117. C.J. Pouchert, 'Aldrich Library of Infrared Spectra', 2nd Ed., Aldrich Chemical Company, 1975.

118. G.D. Lander, J. Chem. Soc., 1902, 591.

119. P.A. Petyunin and A.V. Storozheva, Zh. Obshch. Khim., 1962, 32, 1395. [C.A. 58: 4449b].

120. K. Fukui and R. Sudo, Bull. Chem. Soc. Jpn., 1970, 43, 110.

121. (a) M.D. Bachi and J. Vaya, J. Org. Chem., 1979, 44, 4393.

(b) T. Hiraoka, K. Iino, Y. Iwano, T. Saito and Y. Sugimura, Chem. Soc. Spec. Publ., 1977, No28, 126.

122. M.A. Phillips, J. Chem. Soc., 1928, 172 and 2393.

123. M.A. Phillips, J. Chem. Soc., 1928, 2820.

124. C.J. Pouchert and J.R. Campbell, 'Aldrich Library of ^{1}H NMR Spectra', Aldrich Chemical Company 1974.

125. J.B. Stothers, 'Carbon 13 NMR Spectroscopy', Academic Press, New York 1972, pp.264-5.

126. Chemistry of Carbon Compounds, Ed. E.H. Rodd, Elsevier Publishing Company, Amsterdam-New York, 1962.

127. J. Harley-Mason and T.J. Leeney, Proceedings Chem. Soc., 1964, 368.

128. H. Plieninger, U. Lerch and D. Wild, Angew.Chem, Inter. Ed., 1965, 4, 520.

129. L.H. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance to Organic Chemistry', International Series of Monographs in Organic Chemistry, Ed. D.H.R. Barton and W. Doering, Vol.5, 2nd Ed., Pergamon Press, 1969.

130. B. Chatterjee, J. Chem. Soc., 1929, 2965.

131. R.L. Clark and A.A. Pessolano, J. Am. Chem. Soc., 1958, 80, 1657.

132. J. Davoll and D.H. Laney, J. Chem. Soc., 1960, 314.

133. J. Davoll, J. Chem. Soc., 1960, 308.

134. D. Harrison and H.W. Jones, J. Chem. Soc. (C), 1969, 886.

135. D.J. Brown and R.K. Lynn, J. Chem. Soc. Perkin I, 1974, 349.

136. A. Hunger, J. Kebrle, A. Rossi and K. Hoffmann, Helv. Chim. Acta., 1961, 44, 1273.

137. S. Takahashi and H. Kano, Chem. Pharm. Bull. (Tokyo), 1964, 12, 282. [C.A. 60: 15859e].

138. K.W. Lee and L.A. Singer, J. Org. Chem., 1974, 39, 3780.

139. T.A. Savel'eva and A.V. Belotsvetov, Uch. Zap. Mosk. Gos. Pedagog. Inst., 1971, No.464, 171. [C.A. 77: 113275b].

140. Ibid., Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhol. 1976, 19, 790, [C.A. 86: 42599k].

141. A.C. Satterthwait and F.K. Westheimer, J. Am. Chem. Soc., 1980, 102, 4464.

142. Y. Nomura, Y. Kikuchi and Y. Takeuchi, Chem. Lett. (Tokyo): 1974, 575.

143. N.L. Poznanskaya, S.N. Ivanova, N.N. Mel'nikov and N.I. Shvetsov-Shilovskii, Khim. Geterotsikl. Soedin, 1967, (3), 427, [C.A. 68: 68914k].

144. I. Schuster, Tetrahedron, 1977, 33, 1075.

145. E.D. Bergmann, H. Bendas and Ch. Resnick, J. Chem. Soc. 1953, 2564.

146. R. Bonnett, in 'The Chemistry of the Carbon-Nitrogen Double Bond', Ed. S. Patai, J. Wiley and Sons, 1970.

147. 'The Chemistry of Amidines and Imidates', Ed. S. Patai, J. Wiley and Sons, 1975.

148. A. Sonn and E. Müller, Chem. Ber., 1919, 52, 1927.

J. von Braun and W. Rudolph, Chem. Ber., 1934, 67, 269, and 1735.

149. E. Mosettig, Org. React., 1954, 8, 218.

150. H. Wamhoff, G. Haffmanns and H. Schmidt, Chem. Ber., 1983, 116, 1691.

151. L. Tokes and S.C.K. Wong, Org. Mass Spectrometry 1970, 4 (Suppl.), 59.

152. In reference 6b, Vol.1.

153. A.P. Gara, R.A. Massey-Westropp and J.H. Bowie, Austral. J. Chem., 1970, 23, 307.

R.T. Aplin, A.R. Hands and A.J.H. Mercer, Org. Mass Spectrometry, 1969, 3, 1017.

154. M. Le Corre, Bull. Chim. Soc. Fr., 1974, 2005.

A. Hercouet and M. Le Corre, Tetrahedron Lett., 1979, 5.

B. Begasse, A. Hercouet and M. Le Corre, Tetrahedron Lett., 1979, 2145 and 2149.

A. Hercouet and M. Le Corre, Tetrahedron Lett., 1979, 2995.

Ibid., Tetrahedron, 1981, 37, 2867.

A.P. Uijttewaal, F.L. Jonkers and A. van der Gen, J. Org. Chem., 1978, 43, 3306.

Ibid., J. Org. Chem., 1979, 44, 3157.

P. Babin and J. Dunogues, Tetrahedron Lett., 1983, 3071.

155. A.J.G. Baxter, R.J. Ponsford and R. Southgate, J. Chem. Soc. Chem. Commun., 1980, 429.

156. D.W. Knight and G. Pattenden, J. Chem. Soc. Perkin I, 1979, 62.

157. A. Gossauer, F. Roebler, H. Zilch and L. Ernst, Liebigs Ann. Chem., 1979, 9, 1309.

158. M. Le Corre, A. Hercouet and H. Le Baron, J. Chem. Soc. Chem. Commun., 1981, 14.

J.V. Cooney and W.E. McEwen, J. Org. Chem., 1981, 46, 2570.

159. J.W. Schulenberg and S. Archer, Org. React., 1965, 14, 1.

D55269/85

END