PSUEDOROTATION
IN
PENTACOORDINATE PHOSPHORANES
AS A
MECHANISTIC PROBE

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, 1971 and June, 1974.

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

Signed.

M.W. White

M.W. White.

June, 1975.
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1. **STRUCTURE AND BONDING OF PENTACOORDINATE PHOSPHORANES.**

1.1 **Theoretical Aspects of Structure and Configuration.**

Molecular orbital calculations\(^1\) and electron pair repulsion theory\(^2\) have both shown that the most stable geometry of a pentacoordinate molecule is the trigonal bipyramid (TBP). Other geometries, e.g. the square based pyramid and the two structures (1.1) and (1.2) of \(C_5\) geometry, are all less stable than the TBP structure.\(^{1a,1g}\)

\(\text{(1.1)}\)  \(\text{(1.2)}\)

A consideration of the bonding in a TBP is necessary in order to predict some of the factors which affect the relative stabilities of configurations in pentacoordinate phosphoranes having more than one type of substituent.

A simple molecular orbital (MO) model has been described by Rundle.\(^3\) The equatorial bonds of the TBP are formed from \(sp^2\) hybridized orbitals on phosphorus and the apical bonds are formed from a \(p\) orbital only. The molecular orbitals are then obtained by a linear combination of atomic orbitals (LCAO) of phosphorus and its ligands. Scheme 1 shows the resulting MOs using ligand \(s\) atomic orbitals. The equatorial bonds can be considered as normal, with three two-electron \(\sigma\) bonds. The four remaining valence electrons occupy the bonding three centre MO and the nonbonding MO. The bonding orbital will necessarily withdraw some electron density from phosphorus, placing it on the apical ligands, giving the bond ionic as well as covalent character. For this type of
bond to be stable requires that the apical ligands be more electronegative than the central phosphorus atom. Thus in a phosphorane with more than one type of substituent, the most electronegative ligands should preferentially occupy the apical positions.

A more accurate description of the bonding is that of the completely delocalized MO picture derived from quantum mechanical calculations. Hoffmann, Howell and Muetterties\(^1\) have presented such a scheme which is both simple and informative. The occupied MOs of the TBP were calculated for the model phosphorane PH\(_5\) both with and without the incorporation of 3d orbitals on phosphorus. The occupied MOs are shown in Scheme 2.

Using this scheme Hoffmann\(^1\) was able to predict some of the factors which affect a substituent's preference for the apical positions of the TBP. These are outlined below.
SCHEME 2
Molecular Orbital Scheme for PH$_5$ without 3d Orbitals.

<table>
<thead>
<tr>
<th>Relative Energies</th>
<th>Symmetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a'</td>
<td></td>
</tr>
<tr>
<td>1e'</td>
<td></td>
</tr>
<tr>
<td>1a'_</td>
<td></td>
</tr>
<tr>
<td>1a'</td>
<td></td>
</tr>
</tbody>
</table>

The circle sizes indicate schematically the magnitude of the contribution of the atomic orbital to the MO.

(a) Electronegativity.

The distribution of charge (1.3) on the hydrogen atoms of the PH$_5$ model indicated a relative accumulation of electron density on the apical hydrogens.

$$\text{H} -0.262$$

$$\text{H} \quad \text{P} \quad \text{H} -0.051 \quad \text{(1.3)}$$
Electronegative substituents should therefore prefer to occupy the apical positions where there is most electron density. Other workers using PH$_5$\(^1b,c,4\) and other phosphoranes\(^1d,h,5\) as models came to similar conclusions. Molecular orbital calculations (CNDO/2) on substituted phosphoranes and their isomers has enabled a comparison to be made of ligand preferences for the apical positions over the equatorial positions. The scale (1.4) represents the difference in energy between structures (1.5) and (1.6).

\[
\begin{array}{ccccccc}
F^a & OH^b & H^a & OH^c & OCH$_2$CF$_3$^a & Cl^a & (CH$_3$)$_b^b \\
0 & 10 & 20 & 30 & 40 & 50 & c^-
\end{array}
\]

\(\Delta\text{(Binding Energy)} \text{ kcal mol}^{-1}\)

\[(1.4)\]

\[(1.5)\]

\[
\begin{array}{c}
\text{XPF}_4 \\
(1.7)
\end{array}
\]

\[(1.8)\]

\[(1.9)\]

a. From calculations on (1.7)\(^b\)

b. From calculations on (1.8)\(^h\)

c. From calculations on (1.9)\(^h\).

Huheey\(^6\) has calculated the electronegativities of a wide range of atoms and groups. Some of these are shown on the scale (1.10) below for comparison with the calculated preferences for the apical positions of the TBP shown in (1.4).

Apart from hydrogen, the relative order of ligand preferences for the apical positions appears to be similar to the order of electronegativities.
The anomalous position of hydrogen obviously indicates that there are other factors which affect a ligand's preference for the apical position.

The electronegativities as calculated by Huheey are based on the assumption, originally proposed by Sanderson\(^7\), that electronegativity is equalised by transfer of charge upon covalent bond formation, e.g. for the molecule HCl equalisation of the electronegativities of H and Cl on formation of the covalent H-Cl bond, results in a net negative charge on chlorine of -0.092 of an electron.\(^6\) This equalisation of electronegativities can only occur in a bonding type MO.

In a TBP phosphorane, only the MOs \(1a_2^\pi\) and \(1a_1^\pi\), Scheme 2, would allow equalisation of electronegativity between the phosphorus atom and the apical substituents on covalent bond formation. It is an inherent property of the nonbonding MO \(2a_1^\pi\) that a 'fixed' proportion of charge remains on the apical ligands. Thus Huheey's electronegativity scale cannot be expected to be completely applicable to the apical preferences of substituents in TBP phosphoranes. Account should be taken of a ligand's ability to accommodate a certain fixed amount of negative charge. However, since this charge will be less than one electron it is difficult to visualise a suitable parameter which quantifies this property.
The preference of a group for the apical position should therefore be determined by a ligand's electronegativity and its ability to accommodate a fixed amount of negative charge.

(b) **Ligand \(\pi\) Donors and Acceptors.**

The \(\pi\) orbitals on a ligand can interact with the \(\sigma\) (filled) or \(\sigma^*\) (empty) orbitals on phosphorus. However, there are no low-lying \(\sigma^*\) orbitals in the TBP molecule, and so this type of interaction will be negligible. The symmetry-allowed \(\pi\)-\(\sigma\) interactions for apical and equatorial ligands are shown in Scheme 3.\(^{1a}\)

**Scheme 3**

**Apical**

- \(e_y = p_y + 1\) e
- \(e_x = p_x + 1\) e

**Equatorial**

- \(b_2 = p_e + 1\) e
- \(b_1 = p_a + 1\) e

Pe ligand \(p\) orbital in equatorial plane.
Pa ligand \(p\) orbital in apical plane.

Interaction \(b_2\) will be the weaker since the ligand \(p\) orbital has the least overlap with the two ligand \(s\) orbitals (see arrows). Calculations have shown\(^{1a}\) that the interactions \(e_y\), \(e_x\), and \(b_1\) are of comparable strength. The \(\pi\)-\(\sigma\) interactions will therefore be stronger for apical than for equatorial substitution.
A $p\pi$ acceptor should therefore prefer to occupy the apical position where there is maximum interaction.

Since the $\sigma$-framework is fully occupied, the $p\pi-\sigma$ interaction for a $p\pi$ donor will be destabilising (i.e. an electron-electron repulsive interaction). A $p\pi$ donor should therefore prefer to occupy the equatorial sites where the interactions are weakest.

For a substituent bearing a single $\pi$ system, e.g. OR, SR, NR$_2$, -CR=CR$_2$, -Ar, -COR, etc., in contrast to halogen, -C≡N and -C≡CR, which have two $\pi$ systems, the interactions $b_1$ and $b_2$ in the equatorial position are unequal. This implies that in the equatorial position a single $\pi$ system acceptor should prefer to align its $p\pi$ orbital in the apical plane (1.11), while a single $\pi$ system donor should prefer to align its $p\pi$ orbital in the equatorial plane (1.12).

![Diagram](1.11) ![Diagram](1.12)

This differential interaction of a single $\pi$ system in an equatorial site should lead to an energy barrier to rotation about the equatorial bond. This aspect will be discussed further in a later chapter.

(c) Effect of Phosphorus 3d Orbitals.

The involvement of phosphorus 3d orbitals in the bonding of compounds of the second row p-block elements has long been argued. The 3d orbitals on phosphorus are much higher in energy than the 3p orbitals. The hybridization or directed valency theories require hybrid orbitals of the $sp^3d_{2z}$ type for bonding in a TBP molecule. This implies the use of
a complete \( d_{2z^2} \) orbital. To the other extreme the scheme used by Rundle\(^3\) (Scheme 1) uses a 3-centre 4-electron bonding model which requires no \( d \) orbital participation. Clearly the extent of \( d \) orbital interaction is between these two extremes.

Hoffmann\(^1a\) has probed the effect of phosphorus 3d orbitals by including in the calculations a 'moderate' 3d interaction. The results are outlined below.

(i) Of the occupied MOs only the nonbonding \( 2a_1^1 \) orbital is significantly stabilised. This stabilisation is accompanied by transfer of electron density from the apical ligands to the phosphorus. However, the apical ligands still remain more negative than those in the equatorial position. Thus the preference of electronegative substituents for the apical positions should be unaffected.

(ii) For an equatorial \( \pi \) system, the difference between interactions \( b_1 \) and \( b_2 \) increases. This results in a higher energy barrier to rotation about the equatorial bond for a substituent bearing a single \( \pi \) system.

(iii) The empty 3d orbitals interact with ligand \( \pi \) donors with a stabilising effect. The interaction is found to be strongest in the equatorial positions. A \( \pi \) donor should therefore increase its preference for the equatorial positions, i.e. maximum \( d\pi-p\pi \) bonding and minimum \( \sigma-p\pi \) repulsion. Except for the case of maximum \( d \) orbital participation, the difference between equatorial \( d\pi-p\pi \) and apical \( d\pi-p\pi \) interactions is small compared to the equatorial apical difference of the \( p\pi-\sigma \) interactions. Thus for a \( \pi \) donor ligand its preference for the equatorial position is determined largely by the \( p\pi-\sigma \) repulsive term. However, the difference between the \( d\pi-p\pi \) bonding interaction and \( p\pi-\sigma \) repulsive interaction for an equatorial \( \pi \) donor cannot be determined since it is dependent on the amount of \( d \) orbital participation.
(d) Additional Factors Affecting the Preferred Configuration of a Trigonal Bipyramid.

Steric Effects.

Gillespie\textsuperscript{2} has shown, using Electron Pair Repulsion theory, that for five electron pairs, the TBP will be the favoured structure. The theory also predicts that a nonbonding pair (lone pair) of electrons should preferentially occupy an equatorial position and that electronegative substituents should favour the apical positions. The assumptions used were;

(i) A nonbonding pair of electrons takes up more room on the surface of an atom than a bonding pair.

(ii) The size of a bonding pair decreases with increasing electronegativity of the ligand.

(iii) A 90° interaction of electron pairs is much larger than two 120° interactions.

The theory is thus a reflection of the steric and electrostatic repulsions between the electron pairs. The last assumption (iii) has also been applied to the interactions between substituents in a TBP\textsuperscript{8}. If this extrapolation is valid, then the largest substituents in a TBP should prefer the sterically less hindered equatorial positions.

Effect of Ligand 3d Orbitals.

The involvement of 3d orbitals on phosphorus has already been mentioned. It may therefore be possible to include any vacant ligand 3d orbitals in the overall bonding scheme. The symmetry-allowed interactions for apical and equatorial ligand 3d orbitals are shown in Scheme 4. Interactions (1.13) and (1.14) are of the σ type and should not differ greatly in energy. If it can be assumed that the dπ-σ interactions (1.15) and (1.16) are weak and similar in magnitude then the remaining
interactions (1.17), (1.18), (1.19), and (1.20) are analogous to those reported by Hoffmann for \( \pi-\sigma \) interactions. Thus \( d\pi \) acceptors should preferentially occupy the apical positions of a TBP.

**SCHEME 4**

*Ligand 3d Orbital Interactions.*

**Apical**

(1.13)

(1.15)

(1.17)

**Equatorial**

(1.14)

(1.16)

(1.18)

(1.19)

(1.20)
Apicophilicity.

Although electronegativity appears to be a major factor in determining ligand preferences for the apical position, other factors must obviously be considered. Ugi and Ramirez have introduced the term 'apicophilicity' to describe the preference of any group for the apical position over the equatorial position. The earlier terms used in the literature, 'polarity rule', 'element effect' and 'preference rule' (with reference to electronegativity) are best replaced by the new term 'apicophilicity' since this avoids stating the cause of the effect and is more useful for the description of quantitative variations.

Thus the definition of apicophilicity of a ligand X with reference to some ligand R is the difference in energy ($A_X$) between the two structures (1.21) and (1.22).

\[
A_X = \text{Energy (1.22)} - \text{Energy (1.21)}
\]

A negative value of $A_X$ will therefore be obtained when X is more apicophilic than the reference ligand R.

Effect of Small Rings.

The presence of a small (3, 4 or 5-membered) ring in a TBP molecule will affect the preferred configuration. In a TBP a ring may be accommodated in three ways. The ring may span apical-equatorial

(1.23)  (1.24)  (1.25)  (1.26)
(1.23), diequatorial (1.24) or diapical positions. Except in the case of very large rings or in a fused bicyclic system (1.26) in which there are two rings each sharing the same equatorial site, the diapical orientation would be impossible if the TBP structure were to be maintained.

Inspection of models indicates that for small rings (4 or 5 membered) there is considerably less strain with the ring in an apical-equatorial position compared to a diequatorial position. In the case of the six membered ring, models indicate that there is almost no angle strain in either apical-equatorial or diequatorial positions. Most of the strain in this ring will be a result of eclipsing interactions, which are difficult to estimate using framework molecular models. There is therefore probably little difference in energy between the two possible positions of a six membered ring.

Ugi and Ramirez\textsuperscript{1h}, using semi-empirical MO calculations on a model monocyclic phosphorane have shown that structure (1.27) is destabilised by 40 Kcal mol\textsuperscript{-1} relative to structure (1.28). Although this is rather high when compared to the total strain energy in, for example, cyclobutane (26.9 Kcal mol\textsuperscript{-1})\textsuperscript{9} it does indicate that a five membered ring prefers apical-equatorial placement.

Calculations by Westheimer\textsuperscript{10} have shown that the difference in energy between the two possible TBP intermediates (1.29) and (1.31), formed on hydrolysis of methyl ethylene phosphate (1.30) is 8 - 13 Kcal mol\textsuperscript{-1}
Theoretical arguments would therefore seem to suggest the following preference rule for small rings:

'Small rings prefer to span the apical-equatorial positions of a TBP phosphorane.'

1.2 Structural Investigations.

The structures of several pentacoordinate phosphoranes have been examined by X-ray diffraction\textsuperscript{11-21}, electron diffraction\textsuperscript{22,23}, microwave\textsuperscript{24,25} and vibrational\textsuperscript{26} spectroscopy, nuclear quadrupole resonance\textsuperscript{26}, nuclear magnetic resonance\textsuperscript{27-29}, and vapour phase dipole moment measurements\textsuperscript{30}. The results of such investigations lead, with few exceptions\textsuperscript{18,19}, to the following conclusions.

(i) The most stable geometry for pentacoordination is the TBP\textsuperscript{168}.

(ii) Apical bonds are longer than equatorial bonds for the same substituent.

(iii) The most electronegative substituents prefer to occupy the apical positions of the TBP structure.

(iv) Small rings (four- or five-membered) prefer to span the apical-equatorial positions of the TBP structure.
These generalisations are in agreement with those predicted from theoretical models. Of the exceptions to rules (iii) and (iv) most can be explained in terms of a balance between the apicophilicity of ligands and the preferences of small rings for the apical-equatorial positions.

The low temperature (< -70°) $^{19}$F n.m.r. spectrum of 1,1,1-trifluoro phospholane shows two different fluorine environments in the ratio of 2:1. The fluorines of relative intensity two have a smaller PF coupling constant ($J_{PF}$ 865Hz) than the fluorine of intensity one ($J_{PF}$ 990Hz). Apical PF spin-spin couplings average about 170Hz less than equatorial PF couplings in compounds of the general formula $R_2PF_3$. Thus the preferred structure (1.32) probably has the phospholan ring spanning the diequatorial positions. Thus the apicophilicity of fluorine

$$|A_F - A_{CH_2}| > S_{90-120} \text{(Phospholan)}$$

(1.32)

$A_F$ relative to alkyl is greater than the increase in ring strain, $S_{90-120}$ (phospholan), on changing the ring angle at phosphorus from 90° for apical-equatorial placement to 120° for diequatorial placement. The apicophilicity factor therefore is the dominant factor dictating the preferred structure. This is effectively a violation of the preference rule for small rings.

In the case of the phosphetan system the ring strain is greater and $S_{90-120}$ (phosphetan) is approximately equal to the apicophilicity of fluorine relative to alkyl. This is implied from the observance of two isomers (1.33) and (1.34) for 1,1-difluoro-1-phenyl-2,2,4,4-tetramethyl phosphetan in the ratio of 2.4:1 as observed by low temperature (ca. -100°) $^{31}$P, $^{19}$F and $^1$H n.m.r.
The $^{19}$F n.m.r. data ($J_{PF}$ 829 Hz, $\delta_F$ 21.65 p.p.m.) for (1.35) are comparable to those of phosphoranes (1.36 a-c) which are known to have fluorine apical. The apicophilicity of fluorine then, dominates the structure of (1.35) and the phospholan ring is forced to span the diequatorial positions.

The structures of pentacoordinate phosphoranes with a diequatorial ring will be highly strained and may not therefore exist as perfect TBP's. Structure determinations by X-ray diffraction are therefore desirable for this class of phosphoranes.

If the ring strain is sufficiently large then the highly electronegative and hence highly apicophilic fluorine atom can be forced to occupy
an equatorial position, violating rule (iii), that the most electronegative
groups prefer to be apical. In phosphoranes (1.37), (1.38) and
(1.39), the large PF coupling constants, [(1.37) $\mathcal{J}_{PF}$ 1018Hz, (1.38) $\mathcal{J}_{PF}$
1035Hz, (1.39) $\mathcal{J}_{PF}$ 1038Hz] in the $^{19}$F n.m.r. spectra suggests that in these
phosphoranes the fluorine is probably forced into an equatorial position.

![Chemical structures](image)

A recent X-ray structure determination $^{19}$ on (1.37) in fact shows it to be
distorted, the structure being intermediate between a TBP and a square
based pyramid. This may be a consequence of the unfavourable position of
the fluorine atom.

The anomalous apicophilicity of hydrogen, predicted by theoretical
considerations $^{1h}$, has not been verified experimentally by structural
determinations. The only phosphoranes known which have hydrogen as a
substituent also contain the more apicophilic fluorine substituent, e.g.
(1.40) and (1.41), or the phosphorane is of the spiro type, e.g. (1.42 -
1.45). In both these systems the hydrogen is always constrained to
occupy an equatorial position. The only exception may be the spiro
phosphorane (1.46). The PH spin-spin coupling constant and the PH
stretching frequency are both much lower than those observed in other
hydrido-phosphoranes, Table 1.
TABLE 1

PH Proton Chemical Shifts, Spin-Spin Coupling Constants and Stretching Frequencies for Hydrido-phosphoranes.

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\delta_H$ (p.p.m.)</th>
<th>$J_{PH}$ (Hz)</th>
<th>$\nu_{PH}$ (cm$^{-1}$)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPF$_4$</td>
<td>-7.52</td>
<td>1084</td>
<td>2478</td>
<td>34</td>
</tr>
<tr>
<td>CH$_3$PF$_3$H</td>
<td>-7.4</td>
<td>860</td>
<td>-</td>
<td>35</td>
</tr>
<tr>
<td>(1.42, X=NH)</td>
<td>-7.1</td>
<td>830</td>
<td>2410</td>
<td>36</td>
</tr>
<tr>
<td>(1.43, X=O)</td>
<td>-6.4</td>
<td>730</td>
<td>2360</td>
<td>36</td>
</tr>
<tr>
<td>(1.44)</td>
<td>-8.62</td>
<td>829</td>
<td>2394</td>
<td>37</td>
</tr>
<tr>
<td>(1.45)</td>
<td>-</td>
<td>-</td>
<td>2244</td>
<td>38</td>
</tr>
<tr>
<td>(1.46)</td>
<td>-9.33</td>
<td>482</td>
<td>2096</td>
<td>39</td>
</tr>
</tbody>
</table>

These data are consistent with phosphorane (1.46) having a much weaker PH bond than other hydrido-phosphoranes. This may be a consequence of having four carbon groups for the other substituents. However, the data could also be considered to suggest an apical hydrogen atom as shown.
in structure (1.47). Quantitative data on ring strains and apicophilicities, discussed later, may also be consistent with this structure. However, an X-ray structure determination would be required to test this postulate. If this structure is found to be correct it would be consistent with the high apicophilicity of hydrogen as predicted by theoretical calculations. In view of the low electronegativity of hydrogen, the reason for its high apicophilicity is still not understood. The small size of the hydrogen atom, and its bonding orbitals may be an important factor.

As a final example of anomalous apicophilicity it is of interest to consider the trifluoromethyl group. Calculations\(^1\) and electronegativity scales\(^6\) indicate that fluorine should be more apicophilic than the CF\(_3\) group. Studies on CF\(_3\)PF\(_4\) by microwave\(^2\) and vibrational\(^3\) spectroscopy have led to different conclusions concerning its structure. Microwave studies at -78° (liquid state) have detected the presence of a phosphorane having TBP geometry with an apical CF\(_3\) group. However, vapour phase infrared studies indicate TBP geometry with an equatorial CF\(_3\) group. If both these results are correct then both isomers may be present indicating that there is very little difference in energy between the two structures. Thus the apicophilicity of the trifluoromethyl group may be approximately equal to that of fluorine.

Studies on (CF\(_3\))\(_2\)PF\(_3\) by \(^{19}\)F n.m.r. are consistent with, but do not
establish, a structure with two apical \( \text{CF}_3 \) groups\(^{27} \). However, this may be due to an unusual steric effect. If fluorine is slightly more apicophilic than the \( \text{CF}_3 \) group, structure (1.48) would be most stable.

\[
\text{CF}_3 \quad \text{F} \\
\text{CF}_3 \\
\text{F} \\
\text{F} \\
\text{P} \\
\text{F} \\
\text{F}
\]  

(1.48)

However, the 120° interaction between \( \text{CF}_3 \) groups may be sufficiently large as to favour a 180° separation as in structure (1.49) provided that there is little loss in energy due to the less apicophilic \( \text{CF}_3 \) groups being apical.

\[
\text{F} \quad \text{CF}_3 \\
\text{F} \\
\text{F} \\
\text{F} \\
\text{P} \\
\text{F} \\
\text{CF}_3
\]  

(1.49)

The use of nuclear magnetic resonance techniques often leads to different conclusions concerning the structure of substituted phosphoranes, especially those of the type \( \text{PX}_5 \) and \( \text{YPX}_4 \). For example electron diffraction studies\(^{22} \) on \( \text{MePF}_4 \) indicate a TBP having \( C_{2v} \) geometry, i.e. an equatorial methyl group. However at low temperatures the \(^{19}\text{F} \) n.m.r. spectrum shows all four fluorines to be equivalent, suggesting a structure with \( C_{4v} \) geometry\(^{41,42} \). This aspect of pentacoordinate TBP phosphoranes will be discussed in Chapter 2.
2. LIGAND PERMUTATIONAL ISOMERISATION.

The structure of phosphorus pentafluoride has been studied by infrared spectroscopy and electron diffraction and has been found to be consistent with TBP geometry. However, the $^{19}$F n.m.r. spectrum exhibited only a doublet (PF spin-spin coupling), and was unchanged from 60° to -197°. These results indicate that on the infrared timescale the PF$_5$ molecule is 'frozen' in the geometry of lowest energy, the TBP, whereas on the n.m.r. timescale the fluorine atoms are exchanging rapidly. The exchange process therefore occurs at a frequency of between $10^{-8}$ and $10^{-2}$ s$^{-1}$.

The general term 'Ligand Permutational Isomerisation' (LPI) has been used to describe such rearrangements since it avoids any preconceived ideas as to the mechanism of such an exchange.

2.1 Modes of Rearrangement in Trigonal Bipyramidal Molecules.

Recently Musher has described LPI using combinatorics, which provides a description of all the experimentally distinguishable kinds of rearrangement or 'modes of rearrangement' that a TBP molecule can undergo.

The possible ways that the labelled ligands of the TBP (2.1) can be rearranged among themselves, can be grouped according to the number of ligands which preserve their explicit location. Thus Table 2 lists the permutational notations of all possible rearrangements, leading to different
TBP phosphoranes. The ordering of the letters is in the permutational sense. As an example consider the permutation eaea. This means that an e ligand goes to an a site, that a ligand goes to the next e site and that e ligand goes to the next a site, and finally that a ligand goes to the original e site. This corresponds to the rearrangement (2.2).

**TABLE 2**

**Permutational Rearrangements in a TBP Molecule.**

<table>
<thead>
<tr>
<th>Number of Non-exchanging Ligands</th>
<th>Permutational Operations of Exchanging Ligands</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>ee, aa, ea</td>
</tr>
<tr>
<td>2</td>
<td>aae, aee, eee</td>
</tr>
<tr>
<td>1</td>
<td>(i) eeea, eea, eea</td>
</tr>
<tr>
<td></td>
<td>(ii) aaxee, aexe, aexae (concerted pairs of pairwise rearrangements).</td>
</tr>
<tr>
<td>0</td>
<td>(i) aae, aae</td>
</tr>
<tr>
<td></td>
<td>(ii) aaxee, aexae, exae (concerted pairwise and three ligand rearrangements)</td>
</tr>
</tbody>
</table>

a = apical; e = equatorial

Each stereoisomer can be obtained by more than one of the permutational operations. If all operations which lead to the same isomer are grouped,
only six distinct types of rearrangement are obtained. These are known as 'modes' (M) and are listed in Table 3. The trivial mode $M_0$ leads to

\[
\begin{array}{|c|c|}
\hline
\text{Mode} & \text{Permutational Operations} \\
\hline
M_0 (1) & eee, aaxee \\
M_1 (3) & eaea, aexaee \\
M_2 (6) & ae, eeea, eea, eexae \\
M_3 (1) & aa, ee, aaxee \\
M_4 (6) & aee, ae, aexe, aae \\
M_5 (3) & aexae, aae \\
\hline
\end{array}
\]

the original TBP. The number in parentheses is the number of possible isomers obtainable following one operation on a TBP. For example the operation eaea, belonging to mode $M_1$, has an $e$ ligand which remains fixed. Three possible isomers may therefore be obtained each using a different 'fixed' $e$ ligand. Thus any of the possible 20 isomers of a TBP molecule may be obtained using one or other of the modal rearrangements.

2.2 Berry Pseudorotation.

The anomalous behaviour of PF$_5$ in the $^{19}$F n.m.r. spectrum was explained by Berry\textsuperscript{46} in terms of a purely internal pseudorotation (2.3).
The apical ligands 4 and 5 bend away from the equatorial ligand 3, while remaining in the vertical plane. Simultaneously the equatorial ligands 1 and 2 bend away from each other in the horizontal plane. These motions lead to the square based pyramidal structure in which ligands 1, 2, 4, and 5 are equivalent. Continuation of the above motion leads to a new TBP, which leaves the molecule in a rotated and permuted form of its original state. The ligand 3, which remains equatorial is termed the 'pivot'. This mechanism is generally referred to as Berry Pseudorotation (BPR) and until recently has been widely used to account for the n.m.r. spectra of pentacoordinate phosphoranes. The BPR mechanism is permutationally equivalent to the operation eaea, and belongs to the mode $M_1$.

2.3 Mechanistic Alternatives to Berry Pseudorotation.

Muetteerties has described a number of conceivable mechanisms and symmetries of intermediate states for the isomerisation of TBP molecules, Table 4. The modes to which these mechanisms belong are shown in the table. Mechanisms 4 and 6 have the same stereochemical consequences, i.e. $M_4$, while mechanism 5 is supposed to represent $M_5$ but actually belongs to all modes since it goes through a $D_{5h}$ intermediate which should therefore scramble all the isomers. Mechanism 1 is the BPR mechanism.

The question arises as to what actual mechanism(s) of LPI is in operation. It would seem reasonable that mechanisms 3 and 5 can be eliminated since they go through planar intermediates which would be expected to have very high energies. It could also be argued that mechanisms 2, 4 and 6 contravene the theory of conservation of angular momentum and so may be eliminated. This would leave BPR as the only plausible mechanism.
Table 4

Some Mechanisms for Ligand Permutational Isomerisations in a Trigonal Bipyramidal Molecule

<table>
<thead>
<tr>
<th>Mechanism Number</th>
<th>Intermediate State</th>
<th>Mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><img src="image1" alt="Mechanism 1 Diagram" /></td>
<td>$M_1$</td>
</tr>
<tr>
<td>2.</td>
<td><img src="image2" alt="Mechanism 2 Diagram" /></td>
<td>$M_2$</td>
</tr>
<tr>
<td>3.</td>
<td><img src="image3" alt="Mechanism 3 Diagram" /></td>
<td>$M_3$</td>
</tr>
<tr>
<td>4.</td>
<td><img src="image4" alt="Mechanism 4 Diagram" /></td>
<td>$M_4$</td>
</tr>
<tr>
<td>5.</td>
<td><img src="image5" alt="Mechanism 5 Diagram" /></td>
<td>$M_{1-5}$ (or $M_5$)</td>
</tr>
<tr>
<td>6.</td>
<td><img src="image6" alt="Mechanism 6 Diagram" /></td>
<td>$M_4$</td>
</tr>
</tbody>
</table>
Experiment can only distinguish among the various rearrangement modes if it explicitly involves a one-step process. This is because single-step rearrangements of most of the modes are equivalent to multistep rearrangements of others. The only examples of one step rearrangements so far studied are due to Whitesides and Mitchell on the fluorophosphorane (2.4), and Whitesides and Bunting on the bis(bitolyl) compound (2.5).

Variable temperature $^{31}$P n.m.r. studies on (2.4) showed that in the temperature range studied (-50° to -100°) the two apical fluorines exchange with the two equatorial fluorines in a concerted manner. This indicates rearrangement via mode $M_1$ and/or $M_5$. In principle it is also possible for a fast $M_3$ rearrangement to be occurring but such a process would be undetectable in this experiment.

The $^1$H n.m.r. of (2.5) at 33° showed that the four bitolyl methyl groups are stereochemically non-equivalent (two of the methyl groups are however magnetically equivalent and appeared as two overlapping singlets) and that the isopropyl methyl groups are also non-equivalent due to their proximity to the chiral environment of the phosphorus. The bitolyl methyl groups would be expected to have only two environments. The
observed spectrum being a result of restricted rotation of the
o-iso-propylphenyl group.

On warming the sample to 130° the bitolyl methyl signals were
found to collapse to a singlet and the iso-propyl resonances to a doublet.
Line shape analysis of the spectra showed that both processes had the
same rate constants. The results are consistent with the rearrangement
\((2.5a) \rightleftharpoons (2.5b)\) occurring via a \(M_1\) process, or via all modes with equal
probability\(^{45}\).

\[
\begin{align*}
\text{R} & \rightleftharpoons \text{R} & \rightleftharpoons \text{R} & \equiv \text{R} \\
(2.5a) & \quad (2.5b)
\end{align*}
\]

If all rearrangements of pentacoordinate phosphoranes take place
via a unique mode, independent of substituents, then these two experiments
taken together prove the mode involved must be \(M_1\).

The problem then arises as to which mechanism within \(M_1\) is operative.
The two permutational possibilities are \(\text{aeae}\) and \(\text{aexze}\). The first of
these being the BPR mechanism.

Ugi and Ramirez\(^{1h, 50-53}\) have suggested an alternative mechanism for
LPI which corresponds to the latter operation \(\text{aexae}\) of \(M_1\) and is therefore
also consistent with experiments of Whitesides, Mitchell and Bunting. This
process has been termed 'turnstile rotation' (TR) and corresponds to an
internal rotation of one apical and one equatorial ligand rotating as a
pair against the oppositely rotating trio formed from the other three
ligands.

As a model concept of TR one can visualise it to begin with a
combination of a bending motion \((2.6)\) and an internal rotation \((2.7)\)
as shown in Scheme 5.
The two equatorial ligands 1 and 2 of (2.6), move towards one another until the angle between them is reduced to ca. 90° forming a trio from 1, 2, and 5, of local C₃ symmetry. At the same time the pair of remaining ligands 4 and 3 tilt by ca. 9° in the direction shown, forming a pair of local C₂ symmetry. Furthermore the two symmetry axes C₂ and C₃ are coincident. (The variation of bond lengths has, as in the description of BPR been ignored for simplicity). Superimposed upon these bending motions is an internal rotation of the pair against the trio (2.7). A rotation of +90° by the pair and -60° by the trio (a relative internal
rotation of 30°) leads to the intermediate state (2.8). A further 30°
internal rotation and a reverse of the bending motion leads to the TBP
(2.10).

This process was not considered by Muetteties\textsuperscript{47} although as will
be shown later there are similarities between the TR mechanism and
mechanisms 2 and 4 of Table 4.

Holmes\textsuperscript{26} has argued that the observations of Whitesides, Mitchell
and Bunting\textsuperscript{48,49} are not directly applicable to other phosphoranes, i.e.,
there is no unique mode for all LPI processes. The mechanism suggested
by Holmes\textsuperscript{26} specifically accounts for the equivalence of the fluorine
atoms in pentacoordinate phosphoranes of the type R\textsubscript{2}PF\textsubscript{3}. The mechanism
has two distinct advantages;

(i) The 'intermediate' is a square based pyramidal structure of
the same energy as that involved in the BPR of R\textsubscript{2}PF\textsubscript{3}.

(ii) It is unnecessary to go via the high energy TBP (2.15) with
an apical alkyl group.

The mechanism can be considered as a combination of a 'Berry'
type bending (2.10) with R' as pivot and a simultaneous pairwise rotation
of the fluorines 4 and 2, leading to the square based pyramid (2.12) with
R\textsuperscript{3} at the apex. This equilibrates fluorine atoms 2 and 5. In a similar
way substituents 2 and 4 can be equilibrated, thus equilibrating all three
fluorines, 2, 4, and 5. In the BPR mechanism it is necessary to go via
the high energy TBP (2.15).

Although the square based pyramidal species (2.12) and (2.14) have
the same energy, Holmes does not consider the activation energy necessary
to reach the square based pyramid (2.12), which may be higher than the
high energy TBP (2.15) in the BPR mechanism.
SCHEME 6
Holmes Mechanism for LPI of $R_2PF_3$

\[
\begin{align*}
\text{Holmes Mechanism for LPI of } R_2PF_3 \\
\text{Pivot} & & \text{Pivot} \\
\text{\textcolor{red}{(2.10)}} & + & \text{\textcolor{red}{(2.11)}} & \iff & \text{\textcolor{red}{(2.12)}}
\end{align*}
\]

Berry Pseudorotation Mechanism

\[
\begin{align*}
\text{Berry Pseudorotation Mechanism} \\
\text{Pivot} & & \text{Pivot} \\
\text{\textcolor{red}{(2.13)}} & \iff & \text{\textcolor{red}{(2.14)}} & \iff & \text{\textcolor{red}{(2.15)}}
\end{align*}
\]

The TR mechanism of Ugi and Ramirez has also been postulated to be capable of bypassing high energy TBPs. This is accomplished by the multiple TR mechanisms $TR^2$ and $TR^3$. To visualise these mechanisms it is advantageous to use Newman projections along the coincident $C_2$-$C_3$ axis. Thus a single TR process (from now on TR') is represented by the sequence (2.16) to (2.20), Scheme 7.

Structure (2.18) is termed a $30^\circ$ - (2+3) species since the angle $\delta$ between the pair and trio is $30^\circ$. If (2.20) is a high energy TBP then the relative internal rotation may be continued by a further $60^\circ$, through a $0^\circ$ - (2+3) structure equivalent to (2.19), to a new $30^\circ$ - (2+3) structure and then to the TBP (2.21), Scheme 8. This would be a TR$^2$ process, i.e. two $60^\circ$ internal rotations between the pair and trio.
SCHEME 7

Turnstile Rotation

(2.17) \[ \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \] \rightarrow \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \]

30° Rotation

(2.18) \[ \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \] \rightarrow \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \]

Bending Motion

View here

(2.16) \[ \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \]

- - - - - Simultaneous Process

(2.19) \[ \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \]

(2.20) \[ \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \]

SCHEME 8

TR² Process

(2.21) \[ \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \] \rightarrow \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \]

30° Rotation

(2.22) \[ \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \] \rightarrow \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \]

Bend + Rotation

(2.23) \[ \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \] \rightarrow \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \]

Bend + Rotation

(2.24) \[ \begin{array}{c}
1 \\
2 \\
3 \\
5
\end{array} \]
The TR³ process is basically the same, but involves a 120° rotation from (2.18) and then the simultaneous bending and rotational movements to return to a TBP.

The permutational operations, and the modes to which they belong are shown in Table 5, for all the TR mechanisms. The permutational consequences of TR² and TR³ are the same as mechanisms 4 and 2 respectively, postulated by Muetterties, Table 4.

The complexity of the TR process is further increased by the presence of energetically favourable pathways by which a turnstile species with a certain pair-trio combination can switch over to another turnstile species.
with a different pair-trio combination. Thus for PF$_5$, once the 2+3 structure has been adopted, all the fluorines can be equilibrated before reverting back to a TBP.

### 2.4 Differentiation Between Modes.

As shown by Musher$^{45}$, experiment can only distinguish between modes of rearrangements and not the mechanisms. Even then the results$^{48,49}$ only show that rearrangements via $M_1$ are the most energetically favoured ones. There is no quantitative evidence which excludes the possibility of competition from other modes, which may be prevalent in the rearrangements of distorted TBP molecules. Recently Brocas and Willem$^{54}$ have shown that it is theoretically possible to distinguish between modes by comparison of the relaxation times of the individual isomers of a TBP phosphorane. In principle the method may be applied to any system including a phosphorane with five different ligands. However, in practice the experimental study of systems containing twenty isomers is impossible. In simpler systems however, the method may find important applications.

### 2.5 Differentiation Between Mechanisms.

The accumulation of quantitative data on barriers to pseudorotation is best explained by assuming that all rearrangements take place via the same mode $M_1$, i.e. the BPR and/or the TR' mechanisms. For the purpose of studying the relative energies of TBP phosphoranes the mechanism of rearrangement is irrelevant. It is only the mode which is important. However, the possibility of multiple TR processes, TR$_2$, TR$_3$, and TR switches, makes the interpretation of energy barriers to pseudorotation
an almost impossible task. The evidence in favour of the TR$^2$ and TR$^3$ mechanisms appears to be based on the results of quantum mechanical calculations\textsuperscript{1h}. These indicated that in the phosphorane (2.22) the energy required to place the five membered ring diequatorial (2.23) is 40 Kcal mol$^{-1}$ and secondly, the energy required to exchange an apical oxygen for an equatorial carbon (2.21) is 37 Kcal mol$^{-1}$. A multiple TR process would be capable of avoiding such high energy TBPs.

Denney\textsuperscript{55} has studied the LPI processes in the phosphoranes (2.24)

\begin{align*}
\text{SCHEME 9} \\
\begin{array}{ccc}
\text{(2.24)} & \leftrightarrow & \text{(2.26)} \\
\Delta G^\circ > S_{90-120}(\text{Dioxaphospholan}) + (A_{Ph} - A_0)
\end{array}
\end{align*}

\begin{align*}
\begin{array}{ccc}
\text{(2.25)} & \leftrightarrow & \text{(2.27)} \\
\Delta G^\circ > A_{Ph} - A_0
\end{array}
\end{align*}
and (2.25), by variable temperature $^1$H n.m.r. The coalescence temperatures for the ring protons are very different, (2.24) $T_c > 190^\circ$ and (2.25) $T_c < -60^\circ$. This difference is clearly explained by the BPR mechanism. The coalescence temperatures being associated with the high energy of the TBPs (2.26) and (2.27), Scheme 9. The difference in coalescence temperatures being due to the strain in the dioxaphospholan ring in (2.26). The $T_R^2$ mechanism avoids the high energy TBPs (2.26) and (2.27), Scheme 10, for (2.24). For the monocyclic phosphorane (2.25), oxygen atoms

**SCHEME 10**

2 and 5 are replaced by ethoxy groups. Since the angles between the trio ligands in the (2+3) turnstile species are ca. $90^\circ$, there would seem to be no additional strain in the ring compared to the TBP ground state (2.24). The $0^\circ$ - (2+3) turnstile species for both (2.24) and (2.25) should therefore have similar energies resulting in similar coalescence temperatures for the two phosphoranes. The $T_R^2$ mechanism therefore, does not adequately
explain the observed energy barriers normally associated with ring strain in cyclic phosphoranes.

**Conclusion**

All the experimental data for LPI in TBP phosphoranes are consistent with the assumption that all rearrangement processes proceed via the same mode $M_1$. If only the relative energies of the TBP structures are of interest then the mechanism, BPR or TR', which is operating becomes irrelevant.

Throughout the rest of this thesis all regular (i.e. without bond breaking) LPI processes will be assumed to proceed via the mode $M_1$, and the term pseudorotation will be used to describe this mode.

2.6 **Topological Representation of Trigonal Bipyramidal Stereoisomers and of the Inter-relating Pseudorotations.**

A TBP with five different substituents has a total of 20 different chiral stereoisomers (10 dl-pairs). Each isomer can pseudorotate to

![Graph](image-url)
give one of three possible isomers (each using a different non-permuted equatorial ligand). Thus there is a total of 30 different pseudorotations. In order to visualise all these possibilities a number of topological representations have been presented. The preferred variation of a Balaban\textsuperscript{20} 20-vertex graph projection proposed by Mislow\textsuperscript{57} is shown in (2.28). Each vertex corresponds to one of the 20 possible TBPs. The stereochemistries of the TBPs are designated by the numbers of the groups occupying the apical positions and enantiomers are shown by use of the bar. If the ascending order of numerical index for the equatorial ligands is anticlockwise when viewed from the apical ligand of lowest numerical index, then a bar is used to show this chirality, if clockwise no bar is used. e.g.

![Diagram of graph projection](image)

The interconnecting lines between vertices represent the pseudorotation pathways.

2.7 Irregular Processes.

The rearrangements discussed so far are termed regular processes in that they are unimolecular and involve no bond breaking or bond formation.

Irregular processes may be of three general types;
(i) Fission of a phosphorus-ligand bond to give a tetrahedral phosphorus species, followed by bond formation on a different face of the tetrahedron.

(ii) Bond formation by attack of a nucleophile to form a hexacoordinate species.

(iii) A bimolecular process involving two TBP phosphoranes, or a phosphorane-solvent complex.

Oram has studied the variable temperature $^1$H n.m.r. of the pentacoordinate phosphorane (2.29). At temperatures above 85° the vinyl

![Chemical Structure](image)

and acyl methyl groups became equivalent suggesting rearrangement via the betaine (2.30). This process is an example of the irregular type (i) mechanism.

Ugi and Ramirez have observed a base-catalysed exchange of alkoxy groups in the oxyphosphorane (2.31) via a hexacoordinate species (2.32). Thus contamination from hydrolysis products or thermal decomposition products may possibly result in an irregular LPI process analogous to the mechanism of alkoxy group exchange.

![Chemical Structure](image)
Cowley\textsuperscript{59} has observed an irregular process of type (iii) for the equilibration of fluorine atoms in $\text{Me}_2\text{PF}_3$ and $\text{Me}_3\text{PF}_2$. The rearrangements followed second order kinetics and showed large negative entropies of activation. A fluorine-bridged dimeric intermediate (2.33) was postulated to account for the results. However, Moreland, Doak and Littlefield\textsuperscript{60} have shown that in Teflon n.m.r. tubes the LPI of $\text{Ph}_2\text{PF}_3$ is an intramolecular process with first order kinetics. In Pyrex n.m.r. tubes however, they concluded that the process was intermolecular, but still first order. This was thought to be caused by the involvement of impurities formed by attack of the phosphorane on the glass tubes.

Musher\textsuperscript{61} has postulated that $\text{RPF}_4$ phosphoranes ($\text{R} = \text{NH}_2, \text{NMe}_2, \text{Cl}, \text{F}, \text{and Me}$) can also rearrange via fluorine bridged dimeric species. The possibility of an equilibration of fluorine atoms via a solvent-phosphorane complex (2.34) was also suggested.

Thus when interpreting LPI processes it is important to consider such irregular processes and where possible eliminate them by experiment.
3. **NUCLEOPHILIC SUBSTITUTION AT TETRAHEDRAL PHOSPHORUS.**

The study of TBP phosphoranes and their rearrangements has become increasingly important in the field of phosphorus reaction intermediates and transition states. Pentacoordinate species have been postulated as intermediates in nucleophilic substitution reactions at tetrahedral phosphorus, radical reactions at tervalent phosphorus and recently in the Arbuzov reaction of alkyl halides with phosphites.

3.1 **Mechanisms of Nucleophilic Substitution.**

There are a number of different pathways by which substitution reactions at phosphorus may occur.

(i) **Addition-Elimination.** This involves the attack of a nucleophile on tetrahedral phosphorus to form a discrete pentacoordinate intermediate, which then decomposes by elimination of the leaving group.

(ii) **Direct Displacement.** This is essentially a special case of the addition-elimination mechanism. A pentacoordinate species is formed as a transition state only, and spontaneously breaks down to products. This is analogous to the SN$_2$ mechanism at a tetrahedral carbon atom.

(iii) **Elimination-Addition.** This type of reaction usually occurs in compounds containing an acidic α-hydrogen, e.g. (3.1) and (3.2). The products are formed by solvolysis of the intermediate.

\[
\text{Products}
\]

\[
\text{Products}
\]
The last mechanism does not involve a pentacoordinate species and therefore will not be considered further.

3.2 Pentavalency of Intermediate.

McEwen\(^{70}\) was the first to report on the results of kinetic studies on phosphonium salt hydrolyses. Studies on methylethylphenyl-benzylphosphonium iodide and on a series of p-substituted-benzyl-tribenzyl-phosphonium halides showed all the reactions to be third order, with a first order dependence on the concentration of phosphonium salt and a second order dependence on the concentration of hydroxide ion. Third order kinetics have since been observed for almost all phosphonium salt hydrolyses\(^{71-75}\). Second order kinetics have been observed in a few phosphonium salts which contain an exceptionally good leaving group\(^{73,76}\).

The observed third order kinetics requires that both hydroxyl ions are involved prior to, or during the rate determining step. To account for these kinetic results, McEwen\(^{70}\) proposed the mechanism, Scheme 11, involving the formation of a pentacoordinate intermediate. The fate of the pentacoordinate species \(R_4POH\) is probably not as McEwen originally proposed\(^{72,77}\).

**Scheme 11**

\[
\begin{align*}
R_4^+P + OH & \underset{\text{fast}}{\rightarrow} R_4POH \\
R_4POH + OH & \underset{\text{fast}}{\rightarrow} R_4PO^- + H_2O \\
R_4PO^- & \underset{\text{slow}}{\rightarrow} R_3P=O + R^- \\
R^- + H_2O & \underset{\text{fast}}{\rightarrow} RH + OH
\end{align*}
\]

More direct evidence of a pentacoordinate intermediate has been
due to Allen and Haake.

Allen and coworkers have observed the $^{31}$P n.m.r. spectrum of methyltri-(2-furyl)phosphonium iodide (3.3), in absolute methanol, over a range of concentrations of added sodium methoxide. The $^{31}$P chemical shift changed from $\delta +14.5$ ppm with no added methoxide to $\delta +91.7$ ppm with 30 molar equivalents of added methoxide. No other $^{31}$P resonances were observed. Since pentacovalent phosphoranes are known to have considerably more positive $^{31}$P chemical shifts than other organophosphorus compounds, the results are consistent with a rapid, reversible, equilibrium between the phosphonium ion (3.3) and methoxide ion to form the pentavalent phosphorane (3.4). The $^{31}$P n.m.r. spectrum was also found to be temperature dependent. On progressively cooling a solution of (3.3) and sodium methoxide (0.5 mol. equiv.) in absolute methanol, the $^{31}$P resonance at $\delta +48.5$ ppm gradually broadened until, at $-75^\circ$ it could no longer be observed. On further cooling to $-80^\circ$ two new signals at $\delta +16$ and $\delta +97$ were observed. This was interpreted in terms of a slowing of the equilibration process. Integration of the $^{31}$P n.m.r. signals at $-83^\circ$, enabled the equilibrium constant for the reaction to be evaluated as $11.05 \text{ mol}^{-1}$. This corresponds to a $\Delta G$ of $-0.9 \text{ Kcal mol}^{-1}$.

Haake has recently studied the kinetics of hydrolysis of a series of phosphinate esters. The reactions were shown to follow second order kinetics. The hydrolysis of methyl di-isopropylphosphinate however, was unusual in that an induction period preceeded second order kinetics. Assuming the reaction proceeds according to Scheme 12,
computer analysis of the rate data enabled the rate constants to be evaluated. Therefore, it appears that the induction period corresponds to an initial accumulation of the pentacoordinate intermediate (3.5) and rate determining decomposition of (3.5) to products.

### 3.3 Structure of the Pentacoordinate Intermediate.

As previously mentioned (Chapter 1) many stable pentacoordinate compounds have been isolated and shown to have TBP structures. It has therefore been generally assumed that pentacoordinate reaction intermediates will also have TBP geometry. Most of the evidence has been inferred from the accelerated reaction rates observed for a number of cyclic phosphorus compounds. The nature of reaction products can in some cases only be explained in terms of pseudorotation of a TBP intermediate.

Westheimer and Haake observed that the rate of P-O bond cleavage in the acid hydrolysis of ethylene hydrogen phosphate (3.6) exceeded that
for dimethyl hydrogen phosphate by a factor of ca. $10^6$. It was also found that the acid hydrolysis of (3.6) was accompanied by a rapid incorporation of $^{18}O$ into the unreacted starting material, at a rate of 20% of the hydrolysis rate. Similar results were later obtained for the acid hydrolysis of methyl ethylene phosphate (3.7). The rapid cleavage of the exocyclic methoxy group (30% of product) corresponds to the process responsible for $^{18}O$ incorporation in (3.6).

**SCHEME 13**

\[ \text{H}^+ + \text{H}_2\text{O} + \text{X} \rightarrow \text{P} \]

\[ [(3.7): X = \text{OMe}] \]
\[ [(3.6): X = \text{OH}] \]

\[ \begin{array}{c}
\text{MeO} \\
\text{HO} \\
\text{OH}_2 \\
\end{array} \]

\[ (3.8) \]

\[ \begin{array}{c}
\text{MeO} \\
\text{HO} \\
\text{O} \\
\end{array} \]

\[ (3.9) \]

\[ \begin{array}{c}
\text{MeO} \\
\text{HO} \\
\text{OH} \\
\end{array} \]

\[ (3.10) \]

\[ \begin{array}{c}
\text{MeO} \\
\text{HO} \\
\text{P} \\
\end{array} \]

\[ (3.11) \]

\[ \begin{array}{c}
\text{MeO} \\
\text{HO} \\
\text{OH} \\
\end{array} \]

\[ (3.12) \]

\[ \begin{array}{c}
\text{MeO} \\
\text{HO} \\
\text{OH} \\
\end{array} \]

\[ (3.13) \]

\[ \begin{array}{c}
\text{MeO} \\
\text{HO} \\
\text{OH} \\
\end{array} \]

\[ (3.14) \]

\[ \begin{array}{c}
\text{MeO} \\
\text{HO} \\
\text{OH} \\
\end{array} \]

\[ (3.15) \]

$\text{MeOH} + \text{H}^+$

$\text{OH}^-$
The mechanism shown in Scheme 13 proposed by Westheimer to account for these results, involves the formation of the energetically favoured TBP intermediate (3.8). Proton transfer in (3.8) to give (3.10) followed by elimination leads to the ring opened product (3.11). Exocyclic cleavage is obtained by deprotonation of (3.8) to give (3.9) which can pseudorotate to (3.12). This pseudorotation should readily occur since the energies of (3.9) and (3.12) are similar. Reprotonation of (3.12) will give (3.13) and (3.14) which will decompose to give the ring opened product (3.11) and ring retained product (3.15) respectively. A similar mechanism would apply to the $^{18}O$ exchange in ethylene hydrogen phosphate.

The base hydrolysis of (3.7) and of the anion of (3.6) are also fast with respect to their acyclic analogues. However, no $^{18}O$ exchange in (3.6) or exocyclic cleavage of (3.7) is observed. The mechanism of base hydrolysis of (3.7) is shown in Scheme 14. Exclusive ring opened product is probably due to the fact that decomposition of (3.16) is much faster than its pseudorotation to (3.17).

Molecular orbital calculations by Boyde have confirmed the essential features of Westheimer's mechanism.
The relatively high rates of hydrolyses of these five membered cyclic esters may be due to relief of ring strain in going from the strained tetrahedral phosphorus (preferred ring angle at phosphorus 109.5°) to the intermediate phosphorane containing the relatively strain free ring.

Calculations\(^\text{10}\) indicate that there is a relief in ring strain on going from (3.7) to (3.16) of ca. 3-6 Kcal mol\(^{-1}\). The energetics of five membered cyclic phosphate ester hydrolyses will be discussed again later (Chapter 7).

3.4 Principle of Microscopic Reversibility.

There are two possible modes of attack of a nucleophile at tetrahedral phosphorus, (i) attack on any one of the four faces, or (ii) attack on any one of the six edges. Attack on an edge is termed equatorial attack as the nucleophile occupies an equatorial position in the TBP intermediate and attack on a face is termed apical attack as the nucleophile occupies an apical position in the TBP intermediate. Similarly the leaving group can depart from either an apical or an equatorial position. Thus there are four permutational possibilities for nucleophilic substitution via a TBP intermediate.

<table>
<thead>
<tr>
<th>Position of Attack</th>
<th>Position of Departure</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>a</td>
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<tr>
<td>a</td>
<td>e</td>
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<tr>
<td>e</td>
<td>a</td>
</tr>
<tr>
<td>e</td>
<td>e</td>
</tr>
</tbody>
</table>

In the mechanism proposed by Westheimer\(^\text{64}\) for the hydrolyses of
cyclic phosphate esters, it was necessary to assume apical attack of the nucleophile and apical departure of the leaving group. Westheimer has attempted to rationalise this assumption by application of the 'principle of microscopic reversibility' (pmr). Thus the principle as extended to phosphorus chemistry is postulated by Westheimer to state that:

"If a molecule or reactant enters a TBP at an apical position this (or another) molecule or reactant must likewise leave the TBP from an apical position."

This 'extended' pmr has however, been severely criticized by a number of workers.

The assumption of apical attack and apical departure can however be supported on other grounds. Structural investigations of stable TBP phosphoranes have shown that apical bonds are longer and therefore weaker and should be more readily broken than equatorial bonds. Orbital electronegativity has also been shown to give weight to the above assumption. Equatorial phosphorus orbitals are more electronegative than apical orbitals because the phosphorus 3s orbital is concentrated in the equatorial orbitals. Nucleophiles should therefore prefer apical entry and departure, and electrophiles should prefer equatorial entry and departure. The steric interactions should also be less for attack on the face of a tetrahedral phosphorus molecule (apical attack) as compared to attack on an edge (equatorial attack). Molecular orbital calculations by Boyde are also in agreement with apical entry and apical departure of nucleophiles.

In addition to the theoretical arguments experimental results also favour this assumption. The hydrolysis of optically active benzylethyl-methylphenylphosphonium iodide (3.18) was shown by McEwen to give
ethylmethylphenylphosphine oxide (3.19) with inversion of configuration at phosphorus. This result can only be explained in terms of apical attack and apical departure or equatorial attack and equatorial departure. The latter is however unlikely in view of the theoretical considerations.

The results of Westheimer\(^{64}\) from the hydrolysis of the cyclic phostonate (3.20) can only be explained in terms of apical attack and apical departure. The rate of hydrolysis of (3.20) was found to be 10\(^6\) times faster than its acyclic analogue, and also to proceed with almost complete ring opening (> 99.8%). The rate acceleration indicates the formation of a TBP intermediate in which the ring strain has been reduced by placing the ring apical equatorial, with the ring oxygen apical.

The mechanism of apical attack and equatorial departure, Scheme 15, would lead to predominant exocyclic cleavage. Similarly equatorial attack and apical departure, Scheme 16, would lead to a mixture of ring opened and ring retained products.

\[ \text{Scheme 15} \]
Equatorial attack and equatorial departure can also be eliminated, Scheme 17. The initially formed intermediate has no suitable leaving group in an equatorial position and must therefore pseudorotate to the high energy TBP with a carbon atom apical. This would result in a slower rate of hydrolysis and a mixture of ring opened and ring retained products.

Thus the only plausible mechanism appears to be apical attack followed by apical departure, Scheme 18.
Although these facts and many other results support Westheimer's 'extended' pmr they do not prove that the principle is valid in these reactions but rather that the original assumption of apical attack and apical departure is reasonable. This assumption will be used throughout the rest of this thesis.

3.5 Reaction Pathways.

With the restrictions of TBP geometry for the intermediate and its formation by apical attack and decomposition by apical departure it is possible to determine all the reaction pathways available for nucleophilic substitution at tetrahedral phosphorus which proceed via a pentacoordinate species.

A knowledge of the relative stabilities of isomers of a TBP phosphorane enables a prediction to be made of the preferred reaction pathway, providing the following conditions are met;

(i) thermodynamic control of intermediate formation, i.e. the most stable TBP species is formed fastest.

and (ii) the products are derived from the most stable initially formed TBP intermediate.

Exceptions to these conditions do however occur. Failure of the first condition arises when intermediate formation comes under kinetic control, i.e. the most rapidly formed intermediate is not that predicted to be the most stable.

The alkaline hydrolysis of the diastereomers of ethoxymethoxymethylphenylphosphonium salt (3.21) have been studied by DeBruin and Mislow. The possible initially formed intermediates are;
of these it would be expected that (3.22) would be the most stable on the grounds of electronegativity and steric effects (Chapter 1). The preferred reaction pathway should therefore be via (3.22) followed by loss of \(\text{OEt}\) to give the phosphinate ester with inversion of configuration at phosphorus. However, the product analysis showed only 20% and 27% of the predicted product from (3 - 3.21) and (R - 3.21) respectively.

The large bulk of the menthoxy group decreases the rate of formation of (3.22) by hindering the attacking hydroxide ion. The activation energy to formation of (3.22) is increased sufficiently such that the formation of the less stable intermediate (3.23) becomes the preferred reaction pathway. Thus two of the observed products (R - 3.27) and (S - 3.26) are formed by direct loss of the apical alkoxy groups from (3.22) and (3.23), Scheme 19.

Two further products (R - 3.26) and (S - 3.27) are obtained by pseudorotations of (3.22) and (3.23) as in Scheme 19. However, the relative yields of these products can still be predicted from a knowledge of the relative stabilities of (3.28 - 3.31). Pseudorotation of (3.22) will be less favourable than that of (3.23), since the former places the bulky menthoxy group into the unfavourable apical position whereas the latter places the menthoxy group into the favourable equatorial position. The placing of a carbon atom in the unfavourable apical position is
Scheme 19

Mechanism of Hydrolysis of (S-3.21)

Attack Opposite Ethoxy

Attack Opposite Menthoxy
partially compensated for by formation of the conjugate base from the equatorial hydroxy group. The reverse pseudorotations in Scheme 19 will be very unfavourable as they require the poorly apicophilic $O^-$ group to be apical.

Another kinetically controlled reaction has been observed by Trippett and De'ath. The hydrolysis of benzyl-$t$-butylmethylphenylphosphonium bromide (3.32, $R = \text{CH}_2\text{Ph}; X = \text{Br}$) was shown to give $t$-butylmethylphenylphosphine oxide with predominant retention of configuration, Scheme 20. However, if the apicophilicity of the $R$ group is increased, then the stability of the intermediate (3.33) can be increased sufficiently to make the 'normal' pathway be preferred, and the reaction will revert to thermodynamic control.

SCHEME 20

The hydrolysis of (3.32, $R = \text{OEt}, X = \text{SbCl}_6$) has been shown to go with almost complete inversion of configuration at phosphorus. When $R$ is intermediate in apicophilicity between ethoxy and benzyl (e.g.
In cases where the first condition holds (thermodynamic control), the products may not always be derived from the initially formed phosphorane. This usually occurs when the leaving group is prevented from occupying an apical position in the most stable initially formed phosphorane. This may occur when:

(i) the phosphorus atom is contained in a small ring, and
(ii) the most apicophilic group is not the best leaving group.

The mechanism of the alkaline hydrolysis of the diamidate (3.34) is shown in Scheme 21. The most stable initially formed TBP intermediate (3.35) has the ring apical-equatorial. The energy of activation for loss of ́N(Me)Ar is much higher than that required for (3.35) to pseudorotate to (3.36), from which the products are obtained by apical loss of phenoxide.
There are very few examples where a ligand is highly apicophilic and yet a poor leaving group. This is because the same factors which determine the leaving group ability also contribute to the apicophilicity. The only examples of this effect appear to be fluorine versus chlorine and oxygen versus sulphur.

When the leaving group is prevented from occupying the apical position then pseudorotation of the intermediate usually occurs, placing the leaving group apical. However, if the nucleophile is highly apicophilic then pseudorotation may be unfavourable. This may result in either (i) the formation of a stable phosphorane, or (ii) a reversible loss of the nucleophile, and a slower formation of a less stable intermediate from which the products may be derived.

The reaction of the phosphonium salt (3.3) with methoxide ion is such an example. At low temperatures the intermediate is relatively stable, but is in a slow equilibrium with the phosphonium salt and methoxide.

Wadsworth and coworkers have shown that the phosphorochloridate (3.37) gives different ratios of geometrical isomers depending on the basicity of the nucleophile. The reaction pathways are shown in Scheme 22. Although the intermediate (3.38) is probably most stable with the ring apical-equatorial, pseudorotation to (3.39) becomes less favourable as the apicophilicity of the nucleophile increases. In the case of (3.38, \( R = \text{NO}_2 \)) the intermediate (3.39) becomes less stable than (3.40) and predominant inversion results. The reaction to (3.38) is then merely a parasitic equilibrium.
Conclusion.

The course of a nucleophilic substitution reaction at phosphorus can be predicted providing the relative stabilities of the initially formed TBP intermediates are known and subject to the two conditions outlined in Section 3.5. These reactions may then be considered to proceed via the direct displacement mechanism (Section 3.1), although they may not necessarily proceed by a transition state.

When these conditions do not hold the reaction pathway can still be predicted providing the following can be determined:

(i) the steric factors which may lead to kinetic control of intermediate formation,

(ii) the relative stabilities of all the possible TBP species,
such that the most favourable pseudorotation pathway(s) can be predicted, and (iii) the relative order of leaving group abilities.

These reactions will usually be of the addition-elimination type (Section 3.1) where the lifetime of the intermediate is sufficiently long for pseudorotational processes to occur.

Finally it should be realised that the course of reactions at phosphorus may be influenced by solvent\(^\text{94}\), and whether in heterogeneous or homogeneous conditions\(^\text{90}\).
4. **STABILITY OF PHOSPHORANES.**

4.1 **Absolute Stability.**

The stability of a phosphorane intermediate will determine whether or not it will exist as an intermediate or a transition state, i.e. its lifetime. The factors which influence the stability of a TBP phosphorane intermediate are best determined by examination of the properties of known stable phosphoranes. Their stability is found to be dependent on (a) the presence of a small ring in the molecule and (b) the size and electronic properties of the substituents.

(a) **Ring Effects.**

In a TBP molecule with five substituents there will inevitably be considerable crowding. This is evident from X-ray diffraction studies\(^ {11-21}\). The presence of a small ring may therefore partly offset these crowding difficulties with a resultant stabilisation of the molecule.

Stability can also be measured in terms of the ease of decomposition. The most likely mode of breakdown will be elimination to give a tetrahedral phosphonium centre and an anion. With the ring apical-equatorial in the TBP, the angle at phosphorus in the ring is 90° and there is very little angle strain (4.1). However, if one of the other substituents is lost the ring strain will increase since the preferred ring angle at phosphorus will increase to 109.5° (4.2). Thus the apical-equatorial ring should stabilise the phosphorane by increasing the activation energy to

\[
\begin{align*}
\text{(4.1)} & \quad \text{P} \quad \text{X} \\
\implies & \quad \text{P}^+ \quad \text{X}^- \\
\text{(4.2)} & \quad \text{X} \\
\end{align*}
\]
decomposition. This has been observed by Denney\textsuperscript{95,96} and coworkers for the adducts of diethylperoxide with various phosphines. The stability with respect to the equilibrium (4.1)$\rightleftharpoons$(4.2) was found to be in the order;

\[
\begin{align*}
R'\text{P(OEt)}_2 + \text{PhOEt} & \rightarrow R'\text{P(OEt)}_3 \\
& \rightarrow R'\text{P(OEt)}_4 \\
& \rightarrow R'\text{P(OEt)}_5
\end{align*}
\]

The adducts from tris(dimethylamino)phosphine with $\alpha$-ketones exist predominantly as the open dipolar ion (4.3) in solution while those from a cyclic aminophosphine are stable pentacoordinate species (4.4)\textsuperscript{97-99}.

A number of acyclic and monocyclic phosphoranes have been shown to react with diols to form monocyclic and spirocyclic phosphoranes respectively\textsuperscript{55,100}. It may be argued that these reactions occur due to
the favourable entropy term. Ramirez\textsuperscript{101} and coworkers have measured the enthalpy of reaction of (4.5) with ethylene glycol and have shown it to be exothermic by ca. 2 Kcal mol\textsuperscript{-1}. Assuming solvation changes are negligible then this represents a significant increase in the stability of the phosphorane (4.6), presumably by relief of crowding.

(b) Substituent Effects.

The introduction of large substituents should increase intramolecular crowding and therefore destabilise the molecule. However, there is very little experimental evidence for this effect. Ramirez\textsuperscript{102} and coworkers have studied the base catalysed exchange of alkoxy groups in oxyphosphoranes. The reaction of (4.7) with methanol (3 Molar equiv.) in the presence of pyridine gave a mixture of oxyphosphoranes and 2.11 molar equivalents of benzyl alcohol. However, the analogous reaction of (4.8) with benzyl alcohol under the same conditions produced only 1.19 molar equivalents of methanol. All the oxyphosphorane products
still contained the dioxaphospholen ring. These results would appear
to indicate that large groups destabilise the TBP molecule.

\[
\begin{align*}
\text{Me} & \quad \text{OCH}_2\text{Ph} \\
\text{Me} & \quad \text{OCH}_2\text{Ph} \\
\text{Me} & \quad \text{OCH}_2\text{Ph}
\end{align*}
\]

(4.7) \[ + \text{3 MeOH}_\text{base} \xrightarrow{\text{base}} \text{Mixture of} \quad \text{Oxyphosphoranes} + \text{2.11 PhCH}_2\text{OH} \]

(4.8)

The electronegativity of the substituents also effects the
stability of the phosphorane. In the series of biacetyl adducts (4.9
to 4.12) the tris(dimethylamino)phosphine adduct (4.12) exists as a
dipolar species. However, the difference in steric requirements of
\(\text{NMe}_2\) and \(\text{OMe}\) will also be a contributing factor in this case.

\[
\begin{align*}
\text{Me} & \quad \text{OCH}_2\text{Ph} \\
\text{Me} & \quad \text{OCH}_2\text{Ph} \\
\text{Me} & \quad \text{OCH}_2\text{Ph}
\end{align*}
\]

(4.9) \[ R_1=R_2=R_3=\text{MeO} \]
(4.10) \[ R_1=\text{NMe}_2; R_2=R_3=\text{MeO} \]
(4.11) \[ R_1=R_2=\text{NMe}_2; R_3=\text{MeO} \]
(4.12) \[ R_1=R_2=R_3=\text{NMe}_2 \]

Ref. 103

Molecular orbital calculations on \(\text{PF}_{n}\text{Cl}_{15-n}\) molecules show that the
stability decreases with increasing substitution by chlorine\(^1\).
4.2 Relative Stabilities of Isomers.

In order to predict with any confidence the preferred reaction pathway for a nucleophilic substitution at phosphorus, it is necessary to have quantitative data on the relative stabilities of the isomers of TBP molecules. The qualitative information discussed in Chapter 1 does not allow accurate predictions to be made, especially in cases where the stabilities are determined by a balance of several factors.

The most widely used technique for obtaining the relative stabilities is that of dynamic nuclear magnetic resonance (d.n.m.r.). In this method the rate of interconversion of two TBP conformations is measured and the corresponding energy of activation $\Delta G^*$ for the process is calculated. The value of $\Delta G^*$ is a measure of the energy of the highest-energy species which is traversed in the observed pseudorotation pathway. Other methods which have been used to obtain data on relative stabilities of TBPs include kinetic studies$^{105,106}$ and product analysis of substitution reactions$^{107}$.

Single Step Pseudorotations.

The simplest system is that in which the two TBP structures have the same energy, e.g. PL₅ and RPL₄ (Where R is less apicophilic than L). The reaction coordinates (4.13) show the intermediate state as a transition

![Diagram](image)
state, it may however be a stabilised intermediate, although there is no
evidence to this effect. The magnitude of $\Delta G^\star$ will then represent the
energy of the transition state between the two topomeric TBPs, i.e. the
square based pyramid for a BPR or the $30^\circ$-$(2+3)$ turnstile species for a
TR' process.

Many workers$^{41,29,109,119}$ have studied this type of process to
determine the factors which effect the energy of the transition state.
In most cases, e.g. PF$_5$$^{41}$ and MePF$_4$$^{29}$, the energy barrier is very low
and cannot be measured using d.n.m.r. techniques. The energy barrier
to pseudorotation in PF$_5$ has been calculated from infrared studies$^{26,108}$,
and for a BPR was found to be 3.8 Kcal mol$^{-1}$. The highest energy
barrier yet observed for pseudorotation between topomeric acyclic phospho-
ranes is a $\Delta G^\star > 6.9$ Kcal mol$^{-1}$ for the pseudorotation of (4.14)$^{109}$.

$$
\begin{array}{c}
\text{H} \\
\text{F} \\
\text{F} \\
\text{F} \\
\text{P} \\
\text{F} \\
\text{F} \\
\end{array} \quad \leftrightarrow \quad 
\begin{array}{c}
\text{H} \\
\text{F} \\
\text{F} \\
\text{F} \\
\text{P} \\
\text{F} \\
\text{F} \\
\end{array}
$$

(4.14)

However, for the spirophosphorane (2.5), studied by Whitesides and
Bunting$^{49}$, the energy barrier is very large, $\Delta G^\star = 20.8$ Kcal mol$^{-1}$.
Clearly both steric and electronic effects are important. However, since
in most cases the energy barriers are low, few measurements have been
obtained, and it is therefore difficult to establish any trends.

Pseudorotations between two TBPs of different energies can also
be observed by d.n.m.r. However, if the difference in energy is too
large the concentration of the higher energy TBP may be so low as to be
undetectable by n.m.r. techniques.
Multi step Pseudorotations.

The reaction coordinates (4.15) for the pseudorotation of the spirophosphorane (2.24) proceeds via a high energy TBP structure (2.26), Scheme 9. The ring protons in (2.24) can only become equivalent when pseudorotation via (2.26) is fast on the n.m.r. time scale. Thus $\Delta G^*$ can be calculated from the temperature at which the ring protons become equivalent. The difference in energy $\Delta G$ between (2.26) and (2.24) is,

$$\Delta G = S_{90-120} \text{(dioxaphospholan)} + (A_{Ph} - A_0)$$

and the value of $\Delta G^*$ will be an overestimate of $\Delta G$. As the value of $\Delta G$ increases the difference between $\Delta G$ and $\Delta G^*$ will decrease, as the transition state becomes more like the TBP. In the limit the TBP intermediate may be of such high energy that it becomes a transition state ($\Delta G = \Delta G^*$).

If the phenyl group of (2.24) is replaced by a more apicophilic group (R), then the high energy species will be (4.16), and the
difference in energy between (4.16) and (4.17) will be:

\[ \Delta G^* > \Delta G = S_{90-120} \text{ (dioxaphospholan)} + (A_R-A_O) \]

but now \( \Delta G^* - \Delta G \) will be greater than when \( R \) was phenyl since \( R \) is more apicophilic than phenyl and so (4.16) is of lower energy than (2.26).

The \( \Delta(\Delta G) \) value for these two examples will be,

\[ \Delta(\Delta G) = A_{Ph} - A_R \]

and the difference between the two \( \Delta G^* \)s, \( \Delta(\Delta G^*) \), will be an underestimate of \( \Delta(\Delta G) \). This is best seen by referring to the reaction coordinates (4.18). The ground state energies of the two spirophosphoranes (2.24)

\[ \Delta(\Delta G^*) \]

\[ \Delta(\Delta G) \]

(4.18)

and (4.17) are arbitrarily assigned the same energies. Thus for a series of \( R \) groups a quantitative apicophilicity scale can be obtained.

These data can then be used to estimate the relative energies of TBP reaction intermediates.
5. **DYNAMIC NUCLEAR MAGNETIC RESONANCE STUDIES ON SPIROPHOSPHORANES.**

Most of the reports in the literature on the determination of free energies of activation for multistep pseudorotations have been for single compounds. There are very few examples for which $\Delta G^*$ values are known as a function of one substituent only$^{21,38,110-115}$.

In order to gain additional data on the relative apicophilicities of groups a number of systems were designed for study by dynamic nuclear magnetic resonance. In addition, data were obtained on the increase in ring strain on placing a ring diequatorial, relative to the preferred apical-equatorial placement.

5.1 **Biacetyl Adducts.**

(a) **Introduction**

Ramirez and coworkers$^{103}$ have found that the reaction of phosphites, phosphonites, and phosphinites with $\alpha$-diketones and $\sigma$-quinones gives the unsaturated 1,3,2-dioxaphospholen adducts, e.g. (5.1), Scheme 23.

![Scheme 23](image)

The 1:1 adduct (5.1) was also shown to react rapidly with ethylene glycol to form the spiro-oxyphosphorane (5.2; $A-D = H$)$^{101}$. The pseudorotation pathways available to the adduct (5.2) can
be derived by referring to the Balaban graph (2.28)\(^5\). Using the numbering indicated in (5.2) the graph simplifies to (5.3), since the

![Graph](image)

(5.3)

vertices labelled 12, 15, 34 and 34 correspond to geometrically impossible TBPs, with the rings diapical. There are then three distinct types of pseudorotation (Scheme 24) which may occur. Although the energy of

\[
\begin{align*}
\text{(5.4)} & \quad \text{(5.5)} & \quad \text{(5.6)} & \quad \text{(5.7)} \\
\end{align*}
\]

\text{SCHEME 24}

(5.4) would be expected to be quite high, the pseudorotation (i) cannot be observed by d.n.m.r. since the spectral changes are the same as for the low energy pseudorotation (ii) between the topomeric TBPs (5.5) and (5.6). However, at high temperatures pseudorotation (iii) should be observable since A, B, C, and D will become equivalent when (iii) is fast on the n.m.r. time scale. The \(\Delta \mathcal{G}^*\) for this high energy pseudorotation
(iii) will be a measure of the difference in energy between (5.6) and (5.7).

\[ \Delta G^* = \Delta G = S_{90-120} (\text{dioxaphospholen}) + (A_R - A_o) \]

Ramirez has not reported on the variable temperature \(^1\text{H}\) n.m.r. spectrum of (5.2; A-D = H). The spectrum at ambient temperature is complex due to both H-H and P-H coupling. A determination of the \(\Delta G^*\) for the pseudorotation (iii) would therefore require a full line shape analysis. The pinacol adduct (5.2; A-D = Me) should have a simple spectrum since both H-H and P-H coupling will be largely eliminated. However, attempts to prepare the pinacol adduct by the exchange route (Scheme 23) have been unsuccessful.\(^{116}\)

Denney and coworkers\(^{55}\) have also shown that pinacol does not react analogously to other glycols in their reactions with phosphoranes containing two ethoxy groups. Pentaethoxyphosphorane (5.8) was shown to react with ethylene glycol, neopentyl glycol, propylene glycol, \(\text{d}1\)-2,3-butanediol, and styrene glycol to give monocyclic-(1 mol glycol) or spiro-(2 mol glycol) oxyphosphoranes, Scheme 25. The reactions of 1,4-butanediol and 1,5-pentanediol gave monocyclic oxyphosphoranes which decomposed under the reaction conditions, 0\(^\circ\), to give tetrahydrofuran and tetrahydropyran respectively, and triethylphosphate. This was probably due to the
instability of phosphoranes containing large (seven and eight membered) rings. The reaction of pinacol with (5.8) gave only triethylphosphate, pinacol, and ethanol as the major products. The unreactivity of pinacol may be due to steric hindrance, since the glycols which did give oxyphosphoranes were either primary or secondary alcohols.

The pinacol adduct (5.10; \( R = \text{OMe} \)) was therefore prepared by reaction of molar equivalents of methyl pinacol phosphite (5.9) with biacetyl (Scheme 26, \( R = \text{OMe} \)). The reaction was carried out at ambient temperature in the absence of a solvent and was extremely exothermic. After several hours the yellow colour of the biacetyl disappeared and the reaction mixture crystallised. No 1:2 adducts (5.11) and (5.12), reported by Ramirez\(^{103d} \) for the reaction of acyclic phosphites with biacetyl, were observed by \(^1\text{H} \) n.m.r., Scheme 27.

The hydrolytic instability of (5.10) precluded the obtention of standard analytical data. Furthermore, the molecular ion was never
observed in attempts to obtain mass spectral data. The assignment of a pentacoordinate structure for (5.10) rests therefore on \( ^1H \) and \( ^{31}P \) n.m.r. spectroscopy, the method of preparation and the hydrolysis products.

The \( ^1H \) n.m.r. spectrum of (5.10; \( R = \text{OMe} \)) in chloroform - d, benzene, and o-dichlorobenzene exhibited a sharp singlet of 12H corresponding to the four methyl groups of the dioxaphospholan ring. The equivalence is probably accidental and not due to fast pseudorotation via (5.7; A-D = Me). The spectrum also showed a doublet of 3H, (\( J_{PH} = 14\) Hz) corresponding to a POMe group, and a singlet of 6H corresponding to the two methyls of the dioxaphospholen ring, their equivalence being due to the pseudorotation (ii) between topomeric TBPs being fast at ambient temperature.

The adduct (5.10; \( R = \text{OMe} \)) exhibited a \( ^{31}P \) n.m.r. signal at +34.2 p.p.m., which is at a lower field than that reported (+48.9 p.p.m.) for the trimethyl phosphite adduct (5.1)\(^{103d}\). Lowering of \( ^{31}P \) chemical shifts on the incorporation of a ring have also been observed by Ramirez\(^{101,103d} \) and Denney\(^{55} \).

Exposure of a solution of the adduct (5.10; \( R = \text{OMe} \)) to the atmosphere at ambient temperature led to rapid hydrolysis to methyl pinacol phosphate. The mechanism is probably as postulated by Ramirez\(^{102a} \) for the hydrolysis of (5.1), Scheme 28. No other phosphorus-containing products were observed.*

**Footnote:** The adduct (5.1) has also been reported to react with molecular oxygen\(^{117} \). This reaction is however much slower than hydrolysis.
A range of 1-substituted pinacol phosphites was synthesised and the adducts with biacetyl prepared. Some of the spectroscopic data for these adducts are given below, Table 6.

**TABLE 6**

**Spectroscopic Data for Biacetyl Adducts.**

<table>
<thead>
<tr>
<th>Compound</th>
<th>R group</th>
<th>( \delta^a )</th>
<th>( \tau(CMe_2)^b )</th>
<th>( \tau(MeC=)^b )</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5.10-a)</td>
<td>MeO</td>
<td>+34.2</td>
<td>8.87</td>
<td>8.68</td>
</tr>
<tr>
<td>(5.10-b)</td>
<td>EtO</td>
<td>+36.0</td>
<td>8.82&lt;sup&gt;c&lt;/sup&gt;</td>
<td>8.28&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>(5.10-c)</td>
<td>i-PrO</td>
<td>+37.8</td>
<td>8.85</td>
<td>8.32</td>
</tr>
<tr>
<td>(5.10-d)</td>
<td>t-BuO</td>
<td>+36.8</td>
<td>8.33&lt;sup&gt;d&lt;/sup&gt;</td>
<td>8.33&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>(5.10-e)</td>
<td>EtS</td>
<td>-</td>
<td>8.82</td>
<td>8.37</td>
</tr>
<tr>
<td>(5.10-f)</td>
<td>PhD</td>
<td>-</td>
<td>8.80</td>
<td>8.55</td>
</tr>
</tbody>
</table>


The \( ^{31}P \) chemical shifts were not obtained for the adducts (5.10-e and f) as they were extremely unstable and readily decomposed in solution giving a black colouration. At ambient temperature the half life of the adduct (5.10-e) was about 12h. The adduct (5.10-f) appeared to be even
less stable. Preparation of (5.10-f) in the absence of a solvent gave a colourless crystalline product. However, on making up an n.m.r. sample the compound readily decomposed. The formation of an adduct was confirmed by monitoring the reaction of molar equivalents of biacetyl and phenyl pinacol phosphite in benzene, by $^1$H n.m.r. at ambient temperature. Initially two new signals appeared corresponding to the adduct, however after 2h. additional signals were observed. Finally after 18h. the initial signals corresponding to the adduct had almost disappeared. The resulting spectrum was consistent with that of phenyl pinacol phosphate.

(b) *Dynamic Nuclear Magnetic Resonance Studies.*

Apart from the t-butoxy adduct (5.10-d) the pinacol methyl groups showed chemical shift degeneracy in most n.m.r. solvents. However, in 1-bromonaphthalene both the methoxy (5.10-a) and the t-butoxy (5.10-d) adducts exhibited two broad singlets of equal intensity. On heating the samples to 80°, the signals sharpened, presumably due to the reduced viscosity of the solvent and consequent increase in resolution. Further heating caused the peaks to broaden again and eventually coalesce. Beyond the coalescence temperature Tc the broad absorption sharpened. The process was reversible although after prolonged heating decomposition occurred as evidenced by the n.m.r. spectrum.

The free energies of activation $\Delta G^*$ were then calculated from the coalescence temperatures Tc and the peak separations $\Delta v_e$, at slow exchange, using the Eyring equation

$$k_1 = \frac{(kT/h)}{\exp(-\Delta G^*/RT)}$$

$k = $ Boltzmann's constant
$T = $ Temperature of coalescence
$h = $ Plank's constant
$R = $ Gas constant
where the rate of pseudorotation $k_1$ at the coalescence temperature is given by the Gutowsky-Holm approximation \[ \text{Eq. 118,121} \]

$$k_1 = \frac{\pi \Delta \nu_{\infty}}{\sqrt{2}}$$

Although this approximation is often subject to large errors, it has been shown \[120,121\] to be reliable in the case of processes involving exchange between two equally populated configurations. The equation for $k_1$ is only valid for the coalescence of two signals and not systems involving a change in spin-spin coupling. In order to compare the $\Delta G^*$s for different compounds the corresponding $\Delta S^*$s must differ only slightly. In fact pseudorotations are expected to have small entropies of activation and so any differences would be small compared to $\Delta G^*$. Determinations of $\Delta S^*$s by line shape analysis \[110b\] and by conventional kinetic methods \[105\] have been within experimental error of zero.

The results from the biacetyl adducts are given below, in Table 7.

**TABLE 7**

Dynamic Nuclear Magnetic Resonance Data for Biacetyl Adducts

<table>
<thead>
<tr>
<th>Compound</th>
<th>R-group</th>
<th>$\Delta \nu_{\infty}^b$ (Hz)</th>
<th>$T_c$ (°C)</th>
<th>$\Delta G^a$ (kcal mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5.10-a)</td>
<td>MeO</td>
<td>4 ±0.25</td>
<td>114±5</td>
<td>21.2±0.3</td>
</tr>
<tr>
<td>(5.10-d)</td>
<td>t-BuO</td>
<td>3.5±0.25</td>
<td>144±5</td>
<td>23.0±0.3</td>
</tr>
</tbody>
</table>

a. Error based on $\Delta \nu_{\infty}$ and $T_c$ only. The error due to the Gutowsky-Holm equation is $<\pm0.1$ kcal mol$^{-1}$ at 300°K if $\Delta \nu_{\infty} > 3$Hz. (Ref. 120).

b. At 100MHz.

The $\Delta G^*$s correspond to the free energies of activation for the pseudorotation (iii), Scheme 24. Since the high energy TBP (5.7; A-D = Me) may be a
transition state or an intermediate then, \( \Delta G^* \geq \Delta G \). The methoxy group is therefore more apicophilic than \( t \)-butoxy by:

\[
\Delta(\Delta G) = \Delta(\Delta G^*) = (\Delta G^*_{t-BuO} - \Delta G^*_{MeO}) = 1.8 \pm 0.6 \text{ kcal mol}^{-1}
\]

In addition to the errors already referred to a further error may arise if there is a temperature dependence of the chemical shifts of the coalescing signals. This can only be detected by either, (a) examination of the line widths as a function of temperature, or (b) the comparison of \( \Delta G^* \)s obtained at different temperatures (only if \( \Delta S^* = 0 \)) using an n.m.r. spectrometer operating at a different frequency. Although this phenomenon cannot be shown to be absent in this system, it is probable that the effect will be negligible.

Finally it must be noted that an irregular process, i.e. a reversible opening of the pinacol ring or a reversible loss of the \( R \) group, would also account for the temperature dependence of the n.m.r. spectra of these adducts. If an irregular process is responsible then the results would represent a minimum value of \( \Delta G^* \) for the pseudorotation process. The \( \Delta G^* \) for an irregular process would be expected to be lower in a more polar solvent, due to stabilisation of the intermediate dipolar species. However, the degeneracy of chemical shifts for these adducts in a solvent other than \( 1 \)-bromonaphthalene, precluded the obtention of such data.

(c) Lanthanide Induced Shifts.

Lanthanide shift reagents are paramagnetic metal complexes which in solution associate with organic substrates thereby inducing paramagnetic shifts in the n.m.r. spectra of the organic compounds. The shift reagent usually complexes to a lone pair of electrons in the substrate and the magnitude of the shift depends on the degree of association.
Shift reagents have been frequently used for the simplification of the n.m.r. spectra of organic compounds and especially for the separation of overlapping signals. However, there are very few examples of their application to organophosphorus compounds and only two cases in which a pentacoordinate phosphorus compound has been the substrate.

The $^{1}$H n.m.r. spectrum of (5.13) at ambient temperature was shown to exhibit three signals in the ratio 2:1:1 for the pinacol methyl groups. However, in the presence of the shift reagent Eu(fod)$_3$, (fod = 1,1,1,2,-2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate), four equally intense singlets were observed.

It was found that the degeneracy of chemical shifts from the biacetyl adducts (5.10 a-c) in o-dichlorobenzene solution could be removed using the shift reagent, tri(dipivalomethanato)europium(III), Eu(dpm)$_3$. The results are given in Table 8. The variation of induced shift with molar ratio of shift reagent is very sensitive to the presence of impurities, especially those with functional groups with which the shift reagent will preferentially associate. The phosphorus containing decomposition products of the biacetyl adducts are usually phosphoryl compounds ($\text{P}^+\text{O}^- \rightleftharpoons \text{P}=\text{O}$) which would be expected to associate strongly to the shift reagent. The lower shifts observed for the iso-propoxy adduct (5.10 -c) may be due to the presence of a larger proportion of impurities in the sample.
TABLE 8

N.m.r. Spectra of Biacetyl Adducts in o-Dichlorobenzene

in the Presence of Eu(dpm)₃.

The chemical shift (τ) is followed by the shift (Hz) from the normal position in o-dichlorobenzene.

\[
\begin{array}{cccccc}
R & \text{Eu(dpm)₃} & \text{AB} & \text{CD} & \text{EF} & \text{OTHERS} \\
& \text{(Molar equiv.)} & & & & \\
\text{MeO} & 0.35 & 8.83 & 8.83 & 8.28 & \text{MeO} 6.47 \\
& & 77 & 29 & 35 & 5 \\
\text{EtO} & 0.18 & 8.82 & 8.82 & 8.28 & \text{CH}_2\text{O} 6.12, \text{CMe} 8.85 \\
& & 30 & 10 & 15 & 3 \ 0 \\
\text{i-PrO} & 0.20 & 8.78 & 8.78 & 8.27 & - \\
& & 14 & 2 & 8 & \\
\end{array}
\]

a. At 60 MHz. b. Calculated from spectrum integration.

It is interesting to speculate on the site of coordination of the shift reagent. At ambient temperature the topomeric pseudorotation (ii), Scheme 24, will be fast on the n.m.r. time scale and so the average structure 'seen' by the shift reagent will be the square based pyramid (SBP) structure. The induced shift is inversely proportional to the cube of the distance of the observed nucleus from the europium atom\textsuperscript{124b}. 
From the shifts given in Table 8, it would seem reasonable that the europium atom on average lies nearest to the four basal positions of the SBP (5.14). This is as expected since the four basal ligands of a SBP have more electron density than the axial ligand and should therefore be better electron donors.

The induced shift is not entirely a function of the distance from the europium atom. The complete McConnell-Robertson equation\(^\text{125}\) (5.15) is more useful for accurate structural and conformational analyses\(^\text{124a}\).

\[
\text{Relative Shift } (\Delta H_i/H) = \frac{k(3\cos^2 \theta_i - 1)}{r_i^3}
\]  
(5.15)

\(\Delta H_i/H\) = Relative shift of the \(i\)th atom  
\(r_i\) = Distance of \(i\)th atom from europium atom  
\(\theta_i\) = Angle between the principle magnetic axis and the line represented by \(r_i\)  
k = Scaling constant

Thus assuming the position of coordination of the europium atom and a given structure for the compound a least squares fit can be carried
out between the calculated and observed shifts. If the sum of the squares of the differences between calculated and observed shifts is acceptably small, then the proposed structure and site of coordination are probably correct. A simple graphical method for the calculation of shifts has been suggested by Wing and coworkers

The averaged structure (5.14) of the shift reagent-adduct complex was subjected to a least squares fit between the observed and calculated shifts. The adduct used was the ethoxy compound (5.10-b). The distance of the europium atom from the four basal oxygens was optimised to give a minimum sum of squares R(%). The angles and bond lengths of the SBP were taken from framework molecular models and are assumed to be reasonable. The angle \( \alpha \) between the plane of the rings and the \( C_2 \) axis was chosen to be 110°, and the principle magnetic axis of the \( \text{Eu(dpm)}_3 \) was taken to be coincident with the \( C_2 \) axis of the SBP. With these restrictions the optimised value of the Eu-0 distance, the minimum least squares sum (R%), and the scaling constant \( k \) were determined and are given in Table 9.

### Table 9

**Structural Data of Shift Reagent Complex with Biacetyl Adducts.**

<table>
<thead>
<tr>
<th>Eu-0 Bond Distance</th>
<th>3.5 Å</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \alpha )</td>
<td>110°</td>
</tr>
<tr>
<td>R(%)</td>
<td>2.5%</td>
</tr>
<tr>
<td>( k )</td>
<td>.24</td>
</tr>
</tbody>
</table>

\[ R^2 = \Sigma (\text{shift observed} - \text{shift calculated})^2 / (\text{shift observed})^2 \]

\[ R(\%) = 100 \times R \]
Although this is not a rigorous treatment, the Eu-O distance is close to that expected (3.0 ± 0.5 Å) for coordination to lone pairs. The value of R(%) is also within the limits of those values reported in the literature. The results are therefore consistent with the proposed averaged structure of the complex.

The structure (5.14) may be the average of all possible TBP-Eu(dpm)$_3$ complexes all in rapid equilibrium via a dissociation-association mechanism, or the coordination of the shift reagent may actually restrict the phosphorane to a SBP geometry. The latter explanation is unlikely since there are no known examples of mono- or bichelation of substrates to shift reagents.

(d) Shift Reagents in Chemical Exchange Studies.

There are few reports in the literature in which paramagnetic shift reagents have been employed for chemical exchange studies.

Recently Springer and coworkers have used the lanthanide shift reagent, Eu(fod)$_3$, to increase the time resolution of d.n.m.r. spectroscopy by varying $\Delta \nu^\infty$ (i.e. $\Delta \nu$ in the absence of exchange) at a constant temperature, above the normal coalescence temperature. At ambient temperature the $^1$H n.m.r. spectrum of trimethyl carbamate (TMC) exhibited only one NMe resonance due to fast rotation about the C-N bond. At low temperatures (-46°) however, no splitting of the NMe resonance was observed, i.e. at slow exchange there is accidental degeneracy of chemical shifts ($\Delta \nu^\infty = 0$). The $^1$H n.m.r. spectrum of TMC in CCl$_4$ at 27° for progressively larger mole ratios of Eu(fod)$_3$ showed that the NMe resonance was broadened and then split into two peaks as more shift reagent was added. Further addition of shift reagent caused the peaks to sharpen. The effect is caused by an increase in $\Delta \nu^\infty$ on addition of shift reagent. Measurements
of $\Delta \nu$ and line shape analysis for each spectrum enabled the rate constant for C-N rotation to be determined.

Earlier, Gutowski and Cheng\textsuperscript{127} had studied the variable temperature $^1\text{H}$ n.m.r. of dimethyl formamide (DMF) in the presence of Eu(fod)$_3$. The temperature dependence of the $^1\text{H}$ n.m.r. shift induced by a paramagnetic shift reagent on an organic substrate in a polar solvent is given by equation (5.15)\textsuperscript{226}. Thus a plot of $\Delta \nu$ against $1/T$ should be a straight line of slope $C_s K_j/k$.

$$\Delta \nu = \frac{C_s K_j}{kT} \quad (5.15)$$

$C_s$ = Concentration of complex.
$K_j$ = Contact shift constant (characteristic of the nuclei and applied field).
$k$ = Boltzmann's constant
$T$ = Temperature (K).

Gutowski\textsuperscript{127} observed the dependence of the separation $\Delta \nu$ between cis and trans $\alpha$-Me group resonances in DMF for various mole ratios of shift reagent Graph (5.16). Initially $\Delta \nu$ is linear in $1/T$ at temperatures below the coalescence temperature $T_c$. As $T$ approaches $T_c$, $\Delta \nu$ becomes increasingly dependent on the exchange process, causing the value of $\Delta \nu$ to rapidly fall away from the linear $1/T$ plot. The rate constant at $T_c$ was then determined using the Gutowski-Holm approximation. Two independent determinations of $\Delta \nu$ were made, one from the line width at $T_c$, and the other by extrapolation of the linear portion of the $\Delta \nu$ vs. $1/T$ graph to $1/T_c$. Both values were in good agreement for concentrations of shift reagent below 0.3 molar equivalents.

The method used by Gutowski was applied to the ethoxy and iso-
Graph (5.16)

- DMF + 0.2 molar equiv. Eu(fod)$_3$ (Ref. 127).
- (5.10-a) + 0.35 molar equiv. Eu(dpm)$_3$ in o-Dichlorobenzene.

Calculated Curve

$$\Delta \nu = \left( A/T \right) \exp \left( -\Delta H/RT \right)$$

$$A = 260$$

$$\Delta H/R = -1400$$

Graph (5.17)

- 0.18 molar equiv. Eu(dpm)$_3$ in o-Dichlorobenzene
Graph (5.18)

- 0.2 molar equiv. Eu(dpm)$_3$ in o-Dichlorobenzene.

Graph (5.19)

- 0.35 molar equiv. Eu(dpm)$_3$ in o-Dichlorobenzene
propoxy adducts (5.10 - b,c), which showed accidental chemical shift
degeneracy. The methoxy adduct (5.10 -a) was also studied so that
the results could be compared to those obtained in the absence of shift
reagent. The resulting $\Delta \nu$ vs. $1/T$ plots are shown in the Graphs (5.16 -
5.18).

The results were unexpected since although the plots are linear
the intercepts of the extrapolated linear portion of the curves intercept
the $1/T$ axes at temperatures in the region of the coalescence temperature.
This would seem to imply a $\Delta \nu = < 0$ for the adducts in the presence of
shift reagent. The methoxy adduct (5.10-a; Graph 5.16) shows an inter-
esting anomalous behaviour near $T_c$, in that the $\Delta \nu$ departs from the linear
plot in a direction opposite to that expected. Also extrapolation of the
linear portion gives an intercept in the region of $T = 400^\circ$K instead of at
the origin, i.e. $1/T = 0$, as expected from equation (5.15). These
anomalies may possibly be due to an over simplification of the dependence
of $\Delta \nu$ on $T$ (Equation 5.15). The concentration of the paramagnetic
complex should also vary with temperature, according to equation (5.20),
where $\Delta S$ and $\Delta H$ are the entropy and enthalpy of complex formation in the
equilibrium (5.21).

$$\Delta G = -RT \ln K$$

$$\therefore \ [\text{complex}] = [\text{Eu(dpm)}_3][\text{Adduct}] \exp(\Delta S/R). \exp(-\Delta H/RT) \quad (5.20)$$

$$\text{Eu(dpm)}_3 + \text{Adduct} \xrightarrow{\text{Paramagnetic Complex}} \quad (5.21)$$

The modified equation (5.22) for $\Delta \nu$ will then be:

$$\Delta \nu = (K_j/kT).[\text{Eu(dpm)}_3][\text{Adduct}].\exp(\Delta S/R). \exp(-\Delta H/RT)$$

$$= (A/T). \exp(-\Delta H/RT) \quad (5.22)$$
The calculated curve in Graph (5.16) is derived from this equation. The values of \( A \) and \( \Delta H/R \) were chosen to give the best fit with the linear portion of the plot for the methoxy adduct (5.10 -a), Graph (5.16).

At temperatures above 80\(^\circ\)C the effect of chemical exchange on \( \Delta \nu \) becomes increasingly significant, causing the observed plot to fall away from the calculated curve. Near coalescence the chemical exchange effects are dominant and \( \Delta \nu \) decreases rapidly to zero at the coalescence temperature. The linear plots obtained by Gutowski and Cheng\(^{127}\) (5.16) for DMF, may be due to a smaller value of \( \Delta H \) for complex formation, so that the term \( \exp(-\Delta H/RT) \) in equation (5.22) is closer to unity.

To test this hypothesis the temperature dependence of the full line widths at half height of the pinacol methyl resonances for the adduct (5.10 -a) were studied. The results (Graph 5.19) show the temperature dependence of the sum of the line widths \( (W_{AB} + W_{CD}) \) of the two singlets below coalescence and of the single peak at and above coalescence.

At temperatures up to about 80\(^\circ\) the reduction in line width is due to the temperature dependence of electron relaxation in the paramagnetic complex\(^{127}\). At temperatures above 80\(^\circ\) the broadening caused by the paramagnetic complex is negligible, since at 80\(^\circ\) the sum of the line widths of the two singlets is only twice that of tetramethyldisilane (TMS). At this temperature the effects of chemical exchange broadening must also be negligible. However, above 80\(^\circ\) the line widths increase again to a maximum at the coalescence temperature, above which the line width rapidly decreases to a value approaching that of TMS. If the coalescence process was simply a merging of the two singlets there would be no increase in line width and the dependence on temperature would be as shown in the dashed portion of Graph (5.19).
In the case of the ethoxy (5.10 -b) and iso-propoxy (5.10 -c) adducts the molar ratios of shift reagent to adduct were smaller and so the deviations from the linear plot are not so well defined. Line width studies on these two adducts were not attempted since the ethoxy and iso-propoxy methyl group resonances overlap with the pinacol methyl resonances.

The free energy of activation for pseudorotation of the methoxy adduct (5.10 -a) in the presence of shift reagent was calculated from $\Delta v^\infty$ and $T_c$ as previously described. The value of $\Delta v^\infty$ was determined from the excess line width at coalescence (Graph 5.19). The value of $\Delta G^*$ (Table 10) is larger than that observed in the absence of shift reagent (21.2 ± 0.3 Kcal mol$^{-1}$; Table 7). A similar effect on $\Delta G^*$ was observed by Gutowski and Cheng$^{127}$ and is probably caused by the adduct-shift reagent association and possibly a small contribution from the entropy term $\Delta S^*$ for pseudorotation.

In conclusion then it appears that shift reagents can be applied to dynamic n.m.r. studies of pentacoordinate phosphoranes which normally show accidental chemical shift degeneracy. However, the $\Delta G^*$s so obtained tend to be larger than those for the same process in the absence of shift reagent. Further studies were not therefore carried out since

<table>
<thead>
<tr>
<th>Compound</th>
<th>$T_c$ (°C)</th>
<th>$\Delta v^\infty$ (Hz)</th>
<th>$\Delta G^*$ (Kcal mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.10-a</td>
<td>138 ±5</td>
<td>3.5 ± 0.5</td>
<td>22.7 ± 0.4</td>
</tr>
</tbody>
</table>

TABLE 10

Pseudorotational Energy Barrier in the Presence of Shift Reagent
the increase in $\Delta G^*$ in the presence of shift reagent was found to be too large for accurate data to be obtained on the relative apicophilicities of MeO, EtO, i-PrO, and t-BuO.

(e) Benzil Adduct of Ethyl Pinacol Phosphite.

The accidental chemical shift degeneracy observed in the $^1$H n.m.r. of the adducts (5.10) may be caused by a similarity in the shielding effects of the alkoxy substituent and the equatorial biacetyl oxygen group. An attempt was made to remove this effect by replacing the methyl groups of the dioxaphospholen ring by phenyl groups. The adduct (5.22) from ethyl pinacol phosphite and benzil was therefore prepared. However, the $^1$H n.m.r. showed only one pinacol methyl resonance in aromatic solvents.

![Chemical Structure](5.22)

(f) Carbon-13 Magnetic Resonance.

The $^1$H n.m.r. of the methoxy adduct (5.10-a) in o-dichlorobenzene exhibited only a single resonance for the pinacol methyl groups. However, the $^1$H decoupled Fourier Transform $^{13}$C n.m.r. spectrum at ambient temperature exhibited a pair of doublets, each doublet being due to long range $^{31}$P-$^{13}$C spin-spin coupling. The spectral details are given in Table 11. The resonances due to C-7 and C-8 are obscured by those of the solvent. In the absence of $^{31}$P decoupling it was not possible to distinguish between $\Delta \nu$ and $J_{PC}$ for the pinacol methyl carbons C1-C4.
TABLE II

$^1$H Decoupled Carbon-13 Spectral Data for the Methyl Pinacol
Phosphite-Biacetyl Adduct (5.10-a) in o-Dichlorobenzene.

![Diagram](5.10-a)

<table>
<thead>
<tr>
<th>$\delta$ (ppm)</th>
<th>$J_{PC}$ (Hz)</th>
<th>Integration</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.79</td>
<td>11.7</td>
<td>51</td>
<td>C-9 and C-10</td>
</tr>
<tr>
<td>23.46</td>
<td></td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>23.79</td>
<td></td>
<td>27</td>
<td>Cl - C4</td>
</tr>
<tr>
<td>23.92</td>
<td></td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>24.24</td>
<td></td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>54.47</td>
<td>8.8</td>
<td>27</td>
<td>C-11</td>
</tr>
<tr>
<td>78.77</td>
<td>3.0</td>
<td>57</td>
<td>C-5 and C-6</td>
</tr>
</tbody>
</table>

The assignments were made by comparison of the shifts with those of similar functional groups.$^{133}$

Variable temperature $^{13}$C n.m.r. may enable the $\Delta G^*$ values to be determined for processes which cannot be studied by $^1$H n.m.r. due to accidental chemical shift degeneracy. However, the time required to obtain a $^{13}$C n.m.r. spectrum is considerably longer than that for a $^1$H n.m.r. spectrum. Thus at high temperatures this may lead to extensive decomposition. The absorptions due to decomposition products may then interfere with the observance of coalescence.
There are few examples of dynamic $^{13}$C n.m.r. spectroscopy. Nakanishi and Yamamoto\textsuperscript{134} have studied the Cope rearrangement of bullvalene by F.T.-$^{13}$C n.m.r. A complete line shape analysis of the $^{13}$C n.m.r. spectra of bullvalene at 35 different temperatures enabled the activation parameters $\Delta G^*$ and $\Delta S^*$ to be determined. The results obtained were larger than those previously reported using $^1$H n.m.r. and $^1$H spin echo methods.

5.2 Benzylideneacetylacetone Adducts.

Ramirez\textsuperscript{135} has shown that benzylideneacetylacetone reacts with acyclic phosphines, phosphinites, phosphonites, and phosphites to form 1:1 adducts. Those from phosphines were shown by $^{31}$P n.m.r. to have the structure of open dipolar ions with tervalent phosphorus. The other 1:1 adducts had the pentacovalent structure.

Ramirez\textsuperscript{136}, and Gorenstein and Westheimer\textsuperscript{110}, have studied the variable temperature $^1$H n.m.r. spectra of the benzylideneacetylacetone adducts of trimethylphosphite (5.23), dimethylphenylphosphite (5.24) and dimethyl phenylphosphonite (5.25). The results were interpreted in terms of ring strain and the apical preference of oxygen over carbon in a TBP\textsuperscript{110}. Rupture of the ring P-O bond in (5.25) occurred at temperatures above 70°, and at 125° the structure was that of an open dipolar ion\textsuperscript{136}.

For the adducts (5.23) and (5.24), Gorenstein and Westheimer\textsuperscript{110}
noted three different mechanisms for rearrangement, (i) normal pseudo-rotation processes, (ii) ring opening, and (iii) reversible loss of benzylideneacetylacetone.

The free energy of activation for the latter was found to be large (30-31 Kcal mol$^{-1}$) and will therefore be slow on the n.m.r. time scale. The ring opening process was found to have an energy barrier of $\Delta G^* = 20-21$ Kcal mol$^{-1}$, as observed by collapse of the acetyl and vinyl methyl groups, which are equivalent in the dipolar ion (5.26). The barrier to the high energy pseudorotation of (5.24) via the TBP (5.27) is 22 Kcal mol$^{-1}$ as observed by the collapse of the two methoxy signals.

Although both processes have similar activation energies they are different pathways and have quite different consequences for the n.m.r. spectra and are thus distinct.

The incorporation of a small ring into (5.23) or (5.24) should lead to a more stable phosphorane. Bernard and Burgada$^{137}$ have synthesised the adducts (5.30) and (5.31) by reaction of benzylideneacetylacetone with
the cyclic phosphoramidite (5.28) and phosphite (5.29) respectively. Fractional recrystallisation from ether gave only the trans isomers shown.

The \( ^1 \text{H} \) n.m.r. spectra exhibited four singlets for the pinacol methyl groups since they cannot be equilibrated by pseudorotations at ambient temperatures.

The stereochemistry of the phenyl group was inferred from the large upfield shifts of the trans pinacol methyl resonances, caused by the shielding effect of the phenyl group. The assignments of the pinacol methyl resonances are shown in Table 12. These were obtained by comparison of the shifts with those of (5.32).

\[ \text{Me(a.c.)} = 1.17 \delta \]
\[ \text{Me(a.t.)} = 0.80 \delta \]
Bernard and Burgada also studied the variable temperature $^1$H n.m.r. spectra of (5.30) and (5.31). At 50° for (5.31) and 120° for (5.30) the four singlets of the pinacol methyl groups coalesced and sharpened to two singlets at 120° and 180° respectively. Heating the solutions of (5.31) and (5.30) also led to the formation of an equilibrium mixture of trans and cis isomers. The trans:cis ratios at 20° were 85:15 and 50:50 respectively. Equilibration between the trans and cis isomers was slow on the n.m.r. time scale even at high temperatures. The free energies of activation for the coalescence processes were not reported.

It was therefore decided to use this system in order to gain more data on the relative apicophilicities of groups in pentacoordinate phosphoranes.

A series of phosphoranes was prepared by the reaction of equimolar amounts of the 1-substituted pinacol phosphites with benzylideneacetylacetone in benzene at 40-50° for ca. 16 h. The adducts were usually obtained as viscous oils which could be crystallised from ether. In all cases fractional recrystallisation gave predominantly the trans isomers. Some of the spectral details are given in Table 13.
### TABLE 13

**Spectroscopic Data for the trans-Benzylideneacetylacetone Adducts.**

<table>
<thead>
<tr>
<th>Compound</th>
<th>R-Group</th>
<th>$\delta$ (CH$_2$Cl$_2$) (ppm)</th>
<th>$\tau$ (C$_6$H$_5$Cl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Me (a.c)</td>
<td>Me (e.c)</td>
</tr>
<tr>
<td>(5.33-a)</td>
<td>MeO</td>
<td>+13.5$^a$</td>
<td>8.87</td>
</tr>
<tr>
<td>(5.33-b)</td>
<td>t-BuO</td>
<td>+14.5</td>
<td>8.75</td>
</tr>
<tr>
<td>(5.33-c)</td>
<td>PhO$^c$</td>
<td>+15.5</td>
<td>8.62</td>
</tr>
<tr>
<td>(5.33-d)</td>
<td>EtS$^c$</td>
<td>-</td>
<td>8.67</td>
</tr>
</tbody>
</table>

a. Lit. value +13 (C$_6$H$_5$Cl)$^{137}$. b. Lit. value +17 (C$_6$H$_5$Cl)$^{137}$.

c. $\tau$ (CDCl$_3$). d. $\tau$ (C$_6$H$_4$Cl$_2$).

The $^{31}$P chemical shift for the ethylthio adduct (5.33-d) could not be obtained, although the $^1$H n.m.r. is characteristic of the trans benzylideneacetylacetone adducts. Apart from the alkylthio adduct all were more hydrolytically stable than the corresponding biacetyl adducts and were readily crystallised. The ethylthio adduct however, could not be obtained pure.

**Dynamic Nuclear Magnetic Resonance Studies.**

The pseudorotation pathway responsible for the coalescence observed by Bernard and Burgada is shown in Scheme 29. The high energy TBP (5.35) has the oxaphospholen ring diequatorial with the R group apical.
The free energy of activation for this process is therefore,

$$
\Delta G^* = \Delta G = S_{90-120}^{\text{oxaphospholen}} + (A_R - A_0)
$$

and using the arguments outlined previously (Section 5.1),

$$
\Delta(\Delta G^*) \leq (A_R - A'_R)
$$

when comparing $\Delta G^*$s for different $R$ substituents.

The interconversion of cis and trans isomers must proceed via the high energy TBP (5.37), according to Scheme 30. The free energy of activation for this process is,

$$
\Delta G^* (\text{trans-cis}) > S_{90-120}^{\text{dioxaphospholan}} + (A_R - A_0).
$$
The pseudorotation pathway outlined in Scheme 29 gives rise to two coalescence processes, (i) coalescence of the Me (a.c) and Me (e.t) resonances, and (ii) coalescence of the Me (e.c) and Me (a.t) resonances. Each of these two pairs of singlets have different $\Delta v^\omega$'s and consequently have different coalescence temperatures. The results of the d.n.m.r. experiments are shown in Table 14-a and 14-b. The activation energies $\Delta G^*$ were calculated from $\Delta v^\omega$ and $T_c$ as outlined previously (Section 5.1).

The activation energies in Table 14-b are lower than those in Table 14-a. This is probably due to the difficulty in determining the coalescence temperature when the value of $\Delta v^\omega$ is very large. However, the relative orders are the same, and therefore the order of apicophilicity of the R groups is:

$$A_{\text{PhO}} < A_{\text{t-BuO}} < A_{\text{MeO}} < A_{\text{EtS}} >> A_{\text{Me}_2N}.$$
TABLE 14

Peak Separation, Coalescence Temperature, and Activation Energies
for Pseudorotation in the Benzylideneacetylacetone Adducts in
Chlorobenzene.

(14-a) Coalescence of Me(a.c) and Me(e.t) Resonances.

<table>
<thead>
<tr>
<th>Compound</th>
<th>R-Group</th>
<th>$\Delta v^a$ (Hz)</th>
<th>$T_c$ (°C)</th>
<th>$\Delta G^*$(Kcal mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5.33-a)</td>
<td>MeO</td>
<td>14.5 ±0.25</td>
<td>66 ±5</td>
<td>17.6 ± 0.3</td>
</tr>
<tr>
<td>(5.33-b)</td>
<td>t-BuO</td>
<td>19.0 ±0.25</td>
<td>57 ±5</td>
<td>16.9 ± 0.3</td>
</tr>
<tr>
<td>(5.33-c)</td>
<td>PhO</td>
<td>15.5 ±0.25</td>
<td>52 ±5</td>
<td>16.8 ± 0.3</td>
</tr>
<tr>
<td>(5.33-d)</td>
<td>EtS$^c$</td>
<td>35.0 ±0.25</td>
<td>85 ±5</td>
<td>18.0 ± 0.3</td>
</tr>
<tr>
<td>(5.33-e)</td>
<td>Me$_2$N$^b$</td>
<td>17.5 ±0.25</td>
<td>&gt; 150</td>
<td>&gt; 22.0</td>
</tr>
</tbody>
</table>

(14-b) Coalescence of Me(e.c) and Me(a.t) Resonances.

<table>
<thead>
<tr>
<th>Compound</th>
<th>R-Group</th>
<th>$\Delta v^a$ (Hz)</th>
<th>$T_c$ (°C)</th>
<th>$\Delta G^*$(Kcal mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5.33-a)</td>
<td>MeO</td>
<td>100.5 ±0.25</td>
<td>89 ±10</td>
<td>17.4 ± 0.5</td>
</tr>
<tr>
<td>(5.33-b)</td>
<td>t-BuO</td>
<td>114.5 ±0.25</td>
<td>75 ±10</td>
<td>16.7 ± 0.5</td>
</tr>
<tr>
<td>(5.33-c)</td>
<td>PhO</td>
<td>112.0 ±0.25</td>
<td>67 ±10</td>
<td>16.3 ± 0.5</td>
</tr>
<tr>
<td>(5.33-d)</td>
<td>EtS$^c$</td>
<td>112.0 ±0.25</td>
<td>100 ±10</td>
<td>17.9 ± 0.5</td>
</tr>
<tr>
<td>(5.33-e)</td>
<td>Me$_2$N$^b$</td>
<td>98.5 ±0.25</td>
<td>&gt; 150$^d$</td>
<td>&gt; 20.5</td>
</tr>
</tbody>
</table>

a. At 100 MHz. b. o-dichlorobenzene. c. Decomposition.
d. Limit of temperature range available.

The relative apicophilicities of tertiary butoxy and methoxy
are the opposite to those expected on steric arguments (Chapter 1) and
to the results from the biacetyl system (Section 5.1). This is probably
caused by the presence of the α-phenyl group in the adducts (5.33) and will be discussed in detail later (Chapter 6).

Except for the ethylthio adduct (5.33-d) which was decomposing at the coalescence temperature, the observed coalescences were reversible. It is unlikely that irregular processes are responsible for the observed coalescences. This can be inferred from the following:

(a) The dimethylamino adduct (5.33-e) did not coalesce up to 150°. A nitrogen substituent has a greater destabilising effect than oxygen (Section 4.1) on the TBP with respect to the formation of a dipolar ion. Thus, if this adduct is not undergoing an irregular process it is probable that all the adducts rearrange via a regular process.

(b) The irregular process observed by Westheimer and Gorenstein (5.26) had an activation energy of 20-21 Kcal mol⁻¹. In a spirophosphorane this value should be larger due to the increase in ring strain which would occur on formation of a tetrahedral phosphorus species. From Westheimer's work on relative rates of hydrolysis of methyl ethylene phosphate this increase may be as much as 8.0 Kcal mol⁻¹.

(c) No irregular process via a dipolar ion can give rise to the observed equilibration of methyl groups, i.e. A=D and B=C, in the adducts (5.33). If the assignments of the pinacol methyls are correct then the observed coalescences can only be explained by a regular pseudorotation process.

The decomposition of the ethylthio adduct (5.33-d) probably proceeds via the high energy TBP (5.35). In this structure the ethylthio group is in the apical position. The high energy of the TBP and the fact that ethylthio is a good leaving group (stable anion), probably provides a good 'driving force' for decomposition, Scheme 31. Thus if the high energy TBP is a common intermediate for both pseudorotation and decomposition, it would explain why the rate of decomposition is similar to the rate of pseudorotation.
During the variable temperature n.m.r. experiments on the trans adducts, slow equilibration to the cis adduct was also observed. The equilibrium ratios of cis and trans isomers are given in Table 15. The activation energy for interconversion of cis and trans isomers could be determined by normal kinetic methods. However, it is difficult to obtain accurate concentrations of the isomers due to overlap of peaks in the n.m.r. spectra. An attempt was made to determine the $\Delta G^*$s for

<table>
<thead>
<tr>
<th>Compound</th>
<th>R-Group</th>
<th>Trans (%)</th>
<th>Cis (%)</th>
<th>Decomposition Temp. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5.33-a)</td>
<td>MeO</td>
<td>80$^h$</td>
<td>20$^{a,e}$</td>
<td>171$^g$</td>
</tr>
<tr>
<td>(5.33-b)</td>
<td>t-BuO</td>
<td>77</td>
<td>23$^{a,e}$</td>
<td>&gt; 98$^e$</td>
</tr>
<tr>
<td>(5.33-c)</td>
<td>PhO</td>
<td>&gt; 95</td>
<td>&lt; 5$^{a,f}$</td>
<td>151$^f$</td>
</tr>
<tr>
<td>(5.33-d)</td>
<td>EtS</td>
<td>65</td>
<td>35$^{b,e}$</td>
<td>100$^e$</td>
</tr>
<tr>
<td>(5.33-e)</td>
<td>Me$_2$N</td>
<td>65$^i$</td>
<td>35$^{c,g}$</td>
<td>159$^g$</td>
</tr>
</tbody>
</table>

a. 25°. b. 41°. c. 105°. e. chlorobenzene. f. o-dichlorobenzene. g. 1-bromonaphthalene. h. 85:15 (20°)$^{137}$. i. 65:35 (160°)$^{137}$.

Cis-trans isomerisation by observing the coalescence of the resonances due to cis and trans isomers. However, in all cases decomposition
occurred before any coalescences were observed. The temperatures of decomposition are given in Table 15. The tertiary butoxy adduct was not heated above $98^\circ$ because of the danger of explosive decomposition to give iso-butene.\footnote{114}

Bernard and Burgada\footnote{137} observed the coalescences for the pinacol methyl resonances of the cis isomers of (5.33-a) and (5.33-e) at $10^\circ$ and $80^\circ$ respectively. No similar studies on the cis isomers of (5.33-a-e) were carried out because the signals for the cis isomers tended to be obscured by those of the trans isomers. In the dimethylamino adduct (5.33-e) the resonances for the cis isomer were quite distinct but did not coalesce up to $100^\circ$ in chlorobenzene, o-dichlorobenzene or 1-bromonaphthalene. The lower coalescence temperatures observed by Bernard and Burgada may be due to the use of a 60 MHz n.m.r. spectrometer, lowering $\Delta v^\circ$ and $T_c$. However, the spectrometer frequency was not reported.

5.3 Methylenedehydrobenzoin Adducts.

The unexpected relative apicophilicities of methoxy and tertiary-butoxy in the benzylideneacetylacetone adducts may be caused by the presence of the $\alpha$-phenyl group on the 1,2-oxaphospholen ring. It was therefore of interest to obtain data from another 1,2-oxaphospholen system in which hydrogens were the only $\alpha$-substituents. The only suitable $\alpha,\beta$-unsaturated carbonyl compounds, whose reactions with phosphorus(III) compounds have been studied are acrolein\footnote{138}, methylvinylketone\footnote{110}, methyleneacetylacetone\footnote{110}, and methylenedehydrobenzoin\footnote{139,140}. The latter compound was chosen for its ease of synthesis.

Trippett and Stewart\footnote{139} have used methylenedehydrobenzoin for the preparation of the adducts (5.38-a and b) in order to study the
positional preference of the tertiary-butyl group in a TBP. However, there are no reports in the literature on the reaction of methylenedioxo-benzoin with acyclic or cyclic phosphites.

The reaction of methylenedioxo-benzoin with 1-substituted pinacol phosphites in benzene at 50-60° for 72 h gave the required adducts (5.39) as viscous oils which were extremely difficult to crystallise. All the adducts gave positive $^{31}$P n.m.r. shifts characteristic of a pentacoordinate structure. Some of the spectroscopic data for these adducts are given in Table 16.

At low temperatures when pseudorotation is slow on the $^1$H n.m.r. time scale all four pinacol methyls should be different. However, because there is no α-phenyl group, as in the benzylideneacetylacetone adducts, the range of shifts for the pinacol methyls is small, and consequently overlap of two resonances often occurs.

Attempts to prepare the ethylthio and phenylthio adducts were unsuccessful, presumably because of the extreme conditions required to effect adduct formation. Longer reaction times at lower temperatures may be more successful.
### TABLE 16

**Spectroscopic Data for Methylenedeeoxybenzoin Adducts**

<table>
<thead>
<tr>
<th>Compound</th>
<th>R-Group</th>
<th>$\text{P}^{31}(\text{CH}_2\text{Cl}_2)$</th>
<th>$\tau(\text{Pinacol Methyls})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5.39-a)</td>
<td>MeO</td>
<td>+ 13.5</td>
<td>8.68(6H) 8.76(3H) 8.79(3H)</td>
</tr>
<tr>
<td>(5.39-b)</td>
<td>t-BuO</td>
<td>+ 16.3</td>
<td>7.71(3H) 7.77(3H) 7.90(6H)</td>
</tr>
<tr>
<td>(5.39-c)</td>
<td>PhO</td>
<td>+ 24.0</td>
<td>8.54(3H) 8.63(6H) 8.74(3H)</td>
</tr>
<tr>
<td>(5.39-d)</td>
<td>Me$_2$N</td>
<td>+ 19.5</td>
<td>8.87(3H) 8.89(3H) 8.92(6H)</td>
</tr>
</tbody>
</table>

*a. dichloromethane ($1^\circ$). b. dichloromethane ($-21^\circ$)*

*c. chlorobenzene ($-20^\circ$). d. chlorobenzene ($2^\circ$)*

*e. chlorobenzene (ambient temperature) f. benzene.*

### Dynamic Nuclear Magnetic Resonance Studies.

The pseudorotation pathways are analogous to those of the trans-benzylideneacetylacetone adducts, and are shown below in Schemes 32 and 33. The pseudorotations outlined in Scheme 32 cause a collapse of the four peaks to two, when fast on the n.m.r. time scale. At higher temperatures the pseudorotations in Scheme 33 will cause a further collapse of the two signals to a singlet, all four methyls then being equivalent on the n.m.r. time scale.
The coalescence temperatures, peak separations, and calculated activation energies for the pseudorotations in Scheme 32 are listed in Table 17.

<table>
<thead>
<tr>
<th>Compound</th>
<th>R-Group</th>
<th>$\Delta v_{\text{eq1}}$ (Hz)</th>
<th>$\Delta v_{\text{eq2}}$ (Hz)</th>
<th>$T_c$ (°C)</th>
<th>$\Delta G^*$ (Kcal mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5.39-a)</td>
<td>MeO$^a$</td>
<td>8.0</td>
<td>11.0</td>
<td>23 ± 5</td>
<td>15.5 ± 0.6</td>
</tr>
<tr>
<td>(5.39-b)</td>
<td>t-BuO$^b$</td>
<td>13.0</td>
<td>19.5</td>
<td>21 ± 5</td>
<td>15.1 ± 0.6</td>
</tr>
<tr>
<td>(5.39-c)</td>
<td>PhO$^b$</td>
<td>13.0</td>
<td>15.0</td>
<td>0 ± 5</td>
<td>14.1 ± 0.6</td>
</tr>
<tr>
<td>(5.39-d)</td>
<td>Me$_2$N$^b$</td>
<td>3</td>
<td>6</td>
<td>80 ±10</td>
<td>19.0 ± 0.8</td>
</tr>
</tbody>
</table>

a. dichloromethane. b. chlorobenzene. c. 100 MHz.
The increased errors are largely due to the two different values of $\Delta v^\omega$, one for each pair of singlets. The small difference in chemical shift between the centres of each pair made it impossible to observe the individual coalescences for each pair, with a consequent loss of accuracy. Thus coalescence of one pair is masked by the other. The value of $\Delta v^\omega$ used for the calculations of $\Delta G^*$ was determined from the equation

$$\Delta v^\omega = \frac{\Delta v^\omega_1 + \Delta v^\omega_2}{2} \pm \frac{\Delta v^\omega_2 - \Delta v^\omega_1}{2} \text{ Hz}$$

The absolute assignments of the pinacol methyl resonances could not be made in this system. The assignment of coalescing pairs was made using the peak separation between the two singlets above the coalescence
temperature. In the case of the dimethylamino adduct the assignments may be incorrect, because the four singlets collapsed to one peak. The chemical shift difference between the coalesced peaks may be very small or there may be a small temperature dependence of the shifts. However, other assignments for this adduct would give the same $\Delta G^*$s, within experimental error.

The results indicate that, within experimental error, the apicophilicities of methoxy and tertiary-butoxy are the same. This result is intermediate between those obtained for the biacetyl system and for the benzylideneacetylacetone system.

Irregular processes can be ruled out using similar arguments to those outlined for the benzylideneacetylacetone adducts. In addition the irregular process involving opening of the oxaphospholen ring can also be dismissed by observing the $^1$H n.m.r. of the two $\alpha$-hydrogens. In all cases they remained nonequivalent exhibiting the characteristic A$\beta$X pattern in the $^1$H n.m.r. spectrum. They can only become equivalent if the higher energy pseudorotation (Scheme 33) is fast or if opening of the oxaphospholen ring is fast.

The coalescence for the higher energy pseudorotation (Scheme 33) was observed for the methoxy adduct (5.39-a). The results are given below in Table 18. No decomposition was observed.

| TABLE 18 |
| Complete Coalescence of all Pinacol Methyls of the Methoxy Adduct (5.39-a) in Bromonaphthalene. |
| $R$ | $\Delta v_c$ (Hz) | $T_c$ (°C) | $\Delta G^*$ (Kcal mol$^{-1}$) |
| MeO | $3 \pm 0.25$ | $175 \pm 5$ | $24.9 \pm 0.4$ |
6. **APICOPHILICITY.**

The scale below (6.1) summarises the apicophilicity data obtained for the three systems described in Chapter 5. The methoxy group has arbitrarily been taken as the reference point for each system.

**APICOPHILICITY SCALE**

<table>
<thead>
<tr>
<th></th>
<th>PhO</th>
<th>t-BuO</th>
<th>NMe₂</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PhO</td>
<td>t-BuO</td>
<td>NMe₂</td>
</tr>
<tr>
<td>α. biacetyl system.</td>
<td>b. benzylideneacetylacetone system.</td>
<td>c. methylenedideoxybenzoin system.</td>
<td>d. minimum value.</td>
</tr>
</tbody>
</table>

\[
\Delta(\Delta G^m) \text{ Kcal mol}^{-1}
\]

(6.1)

6.1 **Steric Effects.**

The electronegativity difference between methoxy and tertiary-butoxy would be expected to be small. Huheey's calculations show t-butoxy to be more electronegative than methoxy by 0.76 Mulliken units. However, this large difference is probably a direct result of the assumption of equalisation of electronegativity. It does not take into account the 'dilution' of polar effects of substituents not directly bonded to the terminal atom. Thus the theory yields identical electronegativities for the isomeric
groups, (6.2) and (6.3)$^6$.

\[
\begin{align*}
FCH_2CH_2CH_2 & - \quad CH_3CH_2CHF & \quad (6.2) \quad (6.3)
\end{align*}
\]

If then the electronic contributions to the apicophilicity of methoxy and tertiary-butoxy are the same then their differences in apicophilicity should be primarily due to steric effects. The results from the biacetyl system show that \(t\)-BuO is less apicophilic than MeO- by 1.8 Kcal mol$^{-1}$ which is as expected if the apical positions are the most sterically hindered$^8$. However, in the benzylideneacetylacetone system this steric order is reversed and \(t\)-BuO is more apicophilic than MeO by 0.7 Kcal mol$^{-1}$. A similar preference of bulky alkoxy groups for the apical positions has been found in the phosphorane (6.4)$^{114}$ and the oxyphosphoranyl radical (6.5)$^{148}$. The effect may be due to the increased apical P-O bond lengths in phosphoranes containing an equatorial carbon atom$^{12-14}$. However, substituents on the \(\alpha\)-carbon atom may also have a significant effect on the relative steric requirements of apical and equatorial positions.

In the phosphorane (6.4) a Newman projection (6.6) along the C-P bond for the ground state TBP (6.4), and the high energy TBP (6.7), shows that the \(\alpha\)-CF$_3$ groups interact more strongly with equatorial substituents than apical substituents. This effect however does not directly explain
the preference of bulky alkoxy groups for the apical position in the trans-benzylideneacetylacetone adducts, since both in the ground state TBP (6.8) and the high energy TBP (6.9) the phenyl group is directed away from the alkoxy substituent. The effect of the phenyl group may however be transmitted to the alkoxy group in the ground state TBP, via the pinacol ring. This is best seen by referring to the Newman projection (6.10) along the apical O-P bond of the pinacol ring. The eclipsing interactions between the four ring methyl groups will cause the five membered ring to adopt a puckered conformation, placing the methyls in a
staggered position. There are two possible directions in which the apical methyl groups can be displaced, either towards the alkoxy group or the equatorial carbon atom. The presence of an α-phenyl group prevents the latter, and so the apical methyl groups will be displaced towards the alkoxy group increasing the steric hindrance in the equatorial position.

Replacement of the phenyl group by the smaller hydrogen atom should relieve this constraint on the puckering of the pinacol ring, giving the ground state TBP (6.11). The results from the methylenedeoxybenzoin system would seem to corroborate this hypothesis. They indicate that within experimental error the apicophilicities of methoxy and t-butoxy are the same. The change in apicophilicity of t-butoxy was therefore as expected, although there is still a significant difference in steric factors when compared to the biacetyl adduct. This residual effect may therefore be due to the two other factors previously mentioned.

The results have only been interpreted in terms of the ground state and high energy TBP structures. It is conceivable that energy differences may be a result of different steric interactions in the transition state for pseudorotation. However if ΔG* = ΔG then the structure of the transition state should be similar to the high energy TBP. Thus the arguments proposed should still be valid for the transition state. The same arguments will apply even if the high energy TBP is distorted, provided the distortion is not too large.

The relative apicophilicities of the alkoxy groups are therefore the result of a fine balance between two factors, (i) ratio of apical to equatorial bond lengths, and (ii) the size and stereochemistry of substituents on atoms α to the phosphorus. The small differences in apicophilicity between alkoxy groups may be due to the fact that the bulk of the group is on an atom β to the phosphorus. Steric effects should
therefore be larger for alkyl groups, Me, Et, i-Pr, and t-Bu, which are directly bonded to phosphorus. However, the results of Oram\textsuperscript{11} from (6.12) and Whittle\textsuperscript{21} from (6.13) indicate that the difference in:

\[
|A_{\text{Me}} - A_{\text{i-Pr}}| = 0.9 \text{ Kcal mol}^{-1}
\]

\[
|A_{\text{Me}} - A_{\text{t-Bu}}| = 1.1 \text{ Kcal mol}^{-1}
\]

apicophilicity between alkyl groups is also small. This is also unexpected on electronegativity considerations. The \( \text{t-Bu} \) group is only 0.05 Mulliken units more electronegative than methyl.

Larger steric effects in alkyl groups have however been observed by Westheimer and Gorenstein\textsuperscript{110}. In the phosphoranes (6.14) and (6.15)

\[
\Delta G^* \gg \Delta G = (A_{\text{CMe}_2} - A_{\text{OCMe}}) = 14.5 \pm 0.5 \text{ Kcal mol}^{-1}
\]

\[
\Delta G^* \gg \Delta G = (A_{\text{CMe}_2} - A_{\text{OCMe}}) = 9.6 \pm 0.2 \text{ Kcal mol}^{-1}
\]
the activation energies for the high energy TBPs (6.16) and (6.17), Scheme 34, differ by 4.9 Kcal mol\(^{-1}\). This difference is largely due to the eclipsing interactions in the high energy TBP, since the ring alkyl groups are not free to rotate into a staggered conformation.

The larger steric effect of alkoxy groups compared to alkyl groups may possibly be due to the larger 'volume' of rotation of alkoxy groups.

6.2 Electronic Effects.

The electronegativities of phenoxy, methoxy, ethylthio, and dimethylamino are shown on the scale (1.10) and in Table 19\(^6\).

<table>
<thead>
<tr>
<th></th>
<th>MeO</th>
<th>PhO</th>
<th>EtS</th>
<th>Me2N</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8.59</td>
<td>8.50</td>
<td>7.74</td>
<td>7.75</td>
<td>Mulliken units.</td>
</tr>
</tbody>
</table>

The observed apicophilicities of phenoxy and ethylthio are greater than expected on electronegativity considerations. The deviations may be a result of a combination of other factors mentioned previously (Chapter 1), i.e. the following properties of the ligand;

(i) size
(ii) anion stability,
(iii) \(\pi\)-donor ability
and (iv) \(\pi\)-acceptor ability.

(i) Size. Steric effects have already been discussed and are probably small in comparison to electronic effects.
(ii) Anion Stability. Electronegativities indicate that phenoxy and methoxy should have the same apicophilicities. Similarly ethylthio should be the same as dimethylamino. However, the stabilities of the anions of these groups differ considerably. The relative stabilities are, \( \text{PhO}^- > \text{MeO}^- \) and \( \text{EtS}^- > \text{Me}_2\text{N}^- \). Thus if this property can be applied to apicophilicities in pentacoordinate phosphoranes it would explain the observed deviations.

(iii) \( \pi \)-Donor Ability. Hoffman\(^1\) (Chapter 1) has shown that \( \pi \) donors prefer to occupy the equatorial position, and that there is an energy barrier to rotation about the equatorial bond. A \( \pi \)-donor preferring to align its \( p_\pi \) orbital in the equatorial plane. The \( \pi \)-donor ability of a substituent can be estimated from the energy barrier to rotation about the equatorial bond, since this should increase as \( \pi \)-donor ability increases. The experimentally observed energy barriers to rotation are in the order \( N > S > \text{O} \)\(^{141-143} \). Thus this also accounts for the increased apicophilicity of sulphur relative to nitrogen. The rotational energy barriers for alkoxy and aryloxy groups are small (\( < 8 \text{ Kcal mol}^{-1} \))\(^5 \) and are too small to be measured by n.m.r. techniques. The relative \( \pi \)-donor abilities of phenoxy and methoxy cannot therefore be determined in this way.

(iv) \( \pi \)-Acceptor Ability. \( \pi \)-Acceptors prefer to occupy the apical positions (Chapter 1). However, the methoxy and dimethylamino groups have no low lying vacant orbitals to act as \( \pi \) acceptors. The ethylthio group may be able to make use of the empty 3d orbitals on sulphur, and similarly the phenoxy group should have an empty low lying \( \pi^* \) molecular orbital available. Again this should increase the apicophilicity of S over
N and phenoxy over methoxy.

Thus these electronic effects in addition to group electronegativities would seem to account for the observed order of apicophilicities.

The apicophilicities of alkylthio or arylthio groups may therefore be expected in some cases to be even greater than their corresponding oxygen analogues, depending on the extent to which the other factors are involved. The only factors which will increase the apicophilicity of sulphur relative to oxygen are the \( \pi \)-acceptor ability of the sulphur 3d orbitals, and the increased stability of the thio anion over the oxy anion. Both electronegativity and \( \pi \)-donor ability would lead to sulphur being less apicophilic than oxygen. Trippett, Bone, and Whittle\(^{115} \) have shown that in the phosphorane (6.18) the phenylthio group is more apicophilic than phenoxy by 1.0 Kcal mol\(^{-1} \). DeBruin\(^{107} \) has also found that in the TBP intermediate (6.20) the apicophilicity of methylthio is greater than methoxy. The order of apicophilicity was found to be

\[ \text{NMe}_2<\text{OMe, OEt, O-i-Pr}<\text{SMe=Cl}. \]

This was determined by product analysis of the base hydrolysis of (6.19) according to the simplified Scheme 35. Pseudorotation of (6.20) to put methoxy or X apical is considered to be irreversible since the equatorial hydroxy group is rapidly deprotonated in the basic medium. The reverse pseudorotation would consequently be
of high energy due to the poorly apicophilic O\textsuperscript{-} substituent. The ratio of the two possible products therefore represents the stability of the TBP(s) (6.21) and (6.22), and the effect of leaving group ability is eliminated providing the pseudorotations are irreversible.

In other phosphoranes the apicophilicities of alkyl or arylthio groups are usually equal to or less than the corresponding oxygen analogues\textsuperscript{21,112-115}. Few direct comparisons are, however, available.

The observed order of apicophilicities on the scale (6.1) are in agreement with those of other workers\textsuperscript{21,111-115}. However, the magnitudes differ depending on the nature of the other groups attached to phosphorus. A summary of the apicophilicities of a range of groups is shown by the scale (6.23).

Because the apicophilicity of a group is known to vary with the other substituents on phosphorus it has become increasingly important to study a variety of systems in order to determine the factors
Apicophilicity Scale

- $\text{Me} > \text{i-Pr} > \text{C} = \text{C} > \text{Ph}$
- $\text{Me} > \text{i-Pr} > \text{t-Bu}$
- $\text{Ph}$
- $\text{MeC} = \text{C} > \text{Ph}$

(6.23)

Responsible for this variation.

Whittle has shown that the steric component of a group's apicophilicity is extremely sensitive to the size of the other substituents on phosphorus. Thus in (6.13) where a Me group remains equatorial then

\[ |A_{\text{t-Bu}} - A_{\text{Me}}| = 1.1 \text{ Kcal mol}^{-1} \]  

(6.13)

(6.24)

\[ |A_{\text{t-Bu}} - A_{\text{Me}}| = 3.3 \text{ Kcal mol}^{-1} \]  

(6.25)

(6.26)
(ΔG*<sub>But</sub> - ΔG*<sub>Me</sub>) for (6.13) → (6.24) is only 1.1 Kcal mol<sup>-1</sup>, whereas with the larger t-Bu group the Δ(ΔG*) increases to 3.3 Kcal mol<sup>-1</sup>.

Some of the electronic properties of the substituents on phosphorus which affect the apicophilicity of an alkyl or aryl group can be inferred from the work of Robert<sup>144</sup>, Schmutzler<sup>145</sup>, and Goodrich<sup>146</sup>. For the phosphoranes RPF<sub>3</sub>X (6.27) the highest energy TBP (6.28) is shown in Scheme 36. The energy of this TBP represents the difference in apicophilicities of the R group (methyl or phenyl) and fluorine, and would be expected to be independent of the substituent X. However, ΔG* for equilibration of the fluorines increases in the order:

\[
X = \text{OCH}_2\text{CMe}_3^{114} < \text{H}^{146} < \text{Me}_2\text{N}, \text{SR}^{145}.
\]

Clearly more work is required in this area, especially on the theoretical aspect, before any definite conclusions can be drawn. In addition the possibility of an irregular process in these fluorophosphoranes must be considered.
7. **RING STRAIN.**

The energy required to move various five-membered rings from the preferred apical-equatorial (ae) to the diequatorial (ee) positions varies considerably depending on the nature of the heteroatoms within the ring. When a ring moves from an ae to an ee position (e.g. Scheme 33), of necessity some other group moves from an e to an a position. In the systems discussed in Chapter 5, this is the group R which was varied to obtain apicophilicity data. Even if one allows for the difference in apicophilicity between the R group and the a ring atom, there is still no single value for the increase in strain in all five-membered rings.

It was therefore of interest to obtain data on the energy required to place the five-membered phospholan and phospholen rings diequatorial for comparison with those rings containing endocyclic heteroatoms bonded to phosphorus. In addition the six-membered phosphorinan ring was studied.

7.1 **Phospholan Ring Strain.**

(a) **The Hexafluoroacetone Adduct of 1-Phenylphospholan.**

Hexafluoroacetone (HFA) forms 2:1 adducts with both acyclic and cyclic phosphines. The HFA adduct (7.1) of 1-phenylphospholan was prepared according to the method outlined in Scheme 37. The $^{19}$F and
The pseudorotation pathways available to the adduct (7.1) are shown in Scheme 38 (R = Ph; A-D = CF₃). The pseudorotation (7.2) ⇌ (7.3) is between topomeric TBPs and will therefore have a very low activation energy. The activation energy for the pseudorotation (7.3) ⇌ (7.4) will be representative of the energy difference ΔG between (7.3) and (7.4), and is given by equation (7.5).

\[ \Delta G^\ast > \Delta G = S_{90-120} ( \text{phospholan} ) + (A_{\text{Ph}} - A_{\text{CH}_2}) \] (7.5)

The \(^{19}\text{F}\) n.m.r. spectrum of (7.1) exhibited a singlet which remained unchanged down to -80°. This is consistent with both pseudorotations (7.2) ⇌ (7.3) ⇌ (7.4) being fast (on the n.m.r. time scale) even at -80°. Assuming \(^{38}\) Δν = 100Hz (between the AB pair and the CD pair when (7.3) ⇌ (7.4) is slow on the n.m.r. time scale), then \(\Delta G^\ast < 9.1 \text{ Kcal mol}^{-1}\). Further cooling below -80° was beyond the range of the instrument.
(b) Pinacol Adduct of 1-Phenylphospholan.

Spirophosphoranes containing the perfluoropinacol ring are known to have the effect of reducing the ring strain of the other ring in the molecule. It was therefore decided to make a study of the analogous adduct (7.5).

Denney has shown that acyclic and monocyclic phosphoranes containing two ethoxy groups can be prepared by the reaction of the corresponding phosphorus(III) compounds with diethyl peroxide. These phosphoranes often undergo exchange reactions with 1,2- and 1,3-glycols to give phosphoranes containing one or two rings.

However, the reaction of pinacol with monocyclic oxyphosphoranes containing two ethoxy groups have so far proved unsuccessful. Although Denney has shown that 1-phenylphospholan reacts with diethyl peroxide to form a pentacoordinate phosphorane the exchange reaction with diols was not investigated for this phosphorane.

The adduct (7.6) was prepared by the reaction of diethylperoxide with 1-phenylphospholan in dichloromethane at 0-5° for ca two weeks. The resulting solution when added to one equivalent of anhydrous pinacol gave a quantitative yield (by \( ^1H \) n.m.r.) of the required adduct (7.5) and two moles of ethanol, Scheme 39. It was later found that the

\[
\text{SCHEME 39}
\]

\[
\begin{align*}
\text{EtO}_2 & \xrightarrow{\text{CH}_2\text{Cl}_2, 0-5^\circ} \text{(EtO)}_2 \\
\text{(7.6)} & \xrightarrow{\text{Me}_2\text{COH}} \text{(7.5)} + 2 \text{EtOH}
\end{align*}
\]
preparation of (7.5) could be accomplished in 24h. by the reaction of
the phosphine with diethyl peroxide and pinacol in situ, at 25°. The
reaction in situ is preferred since any decomposition of (7.6) at higher
temperatures is minimised due to its almost instantaneous reaction with
pinacol. The adduct (7.5) was found to be hydrolytically stable and
also stable to sublimation, although after prolonged storage at ambient
temperatures slow decomposition occurred, according to Scheme 40, as shown
by ¹H n.m.r.

SCHEME 40

The pseudorotation pathways for (7.5) are outlined in Scheme 38.
The ¹H n.m.r. spectrum at 25° exhibited a singlet for the four pinacol
methyl groups. On cooling the singlet broadened, and below -96° split
into two. The ¹H n.m.r. data for (7.5) are given in Table 20.

TABLE 20
Data for the Pinacol Adduct of 1-Phenylphospholan (7.5).

<table>
<thead>
<tr>
<th>Tc(°C)</th>
<th>Δν= (Hz)</th>
<th>ΔG° (Kcal mol⁻¹)</th>
<th>³¹P</th>
</tr>
</thead>
<tbody>
<tr>
<td>-96 ± 5</td>
<td>18 ± 1.0</td>
<td>8.9 ± 0.3</td>
<td>+17.1</td>
</tr>
</tbody>
</table>

a. CFCl₃. b. CH₂Cl₂. c. At 100 MHz.

To obtain the ring strain in the phospholan, the difference in
apicophilicity between phenyl and ethyl is required, equation (7.5).
The results of Oram\textsuperscript{38,111} from the adducts (6.12) suggested that phenyl was less apicophilic than ethyl by ca. 4.5 Kcal mol\textsuperscript{-1}. This would make the strain in the phospholan ca. 4.4 Kcal mol\textsuperscript{-1}, which is very much smaller than that expected from the work of Westheimer\textsuperscript{152} and Aksnes\textsuperscript{153} on the relative rates of alkaline hydrolysis of 1-ethoxy-phospholan-1-oxide (7.7) and 1-ethoxy-3-phospholen 1-oxide (7.8), compared to their acyclic analogues. These results are shown in Table 21. If

<table>
<thead>
<tr>
<th>Relative Rates</th>
<th>(\Delta(\Delta G^*))</th>
</tr>
</thead>
<tbody>
<tr>
<td>(7.7) Et\textsubscript{2}PO\textsubscript{2}Et</td>
<td>4\textsuperscript{152}</td>
</tr>
<tr>
<td>(7.8) (CH\textsubscript{2}=CHCH\textsubscript{2}).EtPO\textsubscript{2}Et</td>
<td>60</td>
</tr>
</tbody>
</table>

the mechanism of hydrolysis of (7.7) and Et\textsubscript{2}PO\textsubscript{2}Et is as outlined in Scheme 41, then the relief of ring strain, \(S_{90-109.5}\) (phospholan), in going from the tetrahedral phosphorus in (7.7) to the TBP intermediate (7.9), should be about 0.3-0.9 Kcal mol\textsuperscript{-1} greater than the difference in apicophilicity between ethoxy and ethyl. The value of \(|A_{\text{OEt}}-A_{\text{Et}}|\) is
ca. 9 - 10 Kcal mol\(^{-1}\). It would therefore be expected that 
\(S_{90-120} (\text{phospholan}) \gg 9.3 \text{ Kcal mol}^{-1}\).

\[\text{SCHEME 41}\]

\[
\begin{align*}
\text{(7.7)} & \quad \text{EtO}^- \quad \text{EtO}^- \quad \text{EtO}^- \\
\text{(7.9)} & \quad \text{EtO}^- \\
\text{(7.10)} & \quad \text{EtO}^- \\
\text{(7.11)} & \quad \text{EtO}^- \\
\end{align*}
\]

\[\Delta (\Delta G^*) = \Delta G^*_{\text{acyclic}} - \Delta G^*_{\text{cyclic}} = S_{90-109.5} (\text{phospholan}) - |A_{\text{OEt}} - A_{\text{Et}}| = 0.3 - 0.9 \text{ Kcal mol}^{-1}\]

If (7.10) is the high energy TBP intermediate (i.e. if OEt is less apicophilic than OH) then \(\Delta (\Delta G^*)\) will be given by:

\[\Delta (\Delta G^*) = S_{90-109.5} (\text{phospholan}) - |A_{\text{OEt}} - A_{\text{Et}}| = 0.3 - 0.9 \text{ Kcal mol}^{-1}\]

This would require an even larger value for \(S_{90-109.5}\) (phospholan), and consequently a larger value for \(S_{90-120}\) (phospholan).

The large difference in apicophilicity between phenyl and ethyl obtained by Oram\(^{38,111}\), may possibly be a result of the fact that the adduct (6.12) \((R = p-\text{BrC}_6\text{H}_4^-)\) has since been shown to have a square based pyramid structure in the solid state\(^{18}\).
The results of Whittle\textsuperscript{21} from the adducts (6.13) indicate that the apicophilicity of phenyl and ethyl are the same, within experimental error. Thus this would indicate that the $\Delta G^*$ for (7.5), 8.9 Kcal mol\textsuperscript{-1}, is a direct measure of the ring strain in the phospholan, $S_{90-120}$(phospholan).

(c) Pinacol Adduct of 1-Ethylphospholan.

In order to obtain direct data on $S_{90-120}$(phospholan) the adduct (7.12) was prepared. In this compound no correction for apicophilicity should be required and $\Delta G^*$ will be a direct measure of the strain factor. The adduct was synthesised according to the method outlined in Scheme 42.

**SCHEME 42.**

![Scheme 42](image)

(7.12)

The $^1$H and $^{31}$P n.m.r. spectra of (7.12) were consistent with the proposed structure. However, the $^1$H n.m.r. exhibited a singlet for the pinacol methyls, even at $-117^\circ$ (CFCI\textsubscript{3}). This may be caused by accidental chemical shift degeneracy, since the ethyl group will have a similar
shielding effect to the equatorial CH$_2$ group of the ring. If this is not the case then, assuming $\Delta v_{\text{iso}} = 5$ Hz, then $\Delta G^* \leq 8.3$ Kcal mol$^{-1}$. The lower temperature limit of the $^1$H n.m.r. was determined by the lack of a suitable solvent.

(d) Conclusion.

In the absence of any additional information on the difference in apicophilicity between phenyl and ethyl it is not possible to arrive at any precise value for the $S_{90-120}(\text{phospholan})$. Thus in view of the work of Westheimer and Aksnes the value cannot be much less than the $\Delta G^* = 8.9$ Kcal mol$^{-1}$, observed for the adduct (7.5). A value of ca. 8.0 Kcal mol$^{-1}$ would therefore seem reasonable as a lower limit.

This value for $S_{90-120}(\text{phospholan})$ is in agreement with the results obtained by Muetterties and Schmutzler on (CH$_2$)$_4$PF$_3$ (1.32). The $\Delta G^*$ for equivalence of the fluorine atoms in the $^19$F n.m.r. spectrum of (1.32) was found to be 7 Kcal mol$^{-1}$. The high energy TBP has the phospholan ring $\text{ae}$. Thus $\Delta G^*$ is given by:

$$\Delta G^* \geq \Delta G = |A_F - A_{\text{Et}}| - S_{90-120}(\text{phospholan}) = 7 \text{ Kcal mol}^{-1}.$$  

Thus if $|A_F - A_{\text{Et}}|$ is about 15 Kcal mol$^{-1}$, then this gives the same value of 8.0 Kcal mol$^{-1}$ for $S_{90-120}(\text{phospholan})$.

If the adducts (7.1), (7.5), and (7.12) are rearranging via an irregular process, then the $\Delta G^*$ for (7.5) will be a minimum value for the high energy pseudorotation (Scheme 38), since below coalescence all processes except the topomeric pseudorotation, will be slow on the $^1$H n.m.r. time scale. However, in view of the hydrolytic stability of these adducts irregular processes are unlikely.
7.2 Phospholen Ring Strain.

The adducts (7.18) cannot be synthesised by means of the diethyl peroxide route, as in Scheme 39 since the analogous monocyclic phosphorane (7.14) is known to be unstable, and spontaneously undergoes a retro-Diels-Alder type reaction, giving diethyl phenylphosphonite and the diene \(^95\), Scheme 43.

**SCHEME 43.**

\[
\begin{align*}
\text{PhP} & \quad \rightarrow \quad \text{PhP(OEt)}_2 \\
\text{Ph} & \quad \rightarrow \quad \text{PhP(OEt)}_2 \\
(\text{EtO})_2 & \quad \rightarrow \quad \text{PhP(OEt)}_2 \\
\end{align*}
\]

(7.14)

Razumova and Petrov \(^{154,155}\) have however shown that dienes react with ethylene - (7.15) and o-phenylene - (7.16) phosphonites to give pentacoordinate phosphoranes.
The reaction of pinacol phenylphosphonite (7.17) with 2,3-dimethylbuta-1,3-diene at ambient temperature over 2-3 days gave a quantitative yield of the desired adduct (7.18), Scheme 44. The pseudorotation scheme for (7.18) is analogous to that of Scheme 38. The resulting data for this adduct are given in Table 22.

**TABLE 22.**

Data for the Dimethylbutadiene Adduct of Pinacol Phenylphosphonite.

<table>
<thead>
<tr>
<th>Tc (°C)(^a)</th>
<th>δν∞ (Hz)(^b)</th>
<th>ΔG* (Kcal mol(^{-1}))</th>
<th>(^{31P})(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-76 ± 5</td>
<td>39 ± 1.0</td>
<td>9.6 ± 0.3</td>
<td>+17.5</td>
</tr>
</tbody>
</table>

\(^{a}\) CFCl\(_3\). \(^{b}\) At 100 MHz. \(^{c}\) CH\(_2\)Cl\(_2\).

The activation energy ΔG* for (7.18) is given by equation (7.19).

\[
\Delta G^* > \Delta G = S_{90-120}(\text{phospholen}) + (A_{Ph} - A_{Allyl}) \quad (7.19)
\]

However, since no data is available on the difference in apicophilicity of allyl and phenyl, then no precise value of \(S_{90-120}(\text{phospholen})\) can be derived. The work of Westheimer\(^{152}\) on the relative rates of hydrolysis of (7.7) and (7.8) would indicate that;
A value of 10 Kcal mol$^{-1}$ for $S_{90-120}$ (phospholen), being about 2 Kcal mol$^{-1}$ more than that of the phospholan, would seem reasonable.

In order to gain more data on the relative apicophilicities of phenyl and ethyl, the preparation of the adduct (7.21) was attempted.

However, the pinacol ethylphosphonite (7.20) was less reactive than (7.17) and the only products observed by $^1$H and $^{31}$P n.m.r., appeared to be due to thermal decomposition of (7.21), according to Scheme 45.

7.3 Phosphorinan Ring Strain.

The HFA adduct (7.25) of 1-phenylphosphorinan (7.24) was prepared in order to study the activation energies to pseudorotation in phosphoranes containing the six-membered carbon ring.
The possible pseudorotations are shown in Scheme 46. It is not possible to determine which is the ground state TBP, since the preference of the six-membered ring is not known. Whether the ground state is (7.26) and (7.27) or (7.28), the $^{19}$F n.m.r. should still exhibit two singlets when the pseudorotation $(7.27) \leftrightarrow (7.28)$ is slow on the $^{19}$F n.m.r. time scale.

The $^{19}$F n.m.r. spectrum of (7.25) exhibited a singlet, which did not split into two on cooling to $-129^\circ$. Assuming $\Delta \nu = 100\text{Hz}$, then $\Delta G^* < 6.7 \text{ Kcal mol}^{-1}$. Thus, assuming the apicophilicities of Ph and $\text{CH}_2$ are the same, then whatever the positional preference of the six-membered ring, the difference in energy between the two positions is small.

7.4 Strain in Other Rings.

Table 23 summarises the relevant pseudorotations for the phosphoranes studied in Chapter 4 and above, in which various rings are placed in the unfavourable ee positions of the TBP. In addition to these results a selection of data from other rings obtained by Whittle and Bone are included. The first column gives the $\Delta G^*$s for the indicated pseudorotations, and the second column gives the increase in ring strain.
TABLE 23

<table>
<thead>
<tr>
<th>Pseudorotation</th>
<th>$\Delta G^*$</th>
<th>$\Delta G^*-\Delta A$</th>
<th>$\Delta G^*$(calc.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kcal mol$^{-1}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudorotation$^a$</td>
<td>8.9</td>
<td>8</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>(7.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9.6</td>
<td>10</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>(7.18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17.6$^d$</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>(5.33-a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14.1</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>(5.39-c)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>21.2</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>(5.10-a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24.9</td>
<td>24.5</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>(5.39-a)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE 23 (continued)

Pseudorotation

<table>
<thead>
<tr>
<th>b.</th>
<th>X = F</th>
<th>21.8</th>
<th>22</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>17.4</td>
<td>18</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>c.</td>
<td>OCH(CF₃)₂</td>
<td>21.0</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>6</td>
<td>20.4</td>
<td>29</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

b. Prepared by S.A. Bone.  
d. This result is 4.4 Kcal mol⁻¹ less than that obtained by Westheimer and Gorenstein for the pseudorotation (5.24)⇌(5.27), of the monocyclic phosphorane.
from 90 to 120°, after compensating for any change in apicophilicity. From this data two facts are apparent: (a) the energy required to move five-membered rings containing heteroatoms bonded to phosphorus to an ee position is considerably greater than is needed in the case of a phospholan or phospholen ring and (b) the energy required depends not only on the nature of the heteroatom which moves from an a to an e position but also on the nature of the atom which remains equatorial.

It is possible to rationalise these data by taking into account the preferred orientation of lone-pairs on equatorially bonded heteroatoms. Structural investigations by X-ray diffraction techniques have shown that the heteroatoms attached to phosphorus in TBP molecules are approximately sp2 hybridised, and consequently have a pair of electrons in a π orbital. Hoffmann (Chapter 1) has shown by calculation that for an equatorial substituent bearing a single π-donor system, then the π orbital will prefer to align itself in the equatorial plane.

The preference of a π donor for the equatorial plane over the apical plane has been established by experiment in the case of PN and PS (but not PO) bonds and leads to a barrier to rotation round these bonds of 5 - 12 Kcal mol⁻¹.

The total energy difference between (7.33) and (7.34) is therefore composed of three basic terms; (a) an angle-strain factor, due to increase in the bond angle at phosphorus, (b) the energy required to rotate the lone-pair on X from the e to an a plane, and (c) the difference
in apicophilicity between R and Y, when the lone-pair on Y is constrained to an apical plane. The last is equivalent to the 'normal' difference in apicophilicity between R and Y, as shown in systems in which the lone-pairs on R and Y are free to take up the preferred equatorial orientation, plus the energy required to rotate the lone-pair on Y from the e to an a plane. Thus $\Delta G^*$ for $(7.33) \rightleftharpoons (7.34)$ is given by equation (7.35)

$$\Delta G^* = S_{90-120} + R^X + \Delta A(Y-R) + R^Y$$  \hspace{1cm} (7.35)

The data in the last column were calculated on the following basis:

<table>
<thead>
<tr>
<th>Term</th>
<th>Energy (Kcal mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S_{90-120}$ (phospholan)</td>
<td>8</td>
</tr>
<tr>
<td>$S_{90-120}$ (phospholen)</td>
<td>10</td>
</tr>
<tr>
<td>$\Delta A(Ph0-Alko)$</td>
<td>1</td>
</tr>
<tr>
<td>PN Rotation ($R^N$)</td>
<td>10</td>
</tr>
<tr>
<td>PO Rotation ($R^O$)</td>
<td>5</td>
</tr>
</tbody>
</table>

The only experimental evidence$^{143}$ relating to $R^0$ is that it must be less than about 8 Kcal mol$^{-1}$.

The calculated values of $\Delta G^*$ appear to be in agreement with the experimental results, except in the case of (5.33-a) and (5.39-a) in which steric effects are involved.

The increase in ring strain in the pinacol ring of (5.39-a) over that of the ethylene glycol ring of (7.30) can be explained in terms of an increase in torsional strain. If one assumes, by inspection of models, that the dioxaphospholane ring is able to pucker when in the ae positions, but is constrained to be planar when ee, then the additional strain in the pinacol ring can be represented by the difference in energy, $E_2-E_1$. 
between the equilibria shown in Scheme 47. A value of 6 Kcal mol\(^{-1}\) for \(E_2-E_1\) would make \(\Delta G^*\) (calc.) = 24 Kcal mol\(^{-1}\) which is in agreement with the experimental result.

Other steric effects are found in phosphoranes with branching on atoms attached to phosphorus, e.g. (5.33-a). However, even here the effect of the ring atom which remains equatorial is shown clearly; the pseudorotation (7.35) \(\leftrightarrow\) (7.36) has \(\Delta G^* = 17.6\) Kcal mol\(^{-1}\) (calc. 15), but the pseudorotation (7.36) \(\leftrightarrow\) (7.37), which leads to equilibration of (7.36) with its cis-isomer, is slow on the n.m.r. time scale at 170° (i.e. \(\Delta G^* > 23\) Kcal mol\(^{-1}\)).
8. **THE STEREOCHEMISTRY OF NUCLEOPHILIC SUBSTITUTION AT PHOSPHORUS IN P\textsuperscript{V} PHOSPHOLANS.**

8.1 **Introduction.**

The stereochemistry of the phosphorus heterocycles in this thesis will be described using the Beilstein \( r \)-system\textsuperscript{180,181}. A reference group on phosphorus is specified by the symbol \( r \)- and the ring substituents are related to it. 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.

Trippett and coworkers\textsuperscript{158-161} have shown that nucleophilic substitutions of electronegative groups at the phosphorus of 2,2,3,4,4'-pentamethylphosphetan 1-oxides (8.1) and 1-sulphides (8.2) proceed with retention of configuration.

\[ \begin{align*}
\text{(8.1)} & \quad \begin{array}{c}
\text{X} \\
\text{P} \text{PO}_\text{\textsuperscript{3}} \\
\text{X}
\end{array} \\
\text{(8.2)} & \quad \begin{array}{c}
\text{X} \\
\text{P} \text{PS}_\text{\textsuperscript{3}} \\
\text{X}
\end{array}
\end{align*} \]

Similarly, displacement reactions in phosphetanium salts usually proceed with retention, (for a review see reference 65). This result can be explained in terms of the large energy (ca. 18 Kcal mol\(^{-1}\))\textsuperscript{31,95,111} required to move the phosphetan ring from the ee to the ae positions. Thus in Scheme 48 path \( A_1 \) will be the preferred reaction pathway. Inversion via route \( A_2 \) will usually be unfavourable because the leaving group \( X \) is in most cases more apicophilic than \( Z \).
Marsi and coworkers\textsuperscript{162-165} have studied the stereochemistry of the alkaline hydrolyses of five-\textsuperscript{162,165}, six-\textsuperscript{163}, and seven-membered ring phosphonium\textsuperscript{164} salts. When the leaving group $X$ is benzyl, complete retention of configuration was observed in the case of the phospholan systems and complete inversion of configuration was observed in the phosphepanium (seven-membered) salts. However, the phosphorinanum (six-membered) salts hydrolysed to give a mixture of the two isomeric phosphorinan 1-oxides.

If the initially formed TBPs are of highest energy, Scheme 48, then the difference in activation energies, between the two pathways A and B is given by equation (8.3). When the group $X$ is benzyl it is unlikely

$$\Delta G^*_{B} - \Delta G^*_{A} = 890 - 120 - (A_{CH_2} - A_X)$$  \hspace{1cm} (8.3)
that the difference in apicophilicity between alkyl and benzyl* will
be sufficient to overcome the increase in strain (8 Kcal mol\(^{-1}\), Chapter
7) on moving the phospholan from the \(ae\) to the \(ee\) positions. Thus the
hydrolysis of the phospholanium salts probably proceed via the path \(A_+\),
Scheme 48. The strain in the phosphepan ring, \(S_{90-120}\), will be zero
or possibly negative (i.e. preferentially occupies the \(ee\) position),
and therefore the alkaline hydrolysis of the phosphepanium salt
probably proceeds via path \(B\), Scheme 48, analogous to the acyclic
phosphonium salts\(^{85,86}\). The results from the alkaline hydrolysis of
the phosphorinanium salt were best explained in terms of a competition
between paths \(A_+\) and \(B\)^.164

The energy required to move the phospholan ring from the \(ae\) to
the \(ee\) positions was found to be about 8 Kcal mol\(^{-1}\) (Chapter 7). Thus
if the leaving group \(X\), Scheme 48, is chosen such that \(A_{CH_2}-A_X > 8\) Kcal
mol\(^{-1}\) then nucleophilic substitution at phosphorus in the phospholan
system would be expected to go via path \(B\), and consequently with inversion
of configuration at phosphorus. Such an example has been observed by
Marsi and Mislow\(^{166}\). The deoxygenation of cis- or trans-3-methyl-1-
-phenylphospholan r-1-oxide (8.4) by \(Si_2Cl_6\) gave the phosphine (8.5)
with predominant inversion of configuration. The mechanism\(^{167}\) of this
reaction probably proceeds as shown in Scheme 49. The predominant
inversion of configuration being due to preferential attack of \(\text{"SiCl}_3\)
on phosphorus giving the intermediate (8.6), path \(B\), Scheme 48 (\(Z = \text{Ph},\)
\(X = \text{OSiCl}_3\), and \(N = \text{"SiCl}_3\)). This would imply that:

\[
S_{90-120}(\text{phospholan}) < |A_{CH_2}-A_{\text{OSiCl}_3}|,
\]

* No apicophilicity data are available for the benzyl group. The
electronegativity\(^6\) of benzyl (7.90 Mulliken units) is however greater
than that of ethyl (7.40 Mulliken units).
SCHEME 49

(8.4) Me \(-\) P \(\text{Ph} \rightarrow\) Me \(-\) P Cl\(_3\) Si O \(\text{Ph} \rightarrow\) Cl\(_3\) Si O \(\text{Ph} \rightarrow\) P Si Cl\(_3\) Ph

(8.5) Me \(-\) P \(\text{Ph} \rightarrow\) Me \(-\) P \(\text{Ph} \rightarrow\) Cl\(_3\) Si O S i Cl\(_3\) Ph

(8.6) Me \(-\) P \(\text{Ph} \rightarrow\) Me \(-\) P \(\text{Ph} \rightarrow\) Cl\(_3\) Si O S i Cl\(_3\) Ph

[O Si Cl\(_2\)]\(_n\)
however no data are available on the apicophilicity of OSiCl$_3$.

Electronegativity calculations$^6$ indicate that the group is even more
electronegative than OMe (OSiCl$_3$ = 9.76, and OMe = 8.59 Mulliken units).
Thus since $|A_{CH_2} - A_{OMe}| = 9 - 10$ Kcal mol$^{-1}$ $^{21,110,112}$ then the stereo-
chemical course of the reduction is as expected.

8.2 The 1-Substituted-3-Methyl-Phospholan 1-Oxide System.

In view of the small magnitude (8 Kcal mol$^{-1}$) of $S_{90-120}$(phospholan)
as compared to that of the phosphetan it was decided that a study of the
stereochemistry of nucleophilic substitution of electronegative groups
at phosphorus in $P^V$ phospholans should be undertaken. Thus from
equation (8.3) for groups $X$ which are ca. 8 Kcal mol$^{-1}$ more apicophilic
than CH$_2$ the substitution reactions should proceed with predominant
inversion of configuration, path B, Scheme 48.

The 1-substituted-3-methyl-phospholan 1-oxide was chosen for the

\[
\text{SCHEME 50.}
\]
above study. The synthetic route used to obtain this system is shown in Scheme 50.

The $^1$H n.m.r. spectra of (8.9), (8.10), and (8.11), in a range of solvents, exhibited only a single resonance (excluding H-H and P-H spin-spin coupling) for the 3-methyl group and, in the case of (8.10) and (8.11), for the 1-substituent. In addition, thin layer chromatography of (8.10) and (8.11), gas-liquid chromatography of (8.11), and column chromatography of (8.10) were consistent with single isomers for these compounds.

Corfield$^{132,169}$ has shown that the Lanthanide Shift reagent, Eu(dpm)$_3$, can be used to distinguish between cis- and trans- isomers of 2,2,3,4,4-pentamethylphosphetan 1-oxides (8.1) by the induced paramagnetic shifts of the respective 3-protons in their $^1$H n.m.r. spectra. The spectral data for (8.1; $X = $OEt) are shown below in Table 25. The greater shift

TABLE 25.

N.m.r. Spectra$^a$ of r-1-Ethoxy-2,2-cis- and trans-3,4,4-Pentamethylphosphetan 1-Oxides$^b$ in CDCl$_3$ in the presence of 0.48 Molar Equivalent of Eu(dpm)$_3$.

<table>
<thead>
<tr>
<th></th>
<th>3-Me</th>
<th>3-H</th>
<th>2,4-Me$_2$</th>
<th>2,4-Me$_2$</th>
<th>OCH$_2$</th>
<th>O.C.Me</th>
</tr>
</thead>
<tbody>
<tr>
<td>trans</td>
<td>7.68</td>
<td>6.0</td>
<td>6.92</td>
<td>6.20</td>
<td>2.57</td>
<td>7.58</td>
</tr>
<tr>
<td></td>
<td>86</td>
<td>145</td>
<td>114</td>
<td>155</td>
<td>194</td>
<td>65</td>
</tr>
<tr>
<td>cis</td>
<td>7.50</td>
<td>4.55</td>
<td>6.70</td>
<td>5.80</td>
<td>2.68</td>
<td>7.47</td>
</tr>
<tr>
<td></td>
<td>97</td>
<td>224</td>
<td>131</td>
<td>174</td>
<td>196</td>
<td>76</td>
</tr>
</tbody>
</table>

a. The chemical shift (t) is followed by the shift (Hz) from the normal position in CDCl$_3$. 


b. Beilstein reference nomenclature for cis- and trans-isomers\textsuperscript{180,181} of the 3-proton in the cis isomer implies that the europium coordinates with the phosphoryl oxygen.

The \textsuperscript{1}H n.m.r. of (8.11) was therefore examined in the presence of the more soluble shift reagent Eu(Fod)\textsubscript{3}. The results are shown below in Table 26.

\textbf{TABLE 26.}

\begin{center}
\textbf{N.m.r. Spectrum of l-Methoxy-3-methyl-phospholan 1-Oxide (8.11) in CDCl\textsubscript{3} in the Presence of 0.29 molar equivalents of Eu(Fod)\textsubscript{3}.}
\end{center}

<table>
<thead>
<tr>
<th></th>
<th>3-Me</th>
<th>OMe</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.87</td>
<td>6.23</td>
<td>(\tau) (CDCl\textsubscript{3}) normal shift (TMS)</td>
</tr>
<tr>
<td>26</td>
<td>106</td>
<td>Shift (Hz) from normal</td>
</tr>
</tbody>
</table>

Neither the 3-Me nor the OMe resonances were separated into those of the cis- and trans-isomers. The OMe doublet (P-H spin-spin coupling) may possibly have shown a separation of less than 1Hz, however the observation was not consistently repeatable and may have been due to instrument 'noise'. The other protons remained as a complex multiplet.

All the available experimental evidence therefore appears to be consistent with the presence of single isomers. This was thought to have been caused by the formation of the thermodynamically most stable isomer of (8.9) formed by the reaction of \textsuperscript{3}Cl ions with (8.9), Scheme 51, during its preparation from (8.8). Assuming then that only single isomers are present, the amide (8.10) was also prepared from (8.11), Scheme 52,
and then compared with the sample obtained directly from (8.9) by melting points and mixed melting point. Both samples of (8.10) had the same melting points, and the mixed melting points were not depressed (1:3, 74.5 - 78°; 3:1, 74.5 - 77°) significantly.

The stereochemistry of these substitution reactions should be a function of the leaving group apicophilicity only, Equation (8.3). Thus if both samples of (8.10) are identical, and only a single isomer, then all three reactions, (8.9) $\rightarrow$ (8.10), (8.9) $\rightarrow$ (8.11) $\rightarrow$ (8.10), must proceed with retention of configuration. This result is unexpected in view of the high apicophilicity of the leaving groups Cl and OMe, relative to CH$_2$.

Marsi has reported the $^1$H n.m.r. spectra of the 1-cis- and trans- 3-dimethylphospholanyl-1-oxides (8.12), (absolute assignments of configuration were not made). Using benzene as solvent it was possible to observe two sets of resonances for both the 1- and 3-methyl groups, $[\Delta \delta$ (1-Me) = 0.23 ppm; $\Delta \delta$ (3-Me) $\approx$ 0.19 ppm].
The stereochernical composition of the acid chloride (8.9) was therefore further probed by preparation of (8.12), Scheme 53 (R = Me, X = Cl, Br or I). The $^1$H n.m.r. spectrum of (8.12) obtained from (8.9) was consistent with a single isomer (isomer 2b, m.p. 72 - 73.5°, Ref. 162), however the m.p. (46 - 56°) was much lower than that reported$^{162}$.

Preparation of the 1-benzyl derivative (8.13) from (8.9) however gave a mixture of two isomers. The $^1$H n.m.r. in CDCl$_3$ exhibited two sets of absorptions for the 3-methyl group, consistent with a mixture of cis- and trans- isomers. The P-CH$_2$-Ph group however showed only one set of absorptions.

In view of the above findings the $^1$H n.m.r. of the methyl ester (8.11) was reinvestigated in the presence of the shift reagent Eu(dpm)$_3$. In contrast to the results using Eu(fod)$_3$, the P-OMe resonances were separated into two, each of equal area. However, no separation of the 3-Me resonance was observed. The $^1$H n.m.r. data are shown below in Table 27.

If the europium coordinates with the phosphoryl oxygen then it would be expected that the shift of the OMe resonances would be the same for both isomers since the relative positions of the OMe group to the europium atom should be the same in both cases. The induced shift is, however, also proportional to the concentration of the shift-reagent-substrate complex, Equation (5.15)$^{132}$. The assignments of configuration in Table 27 are therefore based on the assumption that the equilibrium

\[ \text{Scheme 53.} \]

\[ \begin{align*}
\text{Me} & \quad \text{i)RMgX} & \quad 8.12; R = \text{Me} \\
\text{O} & \quad \text{ii)H}_2\text{O} & \quad 8.13; R = \text{PhCH}_2 \\
\end{align*} \]
TABLE 27.

N.m.r. Spectra of r-1-Methoxy-cis- and trans-3-methyl-phospholan 1-Oxides (8.11) in CDCl$_3$ in the Presence of 0.24 Molar Equivalent of Eu(dpm)$_3$.

<table>
<thead>
<tr>
<th></th>
<th>3-Me$^a$</th>
<th>P-OMe$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>cis-3-methyl</td>
<td>8.87</td>
<td>6.23</td>
</tr>
<tr>
<td>trans-3-methyl</td>
<td>21</td>
<td>88</td>
</tr>
</tbody>
</table>

a. The chemical shift ($\tau$) is followed by the shift (Hz) from the normal position in CDCl$_3$.

constant for complex formation for trans (8.11) will be less than that for cis (8.11), due to steric hindrance from the 3-methyl group in the trans isomer. Consequently the induced shift of the OMe resonances should be less for the trans isomer than for the cis isomer.

This result would appear to suggest that a 50:50 mixture of cis and trans isomers is also present in the compounds (8.9) and (8.10) which were originally consistent with single isomers. This result would also account for the similarity of the two samples of (8.10), as indicated by the m.p. data.

8.3 1-Benzyl-1-Ethoxy-3-Methyl-Phospholanium Salt Hydrolyses.

The observance of two isomers for 1-benzyl-3-methyl-phospholan
1-oxide (8.13) prompted a study of the stereochemistry of alkaline hydrolysis of the 1-benzyl-1-ethoxy-3-methyl-phospholanium salt (8.14).

The isomer (8.13-a) was obtained pure (> 90% by $^1$H n.m.r. of the 3-Me group) by fractional recrystallisation from ethyl acetate. The isomer (8.13-b) was obtained isomerically pure (> 90% by $^1$H n.m.r.) from the enriched mother liquors by dry column chromatography.

The tetrafluoroborate salts (8.14-a and b) were prepared by the reaction of (8.13-a and b) with triethyl oxonium tetrafluoroborate. This reaction preserves the stereochemistry of phosphorus, since no bonds to phosphorus are made or broken, Scheme 54.

The cis- and trans- designations for a and b are arbitrary; they represent relative configurations and are not intended to denote absolute stereochemistry.

The alkaline hydrolyses of (8.14-a) and (8.14-b) in aqueous dioxan at 25°, gave the corresponding phospholan oxides (8.13) with predominant retention of configuration at phosphorus (ca. 75% retention as observed by $^1$H n.m.r.).

Nucleophilic attack of OH$^−$ on (8.14) may occur either at phosphorus, Scheme 48 (Z = CH$_2$Ph, X = OEt, and N = OH$^−$), or at the carbon atom adjacent to oxygen, Scheme 55. Since attack at carbon would
also lead to the formation of (8.13) with retention of configuration, it was necessary to determine whether the hydrolysis was in fact occurring

\[
\text{SCHEME 55.}
\]

\[
\begin{array}{c}
\text{Me} \\
\text{CH}_3\text{CH}_2\text{O} \\
\text{CH}_2\text{Ph}
\end{array}
\xrightarrow{\text{H}_2\text{O}^\circ/\text{Dioxan}}
\begin{array}{c}
\text{Me} \\
\text{O} \\
\text{CH}_2\text{Ph}
\end{array}
\]

at phosphorus. This was accomplished by an 18-oxygen tracer experiment. Alkaline hydrolysis of (8.14-a) in H\textsubscript{2} \textsuperscript{18}O enriched aqueous dioxan gave the oxide (8.13-a) with predominant retention of configuration and with incorporation of 74\% of the theoretical amount of \textsuperscript{18}O. The results are shown in Table 28. Although the necessary control experiment in which

\[
\text{TABLE 28.}
\]

Alkaline Hydrolysis of (8.14-a) in H\textsubscript{2} \textsuperscript{18}O/Dioxan at 25\°.

<table>
<thead>
<tr>
<th>% Retention</th>
<th>Atom % \textsuperscript{18}O Theoretical</th>
<th>Atom % \textsuperscript{18}O Found</th>
<th>% Attack at Phosphorus</th>
</tr>
</thead>
<tbody>
<tr>
<td>ca. 75\textsuperscript{a}</td>
<td>23\textsuperscript{b}</td>
<td>17\textsuperscript{c}</td>
<td>74</td>
</tr>
</tbody>
</table>

a. Estimated from \textsuperscript{1}H n.m.r.  
b. Calculated from composition of reaction mixture; 0.447g H\textsubscript{2} \textsuperscript{18}O (25 Atom \%) + 0.086g NaOH.  
c. By mass spectrometry.

(8.13-a) is subjected to the same reaction conditions was not carried out, Mislow\textsuperscript{171} has shown that no \textsuperscript{18}O exchange occurred when either an acyclic phosphine oxide or a phosphetan oxide was subjected to the same reaction conditions as used for the hydrolysis of (8.14-a). Thus
exchange of \(^{18}O\) in (8.13-a) is also unlikely.

These results suggest that the hydrolyses of (8.14-a and b) proceed via path A\(_i\), Scheme 48. This implies that:

\[ S_{90-120} (3\text{-methyl-phospholan}) > |A_{CH_2} - A_{OEt}| \]

This is unexpected in view of the observed ring strain \([S_{90-120} (\text{phospholan}) = 8 \text{ Kcal mol}^{-1}\]) and the expected difference in apicophilicities of CH\(_2\) and OEt, \((9 - 10 \text{ Kcal mol}^{-1})\)\(^{21,110,112}\). However, the results are in agreement with the faster rate of hydrolysis of 1-ethoxy-phospholan 1-oxide (7.7) compared to its acyclic analogue\(^{152,153}\).

8.4 The 1-Substituted-3,4-Dimethyl-Phospholan 1-Oxide System.

(a) Synthetic Methods.

In order to try and overcome the problems of isomer observation encountered in the 3-methyl-phospholan system, the more symmetrical 3,4-dimethyl-phospholan system was studied. However, there are additional problems in the synthesis of this system; these are:

(i) Preparation of the 3-phospholen without isomerisation to the 2-phospholen.

(ii) Hydrogenation of a tetra-substituted double bond.

Hunger\(^{172}\) and Arbuzov\(^{173}\) have shown that in the case of 3,4-di-methyl-phospholen, the position of the double bond on conversion of the pentacoordinate trihalo adducts (e.g. 8.15) into the tetra-coordinate phosphoryl compounds depends on the nature of the halogen. The use of bromides leads exclusively to structures with a double bond in the 3-position, while chlorides give predominantly the 2-isomer.

The preparation of the meso-3,4-dimethyl-phospholan system was
therefore attempted by the route shown in Scheme 56. There are a number of reports on the hydrogenation of various phospholen compounds\textsuperscript{162,165,172} 175-177. Hydrogenations of the 3,4-dimethyl-3-phospholen system have usually been accomplished by the use of activated Raney-Nickel, at moderate pressures (50 p.s.i.) in alcohols\textsuperscript{176,177}. Hydrogenation of (8.16) however, could only be accomplished under quite severe conditions (e.g. Pd/C, 80°, 100 Atm. 21h gave only 50% hydrogenated product). It was therefore decided to investigate the hydrogenation of an ester derivative of (8.16) which in addition would be more readily available. The proposed synthetic scheme is shown below, Scheme 57. Use of the readily available\textsuperscript{178} 2-chloro-1,3,2-dioxaphospholan.
(8.18) gave only the 3-phospholen isomer of (8.20). Various attempts were made to hydrogenate this compound, however, severe conditions were required to effect this reaction (e.g. PtO₂, 75°/110 Atm., 65h. gave 100% hydrogenated product).

The phospholan ester (8.21) was shown by \(^1\)H n.m.r. and g.l.c. to contain two isomers. A third isomer was also observed by g.l.c. Table 29 shows the ratios of isomers, relative g.l.c. retention times, and \(^1\)H n.m.r. data for the ring methyls. Alkaline hydrolysis of (8.21) gave only one acid as shown by \(^1\)H n.m.r. These results suggest that the minor isomer is dl-\(\text{r-1-(\beta\text{-chloroethoxy})-cis-3,trans-4-dimethyl-phospholan 1-oxide (8.21-c).}

<table>
<thead>
<tr>
<th>Isomer</th>
<th>% Isomers</th>
<th>Relative Retention</th>
<th>3,4-Me₂</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(a)</td>
<td>(b)</td>
<td>(r)</td>
</tr>
<tr>
<td>(8.21-a)</td>
<td>66</td>
<td>50</td>
<td>0.94</td>
</tr>
<tr>
<td>(8.21-b)</td>
<td>33</td>
<td>39</td>
<td>1.00</td>
</tr>
<tr>
<td>(8.21-c)</td>
<td>1</td>
<td>11</td>
<td>0.85</td>
</tr>
</tbody>
</table>

a. From g.l.c. peak areas. b. 3% OV-17 column (170°). c. CDCl₃ d. 75°/110Atm., 65h. e. Ambient temperature and pressure.

It was later found that the ester (8.20) could be hydrogenated using Adams catalyst in glacial acetic acid at normal temperature and pressure. This method, although less stereospecific, was subsequently used in synthesising the precursor (8.21) for the 3,4-dimethyl-phospholan system. The isomer composition obtained by this method is shown in Table 29. The yield of the minor isomer (8.21-c) was not constant in
different 'batches' and varied between 10 - 20%.

The reaction of (8.21) with 2 molar equivalents of sodium methoxide in refluxing methanol overnight gave a thermodynamic equilibrium mixture of the methyl ester (8.22), Scheme 58.

SCHEME 58.

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{P} & \quad \text{OCH}_2\text{CH}_2\text{Cl} \\
\text{O} & \quad \text{MeOH} \\
(8.21) & \quad \text{2 MeO}^- \text{Na}^+ \\
\text{Me} & \quad \text{Me} \\
\text{P} & \quad \text{OMe} \\
\text{O} & \quad \text{MeOCH}_2\text{CH}_2\text{OH} \\
(8.22) & \quad \text{NaCl}
\end{align*}
\]

(b) Absolute Stereochemistry.

Isomerically pure samples of (8.22-a) and (8.22-b) were obtained by column chromatography. The absolute stereochemistry of these two isomers was then studied by \(^1\text{H}\) n.m.r. using the shift reagent Eu(dpm)\(_3\). The induced shifts of both the MeO and 3,4-Me\(_2\) resonances were measured as a function of shift reagent concentration. The results shown in graph (8.23) were obtained using pure isomers of (8.22-a) and (8.22-b). Consequently association with the shift reagent is non-competitive. The 3,4-dimethyl resonances are shifted equally for both isomers, and there appears to be only a small difference in the shifts of the OMe resonances, with isomer (8.22-b) the larger.

The induced shifts in the presence of Eu(dpm)\(_3\) were therefore reinvestigated using a mixture of isomers, in which competitive association should be observed. The isomeric mixture of (8.22) was obtained via method (ii), Scheme 59. The results are shown in the Graph (8.24). These results are best explained by a steady increase in steric.
(8.23) Non-competitive Lanthanide Induced Shifts

![Graph showing induced shifts for non-competitive lanthanide induced shifts.]

(8.24) Competitive Lanthanide Induced Shifts

![Graph showing induced shifts for competitive lanthanide induced shifts.]
hindrance to shift reagent-substrate complex formation, from (8.22-b) to (8.22-c) to (8.22-a). This would be expected if the shift reagent coordinates to the phosphoryl oxygen. Thus the absolute stereochemistries of the isomers of (8.22) are probably as shown below.

\[
\begin{align*}
\text{Me} & \quad \text{Me} & \quad \text{Me} & \quad \text{Me} \\
\text{O} & \quad \text{OMe} & & \\
(8.22-a) & & & \\
\end{align*}
\begin{align*}
\text{Me} & \quad \text{Me} & \quad \text{Me} & \quad \text{Me} \\
\text{O} & \quad \text{OMe} & & \\
(8.22-b) & & & \\
\end{align*}
\begin{align*}
\text{Me} & \quad \text{Me} & \quad \text{Me} & \quad \text{Me} \\
\text{O} & \quad \text{OMe} & & \\
(8.22-c) & & & \\
\end{align*}
\begin{align*}
\text{trans-trans} & & & \text{cis-cis} & & \text{dl-trans-cis} \\
\end{align*}

The unexpected order of the induced shifts observed for the 3,4-dimethyl groups of (8.22-a) and (8.22-b) can also be explained in terms of competitive association of shift reagent and substrate.

(c) Stereochemistry of Nucleophilic Substitution.

The methyl ester (8.22) was prepared using two different reagents as shown in Scheme 59. The isomer compositions of (8.22) and methods of preparation are shown in Table 30, along with the equilibrium composition observed for the reaction in Scheme 58.

**TABLE 30.**

Isomer Compositions of 3,4-Dimethyl-1-Methoxy-Phospholane 1-Oxide (8.22)

Prepared by Different Methods.

<table>
<thead>
<tr>
<th>Isomers</th>
<th>% Composition</th>
<th>% Composition</th>
<th>% Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Equilibrium</td>
<td>(i) MeO⁻Na⁺/MeOH</td>
<td>(ii) MeOH/Et₃N</td>
</tr>
<tr>
<td></td>
<td>Mixture</td>
<td>a,b</td>
<td>a</td>
</tr>
<tr>
<td>(8.22-a)</td>
<td>56</td>
<td>33</td>
<td>46</td>
</tr>
<tr>
<td>(8.22-b)</td>
<td>36</td>
<td>48</td>
<td>35</td>
</tr>
<tr>
<td>(8.22-c)</td>
<td>8 c</td>
<td>19 c</td>
<td>19 c</td>
</tr>
</tbody>
</table>

a. By g.l.c. peak areas. b. By \(^1\)H n.m.r. of the OMe resonances in CDCl₃ in the presence of Eu(dpm)₃. c. The increase in the % of (8.22-c)
is due to the use of different samples of (8.21).

**SCHEME 59.**

![Chemical diagram](image)

(i) MeO⁻Na⁺/MeOH

(ii) MeOH/Et₃N in C₆H₆.

The ratios of the two major isomers, (8.22-a):(8.22-b), are almost completely inverted for the two different preparative methods, using the same sample of the acid chloride (8.25). No isomerisation of single isomers was observed under the same conditions.

One possible explanation of these results is shown by the mechanism in Scheme 60. If the mechanism of the reaction of MeOH/Et₃N is as shown then all three substitution steps would be expected to go with inversion of configuration in view of the presence of the highly electronegative leaving groups, Cl and N⁺ Et₃, (Equation 8.3). Trigonal bipyramidal intermediates similar to (8.27) have been observed by Yamazaki and Higashi, and intermediates similar to (8.28) have also been postulated in the reactions of acylchlorides with pyridine.

An alternative mechanism may however be implied from the work of Emsley, on the reaction of 1-chlorophosphetan 1-oxide (8.1, X = Cl), with various alcohols in the presence of triethylamine. Thus in the intermediate (8.26) pseudorotation will be unfavourable since the poorly apicophilic O⁻ and CH₂ groups would be placed apical. However, when the reagent is MeOH/Et₃N, it is postulated that the triethylamine
hydrochloride formed during the reaction would enable the intermediate (8.26) to pseudorotate. The apicophilicity of the \( O^+ \) group being increased by hydrogen bonding with the \( \text{Et}_3\text{NH.CI}^- \), Scheme 61. This would lead to epimerisation of the ester (8.22), by further pseudorotations of the intermediate (8.30). This phenomena would apply equally well to
Graph (8.31) Kinetics of Isomerisation of (8.22-a) by g.l.c.

\[
10 \times \frac{[K]}{[K+1]} \ln \left[ \frac{x_e}{x_e-x} \right]
\]

<table>
<thead>
<tr>
<th>Time (s)</th>
<th>0</th>
<th>5</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Slope = 3.07 \times 10^6 \text{ s}^{-1}

\[ k_1 = 9.30 \times 10^6 \text{ M}^{-1} \text{s}^{-1} \]

\[ k_2 = 1.45 \times 10^5 \text{ M}^{-1} \text{s}^{-1} \]

Graph (8.33), Kinetics of Isomerisation and of Incorporation of CD$_3$O by $^1$H n.m.r. (100MHz) in CD$_3$OD$^+$ / CD$_3$OH.

\[
10 \times \frac{[K]}{[K+1]} \ln \left[ \frac{x_e}{x_e-x} \right]
\]

<table>
<thead>
<tr>
<th>Time (s)</th>
<th>0</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>0</td>
<td>5</td>
<td>10</td>
<td>15</td>
<td>20</td>
</tr>
</tbody>
</table>

\[ k_2 / k_1 = 1.3 \]

T = 50°
either of the two pathways in Scheme 61.

In conclusion then it is not possible to come to any reliable interpretation of these results in the absence of any information on the isomer composition of the 1-chloro compound (8.25), and on the mechanism of the reaction using MeOH-Et$_3$N.

(d) Kinetic Studies on the Rates of Isomerisation and Methoxide Exchange in the Reactions of 1-Methoxy-3,4-Dimethyl-Phospholan 1-Oxides with Sodium Methoxide.

It was shown by g.l.c. that although no measurable amount of isomerisation of the methyl ester (8.22-a) was observed in sodium methoxide-methanol at 0°, the compound was epimerised at higher temperatures. The kinetics of isomer interconversion was then followed by g.l.c. The results in Graph (8.31) were obtained by plotting the isomer concentrations and reaction times as a function of the rate equation (8.32), for opposing reactions, Scheme 62.

$$k_1[\text{MeO}^-\text{Na}^+]t = \frac{K}{(K+1)} \ln \left(\frac{x_e}{(x_e-x)}\right)$$  \hspace{1cm} (8.32)

- $k_1$: Rate constant of forward reaction
- $K$: Equilibrium constant, $[8.22-b]/[8.22-a] = 0.64$ (Table 30)
- $x_e$: Equilibrium concentration of isomer (8.22-b)
- $x$: Concentration of isomer (8.22-b) at time $t$.
- $[\text{MeO}^-\text{Na}^+] = 0.33$ mol l$^-1$

![Scheme 62](image-url)
Thus isomer interconversion must be occurring via either of the pathways B or $A_2$, Scheme 48, $(Z = O^-, X = N = OMe)$. Reaction via path $A_2$ is unlikely because this requires placing the poorly apicophilic $O^-$ group apical. Also Cremer$^{183}$ has shown that in the phosphetan (8.1, $X = OCD_3$) no isomer interconversion was observed under similar conditions, although exchange of $OCD_3$ for $OMe$ did occur. Thus in this compound no inversion of configuration via path $A_2$ can be occurring.

In order to determine whether the reaction of (8.22-a) with methoxide was proceeding with exclusive inversion, or whether the inversion was due to a 'leakage', it was necessary to measure the rate of exchange of the methoxy group, for comparison with the rate of epimerisation.

This was accomplished by observing both the rate of incorporation of $OCD_3$ and the rate of isomerisation by $^1H$ n.m.r. of (8.22-a) in a solution of sodium $d_3$-methoxide in $d_4$-methanol. The rate of incorporation of $OCD_3$ was determined by integration of the $0$-$Me$ region and the results plotted as a function of the rate equation (8.34). The rate of isomerisation

$$k_2.[CD_3O^-Na^+] = \ln \frac{a}{(a-x)}$$

(8.34)

$k_2 = $ Rate constant for incorporation of $OCD_3$.
$a = $ Integral height (mm) of the $OMe$ group at $t = 0$.
$x = $ Integral height (mm) of the $MeOH$ resonance at time $t$.

was determined by observing the change of intensity of the upfield half of the 3,4-dimethyl doublet of the isomer (8.22-b). The results were then plotted as a function of the rate equation (8.32), where,

$x_e = $ Peak intensity at equilibrium ($t = \infty$)
$x = $ Peak intensity at time $t$. 
From the results shown in the Graph (8.33), the plots obtained were not linear, the rate being slower towards the end of the reaction. This may be caused by a small contribution from the reaction (8.35),

\[ \text{Me Me Me Me} \xrightarrow{\text{OCD}_{3}} \text{+ CH}_{3}\text{OCD}_{3} \]

which would reduce both the concentration of the ester and of the \text{d}_{3}-\text{methoxide ions. The slopes were therefore taken from the initial part of the graph.}

The slopes for the two reactions at 50°, are:

\[ k_{2}[\text{CD}_{3}\text{O}^{-}\text{Na}^{+}] = 7.50 \times 10^{-6} \text{ s}^{-1} \text{ (Exchange)} \]
\[ k_{1}[\text{CD}_{3}\text{O}^{-}\text{Na}^{+}] = 5.75 \times 10^{-6} \text{ s}^{-1} \text{ (Isomerisation)} \]

and therefore the ratio of \( k_{2} : k_{1} \) is:

\[ \frac{k_{2}}{k_{1}} = 1.3 \]

The rate constant \( k_{2} \) for \text{MeO} exchange will be the sum of the forward rate constant \( k_{1} \) for inversion and the rate constant \( k_{R} \) for retention of configuration.

\[ \frac{k_{2}}{k_{1}} = \frac{k_{R} + k_{1}}{k_{1}} = 1.3 \]

\[ \frac{k_{1}}{k_{R}} = 3.3 \]

Thus the rate of inversion is 3.3 times faster than the rate of
the retention reaction for the isomer (8.22-a). The preferred reaction path appears then to be the inversion route, path B, Scheme 48. This implies that:

\[ S_{90-120} (3,4\text{-dimethyl-phospholan}) < |A_{\text{CH}_2} - A_{\text{OMe}}| \]

which is contrary to the results in section 8.3, and also to those of Westheimer\(^\text{152}\) and Aksnes\(^\text{153}\), Section 7.1.

It was also shown that the possibility of inversion via path \(A_2\) could be eliminated, since no isomerisation of (8.22-a), as observed from the \(\text{OMe}\) resonances, was observed in \(\text{CD}_3\text{O}^-\text{Na}^+ / \text{CD}_3\text{OD}\), i.e. no isomerisation occurs without exchange. This would have been observed if pseudorotations had occurred in which the \(O^-\) or OD group were placed apical.

8.5 Conclusion.

It appears that nucleophilic substitution of highly apicophilic groups, e.g. Cl and \(\text{NEt}_3\), at the phosphorus(V) of phospholan compounds proceed with predominant inversion, in accord with equation (8.3).

In the case of poorly apicophilic groups, e.g. benzyl\(^\text{162,165}\), predominant retention is observed.

However, for intermediate groups, e.g. \(\text{OMe}\) and \(\text{OEt}\), in which the difference in apicophilicities of the leaving group and \(\text{CH}_2\) is similar to the ring strain in the phospholan, the stereochemistry of substitution is inconsistent. This may be caused by a fine balance between factors other than ring strain and apicophilicity, e.g. other substituents on phosphorus, ring substituents and solvation.
9. HYDROXYPHOSPHORANES.

Nucleophilic substitution in phosphonyl compounds ($\equiv$P=O) and alkaline hydrolyses of phosphonium salts both proceed via TBP intermediates (9.1) with an $O^-$ substituent. The preferred pseudorotation pathways are based on the assumption that the $O^-$ group is poorly apicophilic. Protonation of this group will however enable pseudorotation to occur, e.g. (9.2) $\rightarrow$ (9.3), since the $OH$ group is highly electronegative. Information on the pKa values of equatorial alkoxy groups would therefore be useful for predicting the probability of pathways such as (9.1) $\rightarrow$ (9.2) $\rightarrow$ (9.3).

There are a number of reports in the literature of the preparation of TBP phosphoranes containing an $OH$ or an $O^-$ group. Whittle has recently shown that the equivalence of the fluorines in the $^{19}F$ n.m.r. of (9.4) above $-87^\circ$ is probably due to the process (9.4) $\rightarrow$ (9.5) $\rightarrow$ (9.6) being fast on the n.m.r. time scale. Goldwhite has shown that stable
TBP arsenic compounds containing an OH group can be prepared. The compound (9.7) was shown to react with diazomethane to give (9.8).

Derkach and Kirsanov\textsuperscript{189} have shown that the spirophosphonium hydroxide salt (9.10) is stable at room temperature. However, no \textsuperscript{31}P chemical shift was given. The compound was therefore reinvestigated in view of the possible formation of the pentacoordinate species (9.11) or (9.12). However, the \textsuperscript{31}P shift of (9.10) in methanol (-72 ppm) was almost identical to that of the iodide (-71.6 ppm). In view of the results obtained by Allen\textsuperscript{78} on (3.3) in the presence of methoxide, the \textsuperscript{31}P shift of the iodide of (9.10) was measured in methanol in the presence of 3 molar equivalents of sodium methoxide. However, no shift in the \textsuperscript{31}P signal was observed.

Razumova and Petrov\textsuperscript{190} have shown that hydrolysis of (9.13, X = Cl or Br) gave the hydroxyphosphorane (9.14), whereas (9.13, X = F) gave the ester (9.15). The structure of (9.14) was proved by reaction with
diazomethane followed by hydrolysis in dilute (1:3) hydrochloric acid at 100° for 1.5h, when pyrocatechol was obtained. Reaction of (9.15) with diazomethane, followed by hydrolysis in dilute (1:3) hydrochloric acid at room temperature for 4 days gave guaiacol. The pH values of (9.14) and (9.15) were measured by a potentiometric titration method and found to be 5.36 and 2.96 respectively. The meaning of these figures is uncertain.

The compound (9.14) was therefore reinvestigated. The pKa was determined by titration with sodium hydroxide solution using a pH meter, and was found to be 9.6. This is in the range expected for a phenol. The compound also gave a positive phenol test with ferric chloride. The reaction of (9.14) with diazomethane followed by hydrolysis in 0.1N sodium hydroxide at 100° for 2h gave guaiacol and 1-hydroxy-3-phospholene 1-oxide as the only products.

These results are consistent with the structure (9.15) and are contrary to those of Razumova and Petrov.
The conjugate base of (9.14) was also studied in aprotic solvents. Demethylation of the phosphorane (9.13, X = OMe) with sodium iodide in d₆-acetone gave a ¹H n.m.r. spectrum consistent with the predominant formation of the conjugate base of (9.15). However, demethylation with lithium iodide in d-chloroform gave a ¹H n.m.r. spectrum similar to that of the phosphorane (9.13, X = OMe). These results suggest that the more covalent Li-O bond stabilises the conjugate base of (9.14).

Addition of trifluoroacetic acid to the lithium salt of the conjugate base of (9.14) gave an ¹H n.m.r. spectrum consistent with the structure (9.15).

Thus it appears that pentacoordinate hydroxyphosphoranes are unstable with respect to the phosphonyl compound or phosphonium salt, (9.16).
It may be possible to design a system which would favour an equilibrium towards the hydroxyphosphorane. Such a system may be (9.17) in which the ring strain and poor leaving group ability of fluorine (but high apicophilicity) should favour its formation from the phosphetan oxide and hydrogen fluoride.
10. PHOSPHOLANONE 1-OXIDES (KETO PHOSPHOLANES).

10.1 1-Substituted-3-Phospholanone 1-Oxides.

There are few methods available for the synthesis of 1-substituted-3-phospholanone 1-oxides\textsuperscript{191-193}. These compounds are interesting in that they have a high enolic content (10.1).

![Diagram of keto and enol forms of 1-substituted-3-phospholanone 1-oxide]

(10.1)

The synthetic scheme used by Quin and Caputo\textsuperscript{191} for the synthesis of (10.1, \(R = \text{Me}\)) is shown below. The intermediacy of the vinyl ether

![Chemical reaction scheme for synthesis]

(10.2) initiated the investigation of an alternative synthesis using 2-ethoxy-1,3-butadiene.

The factors which affect the rates of reaction of dienes with
phosphorus(III) compounds have been widely studied. The results indicate that the following factors increase the rate of reaction:

(i) Electron donating groups in the diene.
(ii) Electron withdrawing groups in the phosphorus(III) compound,
(iii) Presence of a small (5-membered) ring in the phosphorus(III) compound.

The reactions of 2-ethoxy-1,3-butadiene with phosphorus(III) compounds however, have not been studied. The electron donating ability of the ethoxy group should give this diene enhanced reactivity. From (ii) and (iii) one would expect the most reactive phosphorus(III) compound, towards 1,3-cycloadditions, to be o-phenylene phenylphosphonite (10.3, R = Ph).

A method for preparing 1-phenyl-phospholan-3-one 1-oxide was therefore devised using the expected high reactivity of 2-ethoxy-butadiene and o-phenylene phenylphosphonite. The synthetic scheme is outlined below, Scheme 63 (R = Ph).

**SCHEME 63.**

\[
\begin{align*}
\text{EtO} & \quad \text{EtO} \\
\text{EtO} & \quad \text{EtO} \\
\text{EtO} & \quad \text{EtO} \\
\text{EtO} & \quad \text{EtO} \\
\text{EtO} & \quad \text{EtO}
\end{align*}
\]
The cycloaddition of 2-ethoxy-butadiene with the o-phenylene phenylphosphonite was found to be complete in 2 - 3 days at room temperature. The adduct (10.4, R = Ph) was obtained as a white crystalline solid. Alkaline hydrolysis of (10.4) gave a mixture of the 2- and 3-phospholenes (10.5, R = Ph), which gave the required 3-keto phospholan (10.1, R = Ph) on acid hydrolysis.

This method was found to be applicable to the synthesis of other 3-keto phospholanes (10.1, R = i-Pr and CHzPh), although in the case of (10.3, R = t-Bu) no cycloaddition product was observed even at 60°, the only products being due to polymerisation of the diene and disproportionation of (10.3, R = t-Bu) to (10.6) and (10.7).

![Chemical structure](image)

(10.6) (10.7)

The tautomerism of the 3-keto-phospholanes (10.1, R = Ph, i-Pr, and CH2Ph) was also investigated. It was found that although in the compounds (10.1, R = Ph and i-Pr) enol formation was observed in the solid state, and in highly concentrated solutions (for R = Ph, by 1H n.m.r.), the compound (10.1, R = CH2Ph) was always observed as the keto form. This is the first example of an enolisable 3-keto phospholan 1-oxide which exists as the keto form irrespective of conditions. The pertinent infrared data are given in Table 31.
TABLE 31.

Infrared Data for 1-Substituted 3-Keto-Phospholan 1-Oxides.

<table>
<thead>
<tr>
<th>R-group</th>
<th>Tautomeric Form</th>
<th>Dilute Solution (cm⁻¹) (C=O)</th>
<th>Dilute Solution (cm⁻¹) (OH)</th>
<th>Solid State (cm⁻¹) (C=C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>keto</td>
<td>1730ᵃ</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>enol</td>
<td>-</td>
<td>2440-2275</td>
<td>1558ᶜ</td>
</tr>
<tr>
<td>Ph</td>
<td>keto</td>
<td>1740ᵇ</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>enol</td>
<td>-</td>
<td>2700-2200</td>
<td>1585ᶜ,ᵈ</td>
</tr>
<tr>
<td>i-Pr</td>
<td>keto</td>
<td>173ᵇᵃ</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>enol</td>
<td>-</td>
<td>2600-2300</td>
<td>1600,1585ᶜ,ᵈ</td>
</tr>
<tr>
<td>CH₂Ph</td>
<td>keto</td>
<td>173ᵃᶜ</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>keto</td>
<td>173ёт</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

a. CHCl₃. b. CH₂Cl₂. c. Nujol. d. KCl (0.5-1% w/w)

Conditions of the enol formation are those where intermolecular hydrogen bonding is enhanced (i.e. high concentrations in aprotic solvents, or the solid state). The tautomeric forms are easily recognised in their i.r. i.e. (C=O, OH, and C = C stretches) and ¹H n.m.r. (=CH- and OH resonances) spectra.

The nature of the hydrogen bonding in the enol form has been postulated to be either a cyclic dimeric structure (10.8) or a chain structure (10.9).

![Diagram](10.8)

![Diagram](10.9)
The phospholan oxide (10.10) is known to form a 1:1 hydrogen-bonded adduct (10.11) with phenols\textsuperscript{194}. The relief of ring strain probably favours the near TBP structure in which the phenolic oxygen is partially bonded to phosphorus. In addition most phospholan oxides are extremely hygroscopic, and presumably form a 1:1 adduct with water similar in structure to (10.11). However, the 1-benzyl-3-methyl-phospholan 1-oxide (8.13-a) was found to be non-hygroscopic.

Thus if all the structures of hydrogen-bonded adducts between phenols, enols, and water with phospholan oxides are analogous to (10.11), then there may be a common explanation for the anomalous behaviour of the 1-benzylphospholan 1-oxide system. One possible explanation may be the large size of the benzyl group which would destabilise a TBP structure.

10.2 1-Substituted-2-phospholan-1-oxides.

An attempt was made to extend the synthesis in Scheme 63 to the preparation of 2-keto phospholan 1-oxides (10.12) using 1-ethoxy-1,3-butadiene.

The \textit{cis}-1-substituted dienes are unreactive towards phosphorus(III) compounds. The reaction of \textit{trans}-1-ethoxy-1,3-butadiene with o-phenylene phenylphosphonite was therefore studied. However, no 1,4-cycloaddition product was observed, even at 60°. The only products were due to polymerisation of the diene and disproportionation of the phosphonite.
EtOEt to give products analogous to (10.6) and (10.7).
In a recent communication\textsuperscript{195}, Burger reported that hexafluoro-acetone azine (11.1) reacts with phosphites and tris(dimethylamino)-phosphine (11.2) to give 1,2-addition products (11.3). These 1:1 adducts exhibited high thermal stability. This is the first report of a pentacoordinate phosphorane in which the phosphorus atom is in a three membered ring. Denney has however postulated the intermediacy of the pentacoordinate phosphorane (11.4) in the reaction of a dithietane with 1-phenylphosphiran at \(-78^\circ\)\textsuperscript{196}.

Thus it would appear that the high thermal stability of (11.3) is contrary to that expected for this type of compound.
The structure of (11.3) has been reinvestigated by Bone\textsuperscript{114}, using both chemical and spectroscopic techniques. The results strongly suggested the structure (11.5) in preference to that of (11.3). The proton-decoupled $^{13}$C n.m.r. spectra of (11.3) and (11.6) exhibited similar P-C coupling constants for the saturated carbon atom directly bonded to two trifluoromethyl groups, Table 32.

**TABLE 32**

*Phosphorus-Carbon Coupling Constants in (11.3) and (11.6).*\textsuperscript{114}

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\delta$ C-(a)</th>
<th>$\gamma_{PC-a}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(11.3)</td>
<td>81.7 p.p.m.</td>
<td>11 Hz</td>
</tr>
<tr>
<td>(11.6)</td>
<td>73.1 p.p.m.</td>
<td>4.5 Hz</td>
</tr>
</tbody>
</table>

Although $\gamma_{PC-a}$ for (11.3) is larger than that for (11.6), it is smaller than expected for a carbon atom directly bonded to phosphorus. There are few reports\textsuperscript{197,198} of $^{13}$C n.m.r. spectra of pentacoordinate phosphoranes.

In order to obtain more data on $\gamma_{PC}$ coupling constants, a number
of pentacoordinate phosphoranes were examined by proton-decoupled Fourier Transform $^{13}$C n.m.r. spectroscopy. The carbon chemical shifts, coupling constants, integrations, and assignments are given in Tables 33-36. Assignments were made on the basis of chemical shifts and intensities of carbon atoms in similar environments.$^{133}$

In those compounds in which the carbon atoms directly bonded to phosphorus are constrained to the equatorial position, the magnitudes of $J_{PC}$ are all close to 150 Hz for saturated carbons and 117.7 Hz in the case of an aryl carbon (Table 34). The alkyl carbons of the phosphorane (11.10), Table 34, are rapidly exchanging between equatorial and apical sites. In this case $J_{PC}$ is only 77.9 Hz. There are no examples of $J_{PC}$ for a carbon atom constrained to the apical position of a TBP. However, it is known that the magnitude of $J_{PC}$ increases with the increase of s-character in the P-C bond.$^{199}$ Thus since apical bonds are longer, and have less s-character (Rundel's$^{3}$ Model) than equatorial bonds then one would expect apical $J_{PC}$ values to be smaller than equatorial. $J_{PC}$ values. This then would account for the reduced phosphorus-carbon (alkyl) coupling constant in (11.10). However, on the same lines the phosphorus-carbon (aryl) coupling constant would be expected to be higher than that observed, due to the sp$^{2}$ nature of the hybrid orbital on carbon.

In conclusion the results in Tables 33 - 36 clearly indicate that large couplings (ca. 150 Hz) would be expected for equatorial $J_{PC}$'s in pentacoordinate phosphoranes. Thus the structure (11.5) suggested from the work of Bone$^{114}$ for the hexafluoroacetone azide-phosphite adduct, would explain the low value (11 Hz) of the phosphorus-carbon (alkyl) coupling constant.

Since this work was finished, Burger has obtained further data on the hexafluoroacetone azine-phosphite adduct which also favours the structure (11.5).$^{200}$
TABLE 33
Carbon-13 N.M.R. Spectrum of 2-tertiary Butyl-2,2'-spirobi[1,3,2-benzo-dioxaphosphole], (11.9), in d-Chloroform.

<table>
<thead>
<tr>
<th>$\delta$ (ppm)</th>
<th>$J_{PC}$ (Hz)</th>
<th>Integration</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.2</td>
<td>0</td>
<td>553</td>
<td>a</td>
</tr>
<tr>
<td>42.2</td>
<td>153.0</td>
<td>77</td>
<td>b</td>
</tr>
<tr>
<td>110.2</td>
<td>13.2</td>
<td>942</td>
<td>c</td>
</tr>
<tr>
<td>121.8</td>
<td>0</td>
<td>1000</td>
<td>d</td>
</tr>
<tr>
<td>144.6</td>
<td>2.9</td>
<td>262</td>
<td>e</td>
</tr>
</tbody>
</table>
Table 34
Carbon-13 N.M.R. Spectrum of 2,2,3,3-Tetramethyl-5-phenyl-1,4-dioxa-5-phospha(5-P^)spiro[4.4]non-7-ene, (11.10), in d-Chloroform.

<table>
<thead>
<tr>
<th>δ (ppm)</th>
<th>$J_{PC}$ (Hz)</th>
<th>Integration</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>24.7</td>
<td>4.4</td>
<td>1427</td>
<td>a</td>
</tr>
<tr>
<td>34.5</td>
<td>77.9</td>
<td>1011</td>
<td>b</td>
</tr>
<tr>
<td>76.7</td>
<td>2.9</td>
<td>395</td>
<td>c</td>
</tr>
<tr>
<td>126.9</td>
<td></td>
<td>884</td>
<td></td>
</tr>
<tr>
<td>127.4</td>
<td></td>
<td>254</td>
<td></td>
</tr>
<tr>
<td>127.8</td>
<td></td>
<td>414</td>
<td>Not</td>
</tr>
<tr>
<td>128.4</td>
<td></td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>129.0</td>
<td></td>
<td>272</td>
<td>assigned</td>
</tr>
<tr>
<td>129.1</td>
<td></td>
<td>470</td>
<td></td>
</tr>
<tr>
<td>130.4</td>
<td></td>
<td>348</td>
<td></td>
</tr>
<tr>
<td>130.9</td>
<td></td>
<td>159</td>
<td></td>
</tr>
<tr>
<td>139.1</td>
<td>117.7</td>
<td>124</td>
<td>d</td>
</tr>
</tbody>
</table>

Diagram: 2,2,3,3-Tetramethyl-5-phenyl-1,4-dioxa-5-phospha(5-P^)spiro[4.4]non-7-ene, (11.10)
TABLE 35

Carbon-13 N.M.R. Spectrum of 8-Acetyl-2,2,3,3,7-pentamethyl-r-5-phenoxy-trans-9-phenyl-1,4,6-trioxa-5-phospha(5-P\(^\dagger\))spiro[4.4.]non-7-ene, (5.33-c) in d-Chloroform.

<table>
<thead>
<tr>
<th>( \delta ) (ppm)</th>
<th>( J_{PC} ) (Hz)</th>
<th>Integration</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.8</td>
<td>7.4</td>
<td>320</td>
<td>a</td>
</tr>
<tr>
<td>23.1</td>
<td></td>
<td>248</td>
<td>b, c, d, e</td>
</tr>
<tr>
<td>23.7</td>
<td></td>
<td>260</td>
<td></td>
</tr>
<tr>
<td>24.1</td>
<td>0</td>
<td>227</td>
<td></td>
</tr>
<tr>
<td>25.3</td>
<td></td>
<td>202</td>
<td></td>
</tr>
<tr>
<td>29.8</td>
<td>0</td>
<td>189</td>
<td>f</td>
</tr>
<tr>
<td>48.0</td>
<td>150.0</td>
<td>312</td>
<td>g</td>
</tr>
<tr>
<td>78.9</td>
<td>2.9</td>
<td>162</td>
<td>h</td>
</tr>
<tr>
<td>82.9</td>
<td>0</td>
<td>116</td>
<td>i</td>
</tr>
<tr>
<td>114.4</td>
<td>11.8</td>
<td>190</td>
<td>j</td>
</tr>
<tr>
<td>121.3</td>
<td>4.4</td>
<td>494</td>
<td>k</td>
</tr>
<tr>
<td>124.3</td>
<td></td>
<td>319</td>
<td></td>
</tr>
<tr>
<td>127.2</td>
<td></td>
<td>223</td>
<td></td>
</tr>
<tr>
<td>127.4</td>
<td></td>
<td>223</td>
<td></td>
</tr>
<tr>
<td>128.5</td>
<td></td>
<td>288</td>
<td></td>
</tr>
<tr>
<td>128.7</td>
<td></td>
<td>477</td>
<td></td>
</tr>
<tr>
<td>129.0</td>
<td></td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>129.2</td>
<td></td>
<td>300</td>
<td></td>
</tr>
<tr>
<td>129.6</td>
<td></td>
<td>277</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Not assigned</td>
</tr>
<tr>
<td>136.1</td>
<td>8.8</td>
<td>306</td>
<td>l</td>
</tr>
<tr>
<td>152.3</td>
<td>11.8</td>
<td>204</td>
<td>m</td>
</tr>
<tr>
<td>165.9</td>
<td>13.2</td>
<td>231</td>
<td>n</td>
</tr>
<tr>
<td>194.5</td>
<td>10.6</td>
<td>235</td>
<td>o</td>
</tr>
</tbody>
</table>
TABLE 36
Carbon-13 N.M.R. of 2,2,3,3-Tetramethyl-5-phenoxy-7,8-diphenyl-1,4,-
6-trioxa-5-phospha(5-P^)$piro[4.4]non-7-ene, (5.39-c), in d-Chloroform.

<table>
<thead>
<tr>
<th>δ (ppm)</th>
<th>Jpc</th>
<th>Integration</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.9</td>
<td></td>
<td>222</td>
<td>a,b,c,d</td>
</tr>
<tr>
<td>24.2</td>
<td>0</td>
<td>217</td>
<td></td>
</tr>
<tr>
<td>24.6</td>
<td>154.4</td>
<td>520</td>
<td></td>
</tr>
<tr>
<td>35.2</td>
<td></td>
<td>183</td>
<td>e</td>
</tr>
<tr>
<td>106.9</td>
<td>8.8</td>
<td>142</td>
<td>f</td>
</tr>
<tr>
<td>121.6</td>
<td>4.4</td>
<td>535</td>
<td>g</td>
</tr>
<tr>
<td>123.9</td>
<td></td>
<td>251</td>
<td></td>
</tr>
<tr>
<td>125.7</td>
<td></td>
<td>155</td>
<td></td>
</tr>
<tr>
<td>127.3</td>
<td></td>
<td>342</td>
<td></td>
</tr>
<tr>
<td>127.6</td>
<td></td>
<td>1000</td>
<td>Not Assigned</td>
</tr>
<tr>
<td>128.1</td>
<td></td>
<td>760</td>
<td>Assigned</td>
</tr>
<tr>
<td>128.4</td>
<td></td>
<td>668</td>
<td>Assigned</td>
</tr>
<tr>
<td>128.9</td>
<td></td>
<td>35</td>
<td>Assigned</td>
</tr>
<tr>
<td>129.1</td>
<td></td>
<td>666</td>
<td>Assigned</td>
</tr>
<tr>
<td>132.8</td>
<td>8.8</td>
<td>127</td>
<td>h</td>
</tr>
<tr>
<td>136.7</td>
<td>19.1</td>
<td>123</td>
<td>i</td>
</tr>
<tr>
<td>148.6</td>
<td>13.2</td>
<td>98</td>
<td>j</td>
</tr>
<tr>
<td>153.2</td>
<td>10.3</td>
<td>108</td>
<td>k</td>
</tr>
</tbody>
</table>

* Not observable.
**EXPERIMENTAL**

**Instrumentation.**

Melting points were determined on a Kofler heating stage and are uncorrected. Infrared spectra are for samples in nujol unless stated otherwise, and were recorded on a Perkin-Elmer 237 or 257 grating spectrometer. 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. Proton magnetic resonance spectra were recorded on a Varian model T60 in deuterochloroform as solvent unless otherwise stated. Proton shifts are relative to tetramethylsilane. Fluorine magnetic resonance spectra were recorded on a Varian model A60 or a Jeol PS100 instrument, with internal $\alpha,\alpha,\alpha$-trifluorotoluene as standard. Phosphorus chemical shifts were determined with a Varian DA60 spectrometer or by heteronuclear INDO R spectroscopy using a modified Varian T60 instrument. Phosphorus chemical shifts are relative to an 85% H$_3$PO$_4$ solution. Variable temperature nuclear magnetic resonance spectra were recorded on a Varian DA60 or a Jeol PS100 instrument. Proton decoupled Fourier Transform 13-Carbon magnetic resonance spectra were performed by the Physico-Chemical Measurements Unit, Harwell, Didcot, Berkshire on a Bruker HX90E instrument at 22.63 MHz, using a pulse length of 7µs and a post delay of 2s. Carbon chemical shifts are relative to tetramethylsilane. Gas-liquid chromatography was carried out on a Pye-Unicam series 104 chromatograph.

**General.**

Solutions in organic solvents were dried over magnesium sulphate
unless otherwise stated. A rotary evaporator was used for reduced pressure solvent removal except in the case of corrosive or air sensitive solutions in which case the 'swirling' technique was used. All operations involving air or moisture sensitive compounds were carried out under an atmosphere of dry, oxygen free, nitrogen. Liquid reagents were distilled prior to use.

Solvents were dried as follows:

Diethyl ether, petroleum spirit, hexane, and benzene were dried over sodium wire. Methanol and ethanol were refluxed over, and distilled from their alkoxides. Pyridine and triethylamine were refluxed over, and distilled from, potassium hydroxide. Chloro-benzene and o-dichloro-benzene were distilled and stored over molecular sieves. Dichloromethane was refluxed over, and distilled from, calcium hydride.

Small scale distillations were carried out using a Kugelrohr and the boiling points quoted are the oven temperatures over which distillation occurred.

'Hyflo' refers to the Koch-Lite Celite preparation, used as a filtering aid.
Preparation of 2-Chloro-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan.

High yields of this cyclic chlorophosphite were obtained from pinacol and phosphorus trichloride in ether using pyridine as base, (88.3%); b.p. 80-89/11 mm

Preparation of 2-Substituted-4,4,5,5-tetramethyl-1,3,2-dioxaphospholans from the 2-Chloro Compound.

General Method of Preparation.

2-Chloro-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan (0.05 mol) in ether (25 ml) was added dropwise to a vigorously stirred solution of the alcohol or thiol (0.05 mol) and pyridine (0.05 mol) in ether (100 ml) over 1 hour at 0°C. The reaction mixture was then refluxed with stirring for 1 - 2 hours and then filtered through 'Hyflo'. The solvent was then removed from the filtrate by distillation and the residue distilled under reduced pressure using a 10 cm Vigreux fractionating column. The following compounds were prepared:

1). 2-Methoxy-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan, (70%); b.p. 60-61°/11 mm; δ 6.47 (3H, d, J<sub>PH</sub> 13 Hz), 8.63 (6H, s), and 8.77 (6H, s).

2). 2-Ethoxy-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan, (55%); b.p. 69-70°/11 mm; δ 6.08 (2H, dq, J 7, J<sub>PH</sub> 11 Hz), 8.62 (6H, s), 8.77 (6H, s), and 8.77 (3H, t, J 7 Hz).

3). 2-iso-Proxoxy-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan; (50%); b.p. 75-77°/11 mm.
4). 2-tertiary-Butoxy-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan; (78%); b.p. 82-83°/11 mm; τ 8.67 (9H, s), 8.68 (6H, s), and 8.80 (6H, s).

5). 2-Ethylthio-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan; (50%); b.p. 97-113/11 mm; τ 7.20 (2H, dq, J 7, JPH 11 Hz), 8.68 (6H, s), 8.70 (3H, t, J 7 Hz), and 8.77 (6H, s).

6). 2-Phenoxy-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan; (75%); b.p. 90-105°/0.5 mm; τ 2.83-3.40 (5H, m), 8.60 (6H, s), and 8.75 (6H, s).

7). 2-Phenylthio-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan; was prepared by S.A. Bone:

8). 2-(N,N-Dimethylamino)-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan; was prepared by S.A. Bone; b.p. 65-68/3 mm.

Reaction of 2-Substituted-4,4,5,5-Tetramethyl-1,3,2-dioxaphospholans with Biacetyl.

General Method.

Biacetyl (0.01 mol) was added dropwise to the rapidly stirred dioxaphospholan (0.01 mol) over 15 minutes. After an induction period of 2-3 minutes after the start of addition, the temperature rose rapidly. A cold water bath was used to keep the temperature below 50°. After the addition the reaction was allowed to go to completion by leaving it overnight at ambient temperature.

The following 1:1 adducts of biacetyl with 2-substituted-4,4,5,5-tetramethyl-1,3,2-dioxaphospholans (5.10 a-f) were prepared (no analyses were obtained for these compounds due to their hydrolytic instability):
1). 5-Methoxy-2,2,3,3,7,8-hexamethyl-1,4,6,9-tetraoxa-5-phospha(5-P^)
Spiro[4.4]non-7-ene (5.10 - a); m.p. 55-60° (40-60 petrol);
δ 6.42 (3H, d,  1J_{PH} 14 Hz), 8.18 (6H, s), and 8.73 (12H, s);
δ (C₆H₆) 6.50 (3H, d,  1J_{PH} 14 Hz), 8.68 (6H, s), and 8.87 (12H, s);
δ (o-C₆H₄Cl₂) 6.47 (3H, d,  1J_{PH} 14 Hz), 8.28 (6H, s), and 8.83
(12H, s); m/e (no mass peak), 194, 179, 165, 152, 147, 138, 136,
121, 113, 100, 99, 82, 67, and 58; ³¹P (CH₂Cl₂) + 34.2 ppm;
¹³C (o-C₆H₄Cl₂) see Chapter 5.

2). 5-Ethoxy-2,2,3,3,7,8-hexamethyl-1,4,6,9-tetraoxa-5-phospha(5-P^)
Spiro[4.4]non-7-ene (5.10-b); viscous oil; δ (o-C₆H₄Cl₂) 6.12
(2H, dq,  1J 7,  2J_{PH} 9.5 Hz), 8.28 (6H, s), 8.67 (3H, dt,  1J 7,  1J_{PH}
1 Hz), and 8.82 (12H, s); ³¹P (CH₂Cl₂) + 36 ppm.

3). 5-iso-Propoxy-2,2,3,3,7,8-hexamethyl-1,4,6,9-tetraoxa-5-phospha(5-P^)
Spiro[4.4]non-7-ene (5.10-c); viscous oil; δ (o-C₆H₄Cl₂) 5.43
(1H, dsept,  1J 6,  3J_{PH} 8 Hz), 8.27 (6H, s), and 8.7 - 8.9 (18H, m);
³¹P (CH₂Cl₂) +37.8 ppm.

4). 5-tertiary-Butoxy-2,2,3,3,7,8-hexamethyl-1,4,6,9-tetraoxa-5-
phospha(5-P^)Spiro[4.4]non-7-ene (5.10-d); m.p. 40-50° (not
recrystallisable); δ (C₆H₆) 8.33 (6H, s), 8.60 (9H, s), 8.80
(6H, s), and 8.83 (6H, s); ³¹P (CH₂Cl₂) +36.8 ppm.

5). 5-Ethylthio-2,2,3,3,7,8-hexamethyl-1,4,6,9-tetraoxa-5-phospha(5-P^)
Spiro[4.4]non-7-ene (5.10-e); very unstable viscous oil; δ (C₆H₆)
7.35 (2H, dq,  1J 7,  2J_{PH} 17 Hz), 8.37 (6H, s), 8.67 - 9.0 (3H,
unresolved dt), and 8.82 (12H). No ³¹P signal could be
detected.

6). 5-Phenoxy-2,2,3,3,7,8-hexamethyl-1,4,6,9-tetraoxa-5-phospha(5-P^)
Spiro[4.4]non-7-ene (5.10-f); very unstable crystalline solid.
No spectroscopic data could be obtained for this compound owing
to the unstable nature of this compound.
Reaction of 2-Phenoxy-4,4,5,5-Tetramethyl-1,3,2-dioxaphospholan with
Biacetyl in Benzene Solution.

Biacetyl (53 mg, 0.62 mmol) was added to a solution of
2-phenoxy-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan (149 mg, 0.62
mmol) in benzene (0.5 ml) in an n.m.r. tube. The reaction was then
monitored by $^1$H n.m.r. at ca. 35°.

After 5 hours there was a build up to a maximum concentration
of a compound whose $^1$H n.m.r. was consistent with the 1:1 adduct,
5-phenoxy-2,2,3,3,7,8-hexamethyl-1,4,6,9-tetraoxa-5-phospha(5-P$^V$)
spiro[4.4]non-7-ene (5.10-f); $\tau$ ($C_6H_6$) 8.55 (6H, s) and 8.80 (12, broad s).

During the formation of this compound its decomposition was
occurring. After ca. 18 hours the major product was consistent with
the $^1$H spectrum expected for 2-phenoxy-4,4,5,5-tetramethyl-1,3,2-
dioxaphospholan 2-oxide; $\tau$ ($C_6H_6$) 8.83 (6H, s) and 8.9 (6H, s).

Hydrolysis of 5-Methoxy-2,2,3,3,7,8-hexamethyl-1,4,6,9-tetraoxa-5-
-phospha(5-P$^V$)spiro[4.4]non-7-ene (5.10-a).

A solution of the adduct (5.10-a) in ether at ambient temperature
was stirred with exposure to the atmosphere for 3-4 hours. Evaporation
of the solvent and other volatiles gave 2-methoxy-4,4,5,5-tetramethyl-1,
3,2-dioxaphospholan 2-oxide, as a white crystalline solid, m.p. 100-101°
(ether); $^{224}$$\nu_{max}$ 1405, 1285, 1275, 1150, 1055, 1020, 970, 900, 835,
805, 780 and 660 cm$^{-1}$; m/e 194, 179, 152, 136, 121, 113, and 82;
$\tau$ 6.28 (3H, d, $J_{PH}$ 11 Hz), 8.58 (6H, s), and 8.63 (6H, s); (Found:
C, 43.5; H, 7.9; P, 15.6. C$\textsubscript{7}$H$\textsubscript{15}$O$_4$P requires C, 43.3; H, 7.8;
P, 15.9%).
Reaction of 2-Ethoxy-4,4,5,5-tetramethyl-1,3,2-dioxaphospholane with Benzil.

A solution of benzil (55 mg, 0.26 mmol) in benzene (1 ml) was added to a solution of 2-ethoxy-4,4,5,5-tetramethyl-1,3,2-dioxaphospholane (50 mg, 0.26 mmol) in benzene (1 ml). The reaction mixture was heated to 50° and left for 3 hours. Evaporation of the solvent gave 5-ethoxy-2,2,3,3-tetramethyl-7,8-diphenyl-1,4,6,9-tetraoxa-5-phospha-(5-P^)spiro[4.4]non-7-ene (5.22) as a colourless viscous oil, \( \tau (C_6H_6) 5.98 \) (2H, dq, \( J 7, 10.5 \) Hz), \( 8.82 (12H, s) \), and \( 8.92 (3H, dt, J 7, J_{PH} 1.5 \) Hz); \( ^{31}P (CH_2Cl_2) +36.5 \) p.p.m. No analysis was obtained for this compound due to its hydrolytic instability.

Reaction of 2-Substituted-4,4,5,5-tetramethyl-1,3,2-dioxaphospholanes with 3-Benzylidene-2,4-pentanedione.

General Method.

A solution of 3-benzylidene-2,4-pentanedione (0.05 mol) and the 2-substituted-4,4,5,5-tetramethyl-1,3,2-dioxaphospholane (0.05 mol) in a mixture of benzene and hexane (4.4 ml of 1:4 v/v) was allowed to react at 40° overnight (ca. 16 hours). Evaporation of the solvent gave the 1:1 adduct. Fractional recrystallisation from ether gave the trans isomer. The following 1:1 adducts were prepared by this method:

1a). \( r-5\)-Methoxy-8-acetyl-2,2,3,3,7-pentamethyl-trans-9-phenyl-1,4,6-trioxa-5-phospha(5-P^)spiro[4.4]non-7-ene (5.33-a), m.p. 129-133° (ether); \( ^{13}C (C_6H_5Cl) 6.12 (1H, d, J_{PH} 21 \) Hz), 6.69 (3H, d, \( J_{PH} 12.5 \) Hz), 7.59 (3H, d, \( J_{PH} 1 \) Hz), 8.28 (3H, s), 8.87 (3H, s), 9.05 (3H, s), 9.19 (3H, s), and 9.87 (3H, s); \( ^{31}P (CH_2Cl_2) +13.5 \) p.p.m.
b). cis-9-phenyl isomer, τ (C₆H₅Cl) 7.02 (3H, d, $\nu_{PH}$ 12.5 Hz), 7.63 (3H, d, $\nu_{PH}$ 1 Hz), 8.23 (3H, s), and 8.9-9.0 (12H, m).

2a). r-5-tertiary-Butoxy-8-acetyl-2,2,3,3,7-pentamethyl-trans-9-phenyl-1,4,6-trioxa-5-phospha(5-P)V spiro[4.4]non-7-ene, (5.33-b), m.p. 147-150° (ether); $\nu_{max}$ 1655, 1570, 1555, 1155, 1140, 1035, 1010, 975, 930, 745, 695, and 655 cm⁻¹; τ (C₆H₅Cl) 5.96 (1H, d, $\nu_{PH}$ 22.5 Hz), 7.52 (3H, d, $\nu_{PH}$ 1 Hz), 8.26 (3H, s), 8.63 (9H, s), 8.75 (3H, s), 9.01 (3H, s), 9.19 (3H, s), and 9.89 (3H, s); $^{31}$P (CH₂Cl₂) +14.5 p.p.m.; (Found: C, 64.7; H, 8.1.

b). cis-9-phenyl isomer, τ (C₆H₅Cl) 5.68 (1H, d, $\nu_{PH}$ 25 Hz), 8.22 (3H, d, $\nu_{PH}$ 1 Hz), 8.11 (3H, s), 8.79 (6H, broad s), and 8.89 (6H, broad s).

3a). r-5-Phenoxy-8-acetyl-2,2,3,3,7-pentamethyl-trans-9-phenyl-1,4,6-trioxa-5-phospha(5-P)V spiro[4.4]non-7-ene, (5.33-c), m.p. 149-150° (ether); $\nu_{max}$ 1655, 1595, 1565, 1215, 1155, 975, 935, 915, 880, 775, and 755 cm⁻¹; τ 2.7-3.3 (10H, m), 5.73 (1H, d, $\nu_{PH}$ 23 Hz), 8.10 (3H, s), 8.35 (3H, d, $\nu_{PH}$ 1 Hz), 8.62 (3H, s), 8.70 (3H, s), 8.97 (3H, s), and 9.75 (3H, s); $^{31}$P (CH₂Cl₂) +15.5 p.p.m.; $^{13}$C (CDCl₃) see Chapter 11. (Found: C, 67.25; H, 6.9. C₂₄H₂₈O₅P requires C, 67.3; H, 6.8%).

b). No cis-9-phenyl isomer was observed, even after heating to over 100°.

4a). r-5-Dimethylamino-8-acetyl-2,2,3,3,7-pentamethyl-trans-9-phenyl-1,4,6-trioxa-5-phospha(5-P)V spiro[4.4]non-7-ene, (5.33-e), m.p. 151-155°. $^{13}$C (C₆H₄Cl₂) 6.17 (1H, d, $\nu_{PH}$ 19 Hz), 7.43 (6H, d, $\nu_{PH}$ 9.5 Hz), 7.57 (3H, d, $\nu_{PH}$ 1 Hz), 8.15 (3H, s), 8.88 (3H, s), 9.02 (3H, s), 9.20 (3H, s), and 9.87 (3H, s); $^{31}$P (CH₂Cl₂) +16.5 p.p.m.
b). cis-9-phenyl isomer, 7.59 (3H, d, $J_{PH} 1$ Hz), 8.18 (3H, s), 8.77 (3H, s), 8.88 (3H, s), 8.92 (3H, s), and 8.96 (3H, s).

5a). r-5-Ethylthio-8-acetyl-2,2,3,3,7-pentamethyl-trans-9-phenyl-1,4,6-trioxa-5-phospha(5-P)spiro[4.4]non-7-ene, (5.33-d), hydrolytically unstable crystalline solid; $\tau$ 2.92 (5H, s), 5.92 (1H, d, $J_{PH} 17.5$ Hz), 7.62 (3H, d, $J_{PH} 1$ Hz), 8.12 (3H, s), 8.67 (3H, s), 8.75 (3H, s), 9.18 (3H, s), 9.77 (3H, s), 8.47-8.83 (3H, m), and 7.0-7.9 (2H, m); No $^{31}$P signal could be detected. This compound could not be obtained in an analytically pure state.

b). cis-9-phenyl isomer, $\tau$ 5.8 (1H, d, $J_{PH} 23$ Hz), 7.65 (3H, d, $J_{PH} 1$ Hz), 8.18 (3H, s), 8.65 (6H, broad s), 8.70 (6H, broad s).

Preparation of 2-Phenyl-acrylophenone.

(a) Preparation of 2-Phenyl-acetophenone.

This was prepared by the method of Allen and Barker, $^{204}$ m.p. 53-54° (methanol).

(b) Preparation of 2-Phenyl-acrylophenone.

Formaldehyde solution (30 ml of 40% w/v) was added to a solution of 2-phenyl-acetophenone (19.6g, 0.1 mol) in methanol (80 ml). The mixture was then heated to reflux and piperidine (0.5 ml) was then added dropwise over 10 minutes. After refluxing for 6 hours the reaction mixture was allowed to cool and then water (100 ml) was added. A colourless oil separated out. The oil was extracted with methylene chloride (3 x 100 ml) and the combined organic layers washed successively with dilute sulphuric acid, dilute sodium bicarbonate solution, and water, and then dried. Evaporation of the solvent and distillation of the residue under reduced
pressure gave 2-phenyl-acrylophenone, (10.2 g, 49%); b.p. 132-136°/0.3 mm; 2.1-2.3 (2H, m), 2.6-2.9 (8H, m), 4.23 and 4.48 (2H, centre of AB, dd).

**Reaction of 2-Substituted-4,4,5,5-Tetramethyl-1,3,2-dioxaphospholans with 2-Phenyl-acrylophenone.**

**General Method.**

A solution of 2-phenyl-acrylophenone (0.05 mol) and the 2-substituted-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan (0.05 mol) in benzene (5 ml) was allowed to react at 50-60° for 72 hours. Evaporation of the solvent gave the 1:1 adduct as a viscous oil which crystallised on standing for several weeks.

The following 1:1 adducts were prepared:

1. 5-Methoxy-2,2,3,3-tetramethyl-7,8-diphenyl-1,4,6-trioxa-5-phospha(5-P^)spiro[4.4]non-7-ene, (5.39-a), τ (CH_2Cl_2) 6.39 (3H, d, J_P 13 Hz), 7.05 (2H, ABX, J' 19.5, J'_PH 18 Hz, τ_A 6.87, τ_B 7.16), and 8.74 (12H, broad s); ^31P (CH_2Cl_2) +13.5 p.p.m. This compound could not be obtained in an analytically pure state.

2. 5-tertiary-Butoxy-2,2,3,3-tetramethyl-7,8-diphenyl-1,4,6-trioxa-5-phospha(5-P^)spiro[4.4]non-7-ene, (5.39-b), viscous oil, τ (C_6H_6) 6.78 (2H, ABX, J'_ 19.2, J'_PH 17.2 Hz, τ_A 6.58, τ_B 7.00), 8.57 (9H, s), and 8.83 (12H, broad s); m/e 428, 372, 455, 328, 314, 290, 272, 256, and 208; ^31P (C_6H_6) +17.1 p.p.m. This compound could not be obtained in an analytically pure state.

3. 5-Phenoxy-2,2,3,3-tetramethyl-7,8-diphenyl-1,4,6-trioxa-5-phospha(5-P^)spiro[4.4]non-7-ene, (5.39-c), m.p. 125-128° (ether);
   τ 2.7-3.8 (15H, m), 6.73 (2H, ABX, J' 19.5, J'_PH 18 Hz, τ_A 6.50, τ_B 6.97), and 8.62 (12H, s); ^31P (CH_2Cl_2) +24.0 p.p.m; ^13C (CDCl_3) see Chapter 11. This compound could not be obtained analytically pure.
4) 5-Dimethylamino-2,2,3,3-tetramethyl-7,8-diphenyl-1,4,6-trioxa-
-5-phospha(5-P\textsuperscript{V})spiro[4.4]non-7-ene, (5.39-d), \( \tau (C_6H_6) 6.71 \)
(2H, d, \( J_{PH} 18 \text{ Hz} \)), 7.03 (6H, d, \( J_{PH} 10 \text{ Hz} \)), 8.61 (6H, broad s),
and 8.70 (3H, broad s); \( ^{31}P (C_6H_6) +19.5 \text{ p.p.m.} \) This compound
could not be obtained in an analytically pure state.
Chapter 7.

Preparation of 1-Phenylphospholan.

Phenyldichlorophosphine (25 g, 0.14 mol) in ether (75 ml) was added dropwise with vigorous stirring to a solution of the di-Grignard reagent of 1,4-dibromobutane (50 g, 0.23 mol) in ether (200 ml) at 0° over 6 hours. The reaction mixture was then filtered and the solvent evaporated to give a grey-white semi-solid residue. This residue was then subjected to flash distillation under reduced pressure. The crude distillate was then fractionated under reduced pressure using a short Vigreux column, to give 1-phenylphospholan, (4.3 g, 19%), b.p. 135-140°/20 mm.

Preparation of 1-phenylphosphorinan.

Phenyldichlorophosphine (14.3 g, 0.08 mol) in ether (50 ml) was added dropwise with vigorous stirring to a solution of the di-Grignard reagent of 1,4-dibromopentane (55.2 g, 0.24 mol) in ether (200 ml) at 0° over 4 hours. The reaction mixture was then refluxed for 0.5 hours, cooled to 0° again and a saturated, deoxygenated aqueous solution of ammonium chloride (100 ml) was slowly added keeping the temperature below 5°. The organic layer was then separated and the aqueous layer further extracted with ether (2 x 100 ml). The combined organic layers were then dried, the solvent evaporated, and the residual oil distilled under reduced pressure to give 1-phenylphosphorinan, (2.6 g, 18%), b.p. 75-79°/0.3 mm.
Reaction of 1-phenylphospholan with Hexafluoroacetone.

Hexafluoroacetone (3 ml) was condensed into a stirred solution of 1-phenylphospholan (1.4 g) in n-hexane (30 ml) at -78°. After 30 minutes the solution was allowed to warm to 0° and the solvent removed under reduced pressure, to give the 2:1 adduct, 5-phenyl-2,2,3,3-tetrakis(trifluoromethyl)-1,4-dioxa-5-phospha(5-P^)spiro[4.4]nonane, (7.1), as a white solid, \( \nu_{\text{max}} \) 1595, 1240, 1210, 1360, 1310, 995, 960, 950, 875, 770, 745, and 690 cm\(^{-1}\); \( \tau \) 1.9-2.56 (5H, m) and 6.34-9.07 (8H, m); \( ^{19}\text{F} \) (toluene) +5.50 (12F, s) p.p.m.; \( ^{31}\text{P} \) (CH\(_2\)Cl\(_2\)) -16.3 p.p.m.; This compound was not obtained in an analytically pure state.

Reaction of 1-phenylphosphorinan with Hexafluoroacetone.

Hexafluoroacetone (3 ml) was condensed into a stirred solution of 1-phenylphosphorinan (1.5 g) in a mixture of n-hexane (30 ml) and ether (10 ml) at -73°. After 30 minutes the solution was allowed to warm to 0° and then left at this temperature for a further 20 minutes. Removal of the solvent under reduced pressure gave the 2:1 adduct, 5-phenyl-2,2,3,3-tetrakis(trifluoromethyl)-1,4-dioxa-5-phospha(5-P^)spiro[4.5]decane, (7.25), as a white solid, m/e 510, 491, 481, 467, 454, 441, 433, 344, and 325; \( ^{19}\text{F} \) (CH\(_2\)Cl\(_2\)) +5.52 (12F, s) p.p.m.; \( ^{31}\text{P} \) (CH\(_2\)Cl\(_2\)) + 3.5 p.p.m. This compound was not obtained in an analytically pure state.

Preparation of Diethyl Peroxide.

This was prepared by the method of Denney.\(^{55}\) The use of an
ordinary flask instead of the preferred creased flask gave lower
yields, (14.7 g, 37%), b.p. 61-66°. This compound was stored in a
deep-freeze at -20° over molecular sieve.

Reaction of 1,1-Diethoxy-1-phenylphospholan(P^) with Pinacol.

A solution of 1-phenylphospholan (95 mg, 0.57 mmol) and diethyl
peroxide (52 mg, 0.65 mmol) in dichloromethane (0.5 ml) in an n.m.r.
tube was kept at 0-5° in a fridge for 2 weeks, to give 1,1-diethoxy-1-
-phenylphospholan(P^), (7.6), \( \tau \) 6.68 (4H, dq, \( J \) 7, \( J_{PH} \) 7 Hz), 7.4-7.9
(CH, m), and 8.74 (6H, t, \( J \) 7 Hz).

Addition of this solution to anhydrous pinacol (67 mg, 0.57 mmol)
and evaporation of the solvent and other volatiles under reduced pressure
gave 2,2,3,3-tetramethyl-5-phenyl-1,4-dioxa-5-phospha(5-P^)spiro[4.4]
nonane, (7.5), m.p. 79-84° (40-60 petrol); \( \nu_{max} \) 1210, 1155, 1115, 975,
915, 780, 750, 705, and 650 cm\(^{-1}\); m/e 280, 180, 152, 139, 134, and 124;
\( \tau \) 1.9-2.73 (5H, m), 7.77-9.17 (8H, m), and 8.98 (12H, s); \( ^{31}P \) (CH\(_2\)Cl\(_2\))
+ 17.1 p.p.m.; (Found: C, 68.7; H, 8.9; P, 11.4. C\(_{16}\)H\(_{25}\)O\(_2\)P requires
C, 68.55; H, 9.0; P, 11.05%).

Reaction of 1-Phenylphospholan with Diethyl Peroxide and Pinacol in situ.

A solution of 1-phenylphospholan (249 mg, 1.52 mmol), diethyl
peroxide (137 mg, 1.52 mmol), and anhydrous pinacol (137 mg, 1.52 mmol)
in dichloromethane (0.5 ml) in an n.m.r. tube was kept at 0-5°, and the
reaction monitored by \( ^{1}H \) n.m.r. After 13 days the reaction had gone to
completion. The solvent and other volatiles were evaporated to give an
almost quantitative yield of 2,2,3,3-tetramethyl-5-phenyl-1,4-dioxa-5-
-phospha(5-$P^V$)spiro[4.4]nonane, (7.5), m.p. and spectral details were identical to the sample prepared previously.

**Preparation of 5-Ethyl-2,2,3,3-tetramethyl-1,4-dioxa-5-phospha(5-$P^V$) spiro[4.4]nonane, (7.12).**

(a) **Preparation of 2-Chloro-1,3,2-dioxaphospholan.**

High yields of this cyclic chlorophosphite were prepared from phosphorus trichloride and ethylene glycol in methylene chloride in the absence of a tertiary amine, using the method of Lucas,\textsuperscript{178} b.p. 45-47°/13 mm.

(b) **Preparation of 1-(\textbeta-Chloroethoxy)-3-phospholene 1-Oxide.**

Butadiene (14.2 g, 0.26 mol) was condensed into a 100 ml Carius tube. 2-Chloro-1,3,2-dioxaphospholan (33.1 g, 0.26 mol) and a polymerisation inhibitor (2 mol % hydroquinone) were then added, the tube sealed, and heated to 100° for 15 hours. Distillation under reduced pressure gave, 1-(\textbeta-Chloroethoxy)-3-phospholene 1-oxide, (22.8 g, 48%); b.p. 110-118°/0.4 mm;\textsuperscript{172} \textnu_max (film) 1610, 1395, 1300, 1250, 1205, 1120, 1080, 1030, 960, 925, 860, 760, 715, and 665 cm\textsuperscript{-1}; \tau 4.03 (2H, d, \textdelta_{PH} 3H Hz), 5.73 (2H, dq, \textdelta 6, \textdelta_{PH} 8 Hz), 6.25 (2H, dt, \textdelta 6; \textdelta_{PH} 1 Hz), and 7.52 (4H, d, \textdelta_{PH} 12 Hz).

(c) **Hydrogenation of 1-(\textbeta-Chloroethoxy)-3-phospholene 1-Oxide.**

Adams catalyst (1.2 g) was added to a solution of 1-(\textbeta-Chloroethoxy)-3-phospholene-1-oxide (20 g) in glacial acetic acid (100 ml) and the mixture hydrogenated at normal temperature and pressure. After one equivalent of hydrogen had been taken up, (ca 2 h) the solution was filtered through 'Hyflo' and the solvent removed under reduced pressure. The residue was taken up in dichloromethane (250 ml) and washed with water (3 x 100 ml), dilute sodium bicarbonate solution and finally water again. The organic layer was then dried, the solvent evaporated and
the residue distilled under reduced pressure to give, 1-(\(\beta\)-chloroethoxy)phospholan 1-oxide (15.8 g, 78%); b.p. 120-130°/0.2 mm; m.p. ambient temperature; \(\nu_{\text{max}}\) (film) 1450, 1410, 1275, 1220, 1190, 1110, 1085, 1025, 960, 920, 880, 730, and 660 cm\(^{-1}\); \(\tau\) 5.60-5.95 (2H, m), 6.33 (2H, dt, \(J_6\) 6, \(J_{\text{PH}}\) 0.5 Hz), and 7.8-8.5 (8H, m).

d) Preparation of 1-Chlorophospholan 1-Oxide.

Phosphorus pentachloride (6 g, 29 mmol) was added to a stirred solution of 1-(\(\alpha\)-chloroethoxy)-phospholan 1-oxide (8 g, 44 mmol) in carbon tetrachloride (40 ml) and then the mixture heated to 70°. After all the phosphorus pentachloride had reacted a further portion of phosphorus pentachloride (3.14 g, 15 mmol) was added and the mixture stirred at 70° until reaction was complete (ca 2 h). The solvent and volatile products were then removed under reduced pressure and the residue distilled to give 1-chlorophospholan 1-oxide (5.3 g, 61%); b.p. 67-75°/0.1 mm; \(\nu_{\text{max}}\) (film) 1460, 1450, 1405, 1275, 1230, 1110, 1060, 1025, 865, 725, and 680 cm\(^{-1}\).

(e) Preparation of 1-Ethylphospholan 1-Oxide.

A solution of ethylmagnesium chloride in ether (23.1 ml, 1.88 N) was added dropwise to a stirred solution of 1-chlorophospholan 1-oxide (5 g, 36 mmol) in ether (25 ml) over 45 minutes at 0°, and then the mixture refluxed for 16 hours. After cooling to 0°, dilute hydrochloric acid (25 ml, 2N), was added and the aqueous layer saturated with ammonium chloride. The ether was removed under reduced pressure and the aqueous solution extracted with dichloromethane (3 x 100 ml). The combined extracts were dried, the solvent evaporated and the residue distilled under reduced pressure to give, 1-ethylphospholan 1-oxide, (2 g, 42%); b.p. 120-130°/0.2 mm; \(\nu_{\text{max}}\) (film) 1460, 1405, 1265, 1175, 1110, 1055, 1030, 1025, 855, 765, 740, 725, and 695 cm\(^{-1}\); \(\tau\) (C\(_6\)H\(_6\)).
8.1-8.9 (10H, m), 9.13 (3H, dt, J = 6, J = 1 Hz). This compound was not analysed due to its extremely hygroscopic nature.

(f) Reduction of 1-Ethylphospholan 1-Oxide.

A mixture of 1-ethylphospholan 1-oxide (1 g) and polymethylhydrogensiloxane (M.S. 1107; 1 ml) was heated slowly to 150°, at which temperature the mixture became a polymeric mass. The mixture was cooled to 120° and held at this temperature for 45 minutes and then the phosphine and water were distilled out of the glass under reduced pressure (120°/100 mm). The phosphine was then redistilled from calcium hydride to give 1-ethylphospholan (0.7 g, 62%), b.p. 99-101°/100 mm; \( v_{\text{max}} \) (film) 1475, 1450, 1105, 1030, 830, and 670 cm\(^{-1}\).

(g) Reaction of 1-Ethylphospholan with Diethyl Peroxide and Pinacol in situ.

A mixture of 1-ethylphospholen (224 mg, 1.93 mmol), diethyl peroxide (178 mg, 2.23 mmol), and anhydrous pinacol (228 mg, 1.93 mmol) in dichloromethane (1 ml) in an n.m.r. tube was kept at 31°, and the reaction monitored by \(^1\)H n.m.r. After 3 hours the reaction was complete. The solvent and other volatiles were then removed under reduced pressure to give 5-ethyl-2,2,3,3-tetramethyl-1,4-dioxa-5-phospha(5-P\(^\gamma\))spiro[4.4]nonane (7.12), in quantitative yield, m.p. ca. -20°, \( v_{\text{max}} \) (film) 1450, 1380, 1370, 1360, 1255, 1210, 1165, 1150, 1110, 1065, 975, 910, 850, 775, and 690 cm\(^{-1}\); m/e (no mass peak), 132, 131, 104, 85, 78, 76, 75, and 59; \( \tau \) 8.0-9.17 (13H, m), and 8.89 (12H, s); \(^{31}\)P (\( \text{CH}_2\text{Cl}_2 \)) +16.9 p.p.m. No analysis was obtained for this compound due to the difficulties of purification.

Preparation of 4,4,5,5-Tetramethyl-2-phenyl-1,3,2-dioxaphospholan.

Solutions of phenyldichlorophosphine (35.8 g, 0.2 mol) in ether
(150 ml) and anhydrous pinacol (23.6 g, 0.2 mol) in ether (150 ml) were added dropwise simultaneously to a stirred solution of pyridine (32 g, 0.4 mol) in ether (11 ml) over 4.5 hours at 0°. The mixture was then left stirring for a further 16 hours at ambient temperature. The reaction mixture was then filtered through 'Hyflo', the solvent distilled, and the solid residue distilled to give 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaphospholan (23.2 g, 52%); b.p. 99-115°/0.5 mm; m.p. 90-100°. This compound reacted slowly with d-chloroform, \( \tau 2.83-3.40 \) (5H, m), 8.6 (6H, s), and 8.75 (6H, s).

**Preparation of 2,3-Dimethyl-1,3-butadiene.**

Good yields of this diene were obtained by dehydration of pinacol using hydrobromic acid.208

**Reaction of 4,4,5,5-Tetramethyl-2-phenyl-1,3,2-dioxaphospholan with 2,3-Dimethyl-1,3-butadiene.**

A mixture of 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaphospholan (1.35 g, 6.04 mmol) and 2,3-dimethyl-1,3-butadiene (1.5 g, 18.3 mmol) was kept at ambient temperature for 3 days. The resulting crystalline product was separated by decantation and triturated with cold 40-60 petrol to give 2,2,3,3,7,8-hexamethyl-5-phenyl-1,4-dioxa-5-phospha(5-P\(^V\))-spiro[4.4]non-7-ene (7.18), in quantitative yield; \( \tau 2.23-2.97 \) (5H, m), 7.63 (4H, d, \( \delta_{\text{ppm}} 14 \) Hz), 8.57 (6H, s), and 9.02 (12 H, s); \(^{31}\)P (CH\(_2\)Cl\(_2\)) + 17.5 p.p.m. An analytical sample could not be obtained due to the hygroscopic nature of this compound.
Reaction of 4,4,5,5-Tetramethyl-2-phenyl-1,3,2-dioxaphospholan with 1,3-Butadiene.

Butadiene (4.3 g) was condensed into a 50 ml Carius tube containing the dioxaphospholan (6.1 g). The tube was sealed and kept at ambient temperature for 2 weeks. The tube was periodically warmed to 50-60° to redissolve the starting phosphonite and product to ensure thorough mixing of reactants. The excess diene was then allowed to evaporate to give 2,2,3,3-tetramethyl-5-phenyl-1,4-dioxa-5-phospa(5-P)V-spiro[4.4]non-7-ene (11.10), m.p. 94-97° (40-60 petrol); τ 2.13-2.93 (5H, m), 4.37 (2H, d, JPH 28 Hz), 7.63 (2H, dd, J 16, JPH 10 Hz), 7.77 (2H, dd, J 16, JPH 10 Hz), and 9.00 (12H, s); 31P (CH2Cl2) +10 p.p.m.

An analytical sample could not be obtained due to the hygroscopic nature of this compound.

Preparation of Ethylidichlorophosphine.

This was prepared by the reduction of the aluminium chloride-phosphorus trichloride-ethyl chloride complex in diethyl phthalate solution by finely powdered antimony according to the method of Perry, Reesor, and Ferron, 209 (45%) b.p. 110-114°/756 mm; τ 7.73 (2H, dq, J 7, JPH 17 Hz), and 8.75 (3H, dt, J 7, JPH 15 Hz).

Preparation of 2-Ethyl-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan.

Solutions of ethylidichlorophosphine (13.1 g, 0.1 mol) in ether (75 ml) and anhydrous pinacol (11.8 g, 0.1 mol) in ether (75 ml) were added dropwise simultaneously to a stirred solution of pyridine (16 g,
0.2 mol) in ether (500 ml) over 4.5 hours at 0°. The mixture was then left stirring for a further 16 hours at ambient temperature. The reaction mixture was then filtered through 'Hyflo', the solvent evaporated, and the residue distilled under reduced pressure to give 2-ethyl-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan, (2.8 g, 16.5%), b.p. 61-5°/8 mm; \( \tau \) (C\(_6\)H\(_6\)) 8.2-8.92 (5H, m), 8.63 (6H, s), and 8.65 (6H, s); \( ^{31}P \) (C\(_6\)H\(_6\)) -210 p.p.m.

Reaction of 2-Ethyl-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan with 2,3-Dimethyl-1,3-butadiene.

A mixture of the diene (0.5 g) and the phosphonite (0.88 g) in an n.m.r. tube was kept at 80° and the reaction monitored by \( ^1H \) n.m.r. and \( ^{31}P \) n.m.r. After 16 hours a singlet appeared at \( \tau \) 8.83 consistent with the 1:1 adduct, 5-ethyl-2,2,3,3,7,8-hexamethyl-1,4-dioxa-5-phospha-(5-P\(^V\))spiro[4.4]non-7-ene (7.21). No \( ^{31}P \) signal could be detected for this compound. On further heating this singlet decayed and a new singlet at \( \tau \) 8.72 was observed consistent with the formation of tetramethylethylene oxide. A new doublet at \( \tau \) 7.77 (J\(_{PH} \) 12 Hz) was also observed. Decoupling of this doublet gave a \( ^{31}P \) shift of -61 p.p.m., consistent with 1-ethyl-3,4-dimethyl-3-phospholene-1-oxide (7.22).
Chapter 8.

Preparation of 1-Hydroxy-3-methyl-2-phospholen 1-Oxide (8.7).

The adduct\textsuperscript{172} from isoprene (100 ml, 1 mol) and phosphorus trichloride (96 ml, 1 mol) was powdered, and slowly added to an ice/water mixture (700 ml) keeping the temperature below 10°. Concentrated hydrochloric acid (100 ml) was then cautiously added and the solution saturated with sodium chloride. Continuous extraction with chloroform gave 1-hydroxy-3-methyl-2-phospholen 1-oxide (8.7), (43.6 g, 33%); m.p. 117.5-120°\textsuperscript{172}, \(\nu_{\text{max}}\) 2400-2200, 1610, 1325, 1255, 1180, 1155, 1115, 955, and 800 cm\(^{-1}\).

\textbf{Hydrogenation of 1-Hydroxy-3-methyl-2-phospholen 1-Oxide.}

Adams catalyst (200 mg) was added to a solution of 1-hydroxy-3-methyl-2-phospholen 1-oxide (43.6 g) in absolute ethanol (350 ml) and the mixture hydrogenated at normal temperature and pressure. Hydrogenation was complete in 6 hours. The solution was filtered through 'Hyflo' and the solvent evaporated to give 1-hydroxy-3-methylphospholan 1-oxide (8.8) as a viscous oil, (40.6 g, 92%). The acid was characterised as its benzylamine salt, m.p. 140-145° (CH\(_2\)Cl\(_2\)/petrol); m/e 268 (phosphinic acid dimer), 250 (phosphinic anhydride), 235, 208, 181, 135, 134, 107 (benzylamine), and 106; \(\tau\) 0.83 (3H, s), 2.3-2.6 (5H, m), 6.03 (2H, s), 7.9-9.2 (7H, m), and 9.07 (3H, d, \(\downarrow\) 5.5 Hz).

Preparation of 1-Chloro-3-methylphospholan 1-Oxide (8.9).

Thionyl chloride (50 ml) was added dropwise to 1-hydroxy-3-methyl-
phospholan 1-oxide (35 g) in the absence of a solvent. The reaction mixture was then heated to 100° for 9 hours. The excess thionyl chloride was then removed by distillation and the residue distilled under reduced pressure to give 1-chloro-3-methylphospholan 1-oxide (8.9), (17.4 g, 44%), b.p. 75-78°/0.4 mm; \( \nu_{\text{max}} \) (film) 1455, 1400, 1375, 1245, 1395, 1100, 860, 775, and 690 cm\(^{-1}\); m/e 154, 152, 139, 137, 126, 124, and 117; \( \tau \) 7.3-7.8 (7H, m), 8.95 (3H, d, \( j = 4 \) Hz). No analysis was obtained due to the hydrolytic instability of this compound.

**Reaction of 1-Chloro-3-methylphospholan 1-Oxide with Benzylamine.**

A solution of 1-chloro-3-methylphospholan 1-oxide (3.1 g, 18.4 mmol) in benzene (25 ml) was added dropwise with stirring to a solution of benzylamine (3.9 g, 36.8 mmol) in benzene (30 ml) over 30 minutes. The reaction mixture was kept at ambient temperature for 4 hours, then filtered and the solvent evaporated. Chromatography of the residue on basic alumina (100 g), yielded on elution with 2% methanol in ether, 1-benzylamino-3-methylphospholan 1-oxide (8.10), (3.0 g, 69%), m.p. 74-78° (ethylacetate/40-60 petrol); \( \nu_{\text{max}} \) 3150, 1215, 1150, 1120, 1050, 1035, 1025, 860, 765, 730, and 695 cm\(^{-1}\); \( \tau \) 2.6 (5H, s), 5.80 (2H, d, \( J_{\text{PH}} = 9.5 \) Hz), 7.6-8.8 (7H, m), and 8.91 (3H, d, \( J = 5 \) Hz). This compound readily hydrolysed to the benzylamine salt of the parent phosphinic acid and so an analytically pure sample could not be obtained.

**Reaction of 1-Chloro-3-methylphospholan 1-Oxide with Sodium Methoxide.**

A solution of sodium methoxide in methanol (20 ml, 1.5N) was added dropwise to a stirred solution of 1-chloro-3-methylphospholan 1-oxide
(4.4 g, 30 mmol) in ether (20 ml) over 30 minutes. The reaction mixture was then stirred for 16 hours. The solvent was then evaporated and the residue partitioned between water (20 ml) and dichloromethane (40 ml). The aqueous layer was extracted with dichloromethane (2 x 40 ml) and the combined extracts dried. Evaporation of the solvent and distillation of the residue under reduced pressure gave 1-methoxy-3-methylphospholan 1-oxide (8.11), (2.5 g, 57%), b.p. 56-7°/0.3 mm; \( \nu_{\text{max}} \) (film) 1455, 1405, 1375, 1270, 1230, 1195, 1105, 1205, 870, 830, and 785 cm\(^{-1}\); m/e 148, 133, 120, 106, 94, and 79; \( \tau \) 6.58 (3H, d, \( J_{\text{PH}} \) 10 Hz), 7.4-8.75 (7H, m), and 8.87 (3H, d, \( J \) 6 Hz). A satisfactory analysis could not be obtained due to the hygroscopic nature of this compound.

Preparation of 1-Benzylamino-3-methylphospholan 1-Oxide (8.10) from 1-Methoxy-3-methylphospholan 1-Oxide.

A solution of n-butyl lithium (18 ml, 1.85N) in hexane was added dropwise to a stirred solution of benzylamine (3.54 g, 33 mmol) in ether (20 ml) at 0°. A deep red coloured solution of the lithium amide was obtained. A solution of 1-methoxy-3-methylphospholan 1-oxide (2.45 g, 16.5 mmol) in ether (20 ml) was then added dropwise over 30 minutes at 0°. The mixture was then allowed to warm to room temperature and then stirred for 1 h. Dilute hydrochloric acid was then added to give a pH of 7 (ca 15 ml, 2N). The organic layers were then evaporated and the residual aqueous solution extracted with chloroform (3 x 50 ml). The combined organic layers were then washed and dried. Evaporation of the solvent gave 1-benzylamino-3-methylphospholan 1-oxide, (2.76 g, 35%), m.p. 76-78° (ethyl acetate-petrol). This sample was identical to that prepared from the acid chloride, mixed m.p.; (1:3) 74.5-78°, (3:1) 74.5-77°.
Reaction of 1-Chloro-3-methylphospholan 1-Oxide with Methyl Grignard Reagent.

A solution of the acid chloride (1.53 g, 10 mmol) in ether (15 ml) was added dropwise to a solution of methylmagnesium iodide in ether (14.4 ml, 0.763N). After stirring for 3 h, dilute sulphuric acid (10 ml, 2N) was slowly added, the ether evaporated and the aqueous layer extracted with chloroform (3 x 20 ml). The combined extracts were dried, the solvent evaporated, and the residue distilled to give 1,3-dimethylphospholan 1-oxide, m.p. 46-56°; $\tau$ (C$_6$H$_5$) 8.91 (3H, d, $\delta$ 12.5 Hz), 7.78-9.17 (7H, m), and 9.28 (3H, d, $\delta$ 6 Hz).

Reaction of 1-Chloro-3-methylphospholan 1-Oxide with Benzyl Grignard Reagent.

A solution of benzylmagnesium chloride in ether (20.5 ml, 1.6N) was added dropwise to a stirred solution of the acid chloride (5g, 33 mmol) in ether (35 ml) at 0°. The mixture was then refluxed for 1 h, cooled and then a saturated ammonium chloride solution (25 ml) was slowly added. The ether was then evaporated and the aqueous solution extracted with chloroform (3 x 50 ml). The combined extracts were washed, dried, and the solvent evaporated. Seven fractional recrystallisations of the residue from ethylacetate gave one isomer (8.13-a) of 1-benzyl-3-methylphospholan 1-oxide, m.p. 137-157°; $\nu_{max}$ 1600, 1500, 1265, 1215, 1175, 1125, 1105, 870, 770, 750, 720, 700, and 660 cm$^{-1}$; m/e 208, 193, 180, 166, 154, 152, 139, and 117, [Ratio M:(M+2)=285:3.1]; $\tau$ 2.62 (5H, s), 6.72 (2H, d, $\delta_{PH}$ 14.5 Hz), 7.37-8.90 (7H, m), and 9.02 (3H, dd, $\delta$ 5.8, $\delta_{PH}$ 1 Hz); (Found: C, 69.2; H, 8.15; P, 15.0. C$_{12}$H$_{17}$OP requires
C, 69.2; H, 8.2; P, 14.9%). Evaporation of the mother liquor from the first crystallisation gave a crude sample of (8.13), (800 mg) enriched in isomer (8.13-b). Dry column chromatography on deactivated alumina (80 g Alumina + 8 g water) gave on elution with chloroform, one isomer (8.13-b) of 1-benzyl-3-methylphospholan 1-oxide; b.p. 140-150°/0.05 mm; m.p. 79-85°; ν max 1600, 1495, 1400, 1260, 1235, 1215, 1160, 1125, 1105, 865, 830, and 695 cm⁻¹; m/e 208, 193, 180, 166, 154, 152, 139, and 117; τ 2.70 (5H, s), 6.76 (2H, dq, J 7, J PH 7 Hz), 6.04 (2H, d, J PH 17.5 Hz), 7.23-8.43 (7H, m), 8.73 (3H, dt, J 7, J PH 0.5 Hz), and 9.04 (3H, d, J 5 Hz). A satisfactory analysis could not be obtained for this isomer.

Preparation and Hydrolysis of 1-Benzyl-1-ethoxy-3-methylphospholanium Tetrafluoroborate (8.14).

(a) Isomer (8.14-a)

A solution of 1-benzyl-3-methylphospholan 1-oxide (8.13-a), (160 mg, 0.77 mmol) in dichloromethane (3 ml) was added to a suspension of triethyl oxonium tetrafluoroborate (164 mg, 0.86 mmol) in dichloromethane (1 ml). The mixture was then stirred at ambient temperature for 17 hours. The solvent was then evaporated to leave 0.5 ml of solution. Ether (8 ml) was then added and the precipitated phospholanium salt (8.14-a) filtered off (218 mg, 88%), τ (CH₂Cl₂) 2.67 (5H, s), 5.85 (2H, dq, J 7, J PH 7 Hz), 6.04 (2H, d, J PH 17.5 Hz), 7.23-8.43 (7H, m), 8.73 (3H, dt, J 7, J PH 0.5 Hz), and 9.04 (3H, d, J 5 Hz). The phosphonium salt (218 mg) was then added to a mixture of dilute sodium hydroxide solution (3 ml, 0.89N) and dioxan (3 ml) and the mixture stirred at ambient temperature for 15 minutes. The solution was then extracted with methylenechloride (3 x 15 ml) and the combined extracts washed and dried.
Evaporation of the solvent gave the phospholan oxide. The n.m.r. spectrum indicated that the sample contained > 75% of the isomer (8.13-a).

(b) Isomer (8.14-b)

A solution of the phospholan oxide (8.13-b) (37 mg, 0.18 mmol) in dichloromethane (2 ml) was added to a stirred suspension of triethyl oxonium tetrafluoroborate (45 mg, 0.23 mmol). The mixture was then stirred for a further 12 hours, and then the volume of solution reduced to 0.5 ml and ether (3 ml) added. The precipitated phosphonium salt (8.14-b) was then filtered off.

\[ \text{CH}_2\text{Cl}_2 \] 2.67 (5H, m), 5.80 (2H, dq, J_7 7 Hz), 6.13 (2H, d, J_{PH} 16 Hz), 7.20-8.67 (7H, m), 8.72 (3H, dt, J 7 Hz, J_{PH} 0.5 Hz), 9.0 (3H, unresolved d).

The phosphonium salt was then added to a mixture of dilute sodium hydroxide (1.5 ml, 0.89 N) and dioxan (1.5 ml) and the mixture stirred at room temperature for 15 minutes. The solution was then extracted with dichloromethane (3 x 10 ml) and the combined extracts washed and dried. Evaporation of the solvent gave the phospholan oxide. The n.m.r. spectrum indicated that the sample contained > 75% of the isomer (8.13-b)

(c) Hydrolysis of (8.14-a) in \textsuperscript{18}O-Water.

The phosphonium salt (8.14-a) was prepared from the phospholan oxide (8.13-a) (149 mg) and triethyl oxonium tetrafluoroborate (150 mg) by the method outlined above. The salt was then hydrolysed in a solution of sodium hydroxide (86 mg, 2.15 mmol) in a mixture of \textsuperscript{18}O-water (0.447 g, 25 Atom %) and dioxan (0.5 ml) at room temperature for 15 minutes. The phospholan oxide was then isolated as described above. m/e 210, 208; Ratio 11:55. This corresponds to an \textsuperscript{18}O content of 17 Atom %.
Preparation of 1-Hydroxy-3,4-dimethyl-3-phospholen 1-Oxide, (8.16).

The adduct from 2,3-dimethyl-1,3-butadiene (8.2 g, 0.1 mol) and phosphorus tribromide (27 g, 0.1 mol) was added slowly to a mixture of ice/water (50 g). The aqueous solution was then saturated with sodium chloride and then continuously extracted with chloroform to give 1-hydroxy-3,4-dimethyl-3-phospholen 1-oxide (8.16), (9.6 g, 65%), m.p. 115-120° (acetone).210

Hydrogenation of 1-Hydroxy-3,4-dimethyl-3-phospholen 1-Oxide.

To a solution of the unsaturated acid (1.68 g, 11.5 mmol) in absolute ethanol (25 ml) was added the hydrogenation catalyst, 10% palladium on carbon (166 mg) and the mixture hydrogenated in an autoclave at 80° with a hydrogen pressure of 100 Atmospheres. After 21 hours the hydrogenation was stopped, the solution filtered through 'Hyflo' and the solvent evaporated, to give a mixture of the saturated and unsaturated acids (50:50 by 1H n.m.r.).

Preparation of 1-(a-Chloroethoxy)-3,4-dimethyl-3-phospholen 1-Oxide (8.20).

A mixture of 2,3-dimethyl-1,3-butadiene (15 g), 2-chloro-1,3,2-dioxaphospholan (23.2 g) and hydroquinone (200 mg) in a Carius tube was kept at 100° for 16 hours. The mixture was then distilled under reduced pressure to give 1-(a-chloroethoxy)-3,4-dimethyl-3-phospholen 1-oxide (8.20), (12.3 g, 32%), b.p. 113-121°/0.1 mm.172
Hydrogenation of 1-(β-Chloroethoxy)-3,4-dimethyl-3-phospholen 1-Oxide.

(a) Adams' catalyst (500 mg) was added to a solution of the ester (10 g) in anhydrous ethanol (40 ml) and the mixture hydrogenated in an autoclave at 75° and a hydrogen pressure of 110-120 Atmospheres for 65 hours. The mixture was then filtered through 'Hyflo', the solvent removed and the residue distilled under reduced pressure to give 1-(β-chloroethoxy)-3,4-dimethylphospholan 1-oxide (8.21), (8.5 g, 84%), b.p. 130-140°/0.5 mm; τ 5.53-5.93 (2H, m), 6.27 (2H, dt, J 5.5, J PH 0.5 Hz), 7.27-8.77 (6H, m), 8.98 and 9.01 (3H, 2 x d, J 6.3 Hz); m/e 212, 210, 197, 195, 175, 170, 168, 161, 133, 131, 129, and 127; isomer ratios 1:66:33, by g.l.c. (3% OV17, 170°). A mixture of the saturated ester (1 g) and sodium hydroxide solution (5 ml, 2N) was refluxed for 4.5 hours. The mixture was then cooled, acidified with concentrated hydrochloric acid and saturated with sodium chloride. The aqueous solution was then extracted with dichloromethane (5 x 10 ml), the combined extracts dried and the solvent evaporated to give 1-hydroxy-3,4-dimethylphospholan 1-oxide as a viscous oil, τ 7.4-8.5 (6H, m) and 8.98 (6H, d, J 6 Hz). The acid was then dissolved in ether (5 ml) and a solution of benzylamine (0.52 g) in ether (5 ml) was slowly added with stirring. The precipitate was then filtered off to give the benzylamine salt of the saturated acid, m.p. 135-7° (chloroform/ethylacetate); τ 1.7 (3H, s), 2.3-2.7 (5H, m), 6.02 (2H, s), 7.57-8.93 (6H, m), and 9.18 (6H, d, J 6 Hz); (Found: C, 61.0; H, 8.7; P, 12.2; N, 5.3. \( \text{C}_{13}\text{H}_{22}\text{N}_{2}\text{O}_{2}\text{P} \) requires C, 61.2; H, 8.7; P, 12.1; N, 5.5%). The n.m.r. spectrum indicates the presence of only one isomer for the acid.
(b) Adams' catalyst (1 g) was added to a solution of the ester (20 g) in glacial acetic acid (100 ml) and the mixture hydrogenated at normal temperature and pressure. Hydrogenation was complete in 1.5 hours. The mixture was then filtered through 'Hyflo' and the solvent removed under reduced pressure. The residual oil was then dissolved in dichloromethane (100 ml) and washed with water, dilute sodium carbonate solution and then water again. The solution was then dried, the solvent removed and the residue distilled under reduced pressure to give 1-(β-chloroethoxy)-3,4-dimethylphospholan 1-oxide (19.1 g, 94.5%), b.p. 90-100°/0.2 mm. The spectral data were identical to those of the sample prepared previously. G.l.c. (3% OV17, 170°) showed an isomer ratio of 11:50:39.

Reaction of 1-(β-Chloroethoxy)-3,4-dimethylphospholan 1-Oxide with Sodium Methoxide in Methanol.

Sodium wire (4.3 g) was added in portions to methanol (100 ml). To this solution was then added the saturated β-chloroethoxy ester (18.3 g) in methanol (25 ml) and the mixture refluxed overnight. The solution was then cooled to 0° and acidified with dilute hydrochloric acid (90 ml, 2N). The mixture was then extracted with dichloromethane (3 x 75 ml), and the combined extracts washed and dried. Evaporation of the solvent and reduced pressure distillation of the residue gave a mixture of isomers of 1-methoxy-3,4-dimethylphospholan 1-oxide (8.22), (8.6 g, 61%), b.p. 110-210°/0.4 mm; v_{max} (film) 1455, 1405, 1380, 1230, 1185, 1130, 1095, 1030, 875, 860, and 810 cm^{-1}; m/e 162, 147, 120, 108, 106, 94, and 79; G.l.c. (3% OV17, 125°) and ^{1}H n.m.r. in the presence of Eu(dpm)$_3$ showed an isomer ratio of trans-trans:cis-cis:cis-trans of 56:36:8. Chromatography of the ester (1.5 g) on basic
alumina (100 g) gave, on elution with 2% methanol in ether, r-1-methoxy-trans-trans-3,4-dimethylphospholan 1-oxide (8.22-a), τ 6.29 (3H, d, J_{PH} 11 Hz), 7.4-8.6 (6H, m), and 9.02 (6H, d, J 6 Hz). Continued elution gave an isomerically impure sample of dl-r-1-methoxy-cis-3-trans-4-dimethylphospholan 1-oxide (8.22-c), (n.m.r. not obtainable), and finally gave r-1-methoxy-cis-cis-3,4-dimethylphospholan 1-oxide (8.22-b), τ 6.33 (3H, d, J_{PH} 11 Hz), 7.4-8.6 (6H, m), and 8.97 (6H, d, J 6 Hz). Analytical samples of these isomers could not be obtained due to their hygroscopic nature.

Preparation of l-Chloro-3,4-dimethylphospholan 1-Oxide.

Phosphorus pentachloride (7 g) was added to a stirred solution of l-(β-chloroethoxy)-3,4-dimethylphospholan 1-oxide (10.53 g, 0.5 mol) in carbon tetrachloride (50 ml) and then the mixture heated to 80°. After all the phosphorus pentachloride had reacted a further portion (3.43 g) was added and the temperature kept at 80° for a further 2 hours. The solvent and volatile products were then removed under reduced pressure and the residue distilled to give l-chloro-3,4-dimethylphospholan 1-oxide (8.25), (7.65 g, 92%), b.p. 75-81°/0.15 mm; ν_{max} 1455, 1405, 1385, 1280, 1245, 1205, 1195, 1145, 1085, 980, 855, 300, 740, and 710 cm^{-1}; τ (C_{6}H_{5}) 7.77-3.93 (6H, m), and 9.42 (6H, d, J 5 Hz). A satisfactory analysis for this compound could not be obtained due to the hydrolytic instability of this compound.

Reaction of l-Chloro-3,4-dimethylphospholan 1-Oxide with Sodium Methoxide in Methanol.

A solution of the acid chloride (0.95 g, 5.7 mmol) in ether (5 ml)
was added dropwise to a stirred solution of sodium methoxide in methanol (7.1 ml, 0.81N) and ether (10 ml), over 10 minutes at -20°. After warming to room temperature, dilute hydrochloric acid (25 ml) was added. The organic layer was then separated and the aqueous layer extracted with dichloromethane (3 x 20 ml). The combined organic layers were then washed and dried. Evaporation of the solvent and distillation of the residue gave a mixture of isomers of 1-methoxy-3,4-dimethylphospholan 1-oxide (8.22), (563 mg, 61%); b.p. 72°/0.2 mm; G.l.c. (3% OV17, 125°) showed an isomer ratio of trans-trans:cis-cis:cis-trans of 33:48:19. No isomerisation of a pure isomer of (8.22) was observed under identical reaction conditions.

Reaction of 1-Chloro-3,4-dimethylphospholan 1-Oxide with Methanol and Triethylamine.

A solution of the acid chloride (317 mg, 1.9 mmol) in benzene (3 ml) was added dropwise to a stirred solution of methanol (61 mg, 1.9 mmol) and triethylamine (101 mg, 1.9 mmol) in benzene (3 ml). The mixture was then heated to 70° and stirred at this temperature for 2 hours. After cooling the mixture was filtered, the solvent evaporated and the residue distilled under reduced pressure to give a mixture of isomers of 1-methoxy-3,4-dimethylphospholan 1-oxide (8.22), (253 mg, 82%), b.p. 70-75°/0.2 mm. Proton n.m.r. in the presence of Eu(dpm)₃ showed an isomer ratio of trans-trans:cis-cis:cis-trans of 46:35:19. No isomerisation of a pure isomer of (8.22) was observed under identical reaction conditions.
Kinetics of Reaction of \(1\text{-methoxy-3,4-dimethylphospholan 1-Oxide}\) with Sodium Methoxide in Methanol.

1. To \(r\)-\(1\text{-methoxy-trans,trans-3,4-dimethylphospholan 1-oxide}\) (107 mg, 0.66 mmol) was added a solution of sodium methoxide in methanol (1 ml, 0.33M) and the mixture kept at 45°. The reaction was followed by removal of an aliquot (0.05 ml) and quenching it with a solution of glacial acetic acid in methanol (0.1 ml, 0.3N). The quenched solution was then analysed by g.l.c. (3% OV17, 125°), the % of each isomer being determined from the peak areas. The results are shown in the graph (8.31).

2. Sodium (0.12 g) was added to a solution of the trans-trans-ester (8.22-a), (80 mg, 0.49 mmol) in \(d_4\)-methanol (0.5 ml) in an n.m.r. tube. After the reaction of the sodium was complete, the tube was sealed and the reaction followed by \(^1\text{H}\) n.m.r. at 50°. The rate of incorporation of CD₃O was determined by integration of the MeO region of the n.m.r. spectrum. The rate of isomerisation was determined by measuring the peak height of the upfield half of the doublet due to the ring methyls of isomer (8.22-b). Integration was not possible due to the poor separation between peaks. The results are shown in the graph (8.32). No isomerisation was observed without incorporation of CD₃O.
Chapter 9.

Preparation of 1,4-Diodomethane.
This was prepared from tetrahydrofuran by the method of Heisig,\textsuperscript{211} (67%), b.p. 55-59°/0.15 mm.

This was prepared from 1,4-diiodomethane by the method of Derkach and Kirsanov,\textsuperscript{189} $^{31}$P (MeOH) -71.6 p.p.m., $^{31}$P (in 3 molar equivalents of NaOMe in MeOH) - 71.5 p.p.m.

This was prepared from the iodide using silver oxide,\textsuperscript{189} $^{31}$P (MeOH) -72 p.p.m.

Preparation of 2-Chloro-1,3,2-benzodioxaphosphole.
This was prepared from catechol and phosphorus trichloride by the method of Crofts, Markes, and Rydon,\textsuperscript{212} (82%), 93-94°/13.5 mm.

Preparation of 2-Chloro-spiro(1,3,2-benzodioxaphosphole-2,1'-phosphol-3'-ene) (9.13, X = Cl).
This was prepared from 2-chloro-1,3,2-benzodioxaphosphole and butadiene, by the method of Razumova and Petrov.\textsuperscript{213}

Hydrolysis of 2-Chloro-spiro(1,3,2-benzodioxaphosphole-2,1'-phosphol-3'-ene) (9.13, X = Cl).
Distilled water (8.5 ml) was added to the adduct (9.13, X = Cl) (1.7 g) and the mixture stirred at ambient temperature for 15 minutes.
The mixture was then extracted with chloroform (3 x 15 ml) and the combined extracts washed and dried. Evaporation of the solvent gave a white solid, m.p. 128-130° (ethyl acetate); v_max 3080 (broad), 1615, 1590, 1510, 1290, 1250, 1200, 1170, 1100, 1030, 935, 915, 865, 825, 755, and 700 cm⁻¹; m/e 210, 193, 156, 139, 116 (metastable), 110, 109, 101, and 81; τ 1.50 (1H, s), 2.96 (4H, m), 3.97 (2H, d, J_P_H 34.5 Hz), 7.33 (4H, d, J_P_H 13.5 Hz); ³¹P (CDCl₃) -85 p.p.m.; (Found: C, 57.3; H, 5.3; P, 15.0. C₁₀H₁₁O₃P requires C, 57.15, H, 5.3; P, 14.7%). A sample of this product (230 mg) was stirred overnight with a solution of diazomethane (0.32-0.35 g) in ether (50 ml). The solvent and excess diazomethane were then evaporated under reduced pressure to give a viscous oil, τ 2.5-3.2 (4H, m), 4.02 (2H, d, J_P_H 35 Hz), 6.17 (3H, s), 7.37 (4H, d, J_P_H 13 Hz). The crude product was then hydrolysed in refluxing sodium hydroxide (25 ml, 0.1N) for 2 hours. The solution was then acidified (to litmus) with dilute sulphuric acid (2N) and then made alkaline with sodium carbonate. The solution was then extracted with ether (3 x 25 ml) and the combined extracts dried. Evaporation of the solvent gave a viscous oil, τ 2.97-3.17 (4H, m), and 6.22 (3H, s). The shift of the MeO resonance was identical to that of a pure sample of guaiacol. The aqueous solution was then acidified with concentrated sulphuric acid and the solution extracted with chloroform (3 x 25 ml). The combined extracts were then dried and the solvent evaporated to give a viscous oil, τ 3.97 (2H, d, J_P_H 34 Hz) and 7.47 (4H, d, J_P_H 13 Hz). The ¹H n.m.r. spectrum was consistent with that expected for 1-hydroxy-3-phospholen 1-oxide.
Preparation of 2-Methoxy-spiro(1,3,2-benzodioxaphosphole-2,1'-phosphol-3'-ene), (9.13, X = OMe).

(a) Preparation of 2-Methoxy-1,3,2-benzodioxaphosphole

This was prepared from 2-chloro-1,3,2-benzodioxaphosphole and methanol in ether in the presence of pyridine (the method was the same as that for the 2-substituted-4,4,5,5-tetramethyl-1,3,2-dioxaphospholans), (60%), b.p. 79-80°/9 mm.²¹⁴

(b) Preparation of the Spiro adduct from 2-Methoxy-1,3,2-benzodioxaphosphole and Butadiene.

This was prepared by the method of Razumova and coworkers,²¹⁵ b.p. 94-110°/0.5 mm, τ 3.13 (4H, s), 4.0 (2H, d, JPH 38 Hz), 6.35 (3H, d, JPH 13.5 Hz), and 7.56 (4H, d, 13 Hz); ³¹P (CDCl₃) -25.3 p.p.m.

Reaction of 2-Methoxy-spiro(1,3,2-benzodioxaphosphole-2,1'-phosphol-3'-ene), (9.13, X = OMe) with Sodium Iodide in d₆-Acetone.

Anhydrous sodium iodide (78 mg) was added to a solution of the adduct (9.13, X = OMe) (87 mg) in d₆-acetone (0.5 ml) in an n.m.r. tube. The reaction was then monitored by ¹H n.m.r. at ca. 35°. After 5 minutes the spectrum was that expected for unreacted (9.13, X = OMe); τ (d₆-acetone) 2.8-7.2 (4H, m), 4.05 (2H, d, JPH 38 Hz), 6.38 (3H, d, 14 Hz), and 7.62 (4H, d, JPH 13 Hz). After 48 hours the spectrum showed a peak due to methyl iodide, τ (d₆-acetone) 7.82, and the following τ (d₆-acetone) 2.4-3.6 (4H, m), 3.9 (2H, d, JPH 33 Hz), and 7.3 (4H, d, JPH 12 Hz). The spectrum was consistent with the presence of the sodium salt of the ester (9.15). An additional doublet at τ 4.2 (2H, d, JPH 44 Hz) was also observed. Addition of trifluoroacetic acid gave the following spectrum, τ (d₆-acetone) 2.6-3.3 (4H, m), 3.97 (2H, d, JPH 34.5 Hz), and 7.29 (4H, d, JPH 12 Hz).
Reaction of 2-Methoxy-spiro(1,3,2-benzodioxaphosphole-2,1'-phosphol-3'-ene), (9.13, X = OMe) with Lithium Iodide in d-Chloroform.

Anhydrous lithium iodide (85 mg) was added to a solution of the adduct (9.13, X = OMe) (90 mg) in d-chloroform (0.5 ml) in an n.m.r. tube. The reaction was monitored by $^1$H n.m.r. at ca 35°. After 43 hours the spectrum exhibited the following features, $\tau$ 2.8-3.5 (4H, m), 4.17 (2H, d, $\Delta_{PH}$ 35 Hz), and 7.57 (4H, d, $\Delta_{PH}$ 13 Hz). The spectrum also exhibited a singlet at 7.87 $\tau$ due to methyl iodide. The spectrum was consistent with the lithium salt of the adduct (9.13, X = OH).
Preparation of 2-Ethoxy-1,3-butadiene.

Finely ground iodine (127 g, 0.5 mol) was added portionwise to a stirred suspension of mercuric oxide (64.8 g, 0.3 mol) in 1,3-butadiene (40.5 g, 0.75 mol) and absolute ethanol (46 g) over 5 hours at -10°. The mixture was then allowed to warm to room temperature and the inorganic salts filtered off and washed with ethanol. Finely powdered potassium hydroxide (56 g, 1 mol) was then added portionwise to the ice cooled filtrate, and then the mixture refluxed for 2 hours. The alcohol-diene mixture was then distilled off at atmospheric pressure (b.p. 72-81°). The distillate was then washed with distilled water (500 ml and then 6 x 50 ml) to remove the ethanol. The upper organic layer was then dried over potassium hydroxide and then distilled to give 2-ethoxy-1,3-butadiene, (22.4 g, 30.5%), b.p. 92-94°. This compound was stored at -20° in the presence of hydroquinone (1% w/w).

Preparation of Benzyldichlorophosphine.

To the Grignard reagent, formed by the reaction of benzyl bromide (171 g, 1.0 mol) with magnesium (24.32 g, 1.0 mol) in ether (450 ml), was added dropwise with stirring at 0° a solution of freshly fused zinc chloride (136 g, 1.0 mol) in ether (260 ml) over 2 hours, and then refluxed for 2 hours. Using a delivery tube and nitrogen pressure this slurry was added slowly to a refluxing solution of phosphorus trichloride (105 ml, 1.2 mol) in ether (200 ml) over 1.5 hours. After the addition the benzylzinc chloride flask was flushed with ether (200 ml), and then the mixture refluxed for a further 2 hours. After
cooling the mixture was filtered, the solvent evaporated, and the residue distilled under reduced pressure to give benzyldichlorophosphine (38 g, 20%), b.p. 123-136°/12 mm.²¹⁸

**Preparation of iso-Propyldichlorophosphine.**

This was prepared from di-iso-propylcadmium and phosphorus trichloride by the method of Fox,²¹⁹ (32%), b.p. 132-3°.²⁰⁹

**Preparation of tertiary-Butyldichlorophosphine.**

This was prepared from the Grignard reagent of tertiary-butyl chloride with phosphorus trichloride by the method of Metzger and co-workers,²²⁰ (37%), b.p. 140-144°.

**Preparation of 2-Phenyl-1,3,2-benzodioxaphosphole.**

A solution of phenyldichlorophosphine (17.9 g, 0.1 mol) in ether (80 ml) was added dropwise to a stirred solution of catechol (11 g, 0.1 mol) and triethylamine (30.5 ml, 0.22 mol) in ether (500 ml) over 2 hours at 0°. The mixture was stirred at room temperature for 2 hours and then filtered through 'Hyflo'. Removal of the solvent by distillation, and reduced pressure distillation of the residue gave 2-phenyl-1,3,2-benzodioxaphosphole, (70.4%), b.p. 106-110°/0.3 mm.²²¹

The following 2-substituted-1,3,2-benzodioxaphospholes were prepared by the same method:

1. 2-Benzyl-1,3,2-benzodioxaphosphole (10.3, R = CH₂Ph), (40%); b.p. 99-108°/0.1 mm; ν_max 1600, 1480, 1300, 1230, 1095, 880,
212.

2.  **2-iso-Propyl-1,3,2-benzodioxaphosphole** (10.3, R = Pr-i), (32.5%); b.p. 99-100°/11 mm; ν_max 1605, 1480, 1330, 1090, 1010, 890, 865, 705, and 665 cm\(^{-1}\); τ 2.9-3.27 (4H, m), 8.1-8.8 (1H, m), and 9.07 (6H, dd, \(J_7, J_\text{PH} 15\) Hz); 31P (CDCl\(_3\)) -206 p.p.m.

**Reaction of 2-iso-Propyl-1,3,2-benzodioxaphosphole with Sulphur.**

Sulphur (0.26 g) was added to a solution of 2-iso-propyl-1,3,2-benzodioxaphosphole (1.0 g) in benzene (5 ml) and the mixture refluxed for 16 hours. The solvent was then removed under reduced pressure and chloroform (5 ml) added. The mixture was then filtered, the solvent evaporated and the residue distilled under reduced pressure to give 2-iso-propyl-1,3,2-benzodioxaphosphole 1-sulphide, b.p. 120-125°/0.3 mm; ν_max 1600, 1480, 1330, 1230, 1095, 1010, 860, 780, and 740 cm\(^{-1}\); m/e 214, 198, 182, 172, 156, 139, 110, and 92; τ 3.03 (4H, s), 7.1-7.9 (1H, m), and 8.7 (6H, dd, \(J_7, J_\text{PH} 22\) Hz); (Found: C, 50.1; H, 5.3. \(\text{C}_9\text{H}_{11}\text{O}_2\text{PS}\) requires C, 50.5; H, 5.2%).

**Preparation of 2-tertiary-Butyl-1,3,2-benzodioxaphosphole.**

This was prepared according to the method of Stewart. Sodium hydride (9.6 g, 50% w/w dispersion in oil), was added in portions to a stirred solution of catechol (11 g, 0.1 mol) in ether (250 ml) and then the mixture refluxed for 1 hour. A solution of tertiary-butyl dichlorophosphine (15.9 g, 0.1 mol) in ether (50 ml) was then added dropwise to the stirred suspension over 1 hour at 0°, and...
then the solution refluxed for 1 hour. After cooling the solution was filtered and the solvent evaporated to give 2-tertiary-butyl-2,2'-spirobi(1,3,2-benzodioxaphosphole), (11.9) as a white crystalline solid, m.p. 175-176° (ether), \( \tau \) 3.13 (8H, m), and 8.83 (9H, d, \( J_{PH} \) 20 Hz); \(^{31}P \) (CDCl\(_3\)) -6.0 p.p.m.; (Found: C, 63.2; H, 5.5; P, 10.5.
C\(_{16}H\)\(_{17}O_4\)P requires C, 63.2; H, 5.6; P, 10.2%). Evaporation of the mother liquor from the crystallisation of the phosphorane (11.9) and reduced pressure distillation of the residue gave 2-tertiary-butyl-1,3,2-dioxaphospholan, b.p. 55-60°/0.5 mm, \(^{140} \tau \) 2.67-3.0 (4H, m) and 9.10 (9H, d, \( J_{PH} \) 13 Hz); \(^{31}P \) (CDCl\(_3\)) -210 p.p.m.

Preparation of 1-Phenyl-3-phospholanone 1-Oxide.

(a) Reaction of 2-Ethoxy-1,3-butadiene with 2-Phenyl-1,3,2-benzodioxaphosphole.

A mixture of 2-phenyl-1,3,2-benzodioxaphosphole (5.45 g, 25.2 mmol), 2-ethoxy-1,3-butadiene (2.47 g, 25.2 mmol), and hydroquinone (50 mg) was kept at ambient temperature for 63 hours, to give 3'-ethoxy-2-phenyl-spiro(1,3,2-benzodioxaphosphole-2,1'-phosphol-3'-ene), (10.4, R = Ph), as a white crystalline solid; m/e 314, 299, 285, 269, 257, 232, 222, 216, 206, 205, 177, 149, 129, 121, 98, and 92; \( \tau \) 1.97-2.77 (5H, m), 3.23 (4H, s), 5.47 (1H, d, \( J_{PH} \) 42 Hz), 6.30 (2H, q, \( J \) 7 Hz), 6.60-7.4 (4H, m), and 8.78 (3H, t, \( J \) 7 Hz).

(b) Alkaline Hydrolysis of the Adduct (10.4, R = Ph).

The adduct (10.4, R = Ph) (3.4 g, 10.8 mmol) was added to dilute sodium hydroxide solution (20 ml, 2N) and the mixture stirred at ambient temperature for 5 hours. The mixture was then extracted with dichloromethane (3 x 50 ml), and the combined extracts washed and dried.
Evaporation of the solvent gave a mixture of isomers of 3-ethoxy-1-
-phenyl-2- and 3-phospheten 1-oxides (10.5, R = Ph) as a viscous oil,
\( \tau 1.9-2.6 \) (5H, m); 5.00 (d, \( J_{PH} 16 \text{ Hz} \)), and 5.20 (d, \( J_{PH} 36 \text{ Hz} \)) (1H);
5.97 (q, \( J 7 \text{ Hz} \)) and 6.08 (q, \( J 7 \text{ Hz} \)) (2H); 6.9-8.1 (4H, m); 8.63
(t, \( J 7 \text{ Hz} \)) and 8.68 (t, \( J 7 \text{ Hz} \)) (3H).
(c) Acid Hydrolysis of 3-Ethoxy-1-phenyl-2 and 3- phospholen 1-Oxides.

Water (25 ml) and dilute hydrochloric acid (1 ml, 2N) was added
to the mixture of phospholen oxides (10.5, R = Ph) and then refluxed for
2 hours. The water was then removed under reduced pressure and then by
azeotropic distillation with benzene (20 ml), to give 1-phenyl-3-phosphol-
anone 1-oxide (10.1, R = Ph), m.p. 155-158° (chloroform/ethyl acetate);
\( \nu_{\text{max}} 2700-2200, 1580, 1440, 1325, 1250, 1200, 1145, 1080, 955, 875, \text{ and}
775 \text{ cm}^{-1}; \nu_{\text{max}} (\text{KCl}) 2700-2200, 1585, 1445, 1330, 1255, 1205, 1140, 1085,
960, 870, \text{ and } 780 \text{ cm}^{-1}; \nu_{\text{max}} (\text{CH}_2\text{Cl}_2) 1740, 1210, 1190, \text{ and } 1120 \text{ cm}^{-1};
\tau (\text{CDCl}_3; \text{keto}) 1.9-2.5 (5H, m), \text{ and } 6.8-7.7 (6H, m); \tau (\text{CDCl}_3; \text{enol})
-2.23 (1H, s), 4.90 (1H, d, \( J_{PH} 21 \text{ Hz} \)), \text{ and } 6.8-8.1 (4H, m); m/e 194,
166, 165, 138, 125, 124, 107, 96, 91, 77, 65, 51, 47, \text{ and } 39; \text{ (Found:}
C, 61.7; H, 5.7; P, 15.8. \text{C}_{10} \text{H}_{11} \text{O}_2 \text{P requires C, 61.8; H, 5.7; P, 15.95%.)}

Preparation of 1-Benzyl-3-phospholanone 1-Oxide.

(a) Reaction of 2-Ethoxy-1,3-butadiene with 2-Benzyl-1,3,2-benzodi-
oxaphosphole.

A mixture of 2-ethoxy-1,3-butadiene (1 g), the phosphorus ester
(10.3, R = \text{CH}_2\text{Ph}) (4 g), and hydroquinone (25 mg) was kept at ambient
temperature for 7 days to give 3'-ethoxy-2-phenyl-spiro(1,3,2-benzodioxa-
phosphole-2,1'-phosphol-3'-ene) (10.4, R = \text{CH}_2\text{Ph}) as a viscous oil,
\( \tau 2.7 \) (5H, m), 3.20 (4H, s), 5.43 (1H, d, \( J_{PH} 42 \text{ Hz} \)), 6.20 (2H, q, \( J 7 \text{ Hz} \)),
\text{ and } 7.10 (2H, d, \( J 7 \text{ Hz} \)) (2H).
6.68 (2H, d, J_{PH} 13 Hz), 7.0-8.2 (4H, m), and 8.7 (3H, t, J_{PH} 7 Hz).

(b) Alkaline Hydrolysis of the Adduct (10.4, R = CH$_2$Ph).

The crude adduct was added to dilute sodium hydroxide solution (20 ml, 2N) and stirred for 5 hours at 40°. The mixture was then extracted with dichloromethane (3 x 25 ml), and the combined extracts washed and dried. Evaporation of the solvent and distillation of the residue gave 1-benzyl-3-ethoxy-2-phospholen 1-oxide, b.p. 200-210°/0.1 mm; m/e 236, 221, 207, 168, 166, 145, 140, 108, 107, 79, and 77; τ (CCl$_4$) 2.7 (5H, s), 5.02 (1H, d, J$_{PH}$ 16 Hz), 6.05 (2H, q, J 7 Hz), 6.73 (2H, d, J$_{PH}$ 16.5 Hz), 7.2-8.4 (4H, m), and 8.72 (3H, t, J 7 Hz); $^{31}$P (CCl$_4$) 60.2 p.p.m.

(c) Acid Hydrolysis of 1-Benzyl-3-ethoxy-2-phospholen 1-Oxide (10.5, R = CH$_2$Ph)

Water (25 ml) and dilute hydrochloric acid (1 ml, 2N) was added to the phospholen oxide (10.5, R = CH$_2$Ph) and the mixture refluxed for 2 hours. The water was then removed under reduced pressure and then by azeotropic distillation with benzene (20 ml) to give a viscous oil. Thick layer chromatography on silica gave on development with methanol-ether (4% v/v) 1-benzyl-3-phospholanone 1-oxide, m.p. 135-151° (Chloroform/ethyl acetate); $\nu_{\text{max}}$ 1730, 1605, 1495, 1260, 1205, 1190, 1170, 1125, 860, 840, 770, and 700 cm$^{-1}$; $\nu_{\text{max}}$ (KCl) 1730, 1600, 1495, 1455, 1415, 1370, 1260, 1200, 1180, 1160, 1120, 860, 840, 770, and 700 cm$^{-1}$; $\nu_{\text{max}}$ (CHCl$_3$) 1735 cm$^{-1}$; m/e 208, 180, 160, 118, 104, 91, 78, 65, and 55; τ 2.77 (5H, s), 3.36 (2H, d, J$_{PH}$ 15.5 Hz), and 7.05-8.13 (6H, m); (Found: C, 63.4; H, 6.25; P, 14.8. C$_{11}$H$_{13}$O$_2$P requires C, 63.5; H, 6.3; P, 14.9%).
Preparation of 1-iso-Propyl-3-phospholanone 1-Oxide.

(a) Reaction of 2-Ethoxy-1,3,2-butadiene with 2-iso-Propyl-1,3,2-benzodioxaphosphole and Alkaline Hydrolysis of the Product.

A mixture of the phosphonite (1 g, 5.5 mmol), 2-ethoxy-1,3-butadiene (0.81 g, 8.25 mmol) and hydroquinone (10 mg) was kept at 75° for 4 days. The reaction mixture was then hydrolysed with dilute sodium hydroxide solution (10 ml, 2N) for 24 hours at ambient temperature. The mixture was then extracted with chloroform (3 x 20 ml) and the combined extracts washed and dried. The solvent was then evaporated and the residue distilled under reduced pressure to give 3-ethoxy-1-iso-propyl-2-phospholen 1-oxide, b.p. 140-145°/0.25 mm; ν\text{\text{max}} (film) 1590, 1465, 1335, 1255, 1210, 1140, 1115, 1030, 880, 865, and 765 cm⁻¹; m/e 188, 173, 159, 156, 146, 117, 113 (meta-stable), 110, 94.5 (meta-stable); τ 5.12 (1H, d, \text{JPH} 16 Hz), 6.02 (2H, q, \text{J} 7 Hz), 7.05-8.38 (5H, m), 8.65 (3H, t, \text{J} 7 Hz), 8.82 (6H, dd, \text{J} 7 Hz, \text{JPH} 15.5 Hz).

(b) Acid Hydrolysis of 3-Ethoxy-1-iso-propyl-2-phospholen 1-Oxide.

A mixture of the phospholen (247 mg), water (2 ml), and dilute hydrochloric acid (0.15 ml, 2N), was kept at ambient temperature for 3 days. The water was then removed under reduced pressure and then by azeotropic distillation with benzene. Thick layer chromatography of the residue on silica gave on development with methanol-ether (4% v/v) 1-iso-propyl-3-phospholanone 1-oxide, m.p. 120-121° (chloroform/ethylacetate); ν\text{\text{max}} 2600-2300, 1600, 1585, 1330, 1250, 1205, 1125, 1105, 1085, 1035, 950, 885, 870, 770, and 660 cm⁻¹; ν\text{\text{max}} (KCl) 2600-2300, 1600, 1585, 1495, 1440, 1415, 1335, 1255, 1210, 1130, 1085, 950, 875, 775, and 665 cm⁻¹; ν\text{\text{max}} (CH₂Cl₂) 1735 cm⁻¹; τ (keto) 7.0-8.2 (7H, m), 8.75 (6H, dd, \text{J} 7, \text{JPH} 16.5 Hz); τ (enol) the following additional peaks were observed for
the enol form, \( -0.58 \) (IH, s), and \( 5.10 \) (IH, d, \( J_{PH} 20\) Hz); m/e 160, 132, 118, 104, 90, 76, 70, and 55; (Found: C, 52.3; H, 8.2; P, 19.5. \( \text{C}_7\text{H}_{13}\text{O}_2\text{P} \) requires C, 52.5; H, 8.2; P, 19.3%).

**Attempted Reaction of 2-Ethoxy-1,3-butadiene with 2-tertiary-Butyl-1,3,2-benzodioxaphospholan.**

A mixture of the phosphonite (0.5 g), 2-ethoxy-1,3-butadiene (0.5 g) and hydroquinone (5 mg) was kept at room temperature and the reaction monitored by \( ^1\text{H} \) n.m.r. After 1 week no reaction had occurred. The mixture was therefore heated to 60°. After 3 days the only products observed by n.m.r. were those due to polymerisation of the diene and disproportionation of the phosphonite to give the pentacoordinate phosphorane (10.5).

**Preparation of trans-1-Ethoxy-1,3-butadiene.**

(a) **Preparation of 1,1,3-Triethoxybutane.**

This was prepared by the method of Wolfgang,\(^{222}\) from crotonaldehyde, b.p. 90-100°/22 mm.

(b) **Preparation of trans-1-Ethoxy-1,3-butadiene.**

This was prepared from 1,1,3-triethoxybutane by the method of Fueno and Furukawa,\(^{223}\) b.p. 108-110°.

**Attempted Reaction of trans-1-Ethoxy-1,3-butadiene with 2-Phenyl-1,3,2-benzodioxaphosphole.**

A mixture of trans-1,3-butadiene (1.96 g), the phosphonite (4.32 g),
and hydroquinone (20 mg) was kept at 60° and the reaction monitored by $^1$H n.m.r. After 1 week the only products were those due to polymerisation of the diene and disproportionation of the phosphonite.
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