SOME ASPECTS

OF

ORGANO-PHOSPHORUS CHEMISTRY.

by

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A Thesis

presented for

the degree of

Doctor of Philosophy

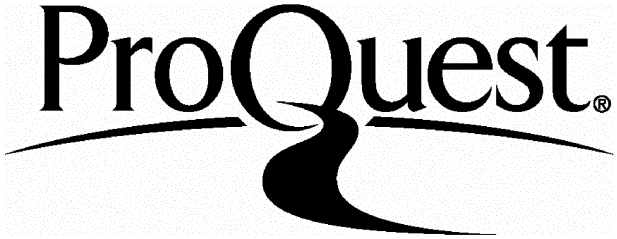
in the

Faculty of Science

of the

University of Leicester.

1976.



TO

MY COUNTRY, EGYPT,

MOTHER AND FATHER,

SORIA, ASSER AND SHADY.

STATEMENT.

The experimental work described in this thesis has been carried out by the author in the laboratories of the Department of Chemistry of the University of Leicester, between November, 1971 and November, 1974.

No part of this work has been presented or is concurrently being presented for any other degree.

Signed.

Hassan Aly
Feb 1976

February, 1976.

H. Abu-El-Seoud Aly.

ACKNOWLEDGEMENTS.

I am indebted to Professor S. Trippett for his ever so kindly encouragement, understanding and helpful suggestions.

I also wish to thank Dr. D.J.H. Smith for his constant supervision, for his many helpful criticisms, and guidance throughout the writing up of this thesis.

In addition I wish to express my thanks to Mrs. Sheila Davies for help in carrying out the n.m.r. spectra and for her cheerful character, to Mrs. N. Johnson for typing the thesis, and to Mrs. M.E. Warner.

I am especially grateful to my late mother and my father for their sacrifices and affection, to my wife, Soria, for being a tower of strength, support, help and comfort, to my daughter, Asser, for her charming smile, and to my brothers, family and colleagues in Egypt.

Finally, it is a pleasure to thank all members of the Chemistry Department, especially my colleague, Mr. S. Bone, and to thank the Egyptian Government for a maintenance grant during my study, which proved to be one of the happiest periods in our life.

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Abbreviations used in this thesis.

TBP = trigonal bipyramid(al)

BPR = Berry pseudorotation

TMP = 2,4,4-trimethyl-2-pentene

TR = turnstile rotation

a = apical

e = equatorial

PMR = principle of microscopic reversibility

d.n.m.r. = dynamic nuclear magnetic resonance

SUMMARY

Chapter 1 represents a review on the synthesis and structure of 1-substituted 2,2,3,4,4-pentamethylphosphetans.

In Chapter 2 the stereochemistry and mechanism of base-catalysed phosphetanium salt hydrolysis are envisaged and shown to depend upon the reaction conditions, in particular the pH of the medium. The results are interpreted in terms of the intermediacy of TBP structural phosphoranes, and the most significant role of the BPR as a viable mechanism for intramolecular isomerization of such intermediates, in determining the products distribution, is discussed. The possibility of a pre-decomposition equilibrium between diastereomeric salts *via* pseudorotation is considered and shown to occur, specifically, in very dilute alkaline media. A change in the reaction rate-limiting step from a slow isomerization process to a phosphorane decomposition is postulated to account for variation in product composition on varying the conditions. The alkaline hydrolysis of *r*-1-substituted acetylenic 2,2,3-*trans*-4,4-pentamethylphosphetanium bromides proceeds, in contrast to the generally reported retention as the stereochemically preferred pathway for phosphetans, with complete inversion of configuration.

Base-catalysed ring expansions of a number of salts are shown to proceed, stereospecifically, to give only one observable product oxide. This is attributed to a very short-lived intermediate phosphorane. In the end a qualitative scale of the relative apicophilicities of the studied groups, is observed.

In Chapter 3, an attempt to synthesise the 1:2 adducts of 1-substituted acetylenic-2,2,3,4,4-pentamethylphosphetan with HFA

resulted in formation of other products for which a probable mechanism and structures, based on spectroscopic and elemental analysis data are discussed and suggested for each product.

A variety of phosphoranes containing phosphetan rings was synthesised. A kinetic study of the rate of reaction of 2-ethoxy--1,3,2-dioxaphospholan with benzil showed the reaction to follow a bimolecular step-wise mechanism.

Relative apicophilicities of a number of groups attached to the phosphorus atom in phosphetan adducts were determined by monitoring the high energy isomerization pathways, accessible to these adducts, in which the five-membered rings span diequatorial positions, using ^{1}H n.m.r. spectroscopy techniques. The values so determined are rationalised in terms of substituent electronegativities and the extent of a probable π-electron interaction with the phosphorus d-orbitals.

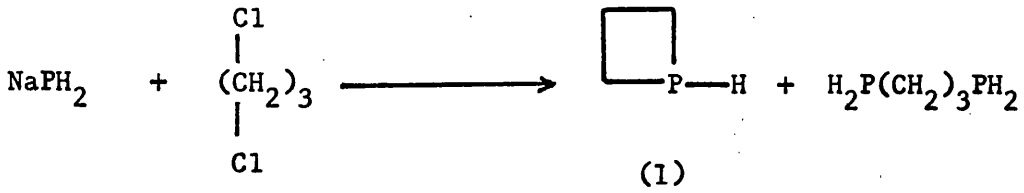
CHAPTER 1

THE SYNTHESIS OF PHOSPHETAN COMPOUNDS.

1.1 General Ring Synthesis.

Phosphetans or phosphacyclobutanes are compounds in which the phosphorus atom and three more carbon atoms form a four-membered ring. Due to the particular characteristics associated with the phosphetan ring (Section 1.2), many attempts to extend well established phosphorus heterocycle synthetic methods to phosphetan preparation resulted in not much success. Hence, there are only a limited number of reports which have described the successful synthesis of the phosphetan ring system.[1-5]

The reaction of substituted phosphines or phosphides with dihalogenoalkanes proceeds generally, to give phosphorus heterocyclic compounds.[3,4,6] Using this same approach, the phosphetan (1) has been successfully obtained[3] by reacting sodium phosphide with 1,3-dichloropropane.

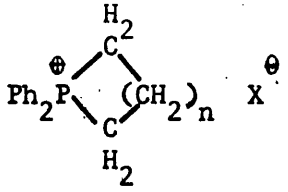


(1)

The reaction of secondary phosphines and phosphides with dihaloalkanes has been shown[7,8,9] to give an intermediate (2), which at once quaternizes intramolecularly to the cyclic phosphonium salts (3).

$XCH_2(CH_2)_nCH_2X$

\+ Ph_2PK (H) $\longrightarrow$ $Ph_2PCH_2(CH_2)_nCH_2X$ (2) $\longrightarrow$ (3)

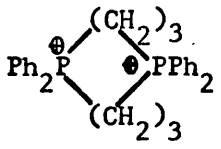


X = Br & I.

n = 2,3 &4.

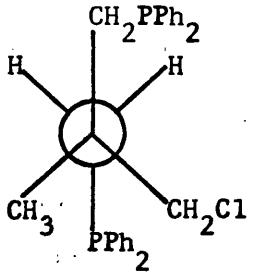
No other product but the bisphosphonium salt (4) has been obtained on reacting diphenyl phosphine with di-iodopropane[9]. The phosphetan

Ph_2PH + $I\text{-}(CH_2)_3\text{-}I$ $\longrightarrow$ (4) $2I^{\ominus}$

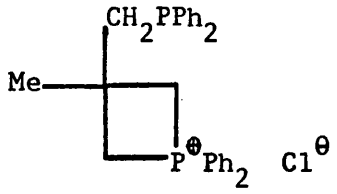


(5), however, has been formed by this route[10]; probably <u>via</u> an intermediate (6).

2 Ph_2PNa + $CH_3C(CH_2Cl)_3$ $\longrightarrow$ $Ph_2PCH_2\text{-}C(CH_2Cl)(CH_3)\text{-}CH_2PPh_2$ (6) $\equiv$



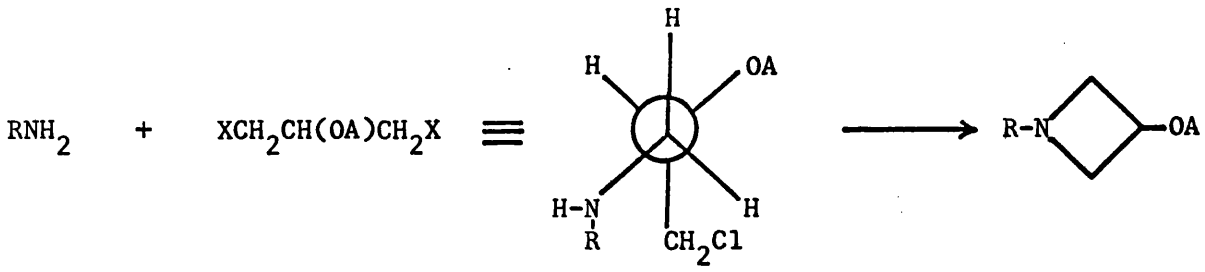
(6) $\longrightarrow$ (5)



Intramolecular quaternization of the intermediates (2) and (6) has been suggested to occur in such reactions. Steric effects seem to

influence the reaction outcome. For the intermediate (6) a Newman projection shows the influence of the large bulky groups present in effecting a favourable and suitable conformation for cyclisation to take place.

Similar argument has been advanced to account for the formation of the analogous azetidines from amines[11,12]. The results obtained are consistent with the azetidine formation being governed by the total bulk of the RNH- and -OA groups. When the sum of the steric bulk is increased, the conformation of the intermediate approaches the eclipsed transition state required for cyclisation, and this promotes azetidine formation.

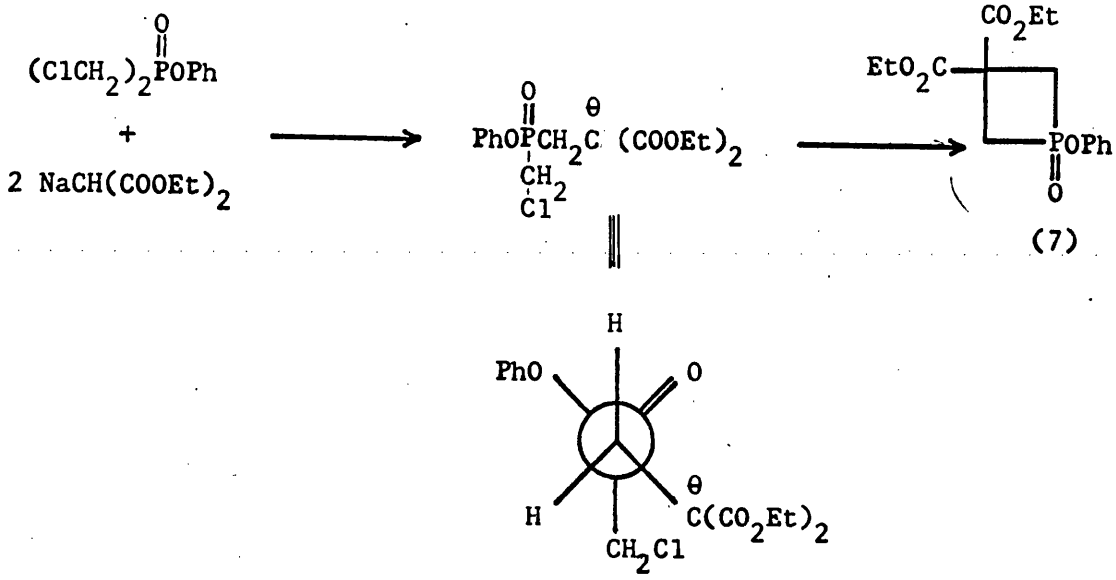


X = Cl or Br.

R = CH_3, n-C_4H_9, $PhCH_2$- & $PhCH_2CH_2$-.

A = H, $OCH_2—CH_3$.

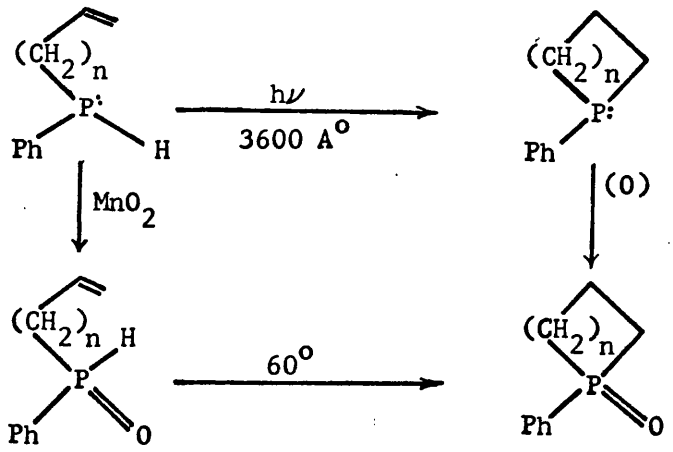
The formation of the phosphetan (7), has also been achieved when bis(chloromethyl)phosphinate was treated with two equivalents of sodiumdiethyl malonate. The cyclisation of the intermediate (8) was also enhanced by bulky substituents[13].



(7)

(8)

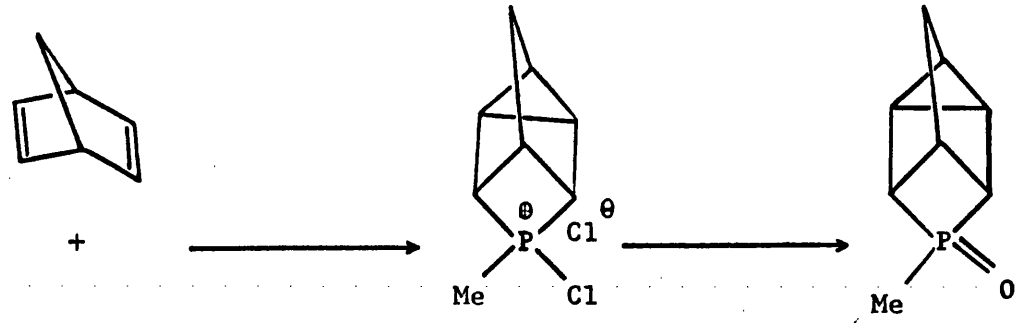
Cyclic phosphines having five, six and seven-membered rings have been prepared from secondary phosphines possessing a terminally unsaturated



n = 2,3&4.

alkenyl group, under the influence of u.v. radiation[14]. However, when n=1, polymeric material resulted under the same conditions.

The highly substituted phosphetan oxide (9) was obtained by allowing methylphosphonous dichloride to react with bicyclo 2,2 heptadiene[2].

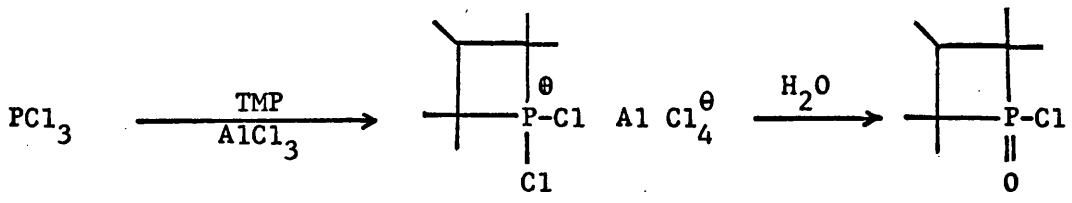


(9)

Attempts to prepare the analogous phenyl phosphetan oxide by Corfield[15], proved to be successful. Catalytic amounts of aluminium chloride had to be added to the reaction mixture to obtain the desired product.

1.2 2,2,3,4,4-Pentamethylphosphetan Oxides.

The successful synthesis of the phosphetan acid chloride (10) by addition of a mixture of phosphorus trichloride and aluminium chloride to 2,4,4-trimethyl-2-pentene (TMP) was first described by Jungermann[4] in 1962.



(10a)

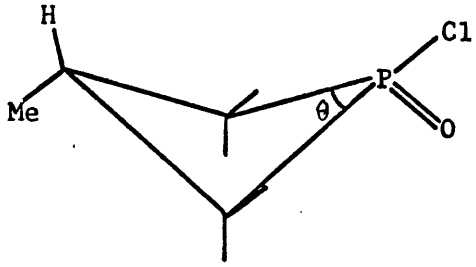
Generalisation of this reaction has led to the preparation of many substituted phosphetans with between three and five methyl substituents on the carbon atoms of the four-membered ring, and groups other than chlorine on the phosphorus atom[16-19].

The substituents on the phosphetan ring 3-carbon allow for two geometrical isomers of (10) to exist. However, only one of them was formed, of which X-ray analysis[20] showed that:

(a) The 3-methyl group was trans to the 1-chloride atom on phosphorus

(b) The four-membered ring was puckered.

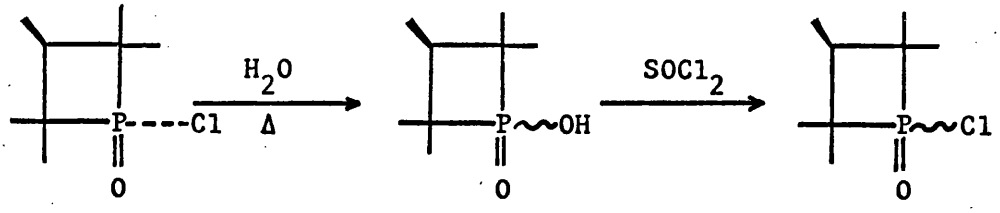
(c) The angle (θ) was considerably distorted from the tetrahedral.



(10a)

The synthesis of the cis-acid chloride (10b) was of interest for the preparation of the cis-isomers of the phosphetan oxides studied in this thesis.

The trans-acid chloride (10a) was reported[4] to give, on refluxing with water for 2 hr, the dihydrated acid (11), which can be converted to its anhydrous form by either vacuum drying or by heating above its melting point. A predominance (3:2) of the cis-acid chloride (10b) was obtained[21] by heating the acid (11) with thionyl chloride in benzene (5hr at reflux temperature).



(10a) (11) (10a+10b)

However, McBride[4] has implied that thionyl chloride treatment of anhydrous acid (11), gave back the starting isomeric acid chloride. Due to this confusion in the literature on the preparation of the isomers of (2), the situation seemed worth re-investigating.

The crystalline anhydrous acid (11) was obtained by vacuum drying the dihydrate for 12hr. Dehydration by refluxing the dihydrate in toluene, using a Dean-Stark apparatus, resulted in less acid being recovered. Refluxing the anhydrous acid with excess thionyl chloride in benzene for 1hr gave only the trans-acid chloride (10a). Hence, the chlorination step was repeated at 60°. The acid consumption and the production of the acid chloride was monitored by ^{1}H n.m.r. spectroscopy. A predominance of the cis-isomer (10b), of ca 65%, was achieved within 4hr. The amount of the cis-isomer (10b) can be increased to ca 80% by reaction of the acid with thionyl chloride at room temperature. This ratio cannot be increased by recrystallisation.

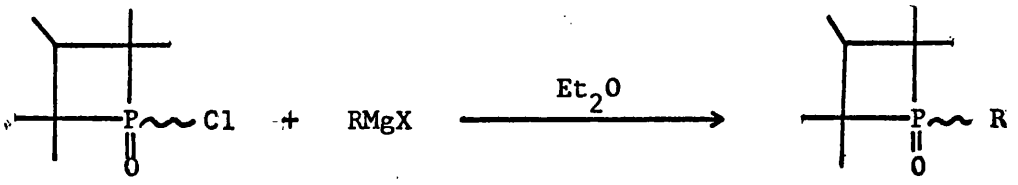
The solid mixture, predominant in the cis-isomer, isomerised completely to the trans-isomer over a period of one month, even when stored at -25°C.

Modification of the Jungermann and McBride synthesis[4] resulted in the preparation of the 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxide as a mixture of stereoisomers[16,17]. When using phenyl phosphonous dichloride in place of phosphorus trichloride, the isomer composition of the product was found to be dependent upon the work-up procedure. The isomer separation has been achieved by fractional recrystallisation and more readily by column chromatography on basic alumina[22]. The structures of the two isomers, examined by X-ray analysis[23,24], show that both isomers have puckered rings and C(2)-P(1)-C(4) angles of ca 82° indicating a

similar distortion to that found in the trans-phosphetan acid chloride (10a). It was found that the isomer having m.p. 126-127°C had the 3--methyl trans- to the 1-phenyl, while the cis-isomer melted at 117-118°C.

As the isomeric oxides are readily distinguishable by ^{1}H n.m.r. spectroscopy, this technique has been used to determine the isomer composition of the products in this and related cases.

The 2,2,3,4,4-pentamethylphosphetan 1-oxides (12-14) used for studies described in this thesis have been readily synthesised by the reaction of Grignard reagents with cis- and trans-1-chloropentamethyl-phosphetan 1-oxide. The reaction proceeds smoothly with retention of configuration.



(10)

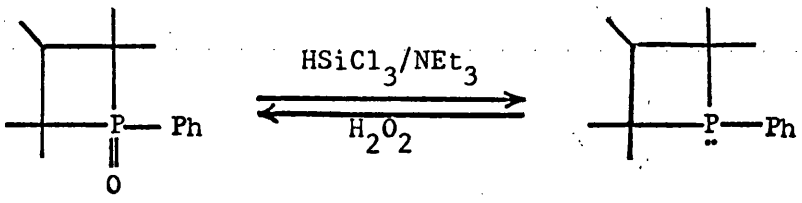
(12) R = Me
(13) R = CH_3-C≡C-
(14) R = Ph-C≡C-

The pure trans-oxides were easily obtained from the trans-acid chloride (10a), but, for the cis-oxides, mixtures of isomers of the acid chloride highly enriched in the cis-isomer have been used and the single isomeric oxides separated by fractional crystallisation.

1.3 Preparation of 2,2,3,4,4-Pentamethylphosphetans by Reduction of 2,2,3,4,4-Pentamethylphosphetan 1-Oxides.

Cremer[16] demonstrated that the isomeric 2,2,3,4,4-pentamethyl-1--phenylphosphetan 1-oxides (15) could be reduced using trichlorosilane

as the reducing agent in the presence of triethylamine to give the phosphetans (16).



(15) (16)

The reduction proceeds with retention of configuration at phosphorus, as oxidation by hydrogen peroxide gives back the starting isomer in each case[25].

The phosphetan oxides (13, 14) can also be reduced stereospecifically by this technique, as shown by ^{1}H n.m.r. spectroscopy and preparation of their adducts with α-diketones (see Section 3.11). In the case of (12), although the reduction of the trans-oxide with trichlorosilane proceeded stereospecifically to give the corresponding phosphetan, the cis-isomer could not be satisfactorily reduced (see Section 3.11). Attempts to reduce the single isomeric oxides or mixtures of both isomers using neat phenylsilane have been tried. This reduction proceeded non-stereospecifically, giving the corresponding phosphetans as mixture of isomers. The reduction in this case proved to be dependent upon the reaction conditions, particularly upon the temperature selected. This may be due to the energy barrier to pyramidal inversion in this compound being relatively low, thus permitting equilibration between the isomeric phosphetans. Mislow[26] has suggested the combination of steric factors and (P-p)π-bonding between the lone pair and the π- orbitals

of the phenyl group in 1-phenylphosphetan, to be responsible for the lower barrier to pyramidal inversion observed in this case.

However, although the reaction of the phosphetans with tetra-chloro-o-benzoquinone gave a mixture of products, the only isolable compound,(R≡Me),was the trans-adduct and some other unknown products. The cis-adduct has not been isolable under these conditions.

CHAPTER 2

ALKALINE HYDROLYSIS OF PHOSPHONIUM SALTS.

2.1 Alkylarylphosphonium Salts.

The alkaline hydrolysis of quaternary phosphonium salts results in the formation of phosphine oxides and hydrocarbons, in contrast to their ammonium analogues which give amines and olefins by β-elimination[27]. These differences are thought to arise because of the nitrogen inability to form a pentaco-ordinate intermediate which is accessible to phosphorus with its greater radius and the possibility of d-orbital participation. Fenton and Ingold[28] investigated the relative extents of hydrolysis and β-elimination in phosphonium salts possessing a β-proton and they suggested that olefin formation depends upon the extent to which the β-hydrogen is activated or deactivated by the substituents on the β-carbon.

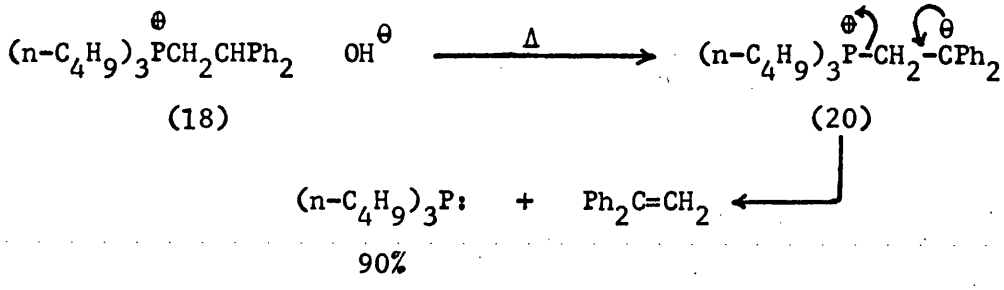
Substituents which would increase the acidity of that proton should favour the formation of an olefin and phosphine. Thus, while the decomposition of (β-phenethyl)triethylphosphonium hydroxide (17) gave essentially phosphine oxide and hydrocarbon with the formation of some olefin, β, β-diphenyl-tri-n-butylphosphonium hydroxide (18) decomposed mainly to olefin and phosphine[28,29]. This is probably due to the

$$PhCH_2CH_2\overset{\oplus}{P}(CH_2CH_3)_3\ OH^{\ominus} \xrightarrow{\Delta} PhCH_2CH_2\overset{O}{\overset{\|}{P}}(CH_2CH_3)_2 + (CH_3CH_2)_3P{=}O$$

(17) 95%

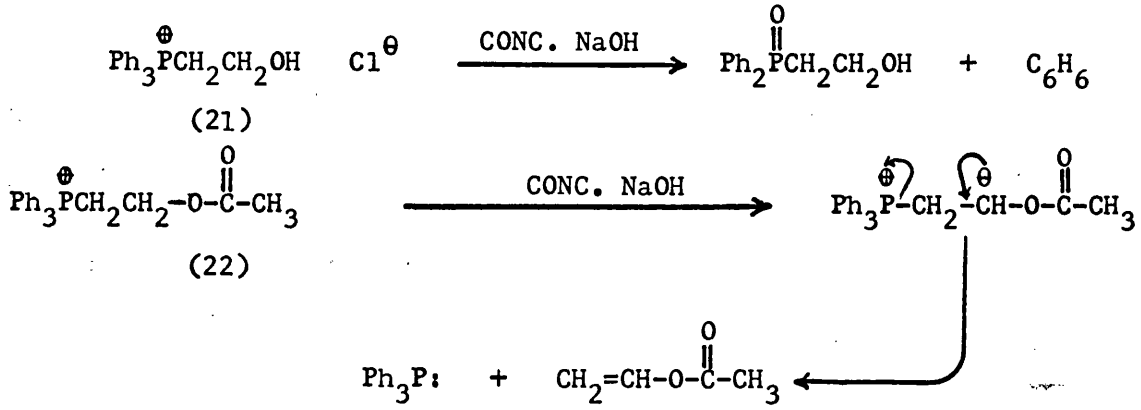
$$PhCH(\overset{\ominus}{\curvearrowleft})\text{-}CH_2\text{-}\overset{\oplus}{P}(CH_2CH_3)_3 \longrightarrow PhCH{=}CH_2 + (CH_3CH_2)_3P:$$

(19) 5%



relative stability of the resonance stabilised intermediate anion (20), compared to (19).

Similar results have been obtained by Aksnes[30], who attributed the difference in behaviour between the phosphonium salts (21) and (22) during decomposition, to the more easy ionization of the β-proton which apparently can be linked to the difference in the relative stability of the intermediates involved.



Considering the ease of elimination of the various groups in phosphonium salt decomposition, Ingold[29] observed the order: allyl, benzyl> phenyl > methyl > β-phenethyl > ethyl and higher alkanes.

Studies on hydrolysis of tetra-arylphosphonium salts[31] have shown that aryl groups containing electron-withdrawing substituents were more easily lost than phenyl in contrast to those bearing electron-releasing substituents which were less readily lost than phenyl. These findings have been confirmed by McEwen and co-workers[32]. Their studies on the

hydrolysis of p-substituted toluene tribenzylphosphonium halide salts, have revealed that the relative ease of elimination of p-substituted toluenes paralleled their anionic stability, which is enhanced by the presence of electron-withdrawing substituents. Therefore, it would seem that the groups most easily eliminated on alkaline hydrolysis is that group most stable as the anion.

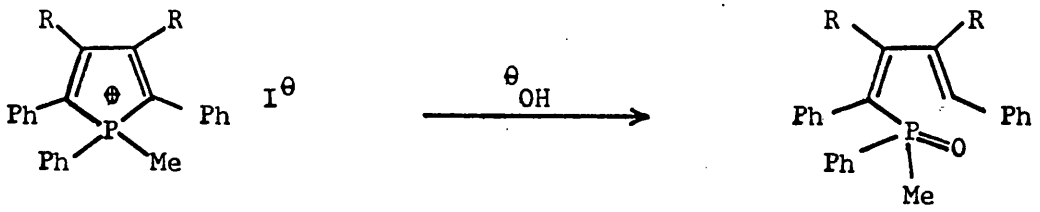
This has been supported by other workers[33,34]. However, the hydrolysis of the phosphonium salts to a mixture of products has been noticed[31,32], where the stability of the different groups present are comparable.

In contrast to earlier suggestions[28,29], McEwen[32] found that the relative ease of departure of a given group is influenced by the nature of the other groups present, but it was suggested[35] that steric factors would prove to be of a minor importance in this context. However, steric effects have been invoked by Trippett and his co-workers[36,37] to account for the deviation from the normal rules of hydrolysis to hydrocarbons and phosphine oxides in sterically crowded phosphonium salts (see Section 2.7).

2.2 Kinetics of Nucleophilic Attack of Hydroxide Ion at Phosphorus.

The alkaline hydrolysis of quaternary phosphonium compounds to give phosphine oxide and hydrocarbon was found to obey third order kinetics, with a first order dependence on the concentration of phosphonium salt and second order dependence on base concentration[32-34,38-40]. However, in cases where the generated anion is exceptionally stable, second order kinetics are observed. The hydrolysis of (p-nitrobenzyl)tribenzylphosphonium hydroxide to give p-nitrotoluene was shown to proceed with second

order kinetics[38]. McEwen[32] reported that the hydrolysis of (p-nitrobenzyl)tribenzylphosphonium chloride did not follow third order kinetics as it decomposed too rapidly to be followed kinetically. Bergesen[41] also observed the formation of the ring-opened phosphine oxides (23) and (24) during the hydrolysis of 1,2,5-triphenyl or 1,2,3,4,5-pentaphenylphospholium iodide salts (25) and (26), via a first order process in both phosphonium salt and hydroxide ion concentrations.

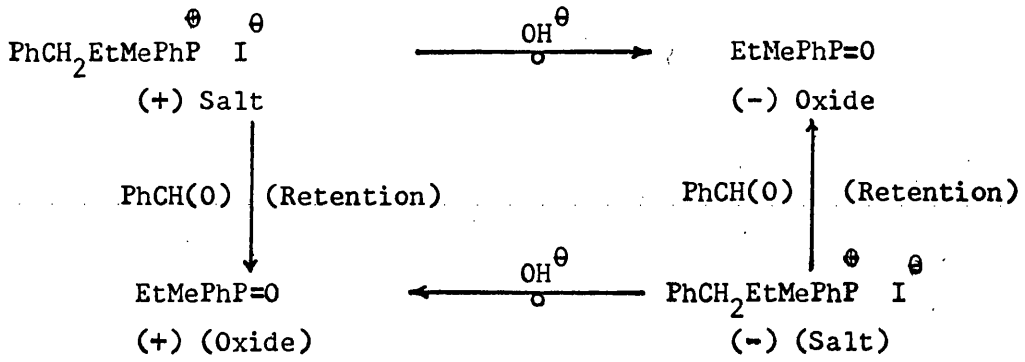


(25) R = H
(26) R = Ph

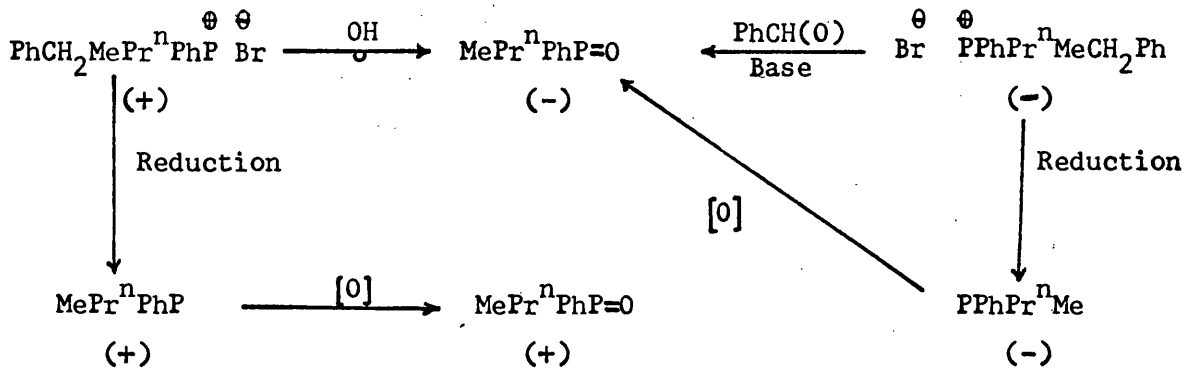
(23) R = H
(24) R = Ph

2.3 Stereochemistry of Phosphonium Salt Hydrolysis.

McEwen and his co-workers[42] reported that optically active benzylethylmethylphenylphosphonium iodide hydrolyses stereospecifically to give toluene and phosphine oxide with inversion of configuration at phosphorus. The pure dextrarotatory phosphine oxide formed by the alkaline hydrolysis of the optically pure leavorotatory salt, had an equal and opposite sign of rotation to that of the phosphine oxide resulted from the Wittig reaction on the same optically pure levorotatory enantiomer. They developed an argument which indicates that the Wittig reaction should proceed with complete retention of configuration at the phosphorus atom via a four-membered cyclic intermediate, consequently, the hydrolysis proceeds with inversion of configuration at phosphorus.

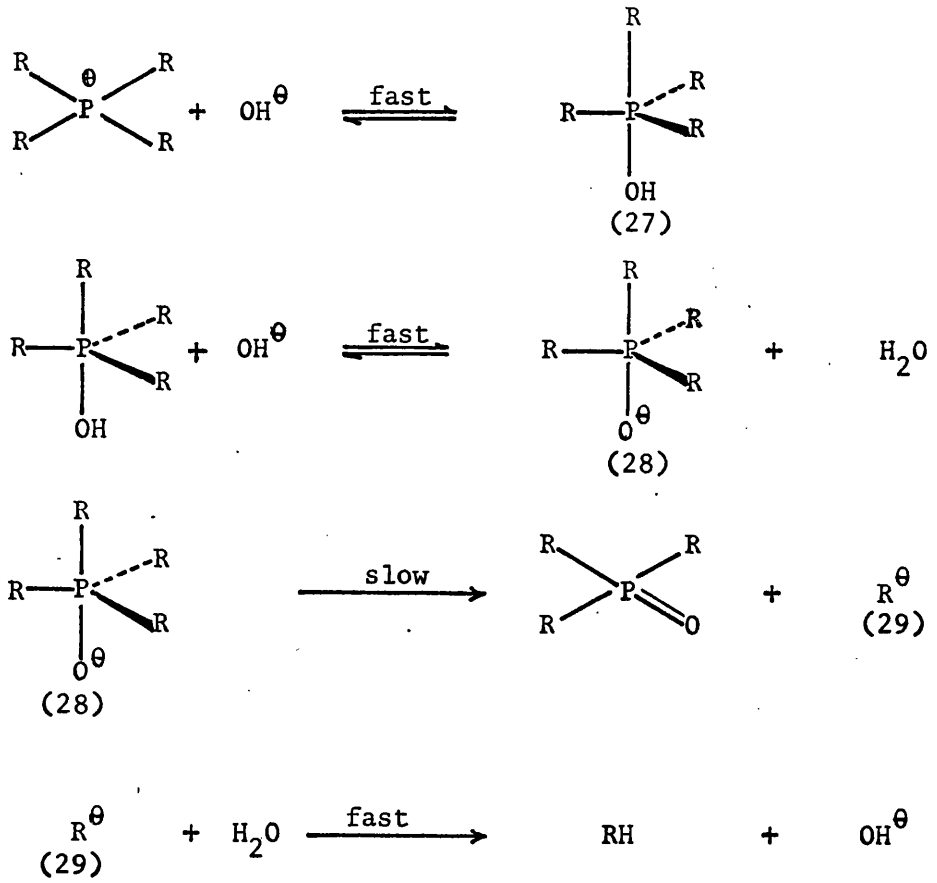


Horner and co-workers[43-45] furnished evidence to show that the two enantiomers of benzylmethylphenyl-n-propylphosphonium bromide, hydrolysed with inversion of configuration at the phosphorus atom. They observed that the oxide resulting from the hydrolysis of the salt had the opposite sign of rotation to that oxide formed by cathodic reduction of the salt followed by peroxide reoxidation of the obtained phosphine. Both oxidation and cathodic reduction are presumed to proceed with retention of configuration. The oxide formed from the Wittig reaction on the leavorotatory enantiomer of the salt and that resulting from hydrolysis of the dextrorotatory salt, both had the same sign of rotation and hence it seems reasonable to conclude that the observed hydrolysis must proceed with inversion of configuration at phosphorus.



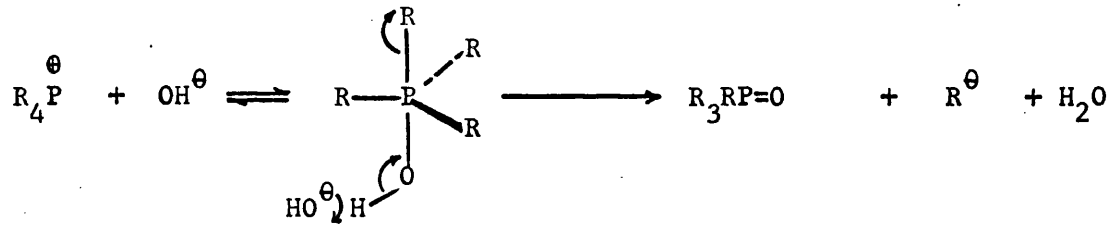
2.4 The Mechanism of Phosphonium Salt Hydrolysis.

The kinetic results indicate the involvement of two hydroxide ions prior to, or during the rate-determining step of the reaction. This can be accounted for by the mechanism suggested by McEwen *et al*[42], which involves four steps. Firstly, a fast reversible formation of a penta-co-ordinate intermediate (27), and secondly a fast reversible formation of the conjugate base (28) by the attack of a second hydroxide ion, followed by the third step, a slow rate-determining formation of the appropriate phosphine oxide and a carbanion (29). The fourth and last step is a very rapid protonation of the carbanion (29) to the hydrocarbon by the aqueous medium.



In cases where only one hydroxide ion is involved during the rate determining step, overall second order kinetics would obviously be expected, as it is the case for p-nitrobenzyl, and butadienyl anions. This may be rationalised by a very fast decomposition of the conjugate base (28) to products , which is fast enough to make the first step, the formation of the pentacovalent intermediate (27), rate-determining step.

McEwen[46] has suggested that in cases where one observes second order kinetics, one has the possibility of synchronous attack of a second hydroxide ion with departure of the leaving anion (i.e. steps 2 and 3 above would become a single concerted step).



He also suggested the possibility of the formation of an unstable tetragonal bipyramid intermediate with two hydroxide groups bonded to the phosphorus. The collapse of this hexaco-ordinate intermediate would yield phosphine oxide, a carbanion and water.

A small kinetic isotope effect (k_H/k_D, ca. 1.2) in the protonation of the carbanions lost from certain phosphonium salts was reported by Corfield and Trippett[47]. They showed that a free carbanion would produce such an isotope effect, which suggests immediate protonation of the leaving anion as it is formed. Consequently, the rate-determining loss of the carbanion and its protonation, i.e. the final two steps of McEwen's mechanism, could well be concerted.

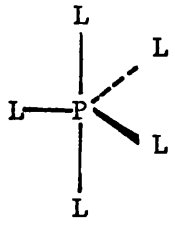
The intermediacy of a pentaco-ordinate phosphorane in bimolecular

nucleophilic substitution at tetraco-ordinate phosphorus via a two-step process has been suggested[48] as an alternative to direct substitution at phosphorus.

The ability of phosphorus, like other second row elements, to achieve higher co-ordination numbers made this suggestion a viable one. There are two main classes of these compounds: those postulated as metastable intermediates in substitution reactions at tetraco-ordinated phosphorus, and those that are relatively stable, characterisable compounds. The evidence for the existence of the first type comes mainly from kinetic or stereochemical studies of the reaction pathway.

The number of isolated stable phosphoranes is increasing rapidly and physical studies on some of these compounds have shown a number of more important observations concerning their structures:

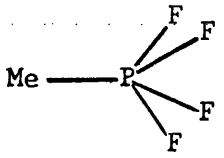
(a) Although there are a number of other possible geometries for the intermediate phosphorane[49], virtually all, as has been shown by X-ray diffraction[50-57], electron diffraction[58] and n.m.r. data[59-62], have essentially a trigonal bipyramidal (TBP) geometry[63,64] (30).



(30)

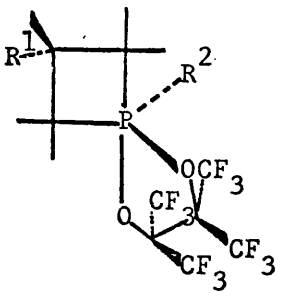
This is found to be the case in acyclic phosphoranes with five identical ligands bonded to the phosphorus atom. There is evidence, however, that small distortions do arise when phosphorus is asymmetrically substituted. The reason for such distortion has been suggested to be

mainly due to steric interactions. The fluorine atoms in phosphoranes (31) are slightly bent away from the carbon ligand.[58]



(31)

For cyclic phosphoranes, in which the phosphorus atom is incorporated in a small ring, the constraint imposed by such systems, in some cases, forces the molecule to be distorted away from the TBP geometry. Recently square pyramidal geometry was confirmed, by X-ray analysis[65], for the adducts (32)



(32)

(33) R^1= H ; R^2 = p-BrC_6H_5

(34) R^1= Me ; R^2= p-BrC_6H_5

However, the energy difference between the TBP and the square pyramidal geometries has been known to be as small as 1.5 Kcal. mol^{-1}.[66]

(b) In four- and five-membered ring cyclic TBP-phosphoranes, the ring is always in the apical-equatorial (ae) position,[50-57] (see Section 2.8).

(c) The apical bonds are longer, and therefore weaker, than the equivalent equatorial bonds, (see Section 2.8).

(d) The more electronegative ligands prefer to occupy the apical position of the TBP. This is known as the polarity rule[59,63], a semi-empirical rule based upon experimental observations and theoretical deductions.

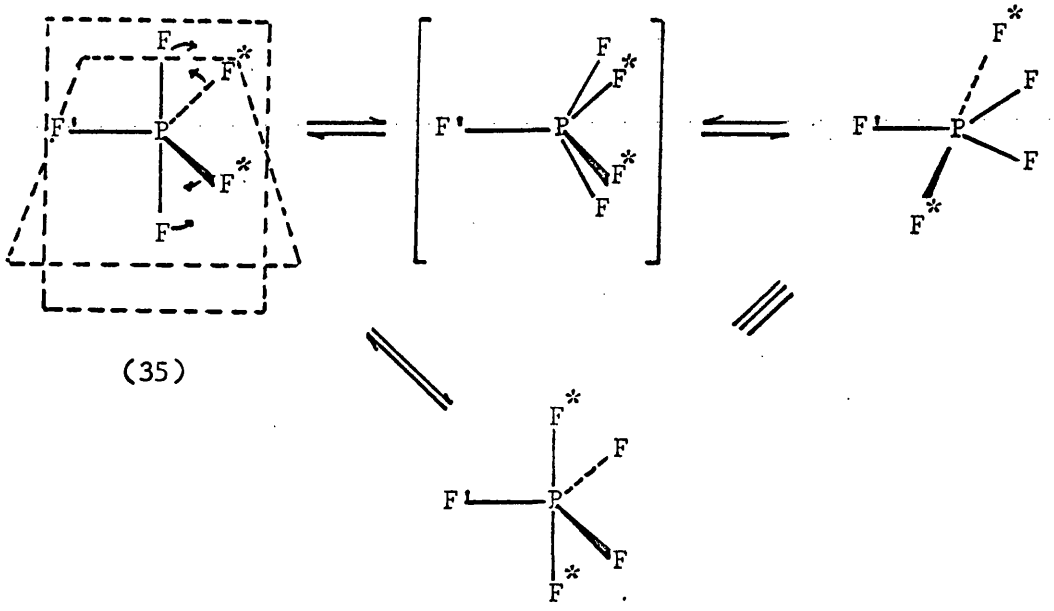
2.5 The Role of Pseudorotation in Phosphonium Salt Hydrolysis.

Trigonal-bipyramidal geometry has been indicated for the pentafluorophosphorane molecule[58,66,67], with three identical equatorial and two identical apical fluorine atoms. However, in spite of the nonequivalence of the two positions in the TBP, which should lead to two kinds of fluorine atoms in the ratio of 3:2 in the ^{19}F n.m.r. spectrum of the molecule, only one type of fluorine[68] can be found in the spectrum at temperatures as low as $-157^{o}C$.

To account for this unexpected observation, Berry[69] postulated that ligand positional exchange in TBP-pentaco-ordinate phosphoranes takes place by pairwise exchange of apical and equatorial ligands; thus, equilibration of apical and equatorial fluorines in PF_5 could occur.

This process, now known as the Berry pseudorotation (BPR) mechanism, is purely a vibrational transformation without any bond rotation; hence, the name'pseudorotation'. A pair of equatorial ligands, move forward while the remaining ligand fixed as a pivot. A continuation of this process leads to another TBP, which appears to have been produced by rotating the first TBP by 90^{o} about the pivotal bond[70]. In the idealized case, the molecule passes through a C_{4v} square-base pyramid before returning to the D_{3h} geometry of a TBP.

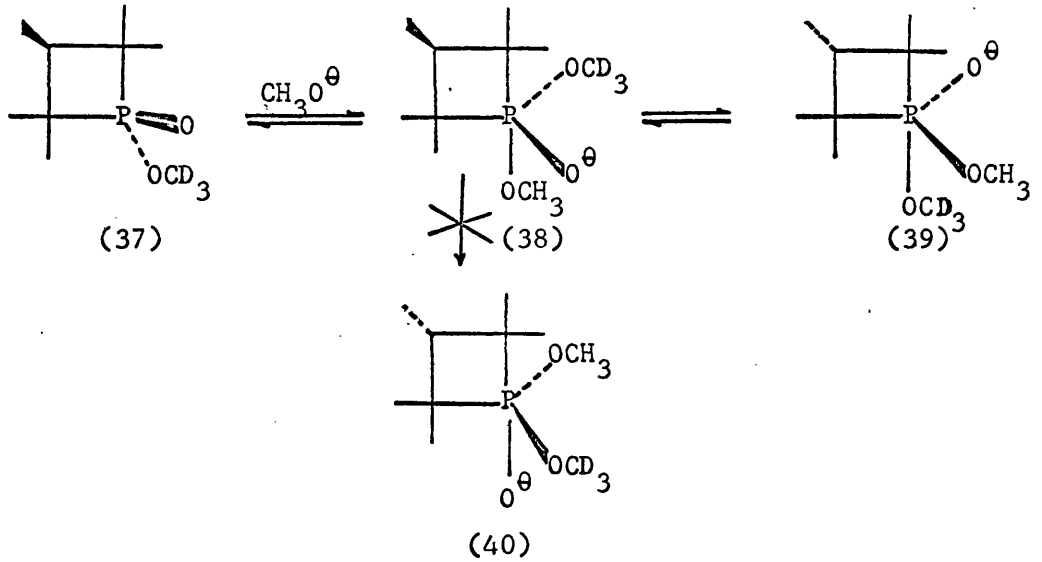
The trigonal bipyramid (35) is identical to (36) except for the individual fluorine atoms positions.



(35)

(36)

Exchange of (CD_3O) by (CH_3O) was observed[21] to occur with each isomer of the ester (37) with retention of configuration at phosphorus. Isomer crossover was shown not to occur between the cis- and trans-



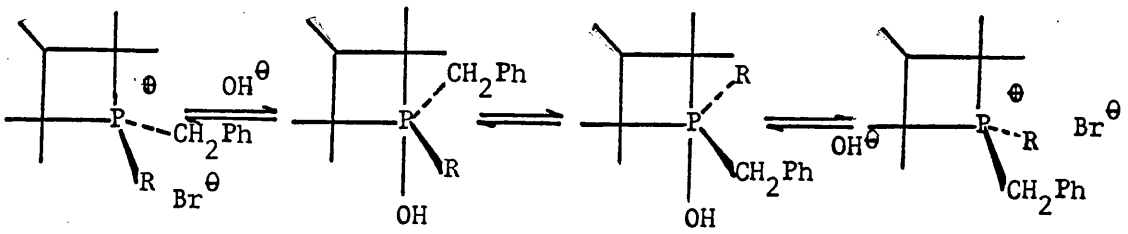
(37) (38) (39)

(40)

isomers; hence, pseudorotation of (38) to (39) was invoked to explain these results.

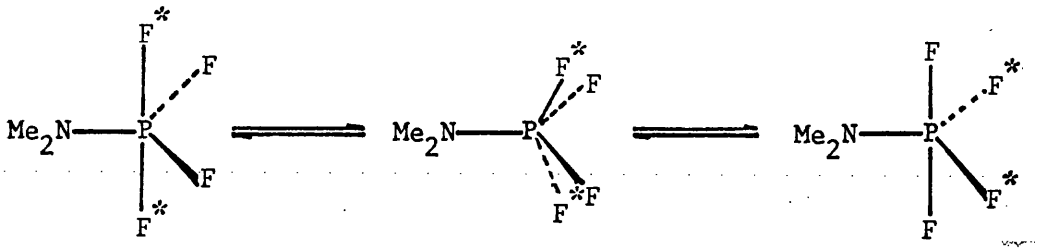
Pseudorotation of (38) to (39) was favoured over (38) to (40), which is inhibited, for placing the electropositive ligand (O^-), in the apical position, would be energetically unfavourable. Thus, the (OCH_3) in TBP (39) can leave from an apical position.

What may be considered as a potential argument in favour of pseudorotation is the reported isomerisation of the cis- and trans-isomers of the phosphetanium bromide salts (41) and (42). Cremer[71] has reported that the pure isomers of both salts on treatment with one drop of (1N) sodium hydroxide solution, gave rise to the immediate equilibration of the individual isomers. Excluding the possibility of equilibration via an 'ylide mechanism', the author favoured pseudorotation between the intermediate phosphoranes, as a pathway to equilibration of the isomeric salts. This has also been confirmed by Corfield[15] (see Section 2.10).



(41) R = Me , (42) R = Ph

Variable temperature ^{31}P n.m.r. spectrum of N,N-dimethylaminotetrafluorophosphorane (43) has been analysed by Whitesides and Mitchell[72], who found that, in the temperature range -50 to -100°C, the apical pair of fluorines were replaced by an equatorial pair in a single concerted step. This led them to conclude that the Berry pseudorotation mechanism provides a satisfactorily and agreeable explanation with the observed exchange process.



(43)

The amino group remains always as the pivot with the P-N bond in the equatorial plane. Swinging this group to an apical position with one fluorine ligand acting as the pivot, can also equilibrate the fluorine atoms, but would generate a TBP intermediate with an apical nitrogen. This violates the polarity rule as nitrogen is less electronegative than fluorine. To avoid such high energy TBP intermediates, Ramirez, Ugi and co-workers[73-74] proposed an alternative mechanism which also explains the observed intramolecular ligand reorganisation and satisfies the conditions needed.

Their mechanism which they termed 'Turnstile Rotation' (TR) in which the five ligands around pentaco-ordinate phosphorus, by undergoing slight but significant angular distortions, divide themselves into two sets, a trio and a pair. In this case stereomutation is postulated to occur by mutual counterrotation of these two sets with subsequent collapse to a new TBP.

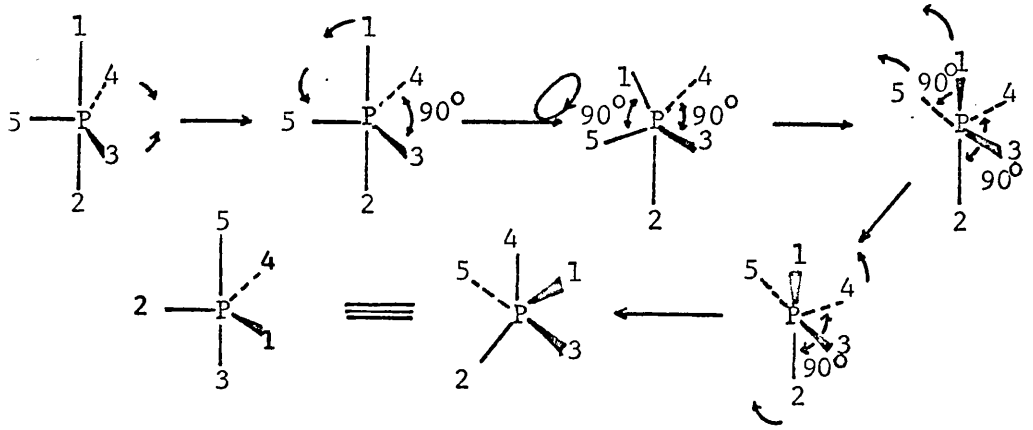
The detailed mechanism as they described it, involves three concerted types of motions of the ligands:

1) A compression of the diequatorial angle 3-P-4 to about 90^{o}.

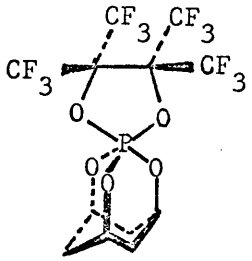
2) A tilt of the pair-ligands (1,5) (in plane) approximately 9^{o} towards ligand 2.

3. Rotating the pair ligands (1,5) 60° in the opposite direction, relative to the trio ligands (2,3,4) rotation.

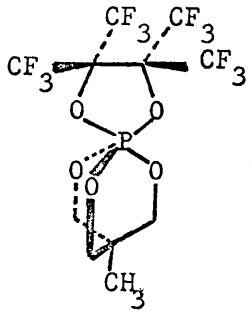
The new TBP would be formed by the concerted reverse of the tilt of the pair-ligands 9° and re-expanding the diequatorial angle to 120°, to give the new TBP, which is identical to that which would be formed by one BPR on the original phosphorane with ligands (4) as the pivot.



The rapid ligand exchange observed in the cage phosphoranes (41) and (42), can be explained by a process of rotating the five-membered ring against the cage system.



(44)



(45)

They suggested that ligand intramolecular reorganisation using Berry's mechanism, *via* a tetragonal-pyramidal intermediate, has a prohibitively high energy barrier due to the high degree of strain involved in the cage structure in the intermediate.

In the case of acyclic phosphoranes, they suggested that both the Berry and TR mechanisms may operate, but for these and other cage systems, it must proceed only by the TR mechanism.

Molecular orbital calculations, by Hoffmann and co-workers[75] have favoured BPR mechanism over TR mechanism in symetrically substituted phosphoranes, suggesting a higher energy barrier for the TR pathway. than for BPR due to the particular intermediate involved in each case.

They further suggested that in some possible cases the TBP ground states are distorted, from the ideal TBP geometry, towards the TR model geometry. In these cases the TR mechanism could operate, even though in the more normal circumstances the BPR route is more likely.

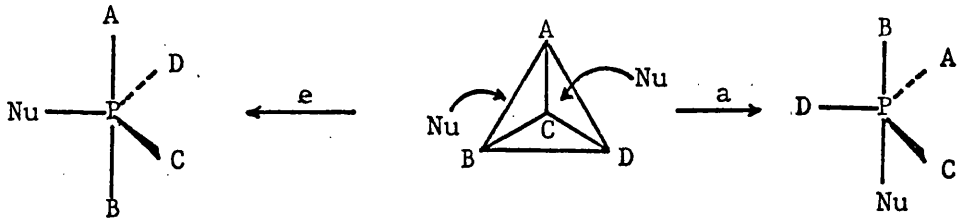
Consequently as most of the published literature uses the BPR mechanism for ligand reorganisation and, as there is no conclusive evidence to the contrary, this mechanism will be assumed to operate whenever intramolecular ligand reorganisation in TBP phosphoranes is considered, throughout this thesis.

2.6 Formation and Decomposition of the Intermediate in Phosphonium Salts Hydrolysis.

A nucleophile can attack a tetrahedral phosphonium cation to form a TBP at any of the four possible faces of a tetrahedron, designated as apical attack, or at any of the six possible edges, designated as equatorial attack.

Apical attack will lead to a TBP in which the nucleophile occupies an apical position with the equatorial positions being occupied by the three groups which form the face under attack. Equatorial attack will lead to a TBP with the attacking nucleophile in an equatorial position and the two groups which form the edge being moved to apical positions.

Similarly, departure of the leaving group can occur from either an apical or an equatorial position.



Apical (≡ Face) attack = a

Equatorial (≡ Edge) attack = e

Mislow[76] has broadly discussed the application of an extended principle of microscopic reversibility (PMR) to displacement reactions at tetraco-ordinate phosphorus, which states in effect that the stereochemistry (apical vs equatorial) of entry and departure must be the same[70,77].

In his discussion he indicated that, according to the PMR, the pathways of forward and reverse reactions at equilibrium (in mechanistic terms), are described by the same energy surface. It decidedly does not state that the profile of such a surface must be symmetrical with respect to the reaction path. Consequently, a nucleophilic apical attack at phosphorus, followed by equatorial departure of the leaving

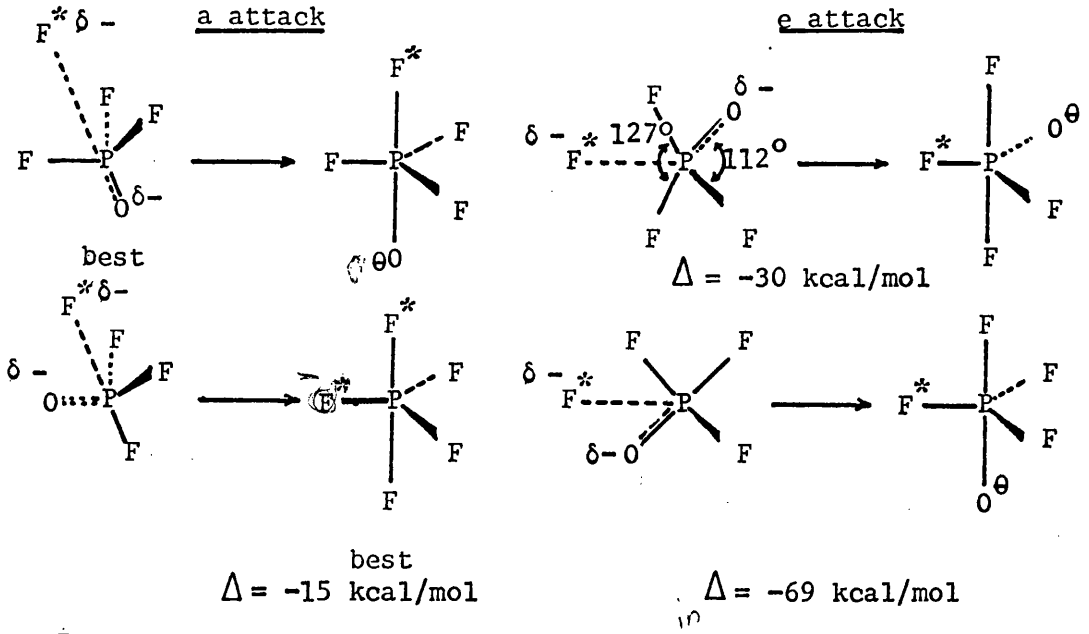
group, only violates the PMR when the energy profile has mirror symmetry. Likewise, equatorial attack (as well as departure) can not be excluded. He then suggested that in the final analysis, all that can be said on the basis of the PMR is that equatorial departure is rendered unfavourable to the extent as apical attack is preferred over equatorial attack. Nevertheless, as a simplifying postulate, apical attack and apical departure should be assumed.

Apical attack and apical departure are the preferential modes of bond making and bond breaking, at least when the ligands in question are relatively electronegative. This can be supported by several lines of argument. Theoretical calculations[74] indicate that an atom in the apical position of TBP phosphorus has a lower capability of donating electron density to the central phosphorus atom, than if the same atom is placed in an equatorial position. In general a reduction of polarity difference between phosphorus and its ligands is achieved by back donation of electron density from the ligand *via* *p* - orbitals into the empty *d*-orbitals of phosphorus. This results in a significant increase in stability. Since there is less back-donation of electrons towards the phosphorus, from the apical than from the equatorial positions (due to the increased *s* character in equatorial bonds)[78], the most electronegative elements will tend to be at the apex where they will be able to support more electronic charge. It follows that there is less double bond character at the apical positions, and this should be reflected in longer apical bonds, as has been found in phosphoranes.

It follows that apical bonds are expected to be weaker, more ionic, and more easily broken than equatorial bonds. Thus, the nucleophile has less distance to travel before it forms an apical bond. At the same time,

it can depart easily from an apical site. Therefore, it is obvious that electronegative nucleophiles will be attracted more to the face of a tetrahedron than to the edge (equatorial orbitals are more electronegative than the apical orbitals in a TBP).

Theoretical calculations were carried out by Ugi, Ramirez and their co-workers[74] to estimate the relative energies for the possible type of attack on phosphoryl fluoride by a fluorine anion. The results favoured the apical attack via an FFF face by 30kcal mol^{-1} relative to an equatorial attack on an FF edge and by approximately 69kcal mol^{-1}, as to an attack on the FO edge.



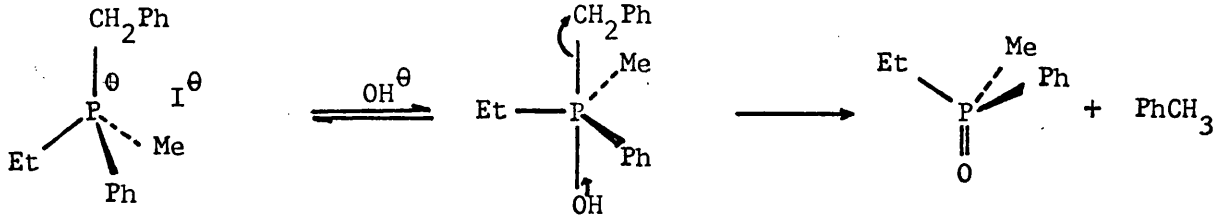
2.7 Stereochemistry of the Intermediate Phosphonium Salt Hydrolysis.

The stereochemistry-consequences of nucleophilic substitution at phosphorus are controlled by the position of entry and exit in the TBP intermediate as shown in the following table:-

Table 1: Stereochemistry of Substitution via TBP.

Entry	Departure	Stereochemistry
a	a	Inversion
a	e	Retention
e	a	Retention
e	e	Inversion

The alkaline hydrolysis of the phosphonium salt (46) has been shown to proceed with inversion of configuration at phosphorus[42]. This can be the result of either apical entry and departure or equatorial entry and departure, as either of apical attack-equatorial loss or the opposite route, would result in retention of configuration at phosphorus.



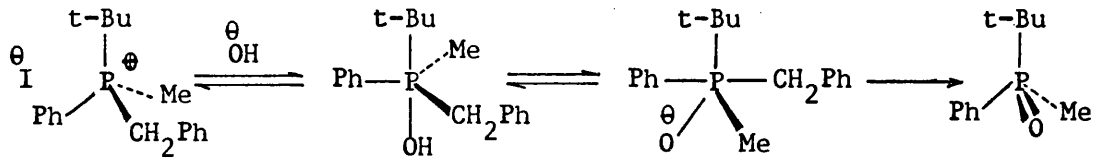
(46)

Formation of a TBP with the most electronegative groups (and hence the most stable anions) in the apical position, corresponds to the most stable phosphorane. When it is possible for the nucleophile to attack opposite any one of the three other groups, the departure of the resonance--stabilised benzyl anion would be then from an equatorial position leading to retention of configuration. The observed overall inversion infers that the intermediate collapses to products faster than undergoing pseudorotation which could lead to racemisation of the phosphorane.

Stereomutation can occur in such cases when the rates of hydrolysis and pseudorotation become comparable. This situation arises when the

leaving group is a poor one. This retards the rate of hydrolysis and hence leads to isomerisation of the intermediate.

The alkaline hydrolysis of the t-butyl salt (47) provides an example in which stereomutation was observed. This salt hydrolyses with predominant retention of configuration at the phosphorus atom[36].



(47) (48)

The t-butyl group exerts hindrance to attack of the hydroxide anion opposite the benzyl group. However it can attack opposite the t-butyl group, which can occupy an apical position in the TBP (48). Loss of the benzyl group from an equatorial position would lead to overall retention. As this mode of departure is not likely, apical loss after at least one pseudo-rotation putting the leaving group in an apical position, is necessary.

This pseudorotation will be energetically feasible, because of removing the bulky and more electropositive ligand from the highly crowded apical position, hence, the observed result.

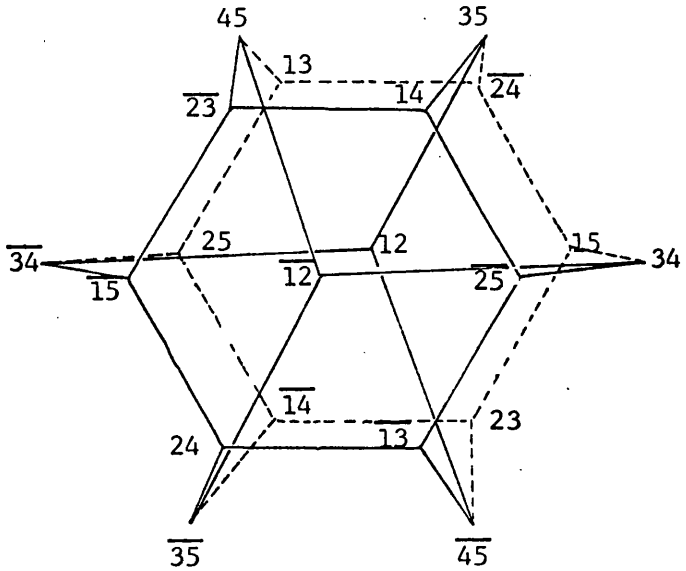
Nucleophilic attack at phosphorus in a phosphonium salt, to give a pentaco-ordinate TBP phosphorane, can occur at any one of four different faces or six different edges of the phosphonium ion. When all five ligands attached to phosphorus are different, and in the absence of special constraints, 10 stereoisomeric phosphoranes can be formed from a given stereoisomeric phosphonium salt, or a total of 20 phosphoranes from both isomers.

For unrestricted pseudorotation processes, five successive pseudo-rotations are required to interconvert enantiomers, which are related by the centre of symmetry of the graph. However, in cases where any ligand is forbidden to occupy an apical position, only isolated pairs of isomers may interconvert, thus racemisation of the phosphoranes can not occur.

Since each isomeric phosphorane has three equatorial ligands, which can serve as pivots, there is the possibility of three initial pseudorotations for each phosphorane. Thus, there should be a total of 60 pseudorotation routes, but since each pseudorotation connects two isomers, this number is reduced to 30 pseudorotation pathways.

To facilitate an orderly and systematic analysis of these complex displacement-rearrangements, a number of topological representations have been suggested.[76,77]

The Desargues-Levi graph (Fig. 1) has been proposed by Mislow[76,77] for this purpose. The vertices represent the twenty possible isomers and pseudorotations are represented by the lines connecting vertices. A given isomeric phosphorane is designated by the indices of its apical ligands and the chirality of each isomer is denoted, arbitrarily, by the ascending numerical ligand indices; if clockwise when viewed from the apical ligand with the lower numerical index, the isomer is unbarred; if counter-clockwise, barred. Thus, the isomer 14 and its enantiomer $\overline{14}$ represent the two possible isomers which have ligands 1 and 4 in the apical positions.

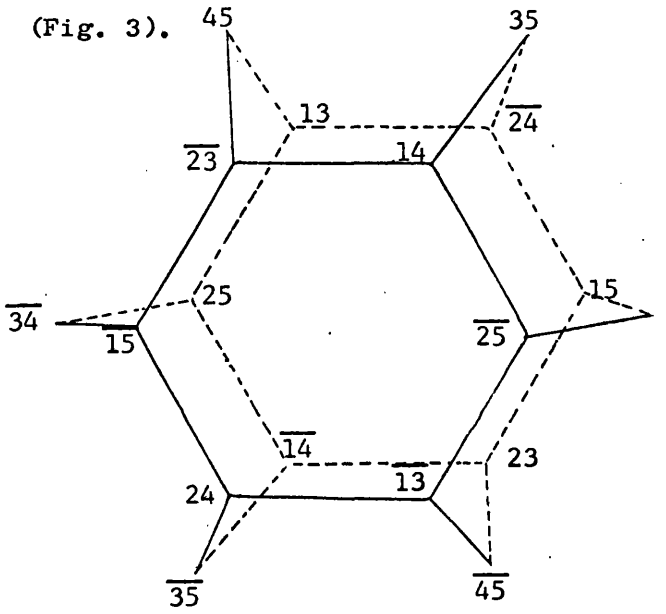


(Fig. 1)

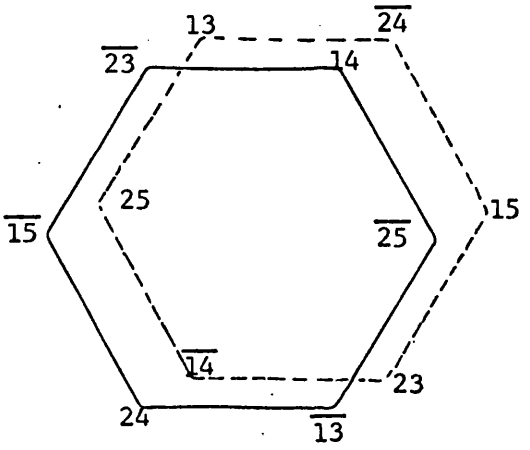
For cyclic phosphoranes, where phosphorus is a part of a small ring, if the ring groupings are designated L_1 and L_2, the diagram (Fig. 1) will be reduced to the "hexaasterane" graph (Fig. 2).[76,77] The effect of the ring incapability to span the diapical positions is to remove isomers (12)

and $(\overline{12})$ as well as the six pseudorotation pathways leading to them.

Furthermore, the considerable strain associated with the ring spanning the diequatorial positions, would lead to neglect all pseudorotation pathways *via* such intermediates. Consequently, the equatorial belt of star-points, representing these high energy phosphoranes, can be eliminated as well. Thus, the graph reduces to unconnected six-membered cyclic pseudorotation pathways, (Fig. 3).



(Fig. 2)



(Fig. 3)

Accordingly, there is no access from one phosphorane to its enantiomer, and racemisation can only occur, by a BPR mechanism, *via* such high energy species represented by the star-points, (see Section 3.12).

2.8 The Hydrolysis of Phosphetanium Salts.

Nucleophilic displacements on tetravalent phosphorus incorporated into a four-membered phosphetan ring are usually held to proceed with retention of configuration at phosphorus[21,79-85]. This is in contrast to the inversion of configuration observed for the acyclic analogues.

The mechanism suggested by McEwen to account for the inversion

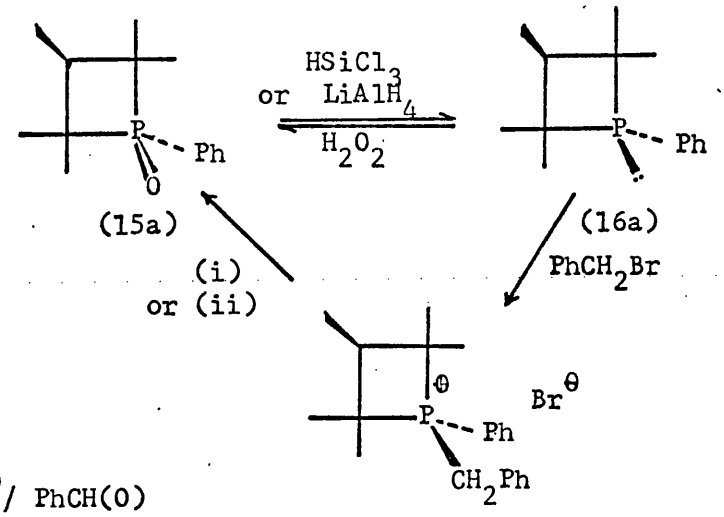
of configuration in the acyclic phosphonium salts demands linearity between the attacking hydroxyl ion and the departing anion. Such a diapical situation would be impossible in cyclic phosphetanium salts, as the ring would have to span a diequatorial position, which would increase the ring strain considerably (see Section 3.12).

It follows that the attacking nucleophile has no alternative but to attack the phosphetanium cation, opposite one of the ring-junctions, to form an intermediate phosphorane with the ring spanning apical-equatorial position. The leaving group would, thus, be placed in an equatorial position. Pseudorotation of the intermediate phosphorane to put the leaving group in an apical position, from where it can be lost, would lead to the observed retention of configuration.

The possibility of more than one pseudorotation arises when the leaving group and the other ligands present have comparable apicophilicities, i.e. their preference for the apical as opposed to the equatorial position in TBP intermediate (see Section 2.10), thus leading to loss of stereospecificity[15].

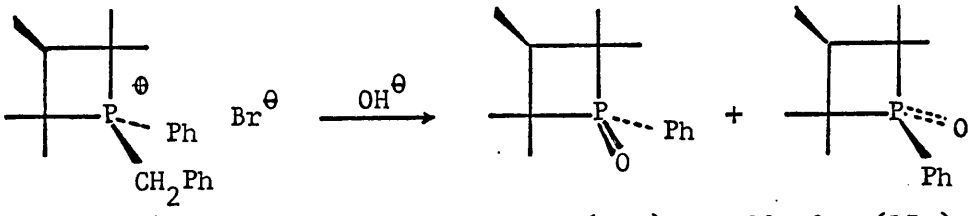
2.9 The Alkaline Hydrolysis of Phosphetanium Salts Involving Expulsion of Groups External to the Ring.

Nucleophilic displacement of the benzyl group in the cis-phosphetanium salt (42a) has been reported to proceed with complete retention of configuration at phosphorus. Both the hydrolysis of the salt and the reduction of trans-oxide (15a) have been shown to proceed with retention of configuration, as oxidation[22] of the phosphetan (16a) and Wittig olefin synthesis[42] also proceed with retention of stereochemistry at phosphorus.



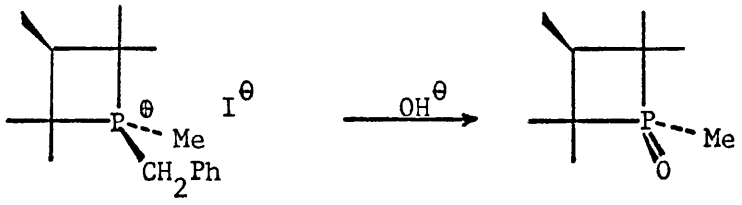
(42a)

This has since been shown to be inconsistent with the results reported by other workers[15,71]. The alkaline hydrolysis of the pure isomeric salts (42) or various mixtures of both[15], gives the same mixture of stereoisomeric (2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxides) (15) (cis:trans = 1:9).

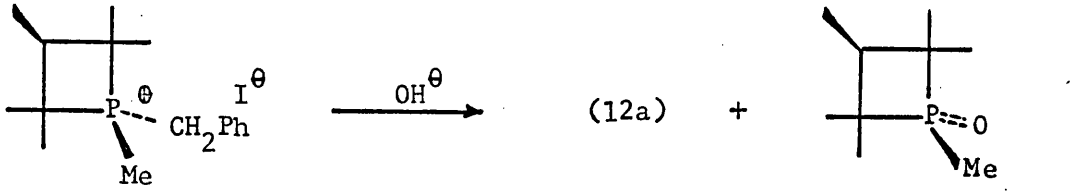


(42a) (15a) (15b)

Trippett and co-workers[15,79] have shown that the hydrolysis of r-1-methyl-2,2-cis-3,4,4-hexamethyl-1-benzylphosphetanium iodide (49a) in aqueous ethanol proceeds with complete retention to give the trans-hexamethylphosphetan 1-oxide (12a). The trans-benzyl salt (49b) hydrolyses to give the oxides (12) as a mixture of stereoisomers in which the cis--oxide (12b) is predominant (i.e. partial inversion)[71]. The ratio of the two isomeric oxides (12) in the hydrolysis products of the trans--benzyl salts (49b) is very sensitive to the reaction conditions.[15] Thus, in aqueous sodium hydroxide, the trans-oxide (12a) is the major product, whereas in ethanolic media the cis-oxide predominates.



(49a) (12a)

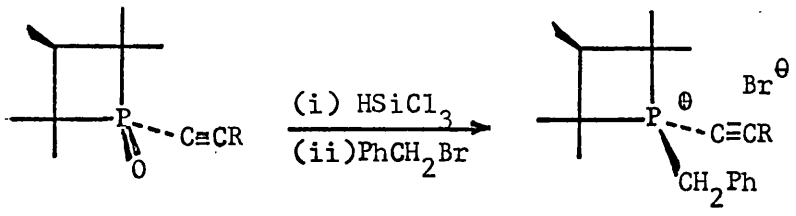


(49b) (12b)

aqueous	70 : 30[15]	
ethanolic	25 : 75[15]	

Cremer and co-workers[71] found that the hydrolysis of both isomers of the analogous bromide salt (41) gives a mixture of the stereoisomeric oxides (12).

These contradicting results, stimulated our interest in preparing and restudying the alkaline hydrolysis of the pure isomers of the 1-benzyl-hexamethylphosphetanium bromide (41) and phosphetanium iodide (49). The <u>trans</u>- isomers of the salts (50) and (51) shown in Table II have also been prepared and studied.



(13) (50)

(14) (51)

K =

TABLE II: The Alkaline Hydrolysis and Equilibrium of the Studied Salts.

	Hydrolysis % Product oxides	Equilibrium(*) % salts in mixture		Hydrolysis % Product oxides	Equilibrium(*) % salts in mixture
Salt	cis:trans	cis:trans	Salt	cis:trans	cis:trans
41a	16:84(AB)	36:64(i)	41b	30:70(A)(i)	36:64(r)
49a	10:90(AB)(r)	64:36(r)	49b	40:60(A)(i)	64:36(i)
	00:100(B)(r)(15)			30:70(A)(i)(15)	
				75:25(B)(r)15	
50	00:100(A)(i)				
51	00:100(A)(i)				

(*) Equilibrium of the pure isomeric salts in very dilute alkali.

(A) Aqueous sodium hydroxide.

(B) Sodium hydroxide in aqueous ethanol.

(r) Partial retention.

(i) Partial inversion.

The salts were synthesised by reducing the corresponding phosphetan oxides with trichlorosilane and quaternization of the phosphetans with benzyl or methyl halides, as appropriate, either *in situ*, (41) and (49), or after being isolated (50) and (51).

The ratio of the phosphetan 1-oxide stereoisomers in the hydrolysis product was determined by ^{1}H n.m.r. spectroscopy.

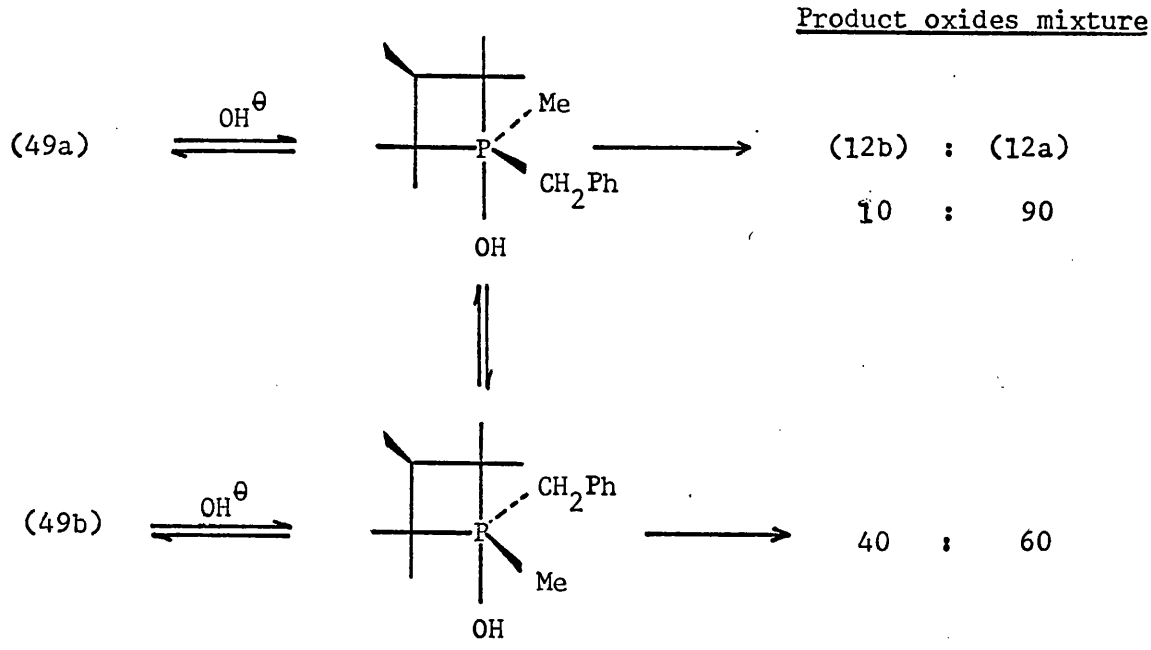
Equilibration of the single isomeric salts studied was achieved by adding one drop of (0.05N) sodium hydroxide solution to a chloroform

solution of the individual salt (40mg/½ml). The equilibrated salts were then extracted and the solvent evaporated. The ratio of the resulting stereoisomeric salts was determined using the ^1H n.m.r. in deuterated chloroform.

(a) 1-Benzyl-1,2,2,3,4,4-Hexamethylphosphetanium Iodide.

In contrast to the report by Corfield[15], it was found that alkaline hydrolysis of the cis-salt (49a) (1-benzyl and 3-methyl cis) gave a mixture of stereoisomers of 2,2,3,4,4-pentamethyl-1-methylphosphetan 1-oxide (12) in which the trans-oxide (12a) was predominant (≃ 90%), while that of the trans-salt (49b) gave a different ratio of the two product oxides (12) (cis:trans = 40:60).

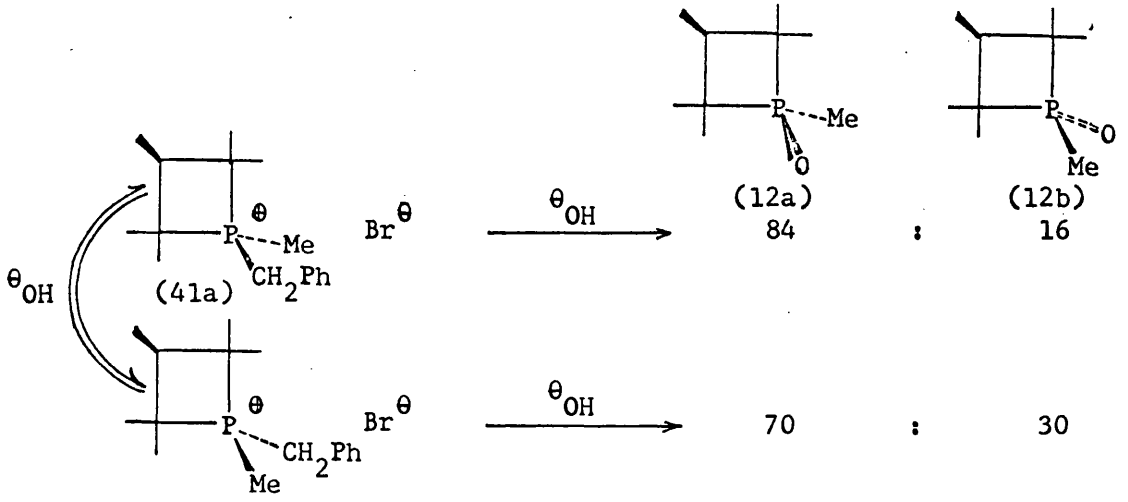
Equilibration of the iodide salts (49) to give mixtures of the two isomeric salts (cis:trans = 64:36), could be achieved by the addition of dilute sodium hydroxide solution as above.



(b) 1-Benzyl-1,2,2,3,4,4-Hexamethylphosphetanium Bromide.

The alkaline hydrolysis in both water and aqueous ethanol of the cis-salt (41a) (1-benzyl and 3-methyl cis), and the aqueous alkaline hydrolysis of the trans-salt (41b), resulted in mixtures of the stereoisomeric oxides (12), in which the trans-oxide (12a) predominated.

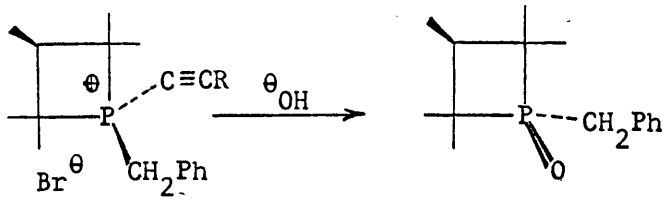
Equilibration of either of the pure isomers (41) gave a mixture of the two isomeric salts (cis:trans = 36:64).



These results are consistent with that reported by Cremer and co-workers[71], as they obtained mainly one isomer of the oxides (12), from the hydrolysis and equilibration of either salts (41).

(c) r-1-Benzyl-2,2-cis-3,4,4-pentamethyl-1-(prop-1-ynyl) and 1-(2-phenylethynyl)phosphetanium Bromide Salts.

Alkaline hydrolysis of the cis-isomeric salt of (50) or (51) gave the trans-oxide (52) (r-1-benzyl-2,2-trans-3,4,4-pentamethyl-1-oxide) as the only identifiable compound in the crude product, as judged by ^{1}H n.m.r. spectroscopy. This was also supported by melting point and the mixed melting point of the products in each case.



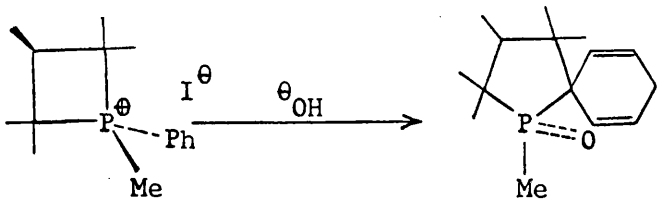
(50) R = Me
(51) R = Ph

(52a)

2.10 Possible Mechanism of Alkaline Hydrolysis of 1-Benzylphosphetanium Salts.

It is for the useful property of the ^{1}H n.m.r. spectra, of the ring methyl region in these phosphetanium compounds, that a distinct differentiation between diastereomers of both reactants and products is possible. Hence, any change in the relationship between the 1-substituent on phosphorus and the methyl group on the 3-carbon of the phosphetanium ring, resulting in different stereochemistry of the products from that of the reactants, can be monitored.

This observed isomer crossover could be attributed to either a change at the phosphorus atom or at the 3-carbon of the ring. Epimerization of the product oxides due to changes at the 3-carbon has been shown to be unlikely[15]. Hydrolysis of r-1-benzyl-1,2,2-trans-3,4,4-hexamethylphosphetanium iodide (49b) and r-1-benzyl-2,2-cis-3,4,4-pentamethyl--1-phenylphosphetanium iodide,in deuterium oxide, has been found by Corfield[15], to result in no deuterium exchange at 3-carbon atom of the resulting oxides. The trans-salt r-1,2,2-trans-3,4,4-hexamethyl-1-phenylphosphetanium iodide (53), rapidly epimerized, however, in dilute solution of sodium deuteroxide in deuterium oxide with the replacement of the 1-methyl hydrogens by deuterium.



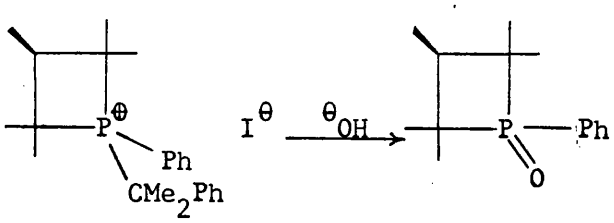
(53) (54)

This deuterium-hydrogen exchange has been also found to occur at the 1-methyl of the product (54), on hydrolysing the salt (53) in deuterium oxide. No exchange occurred when the fully protonated oxide (54) with unknown geometry, was submitted to the reaction conditions[15].

This can be taken to support that both deuterium exchange and the interconversion of the phosphetanium salts can occur prior to hydrolysis, and hence, epimerization is a result of changes at the phosphorus atom.

Intramolecular stereoisomerization observed during the alkaline hydrolysis of 1-benzylpenta- and hexa-methylphosphetanium salts has been suggested to be due to a number of possibilities[15]. The two most likely are ylide isomerization and stereomutation *via* pseudorotation at the phosphorus atom. However, such pre-hydrolysis isomer crossover *via* the ylides as a mechanistic possibility leading to partial inversion of the phosphetanium salts on hydrolysis was suggested to be less likely[15] when compared with stereomutation *via* pseudorotation.

The alkaline hydrolysis of a mixture of stereoisomers of 1-cumyl--2,2,3,4,4-pentamethylphosphetanium iodide (55) gave cumene and a mixture of isomeric oxides (15), in a different ratio from that of the initial isomeric salts.



4 : 1 55 : 45

(55) (15)

Since this salt is incapable of forming an ylide, as it has no α-hydrogen atoms, pseudorotation of the intermediate phosphorane has been favoured by Corfield to be responsible for isomerization in this and similar 1-benzylphosphetanium salts.

The stereochemical relationship between the tetraco-ordinate phosphetan systems, listed in Table I, and the TBP intermediates involved in the displacement reactions can be discussed in the light of Scheme I, page 49 . The results obtained, as shown in Table II, page 36 , may be analysed and rationalised in the light of the set of rules previously advanced in sections 2.4 - 2.7, as well as the following general conclusions, derived in terms of Scheme I, outlined below.

(a) The nucleophile has no alternative but to attack opposite one of the ring groupings, forcing the two potential leaving groups, R and benzyl, to occupy equatorial positions of similar environment. Apical loss of the leaving groups, therefore, necessitates that product formation must be preceded by at least one pseudorotation of the initial phosphoranes (57) and (60).

(b) An equilibrium mixture of topomeric TBP phosphoranes (57) - (62), prior to product formation, may arise under certain conditions. This is because stereoisomeric TBPs are thought to be of comparable energies[86] and the energy barriers for pseudorotations involving them are sufficiently small[75,87,88] that fast equilibration is expected. In such cases, formation or decomposition of the ultimate phosphoranes involved, is the rate-limiting step.

The alkaline hydrolysis of the dibenzylpentamethylphosphetanium salt (56) (R = CH_2Ph, Scheme I), has been reported by Corfield[15], to proceed with complete retention of configuration. On p-deuterating only one of the benzyl groups, the hydrolysis proceeded to give only the trans-oxide (52a), with equal numbers of labelled and unlabelled benzyls.

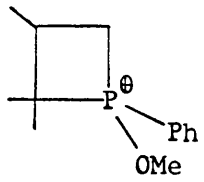
Equilibration of the benzyl groups, prior to a rate-limiting decomposition of the ultimate phosphoranes (58) and (62), would, therefore, arise from a fast pseudorotation process.

It is also evident, from this result, that TBP (58), benzyl and 3-C-methyl trans, is much less stable than its diastereomeric phosphorane (62).

Varying the reaction conditions may, however, develop a variation in the equilibrium mixture under which change in the rate-limiting step from rate-limiting breakdown of an intermediate to rate-limiting isomerization. Thus, the reaction becomes no longer stereoselective and different product ratios can be observed from hydrolysing diastereomeric salts. Under such circumstances pre-product formation equilibrium becomes unattainable. High energy intermediates are assumed to be involved through the reaction pathway, e.g. (59 and 62; R = Me).

It may seem obvious that there would be an area where a combination of both mechanisms could be operative and anomalous results may become observable. This may be invoked to explain the opposite outcomes obtained for the base-catalysed equilibration of 1-benzyl-hexamethyl-phosphetanium salts (41) and (49), on varying the anions from iodide to bromide. However, this must be considered cautiously in view of limited information on anion interaction in such circumstances and its role in stabilizing a particular species.

Kinetic evidence for a change in the rate-limiting step has also been reported by Gorenstein[89] to account for the pH-rate profile obtained for the phosphetanium salt, (64), hydrolysis, on varying the reaction pH. The author, further suggests that it may be possible under suitable conditions to observe the formation and breakdown of the pentacovalent intermediate phosphorane involved.



(64)

(c) The basicity of the hydrolysis medium used, (see Experimental section), apparently is sufficiently high[85] that isomerizations placing the leaving group(s) apical would be of much lower energy barrier than those leading to the nucleophile occupying an apical site[90-92]. Thus. pseudorotations involving (57)⇌(58) or (62) and (60)⇌(59) or (61), would be favourable under these conditions. This may not, however, be so at lower pH values, where rapid equilibration of diastereomeric salts is observable as discussed, later, when considering an appropriate pathway for such equilibration (Section 2.10.1).

(d) A possible mechanism for these reactions can be predicted in the light of the stability and isomerization of the intermediates involved. Consequently, it is of significant importance to establish the factors controlling the geometry of the initially formed TBP's and the relative energetics of the possible isomerization and decomposition pathways available to these intermediates. Of most importance, in this respect, is the effect of the various substituents present, specifically, their 'relative apicophilicities', which, in turn, is the product of three functions, i.e. electronegativity, π-electron interactions and, possibly, steric effects; (see Sections 3.6 and 3.7).

Any of the phosphoranes (58), (59), (61) and (62), in a reaction equilibrium mixture, is capable of decomposing to products, according to the respective equilibrium constants and the relative rate constants for loss of the axial leaving groups.

A comparative analysis of the stereochemical courses available to the initial phosphoranes (57) or (60), to yield either an individual or mixtures of the possible products, becomes apparently achievable. Product analysis of the alkaline hydrolysis of phosphetanium salts (56), on varying the R groups, provided that other factors remain the same, would reflect the relative apicophilicities of R, as compared to that of the benzyl group.

Considering the above discussion, it seems appropriate to envisage the different possibilities, in terms of Scheme I, and the most likely, i.e., of the lowest energy, reaction pathway leading to the observed product(s) under the specific reaction conditions.

(a) Hexamethylphosphetanium Salts.

The stereoisomerization of the 1-benzylphosphetanium salts prior to hydrolysis can be rationalized by an apical reversible attack of the hydroxide ion at the phosphorus atom of the tetrahedral phosphetanium cations, (56, R = CH_3), to give the initial TBPs (57) and (60). The observed predominance of the trans-salt (41b) in the equilibrated products mixture of the bromide salts (41), would be indicative of a lower energy barrier for the decomposition of TBP (60) than for (57). It also suggests possible reversibility of the reaction at every step. This may be explainable by an increasing ability of the equatorial oxy ligand to protonate on decreasing the medium's pH value. Hence, a condition may arise in which the reaction reversibility becomes attainable.

The rate of hydrolysis of the salt (64) is proportional to the hydroxide ion concentration in the alkaline regions, pH > 9, and is independent in dilute acid[89]. It follows that a pre-decomposition equilibrium, via fast pseudorotations, is taking place, allowing the collapse of (57) and (60) to become rate-limiting. The reaction proceeds,

therefore, stereoselectively to give the same equilibrium mixture from both cis- and trans-diastereomers of (41), as well as from (49), though with different product ratios according to the accompanied anions.

By increasing the alkalinity, however, the reaction becomes less stereoselective as different ratios of the hydrolysis product oxides (63) are observed. Under such conditions, apparently, isomerization is relatively slow and the product formation is controlled by the highest energy intermediate involved.

Formation of the oxides (63) and the absence of any observable oxides of (52) indicate that $k_{-2} \gg k_{-3}$ and $k_{-5} \gg k_{-6}$ and the path for pre-hydrolysis equilibrium is blocked. In addition, pseudorotations leading to either (57) or (60) would be exceedingly slow for reasons outlined before.

The overwhelming predominance of the trans-oxide (63a) in the products mixture from both diastereomeric salts is indicative of a higher energy barrier for decomposition of (61) compared to that for (58), i.e. $k_9 \gg k_{10}$; which is also evident on comparing k_{-3} to k_4. As it is expected that $k_4 > k_{-3}$, the above reason becomes an obvious explanation for the observed relative slowness of (60) $\longrightarrow$ (61) compared to (60) $\longrightarrow$ (59) $\longrightarrow$ (58) despite (59). Phosphorane (59) is considered as being a high energy species, as it represents a violation of the Muetterties polarity rule[59,63,93], which requires placing the most electronegative group, benzyl, apical.

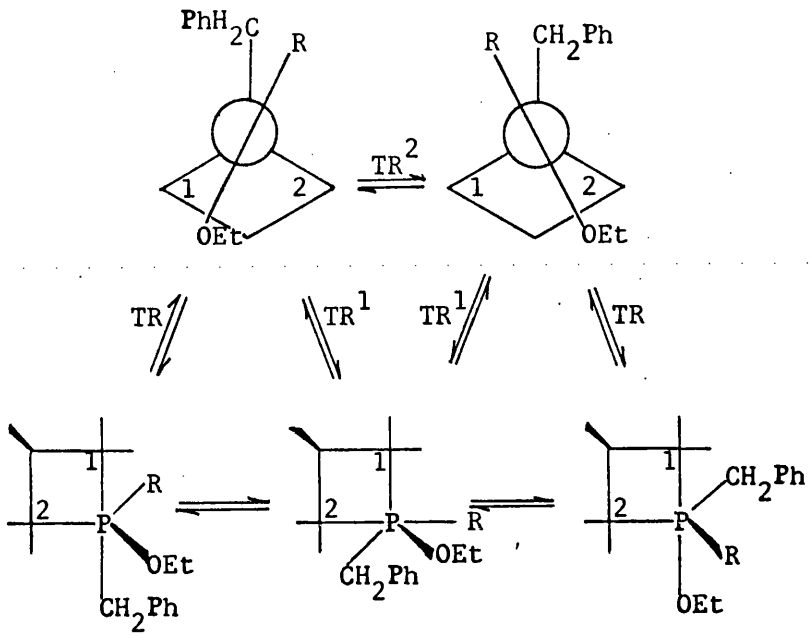
In the alcoholic hydrolysis, the path to equilibrium is still much the same as that outlined for the aqueous alkaline hydrolysis. Replacing the $\bar{O}H$ by the more basic ethoxide anion does, however, affect the analysis. The results can be interpreted in terms of Scheme II, page 50 .

Pre-hydrolysis equilibrium is not expected, under these circumstances, to occur. The path to equilibrium is blocked by the high energy phosphoranes (67) and (70) in which the two more electronegative groups,

benzyl and ethoxide, are in equatorial positions, whereas, the less electronegative methyl occupies the apical site. This represents a triple violation of the polarity rule. Hence the energy barrier to (67) and (70) becomes much higher than the corresponding barriers for (59) and (62), which represent only a single violation of the above rule. Consequently, k_1 and $k_4 \gg k_{-6}$ and k_{-3}; which would explain the unchanged product oxides ratio on hydrolysing the trans-salts (41a) and (49a). Whereas the previous relationship $k_{-3} > k_4$, is now reversed, $k_4 > k_{-3}$, hence, the reversed products ratio observed[15] for the cis-salt (49b).

It may seem worthy, in this respect, to point out that the above analysis is based on the hypothesis that the isomerisation observed proceeds via BPR mechanism. Concurrently, it may be interesting for an analysis based on the TR mechanism[73,74] to be considered. It is apparent from the precedent discussion, Section 2.5, that a principal point in such analysis is that high energy TBPs, such as (59) and (67), are to be avoided as is illustrated below. This means, in effect, that isomerization via TR^2 is, under any conditions, a fast process, i.e. formation and decomposition of the intermediate involved is a rate-limiting step in every case. Such interpretation, clearly, would be in contrast with the observed variable composition of the product mixtures in different media. It is, therefore, additional evidence in support of BPR as the most likely pathway in this regard.

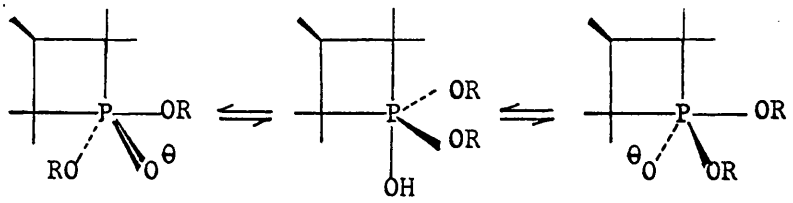
In the end, it seems reasonable to conclude that the benzyl group is more apicophilic than methyl as well as phenyl. A more quantitative approach to the determination of the relative apicophilicities of groups will be discussed later in Section 3.12.



(66) (67) (68)

(b) r-1-Benzyl-2,2-cis-3,4,4-pentamethyl-1-(prop-1-ynyl) and 1-(2-phenylethynyl)phosphetanium Bromide Salts.

The aqueous alkaline hydrolysis of the cis-isomer of either salt (50) or (51) proceeds with complete inversion of configuration at phosphorus, giving the trans-oxide (52a) r-1-benzyl-2,2-trans-3,4,4-pentamethylphosphetan 1-oxide as the only observable product. This complete stereospecificity of the reaction indicates that the decomposition of the ultimate phosphorane (59) is a rate-limiting step. A pre-decomposition equilibrium is evident, in view of the argument advanced for the hydrolysis of the dibenzyl salt (56, section 2.10). Therefore, the formation of the oxide (52, Scheme I) as the exclusive product may be the result of the reaction being thermodynamically, rather than kinetically, controlled, i.e. the formation of (62) can not be ruled out, however, it decomposes very slowly. DeBruin and co-workers[85] have shown that in the alkoxy system (71) there is an inherent

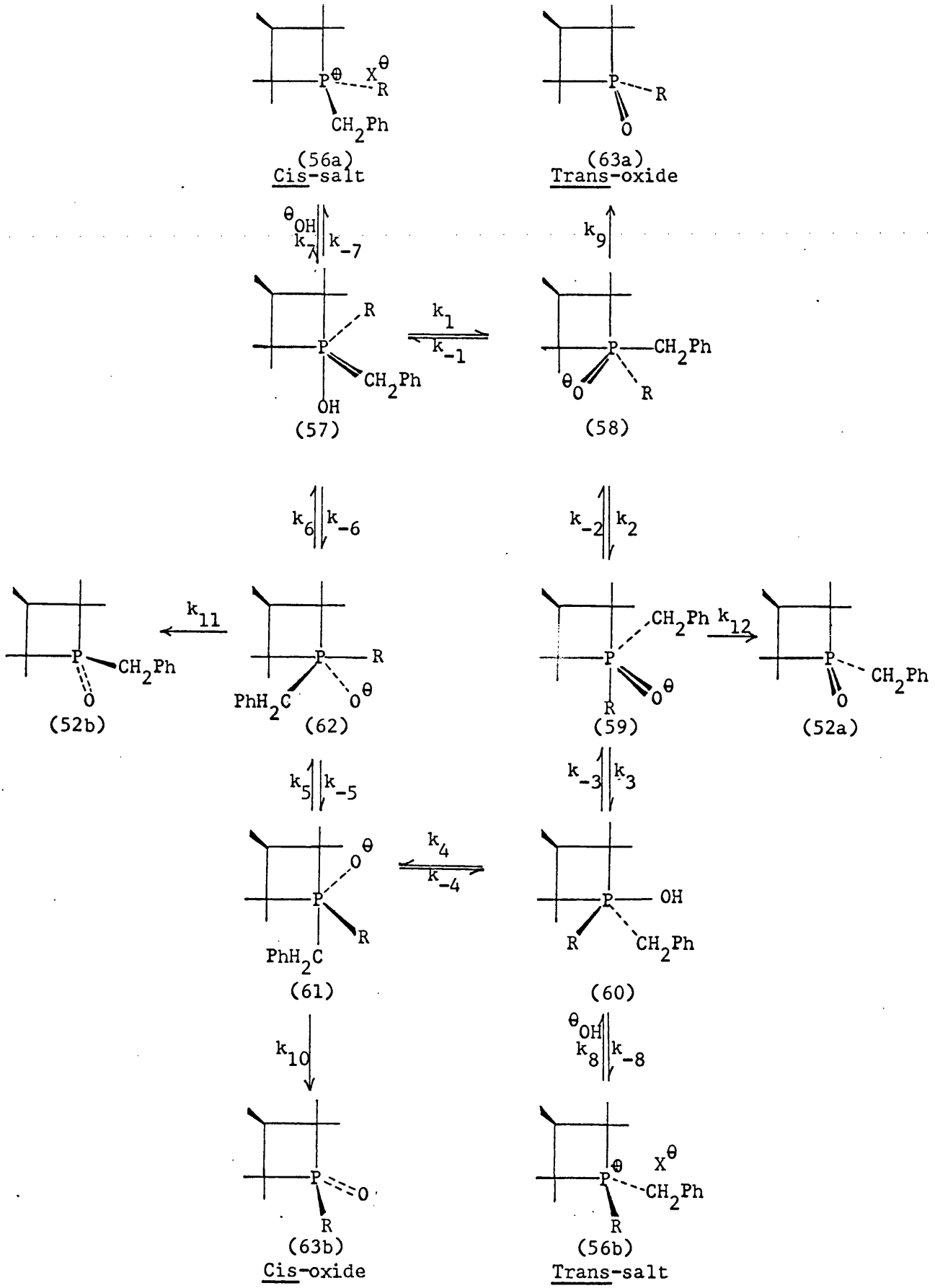


(71b) (71a) (71c)

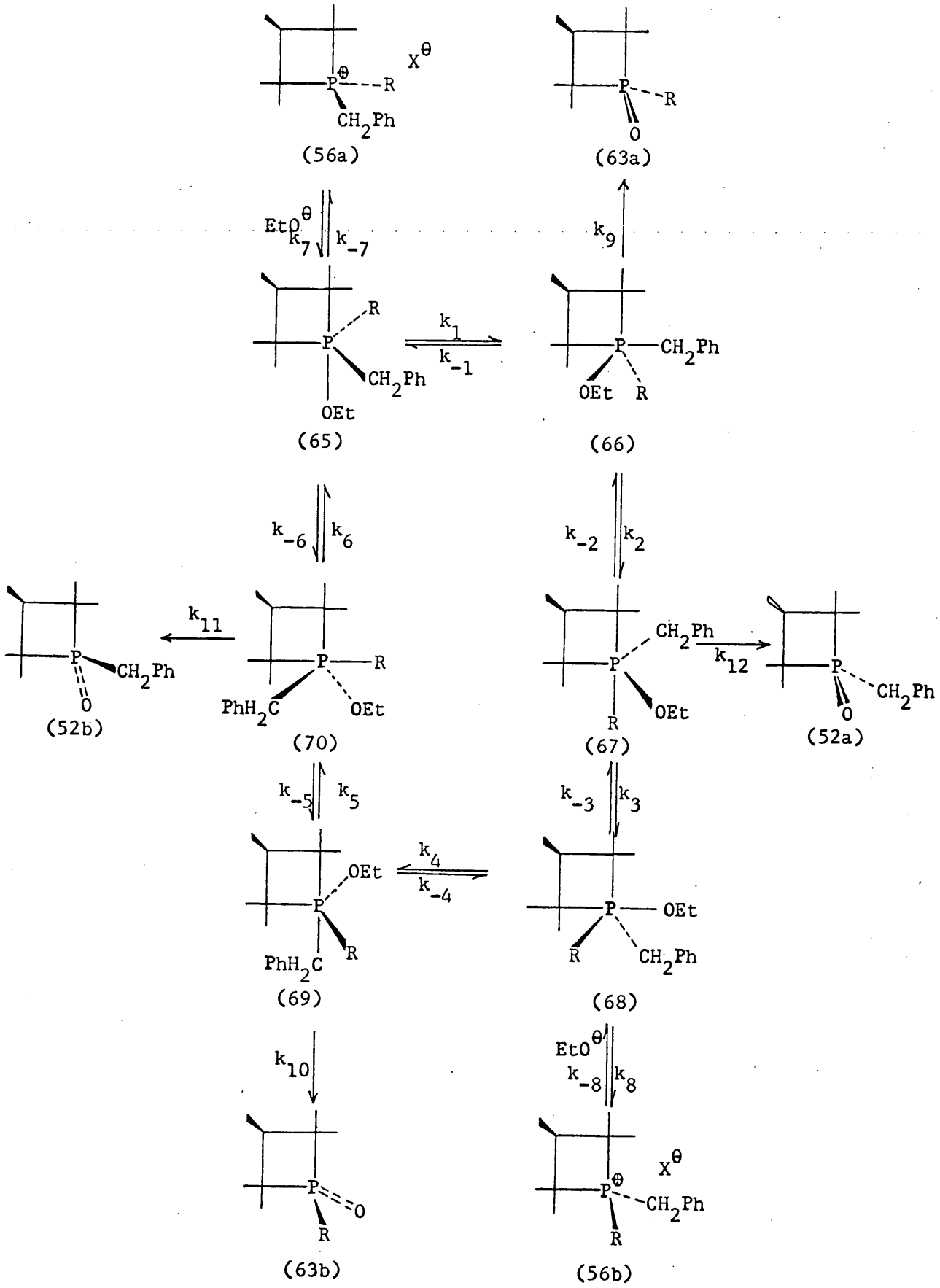
preference for isomerization (a)-(b) over (a)-(c), which has been attributed as being of a steric nature. That there is no observed acetylenic phosphetan oxide (63, R = C≡C-R') product would be taken to indicate a relatively higher apicophilicity value for the acetylenic groups studied than for the benzyl group. This is rather surprising in view of an expected preference for the equatorial site by such a group based upon a large lone-pair interaction with the phosphorus d-orbitals. This, however, will be discussed later in Section 3.10.

The results obtained thus reflect a considerable difference in the leaving ability of the competing groups, which can be attributed to the difference in their stability as the anions. The R-substituted acetylenes seem to be better leaving groups than benzyl. This may be due to the large difference in their pKa values of 18.5 and 35, for phenylacetylene and toluene respectively[94].

In the end it is concluded that the acetylenic groups listed in Table II are more apicophilic than benzyl. Nevertheless, a further study is required to cast some light on the role various factors play in such systems. This has been partly achieved in Section 3.10.


(56a)
Cis-salt
(63a)
Trans-oxide
(57)
(58)
(52b)
(62)
(59)
(52a)
(61)
(60)
(63b)
Cis-oxide
(56b)
Trans-salt

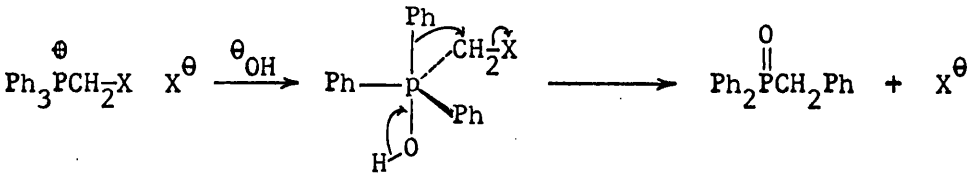
SCHEME I



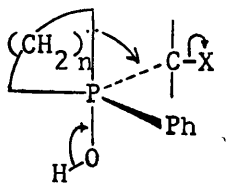
SCHEME II

2.11 Ring Expansion of Phosphetans.

Earlier reports on the hydrolysis of halomethyltriphenylphosphonium salts have indicated that the ease of phenyl migration to the halogen--bearing carbon is dependent upon the ease of loss of the halide ion[95,96].



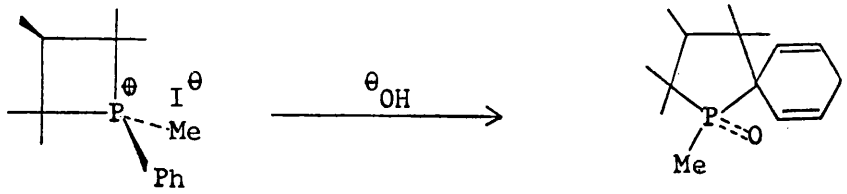
Migration of groups attached to phosphorus was also observed[18] in the hydrolysis of cyclic phosphetanium and phospholanium salts. These salts hydrolyse by nucleophilic attack opposite one of the P-C ring junctions to give a pentaco-ordinate phosphorane, in which the ring occupies an apical-equatorial position. This is considered to reduce the ring strain to less than that associated with the tetrahedral structure. However, evidently the ring still has enough strain to be relieved by ring-opening or ring-expansion. These ring expansions conform to a general pattern (72), where a P-C ring bond migrates to an X-bearing carbon with expulsion of X, which is capable of accommodating a negative charge.



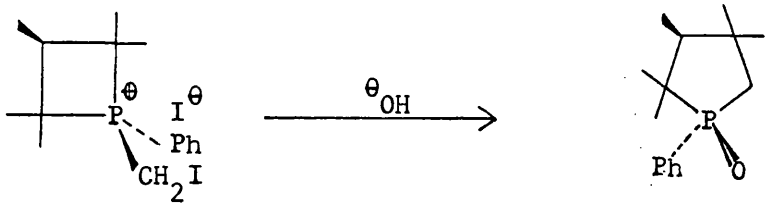
(72)

n = 1 & 2.

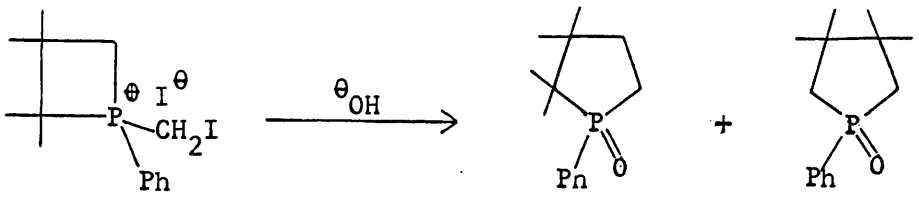
Thus, the phosphetanium iodides (53)[17], (73a)[22], (74)[97] and the phosphaphenanthrene iodide (75)[98,99] hydrolyse with ring expansion to give the corresponding oxides (54), (76a), and (77 - 79), respectively. In contrast, the salt (80) (10-alkylphenoxaphosphine iodide) gives the oxide (81), without ring expansion.[99]



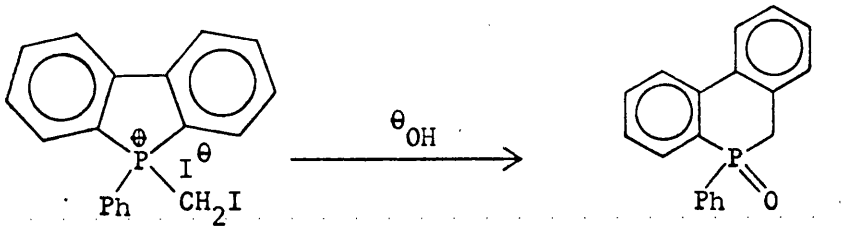
(53) (54)



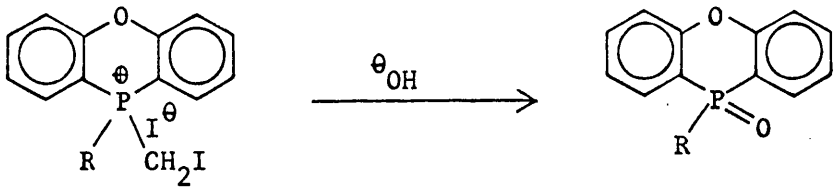
(73a) (76a)



(74) (77) (78)



(75) (79)



(80) (81)

It seems that the different behaviour of salt (80) is a result of a nucleophilic attack, opposite the better leaving iodomethyl group; presumably because the six-membered ring can easily adopt a diequatorial position in the intermediate phosphorane. Six-membered and larger rings are free of the constraints to which the smaller rings are subject[74]. Hence, direct loss of the iodomethyl group becomes the preferential pathway.

(a) The Alkaline Hydrolysis of Isomeric 1-Iodomethyl-2,2,3,4,4-pentamethyl--1-phenylphosphetanium Iodides.

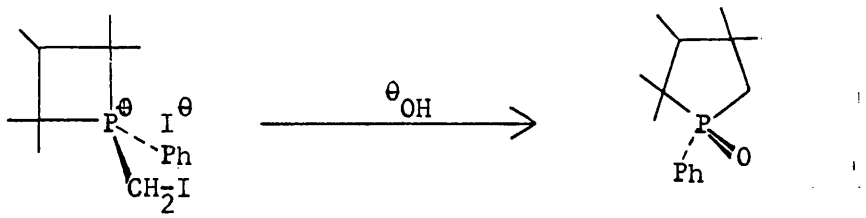
The cis- and trans-isomers of the 1-benzyl-1-phenylphosphetanium bromide (42), have been discussed in Section 2.9, and shown to give the same mixture of isomeric 1-phenylphosphetan 1-oxides (15)[15,71]. Also, both isomers of 1-methyl-1-phenylphosphetanium salts (53) hydrolyse to give the same mixture of isomeric phospholan oxides (54)[17,22,97].

This, and the reported hydrolysis of the cis-salt r-1-iodomethyl--2,2-cis-3,4,4-pentamethyl-1-phenylphosphetanium iodide (73a) to give only (r)-1-phenyl-2,2-trans-3,4,4-pentamethylphospholan-1-oxide (76a), with assumed stereochemical relationship, encouraged the research to investigate the hydrolysis of the trans-isomer (73b) under the same conditions.

Both isomers have been prepared by quaternising the isolated pure isomeric phosphetans with di-iodomethane in benzene.

Alkaline aqueous-ethanolic hydrolysis of the cis-salt (73a) was repeated and found to yield, in accordance with the above result, only the trans-phospholan-1-oxide (76a). Similarly, the pure trans-isomeric salt (73b), gave only the other, assumed, cis-isomer r-1-phenyl-2,2-cis--3,4,4-pentamethylphosphetan-1-oxide (76b).

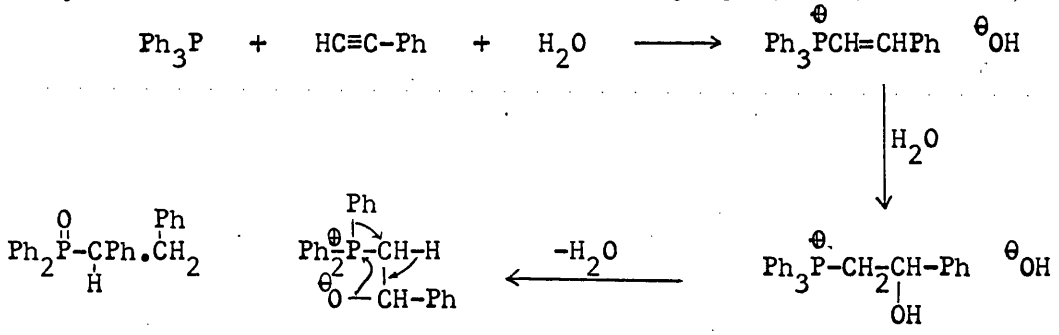
Thus the reaction proceeds completely stereospecifically, with, presumably, retention of configuration at phosphorus.



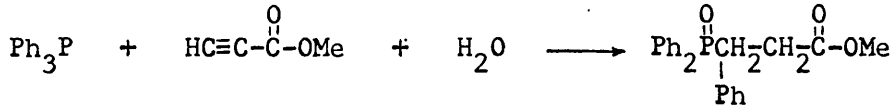
(73a) (76a)

(b) Reaction of Phosphetans and Ethyl Propiolate.

By analogy to the reaction between triphenylphosphine, phenylacetylene and water to give a 1,2-phenyl-shift product[100], Richards and Tebby[101] found that the reaction with methyl propiolate proceeded readily

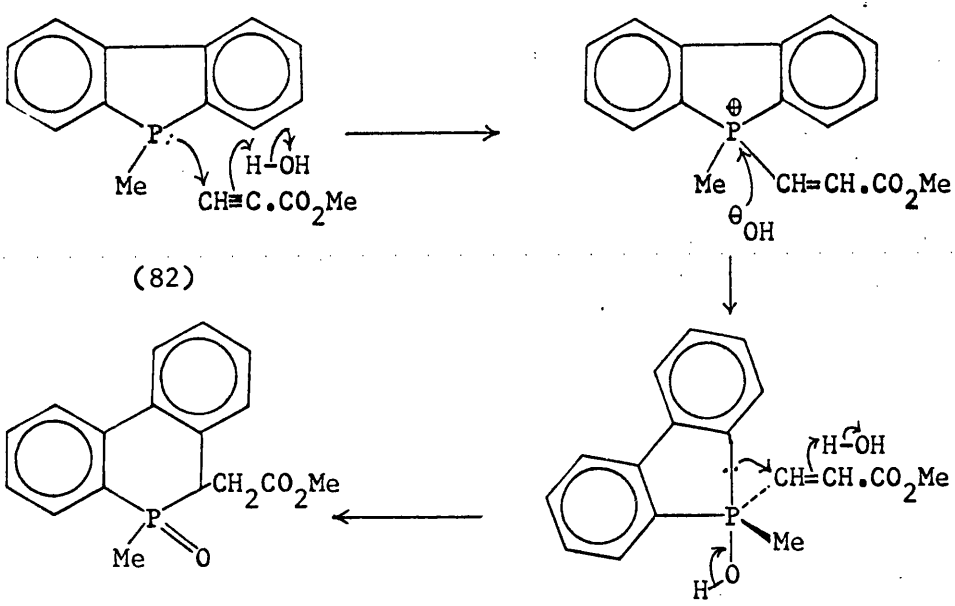


in wet ether to give the corresponding product.



Use was made of this observed 1,2-aryl shift in the reaction between phosphine (82) (9-methyl-9-phosphafluorene), ethyl propiolate and water to give 9,10-dihydro-9-phosphaphenanthrene 9-oxide (83).[100] The mechanism suggested[22] for the reaction involved alkaline hydrolysis of an intermediate phosphonium cation, (Scheme III).

Hawes[22] has investigated the analogous reaction of r-1-phenyl--2,2-trans-3,4,4-pentamethylphosphetan (16a) and ethyl propiolate in moist ether, which proceeds, exothermically, to give the oxide (84).

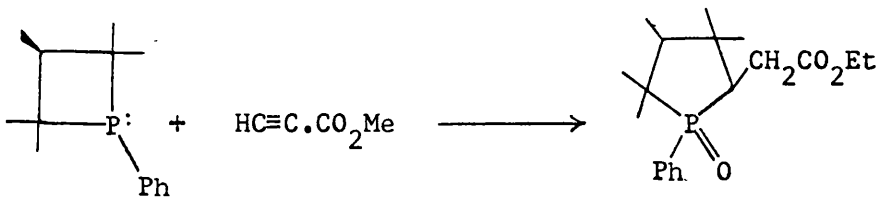


(82)

(83)

SCHEME III

(1-phenyl-2,2,3,4,4-pentamethyl-5-carbethoxyphosphetan 1-oxide).

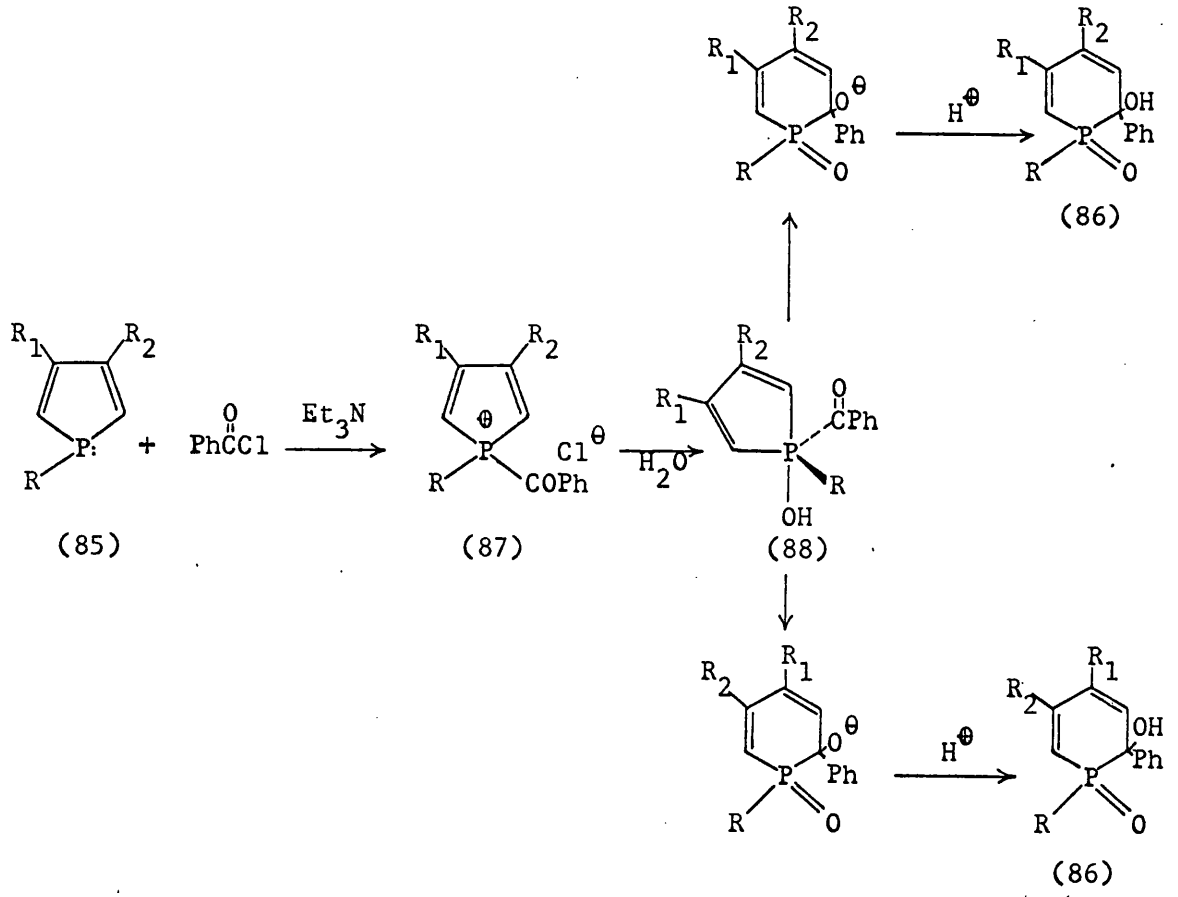


(16a) (84)

The observed complete stereospecificity associated with the above hydrolysis of the iodomethylphosphetanium iodides, invoked investigating the reaction of ethyl propiolate with the isomeric cis-phosphetan (16b) under similar conditions to those used by Hawes. Although one would expect at least four different geometric isomers in the product, only one of these possible oxides could be identified in the n.m.r. spectra, of the crude products, of both reactions. There is no evidence for the formation of any detectable amounts of the other isomeric oxides.

(c) The Reaction of Phosphetans with Benzoyl Chloride.

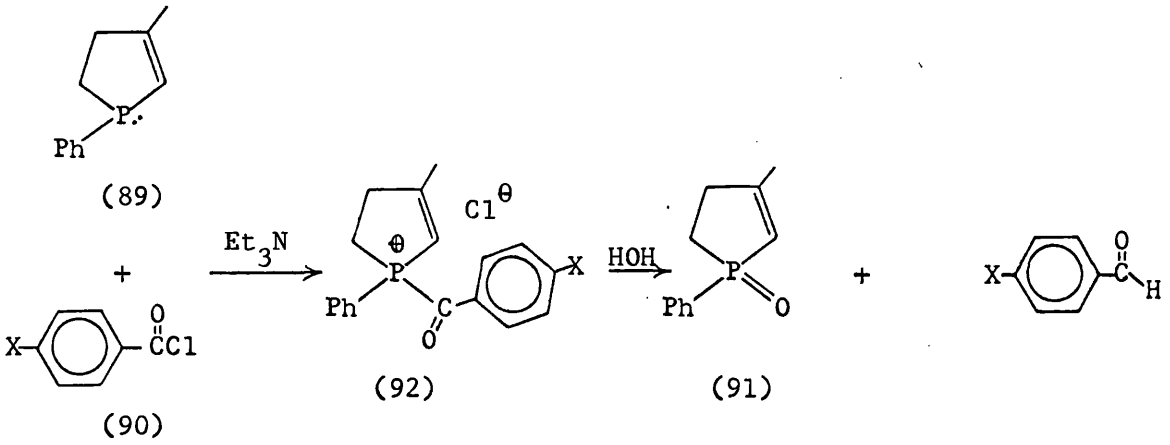
The reaction of the phospholes (85) with benzoyl chloride to give the ring-expanded products (86) was reported by Mathey[102,103] to require the presence of triethylamine for increasing the product yield. This reaction is thought to take place by a nucleophilic attack of hydroxide (or water) at phosphorus in the assumed initial product (87) to give TBP (88) via which the ring-expanded product can be formed. Migration of the P-C ring junction to the carbonyl group followed by protonation of the oxygen anion would give the observed outcome



R = Ph, Me & n-But.

SCHEME IV

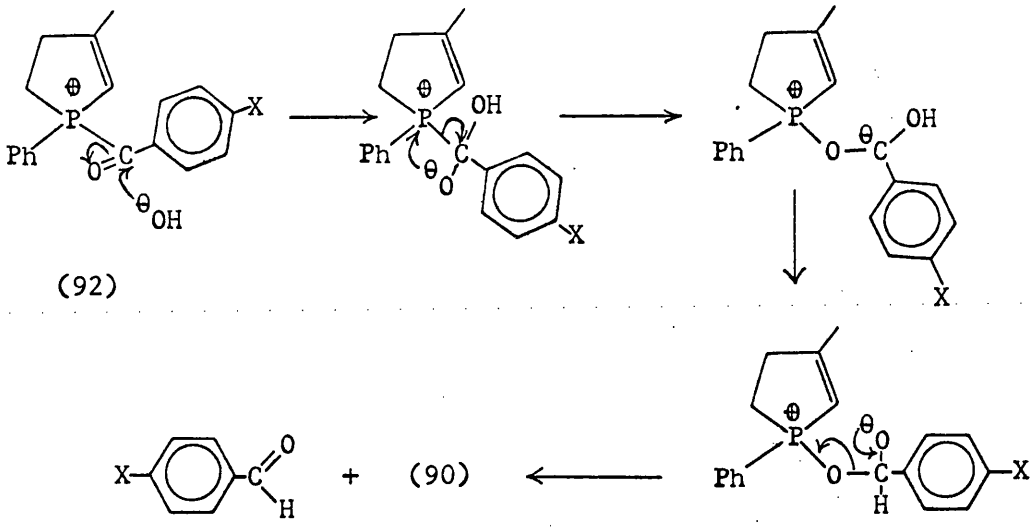
Recently, however, the reaction of the phospholen (89) and the benzoyl chlorides (90) in the presence of Et_3N was found[104] not to give ring-enlarged products; instead phospholen oxides (91) and benzaldehydes were obtained. To account for this different behaviour from phospholes, four possible mechanisms were discussed. Three of these routes arise from attack of base at phosphorus and were based upon the availability of losing the benzoyl group from an apical position. The nucleophile can attack opposite either the leaving group, forcing the ring to the diequatorial position, or one of the P-C ring-junctions. In the latter case, pseudorotation must occur to place the benzoyl group apical; (Scheme V).



X = H, p-$N(CH_3)_2$ & p-OMe.

SCHEME V

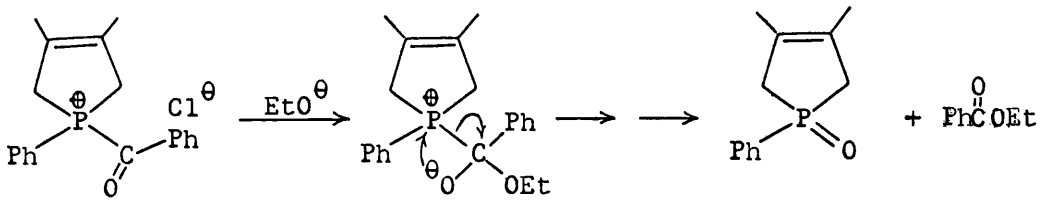
The fourth mechanism involved initial nucleophilic attack of base at the carbonyl carbon of (92), followed by rearrangement of the generated intermediate to give benzaldehyde directly; (Scheme VI). This mechanism was implicated in view of an observed formation of ethyl benzoate and phospholen in the alcoholic decomposition of the salt (93).



(92)

SCHEME VI

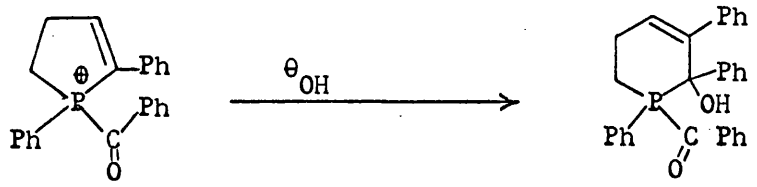
This was explained by a nucleophilic attack of the ethoxide ion at the carbonyl with expulsion of phospholen.



(93)

However, the possibility of this being the result of a kinetic effect was also raised, as due to the slowness of the step involving breakdown of the TBP generated on the oxide attacking the phosphorus atom. An explanation was given for the different products obtained in this case and the phosphole ring compounds, as being due to the relative differences in the stability of the particular TBPs which can be formed in each case.

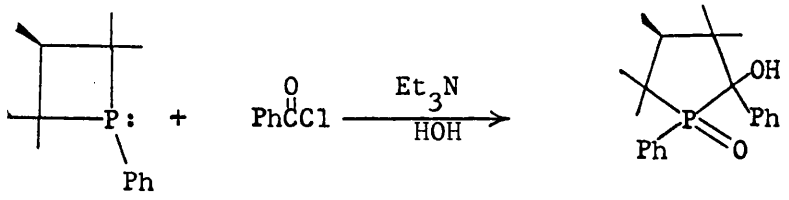
A mixture of ring-enlarged alcohol (95) and benzaldehyde was, on the other hand, observed[104] on hydrolysing the salt (94).



(94) (95)

No clear-cut preference was implicated for any of three possible mechanisms, arising from nucleophilic attack at phosphorus, opposite either of the two ring groupings or the benzoyl group placing the ring diequatorial.

By analogy to the reactions above, the possibility of observing similar behaviour in allowing the isomeric phosphetans (16) to react with benzoyl chloride under similar conditions was investigated. The reaction proceeded smoothly to give nearly quantitative amounts of the ring-enlarged product (96) which was found to be the same from both isomers as shown by n.m.r. and t.l.c. techniques carried out to identify the reaction products.

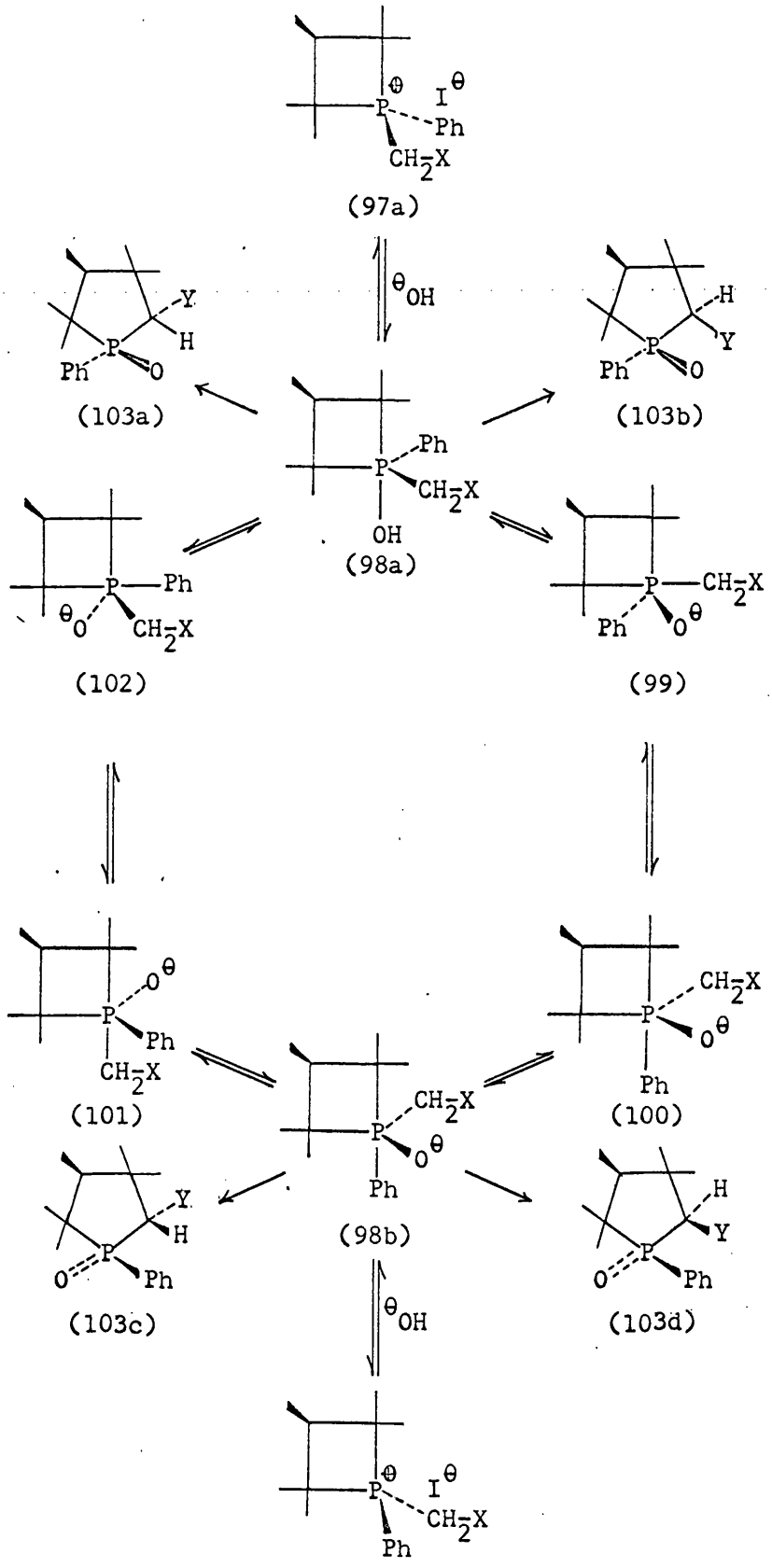


(16) (96)

2.12 Possible Mechanism for Ring Expanding Phosphetans.

The fact that there is only one particular ring enlarged product oxide observable on hydrolysing the corresponding salt, indicates the improbability of crossover between diastereomeric salts concerned.

In terms of Scheme VII, this complete stereospecificity can be explained as due to the incapability of the presumed less strained phosphoranes (98), initially formed by a nucleophilic apical attack on (97) opposite the C-Me_2 ring linkage, to pseudorotate. Pseudorotation



(76) Y = H
(83) Y = CH_2CO_2Me
(96) Y = OH

SCHEME VII

to (100) or (102) would involve a high energy TBP with an apical phenyl group, whereas ring-expansion would be unlikely to take place with the two involved groups occupying the apical sites. Furthermore, this lack of a considerably better leaving group, coupled with the fact that the four-membered ring still experiences some strain, and the possibility of a positive charge residing on the X-bearing carbon, would cause TBPs (98) to exist only for a very short life-time. As a consequence, breakage of the P-CMe_2 bond is, presumably, favoured, with formation of the incipient carbanion which migrates to the X-bearing carbon with expansion to give the observed phospholen 1-oxides (103) with complete retention of configuration at phosphorus.

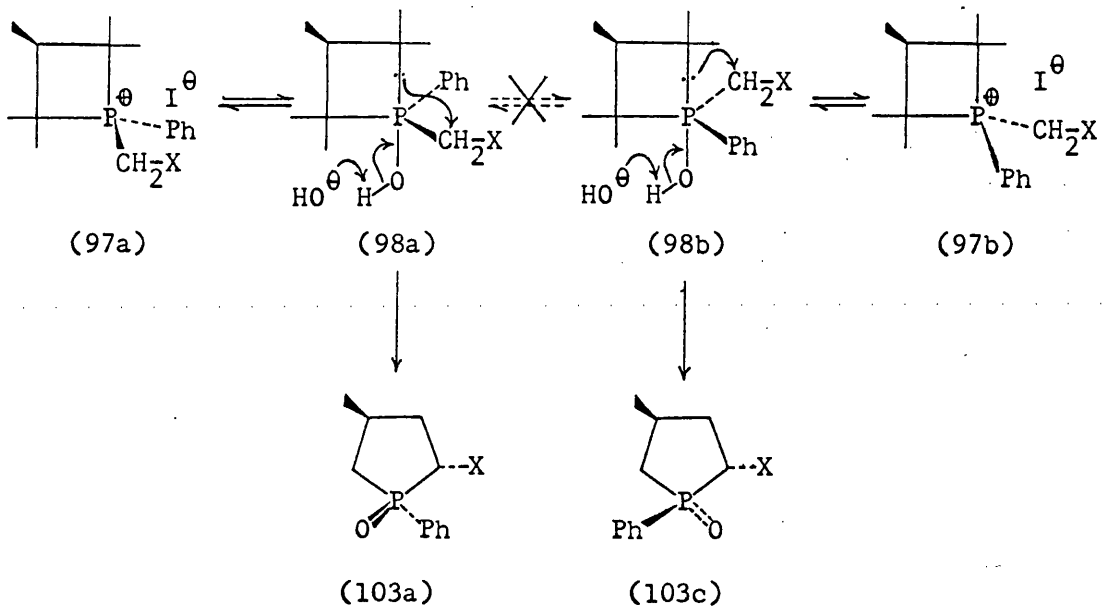
The fact that only one, out of two, product oxides, except where $X \neq I$, is obtained, may be due to steric effects in favour of a trans--stereochemical relationship involving X- and Me-C_5- groups in the product. If this is true, structures (103a,c) are favoured over (103b,d) when $X \neq H$.

Hence, a general pathway for the reaction can be depicted as in Scheme VIII.

In the light of the above discussion, the advancing of an appropriate relevant pathway for each specific reaction may be outlined as follows.

(a) Hydrolysis of 1-Iodomethyl-2,2,3,4,4-pentamethylphenylphosphetanium Iodides.

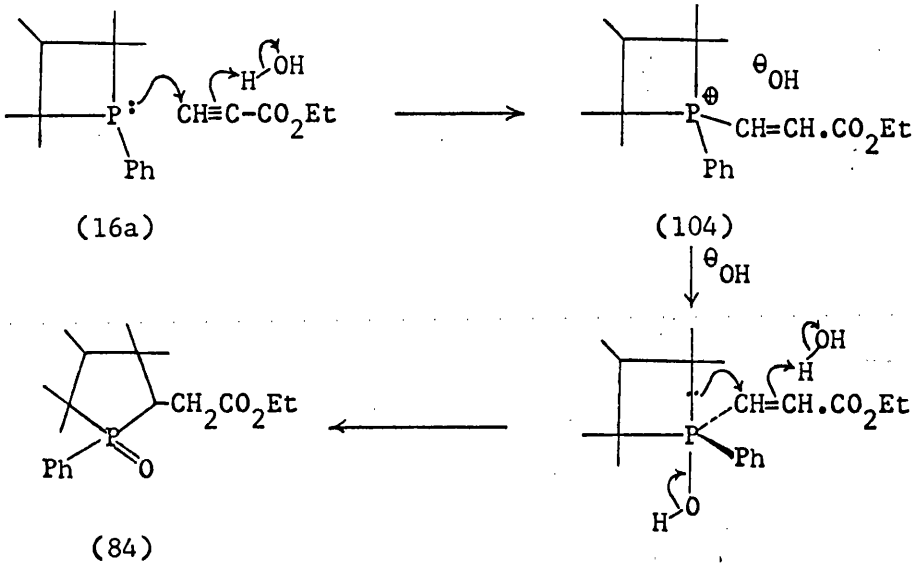
This can be suggested to proceed via the same routes illustrated in Scheme VIII, to give the product oxides, X = H, (103a ≡ b), or (103c ≡ b), according to the starting isomeric salt.



SCHEME VIII

(b) Reaction of Phosphetan with Ethyl Propiolate.

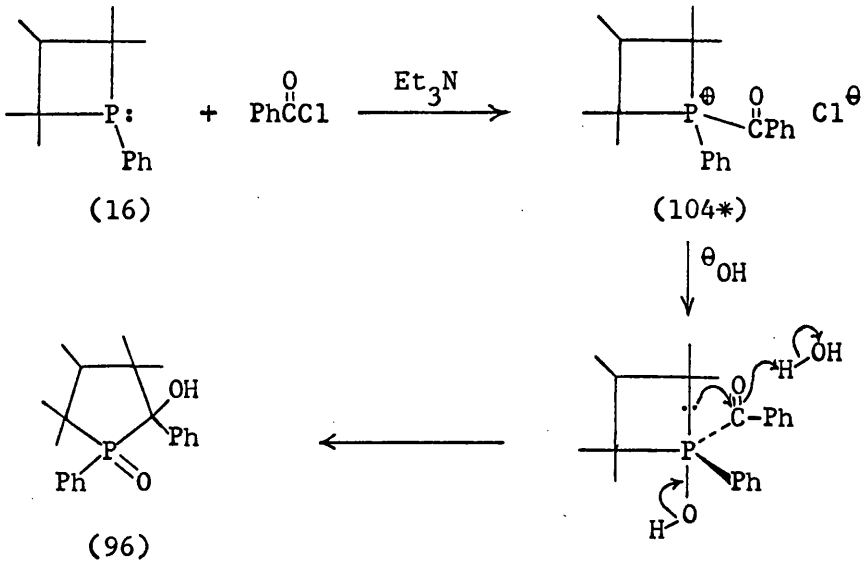
The mechanism of the reaction Scheme IX, is thought to involve an attack of the phosphorus lone pair on the acetylenic bond of the ester and protonation of the generated carbanion gives the un-isolated salt (104). Attack of hydroxide at the phosphonium centre would give TBP intermediate (105). Migration of the ring junction and protonation of the generated anion gives the corresponding product oxides (84), with assumed retention of configuration.



SCHEME IX

(c) Reaction of Phosphetans with Benzoyl Chloride.

It may seem reasonable that the same comments apply regarding the hydrolysis mechanism, Scheme X, of the salt (104*) as put forward for the salts (104) formed on reacting the above pentamethylphenylphosphetans and ethyl propiolate, discussed above.



SCHEME X

In fact, what seemed promising attempts were made to isolate the assumed intermediate salt (104*); however, due to its extreme sensitivity towards moisture, and lack of time, unfortunately, this was not proceeded further.

CHAPTER 3

3. OXYPHOSPHORANES

3.1 Pentaco-ordinate Phosphorus Compounds.

Oxyphosphoranes are derivatives of pentaco-ordinated phosphorus having at least one(P-O)bond. These compounds have long been thought of as intermediates in nucleophilic substitution reactions at tetraco--ordinated phosphorus centres. However, only recently have they become available in sufficient variety to allow their stereochemistry to be studied. Although a very large number of acyclic phosphoranes have been synthesised, the most comprehensive stereochemical studies in the oxyphosphorane field were achieved with cyclic compounds of the 1,3,2-dioxaphospholan and 1,3,2-dioxaphospholen type. This is partly due to their relatively increased stability compared to their acyclic analogues, attributed to the incorporation of small rings.[74] (see section 3.3). Hence, the ease by which they can be synthesised.

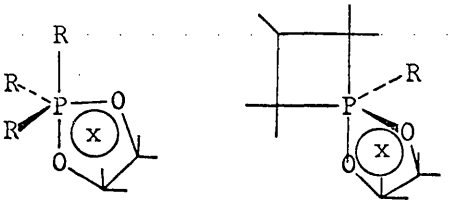
3.2 Synthesis of Oxyphosphorane Compounds.

The most widely used methods of preparation of the oxyphosphoranes studied in this thesis can be summarized as follows:

(a) Reaction of Tervalent Phosphorus Compounds with Mono-functional Carbonyl Compounds.

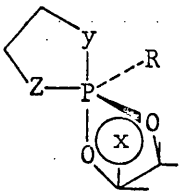
Tervalent phosphorus compounds react with suitably activated mono-carbonyl compounds, in which the substituents around the carbonyl group stabilize a negative charge, in a 1:2 ratio, to form, usually, 1,3,2-dioxaphosphoranes.[105] In contrast, inactivated aliphatic mono--aldehydes give an alternative 1,4,2-dioxaphosphorane. Thus,

ninhydrin,[106] fluorenone,[107,108] and hexafluoroacetone (HFA)[109-112] react with the appropriate phosphorus compounds to give 2:1 mono- and spiro-cyclic 1,3,2-dioxaphosphorane adducts, e.g., the hexafluoroacetone adducts (32), (106) - (109).



(106)

(32)

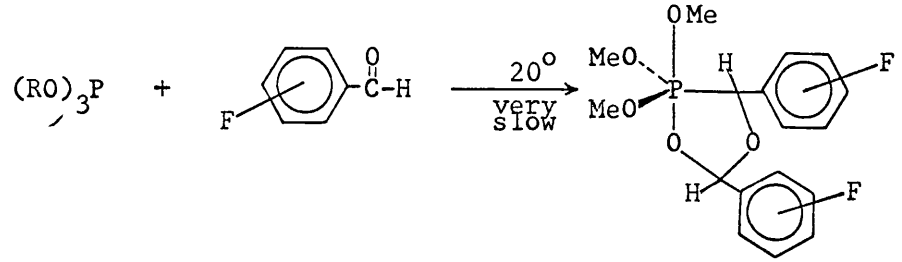


(107) y = Z = C,O & NMe.

(108) (109) y = O, Z = O & NMe.

x = CF_3

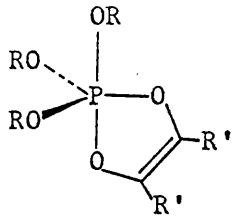
The 2:1, 1,4,2-dioxaphosphorane adducts (110), however, have resulted in reacting certain less activated aliphatic aldehydes,[109] e.g. pentafluorobenzaldehyde, with phosphite esters.



(110)

(b) Reaction of Tervalent Phosphorus Compounds with α-Dicarbonyl Compounds.

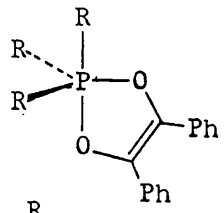
The 1,3,2-dioxaphosphoranes (111) have been prepared from the condensation of trialkyl phosphites with o-quinones and α-diketones.[113,114]



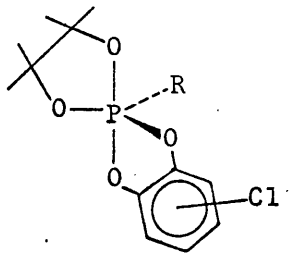
(111)

The chemistry of these compounds has been largely developed by Ramirez and his co-workers.[109,113] They have shown that the reaction proceeds under mild conditions and that these adducts can combine with a second carbonyl molecule to form 1,3,2-dioxaphospholan adducts.

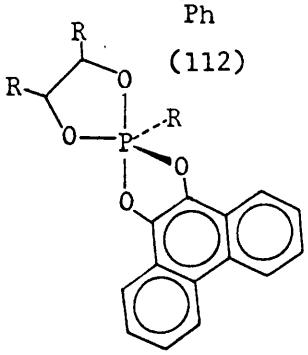
However, due to the increasing interest of many other workers in this field, recent examples of such adducts have since been developed. The adducts (112 - 115) have been synthesised from suitable tervalent phosphorus compounds and benzil,[114] biacetyl,[115] o-tetrachlorobenzo-,[111] phenathra-,[116] and naphtha-quinones.[117]



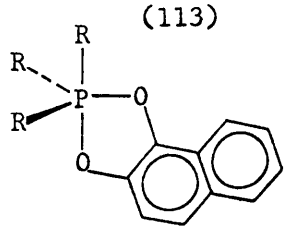
(112)



(113)



(114)

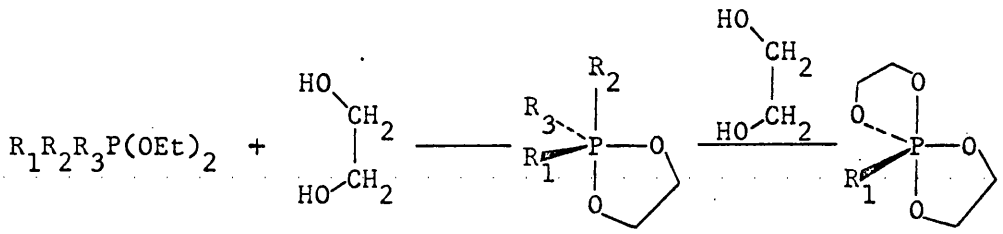


(115)

(c) Exchange Reactions of Diethoxyphosphorane Compounds with Diols.

The reaction of acyclic phosphoranes which contain, at least, two alkoxy groups with simple or substituted 1,2- and 1,3-glycols has been reported to form cyclic oxyphosphoranes containing one or two rings.

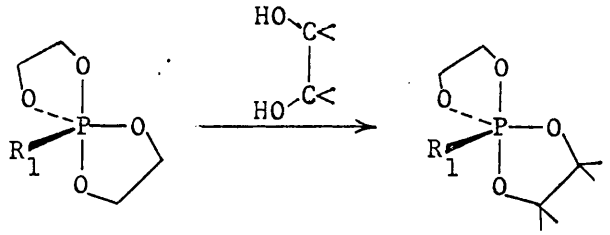
This exchange route has enabled a wide range of these compounds of the general types (116) and (117), to be prepared.



(116) (117)

$R_1R_2R_3$ = alkyl, aryl & ethoxy. $R_1 = R_2 = OEt$.

The ethylene glycol rings, also, can be replaced[119] by more substituted rings, forming a new spiro-oxyphosphorane (118).



(117) (118)

3.3 Stability of Phosphoranes.

The stability of phosphoranes varies considerably and it seems that stabilisation of the pentaco-ordinate structure comes from two main sources: (a) by increasing the electronegativity of the substituents attached to phosphorus and (b) by the incorporation of phosphorus into a small ring.

(a) The electronegativity of the elements attached to phosphorus can bear a major influence on the stability of the formed phosphorane, for example, in reactions between a trivalent phosphorus compound and a carbonyl compound, relative to the ease of decomposition to a phosphonium species.

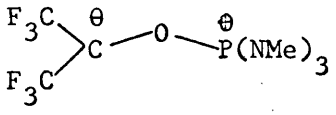
Thus, it may exist as an oxyphosphorane or in the open dipolar

form, as expressed by the following equation, derived from studies on a variety of phosphoranes.[75]

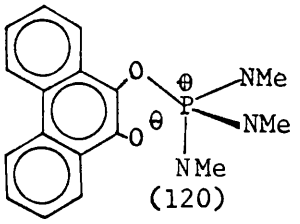
$$PX_5 \rightleftharpoons PX_4^{\oplus} + X^{\ominus} \qquad (1)$$

The more electronegative ligands favour the pentacovalent structure, hence, shifting the equilibrium to the left side of equation (1), i.e. towards phosphorane formation.

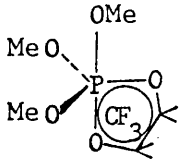
On reacting HFA[115] and phenanthraquinone[120] with tris(dimethylamino)phosphine, the zwitterions (119) and (120) were obtained, while with trimethylphosphite, the adducts isolated were the stable oxyphosphoranes (121) and (122).



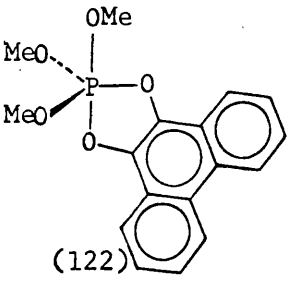
(119)



(120)

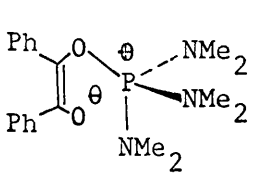


(121)

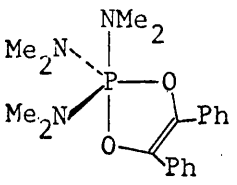


(122)

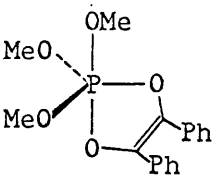
Likewise, on reacting benzil with trimethyl phosphite[120] or tris(dimethylamino)phosphine,[121] the product in the first case is formed in two crystalline forms (123) and (124). These are in equilibrium in solution giving a single solvent-dependent ^{31}P n.m.r. signal.



(123)



(124)



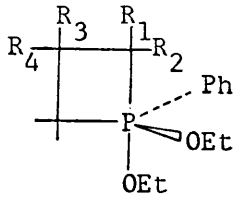
(125)

In contrast, the adduct (125), formed in the second case, is a very stable oxyphosphorane. This, also, is consistent with the observed decrease in the stability of oxyphosphoranes on replacing the alkoxy groups for amino or alkyl groups.[105] This was suggested to be, in part, due to the difference in electronegativity between the oxygen and the nitrogen or carbon ligands, with the less electronegative groupings favouring the dipolar structure.

Steric effects, however, may also be operative due to the larger steric requirements of the dialkylamino groups vs. the alkoxy groups.[105] This would destabilise the adducts formed, which have been shown to have intramolecular crowding within the molecule.[52,54,55,105]

(b) The enhanced stability conferred by the ring may be attributed to the intramolecular crowding due to several non-bonded distances[105] in the TBP structure,[74,108,122] being offset by the ring,[123] and also to the ring being less strained when achieving an apical-equatorial position in the TBP phosphorane. This effect would also shift the equilibrium in the above equation to the left.

Dimethylphenyl- and trimethylphosphines react with diethyl peroxide to give an equilibrium mixture of pentaco-ordinate compounds and phosphonium ethoxide.[102] In contrast, TBP phosphoranes (126) can be formed on reacting the appropriate phosphine with diethyl peroxide.[124]

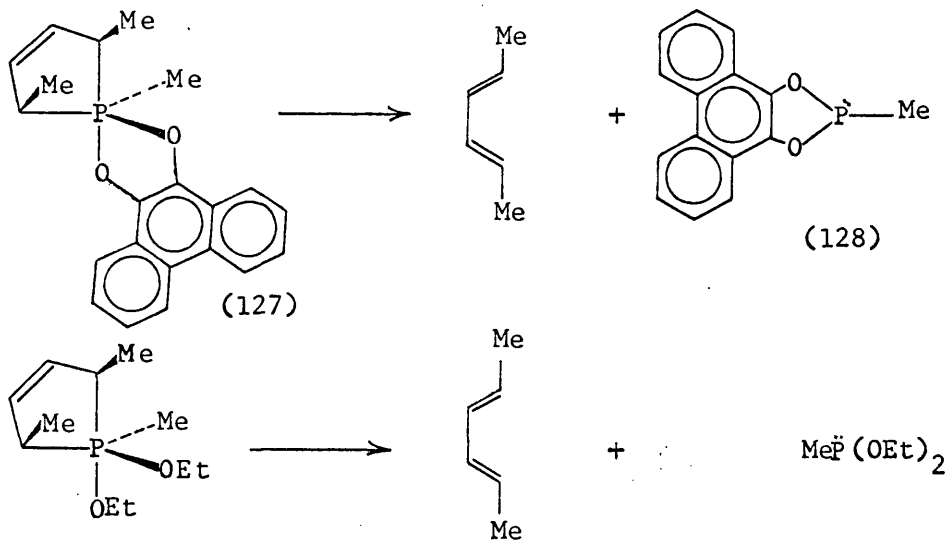


(126)

$R_1 = R_2 = H$,

Or $R_3 = R_4 = H$.

The phosphorane (127) fragments,[125] stereospecifically, to trans,trans-hexa-2,4-diene and the cyclic phosphonite (128), with $\Delta G^* \simeq 25$ kcal mol^{-1}. whereas phosphorane (129) fragments spontaneously at room temperature to the products shown.



(127)

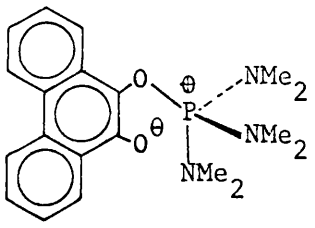
(128)

(129)

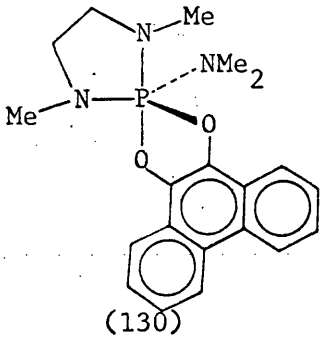
The barrier to decomposition is apparently due to the increased ring strain on forming (128).

Thus, it seems that oxyphosphoranes with two five-membered rings are more stable than the analogous monocyclic compounds.[126] The adduct (120) is an open dipolar species, while (130) is a stable

phosphorane.[105,121]

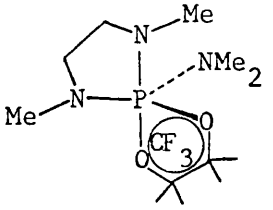


(120)



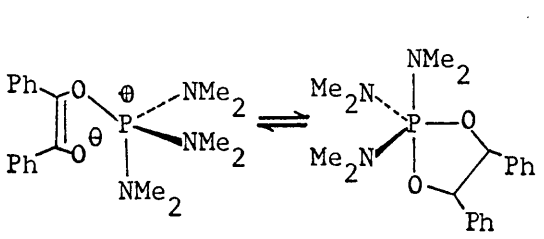
(130)

This also appears to be true when comparing the unstable HFA adduct (119) with the stable spirophosphorane (131).[105]

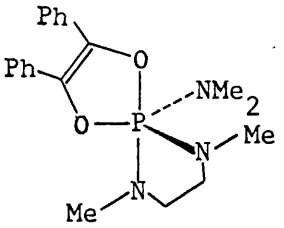


(131)

Similarly, although the phosphorane (123) exists, in solution, as an equilibrium between the dipolar and the phosphorane forms, (132) assumes the TBP structure.[105,121]



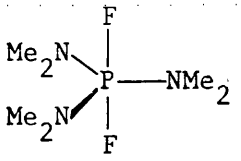
(123)



(132)

It would be more likely to suggest that the TBP structure, in this case, is due to decreased ring strain, relative to that of TBP (123), i.e. ring-containing oxyphosphoranes are, thermodynamically, more stable than their acyclic counterparts. However, it is not necessarily true that all cyclic oxyphosphoranes are more stable than acyclic oxyphosphoranes, e.g. the reaction of HFA with tri(dimethylamino)phos-

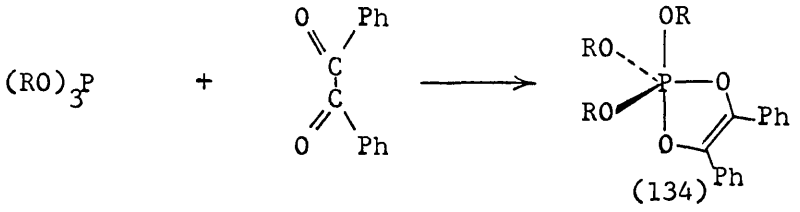
phine to give the 1:1 adduct (119) and a variety of products of molecular fragmentations, among them the fluoroaminophosphorane[105] (133). The 2:1 adduct in this case can not achieve stabilisation by forming an oxyphosphorane.



(133)

3.4 Mechanism of Oxyphosphorane Adduct Formation.

The reaction of trialkyl phosphite with benzil, in anhydrous dioxane to form the cyclic adducts (134), has been studied kinetically by Ogata and Yamashita.[114,127,128]



(134)

R = Me, Et, i-Pr & sec-But.

The rate-reaction was measured, by means of uv spectroscopy of produced adduct phosphorane, for the effects of acid, base, and solvent and also structural effects. Some of their most pertinent results can be summarised as below.

(a) The overall reaction is irreversible. However, the first step was suggested to be reversible in view of a low value of the energy of activation (8.41 kcal. mol^{-1}) which is supported by previous examples.

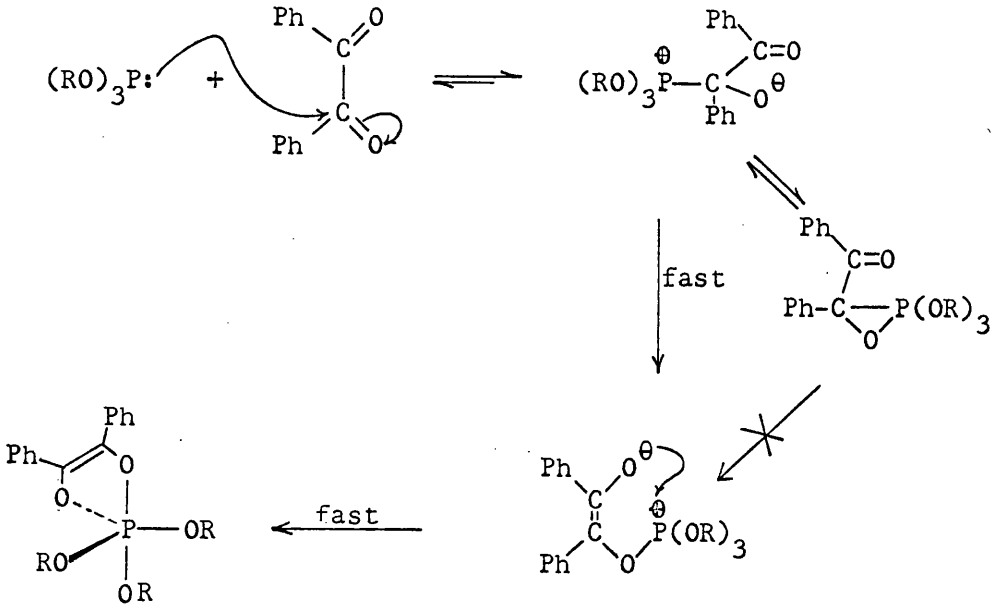
(b) The reaction was found to be second order, first order in both

phosphite and in benzil.

(c) The rate increased with increase in the dielectric constant of the solvent to a limited extent, and with increasing acidity of the reaction mixture. In contrast, it decreased on adding tertiary aliphatic amines.

(d) Varying the R groups of the phosphite generally increased the rate constant in the order Me < sec-Bu < Et < i-Pr. This may reflect an increase of the phosphite nucleophilicity as a result of inductive effects. Steric effects, however, were also suggested to operate, e.g. with tri-sec-butyl phosphite.

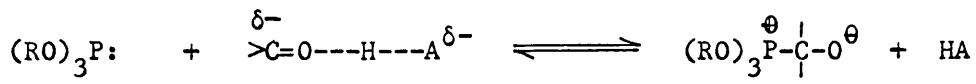
In view of the above findings, the authors proposed the following mechanism, which involves nucleophilic attack of phosphorus on the carbonyl carbon of benzil. Rearrangement of the phosphorus atom from carbonyl carbon to oxygen <u>via</u> a concerted three-membered cyclic mechanism was disfavoured[127] as the course to the product.



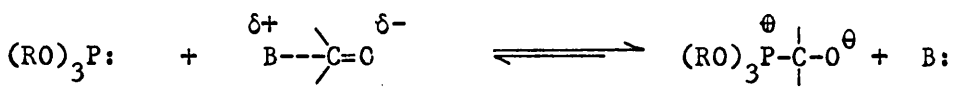
(134)

The value of the activation energy was taken to indicate that, in the rate-determining step, no large energy is needed, hence, it probably involves no C-P bond fission.[129] The large negative entropy of activation (-47.5 eu), was taken to exclude a concerted Diels-Alder type of mechanism. In general, Diels-Alder reactions exhibit entropies of activation not less than -30 eu, and should not be activated by both organic acids or bases.[130]

In the presence of acetic acid, the extinction coefficient of benzil uv carbonyl absorption varies. This was suggested to indicate the presence of hydrogen bonding between the acid and benzil carbonyl oxygen. Hence, the accelerating effect is due to a polarizable carbonyl group which activates the carbon for nucleophilic attack of the phosphite as shown below:

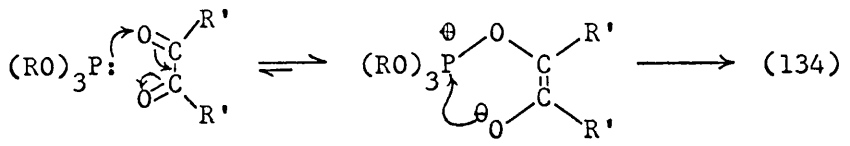


On the other hand, the retarding effect of tertiary amines was attributed to the base being co-ordinated to the carbonyl carbon, i.e. weakening its electrophilicity.



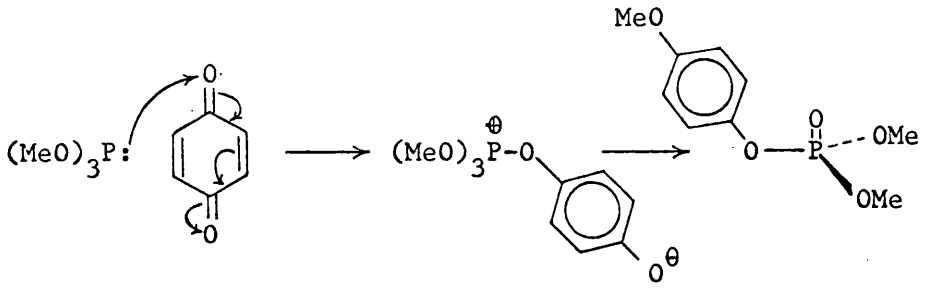
This type of pathway was also suggested by Mukayama et al.[131,132]

Another mechanism, however, was advanced by Ramirez et al[105,121,133,134] which favours attack on the carbonyl oxygen rather than on carbon. Cyclization of the intermediate zwitterion (135) would give the product.



(135)

The argument for this rests on a suggested nucleophilic attack of phosphorus on the oxygen of p-benzoquinone.[105,121,133]

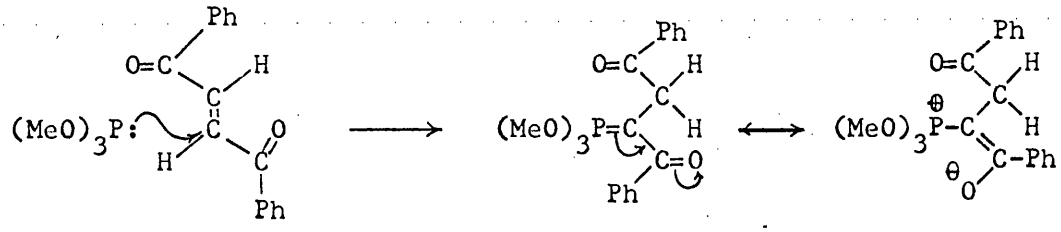


(136) (137)

The dipolar ion (136) undergoes rapid alkyl translocation leading to ether (137). The phosphite tends to attack the oxygen atom whenever the latter is surrounded by groups which are capable of stabilizing a negative charge at the carbonyl carbon.[133] The reaction of phosphites and monocarbonyl compounds is generally accepted to proceed via such a pathway.

The mechanism advanced by Ogata and Yamashita[114,127,128] is based, mainly, on the observed effects of acid, base, and substituents on the reaction rate. The rate decreases with an increase of electron--releasing power of alkyl groups on the ketone. Furthermore, they suggested that the resonance of negative charge with substituent is forbidden in the transition state.

Ramirez and co-workers, however, invoked a similar mechanism,[126] to that of Ogata and Yamashita, to explain the reaction of phosphines and phosphites with the α,β -unsaturated ketone; trans-3-benzylidene--2,4-pentanedione to give the 1:1 adduct (138).



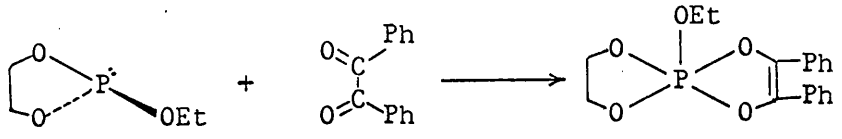
(138)

Ogata and Yamashita rejected the possibility of concerted, and of one-electron transfer from phosphorus to carbonyl, mechanisms because of an observed substituent steric effect,[114] i.e. two bulky t-Bu groups in t-BuCOCOBut-t inhibit the reaction, as well as for reasons discussed above.

It seems, from this discussion, that either mechanism may operate under certain conditions, decided by the nature of the reaction, (see Section 3.10).

3.5 Kinetics of The Reaction of 2-Ethoxy-1,3,2-Dioxa-phospholan with Benzil.

In the light of the mechanism of Ogata and Yamashita, discussed above, the question whether the reaction of benzil with cyclic phosphites follows a step-wise or a concerted mechanism remained an open one. This, therefore, provoked the attempt to find out an answer by looking at the reaction of benzil with 2-ethoxy-1,3,2-dioxaphospholan (139),[135,136] to give the adduct (140).



(139) (140)

The reaction was conducted in anhydrous dioxane at 25° and 45°C, with the phospholan in excess, to shift the reaction towards completion. Equal volumes of benzil and phospholan solutions were mixed together. Aliquots of 1 ml. were then taken at appropriate intervals and the reaction is stopped by diluting with light-petroleum (60-80°).

The u.v. spectrum of the product was measured at the experimentally estimated λ_{max} 318 m u.

The rate-law is expressed by the bimolecular equation:

$$r = k \left[\text{phospholan}\right] \left[\text{benzil}\right]$$

The observed second-order rate constant k was calculated using the formula (2):

$$k = \frac{1}{t(a-b)} \ln \frac{b(a-x)}{a(b-x)} \qquad (2)$$

where t = time in seconds

a & b = initial concentrations of phospholan and benzil respectively

x = concentration of product after time, t.

The concentration of the product (x) is determined from the formula (3):

$$x = \frac{D}{E} = \frac{D}{9100} \qquad (3)$$

where D = optical density of the product at λ_{max} 318 m u

E = molar extinction coefficient of the product at the above wave length.

The kinetic data so obtained are shown in Table III

Table III. Second-order Rate-constant for the Reaction of 2-Ethoxy-1, -3,2-dioxaphospholan with Benzil in Dioxane.

Phospholan M	Benzil M	Temp. °C	$10^3 k$, M^{-1} sec^{-1}
0.1370	.050	25	0.1317
0.0657	.050	25	0.1524
0.1033	.050	45	0.4060
0.0657	.050	45	0.4075
Triethylphosphite:			
0.0966	.050	25	13.88*
-	-	25	11.3 **[124]

* Calculated for E = 11,300 at λ_{max} 322 m u, (light-petroleum)

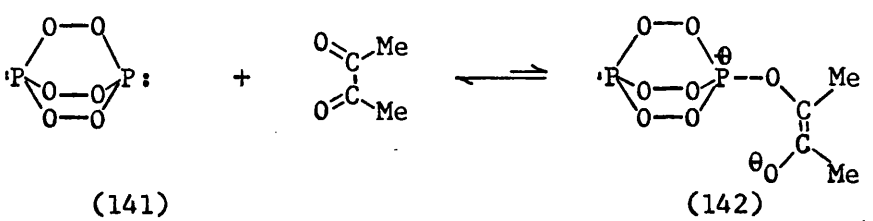
** Calculated for E = 11,800 at λ_{max} 321 m u (n-hexane).[127]

The oxyphospholan adducts formed by reaction of phosphite and benzil are expected to be, for the reasons described in the previous section, reasonably stable.

A conjugation of the double bond with the aromatic rings has been suggested[121] to occur in such adducts which would tend to favour the phospholen structure. These adducts, however, tend to be highly hygroscopic;[127] thus, their separation would sometimes be rather difficult. This, probably, is the reason for the many unsuccessful attempts to crystallise the product from the reaction mixture. Consequently, no standard analytical data could be presented to support the structural assignments, other than ^{1}H, ^{31}P, and ir spectra. The conclusion derived from these data (see experimental section) is in favour of a TBP phosphorane structure.

It is clearly evident, when comparing the observed reaction rate-constants for benzil with trialkyl phosphites to that with the dioxa-phospholan, that the latter is approximately one hundred times slower at 25°C. This observed decrease in the rate-constant of the cyclic phosphite can be attributed to the stability of the intermediates involved. One factor, which may be of most important effect on the reaction rate and the energy barrier to the intermediate, is ring strain.

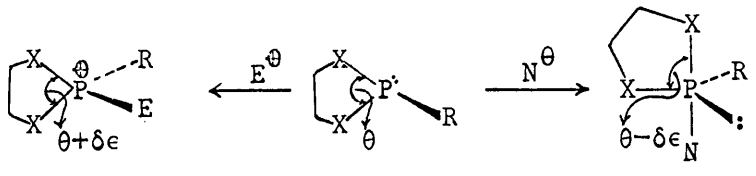
Ring strain has been held responsible for the failure of the bicyclic system (141) to react with biacetyl, even at high temperature, to give a phosphorane. The monocyclic phosphite, methyl ethylene phosphite, as well as trimethyl phosphite, however, reacts rapidly with biacetyl.[137]



(141) (142)

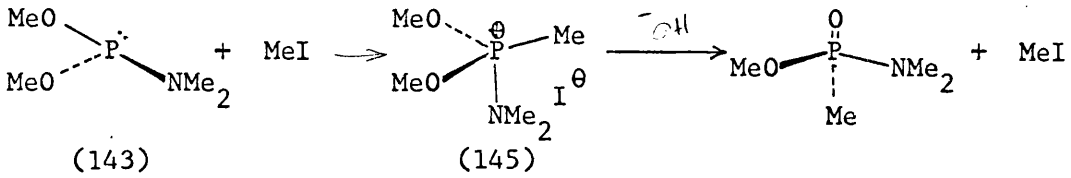
This reluctance of the caged phosphites to form the desired adducts, has been suggested as probably due to the reversibility of the reaction at all steps. This could well be the result of increased ring strain in the intermediate (142) with more tetrahedral geometry, and intramolecular crowding in the TBP products, thence precluding their formation.

The reactions of cyclic and acyclic phosphoramidites have been studied extensively by Hudson and co-workers[137,138] and their relative reactivity interpreted in terms of ring strain in the ground and transition states. Hybridisation in tertiary phosphorus compounds is, in principal, between 3 p-levels, due to the large difference in energy of the s- and p-levels.[139] Hence these compounds are pyramidal, with bond-angles ca. 100°. Due to the electron-pair, trivalent phosphorus compounds have a strong tendency to act as nucleophiles; this should increase the bond-angles as a result of the change in hybridisation on formation of sp^3 hybridised phosphonium ion to ca. 109°. This led Hudson to advance the following hypothesis[137] to account for the relative reactivity of phosphoramidites. Tervalent phosphorus compounds may react as powerful electrophiles as well as nucleophiles. In the case of cyclic compounds, in which phosphorus acts as a nucleophile, the ring strain should be increased. On the other hand, reactions in which phosphorus acts as an electrophile involve decrease in ring strain on formation of the transition state. This can be shown, schematically, as below:

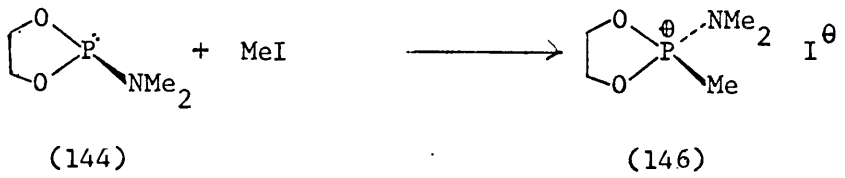


Consequently, the cyclic compound should be less reactive than the acyclic analogue, as the ring strain increases, whereas a decreased ring strain should enhance the cyclic compound reactivity.

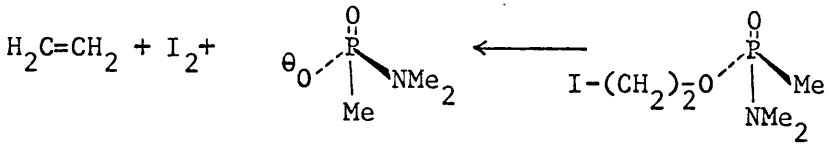
The reactions of amidite (143) and the corresponding cyclic compound (144), with methyl iodide have been investigated.[137,139] The cyclic compound is less reactive than



(143) (145)



(144) (146)

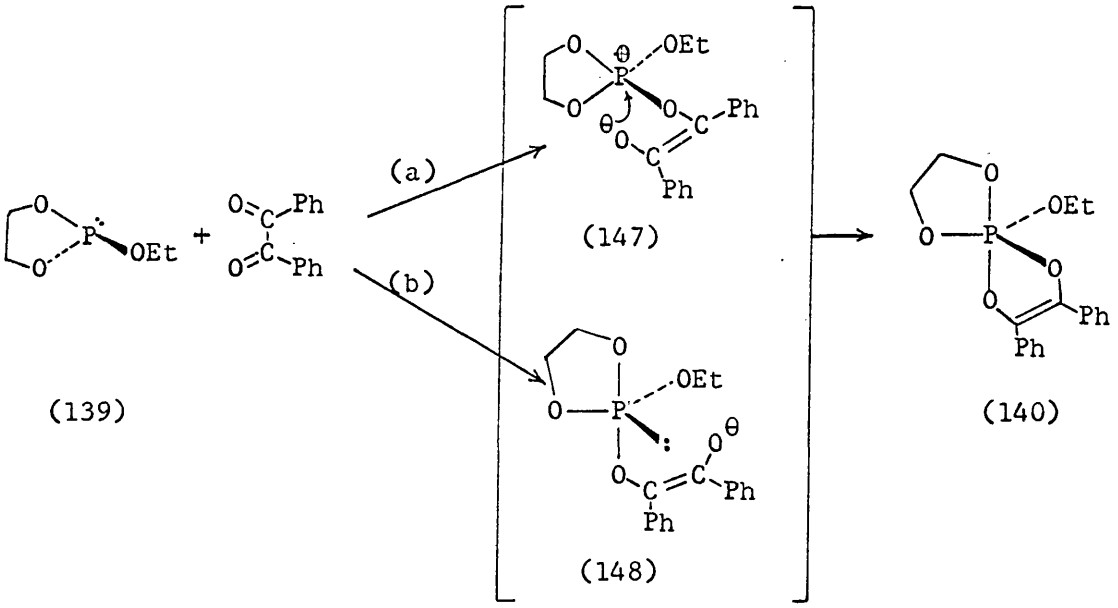


the acyclic analogue, which is consistent with a mechanism *via* the tetrahedral acyclic intermediate (145) and the cyclic intermediate (146), in which the ring strain is regarded to be of substantial magnitude. Hence, it is of a higher energy relative to the strain free species (145).

In the light of the above discussion and of the conclusions deduced by Ogata and Yamashita,[114,127] that the triethyl phosphite-benzil reaction proceeds *via* a step-wise pathway, the energy of activation of

the phospholan-benzil reaction was estimated. Conventional calculations produced an estimated value of $\Delta E \simeq 11$ kcal. mol^{-1}. The certainty of this figure, however, is limited, due to the limited number of temperatured studied. Hence, it may serve as an estimate of the true ΔE.

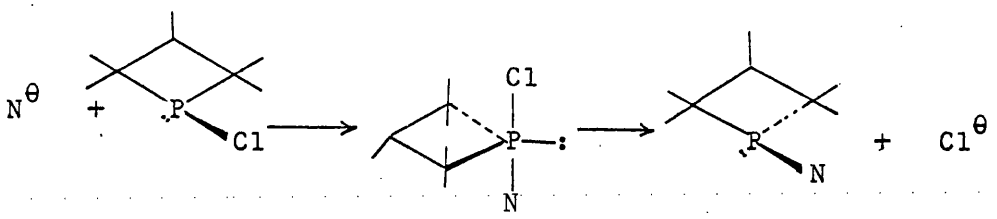
The mechanism for the cyclic reaction can proceed via either the tetrahedral (147) or via a 10-electron TBP intermediate (148) with the lone-pair in an equatorial position. Intermediates, formed by



SCHEME XI

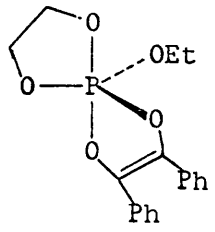
nucleophilic addition to trivalent phosphorus, have not been isolated; however, their existence can be postulated by analogy to the corresponding species in sulphur and selenium chemistry, where in some cases accurate structural determinations have been carried out.[138]

Such a transition state has been suggested by Trippett[83] for the reactions of the phosphetan (149).

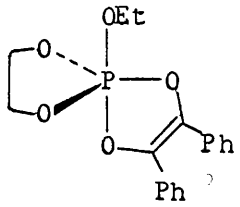


(149)

Intermediates such as (148), in which ring strain is greatly relieved by assuming an apical-equatorial position with an O-P-O ca. 90°, would be of much lower energy compared to (147). Furthermore, the reaction-rate would be enhanced *via* (148), as it has been pointed out above. Hence, when the reaction-rate is slower, and ΔE is larger, comparing to the acyclic reaction, a mechanism *via* an intermediate (147). is, probably, more favourable. Cyclisation of (147) by apical attack of the negatively charged oxygen would give either TBP (140) or (150).

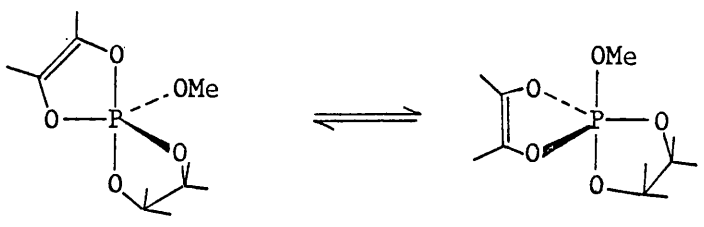


(140)



(150)

TBP (150) is regarded to be of higher energy barrier relative to (140). Recently, a value of $\Delta G^* = 20$ kcal. mol^{-1} has been estimated for pseudorotation of (151) to (152).[112]



(151) (152)

In view of the above energy of activation of 11 kcal. mol^{-1}, determined for the cyclic reaction, and of the widely preferred nucleophilic attack of phosphorus, being a 'soft' base, on the carbonyl 'soft acid' oxygen, a reasonable mechanism for the reaction can be suggested as to involve a nucleophilic attack of phosphorus, on carbonyl oxygen, to give (147), which cyclises to the 1,3,2-dioxaphosphorane (140), i.e. path (a) in Scheme XI.

3.6 Apicophilicity in Pentaco-ordinate Phosphoranes.

The role of electronegativity of the groups attached to the central phosphorus atom in TBP phosphoranes has been detailed in Chapter 2.

A knowledge of the substituents electronegativity around the phosphorus atom, is very useful in forming a rough estimate of the preference of a group for a particular location in a TBP and hence of the relative stabilities of comparable phosphoranes. Theoretical, as well as experimental observations, have shown that it is important, for safer and reliable predictions, that factors other than electronegativity are to be considered as well. In order to take into account the effects of all other possibly relevant factors, Ramirez[140] has suggested that the tendency of a group to reside in an apical, as opposed to an equatorial, position be termed its 'apicophilicity'.

In practice, substituents apicophilicities, and hence their preference for a particular site in a TBP, seem to be determined by a balance of a number of factors. In addition to electronegativity, which usually predominates, polarisability, π-bonding and possibly steric effects are to be taken into account.

Semi-empirical molecular orbital calculations[74,75,78, 140-142]

have been performed for a number of hypothetical phosphoranes, including PH_5 and PF_5, in order to probe their electronic structures and the possibility of extending such predictions to other substituted phosphoranes.

Although there is a wide controversy as to the origin of these conclusions, and in particular the part played by the phosphorus 3d--orbitals, different calculations agree on some of the most significant predictions which can be summarised as follows:

(a) The more electronegative groups prefer the apical positions.

(b) There is an increased stability of phosphoranes with the more electronegative substituents in apical positions.

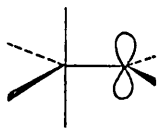
(c) Apical substituents can accommodate more negative charge than the equatorial substituents. Hence, any property, such as electronegativity and polarisability, which helps to achieve this will influence the substituent to prefer an apical site.

(d) There is a greater double bond shortening in the equatorial relative to the apical positions.

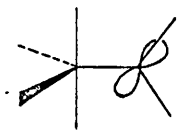
The argument over the role of 3d-orbitals in bonding of second--row elements stems, largely, from the lack of a reliable way to estimate the true degree of d-orbital participation. In this regard, Ramirez, Ugi, and their co-workers[140] predicted a substantial role for phosphorus 3d-orbitals in determining the placement of the substituents in TBP phosphoranes. Their calculations indicated an increased stability of a TBP as due to possible back-donation of electron-density from the substituent *via* p-orbitals into the empty phosphorus d-orbitals. This p-d π-interaction is less in the apical, than in the equatorial, positions. Consequently, substituents in the apical sites are expected to accommodate more negative charge, than those

in the equatorial positions. Hence, the greater the electronegativity of a group becomes, the more its preference for the apical position will be. This, also, would explain the observed double bond shortening in the equatorial relative to the apical positions. It follows that the more electropositive substituents, being more capable of greater d-π interactions, would prefer to occupy the equatorial positions.

Hoffmann, Howell, and Muetterties,[75] on the other hand, predicted that 3d-orbital participation is effectively limited and less important in phosphorane formation. Interactions between the substituent's donor- or acceptor- orbitals and phosphorus framework σ -orbitals are stronger for apical than for equatorial substituents. Consequently, and because of the 3d-orbitals limited role, π-acceptors will prefer apical sites whereas π-donors will prefer equatorial sites. They further concluded that, for a substituent with a single π-system, an equatorial acceptor will prefer to have its acceptor orbitals perpendicular to the equatorial plane, as in (153), while an equatorial donor will prefer to have its donor orbitals in the equatorial plane, as in (154), whereas there is no preferential orientation of the π-system in an apical substituent.



(153)



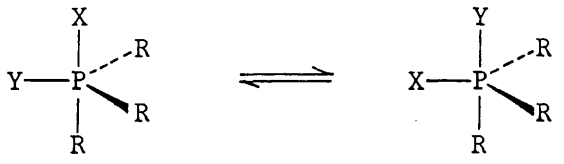
(154)

For a model equatorial amino group in PF_4NH_2, configuration (154) was calculated to be more stable than (153). Finally, they pointed out that the balance of electronegativity and π-donating or accepting capability must be judged individually in each case, e.g. fluorine is

more electronegative, as a substituent, and so would favour the apical site; on the other hand, it is also a π-donor, which would be expected to prefer an equatorial site. The fact that fluorine usually occupies an apical position indicates that the electronegativity effect is dominant.

3.7 Substituents' Relative Apicophilicities.

Ligand apicophilicities can be quantitatively measured, in energetic terms, (see Section 3.12). The relative apicophilicity value of two different groups, in a particular TBP, is an estimate of the energy difference resulting when they exchange apical and equatorial positions. The energy difference between (155) and (156) is a reflection of the varying apicophilicities of group X relative to Y and possibly of varying steric effects.



(155) (156)

Nucleophilic substitution at tetraco-ordinated phosphorus can give four possible TBP intermediates, (see Section 2.7), and each of these, if sufficiently long-lived, may also pseudorotate to form up to 20 possible phosphoranes.

In order to simplify and understand the process of substitution, and assuming that it is directed by thermodynamic considerations, i.e. the most stable TBP is formed the fastest, which seems so in constraint free reactions, it is therefore necessary to be able to predict the relative stabilities of these possible intermediates and assess the

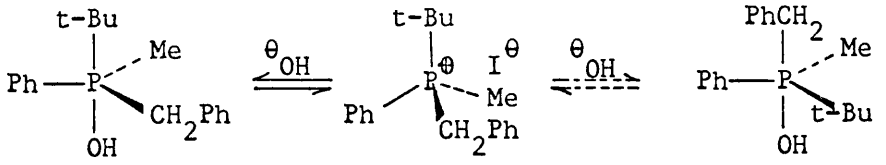
barriers to their interconversions. Apicophilicity values of the groups present in a TBP, if known, would provide a way of predicting the energetically most stable arrangement of substituents in a particular phosphorane. Hence, a more accurate prediction of the preferred reaction pathway becomes possible, especially in cases where the stabilities of the probable intermediates involved are determined by a balance of several factors.

It is possible, in theory, to build up a tentative 'apicophilicity scale' from the accumulated apicophilicities data of a wide spectrum of groups. If this is so, the relative importance of any factor, on the overall apicophilicity value, could then be estimated. A limited number of such 'apicophilicity scales' have been recently reported.[61,111,115]

In comparing the relative apicophilicities of groups in a certain phosphorane with those obtained from data on other phosphoranes it must be realised that both electronegativity and, in particular, $\underline{p}_{\pi}$ -$\underline{d}$ -bonding are dependent on the nature of the other substituents attached to phosphorus. It would, therefore, be unreasonable to expect one general scale of relative apicophilicities to apply in all circumstances.

In this respect, predictions based on such scales would not always be consistent with experimental observations. This would result, in cases where there are imposed constraints, in the formation of unexpected intermediates which would cause the reaction to be under kinetic rather than thermodynamic control.

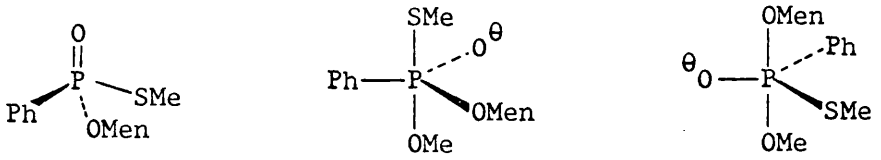
The alkaline hydrolysis of the t-butyl salt (47) would be predicted, on apicophilicity grounds, to proceed *via* (157). However, as has been discussed in section 2.7, this reaction is suggested to take place *via* (48).[36]



(48) (47) (157)

This is because apicophilicity values give no information on the individual factors such as steric hindrance and the strength of lone--pair interactions from the substituents to phosphorus.

Methanolysis of the phosphonate (158), could occur via (159) or (160). In this respect apicophilicity values would favour (160), on the grounds that sulphur is expected to be poorly apicophilic relative to oxygen. The observed inversion,[143] however, suggests (159) as the involved intermediate.

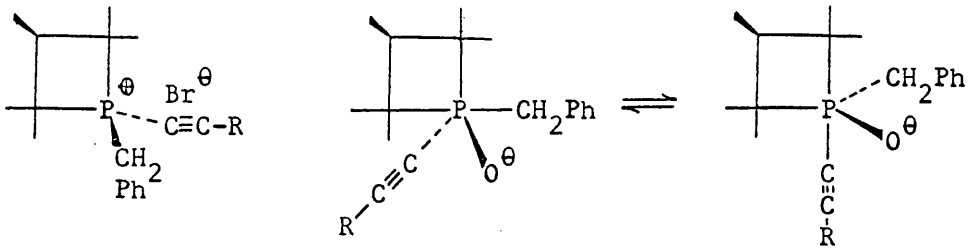


(158) (159) (160)

Trippett[111] has shown that arylthio- and aryloxy- groups have similar apicophilicities, with the balance affected by the nature of the other phosphorus substituents.

The correct prediction would have then been made, if information about the energy barriers involved in the formation, decomposition and pseudorotation of the intermediates, were available. This is not so, because the energy barriers in such cases as estimated from the relative apicophilicities, include an energy of activation term which

is inextricable from the overall value. Consequently, the overall value obtained tends to be either a minimum or a aximum, depending upon the relative magnitude of the energy of activation involved. Similarly, the outcome of the alkaline hydrolysis of phosphetanium salts (50) and (51), discussed in section 2.10, could have been differently predicted on relative apicophilicity considerations alone which favour (161a), rather than (161b), as the ultimate intermediate.



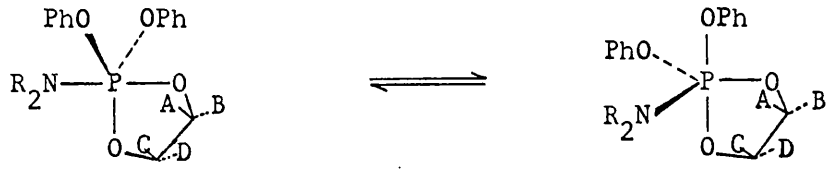
(50) R = Me,
(51) R = Ph.

(161a) (161b)

Intermediate (161a) is favoured on the grounds that extensive π-donation from the acetylene group to phosphorus is involved. The observed experimental outcome seems to suggest that this is not the case.

Oram,[19] in considering the electronegativity of the $OC(CF_3)_2$ group in phosphetans, suggested that the effect of the ring is uncertain but may also affect the group's π-bonding abilities and the effective electronegativity of the substituents in the TBP.

The insensitivity of the energy barrier for pseudorotation (162) $\rightleftharpoons$ (163) to the nature of the groups attached to the nitrogen atom, has been noticed by Trippett.[144] This was somewhat surprising in view of an expected variation in the extend of back-bonding from the equatorial N atoms.



(162) (163)

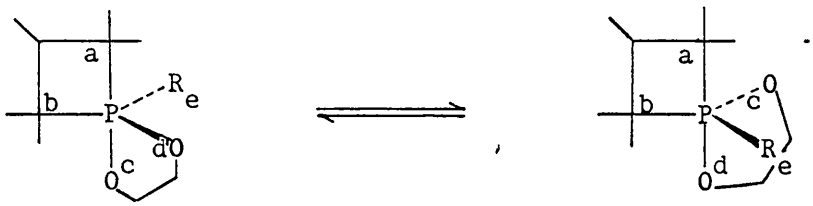
In the light of these considerations, and the suggestion that the electronegativity functions dominate when they are in balance with π -interactions,[75] TBP (161b) would be favoured. This seems to be the case, considering the acetylene group to be more electronegative than benzyl as well as the alkylene group is lost in the gaseous state, hence, pushing the reaction towards the observed result.

Thus, it is of most significance if the relative importance of the individual factors determining an apicophilicity value could be extricated from the other factors and quantitatively evaluated.

3.8 Apicophilicity and Ring-Strain in Five-co-ordinate Phosphetan Compounds.

Phosphetan chemistry can readily be explained in terms of ring strain and the relative apicophilicities of the other groups present.

Pentacovalent phosphetan compounds studied in this thesis can generally be described by the bicyclo-oxyphosphoranes (164).



(164a) (164b)

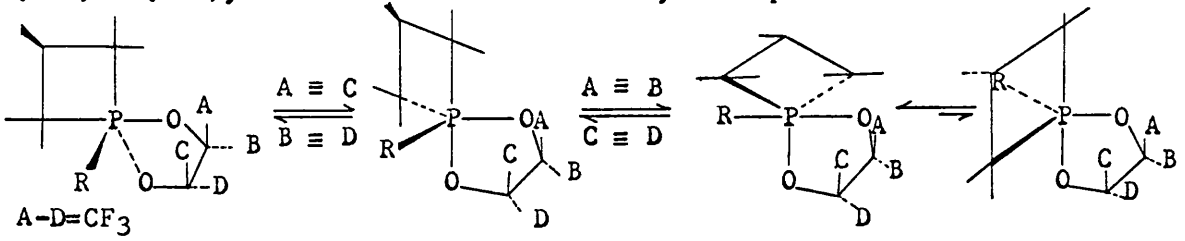
Pseudorotation between these diastereomers can be dicussed in the light of Scheme XII, page 96.

In order to understand the process of isomerisation between these phosphoranes, it is necessary to be able to predict the relative stabilities of the possible intermediates involved and to assess the barriers to their interconversion. Quantitative data on the substituents relative apicophilicities and the preference of small membered rings for the apical-equatorial position in the TBP, would be very useful in this connection.

These can be achieved by using either the ^{1}H or ^{19}F variable temperature n.m.r. spectroscopy techniques for the appropriate phsphoranes.

Pseudorotations which place small-membered rings diequatoril, without compensating gain in the apicophilicity of the groups occupying the apical position, have been shown to be of high energy and slow on the n.m.r. time-scale at room temperature. Such pseudorotations have been shown by Trippett and co-workers[110,144] to be amenable to varible n.m.r. studies.

Their data on pseudorotations (32b-b'), using ^{19}F n.m.r. to monitor the signals due to groups A-D show that the two signals in the n.m.r. spectrum coalesce at 140°. At room temperature, pseudorotation (32b) ⇌ (165), which makes A≡C and B≡D, is rapid on the n.m.r. time sccale.



(32a) (165) (166) (32b)

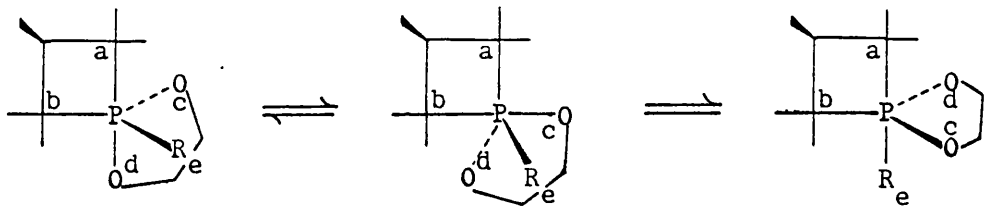
The coalescence at higher temperature is due to a rapid equilibration of (165) and (32b') via the high energy intermediate (166), with ΔG^{*} of 19.6 kcal. mol.$^{-1}$, causing A≡B and C≡D. It follows that if all BPR's are fast on the n.m.r. time-scale, groups A-D are all equivalent. The energy

difference between (165) and (166) or (164-da) and (164-ce), Scheme XII, corresponds to the energy required to overcome the ring strain on forcing the phosphetan ring to the diequatorial position, the difference in apicophilicity between R and the CMe_2, and possibly steric effects.

In this respect, placing the 1,3,2-dioxyphospholan ring diequatorial would lead to equilibration between (32-b) and its trans-isomer, which has not been observed even at 160°. This demonstrates that forcing the dioxaphospholan ring to the diequatorial position would require higher energy, compared to the phosphetan ring. It follows that, in order to gain information on this process, suitable systems and techniques must be developed where such high energy processes can be monitored. To this end, a number of oxyphosphoranes corresponding to the general system (164) were synthesised and pseudorotations (164-b) sudied using high temperature ^1H n.m.r., as described in Section 3.11.

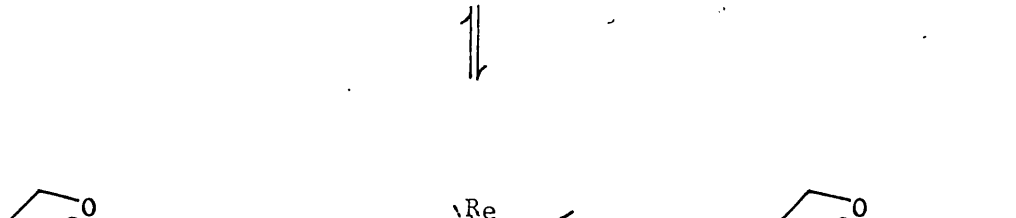
Pseudorotations between these diastereomers can be discussed in the light of Scheme XII, page 96. Each of these phosphoranes can pseudorotate in three directions as shown for the trans-isomer (164-ac) which can pseudorotate eiter to (164-bd) or to (164-ce). However, from the above discussion concerning (32b), it is plain that pseudorotation of (ac) to (ce) would not lead to the equilibration between the diastereomeric phosphoranes (164). Pseudorotation of (ac) to (ce) is presumably very fast on the n.m.r. time-scale under the conditions described in Section 3.11.

Pseudorotations which involves (ac) $\rightleftharpoons$ (bd) is between topomeric TBP's of identical energies.[151] Such pseudorotations have never been slowed on the n.m.r. time-scale[70] even at temperatures as low as -60°.[107,144] Theoretical calculations[75,88] have predicted that they are of small energy barriers (ca. 4 kcal. $mol.^{-1}$), which would not be expected to icrease by the presence of small-membered rings as there is no change in angle strain at any point. It follows that the interconversion of isomers (164a) and (164b) can be achieved only via the pseudorotation of (164-ac) to

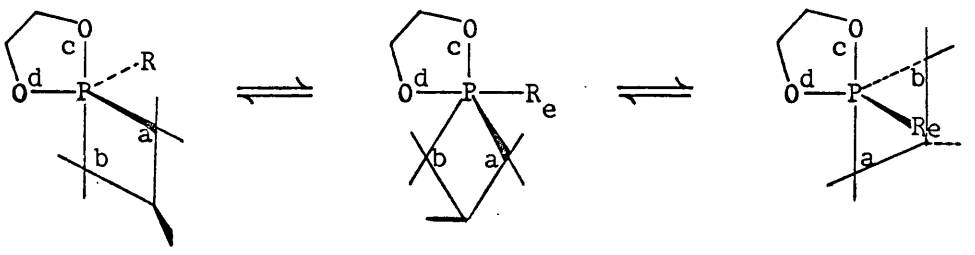


(ad) ≡ (164b) (bc) (ae)

(be) (ac) ≡ (164a) (bd)



(da) (ce) (db)



(cb) (de) (ca) ≡ (164b)

SCHEME XII

(164-be) and cycle (A).

If the R group in (164) were replaced by a series of different substituents, the strain factors and the apicophilicity of CMe_2, would remain constant. Thus, the variation in the free energy of activation for the above pseudorotations, would then be a reflection of the varying apicophilicities of the groups attached to phosphorus and possibly of varying steric effects.

3.9 Determination of Apicophilicity Values.

Most of the information on groups relative apicophilicities has been determined by monitoring the rate of BPR between two conformations using ^{1}H and ^{19}F d.n.m.r. spectroscopy; the results being interpreted in terms of ΔG^* energy of activation required for switching the apical substituents for any two of the equatorial substituents. The value of ΔG^* is calculated and taken as a measure of the barrier for the highest-energy species involved in the observed pseudorotation pathway (164-ac or-be). However, in cases where the activation energy is of a higher magnitude, i.e. outside the limits of d.n.m.r. studies, conventional kinetic techniques have been used.[145]

From product analysis of substitution reactions and prior knowledge of the reaction pathway, a qualitative apicophilicity scale has been constructed[85] (see also Section 2.10). A qualitative apicophilicity series, for some substituent groups, has also been established[61] by studying low temperature n.m.r. spectroscopy of TBP trifluorophosphoranes. At low temperatures the compound becomes frozen in the sense that the positional exchange of the groups is relatively slow, under these conditions, on the n.m.r. time scale. Hence, it becomes possible to distinguish the axial and equatorial groups.

It is important, when comparing ΔG^* of different compounds or at different temperatures, that the entropies of activation must be small. In fact pseudorotations are expected to have small ΔS^*s, and so any difference would be small and within experimental error of zero.[145,146] It is also very significant, when applying such techniques, to make sure that the observed phenomenon is due, actually, to a slow BPR process and not to other mechanisms. Most important in this respect, the possibility that the observed phenomenon is due to an accidental magnetic equivalence of the monitored group's n.m.r. signals or to an irregular isomerisation process. The first of these two routes can be identified where there is no observable variation in the line width of the n.m.r. signals, in contrast to a true BPR, by varying the temperature. Whereas an irregular process should give rise to different ^{31}P n.m.r. chemical shift values in various solvents with different polarities. Consequently, where there is no major change in the ^{31}P value of a particular phosphorane in different media, a true BPR mechanism is considered to be operative.[74] This can also be supported by observing different ^{31}P values for diastereomeric phosphoranes in polar solvents.

(a) Dynamic nuclear magnetic resonance studies.

The rate of isomerisation of two TBPs is obtained by measuring the coalescence temperature (Tc), which can be brought about by cooling or heating the sample. The peaks tend to broaden and move towards each other and eventually coalesce. Beyond Tc, the broad signal sharpens again, although after prolonged heating decomposition may occur.

The free energy of activation ΔG^* can then be calculated from the Tc value and the maximum peak separation $\Delta\nu_{max}$, using the Eyring equation:[147]

$$K_1 = \frac{k\,Tc}{h}\, e^{-\Delta G^*/RT} \qquad (4)$$

where k, h and R represent Boltzmann, Planck, and the gas constants, respectively.

The rate of pseudorotation K_1 at Tc is given by the Gutowsky--Holm approximation,[148]

$$K_1 = \frac{\pi\,\Delta\nu_\infty}{\sqrt{2}} \qquad (5)$$

In this eq. $\Delta\nu_\infty$ = maximum frequency separation of signals below Tc. Such approximation has been shown[149,150] to be reliable in processes involving exchange between two equally populated configurations.

(b) <u>High energy kinetic studies using ^{1}H n.m.r. techniques</u>.

Most of the published studies concerning the determination of the relative apicophilicity of different substituents on phosphorus have been confined to variable temperature ^{19}F d.n.m.r. techniques. Few attempts have been reported[145] on the use of ^{1}H n.m.r. spectroscopy to monitor the isomerisation of pentaco-valent phosphorus compounds at a constant temperature. It is for the limited ΔG^* range of $\simeq$ 10 - 21 kcal. mol^{-1} within which d.n.m.r. spectroscopy can be used for such studies, that the value of the latter techniques becomes apparent. This is due to the limited temperature range over which the n.m.r. machine is operative and the maximum frequency separation $\Delta\nu_\infty$ attainable as well as possible solubility problems at low temperatures. Constant temperature n.m.r. studies become, therefore, a viable alternative for monitoring processes with $\Delta G^* > 21$ kcal. mol^{-1}.

Isomer cross-over processes can be followed by monitoring the n.m.r. spectra of the compound at a pre-selected constant temperature and different intervals over a period sufficient to observe equilibrium.

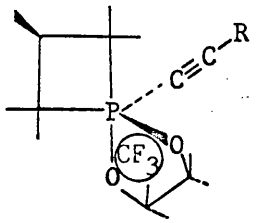
By integrating the area of the signals corresponding to the groups giving rise to the change in the n.m.r. spectra, for each isomer in the mixture, for a number of temperatures, the activation energy for the process can be determined from the formulae.

$$\Delta G^{*} = -RT \ln \frac{h}{kT} K \qquad (6)$$

where K stands for the observed reaction rate constant, whereas the rest remain the same as in eq. (4), above.

3.10 The Reaction Between 1-(2-substituted Ethynyl)-Pentamethyl-phosphetan Compounds with Hexafluoroacetone.

The ^{19}F d.n.m.r. data on the free energies of activation of the pseudorotations (165) ⟹ (166) have been interpreted[144] as being a function of both electronegativity and ability to back-bond into phosphorus d-orbitals. The application of these ideas would imply the p-d- π -bonding from, for example, the phenyl group in (165; R = Ph and p-BrPh), to be sensitive to substituent effects. Trippett and co-workers[144] have found no evidence on this for the above adducts. This encouraged research to seek such evidence for the adducts (167) and (168) as well as the analogous systems discussed in Section 3.11.



(167) R = Ph

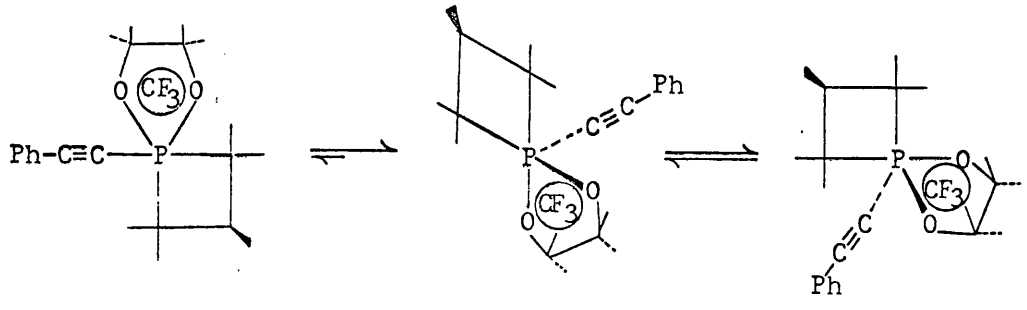
(168) R = Me

(Not isolated)

The reaction of two equivalents of HFA with one equivalent of either r-1-(2-phenylethynyl)- or r-1-(prop-1-ynyl)-2,2-trans-3,4,4-pentamethylphosphetan, (see Section 1.3), was therefore investigated in an attempt to prepare the 2:1 adducts expected.

The reactions proceed smoothly at -76° to give, in both cases, a mixture of one major and at least four other minor products, which are separable on basic alumina. Although it was hoped that the reactions would yield pentaco-ordinate adduct phosphoranes, the ^{1}H, ^{19}F and negative ^{31}P of the major products isolated (-31.59 p.p.m. for 167 and - 32.58 p.p.m. for 168) are inconsistent with such structures. The molecular ion found for the major products, however, indicates the involvement of one mole of phosphetan and two moles of the ketone in the reaction.

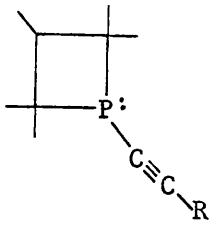
The ^{19}F n.m.r. signals of the products lacked the fine structure usually associated with this type of adducts[110,114] Furthermore, the ^{19}F n.m.r. spectrum of the major product (167), in 1-bromonaphthalene, did not vary between -60 and +160°, and showed the trifluoromethyl signals as a pair of overlapping doublets, $\Delta\nu$ 160 Hz, of equal intensity. This, if the adducts were TBPs, would imply that at -60° ($\simeq \Delta G^{*}$ of 9.8 kcal. mol^{-1}), pseudorotation between the equivalent TBPs (167) and (169) is fast on the n.m.r. time-scale. At 160° no



(170) (167) (169)

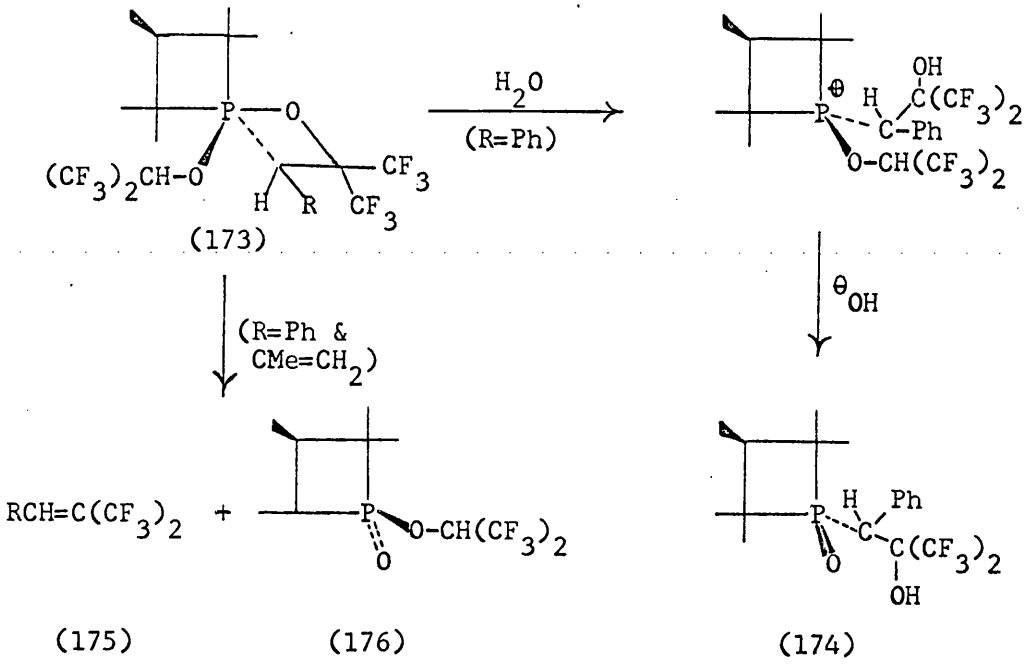
isomer cross-over occurred showing that the pseudorotation (167) $\rightleftharpoons$ (170) is of high energy, i.e., $\Delta G^{*} > 20.55$ kcal. mol^{-1}.

The possibility of the products being dipolar ions can also be ruled out on the grounds of a rather simple pattern of ^{1}H n.m.r. spectra which are the same in different polar solvents. This is confirmed by the similarity of i.r. spectra obtained either in the solid state or in solution. Furthermore, the characteristic i.r. absorptions of the acetylene moiety were absent from the spectra of all products. In this respect, it is notable that this also was observed for the 1-(2-phenylethynyl)-pentamethyl phosphetans, (171). In the latter case, this may be due to either a $\underline{p}_{\pi} - \underline{p}_{\pi}$ interaction[151] between the triple bond and trivalent phosphorus or to an accidental balanced vibrational stretching across the triple bond. However, the acetylenic band reappears in the spectra of the corresponding methyl derivative (172) and on forming the α-diketone adducts of (171) (see Section 3.11).



(171) R = Ph
(172) R = Me

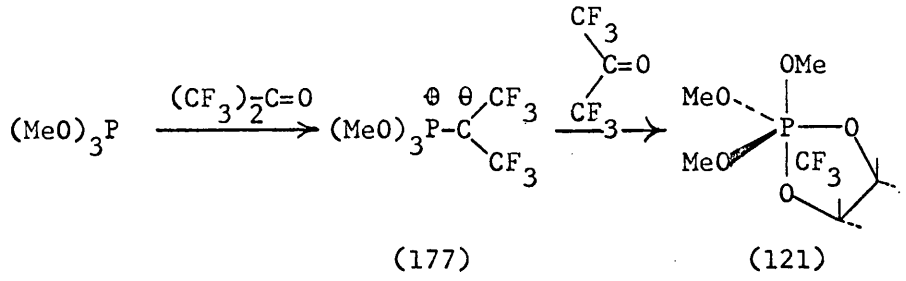
A third possible structure can be designated as an asymmetric phosphorane analogous to (173; R = Ph) which was the only product, out of four possible isomers, isolated from the trans-1-benzylphosphetan and HFA.[110] However, hydrolysis of (173; R = Ph) gave the alcohol (174) as a single isomer, whereas heating above 70° gave the olefin



(175) and the cis-phosphetan (176). With (173; R = $CMe:CH_2$) only the olefin (175; R = $CMe:CH_2$) and the phosphinate (176) were isolated. This, however, proved to be unsuccessful with the presumed adduct (167) which is extremely resistant to hydrolysis and ozonolysis. Under drastic conditions for prolonged times as well as different media only minor changes could be observed in the crude ^1H n.m.r. spectra. Therefore, the asymmetric structure could also be ruled out for the major isolated product (167); however it may be suggested for the other minor products, as discussed below.

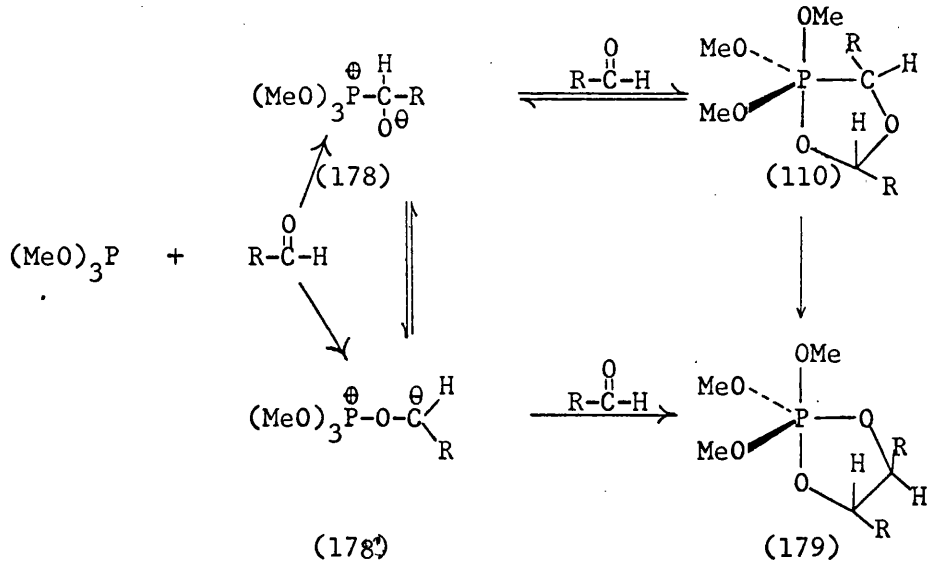
Mechanism of the Reaction.

The reaction between trimethyl phosphite and HFA to give the 1,3,2-dioxaphospholan 1:2 adduct (121) has been suggested[109] to involve the step-wise formation of the product via the unstable betaine (177).



(177) (121)

On the contrary, the reaction of perfluorobenzaldehyde and trimethyl phosphite at 0° yields the alternative 1,4,2-dioxaphospholan 2:1 adduct (110). In this case the phosphite adds to the carbonyl carbon to give the 1:1 betaine (178). Nucleophilic attack of (178) on a second aldehyde molecule followed by ring-closure would give the product. Raising the reaction temperature to 80° results, however, in forming the analogous 1,3,2-dioxaphospholan (179).

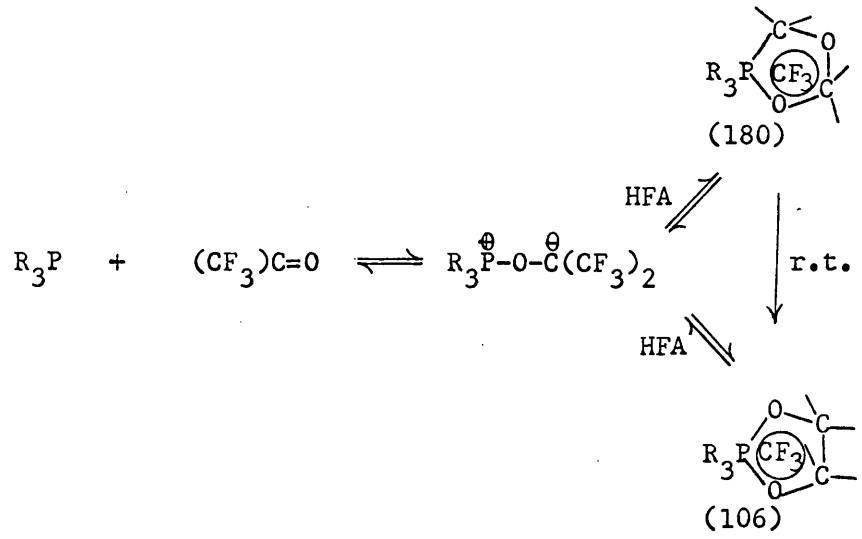


(178) (179)

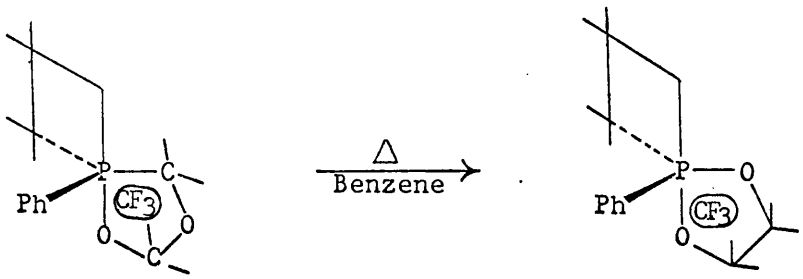
R = C_6F_5

In solution, (110) can also isomerize into (179). Most of these syntheses can be explained by attack of the phosphorus lone-pair on the oxygen of the carbonyl group, however, there exists compelling

evidence that equilibria between P-O and P-C primary adducts also play an important role.[114,127,152] Consequently, the transformation of (110) into (179) may be occurring via the route involving equilibration between (177) and (178). Formation of (177) has been suggested by Ramirez[105] to be more likely in reactions of activated ketones where only the 1,3,2-dioxaphospholans are detectable. Trippett and co-workers[110,153] on the other hand, have suggested the 1,3,4-dioxaphospholan (180) to be the initial and kinetically favoured product in the reaction between HFA and phosphines at low temperatures. They further suggest that, at room temperature, (180) rearranges to the thermodynamically favoured 1,3,2-dioxaphospholan (106).



They have also reported[110] that although (181) is stable at room temperature, in refluxing benzene it gives the 1,3,2-dioxaphospholan (182).

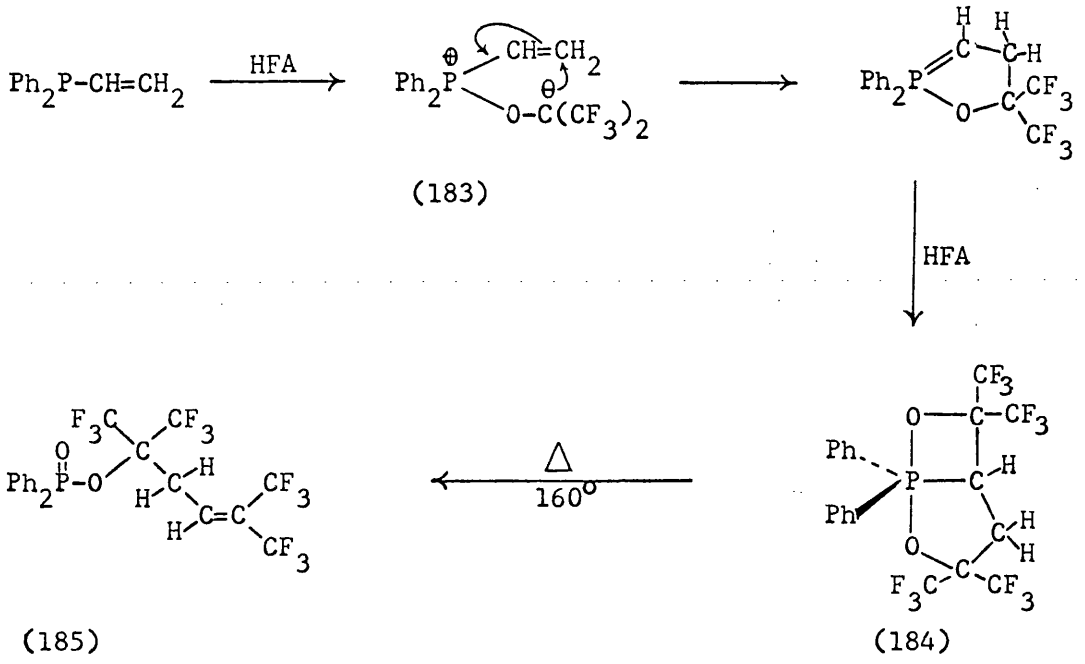


(181) (182)

In view of this discussion, both possibilities will be considered for the initial 1:1 adduct of HFA and phosphetans (171) and (172), with reference to Scheme XIII, page 110.

Acetylene carbon atoms are more susceptible to nucleophilic as to electrophilic attack than ethylenic carbons.[154] The addition of nucleophiles to olefins and acetylenes which are activated by electron-withdrawing groups has been shown[155] to give intermediates which are not sufficiently stable to be isolated, but can be stabilized by rearrangement, cyclization or further addition. Protonation of the resulting intermediate occurs when 'mobile' protons can be supplied by the solvent or, in aprotic media, by prototropy.

In agreement with these ideas the reported reaction, by Trippett and co-workers,[153] of HFA and diphenylvinylphosphine to give a stable 2:1 adduct formulated as the bicyclic phosphorane (184), formed via cyclisation of the intermediate vinylphosphonium salt (183). At 160° the adduct smoothly collapsed to the phosphinate (185).



(183)

(185)

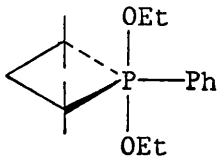
(184)

With reference to Scheme XIII, the assumption of the betaines (186) as the first step in the reaction is justified by the smooth formation of the expected adducts obtained from the same phosphines and α -diketones as will be shown later in Section 3.11. Furthermore, there is no apparent reason to explain the different products being produced with HFA, other than steric effects exerted by the bulky CF_3 groups. This also is expected to be more dominant in (186a) than (186b). The linear array of the acetylene group and the high electron density around the triple bond force the carbons to become closer together. Furthermore, the single bonds attached to the acetylenic carbon are also shortened.[154] Thus, (186b) would be favoured over (186a).

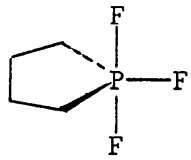
The formation of the anion (187) and its subsequent protonation to give (188) can be assumed as a viable pathway for the formation of the stable 1:1 adducts (189) or (190), however, in a very small yield, i.e. <5%. This seems to suggest that the protonation and subsequent hydrolysis of (188) are due to traces of moisture in the medium, in

spite of the rigorous conditions applied, rather than to the involvement of the solvent itself which would increase their yield substantially.

The structure of the isolated 1:1 adducts can be formulated as (189) or (190). This is based on their negative ^{31}P chemical shifts, the presence of one sharp signal in their ^{19}F n.m.r. spectra (for R=Ph, see Experimental Section), the absence of characteristic i.r. absorptions of the acetylenic moiety, as well as the formation of the expected molecular ion peaks in the mass spectra. The major fragmentation involved loss of an HFA molecule. In cases where ^{1}H n.m.r. spectra of the pure samples were obtainable, down field absorptions suggested the presence of one proton only coupled to phosphorus. On the other hand, there was no evidence to support an OH absorption; however, this may be due to a hydrogen bonding in (190). It is also notable, in respect of the number of isomers (189 or 190) isolated, that only the route (187b) (188c) → (190) would account for the formation of more than two isomers, arising from the stereochemical relationship between the C_3-ring methyl and the 1-substituent on phosphorus as well as between the H and R groups across the double bond. In order to achieve this number, loss of geometry between C-3-Me and α-carbon must be invoked <u>via</u> (188c). Similar examples to (188c) have been reported for (126)[124] and (193).[118]



(126)



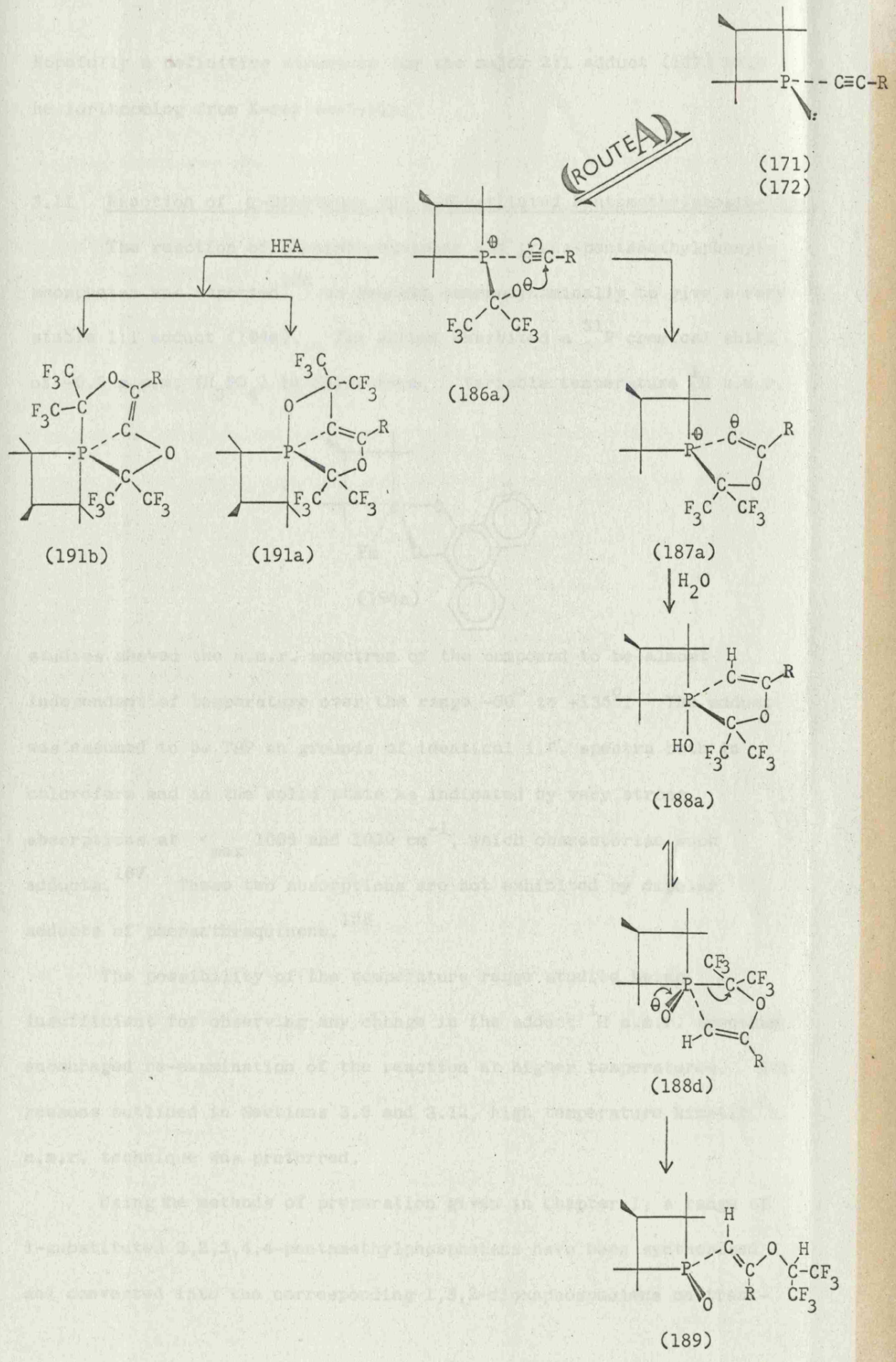
(193)

The structure of the major adducts can be formulated as (191) or (192), however, (191a and b) are inconsistent with the ^{19}F n.m.r. spectra which suggest that the CF_3 groups experience very similar environments, especially for (191; R = Me). In view of these

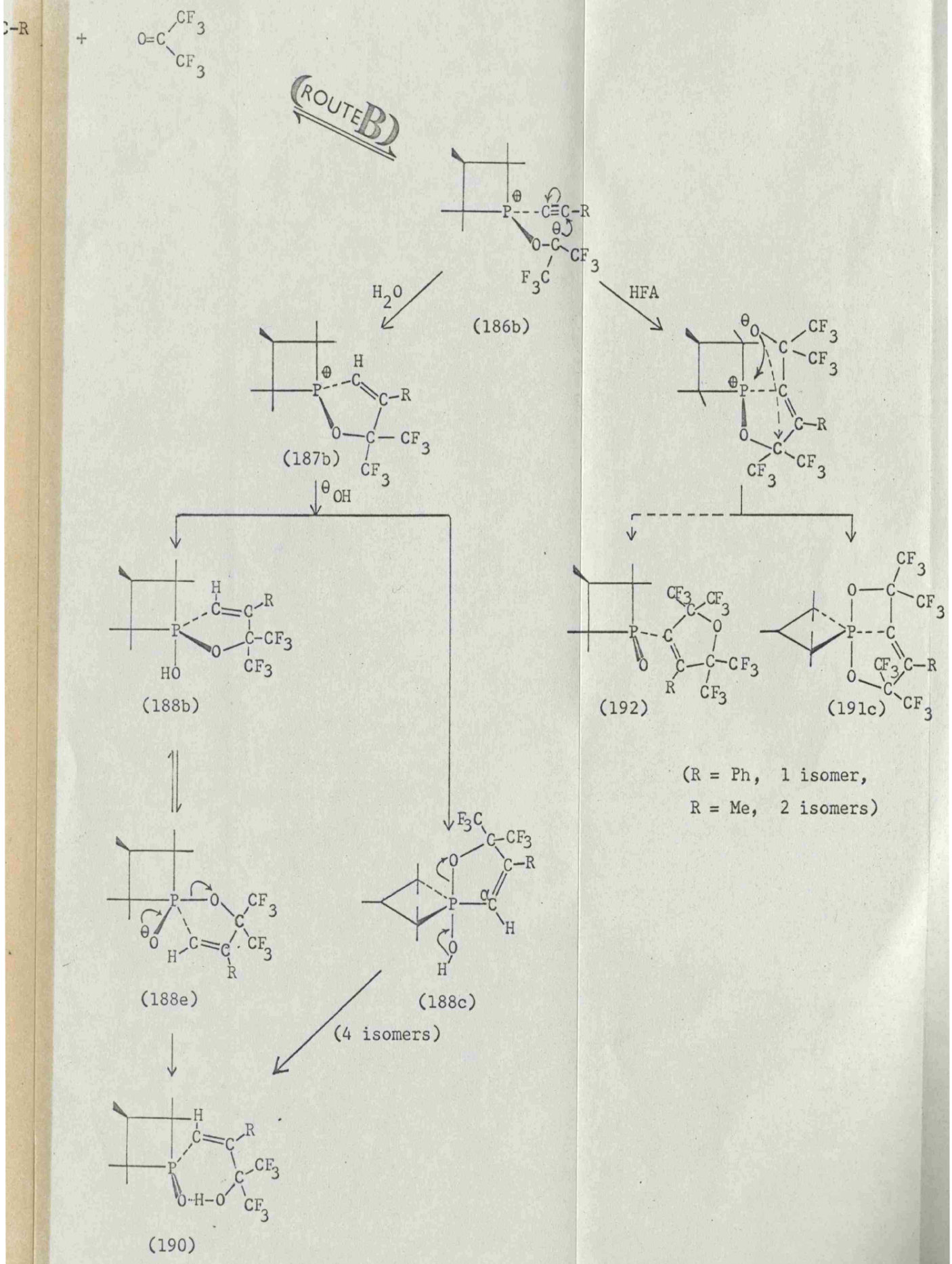
findings and the work by Trippett and co-workers, it seems reasonable to suggest the reaction as proceeding *via* route (B) as shown in Scheme XIII.

In considering the possibility of (192) as compared to (191c), as a viable structure for the major adduct, it is notable that the negative ^{31}P chemical shift, coupled with the assumed considerable strain associated with (191c), would be in favour of (192). On the other hand (191c) is supported by (a) the ^{19}F n.m.r. spectrum, (b) cyclization *via* attack of oxygen on the P-O-C carbon in (187c) is expected to be much hindered, for the sp^2 hybridisation of the double bond causes the molecule, in this region, to be planar, and (c) the exceptionally low and even negative values of the ^{31}P chemical shifts of some 1,3,2- dioxaphospholan HFA adducts which have been reported by Ramirez and co-workers,[109] as well as those found for some of the assumed TBP adducts discussed in Section 3.11, would increase the possibility of the adduct being formulated as (191c).

In the end it may be reasonable to suggest the pathway for the 1:1 adducts to involve the formation of (186b)$\longrightarrow$(187b)$\longrightarrow$(188c) leading to (190). However, in the case of themajor 2:1 adducts, it is difficult to decide with reasonable certainty as to which of the structures (191c) or (192) could be representing the true adduct. This may be verified by thermal decomposition of the compound at higher temperatures than 160°. Structure (191c) is expected to isomerise or decompose easier than the oxide (192). It is also unfortunate, due to the very limited yields of the adducts (190), that no further study could be carried out to ascertain the structure other than the elementary analysis for one of theproducts (191, R = Ph).



SCHEM

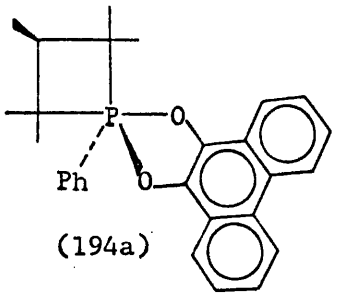

(ROUTE B)
H2O
HFA
(186b)
(187b)
(188b)
(188e)
(188c)
(4 isomers)
(190)
(192)
(191c)
(R = Ph, 1 isomer,
R = Me, 2 isomers)

SCHEME XIII

Hopefully a definitive structure for the major 2:1 adduct (167) will be forthcoming from X-ray analysis.

3.11 Reaction of α-Diketones and 1-Substituted Pentamethylphosphetans.

The reaction of phenanthraquinone and trans-pentamethylphenylphosphetan was reported[156] to proceed thermodynamically to give a very stable 1:1 adduct (194a). The adduct exhibited a ^{31}P chemical shift of -0.5 p.p.m. (H_3PO_4) in chloroform. Variable temperature ^{1}H n.m.r.



(194a)

studies showed the n.m.r. spectrum of the compound to be almost independent of temperature over the range -60° to +135°. The adduct was assumed to be TBP on grounds of identical i.r. spectra both in chloroform and in the solid state as indicated by very strong absorptions at ν_{max} 1055 and 1030 cm^{-1}, which characterise such adducts.[157] These two absorptions are not exhibited by dipolar adducts of phenanthraquinone.[158]

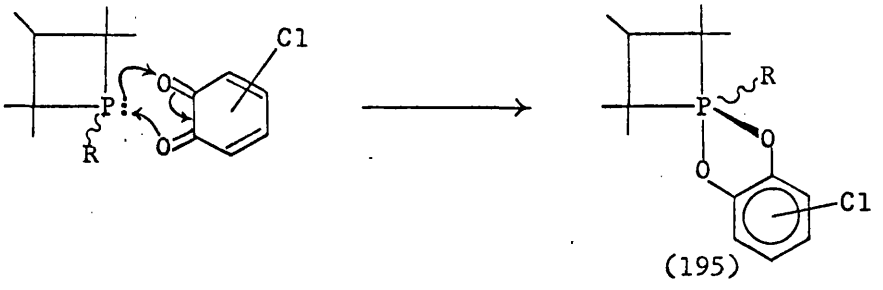
The possibility of the temperature range studied being insufficient for observing any change in the adduct ^{1}H n.m.r. spectrum encouraged re-examination of the reaction at higher temperatures. For reasons outlined in Sections 3.9 and 3.12, high temperature kinetic ^{1}H n.m.r. technique was preferred.

Using the methods of preparation given in Chapter I, a range of 1-substituted 2,2,3,4,4-pentamethylphosphetans have been synthesised and converted into the corresponding 1,3,2-dioxaphospholens on treat-

ment with o-phenanthra- or tetrachloro-o-benzo-quinones, (Table IV, page 121).

Except for the 1-phenylphosphetan oxide, where pure cis- and trans-isomers are separable on alumina, the preparation of the pure or highly enriched mixture of the cis-isomeric oxide was achieved via the corresponding highly enriched cis-acid chloride mixtures. The adducts so obtained are all very stable, crystalline compounds and can be recrystallised readily from ether-light petroleum mixtures.

The path for the reaction at room temperature presumably involves attack of the phosphorus lone pair on the quinone oxygen, as shown below, in the case of (195).



(195)

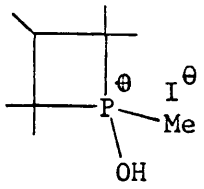
In an attempt to prepare the corresponding (195, R = Me) adducts the reaction proceeded differently as can be outlined below.

The trans-oxide (12a) was prepared as described by Corfield[15] by addition of ethereal methyl-magnesium iodide to r-1-chloro-2,2--trans-3,4,4-pentamethylphosphetan 1-oxide in ether at room temperature.

(10a) (12a)

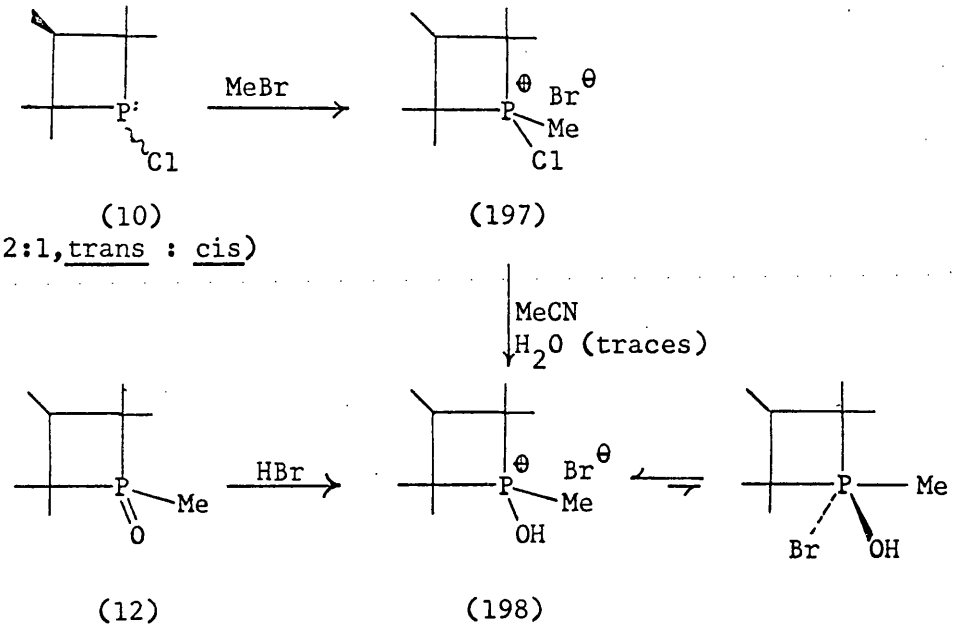
However, reversing the order by the dropwise addition of the acid chloride to the Grignard reagent, at 0^{o} following the procedure described in the Experimental Section and fractional crystallisation gave the trans oxide (12a, 72%) and an unknown white crystalline compound (2.5%). The latter was soluble in water and caused turbidity with dilute acidic silver nitrate solution. Adding one drop of H_2O or D_2O caused the ^{1}H n.m.r. spectrum to become identical to that of the trans-oxide (12a). The process is reversible, i.e. the original substance may be recovered on removal of the volatile solvents under high vacuum. Sublimation, chromatography on basic alumina, or washing with sodium hydroxide, effect an irreversible formation of the oxide. Moreover the mass spectrum was similar to that of the oxide.

In the light of this evidence, the compound was formulated as the salt (196), arising by addition of methyl magnesium iodide to the acid chloride and subsequent hydration during the working up procedure.



(196)

While the research was in progress, Cremer and co-workers[84] reported the formation of (198) during recrystallisation of the salt (197) from acetonitrile (which was not rigorously dried) and also by treatment of both isomeric oxides (12), with dry HBr in chloroform or benzene.



(10)
(2:1, trans : cis)

(197)

(12)

(198)

By a similar series of reactions starting from cis-rich acid chloride the cis-oxide (12b) was obtained. However, attempts to reduce this oxide using trichlorosilane or phenylsilane proceeded nonstereospecifically to give different mixtures of the presumed phosphetans. Reduction of the trans-oxide (12a) in mixture of cis- and trans- oxides is evident from the ^1H n.m.r. of the reduction mixture. It is also supported by the formation of the corresponding o- tetrachlorobenzoquinone adduct (195; R = CH_3) on reacting the crude mixture with the quinone. No cis-adduct was isolated or could be identified in the crude reaction mixture which produced complex ^1H n.m.r. spectra. Furthermore, fractional crystallisation and chromatography on basic alumina of the crude reaction mixture produced no cis-adduct. This may be attributable to lack of stability or reactivity of the cis-phosphetan. It is notable that the presence of triethylamine causes the formation of a green sludgy precipitate which may be attributable to the formation of

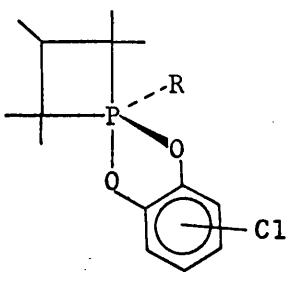
addition compounds with the reduced product. Attempts to remove the volatile materials under vacuum resulted in severe loss of product.

In view of this discussion a close look at the reaction is indeed required to clarify the situation.

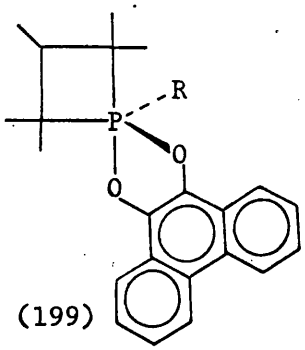
3.12 The Relative Apicophilicities of 1-Substituents in Pentamethyl-phosphetan Adducts.

(a) Determination.

The 1:1 adduct of tri-[156], tetra- and penta-[19] methyl phosphetan with phenanthraquinone have been reported to exhibit spectroscopic properties characteristic of pentaco-ordinate adducts. The structure of such adducts was unchanged over a long range of temperature, which revealed that the energy barriers to pseudorotation forcing the phospholan ring diequatorial, is of > 25 kcal. mol^{-1}. Consequently, monitoring such process is outside the range of variable temperature d.n.m.r. techniques. Therefore, to gain the required data, conventional kinetic techniques using ^{1}H n.m.r. constant temperature spectroscopy were selected and adopted to determine the relative apicophilicity values for a number of alkyl and aryl groups. The phosphoranes shown in Table IV, page 121, which conform to a general formulae (195) and (199), were



(195)



(199)

200 R = Ph

201 R = Ph-C≡C-

202 R = CH_3-C≡C

203 R = CH_3 (trans-isomer)

194 R = Ph

204 R = PhC≡C-

205 R = CH_3C≡C

synthesised in an attempt to gain information about the availability and extent of p-d π-interaction between the phenyl as compared to the methyl group and phosphorus. However, this was hampered by the inability to prepare the cis-isomeric adduct (203b) for reasons outlined in Section 3.11. To overcome such problems, as well as the fact that there have been no previous reports on phosphoranes with alkynyl groups attached to phosphorus, the preparation of both isomers of the adducts (195) and (199) was carried out. The adduct in each case is assumed to be a TBP, as evidenced by (a) their spectroscopic data (b) different ^{31}P n.m.r. values for both diastereomers and (c) the observed high energy isomer cross-over barriers (26-31 kcal. mol^{-1}). Thus, mechanisms other than BPR, which are known to require lower energy barriers, would be excluded.

Preliminary experiments performed to probe the temperature range suitable to achieve isomerisation of the cis-phenanthraquinone adduct (194b) indicated this to be around 130^{o} for a period of $\frac{1}{2}$h. On heating the corresponding trans-adduct (194a), as well as (203≡195, R = CH_3), at 100^{o} overnight, the ratio of the cis-isomer in the equilibrated mixture was too small for an accurate measurement to be made. Accordingly, isomeric exchange determination was performed only on the cis-isomers of (195) and (199).

The isomer cross-over process was monitored in the n.m.r. machine by heating the sample (in the n.m.r. tube) at three constant pre-selected temperatures over a sufficient period for equilibrium to be observed, which ranged from 20 minutes to 72 h.

The equilibrium ratio is computed from the data obtained by integrating the area of the ^{1}H n.m.r. signals corresponding to the phosphetan ring methyls, for each isomer in the monitored mixture, at

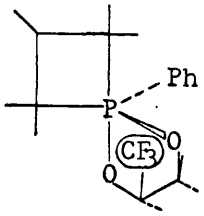
appropriate intervals. Thus the activation energy required for the process is determined using eq. 5 p. 99.

(b) Discussion.

From the data in Table IV and with reference to Graph I page 120, it can be seen that the 1-alkynyl substituents in the tetrachlorobenzoquinone adducts (200) and (201) are more apicophilic than in the corresponding phenanthraquinone adducts.

As it has been discussed in Sections 3.6 - 3.8, the difference in relative apicophilicity of the groups studied can be explained in terms of their electronegativity, p-d π-bonding and steric effect.

On considering the o-tetrabenzoquinone adducts, the relative apicophilicity of the groups studied are in the order MeC≡C- > ph-C≡C- > ph. This suggests an increasing p_π -d_π back-bonding in the reverse order. Trippett and co-workers[110] suggested such interaction between ph and phosphorus d-orbitals, in (206) to be substantial.



(206)

Such interaction seems to be encouraged by the presence of the electron-withdrawing chlorine groups in (195), which would suppress the interaction between the phospholen ring-oxygens and phosphorus. On replacing an alkynyl for phenyl group such interaction through the C-P bond is decreased. Several lines of evidence indicate that the alkynyl unit (-C≡C-) is a poorer transmitter of electronic effects than for example the trans-ethylenic group (H-C=C-H),[154,159] thus suggesting that π-bond interactions involving sp hybridised carbons are weaker

than those of sp^2 carbon under similar conditions. Consequently, the least interaction would be that between CH_3-C≡C-, and phosphorus, whereas the strongest is that of the phenyl group. The latter is in accord with the observed higher group apicophilicities in the phenanthraquinone system as compared with those in the tetrachlorobenzoquinone system. However, there is the possibility of this being partly due to steric effects.

For the phenanthraquinone adducts (194,204-5), a less effective back-bonding is expected to develop between the phospholen ring-oxygens and phosphorus, thus allowing for an increased parallel interaction between phenyl and phosphorus. However, this effect would be rather limited in the case of an alkynyl unit, which causes the Ph-C≡C- to become less apicophilic in the tetrachloro-o-benzoquinone system. The Ph group is capable of acting, however, to a certain extent, as an electron sink, thus releasing or withdrawing electrons according to the variable conditions. The phenanthraquinone-triisopropyl phosphite adduct was indicated by X-ray analysis[95] to be very crowded. This seems also to participate in raising the energy barrier for the same group in thephenanthraquinone (204, 205) as opposed to the benzoquinone (201, 202) phosphoranes.

The activation energy values found for the Ph group seem to agree with that estimated by Trippett and co-workers[110] as being >20 kcal. mol^{-1}. It is also evident from their work that the vinyl group Me_2C=CH- is more apicophilic than the Ph group for the HFA adducts (32), which supports the above explanation for the energy difference found for the Ph and alkynyl groups.

To sum up, the main points can be outlined below:

(a) There is p-d π-bonding between the phospholen ring-oxygens and

phosphorus in the tetrachlorobenzoquinone adducts due to the electron--withdrawing effect exerted by the chlorine atoms in comparison to an opposite electron-inductive effect from the phenanthrene ring, encouraging such bonding.

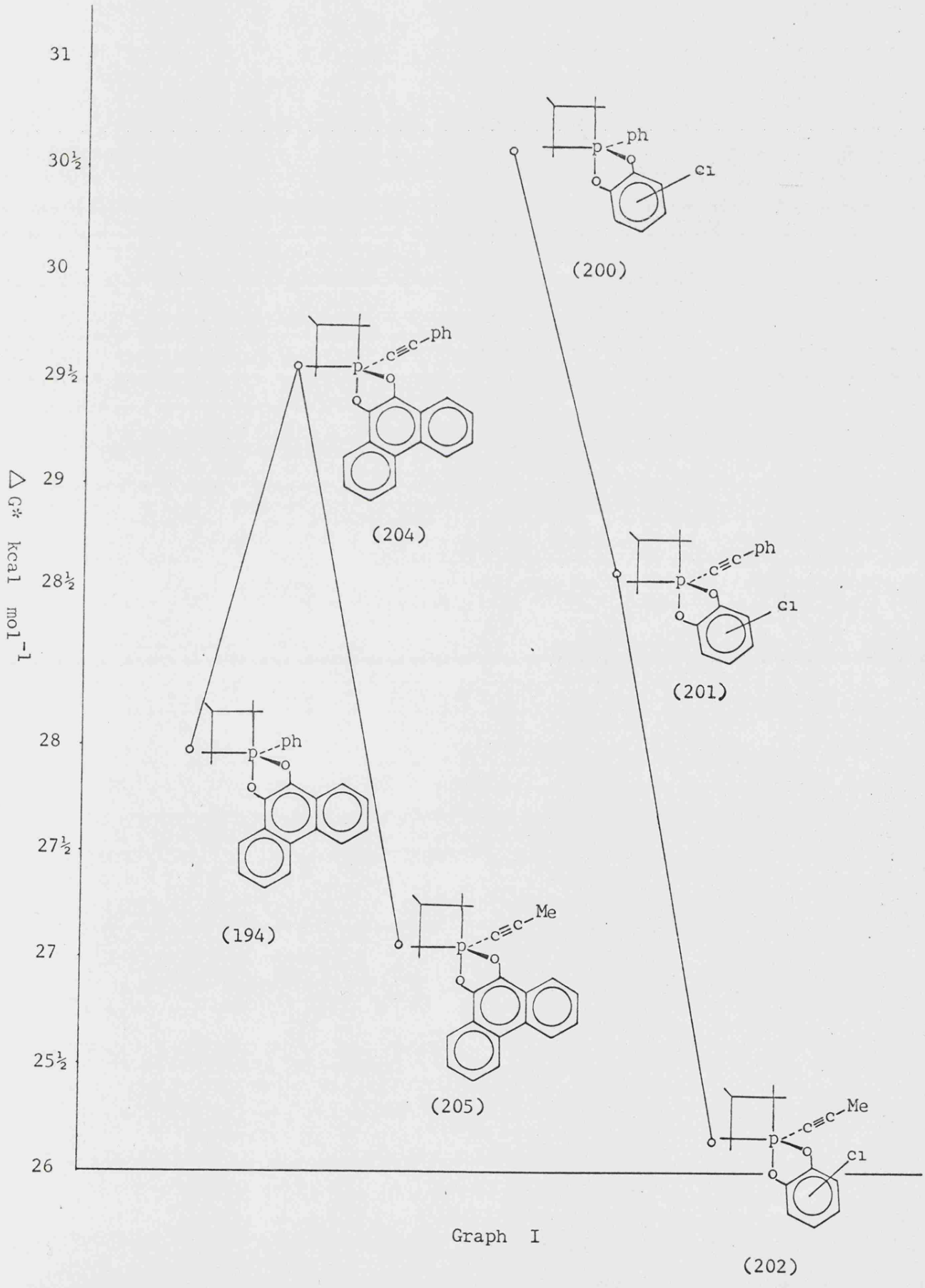
(b) There is substantial back-bonding between the phenyl and phosphorus. However, this can vary according to conditions due to the phenyl group capability to act as an electron-sink.

(c) Several lines of evidence suggest that the alkynyl moiety is a poor transmitter of electronic effects. This suggests that π-bond interactions involving sp hybridised carbon are weaker than those of sp^2 carbon under similar conditions.

(d) The apical position in TBP is more hindered than the equatorial position and phenanthraquinone adducts are expected to be much more crowded than their benzoquinone counterparts.

It is important to emphasise that the evaluated ΔG^*'s are expected to differ from the true values. This is due to the error arising from temperature fluctuation of $\pm 0.05^{\circ}$, the variation in personal judgement of measurements on the n.m.r. spectra, as well as the point of equilibrium, which are expected to be constant for each adduct.

It is also notable, on comparing groups' apicophilicity values, that due to the inability to measure the actual difference in apicophilicity, the measured ΔG^* value is an underestimate of the true value. However, such error is likely to be small, hence, the validity of the comparison is expected not to be signigicantly affected.


31
30½
30
29½
29
28½
28
27½
27
25½
26
Δ G* kcal mol⁻¹
(200)
(204)
(201)
(194)
(205)
(202)

Graph I

Table IV. Data for 1-Substituted Pentamethylphosphetan Adducts with

(a) o-Tetrachlorobenzoquinone.

1-Substituent & Adduct No.	^{31}P (H_3PO_4) δ p.p.m. trans	cis	Temperature studied C°		Δ G* kcal. mol^{-1}
Ph (200)	-10.7	-18.5	122		30.79
			152		30.55
				av.	30.67
Ph-C≡C- (201)	+6.5	+. 8.5	80		28.60
			100		28.60
			120		28.77
				av.	28.66
Me-C≡C- (202)	+6.9	+ 8.4(a)	50		26.26
			70		26.34
			90		26.27
				av.	26.29
Me (203)		-	100		-

(b) o-Phenanthraquinone

Ph (194)	+.02(b)	-7.7(b)	80		27.96
			100		28.00
			120		27.87
				av.	27.94
Ph-C≡C- (204)	+13.0		90		29.37
			110		29.54
			130		29.39
				av.	29.62
Me-C≡C-(d) (205)	+12.8	+12.4(c)	60		26.94
			80		27.14
			100		27.28
				av.	27.12

(1) All ^{31}P n.m.r. were performed in $CDCl_3$ and all kinetic studies were performed in o-dichlorobenzene; otherwise specified. (a) CCl_4, (b) -o-dichlorobenzene, (c) CH_2Cl_2 & (d) 1-Bromonaphthalene.

EXPERIMENTAL

Solvents and Reagents.

Diethyl ether and hydrocarbons were dried over sodium wire, dichloromethane was refluxed over, and distilled from, calcium hydride, chloroform was washed with concentrated sulphuric acid and distilled from anhydrous calcium chloride; methanol and ethanol were refluxed over their magnesium alkoxides and distilled, tetrahydrofuran was refluxed over, and distilled from, lithium aluminium hydride. Triethylamine was refluxed over, and distilled from calcium hydride.

Reactions.

All reactions involving air-sensitive reactants or products were carried out under an atmosphere of dry, oxygen-free nitrogen. Evaporation was performed with a rotary evaporator and solutions in organic solvents were dried over magnesium sulphate.

Instrumentation.

Melting points were recorded on a Koler heating stage and are uncorrected.

^{1}H n.m.r. spectra were recorded on a Varian T-60 spectrometer with tetramethylsilane (TMS) as internal standard and deuteriochloroform as solvent; high-temperature ^{1}H n.m.r. spectra were recorded on a Jeol JNM-PS-100 spectrometer; ^{31}P n.m.r. spectra were recorded by decoupling ^{1}H spectra using an HD-60 heteronuclear decoupler (N.M.R. specialities) and are relative to external 85% phosphoric acid, with ($CDCl_3$) as solvent and ^{19}F n.m.r. spectra were recorded on a Varian A-60 or a Jeol JNM-PS-100 spectrometer with benzotrifluoride as internal standard.

Infrared spectra were recorded on Perkin-Elmer 237 or 257 spectrometers as Nujol mulls, except where otherwise stated. Mass spectra were determined with an A.E.I. MS9 spectrometer, in each case the molecular ion is given first (except where otherwise stated), followed by peaks of structural significance.

Preparation of 2,2-trans-3,4,4-Pentamethyl-r-1-phenylphosphetan 1-Oxide.

This was prepared by the method of Hawes[18]. M.p. and mixed m.p. 126-127°. ^{31}P δ- 57.18 p.p.m.

Preparation of 2,2-cis-3,4,4-pentamethyl-r-1-phenylphosphetan 1-Oxide.

This was prepared by the method of Corfield[15]. M.p. and mixed m.p. 117-118°. ^{31}P δ- 56.0 p.p.m.

Preparation of r-1-Chloro-2,2-trans-3,4,4-pentamethylphosphetan 1-Oxide.

This was prepared by the method of McBride and co-workers[5]. M.p. 73-74°.

Preparation of r-1-Chloro-2,2-cis-3,4,4-pentamethylphosphetan 1-Oxide.

This was prepared by the method of McBride and co-workers[4]. The trans-1-chlorophosphetan 1-oxide (17.5g., 0.09 mol) was refluxed with water (150 ml) for 1.5 hours. The reaction mixture was extracted with dichloromethane and the combined organic layers evaporated. The solid product was dried in a desiccator under vaccuum for 15 hours to give 1,1,2,3,3-pentamethylphosphetanic acid (16.5g), m.p. 75-76°, τ (CCl_4) -2.74 (1H,s), 8.52 (1H, dq, J7, J_{PH} 1.5Hz), 8.82 (6H, d, J_{PH} 18Hz), 8.85 (6H, d, J_{PH} 18Hz), and 9.13 (3H, dd, J 7, J_{PH} 1Hz).

The acid obtained (16.5 g) was stirred with excess thionyl chloride (10 ml) in benzene (100 ml) for 4 hours at room temperature. Removing volatile materials by rotary evaporation and fractional crystallisation from ether-light petroleum gave the acid chloride as a mixture of isomers (11g, 56%; cis:trans = 3.2:1). The stereoisomeric compositions of the 1-chloro-2,2,3,4,4-pentamethylphosphetan 1-oxide products were determined by integration of the n.m.r. spectrum due to the 2,2,4,4-methyls (at τ 8.46 and 8.86 in the trans isomer, and τ 8.6 and 8.76 in the cis isomer), in the n.m.r. spectrum of the mixture. The cis isomer exhibited signals in the n.m.r. spectrum at τ 7.8 - 8.36 (1H,m). 8.6 (6H, d, J_{PH} 22Hz), 8.76 (6H, d, J_{PH} 23Hz) and 9.26 (3H, dd, J7, J_{PH} 1Hz).

Preparation of Phosphetan Oxides from Grignard Reagents and 1-Chloro--2,2,3,4,4-pentamethylphosphetan 1-Oxide.

1. r-1,2,2-trans-3,4,4-Hexamethylphosphetan 1-Oxide.

This was prepared by two routes:

(i) The method of Corfield[15] gave an identical oxide m.p. and mixed m.p. 169-171°.

(ii) r-1-Chloro-2,2-trans-3,4,4-pentamethylphosphetan 1-oxide (9.7 g, 0.05 mol) in ether (60 ml) was added dropwise to stirred ethereal methylmagnesium iodide prepared from magnesium (1.2 g, 0.05 g-atom) and methyl iodide (7.1 g, 0.05 mol) with the temperature maintained at 0°. The solution was kept stirring for a further 1 hour at room temperature before being poured onto a slurry of hydrochloric acid (2.0N; 100 ml) and crushed ice (300 g). The reaction mixture was extracted with dichloromethane and the organic layers were combined together, dried and evaporated. Fractional crystallisation from chloroform - light petroleum gave the trans-1-methylphosphetan oxide (6.5 g;

72%) and an unknown white crystalline compound (0.3g), which was soluble in water and caused turbidity with dilute acidic silver nitrate solution, m.p. around 160°, ν_{max}: 1380, 1240, 1190, 1160, 890, and 770 cm^{-1}; τ 8.13 (3H, d, J_{PH} 12 Hz), 8.66 (6H, $\underline{J}_{PH}$ 17 Hz), 8.76 (6H, d, $\underline{J}_{PH}$ 20 Hz) and 9.03 (3H, dd, $\underline{J}7$, $\underline{J}_{PH}$ 1.5 Hz), the signal from the ring proton was hidden under that from the lower field methyl protons, m/e; 174, 173, 159, 132, 118, 106, 105, 104 and 62. Adding one drop of H_2O or D_2O to the n.m.r. tube caused the spectrum to become identical to that of the oxide. The original substance may be recovered by removal of the volatile materials under high vaccuum. The mass-spectrum was similar to that of the oxide. Sublimation at 90°/0.1 mm, chromatographing on basic alumina or washing with sodium hydroxide solution (0.1N) gave the oxide.

2. r-1,2,2-cis-3,4,4-Hexamethylphosphetan 1-Oxide.

This was prepared by both methods as for the trans oxide.

(i) Ethereal methyl magnesium iodide (0.026 mol) was added dropwise to a stirred solution of 1-chloro-2,2,3,4,4-pentamethylphosphetan 1-oxide stereoisomeric mixture (0.5 g, 0.026 mol, cis:trans = 4:1) in ether (100 ml) at 0°C. The reaction mixture was kept stirring for 2 hours at room temperature, ammonium chloride solution (6%, 500 ml) was added dropwise, with the temperature maintained at 0°C. The ether layer was separated, dried and evaporated to give the 1,2,2,3,4,4-hexamethylphosphetan oxide as a mixture of stereoisomers (20g, cis:trans = 1:1). The aqueous layer was extracted with dichloromethane, and the organic layers combined together, dried, evaporated and sublimed at 80°/0.01 mm, to give a mixture of hexamethylphosphetan oxide stereoisomers (2.4 g, cis:trans = 9:1). The isomeric ratio was determined

by integration of the n.m.r. spectrum due to the 1,2,2,4,4-methyls (at τ 8.45, 8.73 and 8.83 in the trans isomer and τ 8.50, 8.66 and 8.90 in the cis isomer), in the n.m.r. spectrum of the mixture.

(ii) A mixture of stereoisomers of 1-chloro-2,2,3,4,4-pentamethylphosphetan 1-oxide (65 g, 0.033 mol; cis:trans = 3.2:1); in ether (100 ml), was added dropwise to a stirred ethereal methylmagnesium iodide prepared from magnesium (0.65 g, 0.027 g. atom) and methyl iodide (0.82 g, 0.057 mol) with the temperature maintained at 0°. The solution was kept stirring for $1\frac{1}{2}$ hours at room temperature. The reaction mixture was poured on a slurry of hydrochloric acid (2.0N, 100 ml) and crushed ice (300 g), extracted with dichloromethane and the organic layers combined together, dried, evaporated. Fractional crystallisation from dichloromethane-light petroleum gave unreacted acid chloride (2.5 g; having the same ratio of isomers) as well as an identical compound to the trans-hexamethylphosphetan oxide (3.5 g), a mixture of the phosphetan oxide stereoisomers (1.8 g, cis:trans = 2.3:1) and an unknown white crystalline compound (1.0 g), m.p. around 120°, ν_{max} 1380, 1305, 1260, 1240, 1020, 890 and 766 cm^{-1}; τ 7.76 (1H, dq, J7, J_{PH} 1.5 Hz), 8.1 (3H, d, J_{PH} 12 Hz), 8.6 (6H, d, J_{PH} 17 Hz), 8.75 (6H, d, J_{PH} 20 Hz) and 9.03 (3H, dd, J7, J_{PH} 1.5 Hz), m/e 174, 173, 159, 132, 118, 106, 105, 104 and 62. It had the same characteristics ascribed for the unknown compound in the trans-hexamethylphosphetan oxide case, except that sublimation at $60\text{-}70^{\circ}/0.01$ mm. or chromatographing on basic alumina caused no change in the n.m.r. spectra of the compound.

r-1,2,2-cis-3,4,4-Hexamethylphosphetan 1-oxide was obtained by washing an ethereal solution of the unknown (0.2 g) with sodium hydroxide solution (2.0 N). Extraction with dichloromethane, drying and removal of solvent gave the cis-hexamethylphosphetan oxide, (0.2 gm), m.p. $100\text{-}102^{\circ}$, ν_{max} 1395, 1300, 1233, 1185, 1155, 935, 880, 778, and 740 cm^{-1},

τ 7.95 (1H, dq, J8, J_{PH} 1 Hz), 8.50 (3H, d, J_{PH} 11 Hz), 8.66 (6H, d, J_{PH} 16 Hz), 8.90 (6H, d, J_{PH} 18 Hz), and 9.10 (3H, dd, J7, J_{PH} 1.5 Hz), m/e: 174, 159, 132 and 104, (Found: C, 61.87; H, 11.02%. $C_9H_{19}OP$ requires C, 62.1; H, 10.9 %).

3. r-1-(Prop-1-ynyl)-2,2-trans-3,4,4-pentamethylphosphetan 1-Oxide.

Excess methylacetylene (2 ml) was allowed to react with a stirred ethereal ethylmagnesium iodide solution (0.03 M) at -76°C. The reaction mixture was allowed to warm up to room temperature and stirring continued for a further 6 h. The reaction mixture was added dropwise to a stirred solution of trans-pentamethylphosphetan acid chloride (5 g., 0.025 M) in ether (20 ml) at 0°C. The reaction mixture was kept stirring for 1½ h. at room temperature before being cooled down to 0°C and saturated ammonium chloride solution (150 ml) added dropwise. The separation of the layers was achieved by adding excess water (300 ml). Extraction with dichloromethane, drying, solvent evaporation, and distillation at 108-110°/0.1 mm. gave r-1-(prop-1-ynyl)-2,2-trans-3,4,4--pentamethylphosphetan 1-oxide, m.p. 43-45°C, ν_{max} (film): 2200, 1387, 1373, 1248, 1200, 1170, 1045, 930 and 752 cm^{-1}, τ 7.92 (3H, d, J_{PH} 4 Hz), 8.33 (1H, dq, J8, J_{PH} 2 Hz), 8.70 (6H, d, J_{PH} 21 Hz), 8.73 (6H, d, J_{PH} 18 Hz) and 9.13 (3H, dd, J8, J_{PH} 1.5 Hz); the signal from the ring proton was partially hidden under that from the lower-field methyl protons. M/e: 198, 197, 184, 183, 156, 141, 130, 128 and 97, (Found: C, 66.78; H, 9.72; P, 15.4%. $C_{11}H_{19}PO$ requires C, 66.66; H, 9.59; P, 15.25%). ^{31}P δ-57 p.p.m.

4. r-1-(Prop-1-ynyl)-2,2-cis-3,4,4-pentamethylphosphetan 1-Oxide.

This was prepared as for r-1-(prop-1-ynyl)-2,2-trans-3,4,4-pentamethyl-phosphetan 1-oxide; using a mixture of 1-chloro-2,2,3,4,4-pentamethylphos-phetan 1-oxide stereoisomers (cis:trans = 2:1). Chromatography on

Kieselguhr or basic alumina failed to separate the products. Distillation at 70°/0.05 mm. gave 1 - (prop -1-ynyl-2,2,3,4,4-pentamethylphosphetan 1-oxide as a mixture of stereoisomers (60%; cis:trans = 1.7:1). The ratio of the stereoisomers was determined by integration of the n.m.r. spectrum of the distilled mixture, due to the 1-(prop-1-ynyl) and the 2,2,4,4-methyls (at τ 7.92, 8.88 and 8.70 in the trans-isomer and τ 7.96 8.76 and 8.80 in the cis-isomer).

The cis-isomer exhibited signals in the n.m.r. spectrum of the mixture at τ 7.96 (3H, d, J_{PH} 1.5 Hz), 8.76 (6H, d, J_{PH} 17 Hz), 8.80 (6H, d, J_{PH} 22 Hz) and 9.06 (3H, dd, J7, J_{PH} 2 Hz); the signal from the ring proton was hidden under that from the lower-field methyl protons.

5. r-1-(2-Phenylethynyl)-2,2-trans-3,4,4-pentamethylphosphetan 1-Oxide.

Phenylacetylene (4.5 g, 0.04 mol) in ether (20 ml) was added to an ethereal ethylmagnesium solution (0.04 mol) and the mixture refluxed for 2 h. The reaction mixture was added dropwise to a stirred solution of trans-pentamethylphosphetan acid chloride (7.7 g, 0.04 mol) in ether (100 ml) at 0°. After being stirred for 4h at room temperature, a saturated ammonium chloride solution (150 ml) was added dropwise at 0°C. The aqueous layer was extracted with dichloromethane. The organic layers were combined, dried and evaporated.

The crude product was crystallised from chloroform-ether to give r-1-(2-phenylethynyl)-2,2-trans-3,4,4-pentamethylphosphetan 1-oxide, (8.3 g, 80%), m.p. 147°, ν_{max} (CCl_4) 2185, 1490, 1470, 1440, 1382, 1370, 1240, 1220, 1200, 1128, 840 cm^{-1}, τ 2.4-2.86 (5H, m), 8.25 (1H, dq, J7, J_{PH} 1.5 Hz), 8.65 (6H, d, J_{PH} 22 Hz), 8.68 (6H, d, J_{PH} 18 Hz) and 9.10 (3H, dd, J7, J_{PH} 1.5 Hz); the signal from the ring proton was partially

hidden under that of the lower-field methyl protons, m/e 260, 245, 218, 190, 143, 132 and 97. (Found: C, 73.63; H, 8.22; P, 12.04%. $C_{16}H_{21}OP$ requires C, 73.85; H, 8.08; P, 11.92%).

6. r-1-(2-Phenylethynyl)-2,2-cis-3,4,4-pentamethylphosphetan 1-Oxide.

This was prepared as for r-1-(2-phenylethynyl)-2,2-trans-3,4,4--pentamethylphosphetan 1-oxide, using a mixture of isomers of 1-chloro--2,2,3,4,4-pentamethylphosphetan 1-oxide (cis:trans = 1.6:1). Fractional crystallisation from dichloromethane-light petroleum gave r-1-(2-phenylethynyl)-2,2-cis-3,4,4-pentamethylphosphetan 1-oxide, (32%), m.p. 100-103°, ν_{max} 2189, 1494, 1378, 1240, 1195, 1075, 1022, 895, 883, 842, 770 and 694 cm^{-1}, τ (CCl_4), 2.5-2.95 (5H, m), 7.83-7.67 (1H,m), 8.7 (6H, d, J_{PH} 17 Hz), 8.76 (6H, d, J_{PH} 21 Hz) and 9.06 (3H, dd, J7, J_{PH} 1.5 Hz), m/e 260, 245, 218, 143 and 132, (Found: C, 73.91; H, 8.22%. $C_{16}H_{21}OP$ requires C, 73.85; H, 8.08%).

7. r-1-Benzyl-2,2-trans-3,4,4-pentamethylphosphetan 1-Oxide.

This was prepared by the method of Corfield[15], m.p. and mixed m.p. 177-178° (reported 180-182°).

General Procedure for the Reduction of 1-Substituted-2,2,3,4,4-pentamethylphosphetan Oxides with Trichlorosilane.

Trichlorosilane (1 equivalent) in ether (200 ml) was added dropwise to a stirred solution of triethylamine (1 equivalent) and the phosphetan oxide (0.9 equivalent) in ether (150 ml) at 0°. The reaction mixture was stirred for 1½ hours, then recooled, and sodium hydroxide (5N, 100 ml) added dropwise. The organic layer was separated, washed with a saturated sodium chloride solution (100 ml), dried, filtered and the solvent removed under reduced pressure giving quantitative amounts

of the 1-substituted pentamethylphosphetans.

Reduction of 2,2,3,4,4-Pentamethyl-1-phenylphosphetan 1-Oxide.

Pure cis and trans isomers were reduced as above giving compounds identical with that described by Corfield[15].

Reduction of 2,2,3,4,4-Pentamethyl-1-(prop-1-ynyl)-phosphetan 1-Oxide.

Reduction of pure trans isomer gave 2,2-trans-3,4,4-pentamethyl--r-1-(prop-1-ynyl)phosphetan as a white crystalline solid, m.p. slightly above ambient, ν_{max} 2180, 1385, 1370, 1265, 1250, 1205, 1110 and 1035 cm^{-1}, τ(neat), 7.32 (1H, dq, J7, J_{PH} 1 Hz), 8.00 (3H, s), 8.80 (6H, d, J_{PH} 16 Hz), 8.90 (6H, d, J_{PH} 12 Hz) and 9.23 (3H, d, J_{PH} 6 Hz). A mixture of stereoisomers of 2,2,3,4,4-pentamethyl-1-(prop-1-ynyl)phosphetan was prepared by reducing a mixture of phosphetan oxides (cis:trans = 1.7:1). The cis phosphetan exhibited signals in the n.m.r. spectrum of the mixture of τ(neat) 7.73 (1H, dq, J7, J_{PH} 2 Hz), 7.96 (3H, s), 8.72 (6H, d, J_{PH} 12 Hz), 8.82 (6H, d, J_{PH} 14 Hz), and 9.08 (3H, dd, J7, J_{PH} 1.5 Hz), the signal from the ring proton was hidden under that from the lower-field methyl protons.

Reduction of 2,2,3,4,4-Pentamethyl-1-(2-phenylethynyl)phosphetan Oxides.

Reduction of the trans isomer in the manner mentioned above gave r-1-(2-phenylacetylenyl)-2,2-trans-3,4,4-pentamethylphosphetan as a white solid, ν_{max} 1378, 1368, 835, and 755 cm^{-1}, τ2.50-2.93 (5H, m), 8.35 (1H, dq, J7, J_{PH} 1 Hz), 8.70 (6H, d, J_{PH} 15 Hz), 8.82 (6H, d, J_{PH} 14 Hz) and 9.26 (3H, d, J7 Hz), m/e 244, 229 and 201.

r-1-(2-phenylethynyl)-2,2-cis-3,4,4-pentamethylphosphetan 1-oxide was reduced to give the corresponding cis phosphetan as a white solid. τ 2.63-3.10 (5H, m), 7.73 (1H, dq, J7, J_{PH} 2 Hz), 8.68 (6H, d, J_{PH} 11 Hz),

8.80 (6H, d, J_{PH} 16 Hz) and 9.13 (3H, dd, J7, J_{PH} 1 Hz).

Preparation of Phosphetanium Salts by Quaternization of Phosphetans.

1. 1-Benzyl-1,2,2,3,4,4-hexamethylphosphetanium Iodide.

r-1-Benzyl-1,2,2-cis-3,4,4-hexamethylphosphetanium iodide salt, m.p. and mixed m.p. 305-307°; and r-1-benzyl-1,2,2-trans-3,4,4-hexamethylphosphetanium iodide salt, m.p. and mixed m.p. 295-297°, were prepared by the method of Corfield[15].

2. r-1-Benzyl-1,2,2-cis-3,4,4-hexamethylphosphetanium Bromide.

To a stirred solution of triethylamine (2.5 g, 0.025 mol) and the phosphetan 1-oxide (4.5 g, 0.025 mol) in benzene (100 ml) was added a solution of trichlorosilane (3.5 g, 0.025 mol) in benzene (50 ml). After stirring for 1h. excess benzyl bromide (6.0 g, 0.035 mol) was added to the phosphetan solution and the mixture set aside for 24 hours. Water (40 ml) was added and the mixture stirred for a further 1 h. The phosphetanium salt and silica were filtered off, washed with benzene, dried and taken up in boiling chloroform. The silica was removed by filtration and the filtrate treated with ether to give the crystalline phosphetanium bromide, (81%), m.p. 228-30°, ν_{max} 1585, 1432, 1378, 1168, 1157, 783, 775, 747 and 610 cm^{-1}, τ 2.23-2.73 (5H, m), 5.23 (2H, d, J_{PH} 15 Hz), 7.36 (1H, dq, J7, J_{PH} 2 Hz), 7.80 (3H, d, J_{PH} 14 Hz), 8.33 (6H, d, J_{PH} 19 Hz), 8.53 (6H, d, J_{PH} 20 Hz) and 8.93 (3H, dd, J7, J_{PH} 1.5 Hz).

3. r-1-Benzyl-1,2,2-trans-3,4,4-hexamethylphosphetanium Bromide.

This was prepared as for the trans-salt. Crystallisation from chloroform-light petroleum gave the cis-salt, (40%), m.p. 226°.

ν_{max} 1585, 1430, 1379, 1168, 1155, 781, 773, 747 and 692 cm^{-1}, τ 2.16-2.43 (2H, m), 2.43-2.76 (3H, m), 5.26 (2H, d, J_{PH} 15 Hz), 7.0 (1H, dq, J7 J_{PH} 2 Hz), 7.83 (3H, d, J_{PH} 14 Hz), 8.30 (6H, d, J_{PH} 19 Hz), 8.60 (6H, d, J_{PH} 20 Hz) and 8.96 (3H, d, J7). $^{31}P\delta$-61 p.p.m.

r-1-Benzyl-2,2-cis-3,4,4-pentamethyl-1-(prop-1-ynyl)phosphetanium Bromide.

r-1-(Prop-1-ynyl)-2,2-trans-3,4,4-pentamethylphosphetan 1-oxide was reduced and the phosphetan (0.80 g, 0.044 mol) in benzene (10 ml), quaternized by benzyl bromide (2.8 g, 0.016 mol) in benzene (10 ml). The reaction mixture was kept stirring overnight, the solid filtered off and crystallised from dichloromethane-light petroleum to give the phosphetanium bromide (1.5 g, 92%), m.p. 199-200°, ν_{max} 2203, 2108, 1600, 1492, 1070, 845, 811, 795, and 709 cm^{-1}, τ 2.34-2.16 (5H, m), 5.10 (2H, d, J_{PH} 13 Hz), 7.13-7.50 (3H, d, J_{PH} 5 Hz), 8.30 (6H, d, J_{PH} 22 Hz), 8.53 (6H, d, J_{PH} 23 Hz), and 8.95 (3H, d, J 7 Hz). (Found: C, 61.15; H, 7.34; P, 7.90%. $C_{18}H_{26}BrP$ requires C, 61.19; H, 7.42; P, 8.77%).

r-1-Benzyl-2,2-cis-3,4,4-pentamethyl-1-(2-phenylethynyl)phosphetanium Bromide.

r-1-(2-phenylethynyl)-2,2-trans-3,4,4-pentamethylphosphetan 1-oxide was reduced and the phosphetan (0.73g, 0.003 mol) in benzene (10 ml), quaternized by benzyl bromide (0.60 g, 0.0034 mol) in benzene (10 ml). The reaction mixture was refluxed for 1 h, the solid filtered off and crystallised from chloroform-light petroleum to give the phosphetanium bromide (1.1 g, 92%), m.p. 190°, ν_{max} 2188, 1600, 1370, 1170, 1160, 1072, 1029, 874, 782, 770, 700 and 690 cm^{-1}, τ 2.23-2.86 (10H, m), 5.02 (2H, d, J_{PH} 12 Hz), 7.06-7.53 (1H, m), 8.23 (6H, d, J_{PH} 22 Hz), 8.45 (6H, d, J_{PH} 22 Hz) and 8.90 (3H, d, J7 Hz),

(Found: C, 66.47; H, 6.84; P, 7.47%. $C_{23}H_{28}BrP$ requires, C, 66.51; H, 6.79; P, 7.46%).

r-1-Iodomethyl-2,2-cis-3,4,4-pentamethyl-1-phenylphosphetanium Iodide.

This was identical with the compound reported by Hawes.[18] r-2,2-trans-3,4,4-pentamethyl-1-phenylphosphetan 1-oxide was reduced and the phosphetan (1.2 g, 0.0053 mol) in benzene (2 ml), was quaternized with excess diiodomethane (3 g, 0.011 mol) in benzene (2 ml). The reaction mixture was set aside for 24 hours, the precipitate was filtered off, washed well with benzene, dried and crystallised from methanol-light petroleum to give trans-phosphetanium iodide (92%), m.p. 226° (reported 234-5°, with decomposition), ν_{max} 110 and 910 cm^{-1}, τ (CF_3CO_2H) 2.06 (3H, s), 2.13-2.40 (3H, m), 5.98 (2H, d, J_{PH} 7 Hz), 6.92 (1H, dq, J7, J_{PH} 3 Hz), 8.28 (6H, d, J_{PH} 21 Hz), 8.35 (6H, d, J_{PH} 21 Hz) and 8.80 (3H, dd, J7, J_{PH} 1 Hz).

r-1-Iodomethyl-2,2-trans-3,4,4-pentamethyl-1-phenylphosphetanium Iodide.

This was prepared as for cis-phosphetanium iodide. Quaternization of r-1-phenyl-2,2-cis-3,4,4-pentamethylphosphetan with diiodomethane and crystallisation from methanol-light petroleum yielded trans-phosphetanium iodide (97%), m.p. 202-204°, ν_{max} 1585, 1378, 1157, 1124, 1000 and 747 cm^{-1}, τ (CF_3CO_2H) 1.58-2.20 (5H, m), 5.95 (2H, d, J 6 Hz), 7.0 (1H, dq, J7, J_{PH} 1.5 Hz), 8.19 (6H, d, J_{PH} 20 Hz), 8.33 (6H, d, J_{PH} 20 Hz) and 8.73 (3H, d, J7 Hz). (Found: C, 36.85; H, 4.79%. $C_{15}H_{23}I_2P$ requires C, 36.9; H, 4.75%).

Alkaline Hydrolysis of 1-Benzylphosphetanium Salts.

General.

The salt (0.013 mol) was stirred for 24 h. in either a mixture

of ethanol (20 ml) and sodium hydroxide (1N, 20 ml), or in aqueous sodium hydroxide (1N). Most of the solvent was evaporated and the residue taken up in water (20 ml). The aqueous layer was extracted with dichloromethane (3 x 30 ml), the combined extracts were dried and solvent evaporated to give the 1,2,2,3,4,4-hexamethylphosphetan 1-oxide. The stereoisomeric compositions of the oxide products were determined by comparison of the n.m.r. spectra of mixtures of known composition. The stereoisomeric compositions of the 1,2,2,3,4,4-hexamethylphosphetan 1-oxide products were determined by integrating the n.m.r. spectra due to the 2,2,4,4-methyls (at τ (TFA), 8.66 and 8.90 in the cis-isomer and τ 8.73 and 8.83 in the trans-isomer) in the spectra of the total crude hydrolysis products.

Equilibrium of the pure cis- and trans- salts was achieved by stirring the individual salt (0.02 mol) in a mixture of ethanol (15 ml) and sodium hydroxide (0.1N, 0.2 ml) at room temperature for 1h. The residue after removing most of the solvent were dried at the oil pump for 24 h. The stereoisomeric compositions of the salts in the equilibrium mixtures were determined by integrating the n.m.r. spectra due to the signals from the 1-benzyl or the 1,2,2,3,4,4-methyls in the n.m.r. spectra of the total crude.

1. 1-Benzyl-1,2,2,3,4,4-hexamethylphosphetanium Iodide.

The cis salt (1-benzyl and 3-methyl cis) was hydrolysed as above in different conditions:

(i) stirring at reflux for 15 minutes or stirring at room temperature for 24h. in aqueous sodium hydroxide (0.05N), (ii) for 12 days in aqueous sodium hydroxide (1N), to give in every case the same mixture of isomers of the 1-methylphosphetan oxide (cis:trans = 10:90).

The trans-salt was hydrolysed in aqueous sodium hydroxide (1N) to give a different isomer composition of the oxide (cis:trans = 40:60). Equilibration of both cis and trans salts gave the same mixture of isomers of 1-benzyl-1,2,2,3,4,4-hexamethylphosphetanium iodide salt (cis:trans = 64:36), as determined by integrating the spectrum of the product (at τ (TFA) 6.00 in the trans-salt and 5.90 in the cis-salt).

2. 1-Benzyl-1,2,2,3,4,4-hexamethylphosphetanium Bromide.

The cis-salt was hydrolysed as above and also in aqueous sodium hydroxide (1N), to give the same mixture of the 1-methylphosphetan oxide stereoisomers (cis:trans = 16:84). The aqueous hydrolysis of the trans--salt gave a different mixture of isomers of the oxide products (cis: trans = 30:70). Equilibration of both salts gave the same isomeric mixture of the 1-benzylpentamethylphosphetanium bromide salt (cis:trans = 36:64), as determined by the integration of 1,2,2,3,4,4-methyls (at τ 7.8, 8.33, 8.53 and 8.93 in the cis-salt, and τ 7.83, 8.30, 8.60 and 8.96 in the trans-salt).

Alkaline Hydrolysis of 1-Iodomethyl-2,2,3,4,4-pentamethylphosphetanium Iodide.

The cis-salt was hydrolysed as reported by Hawes[18] to give r-1-phenyl-2,2-trans-3,4,4-pentamethylphospholan 1-oxide (90%), m.p. 156° (from ether-light petroleum), reported m.p. 140-1°. ν_{max} 1410, 1385, 1325, 1298, 1243, 1160, 1110, 1084, 1030, 886, 830 and 798 cm^{-1} τ 1.93-2.6 (5H, m), 7.27-8.07 (3H,m), 8.53-8.92 (9H,m), 9.12 (3H,s) and 9.22 (3H, d, J_{PH} 26 Hz). m/e 250, 235, 194, 180 and 125.

The trans-salt was hydrolysed in a similar way to give r-1-phenyl-2,2-cis-3,4,4-pentamethylphospholan 1-oxide (93%),

m.p. 145° (from ether-light petroleum), ν_{max} 1413, 1395, 1380, 1370, 1254, 1217, 1094, 1075, 877, 830 and 800 cm^{-1}, τ 1.93-2.53 (5H, m), 7.87 (2H, d, J_{PH} 12 Hz), 8.2-8.9 (10H, m), 9.12 (3H, s), and 9.18 (3H, d, J_{PH} 24 Hz), m/e 250, 235, 194, 180, and 125, (Found: C, 72.24; H, 9.28%. $C_{15}H_{23}OP$ requires C, 72.0; H, 9.2%). ^{31}P δ-61.46.

Alkaline Hydrolysis of r-1-Benzyl-2,2-cis-3,4,4-pentamethyl-1-(prop-1-ynyl)phosphetanium Bromide.

The salt (0.1 g) was stirred in a mixture of ethanol (10 ml) and sodium hydroxide (2N, 10 ml) for 2h at room temperature. Most of the solvent was evaporated and the residue taken up in water (30 ml). The aqueous layer was extracted with dichloromethane, the combined extracts were dried and solvent evaporated to give a quantitative amount of r-1-Benzyl-2,2-trans-3,4,4-pentamethylphosphetan 1-oxide as the only product shown by the n.m.r. spectrum of the crude which was identical with that of an authentic sample. M.p. and mixed m.p. 177-8°.

Alkaline Hydrolysis of r-1-Benzyl-2,2-cis-3,4,4-pentamethyl-1-(2-phenylethynyl)phosphetanium Bromide.

This was hydrolysed as for the 1-benzyl-1-(prop-1-ynyl)pentamethylphospholanium bromide salt. The hydrolysis gave r-1-benzyl-2,2-trans-3,4,4-pentamethylphosphetan 1-oxide as the only product shown in the n.m.r. spectrum of the crude product which was identical with that of an authentic sample. M.p. and mixed m.p. 177-8°.

Reaction of 1-Phenyl-2,2,3,4,4-pentamethylphosphetan with Ethyl propiolate.

Ethyl propiolate was reacted with pure cis and trans-phenyl pentamethylphosphetan as reported by Hawes[18]. Both reactions gave the same product.

Crystallisation from ether-light petroleum gave 1-phenyl-2,2,3,4,4-pentamethyl-5-acetoxyethylphospholan 1-oxide, (90%), m.p. 125-7° (reported 131-2°), τ 2.16-2.5 (2H, m), 2.5-2.76 (3H, m), 6.2 (2H, qd, J 7 Hz), 7.06-7.3 (1H, m), 7.4-7.9 (2H, m), 8.46 (1H, dq, J 6 J_{PH} 1.5 Hz), 8.73-0.36 (18H, m). ^{31}P δ -62.1.

Reaction of r-1-Phenyl-2,2-trans-3,4,4-pentamethylphosphetan with Benzoyl Chloride.

Benzoyl chloride (0.9 ml) in ether (40 ml) was added dropwise to a stirred mixture of the trans-phenylpentamethylphosphetan (1.7 g, .077 mol) and triethylamine (1.1 ml) in ether (130 ml) at room temperature. The reaction mixture was stirred for 3h, before water (300 ml) added with cooling. The aqueous layer was extracted with chloroform, the combined organic extracts dried and evaporated. Crystallisation from chloroform gave 1-phenyl-2,2,3,4,4-pentamethyl-5-hydroxy-5-phenyl-phosphetan 1-oxide (70%), m.p. 285-7°, ν_{max} 3192, 3050, 1372, 1323, 1150, 1084, 1037, 950 870, 796, 710, 700 and 690 cm^{-1}, m/e 342, 272, 168, 105 and 40, τ (TFA) 1.8-2.63 (10H, m), 7.4 (1H, dq, J 7, J_{PH} 2 Hz), 8.43 (3H, d, J_{PH} 2 Hz), 8.2-8.93 (15H, m), (Found: C, 73.72; H, 8.02; P, 9.06%. $C_{21}H_{27}O_2P$ requires C, 73.68; H, 7.89; P, 9.06%).

Reaction of r-1-Phenyl-2,2-cis-3,4,4-pentamethylphosphetan with Benzoyl Chloride.

Benzoyl chloride was reacted with the cis-phosphetan as for the trans-isomer to give an identical product with that obtained in the above reaction.

Reaction of 2-Ethoxy-1,3,2-dioxaphospholan with Benzil.

2-Ethoxy-1,3,2-dioxaphospholan was prepared by the method of Lucas and co-workers[135]. B.p. 60-66° (21 mm). Reaction of benzil with excess phosphite was carried out in the absence of solvent under nitrogen atmosphere. Attempts to crystallize the product from n-hexane were unsuccessful. ν_{max} (film), 1608, 1505, 1455, 1280, 1140, 1060, 960 and 865 cm^{-1}, τ ($CDCl_3$) 2.54-2.9 (10H, m), 5.34-6.3)6H, m), 8.77 (3H, t, J 6 Hz), m/e 346, 342, 286, 269, and 192. ^{31}P δ(CCl_4) +34 p.p.m.

Kinetic Measurements.

The reaction was started by the rapid addition of dioxane solution of the phospholan to an equimolar dioxane solution of benzil, both of which had reached the temperature of equilibrium in a thermostat (25 and 45°). The reaction was carried out as a homogeneous system with stirring in a glass-stoppered flask. Aliquots (1 ml) were taken out at appropriate intervals of time. The reaction was stopped by diluting it to 100 ml with light petroleum. Products were estimated by means of ultraviolet spectrometry at wave length 318 nm. Product ϵ_{max} = 9100.

Reaction of r-1-(2-Phenylethynyl)-2,2-trans-3,4,4-pentamethylphosphetan with Hexafluoroacetone.

Hexafluoroacetone (10 ml) was condensed into a stirred solution of the phosphetan (1.2 g, .005 mol) in dichloromethane (20 ml) at -78°. After 3h. the solution was allowed to warm to room temperature. The solvent was removed under reduced pressure. Fractional crystallisation from dichloromethane-ether gave a crystalline solid (1.65 g, 60%), m.p. 160°, ν_{max} (CCl_4, 4%), 1450, 1375, 1312, 1288, 1265, 1228, 1160, 1144, 1112, 1080, 975, 963, 885, 720 and 687 cm^{-1}, τ 2.6-2.86 (3H, m), 2.86-3.16 (2H, m), 7.72 (1H, dq, J7, J_{PH} 3 Hz), 8.62 (6H, d, J_{PH} 24 Hz), 8.70 (6H, d, J_{PH} 24 Hz), and 9.1 (3H, dd, J7, J_{PH} 1.5 Hz), m/e 576, 557, 505, 448, 437, 382, 379, 345, 313 and 241 cm^{-1}, (Found: C, 46.10; H, 3.48; F, 40.75; P, 5.44%. $C_{22}H_{21}O_2F_{12}P$ requires C, 45.84; H, 3.65; F, 39.58; P, 5.38%), ϵ_λ = 283 (Ethanol) = 920, ^{19}F ($CDCl_3$) +9.70 (6F, s), +11.52 (6F, d, 4 Hz); ^{31}P δ -31.59 p.p.m.

The mother-liquor was chromatographed on preparative basic alumina plates. Elution with ether-light petroleum (1:1) yielded four different isomers (< 5%) having the same molecular ion. The product eluted after the major compound has been characterized as a crystalline solid, m.p. 100°, ν_{max} (CCl_4), 1605, 1580, 1800, 1387, 1342, 1288, 1225, 1708, 1107, and 838 cm^{-1}, τ (CCl_4), 2.6-3.0 (5H, m), 4.8 (1H, d, J_{PH} 12 Hz), 8.8 (6H, d, J_{PH} 16 Hz), and 8.9 (6H, d, J_{PH} 18 Hz), the signal from the ring proton was partly hidden under that from the lower-field methyl protons, m/e 428, 413, 409, 358, 343, 311, 277, 262, 207, and 149, (Found: C, 52.36; H, 5.30; F, 25.63; P, 8.08%. $C_{19}H_{23}O_2PF_6$ requires C, 52.27; H, 5.30, F, 25.63; P, 7.24%). ^{19}F δ(CCl_4) +9.20 (6F, d, 7 Hz), ^{31}Pδ(CCl_4) -37.8 p.p.m.

Reaction of r-1-(Prop-1-ynyl)-2,2-trans-3,4,4-pentamethylphosphetan with Hexafluoroacetone.

Hexafluoroacetone (1 ml) was condensed into a stirred solution of the phosphetan (1.1 g, 0.0056 mol) into dichloromethane (5 ml) at -78°. After ½ hour the solution was allowed to warm to room temperature. The solvent was removed under reduced pressure and the crude was chromatographed on preparative basic alumina plates. Elution with ether-light petroleum (1:1) yielded three compounds, two of which were identified. The major compound (first band, 63%), m.p. 64-66°, ν_{max} 1720, 1705, 1370, 1145, 1110, 1090, 965 and 910 cm^{-1}, m/e 514, 499, 495, 444, 384, 332, 283, and 216, τ 7.6-7.93 (4H, m), 8.66 (6H, d, J_{PH} 24 Hz), 8.73 (6H, d, J_{PH} 22 Hz), and 9.1 (3H, dd, J7, J_{PH} 1.5 Hz), (Found: C, 39.54; H, 3.39; F, 44.53; P, 5.98%. $C_{17}H_{19}O_2F_{12}P$ requires C, 39.69; H, 3.70; F, 44.36; P, 6.03%). ^{19}F $\delta(CCl_4)$ +9.61 (6F, d, 4 Hz), +9.68 (6F, s); ^{31}P δ -32.58 p.p.m.

The minor product (second band, 0.7%), m.p. 64-65°, ν_{max} 1715, 1375, 1160, 1110, 1025, 965 and 900 cm^{-1}, τ 7.16 (1H, dq, J 7, J_{PH} 1.5 Hz), 7.83 (3H, s), 8.55 (12H, d, J_{PH} 26 Hz) and 9.1 (3H, dd, J 7, J_{PH} 1.5 Hz), m/e 514, 495, 444, 384, and 332, (Found: C, 39.51; H, 4.46; F, 44.57; P, 5.9%. $C_{17}H_{19}O_2F_{12}P$ requires C, 39.69; H, 3.70; F, 44.36; P, 6.03%), ^{19}F δ (CCl_4) -0.3 (6F, s), +9.22 (6F, s); ^{31}P δ (CCl_4) -49.78 p.p.m.

General Procedure for the Preparation of Dione Adducts of 1-Substituted-2,2,3,4,4-pentamethylphosphetans.

Equimolar quantities of the phosphetan in ether (20 ml) and the dione in ether (70 ml), were reacted at 0°, stirred for 1 h and solvent removed under reduced pressure to give the crude 1:1 adduct. In the case of the reaction of pentamethylphosphetan-1-phenyl with 9,10-phenanthraquinone, ether was replaced by benzene (2 ml) as a reaction medium.

1. o-Tetrachlorobenzoquinone Adducts.

Reaction of r-1-Phenyl-2,2-trans-3,4,4-pentamethylphosphetan with o-Tetrachlorobenzoquinone.

The trans phosphetan was reacted with the quinone as above. Crystallisation from ether-light petroleum gave the trans 1:1 adduct (91%), m.p. 160-161°, ν_{max} 1385, 1305, 1255,1240,1115 and 995 cm^{-1}, τ 1.96-2.40 (2H, m), 2.4-2.63 (3H, m), 8.50 (6H, d, J_{PH} 18 Hz), 8.63 (6H, d, J_{PH} 20 Hz) and 9.13 (3H, dd, J 7, J_{PH} 2 Hz); the signal from the ring proton was hidden under that from the lower-field methyl protons. M/e: 466, 364, 398, 396, 394, 279, 277 and 275, (Found: C, 51.07; H, 4.42; Cl, 30.11; P, 6.70%. $C_{20}H_{21}O_2Cl_4P$ requires C, 51.5; H, 4.50; Cl, 30.02; P, 6.65%). ^{31}P δ -10.7 p.p.m.

Reaction of r-1-Phenyl-2,2-cis-3,4,4-pentamethylphosphetan with o-Tetrachlorobenzoquinone.

The cis-phosphetan was reacted with the quinone as above. Crystallisation from ether-light petroleum gave the cis 1:1 adduct, 93%, m.p. 146-147°, ν_{max} 1380, 1375, 1320, 1260, 816 and 720 cm^{-1}, τ 2.17-2.44 (2H, m), 2.44-2.77 (3H, m), 7.80 (1H, dq, J 7, J_{PH} 1.5 Hz), 8.47 (6H, d, J_{PH} 14 Hz), 8.78 (6H, d, J_{PH} 21 Hz) and 9.2 (3H, dd, J 7,

J_{PH} 1.5 Hz). M/e: 466, 398, 396, 394, and 344, (Found: C, 51.48; H, 4.66; Cl, 29.94; P, 6.60%. $C_{20}H_{21}O_2Cl_4P$ requires C, 51.5; H, 4.50; Cl, 30.02; P, 6.815%). ^{31}P δ -18.50 p.p.m.

Reaction of r-1-(Prop-1-ynyl)-2,2-trans-3,4,4-pentamethylphosphetan with Tetrachlorobenzoquinone.

The phosphetan was reacted with the quinone as above. Crystallisation from dichloromethane-ether gave the trans 1:1 adduct, 88%, m.p. 215.5-217.5°, ν_{max} 2200, 1385, 1370, 1230, 1045, 995, 818, 805 and 670 cm^{-1}, τ 8.06 (3H, d, J_{PH} 3 Hz), 8.66 (6H, d, J_{PH} 23 Hz), 8.68 (6H, d, J_{PH} 19 Hz) and 9.13 (3H, dd, J 7, J_{PH} 2 Hz); the signal from the ring proton was hidden under that from the lower-field methyl protons. M/e, 428, 366, 296, 196, 183 and 166, (Found: C, 47.65; H, 4.44; Cl, 33.20; P, 7.21%. $C_{17}H_{19}O_2Cl_4P$ requires: C,47.75; H, 4.44; Cl, 33.10; P, 7.24%). ^{31}P δ +6.9 p.p.m.

Reaction of r-1-(Prop-1-ynyl)-2,2-cis-3,4,4-pentamethylphosphetan with o-Tetrachlorobenzoquinone.

The phosphetan (isomers mixture cis:trans = 1.7:1), was reacted with the quinone as above. Fractional crystallisation from dichloromethane-light petroleum gave the 1:1 adduct as a mixture of isomers (cis:trans = 3.1:1) as determined by the integration of the n.m.r. spectrum of the mixture due to the signals from 2,2,4,4-methyls (at τ:8.66 and 8.68 in the trans-isomer and τ 8.46 and 8.70 in the cis isomer).

The cis adduct exhibited signals in the n.m.r. spectrum of the mixture at τ 8.8 (3H, d, J_{PH} 3 Hz), 8.46 (6H, d, J_{PH} 17 Hz), 8.70 (6H, d, J_{PH} 23 Hz), and 9.06 (3H, d, J 7). The signals from the ring proton

were hidden under that from the lower-field methyl protons, ^{31}P δ (CCl_4) + 8.4 p.p.m.

Reaction of r-1-(2-phenylethynyl)-2,2-trans-3,4,4-pentamethylphosphetan with o-Tetrachlorobenzoquinone.

The phosphetan was reacted with the quinone as above. Crystallisation from dichloromethane-light petroleum gave the 1:1 adduct, 93%, m.p.166-9°, ν_{max} 2190, 1370, 1395, 1192, 1080, and 868 cm^{-1}, τ 2.50-2.90 (5H, m), 8.53 (6H, d, J_{PH} 23 Hz), 8.60 (6H, d, J_{PH} 18 Hz) and 9.10 (3H, dd, J 7, J_{PH} 1.5 Hz). The signals from the ring proton were hidden under that from the lower-field methyl protons, m/e 490, 420, 231 and 143, (Found: C, 53.75; H, 4.18; P, 6.40; Cl, 29.07%. $C_{22}H_{21}O_2PCl_4$ requires: C, 53.88; H, 4.29; P, 6.33; Cl, 28.98%). ^{31}P δ +6.5 p.p.m.

Reaction of r-1-(2-phenylethynyl)-2,2-cis-3,4,4-pentamethylphosphetan with o-Tetrachlorobenzoquinone.

The phospholan (isomers mixture cis:trans = 1.6:1) was reacted with the quinone as above. Fractional crystallisation from dichloromethane-light petroleum gave the cis adduct, m.p. 160°, ν_{max} 2200, 1375, 1360, 1252 and 800 cm^{-1}, τ 2.43-2.85 (5H, m), 7.80 (1H, dq, J 7, J_{PH} 1.5 Hz), 8.40 (6H, d, J_{PH} 18 Hz), 8.62 (6H, d, J_{PH} 24 Hz) and 9.0 (3H, d, J 7), m/e 490, 420, 231 and 143, (Found: C, 54.01; H, 4.36; Cl, 28.92%. $C_{22}H_{21}O_2PCl_4$ requires C, 53.88; H, 4.29; Cl, 28.98%), ^{31}P δ 8.5 p.p.m.

Reaction of r-1-Methyl-2,2-trans-3,4,4-pentamethylphosphetan with o-Tetrachlorobenzoquinone.

(a) The phosphetan oxide was reduced with trichlorosilane and tri-

ethylamine in ether and the phosphetan solution was reacted with the quinone as above. Chromatography on alumina and eluting with dichloromethane gave the trans 1:1 adduct (10%), m.p. 211-212° (dichloromethane-light petroleum). ν_{max} 1390, 1380, 1302, 1240, 1005, 900 and 825 cm^{-1}, τ 8.42 (3H, d, J_{PH} 9 Hz), 8.72 (6H, d, J_{PH} 16 Hz), 8.75 (6H, d, J_{PH} 20 Hz) and 9.15 (3H, dd, J 7, J_{PH} 2 Hz). The signal from the ring proton was hidden under that from the lower-field methyl protons, m/e 428, 360, 358, 338, 336, 316 and 314, (Found: C, 44.62; H, 4.62; Cl, 35.13%. $C_{15}H_{19}O_2Cl_4P$ requires C, 44.58; H, 4.74; Cl 35.10%). ^{31}P $\delta(CH_2Cl_2)$ -62.84 p.p.m.

(b) The phosphetan oxide (1.4 g, .008M) and excess phenylsilane (0.7 g, .0065M) were mixed together and kept at 60°C for 8h. The product was distilled by gradually raising the temperature to 140°. The phosphetan was dissolved in ether (40 ml) before adding the quinone at -10°. Warming the crude mixture up to room temperature and the solvent was removed to give a solid. Chromatography on alumina and eluting with dichloromethane gave a product which was identified as the trans-adduct above (1.7 g, 52%).

Attempted reaction of r-1-Methyl-2,2-cis-3,4,4-pentamethylphosphetan with o-Tetrachlorobenzoquinone.

(a) Following the above procedure as for the trans-phosphetan and varying the conditions of the reduction procedure either by varying the concentration of the reduction reagents, solvent or the reaction time gave a complexed dark solid and oily residue from which no adducts could be isolated.

(b) Phenylsilane (1 g, .009 M) was added to an enriched cis-phosphetan oxide mixture (= 90%) (1.3 g, .007 M) at room temperature. The

reaction mixture was stirred for 5 h at 60-70°. The product was dissolved in ether (50 ml). The quinone (2 g, .008M) in ether (100 ml) was added dropwise to the phosphetan mixture at 0° giving a deep green precipitate. Chromatography on alumina and eluting with dichloromethane gave a product which was identified as the trans-adduct above (0.9 g, 32%).

2. 9.10-Phenanthraquinone Adducts.

Reaction of r-1-Phenyl-2,2-trans-3,4,4-pentamethylphosphetan with 9,10--Phenanthraquinone.

The adduct was prepared as reported by Shutt[156]. M.p. 195° (from ether-light petroleum, reported m.p. 198-199°). τ 1.26-2.83 (13H, m), 7.90-7.60-2.40 (1H, m), 8.43 (6H, d, J_{PH} 16 Hz), 8.62 (6H, d, J_{PH} 19 Hz) and 9.10 (3H, dd, J 7, J_{PH} 2 Hz). m/e 428, 356, 341 and 239, ^{31}P δ (o-Dichlorobenzene) + .02 p.p.m.

Reaction of r-1-Phenyl-2,2-cis-3,4,4-pentamethylphosphetan with 9,10-Phenanthraquinone.

The adduct was prepared as for the trans-isomer (95%). M.p. 161° (from ether-light petroleum), ν_{max} 1645, 1348,1129, 1100, 1055 and 1030 cm^{-1}; τ 1.26-2.86 (13H, m), 7.46-7.93 (1H, m), 8.42 (6H, d, J_{PH} 19 Hz), 8.73 (6H, d, J_{PH} 23 Hz) and 9.20 (3d, dd, J 7, J_{PH} 1.5 Hz), m/e 428, 356, 341, 314, and 239. (Found: C, 78.10; H, 6.97%. $C_{28}H_{29}O_2P$ requires C, 78.50; H, 7.77%). $^{31}P\delta$(o-Dichlorobenzene) -7.7 p.p.m.

Reaction of r-1-(Prop-1-ynyl)-2,2-trans-3,4,4-pentamethylphosphetan with 9,10-Phenanthraquinone.

The phosphetan was reacted with the quinone as above to yield the

crystalline 1:1 adduct (87%), m.p. (ether-light petroleum). ν_{max} 2205, 1655, 1600, 1380, 1290 and 930 cm^{-1}, τ 1.33-2.86 (8H, m), 8.16 (3H, d, J_{PH} 3 Hz), 8.52 (6H, d, J_{PH} 23 Hz), 8.56 (6H, d, J_{PH} 19 Hz) and 9.13 (3H, dd, J 7, J_{PH} 1.5 Hz). The signal from the ring proton was hidden under that from the lower-field methyl protons, m/e 390, 318, 303, 276 and 176, (Found: C, 76.82; H, 6.80; P, 7.91%. $C_{25}H_{27}O_2P$ requires: C, 76.92; H, 6.92; P, 7.95), $^{31}P\delta$+12.8 p.p.m.

Reaction of r-1-(Prop-1-ynyl)-2,2-cis-3,4,4-pentamethylphosphetan with 9,10-phenanthraquinone.

A mixture of the phosphetan isomers (cis:trans = 1.7:1), was reacted with the quinone as above to give the adduct as a mixture of isomers of the same ratio. A mixture of the adduct isomers (cis:trans = 3.1:1) was obtained by fractional crystallisation from ether-light petroleum. The cis:trans isomer ratio was determined by integrating the n.m.r. spectrum of the adducts mixture due to 2,2,4,4-methyls (at τ 8.52 and 8.56 in the trans isomer and τ 8.53 and 8.62 in the cis-isomer).

The cis-adduct exhibited signals in the n.m.r. spectrum of the mixture at τ 1.30-2.90 (8H, m), 8.16 (3H, d, J_{PH} 3 Hz), 8.53 (6H, d, J_{PH} 20 Hz), 8.62 (6H, d, J_{PH} 16 Hz) and 8.96 (3H, dd, J 7, J_{PH} 1.5 Hz). The signal from the ring proton was hidden under that from the lower-field methyls. ^{31}P δ (CH_2Cl_2) +12.4 p.p.m.

Reaction of r-1-(2-phenylethynyl)-2,2-trans-3,4,4-pentamethylphosphetan with 9-10-phenanthraquinone.

The 1:1 adduct was prepared as above (89%), m.p. (dichloromethane-light petroleum), ν_{max} 1190, 1655, 1380, 1060 and 960 cm^{-1}, τ 1.46-3.06 (13 H, m), 8.10 (6H, d, J_{PH} 22 Hz), 8.52 (6H, d, J_{PH} 19 Hz)

and 9.10 (3H, dd, $\underline{J}$ 7, $\underline{J}_{PH}$ 1.5 Hz). The signal from the ring proton was hidden under that from the lower-field methyls, m/e 452, 380, 364, 238 and 138, (Found: C, 79.53; H, 6.31; P, 6.88%. $C_{30}H_{29}O_2P$ requires C, 79.65; H, 6.42; P, 6.89%). ^{31}P δ +13.0 p.p.m.

Reaction of r-1-(2-Phenylethynyl)-2,2-cis-3,4,4-pentamethylphosphetan with 9-10-phenanthraquinone.

The phosphetan isomers mixture (cis:trans = 1.6:1) was reacted, as above. Fractional crystallisation from dichloromethane-light petroleum gave the adduct as a mixture of isomers (cis:trans = 2:1). The cis adduct exhibited signals at τ 1.36-2.96 (13H, m), 8.23 (6H, d, $\underline{J}_{PH}$ 17 Hz), 8.46 (6H, d, $\underline{J}_{PH}$ 23 Hz), and 8.93 (3H, d, $\underline{J}$ 7). The signal from the ring proton was hidden under that from the lower-field methyl protons.

High Temperature Kinetic Measurements.

The appropriate sample of the adducts shown in Table V in o-dichlorobenzene in a sealed n.m.r. tube was heated in the probe of the n.m.r. machine with TMS as internal reference. The isomerisation reaction was followed at pre-selected constant temperatures by scanning the n.m.r. spectra at appropriate time intervals. The height of the peaks in the region corresponding to the phosphetan ring methyls were measured and taken to indicate the percentage concentration of the particular isomer. The ratio of the two isomers in the reaction mixture was followed over a sufficient period to observe equilibrium.(X_{eq}). The slope of the curve of log concentration vs time was determined and the reaction rate (K) calculated from the formula:

$$K = \frac{2.303 \times \text{slope} \times X_{eq}}{100}$$

Table V: Data for 1-Substituted Pentamethylphosphetan Adducts with:

(a) o-Tetrachlorobenzoquinone.

1-Substituent & Adduct No.	Temperature C°	% Trans at equilibrium (Xe)	10^6 Slope sec^{-1}	$10^5 k$ sec^{-1}	ΔG^* kcal. mol^{-1}
Ph	122	77.35	58.64	10.45	30.79
(200)	142	78.57	286.00	51.75	30.55
	152	79.75	517.50	173.90	30.54
PhC≡C-	80	88.38	6.78	1.38	28.60
(201)	100	87.57	64.24	12.95	28.60
	120	86.22	414.00	82.20	28.77
MeC≡C-	50	87.00	5.84	1.17	26.26
(202)	70	89.01	57.90	11.87	26.34
	90	85.39	593.40	116.60	26.27
Me	100	-	-	-	-
(203)					

(b) o-Phenanthraquinone.

Ph	80	85.9	1.87	3.7	27.96
(194)	100	84.2	14.44	28.0	28.00
	120	85.7	131.74	260.0	27.87
PhC≡C-	90	78.26	8.88	1.60	29.37
(204)	110	77.53	63.12	11.27	29.54
	130	80.77	523.20	97.73	29.39
MeC≡C-(a)	60	73.00	8.72	1.47	26.94
(205)	80	77.80	65.21	11.68	27.14
	100	82.00	431.30	81.50	27.28

All kinetic studies were performed in o-dichlorobenzene; otherwise specified: (a) 1-Bromonaphthalene.

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SUMMARY

Chapter 1 represents a review on the synthesis and structure of 1-substituted 2,2,3,4,4-pentamethylphosphetans.

In Chapter 2 the stereochemistry and mechanism of base-catalysed phosphetanium salt hydrolysis are envisaged and shown to depend upon the reaction conditions, in particular the pH of the medium. The results are interpreted in terms of the intermediacy of TBP structural phosphoranes, and the most significant role of the BPR as a viable mechanism for intramolecular isomerization of such intermediates, in determining the products distribution, is discussed. The possibility of a pre-decomposition equilibrium between diastereomeric salts *via* pseudorotation is considered and shown to occur, specifically, in very dilute alkaline media. A change in the reaction rate-limiting step from a slow isomerization process to a phosphorane decomposition is postulated to account for variation in product composition on varying the conditions. The alkaline hydrolysis of *r*-1-substituted acetylenic 2,2,3-*trans*-4,4-pentamethylphosphetanium bromides proceeds, in contrast to the generally reported retention as the stereochemically preferred pathway for phosphetans, with complete inversion of configuration.

Base-catalysed ring expansions of a number of salts are shown to proceed, stereospecifically, to give only one observable product oxide. This is attributed to a very short-lived intermediate phosphorane. In the end a qualitative scale of the relative apicophilicities of the studied groups, is observed.

In Chapter 3, an attempt to synthesise the 1:2 adducts of 1-substituted acetylenic-2,2,3,4,4-pentamethylphosphetan with HFA

resulted in formation of other products for which a probable mechanism and structures, based on spectroscopic and elemental analysis data are discussed and suggested for each product.

A variety of phosphoranes containing phosphetan rings was synthesised. A kinetic study of the rate of reaction of 2-ethoxy--1,3,2-dioxaphospholan with benzil showed the reaction to follow a bimolecular step-wise mechanism.

Relative apicophilicities of a number of groups attached to the phosphorus atom in phosphetan adducts were determined by monitoring the high energy isomerization pathways, accessible to these adducts, in which the five-membered rings span diequatorial positions, using ^{1}H n.m.r. spectroscopy techniques. The values so determined are rationalised in terms of substituent electronegativities and the extent of a probable π-electron interaction with the phosphorus d-orbitals.