SOME ASPECTS

OF

PHOSPHETAN CHEMISTRY

by

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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 October 1968 and June 1971.

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

Signed

J. R. Corfield.

September 1971

J. R. Corfield

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Parts of this thesis have been reported in the following publications :

"The Stereochemistry of the Alkaline Hydrolysis of Phosphetanium Salts. Change in Configuration at Phosphorus on Ylide Formation". J. R. Corfield, J. R. Shutt, and S. Trippett, Chem. Comm., 1969, 789.

"The Nature of the Carbanion formed in the Hydrolysis of Phosphonium Salts". J.R. Corfield and S. Trippett, Chem. Comm., 1970, 1267.

"The Reactions of Phosphetans with Halogens. A New Phospholen Synthesis". J. R. Corfield, M. J. P. Harger, R. K. Oram, D. J. H. Smith, and S. Trippett, Chem. Comm., 1970, 1350.

"Displacement at Phosphorus in a Four-membered Ring." J.R. Corfield, N. J. De'Ath, and S. Trippett, Chem. Comm., 1970, 1502.

"The Assignment of Configuration to 2,2,3,4,4-Pentamethyl-phosphetan Oxides Using Tris(dipivalomethanato)europium(III)." J.R. Corfield, and S. Trippett, Chem. Comm., 1971, 721.

"Further Ring Openings and Ring Expansions of Phosphetans". J. R. Corfield, M.J.P. Harger, J. R. Shutt, and S. Trippett, J. Chem. Soc.(C), 1970, 1855.

"Reactions of Phosphine Sulphides with Aryl-lithiums". J. R. Corfield and S. Trippett, J. Chem. Soc. (C), 1971, 334.

"The Alkaline Hydrolysis of Sterically Crowded Phosphonium Salts". J. R. Corfield, N. J. De'Ath, and S. Trippett, J. Chem. Soc.(C), 1971, 1930.

CONTENTS

RING OPENINGS AND RING EXPANSIONS OF PHOSPHETANS

SUMMARY

A study of the stereochemistry of substitution reactions at the phosphorus atom of 2,2,3,4,4-pentamethylphosphetans has been made. It is proposed that all such displacements proceed *via* trigonal bipyramidal intermediates in which the ring spans an apical-equatorial position.

Walden cycles in which substitution at the phosphoryl centre of phosphetans proceeds with retention of configuration are described and a mechanism involving pseudorotation of the intermediates is proposed. *Cis* and *trans* isomers of 2,2,3,4,4-pentamethylphosphetan 1-oxides can be distinguished by the paramagnetic shifts of the respective 3-protons in their n.m.r. spectra in the presence of tris(dipivalomethanato)europium(III).

Following a discussion of the mechanism of the alkaline hydrolysis of phosphonium salts, the hydrolysis of three salts in D_2O-H_2O (1:1) is described. The kinetic isotope effects observed show that the carbanions involved in these hydrolyses are not free in the rate-determining transition state. The alkaline hydrolysis of a 3-phospholenium salt is described in which the normal rule, that hydrocarbon will be formed from the group most stable as the anion, does not apply. 2,2,3,4,4-Pentamethylphosphetanium salts undergo alkaline hydrolysis with complete retention or with partial inversion of configuration at phosphorus. These differences are discussed in terms of the energy barriers to pseudorotation of the intermediates involved.

Other substitution reactions at the phosphorus of phosphetans bring about either ring expansion or ring opening.

All the reactions are governed by the preference of the four-membered ring for the apical-equatorial position in the trigonal bipyramidal intermediates. Attempts to generate the ylide from 1,2,2,3,4,4-hexamethyl-1-phenylphosphetanium iodide lead to ring opening *via* pentacovalent intermediates as also do the action of cyanide ion on this salt. 2,2,3,4,4-Pentamethyl-1-phenylphosphetan 1-sulphide with two molar proportions of phenyl-lithium gave (1,1,2,3-tetramethyl-3-phenylbutyl)diphenylphosphine. 2,2,3,4,4-Pentamethyl-1-phenylphosphetan with chlorine or bromine gave (1,1,2,3-tetramethyl-but-3-enyl) halogenophosphines which cyclised to phospholens on heating, and to phospholens and phosphetan 1-oxides on treatment with aluminium chloride.

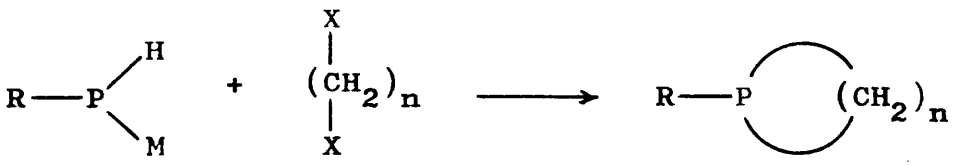
A study was made of the conversion of thiophosphoryl compounds into phosphoryl compounds.

The Synthesis of Phosphetan Compounds

1.1 General Ring Synthesis.

Only a small number of successful syntheses of phosphetans, four-membered rings containing one phosphorus and three carbon atoms, have so far appeared in the literature. One of the reasons for this is that when the general methods of phosphorus heterocycle synthesis were extended to phosphetans it was found that ring formation was suppressed in favour of formation of polymers, open-chain phosphines, or cyclodimerization.

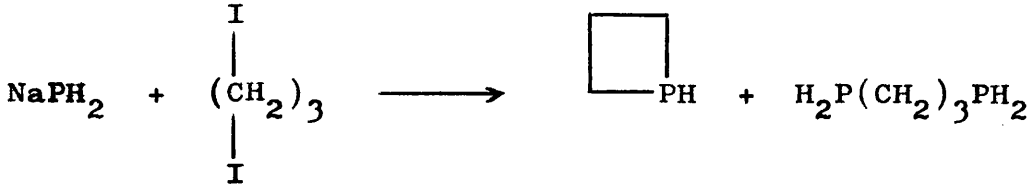
One general method of phosphorus heterocycle synthesis involves the reaction of substituted phosphines or phosphides with dihalogenoalkanes.[1,2,3]



X = Cl, Br, I R = H, Alkyl, Aryl

M = H, Li, Na, K n = 4, 5

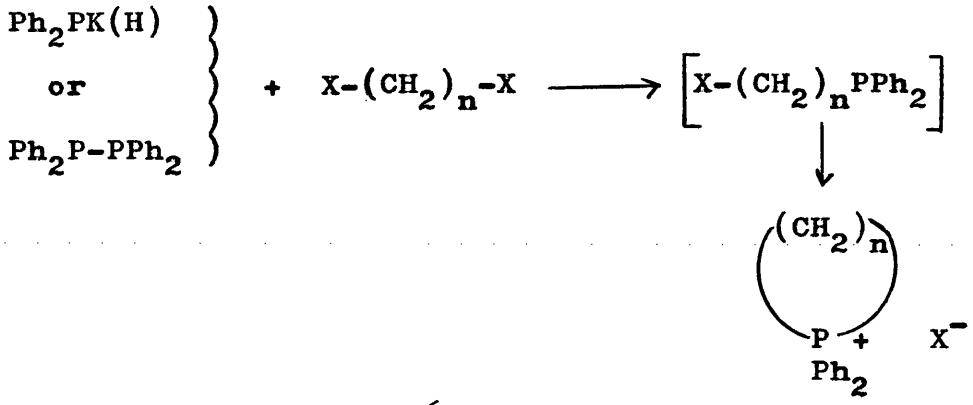
Wagner[1] produced only the simplest phosphetan (1) together with the open-chain phosphine (2) by this method from sodium phosphide and 1,3-di-iodopropane. Replacement of one hydrogen of the phosphide with a methyl or phenyl group



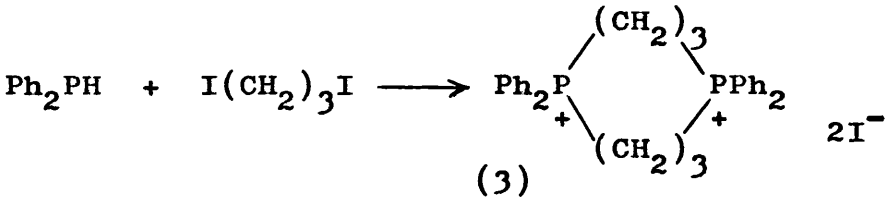
(1) (2)

resulted in formation of only biphosphines analogous to (2).

Phosphorus heterocycles have also been synthesised by the intramolecular formation of quaternary salts from bromoalkylphosphines formed by the reaction of secondary phosphines and phosphides, or diphosphines, with dihalogenoalkanes.[4,5]



Attempts by Grim and Schaaff[6] to synthesise phosphetans by this route proved unsuccessful. They found that the intermediate iodopropylphosphine underwent cyclodimerization to give the bisphosphonium salt (3).



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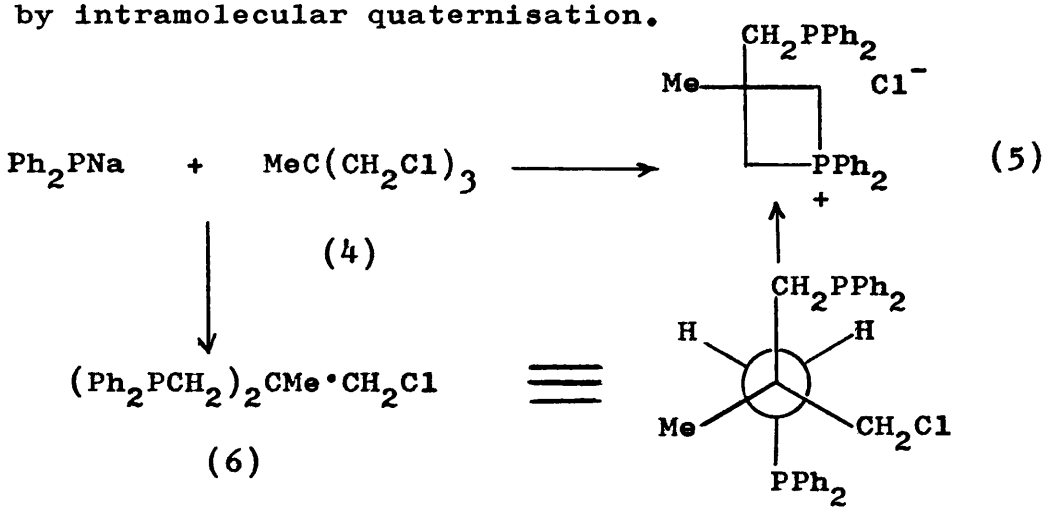
In contrast, Berglund and Meek[7] found that the trichloride (4) and sodium diphenylphosphide gave the salt (5) by intramolecular quaternisation.



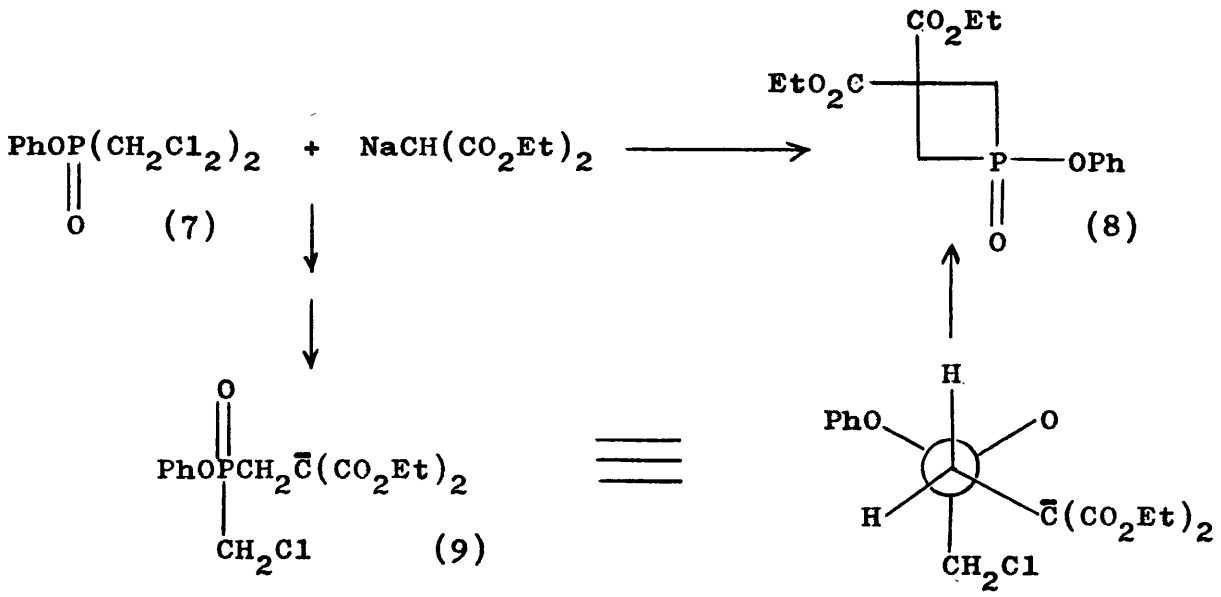
(4)

(6)

(5)

The intramolecular cyclisation reaction occurs in this case because the large groups present force the intermediate (6) into a conformation favouring cyclisation rather than polymerisation. It has been found[8] in the synthesis of the analogous azetidines from amines that certain bulky substituents aid the cyclisation process and this also has been explained by suggesting that the intermediates are forced by the bulky groups into those conformations favouring cyclisation.

Russian workers[9] found that the treatment of the phosphinate (7) with two equivalents of sodiodiethylmalonate gave the phosphetan (8). Again cyclisation occurs

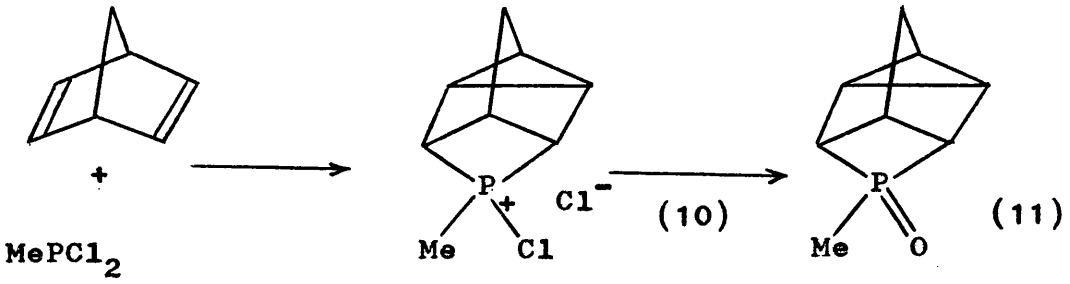


because of the conformation forced on the intermediate (9) by the large substituents.

1.2 Highly Substituted Phosphetans.

Green[10] synthesised the adduct (10), which contains a four-membered ring, from the reaction of methylphosphonous

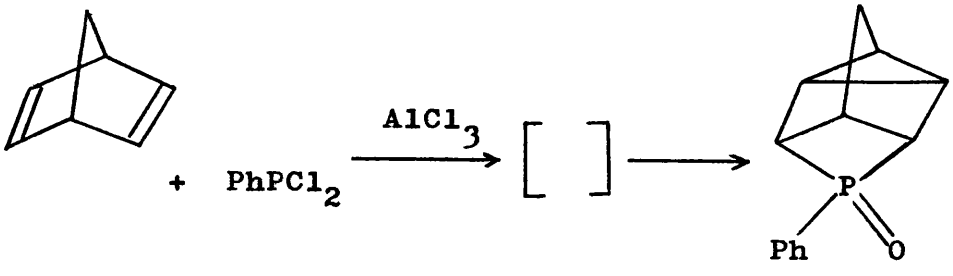
dichloride and bicyclo[2,2,1]heptadiene in the absence of light and oxygen. When treated with aqueous sodium hydrogen



carbonate it gave the phosphine oxide (11). Geometric isomers arising from the arrangement of the substituents on phosphorus with reference to those of the four-membered ring are possible in this oxide. A close examination (n.m.r. spectroscopy) of the hydrolysis product indicated the presence of only one isomer, that described by Green.

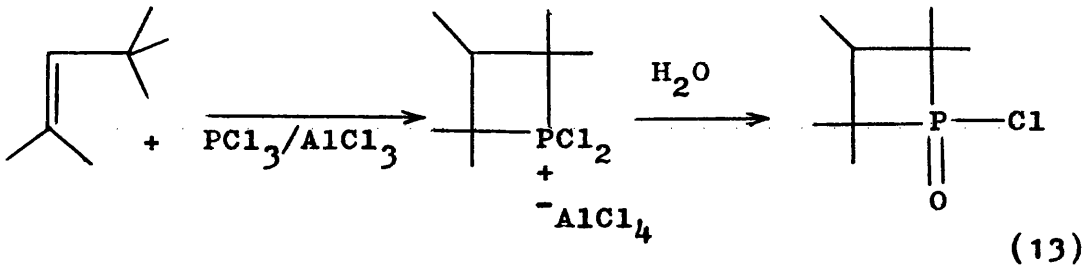
Attempts to prepare phosphetans from phosphines and cyclopentadiene in a similar manner have been unsuccessful.[11,12]

An attempt was made to extend Green's synthesis using phosphorus trichloride and phenylphosphonous dichloride but no adducts formed. On addition of a small quantity of aluminium chloride to a mixture of the latter phosphine and the diene a small quantity of crystals formed slowly over a period of months. Treatment of the crystals with aqueous sodium hydrogen carbonate gave the phosphine oxide (12).



(12)

In a group of papers Jungermann and coworkers[13] presented data in support of formation of the phosphetan (13) in good yield from the cycloaddition of 2,4,4-trimethylpent-2-ene and phosphorus trichloride in the presence of aluminium chloride. The reaction gave only one acid chloride (13) even though the substituents on the 3-carbon of the



(13)

ring allow the possibility of geometrical isomers.

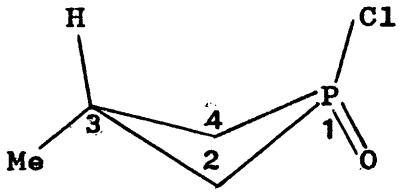
The generality of this cyclisation reaction was demonstrated later by variation of the olefin[14] and the use of other phosphonous dihalides.[11,14,15] In this way phosphetans with between three and five methyl substituents on the ring and groups other than chlorine on phosphorus have been synthesised.

1.3 2,2,3,4,4-Pentamethylphosphetan Compounds.

The stereochemistry of the phosphetans in this thesis will be described using the Beilstein r-system.[16,17] A reference group in the molecule is specified by the symbol r- and the ring substituents are related to it. The reference group is a substituent attached to the lowest-numbered ring member, i.e. the phosphorus atom in phosphetans. When more than one substituent is attached to the phosphorus atom, the one having preference in the IUPAC nomenclature system is taken as the reference group.

1.4 2,2,3,4,4-Pentamethylphosphetan 1-Oxides.

The acid chloride (13) isolated by Jungermann[13] was the first pentamethylphosphetan 1-oxide synthesised. The structure and stereochemistry of the one diastereoisomer isolated was determined by X-ray analysis.[18] This revealed that (a) the 3-methyl group was trans to the 1-chlorine atom on phosphorus, (b) the four-membered ring was puckered, and (c) the ring C(2)-P(1)-C(4) angle of 85.9° was considerably distorted from the tetrahedral.



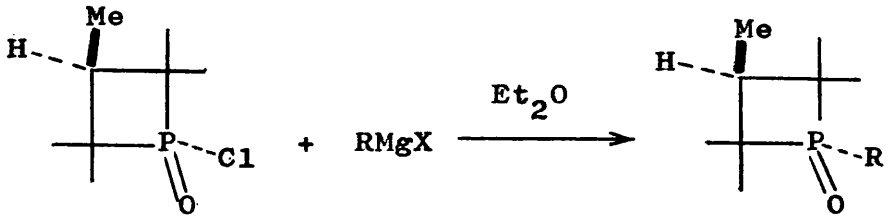
Modification of the phosphetan synthesis by use of phenylphosphonous dichloride in the place of phosphorus trichloride gave the 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxide as a mixture of stereoisomers.[14,15] The isomer composition of the product was found to be dependent on the work-up procedure. Separation of the isomers has been achieved by fractional recrystallisation and more readily by column chromatography on alumina.[19] The structures of the two isomers have been investigated by X-ray analysis.[20,21]. Both isomers have puckered rings, and C(2)-P(1)-C(4) angles of ca. 82° indicating a distortion by the ring ofatetrahedral arrangement of groups around phosphorus similar to that found in r-1-chloro-2,2,trans - 3,4,4-pentamethylphosphetan 1-oxide. It was found in the isomer having m.p. 126-127° that the 3-methyl was trans to the phenyl on phosphorus and in the isomer m.p. 117-118°

there was a cis arrangement of the two groups.

The isomers are readily distinguished by ^{1}H n.m.r. spectroscopy and this has been used to determine the isomer composition of reaction products.

1.5 The Preparation of 2,2,3,4,4-Pentamethylphosphetan 1-Oxides.

When Grignard reagents were added to the diastereoisomerically pure r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide a smooth reaction occurred giving the phosphetan oxides (14) in good yield. The reactions



(14)

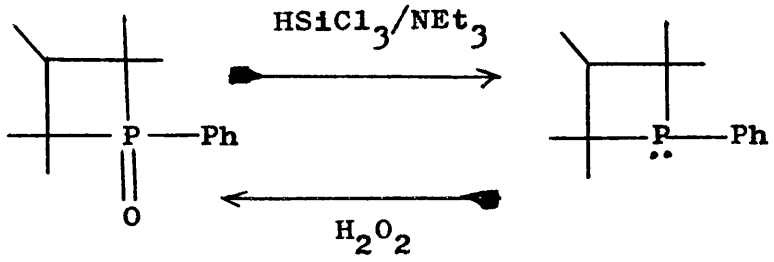
R = Me, $PhCH_2$, 1-Nap

occurred without any interference from ring-opening reactions as was observed with phenyl-lithium.[19,22] The ^{1}H n.m.r. spectrum of each oxide product revealed that it was one stereoisomer, in fact the trans-phosphetan oxide, the reaction proceeding with retention of stereochemistry around phosphorus. The stereochemical direction of this reaction will be discussed in a later chapter.

1.6 The Reduction of 2,2,3,4,4-pentamethylphosphetan 1-Oxides.

Cremer[14] showed that the isomeric 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxides could be reduced with

trichlorosilane in the presence of triethylamine to give the phosphetans (15). The reduction was shown to proceed

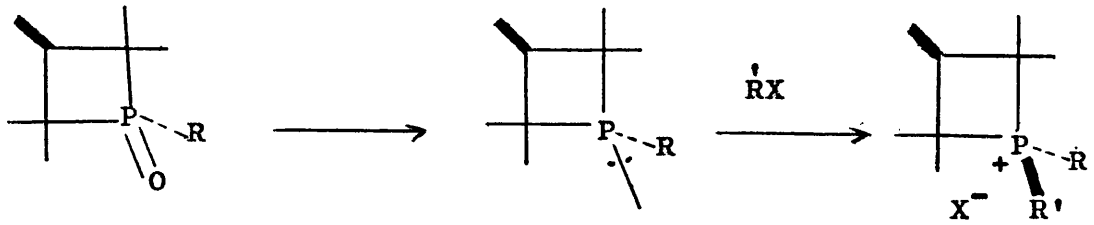


(15)

with retention of stereochemistry at phosphorus as oxidation gave back the starting isomer in each case. Oxidation occurs with retention of configuration.[23] The isomeric phosphetans had distinct ^{1}H n.m.r. spectra and as the stereochemical direction of the deoxygenation has been established configurations could be assigned to them. 1-Phenyl-phosphetan oxides have also been reduced with lithium aluminium hydride.[19]

The trichlorosilane and lithium aluminium hydride reduction of phosphetan oxides provided the phosphetans only in moderate yields so alternative reducing agents were investigated. It was found that phenylsilane and polymethyl-siloxane[24] converted the 1-phenylphosphetan 1-oxide in almost quantitative yield to the phosphetan, the former reagent reducing both isomers of the oxide with retention of configuration. It has since been shown that phenylsilane reduces phospholan oxides[25, 26] and phosphorinan oxides[27] with retention of configuration. The phosphetans undergo smooth quaternisation with alkyl halides such as methyl iodide and benzyl bromide to give phosphetanium salts.

The phosphetan 1-oxides from the reaction of the acid chloride with Grignard reagents were also readily deoxygenated by trichlorosilane in the presence of triethylamine to give the corresponding phosphetans (16). The reduction



R = Ph, $PhCH_2$, Me, 1-Nap (16) (17)

of these oxides also occurred with retention of configuration e.g. reoxidation of the crude phosphetan solution, from reduction of the 1-benzylphosphetan 1-oxide, with hydrogen peroxide gave back the starting oxide.

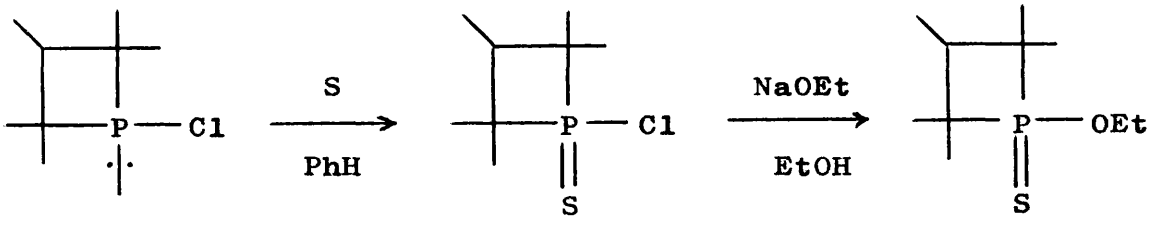
Quaternisation of the crude phosphetan solutions with a series of alkylhalides gave a series of phosphetanium salts (17) of known stereochemistry, as the quaternisation of phosphines is known to proceed with retention of configuration at phosphorus.[23]

1.7 Preparation of 2,2,3,4,4-Pentamethylphosphetan 1-Sulphides.

The reaction of sulphur with a mixture of stereoisomers of 2,2,3,4,4-pentamethyl-1-phenylphosphetan in boiling benzene gave an oily product containing the two isomeric 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-sulphides. Separation of the isomers was achieved by chromatography on alumina. The mixture of phosphetans consisted largely of the trans isomer and as the isomer ratio would be unaffected by the reaction conditions and sulphurization reactions of

phosphines proceed with retention of configuration[29,30] the major phosphetan sulphide isolated, m.p. 102-103°, was assigned a <u>trans</u> configuration. The minor <u>cis</u> isomer had m.p. 92-93°. These two sulphides were distinguished by their n.m.r. and i.r. spectra.

Similarly, 1-chloro-2,2,3,4,4-pentamethylphosphetan[31] (18) has been reacted with sulphur and the product chromatographed on alumina to give one stereoisomer of 1-chloro-2,2,3,4,4-pentamethylphosphetan 1-sulphide (19).[32] Treatment of this with sodium ethoxide gave one isomer of 1-ethoxy-2,2,3,4,4-pentamethylphosphetan 1-sulphide (20).

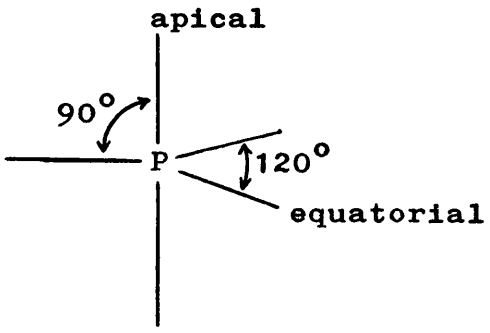


(18) (19) (20)

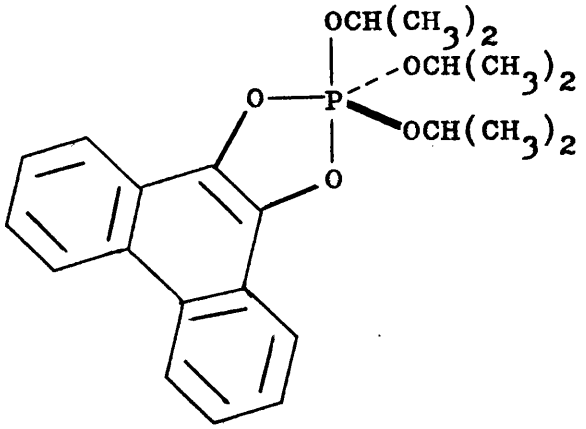
Phosphoranes

2.1 Structure and Stereochemistry.

All structure determinations by electron diffraction and X-ray crystallographic techniques of stable pentacovalent phosphorus compounds have shown that they have trigonal bipyramidal geometries. In the idealised case, the phosphorus atom lies within a triangle defined by three of the nearest bonding atoms which form the basal plane of the trigonal bipyramid. Bonds between phosphorus and these three ligands are designated as 'equatorial' and subtend an angle of 120°. The remaining two ligands, situated above and below the basal plane, are designated as 'apical'. The apical bonds subtend an angle of 180° with the phosphorus atom, and the axis connecting the three atoms is perpendicular to the basal plane.



The compounds studied include pentafluorophosphorus,[33] a stable Wittig intermediate,[34] pentaphenylphosphorus,[35] and the two allotropic forms of the phenanthrenequinone-triisopropyl phosphite adduct (21).[36] These studies also revealed that apical bonds are longer than the corresponding equatorial bonds, e.g. in pentaphenylphosphorus the apical and equatorial P-C lengths are 1.987 A° and 1.850 A° respectively.



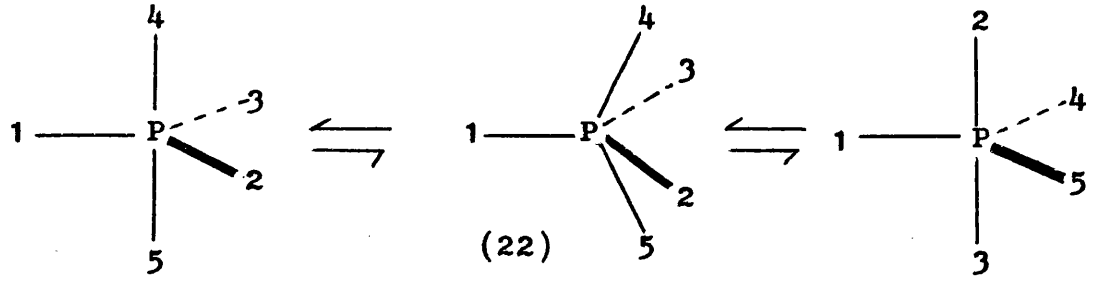
(21)

These structure determinations, together with ^{19}F and ^{1}H n.m.r. studies of alkyl and aryl derivatives of PF_5[37] and oxyphosphoranes[38, 39, 40, 41] clearly indicated that the more electronegative ligands (such as fluorine and oxygen) assume apical positions, and the more electropositive ligands (alkyl and aryl groups) equatorial positions in the phosphoranes. Van Der Voorn and Drago[51] demonstrated theoretically that this was because apical phosphorus orbitals are more electropositive than the equatorial orbitals due to different amounts of s character in them.

2.2 Pseudorotation.

The study of the n.m.r. spectra of fluorophosphoranes,[37] oxyphosphoranes,[38, 39, 40, 41] and penta-arylphosphoranes,[42,43] also demonstrated that phosphoranes may undergo intramolecular ligand exchange by pseudorotation such that one trigonal bipyramid is converted into another trigonal bipyramid. The process was first invoked by Berry[44] to explain the ^{19}F n.m.r. spectrum of pentafluorophosphorane which consisted of only one kind of fluorine although electron diffraction had shown that it has a trigonal bipyramidal structure. In pseudorotation by the Berry mechanism pairwise exchange of apical and equatorial ligands in the trigonal bipyramidal molecule takes place by way of a tetra-

gonal pyramidal transition state (22). The bond which



remains equatorial in the process and occupies the apex of the pyramid in the transition state, has been designated the 'pivot'. Since there are three equatorial ligands which may serve as pivots, there are three pathways which lead, by a single step, from a phosphorane to three others.

2.3 Phosphoranes as Reaction Intermediates.

Phosphoranes (23) have been thought of as intermediates in bimolecular nucleophilic substitution at tetra-coordinate phosphorus.[45,46] Displacement at phosphorus by a two-step

$$N^- + R_3\overset{+}{P}X \longrightarrow \underset{(23)}{NR_3PX} \longrightarrow NR_3\overset{+}{P} + X^-$$

N = nucleophile X = leaving group

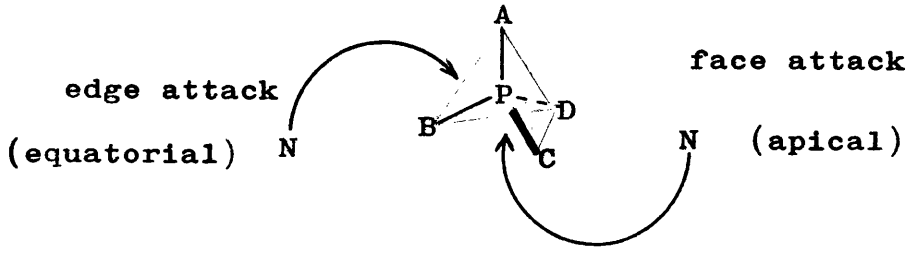
mechanism is a viable alternative to direct substitution because of the capacity of phosphorus, like other second-row elements, to achieve higher coordination numbers.

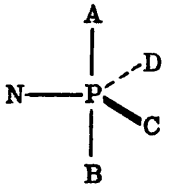
There are several possible geometrical structures which an intermediate phosphorane can adopt.[47] Muetterties and Schunn[48] in their critical review of pentacoordinate species record that most exist in the trigonal bipyramidal form and one other form, the tetragonal pyramid, is adopted

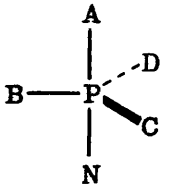
primarily in the solid state for a small number of compounds. All stable phosphoranes studied have been found to have trigonal bipyramidal structures. Consequently, it has been assumed, and it will be assumed, in this thesis, that phosphorane intermediates such as (23) have a trigonal bipyramidal geometry. However, it is generally conceded that the energy difference between the trigonal bipyramidal and tetragonal pyramidal forms is small, evidence for this coming from the n.m.r. studies of pseudorotation in phosphoranes and optically active ate complexes;[42] the Berry mechanism for pseudorotation involving conversion of a trigonal bipyramid into another via a tetragonal pyramidal transition state.

2.4 Formation and Decomposition of Phosphorane Intermediates.

Four-coordinated phosphorus compounds invariably have a tetrahedral phosphorus atom and unlike phosphoranes are stereochemically rigid.[46] Hence there are two possible modes of attack for a nucleophile upon a four-coordinated phosphorus compound, edge and face attack. Attack on the face







of a tetrahedron is referred to as apical attack as the nucleophile occupies an apical position in the trigonal bipyramidal phosphorane so formed, the equatorial positions being occupied by the three groups which bound the face under attack. Attack on the edge of a tetrahedron is equatorial attack as the nucleophile occupies an equatorial position in the phosphorane formed. The two groups defining the edge under attack occupy the apical positions. Similarly a leaving group can depart from two possible positions in the phosphorane, an apical or an equatorial position.

An extended principle of microscopic reversibility (PMR) has been broadly applied to displacement reactions at tetracoordinate phosphorus.[19, 39, 49] It states in effect that the stereochemistry (apical vs. equatorial) of entry and departure must be the same. Mislow has discussed this simplifying assumption,[50] and indicated that apical attack at phosphorus by a nucleophile followed by equatorial departure of a group (and the reverse process) does not violate the PMR in every circumstance. Nevertheless, as a simplifying postulate, apical attack and apical departure will be assumed throughout this thesis.

That apical attack and apical departure are the preferential modes of bond making and breaking follows from several independent lines of argument. Structural analyses of stable phosphoranes[33,34,35,36] have shown that apical bonds are longer and therefore weaker than equatorial bonds. Van Der Voorn and Drago[51] showed by theoretical calculations that equatorial phosphorus orbitals are more electronegative than the axial orbitals because the phosphorus s orbital is

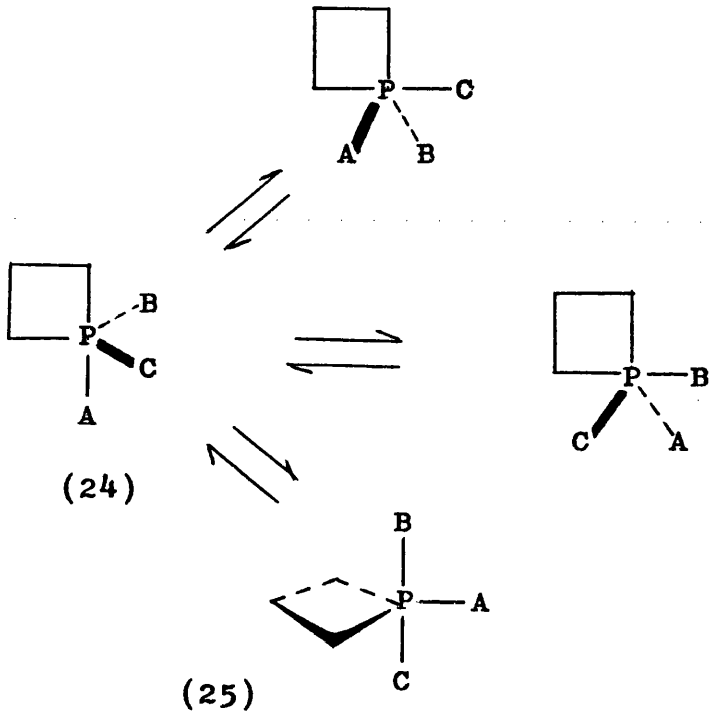
concentrated in the equatorial orbitals. This gives rise to equatorial bonds which are stronger than axial bonds, and to the preference of electronegative substitutents for the electropositive phosphorus orbitals, the apical ones. It is obvious, therefore, that nucleophiles should prefer axial entry and departure. Westheimer's mechanism[39] of the hydrolysis of cyclic phosphate esters included a preference for apical attack and loss and molecular orbital calculations by Boyd[52] bear out this and other essential features of the mechanism.

In another approach to the problem Sommer[53] has argued that the Principle of Least Motion rules out certain modes of attack on a tetrahedron. It indicates an energy preference for forming the trigonal bipyramid by apical attack, and decomposition by apical loss.

2.5 Phosphoranes Containing Small Rings.

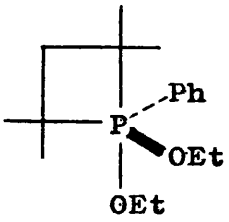
X-ray structure determinations[34,36] of phosphoranes with small four- or five-membered rings containing the phosphorus atom have shown that the ring occupies one apical and one equatorial position in the trigonal bipyramidal structure. The preference for the apical-equatorial position is due to the difference in bond angles between apical-equatorial (90°) and diequatorial positions (120°), the small rings occupying the positions of least ring strain. Consequently, it has been assumed, and will be assumed in this thesis, that if the phosphorus atom is present in a small strained ring in a pentacovalent intermediate the ring will occupy one apical and one equatorial position so as to keep ring strain to a minimum.[15,19]

There are three pseudorotational pathways open to a phosphorane. If the phosphorus atom is part of a small ring (24) one of these pseudorotations, the one with the ring as



the pivot ligand, places the ring in a diequatorial position (25). In small ring systems structures displaying 120° ring angles, e.g. (25), are evidently energetically unfavourable and are thought not to enter into the pseudorotation processes.[25, 39, 41] As a simplifying postulate the pseudorotational process of phosphoranes, with phosphorus as part of a four-membered ring studied here, which leads to diequatorial placing of the ring has been assumed to be of higher energy than the other two possible pseudorotations, in which the ring retains its relatively strain free apical-equatorial position, such that only the latter pseudorotational processes occur.

Mislow[50] however has pointed out that in certain circumstances, when relief of stereoelectronic strain balances the increase in ring strain, it may be possible to place a small ring diequatorial. Recently Denny and co-workers[54] have demonstrated by a variable temperature ^{1}H n.m.r. study of the phosphorane (26) that the energy difference between a pseudorotation that passes through a structure with a diequatorial ring, such as (27), and one in which the ring remains in the apical-equatorial position (26) was of the order of 15 kcal. $mol.^{-1}$ In (27) the



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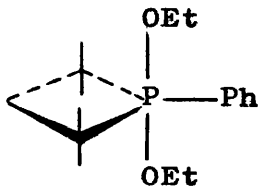


(27)

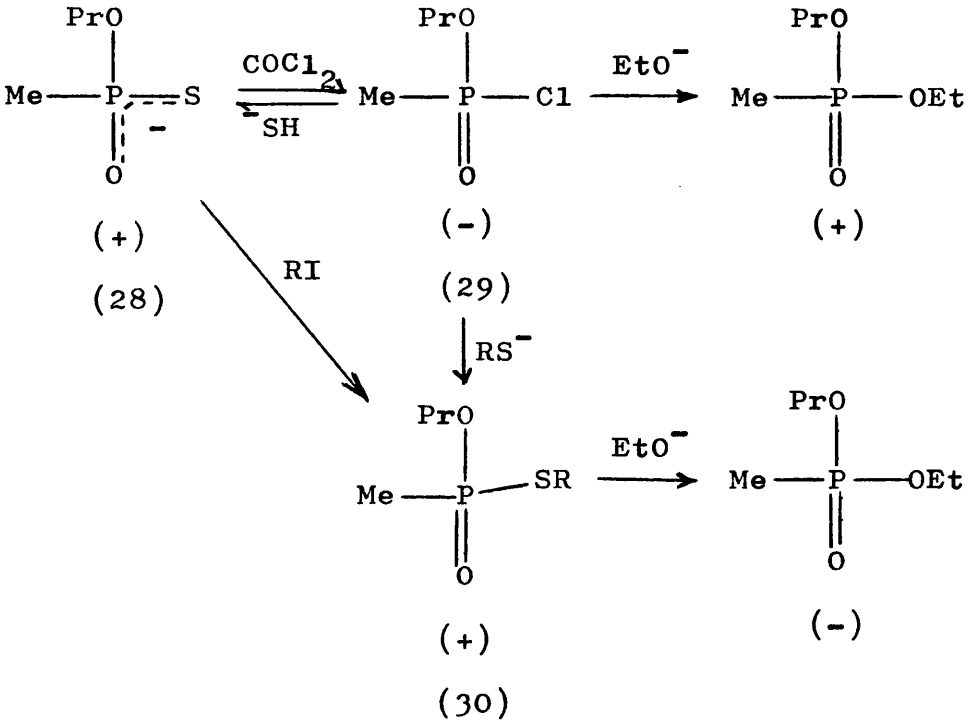
electronegative ethoxy-groups occupy the preferred apical positions, but the relief of stereoelectronic strain still does not balance out the increase in ring strain. Hence the pseudorotational process of highest energy is still the one which passes through (27) with the diequatorial ring.

Nucleophilic Substitution at Phosphoryl and Thiophosphoryl Centres

3.1 Stereochemistry of Displacement at Acyclic Centres.

Nucleophilic substitution at phosphoryl and thiophosphoryl centres generally occurs with a high degree of stereospecificity and inversion of configuration at phosphorus.[46]

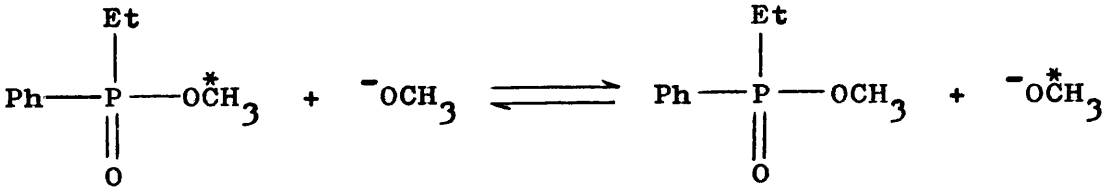
Aaron[56] treated the phosphonothionic acid (28) with phosgene to give the optically active phosphonochloridate (29) and showed that substitution at the phosphoryl centre in this occurred with inversion of configuration. It was



assumed that the steric courses of the substitutions involving ethoxide ion were the same, and as they gave phosphonates of opposite configuration it followed that the phosphonthiolate (30) and phosphonochloridate (29) had opposite configurations. Hence reaction of the alkyl-

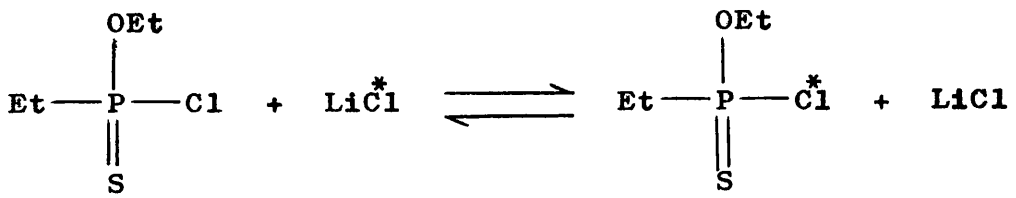
thioxide ion with the chloridate (29) must have occurred with inversion of configuration. Moreover, since the alkylation of the sodium salt (28) must have occurred with retention of configuration (no bonds around the phosphorus atom being broken) the reaction of the chloridate with hydrogen sulphide must have occurred with inversion of configuration.

Hudson and Green[57] have obtained direct proof of inversion at the phosphoryl centre. They showed that the rate of isotopic exchange was exactly equal to the rate of inversion (i.e. half the rate of racemisation) in the optically active methyl ethylphenylphosphinate (31),



(31)

Michalski[58] has investigated the stereochemistry of substitution at the thiophosphoryl centre using a similar technique. The rate of racemisation of optically active O-ethyl ethylphosphonochloridothionate (32) was found to be twice the rate of isotopic exchange.

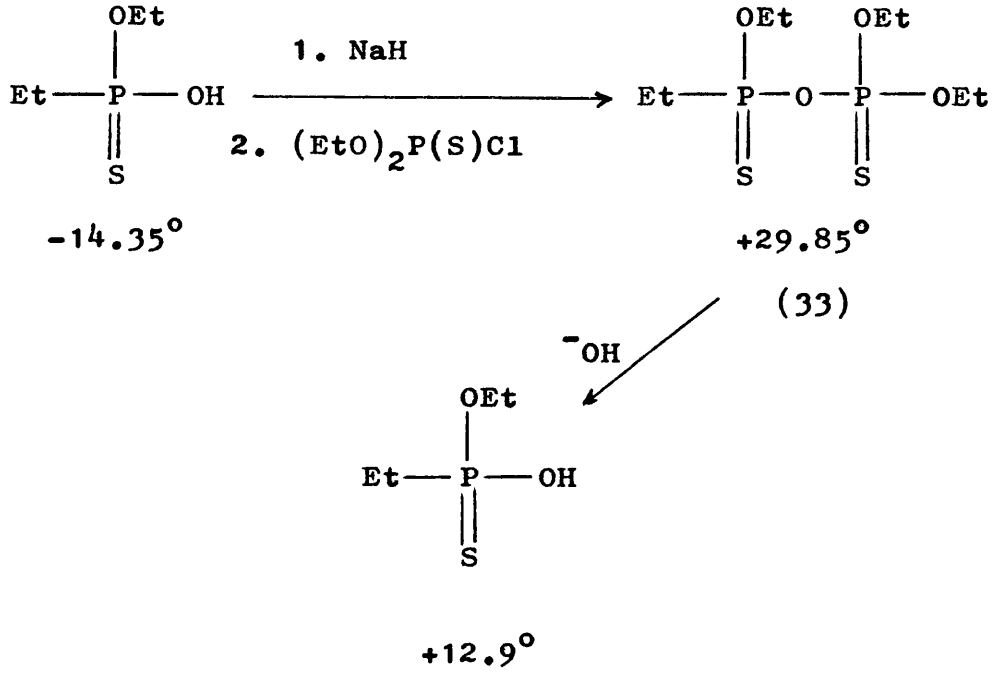


(32)

Most of the substitution studies have been carried out on thiophosphoryl compounds, mainly because they are much more optically stable than phosphoryl compounds

[Aaron[56] found that his products were considerably racemised due to the ready racemisation of the chloridate (19)], and are easily prepared from the readily resolvable phosphonothionic acids.[55]

The alkaline hydrolysis of triethyl ethylpyrophosphonodithionate (33) has been shown to proceed with inversion of configuration by the Walden-type inversion cycle outlined,[59] nucleophilic attack occurring exclusively at the phosphorus atom bearing the carbon function.



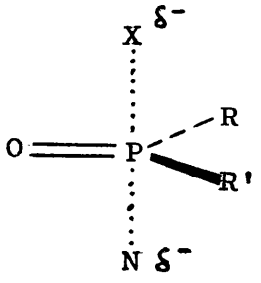
3.2 The Mechanism of Displacement at Acyclic Centres.

The generally observed inversion of configuration in nucleophilic substitution at tetrahedral phosphoryl or thiophosphoryl centres can be accounted for by a transition state or intermediate of trigonal bipyramidal geometry. If a direct displacement is involved the stereochemistry of the reaction is governed by the position of entry of the

nucleophile and the position of loss of the departing group. With a transition state of trigonal bipyramidal geometry it is theoretically possible for the nucleophile to enter, or a group to leave, from either apical or equatorial positions. The stereochemical consequences of the various modes of substitution via a trigonal bipyramid are given in the following table :

Entry	Exit	Stereochemistry
Apical	Apical	Inversion
Apical	Equatorial	Retention
Equatorial	Apical	Retention
Equatorial	Equatorial	Inversion

As inversion of configuration at phosphorus is the observed steric course of nucleophilic substitution at phosphoryl and thiophosphoryl centres the two pathways by which direct substitution is proceeding are either apical attack and apical loss (34), or equatorial attack and equatorial loss (35). Which is preferred comes from a



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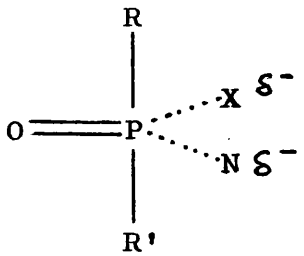


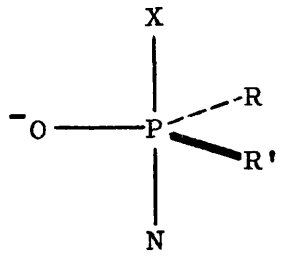
(35)

comparison of transition state energies. The fact that the entering and leaving groups are generally the most electro-negative of the groups around phosphorus and that these

prefer to occupy the apical positions in phosphoranes indicates that apical attack and loss is the probable course of substitution.

Pathways involving apical attack and equatorial loss, and vice versa, would result in retention of configuration, which was not observed and hence cannot be occurring. Consideration of vibration theory also limits the choice of pathways for direct displacement to those involving changes of the apical positions or the equatorial positions.[60] The stereochemical result is inversion in both cases.

The inversion of configuration on substitution can also be explained by proposing that it occurs by an addition-elimination mechanism via a trigonal bipyramidal intermediate (36) whose lifetime is so short or the energy



X = leaving group

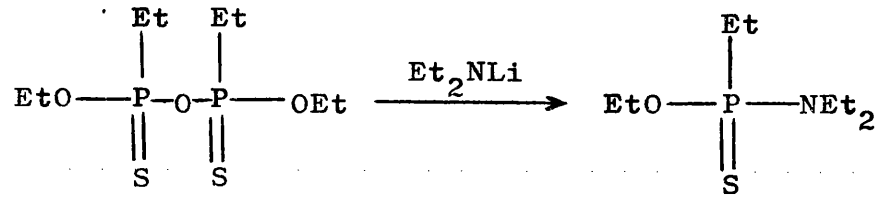
N^- = nucleophile

(36)

barriers to conversion to other pyramids so high that it decomposes before any rearrangements can occur. The trigonal bipyramidal intermediate is formed by apical attack of the nucleophile opposite that group to be lost from its apical position so giving the most stereoelectronically stable phosphorane. The attacking and leaving groups being electronegative prefer to occupy the apical positions.

Recent results indicate that substitution does involve

an intermediate; in these cases the intermediates can be recognised by their stereochemical nonrigidity. Michalski[61] found that the optically active dithiopyrophosphonate (37) gave, as expected, optically active products with methoxide, but with lithium diethylamide a racemic amide was produced.

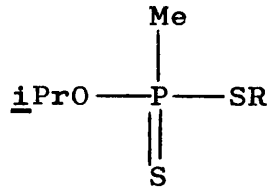


(37) (+) ($\bar{+}$)

It was suggested that a pentacovalent intermediate was formed whose rate of breakdown was slow compared to the rate of pseudorotation.

Similarly Aaron[62] suggested that the alkaline hydrolysis of the phosphonodithioates (38) gave racemic products because of pseudorotation of the intermediates and that other cases of non-stereospecific substitution may be due to pseudorotation of intermediates.[63,64]

R = Ph, iPr

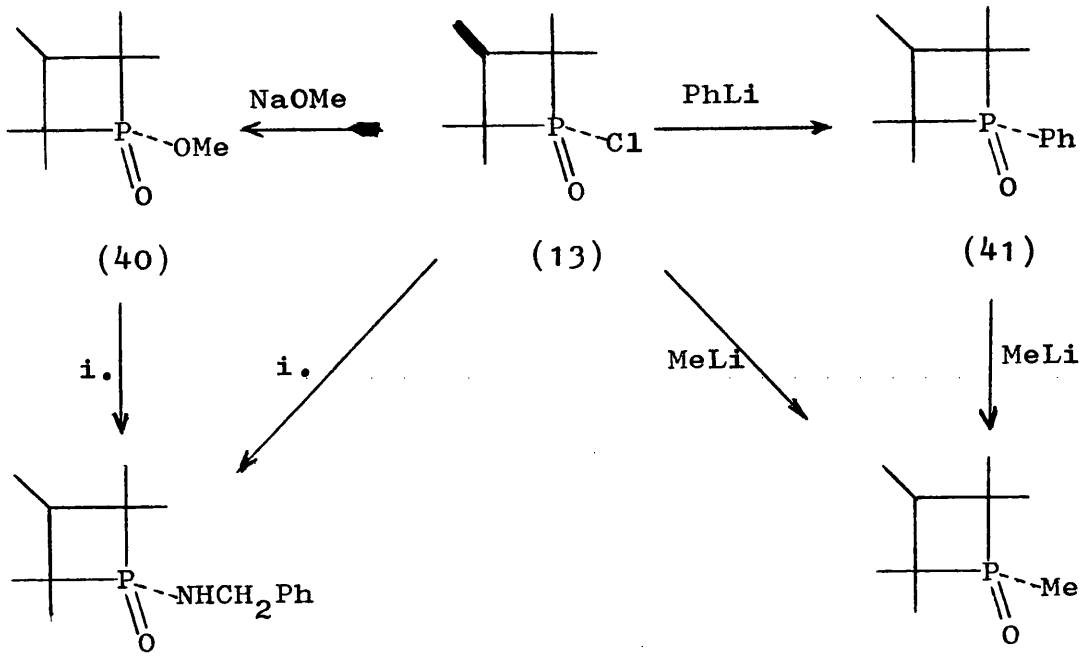


(38)

3.3 Stereochemistry of Displacement at the Phosphoryl Centre in a Four-membered Ring.

Hawes and Trippett[19] showed that r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (13) gave the same crystalline amide (39) on treatment with benzylamine as

was obtained from a two step process by formation of the ester (40) followed by treatment with N-lithiobenzylamine.

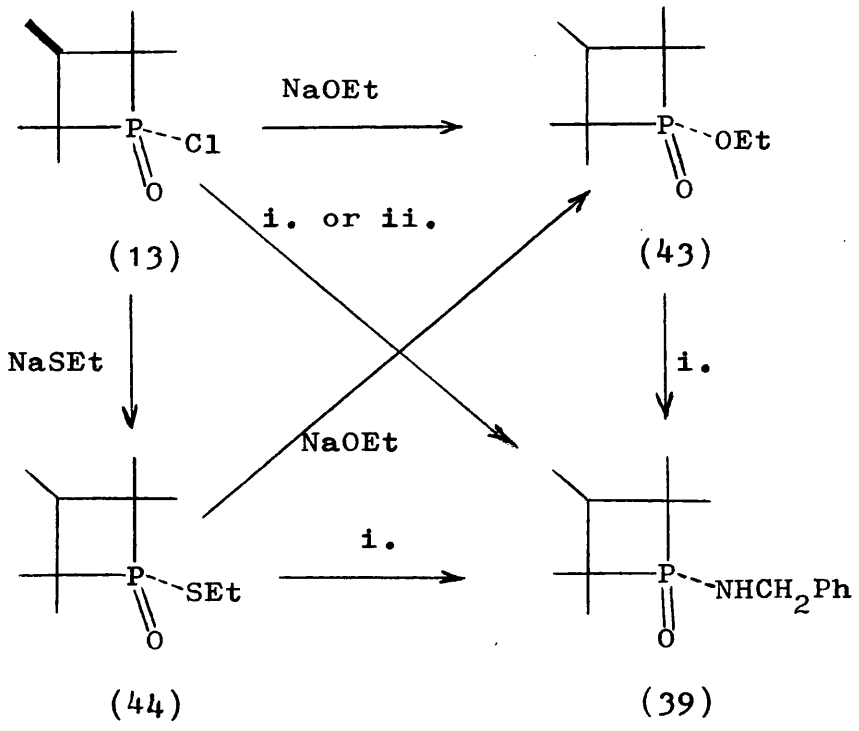


Again the acid chloride (13) with phenyl-lithium gave the phenylphosphine oxide (41), m.p. 127°, free of its isomer, and with methyl-lithium gave the methylphosphine oxide (42). The same oxide (42) was obtained on treatment of the oxide (41) with methyl-lithium. In this second cycle the actions of phenyl- and methyl-lithium on the acid chloride (13) presumably involved the same stereochemistry. Whether this was retention or inversion, the action of methyl-lithium on the phenylphosphine oxide must involve retention of configuration at phosphorus. X-ray analyses[18,20] have since shown that in the acid chloride (13) and the phenylphosphine oxide (41), m.p. 127°, there is a trans relation of the substituent on phosphorus and the 3-methyl ring substituent. The reaction of the acid chloride with phenyl-

lithium is proceeding with retention of configuration about phosphorus. Hence all three displacements occurred with retention of configuration.

Treatment of the first cycle, involving the formation of the amide (39), in the same manner indicated that the action of sodium methoxide on the acid chloride (13) to give the ester (40) involved retention of configuration.

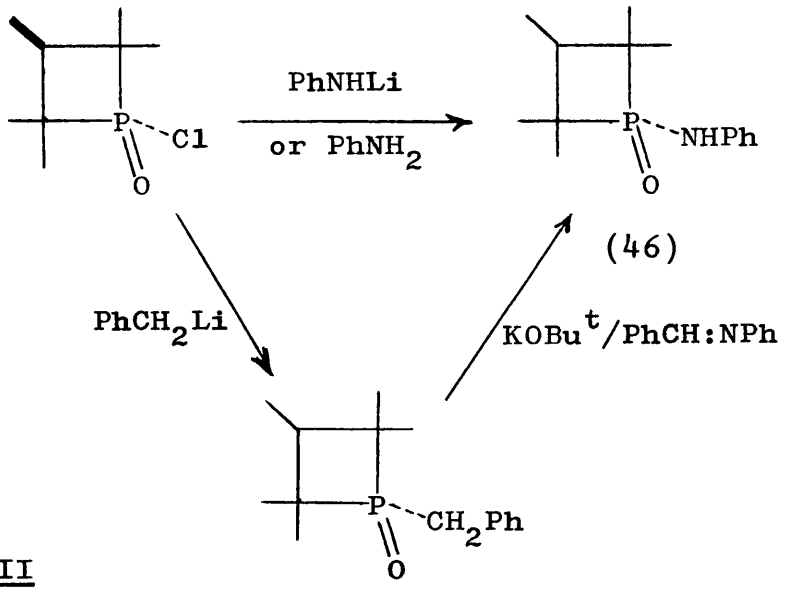
In view of the importance of the stereochemical course of substitutions at phosphetan 1-oxides in understanding the mechanism, other Walden cycles were investigated. r-1-Chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (13) with sodium ethoxide gave one isomer of the ethoxy ester (43), and reaction with sodium ethylthioxide gave one ethylthio ester (44). Both esters gave the same 1-benzylaminopentamethylphosphetan 1-oxide (39) on treatment with N-lithiobenzylamine. This amide was identical to that



i. = $PhCH_2NHLi$ ii. = $PhCH_2NH_2$

obtained by Hawes and Trippett. Treatment of the ethylthio ester (44) with sodium ethoxide gave one ethoxy ester (43) identical with that obtained from the acid chloride (13). These results also agree with the view that retention of configuration is the mode of displacement.

Treatment of one diastereoisomer of 1-benzyl-2,2,3,4,4-pentamethylphosphetan 1-oxide (45), obtained from the reaction of benzyl-lithium with the acid chloride, with potassium t-butoxide and N-benzylideneaniline gave one 1-anilinophosphetan 1-oxide (46). The same 1-anilinophosphetan oxide was isolated from the reaction of the acid chloride with aniline or with N-lithioaniline. It is known that the



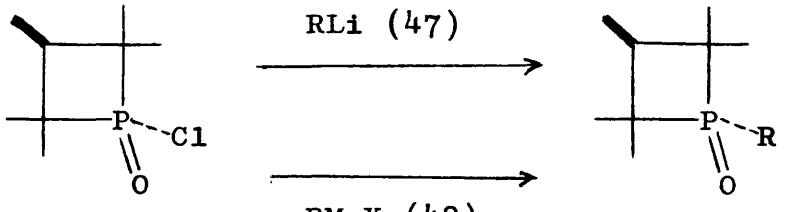
SCHEME II

(45)

reaction of phenyl-lithium with r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide proceeds with retention of configuration at phosphorus, and if one assumes that the corresponding reaction with benzyl-lithium has the same stereochemistry, then Scheme II establishes that reactions

of the acid chloride with aniline and with N-lithioaniline also involve retention of configuration. Since Horner and Winkler[65] have demonstrated that an optically active benzylphosphine oxide was converted stereospecifically and with retention of configuration to an amide presumably via a cyclic Wittig-type intermediate, the ring would not affect the stereochemistry of this reaction.

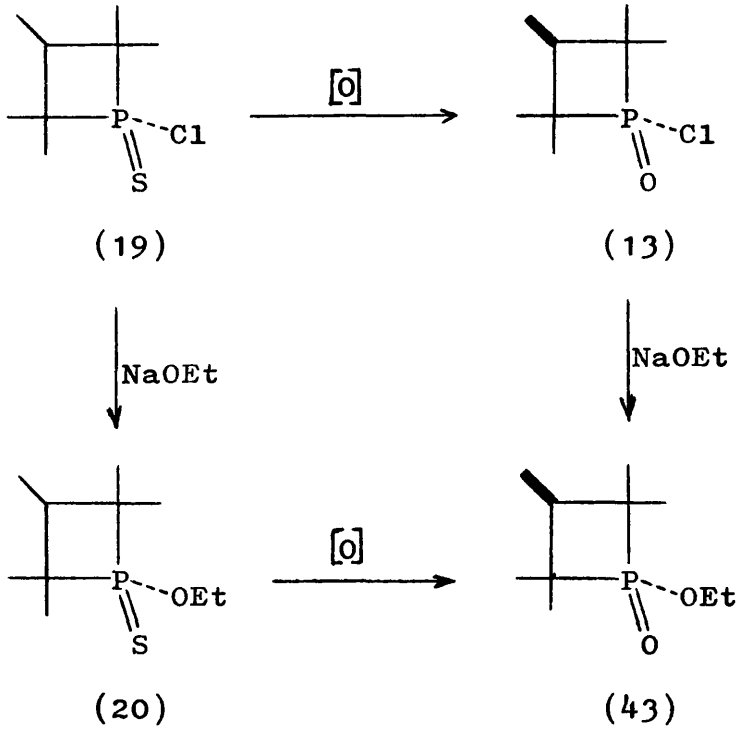
The fact that the lithium compounds (47; R = Me, CH_2Ph, Ph) react with stereoisomerically pure r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (13) to give the corresponding oxides (49; R = Me, CH_2Ph, Ph) with complete retention of configuration establishes that retention is also the steric course of the corresponding reactions with Grignard reagents. The Grignard reagents (48; R = Me, CH_2Ph) gave in good yield phosphetan 1-oxides (49; R = Me, CH_2Ph), identical in every respect to those obtained using the corresponding lithium compound.



(13) (49)

Substitution at the thiophosphoryl centres of phosphetans also proceeds with retention of configuration; treatment of the one diastereoisomer of 1-chloro-2,2,3,4,4-pentamethylphosphetan 1-sulphide (19), obtained from the sulphurization of the 1-chlorophosphetan[32], with sodium ethoxide gives one

isomer of 1-ethoxy-2,2,3,4,4-pentamethylphosphetan 1-sulphide (20) m-chloroperbenzoic acid oxidation converts these 1-sulphides with retention of configuration into r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (13) and the ethoxy ester (43). The ethoxy ester (43) is identical to that obtained from reaction of sodium ethoxide with the trans acid chloride (13). This reaction occurs with the retention of configuration, therefore the 1-ethoxyphosphetan 1-sulphide (20) must be formed stereospecifically from the 1-chlorophosphetan 1-sulphide with retention of configuration.



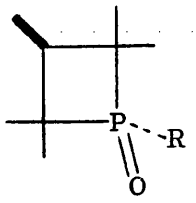
(19) (13)

(20) (43)

3.4 The Assignment of Configuration to 2,2,3,4,4-Pentamethylphosphetan 1-Oxides Using Tris(dipivalomethanato)-europium (III).

Nucleophilic substitution at the phosphoryl and thio-

phosphoryl centres of phosphetans is stereospecific proceeding with retention of configuration at phosphorus although definitive proof has been produced in few cases. In other cases the assumption of retention at phosphorus leads to a consistent picture, but in view of the importance of the stereochemical course of these substitutions in their mechanistic interpretation a method of assigning the configuration of the phosphetans (49) and (50) was sought.



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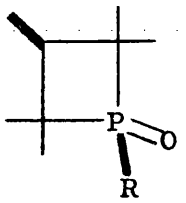


(50)

It was found that this assignment could be made using the europium shift reagent, tris(dipivalomethanato)europium(III), $Eu(DPM)_3$.[66]

Shift reagents are paramagnetic metal complexes which in solution associate with organic substrates thereby inducing paramagnetic shifts in the ^1H n.m.r. spectra of the organic compounds. Recently $Eu(DPM)_3$ has attracted special attention because it produces magnified chemical shifts of the protons of lone pair-containing organic compounds, with little line broadening, so providing valuable information for assignment of configuration or structure.

Addition of an 0.48 molar equivalent of the reagent to deuteriochloroform solutions of 2,2,3,4,4-pentamethylphosphetan 1-oxides produced considerable downfield shifts of all the proton signals in their n,m.r. spectra. The results are given in the Table. Those isomers which are

Table

N.m.r. Spectra of Phosphetan Oxides (49) and (50) in $CDCl_3$ in the Presence of a 0.48 Molar Equivalent of $Eu(DPM)_3$.

The chemical shift (τ) is followed by the shift (Hz) from the normal position in $CDCl_3$.

R	ISOMER	3-CH_3	3-H	2,4-CH_3	2,4-CH_3	OTHERS			
Ph	49	7.58	5.25	6.92	5.73				
		82	160	118	166				
Ph	50	7.58	3.33	6.78	5.68				
		83	224	119	174				
Me	49	7.80	6.25	7.35	6.1	P-Me	5.83		
		78	140	89	158		158		
Me	50	7.73	4.80	7.22	5.85		5.97		
		81	187	100	169		150		
OEt	49	7.68	6.0	6.92	6.20	O·CH_2	2.57	O·C·CH_3	7.58
		86	145	114	155		194		65
OEt	50	7.50	4.55	6.70	5.80		2.68		7.47
		97	224	131	174		196		76
NHBz	49	7.70	6.17	7.17	6.03	N·CH_2	3.52		
		84	135	99	162		133		
NHBz	50	7.73	4.33	7.10	5.90		3.87		
		84	234	112	171		117		
SEt	49	7.63	5.73	6.82	5.83	S·CH_2	4.08	S·C·CH_3	7.70
		87	154	115	171		177		51
SEt	50	7.27	3.58	6.43	5.50		4.13		7.33
		108	262	145	191		180		81
Bz	49	7.63	5.83	7.23	5.83	P·CH_2	3.83		
		88	144	96	176		173		

Bz = CH_2Ph

known (49; R = Ph) or have been assumed (49; R = OEt, SEt, Me, CH_2Ph, and $NHCH_2Ph$) to be <u>trans</u> show a shift in the position of the 3-proton of 135-160 Hz, while in those isomers which are known (50; R = Ph) or have been assumed (50; R = OEt,[32] SEt, Me, and $NHCH_2Ph$[31]) to be <u>cis</u> the shift of these protons is 187-262 Hz. This difference allows assignment of configuration to 2,2,3,4,4-pentamethylphosphetan 1-oxides. Other shifts, e.g. of one pair of α-methyls, are less definitive but show a consistent difference in the two series.

The proton assignments were based on observed signal intensities and splitting patterns. Information reported in the literature[66] that the induced shift decreases with increasing distance between a proton and the complexed functional group indicates that in the phosphetan 1-oxides the europium coordinates with the phosphoryl oxygen in all cases as the shift of the 3-proton in the <u>cis</u>-isomers is greater than that for the <u>trans</u>-isomers. Inspection of molecular models shows that the 3-proton in the <u>cis</u>-isomer is located closer to the phosphoryl oxygen than the 3-proton of the <u>trans</u> isomer. As the phosphetan ring is puckered two conformations are possible through ring flipping; molecular models show that in both the possible conformations the distances between the phosphoryl oxygen and 3-proton of the <u>cis</u> isomer (50) are smaller than those of the <u>trans</u> isomer (49).

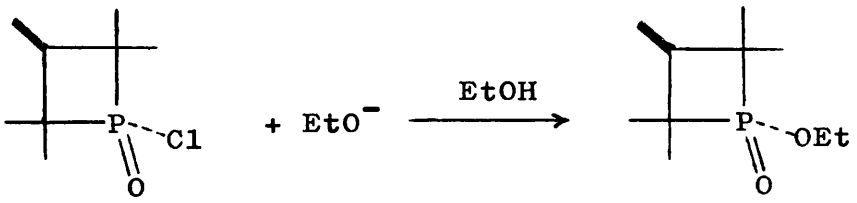
The complexes formed with the europium reagent and phosphetan sulphides were insoluble in deuteriochloroform.

The n.m.r. reagent, $Eu(DPM)_3$, establishes that all the

compounds from the cycles investigated have trans relations of the substituents on phosphorus (49; R) and the 3-methyl. As they are all initially derived from r-1-chloro-2,2, trans-3,4,4-pentamethylphosphetan 1-oxide displacement was occurring with retention of configuration.

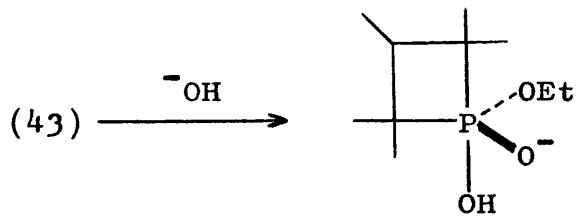
3.5 Kinetics of Displacement at the Phosphoryl Centre in a Four-membered Ring.

Reaction of r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan oxide (13) with sodium ethoxide gives one isomer of 1-ethoxy-2,2,3,4,4-pentamethylphosphetan 1-oxide (43). Bergesen,[67] Trippett,[68] and Haake[69] have studied the rate of



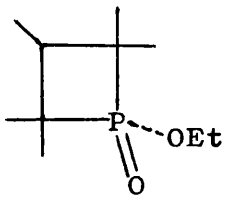
(13) (43)

alkaline hydrolysis of this phosphinate ester (43) and found it approximately equal to that of triethyl phosphate. The hydrolysis exhibited second order kinetics, first order in ester and first order in base, and experiments with water enriched in ^{18}O have established that the hydroxide ion attacks completely at phosphorus. As the C-P-C angle is approximately 82° in the ester the relief of ring strain on going to the intermediate trigonal bipyramid (51) in which



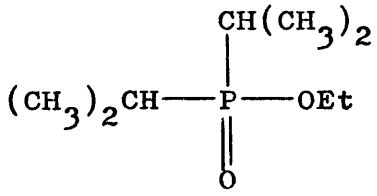
(51)

the four-membered ring will occupy an apical-equatorial position, would be expected to lead to rapid hydrolysis[70] compared with that of triethyl phosphate in which there is no comparable release of strain. Trippett speculated that the 'normal' rate of hydrolysis was the net result of acceleration due to this relief of steric strain, and retardation due to steric hindrance to attack of hydroxyl anion on phosphorus from the 2,2,4,4-methyls. It was also shown that the phosphetan ester undergoes hydrolysis more rapidly than the di-isopropyl phosphinate ester (52).



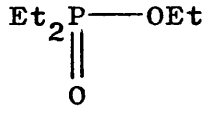
(43)

300/70°



(52)

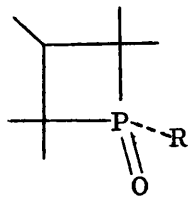
10/100°



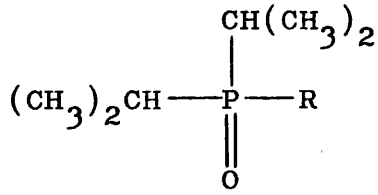
260/70°

Alkaline hydrolysis of phosphinate esters, second order rate constants (l. mole^{-1} sec^{-1} x 10^6).[68]

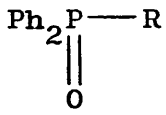
In contrast to these results Haake et al[71] have shown that both the solvolysis of the chloride (53; R = Cl) and the acid-catalysed hydrolysis of the amide (53; R = $N(CH_3)_2$) proceed much more slowly than hydrolyses of the corresponding acyclic compounds (54; R = Cl and $N(CH_3)_2$). Both reactions



(53)

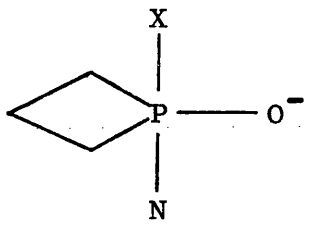


(54)



(55)

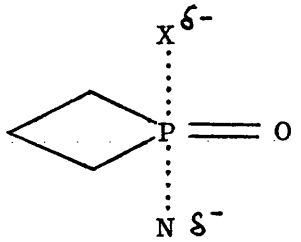
were shown to involve nucleophilic attack by water on phosphorus. The slower hydrolyses of the cyclic phosphetan chloride and amide were ascribed to increased angle strain in intermediates (56) or transition states (57) involving direct displacement, similar to S_N2 reactions, with the entering and leaving groups colinear with phosphorus.



(56)

N^- = nucleophile

X^- = leaving group



(57)

The comparison of rates of displacement of phosphetans (53) with those of the corresponding di-isopropyl compounds (54) and/or the diphenyl compounds (55) was suggested[71] as a criterion for the mechanism of reaction at phosphorus. Reaction through an intermediate in which the ring occupies an apical-equatorial position can result in rate enhancement when the phosphorus atom is part of a strained ring. Direct displacement results in decreased rates with strained rings.

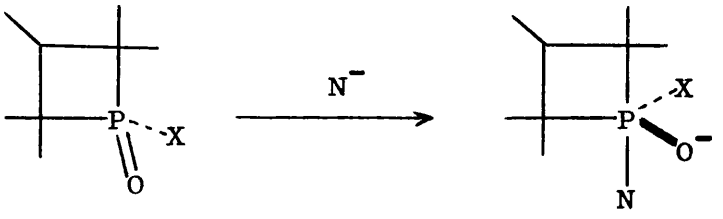
The choice of the di-isopropyl compounds (52 and 54) for comparison purposes is arguable; a true standard might include some di-t-butyl character and as derivatives of di-t-butylphosphinic acid are extremely inert[68] this might invalidate the criterion. Also a colinear theory for substitutions of phosphetans predicts that such substitutions will involve inversion of configuration at phosphorus, as is observed in substitution at phosphoryl and thiophosphoryl centres which are thought to proceed through intermediates

with the entering and leaving groups colinear with phosphorus. In fact retention is the steric course of substitution at phosphorus which is part of a four-membered ring. To overcome these objections an alternative explanation of substitution at the phosphorus of phosphetan 1-oxides was evolved.

3.6 Mechanism of Displacement at the Phosphoryl Centre in a Four-membered Ring.

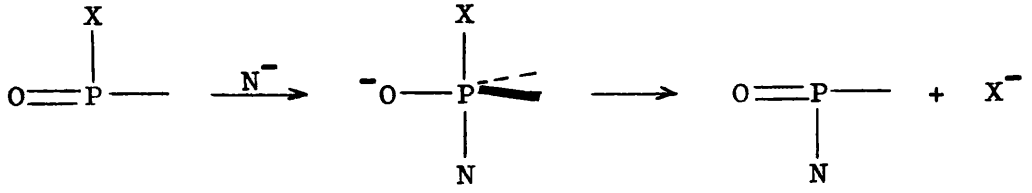
a) Kinetics

This explanation of substitution at the phosphorus of phosphetans assumes that all such substitutions involve the formation of an intermediate (58) in which the four-membered ring is apical-equatorial. In comparison with the similar



(49) (58)

substitution of an acyclic compounds (59) which involves an intermediate (60) in which the entering and leaving groups are colinear with phosphorus, the phosphetan substitution is

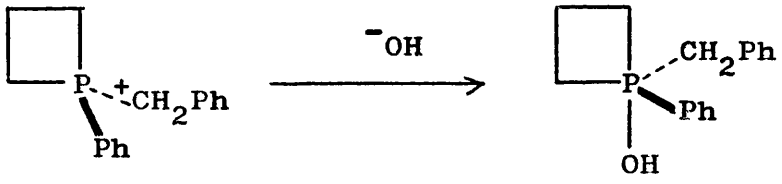


(59) (60)

speeded up by relief of ring strain in going to the intermediate (58) but is retarded by the fact that, whereas (60)

has two electronegative groups in apical positions, (58) has only one, the electronegative groups preferring the apical positions.[57,72] The more electronegative is X, i.e. in general the better the leaving group, the greater will this retardation be and when X = Cl and $\overset{+}{N}HMe_2$ the net effect when compared with the corresponding di-isopropyl compounds (54) is a retardation. With the less electronegative ethoxy group the effects almost balance resulting in the 'normal' rate of alkaline hydrolysis.

The theory predicts that with a poor leaving group the net result should be an acceleration and this is indeed the case with benzylphosphetanium salts.[73] The intermediates involved in the hydrolysis of benzylphosphetanium (61) and acyclic benzylphosphonium (62) salts are directly comparable with those involved in substitution at phosphoryl centres (58 and 60). The relative rates for alkaline hydrolyses of (63), (64) and (65) in 75% ethanol at 45° are 6×10^7 : 2×10^5 : 1.



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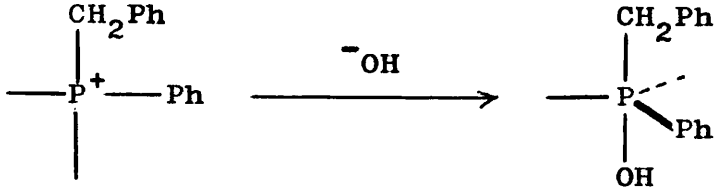
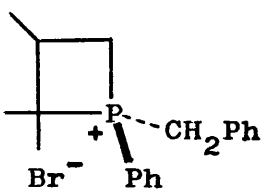
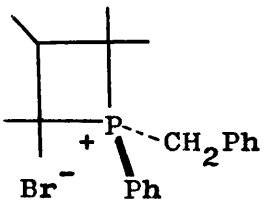


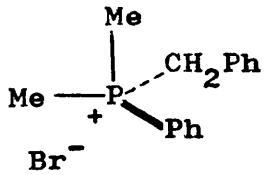
(62)



(63)



(64)



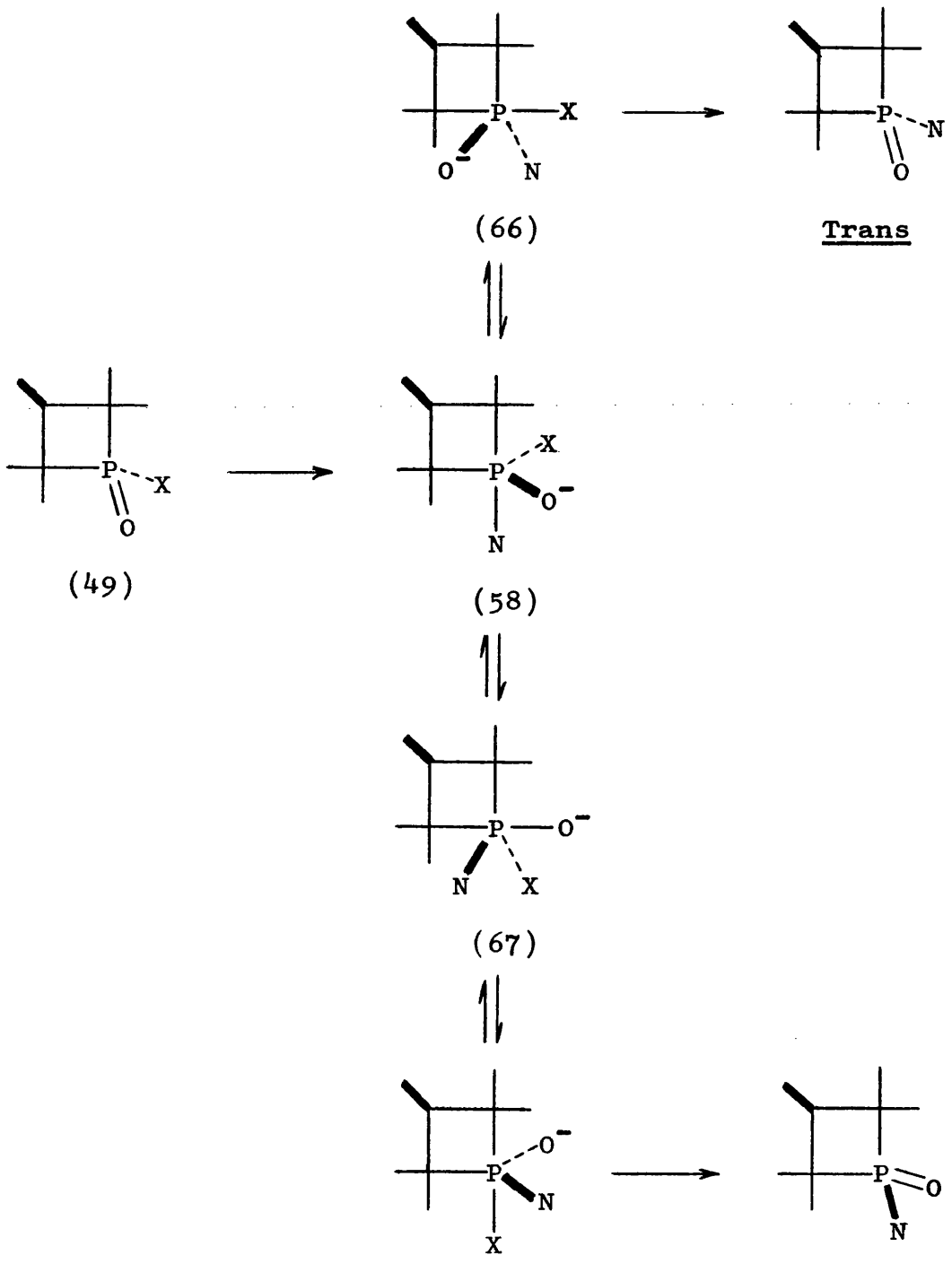
(65)

b) Stereochemistry.

Displacement proceeds with retention of stereochemistry at phosphorus so a colinear transition state cannot be involved as this would lead to inversion of configuration as is observed in displacements at acyclic phosphoryl centres.

The following analysis indicates that a nucleophilic displacement pathway via the apical positions is preferred over one involving the equatorial positions. Equatorial attack and loss should lead to similar stereochemical results for the acyclic and phosphetan systems, namely inversion of configuration. The fact that the acyclic and phosphetan systems give different stereochemical results is therefore indicative of apical attack, for it is only thus that the four-membered ring can play its distinctive role.

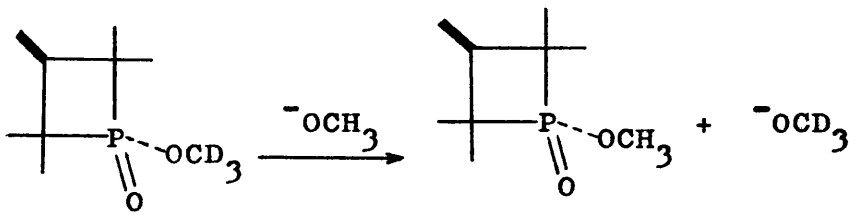
Apical attack of a nucleophile, N^-, on the phosphetan (49) gives the trigonal bipyramidal intermediate (58) in which the ring spans the equatorial-apical positions; an equatorial-equatorial relation (120°) would be highly strained. Apical attack along the other P-C bond produces the mirror image of (58). For the leaving group, X, to depart from an apical position the intermediate (58) must pseudorotate. Using O^- as a pivot group leads to (66). Because of the clear-cut distinction between the stereoelectronic preferences of the groups X and O^- this is the preferred pseudorotation, the electronegative group X being placed in the favoured apical position in (66) and the electron-donating O^- in the favoured equatorial position.[39,52,75] The loss of X from the apical position yields the trans phosphetan oxide. The alternative pseudorotation of (58) to



give (67) is unlikely for it places the groups X and O^- in energetically unfavourable positions. Also, (67) would ultimately lead (by further pseudorotation) to the cis isomer which is not observed.

Treatment of nucleophilic substitution reactions of

cis phosphetan 1-oxides in a similar manner leads to a parallel conclusion, displacement gives cis products. Cycles involving three cis-phosphetan 1-oxides have been established demonstrating that substitution is stereospecific and proceeding with retention of configuration.[32] Cremer and Trivedi[74] have demonstrated, using a deuterium labelled substrate (68), that both isomers of 1-methoxy-2, 2,3,4,4-pentamethylphosphetan 1-oxide undergo methoxy-group exchanges with retention of configuration.

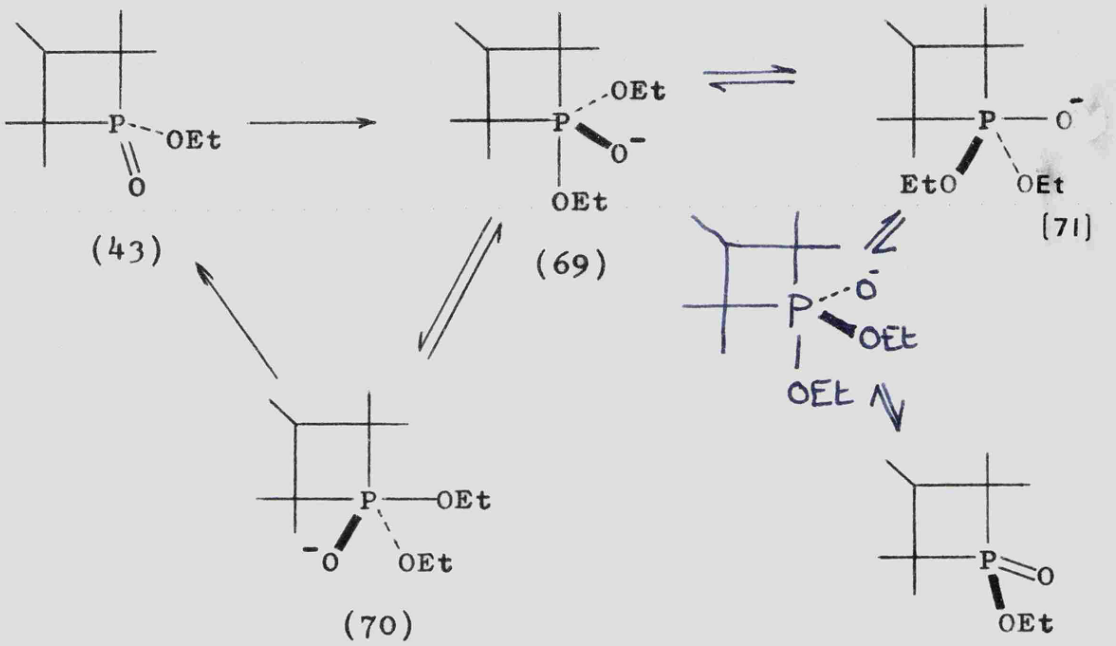


(68)

Treatment of r-1-ethoxy-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (43), and a mixture of the isomeric esters rich in the cis ester, with sodium ethoxide in ethanol did not affect their stereoisomeric compositions. This demonstrates that ethoxy-group exchanges in both ethyl esters occurred with retention of configuration.

The stereospecific courses of these group exchanges indicate that the phosphorane intermediates exist as the mono-anions under the reaction conditions. The ethoxy ester (43) is attacked apically by the ethoxide ion to give the anion (69) which undergoes pseudorotation to (70), followed by loss of ethoxide, to yield the ester (43). The alternative pseudorotation of (69) to (71) would, after loss of

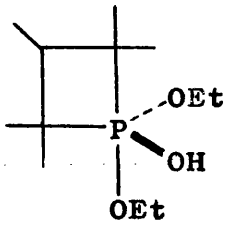
ethoxide, lead to (72), resulting in inversion of configuration. This pseudorotation is energetically unfavourable as it involves placing of the relatively electropositive O^- in an unfavourable apical position,[39] hence only retention is observed. If the initial anion (69) was protonated the



pseudorotation (69) to (71) is energetically favourable as it involves the favourable movement of an electronegative hydroxy group from an equatorial to an apical position. Loss of ethoxy would then give the ester (72) of inverted configuration. That retention is the stereochemical course rules out the intermediacy of protonated anions. The completely stereospecific displacements, with retention of configuration, of chloride in r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide by nucleophiles similarly indicates anion intermediates.

An attempt to generate the protonated form (73) of the anion (69) was made by heating each isomeric ester in ethanol

containing p-toluenesulphonic acid. The reactions produced no stereochemical changes which indicates that if (73) was formed only those pseudorotation pathways leading to retention were followed. More probably the phosphorane (73) was not formed.



(73)

Alkaline Hydrolysis of Phosphonium Salts

4.1 Alkylarylphosphonium Salts.

Quaternary phosphonium salts are decomposed by aqueous base to give tertiary phosphine oxides and hydrocarbons. In contrast the alkaline decomposition of ammonium salts gives amines and olefins by β-elimination.[76] Fenton and Ingold[77] suggested that this difference was due to the inability of nitrogen to form a pentacovalent intermediate. They further suggested that substituents on the β-carbon of phosphonium salts which increased the acidity of the β-proton should favour the formation of olefin and phosphine. Consequently they found that a β-phenylethylphosphonium salt gave mainly hydrocarbon and some olefin whereas a β,β-diphenylethylphosphonium salt (74) gave mainly olefin and phosphine.

$$(C_4H_9)_3\overset{+}{P}\text{-}CH_2\cdot CH\cdot Ph_2\ Br^- \xrightarrow{-OH} (C_4H_9)_3P + CH{:}CPh_2$$

(74)

In the decomposition to hydrocarbon the following order for ease of elimination of various groups was observed:[77] allyl, benzyl ⟩ phenyl ⟩ methyl ⟩ β-phenethyl ⟩ ethyl and higher alkanes.

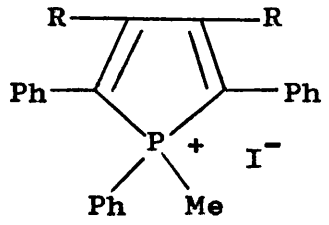
More recent work by Horner[78] on tetra-arylphosphonium salts has shown that aryl groups containing electron withdrawing substituents were more easily lost than phenyl, whereas aryl groups bearing electron releasing substituents were less easily lost than phenyl. A similar pattern has been found for substituted benzyl groups in the hydrolysis of monosubstituted tetra-benzylphosphonium salts.[79] There-

fore, the group most easily eliminated on alkaline hydrolysis is that which is most stable as the anion. This conclusion has been confirmed by other investigations.[80,81] In salts where there was no clear-cut distinction between the stabilities of the groups as anions hydrolysis yielded a mixture of phosphine oxides and their corresponding hydrocarbons.[78,79]

It has also been found that the ease of elimination of a group was partially dependent upon the nature[79] and the steric bulk[82] of the other groups attached to phosphorus.

4.2 Kinetics and Mechanism.

Kinetic studies on the alkaline hydrolysis of phosphonium salts have demonstrated that almost all show third order kinetics, with a first order dependence on concentration of the phosphonium salt and a second order dependence on the concentration of hydroxyl ion.[79-81,83-85] Second order kinetics, first order in hydroxide ion and phosphonium cation, have been observed when the leaving group was an exceptionally stable anion such as p-nitrobenzyl[83] or 1,4-diphenyl-1,3-butadienyl anion. The latter anion was lost in the hydrolyses of both 1,2,5-triphenyl- (75) and 1,2,3,4,5-pentaphenyl-1-methylphospholium iodides (76)[86] to give ring opened phosphine oxides.



(75) R = H

(76) R = Ph

The demonstration of a third-order rate law for alkaline

hydrolysis indicates that two hydroxide ions and one phosphonium cation are involved during or prior to the rate-determining step of the reaction. The mechanism proposed by McEwen[81] to account for the kinetics involved fast, reversible, addition of hydroxide ion to the phosphonium ion giving a pentacoordinate species (77). The rate-determining

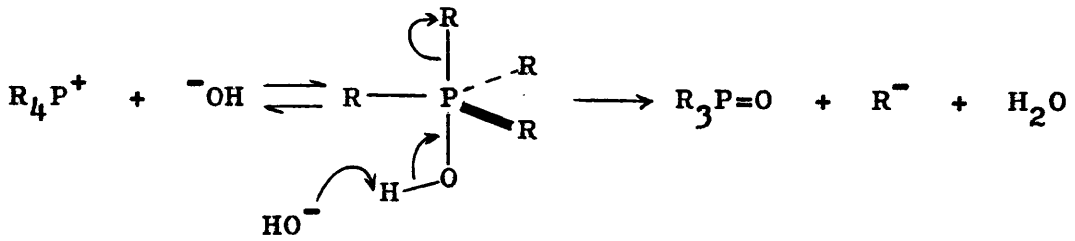
$$R_4P^+ + {}^-OH \rightleftharpoons \underset{(77)}{R_4POH} \overset{{}^-OH}{\rightleftharpoons} R_4PO^- \longrightarrow R_3P{=}O + R^-$$

$$R^- + H_2O \longrightarrow RH + {}^-OH$$

step was the formation of the phosphine oxide and a carbanion from the conjugate base of (77) formed by a fast reversible step. The final step was the conversion of the carbanion to the appropriate hydrocarbon by the action of water.

In the case of the p-nitrobenzyl and butadienyl anion decomposition of the pentacovalent intermediate is sufficiently rapid to make the first step, the formation of the intermediate, rate-determining.

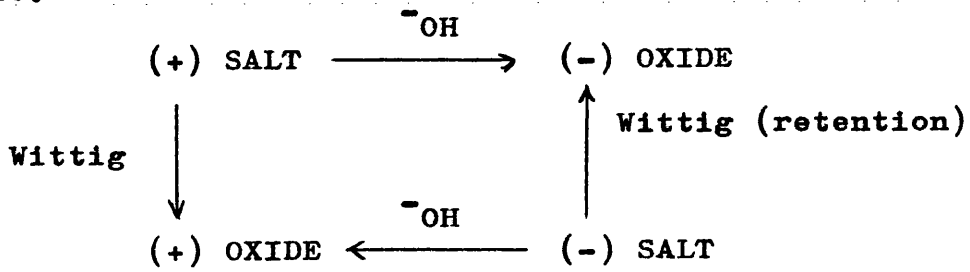
Two variations of the general mechanism have been proposed by McEwen[79] which are consistent with the stereochemical and kinetic data. There could be synchronous attack of the second hydroxide ion and departure of the anion:



There could also be rapid formation of an unstable hexacoordinate intermediate with two hydroxyl groups bonded to phosphorus.

4.3 Stereochemistry.

The alkaline hydrolysis of benzylethylmethylphenylphosphonium iodide has been demonstrated to be completely stereospecific[81] proceeding with inversion of configuration at phosphorus.[87,88] The oxide obtained from alkaline hydrolysis of a sample of optically pure phosphonium salt had exactly the opposite rotation to the phosphine oxide obtained from a Wittig reaction on the same enantiomer of the salt.

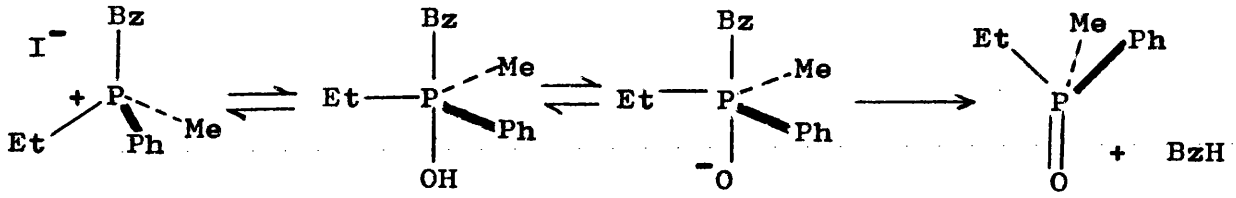


Since the Wittig reaction proceeds *via* a four-membered cyclic intermediate the reaction is thought to occur with retention of configuration.[88] Inversion at phosphorus could only occur if the intermediate underwent the unlikely pseudorotation that places the ring in a diequatorial position.

Evidence furnished by Horner and coworkers[89] also indicates that the phosphonium hydroxide decomposition reaction leads to inversion of the configuration of the phosphorus atom. They showed that the phosphine oxide from the hydrolysis of optically active benzylethylmethylphosphonium iodide had the opposite rotation to the phosphine oxide produced by hydrogen peroxide oxidation of the phosphine obtained by cathodic reduction of the iodide, both processes proceeding with retention of configuration.

As the hydrolysis proceeds with 100% inversion of configuration at phosphorus the two possible pathways of

reaction are via either apical departure of the benzyl anion and apical attack of hydroxide or equatorial departure and equatorial attack. Although both processes are possible it has been assumed that substitution proceeds through apical attack-apical loss.[90]



In the phosphorane intermediate resulting from this S_N2-type displacement at phosphorus, the electronegative hydroxy and the benzyl group (the most stable anion and hence the most electronegative of the groups on phosphorus) occupy apical positions corresponding to the structure of lowest energy.

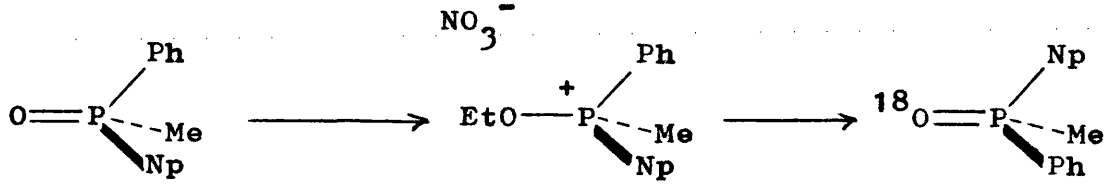
In apical attack, addition of hydroxide ion can occur at each of the four faces of the phosphonium cation giving four stereoisomeric trigonal bipyramids. However, decomposition of the intermediate is dependent upon the stability of the anion leaving group; loss of the resonance stabilised benzyl anion occurs at a much faster rate than loss of phenyl, ethyl, or methyl anion and must occur from an apical position to give the observed stereochemistry.

If no good leaving group was present then the rate of decomposition of the intermediate phosphorane would decrease and a situation might then arise when the rate of pseudorotation was comparable with the rate of hydrolysis. In such a case an optically active phosphonium salt could hydrolyse with racemisation.

4.4 Alkoxy- and Alkylthio-phosphonium Salts.

Monoalkoxy- and monoalkylthio-phosphonium salts have been shown to undergo alkaline hydrolysis with complete inversion of configuration at phosphorus to give the corresponding phosphine oxides.[91]

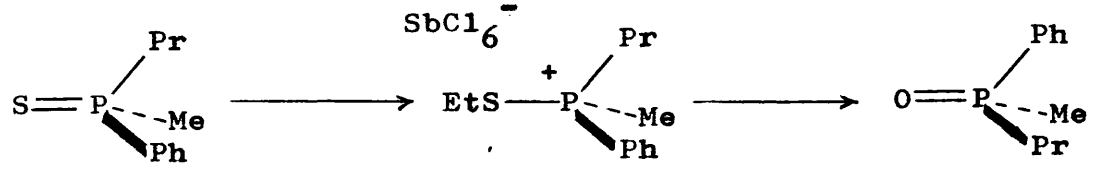
The phosphonium nitrate (79) prepared by ethylation of the (S)-phosphine oxide (78) underwent alkaline hydrolysis in ^{18}O enriched water to give the (R)-phosphine oxide (80),



(+) S-oxide (-) R-oxide

(78) (79) (80)

with complete incorporation of the ^{18}O. Similarly, alkaline hydrolysis of the salt (82), derived from the (S)-sulphide (81) yielded the (R)-oxide (83).



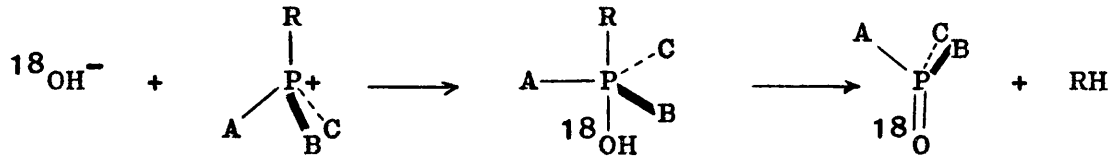
(S)-sulphide (R)-oxide

(81) (82) (83)

In contrast Horner[29] observed a considerable degree of racemisation in the conversion of (81) into (83) by treatment with iodomethane followed by hydrolysis. Mislow[91] has suggested that this may be due to partial racemisation of the iodide before the hydrolysis step which is stereospecific.

The mechanism proposed for these base-catalysed hydrolyses which is consistent with the observed complete inversion

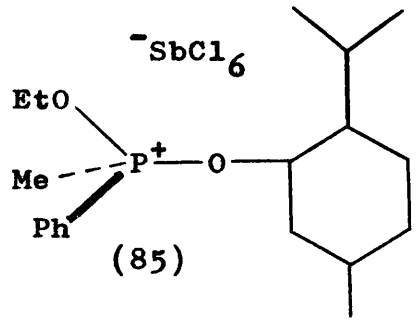
of configuration and incorporation of ^{18}O tracer, and similar to those proposed for the related hydrolyses of alkylarylphosphonium salts, involves apical attack of hydroxide opposite the leaving group (OEt or SEt) which departs from an apical position:



(84)

R = OEt or SEt

In the hydrolysis of the acyclic monoalkoxyphosphonium salt the intermediate phosphorane (84) has electronegative hydroxy and ethoxy groups occupying apical positions, corresponding to the structure of lowest energy. Loss of alkoxy from the apical position then gives the observed high stereospecificity. Pseudorotation of the intermediate, which would result in loss of stereospecificity, does not occur since the elctronegative alkoxy and hydroxy groups would be placed in energetically unfavourable equatorial positions, and a relatively electropositive group in the apical position. However, the presence of a second alkoxy group would give an intermediate containing one apical and one equatorial alkoxy group. In this case the barrier to the pseudorotation with one alkyl group as pivot would be greatly reduced as only change in the positions of alkoxy groups would be involved. In order to test this hypothesis, Mislow and DeBruin[92] made a careful study of the product ratios from the alkaline hydrolyses of the diastereoisomers of the salt (85) and found evidence for pseudorotation and

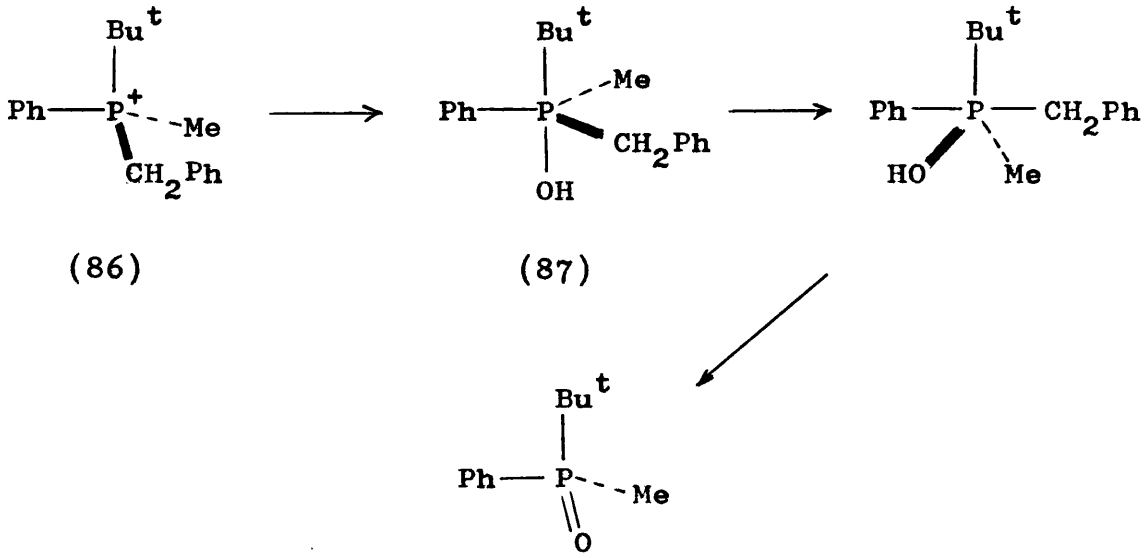


(85)

steric control of product formation. The attack of hydroxide ion opposite the bulky menthoxy was kinetically preferred to attack opposite the ethoxy group.

4.5 t-Butylphosphonium Salts.

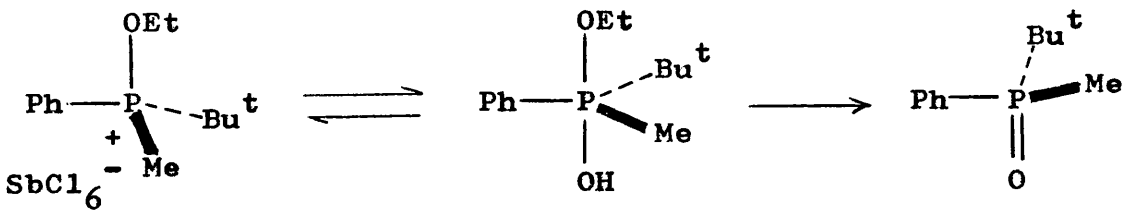
De'Ath and Trippett[93] reported that the benzyl-t-butylphosphonium salt (86) was hydrolysed with predominant retention of configuration at phosphorus because of apical attack of hydroxyl opposite the t-butyl group to give (87),



(86) (87)

pseudorotation followed by loss of benzyl from an apical position resulting in inversion at phosphorus. Attack occurred preferentially opposite the t-butyl group because of its steric bulk.

Mislow[94] has reported that the alkaline hydrolysis of the ethoxy salt (88) proceeds with complete inversion of



(88)

configuration. It was suggested that as the attacking nucleophile ($^{-}$OH) and the displaced group ($^{-}$OEt) are both appreciably more electronegative than alkyl or aryl the lowest energy pathway leads by apical attack to an intermediate phosphorane in which hydroxy and ethoxy occupy apical positions. Loss of ethoxy from the apical position will then give the observed inversion. In this case the stereoelectronic factors are more important than the steric effect of the t-butyl group in controlling displacement stereochemistry.

The Decomposition of the Phosphorane Intermediate Involved in the Alkaline Hydrolysis of Phosphonium Salts.

5.1 The Nature of the Carbanion Formed in the Hydrolysis of Silicon and Tin Compounds.

The alkaline hydrolysis of phosphonium salts is thought to involve, in the rate-determining step, loss of that group most stable as the anion from the conjugate base (90) of the initial adduct (89). The free carbanion is then protonated to give the corresponding hydrocarbon (91).

$$R_4P^+ + {}^-OH \rightleftharpoons R_4POH \rightleftharpoons R_4PO^- \longrightarrow R_3PO + R^- \longrightarrow RH$$

(89) (90) (91)

It has been shown[95] that in the similar base-catalysed cleavage of benzyl-silicon, benzyl-tin, and aryl-tin bonds in methanol, free carbanions are not involved. This conclusion was reached by establishing the isotopic content of the aromatic products formed by cleavage in a MeOH-MeOD mixture. A free carbanion would not discriminate significantly between the isotopes and the H/D ratio in the products from the reaction between a free carbanion and solvent would be the same as that of the hydroxyl groups of the MeOH-MeOD mixture. Kinetic isotope effects, k^H/k^D, of 1.4-4.6 were observed when the base-catalysed cleavages were carried out in MeOH-MeOD (1:1). These would be unity for reactions involving a free carbanion; benzene produced by addition of ethereal phenyl-lithium to the reaction medium showed such a ratio. The observed isotope effect indicates that proton transfer from the solvent to the carbon atom of the incipient carbanion was synchronous with breaking

of the metal-carbon bond, for then the product would be expected to contain a lower proportion of deuterium.

This report prompted an investigation to find if kinetic isotope effects could be observed when phosphonium salts were hydrolysed in equimolar mixtures of water and deuterium oxide.

5.2 Kinetic Isotope Effects in the Alkaline Hydrolysis of Phosphonium Salts.

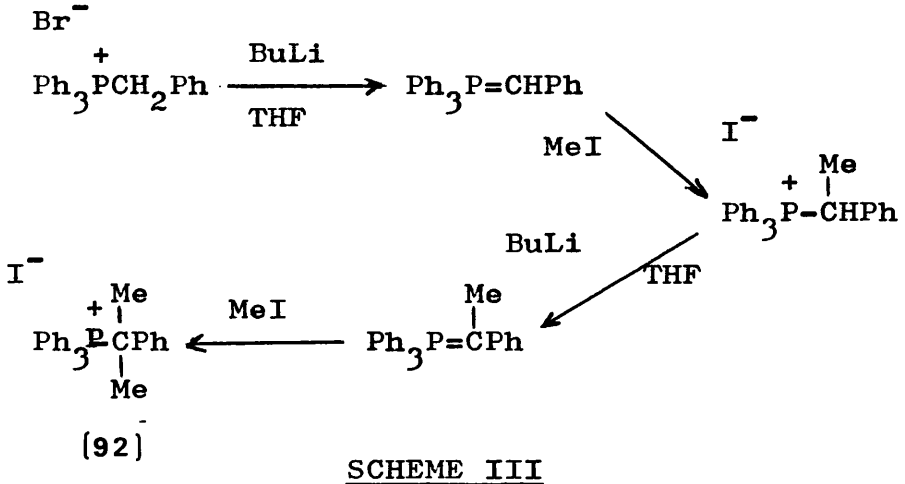
Because the α-hydrogens of phosphonium salts undergo rapid exchange in alkaline solution only phosphonium salts without such hydrogens could be studied.

a) Tetraphenylphosphonium Chloride.[96]

Alkaline hydrolysis of this salt in H_2O-D_2O (1:1) gave benzene, analysis of which by mass spectrometry showed k^H/k^D = 1.22±0.05 for protonation-deuteration of the phenyl anion.

b) Cumyltriphenylphosphonium Iodide.

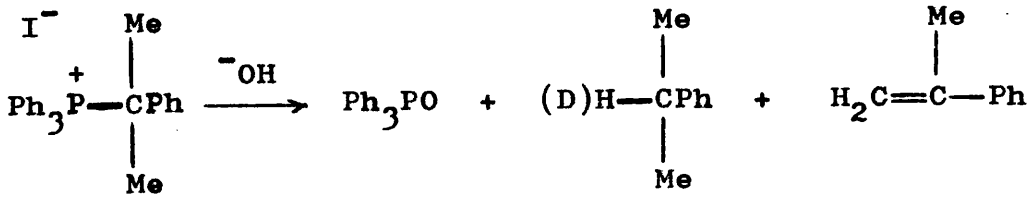
The salt (92) was synthesised as shown in Scheme III by successive methylation of the ylides derived from benzyltriphenylphosphonium bromide.



[92]

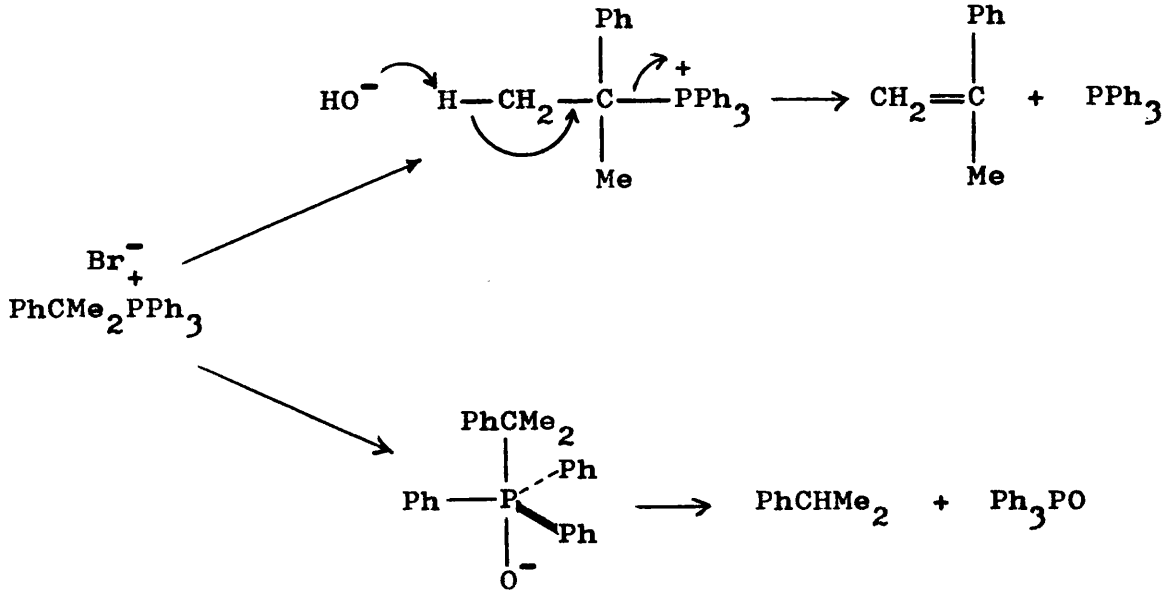
SCHEME III

The hydrocarbon product formed on alkaline hydrolysis of the salt in a mixture of D_2O-H_2O (1:1) was shown by g.l.c. and n.m.r. to be a mixture of 44% cumene (93) and 56% ∝-methylstyrene (94). In this hydrolysis Hofmann

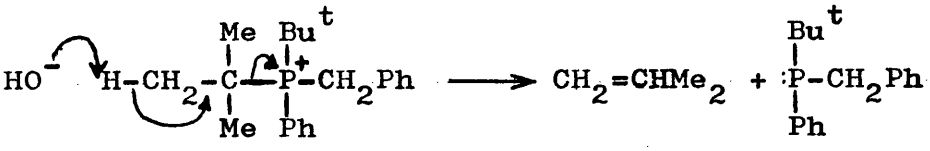


(92) (93) (94)

elimination giving ∝-methylstyrene is competing with the 'normal' hydrolysis reaction, loss of the cumyl anion to give cumene, because the phenyl group on the ∝-carbon can stabilise the transition state leading to olefin formation. Also triphenylphosphine is a good leaving group, and the stoichiometry of the reaction favours the olefin elimination, which is first order in hydroxide ion over the 'normal' hydrolysis involving loss of a cumyl anion which is second order in hydroxide ion.

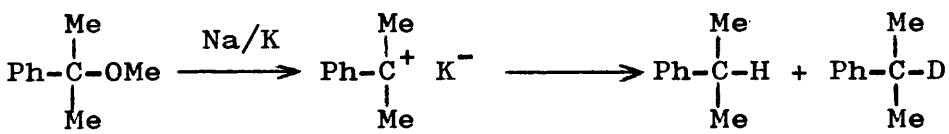


Olefin elimination has been reported[93] in the alkaline hydrolysis of benzyldi-t-butylphenylphosphonium bromide (95) where the two t-butyl substituents inhibit the attack of hydroxyl ion at phosphorus. In this case, olefin elimination is very slow as neither the α- nor β-carbons bear substituents capable of stabilising the transition state.



(95)

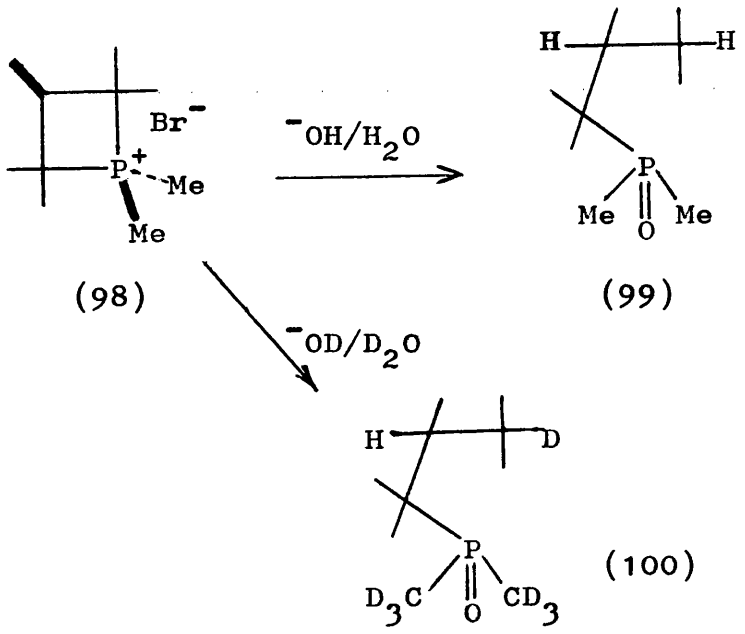
The components of the hydrocarbon product obtained on alkaline hydrolysis of the cumyl salt (92) were separated by preparative g.l.c., fractionation of the cumenes being avoided. Analysis by mass spectrometry of the cumenes showed $k^H/k^D = 1.21 \pm 0.05$ for protonation-deuteration of the cumyl anion, and integration of the n.m.r. spectrum of the cumenes gave a comparable although less accurate figure. The n.m.r. signal due to the methyls of d-cumene was a triplet (J_{HD} = ca. 1 Hz) whose components were of almost equal intensity presumably due to coupling between the deuterium atom and methyl protons.[97] The free cumyl carbanion did not differentiate significantly between the isotopes; the cumene produced by addition of the cumyl anion of cumylpotassium (97) to a mixture of H_2O-D_2O (1:1) showed k^H/k^D = 1.0. The cumylpotassium was prepared by reaction of the ether (96) with a sodium-potassium alloy.



(96) (97) 50% 50%

c) 1,1,2,2,3,4,4-Heptamethylphosphetanium Iodide.

This salt (98) prepared by quaternisation with iodomethane of the phosphetan produced on trichlorosilane reduction of r-1,2,2,trans-3,4,4-hexamethylphosphetan 1-oxide underwent alkaline hydrolysis with ring opening to give the phosphine oxide (99). Hydrolysis in deuterium



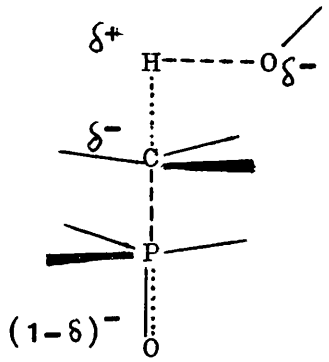
oxide gave the ring opened phosphine oxide (100). The phosphine oxides (99) and (100) were readily distinguished by n.m.r. spectroscopy. N.m.r. integration of the mixture of these phosphine oxides obtained on alkaline hydrolysis of the salt (98) in H_2O-D_2O (1:1) gave $k^H/k^D = 1.1 \pm 0.1$. The same value was indicated by comparison of the n.m.r. spectrum of the oxides with known mixtures of the oxides (99) and (100).

5.3 The Nature of the Carbanion Formed in the Hydrolysis of Phosphonium Salts.

The kinetic isotope effect, k^H/k^D, observed in the

protonation of carbanions formed in phosphonium salt hydrolysis show that these carbanions are not free in the rate-determining transition state, but that transfer of a proton from the solvent to the carbon atom is synchronous with breaking of the phosphorus-carbon bond. The low kinetic isotope effect observed can be interpreted mechanistically in terms of a transition state (101) for the rate-determining step in which little breaking of the phosphorus-carbon bond has occurred and there is correspondingly little transfer of a proton to the incipient carbanion.

(101)

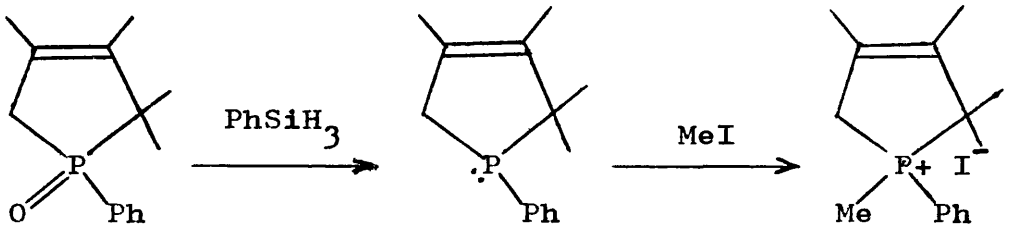


This view is supported by the observed[73] overall kinetic isotope effect for the hydrolysis of benzyltriphenylphosphonium bromide in 50% ethanol of k^H/k^D = 0.6, the relatively small difference between the rates of hydrolysis of comparable benzyl- and phenyl-phosphonium salts,[83] and the small partial rate factors for loss of p-substituted benzyls.[79]

5.4 Alkaline Hydrolysis of 3-Phospholenium Salts.

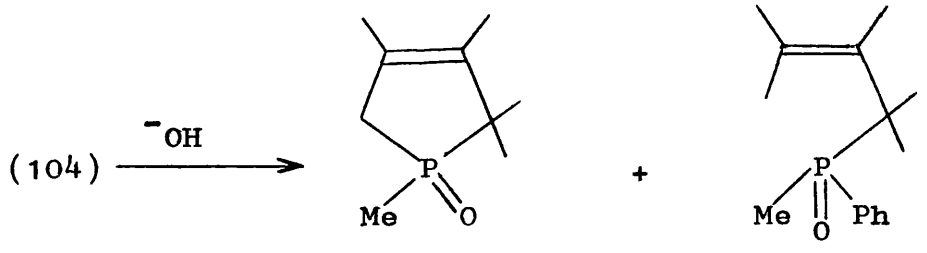
In the hydrolysis of phosphonium salts the ease of loss of groups parallels their anionic stability.[77-78,81] In general only one group is lost unless the anionic stabilities of the various potential leaving groups are similar.[79]

Phenylsilane reduction of 1-phenyl-2,2,3,4-tetramethyl-3-phospholen 1-oxide (102) gave the phospholen (103) which was quaternised with iodomethane to give 1,2,2,3,4-pentamethyl-1-phenyl-3-phospholenium iodide (104). The alkaline



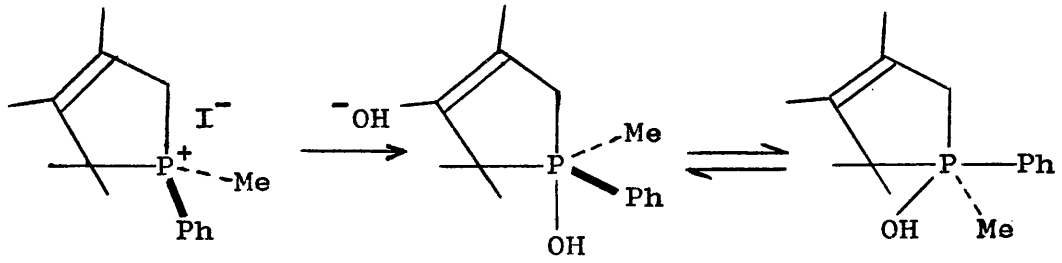
(102) (103) (104)

hydrolysis of this 3-phospholenium salt gave predominantly the 3-phospholen oxide (105), plus some ring opened phosphine oxide, (106). The much greater stability of the allyl



(105) 86% (106) 14%

over the phenyl anion and the preference of the five-membered ring for the apical-equatorial position in the intermediate (107) suggests that the reaction should give only the ring opened oxide (106) which in fact is the minor product. Presumably here the ring constraint leads to poor overlap of the π-bond with the essentially orthogonal p-orbital of the incipient carbanion in the transition state (109) leading to ring opening. Because the ring



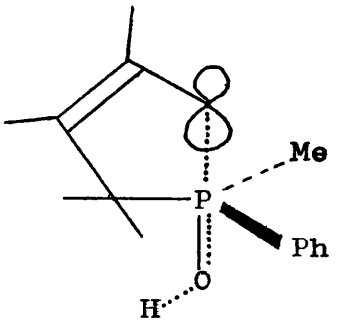
(107) (108)

(106) (105)

prevents the phosphorane adopting a conformation which allows maximum stabilisation of the departing anion pseudo-rotation of the initial adduct (107) to (108) followed by loss of phenyl from an apical position therefore becomes competitive.

It has been shown[98] that the alkaline hydrolysis of 3-methyl-1-phenyl-1-tetradecyl-3-phospholenium bromide proceeds with both ring cleavage and ring retention. In contrast Hawes[11] observed exclusive ring cleavage in the alkaline hydrolysis of 1-phenyl-1,3,4-trimethyl-3-phospholenium iodide.

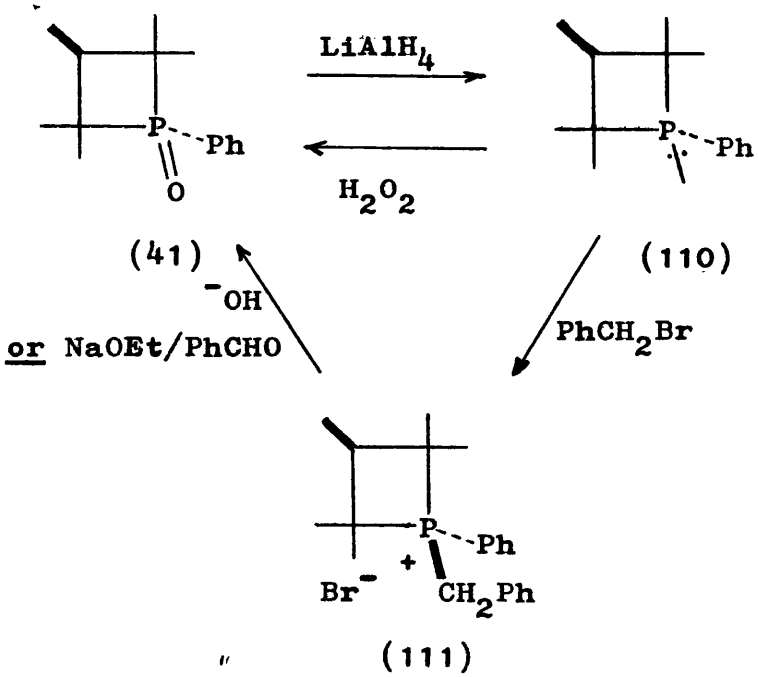
(109)



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

6.1 1-Benzylphosphetanium Salts.

Hawes and Trippett[19] reduced 2,2,trans-3,4,4-pentamethyl-r-1-phenylphosphetan 1-oxide (41), m.p. 127°, with lithium aluminium hydride to the phosphetan (110), which on quaternisation with benzyl bromide gave r-1-benzyl-2,2,cis-3,4,4-pentamethyl-1-phenylphosphetanium bromide (111). The reduction was shown to proceed with retention of stereochemistry at phosphorus as oxidation gave back the starting isomer (41). Both alkaline hydrolysis of, and Wittig olefin



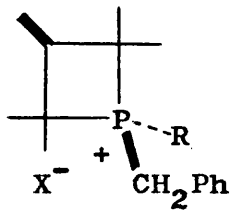
(111)

synthesis with ethanolic sodium ethoxide and benzaldehyde gave the original trans-1-phenylphosphetan 1-oxide (41), m.p. 127°. As the olefin synthesis with optically active acyclic benzylphosphonium salts had been previously shown to proceed with retention of configuration at phosphorus[88] they concluded that the alkaline hydrolysis of the salt (111)

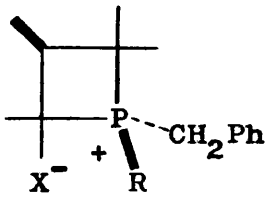
proceeded with retention of configuration.

Later it was demonstrated[99,100] that various mixtures of the stereoisomers of 1-benzyl-2,2,3,4,4-pentamethyl-1-phenylphosphetanium bromide when decomposed with aqueous base always gave the same mixture of stereoisomers of 2,2,3,4,4-pentamethyl-1-phenyl-phosphetan oxide (cis:trans = 1:9), and that olefin synthesis with the ylide from a mixture of isomeric salts rich in the trans salt gave a mixture of oxides rich in the trans-1-phenyl-phosphetan 1-oxide.[100]

The unusual stereochemical courses of alkaline hydrolysis and olefin synthesis of these phosphetanium salts prompted the preparation of the stereoisomerically pure 1-benzylphosphetanium salts (113; R = Me, Ph, CH_2Ph) and (112; R = Me, Ph) and the study of their alkaline hydrolyses and olefin syntheses. The salts were synthesised by



(113)



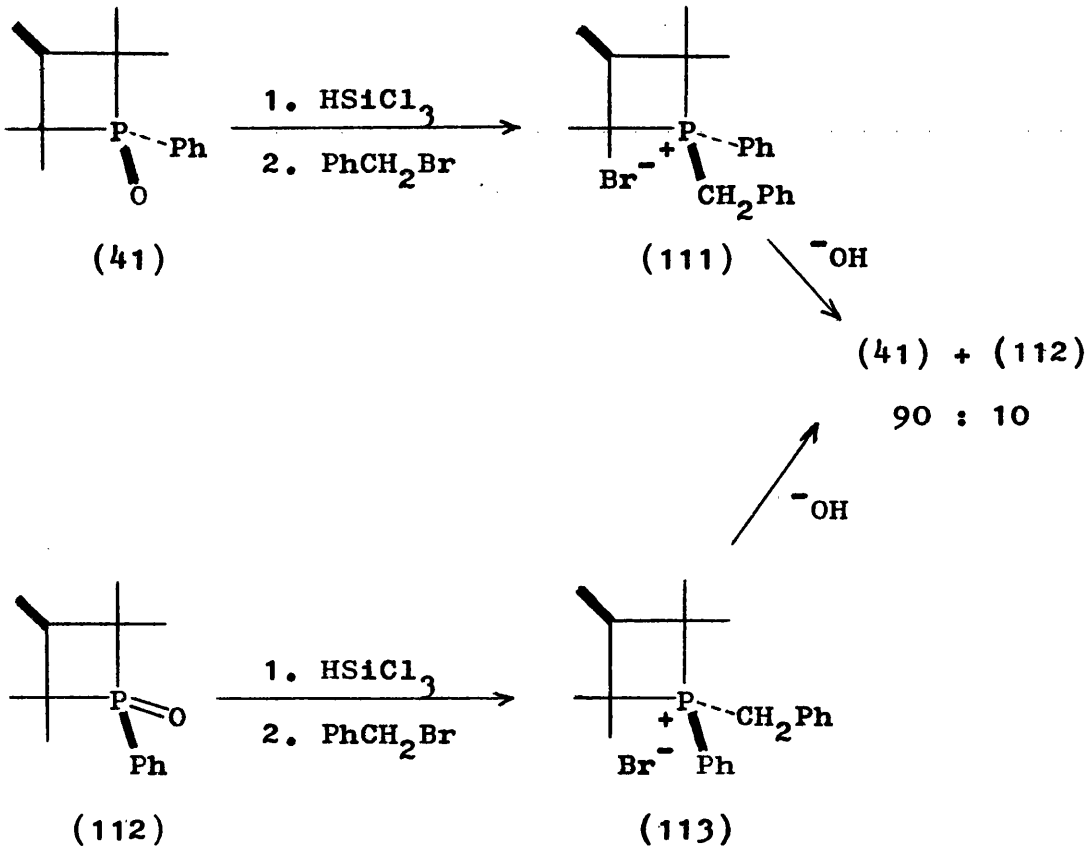
(112)

trichlorosilane reduction of phosphetan 1-oxides and quaternisation of the resultant phosphetans with alkyl halides. The stereoisomer compositions of the phosphetan 1-oxide products were determined by ^1H n.m.r. spectroscopy.

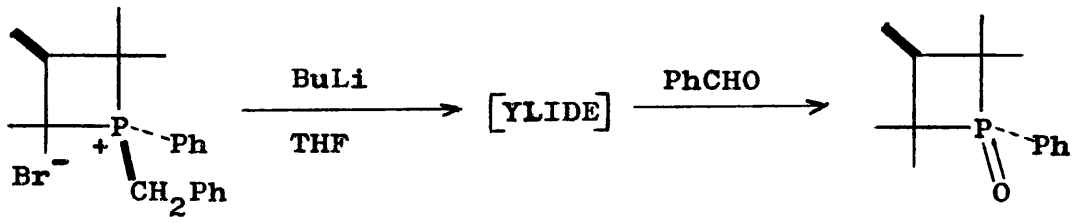
a) 1-Benzyl-2,2,3,4,4-pentamethyl-1-phenylphosphetanium Bromide.

In contrast to the report of Hawes[19] it was found that alkaline hydrolysis of the cis salt (111) (1-benzyl and

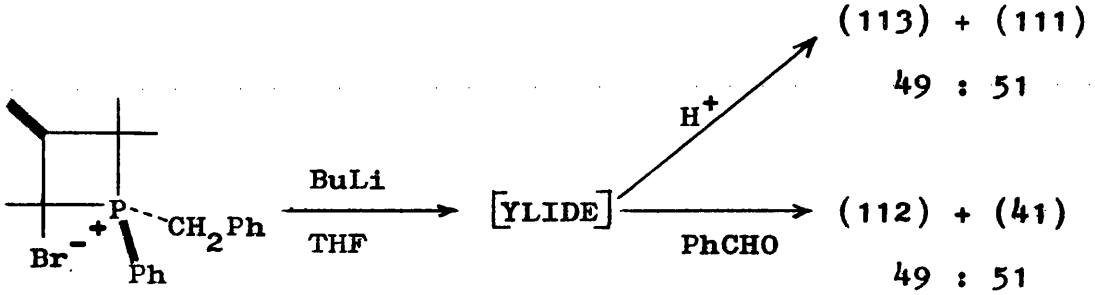
3-methyl cis) gave a mixture of stereoisomers of 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxide (41) and (112) in which the trans oxide (41) was predominant (cis:trans = 1:9). Alkaline hydrolysis of the trans salt (113) gave the same ratio of the two product phosphine oxides.



Wittig olefin synthesis with the cis salt (111) gave only the trans oxide (41), whereas the trans salt (113) gave mixtures of the isomeric oxides (41) and (112). Stereomutation in the olefin synthesis with (113) occurred at the ylide stage: regeneration of the salt from an ylide solution prepared from the pure isomer (113) and butyl-lithium in tetrahydrofuran gave a mixture of salts (113) and (111) corresponding to the mixture of oxides (112) and (41) produced when this ylide solution was used in the olefin synthesis.



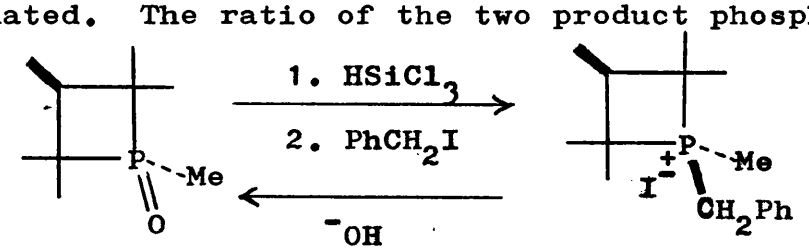
(111) (41)



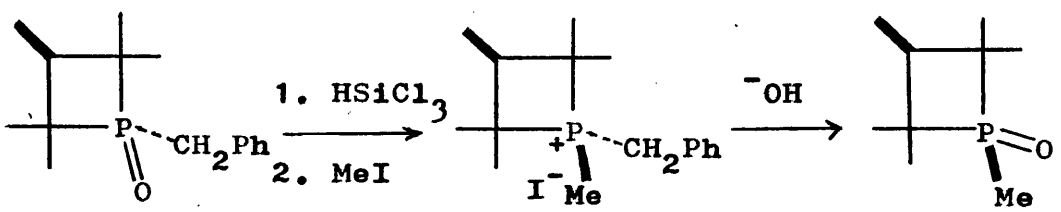
(113)

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

Hydrolysis of the cis salt (114) (1-benzyl and 3-methyl cis) in ethanolic sodium hydroxide proceeded with retention of configuration giving entirely trans-1-methylphosphetan 1-oxide (42), in contrast the trans salt (115) gave a mixture of stereoisomers of 1,2,2,3,4,4-hexamethylphosphetan 1-oxide (42) and (116) in which the cis-1-methylphosphetan 1-oxide predominated. The ratio of the two product phosphines oxides



(42) (114)

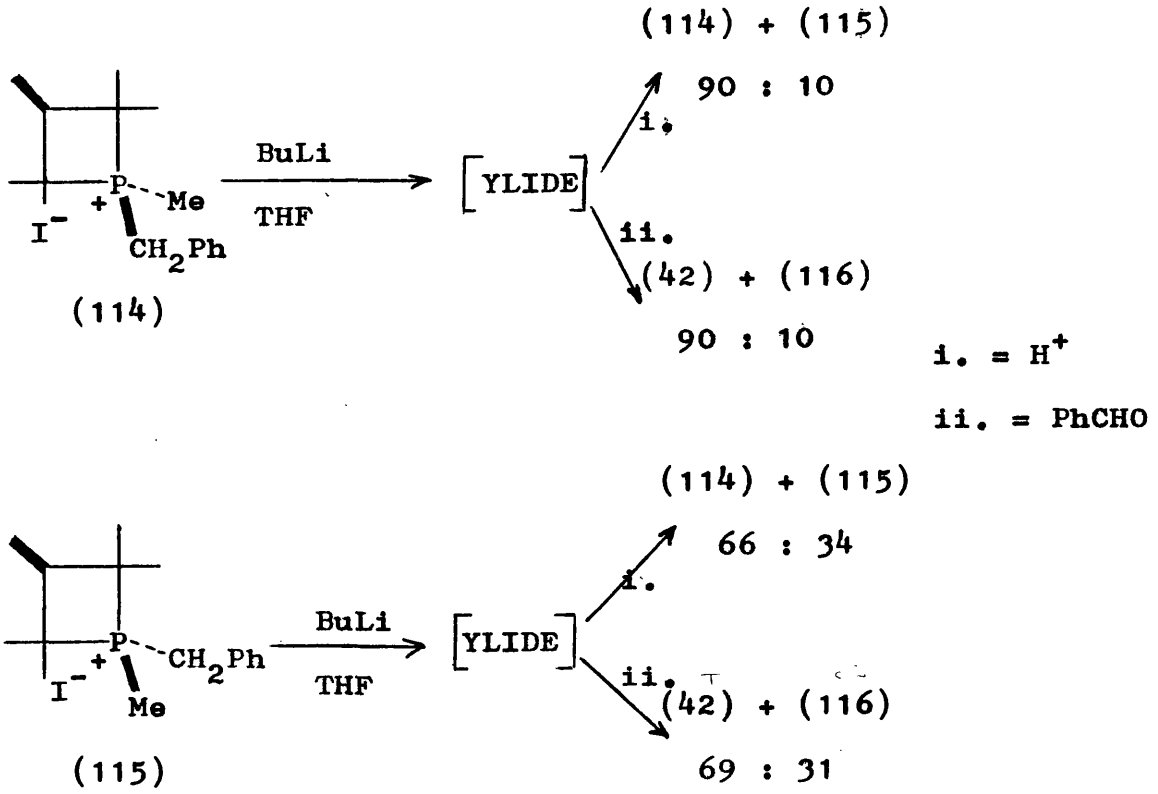


(115) (116) + (42)

75 :25

(116) and (42) from the hydrolysis of the trans salt (115) was very sensitive to the reaction conditions, e.g. hydrolysis of the salt in aqueous sodium hydroxide gave an oxide whose stereoisomer composition was cis-trans = 30:70.

Olefin synthesis with the cis salt (114) and with the trans salt (115) gave mixtures of the isomeric oxides (116) and (42). Regeneration of the salt from an ylide solution again demonstrated that stereomutation was occurring at the ylide stage. The relative amounts of the oxides (42) and



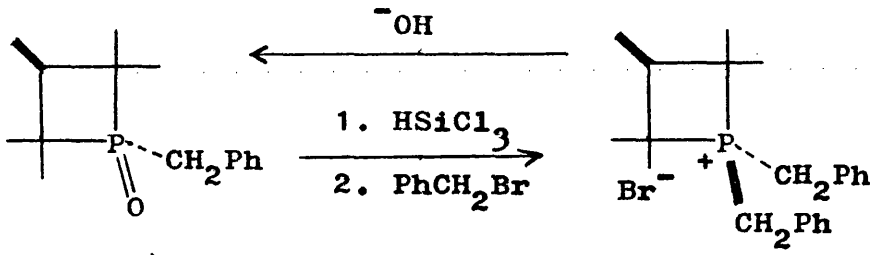
(116) produced from the ylide solution increased with time, after stirring for 18 h a 83:17 trans:cis mixture of oxides was isolated. Shutt[100] also observed this change in isomer composition with time in ylides generated from r-1-benzyl-2,2,trans-3,4,4-pentamethyl-1-phenylphosphetanium bromide, although in this case, the salt used was not completely free of its isomer.

A Wittig olefin synthesis with the trans salt (115),

ethanolic sodium ethoxide and benzaldehyde also gave a mixture of the stereoisomeric phosphine oxides (42) and (116), (cis:trans = 35:65).

c) 1,1-Dibenzyl-2,2,3,4,4-pentamethylphosphetanium Bromide.

Alkaline hydrolysis of this salt (117) gave only one oxide product, the trans oxide (118).



(118) (117)

6.2 Possible Mechanisms of Alkaline Hydrolysis of 1-Benzylphosphetanium Salts.

a) Stereomutation at the 3-carbon.

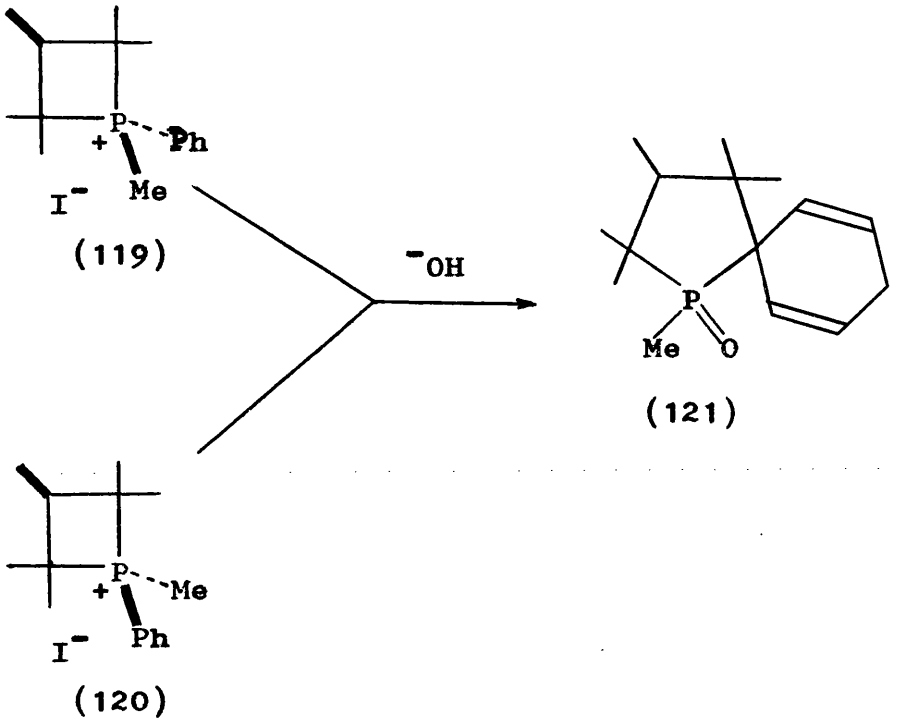
The stereochemical courses of the reactions were determined by analysis of the products by ^{1}H n.m.r. spectroscopy. The isomerism of the product oxides being due to different relationships between the substituents on phosphorus and those on the 3-carbon of the ring. Hence changes in stereochemistry on reaction could be due to changes at phosphorus or the 3-carbon. Hydrolysis of r-1-benzyl-1,2,2,trans-3,4,4-hexamethylphosphetanium iodide and r-1-benzyl-2,2,cis-3,4,4-pentamethyl-1-phenylphosphetanium iodide[100] in deuterium oxide did not lead to deuterium incorporation at the 3-position of the resulting oxide, thus epimerization which involves stereomutation at this carbon atom can be

ruled out. Thus the changes in stereochemistry on alkaline hydrolysis and ylide formation were due to changes at the phosphorus atom.

(b) Ylide Isomerisation.

Isomer cross-over of the ylides derived from the phosphetanium salts suggested that this phenomena might also be responsible for the observed partial inversions of the salts on hydrolysis. The salts being partially converted, *via* ylides, into their isomers prior to hydrolysis. Snyder and Priestley[98] have proposed that ylide formation can compete with phosphorane generation (by attack of hydroxide ion on the phosphonium ion) in the base-catalysed decomposition of 2- and 3-phospholenium bromides.

This mechanistic possibility was supported by the observation that addition of *r*-1,2,2,*trans*-3,4,4-hexamethyl-1-phenylphosphetanium iodide (119) to a dilute solution of sodium deuterioxide in deuterium oxide resulted in rapid isomerisation of the salt into its isomer and replacement of the 1-methyl hydrogens by deuterium. Also alkaline hydrolysis of the salt (119) and its isomer (120) gives the same ring expanded phosphine oxide (121) of unknown geometry (this is considered in more detail in Chapter 7.). Alkaline hydrolysis of the salt in deuterium oxide gave the same ring expanded oxide except that all the hydrogens of the methyl group attached to phosphorus had been replaced by deuterium. No exchange occurred when the fully protonated oxide (121) was submitted to the reaction conditions. These experiments show that deuterium exchange and interconversion of phosphetanium salts can occur prior to hydrolysis. As benzylic protons are more



acidic than methyl protons formation of ylides from 1-benzyl-phosphetanium salts will also occur prior to hydrolysis. Cremer[99] reported that traces of sodium hydroxide produced immediate equilibration of the individual isomers of 1-benzylphosphetanium salts. Hence the salts could presumably be interconverted via ylides prior to decomposition to phosphine oxide products.

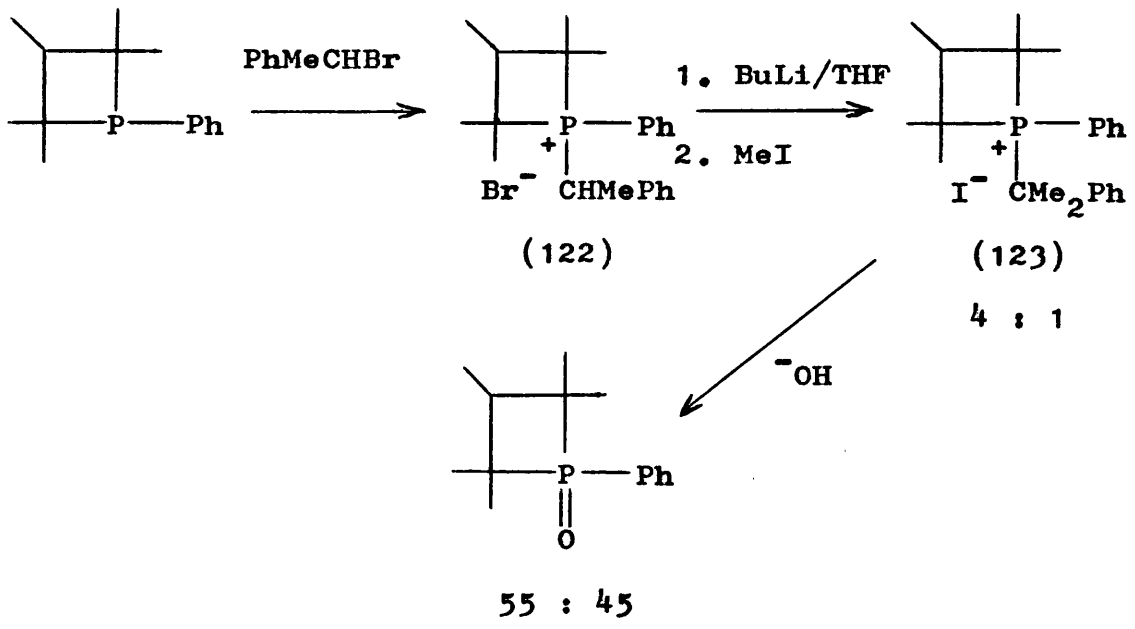
c) Intermediate Pentacovalent Phosphoranes.

The intermediacy of phosphoranes has long been recognised in the alkaline hydrolysis of phosphonium salts,[45] and phosphoranes are known to be stereochemically non-rigid undergoing ligand exchange by pseudorotation. Therefore, an alternative explanation of the stereochemistry of hydrolysis of 1-benzylphosphetanium salts may involve pseudorotation of intermediates prior to their decomposition to products.

To distinguish between the two possible mechanisms of base-catalysed decomposition of 1-benzylphosphetanium salts

a salt incapable of ylide formation was investigated.

Quaternisation of a mixture of stereoisomers of 2,2,3,4,4-pentamethyl-1-phenylphosphetan with 1-phenylethyl-bromide gave the phosphetanium salt (122). Methylation, with iodomethane, of an ylide solution prepared from the salt (122) and butyl-lithium in tetrahydrofuran gave a mixture of stereoisomers (4:1) of 1-cumyl-2,2,3,4,4-pentamethyl-1-phenylphosphetanium iodide (123). Alkaline hydrolysis of this salt gave cumene and a mixture of isomeric

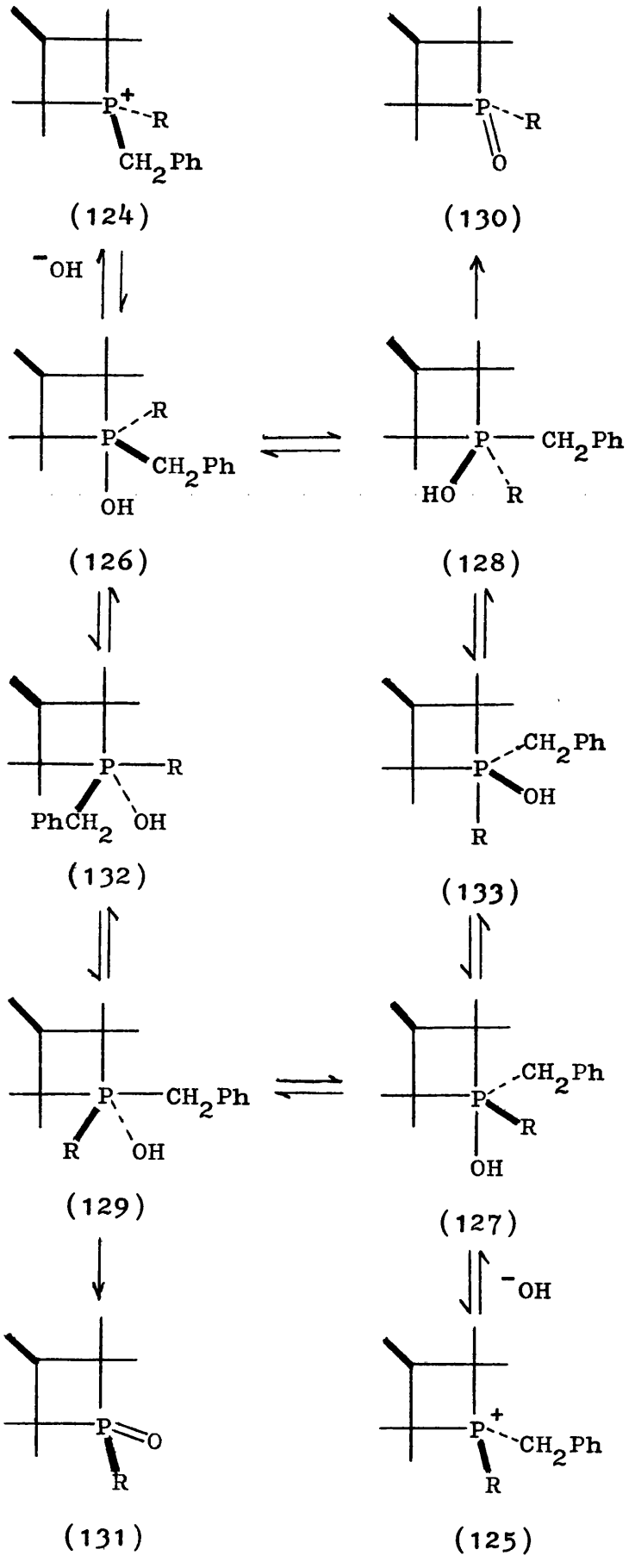


2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxides (cis:trans = 55:45). Since the ratio of the two product phosphine oxides was different to that of the initial stereoisomeric salts (123) which cannot form ylides stereomutation presumably occurred by pseudorotation of intermediates. Presumably the same phenomena was responsible for the stereochemical courses of the alkaline hydrolysis of 1-benzylphosphetanium salts.

6.3 Mechanism of Alkaline Hydrolysis of 1-Benzylphosphetanium Salts.

McEwens basic hydrolysis mechanism,[88] which was proposed for acyclic phosphonium salts, and explains configuration inversion, demands linearity between the hydroxide and departing benzyl anion. Such a diapical situation is impossible in phosphetanium salts (and in other phosphonium salts with phosphorus as part of a small ring) because of the increase in ring strain; the ring would have to occupy a diequatorial position. Therefore, the hydrolysis of phosphetanium salts takes a different course resulting in partial inversion of configuration.

The stereomutation during hydrolysis of 1-benzyl-phosphetanium salts may be rationalised by reversible apical attack of hydroxide ions on the stereoisomeric phosphetanium ions (124) and (125) to give the phosphoranes (126) and (127), of trigonal bipyramidal geometry in which the ring occupies an apical-equatorial position, which pseudorotate to allow benzyl to depart from an apical position. The pseudorotation pathways open to these phosphoranes are shown in Scheme IV, those involving the unfavourable spanning by the ring of the diequatorial position being avoided. The energy barriers for the two pseudorotations open to these initial phos-phoranes are similar because of the similar stereoelectronic preferences of the benzyl and R groups on phosphorus, hence the reactions are not stereospecific. In contrast the energy barriers for the two corresponding pseudorotations which are open to the initial phosphoranes involved in nucleophilic displacements of phosphetan 1-oxides are distinctly different due to clear-cut differences in the stereoelectronic



SCHEME IV

preferences of the groups on phosphorus. In that case only the lowest energy pseudorotation, leading to the observed retention of configuration, occurs.

Three consecutive pseudorotations inter-convert the phosphoranes (126) and (127), then loss of hydroxide regenerates the starting phosphonium ion with inverted configuration at phosphorus. Irreversible loss of the benzyl anion from the phosphoranes (128) and (129) give the trans- and cis- phosphetan 1-oxides, (130) and (131), respectively.

a) 1-Benzyl-2,2,3,4,4-pentamethyl-1-phenylphosphetanium Bromide.

The alkaline hydrolysis of the cis and trans bromides (124 and 125; R = Ph) is stereoselective (a predominance of the trans oxide is obtained from either isomer of the salt) though not stereo-specific. That the same mixture of phosphetan 1-oxides (130 and 131; R = Ph) is obtained from either isomer indicates that epimerization of (124) and (125) is faster than hydrolysis; this, and the observation that addition of sodium hydroxide to solutions of the cis or trans salts catalysed immediate equilibration of the individual isomers,[99] implies that pseudorotation, and attack and loss of hydroxide ion are successfully competing with rate-limiting loss of the benzyl anion from (128) and (129). This situation can only arise if the clockwise and anticlockwise pathways between the initial phosphoranes (126 and 127; R = Ph), which involve three pseudorotational steps and interconvert the cis and trans phosphetanium ions (124 and 125; R = Ph), are of lower energy than those for loss of the benzyl anions from the ultimate phosphoranes (128 and 129; R = Ph). The actual ratio of the two product

phosphine oxides reflects the relative energy barriers for decomposition of these phosphoranes.

If the phosphorane intermediates existed as the mono-anions, similar to the intermediates involved in displacements at phosphoryl phosphetan centres, the pseudorotations from (126) to (128) and (132) as well as from (127) to (129) and (133) would be irreversible. Since the isomeric phosphetanium ions are interconverted prior to hydrolysis these pseudorotations are clearly reversible, thus the intermediates do not exist as the anions under these alkaline conditions.

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

The alkaline hydrolysis of the cis and trans phosphetanium iodides (124 and 125; R = Me) can also be analysed by reference to Scheme IV. Since different ratios of the two product phosphetan oxides (130 and 131; R = Me) are obtained from the cis and trans salts it follows that decomposition of the ultimate phosphoranes (128 and 129; R = Me) is not the rate-limiting step in this displacement. The energy barriers for pseudorotation are now comparable to those for loss of benzyl, whereas the energy barriers for pseudorotation of the intermediates involved in the hydrolysis of the isomeric 1-benzyl-2,2,3,4,4-pentamethyl-1-phenylphosphetanium bromides were clearly lower than those for loss of benzyl. This difference is presumably a consequence of changes in energy barriers for pseudorotation caused by a change in steric and/or stereoelectronic factors on replacing phenyl by methyl, e.g. methyl is less electronegative than phenyl therefore, the barriers for pseudorotations that place methyl apical will be higher than the

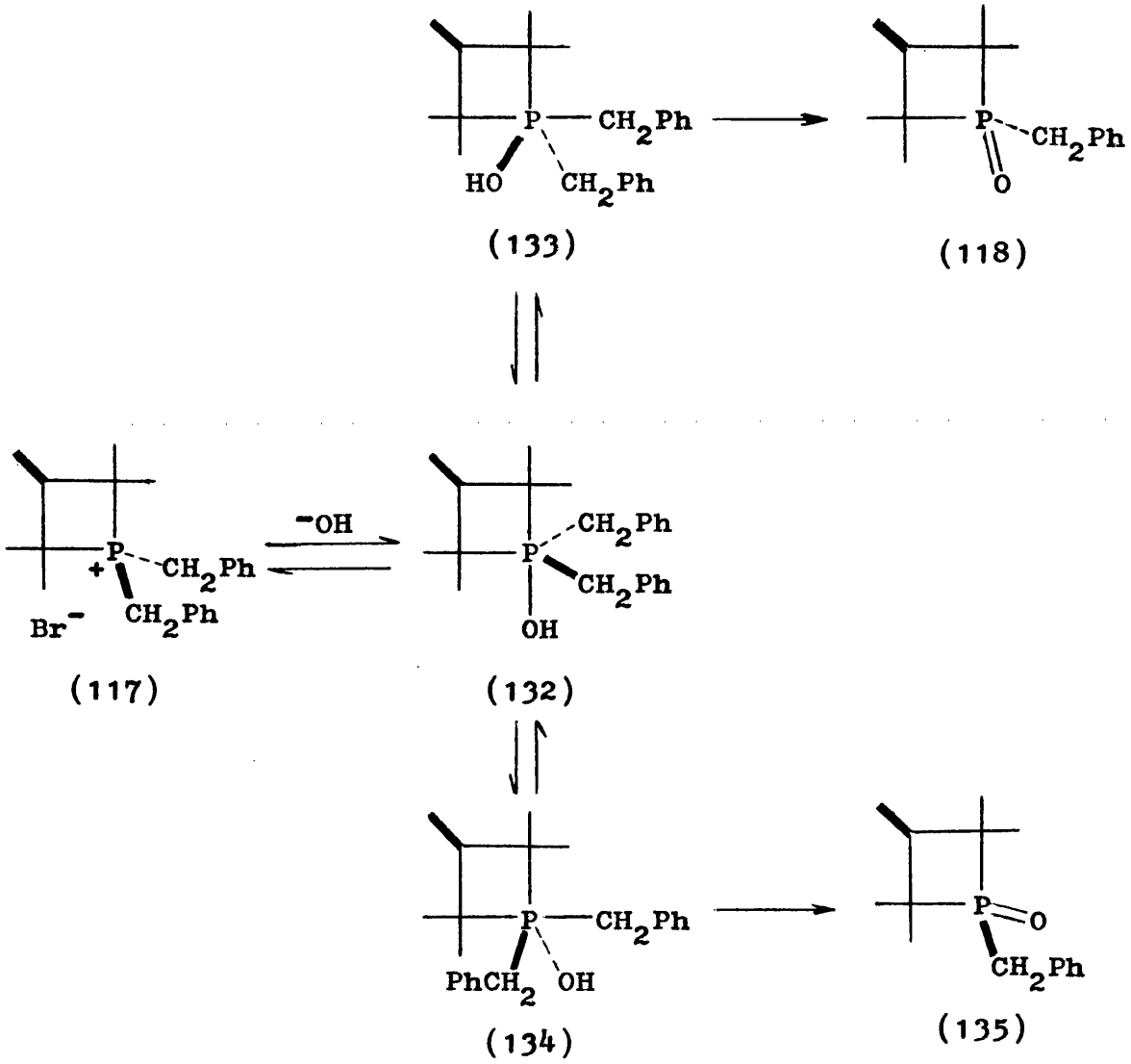
comparable ones that place phenyl apical.

However, the pseudorotations must still be of lower energy in order to explain the degree of equilibration observed (the displacements are not stereospecific) and the immediate equilibration of the individual isomers caused by addition of a drop of sodium hydroxide to solutions of the isomers.[99]

Alkaline hydrolysis of the trans salt (125; R = Me) in ethanolic sodium hydroxide produced a phosphine oxide whose stereoisomeric composition (cis:trans = 75:25) was considerably different to that obtained by hydrolysis in aqueous sodium hydroxide (cis:trans = 30:70). This dramatic realignment of product ratio is presumably a consequence of a delicate balance existing between the energies of various processes. A different reaction medium alters the relative energies of the processes.

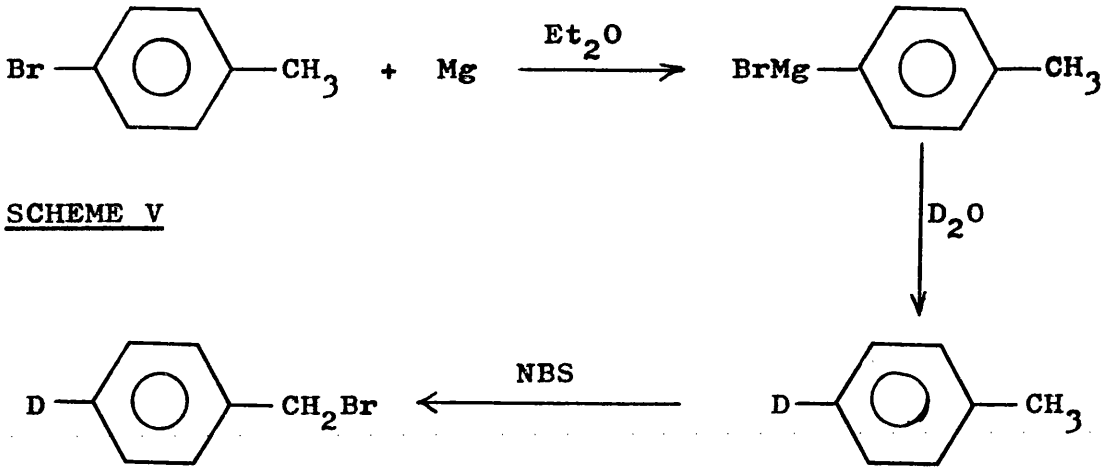
c) 1,1-Dibenzyl-2,2,3,4,4-pentamethylphosphetanium Bromide.

Alkaline hydrolysis of the dibenzyl salt (117) was completely stereospecific giving only the trans oxide (118). Apical attack of hydroxide ion on the salt gives the phosphorane (132). Attack along the other ring phosphorus-carbon bond produces the mirror image of (132). Pseudorotation of (132) gives the phosphoranes (133) and (134) which on loss of a benzyl anion give the trans and cis phosphetan 1-oxides (118) and (135). The stereospecificity of the reaction implies that (a) the relative energy barriers for pseudorotation of (132) to (133) and (134) are lower than those barriers for decomposition of these ultimate phosphoranes, and that loss of benzyl from the phosphorane (133)



is a lower energy pathway than loss of benzyl from (134); or alternatively (b) pseudorotation is the rate-limiting process and the energy barrier for the pseudorotation (132) to (133) is lower than that for the pseudorotation of (132) to (134).

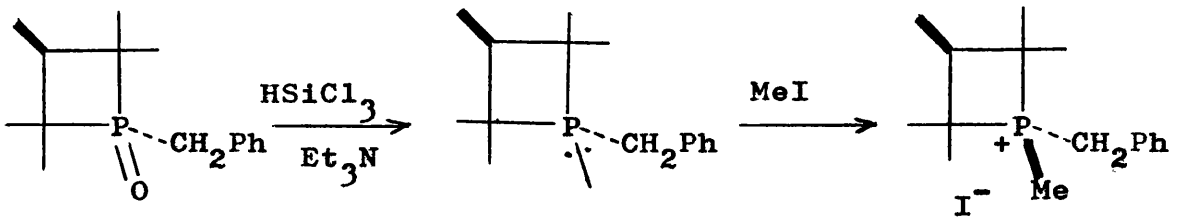
To distinguish between these two mechanistic possibilities r-1-benzyl-1-p-deuteriobenzyl-2,2,trans-3,4,4-pentamethylphosphetanium iodide (136) was synthesised. p-Deuteriobenzyl bromide was prepared by the route outlined in Scheme V. Mass spectral analysis showed that the toluene was 92% deuterated. Quaternisation of the bromide with r-1-benzyl-



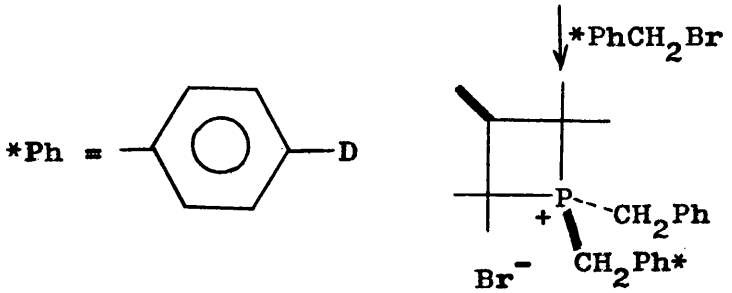
SCHEME V

NBS = N-bromosuccinimide

2,2,trans-3,4,4-pentamethylphosphetan (137), prepared by reduction of the corresponding phosphetan 1-oxide (118) with trichlorosilane in the presence of triethylamine, gave the phosphetanium salt (136). The reduction was shown to proceed with complete retention of configuration at phosphorus as quaternisation of a sample of the phosphetan (137) with iodomethane gave only r-1-benzyl-1,2,2,trans-3,4,4-hexamethylphosphetanium iodide (115).



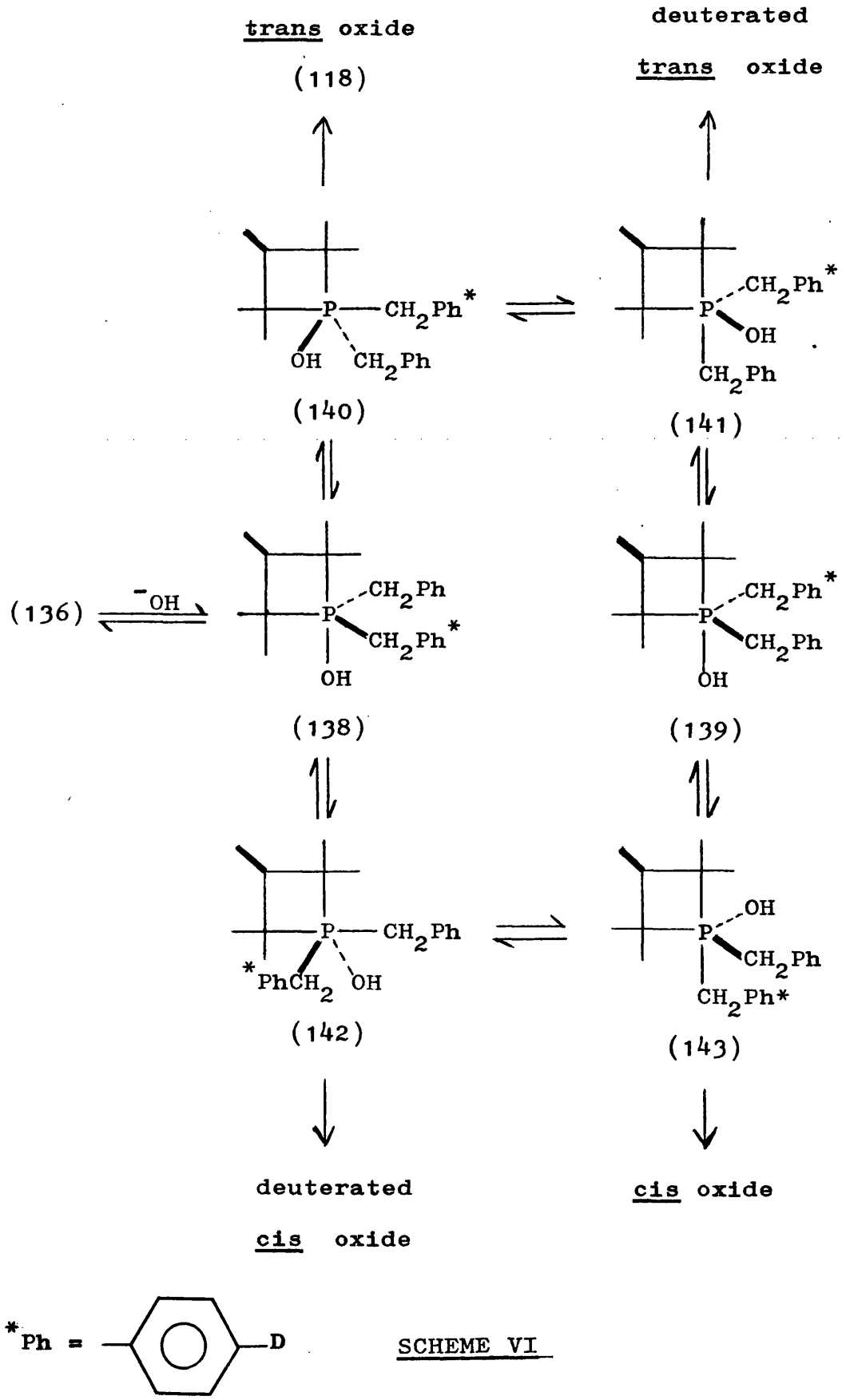
(118) (137) (115)



(136)

Alkaline hydrolysis of the dibenzyl salt (136) gave a phosphine oxide whose n.m.r. spectrum was identical with that of r-1-benzyl-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide except that the aromatic region integrated for less than five protons. Mass spectral analysis of the oxide showed that 43% of the benzyl groups were labelled with deuterium. Therefore, the benzyl groups had become equivalent during the course of the hydrolysis. This can be explained by the first of the two proposed mechanisms (a): rapid pseudorotation and rate-limiting decomposition of the ultimate phosphoranes.

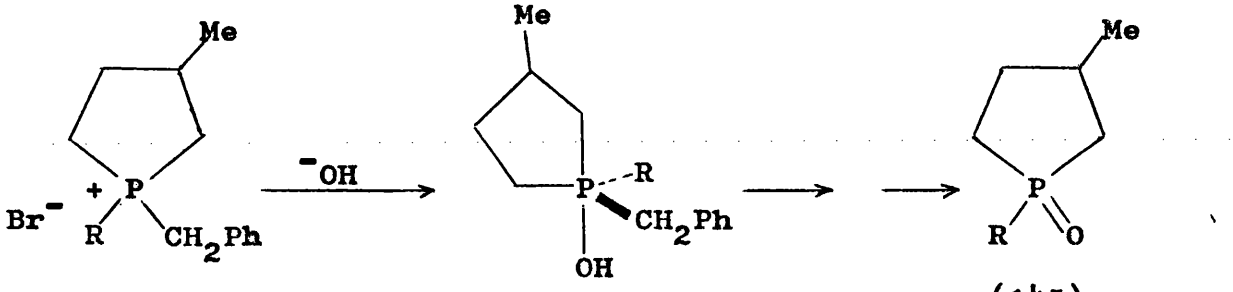
In the salt (136) the benzyl groups are distinguishable so Scheme VI shows the pseudorotation pathways open to the initial phosphorane (138) formed by apical attack of hydroxide ion on the salt. Equilibration of the benzyl groups arises by rapid interconversion of the phosphoranes (138) and (139), by the clockwise and anticlockwise pathways involving three pseudorotations, prior to rate-limiting decomposition of the ultimate phosphoranes to product. The fact that hydrolysis gives only the trans oxide suggests that the energy barrier for decomposition of the phosphoranes (140) and (141) is lower than that for decomposition of (142) and (143). The phosphoranes (140) and (141) being mirror images of each other [this is also true for the phosphoranes (142) and (143)] decompose at the same rate thus the trans oxide product contains equal numbers of labelled and unlabelled benzyl groups.


trans oxide
(118)
deuterated
trans oxide
(140)
(141)
(136)
-OH
(138)
(139)
(142)
(143)
deuterated
cis oxide
cis oxide
*Ph =
D

SCHEME VI

6.4 The Alkaline Hydrolysis of other Cyclic Phosphonium Salts.

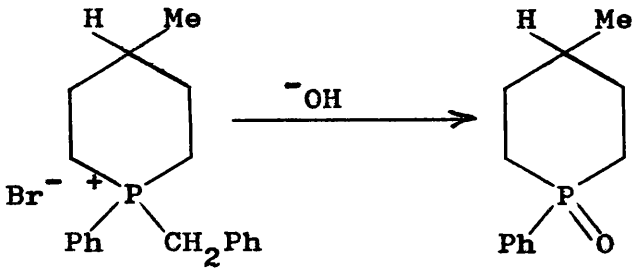
The alkaline hydrolysis of both the cis and trans isomers of the 1-benzyl-3-methylphospholanium bromides (144; R = Me, Ph) to the oxides (145; R = Me, Ph) have been reported to proceed with complete retention of configuration



(144) (146) (145)

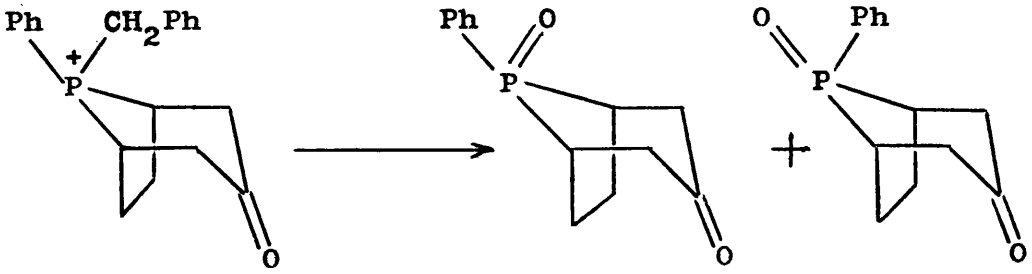
at phosphorus.[25,26] The phospholan ring is similar to the phosphetan ring in its stereochemical requirement, in that during hydrolysis of the phospholanium salt, the ring will occupy an apical-equatorial position in the trigonal bipyramidal intermediate (146) formed by apical attack of hydroxide ion. The stereochemical course of the phospholanium salt hydrolysis has been explained by equatorial departure of the benzyl anion from this intermediate,[25] or alternatively, by loss of a proton from (146) to give the mono-anion, followed by pseudorotation (to place the electropositive O^- group in the preferred equatorial position) and loss of the benzyl anion from the apical position.[50,102]

The pure cis and trans isomers of the 1-benzyl-4-methyl-1-phenylphosphorinanium bromide (147) undergo alkaline hydrolysis to mixtures of different proportions of cis-and trans-4-methyl-1-phenylphosphorinan 1-oxide (148).[27] Similarly both isomers of the bicyclic phosphonium salt (149)



(147) (148)

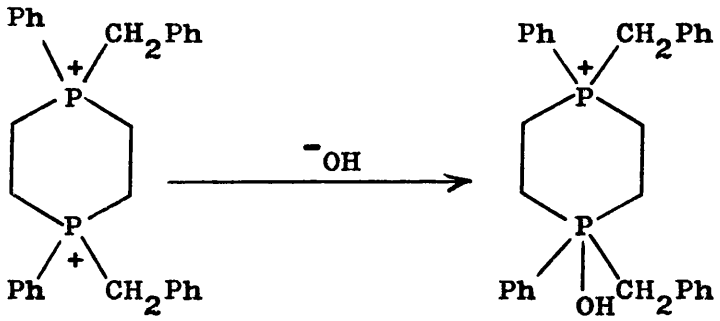
have been shown to undergo hydrolysis to give mixtures of different proportions of the isomeric oxides (150) and (151).[103]



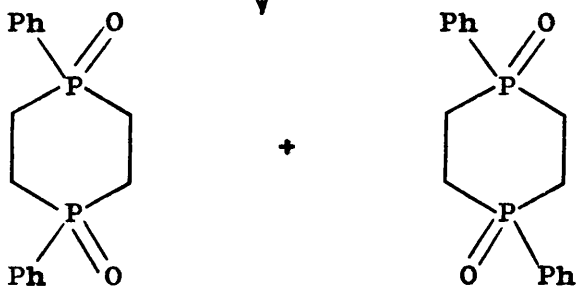
(149) (150) (151)

These hydrolyses are envisaged to occur in the same manner as the hydrolysis of the 1-benzylphosphetanium salts: the rings occupy apical-equatorial positions in the initial trigonal bipyramidal intermediates formed by apical attack of hydroxide ion on the phosphonium ions. Pseudorotations must then occur to place the benzyl group in its apical departing position. Mixtures of isomeric oxides are formed as the two pseudorotation pathways (one leading to retention and the other to inversion) open to the initial phosphoranes are of equal energy.

Driver and Gallagher[104] found that one isomer of the salt (152) gave a mixture of the oxides (153) and (154) when decomposed with aqueous base. They explained this by proposing pseudorotation of the monophosphorane intermediate (155).



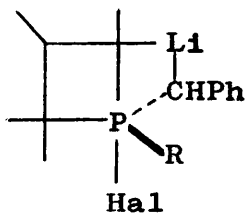
(152) (155)



(153) (154)

6.5 Mechanism of Ylide Isomerisation.

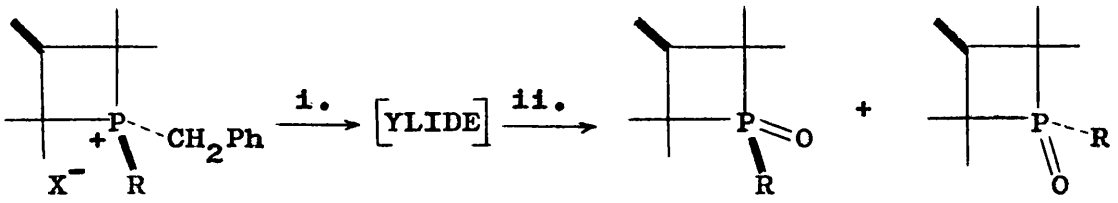
Ylides obtained by the action of strong bases on phosphonium salts are known to be complexed with salts.[105] Thus the ylides derived from the 1-benzylphosphetanium halides using butyl-lithium were complexed with lithium halides. These adducts could have a pentacoordinate phosphorus atom, e.g. (156), and the observed ylide isomerisation could then



(156)

be due to pseudorotation of this phosphorane in a manner similar to that of the phosphorane intermediates involved in the alkaline hydrolysis of the 1-benzylphosphetanium salts.

To investigate this proposal the pure tetraphenylborate phosphetanium salts (157) and (158) were synthesised and the ylides derived from them by the action of butyllithium in tetrahydrofuran, were used in an olefin synthesis. The stereoisomeric compositions of the product phosphine oxides, were determined and compared with the composition of the oxides obtained from olefin syntheses with the corresponding phosphetanium halides (113) and (115).



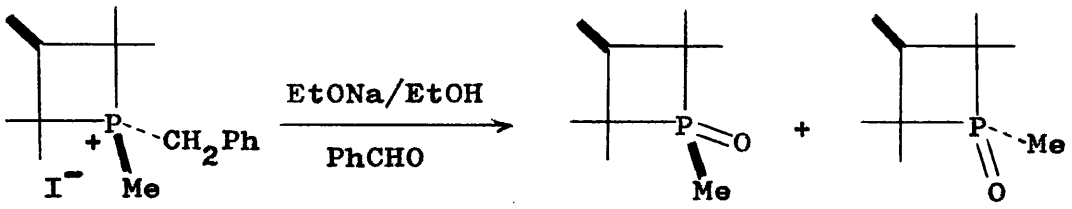
i. = BuLi/THF ii. = PhCHO

SALT	OXIDE PRODUCTS (42) + (116)			
(115) R = Me; X = I	69	:	31	R = Me
(157) R = Me; X = BPh_4	45	:	55	
	(41) + (112)			
(113) R = Ph; X = Br	49	:	51	R = Ph
(158) R = Ph; X = BPh_4	20	:	80	

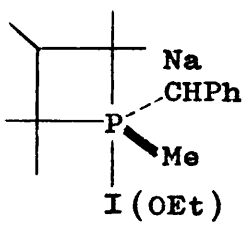
The ylides obtained from the tetraphenylborate salts (157) and (158) would not form phosphoranes involving the non-nucleophilic tetraphenylborate anion and hence no ylide isomerisation *via* phosphoranes of this type could occur.

The results show that there was less interconversion of the ylides derived from the tetraphenylborate salts (157) and (158) than with those derived from the halide salts (115) and (113). Thus ylide isomerisation occurs *via* pseudorotation of ylide-lithium halide adducts. The small amount of interconversion that did occur with the ylides derived from the tetraphenylborate salts is presumably due to some other mechanism or alternatively other anionic species complexed with the ylide to form a phosphorane capable of pseudorotation.

Similarly, Wittig olefin synthesis with *r*-1-benzyl-1,2,2, *trans*-3,4,4-hexamethylphosphetanium iodide (115), benzaldehyde and ethanolic sodium ethoxide gave in high yield a mixture of phosphetan 1-oxides. Presumably pseudorotation of an intermediate adduct, e.g. (159), was also responsible for this non-stereospecific reaction.



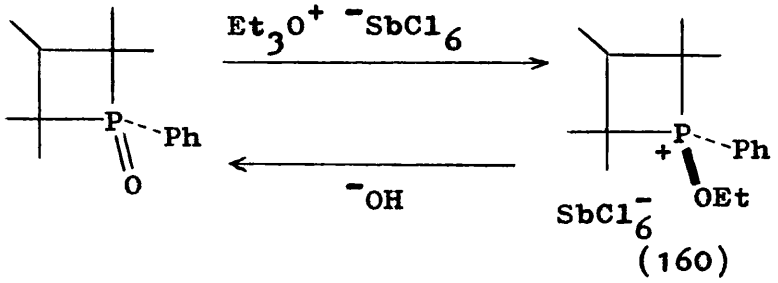
(115) 35 : 65



(159)

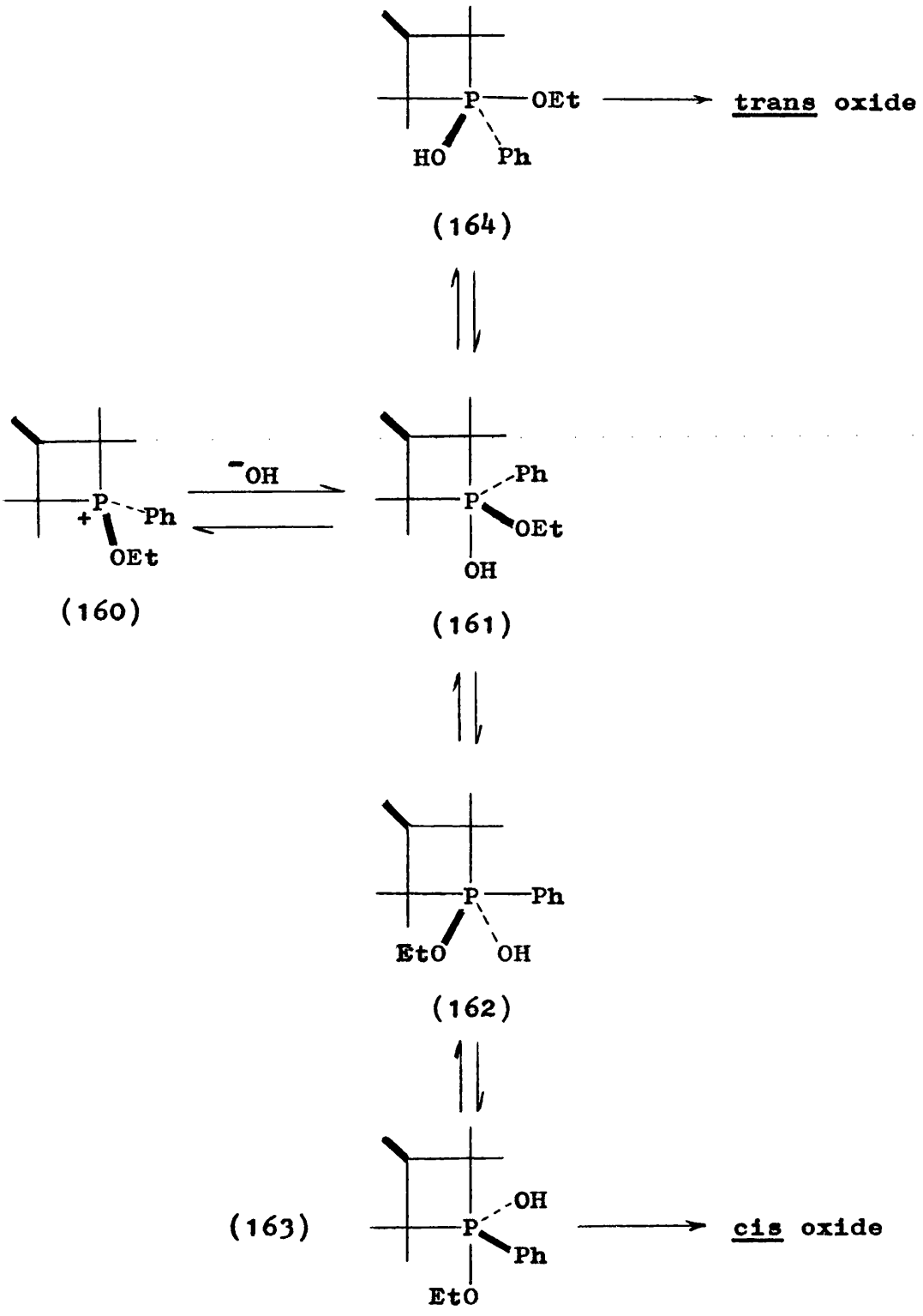
6.6 Ethoxyphosphetanium Salts.

Whereas the base-catalysed hydrolysis of ethoxyphosphonium ions derived from acyclic phosphine oxides proceed with overall inversion of configuration,[91] the same nucleophilic displacement reaction proceeds with overall retention of configuration when the phosphorus atom is constrained in the phosphetan system; Mislow[101] showed that hydrolysis of both isomers of 1-ethoxy-2,2,3,4,4-pentamethyl-1-phenylphosphetanium hexachloroantimonate (160) produced oxides by phosphorus-oxygen cleavage whose stereoisomeric composition was the same as the oxides from which the salts were synthesised by O-ethylation.



(160)

The mechanism proposed to explain the retention of configuration at phosphorus on hydrolysis involves apical attack on the phosphetanium ion (160) to give the intermediate (161) of trigonal bipyramidal geometry. Two pseudorotation pathways are open to the intermediate; retention requires one pseudorotation about phenyl. Inversion requires two pseudorotations, the last step, (162) to (163), involving rearrangement from relatively unfavourable placements to favourable, since equatorial and apical positions are positions of relative preference for more electropositive and



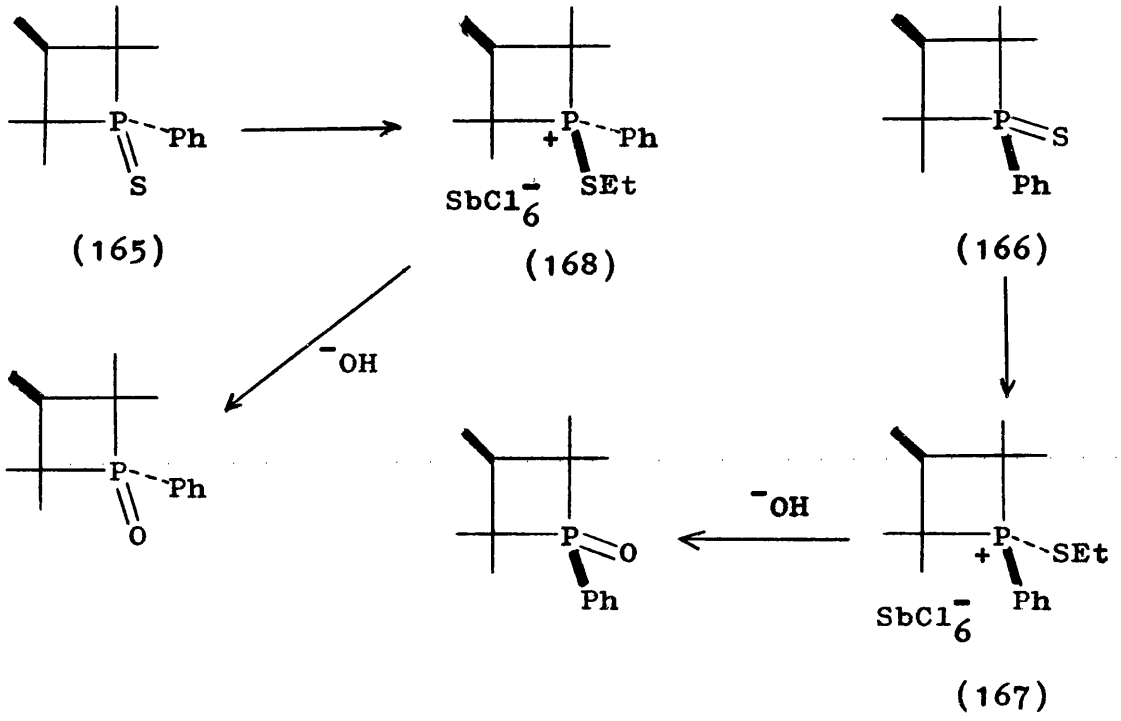
electronegative groups respectively.[39] It is likely, therefore, that this step is a fast one and that the first pseudorotations are rate-determining. In the reaction of the r-1-ethoxy-2,2,cis-3,4,4-pentamethyl-1-phenylphosphetanium salt (160) pseudorotation about phenyl (retention) to (164)

merely exchanges the apical and equatorial positions of the electronegative ethoxy and hydroxy groups, whereas pseudorotation about ethoxy (inversion) to (162) places both electronegative groups in equatorial positions and the relatively electropositive in the apical position, an energetically unfavourable arrangement. It follows that retention is the preferred pathway. In the reaction of the isomeric salt a similar argument leads to the same conclusion.

6.7 Ethylthiophosphetanium Salts.

Retention is the stereochemical course followed when ethoxyphosphetanium salts are decomposed by base because of the clear-cut distinction between the stereochemical preferences of the groups on phosphorus and the preference of the small ring for the apical-equatorial position in the intermediate phosphoranes. The same factors are held responsible for the observed retention of configuration in displacements at the phosphoryl group of phosphetans. In contrast, the similar electronegativities of the groups occupying the equatorial positions in the initial phosphoranes involved in the base-catalysed decompositions of 1-benzyl-1-methyl- and 1-benzyl-1-phenyl-phosphetanium salts, leads to the observed non-stereospecific displacements.

Sulphur and carbon are held to have similar electronegativities[106] and therefore one might expect alkylthio-phosphetanium salts to undergo non-stereospecific hydrolysis. The isomeric salts (167) and (168) were synthesised by S-ethylation with triethyloxonium hexachloroantimonate of the cis phosphetan sulphide (166) and the trans phosphetan sulphide (165), respectively.



Whereas Mislow[91] has shown that the alkaline hydrolysis of ethylthiophosphonium ions derived from acyclic phosphine sulphides proceed with overall inversion of configuration the alkaline hydrolysis of these stereoisomeric ethylthiophosphetanium salts occurred stereospecifically with complete retention of configuration. The salt (168) derived from the trans sulphide (165) gave only the trans oxide and the salt (167) derived from the cis sulphide (166) gave only the cis oxide.

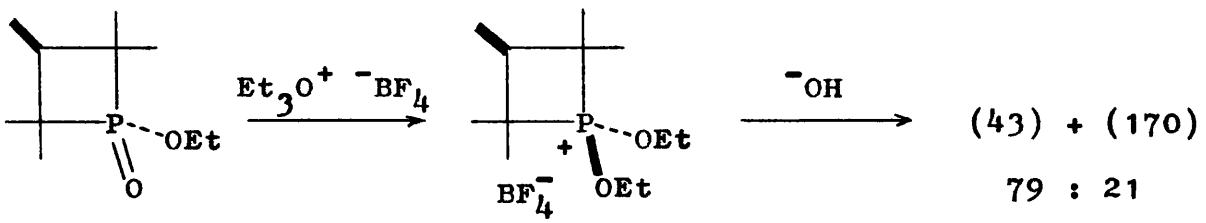
On the basis of the assumption that the mechanism of the alkaline hydrolysis of the ethylthiophosphetanium salts (167) and (168) parallels that proposed[101] for the alkaline hydrolysis of the ethoxyphosphetanium salts the initial phosphorane formed by apical attack of hydroxide ion on the ethylthiophosphetanium ion, follows the pseudorotation pathway leading to retention because of the difference in stereochemical preferences of its two equatorial groups. The

stereospecific hydrolysis of the isomeric ethylthio salts shows that there is a distinct preference by the ethylthio group, relative to the phenyl group, for the apical position in phosphoranes.

Similarly the reduction of phosphetan 1-oxides with trichlorosilane in the presence of triethylamine affords phosphetans with retention of configuration[14], in contrast to the inversion observed in the analogous reduction of acyclic phosphine oxides.[107] In the phosphetan reduction the stereochemical preferences of the groups of the phosphorane involved favour the pseudorotation pathway leading to retention of configuration.[101]

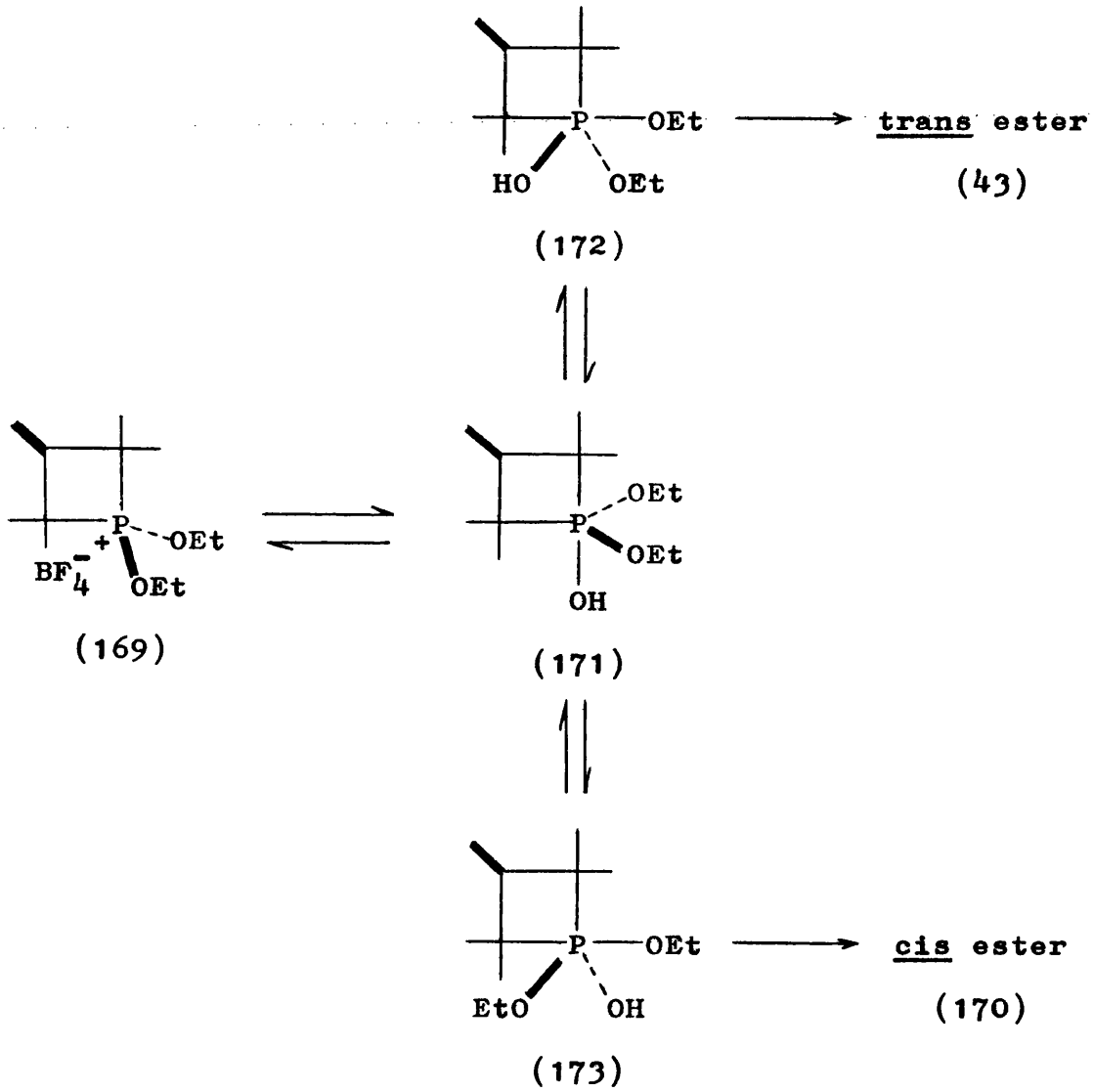
6.8 1,1-Diethoxy-2,2,3,4,4-pentamethylphosphetanium Tetrafluoroborate.

O-ethylation of r-1-ethoxy-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (43) with triethyloxonium tetrafluoroborate gave the diethoxyphosphetanium salt (169) in good yield. Alkaline hydrolysis of the salt gave 1-ethoxy-2,2,3,4,4-pentamethylphosphetan 1-oxide whose stereoisomeric composition was cis (170): trans (43) = 21:79. Known ratios of the products were unaffected when submitted to the reaction conditions.



(43) (169)

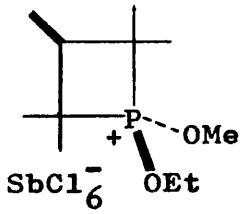
Apical attack of hydroxide ion on the phosphetanium ion gives the initial phosphorane (171), or its mirror image, in which the ring occupies an apical-equatorial position. For departure to occur from an apical position the phosphorane must pseudorotate to give the phosphoranes (172) and (173) which decompose to give the esters (43) and (170) respectively.



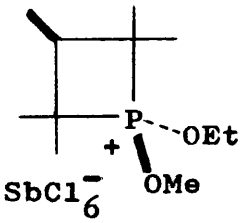
Thus in order for the salt (169) to give both ester products upon hydrolysis, pseudorotation from (171) to (172) and (173) must occur. This is reasonable as the stereoelectronic transformations involved in these two pseudorotations are identical.

If loss of ethoxide from the ultimate phosphoranes (172) and (173) is the rate-limiting step, as was loss of the benzyl anion in the analogous hydrolysis of 1,1-dibenzyl-2,2,3,4,4-pentamethylphosphetanium bromide, then the product ratio reflects the relative energy barriers for these processes. As in the dibenzyl case the energy barrier for decomposition to the trans oxide is lower than that for decomposition to cis oxide. Alternatively, if the pseudorotations to (172) and (173) are the rate-limiting steps then the product ratio indicates the relative energy barriers for these pseudo-rotations. As the electronic factors involved in these pseudo-rotations are identical the preference for the pseudorotation leading to the trans ester (43) must be due to a steric factor.

DeBruin and Jacobs[108] studied the alkaline hydrolysis of the isomeric 1-ethoxy-1-methoxy-phosphetanium salts (174) and (175) which give four ester products. On the basis of



(174)



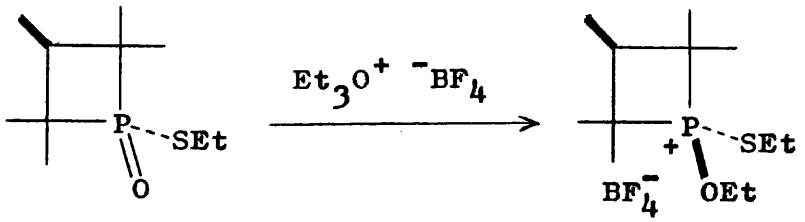
(175)

the results obtained by Cremer and Trivedi,[73] that indicate that the phosphorane intermediates involved in the methoxy-group exchanges of both isomers of 1-methoxy-2,2,3,4,4-pentamethylphosphetan 1-oxide exist as the mono-anions, they assumed that the intermediates involved in the alkaline hydrolysis of (174) and (175) existed as the mono-anions. Hence the pseudorotations of the initial intermediates formed

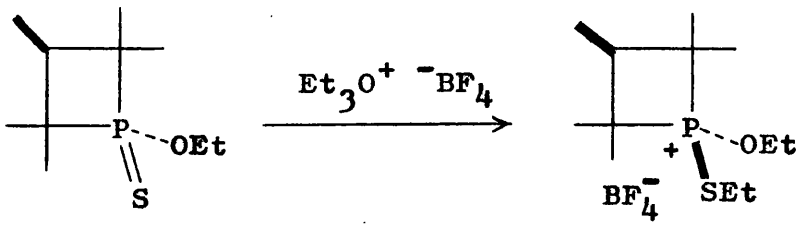
by apical attack of hydroxide ion on the salts (174) and (175) were postulated to be irreversible. This view is in conflict with the observation that hydroxide ion interconverts isomeric alkylarylphosphetanium salts. In spite of this objection, their conclusion, from an analysis of product ratios, that the pseudorotations of the phosphoranes involved in the hydrolysis were not the rate-limiting steps still stands.

6.9 Ethoxyethylthiophosphetanium Salts.

O-ethylation of r-1-ethylthio-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (44) with triethyloxonium tetrafluoroborate gave the phosphetanium salt (176). The isomeric salt (177) was produced by S-ethylation of r-1-ethoxy-2,2,trans-3,4,4-pentamethylphosphetan 1-sulphide[32] (20) with the same oxonium salt. Alkaline hydrolysis of



(44) (176)



(20) (177)

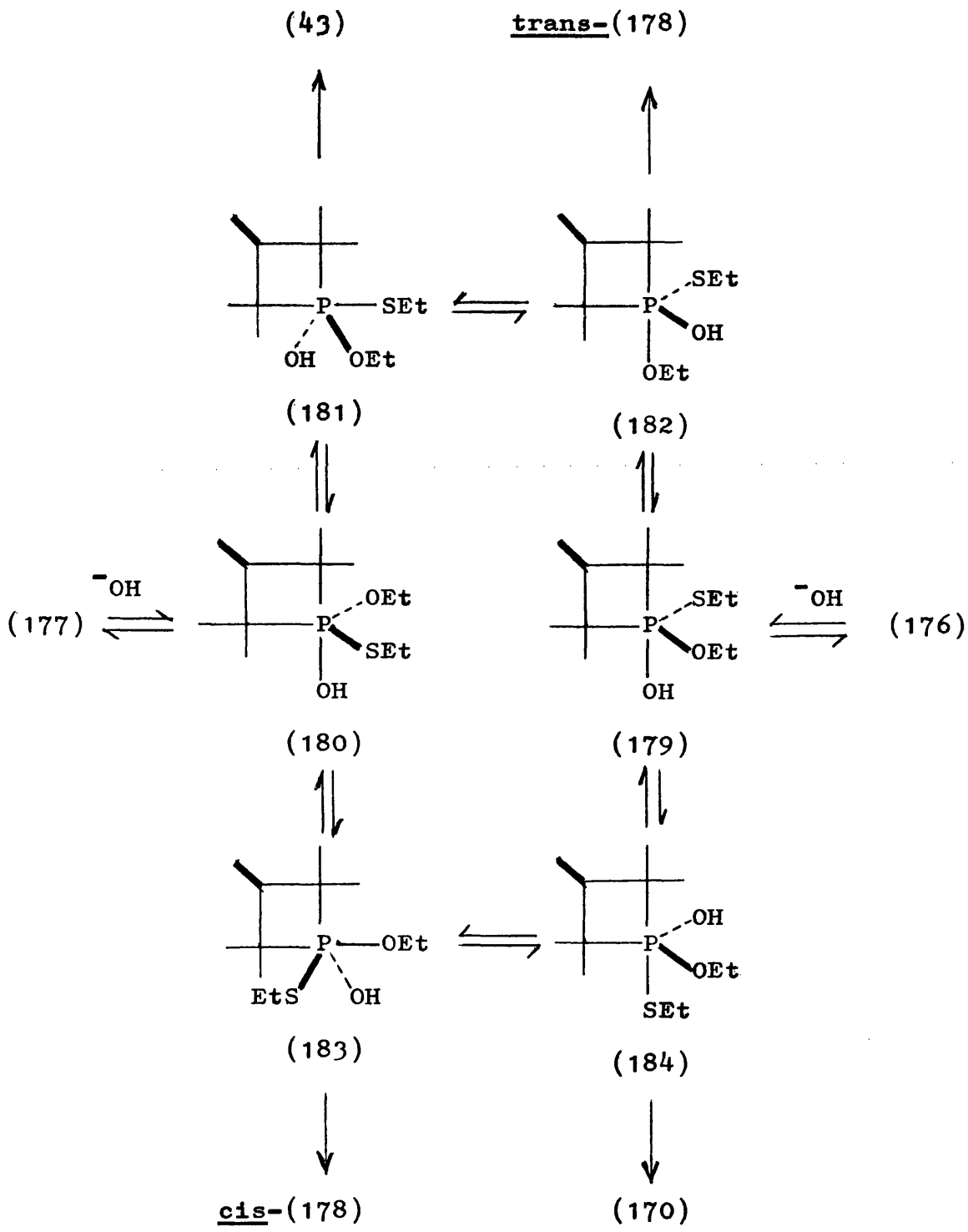
these isomeric salts under identical conditions yielded different mixtures of both the esters (43) and (170) and 1-ethylthio-2,2,3,4,4-pentamethylphosphetan 1-oxide (178). The relative amounts of the products were obtained by n.m.r. integration. In the hydrolysis products the isomeric thio esters could not be distinguished by n.m.r. spectroscopy. Known ratios of the products were unaffected when submitted to the reaction conditions.

Products from hydrolyses of phosphetanium Salts

SALT	YIELD OF PRODUCTS (%)		
	(43)	(170)	(178)
(176)	45%	43%	12%
(177)	53%	32%	15%

Scheme VII shows the phosphoranes and their relation to the products, involved in these hydrolyses. If one assumes apical attack then (179) and (180) are the initial phosphoranes formed from (176) and (177). Apical departure necessitates pseudorotation to give the ultimate phosphoranes (181), (182), (183), and (184) which decompose to give (43), trans-(178), cis-(178), and (170) respectively.

Since different ratios of the products are obtained from the isomeric salts it follows that decomposition of the ultimate phosphoranes is not the rate-limiting step, and that the stereoelectronic preferences of ethoxy and ethylthio groups are similar even though sulphur and oxygen have very different electronegativities.[106]

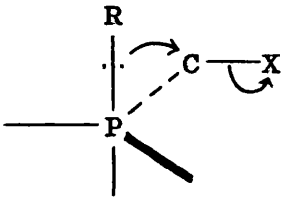

(43)
trans-(178)
SEt
OH
OEt
(181)
(182)
(177)
-OH
(176)
(180)
(179)
EtS
(183)
(184)
cis-(178)
(170)

SCHEME VII

Ring Openings and Ring Expansions of Phosphetans

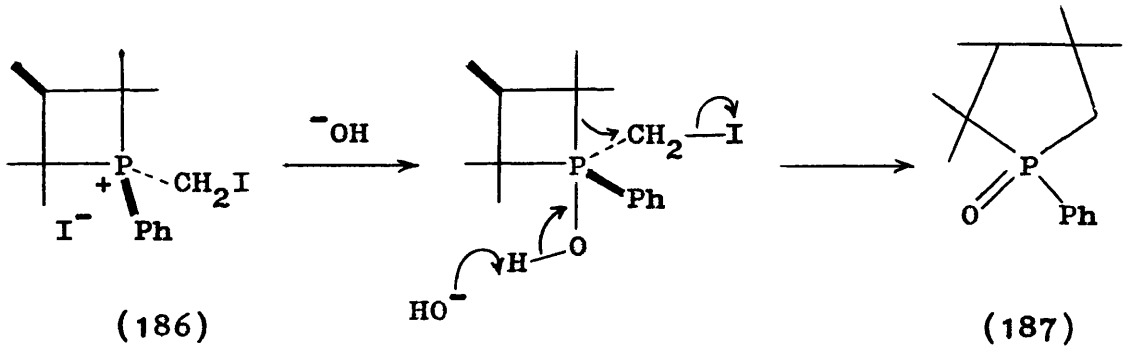
7.1 The Alkaline Hydrolyses of Phosphetanium Salts giving Ring-expanded Products.

A number of rearrangements are known which conform to the general pattern (185) in which a group occupying an apical position in a trigonal bipyramidal intermediate migrates to an α-carbon bearing a substituent which can accommodate a negative charge.[109] When R is part of a four-



(185)

or five-membered ring preference of the ring for an apical-equatorial position and relief of ring strain leads to ring expansion. Thus alkaline hydrolysis of the iodomethyl salt (186) gave the phospholan oxide (187).[15]

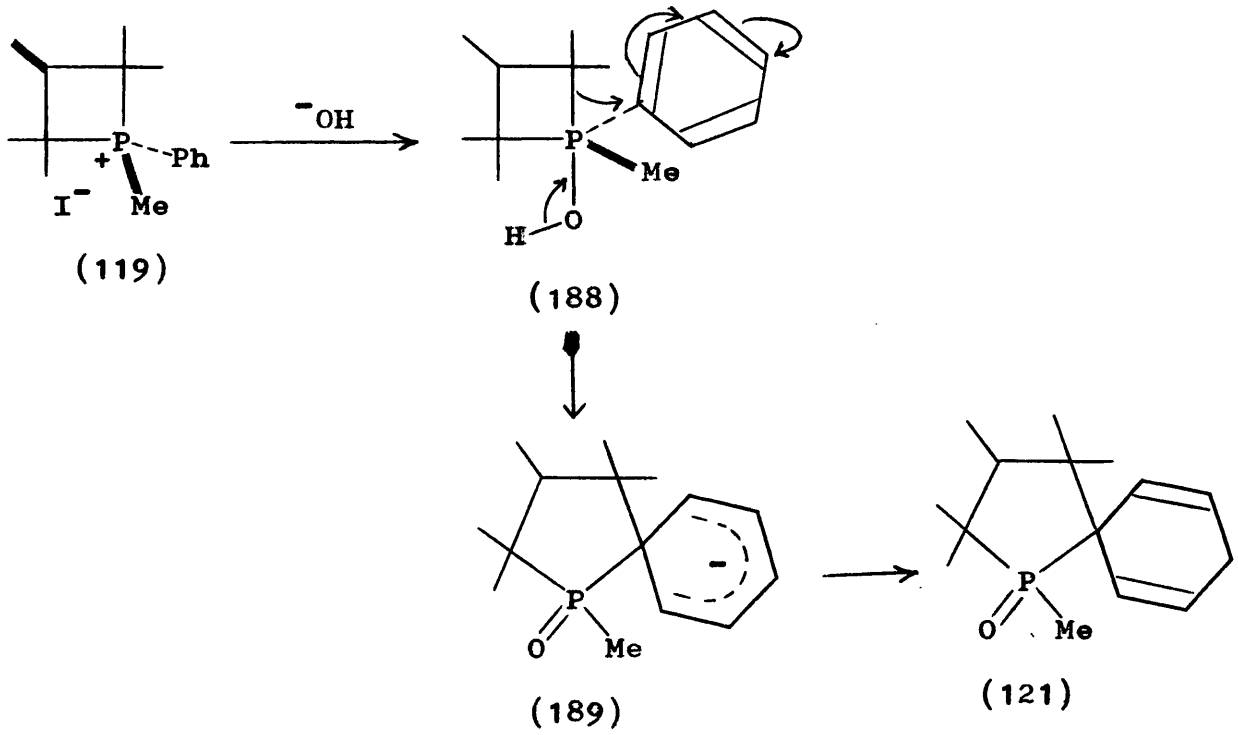


(186) (187)

a) 1,2,2,3,4,4-Hexamethyl-1-phenylphosphetanium Iodide.

Also conforming to the general pattern (185) was the alkaline hydrolysis of r-1,2,2,cis-3,4,4-hexamethyl-1-phenyl-phosphetanium iodide (119) which gave a phosphine oxide whose structure was shown to be the spirophospholan oxide (121) by

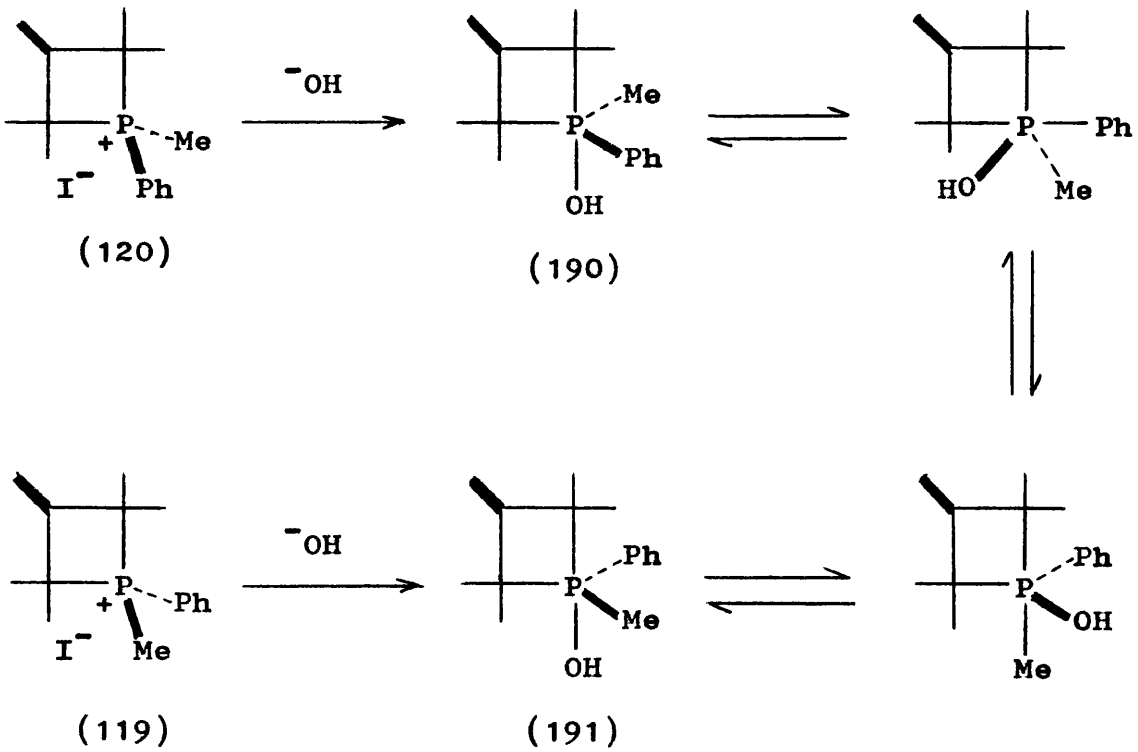
spectroscopic[15] and deuterium labelling experiments.[19,110] The reaction was postulated as going via the intermediate (188) whose apical position was occupied by a poor leaving group so that the most favourable process was migration of the apical $-CMe_2$ group to give the intermediate cyclohexadienyl anion (189) which was rapidly protonated to give the non-conjugated oxide (121). Even though there are two possible stereoisomers of the phospholan oxide only one was isolated.



The isomeric salt, r-1,2,2,trans-3,4,4-hexamethyl-1-phenylphosphetanium iodide (120), was prepared and hydrolysed to determine whether it gave the stereoisomeric phospholan oxide. It was found that both pure stereoisomeric phosphetanium salts (119) and (120) afforded the same ring-expanded oxide (121), the geometry of which is unknown. There was spectroscopic evidence of the presence of a small

amount ($\langle 3\%$) of a second isomer of (121) in the hydrolysis product of both salts but it could not be isolated.

As the isomeric salts undergo hydrolysis to give the same phosphine oxide products it is likely that they are equilibrated prior to ring expansion of the hydrolysis intermediate. Presumably rapid pseudorotation leads to equilibration of the intermediates (190) and (191) formed by apical attack of hydroxide ion on the isomeric salts. Migration of the ring from the apical position of the predominant intermediate then gives the phospholan oxide (121).

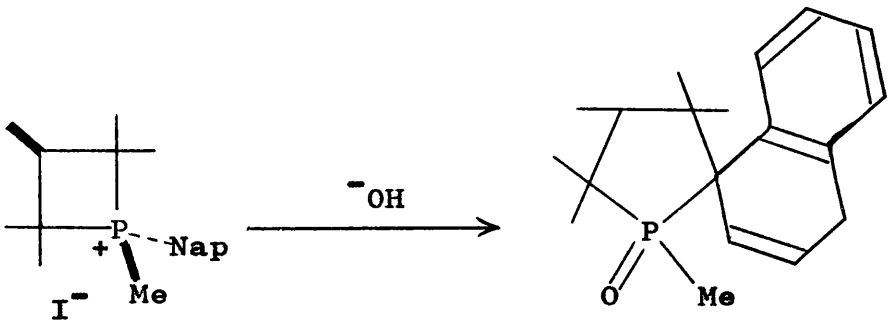


(120) (190)

(119) (191)

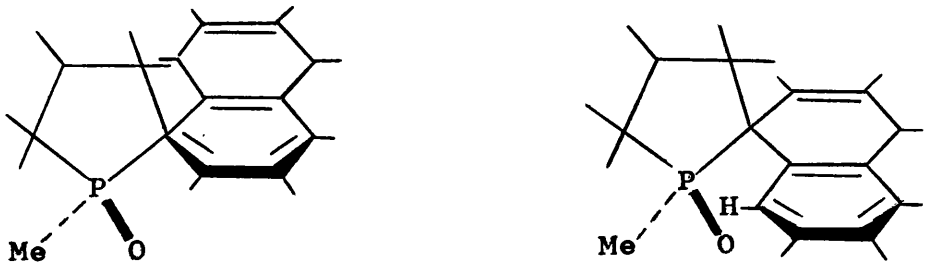
b) <u>1,2,2,3,4,4-Hexamethyl-1-(1-naphthyl)phosphetanium Iodide</u>.

Hydrolysis of this salt (192) occurred in an analogous manner to give the spirophospholan oxide (193), whose ^{1}H n.m.r. spectrum showed that only one stereoisomer was formed. The



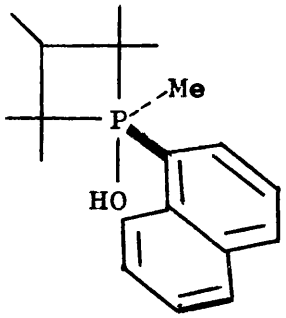
(192) (193)

aromatic region of the spectrum is of interest in that one aromatic proton (τ1.38-1.70) had quite a different chemical shift to the other three (τ2.62-2.93). That only one proton is shifted downfield can be related to the stereochemistry of the product. Only in the structure (195) is one aromatic proton close enough to the phosphoryl oxygen to be shifted. In the alternative structure (194) all the aromatic protons would have similar chemical shifts. The relationship of the substituents on the 3-carbon to those on phosphorus is unknown.

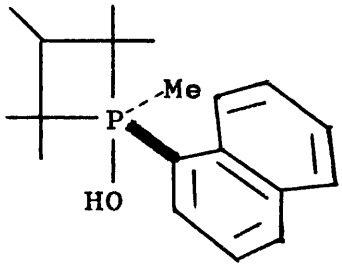


(194) (195)

Hydrolysis gives the oxide (195) because of the difference in steric crowding in the intermediate phosphoranes (196) and (197), which can be formed by apical attack of hydroxide ion on the phosphetanium ion. Molecular models



(196)

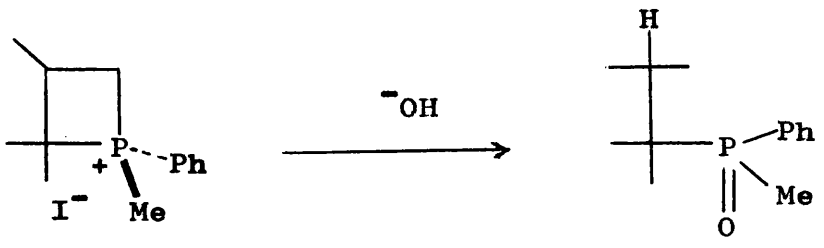


(197)

show there is more crowding in (197) than in (196), thus attack of hydroxide to form (196) is kinetically preferred. The intermediate (196) decomposes by apical migration of the ring $-CMe_2$ to give (195); (197) would give the isomeric oxide (194).

7.2 <u>The Alkaline Hydrolysis of Phosphetanium Salts giving Ring-opened Products</u>.

Whereas the isomeric 1-methyl-1-phenylphosphetanium salts (119) and (120) underwent ring expansion on alkaline hydrolysis, Fishwick and Flint[111] showed that the corresponding 1,2,2,3-phosphetanium salt (198) gave the ring-opened phosphine oxide (199) presumably because the $-CH_2$ carbanion is more stable than the $-CMe_2$ carbanion. The more stable $-CH_2$ carbanion does not attack the phenyl group to

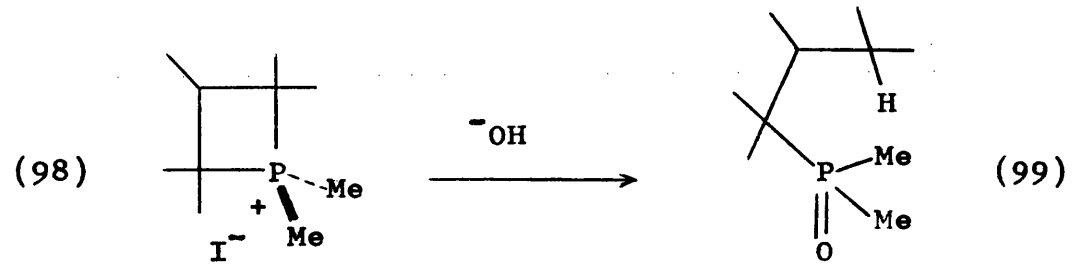


(198) (199)

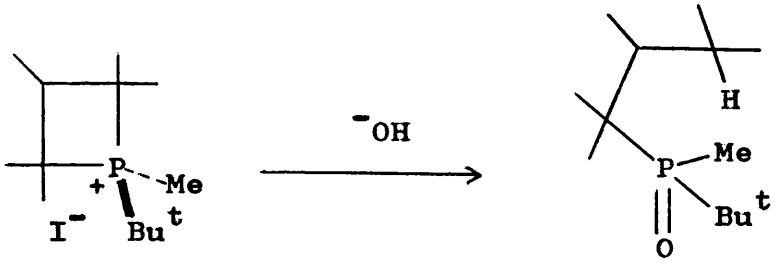
give a spirophospholan oxide but separates and is protonated to give the ring-opened product.

a) 1,1,2,2,3,4,4-Heptamethylphosphetanium Iodide.

It has previously been shown in this thesis that base decomposition of the heptamethylphosphetanium salt (98) occurs with expulsion of the $-CMe_2$ carbanion from the intermediate phosphorane to give the ring opened oxide (99).

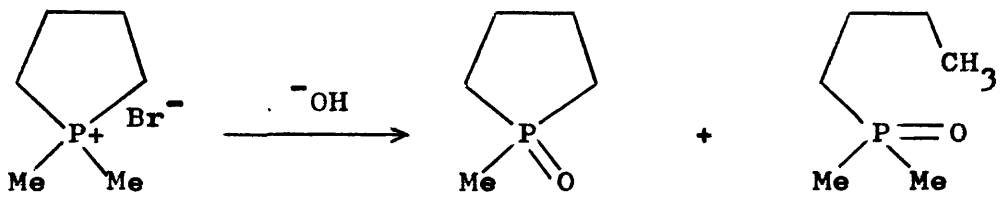


Similarly, Cremer[112] has shown that both the isomers of the salt (200) decompose in base with ring opening to give the oxide (201).



(200) (201)

Marsi[25] found that base decomposition of (202) resulted in expulsion of methyl external to the ring to give (203), ring cleavage giving (204) being a minor reaction.

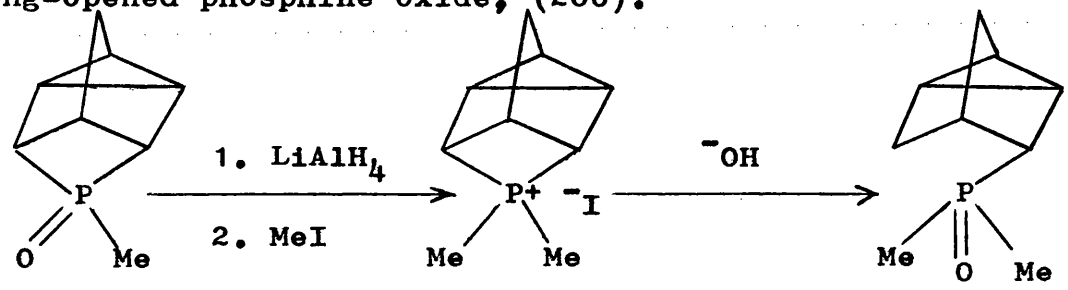


(202) (203) (204)

80% 20%

b) 2,2,-Dimethyl-2-phospha(IV)tetracyclo[3,2,1,$O^{3,6}$, $O^{3,6}$,$O^{4,7}$]octane Iodide.

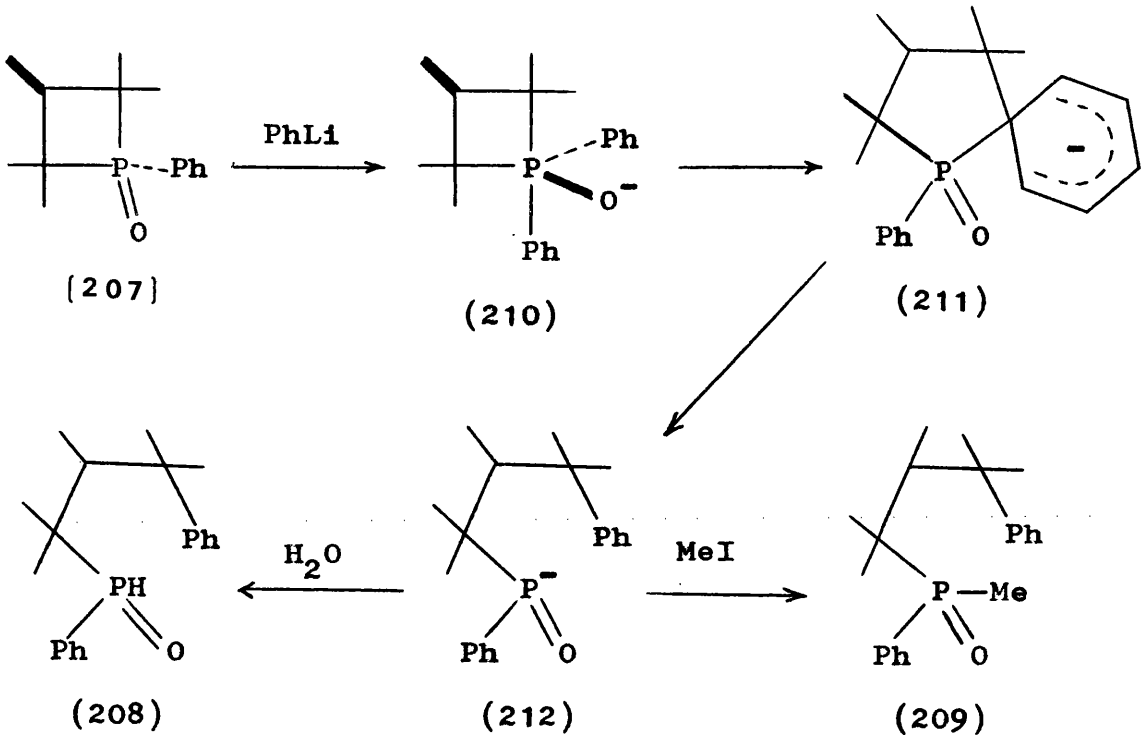
This phosphetanium salt (205) was prepared by quaternisation with iodomethane of a solution of the phosphine obtained by lithium aluminium hydride reduction of the phosphine oxide (11).[10] On treatment with sodium hydroxide solution this salt was hydrolysed in the same manner as the heptamethylphosphetanium salt (98) giving the hygroscopic ring-opened phosphine oxide, (206).



(11) (205) (206)

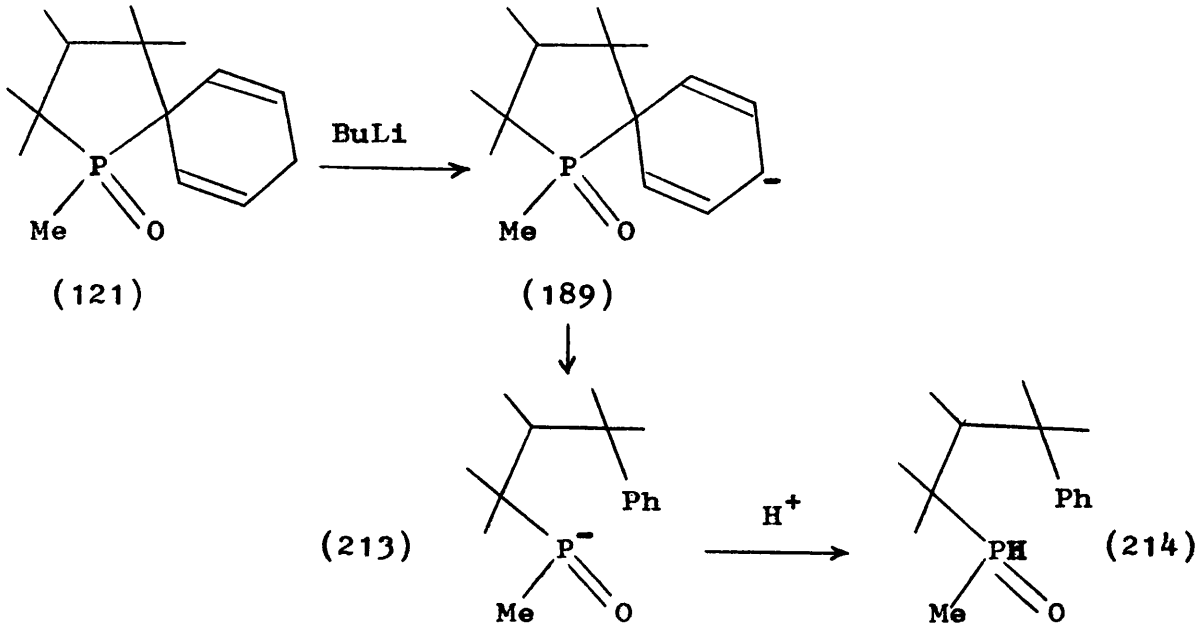
7.3 Reaction of Phenyl-lithium with 2,2,3,4,4-Pentamethyl-1-phenylphosphetan 1-oxide.

Hawes and Trippett[19] found that protonation of the product from thereaction of phenyl-lithium with the phosphetan 1-oxide (207) gave the secondary phosphine oxide (208), while addition of iodomethane to the mixture gave the oxide (209). They proposed that the reaction occurred by initial attack of phenyl-lithium at phosphorus to give a pentacovalent species (210) which subsequently underwent ring expansion to a cyclohexadienyl anion (211), analogous to the intermediate anion (189) postulated in alkaline hydrolysis of the salt (119). Since in this reaction mixture the anion (211) cannot be protonated it rearomatises with ring opening to form the anion (212), which on protonation and methylation gives the oxides (208) and (209) respectively.



(207) (210) (211) (208) (212) (209)

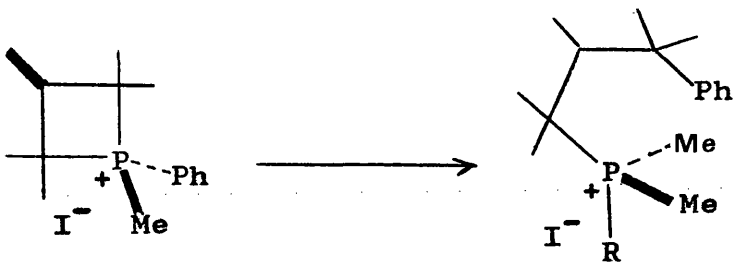
The intermediacy of the cyclohexadienyl anion (211) was demonstrated by treatment of the spirophospholan oxide (121), the oxide formed on hydrolysis of 1,2,2,3,4,4- hexamethyl-1-phenylphosphetanium iodide (119), with butyl-lithium. This generated the cyclohexadienyl anion (189), by removal of an allylic proton, which rearranged to the acyclic anion (213) as protonation of the reaction mixture gave the secondary phosphine oxide (214).



(121) (189) (213) (214)

7.5 Reaction of Butyl-lithium with r-1,2,2,cis-3,4,4-Hexamethyl-1-phenylphosphetanium Iodide.

Reaction of the salt (119) with butyl-lithium in an attempt to generate the methylene ylide gave, after methylation of the reaction product with iodomethane, the acyclic phosphonium salt (215; R = Bu). This reaction probably

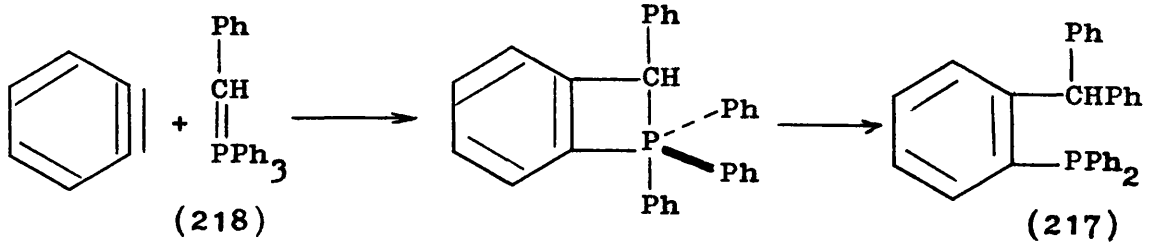


(119) (215)

occurred via ring-expansion of the pentacovalent intermediate formed by nucleophilic attack of butyl-lithium on the phosphorus atom of the salt (119), to give a cyclohexadienyl anion that rearomatised with ring opening to give, after quaternisation with iodomethane, the salt (215). It has been shown[22] that the same reaction with phenyl-lithium gives the analogous salt (215; R = Ph).

The formation of products derived from intermediate pentacovalent phosphoranes has previously been noted[113] in the action of alkyl-lithiums on acyclic phosphonium salts.

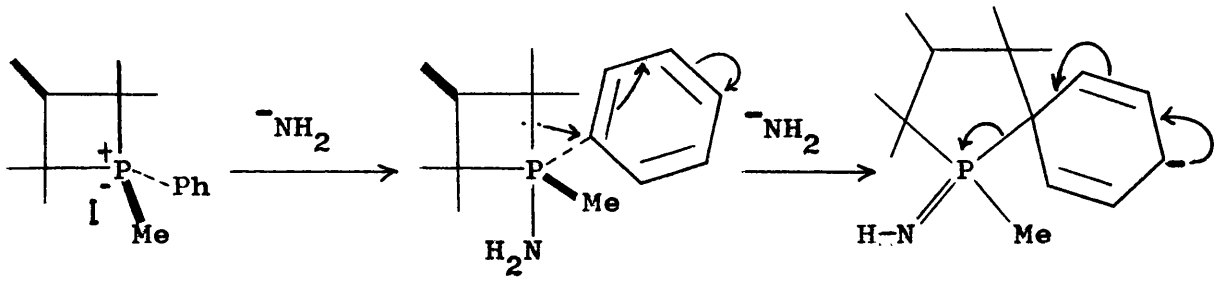
Zbiral has proposed[114] a similar rearrangement of the phosphorane intermediate (216) to account for the product (217) afforded by the reaction of benzyne with the ylide (218).



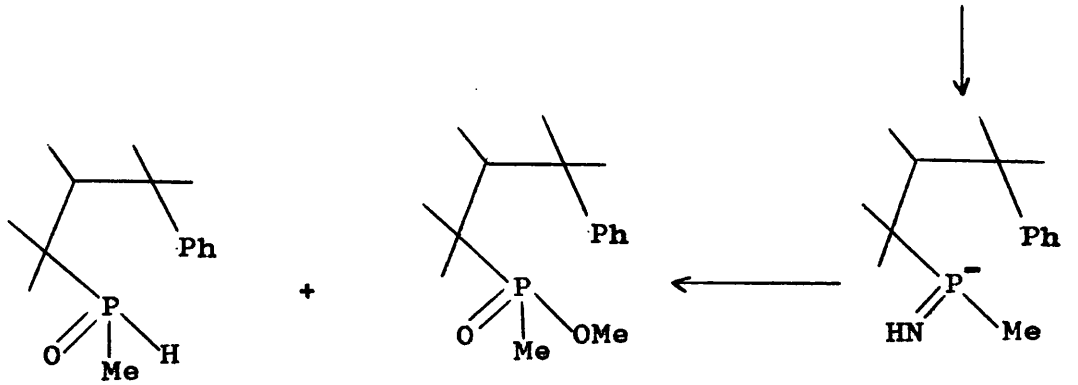
(218) (216) (217)

7.6 Reaction of Sodamide with r-1,2,2,cis-3-4,4-Hexamethyl-1-phenylphosphetanium Iodide.

All attempts to generate the methylene ylide from the salt (119) with sodamide in liquid ammonia also failed because of ring opening of the pentacovalent intermediate (218) formed by nucleophilic attack on phosphorus. After hydrolysis and methylation with diazomethane of the reaction product three crystalline compounds were isolated: the secondary phosphine oxide (214) and two diastereoisomers of the methyl phosphinate (219). These arise from the intermediate phosphorane (218) by ring-expansion to the anion (220) followed by feed-back of the negative charge leading to opening of the expanded anion to give the anion of the secondary phosphine imine (221), which on work-up gives the crystalline products (214) and (219).

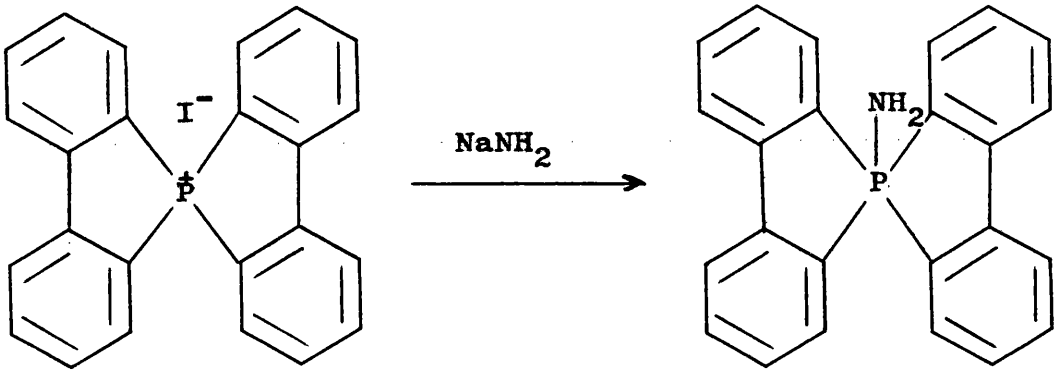


(119) (218) (220)



(214) (219) (221)

That the reaction involves initial formation of an aminophosphorane is supported by the recent observation of Hellwinkel and Wilfinger[115] that addition of sodamide to the phosphonium salt (222) gives the crystalline aminophosphorane (223). The structure is stabilised by the two small rings.



(222) (223)

Similarly formation of the intermediate imine (220) is supported by the observation that reaction of a tetraphenylphosphonium ion with sodamide gives the imine (224) plus benzene, presumably <u>via</u> expulsion of a phenyl anion from the intermediate aminophosphorane (225).[115,116]

$$Ph_4P^+ \xrightarrow{NaNH_2} Ph_4P\text{-}NH_2 \longrightarrow Ph_3P{=}NH + PhH$$

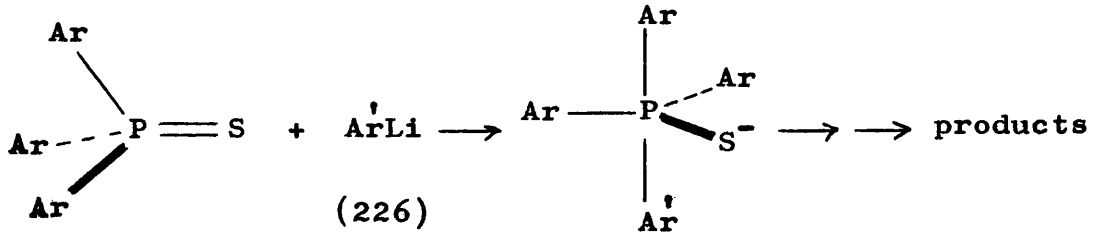
(225) (224)

7.7 <u>Reaction of Phenyl-lithium with 2,2,trans-3,4,4-Pentamethyl-r-1-phenylphosphetan 1-sulphide.</u>

Wittig and Cristau[117] showed that treatment of triphenylphosphine sulphide with phenyl-lithium gave triphenylphosphine and, after acidification, benzenethiol isolated as the disulphide. They envisaged the reaction as proceeding

via attack of the phenyl-lithium on sulphur.

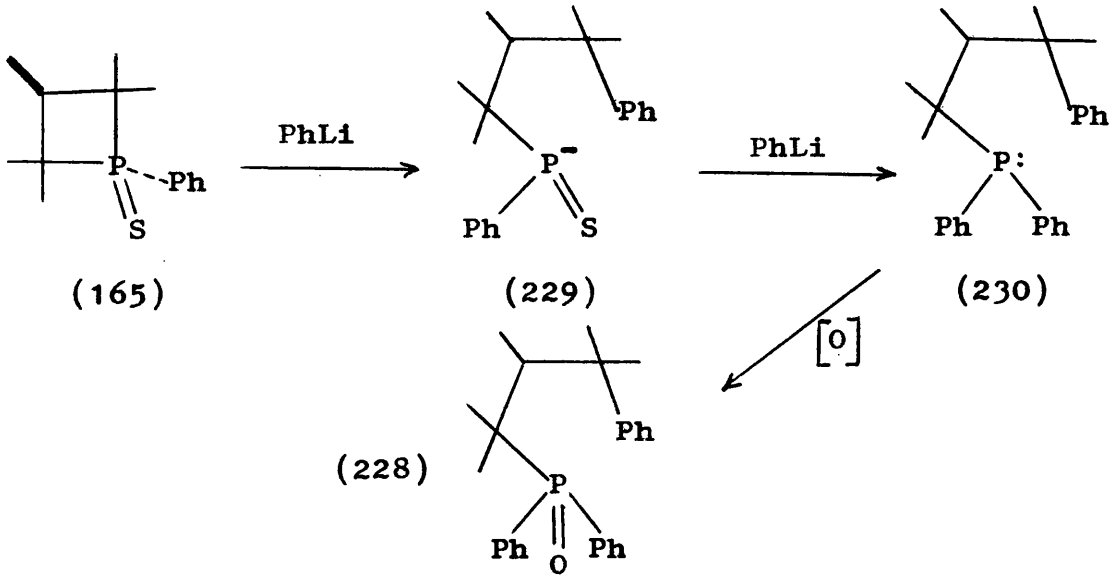
In order to determine the mechanism of the reaction p-tolyl-lithium was reacted with triphenylphosphine sulphide. It gave a 1:1 mixture of triphenylphosphine and diphenyl-p-tolylphosphine together with, after oxidation by air, a mixture of disulphides containing equal numbers of phenyl and p-tolyl residues. Correspondingly tri-p-tolylphosphine sulphide with phenyl-lithium, gave a 1:1 mixture of tri-p-tolylphosphine and phenyl-di-p-tolylphosphine. Apparently these reactions involve attack of the aryl-lithium (226) entirely on the phosphorus atom, to give a pentacovalent intermediate (227) in which the entering aryl group becomes equivalent to only one of the three original aryl residues, followed by loss of one of these two equivalent groups with sulphur. This situation could arise by apical attack of the



(227)

aryl-lithium opposite one of the aryl groups of the phosphine sulphide to give the phosphorane (227), which does not pseudo-rotate and decomposes only by loss of the aryl groups from the apical positions. Alternatively attack could occur only partly on the phosphorus atom and partly (ca. 30%) on sulphur. In this case the phosphorane intermediate (227) would be undergoing rapid pseudorotation making all the four aryl residues equivalent.

As the aryl group lost from the phosphorus atom probably occupied an apical position in the trigonal bipyramidal intermediate, it was of interest to study the behaviour of 2,2,trans-3,4,4-pentamethyl-r-1-phenylphosphetan 1-sulphide (165) in the same reaction in the expectation that a ring expansion or ring opening with migration to the sulphur atom might occur. When the sulphide (165) was treated with one molar proportion of phenyl-lithium, half the sulphide was recovered unchanged and the phosphine oxide (228) was isolated. Presumably opening of the phosphetan ring with migration of the phenyl group from phosphorus to carbon occurred via an intermediate cyclohexadienyl anion as occurs in the analogous reaction of 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxide with phenyl-lithium.[19,22] This would give the secondary phosphine sulphide anion (229). That treatment of diphenylphosphine sulphide with two molar proportions of phenyl-lithium gave a high yield of triphenylphosphine makes the assumption that the anion (229) will then react further with phenyl-lithium to give the phosphine (230) reasonable. Air oxidation of the phosphine gives the phosphine oxide product (228) isolated.



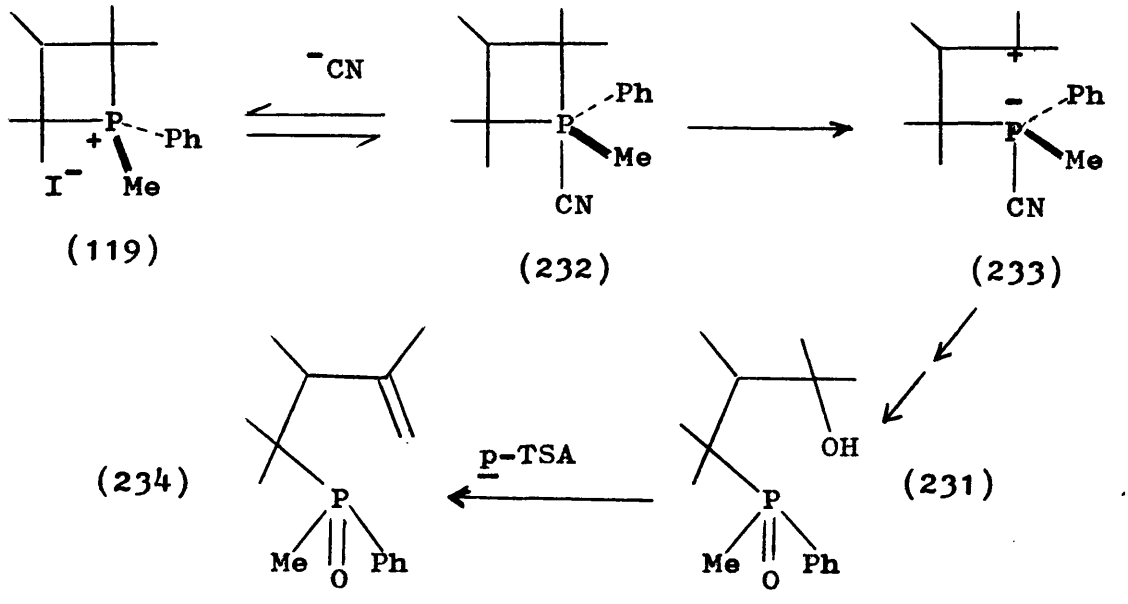
(165) (229) (230)

(228)

Wittig and Cristau[117] also showed that treatment of methylthiotriphenylphosphonium tetraphenylborate with phenyl-lithium gave triphenylphosphine and methyl phenyl sulphide. They also envisaged this reaction as proceeding *via* attack onsulphur. Treatment of ethylthiotriphenylphosphonium tetraphenylborate with *p*-tolyl-lithium gave triphenylphosphine and diphenyl-*p*-tolylphosphine in the ratio of 9:1. Here the predominant attack of the aryllithium is on the sulphur atom.

7.8 Reaction of Potassium Cyanide with 1,2,2,3,4,4-Hexamethyl-1-phenylphosphetanium Iodide.

Treatment of the salt (119) with potassium cyanide gave, after oxidation, two diastereoisomers of the tertiary alcohol (231). The nature of the products indicated that this ring opening mechanism did not involve an intermediate cyclohexadienyl anion or cleavage of a phosphorus-carbon ring bond by expulsion of a $-CMe_2$ carbanion. If the formation of the alcohols (231) involves the pentacovalent intermediate (232) the powerful inductive effect of the nitrile group induces ring opening to give the carbonium ion (233).



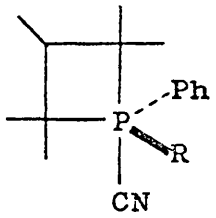
Support for formation of an intermediate was obtained experimentally: the unreacted salt recovered from a partial reaction involving stereoisomerically pure r-1,2,2,trans-3,4,4-pentamethyl-1-phenylphosphetanium iodide was a 1:1 mixture of stereoisomers, presumably because of pseudorotation of (232) formed by reversible attack of cyanide on phosphorus.

In the mass spectra of both isomers of the tertiary alcohol (231) the molecular ion was not observed. Dehydration of the major isomer gave an olefin (234) whose mass spectrum was identical with that of the alcohol. Thus the alcohols were being dehydrated in the mass spectrometer.

The Reactions of Halogens with 2,2,3,4,4-Pentamethyl-1-phenylphosphetan

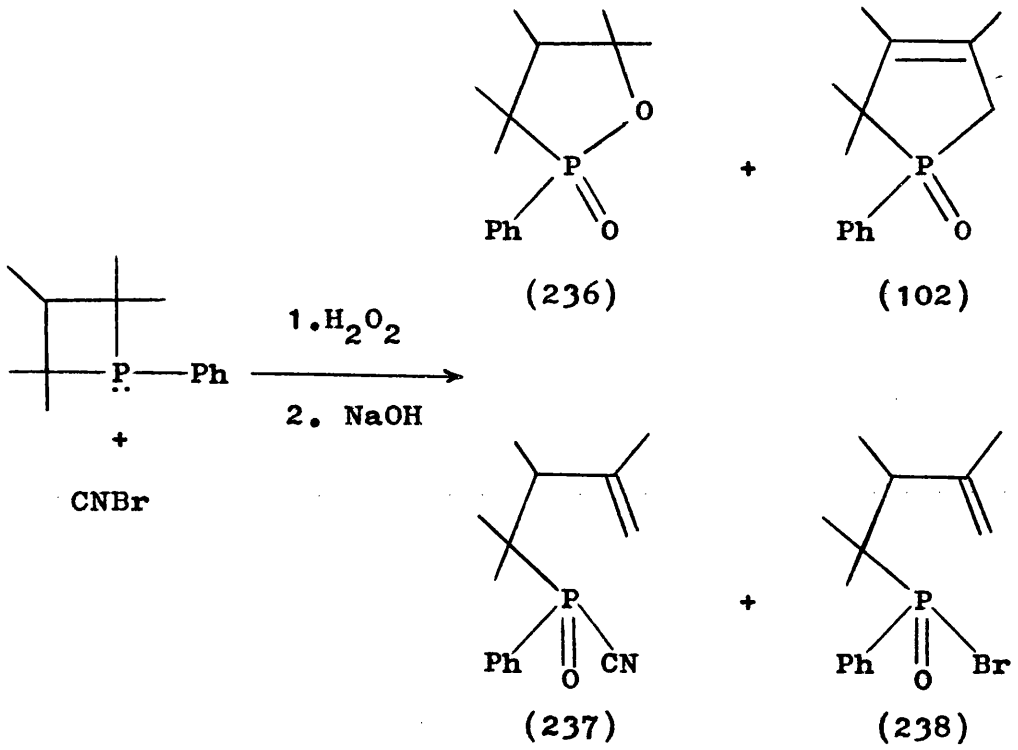
8.1 Cyanogen Bromide.

Finding that reaction of potassium cyanide with 1,2,2,3,4,4-hexamethyl-1-phenylphosphetanium iodide gave, *via* the phosphorane intermediate (235; R = Me), ring opened products prompted an investigation of the reaction of cyanogen bromide with 2,2,3,4,4-pentamethyl-1-phenylphosphetan to see if a similar ring opening occurred *via* the analogous intermediate (235; R = Br).



(235)

Surprisingly equimolar quantities of these reactants gave, after oxidation, alkaline hydrolysis and chromatography on acidic silica, 3,3,4,5,5-pentamethyl-2-phenyl-1,2-oxaphospholan 2-oxide (236) (30%) as a 1:1 mixture of stereoisomers, 1-phenyl-2,2,3,4-tetramethyl-3-phospholen 1-oxide (102) (7%), and the acyclic cyanophosphine oxide (237) (13%) as a 1:1 mixture of diastereoisomers. There was also evidence (mass spectrometry of the crude cyanophosphine oxide) for the formation of the bromophosphine oxide (238) but it could not be isolated. The products isolated were all identified by their physical properties and analysis. The structure of the cyanophosphine oxide was confirmed by its alkaline hydrolysis to the phosphinic acid (239). The mass spectrum of this acid showed peaks corresponding to dimeric

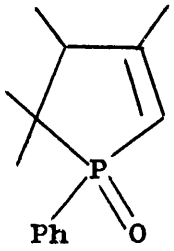


species. This behaviour of phosphinic acids has previously been noted by Dimroth[136] and Shutt.[100]

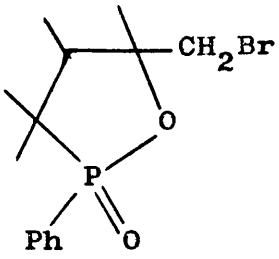
The 3-phospholen oxide (102) was unaffected by exposure to refluxing aqueous sodium hydroxide (4N) for two days, although this would cause the rearrangement of the double bond of certain other 3-phospholens to the 2,3 position.[118,119] This result agrees with the observation of Quin[118] that two methyl substituents on the double bond of a 3-phospholen prevents rearrangement.

A similar reaction of the phosphetan with a 1.5 molar equivalent of cyanogen bromide gave acidic and neutral products. The neutral products were identified as the 3-phospholen oxide (102) (42%) and a mixture of stereoisomers of 1-phenyl-3,4,5,5-tetramethyl-2-phospholen 1-oxide (240) (10%). The acidic product gave, after chromatography on acidic silica, one isomer of the neutral 5-bromomethyl-2-

phenyl-3,3,4,5-tetramethyl-1,2-oxaphospholan 2-oxide (241) (13%). This suggested that the bromomethyl-oxaphospholan oxide was formed by acid-catalysed cyclisation of an acyclic

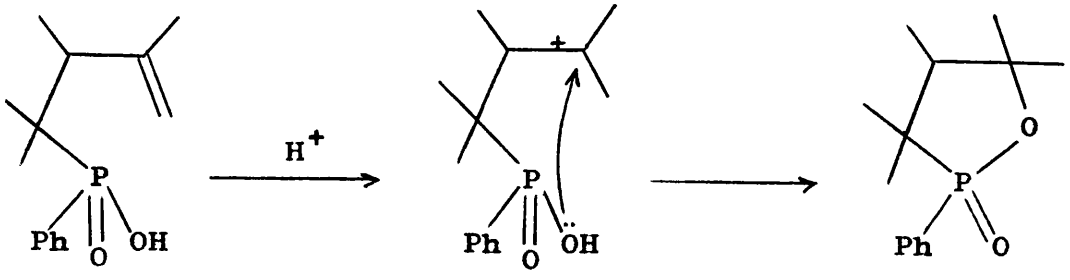


(240)



(241)

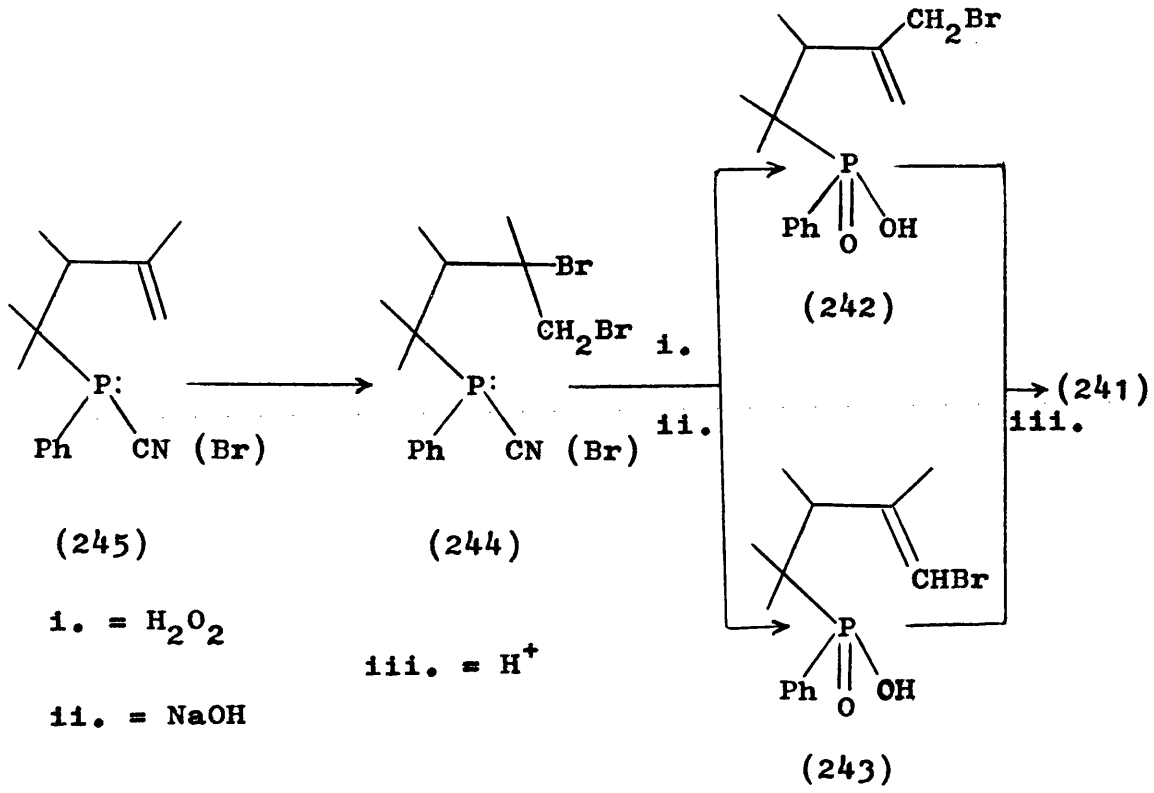
phosphinic acid, and presumably the oxaphospholan oxide (236) had a similar origin. In fact the phosphinic acid (239) cyclised readily on treatment with dilute hydrochloric acid and on chromatography on acidic silica to a 1:1 mixture of stereoisomers of the oxaphospholan (236), presumably by the mechanism illustrated: protonation giving the tertiary carbonium ion rather than the less stable primary ion.



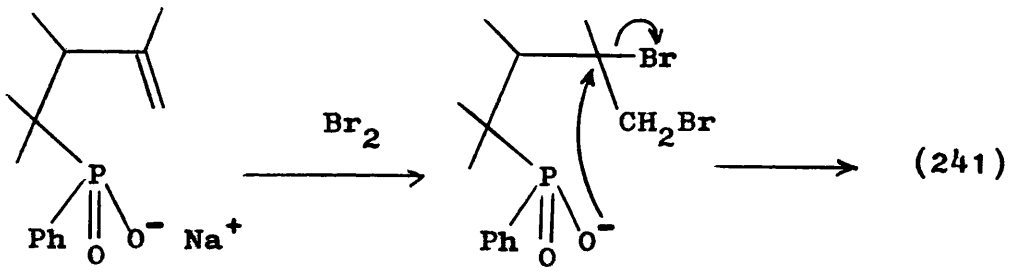
(239) (236)

By analogy the bromomethyl-oxaphospholan oxide (241) has its origin in the phosphinic acids (242) or (243). The formation of these acids might well be the result of dehydrobromination, during the alkaline work-up, of a dibromo compound (244) formed by bromination of but-3-enylphosphine (245) products in the reaction mixture. This is consistent with the isolation of the bromomethyl-oxaphospholan oxide only from

the reaction of the phosphetan with an excess of cyanogen bromide.



The bromomethyl-oxaphospholan (241) was also formed when bromine was added to the salt (246) of the phosphinic acid (239), presumably by intramolecular nucleophilic attack.



Finding that reaction of cyanogen bromide resulted in unusual ring openings and ring expansions prompted the investigation of the reaction of other halogens with 2,2,3,4,4-pentamethyl-1-phenylphosphetan.

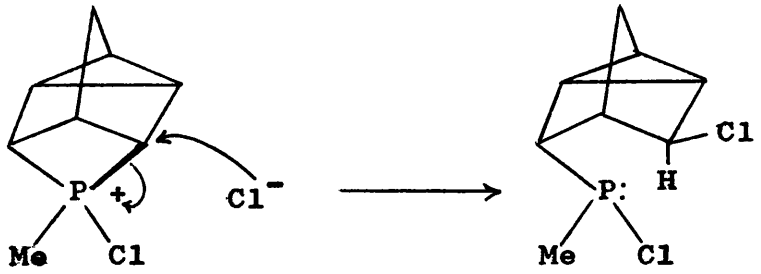
8.2 Chlorine.

Treatment of the liquid 2,2,3,4,4-pentamethyl-1-phenylphosphetan with one mole of chlorine in 1,2-dichloroethane at -20° gave, after evaporation of the solvent, the crystalline addition compound (247).[120,121] Pyrolysis of which gave in quantitative yield the but-3-enylchlorophosphine (248) as a 1:1 mixture of diastereoisomers. The chlorophosphine was also obtained on pyrolysis of the adduct from the reaction of the phosphetan with phosgene. The structure

(247) (248)

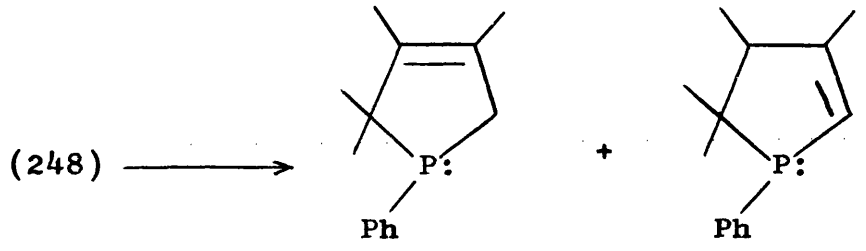
(248) was confirmed by the oxidation and alkaline hydrolysis to the phosphinic acid (239).

Green[10] observed a different ring opening reaction when the analogous phosphetan adduct (249) was pyrolysed. He found that it decomposed in the same manner as the halogen adducts of acyclic trialkylphosphines[122] to give the chlorophosphine (250) by the nucleophilic displacement illustrated.



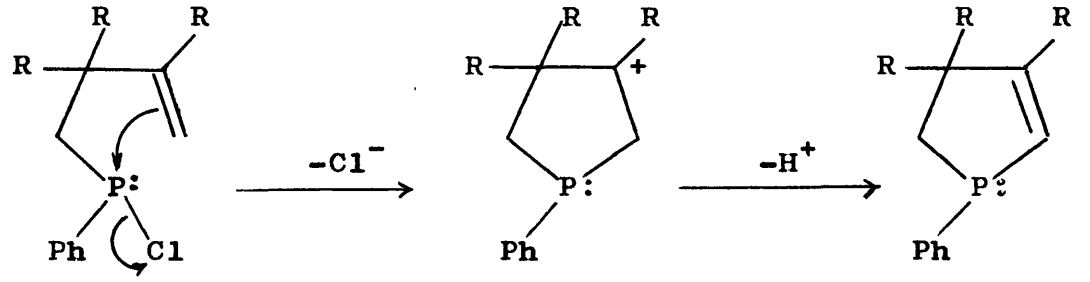
(249) (250)

At 150° the but-3-enylchlorophosphine (248) cyclised, with evolution of hydrogen chloride, to the 3-phospholen (103) containing 3% of the 2-phospholen (251). The structure of the major product was confirmed by preparation of an authentic sample by phenylsilane reduction[24] of 1-phenyl-2,2,3,4-tetra methyl-3-phospholen 1-oxide (102).



(103) (251)

Similarly, Oram[123] found that at 150° the phosphine (252; R = Me) gave the 2-phospholen (253; R = Me), whereas the phosphine (252; R = H) did not cyclise at 190°. Thus the cyclisation of but-3-enylchlorophosphines is aided by a 3-methyl substituent. This and the nature of the products from the cyclisation of (248) suggests the mechanism shown.



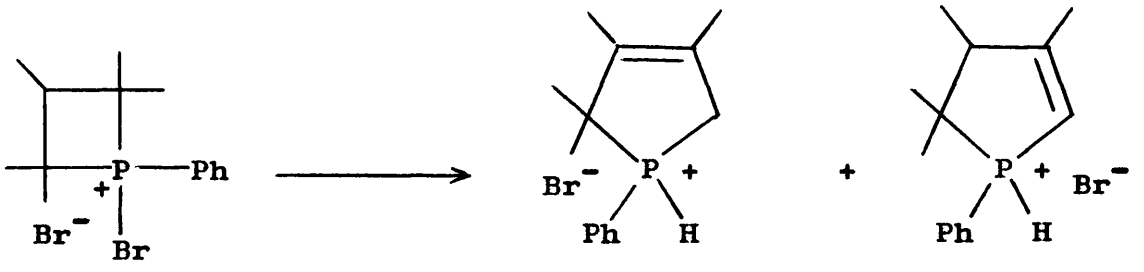
(252) (253)

Cyclisation of the but-3-enylchlorophosphine (248) was also catalysed by aluminium chloride; aqueous work-up gave a mixture of stereoisomers of 2,2,3,4,4-pentamethyl-1-phenyl-phosphetan 1-oxide (37% of 1:1 = cis:trans) and a mixture of 2- and 3-phospholens (103 and 251) (36% of a

1:5 mixture) which were isolated as the oxides. Similarly, aluminium chloride-catalysed cyclisation of the chlorophosphine (252; R = Me) gave 1-phenyl-2,2,3,3-tetramethylphosphetan 1-oxide and the 2-phospholen (253; R = Me), whereas the chlorophosphine (252; R = H) gave only the 2-phospholen (253; R = H).[123] Thus phosphetan formation is favoured by a 3-methyl substituent. Hence in these reactions formation of the phospholen ring presumably involves co-ordination of the aluminium chloride to the phosphorus, and phosphetan formation involves coordination to the olefin.

8.3 Bromine.

Treatment of 2,2,3,4,4-pentamethyl-1-phenylphosphetan with one mole of bromine in dichloromethane gave the crystalline adduct (254) which on pyrolysis gave a crystalline mixture of the 2- and 3-phospholen hydrobromides (255) and (256) (77% of a 2:9 mixture). The presence of a phosphorus-hydrogen

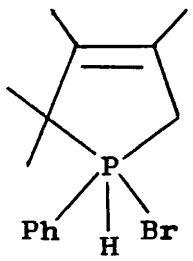


(254) (255) (256)

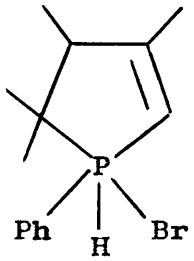
bond follows from the i.r. spectrum which showed $\nu_{max.}$ 2440 and 2220 cm^{-1}, and the ^1H n.m.r. spectrum which showed a very broad doublet centred at τ 0.67 (J_{PH} = 512 Hz). The structure of the 3-phospholen hydrobromide (255), the major product, was confirmed by its synthesis from hydrogen bromide and 1-phenyl-2,2,3,4-tetramethyl-3-phospholen (103) produced

by phenylsilane reduction of the corresponding oxide (102).

The ^{1}H n.m.r. spectrum of the mixture of hydrobromides was of interest in that the signals due to the 3-phospholen hydrobromide were shifted downfield relative to those of the corresponding oxide (102) and phospholen (103). These downfield shifts resemble those of 1,2,2,3,4-pentamethyl-1-phenylphospholenium iodide (104). Similarly, the doublet due to the vinylic proton of the 2-phospholen hydrobromide (τ3.68, J_{PH} 28 Hz) was well downfield relative to the corresponding signal of the 2-phospholen oxide (τ4.08, J_{PH} 22 Hz) (240) and the 2-phospholen (τ4.1, J_{PH} 22 Hz) (251). This suggested that, at least in solution, the phosphorus is ionic (255 and 256) in these adducts rather than covalent (257 and 258).[118] Unfortunately no signal could be detected in the



(257)



(258)

^{31}P n.m.r. spectra of these hydrobromides. The large coupling constant between phosphorus and the vinylic proton appears to be characteristic of 2-phospholens.[118, 124]

The structures (255 and 256) were further proved by titration with sodium hydroxide; one mole of hydroxide neutralised one mole of phospholen hydrobromide. Oxidation of the resultant mixture gave a mixture of 2- and 3-phospholen oxides (85% of a 2:9 mixture) (102) and (240).

The thermal cyclisation of but-3-enylchlorophosphines

suggests that phospholen hydrobromide formation occurs *via* intermediate acyclic bromophosphines but these could not be isolated. In fact, one would, on the basis of the proposed mechanism (252) for this cyclisation, expect the but-3-enylbromophosphines to cyclise more readily than the corresponding chlorophosphine; bromide being a better leaving group than chloride.

Oxidation of Thiophosphoryl Compounds

9.1 Methods of Oxidation.

Thiophosphoryl compounds are easily converted to the corresponding phosphoryl compounds by oxidising agents such as nitric acid,[125, 126, 127] bromine in alkaline solution,[126] potassium permanganate in pyridine,[125,128] and thionyl chloride.[125, 129] In some cases the oxidation affects the groups on phosphorus as well as the thiophosphoryl function. Thus, bis(p-carboxy-phenyl)phenylphosphine oxide (259) was obtained by oxidation of bis(p-tolyl)phenylphosphine sulphide (260) with potassium permanganate in pyridine.[128] Similarly,

$$(\underline{p}\text{-}CH_3C_6H_4)_3PS \xrightarrow[\text{pyridine}]{KMnO_4} (\underline{p}\text{-}HO_2CC_6H_4)_3PO$$

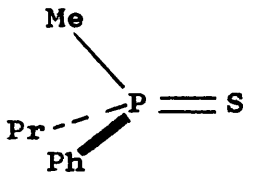
(260) (259)

nitration of triphenylphosphine sulphide resulted in formation of tris(m-nitrophenyl)phosphine oxide (261).[125]

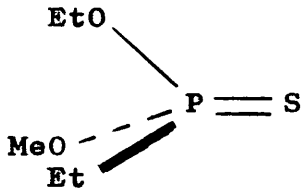
$$(C_6H_5)_3PS \xrightarrow[H_2SO_4]{HNO_3} (\underline{m}\text{-}NO_2C_6H_4)PO$$

(261)

Stereochemical studies have been limited to the oxidations of optically active methylphenylpropylphosphine sulphide (262) and O-ethyl O-methyl ethylphosphonothionate (263). Horner[29] demonstrated that oxidation of the former sulphide by



(262)



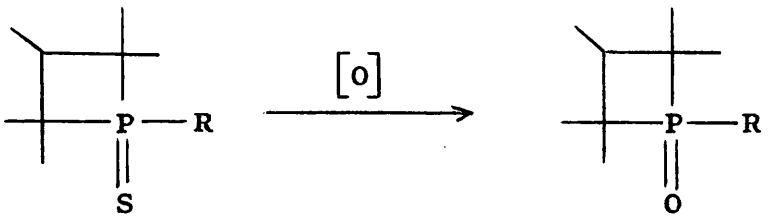
(263)

potassium permanganate in pyridine proceeded with complete retention of configuration. In contrast Michalski[130] demonstrated that oxidation of (262) and (263) by nitric acid led to largely inversion of configuration, and that oxidation by dinitrogen tetroxide led to retention with considerable racemisation.

9.2 m-Chloroperbenzoic Acid.

It was found that addition of one molar equivalent of the peracid to triphenylphosphine sulphide in dichloromethane at 0^{o} resulted in the immediate formation of collodial sulphur (>90%) and triphenylphosphine oxide in good yield.

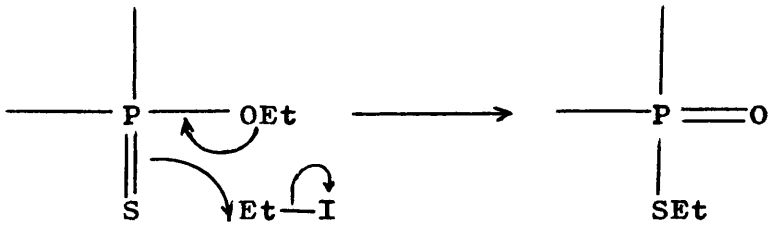
The stereochemical direction of the reaction was investigated by examination of the behaviour of the stereoisomerically pure 2,2,3,4,4-pentamethylphosphetan 1-sulphides (264) on oxidation to the phosphetan 1-oxides (265).



(264) (265)

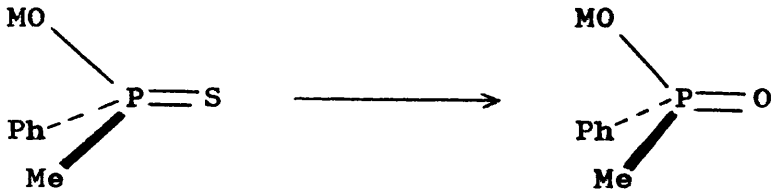
Oxidation of cis- or trans- 1-phenylphosphetan 1-sulphide (264; R = Ph) with m-chloroperbenzoic acid gave cis- or trans-1-phenylphosphetan 1-oxide (265; R = Ph), respectively, in quantitative yield. Thus the reaction proceeds with complete retention of configuration at phosphorus. On the basis of this conclusion the isomerically pure 1-chloro-2,2,3,4,4-pentamethylphosphetan 1-sulphide (264; R = Cl) and 1-ethoxy-2,2,3,4,4-pentamethylphosphetan 1-sulphide (264; R = OEt) synthesised by Smith[32] were assigned trans

configurations, as on oxidation with m-chloroperbenzoic acid they gave the corresponding trans phosphetan 1-oxides (265; R = Cl and OEt respectively). The trans configuration of the ethoxy ester was confirmed by its conversion by ethyl iodide (Pishschimuka reaction) to the ethylthio ester (265; R = SEt) which was isomeric with r-1-ethylthio-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide. The Pishschimuka reaction does not involve breaking any bonds around phosphorus (266) and therefore, proceeds with retention of configuration.[131]



(266)

It has since been shown that O-menthyl $(S)_p$-methylphenylthiophosphinate (267) is oxidised by m-chloroperbenzoic acid or hydrogen peroxide in refluxing ethanol stereospecifically with retention of configuration to the phosphinate (268).[132]

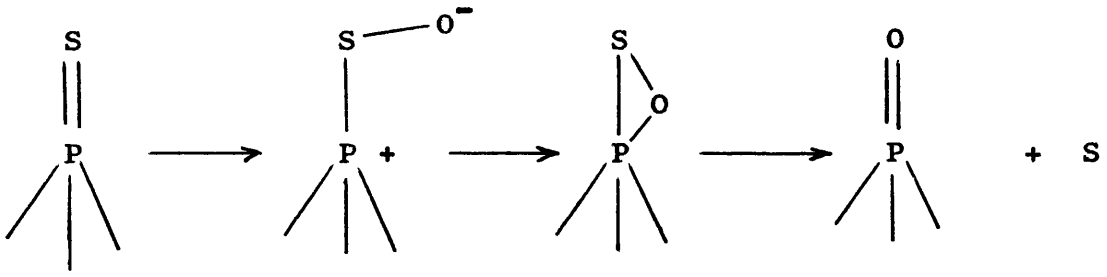


(267) (268)

M = (-)-Menthyl

Herriott[137] has confirmed the peracid oxidation of (267) and suggested that by analogy with the oxidation of thiocarbonyl groups to sulphines[138] the S-oxide (269) is a

plausible intermediate in the retention reaction. Closure to a three-membered ring (270) and concomitant or successive

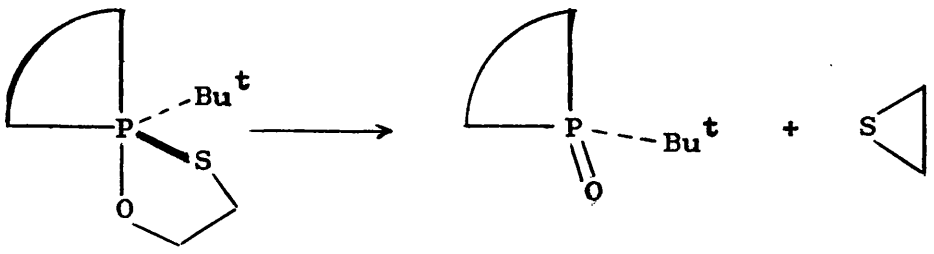


(269) (270) (271)

loss of sulphur produces (271). He found that oxidation with peroxytrifluoroacetic acid occurred with predominant inversion, as did oxidation with m-chloroperbenzoic acid in the presence of strong acids. In this case a mechanism involving nucleophilic attack of peroxy acid on the protonated sulphide was postulated.

9.3 Styrene Oxide.

It has been shown[133] that phosphoranes of the type (272) readily eliminate ethylene sulphide on warming, to give the corresponding phosphoryl compounds (273). A similar

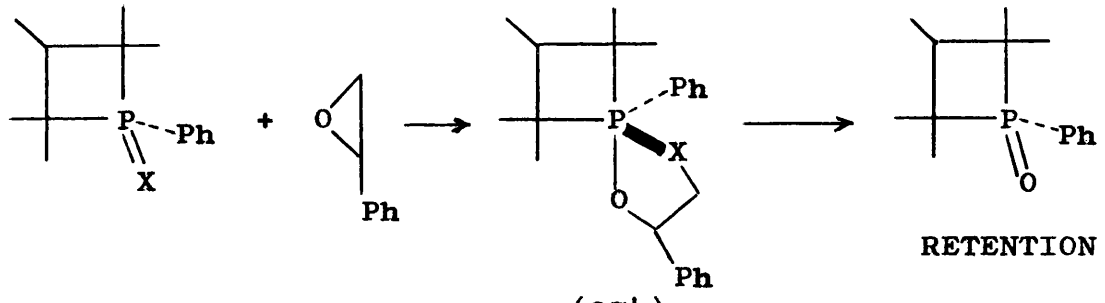


(272) (273)

elimination has been postulated in certain five-coordinate intermediates.[134] As a consequence of these results, phosphine sulphides were treated with styrene oxide in the hope that the corresponding phosphine oxides would be produced via an

intermediate phosphonothioite. Heating styrene oxide with 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-sulphide at 190° for 1 h completely converted the sulphide to the corresponding phosphetan 1-oxide. The reaction was not stereospecific; trans-1-phenylphosphetan 1-sulphide gave an oxide whose stereoisomeric composition was cis:trans = 1:9. Similarly cis-1-phenylphosphetan 1-sulphide gave a cis:trans = 1:1 mixture of oxides.

If the mechanism of the oxidation involves a phosphonothioite intermediate (274; X = S), formed by nucleophilic attack of the thiophosphoryl sulphur on styrene oxide, decomposition of this initial intermediate leads to retention of configuration.



Pseudorotation of (274; X = S) as shown in Scheme VII leads to inversion of configuration. Both processes must be occurring to explain the lack of stereospecificity. Isomer cross-over can only occur *via* the intermediate (275; X = S) where the five-membered phosphonothioite ring occupies a diequatorial position. Such a high energy intermediate is possible at the elevated temperature of the reaction.[135]

Alternatively, stereomutation could have occurred by the action of styrene oxide on the phosphetan 1-oxide product to give the phosphorane (274; X = O), which could pseudorotate to the intermediate (275; X = O) and so to the isomeric oxide. To test this possibility 2,2,*cis*-3,4,4-pentamethyl-*r*-1-phenylphosphetan 1-oxide was heated at 190° for 1h with styrene oxide. The phosphetan 1-oxide recovered from the reaction had a stereoisomer composition of *cis*:*trans* 1:1.

Triphenylphosphine sulphide was only partially converted (65%) to triphenylphosphine oxide when heated with one molar equivalent of styrene oxide at 190° for 2 h. Heating the sulphide for longer periods and with more than one equivalent of styrene oxide still did not result in the sulphides complete conversion to the oxide.

EXPERIMENTAL

General.

I.r. spectra were recorded on a Perkin-Elmer 237 grating spectrometer for samples in Nujol except as otherwise noted. Mass spectra were determined with an A.E.I. MS9 instrument; in each case the molecular ion is given first followed by peaks of structural significance. Except as otherwise noted ^{1}H n.m.r. spectra were recorded with a Varian T-60 spectrometer with tetramethylsilane as internal standard and deuteriochloroform as solvent. Analytical g.l.c. was carried out on a Perkin-Elmer F11 instrument. Preparative g.l.c. was carried out on a Aerograph Autoprep A-700 instrument.

Evaporation was performed with a rotary evaporator, and solutions in organic solvents were dried over magnesium sulphate. All reactions involving air sensitive reactants or products were carried out under an atmosphere of dry, oxygen free, nitrogen. The butyl-lithium used was a solution in pentane supplied by The Aldrich Chemical Company. Light petroleum had b.p. 40-60.

Solvents were dried as follows. Tetrahydrofuran was refluxed over calcium hydride and distilled onto sodium wire; when required a portion was refluxed over, and distilled from, lithium aluminium hydride. Diethyl ether when required very dry was purified in a similar manner; otherwise it was dried over sodium as was petroleum spirit. Methanol and ethanol were refluxed over their magnesium alkoxides and distilled. Benzene and dichloromethane were refluxed over calcium hydride and distilled.

2-Phenyl-2-phosphatetracyclo[3,2,1,$O^{3,6}$,$O^{4,7}$]octane 2-Oxide.

Aluminium chloride (0.2 g) was added to an equimolar mixture of phenylphosphonous dichloride (12.5 g, 0.07 mol) and freshly distilled bicyclo[2,2,1]heptadiene (6.5 g, 0.07 mol). After standing for 6 months a small amount of a crystalline solid formed. The solid was filtered off and shaken with aqueous sodium hydrogen carbonate for 1 h. Extraction of the mixture with chloroform gave the phosphine oxide (1.7 g), m.p. 154-155° (from carbon tetrachloride), $\nu_{max.}$ 1434, 1206, 1200, 1192, 1118, 946, and 800 cm^{-1}, m/e 216, 215, 169, 167, 165, 125, 92, 91, and 77, τ 1.9-2.7 (5H, m), 7.25 (2H, broad s), 8.05 (2H, s), 8.15 (2H, broad s), and 8.48(2H, s) (Found: C, 72.45; H, 6.2; P, 14.2. $C_{13}H_{13}OP$ requires C, 72.2; H, 6.05; P, 14.3%).

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

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

Ethereal benzylmagnesium chloride prepared from magnesium (2.4 g, 0.1 g-atom) and benzyl chloride (12.6 g, 0.1 mol) was added dropwise to a stirred solution of the phosphinyl chloride (19.45 g, 0.1 mol) in ether (100 ml)

with the temperature maintained at 0°. The solution was refluxed for 0.5 h, cooled to room temperature, and poured onto a slurry of sulphuric acid (2.0N;100 ml) and crushed ice (300 g). The organic layer was washed successively with water, dilute sodium hydrogen carbonate, and water, dried, and evaporated. The residue recrystallised from benzene gave the 1-benzylphosphetan oxide (18.5 g, 74%), m.p. and mixed m.p. 180-182°, n.m.r. spectrum identical with that of a sample of the oxide prepared from benzyllithium and the phosphinyl chloride.

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

Ethereal methylmagnesium iodide (0.1 mol) was reacted with the phosphinyl chloride (19.45 g, 0.1 mol) as above. Recrystallisation of the residue from light petroleum gave the hexamethylphosphetan oxide (14.2 g, 82%), m.p. 171-172° (sealed, completely immersed capillary tube), $\nu_{max.}$ 1304, 1159, 890 and 770 cm^{-1}, τ 8.45(3H, d, J_{PH} 11.5 Hz), 8.73 (6H, d, J_{PH} 16 Hz), 8.83 (6H, d, J_{PH} 18.5 Hz), and 9.08 (3H, dd, J 7, J_{PH} 1 Hz); the signal from the ring proton was hidden under that from the lower-field methyl protons.

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

Ethereal 1-naphthylmagnesium bromide (0.1 mol) was reacted with the phosphinyl chloride (19.45 g, 0.1 mol) as above. The residue was chromatographed on basic alumina (500 g). Elution with ether-methanol (50:1) gave the crystalline 1-(1-naphthyl)phosphetan oxide (15.0 g, 49%),

m.p. 250-252° (from cyclohexane), $\nu_{max.}$ 1179, 1158, 1142, 984, 808, 781, and 679 cm^{-1}, τ 1.67-2.70 (7H, m), 7.43 (1H, dq, $\underline{J}$ 7, $\underline{J}_{PH}$ 3Hz), 8.47 (6H, d, $\underline{J}_{PH}$ 17Hz), 8.83 (6H, d, $\underline{J}_{PH}$ 18 Hz), and 9.07 (3H, dd, $\underline{J}$ 7, $\underline{J}_{PH}$ 1.5 Hz) (Found: C, 75.3; H, 8.1; P, 10.7. $C_{18}H_{23}OP$ requires C, 75.5; H, 8.1; P, 10.8%).

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

High yields of this phosphetan oxide were obtained by the method of Hawes and Trippett,[19] m.p. and mixed m.p. 126-127°, τ 1.80-2.18 (2H, m), 2.30-2.55 (3H, m), 7.92 (1H, dq, $\underline{J}$ 7, $\underline{J}_{PH}$ 1.5 Hz), 8.57 (6H, d, $\underline{J}_{PH}$ 16 Hz), 8.88 (6H, d, $\underline{J}_{PH}$ 19 Hz), and 8.95 (3H, dd, $\underline{J}$ 7, $\underline{J}_{PH}$ 1.5 Hz).

2,2,cis-3,4,4-Pentamethyl-r-1-phenylphosphetan 1-Oxide

2,4,4-Trimethylpent-2-ene (28.0 g, 0.25 mol) was added slowly to a solution of aluminium chloride (33.3 g, 0.25 mol) and dichlorophenylphosphine (45.0 g, 0.25 mol) in dichloromethane (150 ml), the temperature was maintained below 10°. After stirring for 2 h the solution was added slowly to ice-water (2kg). The organic layer was washed with water, aqueous sodium hydroxide (1N; 50 ml), and water, dried, and evaporated. The residue was chromatographed on basic alumina (750 g). Elution with ether-light petroleum (1:1; 500 ml) gave the trans-1-phenylphosphetan oxide (2.5 g), m.p. and mixed m.p. 126-127°, n.m.r. spectrum identical with that of an authentic sample. Elution with ether-methanol (100:1; 2.5 l) gave

the cis-1-phenylphosphetan oxide (12.2 g, 21%), m.p. and mixed m.p. 117-118°, τ 2.0-2.6 (5H, m), 7.62 (1H, dq, J 7, J_{PH} 7 Hz), 8.58 (6H, d, J_{PH} 17 Hz), 8.77 (6H, d, J_{PH} 19 Hz), and 8.97 (3H, d, J 7 Hz).

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

1. With Trichlorosilane.

The phosphetan oxide (11.8 g, 0.05 mol) in benzene (100 ml) was added to a stirred, cooled solution of dry triethylamine (5.1 g, 0.05 mol) and trichlorosilane (6.9 g, 0.05 mol) in benzene (50 ml). The solution was stirred for 0.5 h, then recooled, and sodium hydroxide (5N; 100 ml) added dropwise to it. The organic layer was separated and washed with a saturated sodium chloride solution. The benzene was distilled off and the residue distilled under reduced pressure giving 2,2,3,4,4-pentamethyl-1-phenylphosphetan (5.7 g, 52%), b.p. 82-84°/0.3 mm. Reduction of 2,2,trans-3,4,4-pentamethyl-r-1-phenylphosphetan 1-oxide in this manner gave 2,2,trans-3,4,4-pentamethyl-r-1-phenylphosphetan, τ (neat) 2.1-2.9 (5H, m), 7.18 (1H, q, J 7 Hz), 8.68 (6H, d, J_{PH} 19.5 Hz), 8.98 (6H, d, J_{PH} 7 Hz), and 9.19 (3H, d, J 7 Hz). The cis-1-phenylphosphetan 1-oxide gave cis-1-phenylphosphetan, τ (neat) 2.1-3.0 (5H, m), 7.70 (1H, dq, J 7, J_{PH} 4 Hz), 8.68 (6H, d, J_{PH} 20 Hz), 8.90 (6H, d, J_{PH} 7 Hz), and 9.22 (3H, dd, J 7, J_{PH} 1.5 Hz).

2. With Phenylsilane.

The phosphetan oxide (2.3 g, 0.01 mol) was added in small portions to phenylsilane (1.08 g, 0.01 mol), a smooth reaction occurring at room temperature. After all the oxide

had been added the mixture was heated to 80°. Distillation under reduced pressure gave the phosphetan (2.02 g, 92%). The trans-1-phenylphosphetan 1-oxide gave the trans-phosphetan and cis-1-phenylphosphetan 1-oxide gave the cis-phosphetan.

3. With Polymethylhydrogensiloxane.

A stirred mixture of the phosphetan oxide (23.6 g, 0.1 mol) and polymethylhydrogensiloxane (25 g) was slowly heated over 3 h to 100°. At 100° the mixture became a polymeric mass. Distillation under reduced pressure gave 2,2,3,4,4-pentamethyl-1-phenylphosphetan (17.6 g, 74%), b.p. 100°/0.6 mm.

The stereoisomer composition of mixtures of the phosphetans was determined by integration of the n.m.r. spectra (neat) due to the ring proton at τ 7.18 in the trans-phosphetan and τ 7.70 in the cis-phosphetan.

2,2,3,4,4-Pentamethyl-1-phenylphosphetan 1-Sulphide.

A mixture of stereoisomers of 2,2,3,4,4-pentamethyl-1-phenylphosphetan (cis:trans 1:4) was prepared by trichlorosilane reduction of a mixture of phosphetan oxides. The mixture (11.0 g, 0.05 mol) and sulphur (1.6 g, 0.05 mol) were refluxed in benzene (50 ml) for 6 h. The benzene was evaporated and the residue chromatographed on basic alumina (300 g). Elution with light petroleum-ether (10:1) gave 2,2,trans-3,4,4-pentamethyl-r-1-phenylphosphetan 1- sulphide (8.0 g, 70%), m.p. 102-103° (from light petroleum), $\nu_{max.}$ 1430, 1308, 1090, 753, 710,

701, and 695 cm^{-1}, m/e 252, 237, 236, 220, 182, 166, 150, 135, 119, and 108, τ 1.57-2.03 (2H, m), 2.37-2.57 (3H, m), 7.37 (2H, dq, J 7, J_{PH} 2 Hz), 8.65 (6H, d, J_{PH} 20 Hz), 8.91 (6H, d, J_{PH} 20 Hz), and 8.99 (3H, dd, J 7, J_{PH} 1 Hz) (Found: C, 66.6; H, 8.9; P, 12.2. $C_{14}H_{21}PS$ requires C, 66.65, H, 8.95; P, 12.25%). Elution with light petroleum-ether (5:1) gave 2,2,cis-3,4,4-pentamethyl-r-1-phenyl-phosphetan 1-sulphide (2.0 g, 17%), m.p. 92-93° (from light petroleum), $\nu_{max.}$ 1430, 1310, 1110, 749, 721, 703, and 687 cm^{-1}, m/e identical with data for the trans-isomer, τ 2.17-2.74 (5H, m), 7.60 (1H, dq, J 7, J_{PH} 4 Hz), 8.63 (6H, d, J_{PH} 20 Hz), 8.67 (6H, d, J_{PH} 18 Hz), and 9.03 (3H, dd, J 7, J_{PH} 1.5 Hz) (Found: C, 66.7; H, 8.9; P, 12.0%).

General Procedure for the Preparation of Phosphetanium Salts by Quaternisation of Phosphetans formed by the Trichlorosilane Reduction of Phosphetan 1-Oxides.

To a stirred solution of triethylamine (5.1 g, 0.05 mol) and the phosphetan 1-oxide (0.05 mol) in benzene (100 ml) was added a solution of trichlorosilane (6.9 g, 0.05 mol) in benzene (50 ml). After stirring for 1h excess alkyl halide was added to the phosphetan solution and the mixture set aside for 24 h. Water (40 ml) was added and the mixture stirred for a further 1h. The phosphetanium salt and silica were filtered off, washed well with benzene, dried, and taken up in boiling chloroform. The silica was removed by filtration and the filtrate treated with ethyl acetate to give the crystalline phosphetanium salt. In some cases the filtrate was evaporated and the residue recrystallised from another solvent.

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

r-1-Benzyl-2,2, trans-3,4,4-pentamethylphosphetan 1-oxide was reduced, and quaternised with iodomethane to give the phosphetanium iodide (77%), m.p. 295-297° (from n-butanol), $\nu_{max.}$ 1296, 913, 873, and 698 cm^{-1}, $\tau(CF_3CO_2H)$ 2.57 (5H,s), 5.83(3H,d, J_{PH} 14 Hz), 7.03 (1H, dq, J 7, J_{PH} 5Hz), 8.12 (3H, d, J_{PH} 13.5 Hz), 8.37 (6H, d, J_{PH} 19 Hz), 8.55 (6H, d, J_{PH} 20 Hz), and 8.90 (3H, dd, J 7, J_{PH} 1 Hz) (Found : C, 50.95; H, 6.9; P, 8.1. $C_{16}H_{26}IP$ requires C, 51.05; H, 6.95; P, 8.25%).

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

r-1,2,2,trans-3,4,4-Hexamethylphosphetan 1-oxide was reduced, and quaternised with benzyl iodide to give the phosphetanium iodide (73%), m.p. 305-307° (from chloroform-ethyl acetate, acetonitrile, or butanol), $\nu_{max.}$ 1300, 923, and, 703 cm^{-1}, $\tau(CF_3CO_2H)$ 2.37-2.83(5H, m), 6.03 (2H, d, J_{PH} 13 Hz), 7.23 (1H, dq, J7, J_{PH} 1.5 Hz), 8.13 (3H, d, J_{PH} 13.5 Hz), 8.30 (6H, d, J_{PH} 20 Hz), 8.62 (6H, d, J_{PH} 19 Hz), and 8.85 (3H, dd, J 7, J_{PH} 1.5 Hz) (Found: C, 50.9 ; H, 6.9; P, 8.0. $C_{16}H_{26}IP$ requires C, 51.05; H, 6.95; P, 8.25%).

3. r-1,2,2,cis-3,4,4-Hexamethyl-1-phenylphosphetanium Iodide.

2,2,trans-3,4,4-pentamethyl-r-1-phenylphosphetan 1-oxide was reduced and quaternised with iodomethane to give the phosphetanium iodide (86%), m.p. 279-280° (from chloroform-ethyl acetate), $\nu_{max.}$ 1435, 1300, 1110, 914, 895, and 786 cm^{-1}, $\tau(CF_3CO_2H)$ 1.85-2.26(5H, m), 6.97 (1H, dq, J 7, J_{PH} 7 Hz), 7.65 (3H, d, J_{PH} 13 Hz), 8.34 (6H, d, J_{PH} 20 Hz), 8.49 (6H, d, J_{PH} 20 Hz), and 8.79 (3H, dd, J 7, J_{PH} 1.5 Hz) (Found: C, 49.6; H, 6.6; P, 8.4. $C_{15}H_{24}IP$ requires C, 49.75; H, 6.7; P, 8.55%).

4. r-1,2,2,trans-3,4,4-Hexamethyl-1-phenylphosphetanium Iodide.

2,2,cis-3,4,4-Hexamethyl-r-1-phenylphosphetan 1-oxide was reduced and quaternised with iodomethane to give the phosphetanium iodide (89%), m.p. 296-297°

(from chloroform-ethyl acetate), $\nu_{max.}$ 1301, 1112, 908, 897, 783, 744, and 693 cm^{-1}, τ (CF_3CO_2H) 2.0 - 2.33 (5H, m), 7.0 (1H, dq, J 7, J_{PH} 2 Hz), 7.60 (3H, d, J_{PH} 13.5 Hz), 8.36 (12H, d, J_{PH} 20 Hz), and 8.80 (3H, dd, J 7, J_{PH} 1.5 Hz) (Found: C, 49.7; H, 6.7, P, 8.3. $C_{15}H_{24}IP$ requires C, 49.75; H, 6.7; P, 8.55%).

5. 1,1,2,2,3,4,4-Heptamethylphosphetanium Iodide.

r-1,2,2,trans-3,4,4-Hexamethylphosphetan 1-oxide was reduced and quaternised with iodomethane to give the phosphetanium iodide (88%), m.p. $>$ 335° (from water), $\nu_{max.}$ 1290, 965, 945, 910, 870, 770, and 735 cm^{-1}, τ (CF_3CO_2H) 7.22 (1H, dq, J 7.5, J_{PH} 1.5 Hz), 7.84 (3H, d, J_{PH} 14 Hz), 7.90 (3H, d, J_{PH} 14 Hz), 8.50 (6H, d, J_{PH} 20 Hz), 8.57 (6H, d, J_{PH} 20 Hz), and 8.92 (3H, dd, J 7.5, J_{PH} 1.5 Hz) (Found: C, 40.0; H, 7.5; P, 10.2. $C_{10}H_{22}IP$ requires C, 40.0; H, 7.4; P, 10.3%).

6. 1,1-Dibenzyl-2,2,3,4,4-pentamethylphosphetanium Bromide.

r-1-Benzyl-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide was reduced and quaternised with benzyl bromide to give the phosphetanium bromide (81%), m.p. 214 - 216° (from chloroform-ethyl acetate), $\nu_{max.}$ 1493, 1450, 1243, 1165, 1070, 852, 774, 750, 703, and 688 cm^{-1}, τ (CF_3CO_2H) 2.47-3.57(10H, m), 6.33(2H, d, J_{PH} 13 Hz), 6.40 (2H, d, J_{PH} 13 Hz), 7.30 (1H, dq, J 7, J_{PH} 3 Hz), 8.63 (6H, d, J_{PH} 19 Hz), 8.68 (6H, d, J_{PH} 19 Hz), and 8.95 (3H, dd, J 7, J_{PH} 1 Hz) (Found: C, 65.2; H, 7.4; P, 7.3. $C_{22}H_{30}BrP$ requires C, 65.2; H, 7.45; P, 7.65%).

7. r-1-Benzyl-1-p-deuteriobenzyl-2,2,trans-3,4,4-pentamethylphosphetanium Bromide.

r-1-Benzyl-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide was reduced and quaternised with p-deuteriobenzyl bromide to give the phosphetanium bromide (80%), m.p. 214-216° (from chloroform-ethyl acetate). The n.m.r. spectrum was the same as the dibenzyl analogue except that the aromatic region only integrated for nine protons. The p-deuteriobenzyl bromide was synthesised by N-bromosuccinimide bromination of p-deuteriotoluene produced by adding deuterium oxide to an ethereal solution of the Grignard from p-bromotoluene. The p-deuteriotoluene was shown by mass spectrometry to be 92% deuterated.

8. r-1,2,2,cis-3,4,4-Hexamethyl-1-(1-naphthyl)phosphetanium Iodide.

r-1-(1-Naphthyl)-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide was reduced and quaternised with iodomethane to give the phosphetanium iodide (79%), m.p. 178-179° (from chloroform-ethyl acetate), $\nu_{max.}$ 1146, 902, 804, and 774 cm^{-1}, τ 1.43-2.63 (7H, m), 6.50 (1H, dq, J7, J_{PH} 2 Hz), 7.27 (3H, d, J_{PH} 13 Hz), 8.08 (6H, d, J_{PH} 21 Hz), 8.43 (6H, d, J_{PH} 19 Hz), and 8.87 (3H, dd, J7, J_{PH} 1 Hz)(Found: C, 55.4; H, 6.5; P, 7.55. $C_{19}H_{26}IP$ requires C, 55.35; H, 6.35; P, 7.5%).

9. r-1-Benzyl-2,2,cis-3,4,4-pentamethyl-1-phenylphosphetanium Bromide.

2,2,trans-3,4,4-Pentamethyl-r-1-phenylphosphetan 1-oxide was reduced and quaternised with benzyl bromide

to give the phosphetanium bromide (83%), m.p. 218-220° (from chloroform-ethyl acetate), Lit. value 220-221°,[19] $\nu_{max.}$ 1437, 1115, and 865 cm^{-1}, τ 1.87-2.63 (5H, m), 2.95 (5H, s), 5.08 (2H,d, J_{PH} 13.5 Hz), 7.32 (1H, dq, J 7, J_{PH} 2 Hz), 8.07 (6H, d, J_{PH} 20 Hz), 8.38 (6H, d, J_{PH} 18 Hz), and 8.85 (3H, dd, J 7, J_{PH} 1.5 Hz).

10. r-1-Benzyl-2,2,trans-3,4,4-pentamethyl-1-phenyl-phosphetanium Bromide.

2,2,cis-3,4,4-Pentamethyl-r-1-phenylphosphetan 1-oxide was reduced and quaternised with benzyl bromide to the phosphetanium bromide (87%), m.p. 232-233° (from chloroform-ethyl acetate), τ 2.2-2.7 (5H, m), 2.98 (5H, s), 4.90 (2H, d, J_{PH} 14 Hz), 6.32 (1H, dq, J7, J_{PH} 2 Hz), 8.07 (6H, d, J_{PH} 20 Hz), 8.58 (6H, d, J_{PH} 19 Hz), and 8.97 (3H, d, J 7 Hz) (Found: C, 65.0; H, 6.9; P, 7.9. $C_{21}H_{28}BrP$ requires C, 645; H, 7.2; P, 7.9%).

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

This was synthesised according to the method of McBride and co-workers.[13] M.p. 73-74°, reported 72-75°.

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

A solution of sodium (2.3 g, 0.1 mol) in ethanol (100 ml) was added slowly to a stirred solution of r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (19.6 g, 0.1 mol) in ethanol (50 ml), and the mixture refluxed for 1 h. The ethanol was evaporated and the residue partitioned between dichloromethane and water. The organic layer was dried and evaporated and the residue distilled to give the ethyl ester (17.2 g, 84%), b.p. 73 - 75°/1.5 mm, $\nu_{max.}$ (film) 1257, 1218, 1040, 950, 764, and 674 cm^{-1}, τ 5.83 (2H,dq, J7, J_{PH} 7 Hz), 8.67 (3H,t, J 7 Hz), 8.78 (6H, d, J_{PH} 19 Hz), 8.82 (6H, d, J_{PH} 18 Hz), and 9.12 (3H, dd, J 7, J_{PH} 1.5 Hz); the signal from the ring proton was partially hidden under that from the lower-field methyl protons.

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

The suspension formed from sodium hydride (2.4 g, 0.1 mol) and ethanethiol (6.2 g, 0.1 mol) in ether (50 ml) was added to a stirred, ice-water cooled, solution of r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (19.6 g, 0.1 mol) in ether (100 ml). The mixture was refluxed for 1 h, filtered and treated with water (100 ml).

The organic layer was dried and evaporated and the residue distilled to give the ethylthio ester (16.7 g, 76%), b.p. 104°-106°/0.6 mm, $\nu_{max.}$ (film) 1260, 1200, and 646 cm^{-1}, m/e 220, 205, 191, 161, 150, 108, and 97, τ 7.02 (2H, dq, J 7, J_{PH} 8 Hz), 8.30 (1H, dq, J 7, J_{PH} 4 Hz), 8.60 (3H, t, J 7 Hz), 8.67 (6H, d, J_{PH} 19 Hz), 8.73 (6H, d, J_{PH} 21 Hz), and 9.08 (3H, dd, J 7, J_{PH} 1.5 Hz) (Found : C,54.4; H, 9.6; P, 13.9; S, 14.3. $C_{10}H_{21}OPS$ requires C, 54.5; H, 9.6; P, 14.05; S, 14.55%).

Reaction of Sodium Ethoxide with r-1-Ethylthio- 2,2,trans-3,4,4-pentamethylphosphetan 1-Oxide.

The ethylthio ester (2.2 g, 0.01 mol) was added to a solution of sodium (0.23 g, 0.01 mol) in ethanol (20 ml) and the mixture stirred for 2h. The ethanol was evaporated and the residue partitioned between dichloromethane and water. The organic layer was dried and evaporated and the residue (1.9 g) was shown by n.m.r. to contain only r-1-ethoxy-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (77%) and unreacted thio ester (23%).

Preparation of 1-Benzylamino-2,2,3,4,4-pentamethylphosphetan 1-Oxide.

1. r-1-Ethoxy-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (2.04 g, 0.01 mol) in ether (25 ml) was added to a solution of benzylamine (5.35 g, 0.05 mol) and butyllithium (2.5N; 4.0 ml) in ether (50 ml), and the solution was stirred at room temperature for 1h. Hydrochloric acid (2N; 10 ml) was then added and the organic layer was

washed with water, dried, and evaporated. The residue gave the r-1-benzylamino-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (2.2 g, 83%), m.p. and mixed m.p. 159°-160°, ^{19} n.m.r. spectrum identical with that of an authentic sample.

2. r-1-Ethylthio-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (2.2 g, 0.01 mol) was treated with N-lithiobenzylamine as described above. The residue gave the r-1-benzylamino-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (2.1 g, 79%), m.p. and mixed m.p. 159°-160°, n.m.r. spectrum identical with that of an authentic sample.

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

A solution of benzyl-lithium (3.05 g, 0.031 mol) in tetrahydrofuran (320 ml), prepared by the method of Gilmann and McNinch,[139] was added dropwise to a stirred solution of r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (6.0 g, 0.031 mol) in tetrahydrofuran (80 ml) at -19°. After stirring for 1h at room temperature the mixture was hydrolysed with water (200 ml) and extracted with ether (4 x 150 ml). The combined extracts were dried and the solvent evaporated giving the phosphetan oxide (6.2 g, 76%), m.p. 180°-182° (from benzene), $\nu_{max.}$ 1247, 1190, 1169, 1146, and 704 cm^{-1}, m/e 250, 235, 182, 181, 165, 159, 122, and 97, τ 2.40-2.92 (5H, m), 6.75 (2H, d, J_{HH} 11 Hz), 8.25 (1H, dq, J 7, J_{PH} 1.5 Hz), 8.76 (6H, d, J_{PH} 16 Hz), 8.84 (6H, d, J_{PH} 17.5 Hz) and 9.11

(3H, dd, J 7, J_{PH} 1.5 Hz) (Found : C, 71.95; H, 9.2; P, 12.7; $C_{15}H_{23}OP$ requires C, 72.0; H, 9.25; P, 12.4%).

Preparation of 1-Anilino-2,2,3,4,4-pentamethylphosphetan 1-Oxide.

1. r-1-Chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (7.78 g, 0.04 mol) and aniline (7.3 g, 0.08 mol) in benzene (50 ml) were refluxed for 48 h. The solution was then washed with hydrochloric acid (2N; 25 ml), water, and dried. After evaporation the residue was chromatographed on basic alumina (300 g). Elution with ether-methanol (30:1) gave the required 1-anilinophosphetan oxide (144 mg, 14%), m.p. 172°-173° (from petrol, b.p. 60°-80°), $\nu_{max.}$ 3290, 1604, 1285, 1239, 1190, 1163, 912, and 744 cm^{-1}, m/e 251, 236, 181, 140, 123, and 112, τ 2.60-3.30 (5H, m), 4.43 (1H, d, J_{PH} 11 Hz), 8.28 (1H, dq, J 7, J_{PH} 3 Hz), 8.72 (6H, d, J_{PH} 18.5 Hz), 8.82 (6H, d, J_{PH} 18.5 Hz), and 9.12 (3H, dd, J 7, J_{PH} 1.5 Hz) (Found : C, 66.4; H, 9.05; N, 5.6; P, 12.5. $C_{14}H_{23}NOP$ requires C, 66.6; H, 9.2; N, 5.55; P, 12.25%).

2. r-1-Chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (5.84 g, 0.03 mol) in ether (25 ml) was added to a solution of aniline (8.4 g, 0.09 mol) and butyl-lithium (2.5N; 3.6 ml) in ether (50 ml) and the solution was stirred at room temperature for 1 h. Hydrochloric acid (2N; 30 ml) was then added and the organic layer was separated, washed with water, dried, and evaporated. The residue gave the 1-anilinophosphetan oxide (6.0 g, 79%),

m.p. and mixed m.p. 172-173°, n.m.r. spectrum identical with that described above.

3. r-1-Benzyl-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (7.5 g, 0.03 mol) and potassium t-butoxide (5.05 g, 0.045 mol) in benzene (150 ml) were refluxed together for 0.5 h. The mixture was then treated dropwise with a solution of N-benzylideneaniline (5.4 g, 0.03 mol) in benzene (50 ml) and refluxed for a further 4 h. The benzene was evaporated and the residue partitioned between water and dichloromethane. The organic layer was dried and evaporated and the residue chromatographed on basic alumina (300 g). Elution with light petroleum gave crystalline trans-stilbene (3.6 g, 62%) whose i.r. was identical with that of an authentic sample. Elution with ether-methanol (50:1) gave unreacted 1-benzylphosphetan oxide (0.9 g, 12% recovery), m.p. and mixed m.p. 180-182°. Elution with ether-methanol (20:1) gave the 1-anilinophosphetan oxide (4.6 g, 61%), m.p. and mixed m.p. 172-173°, n.m.r. spectrum identical with that described above.

Reaction of Sodium Ethoxide with 1-Ethoxy-2,2,3,4,4-pentamethylphosphetan 1-Oxide.

The trans ester (1.02 g, 5 mmol) was added to a solution of sodium (0.12 g, 5 mmol) in ethanol (25 ml) and the mixture refluxed for 16 h. The ethanol was evaporated and the residue partitioned between dichloromethane and water. The organic layer was dried and the residue (0.92 g, 90% recovery) was shown by n.m.r. to

contain only *trans* ester.

Similarly, the stereoisomeric composition of a mixture rich in the *cis* ester (*cis*:*trans* = 65:35) was unaffected by sodium ethoxide under the same conditions.

Reaction of Toluene-p-*sulphonic acid with 1-Ethoxy-2,2,3,4,4-pentamethylphosphetan 1-Oxide*.

A mixture of the acid (0.2 g) and the *trans* ester (0.51 g) in ethanol (25 ml) was refluxed for 16 h. The ethanol was evaporated and the residue in chloroform washed with aqueous sodium hydrogen carbonate and then water. The organic layer was dried and evaporated and the residue (0.43 g, 85% recovery) was shown by n.m.r. to be only the *trans* ester.

Similarly, the stereoisomeric composition of a mixture rich in the *cis* ester (*cis*:*trans* = 65:35) was unaffected by the acid.

Alkaline Hydrolysis of Tetraphenylphosphonium Chloride.

The salt[96] (36.0 g) was refluxed for 16 h in a mixture of water (12.60 g, 0.70 mol), deuterium oxide (15.0 g, 0.75 mol), and sodium hydroxide (4.00 g, 0.10 mol). The organic layer was separated from the warm mixture and the benzene separated from the triphenylphosphine oxide in it under reduced pressure (water pump). The benzene was collected in a cold trap (dry ice-acetone), dried, and distilled. Analysis by mass spectrometry of the benzene fraction (6.4 g, 81%), at an ionising potential of 14eV to avoid (M-1) fragments, showed a ratio of benzene to d-benzene of 1.22 ± 0.05.

Alkaline Hydrolysis of Cumyltriphenylphosphonium Iodide.

To a slurry of benzyltriphenylphosphonium bromide (50.0 g, 0.115 mol) in tetrahydrofuran (200 ml) at 0° was added butyl-lithium (2N; 58 ml) and the mixture stirred for 1 h. The deep red solution was re-cooled and iodomethane (21.3 g, 0.15 mol) added. The resultant suspension was stirred for 3 h, the solvent evaporated, and the residue dissolved in chloroform was washed with water, dried, and concentrated. Ethyl acetate was added to the hot, concentrated chloroform solution which on cooling gave triphenyl-1-phenylethylphosphonium iodide, (51.0 g, 89%), m.p. 209-211°; $\nu_{max.}$ 1440, 1113, and 998 cm^{-1}, τ ($CF_3 \cdot CO_2H$) 1.9-2.9 (20H, m), 4.85 (1H, dq, J 7, J_{PH} 14 Hz), and 7.98 (3H, dd, J 7, J_{PH} 19 Hz) (Found: C, 63.5; H, 4.95; P, 6.4. $C_{26}H_{24}$ IP requires C, 63.2; H, 4.9; P, 6.25%).

Similarly this phosphonium iodide (49.4 g, 0.1 mol) in

tetrahydrofuran (150 ml) was treated with butyl-lithium (2N; 50 ml) and iodomethane to give cumyltriphenylphosphonium iodide (43 g, 84%), m.p. 170-171°(decomp.), $\nu_{max.}$ 1438, 1105, 1097, 1084, and 993 cm^{-1}, $\tau(CF_3 \cdot CO_2H)$ 1.9-2.9 (20H, m), and 7.83 (6H, d, J_{PH} 17 Hz) (Found: C, 63.75; H, 5.2; P, 6.2. $C_{27}H_{26}IP$ requires C, 63.8; H, 5.15; P, 6.1%).

The salt (37.5 g) was refluxed for 16 h in a mixture of water (14.625 g), deuterium oxide (17.00 g) and sodium hydroxide (3.00 g). The hydrocarbon product (5.5 g), b.p. 130-160°, was isolated from the reaction mixture using a cold trap. G.l.c. analysis (DE 201 column) showed that the hydrocarbon product was a mixture of α-methylstyrene (56%) and cumene(44%), this was confirmed by n.m.r. The cumenes were separated from the α-methylstyrene by preparative g.l.c., fractionation of the cumenes being avoided. Analysis by mass spectrometry indicated a ratio of cumene to d-cumene of 1.21 ± 0.05. This ratio was confirmed by n.m.r. integration of the signals due to the methyl groups of cumene at τ 8.75 (6H, d, J 7 Hz) with those of d-cumene at τ 8.75 (6H, triplet whose components were of equal intensity, J_{HD} 1 Hz). This gave a comparable though less accurate figure.

Reaction of Cumylpotassium.

Cumylpotassium, prepared by the method of Brown, Mighton and Senkus[140] from 2-phenyl-2-methoxypropane and sodium-potassium alloy, was added to an equimolar mixture of water and deuterium oxide. The mixture was filtered, the organic layer separated and dried. Fractional distillation gave a

mixture of cumenes (85%), b.p. 149-151°, mass spectral analysis showed that it was an equimolar mixture of cumene and d-cumene.

Alkaline Hydrolysis of 1,1,2,2,3,4,4-Heptamethylphosphetanium Iodide.

The salt (3.0 g, 0.01 mol) was stirred with aqueous sodium hydroxide (2N; 20 ml) at room temperature for 16 h. Ether extraction gave dimethyl(1,1,2,3-tetramethylbutyl)phosphine oxide (1.6 g, 84%), b.p. ca.35°/2mm, $\nu_{max.}$ (film) 1303, 1290, 1145, 930, 857, and 734 cm^{-1}, m/e 190, 147, 120, 77, and 43, τ 7.64(1H, quintet, J 7, 7 Hz), 8.32 (1H, dq, J 7, J_{PH} 2 Hz), 8.57 (6H, d, J_{PH} 12.5 Hz), 8.83 (3H, d, J_{PH} 17 Hz), 8.90 (3H, d, J_{PH} 18 Hz), 9.03 (3H, d, J 7 Hz), 9.06 (3H, d, J 7 Hz), and 9.13 (3H, d, J 7 Hz) (Found: C, 62.9; H, 12.1; P, 16.1. $C_{10}H_{23}OP$ requires C, 63.1; H, 12.1, P, 16.3%).

Hydrolysis of the salt in a deuterium oxide solution of N-sodium deuteroxide gave di-trideuteriomethyl(3-d-1,1,-2,3-tetramethylbutyl)phosphine oxide, whose n.m.r. spectrum was the same as that of the non-deuterated oxide except that the doublets at τ 9.06 and 9.13 had been replaced by singlets (3H) at those values, and there was no quintet at τ 7.64 and no doublet at τ 8.57.

Hydrolysis of the salt (0.9 g, 30 mmol) in a solution of sodium (0.63 g) in an equimolar mixture of water (7.262 g) and deuterium oxide (6.535 g) gave a mixture of the deuterated and non-deuterated phosphine oxides (0.37 g, 83%). The oxide composition was estimated by integration of the n.m.r. spectrum due to the 1-methyls at τ 8.76 and τ 8.69

(these signals are parts of the doublets centred at τ 8.83 and 8.90 and occur in the n.m.r. spectra of both the phosphine oxide products), and the 3-methyl at τ 9.21 (part of the doublet at τ 9.13 which is not seen in the n.m.r. spectrum of the deuterated phosphine oxide). The n.m.r. integration indicated a ratio of non-deuterated phosphine oxide to deuterated phosphine oxide of 1.1 ± 0.1; a similar value was indicated by comparison of the n.m.r. spectrum of the hydrolysis product with those of mixtures of known composition.

Alkaline Hydrolysis of 1,2,2,3,4-Pentamethyl-1-phenyl-3-phospholenium Iodide.

Excess iodomethane was added to a solution of 2,2,3,4-tetramethyl-1-phenyl-3-phospholen (0.87 g, 4 mmol; prepared by phenylsilane reduction of the phospholen 1-oxide) in benzene (10 ml). After stirring for 18 h filtration gave the phospholenium iodide (1.3 g, 90%), m.p. 153-154° (from chloroform-ethyl acetate), $\nu_{max.}$ 1440, 1120, 898, 857, 804, 778, 746, and 692 cm^{-1}, τ 1.80-2.47 (5H, m), 5.94 - 6.40 (2H, m), 7.30 (3H, d, J_{PH} 13 Hz), 7.99 (3H, d, J 1 Hz), 8.27 (3H, s), 8.42 (3H, d, J_{PH} 16 Hz), and 8.88 (3H, d, J_{PH} 18 Hz) (Found : C, 50.3; H, 6.1; P, 8.3. $C_{15}H_{22}IP$ requires C, 50.0; H, 50.0; H, 6.15; P, 8.6%).

The phospholenium iodide (1.08 g, 3 mmol) was refluxed with aqueous sodium hydroxide (2N; 5 ml) for 10 h. The mixture was extracted with ether, and the combined extracts were washed with water and dried. The solvent was evaporated and the residue (0.52 g) chromatographed on basic alumina (100 g). Elution with ether-ethyl acetate (9:1) afforded

methylphenyl(1,1,2,3-tetramethylbut-2-enyl)phosphine oxide (0.06 g, 8%), b.p. 85° (bath)/2.0 mm, $\nu_{max.}$ (film) 1444, 1300, 1180, 1120, 884, 748, and 702 cm^{-1}, m/e 250, 235, 219, 182, 181, 154, 140, 125, 111, and 95, τ 2.20-2.73 (5H, m), 8.13-8.43 (15, m), and 8.77 (3H,s) (Found: C, 71.8; H, 9.1; P, 12.2. $C_{15}H_{23}OP$ requires C, 71.95; H, 9.25; P, 12.35%). Elution with ether-ethyl acetate (1:4) afforded 1,2,2,3,4-pentamethyl-3-phospholen 1-oxide (0.42 g, 80%), b.p. 65° (bath)/2.0 mm, $\nu_{max.}$ (film) 1298, 1210, 1179, 1150, 1107, 880, and 835 cm^{-1}, m/e 172, 157, 139, 110, and 95, τ 7.23-7.87 (2H, m), 8.23 (3H, s), 8.34 (3H, d, J 1 Hz), 8.49 (3H, d, J_{PH} 13 Hz), 8.70 (3H, d, J_{PH} 12 Hz), and 8.80 (3H, d, J_{PH} 15 Hz) (Found : C, 62.6; H, 9.9; P, 17.9. $C_9H_{17}OP$ requires C, 62.75; H, 9.95; P, 18.0%).

Alkaline Hydrolyses of 1-Benzylphosphetanium Salts.

The salt (5 mmol) was stirred for 15 h in a mixture of ethanol (20 ml) and sodium hydroxide (1N;20 ml). Extraction with dichloromethane gave the phosphine oxide products. The stereoisomeric compositions of the 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxide products were determined by comparison of the n.m.r. spectra (CCl_4) of the total crude products with n.m.r. spectra (CCl_4) of mixtures of known composition. The stereoisomeric compositions of the 1,2,2,3,4,4-hexamethylphosphetan 1-oxide products were determined by integration of the n.m.r. spectra due to the 2,2,3,3-methyls [at τ 8.68 and 8.87 in the trans isomer, and τ 8.73 and 8.80 in the cis isomer] in the n.m.r. spectra of the total crude products. A pure sample of r-1,2,2,cis-3,4,4-hexamethylphosphetan 1-oxide (obtained by fractional recrystallisation of a mixture of cis and trans isomers from light petroleum, the cis isomer being concentrated in the mother liquors) exhibited signals in the n.m.r. at τ 7.93 (1H, dq, J 7, J_{PH} 7 Hz), 8.50 (3H, d, J_{PH} 11.5 Hz), 8.65 (6H, d, J_{PH} 16 Hz), 8.88 (6H, d, J_{PH} 19 Hz), and 9.08 (3H, dd, J 7, J_{PH} 1.5 Hz).

1. 1-Benzyl-2,2,3,4,4-pentamethyl-1-phenylphosphetanium Bromide.

The alkaline hydrolyses of the cis- and trans-salts gave the same product, namely the 1-phenylphosphetan oxide ( ) 90% yield; cis:trans = 10:90).

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

The alkaline of hydrolysis of the cis-salt (1-benzyl

and 3-methyl cis) gave only r-1,2,2,trans-3,4,4-hexamethylphosphetan 1-oxide (0.8 g, 92%). The trans-salt gave a mixture of isomers of the 1-methylphosphetan oxide (0.77 g, 89%; cis:trans = 75:25). When this salt was hydrolysed in aqueous sodium hydroxide (1N) the oxide product was of a different isomer composition (cis:trans = 30:70).

3. 1,1-Dibenzyl-2,2,3,4,4-pentamethylphosphetanium Bromide.

Alkaline hydrolysis of this salt gave r-1-benzyl-2,2, trans-3,4,4-pentamethylphosphetan 1-oxide (1.16 g, 93%), m.p. and mixed m.p. 180-182°, n.m.r. spectrum identical with that of an authentic sample.

Similarly, hydrolysis of the r-1-benzyl-1-p-deuteriobenzyl-2,2,trans-3,4,4-pentamethylphosphetanium bromide gave the trans-1-benzylphosphetan which was shown by mass spectrometry to contain 43% of labelled benzyl group.

Investigation of the Ylides formed from 1-Benzylphosphetanium Salts.

The 1-Benzyl-1-phenylphosphetanium salt (5 mmol) was stirred with butyl-lithium (2.0N; 2.5 ml) in dry tetrahydrofuran (50 ml) at room temperature for 1h; the 1-benzyl-1-methyl-phosphetanium salt was treated similarly for 0.75 h.

Half the solution (26 ml) was then added to 66% hydriodic acid (20 ml) at 0°. The solution was diluted with water (150 ml) and extracted with dichloromethane. The combined extracts were dried, the solvent evaporated, and the residue triturated with ether (300 ml) giving the

crystalline phosphetanium salt which was washed with more ether. The stereoisomer composition of the product was determined by integration of the n.m.r. spectra ($CF_3 \cdot CO_2H$) due to the benzylic protons, those of the cis isomers being ca. 8 Hz upfield of the trans isomers.

The remaining half of the ylide solution was treated with benzaldehyde (1.5 g) and stirred for 18 h. Stilbenes were estimated by g.l.c. (DE 120 column), the solvent evaporated, and the residue in dichloromethane was washed with water and dried. The solvent was evaporated and the residue chromatographed on basic alumina (100 g). Elution with light petroleum gave mixtures of stilbenes. Elution with ether-methanol (50:1) gave the phosphine oxide product whose stereoisomer composition was determined by n.m.r.

1. 1-Benzyl-2,2,3,4,4-pentamethyl-1-phenylphosphetanium Bromide.

The red ylide solution from the cis-salt (1-benzyl and 3-methyl cis) (1.95 g) with hydriodic acid gave only cis-phosphetanium salt (0.9 g). The reaction with benzaldehyde gave stilbene (90%; cis:trans = 84:16) and the trans-1-phenylphosphetan oxide (0.55 g, 93%).

The red ylide solution from the trans-salt gave a mixture of isomers of the 1-benzyl-2,2,3,4,4-pentamethyl-1-phenylphosphetanium salt (cis:trans = 51:49) and 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxide (91%; cis:trans = 51:49).

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

The pale yellow ylide solution from the cis-salt

(1.88 g)(1-benzyl and 3-methyl cis) gave the 1-benzyl-1,2,2,3,4,4-hexamethylphosphetanium salt (0.9 g; cis-trans = 90:10), and 1,2,2,3,4,4-hexamethylphosphetan 1-oxide (0.4 g, 87%; cis:trans = 10:90) and stilbene (cis:trans = 55:45).

The solution of the ylide from the trans-salt gave the benzylhexamethylphosphetanium salt (0.85 g: cis:trans = 66:34) and the hexamethylphosphetan oxide (0.41 g, 89%; cis:trans = 31:69). When the ylide solution was left at room temperature for 18 h the same oxide product was formed but with a different composition (cis:trans = 17:83).

r-1-Benzyl-1,2,2,trans-3,4,4-hexamethylphosphetanium iodide was used in an olefin synthesis with sodium ethoxide as the base. The salt (3.15 g, 5 mmol) and benzaldehyde (3 g) were added to a solution of sodium (0.12 g, 5 mmol) in very dry ethanol (25 ml) and the solution was set aside at room temperature for 18 h. G.l.c. analysis (DE 120 column) of the crude reaction mixture showed the presence of stilbene (65%; cis:trans = 1:1). The solvent was removed and the residue in dichloromethane was washed with water, dried, and the solvent evaporated. The residue was chromatographed on basic alumina (100 g). Elution with ether-methanol (100:1) gave 1,2,2,3,4,4-hexamethylphosphetan 1-oxide (91%; cis:trans = 35:65).

r-1-Benzyl-2,2,trans-3,4,4-pentamethyl-1-phenylphosphetanium Tetraphenylborate.

The trans-phosphetanium bromide (3.9 g, 0.01 mol) and sodium tetraphenylborate (3.4 g, 0.01 mol) were stirred in dry methanol (50 ml) for 3 h. The precipitate was filtered

off giving the phosphonium salt (5.4 g, 85%), m.p. 195-198°(from chloroform-ethyl acetate), $\nu_{max.}$ 1440 and 1120 cm^{-1}, τ ($CF_3 \cdot CO_2H$) 2.2-3.3 (30H, m), 6.03 (2H, d, J_{PH} 12 Hz), 6.98 (1H, dq, J 7, J_{PH} 2 Hz), 8.32 (6H, d, J_{PH} 20 Hz), 8.52 (6H, d, J_{PH} 19 Hz), and 8.90 (3H, dd, J 7, J_{PH} 1 Hz) (Found : C, 85.65; H, 7.7; P, 4.65. $C_{45}H_{48}BP$ requires C, 85.7; H, 7.7; P, 4.9%).

A suspension of the salt (3.15 g, 5 mmol) in tetrahydrofuran (50 ml) was stirred with butyl-lithium (2.0N; 2.5 ml) for 1 h. Excess benzaldehyde was added to the deep red ylide solution and the mixture stirred for 18 h. The solvent was evaporated and the residue chromatographed on basic alumina,(100 g). Elution with ether-methanol (100:1) gave 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxide (1.06 g, 90%; cis:trans = 80:20).

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

The trans-phosphetanium iodide (3.7 g, 0.01 mol) and sodium tetraphenylborate (3.4 g, 0.01 mol) gave the phosphonium salt (4.6 g, 81%), m.p. 205-208° (from acetonitrile-water), $\nu_{max.}$ 1435, 1300, 1042, and 911 cm^{-1}, τ (d_6-DMSO) 2.5-3.3 (25H, m), 5.83 (2H, d, J_{PH} 15 Hz), 8.20 (3H, d, J_{PH} 14 Hz), 8.58 (6H, d, J_{PH} 20 Hz), 8.73 (6H, d, J_{PH} 20 Hz), and 9.07 (3H, d, J 7 Hz).

The olefin synthesis with the salt (2.84 g, 5 mmol) in tetrahydrofuran (50 ml) and butyl-lithium (2.0N; 2.5 ml) gave 1,2,2,3,4,4-hexamethylphosphetan 1-oxide (0.77 g, 88%; cis:trans = 55:45).

1-Cumyl-2,2,3,4,4-pentamethyl-1-phenylphosphetanium Iodide.

A solution of 2,2,3,4,4-pentamethyl-1-phenylphosphetan (1.65 g, 7.5 mmol) and 1-bromo-1-phenylethane (1.85 g, 10 mmol) in benzene (20 ml) was refluxed for 16 h. Recrystallisation of the precipitate formed from chloroform-ethyl acetate gave a mixture of isomers of 2,2,3,4,4-pentamethyl - 1-phenyl-1-(1-phenylethyl)phosphetanium bromide (2.3 g, 75%), m.p. 229-233°, $\nu_{max.}$ 1438 and 1110 cm^{-1} (Found: C, 65.0; H, 7.6; P, 7.45. $C_{22}H_{30}BrP$ requires C, 65.2; H, 7.45; P, 7.65%).

To a stirred slurry of the phosphetanium bromide (2.02 g, 5 mmol) in tetrahydrofuran (20 ml) was added butyl-lithium (2N; 2.5 ml) and the mixture stirred for 1 h. The deep red solution was cooled to 0° and iodomethane (1.5 g) added. After stirring for 1 h the solvent was evaporated, and the residue dissolved in chloroform washed with water, dried, and concentrated. Ethyl acetate was added to the hot concentrated chloroform solution which on cooling gave a mixture of isomers of 1-cumyl-2,2,3,4,4-pentamethyl-1-phenylphosphetanium iodide (1.9 g, 81%), m.p. 174-175°, $\nu_{max.}$ 1317, 1157, 1108, and 998 cm^{-1} (Found : C, 59.2; H, 7.05; P, 6.45. $C_{23}H_{32}$ IP requires C, 59.25; H, 6.9; P, 6.65%). The n.m.r. spectrum showed peaks due to the major isomer at τ 2.1-3.2 (10H, m), 6.65 (1H, dq, $\underline{J}$ 7, $\underline{J}_{PH}$ 2 Hz), 7.78 (6H, d, $\underline{J}_{PH}$ 16.5 Hz), 7.98 (6H, d, $\underline{J}_{PH}$ 18 Hz), 8.48 (6H, d, $\underline{J}_{PH}$ 17.5 Hz), and 8.88 (3H, dd, $\underline{J}$ 7, $\underline{J}_{PH}$ 1 Hz), and peaks due to the minor isomer at 7.87 (d, $\underline{J}_{PH}$ 18 Hz), 7.92 (d, $\underline{J}_{PH}$ 16 Hz), and 8.42, the other peaks were obscured by those of the major isomer. N.m.r. integration indicated a 4:1 isomer

ratio.

The phosphetanium iodide (0.5 g) in a mixture of ethanol (5 ml) and sodium hydroxide (1N; 5 ml) was refluxed for 15 h. G.l.c. analysis (DE 120 column) of the reaction mixture showed the presence of cumene (75%). The solvent was evaporated and the residue partitioned between water and chloroform. The organic layer was dried and evaporated and the residue (0.24 g, 92%) was shown by n.m.r. to be a mixture of stereoisomers of 2,2,3,4,4-pentamethyl-1-phenyl-phosphetan 1-oxide (*cis*:*trans* = 55:45).

Preparation and Alkaline Hydrolyses of Alkoxy- and Alkylthio-phosphetanium Salts.

General Method of Preparation : A mixture of an oxonium salt (0.01 mol) and phosphetan sulphide or ester (0.01 mol) in dichloromethane (25 ml) was stirred at room temperature for 15 h. Addition of the solution to ether (250 ml) precipitated the crystalline phosphetanium salt. All the tetrafluoroborate salts readily decomposed and could only be kept for a few weeks over concentrated sulphuric acid.

1. r-1-Ethylthio-2,2,cis-3,4,4-pentamethyl-1-phenyl-phosphetanium Hexachloroantimonate.

2,2,trans-3,4,4-Pentamethyl-r-1-phenylphosphetan 1-sulphide (2.52 g, 0.01 mol) and triethyloxonium hexachloroantimonate (4.38 g, 0.01 mol) gave the phosphetanium salt (5.4 g, 87%), m.p. 188-189° (decomp.) (from acetone-ethyl acetate), $\nu_{max.}$ 1270, 1160, 1100, 998, 748, 718, and 692 cm^{-1}, τ (d_6-acetone) 1.57-2.20 (5H, m), 6.68-7.45 (3H, m), 8.20 (6H, d, J_{PH} 21 Hz), 8.27 (6H, d, J_{PH} 23 Hz), 8.73 (3H, dd, J 7, J_{PH} 1 Hz), and 8.75 (3H, t, J 7 Hz)(Found: C, 31.0; H, 4.2; P, 4.95. $C_{16}H_{26}Cl_6PSSb$ requires C, 31.2; H, 4.25; P, 5.05%).

A mixture of the salt (1.04 g, 1.7 mmol), sodium hydroxide (0.5N; 20 ml), and dioxane (20 ml) was stirred at room temperature for 5 minutes. The reaction mixture was extracted with dichloromethane and the combined organic layers dried. Evaporation of the solvent gave 2,2,trans-3,4,4,-pentamethyl-r-1-phenylphosphetan 1-oxide (n.m.r. spectroscopy).

2. r-1-Ethylthio-2,2,trans-3,4,4-pentamethyl-1-phenylphosphetanium Hexachloroantimonate.

2,2,cis-3,4,4-Pentamethyl-r-1-phenylphosphetan 1-sulphide (2.52 g, 0.01 mol) and triethyloxonium hexachloroantimonate (4.38 g, 0.01 mol) gave the phosphetanium salt (5.1 g, 82%), m.p. 174-176° (decomp.) (from acetone-ethyl acetate), $\nu_{max.}$ 1270, 1162, 1106, 998, 747, 772, and 692 cm^{-1}, τ (d_6-acetone) 1.67-2.10 (5H, m), 6.73-7.37 (3H, m), 8.25 (6H, d, J_{PH} 22 Hz), 8.27 (6H, d, J_{PH} 21 Hz), 8.77 (3H, t, J 7.5 Hz), and 8.82 (3H, dd, J 7, J_{PH} 1.5 Hz) (Found: C, 31.1; H,4.1; P, 4.9%).

The alkaline hydrolysis of this salt was carried out as described above and gave 2,2,cis-3,4,4-pentamethyl-r-1-phenylphosphetan 1-oxide (n.m.r. spectroscopy).

3. 1,1-Diethoxy-2,2,3,4,4-pentamethylphosphetanium Tetrafluoroborate.

r-1-Ethoxy-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (2.04 g, 0.01 mol) and triethyloxonium tetrafluoroborate (1.9 g, 0.01 mol) gave the phosphetanium salt (2.6 g, 81%) m.p. 121-125°, $\nu_{max.}$ 1281, 1047 br, 782, 751, 668, and 657 cm^{-1}, τ 5.37(3H, dq, J 7, J_{PH} 7 Hz), 5.40 (3H, dq, J 7, J_{PH} 7 Hz), 7.77 (1H, m), 8.45 (3H, t, J 7 Hz), 8.48 (3H, t, J 7 Hz), 8.52 (6H, d, J_{PH} 22 Hz), 8.60 (6H, d, J_{PH} 22 Hz), and 8.92 (3H, dd, J 7, J_{PH} 1.5 Hz).

The salt (1.6 g, 5 mmol) was stirred with sodium hydroxide (0.5N; 30 ml) for 1 minute. The reaction mixture was extracted with dichloromethane and the combined organic layers dried. Evaporation of the solvent gave a mixture of isomers of 1-ethoxy-2,2,3,4,4-pentamethylphosphetan 1-oxide

(0.92 g, 90%). Integration of the signals of the POCH protons (τ5.7-6.2) in the n.m.r. spectrum of the crude product indicated a stereoisomeric composition of cis:trans = 21:79. The signals due to the trans isomer (τ5.83) were ca. 2 Hz downfield from those of the cis isomer.

4. r-1-Ethoxy-1-ethylthio-2,2,trans-3,4,4-pentamethylphosphetanium Tetrafluoroborate.

r-1-Ethoxy-2,2,trans-3,4,4-pentamethylphosphetan 1-sulphide[32] (2.2 g, 0.01 mol) and triethyloxonium tetrafluoroborate (1.9 g, 0.01 mol) gave the phosphetanium salt (2.6 g, 77%), m.p. 116-118°, $\nu_{max.}$ 1285, 1055 br, 783, 752, 671, and 660 cm^{-1}, τ 5.42 (2H, dq, J 7, J_{PH} 6 Hz), 6.72 (2H, dq, J 7, J_{PH} 7 Hz), 7.62 (1H, dq, J 7, J_{PH} 4 Hz), 8.43 (3H, t, J 7 Hz), 8.47 (3H, t, J 7 Hz), 8.50 (6H, d, J_{PH} 20 Hz), 8.53 (6H, d, J_{PH} 23 Hz), and 8.93 (3H, dd, J 7, J_{PH} 1 Hz).

The alkaline hydrolysis of this salt was carried out as described above and gave a mixture of 1-ethoxy-2,2,3,4,4-pentamethylphosphetan 1-oxide (85%; cis:trans = 37:63) and 1-ethylthio-2,2,3,4,4-pentamethylphosphetan 1-oxide (15%). Integration of the signals of the POCH protons (τ5.7-6.2) and the PSCH protons (τ6.8-7.3) in the n.m.r. spectrum of the crude product gave the ratio of the ethoxy and ethylthio esters. The stereoisomeric composition of the ethoxy ester was determined as stated above. As the PSCH signals of the isomeric ethylthio esters could not be distinguished the stereoisomeric composition could not be determined.

5. r-1-Ethoxy-1-ethylthio-2,2,cis-3,4,4-pentamethylphosphetanium Tetrafluoroborate.

r-1-Ethylthio-2,2,trans-3,4,4-pentamethylphosphetan

1-oxide (2.2 g, 0.01 mol) and triethyloxonium tetrafluoroborate (1.9 g, 0.01 mol) gave the phosphetanium salt (3.1 g, 91%), m.p. 113-116°, $\nu_{max.}$ 1281, 1045 br, 782, 751, 669, and 657 cm^{-1}, τ 5.37 (2H, dq, J 7, J_{PH} 15 Hz), 6.72 (2H, dq, J 7, J_{PH} 7 Hz), 7.68 (1H, dq, J 7.5, J_{PH} 1.5 Hz), 8.43 (3H, t, J 7 Hz), 8.45 (3H, t, J 7 Hz), 8.48 (6H, d, J_{PH} 21 Hz), 8.50 (6H, d, J_{PH} 24 Hz), and 8.92 (3H, dd, J 7.5 Hz), J_{PH} 1.5 Hz).

The alkaline hydrolysis was carried out in the same manner as the hydrolysis of the stereoisomeric salt, and gave a mixture of 1-ethoxy-2,2,3,4,4-pentamethylphosphetan 1-oxide (88%; cis:trans = 49:51) and 1-ethylthio-2,2,3,4,4-pentamethylphosphetan 1-oxide (12%). Product composition was determined by n.m.r. integration.

Alkaline Hydrolysis of 1,2,2,3,4,4-Hexamethyl-1-phenylphosphetanium Iodide.

r-1,2,2,cis-3,4,4-Hexamethyl-1-phenylphosphetanium iodide (2 g, 5.5 mmol) was stirred at room temperature with sodium hydroxide (1N; 20 ml) for 15 h. Ether extraction then gave a mixture of phosphine oxides (1.35 g, 97%).

Recrystallisation from ether-light petroleum gave the pure major phosphine oxide (121) (1.23 g, 88%), m.p. 155-162° (freshly sublimed sample), n.m.r. and i.r. spectra identical with those described.[15] The n.m.r. spectrum of the mother liquors showed peaks due to the minor isomer at τ 8.44 (d, J_{PH} 12.5 Hz, P-Me), 8.62, 8.78, 8.83, 8.92, 8.99, and 9.10; The other peaks were obscured by those of the major isomer.

Hydrolysis of the isomeric trans-phosphetanium iodide in an identical manner gave a mixture of phosphine oxides (1.34 g, 96%) whose n.m.r. spectrum was identical with that of the phosphine oxides obtained from hydrolysis of the cis-phosphetanium iodide. The pure major isomer ($\rangle$ 90%) was obtained on recrystallisation from ether-light petroleum (1.21 g, 87%), m.p. and mixed m.p. 156-162° (freshly sublimed samples).

r-1,2,2,cis-3,4,4-Hexamethyl-1-phenylphosphetanium Iodide with Sodium Deuteroxide in Deuterium Oxide.

The salt (0.2 g) was stirred for 10 minutes in a solution of deuterium oxide (25 ml) containing sodium deuteroxide (1N; 1 ml). The solution was neutralised with

hydriodic acid and extracted with chloroform. The combined extracts were dried and evaporated. The residue was washed with ether giving 1,2,2,3,4,4-hexamethyl-1-phenylphosphetanium iodide (0.17 g, 85%); integration of the n.m.r. spectra ($CF_3 \cdot CO_2H$) due to the 2,2,4,4-methyls showed it to be a mixture of isomers (cis:trans = 65:45). There were no P-$\underline{C}H_3$ resonances in the spectrum.

When the salt (0.3 g) was stirred with N-sodium deuteroxide in deuterium oxide (10 ml) for 16 h ether extraction gave the spiro phosphine oxide (121), m.p. 155-162°, the n.m.r spectrum of which was identical with that described by Trippett and coworkers[15] except that integration indicated the presence of only one proton in the allylic region around τ 7.3, and the complete absence of any resonance in the P-$\underline{C}H_3$ region at τ 8.61.

Alkaline Hydrolysis of 1,2,2,3,4,4-Hexamethyl-1-(1-naphthyl)-phosphetanium Iodide.

The salt (1.0 g) was stirred for 15 h in a mixture of ethanol (10 ml) and sodium hydroxide (1N; 10 ml). The ethanol was evaporated off and water (20 ml) added to the residue. Ether extraction gave the phosphine oxide (193) (0.67 g, 91%), m.p. 123-124° (from light petroleum), $\nu_{max.}$ 1300, 1182, 1154, 928, 890, 865, 766, and 746 cm^{-1}, m/e 302, 301, 287, 212, 211, 196, 191, 189, 155, 141, 129, 128, and 106, τ 1.38-1.70 (1H, m), 2.62-2.93 (3H, m), 3.45-4.62 (2H, m), 6.43-6.73 (2H, m), 8.05 (1H, q, $\underline{J}$ 7, Hz), 8.56 (3H, d, $\underline{J}_{PH}$ 12 Hz), 8.66 (3H, d, $\underline{J}_{PH}$ 15.5 Hz), 8.70 (3H, d, $\underline{J}_{PH}$ 12.5 Hz), 8.87 (3H, s), 9.03 (3H, d, $\underline{J}$ 7 Hz), and 9.26 (3H, s) (Found : C, 75.5; H, 9.0; P, 10.2. $C_{19}H_{27}OP$ requires C, 75.45; H, 9.0; P, 10.25%).

Alkaline Hydrolysis of 2,2,-Dimethyl-2-phospha(IV)tetracyclo[3,2,1,$O^{3,6}$,$O^{3,6}$,$O^{4,7}$]octane Iodide.

2-Methyl-2-phosphatetracyclo[3,2,1,$O^{3,6}$,$O^{4,7}$]octane 2-oxide[10] (4.62 g, 0.03 mol) in benzene (20 ml) was added dropwise to a suspension of lithium aluminium hydride (2.3 g, 0.06 mol) in dibutyl ether (20 ml) at 100°. After reluxing for 4 h, water (10 ml) was added very cautiously, followed by hydrochloric acid (2N; 100 ml). The organic layer was dried, filtered, and stirred with iodomethane (7.1 g, 0.05 mol) for 16 h. Filtration gave the phosphonium iodide (4.3 g, 51%), m.p. 286-289° (decomp.) (from chloroform-ethyl acetate), $\nu_{max.}$ 1300, 985, 973, and 806 cm^{-1}, τ 7.20-7.50 (2H, m), 7.22 (6H, d, J_{PH} 14 Hz), 8.13-8.37 (2H, m), and 8.39-8.57 (4H, m) (Found :C, 38.2; H, 5.0; P, 10.8. $C_9H_{14}IP$ requires C, 38.6;H, 5.05; P, 11.05%).

The salt (2.8 g) was stirred in sodium hydroxide (2N; 30 ml) for 48 h. Ether extraction gave the hygroscopic 5-dimethylphosphinyltricyclo[2,2,1,$O^{2,6}$]heptane (1.3 g, 77%), m.p. 117-122° (from petrol, b.p. 60-80°), $\nu_{max.}$ 1298, 1290, 1155 br, 970, 938, 862, 810, 794, 740, and 702 cm^{-1}, m/e 170, 169, 155, 143, 142, 129, 105, 104, 92, 91, 79, 78, and 77. The n.m.r. spectrum was a complex series of multiplets, τ7.3-8.9, the only outstanding feature being at 8.52 (6H, d, J_{PH} 12.5 Hz) (Found: C, 63.1; H, 8.9; P, 18.0. $C_9H_{15}OP$ requires C, 63.5; H, 8.9; P, 18.2%).

Reaction of the Butyl-lithium with theSpirophospholan Oxide(121).

A mixture of the oxide (2.52 g, 0.01 mol) and n-butyl-lithium (2.5N; 4 ml) in ether (20 ml) was refluxed for 0.5 h. Hydrochloric acid (2N; 10 ml) was added, the organic

layer separated, dried, and evaporated. Recrystallisation of the residue from ether-light petroleum gave methyl-(3-phenyl-1,1,2,3-tetramethylbutyl)phosphine oxide (2.1 g, 83%), m.p. and mixed m.p. 127-131° (from ether-light petroleum), $\nu_{max.}$ 2290, 1185, 1158, 760, and 710 cm^{-1}, m/e 252, 124, 133, 119, and 91, τ 2.4-3.0 (5H, m), -0.10 and 7.61 (1H, d, J_{PH} 468 Hz), 7.13 (1H, dq, J 7, J_{PH} 6 Hz), 8.53 (3H, s), 8.55 (3H, d, J_{PH} 11.5 Hz), 8.73 (3H, d, J 6.5 Hz), 8.75 (3H, s), 8.81 (3H, d, J_{PH} 20 Hz), and 9.36 (3H, d, J_{PH} 20.5 Hz) (Found : C, 71.3; H, 9.8; P, 12.2. $C_{15}H_{25}OP$ requires C, 71.4; H, 10.0; P, 12.3%).

Reaction of Butyl-lithium with r-1,2,2,cis-3,4,4-Hexamethyl-1-phenylphosphetanium Iodide.

The phosphetanium iodide (0.5 g, 1.38 mmol) was stirred with butyl-lithium (1.8 N; 0.08ml) in dry tetrahydrofuran (15 ml) at room temperature for 0.25 h. Excess of iodomethane was then added and the solution was stirred for a further 0.5 h. The solvent was evaporated and the residue, in chloroform (30 ml), was washed, dried, and evaporated. Successive recrystallisation of the residue gave butyldimethyl-(3-phenyl-1,1,2,3-tetramethylbutyl)phosphonium iodide, (0.37 g, 61%), m.p. 119-121° (from chloroform-ethyl acetate), $\nu_{max.}$ (KBr) 1095, 770, and 710 cm^{-1}, τ 2.1-3.0 (5H, m), 6.64-ca.8.4 (7H, m, $[CH_2]_3$ and $PhCMe_2 \cdot CH$), 7.96 (6H, d, J_{PH} 13 Hz), 8.47 (3H, d, J 6 Hz), 8.53 (3H, s), 8.74 (3H, s), 8.90 (3H, d, J_{PH} 20 Hz), and 9.23 (3H, d, J_{PH} 20 Hz); the Me $[CH_2]_3$ signal was hidden under that from the other methyl protons (Found: C, 55.5; H, 8.3; P, 7.05. $C_{20}H_{36}IP$

requires C, 55.3; H, 8.35; P, 7.1%).

Reaction of Sodamide with r-1,2,2,cis-3,4,4-Hexamethyl-1-phenylphosphetanium Iodide.

The phosphetanium iodide (2.5 g, 7.0 mmol) was dissolved with stirring in a solution of sodamide (0.28 g, 7.0 mmol) in liquid ammonia (50 ml; freshly distilled from sodium). After 1h under reflux, the ammonia was evaporated off and dry benzene (50 ml) was added. The benzene solution was refluxed for 0.5 h, filtered, and added with stirring to 66% hydriodic acid (20 ml). The organic layer was separated, dried, and evaporated. The resulting viscous oil (0.63 g) was dissolved in dry methanol (15 ml) and treated with an excess of diazomethane. The residue, after evaporation of the methanol, was chromatographed on basic alumina (75 g). Elution with ether-ethyl acetate (1:1) afforded one isomer of methyl methyl-(3-phenyl-1,1,2,3-tetramethylbutyl)-phosphinate (0.167 g, 21%), m.p. 58-59° (from ether-light petroleum), $\nu_{max.}$ 1210, 1190, 1045, 885, 760, and 710 cm^{-1}, m/e 283, 282, 173, 164, 163, 119, 94, and 93, τ 2.44-2.90 (5H, m), 6.36 (3H, d, J_{PH} 10 Hz), 7.15 (1H, sextet), 8.54 (3H, s), 8.68 (3H, d, J 7 Hz), 8.70 (3H, d, J_{PH} 12.5 Hz), 8.82 (3H, d, J_{PH} 17 Hz), 8.83 (3H, s), and 9.39 (3H, d, J_{PH} 19 Hz) (Found: C, 67.95; H, 9.7; P, 10.9. $C_{16}H_{27}O_2P$ requires C, 68.05; H, 9.65; P, 10.95%). Elution with ether-ethyl acetate (1:3) afforded the other isomer (0.18 g, 24%), m.p. 66-67° (from ether-light petroleum), i.r. and mass spectra as described above, τ 2.47-3.05 (5H, m), 6.28 (3H, d, J_{PH} 10 Hz), 7.17 (1H, sextet), 8.54 (3H, s), 8.68 (3H, d, J_{PH} 12.5 Hz), 8.70 (3H, d, J 7 Hz), 8.80 (3H, d, J_{PH} 18 Hz),

8.82 (3H, s), and 9.36 (3H, d, J_{PH} 18.5 Hz) (Found : C, 68.0; H, 9.6; P, 10.8%). Elution with ethyl acetate afforded methyl-(3-phenyl-1,1,2,3-tetramethylbutyl)phosphine oxide (0.23g, 40%), m.p. 127-131°, whose n.m.r spectrum was identical with that of an authentic sample.

Reaction of p-Tolyl-lithium with Triphenylphosphine Sulphide.

Ethereal p-tolyl-lithium (0.65 N; 15.4 ml) was stirred for 18 h with triphenylphosphine sulphide (2.9 g, 0.01 mol) in ether (50 ml). Hydrochloric acid (1.0N; 20 ml) was added and the mixture was stirred for 0.25 h. The organic layer was dried and evaporated and the residue was chromatographed on basic alumina (100 g). Elution with light petroleum-benzene (5:1) gave a mixture of triphenylphosphine and diphenyl-p-tolylphosphine (2.1 g), whose ^1H n.m.r. spectrum showed a singlet, τ 7.75, attributable to the methyl protons of a p-tolyl group, the peak area of which was in the ratio 1:9.7 to that of the aromatic protons. This exidence is compatible with the presence of a 1:1 mixture of the phosphines. Elution with light petroleum-benzene (1:1) gave a mixture of disulphides (0.2 g) whose n.m.r. spectrum indicated the presence of equal numbers of phenyl and p-tolyl groups. Elution with benzene gave triphenylphosphine sulphide (0.15 g, 5% recovery), m.p. and mixed m.p. 162-163°. Elution with chloroform gave a mixture of triphenylphosphine oxide and diphenyl-p-tolyl-phosphine oxide (0.3 g) in the ratio 1:1 (n.m.r. spectrum). The products were characterised by t.l.c. and i.r. spectroscopy where possible.

Reaction of Phenyl-lithium with Tri-p-tolylphosphine Sulphide.

Ethereal phenyl-lithium (0.7N; 14.4 ml) was stirred for 18 h with the sulphide (3.36 g, 0.01 mol) in ether (50 ml). Hydrochloric acid (1.0N; 20 ml) was added and the mixture stirred for 0.25 h. The organic layer was dried and evaporated and the residue was chromatographed on basic alumina (100 g). Elution with light petroleum-benzene (5:1) gave a 1:1 mixture of tri-p-tolylphosphine and phenyldi-p-tolylphosphine (2.4 g). Elution with light petroleum-benzene (1:1) gave a mixture of disulphides. Elution with benzene gave tri-p-tolylphosphine sulphide (0.27 g, 8% recovery), m.p. and mixed m.p. 181-182°. Elution with chloroform gave a 1:1 mixture of tri-p-tolylphosphine oxide and phenyldi-p-tolylphosphine oxide (0.13 g). The compositions of the mixtures were determined from their n.m.r. spectra by comparing the peak areas of the signals attributable to the methyl protons of the p-tolyl group with those of the aromatic protons.

Ethylthiotriphenylphosphonium Tetrafluoroborate.

Triphenylphosphine sulphide (15.0 g, 0.051 mol) in dichloromethane (30 ml) was added to a solution of triethyloxonium tetrafluoroborate (9.5 g, 0.05 mole) in dichloromethane (50 ml). The mixture was stirred at room temperature for 12 h and poured into ether (500 ml). The phosphonium salt (19.3 g, 93%) was filtered off and crystallised from chloroform-ethyl acetate giving needles, m.p. 165-166°, $\nu_{max.}$ 1438, 1105, 1050, 994, 754, 723, and

690 cm^{-1}, $\tau(CF_3 \cdot CO_2H)$ 1.97-2.40 (15H, m), 6.97 (2H, dq, J 7, J_{PH} 11 Hz), and 8.63 (3H, t, J 7 Hz); because of its instability it was converted into the stable tetraphenylborate.

Ethylthiotriphenylphosphonium Tetraphenylborate.

The tetrafluoroborate (8.2 g, 0.02 mol) in acetone (50 ml) was poured into a solution of sodium tetraphenylborate (6.8 g, 0.02 mol) in water (100 ml) giving a white precipitate of the phosphonium salt (12.4 g, 95%), m.p. 180-181° (from nitromethane), $\nu_{max.}$ 1580, 1435, 1375, 1104, 743, 723, 700, and 684 cm^{-1}, $\tau(CF_3 \cdot CO_2H)$ 2.13-2.79 (35H, m), 7.27 (2H, dq, J 7, J_{PH} 11 Hz), and 8.35 (3H, d, J 7 Hz). A satisfactory analysis could not be obtained.

Reaction of p-Tolyl-lithium with Ethylthiotriphenylphosphonium Tetraphenylborate.

Ethereal p-tolyl-lithium (0.85N; 11.8 ml) was stirred for 48 h with a suspension of the phosphonium salt (6.42 g, 0.01 mol) in ether (50 ml). The solution was filtered under an atmosphere of nitrogen and the filtrate was stirred for 0.5 h with hydrochloric acid (1.0N; 11.8 ml). The ether layer was dried and evaporated and the residue was chromatographed on basic alumina (100 g). Elution with light petroleum-benzene (20:1) gave a mixture of ethyl phenyl sulphide and ethyl p-tolyl sulphide (1.0 g), b.p. 90-94°/9.5 mm, whose n.m.r. spectrum showed a singlet, τ 7.72, attributable to the methyl protons of a p-tolyl group, as well as signals for thioethyl and aromatic groups; integration

of the methyl and aromatic proton signals indicated the presence of a 1:9 mixture of the sulphides. Elution with light petroleum-benzene (4:1) gave a mixture of triphenylphosphine and diphenyl-p-tolylphosphine (2.0 g) in the ratio 9:1 (n.m.r. spectrum). Elution with chloroform gave a mixture of triphenylphosphine oxide and diphenyl-p-tolylphosphine oxide (0.25 g) in the ratio 9:1 (n.m.r. spectrum). All the products were characterised by t.l.c.

Reaction of Phenyl-lithium with 2,2,trans-3,4,4-Pentamethyl-r-1-phenylphosphetan 1-Sulphide.

Ethereal phenyl-lithium (1.5N; 6.7 ml) was added to a stirred solution of the sulphide (2.52 g, 0.01 mol) in ether (50 ml). After 0.5 h hydrochloric acid (1.0N; 20 ml) was added and the mixture stirred for 0.5 h. The organic layer was dried and evaporated and the residue was chromatographed on basic alumina (100 g). Elution with light petroleum-ether (10:1) gave unchanged phosphetan sulphide (1.3 g, 51% recovery), m.p. and mixed m.p. 102-103°, n.m.r. spectrum identical with that of an authentic sample. Elution with ether-methanol (50:1) gave (3-phenyl-1,1,2,3-tetramethyl-(butyl)diphenylphosphine oxide (1.8 g, 47%), m.p. 128-129° (from light petroleum), $\nu_{max.}$ 1437, 1170, 1105, 1089, 750, 720, 700, and 660 cm^{-1}, m/e 391, 390, 320, 271, 244, 202, 201, 183, 119, and 117, τ(CCl_4) 1.93-2.83 (10H,m), 2.99 (5H, s), 7.29 (1H, sextet), 8.62 (3H, s), 8.70 (3H, d, J 7 Hz), 8.74 (3H, d, J_{PH} 15 Hz), 9.00 (3H, s), and 9.40 (3H, d, J_{PH} 19 Hz) (Found : C, 79.9; H, 7.9; P, 8.0. $C_{26}H_{31}OP$ requires C, 79.95; H, 8.0; P, 7.95%).

Reaction of Phenyl-lithium with Diphenylphosphine Sulphide.

Ethereal phenyl-lithium (1.5 N; 13.4 ml) was added to a stirred solution of the sulphide (2.18 g, 0.01 mol) in ether (50 ml). After the initial red colouration had disappeared hydrochloric acid (1.0N; 20 ml) was added and the mixture stirred for 0.25 h. The organic layer was dried and evaporated and the residue was chromatographed on basic alumina (100 g). Elution with light petroleum-ether (20:1) gave triphenylphosphine (2.1 g, 83%), m.p. and mixed m.p. 80°. Elution with ether-methanol (20:1) gave triphenylphosphine oxide (0.28 g, 10%), m.p. and mixed m.p. 156-157°. The products were further characterised by t.l.c. and comparison of their i.r. spectra with those of authentic samples.

Reaction of Potassium Cyanide with 1,2,2,3,4,4-Hexamethyl-1-phenylphosphetanium Iodide.

The phosphetanium salt (4.7 g, 13.0 mmol; 3:2 isomer ratio) and potassium cyanide (0.85 g, 13.0 mmol) in ethanol (100 ml) were refluxed for 60 h. The solvent was removed and a solution of the residue in chloroform was washed, dried, and evaporated. The residue was chromatographed on basic alumina (300 g). Elution with ether-methanol (100:1) gave one isomer of (3-hydroxy-1,1,2,3-tetramethylbutyl)methyl(phenyl)phosphine oxide (1.24 g, 35%), m.p. 141-142° (from ether-light petroleum), $\nu_{max.}$ 3280, 1440, 1292, 1173, 1143, 1105, 1078, 882, 755, and 705 cm^{-1}, m/e (no molecular ion) 250, 182, 181, 140, 125, and 58, τ 2.03-2.63 (5H, m), 3.38 br (1H, s, which collapsed on the addition of one drop of D_2O), 8.07 (3H, d, J_{PH} 12 Hz), 8.67 (3H, s), 8.72 (3H, d, J 7 Hz), 8.82 (3H, d, J_{PH} 19 Hz), 8.89 (3H, d, J_{PH} 19 Hz), and 9.10 (3H, s); the $HO{\cdot}CMe_2{\cdot}C\underline{H}$ signal was hidden under that from the lower-field methyl protons (Found: C, 67.3; H, 9.5. $C_{15}H_{25}O_2P$ requires C, 67.15; H, 9.4; P, 11.55%). Elution with ether-methanol (100:2) afforded the other isomer (0.93 g, 28%), m.p. 140-141° (from ether-light petroleum), $\nu_{max.}$ 3320, 1435, 1152, 1104, 1078, 868, 745, and 700 cm^{-1}, mass spectrum identical with that just described, τ 2.08-2.95 (5H, m), 3.76 br (1H, s, which collapsed on the addition of one drop of D_2O), 8.13 (3H, d, J_{PH} 12 Hz), 8.68 (3H, d, J_{PH} 20 Hz), 8.75 (3H, s), (3H, d, J 5 Hz), 8.84 (3H, d, J_{PH} 17 Hz), and 9.12 (3H, s); the $HO{\cdot}CMe_2{\cdot}C\underline{H}$ signal was

hidden under that of the lower-field methyl protons (Found: C, 67.0; H, 9.2; P, 11.55%). Elution with ether-methanol (100:3) gave the spiro phosphine oxide (121) (0.16 g, 5%), i.r. and n.m.r. spectra identical with those of an authentic sample.

A solution of the above alcohol (m.p. 141-142°; 0.5 g, 1.87 mmol) and toluene-p-sulphonic acid mono-hydrate (0.2 g, 1.0 mmol) in benzene (150 ml) was boiled under reflux for 6 h with azeotropic separation of water (Dean-Stark). The solution was cooled and washed with a 5% aqueous solution of sodium hydrogen carbonate and with water. The dried benzene extract was evaporated to give (methyl)phenyl-(1,1,2,3-tetramethylbut-3-enyl)-phosphine oxide (0.34 g, 72%)m.p. 99-101° (from light petroleum), $\nu_{max.}$ 1630, 1435, 1298, 1160, 895, and 878 cm^{-1}, mass spectrum identical with that of the alcohol, τ 2.1-2.65 (5H, m), 5.17 br (2H, s), 7.17 (1H, dq, J 7, J_{PH} 9 Hz), 8.15 (3H, d, J 0.5 Hz), 8.23 (3H, d, J 12 Hz), 8.84 (3H, d, J 17 Hz) (Found: C, 71.9; H, 9.3. $C_{15}H_{23}OP$ requires C, 72.0; H, 9.5%).

Reaction of Cyanogen Bromide with 2,2,3,4,4-Pentamethyl-1-phenylphosphetan.

1. Cyanogen bromide (1.7 g, 16 mmol) in benzene (20 ml) was added to a solution of 2,2,3,4,4-pentamethyl-1-phenyl-phosphetan (3.5 g, 16 mmol) in benzene (20 ml). On warming a crystalline precipitate formed which disappeared after the mixture had been heated under reflux for 48 h. The resultant solution was stirred with sodium hydroxide

(2N; 10 ml) for 15 h, hydrogen peroxide (28%; 10 ml) was added and the mixture stirred for a further 1 h. The benzene layer was separated and the aqueous layer acidified with hydrochloric acid (2N) and extracted with chloroform (3x40 ml). The combined organic extracts were dried and evaporated to give a viscous oil which was chromatographed on silica (140 g). Elution with ether-light petroleum (1:1) afforded 3,3,4,5,5-pentamethyl-2-phenyl-1,2-oxaphospholan 2-oxide (1.2 g, 30%), b.p. 110-120° (bath)/2 mm as a 1:1 mixture of stereoisomers, $\nu_{max.}$ (film) 1440, 1238, 1123, 960, 915, 833, 736, and 698 cm^{-1}, m/e 252, 237, 194, 184, 183, 167, 125, 112, and 97 (Found: C, 66.4; H, 8.35; P, 12.0. $C_{14}H_{21}O_2P$ requires C, 66.65; H, 8.4; P, 12.3%). Repeated chromatography gave a mixture enriched in one isomer whose n.m.r. spectrum showed peaks at τ 2.1-2.5 (5H, m), 7.52 (1H, q, J 7 Hz), 8.43 (3H, s), 8.58 (3H, s), 8.73 (3H, d, J_{PH} 16 Hz), 9.02 (3H, d, J 7 Hz), and 9.25 (3H, d, J_{PH} 19 Hz); the minor component had peaks at τ 7.93 (1H, q, J 7 Hz) and 9.22 (3H, d, J_{PH} 18 Hz); the other peaks were obscured by the major isomer. Elution with ether-light petroleum (2:1) afforded (cyano)phenyl-(1,1,2,3-tetramethylbut-3-enyl)phosphine oxide (0.54 g, 13%), m.p. 75-85° (from light petroleum) as a mixture of diastereoisomers, $\nu_{max.}$ 2200, 1640, 1440, 1228, 1218, 1112, 900, 757, 730, and 702 cm^{-1}, m/e 261, 221, 193, 151, 125, 111, and 110, τ 1.90-2.57 (5H, m), 4.95-5.27 (2H, m), 6.75-7.37 (1H, m) and 8.1-9.0 (12H) (Found: C, 68.9; H, 7.7; P, 11.8. $C_{15}H_{20}NOP$ requires C, 68.95; H, 7.7; P, 11.85%); the mass

spectrum of the crude cyanophosphine oxide also had peaks at 314 and 316 attributable to (bromo)phenyl-(1,1,2,3-tetramethylbut-3-enyl)phosphine oxide but this could not be isolated. Elution with ether-methanol (95:5) afforded 1-phenyl-2,2,3,4-tetramethyl-3-phospholen 1-oxide (0.27 g, 7%), m.p. 118-119° (from petrol b.p. 60-80°), $\nu_{max.}$ 1435, 1213, 1145, 1102, 752, and 700 cm^{-1}, m/e 234, 219, 192, 166, 141, 125, 110, and 95, τ 2.10-2.67 (5H, m), 7.27 br (2H, d, J_{PH} 11 Hz), 8.17 (3H, s), 8.37 (3H, s), 8.65 (3H, d, J_{PH} 14 Hz), and 9.20 (3H, d, J_{PH} 16 Hz) (Found: C, 71.7; H, 8.25; P, 13.0. $C_{14}H_{19}OP$ requires C, 71.75; H, 8.15; P, 13.2%).

2. Cyanogen bromide (10.6 g, 0.1 mol) and 2,2,3,4,4-pentamethyl-1-phenylphosphetan (14.5 g, 0.065 mol) in benzene (200 ml) were heated under reflux for 60 h, by which time the initial precipitate had gone into solution. Sodium hydroxide (2N; 100 ml) was added and the mixture stirred for 2h, and then cooled during the cautious addition of hydrogen peroxide (28%, 50 ml). After stirring for 1h, the benzene layer was separated, dried, and evaporated to give a viscous oil (12 g) which was chromatographed on alumina (300 g). Elution with ether-ethyl acetate (2:3) gave 1-phenyl-2,2,3,4-tetramethyl-3-phospholen 1-oxide (6.5 g, 42%), m.p. and mixed m.p. 118-119°, n.m.r. spectrum identical with that of an authentic sample. Elution with ether-ethyl acetate (1:4) gave a mixture of stereoisomers of 1-phenyl-3,4,5,5-tetramethyl-2-phospholen 1-oxide (1.6 g, 10%), b.p. 140-150° (bath)/2.0 mm, $\nu_{max.}$ (film) 1437, 1182,

1150, 1110, 845, 803, 745, 710, and 696 cm^{-1}, m/e 234, 219, 205, 191, 141, 125, and 110; the major component exhibited peaks τ 2.15-2.70 (5H, m), 4.08 (1H, dd, J 1, J_{PH} 22 Hz), 7.28 (1H, q, J 7 Hz), 7.95 (3H, d, J 1 Hz), 8.67 (3H, d, J_{PH} 14 Hz), 9.03 (3H, d, J 7 Hz), and 9.28 (3H, d, J_{PH} 16 Hz) (Found: C, 71.6; H, 8.0; P, 13.2. $C_{14}H_{19}OP$ requires C, 71.75; H, 8.15; P, 13.2%).

The alkaline aqueous layer was acidified with hydrochloric acid (2N) and extracted with chloroform (3x150 ml). The combined extracts were dried and evaporated to give a viscous oil (3.7 g) which was chromatographed on silica (100 g). Elution with ether gave 5-bromomethyl-2-phenyl-3,3,4,5-tetramethyl-1,2-oxaphospholan 2-oxide (2.8 g, 13%), m.p. 135-138° (from ether-light petroleum), $\nu_{max.}$ 1440, 1240, 1212, 1199, 1120, 1037, 947, 900, 886, 817, 762, 738, 700, and 636 cm^{-1}, m/e (for ions containing bromine only the peaks due to ^{79}Br are quoted) 331, 330, 329, 315, 261, 251, 237, 221, 194, 193, 183, 141, 125, 113, 111, and 97, τ 1.93-2.60 (5H, m), 6.27 (2H, s), 7.40 (1H, q, J 7 Hz), 8.40 (3H, s), 8.68 (3H, d, J_{PH} 15 Hz), 8.87 (3H, d, J 7 Hz), and 9.20 (3H, d, J_{PH} 18 Hz) (Found: C, 50.6; H, 6.1; Br, 24.0; P, 9.3. $C_{14}H_{20}BrO_2P$ requires C, 50.75; H, 6.1; Br, 24.15; P, 9.35%).

Hydrolysis of (Cyano)phenyl-(1,1,2,3-tetramethylbut-3-enyl)-phosphine Oxide.

The oxide (0.26 g, 1.0 mmol) was refluxed in sodium hydroxide (2N; 2 ml) and ethanol (5 ml) for 18 h. The solution was diluted with water (30 ml) and extracted with

dichloromethane (20 ml) to remove any unchanged oxide. Acidification of the aqueous layer followed by extraction with dichloromethane gave phenyl-(1,1,2,3-tetramethylbut-3-enyl)phosphinic acid (0.21 g, 83%), m.p. 89-90° (from ethanol-water), $\nu_{max.}$ 2200 br, 1440, 1196, 1130, 1087, 1071, 975, 955, 893, 757, 744, and 700 cm^{-1}, m/e 504, 394, 252, 237, 197, 183, 156, 142, and 108, τ -0.75 br (1H, s, collapsed on the addition of one drop of D_2O), 2.03-2.73 (5H, m), 5.30 (2H, d, J 8 Hz), 7.42 (1H, dq, J 7, J_{PH} 11 Hz), 8.38 (3H, s), 8.85 (3H, d, J 7 Hz), 8.93 (3H, d, J_{PH} 17 Hz), and 9.08 (3H, d, J_{PH} 16 Hz) (Found: C, 66.7; H, 8.4; P, 12.2. $C_{14}H_{21}O_2P$ requires C, 66.65; H, 8.4; P, 12.3%).

Acid Catalysed Cyclisation of Phenyl(1,1,2,3-tetramethylbut-3-enyl)phosphinic Acid.

The phosphinic acid (0.25 g, 1.0 mmol) was refluxed in hydrochloric acid (0.1N; 10 ml) for 2 h. The mixture was extracted with ether, and the combined extracts were washed with water and dried. The solvent was evaporated off giving a 1:1 mixture of isomers of 3,3,4,5,5-pentamethyl-2-phenyl-1,2-oxaphospholan 2-oxide (0.22 g, 87%), b.p. 110-120° (bath)/2 mm, n.m.r. and i.r. spectra identical with those of an authentic sample of a 1:1 mixture of isomers.

Reaction of Bromine with theSodium Salt of Phenyl(1,1,2,3-tetramethylbut-3-enyl)phosphinic Acid.

Bromine (0.32 g, 2.0 mmole) was added slowly dropwise to a stirred solution of the acid (0.5 g, 2.0 mmol) in sodium hydroxide (0.1N; 20 ml) and the mixture stirred for

2h. The mixture was extracted with chloroform (3x15 ml). The combined extracts were dried and evaporated and the residue chromatographed on silica (50 g). Elution with ether-methanol (100:1) gave 5-bromomethyl-2-phenyl-3,3,4,5-tetramethyl-1,2-oxaphospholan 2-oxide (0.25 g, 39%), m.p. and mixed m.p. 135-138°, n.m.r. spectrum identical with that of an authentic sample.

Reaction of Bromine with 2,2,3,4,4-Pentamethyl-1-phenyl-phosphetan.

Bromine (8.0 g, 0.05 mol) in dichloromethane (25 ml) was added dropwise to a stirred solution of the phosphetan (11.0 g, 0.05 mol; cis:trans = 1:1) in dichloromethane (25 ml) at -20°. The solution was allowed to warm to room temperature (1h) and then the solvent was removed under reduced pressure leaving a white crystalline residue which was heated at 160°/0.6 mm. The pale yellow solid which distilled was a mixture of phospholen hydrobromides (11.6 g, 77%), b.p. 108°/0.6 mm, m.p. 120-135°, $\nu_{max.}$ ($CHCl_3$) 2440, 2220, 1590, 1440, and 1120 cm^{-1}. The n.m.r. spectrum due to the major component, 1-phenyl-2,2,3,4-tetramethyl-3-phospholen hydrobromide (82%), had signals at τ 1.47-2.53 (5H, m), -3.6 and 4.93 (1H, very broad d, J_{PH} 512 Hz), 6.22 (2H, d, J_{PH} 11 Hz), 8.03 (3H, s), 8.27 (3H, s), 8.30 (3H, d, J_{PH} 19 Hz), and 8.82 (3H, d, J_{PH} 17 Hz). That of the minor component, 1-phenyl-3,4,5,5-tetramethyl-2-phospholen hydrobromide (18%), had peaks at τ 3.68 (d, J_{PH} 28 Hz), 7.67, 8.78 and 9.13; the other peaks were obscured by those of the 3-phospholen hydrobromide.

Addition of the mixture of hydrobromides (9.0 g, 0.03

mol) to water (25 ml) gave an acidic solution which was neutralised with aqueous sodium hydroxide (1N; 31.6 ml). Hydrogen peroxide (100 vol; 15 ml) was added and after stirring for 2h the solution was extracted with chloroform (3x50 ml). The combined extracts were washed with water, dried, and evaporated giving a viscous oil (6.6 g) which was chromatographed on alumina (300 g). Elution with ether-ethyl acetate (2:3) gave 1-phenyl-2,2,3,4-tetramethyl-3-phospholen 1-oxide (4.9 g, 70%), m.p. and mixed m.p. 118-119°. Elution with ether-ethyl acetate (1:4) gave a mixture of isomers of 1-phenyl-3,4,5,5-tetramethyl-2-phospholen 1-oxide (1.1 g, 15%), b.p. 115°/0.2 mm. The phospholen oxide products were further characterised by t.l.c. and comparison of their n.m.r. and i.r. spectra with those of authentic samples.

Preparation of 1-Phenyl-2,2,3,4-tetramethyl-3-phospholen Hydrobromide.

A mixture of 1-phenyl-2,2,3,4-tetramethyl-3-phospholen 1-oxide (1.17 g, 5.0mmol) and phenylsilane (0.54 g, 5.0 mmol) was kept at 90° for 1 h and distilled to give 1-phenyl-2,2,3,4-tetramethyl-3-phospholen (0.97 g, 89%), b.p. 104°/0.2 mm, τ (neat) 2.43-2.95 (5H, m), 6.82-8.1 (2H, m), 8.25 (3H, s), 8.53 (3H, d, J 1.5 Hz), 8.77 (3H, d, J_{PH} 20 Hz), and 9.29 (3H, d, J_{PH} 9 Hz).

Hydrogen bromide was passed into a solution of the phospholen (0.87 g, 4.0 mmol) in ether (20 ml) to give white crystals of the 3-phospholen hydrobromide (1.1 g, 91%),

m.p. 153-156°, b.p. 85°/0.2 mm, $\nu_{max.}$ ($CHCl_3$) 2440, 2220, 1590, 1440, and 1120 cm^{-1}. The nmr. spectrum was identical with that of the major product from the reaction of bromine with 1-phenyl-2,2,3,4,4-pentamethylphosphetan. An analysis was not obtained because of the extremely hygroscopic nature of the compound.

Reaction of Chlorine with 2,2,3,4,4-Pentamethyl-1-phenylphosphetan.

Chlorine (7.1 g, 0.1 mol) in 1,2-dichloroethane (40 ml) was added dropwise to a stirred solution of the phosphetan (22.0 g, 0.1 mol; trans:cis = 1:1) in 1,2-dichloroethane (50 ml) at -20°. The solution was allowed to warm to room temperature (1 h) and the solvent distilled off leaving a white crystalline residue which on pyrolysis under reduced pressure (0.6 mm) gave (chloro)phenyl-(1,1,2,3-tetramethylbut-3-enyl)phosphine (23.5 g, 93%), b.p. 124°/0.6 mm as a mixture of diastereoisomers, τ 2.23-2.77 (5H, m), 5.03-5.27 (2H, m), 7.52 (1H, sextet, J 7, J_{PH} 14 Hz), 8.23 (3H, s), and 8.5-9.3 (9H); the n.m.r. spectrum indicated a 1:1 mixture ofisomers, this ratio was always obtained independent of the phosphetan isomer ratio. The chlorophosphine was obtained in similar yields when the reaction was carried out in carbon tetrachloride or dichloromethane.

Reaction of Phosgene with 2,2,3,4,4-Pentamethyl-1-phenylphosphetan.

A solution of phosgene (5.0 g, 0.05 mol) in dichloromethane (50 ml) was reacted with a solution of the phosphetan

(11.0 g, 0.05 mol) in dichloromethane as above. Distillation gave the acyclic chlorophosphine (11.6 g, 90%), b.p. 101°/0.1 mm, as a 1:1 mixture of diastereoisomers whose n.m.r. was identical with that of the chlorophosphine obtained from chlorine and the phosphetan.

Reactions of (Chloro)phenyl-(1,1,2,3-tetramethylbut-3-enyl)-phosphine.

1. Thermal Cyclisation.

Heating the chlorophosphine (4.0 g) to 150° caused the evolution of a gas which stopped after the phosphine had been heated at 200° for 2 h. Distillation gave a mixture of phospholens (3.0 g, 87%), b.p. 84°/0.1 mm. The n.m.r. spectrum due to the major isomer (97%) was identical with that of 1-phenyl-2,2,3,4-tetramethyl-3-phospholen . That of the minor isomer (3%) had a peak at τ4.1 (d, J_{PH} 22 Hz) which identified it as 1-phenyl-3,4,5,5-tetramethyl-2-phospholen ; the other peaks were obscured by those of the major isomer.

2. Aluminium Chloride-Catalysed Cyclisation.

The chlorophosphine (2.54 g, 0.01 mol) was stirred with aluminium chloride (1.33 g, 0.01 mol) in dichloroethane (25 ml) at room temperature for 24 h. Hydrogen peroxide (20 vol., 20 ml) was then added and the mixture stirred for a further 2h. The organic layer was washed with water, dried, and evaporated. The residue was chromatographed on basic alumina (100 g). Elution with ether-ethyl acetate (2:1) gave a mixture of stereoisomers of 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxide (0.88 g, 37%; cis:trans = 1:1). Elution with ether-ethyl acetate (2:3) gave

1-phenyl-2,2,3,4,4-tetramethyl-3-phospholen 1-oxide (0.7 g, 30%), m.p. and mixed m.p. 118-119°. Elution with ether-ethyl acetate (1:4) gave 1-phenyl-3,4,5,5-tetramethyl-2-phospholen 1-oxide (0.14 g, 6%), b.p. 110/0.1 mm. The products were characterised by comparison of their n.m.r. spectra with those of authentic samples.

3. Alkaline Hydrolysis.

Hydrogen peroxide (20 vol., 20 ml) was added to the chlorophosphine (5.1 g) dissolved in ethanol (20 ml) and the solution stirred for 2 h. Sodium hydroxide (2N; 20 ml) was then added and the solution was boiled under reflux for 18 h. The aqueous solution was extracted with ether (2x50 ml), acidified with hydrochloric acid (2N), and then extracted with chloroform (3x50 ml). The combined chloroform extracts were washed, dried, and evaporated giving phenyl-(1,1,2,3-tetramethylbut-3-enyl)phosphinic acid (1.5 g, 30%), m.p. and mixed m.p. 89-90°, the n.m.r. spectrum was identical with that of an authentic sample.

m-Chloroperbenzoic Acid Oxidation of Triphenylphosphine Sulphide.

A solution of the acid (0.69 g, 0.04 mol) in dichloromethane (50 ml) was added dropwise to a stirred solution of triphenylphosphine sulphide (1.18 g, 0.04 mol) in dichloromethane (20 ml) at 0°, a pale yellow precipitate forming instantly. After stirring for 1 minute the solvent was evaporated and the residue chromatographed on basic alumina (100 g). Elution with light petroleum gave crystalline sulphur (0.11 g, 86%). Elution with benzene gave triphenylphosphine sulphide (50 mg, 4% recovery). Elution with chloroform gave triphenylphosphine oxide (1.05 g, 90%).

The products were characterised by mixed melting points, t.l.c., and i.r. spectroscopy.

m-Chloroperbenzoic Acid Oxidations of Phosphetan Sulphides.

General Procedure: A solution of the acid (6.0 mmol) in dichloromethane (30 ml) was added dropwise to a stirred solution of the phosphetan sulphide (5 mmol) in dichloromethane (20 ml) at 0° and the solution stirred for 1 minute. The products isolated were identified by comparison of their n.m.r. spectra with those of authentic samples.

1. 2,2,trans-3,4,4-Pentamethyl-r-1-phenylphosphetan 1-Sulphide.

The dichloromethane solution was evaporated and the residue chromatographed on basic alumina (100 g). Elution

with light petroleum gave sulphur (140 mg, 88%). Elution with ether gave 2,2,trans-3,4,4-pentamethyl-r-1-phenylphosphetan 1-oxide (1.02 g, 93%), m.p. and mixed m.p. 126-127°.

2. 2,2,cis-3,4,4-Pentamethyl-r-1-phenylphosphetan 1-Sulphide.

The reaction was carried out in an identical manner to that of the trans-phenylphosphetan sulphide. Elution with ether gave 2,2,cis-3,4,4-pentamethyl-r-1-phenylphosphetan 1-oxide (0.95 g, 85%), m.p. and mixed m.p. 117-118°.

3. r-1-Chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-Sulphide.[32]

The dichloromethane solution was filtered, the acid removed from it by extraction with aqueous sodium hydrogen carbonate, washed with water, and dried. Evaporation gave r-1-chloro-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (0.77 g, 79%), m.p. and mixed m.p. 73-74°.

4. r-1-Ethoxy-2,2,trans-3,4,4-pentamethylphosphetan 1-Sulphide.[32]

The acid was removed from the reaction mixture using aqueous sodium hydrogen carbonate. Distillation gave r-1-ethoxy-2,2,trans-3,4,4-pentamethylphosphetan 1-oxide (0.83 g, 81%), b.p. 70°/1.0 mm.

Reaction of Styrene Oxide with 2,2,3,4,4-Pentamethyl-1-phenylphosphetan 1-Sulphide and 1-Oxide.

A mixture of the trans-1-phenylphosphetan 1-sulphide (2.52 g, 0.01 mol) and styrene oxide (1.2 g, 0.01 mol) was heated at 190° for 1 h. The resultant red solution was

chromatographed on basic alumina (200 g). Elution with ether-methanol (100:1) gave 2,2,3,4,4-pentamethyl-1-phenylphosphetan 1-oxide (2.04 g, 86%) which was shown by n.m.r. spectroscopy to be a mixture of isomers (cis:trans = 1:9).

Similarly the cis-1-phenylphosphetan 1-sulphide gave a mixture of stereoisomers of the phosphetan oxide (2.15 g, 91%; cis:trans = 1:1).

The reaction of cis-1-phenylphosphetan 1-oxide (2.36 g, 0.01 mol) and styrene oxide (1.2 g, 0.01 mol) under the conditions described above gave a mixture of stereoisomers of the phenylphosphetan oxide (2.1 g, 89%; cis:trans = 1:1).

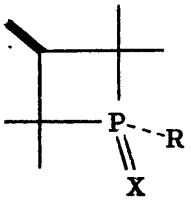
Reaction of Styrene Oxide with Triphenylphosphine Sulphide.

A mixture of the sulphide (2.94 g, 0.01 mol) and styrene oxide (1.2 g, 0.01 mol) was heated at 190° for 2 h. The red solution produced was chromatographed on basic alumina (200 g). Elution with benzene gave triphenylphosphine sulphide (0.74 g, 25% recovery). Elution with chloroform gave triphenylphosphine oxide (1.8 g, 65%). The products were characterised by i.r. spectroscopy.

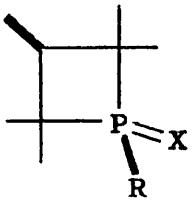
A mixture of the sulphide (2.94 g, 0.01 mol) and styrene oxide (2.4 g, 0.02 mol) also gave triphenylphosphine oxide (1.95 g, 70%).

^{31}P Chemical Shifts (δ ppm from 85% phosphoric acid).

Recorded using a Varian D.A. 60 spectrometer for samples in chloroform except as otherwise noted.

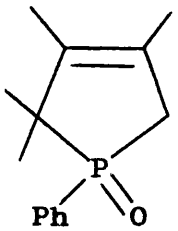


(274)

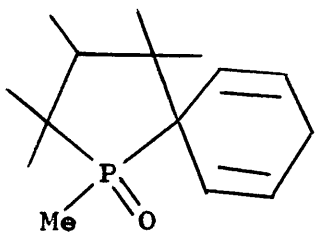


(275)

COMPOUND		δ	
(274; X = O, R = Ph)	(41)	-64.9	
(275; X = O, R = Ph)	(112)	-67.4	
(274; X = O, R = Nap)		-72.0	
(274; X = O, R = OEt)	(43)	-53.0	(neat)
(274; X = O, R = SEt)	(44)	-73.0	(neat)
(275; X = O, R = SEt)	(265)	-74.8	(neat)
(274; X = S, R = Ph)	(165)	-94.5	
(274; X = S, R = Cl)	(19)	-133.7	
(274; X = S, R = OEt)	(20)	-120.6	(neat)

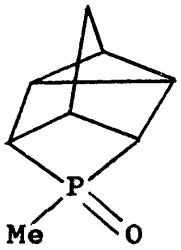
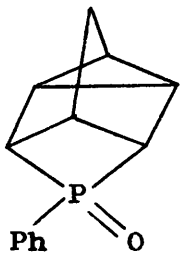


(102) -58.4



(121) -83.0

^{31}P Chemical Shifts.

COMPOUND		δ
	(11)	-55.6
	(12)	-51.9

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J. R. Corfield Ph. D. Thesis

SUMMARY

A study of the stereochemistry of substitution reactions at the phosphorus atom of 2,2,3,4,4-pentamethylphosphetans has been made. It is proposed that all such displacements proceed *via* trigonal bipyramidal intermediates in which the ring spans an apical-equatorial position.

Walden cycles in which substitution at the phosphoryl centre of phosphetans proceeds with retention of configuration are described and a mechanism involving pseudorotation of the intermediates is proposed. *Cis* and *trans* isomers of 2,2,3,4,4-pentamethylphosphetan 1-oxides can be distinguished by the paramagnetic shifts of the respective 3-protons in their n.m.r. spectra in the presence of tris(dipivalomethanato)europium(III).

Following a discussion of the mechanism of the alkaline hydrolysis of phosphonium salts, the hydrolysis of three salts in D_2O-H_2O (1:1) is described. The kinetic isotope effects observed show that the carbanions involved in these hydrolyses are not free in the rate-determining transition state. The alkaline hydrolysis of a 3-phospholenium salt is described in which the normal rule, that hydrocarbon will be formed from the group most stable as the anion, does not apply. 2,2,3,4,4-Pentamethylphosphetanium salts undergo alkaline hydrolysis with complete retention or with partial inversion of configuration at phosphorus. These differences are discussed in terms of the energy barriers to pseudorotation of the intermediates involved.

Other substitution reactions at the phosphorus of phosphetans bring about either ring expansion or ring opening.

All the reactions are governed by the preference of the four-membered ring for the apical-equatorial position in the trigonal bipyramidal intermediates. Attempts to generate the ylide from 1,2,2,3,4,4-hexamethyl-1-phenylphosphetanium iodide lead to ring opening *via* pentacovalent intermediates as also do the action of cyanide ion on this salt. 2,2,3,4,4-Pentamethyl-1-phenylphosphetan 1-sulphide with two molar proportions of phenyl-lithium gave (1,1,2,3-tetramethyl-3-phenylbutyl)diphenylphosphine. 2,2,3,4,4-Pentamethyl-1-phenylphosphetan with chlorine or bromine gave (1,1,2,3-tetramethyl-but-3-enyl) halogenophosphines which cyclised to phospholens on heating, and to phospholens and phosphetan 1-oxides on treatment with aluminium chloride.

A study was made of the conversion of thiophosphoryl compounds into phosphoryl compounds.