ASPECTS OF ORGANOPHOSPHORUS CHEMISTRY

A thesis, submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy, University of Oxford, by

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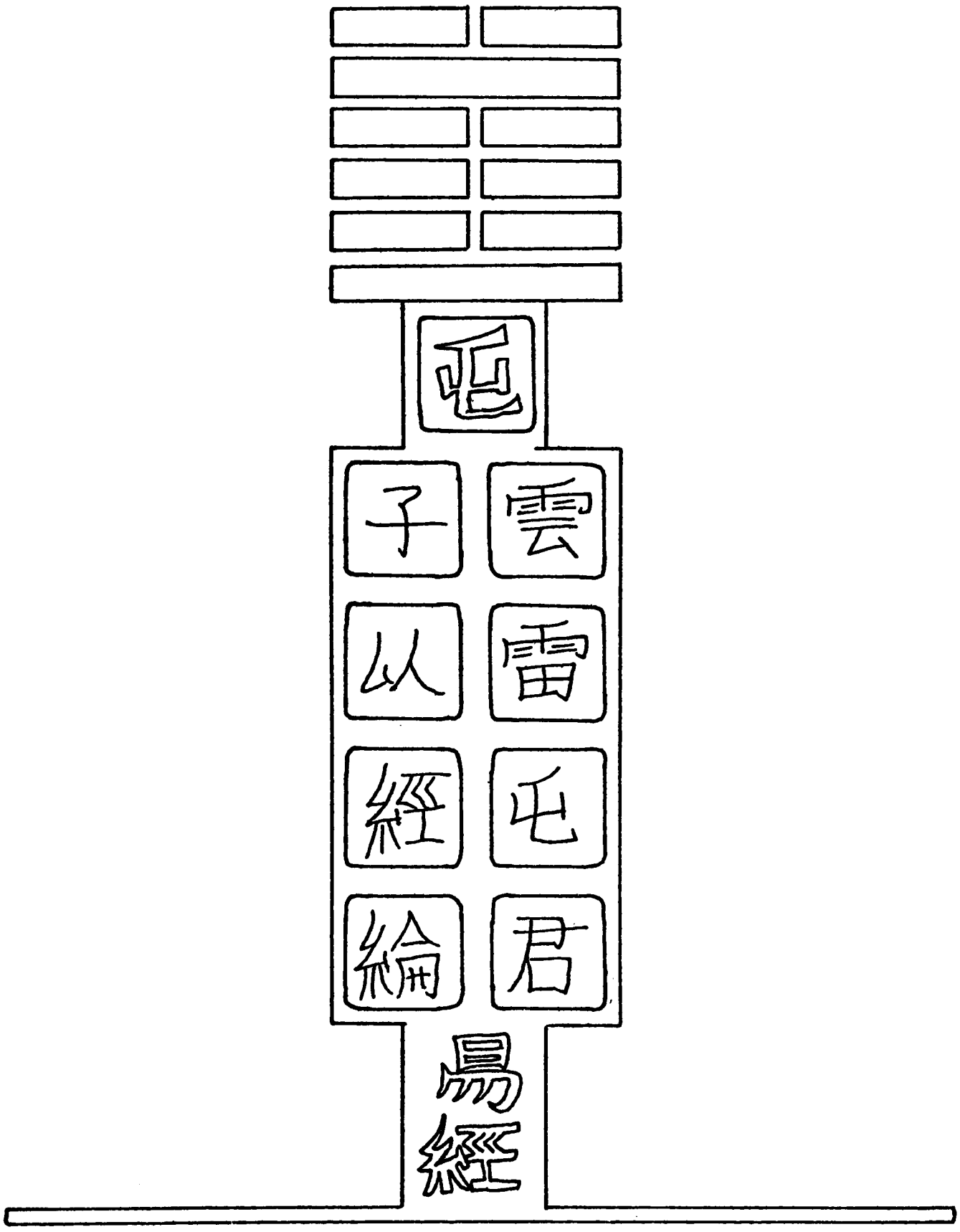
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DEDICATION.

This thesis is respectfully dedicated to Guru Maharaj Ji, whose influence upon me words fail to describe.

ACKNOWLEDGEMENTS.

I should like to extend my thanks to the following:

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January 1976. S.R. Postle.

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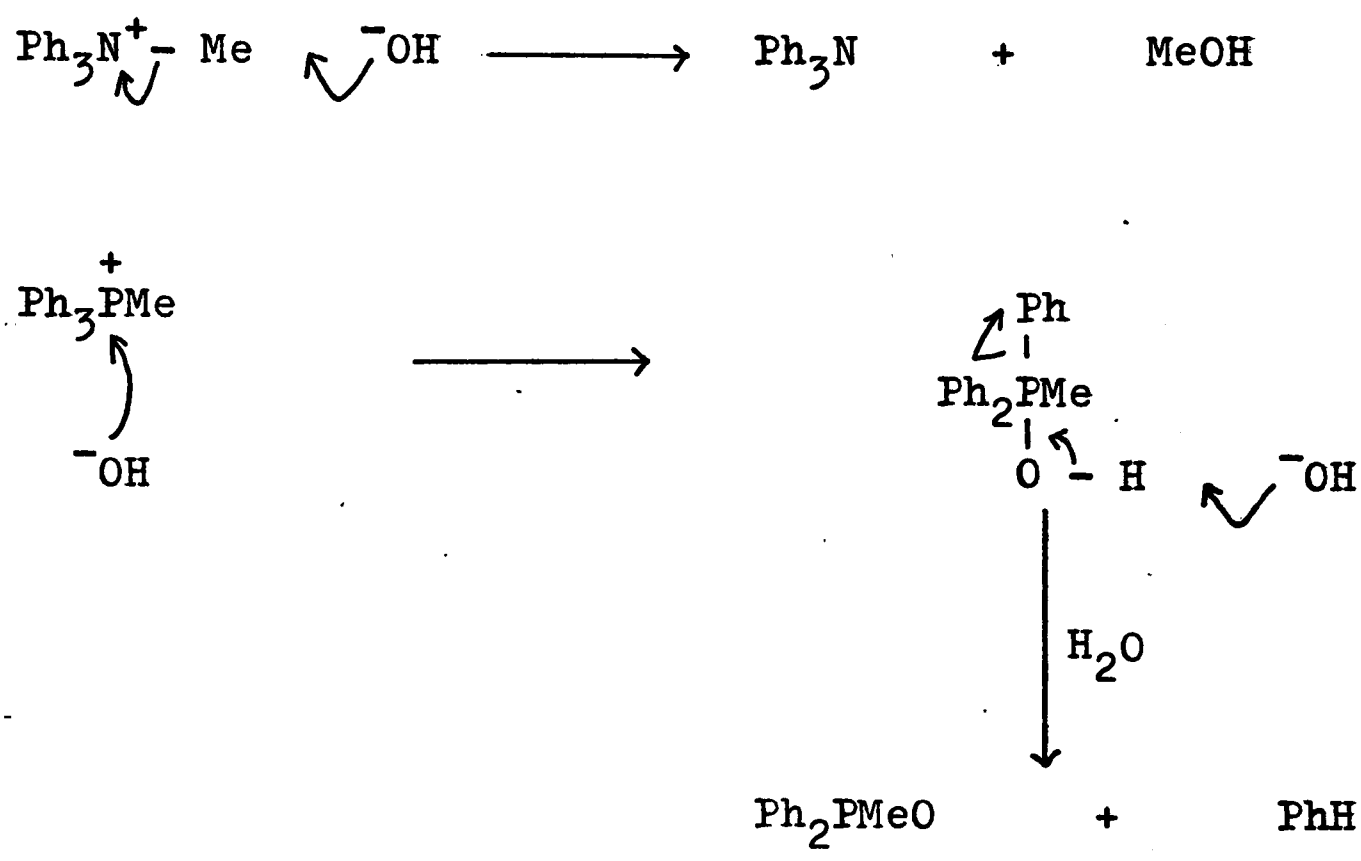
GENERAL INTRODUCTION

Quaternary ammonium and phosphonium salts are formally similar classes of compounds. Both are derived from the +4 oxidation state of the central element; both are ionic, typically being formed by the quaternisation of a tertiary amine (phosphine) with (for example) a haloalkane. One major difference in their behaviour is in reaction with alkali (Scheme 1).



Scheme 1

A similar difference can be seen in the varying abilities of N(IV) and P(IV) to stabilise an adjacent carbanion. A nitrogen ylid, such as $Me_3N^+-CH_2^-$, is unstable at room temperature with respect to amine and poly(alkylidene)[1]: the corresponding phosphorus ylid, $Me_3P^+-CH_2^-$, is a distillable liquid[2].**

** Throughout this thesis, the term 'ylid' will be used to denote a compound having adjacent positively- and negatively- charged centres. A carbanion such as $Ph_2POCH_2^-$, where a negative charge resides next to a formally positively-charged centre, will be termed a 'phosphinyl ylid', and the corresponding phosphine sulphide anion a 'thiophosphinyl ylid'.

These differences in behaviour of corresponding phosphorus and nitrogen compounds highlight a major dissimilarity in the chemistry of these neighbouring Group Vb elements (another difference, which will not be discussed in this thesis, is found in the very different nucleophilicities of corresponding N(III) and P(III) compounds). Phosphorus, for whatever reason, is capable of 'expanding its octet'; that is, it can form stable compounds in which (formally, at least) phosphorus is in the +5 oxidation state. In the types of compounds discussed in this thesis, ylids and phosphinyl ylids, and phosphine oxides and sulphides, one element is (or, can be regarded as being) double-bonded to phosphorus. Consider amine N-oxides and the corresponding phosphine oxides. The bond energy of $N^{+}\text{-}O^{-}$(50-70 Kcal mol^{-1}) is considerably lower than $P^{+}\text{-}O^{-}$(130-40 Kcal mol^{-1})[3]. Additionally phosphine oxides have smaller dipole moments than corresponding amine N-oxides: the opposite result might have been expected upon electronegativity grounds[3]. The differences in energy and polarity of the $N^{+}\text{-}O^{-}$ and $P^{+}\text{-}O^{-}$ bonds is explicable thus: phosphorus, unlike nitrogen, has low-lying unfilled orbitals (the 3d orbitals) of appropriate symmetry such that the lone pairs on oxygen can back-donate into them to form π-bonds. Such back-donation can give rise to three canonical forms: amine N-oxides are representable only by a zwitterionic form (Scheme 2)

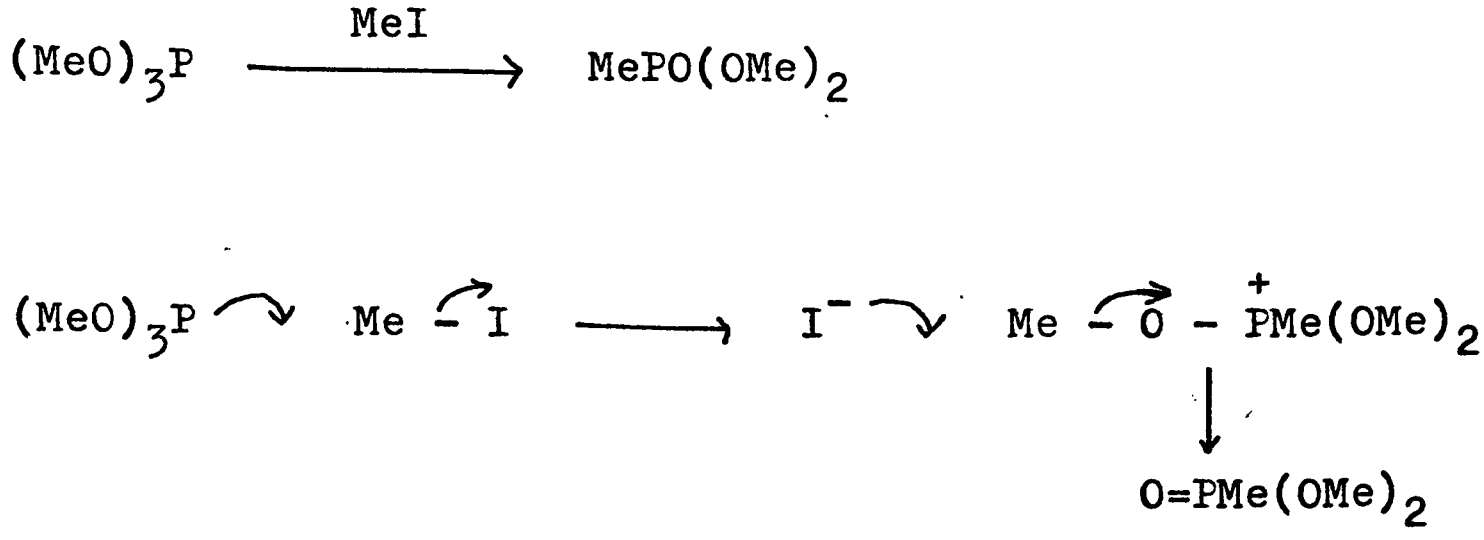
$$Et_3N^{+}- O^{-}$$

$$\left[Et_3P^{+}- O^{-} \longleftrightarrow Et_3P{=}O \longleftrightarrow Et_3P^{-}{\equiv} O^{+}\right]$$

Scheme 2.

This $d\pi$ -$p\pi$ bonding has been used to explain the strength, and consequent readiness of formation, of the phosphinyl group in several reactions in phosphorus chemistry. A famous reaction in this class,

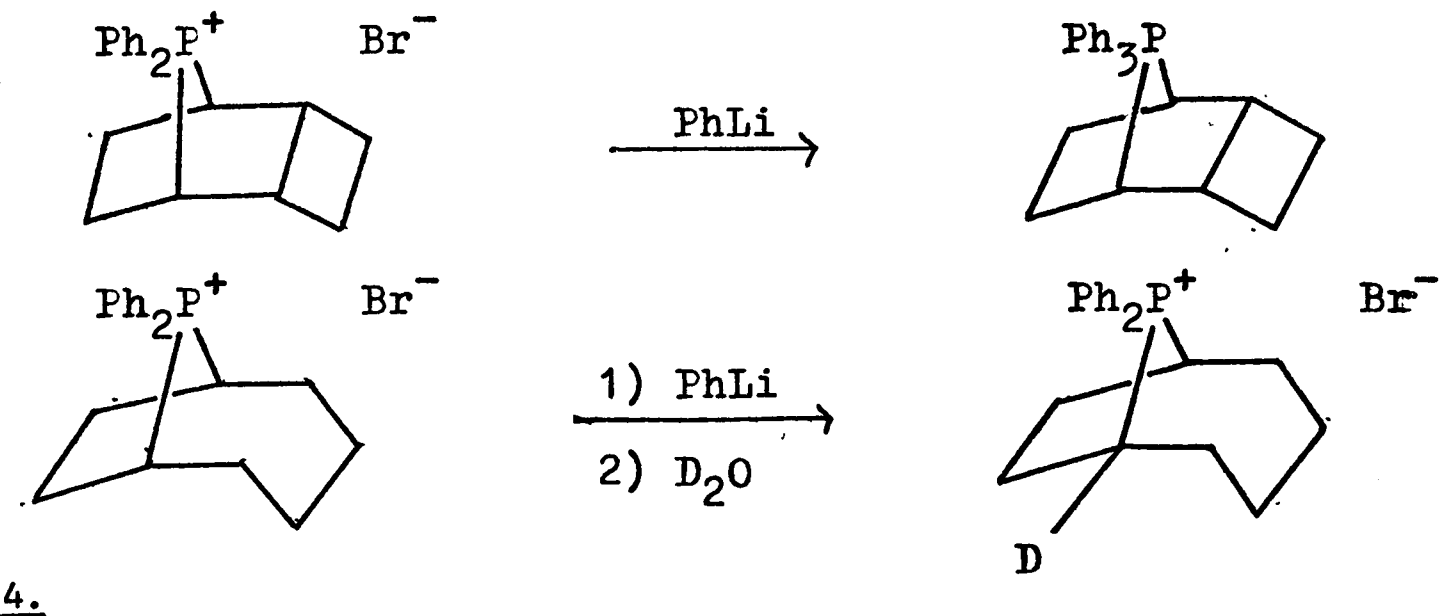
the Arbusov reaction[4], is illustrated in Scheme 3.



Scheme 3

(Other factors undoubtedly contributing to the success of the Arbusov reaction are the high nucleophilicity of P(III) and the biphilicity of iodide ion). As for phosphinyl compounds, the stability of the phosphorus - alkylidene in ylids bond is attributable to the presence of $d\pi - p\pi$ bonding.

An X-ray diffraction study upon methylene triphenylphosphorane[5] has revealed that the phosphorus - methylene bond length is 1.661Å: the sum of the Pauling double bond radii for carbon and phosphorus is 1.665Å [6]. Clearly, this does not constitute 'proof' that the bond may be formulated as "P=C" rather than "P^{+}-C^{-}", as polarisation effects may yield a similar overall result. Work by Katz, summarised in Scheme 4, may possibly be interpreted as evidence for the double bond character of the phosphorus - alkylidene linkage in ylids[7].



Scheme 4.

In the more strained ring system, the (hypothetical) ylid could not (by Bredt's rule) obtain stability by the delocalisation of charge onto phosphorus: in the less strained system, an ylid is formed, and deuterated, normally.

Against this, theoretical calculations, both extended Huckel[8] and ab initio[9], indicate that the 3d orbitals on phosphorus are unimportant in the bonding of the hypothetical compound methylenephosphorane. The barrier to rotation about the phosphorus - methylene bond is estimated at 3 cal. mol^{-1} without the inclusion of a set of 3d orbitals, and 16 cal. mol^{-1} when a set of d orbitals is included. Similar calculations do, however, indicate that a d orbital participation is of some importance in the phosphinyl linkage of the unknown compound, phosphine oxide[9].

The question thus poses itself: is the stabilisation of a carbanion adjacent to phosphorus, relative to a carbanion adjacent to nitrogen, a function of d orbital participation, or merely of the greater polarisability of phosphorus (i.e. phosphorus is less electronegative than nitrogen, and thus its outer shell of electrons can move more easily in response to other electronic influences)?

Most of the theoretical investigations undertaken on ylid systems have concentrated upon the stabilisation of negative charge adjacent to sulphur. It is probably valid to assume that similar factors are responsible for ylid stability in phosphorus and sulphur chemistry. $\Delta G^{\ddagger}_{298}$ for deuterium - hydrogen exchange in sulphonium and phosphonium salts is very similar (Table 1)[10].

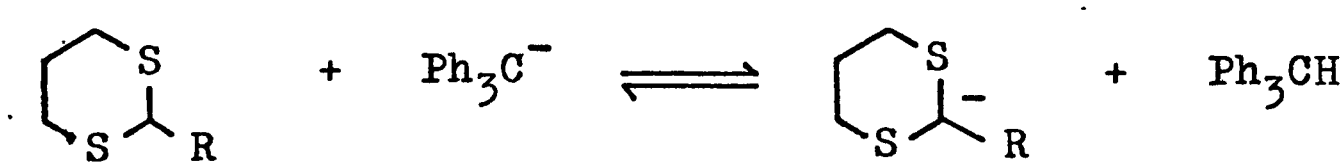
$\Delta G^{\ddagger}_{298}$ for $(CH_3)_nX^+ \xrightarrow[NaOD]{D_2O} (CH_3)_{n-1}X^+ -CH_2D$

X	n	$\Delta G^{\ddagger}_{298}$[a]
N	4	36.7
P	4	24.4
S	3	22.7

[a] in Kcal. mol^{-1}

Table 1.

The stereochemical properties of 1,3-bis sulphonium salts are explicable without assuming any d orbital contribution from sulphur[11]. Recent ab initio calculations on the system $CH_3SH \rightleftharpoons {}^{-}CH_2SH + H^+$, by Streitwieser[12] and Wolfe[13], indicate further that d orbital participation is not important in sulphonium ylids. The differences in stability between such ylids and their (hypothetical) oxygen equivalents may be explained upon grounds of bond lengths and polarisability. Preliminary calculations for phosphorus reach similar conclusions[14]. Streitwieser has produced evidence to support his calculations[15]. The pK_a's of sulphur compounds of the type shown in Scheme 5 have been measured. ΔpK_a for the cases R = H and R = Me is 5.9 units. It is considered that this value is consistent with there being little or no actual delocalisation of charge onto sulphur.



Scheme 5.

Caution should be exercised in the application of several of the

results obtained from an examination of sulphur ylids, as sulphur cations derived from both the +3 and +5 oxidation states will form ylids, whereas phosphorus only forms ylids derived from the +4 state. In any event, whether or not there is actual involvement of the 3d orbitals in ylids and related compounds, the fact remains that the stabilisation of an adjacent negative charge by P(IV) is an important feature of organophosphorus chemistry. From the view point of the synthetic organic chemist, the important thing is that such a stabilisation occurs, and can be exploited. The theme of stabilisation of negative charge in phosphinyl compounds and in ylids will, accordingly, echo through this thesis.

A class of reactions dependent upon the aforementioned properties of phosphorus, and having relevance to some sections of this thesis, are those grouped under the generic title of 'the Wittig reaction'. Typically a phosphorus-stabilised carbanion adds nucleophilically to a carbonyl group, and the adduct decomposes to give a phosphinyl-containing fragment and an olefin. Examples of this are the Wittig reaction proper[16], and the Horner-Emmons[17,18], Horner[19], and Corey-Kwiatkowski[20] reactions, respectively (Scheme 6).

$Ph_3P^+-Me\ \ I^-$ —(1) BuLi/Et_2O, (2) Ph_2CO→ $CH_2=CPh_2$ + Ph_3PO

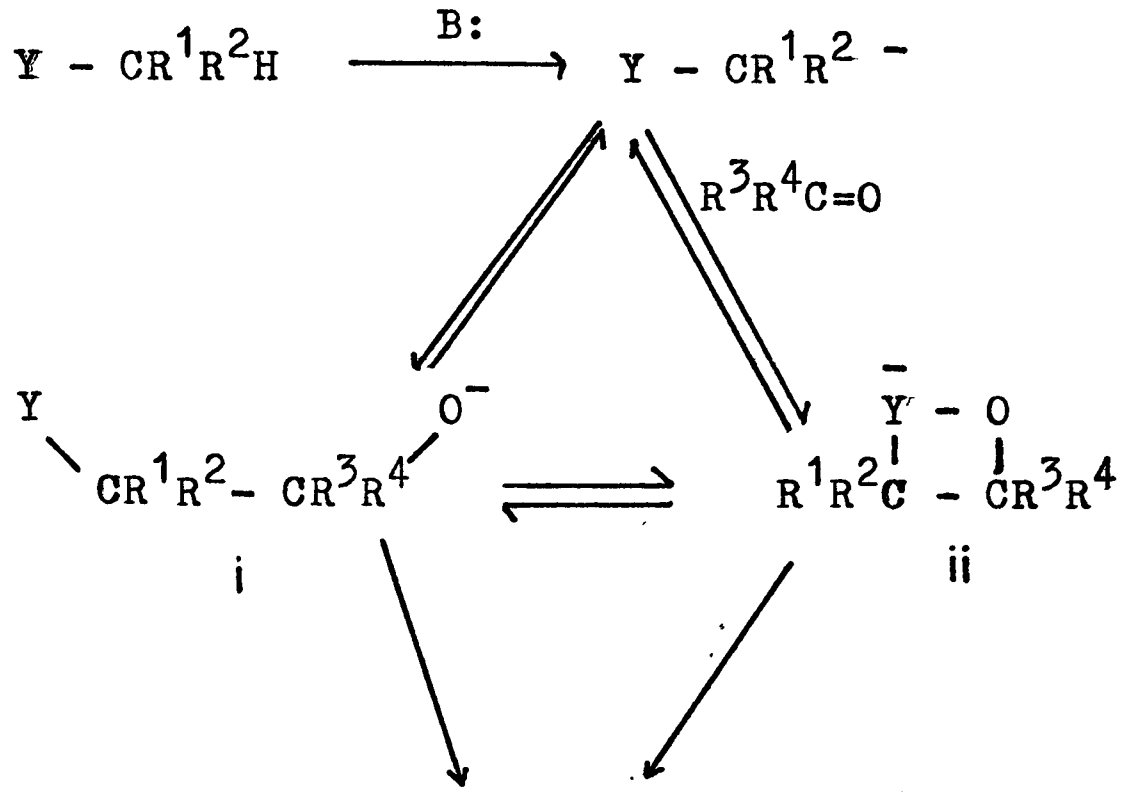
$(EtO)_2P(O)CH_2CO_2Et$ —(1) NaH/$(MeOCH_2)_2$, (2) PhCHO→ $PhCH=CHCO_2Et$ + $(EtO)_2PO_2Na$

Ph_2PMeO —$KO^tBu/Ph_2CO/C_6H_6$→ $Ph_2C=CH_2$ + Ph_2PO_2K

$(Me_2N)_2PMeO$ —(1) BuLi/C_4H_8O, (2) $PhCOCH_3$, (3) H_2O, (4) C_6H_6/SiO_2→ $PhMeC=CH_2$ + $(Me_2N)_2PHO$

Scheme 6.

A general mechanism for each of these reactions may be advanced (Scheme 7)



(Y = Ph_3P^+, $POPh_2$, $PO(OEt_2)_2$, etc.)

Scheme 7.

A large amount of mechanistic investigation has been carried out on these various steps, and some of this will be discussed below, mainly in relation to the Wittig reaction. Until recently, the existence of a betaine intermediate (i in Scheme 7) was assumed by most investigators and empirical observations interpreted in terms of a pathway involving it. As we shall see, however, some recent evidence suggests that an oxaphosphetan (ii in Scheme 7) may be formed directly. In this brief survey of the Wittig reaction, though, I shall continue to assume the existence of betaine intermediates, and reserve until the final section evidence supporting the direct formation of oxaphosphetans. The main areas of investigation have been:

a) reversibility of formation of the betaine.

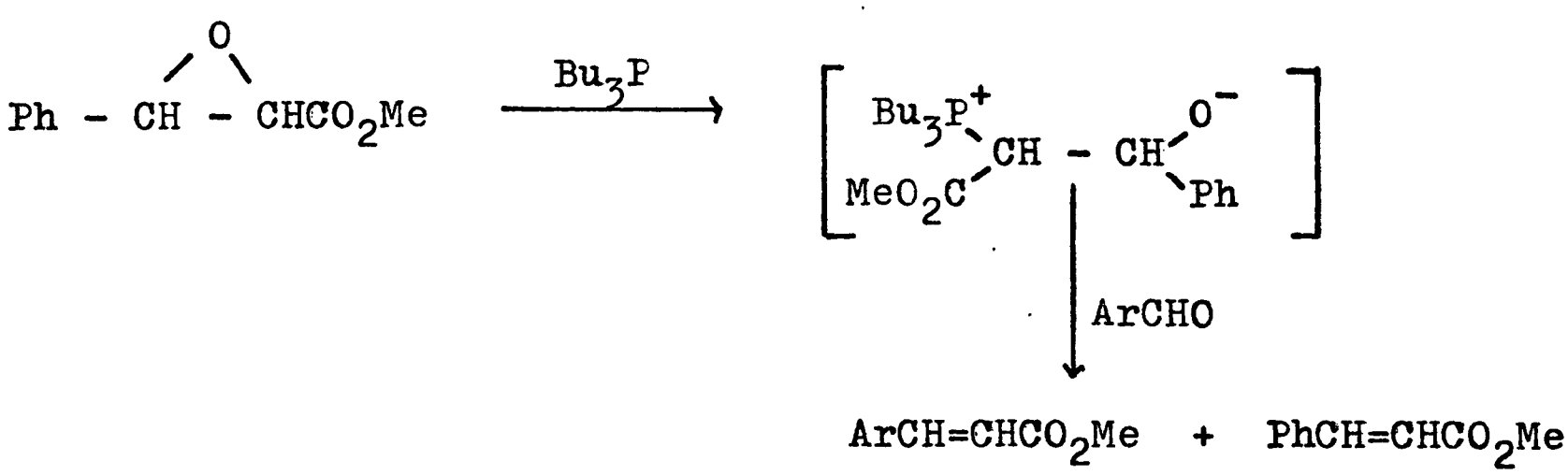
b) stereochemistry of formation and decomposition of the betaine.

c) stereochemistry at phosphorus.

d) involvement of an oxaphosphetan.

e) comparison of the Wittig and Horner reactions.

a) The reversibility of betaine formation has been shown in the Wittig reaction, where the ylid is a 'stabilised' one - that is, where the carbon α- to phosphorus bears an additional group able to effectively stabilise a carbanion[21,22] (e.g. Scheme 8).

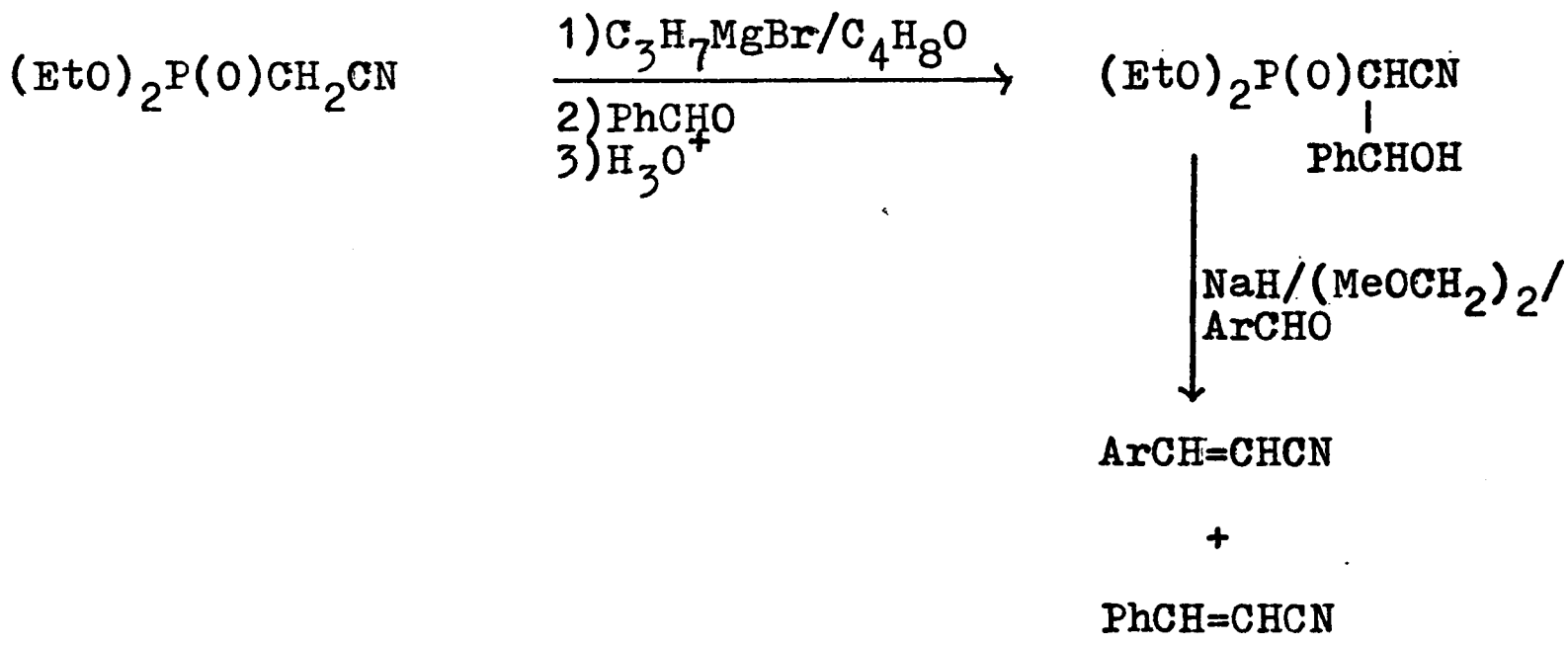


(Ar = 3-chlorophenyl)

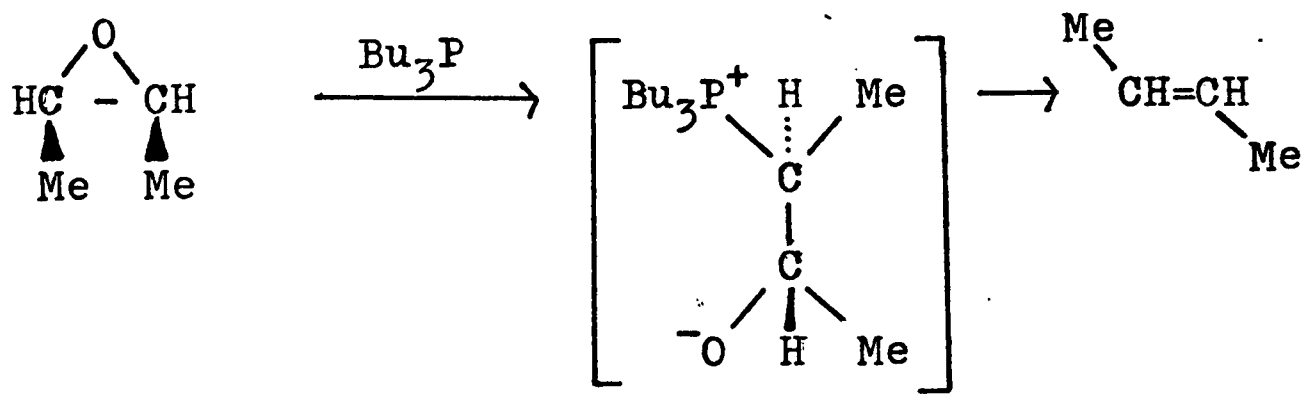
Scheme 8.

Reversibility of betaine formation has also been demonstrated in the Horner-Emmons reaction[23] (Scheme 9). Here, after acidification, the threo and erythro hydroxyphosphonates may be isolated (as the presence of Mg^{+2} inhibits the completion of the Horner reaction). Decomposition of these intermediates in the presence of a second aldehyde gives a mixture of olefins.

For 'non-stabilised', or 'reactive', ylids, betaine formation does not seem to be reversible[96] (Scheme 10), except in the presence of large amounts of lithium cations, or protic additives[24].

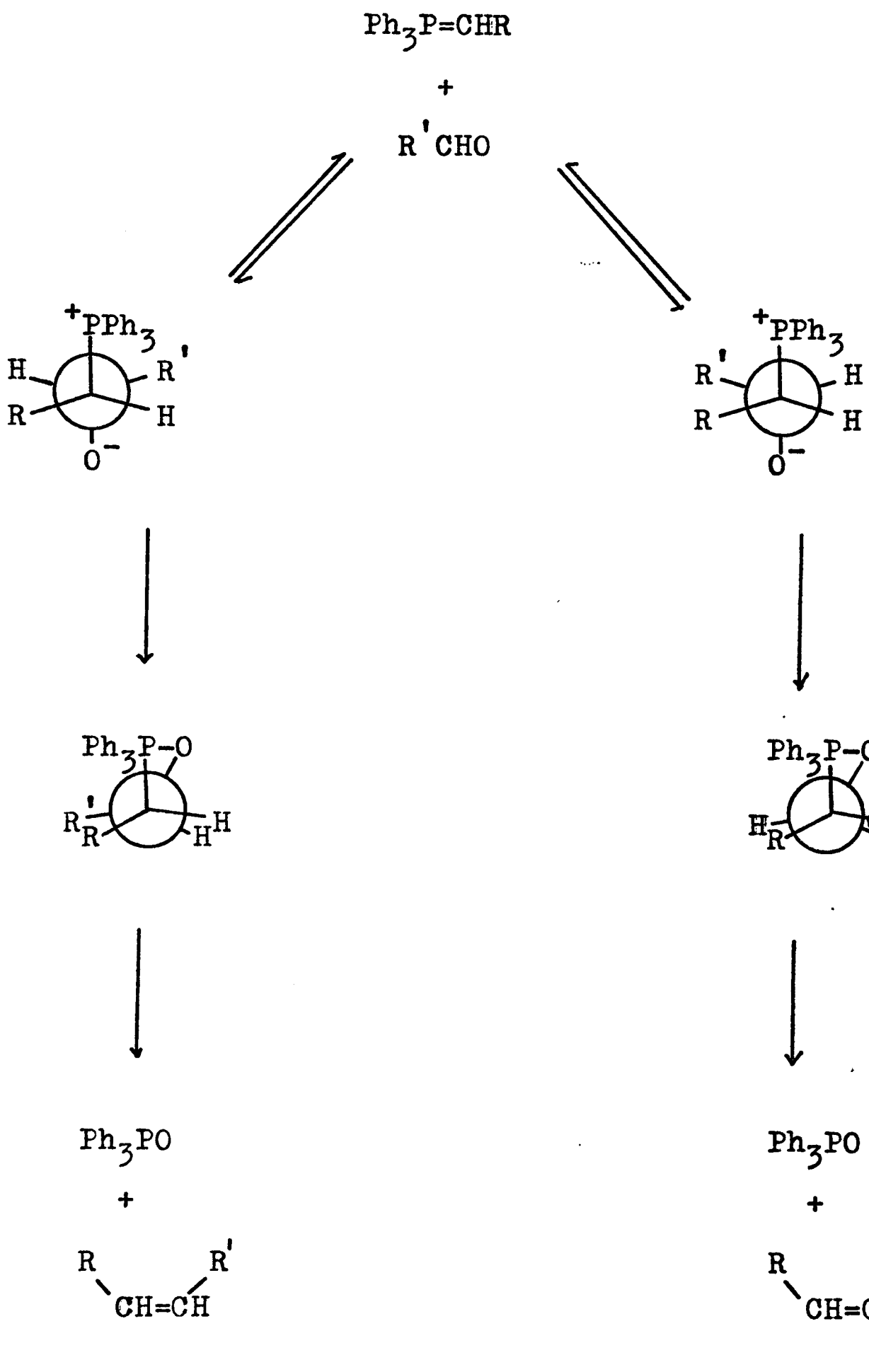


Scheme 9.



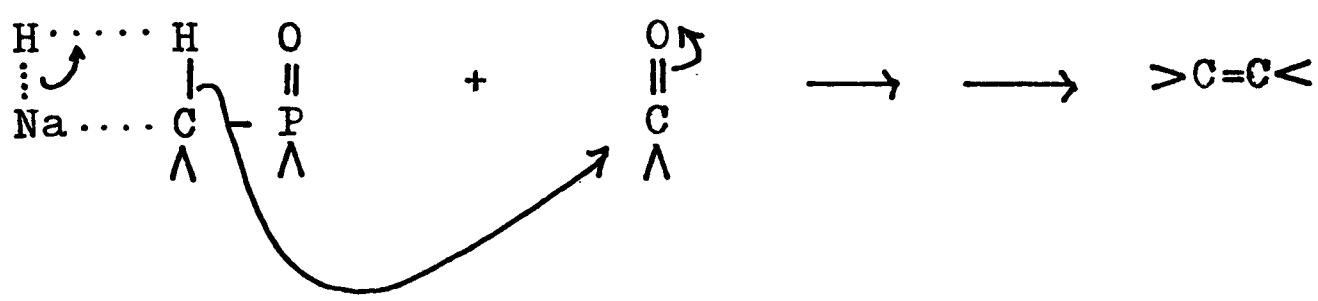
Scheme 10.

b) As a general rule of thumb, olefins derived from 'reactive' ylids are of cis stereochemistry, and those derived from 'stabilised' ylids trans[25]. Scheme 11 shows addition of the ylid to give the erythro betaine, which, in turn, decomposes to the cis olefin. Reversibility of formation of the erythro betaine will lead to formation of the more stable threo betaine, which, in turn, decomposes to trans olefin. In the case of Wittig reactions involving 'stabilised' ylids, factors leading to stabilise the erythro betaine relative to the threo, and thus lead to the formation of a higher proportion of cis olefin, are the presence of Lewis acids (e.g. Li^+) and protic solvents[26].
The Horner and Horner-Emmons reactions generally give the thermodynamically most stable olefin[18],(but exceptions have been noted[27]). This is perhaps because the only examples of successful Horner reactions have been where 'stabilised' phosphinyl ylids have been employed, where betaine formation appears to be reversible (but see Chapter 3).
'Reactive' phosphinyl ylids will react with carbonyl compounds to give betaines, but, where the phosphinyl grouping is part of a phosphonate moiety, these are stable[28]. This may be interpreted as showing that, in the decomposition of the betaine (or related species) to olefin, there is considerable build-up of negative charge on the carbon atom; α- to phosphorus: PPh_3^+ is able to stabilise this charge sufficiently for betaine decomposition to proceed, but $PO(OEt)_2$ is not.


Ph3P=CHR
+
R'CHO
+PPh3
H
R
R'
H
O−
+PPh3
R'
R
H
H
O−
Ph3P-O
R
R'
H
H
Ph3P-O
H
R
R'
H
Ph3PO
+
R
R'
CH=CH
Ph3PO
+
R
CH=CH
R'

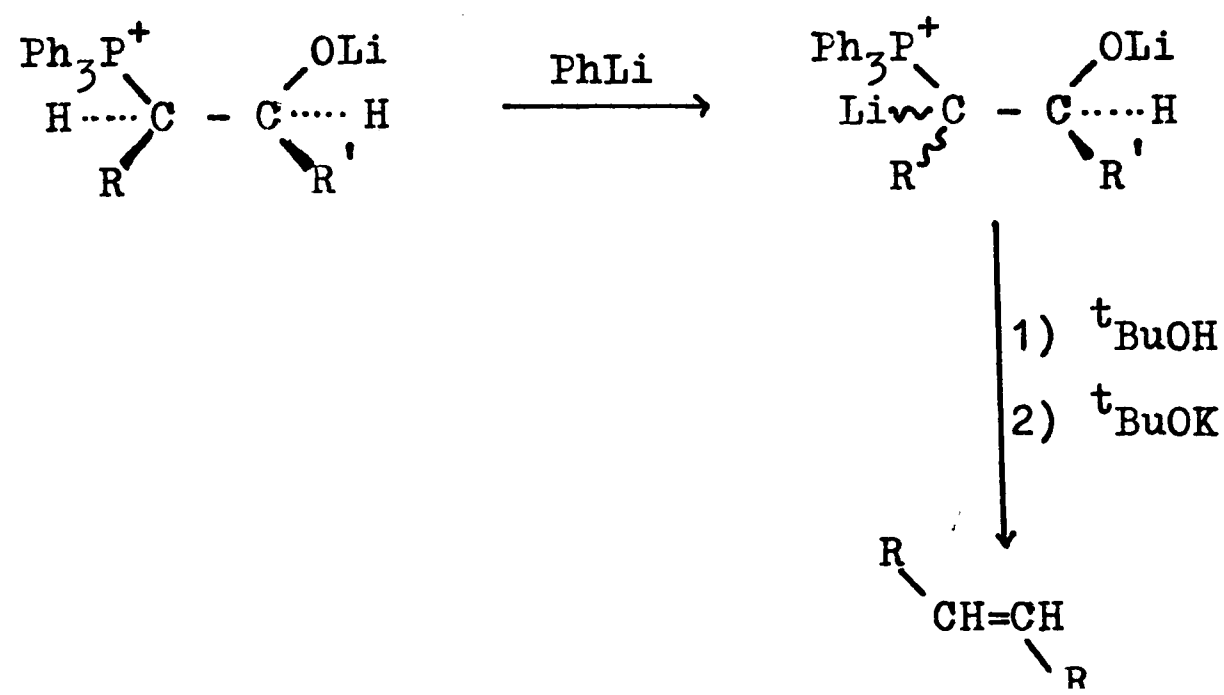
Scheme 11.

Mention should also be made of the Horner-Emmons reaction involving phosphonates where the α-carbon atom bears a substituent which is only slightly electron-withdrawing i.e. where the conjugate base of such a phosphonate would be intermediate in nature between a 'reactive' and 'stabilised' phosphinyl ylid. Such phosphonates can be deprotonated by sodium hydride (in hexamethylphosphoramide/benzene) only in the presence of the carbonyl compounds: the Horner-Emmons reaction then proceeds. It is thought that the base and phosphonate form a complex which is broken down with deprotonation only on addition of the ketone (Scheme 12)[29]:



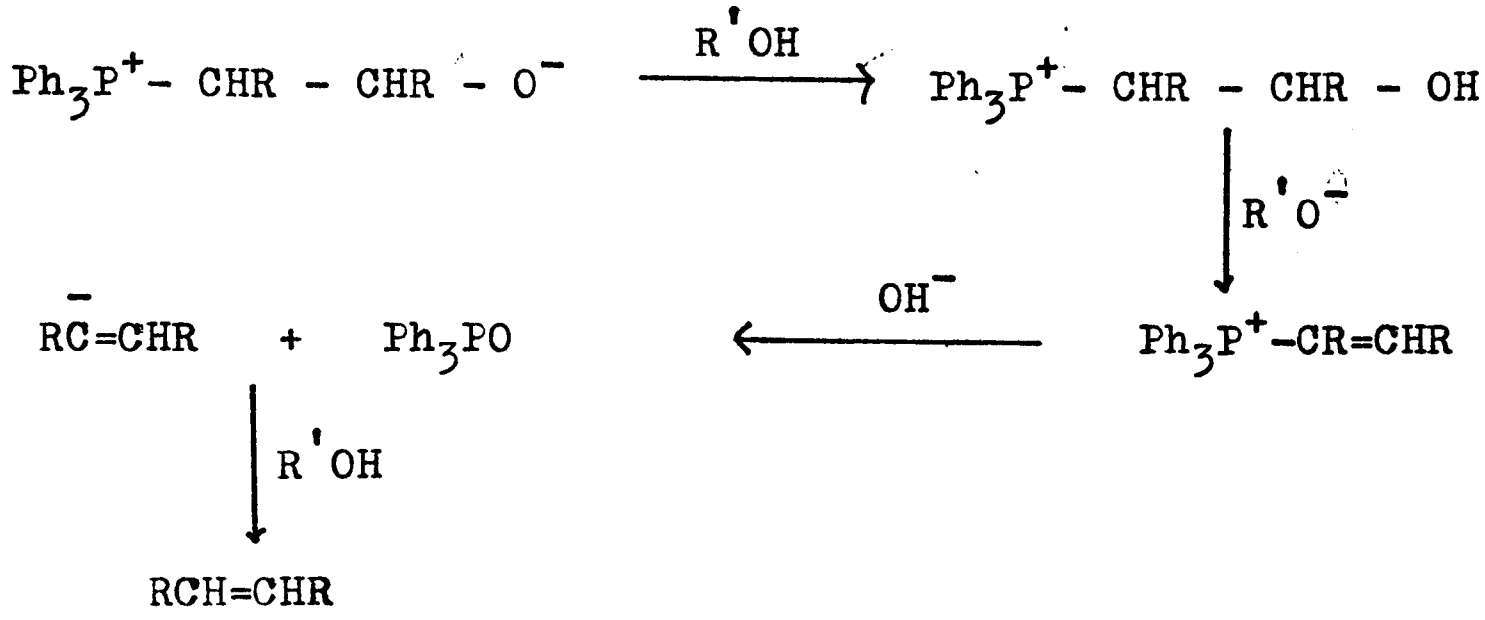
Scheme 12.

As has been shown above, the Wittig reaction employing 'stabilised' ylids may be made to yield a percentage of <u>cis</u> olefin. Schlosser's modification of the Wittig reaction yields, selectively, <u>trans</u> olefins[30] (Scheme 13).



The intermediate betaine is lithiated by more base to yield a β-oxidoylid: this rapidly equilibrates to yield the threo betaine upon reprotonation, and, with potassium tert-butoxide this yields trans olefin. The intermediate β-oxidoylid will itself react with carbonyl compounds to yield allylic alcohols[31]. Save when formaldehyde is used, the carbonyl group of the second carbonyl compound is the one which undergoes Wittig reaction to the olefin.

c) Schweizer has suggested that, in protic solvents, the Wittig reaction occurs via a vinylphosphonium salt intermediate[32]. (Scheme 14)

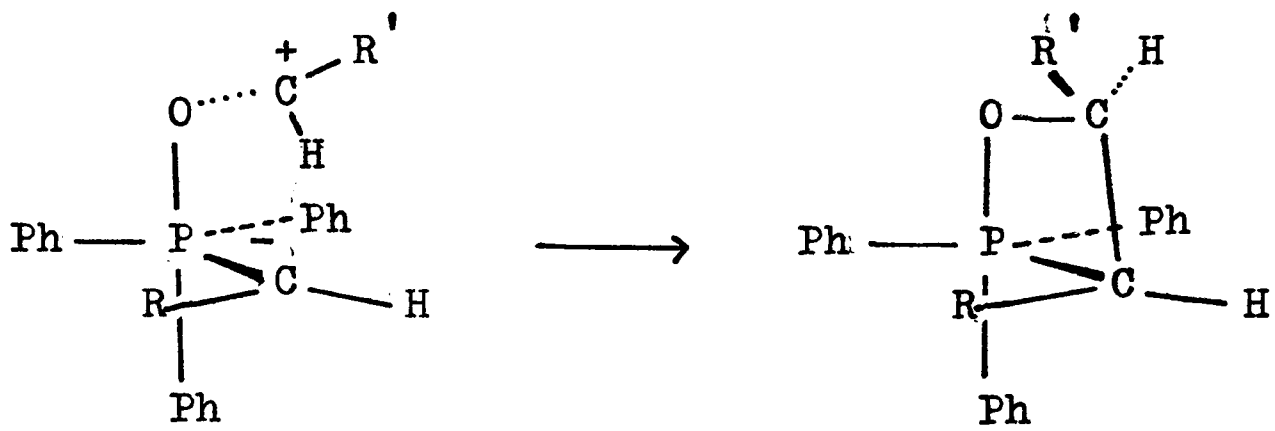


Scheme 14

Such a mechanism, however, predicts inversion of configuration at phosphorus: retention of configuration at this centre has subsequently been demonstrated using ethanol as solvent[33].

d) Schneider has suggested that some co-ordination by the oxygen of the carbonyl component onto phosphorus occurs before nucleophilic attack by the ylidic carbon onto carbonyl carbon[34], at least in the reactions of 'reactive' ylids in non-polar solvents. If the stereochemistry of such an intermediate about phosphorus is trigonal bipyramidal, then the

first-formed species in Scheme 15 (itself the principal conformer, for steric reasons) will undergo preferentially anti-clockwise rotation about the O-C bond (clockwise rotation would bring R' very close to a phenyl group) to give the erythro oxaphosphetan. The very reasonable assumptions are made that the carbonyl oxygen co-ordinates axially to phosphorus, and that the ylidic carbon is equatorially situated (as it surely must be for the four-membered oxaphosphetan ring to be formed).



Scheme 15

If such a mechanism were true, then an oxaphosphetan is formed directly, without the intervention of a betaine species. CNDO/MO calculations support the possible existence of oxaphosphetans as discrete intermediates, and, further, indicate that in the decomposition of such oxaphosphetans, P-C cleavage occurs at an earlier stage than does C-O cleavage[35]. Possible experimental evidence for the latter conclusion comes from the failure of 'reactive' phosphinyl ylid/carbonyl compound adducts to give olefins (see above)[28] and from the mild positive acid catalysis

to which the Wittig reaction of (carboxymethyl)methylene phosphoranes are subject[36].

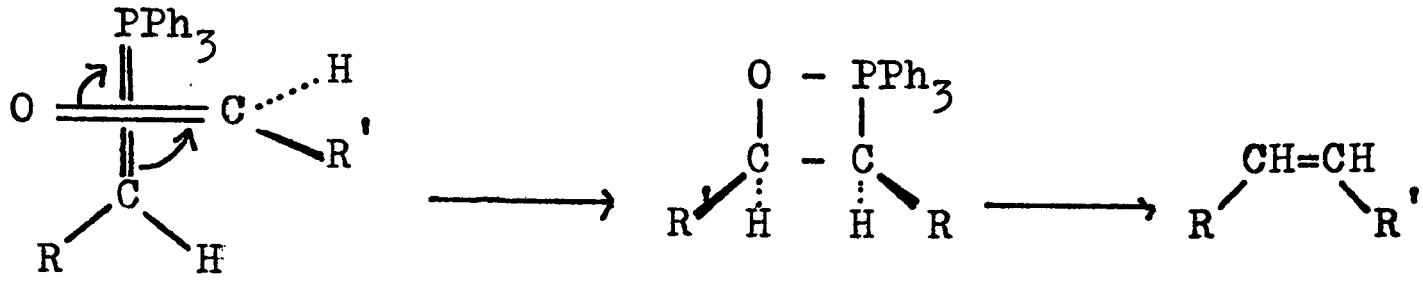
Kinetic evidence for the direct formation of an oxaphosphetan has been presented by Asknes and others[37]. For instance, in the reaction between para-nitrobenzaldehyde and phenacylidenetriphenylphosphorane, $\Delta S^{\ddagger}$ is negative, and varies little with solvent (32.6 cal. deg.$^{-1}$ mol.$^{-1}$ in hexane; 24.4 in ethan-1,2-diol). This suggests the absence of zwitterionic intermediates. The rate constants for this reaction in various solvents correlate linearly with various solvent parameters (e.g. the Kosower Z parameter) only if a group of solvents of similar type (e.g. hydrocarbons or glycols) are chosen.

Against this, the rate constants for the reactions of (carboxyethyl) methylenetriphenylphosphorane and P-ethoxycarbonylmethylene P-phenyldibenzophosphole with benzaldhyde in benzene at 25° are nearly the same (1.73×10^{-3} dm^{-3} mol s^{-1} and 2.8×10^{-3}, respectively), though strongly dependent upon the method of purification of benzene.

It might have been expected that, if an oxaphosphetan were formed immediately, the latter ylid, with its phosphorus already in a five-membered ring, would show a larger rate constant[38].

Vedejs claims to have observed the direct formation of an oxaphosphetan by ^{31}P n.m.r. in the reaction of ethylidenetriphenylphosphorane with cyclohexanone in tetrahydrofuran at -70°[39]. He suggests that reaction between ylid and carbonyl compound proceeds by a $\pi^2_s + \pi^2_a$ cycloaddition, with orthogonal approach of the two π-systems (Scheme 16). Steric repulsion between R' and the bulky triphenylphosphine group will lead to preferential formation of the erythro betaine. With 'reactive' ylids, the greater proportion of trans olefin isolated on addition of lithium salts[24] is considered due to a competing betaine/lithium halide

complex pathway. In these terms, the reason why the reaction of β-oxido ylids with aldehydes gives olefins derived from the second carbonyl fragment (see above) now also becomes clear.

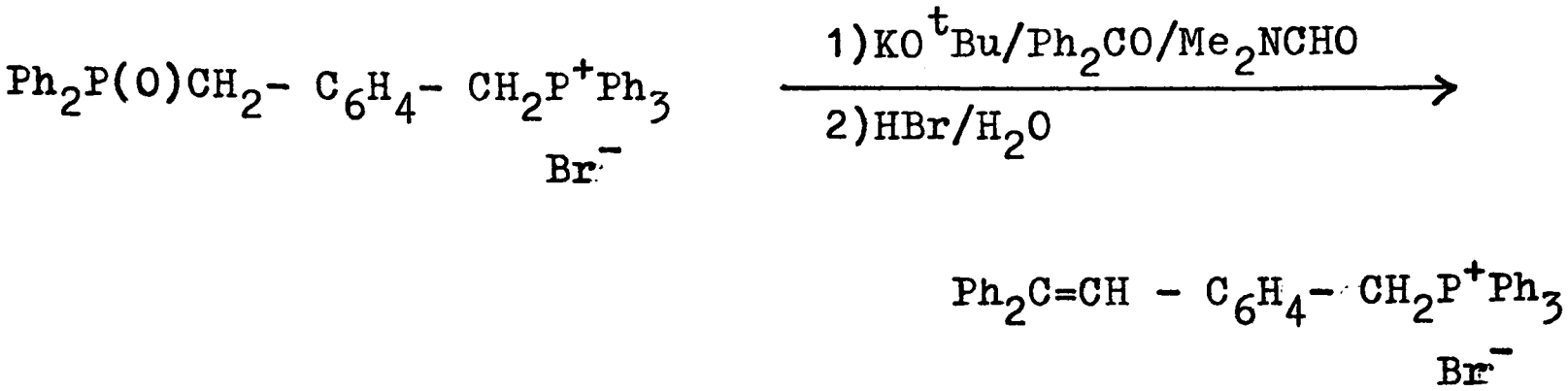


Scheme 16

It should be made clear that Vedejs' experiment does not eliminate the possibility of prior betaine formation and cyclisation to an oxaphosphetan occuring at a rate rapid even on the n.m.r. time-scale.
An oxaphosphetan has been isolated from the reaction of hexafluoroacetone with hexaphenylcarbodiphosphorane[40]: at 110° the Wittig reaction is completed to give triphenylphosphine oxide and 2,2 - bis (trifluoromethyl) vinylidenetriphenylphosphorane.

e) Little direct comparative work has been done on the various phosphorus-containing groups able to effect a Wittig or Horner reaction. Alkylidenetricyclohexylphosphoranes give a higher percentage of <u>trans</u> olefin than do alkylidenetriphenylphosphoranes: the former contain a less electrophilic phosphorus atom, and the reversion of the intermediate to ketone and ylid will thus occur more readily[41]. In a competitive situation, the Horner reaction takes precedence over the Wittig

reaction (Scheme 17).



Scheme 17.

An idea of the relative nucleophilicities of carbanions adjacent to the various phosphorus-containing groups may perhaps be drawn from σ^- values (Table 2). Two assumptions have to be made: that, in the group of ylids and phosphinyl ylids, basicity and nucleophilicity are correlateable, and that stabilisation of charge on a remote heteroatom via a delocalised π-system is related to the stabilisation of charge on adjacent carbon. Neither of these assumptions are particularly attractive, though.

σ^- values of various phosphorus-containing groups.

X	ref. a	ref. b	ref. c
Ph_2P	0.32		0.26
Ph_2PO	0.88	0.85	0.68
Ph_2PS	0.73		0.63
Ph_2PMe^+	1.09		1.28
$(EtO)_2PO$		0.83	
NO_2	1.24		

[a] from the half-neutralisation potentials of $XC_6H_4NMe_2$ [43]

[b] from the alkaline hydrolysis rates of $XC_6H_4CH_2SiMe_3$ [44]

[c] from pK_a values of XC_6H_4OH [45]

Table 2.

There are no literature reports of actual pK_a measurements on ylids. Preliminary measurements by Streitwieser's group[46] give the value of 24 to the pK_a of the methyltriphenylphosphonium cation in dimethylsulphoxide (relative to pK_a DMSO = 35), and a value of 18 for the methyldiphenylsulphonium cation.

Data in this area is sparse, and reliable predictions cannot yet be made about the relative abilities of ylids and phosphinyl ylids to undergo a Wittig-type reaction.

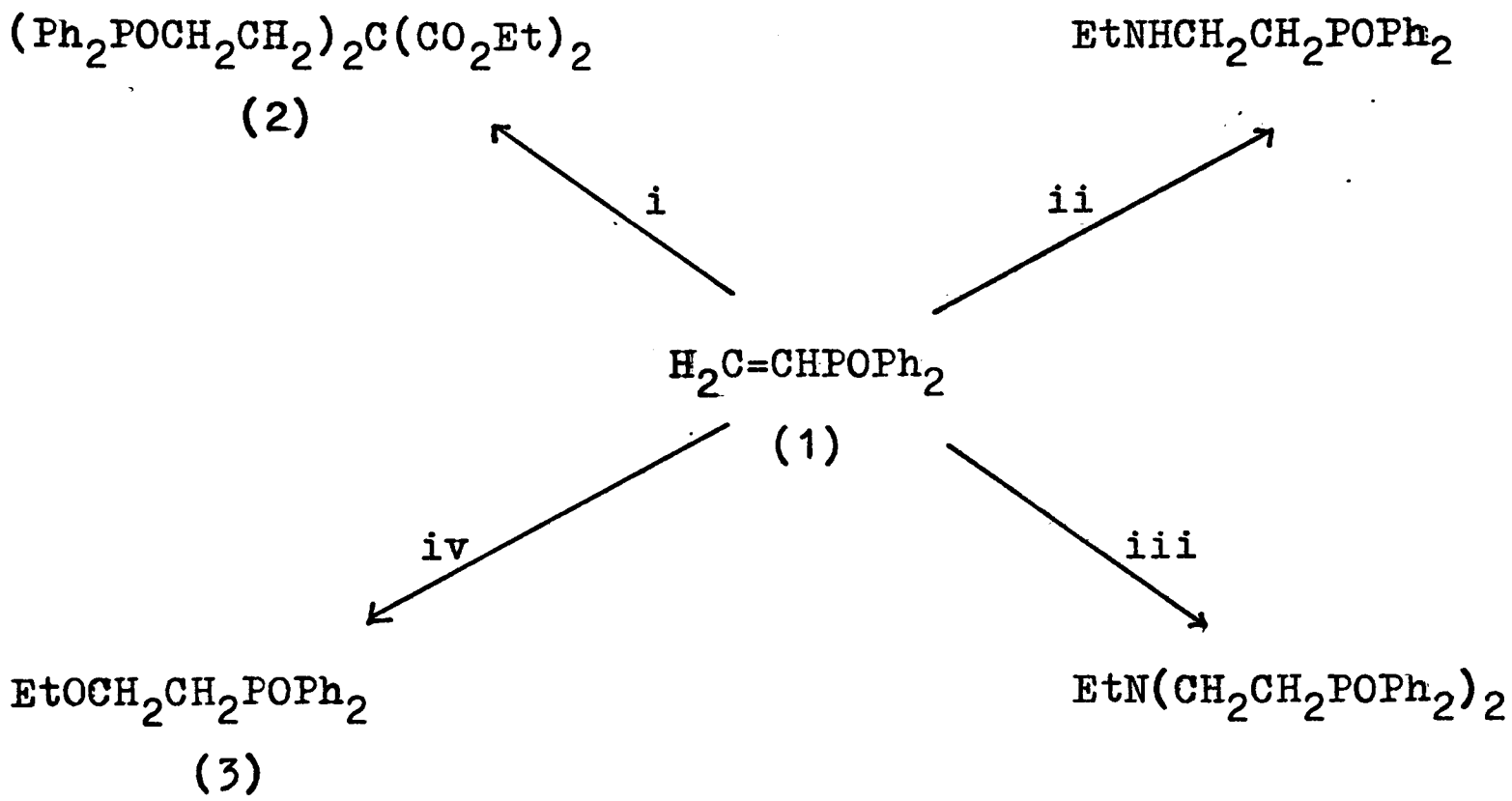
The research reported in this thesis has been arranged into five chapters. Chapter 1 deals with Michael-type additions to diphenyl vinylphosphine oxide; Chapter 2 with an investigation of the stereochemical properties of a carbanion adjacent to the phosphinyl group; Chapter 3 with the synthesis and transformations of 2-hydroxyethyldiphenylphosphine sulphides and oxides; Chapter 4 with an attempted route to cyclobutane synthesis via a modification of the Horner reaction; and Chapter 5 with sequential lithiations at phosphorus (III). The experimental work has been collated into a single section, and the results of carbon-13 spectroscopy have been grouped together as a separate short chapter. Each of the main chapters includes a more specialised introduction.

Chapter I

SOME NUCLEOPHILIC ADDITIONS TO DIPHENYLVINYLPHOSPHINE OXIDE.

Introduction

Diphenylvinylphosphine oxide (1) has been found to undergo several nucleophilic additions[47] analogous to the Michael addition[48]. Some of these are shown in Scheme 18.



i = $Na/CH_2(CO_2Et)_2/C_6H_6/reflux/4h$

ii = $EtNH_2/20^{\circ}/24h$

iii = $EtNH_2/180^{\circ}/3h$

iv = $EtOH/trace\ KOH/20^{\circ}/24h$

Scheme 18

Nucleophilic addition to (1) proceeds because the intermediate carbanion is a phosphinyl ylid, and is thus stabilised. The position of the

equilibrium between reagents and adduct appears to be more on the side of product, in additions to (1), than in corresponding additions of simple nucleophiles to α,β-unsaturated ketones. Thus adduct (3) is formed in 100% yield, where-as methanol and ethanol add to methyl vinyl ketone, to give 4-methoxy- and 4-ethoxy-butan-2-one, respectively, in only about 70% yield[49]. A possible conclusion of this is that the conjugating effect of the phosphinyl group upon adjacent C=C is much less than that of neighbouring carbonyl. We shall see (Chapter 3) that (1-diphenylphosphinyl) bicyclo[4.4.0]dec-9-ene does not tautomerise to the $\Delta^{1,2}$ or $\Delta^{1,9}$ isomer upon treatment with strong base. Corresponding sulphur compounds, sulphoxides and sulphones, prefer to keep the S=0 <u>out of</u> conjugation with C=C (Table 3).

Position of equilibrium in $XCH_2CH{=}CHCH_3 \rightleftharpoons XCH{=}CHC_2H_5$

X	% α,β	% β,γ	Base
PhS	44	56	a
PhS(O)	4	96	a
$PhS(O)_2$	1	99	a
$(EtO)_2P(O)$	25	7	b

a = $^{t}BuOH/^{t}BuOK$ [50]

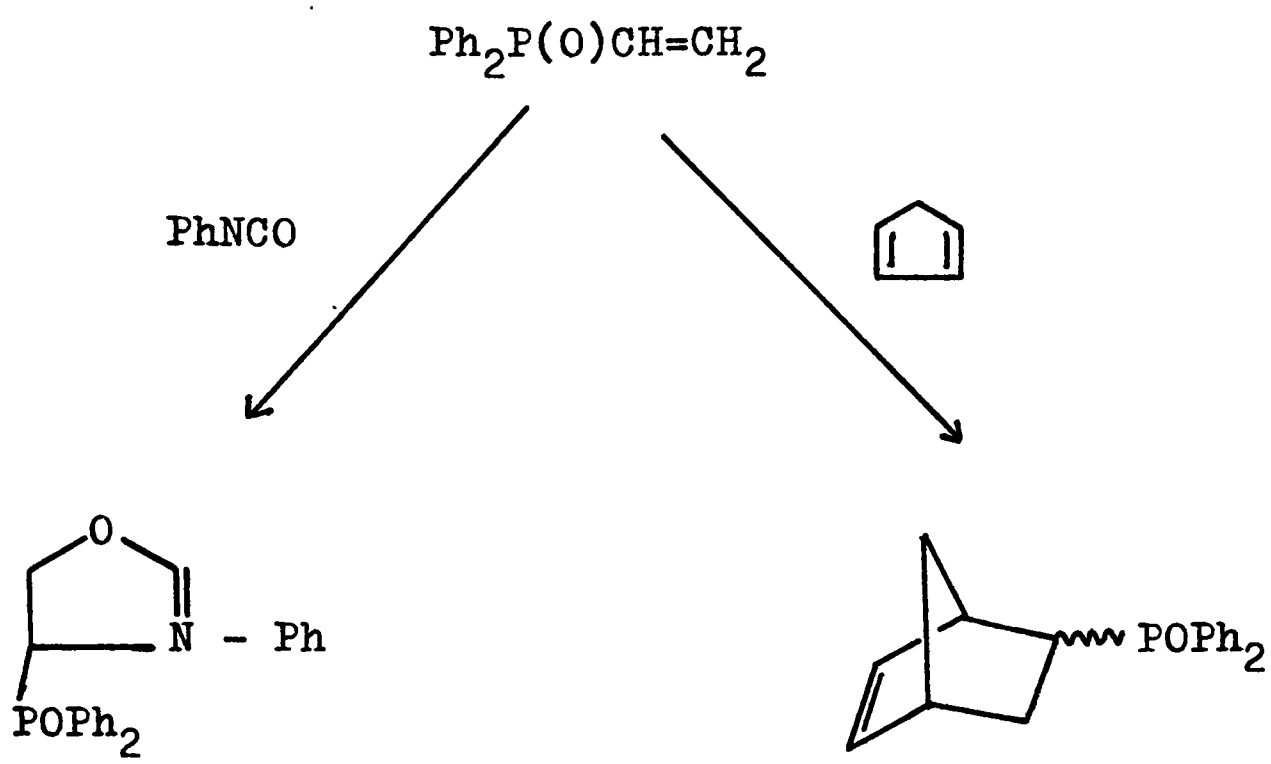
b = EtOH/KOH:

the figures are <u>isolated</u> yields[51]

Table 3

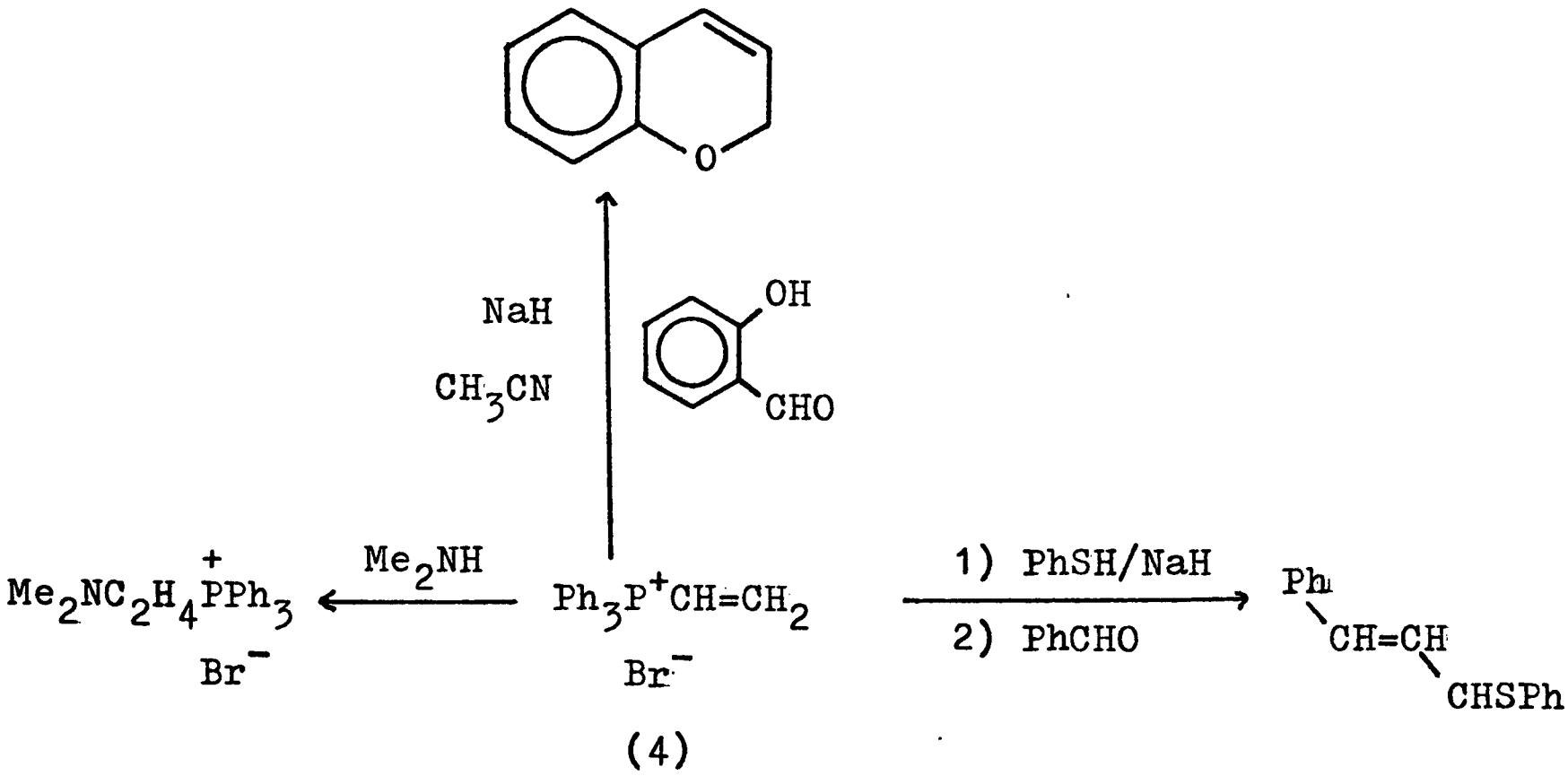
The conclusion is drawn[50] that the sulphur 3d orbitals are not involved in conjugation in the α,β-isomers.

Diphenylvinylphosphine oxide (1) has also been used as a dieneophile[47] and a 1,3-dipolarophile[52] (Scheme 19).



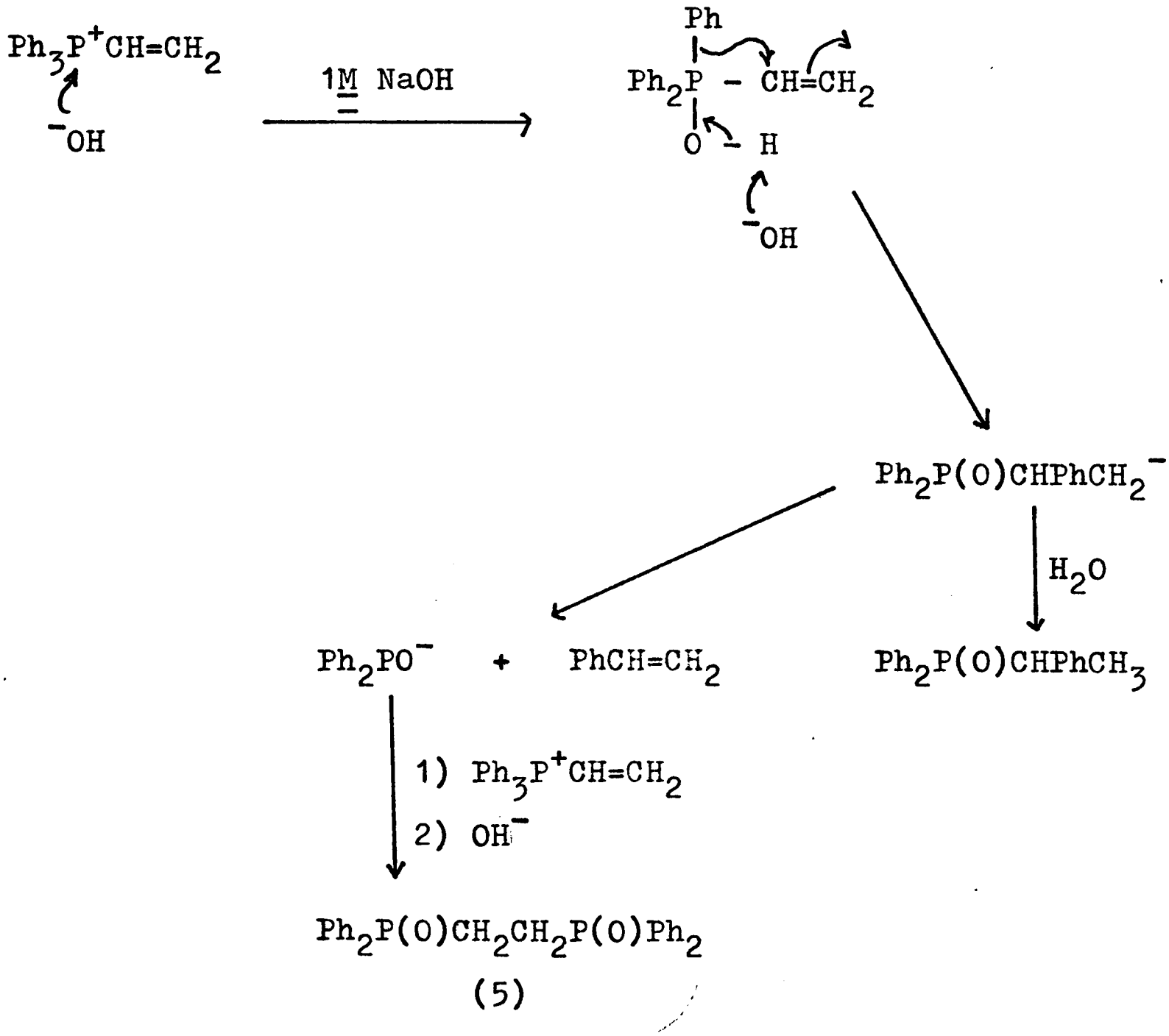
Scheme 19

Now, in principle, any molecule containing a carbon-carbon multiple bond with an α- P(IV) substituent capable of stabilising an adjacent carbanion should undergo a Michael-type addition, to produce an ylid, which might then react further under suitable conditions. The phosphonium salt analogous to phosphine oxide (1), triphenylvinyl-phosphonium bromide (4), has been used synthetically in this way: the ylid resulting from nucleophilic additions to the β- carbon has been trapped by protonation (to give β- substituted ethylphosphonium salts[53]), Wittig reaction with carbonyl compounds (to give olefins[54]) or intramolecular Wittig reaction with a carbonyl group on the nucleophilic species (the Schweizer reaction, to give a variety of carbocyclic and heterocyclic species[55]). Scheme 20 illustrates some of these reactions. The alkaline hydrolysis of salt (4) is also noteworthy (Scheme 21) [56].



(4)

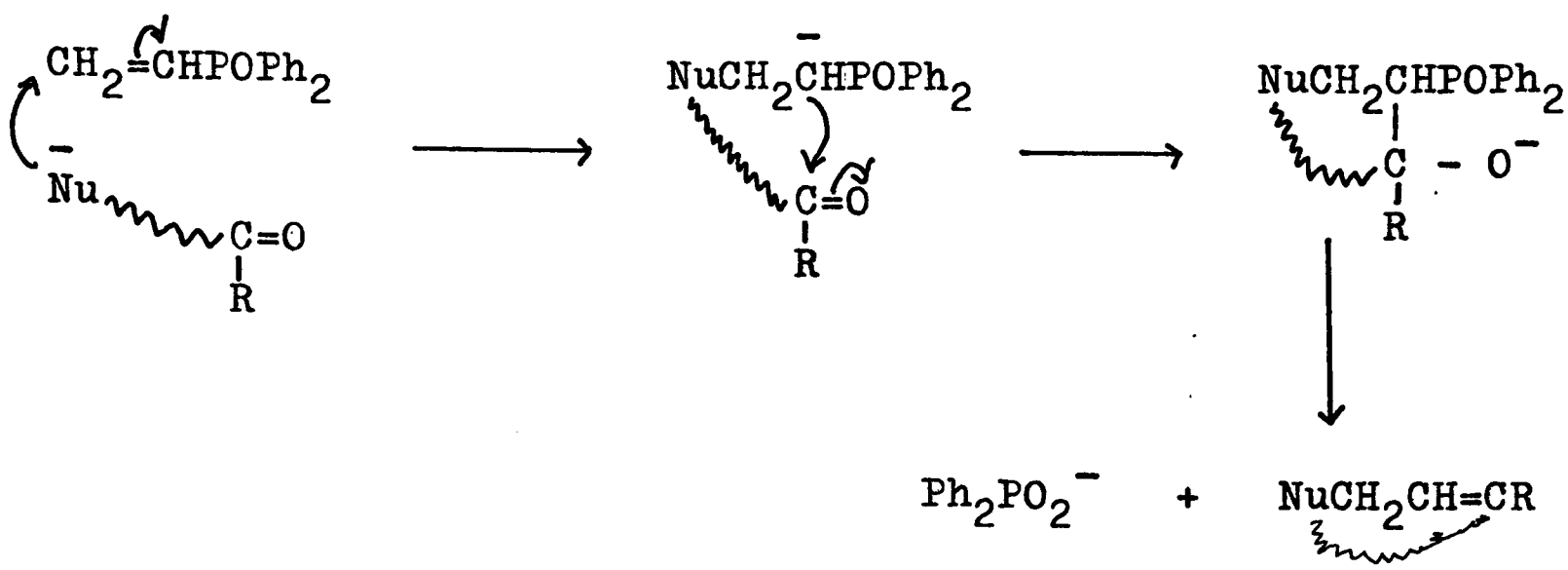
Scheme 20.



(5)

Scheme 21.

It was hoped that the Schweizer reaction could be mimicked by the use of phosphine oxide (1) (for example, see Scheme 22).



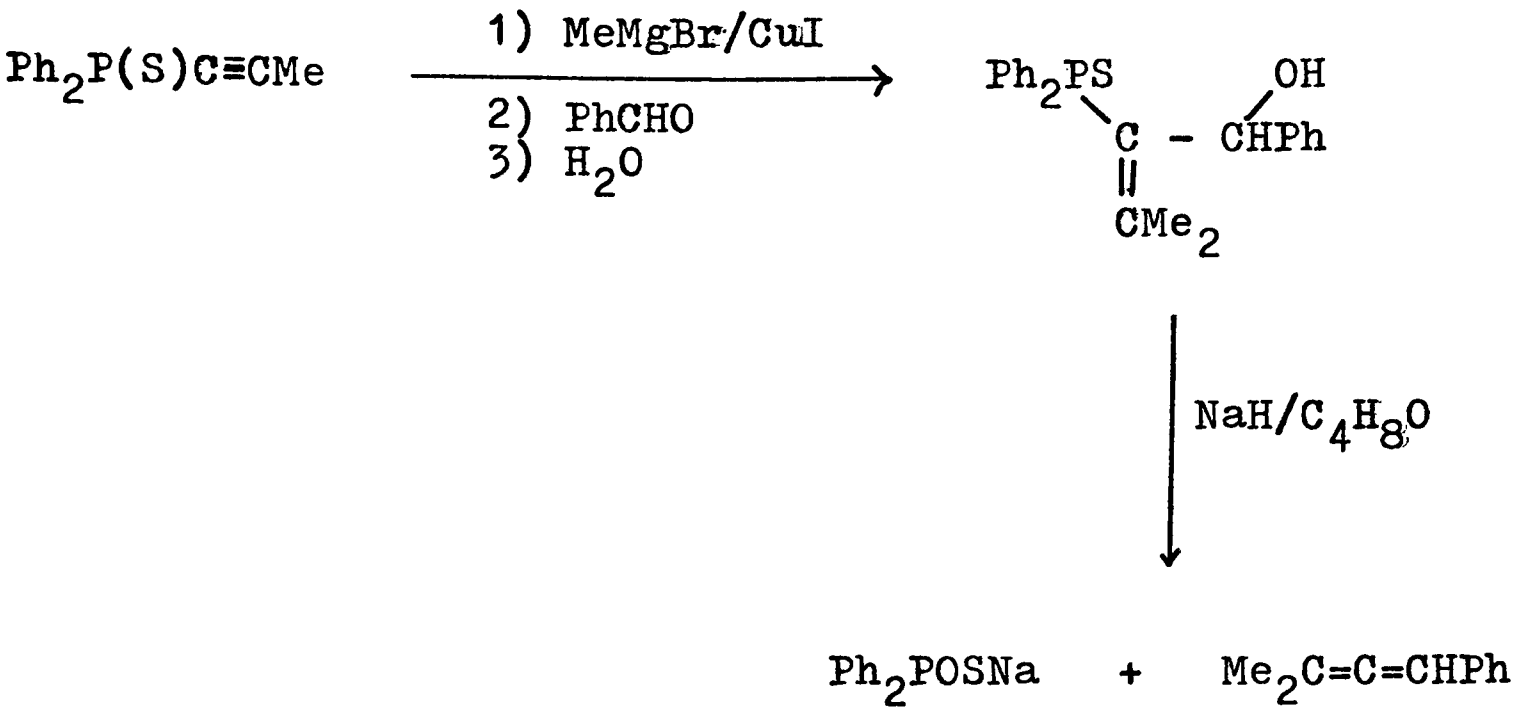
(Nu = a nucleophilic centre)

Scheme 22.

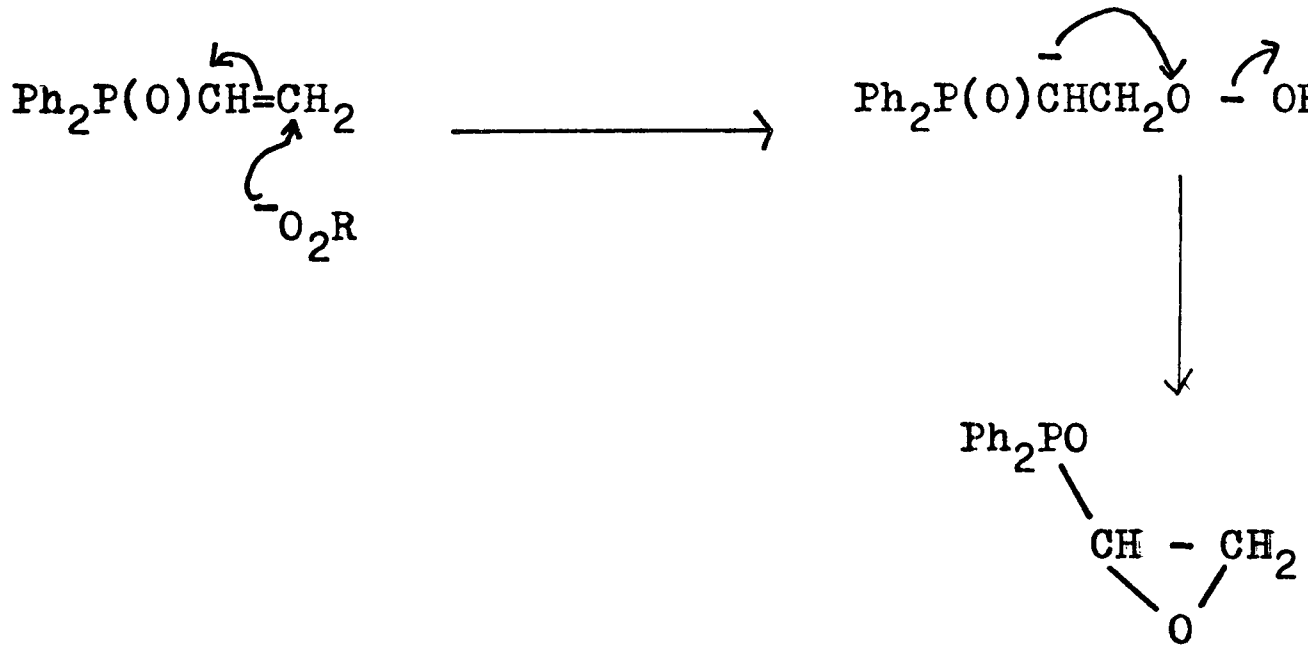
A further group of compounds related to phosphine oxide (1) are the ethynyl phosphine oxides and sulphides. Such compounds undergo Michael-type addition of amines to yield trans-enamines[57]. The ethynyl phosphine sulphides undergo nucleophilic addition of Grignard reagents to yield thiophosphinyl ylids, which may be treated with carbonyl compounds, and subsequently converted to allenes (Scheme 23)[58].

A group of reactions studied at some length in the present work were those of oxide (1) with peroxide-containing nucleophiles. It was hoped that such a reaction would lead to the preparation of epoxyvinyl-diphenylphosphine oxide (6) (Scheme 24: the outlined mechanism is analogous to the generally accepted mechanism for the epoxidation

of α,β - unsaturated carbonyl compounds by alkaline tert-butyl hydroperoxide[59,60] and by alkaline hydrogen peroxide[61]).



Scheme 23.



(6)

Scheme 24

Epoxide (6) could, in principle, be useful as a two-carbon synthon (for example, for the production of allene oxides and their derivatives[62]) An epoxide closely related to (6), diethylepoxyvinylphosphonate (7) has been prepared from diethylvinylphosphonate (8) by a variety of routes[63,64]. These are presented in Table 4.

The conversion of diethylvinylphosphonate to diethylepoxyvinylphosphonate

Reagent	% Yield
H_2O_2/NaOH	10[a]
$^tBuO_2H$/Triton B[b]	61[c]
$H_2O_2/CH_2(CO_2H)_2$	10
$CF_3CO_2H/H_2O_2/CH_2Cl_2$	72

[a] 2-(diethoxyphosphinyl) ethanal (80%) also isolated

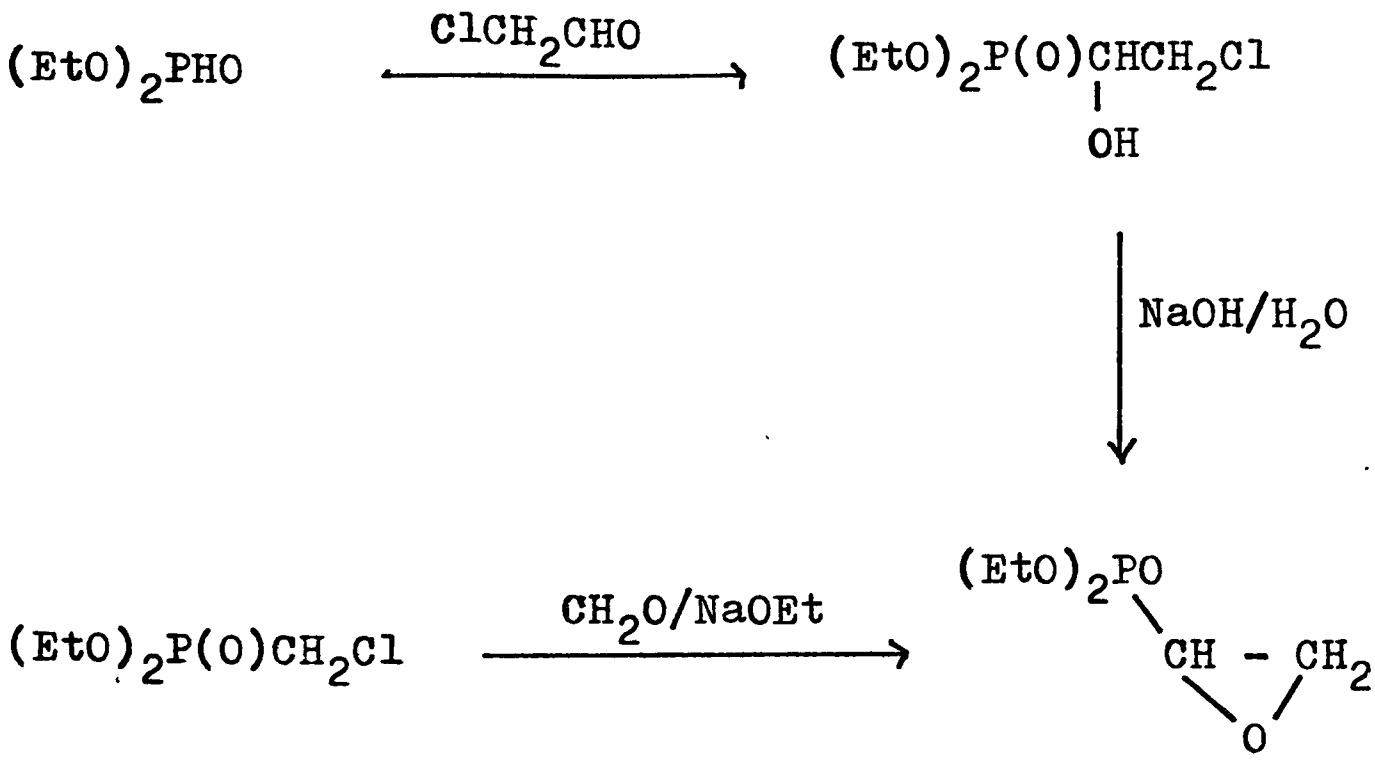
[b] benzyltrimethylammonium hydroxide 40% w/v in methanol

[c] 2-(t-butoxyethyl)diethylphosphonate (23%) also isolated.

Table 4

Other common epoxidising conditions, such as buffered trifluorperoxy-acetic acid[65] or buffered peroxyacetic acid[66], have failed to effect the conversion of (7) to (8). It should also be pointed out that, in the conversion of vinylphosphonates to epoxyvinylphosphonates with t-butyl hydroperoxide/Triton B[63], dimethylvinylphosphonate was epoxidised only to the extent of 18% and diphenylvinylphosphonate not at all.

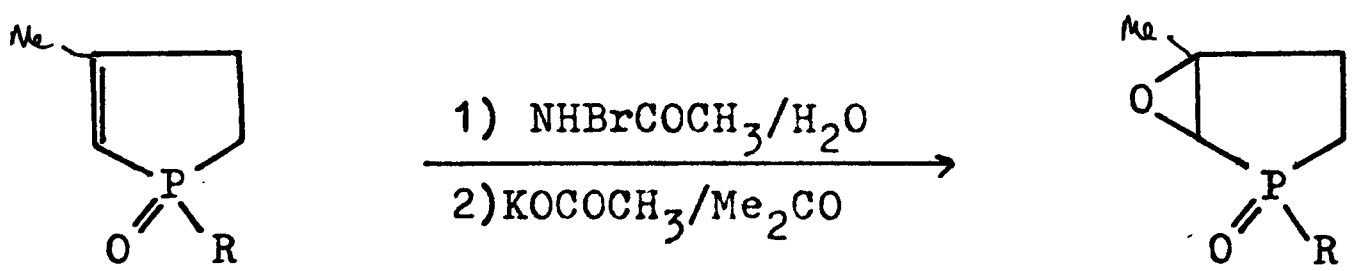
Epoxide (8) has also been prepared via halohydrins [67,68] (Scheme 25).



(8)

Scheme 25

2-Phospholenes have been epoxidised by a related procedure (Scheme 26)[69], although the orientation of the intermediate bromohydrin was not rigorously proven[70].

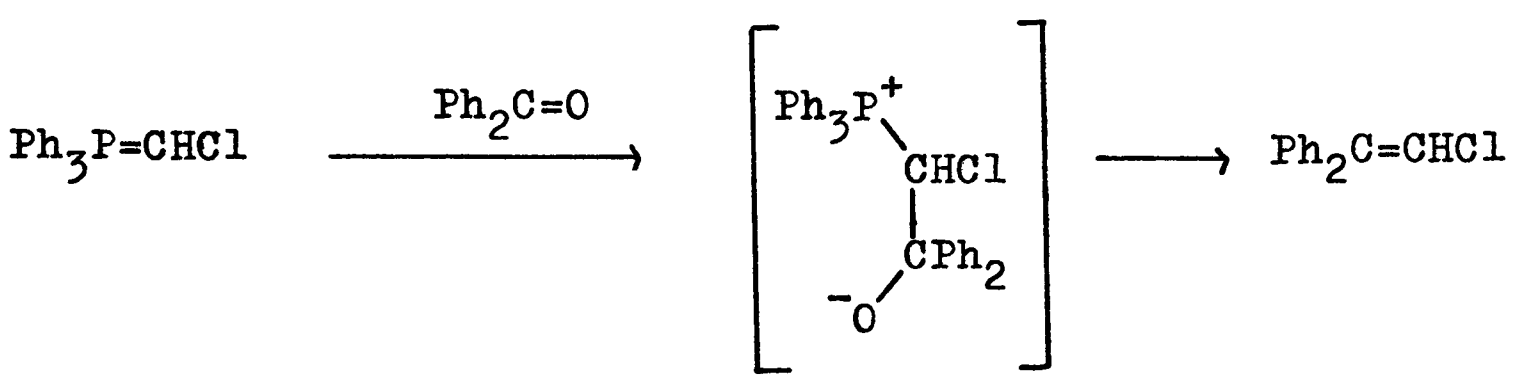


(R = Ph, OEt)

Scheme 26

It is to be expected, though, that the dialkylsubstituted double bond will undergo electrophilic attack much more readily than the carbon-carbon double bond in phosphine oxide (1).

It should be borne in mind that haloalkylidenephosphoranes react with ketones to give vinyl halides[71] (Scheme 27), and that the applicability of a similar approach to the second route in Scheme 25 for the synthesis of phosphine oxide (6) was therefore in some doubt.



Scheme 27

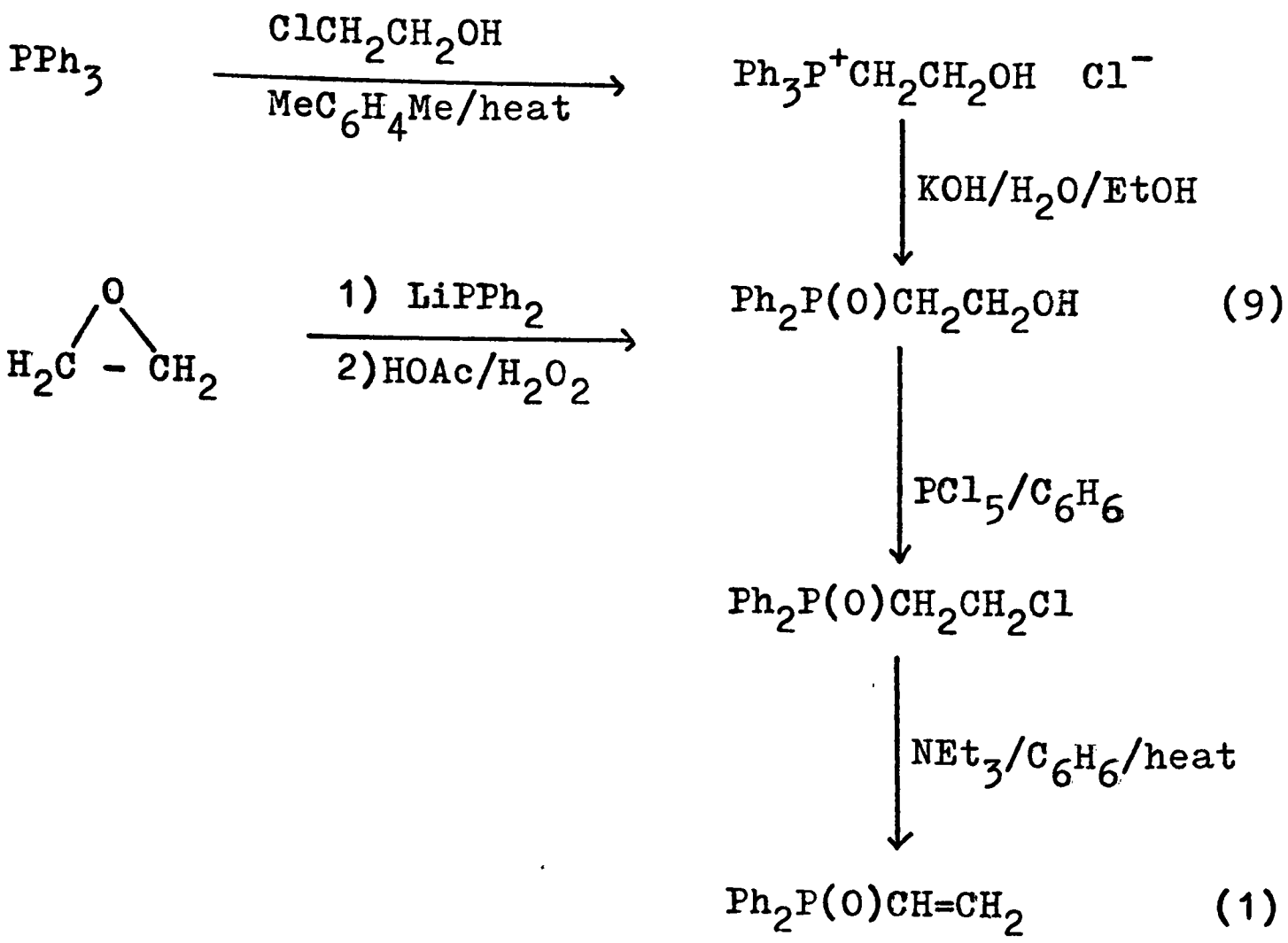
In addition to the doubt hanging over a halohydrin-type approach to epoxide (6), it was not clear, in the light of the above information, whether the carbon-carbon double bond in phosphine oxide (1) would be activated enough in a Michael sense for a base-catalysed epoxidation to occur, or so electron-deficient that a peroxyacid procedure would fail.

The reaction of epoxide (8) with base, and then ketones, was not studied here: simple alkylphosphonates are not acidic enough to be deprotonated under the conditions of the Emmons reaction (sodium hydride/1,2-dimethoxyethane/20°)[17], and rapidly polymerise with base, upon heating.

It may be noted briefly that epoxide (8) is stable to 240°, and that it reacts with nucleophiles and with boron trifluoride to give β- opened products[63].

Results and Discussion

Diphenylvinylphosphine oxide (1) was prepared as shown in Scheme 28.



Scheme 28

2-Hydroxyethyldiphenylphosphine oxide (9) was obtained pure in 74% yield by the lithium diphenylphosphide route[72], and as a non-purifiable oil in about 60% overall yield by the phosphonium salt route[73]. 2-Chloroethyldiphenylphosphine oxide was obtained in 90% yield, and oxide (1) was obtained in 66% yield from this. The recrystallisation

of crude (1) presented a problem in that no common solvent or solvent mixture appeared to be satisfactory for such a process. The method adopted was this: recrystallisation of crude (1) from ethyl acetate, followed by three to four re-workings of the mother liquors to obtain more crystals. These were pure enough for further reactions. Phosphine oxide (1) did not react with lithium triphenylmethide to give an ylid: quenching of such an attempted reaction with iodomethane or benzophenone gave only starting materials, and no evidence for the production of a phosphinyl ylid could be obtained. A similar lack of reactivity towards bases has been noted for the phosphonium salt (4). The ylid derived by deprotonation of (4) has been methylated and benzylated in poor yield[74], but attempts to carry out a Wittig reaction with pentan-3-one[75] or benzophenone[74,75] failed (but see ref. 141). Conditions were not found under which oxide (1) would take part in a Schweizer-type reaction (Scheme 22). Treatment of (1) with the sodium anions of either salicylaldehyde or benzoin, using ether, acetonitrile, or dimethylformamide as solvent, gave only very polar products, which were not further examined. 3,4-Chromene and 2,3-diphenyl 2,5-dihydrofuran, respectively, were not isolated. These are the major products obtained by treating phosphonium salt (4) with the sodium anions of salicylaldehyde[76] and benzoin[77], respectively. Attention was then focussed upon attempts to prepare epoxide (6). The approaches divide themselves into two classes: those starting from phosphine oxide (1), and other attempts. Results are summarised in Tables 5 and 6.

Reagents tried for the conversion of (1) to (6)[a].

1) $BrNHCOCH_3/NaOAc/Me_2CO/H_2O/20^o$ [b]

2) I_2/powdered $KOH/C_4H_8O/20^o$

3) $^tBuO_2H/C_6H_6$ or C_4H_8O/Triton B (trace)/20° [c]

4) $^tBuO_2H/C_4H_8O$/NaH (trace)/20°

5) $ArCO_3H/NaH/C_4H_8O/20^o$ [d]

6) $ArCO_3H/NaOH/MeOH/H_2O/20^o$

7) $ArCO_3H/CH_2ClCH_2Cl$ or $CHCl_3$/reflux

8) CF_3CO_2H/H_2O_2 (85%)/CH_2Cl_2/reflux[e]

9) $BrNHCOCH_3/H_2O/80^o$ [f]

a. In all cases, oxide (1) was recovered in good yield.

b. After ref 78

c. After ref 59

d. Ar = 3-chlorophenyl

e. After ref. 64

f. After ref 69

Table 5.

Reactions 1) and 3) are the standard conditions for epoxidising α,β - unsaturated carbonyl compounds (Table 4), and reactions 4), 5) and 6) were variations on these. It seems likely, now, that no nucleophilic addition to oxide (1) was taking place.

Attempts to synthesise possible precursors for epoxide (6)

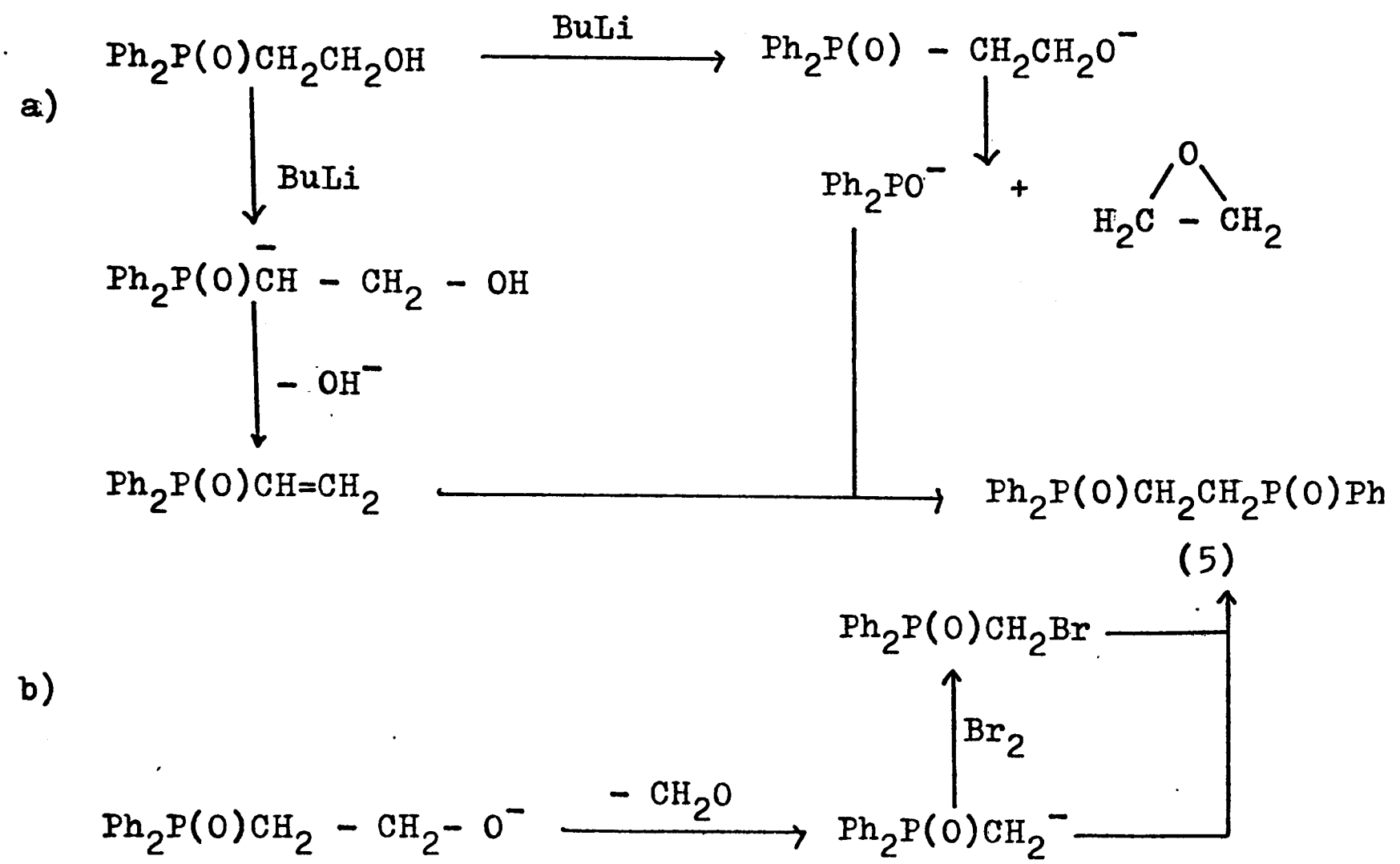
Reaction		Product.
10) Ph_2PLi	1) HCO_2Et/C_4H_8O 2) $HOAc/H_2O_2$	Ph_2PO_2H
11) $Ph_2P(S)CH_2Li$	1) $Br/C_4H_8O/20^{\circ}$ 2) H_2O	Ph_2POSH
12) Ph_2PCl	1) $CH_2O/C_{10}H_{16}$/reflux 2) H_2O	Ph_2PO_2H
13) $Ph_2P(O)CH_2CH_2OH$	1) $BuLi/C_4H_8O/-78^{\circ}$ 2) Br_2 3) H_2O	$(Ph_2POCH_2)_2$ (5)

Table 6

Reaction 10) was an intended synthesis of the unknown species, diphenylphosphinylmethanal. Reaction 11) was an attempted preparation of bromomethyldiphenylphosphine sulphide. It was intended that this be used to prepare the phosphine sulphide analogue of epoxide (6), by treatment with base and methanal (Schemes 25 to 27). Reaction 12) was an intended synthesis of chloromethyldiphenylphosphine oxide[74]. It would not, however, work in our hands.

Phosphine oxide (9) has been treated at -78° with two mole equivalents of butyllithium, to generate (presumably) the dianion (alkoxide phosphinyl ylid), which was methylated with iodomethane selectively in the α- position to give 2-diphenylphosphinylpropanol[72]. In

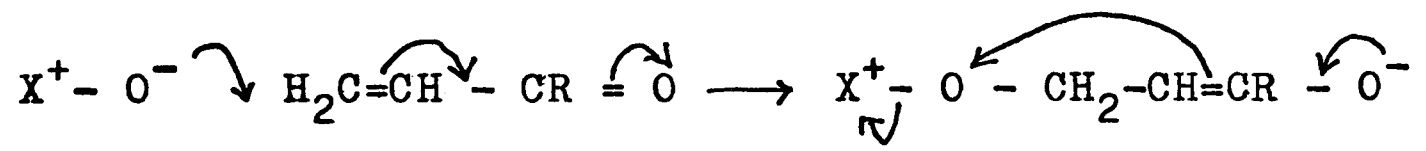
reaction 13), therefore, a similar approach on oxide (9) was tried. Treatment of (9) with, successively, two mole equivalents of butyllithium and bromine did not give (1-bromo 2-hydroxyethyl)diphenylphosphine oxide. Instead, a gum was obtained from which crystals of 1,2-bis (diphenylphosphinyl)ethane (5) separated upon standing, in 19% yield. Two possible mechanisms for the production of (5) are shown in Scheme 29.

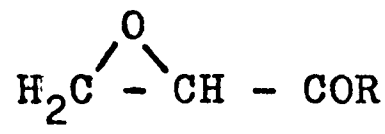


Scheme 29

As lithiomethyldiphenylphosphine oxide is converted to (5) upon treatment with copper (1) chloride and oxygen[142], mechanism b) is preferred.

In an attempt to find a new reagent capable of epoxidising an α,β - unsaturated carbonyl compound, mesityl oxide and chalcone were each treated in turn with trimethylamine oxide, pyridine N-oxide, and dimethylsulphoxide. In principle, a mechanism such as in Scheme 30 can be envisaged. No conditions were found, however, which gave any epoxides. It is not even clear as to whether any Michael-type addition occured. If it did, then the X^+-O^- bond may be too strong for fission to be effected: the peroxide linkage in hydroperoxides is a weaker bond. Some analogy for the feasibility of such a process shown in Scheme 30 is found in the conversion of activated bromoalkanes to aldehydes with trimethylamine N-oxide[80]: O-N cleavage is effected here. Phosphine oxide (1) was not affected by refluxing with trimethylamine oxide in 1,2-dichloromethane.

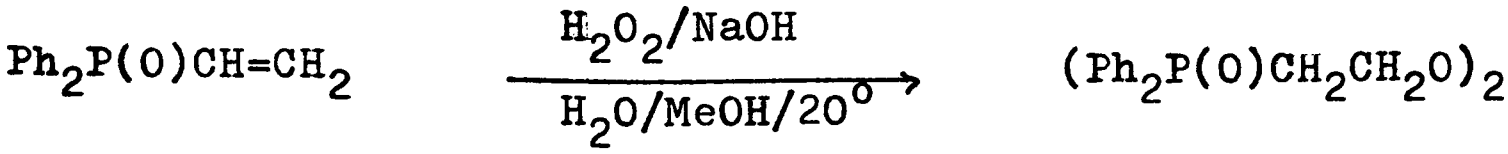




(X = Me_2S, Me_3N, C_5H_5N)

Scheme 30

Another standard procedure for the epoxidation of α,β - unsaturated carbonyl compounds is treatment with alkaline hydrogen peroxide[81]. Phosphine oxide (1) was treated with 30% hydrogen peroxide in dilute aqueous methanolic sodium hydroxide, and a high-melting crystalline product was obtained, in 79% yield. This was identified as bis (2-diphenylphosphinylethyl) peroxide (10) (Scheme 31).



(10)

Scheme 31.

The evidence for the structure of (10) may be summarised thus:

a) The i.r. spectrum contains a weak band at 827cm^{-1}. The literature value for dialkyl peroxides is 826 - 8cm^{-1} [82]. There is no band in this region in the i.r. spectra of phosphine oxide (9) or bis (2-diphenylphosphinylethyl) ether (11)

b) Both the ^{1}H and ^{13}C n.m.r. spectra of (10) are of the same general type as those of phosphine oxides (9) and (11). (^{1}H: τ 2.15 - 65 (10H), 5.75 (dt, J_{P-H} = 12Hz, J_{H-H} = 8Hz, 2H), 7.27 (dt, J_{P-H} = 14Hz, 2H). ^{13}C: aliphatic carbons only: ρ29.1 (d, J_{P-C} = 70.7Hz), 69.7 (s)).

c) Treatment of peroxide (10) with lithium aluminium hydride in ether at 20° gave phosphine oxide (9) in 84% yield.

d) The molecular ion does not appear in the same mass spectrum; the highest mass peak corresponds to $M^{+}/2$.

e) Satisfactory analytical data for (10) were not obtained; the nearest 'fit' being for a dihydrate of (10). A rough determination of the molecular weight was carried out thus: (10) gave an immediate brown colour upon treatment with potassium iodide in acetic acid, as expected for a peroxide. Titration of liberated iodine against standard aqueous sodium thiosulphate gave a molecular weight of 525 for (10). (10) corresponds to a molecular weight of 490; a dihydrate would have molecular weight 526.

f) In support of the presence of water of crystallisation in (10) as

isolated, the i.r. spectrum showed a small peak at 3360cm^{-1}. Recrystallisation of phosphine oxides from di-n-butyl ether is supposed to render them anhydrous[46]: on attempted recrystallisation of (10) from this solvent, a red oil was obtained.

The ether (11) was prepared (Scheme 32) for spectroscopic comparison with peroxide (10). It was isolated in 94% yield. An earlier attempt to prepare (11) by the Michael-type addition of the lithium anion of phosphine oxide (9) to phosphine oxide (1) gave only a complex mixture of products.

$$(TsOCH_2CH_2)_2O \xrightarrow[2)\ H_2O_2/MeOH]{1)\ LiPPh_2/C_4H_8O} (Ph_2P(O)CH_2CH_2)_2O$$

(11)

(Ts = p-$MeC_6H_4SO_2$)

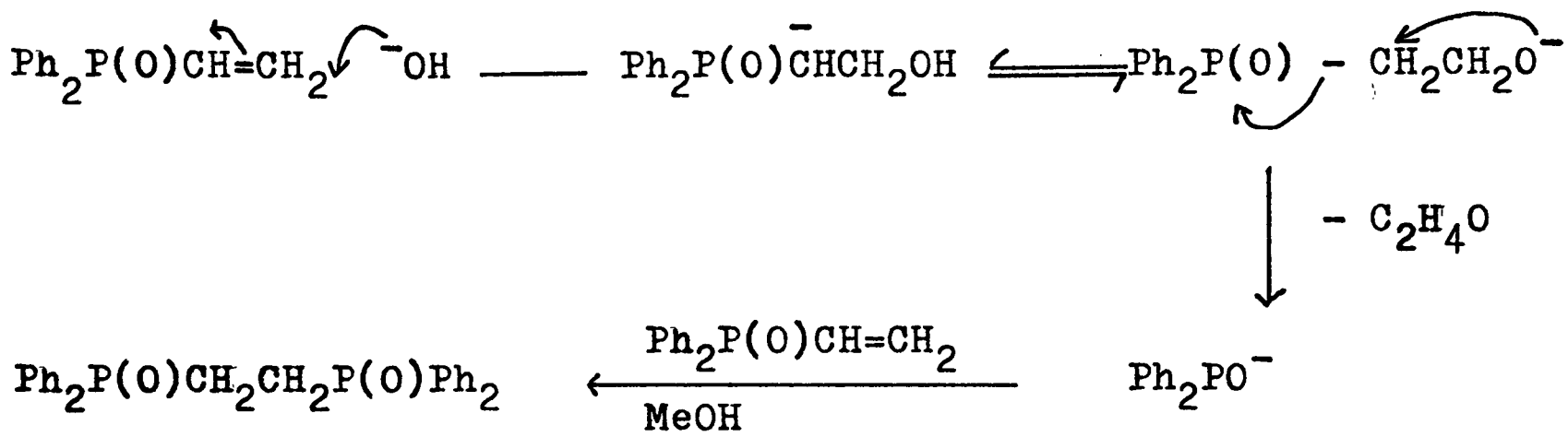
Scheme 32.

On the face of it, the production of peroxide (10) (Scheme 31) is not very surprising: it is merely the result of two Michael-type additions to phosphine oxide (1). Dialkylperoxides, though, are usually unstable species which decompose upon heating. A similar reaction to Scheme 31 reported in the literature involves a vinyl sulphonate[82] (Scheme 33).

$$PhOSO_2CH{=}CH_2 \xrightarrow{Na_2O_2} (PhOSO_2CH_2CH_2O)_2 \qquad (28\%)$$

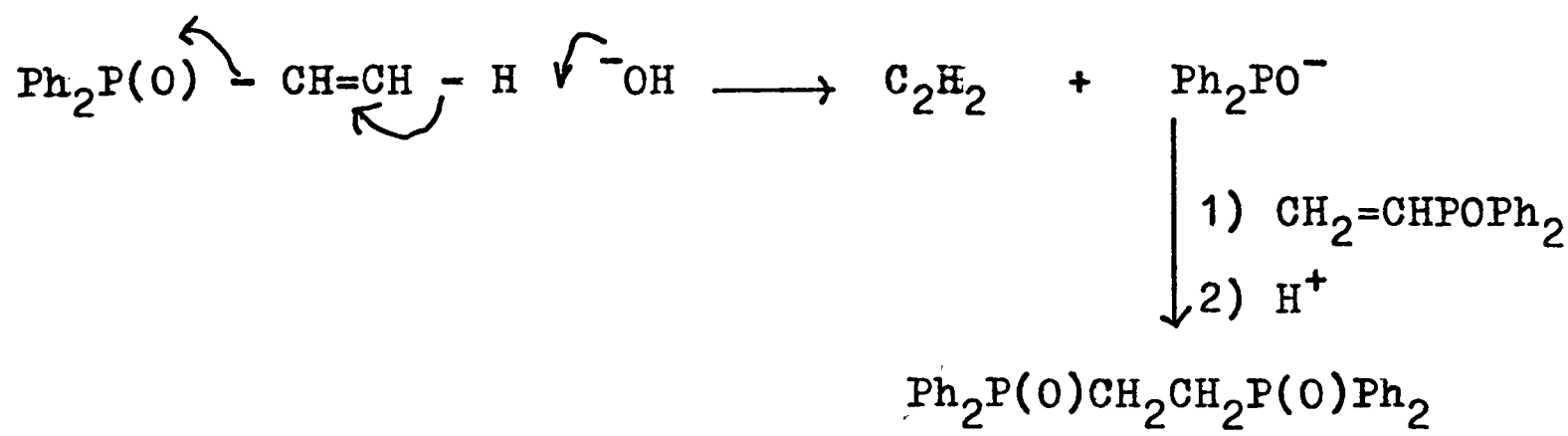
Scheme 33.

At a time when the structure of peroxide (10) was still uncertain, the phosphine oxide (1) was treated with 2M sodium hydroxide/methanol. The product was phosphine oxide (5), isolated in 96% yield. This product had also been isolated in the alkaline hydrolysis of phosphonium salt (4)[54]. A possible mechanism for the production of (5) from (1) is shown in Scheme 34.



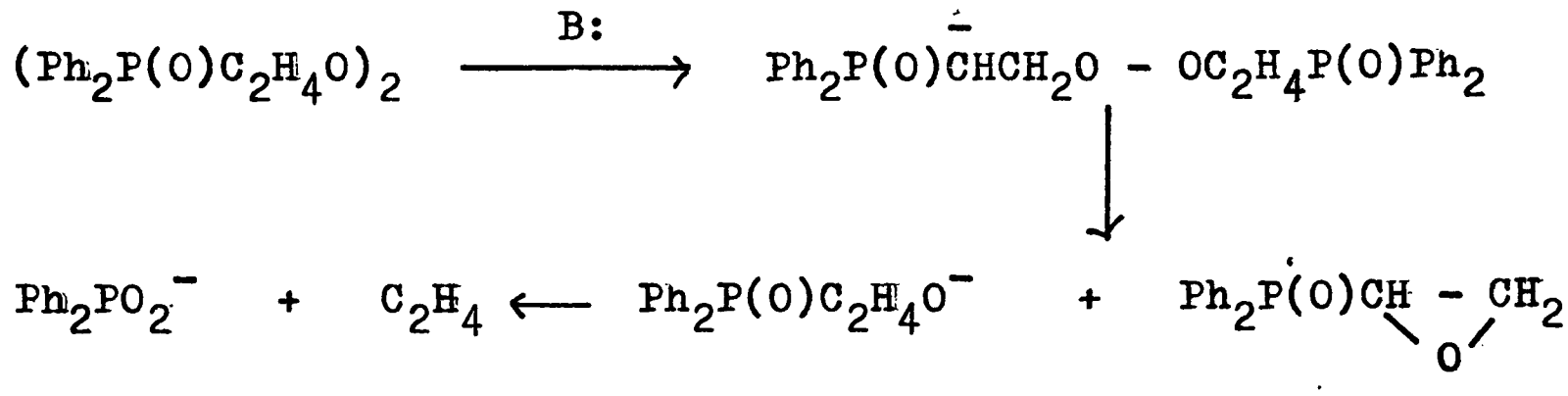
Scheme 34

2-Hydroxyethyldiphenylphosphine oxide (9) was recovered unchanged in quantitative yield after treatment with methanolic sodium hydroxide, under identical conditions to those in which phosphine oxide (1) is converted to phosphine oxide (5) (1.0g of phosphine oxide (9) + 20 ml 2M sodium hydroxide + 20 ml methanol at 20° for 24h). It is unlikely, therefore, that the conjugate base of (9) (as alkoxide anion or phosphinyl ylid) is an intermediate in the production of (5) from (1) A possible alternative mechanism is outlined in Scheme 35.



Scheme 35.

Peroxide (10), upon treatment with suitable base, could, in principle, lead to the production of epoxide (6) (Scheme 36 - the decomposition of the putative alkoxide to ethylene and diphenylphosphinate anion might lend driving force to the reaction).



Scheme 36.

Upon treatment with potassium t-butoxide in dimethylsulphoxide at 20°, peroxide (10) furnished phosphine oxide (9) in low yield, together with another, unidentified, phosphine oxide, of which the n.m.r. showed no signals above 3.5τ. The two products could not be separated, and (9) was identified by n.m.r. Most of the reaction product was removed by aqueous work-up, perhaps suggesting that the other products of the reaction were not themselves stable to the reaction conditions. In general, dialkylperoxides cleave with base by loss of an α- proton to give an alcohol and an aldehyde[83].

In conclusion, then, diphenylvinylphosphine oxide (1) has not proved to be as reactive an electrophile as was hoped. Its reaction with alkaline hydrogen peroxide to give the stable dialkylperoxide (10) is, however, of some interest.

Chapter 2

POSSIBLE ROUTES TO SOME BICYCLIC PHOSPHONATES.

Introduction

The stabilisation of a carbanion by an adjacent phosphinyl group is known in the conjugate bases of phosphonates[17], phosphine oxides[84], and phosphonamides[20]. Little work, however, has been done on the stereochemical implications of a phosphinyl group adjacent to a carbanion. Cram studied phosphinyl and sulphur ylids derived from optically active precursors $XCHMeC_6H_{13}$ (X = Ph_2PO etc)[85]. The details are outlined in Table 7.

The effect of some $P^+ - O^-$ and $S^+ - O^-$ -containing groups on an adjacent asymmetric carbanion.

Asymmetry preserved	Asymmetry not preserved
$PhSO_2$	PhSO
$MeOSO_2$	SO_3^-
$PhNMeSO_2$	Ph_2PO
$PhPO_2^-$	$(RO)_2PO$

Table 7

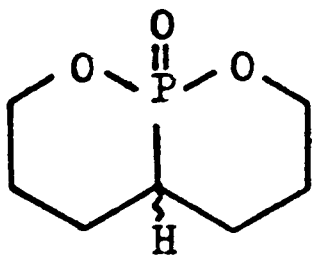
Cram measured the ratio k_e/k_a (where k_e is the rate constant for deuterium-hydrogen exchange, catalysed by potassium t - butoxide/t -(D)butanol, in $XCHMeC_6H_{13}$, and where k_a is the rate constant for racemisation of optically active substrate by potassium t -butoxide/t-butanol) for each substituent X. He found that, in the first group in Table 6, $17 \leqslant k_e/k_a \leqslant 37$, and, in the second, $k_e/k_a \approx 1$. That is, in the first group, stereochemical integrity is retained, and in the second it is not.

It should be noted that those substituents preserving asymmetry in the adjacent carbanion all have two oxygen atoms not bonded to any other atom other than the central phosphorus or sulphur: those substituents not preserving asymmetry possess either one or three such oxygens. Cram offered two explanations:

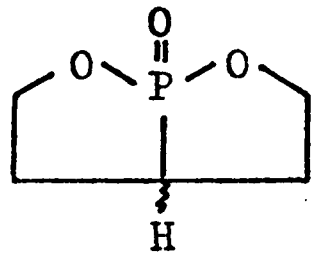
a) 'The carbanion is tetrahedral, and the partial charge on the oxygens provides electrostatic inhibition of this asymmetric species, or,

b) The carbanion is planar, is formed and captured in an asymmetric conformation for electrostatic and steric reasons, and electrostatic and steric inhibition of rotation effects maintain the asymmetric conformation'.**

In order to obtain further information about the stereochemical consequences of a carbanion α - to a phosphinyl group, it was decided to repeat Chérest and Whitham's preparation of the bicyclic phosphonate (12)[86], and fully characterise the compound. For comparison purposes, it was decided also to synthesise the bicyclic phosphonate (13) which would be expected to exist preferentially in the cis form.



(12)



(13)

It was hoped to ascertain the stereochemistry of (12) and (13) by variable-temperature ^{13}C n.m.r. and then to study their behaviour to base-catalysed deuteration and isomerisation.

** Current opinion[150] favours the second of these alternatives.

Chérest and Whitham tried several possible routes to phosphonate (12)[86] (Table 8)

Attempted routes to phosphonate (12)[a].

Reagent 1	Reagent 2
$MePO(OMe)_2$	$CH_2=CHCH_2Br/B$[b,c]
" "	$\overbrace{CH_2CH_2CH_2}O/B$
" "	$CH_2=CHCH=O/B$[d]
(14)[e]	BrC_3H_6OTHP/B[f]
" "	$\overbrace{CH_2CH_2CH_2}O/B$
" "	BrC_3H_6Br/B
" "	$TsOC_3H_6OTHP/B$[g]
(15)[h]	B
$MePO(OC_3H_6OTs)_2$[j]	B

a unless otherwise noted, starting materials were recovered

b B means prior treatment of the phosphonate with $BuLi/C_4H_8O/-78^o$

c mono-, di-, and tri-alkylated products isolated

d $(MeO)_2POCH_2CH(OH)CH=CH_2$ isolated

e for the synthesis of phosphonate (14), see Scheme 37,

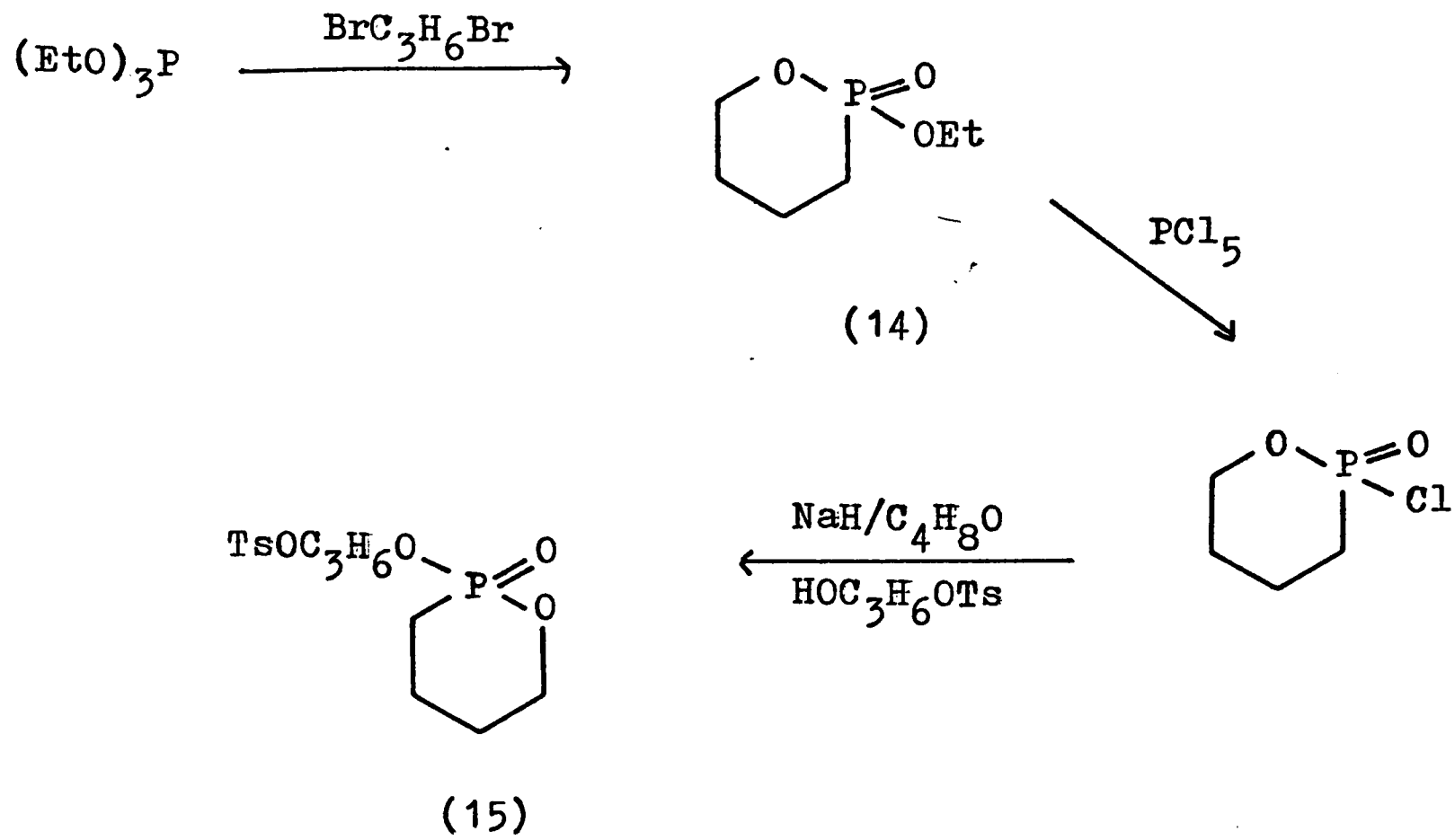
f THP = tetrahydropyranyl

g Ts = tosyl (p-tolylsulphonyl)

h for the synthesis of phosphonate (15), see Scheme 37.

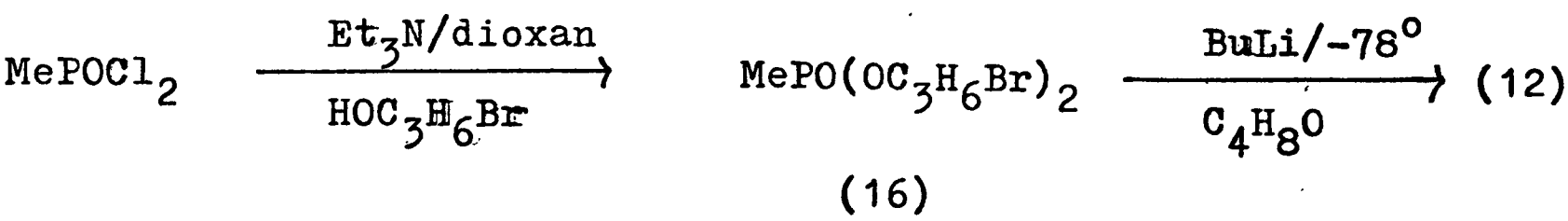
j from $MePOCl_2/HOC_3H_6OTs/NaH/C_4H_8O$

Table 8



Scheme 37

Finally, a compound was obtained[87] in yields of 30 - 50% of which the n.m.r. was compatible with structure (12) ($\tau(C_3D_6O)$ 5.55 - 95 (4H), 7.75 - 95, 7.95 - 8.40 (9H)). The route to (12) is shown in Scheme 38.



Scheme 38

The ^1H n.m.r. spectrum of (12), even at -30° was not, however, informative enough to elucidate the stereochemistry.

It was considered that, both for the synthesis of (12) and (13), and for their reaction with base, a knowledge of the conditions necessary

to metallate then alkylate an unactivated alkylphosphonate was needed. The removal of a proton from the α- carbon atom of an 'activated' alkylphosphonate (i.e. one bearing an additional electron-withdrawing group on the α- carbon atom) is well-known[17], but the conditions used to generate such phosphinyl ylids (sodium hydride in 1,2-dimethoxy-ethane at 20°) are not stringent enough to metallate, say, dimethyl methylphosphonate, and at reaction temperatures where proton removal becomes facile, polymerisation of the carbanion occurs[17]. Büchi has recently established conditions for the metallation and subsequent alkylation of simple alkylphosphonates (Scheme 39)[88].

$$(EtO)_2P(O)CH_2CH_3 \xrightarrow[2)\ HC{\equiv}CCH_2Br]{1)\ BuLi/C_4H_8O/-40^\circ} HC{\equiv}CCH_2CH(CH_3)P(O)(OEt)_2$$

Scheme 39.

Chérest and Whitham, however, have found that metallation and alkylation of simple alkylphosphonates gives mixtures of products, in approximately equal proportions[86]. (Scheme 40.)

$$CH_3PO(OMe)_2 \xrightarrow[2)\ BuBr]{1)BuLi/C_4H_8O/-78^\circ} CH_3PO(OMe)_2 + BuCH_2PO(OMe)_2 + Bu_2CHPO(OMe)_2 + Bu_3CPO(OMe)_2$$

Scheme 40

Either there is little difference between the pKa's of the various phosphonate anions (but see Introduction), or the increased nucleophilicity of the more alkylated anions compensates for the higher pKa's of their conjugate acids.

Results and Discussion

A possible precursor for phosphonate (13) was prepared as outlined in Scheme 41.

$$MePO(OMe)_2 \xrightarrow[2)\ PCl_5]{1)\ HCl} MePOCl_2 \xrightarrow[2)\ HOCH_2CH_2Br]{1)\ Et_3N/(MeOCH_2)_2} MePO(OC_2H_4Br)_2 \quad (17)$$

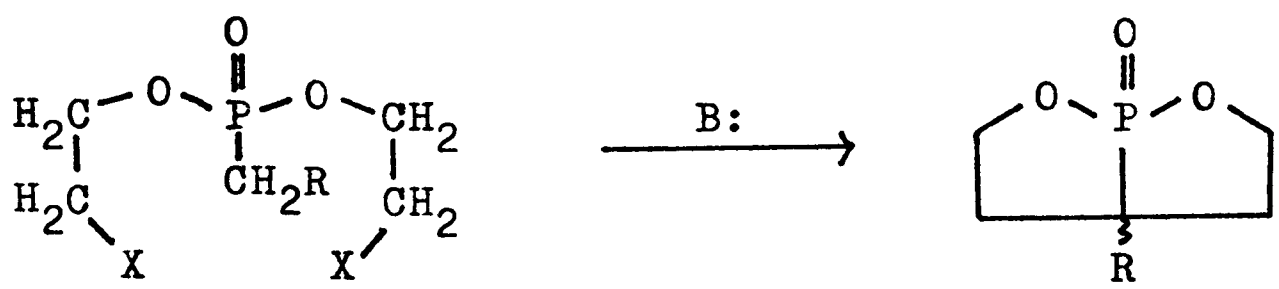
Scheme 41.

Dimethylmethylphosphonate was hydrolysed by refluxing with concentrated hydrochloric acid, to give methylphosphonic acid, which was treated with phosphorus pentachloride to yield methylphosphonyl chloride in 99% overall yield. Thionyl chloride was found to be a much inferior reagent for the chlorination step, even with prolonged refluxing together of the reagents.

Methylphosphonyl chloride was converted to di(2-bromoethyl)methyl phosphonate (17) (63% yield) by treatment with a solution of triethylamine in 1,2-dimethoxyethane at below 10°, followed by heating with 2-bromoethanol. Lower yields of phosphonate (17) were obtained using ether, tetrahydrofuran, or 1,4-dioxan as solvent. In addition, all other permutations of mixing the three reagents were tried, and found to give (17) in lower yield. The use of DABCO (diazabicyclooctane) resulted in no (17) being formed. The optimum conditions for the production of (17) were investigated quite thoroughly as a model for

the similar synthesis of di(3-bromopropyl)methylphosphonate (16), involving the more expensive reagent, 3-bromopropanol.

It was hoped that phosphonate (17) might be converted to phosphonate (13), as outlined in Scheme 42.



(17) (R = H; X = Br)

(18) (R = CO_2Et; X = Cl)

(13) (R = H)

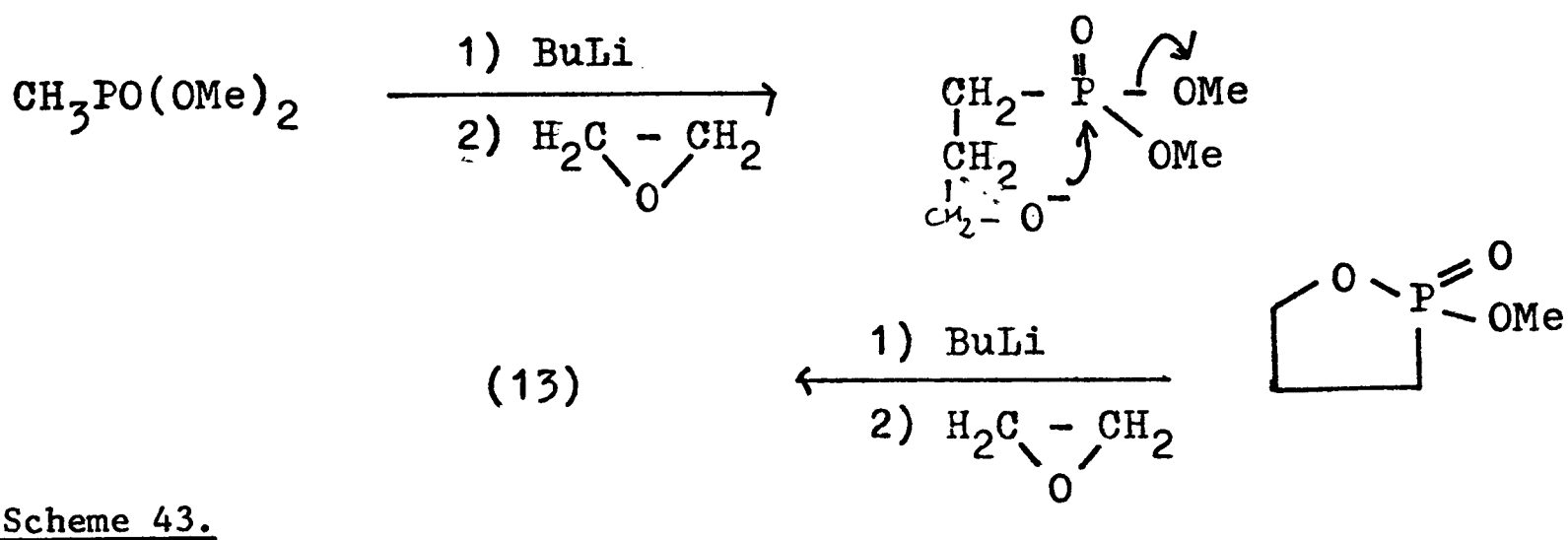
(19) (R = CO_2Et)

Scheme 42

Several sets of conditions were employed in an attempt to effect the cyclisation of (17) to (13). After adding (17) to a threefold molar equivalent of butyllithium in tetrahydrofuran at -78°, and stirring the mixture for a day or more, starting material was recovered in good yield. At -40° or 20°, products were obtained, the n.m.r. of which indicated that they contained n-butyl groups. They were not further examined. Lithium triphenylmethide in tetrahydrofuran at 20°, or lithium N-2-propylcyclohexylamide in tetrahydrofuran, at 20° or at reflux, also failed to effect any cyclisation. Only low yields of starting material were recovered when the amide base was employed.

It is known from Chérest's and Büchi's work[86,88] that simple alkylphosphonates can be lithiated by butyllithium and subsequently alkylated. The failure of phosphonate (17) to self-alkylate is possibly best explained by the degree of ring-strain that would be inherent in phosphonate (13). Such an argument should not, however, preclude the formation of a monocyclic product. Intermolecular alkylation, which might have been a competing reaction, was disfavoured by carrying out all experiments at high dilution.

Attention was then turned to the alternative route outlined in Scheme 43. Although oxetan had failed to react with dimethyllithiomethyl-phosphonate[86] (Table 8), oxirane is a more reactive electrophile.



Scheme 43.

Stepwise addition of butyllithium and oxirane to methyldimethyl-phosphonate in tetrahydrofuran at -78° did not lead to the isolation of any (13). In fact, no evidence for cleavage of oxirane was obtained, even in the presence of two mole equivalents of lithium bromide.

It is known that substituted enolate anions (e.g. those derived from a β- ketoester or β- diketone) are alkylated more readily than unstabilised enolates. By analogy, it was considered that there might be a greater chance of success of cyclisation (Scheme 42) if the

phosphinyl ylid were more stabilised. Accordingly, di(2-chloroethyl) (carboxyethyl)methylphosphonate (18) was prepared (Scheme 44).

$$PCl_3 \xrightarrow[2)\ HOC_2H_4Cl]{1)\ Et_3N/C_4H_8O} P(OC_2H_4Cl)_3 \xrightarrow[100^o]{BrCH_2CO_2Et} EtO_2CCH_2PO(OC_2H_4Cl)_2$$

(18)

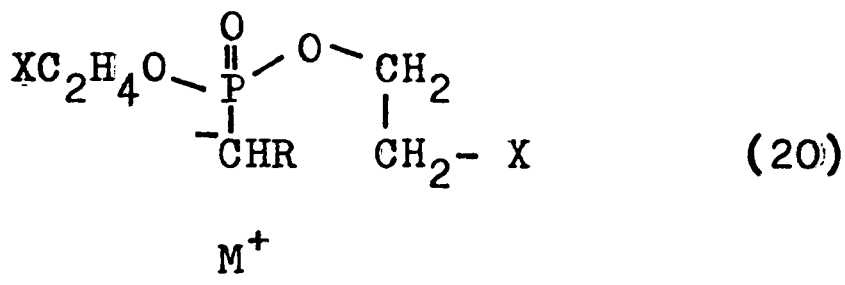
Scheme 44.

Tris(2-chloroethyl)phosphite was isolated in 57% yield from the treatment of phosphorus trichloride with triethylamine and 2-chloroethanol: the yield was considerably lowered if a rapid distillation was not carried out. Orange, water-soluble, polymeric material was always obtained. The Arbusov reaction of this phosphite with ethyl bromoacetate proceeded smoothly at 100° to yield phosphonate (18) in 80% yield. A reaction time of three hours was found to optimise the yield. The structure of (18) was proved by n.m.r. (τ 5.35 - 5.90 (m,6H: $\underline{CH}_2$-O), 6.28(t,J_{H-H} = 7Hz, 4H: $\underline{CH}_2$-Cl), 6.93 (d,J_{P-H}=22Hz, 2H: $\underline{CH}_2$-P), 8.72 (t,J_{H-H} = 8Hz, 3H: $\underline{CH}_3$-CH_2)).

Wadsworth and Emmons have alkylated stabilised phosphinyl ylids by treatment with haloalkanes in refluxing 1,2-dimethoxyethane[17]. Thus attempts were made to effect the cyclisation of phosphonate (18) to bicyclic phosphonate (19). It was hoped that the latter could be hydrolysed and decarboxylated to yield phosphonate (13). However, phosphonate (18) failed to undergo intramolecular (or, indeed, intermolecular) alkylation. (18) reacted with sodium hydride in 1,2-dimethoxyethane to liberate hydrogen and give a white solid (presumably

the sodium salt), but further reaction did not occur, even after prolonged reflux, and (18) could be recovered in good yield after work-up. No cyclisation was observed on changing the conditions to sodium hydride/tetrahydrofuran or potassium tert-butoxide/benzene or toluene/ reflux. Again, starting material was recovered in good yield in all cases.

Again, it is not clear why phosphonate (18) failed to self-alkylate. It is unlikely that the sodio- or potassio- derivative is too stabilised to be alkylated. A possible explanation (also applying to phosphonate (13)) is this: the metallo-anion (20) is a phosphinyl ylid, and for its stabilisation, a peri- or antiperi- planar relationship between the lone pair on carbon and the phosphinyl group may have to be maintained. From models of anion (20), it can be seen that much strain is involved on cyclisation if the 2 - haloethyl side chain approaches the carbanionic centre, such that a 180° relationship is maintained between the lone pair on carbon, the CH_2 α - to halogen, and the halide leaving group.

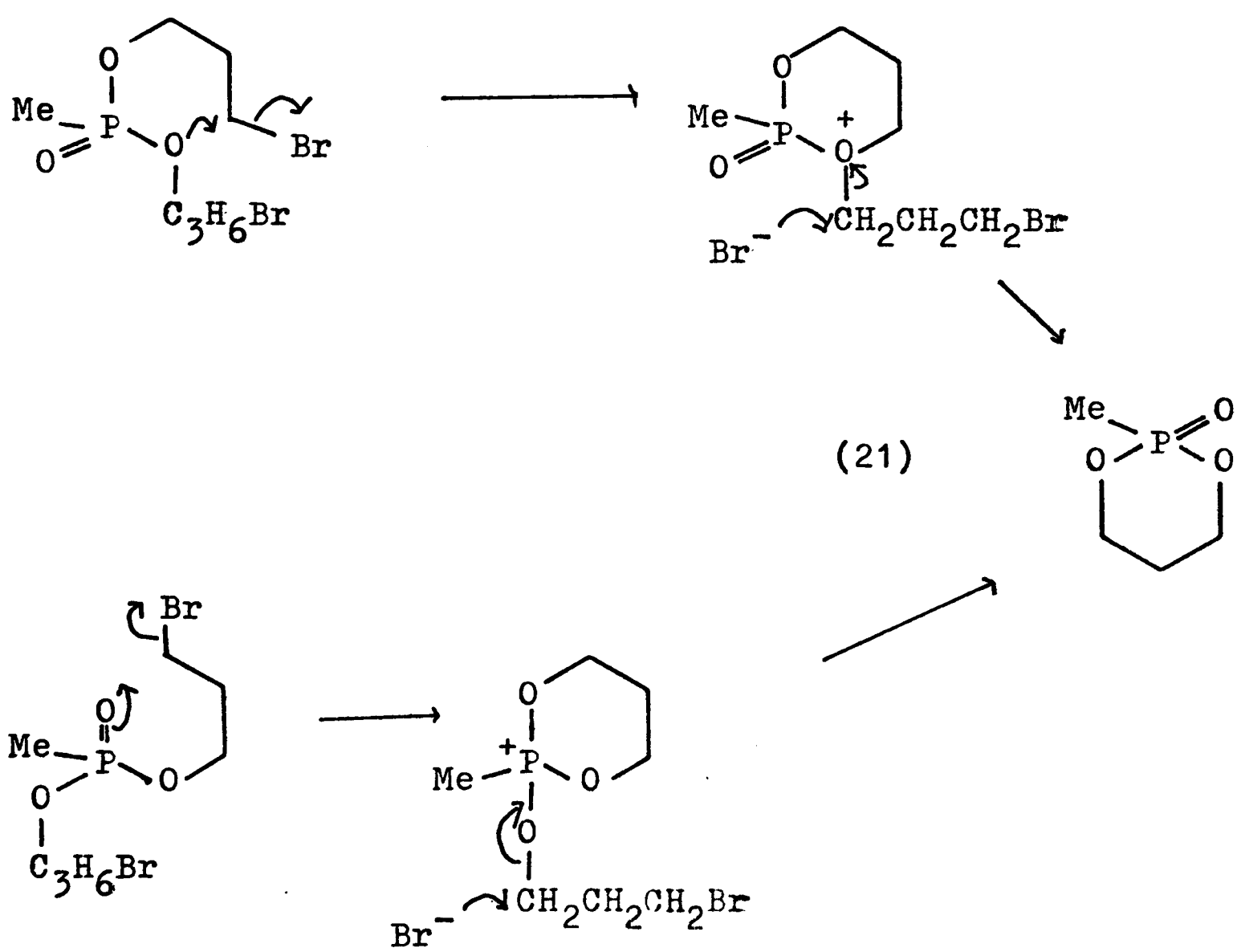


(20)

($R = CO_2Et$, $X = Cl$; $R = H$, $X = Br$)

Attempts to synthesise phosphonate (13) were then abandoned, and a repetition of Chérest's preparation of phosphonate (12)[87] was attempted (Scheme 38).

Di(3-bromopropyl)methylphosphonate (16) was prepared in 79% yield by the treatment of methylphosphonyl chloride with triethylamine/ tetrahydrofuran/3-bromopropanol (Scheme 25). Distillation of crude (16) led to partial decomposition to 2-methyl 1,3,2,-dioxaphosphorinan 2-oxide (21). This reaction had not been reported by Chérest[87]. Volatile impurities were thus removed from crude (16) at 20 mmHg on a boiling water bath, to give material of which the n.m.r. was identical to that reported by Chérest. Two possible mechanisms for the thermal conversion of (16) to (21) are shown in Scheme 45, of which the second seems preferable.



Scheme 45.

The structure of (21) was shown by n.m.r. (τ 5.22 - 86 (m, 4H: $C\underline{H}_2$-O), 7.89 (m, 2H: CH_2-$C\underline{H}_2$-CH_2), 8.49 (d, J_{P-H} = 18Hz, 3H: $C\underline{H}_3$-P).

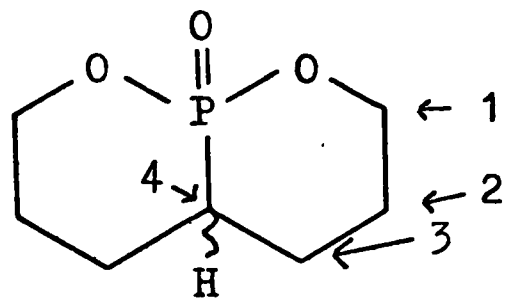
Several attempts were made to effect the conversion of phosphonate (16) to bicyclic phosphonate (12), under the conditions given by Chérest. Treatment of (16) with three mole equivalents of butyllithium in tetrahydrofuran at -78°, followed by stirring for 28h, gave no (12) on quenching, and starting material could be recovered in good yield. Repetition of the procedure at -40° or 20° gave products containing (by n.m.r.) n-butyl groups and the P-CH_3 moiety.

It was considered that a hindered amide base might prove more effective at effecting the cyclisation, notwithstanding the failure of such a base to effect the conversion of phosphonate (17) to bicyclic phosphonate (13). A brief study was carried out on the lithiation and alkylation of dimethylmethylphosphonate using lithium amides in tetrahydrofuran or ether as solvent. Treatment of dimethylmethylphosphonate at -78° with one mole equivalent of lithium N-2-propylcyclohexylamide and quenching with n-bromobutane produced mixtures of mono-, di-, and tri-substituted products. This is analogous to the results of alkylation experiments performed using butyllithium as base (Scheme 40). The major product isolated from the treatment of dimethylmethylphosphonate with lithium N-2-propylcyclohexylamide at 20° was a white, extremely water-soluble solid. The n.m.r. of this material was consistent with it being a mixture of phosphonamides. Again, after quenching with n-bromo-butane, mixtures of alkylated products were obtained, in low yield. The base LiTMP (lithium 2,2,6,6,-tetramethylpiperidide)[89] gave good yields of (mixtures of) alkylated products, and water-soluble products were no longer obtained.

Polylithiation and polyalkylation should not be a problem in the conversion of (16) to (12) as dialkylation is required anyway, and intermolecular alkylation can be retarded by performing the reaction at high dilution. Accordingly, phosphonate (16) was treated with LiTMP in tetrahydrofuran at 20°, and the mixture stirred for 24h. Starting phosphonate was recovered in good yield. At 60° a small amount of yellow oil was obtained after distillation. The n.m.r. of this product was, however, very complex, and did not correspond to that of phosphonate (12)[87]
It may have been possible to effect the cyclisation of (16) to (12) after much further experimentation with conditions. Time, however, did not permit such an investigation, and the route was abandoned.
It is still not clear why phosphonate (16) should, in the hands of one empiricist, distil satisfactorily and cyclise to (12) in the presence of butyllithium, yet, in the hands of another, decompose upon distillation and fail to cyclise.

Despite the failure of phosphonate (18) to cyclise with base to (19), it was considered that an analogous route, via a stabilised phosphinyl ylid, might still be feasible for the larger bicyclo[4.4.0] ring system. Attempts were thus made to prepare a phosphonate analogous to (18). Tris(3-chloropropyl)phosphite was obtained in 45% yield (not optimised) by the reation of phosphorus trichloride with triethylamine/tetrahydrofuran/3-chloropropanol. However this phosphite failed to undergo an Arbusov reaction with methyl bromoacetate, at 100° or at reflux, or with chloroacetonitrile after prolonged refluxing.
The low nucleophilicity of tris(3-chloropropyl)phosphite compared to tris(2-chloroethyl)phosphite (Scheme 31) is remarkable. A possible explanation relates to Newman's 'rule of six'[90]. Substituents on the γ- carbon atom could hinder the approach of electrophiles to the central phosphorus atom.
Finally, a crystalline sample of phosphonate (12) was obtained from Dr. M. Chérest. The low temperature ^{13}C n.m.r. spectrum was

recorded, using ^{2}H-chloroform as solvent.



(12)

C_1 70.1 (J = 6.1), C_4 31.2 (J = 114.8), C_2, C_3 26.7 (J = 6.1) and 24.0 (J = 6.9).

C_4 was distinguished from C_2 and C_3 with the aid of the off-resonance decoupled spectrum, in which C_4 resonates as a doublet of doublets, and C_2, C_3 as doublets of triplets.

A sample was also obtained from Dr. Chérest of a concentrate of mother liquors from the recrystallisation of phosphonate (12). The room temperature ^{13}C n.m.r. spectrum of this material showed several signals in addition to those due to (12), and little useful information could be extracted from it.

The ^{31}P n.m.r. spectrum of (12), in ^{2}H-chloroform, showed a signal 29.7 p.p.m. downfield from external trimethylphosphate. The mother liquors showed three additional signals in the same region.

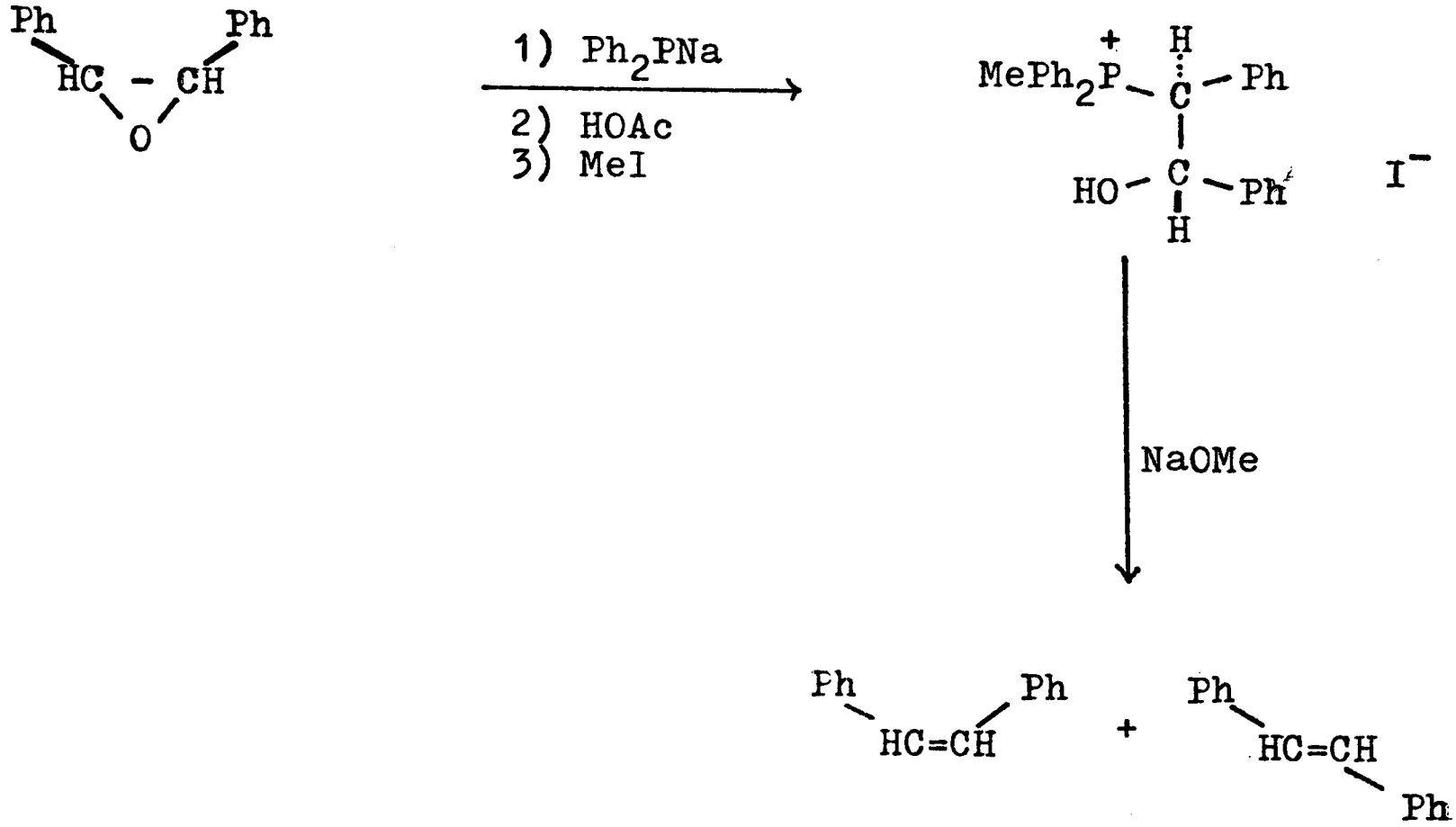
The ^{13}C and ^{31}P m.n.r. spectra together provide good evidence that the structure of the bicyclic phosphonate is indeed (12), but do not

distinguish between <u>cis</u> and <u>trans</u> isomers.

Chapter 3.

THE SYNTHESIS AND TRANSFORMATIONS OF 2-HYDROXYALKYLDIPHENYLPHOSPHINE SULPHIDES AND RELATED COMPOUNDS.

Treatment of epoxides with diphenylphosphide anion, followed by acidification and quaternisation, gives 2-hydroxyalkylphosphonium salts (Scheme 46), which are the conjugate acids of the betaine intermediates produced in the Wittig reaction. These phosphonium salts may be converted to olefins by treatment with base[91,92,93].

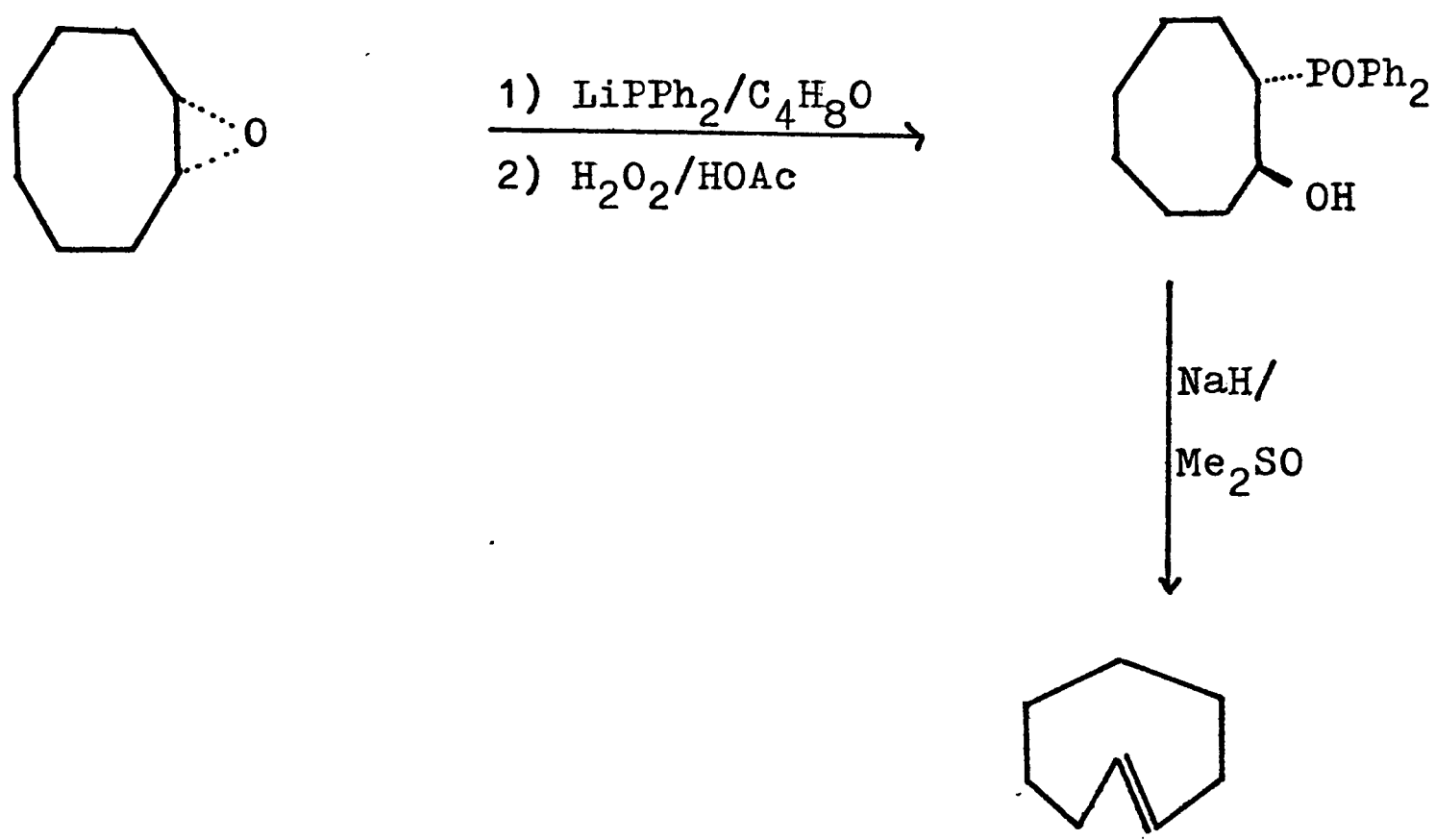


Scheme 46.

Analogously, an olefin-forming reaction which mimics the Horner reaction has been reported[72,94] (Scheme 47).

By this procedure, the intermediate 2-hydroxyalkylphosphine oxide is isolated, and fragmented, after purification. Such phosphine oxides

are easier to purify than their phosphonium salt counterparts (Scheme 46) and this reaction has re-stimulated interest in the Horner reaction which, otherwise, shows few advantages over the Wittig reaction.



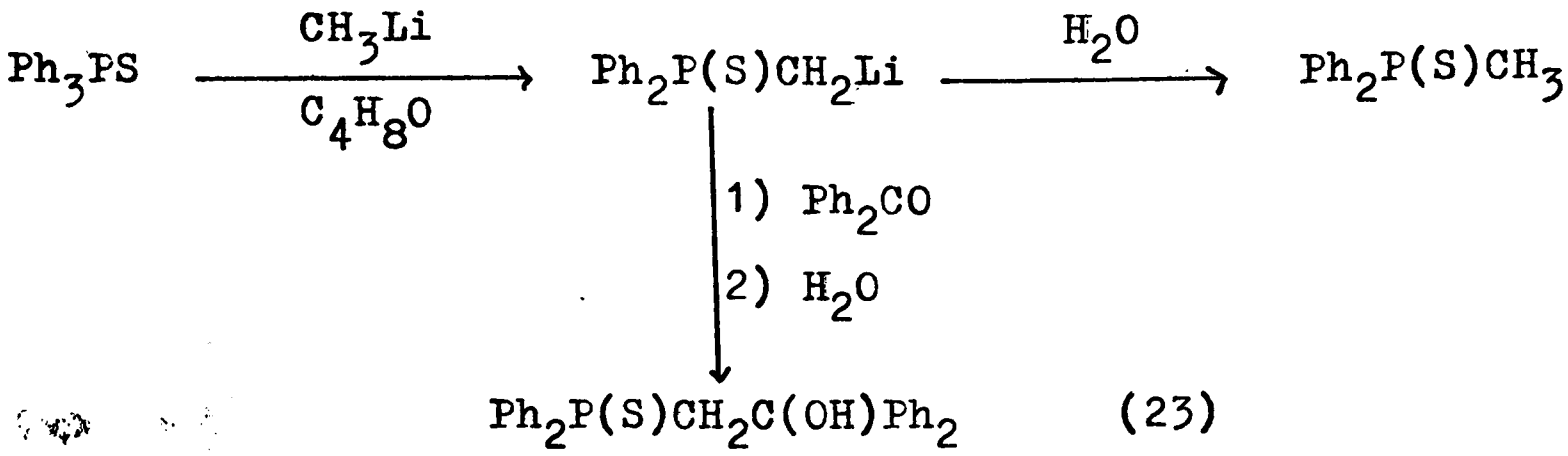
Scheme 47.

Interestingly, Horner has noted a cation dependence for the fragmentation of the 2-hydroxyalkylphosphine oxides.[42]. The lithium derivative is stable under the conditions of its formation (from alkyldiphenyl phosphine oxide/phenyllithium/tetrahydrofuran/ketone/20°), whereas the sodium and potassium derivatives decompose under such conditions to olefin and diphenylphosphinate. Possibly, the comparison is not strictly valid, as, in the lithium derivative, there may be other species present which could have an effect on the equilibrium position of the reaction.

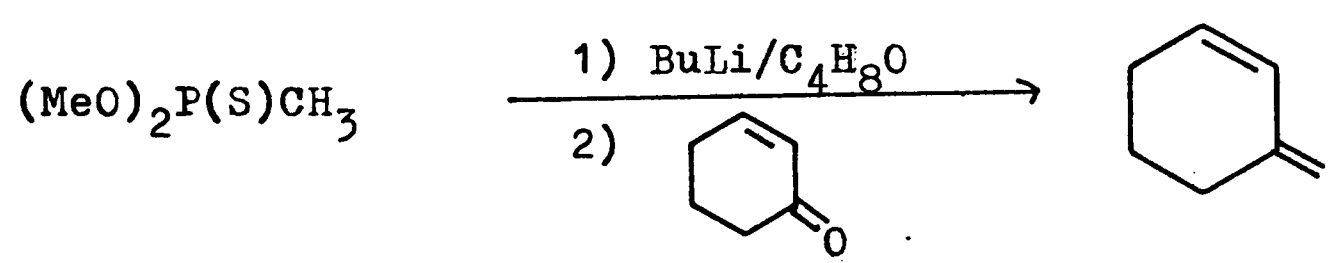
The reaction outlined in Scheme 47, which may be termed a 'modified Horner reaction' is, in general, stereoselective if aryl groups are α- to the epoxide, and stereospecific if only alkyl groups are α- to the epoxide[94].

It was considered that a comparative study of the 2-hydroxyalkylphosphine sulphides and oxides might be of value. The thiophosphinyl bond is

polarised in the same sense as the phosphinyl bond, and is known to stabilise an adjacent carbanion[95] (Scheme 48) and to promote a 'thio-analogue' of the Horner-Emmons reaction (Schemes 23 and 49)[28,58].



Scheme 48.



Scheme 49

The thiophosphinyl linkage is weaker than the phosphinyl linkage: this is illustrated in Table 9. It is not immediately apparent what effect the lower bond energy of P=S would have upon a 'thio-analogue' of the Horner reaction. There is, however, no a priori reason to suppose that 2-hydroxyalkylphosphine sulphides would not undergo such a reaction.

Bond energies of phosphine oxides and sulphides[3]

Compound	X = O[a]	X = S[a]
Cl_3PX	128	69
$(EtO)_3PX$	151	91
Me_3PX	139	92
$^nBu_3PX$	137	92

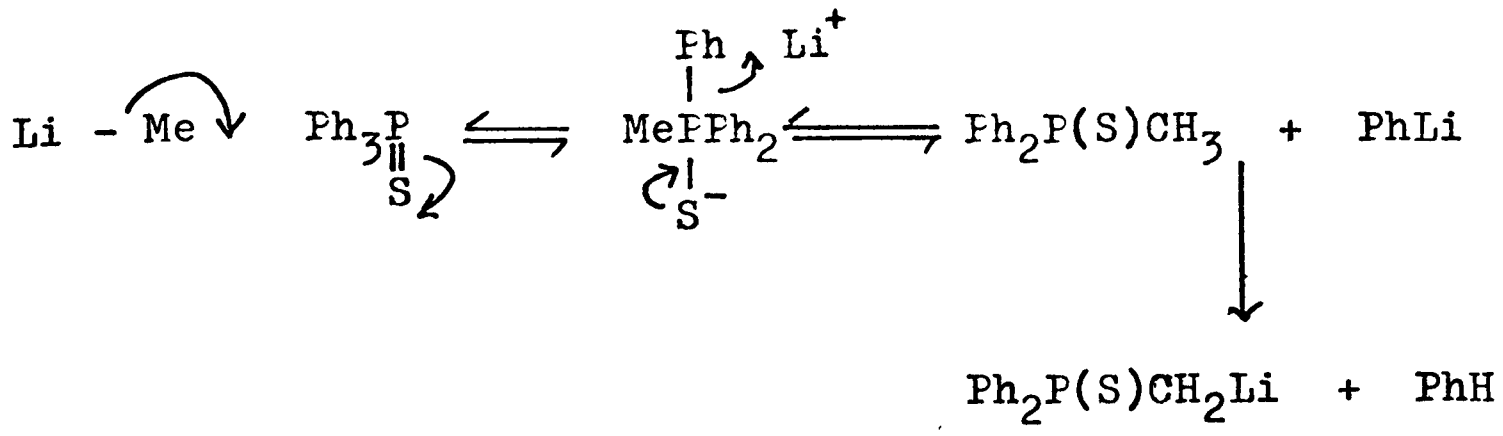
[a] in $Kcal.mol^{-1}$

Table 9

One incentive for this investigation is that the general method for formation of 2-hydroxyalkalphosphine oxides involves alkylation of lithium diphenylphosphide with an epoxide, followed by treatment with acetic acid and hydrogen peroxide[72]. These conditions might be too powerful for some groups to survive, and reaction of the intermediate 2-hydroxyalkylphosphine with elemental sulphur might provide a mild alternative.

Results and Discussion

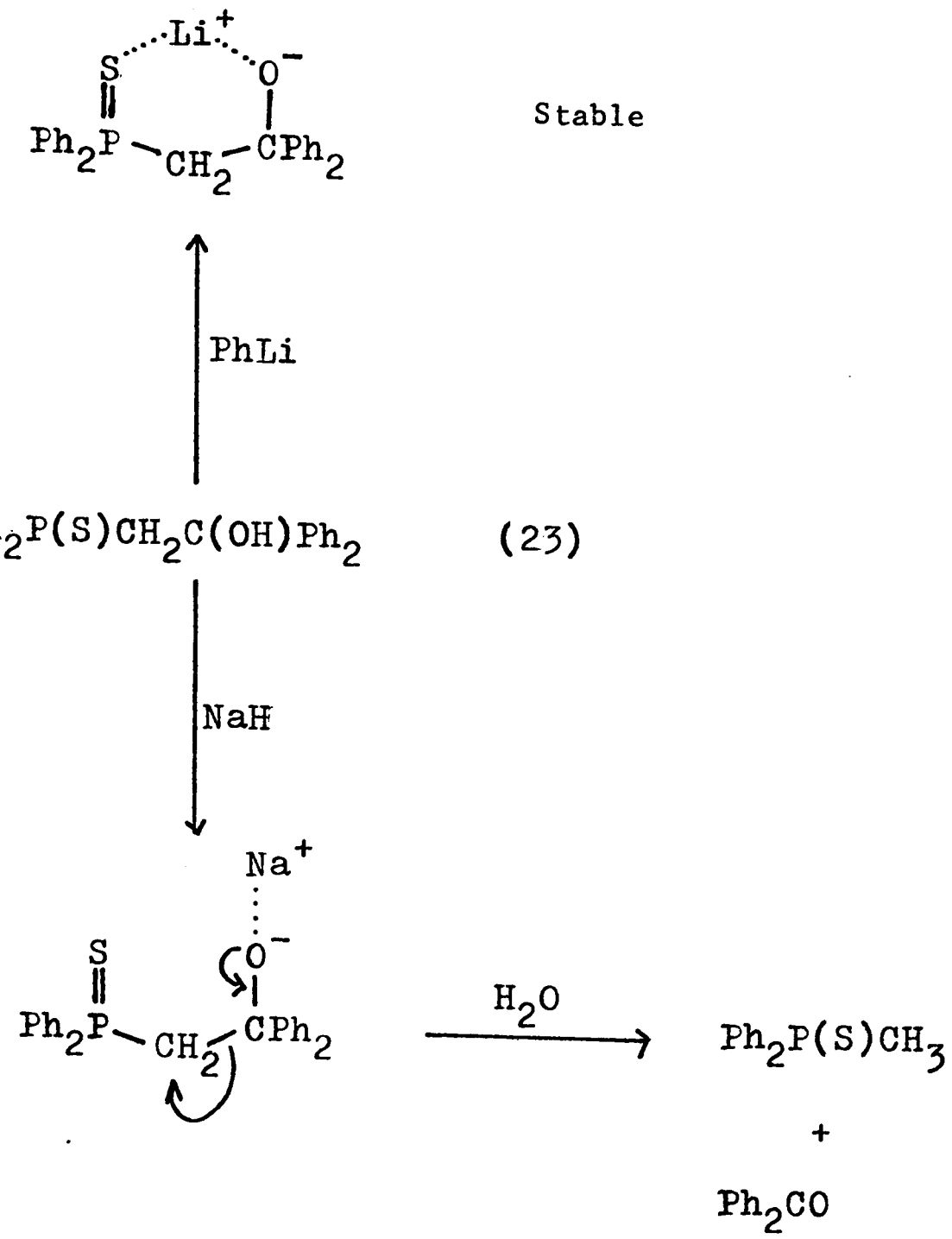
The compound chosen initially to study the transformations of 2-hydroxyalkylphosphine sulphides was (2-hydroxy 2,2-diphenylethyl)-diphenylphosphine sulphide (23). This was prepared by the known route[95] (Scheme 48) and isolated in 80% yield. The mechanism of the first step is shown in Scheme 50: the overall reaction proceeds because benzene is a weaker acid than methyldiphenylphosphine sulphide.



Scheme 50

Phosphine sulphide (23) was found to be quite stable thermally. It was unaffected by prolonged refluxing in benzene or toluene: pyrolysis at 220°/0.1mmHg gave a distillate containing benzophenone and methyldiphenylphosphine sulphide, corresponding to a 7.5% decomposition of (23). The reaction of (23) with bases was more interesting. It was recovered unchanged from treatment with sodium hydride in dimethylformamide at 20° or 80° (conditions under which 2-hydroxyalkyldiphenylphosphine oxides decompose to diphenylphosphinate and olefin)[72]. Upon changing the solvent (at 20° or at reflux) to tetrahydrofuran, methyldiphenylphosphine sulphide (60%) and benzophenone (66%) were isolated. No 1,1-diphenylethene was detected or isolated. Phosphine sulphide (23) gave under the 'normal' conditions of the Horner reaction (that is, potassium t - butoxide in refluxing benzene or toluene) methyldiphenylphosphine sulphide (68%) and benzophenone (67%) after quenching.

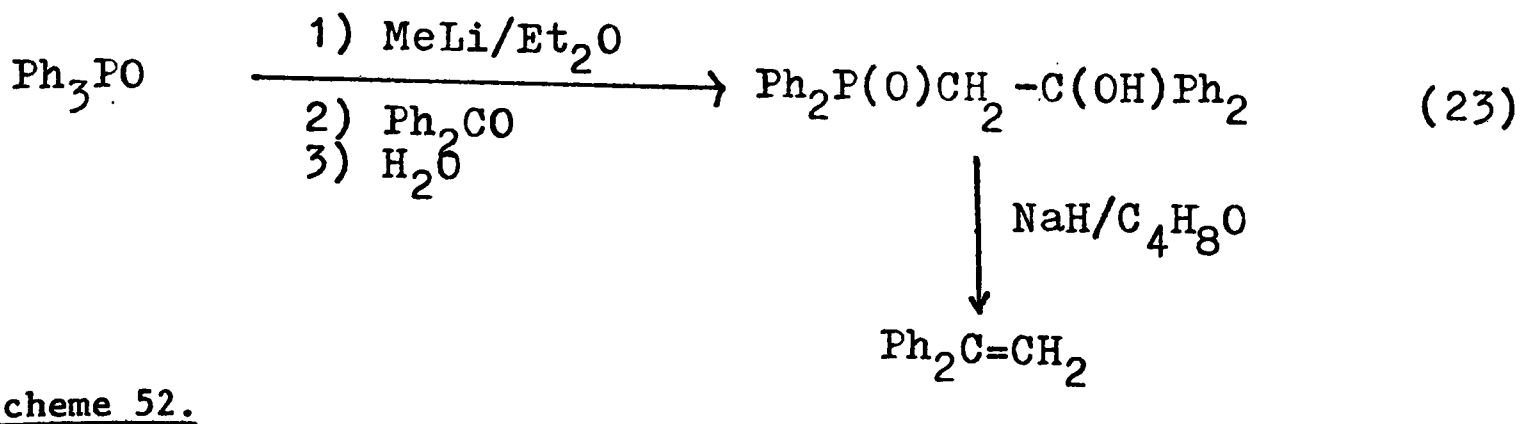
Two points are worth noting at this stage. Firstly, the phosphine oxide analogous to (23) would be expected to fragment differently under the conditions described to give 1,1-diphenylethene. Secondly, there seems to be a cation- (and solvent-) dependence to the cleavage of (23), similar to that noted by Horner for the analogous phosphine oxide fragmentation[42]. The lithium alkoxide of (23) is stable under the conditions (tetrahydrofuran at reflux) where the sodium alkoxide fragments, as shown in the preparation of (23): the lithium cation binding more strongly to the alkoxide and sulphur residues, and thus inhibiting the formation of 'free' alkoxide ion necessary (?) for cleavage (Scheme 51).



Scheme 51.

Phosphine sulphide (23) was also recovered unchanged after treatment with phenyllithium/tetrahydrofuran/20°.

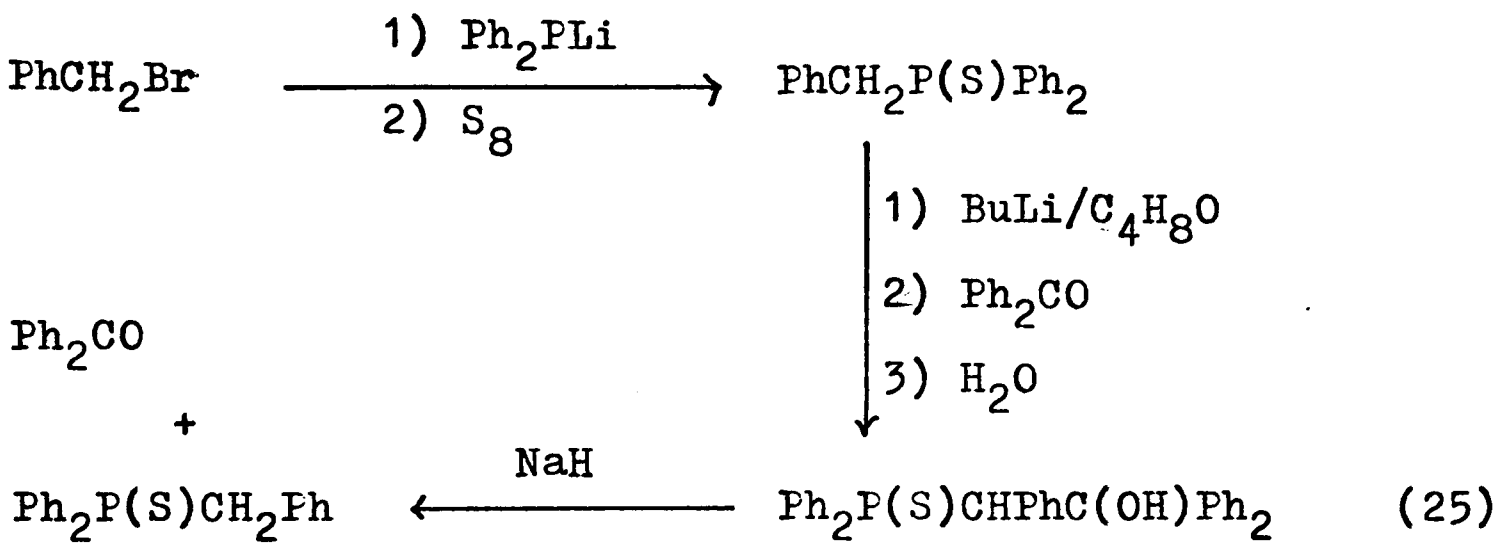
The test of the first-mentioned point was to prepare the corresponding oxide, (2-hydroxy 2,2-diphenylethyl)diphenylphosphine oxide (24), and to treat it with base (Scheme 52).



Scheme 52.

Phosphine oxide (24) was isolated in 75% yield, and 1,1-diphenylethene in 67% yield from the reaction of (24) with sodium hydride in tetrahydrofuran. Interestingly, the corresponding phosphonium salt, (2-hydroxy 2,2-diphenylethyl)methyldiphenylphosphonium iodide, produces a mixture of benzophenone (37%) and 1,1-diphenylethene (35%) upon treatment with potassium t-butoxide/1,2-dimethoxyethane at reflux[97].

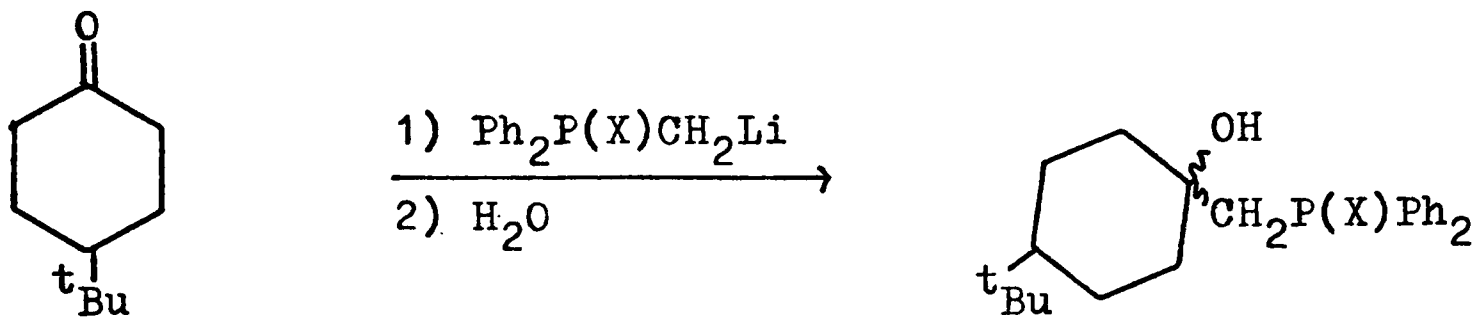
(2-hydroxy 1,2,2-triphenylethyl)diphenylphosphine sulphide (25) was prepared in 97% yield from benzyldiphenylphosphine sulphide (Scheme 53).



Scheme 53.

Upon refluxing (25) with potassium t-butoxide in benzene, benzophenone (92%) and benzyldiphenylphosphine sulphide (97%) were isolated. These two products were also obtained by treating (25) with sodium hydride in tetrahydrofuran or dimethylformamide at 20°. The difference in reactivities of phosphine sulphides (23) (which was stable to the conditions of sodium hydride/dimethylformamide) and (25) is presumably a function of the stabilities of the two thiophosphinyl ylids produced in the cleavage reaction.

To study the reaction of a 2-hydroxyalkylphosphine sulphide containing no aryl group on the 1- or 2-position with base the preparations of 4-t-butyl(1-diphenylphosphinthioyl)cyclohexanol (26) and its corresponding oxide (27) were undertaken (Scheme 54).



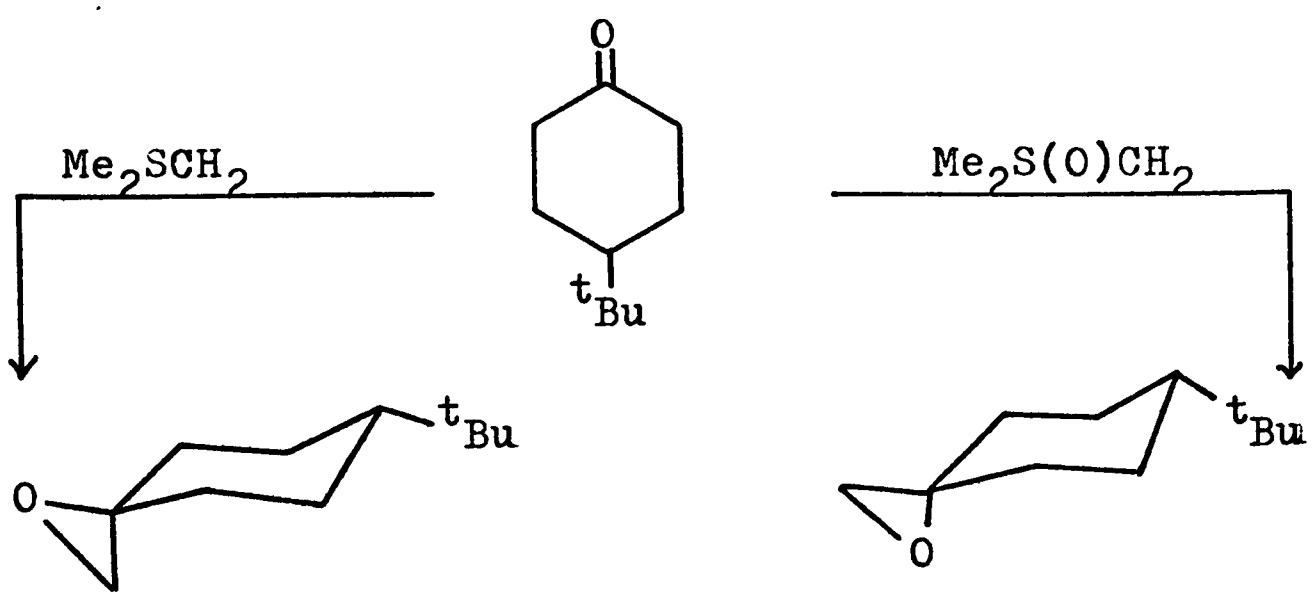
(26) (X = S)

(27) (X = O)

Scheme 54.

Phosphine sulphide (26) was produced in 80% yield and phosphine oxide (27) in 75% yield. The thiophosphinyl ylid, lithiomethyldiphenylphosphine sulphide, appeared to add much more rapidly to 4-t- butylcyclohexanone than it did to benzophenone. Reaction, as judged colorimetrically, was complete in five minutes at 20° in the former case, but needed refluxing for three hours in the latter.

The ^{1}H n.m.r spectra of phosphine sulphide (26) and oxide (27) indicate that the former had been obtained as a single diastereoisomer (one doublet centred at 7.16τ, -C$\underline{H}_2$-P; one t-butyl signal at 9.33τ), but that the latter was a mixture of two diastereoisomers (two doublets at 7.36 and 7.46τ, -C$\underline{H}_2$-P: two t-butyl signals at 9.18, 9.24τ). Johnson[98] and Corey[99] have investigated the orientation of attack of sulphur ylids at cyclohexanones (e.g. Scheme 55). Although the adducts of nucleophilic attack by the ylid at the carbonyl group react further and the nature of the products does not thus give direct evidence on the stereochemistry of the additional addition step, it can be seen that the stereochemistry of the epoxides produced is highly dependant on the nature of the attacking ylid. In the case of the production of (26) and (27), the reaction of the phosphinyl ylids is not complicated by a further cyclisation step.

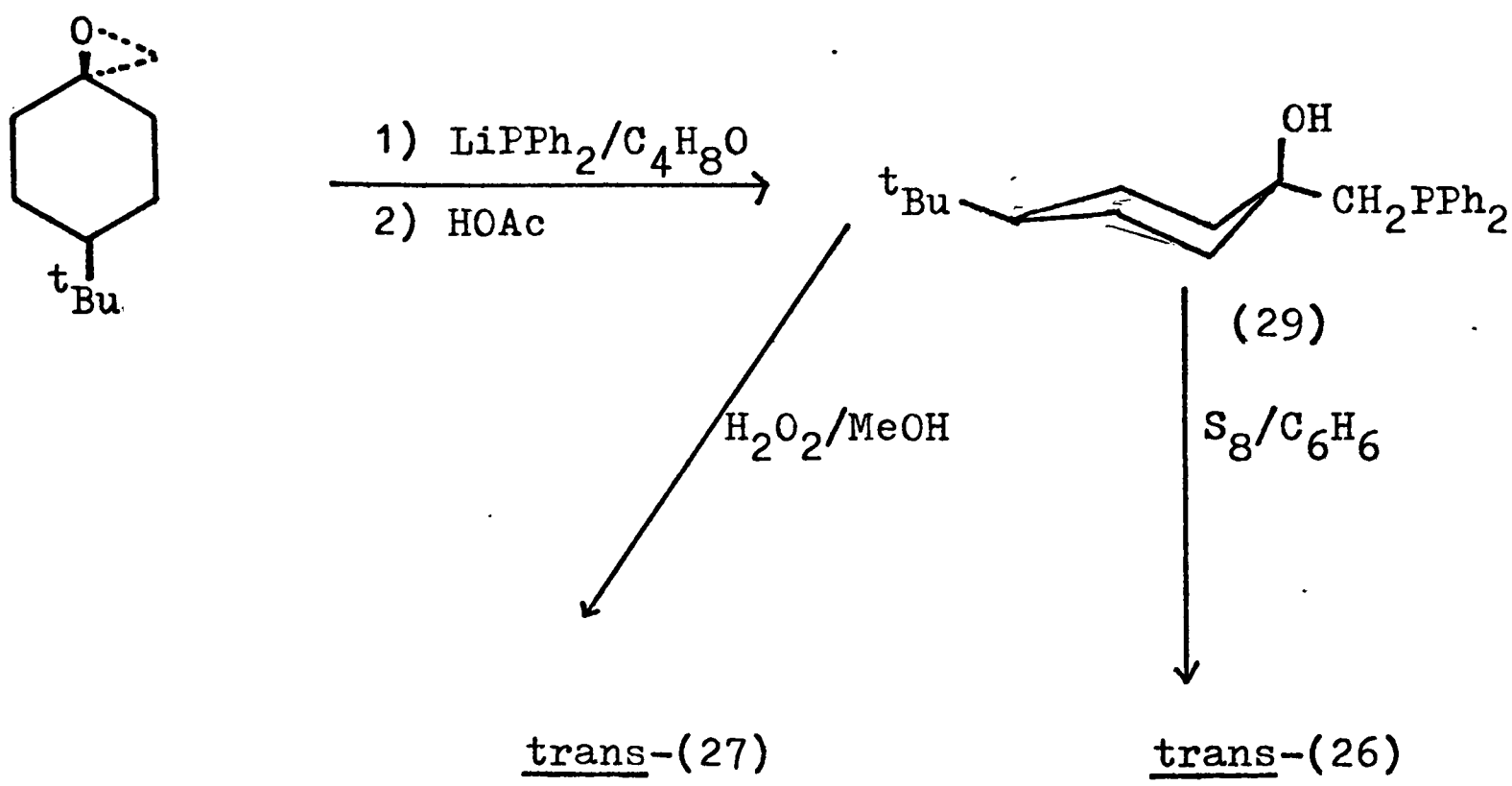


(83% + (28) 17%) (100%) (28)

Scheme 55.

To investigate the stereochemistry of addition of the phosphinyl ylids to 4-t-butylcyclohexanone, the trans isomers of (26) and (27)* were prepared stereospecifically by the reaction of lithium diphenylphosphide with trans-4-t-butyl 1-epoxymethylcyclohexane (28), followed by treatment with, respectively, sulphur or hydrogen peroxide. It is considered that the opening of epoxide (28) occurs by attack at $-CH_2-$, to give an axial hydroxyl group: equilibration of the alkoxide of (29) does not seem feasible at this oxidation level of phosphorus) (Scheme 56).

* trans (26) and (27) are defined as being the geometrical isomers having the t-butyl and diphenylchalcophosphinyl groups trans (i.e. equatorial chalcophosphinyl residue).



Scheme 56.

The trans isomer of (26) gave an n.m.r. spectrum containing a doublet at 7.24 and a t-butyl signal at 9.18τ. Clearly, therefore, the isomer of (26), produced as shown in Scheme 54 is cis, with axial diphenylphosphinthioylmethyl group. The trans isomer of (27) gave an n.m.r. spectrum containing a doublet at 7.46 and a t-butyl signal at 9.18τ. Thus (27) produced as shown in Scheme 54 an approximately 2:1 mixture of the trans and cis isomers, respectively (deduced by the ratio of the integrals of t-butyl group signals in the n.m.r. spectrum). (Recrystallisation of the cis/trans mixture of (27) from ethyl acetate gave pure trans isomer).

In any rationalisation of the observation that lithiomethyldiphenylphosphine sulphide leads to product derived from axial attack on 4-t-butylcyclohexanone, whilst the superficially similar nucleophile lithiomethyldiphenylphosphine oxide gives products derived from predominantly equatorial attack on the ketone, the following considerations should be noted:

a) The main mode of attack of relatively small nucleophiles on sterically unhindered cyclohexanones is from the axial side, leading to the production of equatorial alcohols[143].

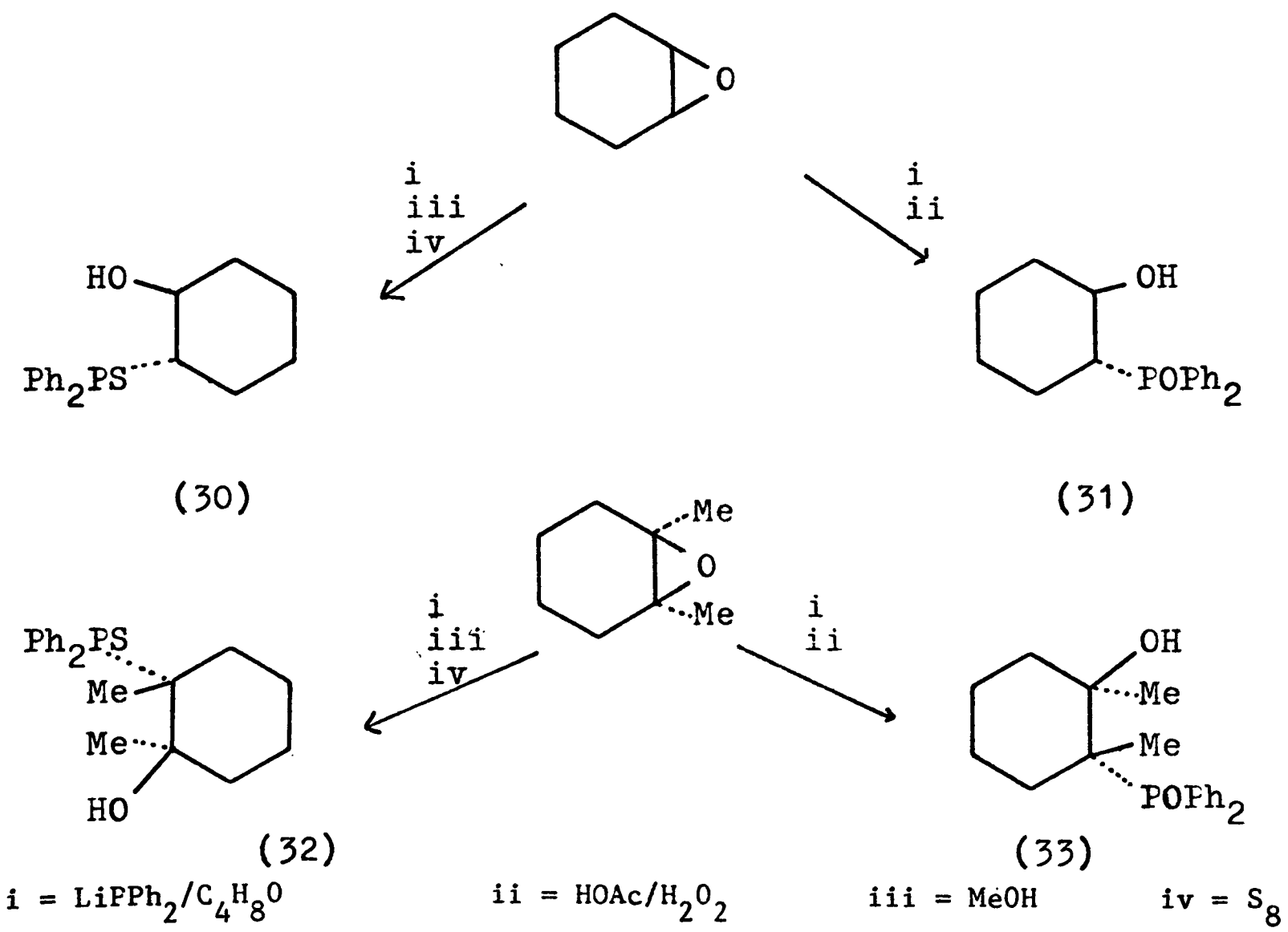
b) The trans-isomers of (26) and (27), with axial hydroxyl groups, should be more stable than the cis-isomers, owing to the greater steric demands of the Ph_2PXCH_2 - grouping: thus any degree of thermodynamic control of the reactions will tend to favour formation of the trans isomers.

It seems clear, therefore, that, in the case of the phosphine sulphide nucleophile, the addition step is irreversible under the conditions of reaction. It is interesting to note the high proportion of adduct derived from axial attack in this reaction, when contrasted with the reactions of other alkyllithium reagents with 4-t-butylcyclohexanone[143]. The case of the phosphine oxide nucleophile is more normal, and the ratio of products is in reasonable accord with those formed in additions of other alkyllithiums of moderate bulk to the ketone.

Oxide (27) and sulphide (26) were both treated with potassium t-butoxide in refluxing benzene: oxide (27) gave 4-t-butylmethylenecyclohexane in 84% yield, whilst sulphide (26) gave 4-t-butylcyclohexanone and methyldiphenylphosphine sulphide. The fragmentation of (27) to olefin and phosphinate is the expected Horner reaction. The fragmentation of (26) to ketone and phosphine sulphide, being in the same mode as the base-induced fragmentations of phosphine sulphides (23) and (25), shows perhaps that the nature of the substituents on the 2- position of the phosphine sulphide does not influence the pathway of fragmentation.

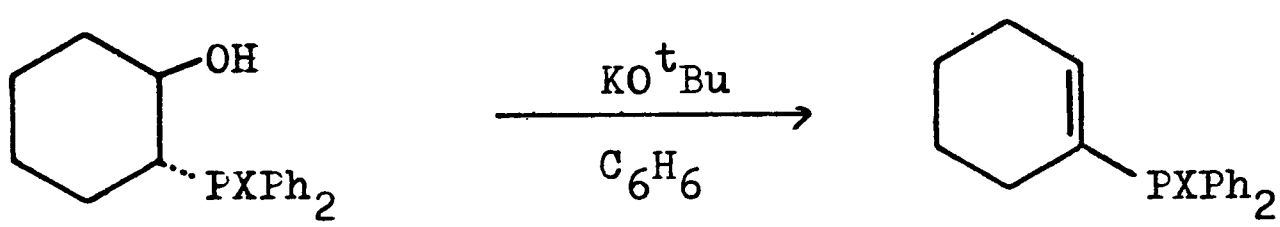
Although no reaction was, by this stage, expected benzyldiphenylphosphine sulphide and 4-t-butylcyclohexanone were refluxed together with potassium t-butoxide in benzene. After quenching, both reagents were cleanly recovered.

The idea was now advanced that, if the 2-hydroxyalkylphosphine sulphides could be generated in a way other than from alkylphosphine sulphide and ketone their cleavage reaction with base might prove useful, synthetically. Accordingly, trans-2-diphenylphosphinthioylcyclohexanol (30) and its 1,2-dimethyl analogue (32) were synthesised (Scheme 57) from the epoxides in 90% and 60% yields. For comparison purposes, the corresponding phosphine oxides (31) and (33) were also prepared, in 91% and 60% yields, respectively.



Scheme 57

Unexpectedly, phosphine sulphide (30) was not cleaved by base to the ω-aldehydophosphine sulphide. On treatment with potassium tert-butoxide in refluxing benzene or 1,2-dimethoxyethane, (30) was dehydrated to 1-diphenylphosphinthioylcyclohexene (34), which was isolated in 96% yield. Phosphine sulphide (30) was stable to the conditions of sodium hydride or potassium t-butoxide in tetrahydrofuran or 1,2-dimethoxyethane at 20°, with none of the cis isomer being detected by t.l.c. after quenching. Phosphine oxide (31) was also dehydrated by refluxing with potassium t-butoxide in benzene, to yield 1-diphenylphosphinylcyclohexene (35) in 80% yield (Scheme 58).



(30) (X = S) (34) (X = S)

(31) (X = O) (35) (X = O)

Scheme 58.

The dehydration of phosphine oxide (31) is analogous to the dehydration of trans-2-hydroxy-2-diphenylphosphinylcycloheptane to 1-diphenylphosphinylcycloheptene with sodium hydride in refluxing 1,4-dioxan[72] *. Both sulphide (32) and oxide (33) were stable to the conditions of potassium

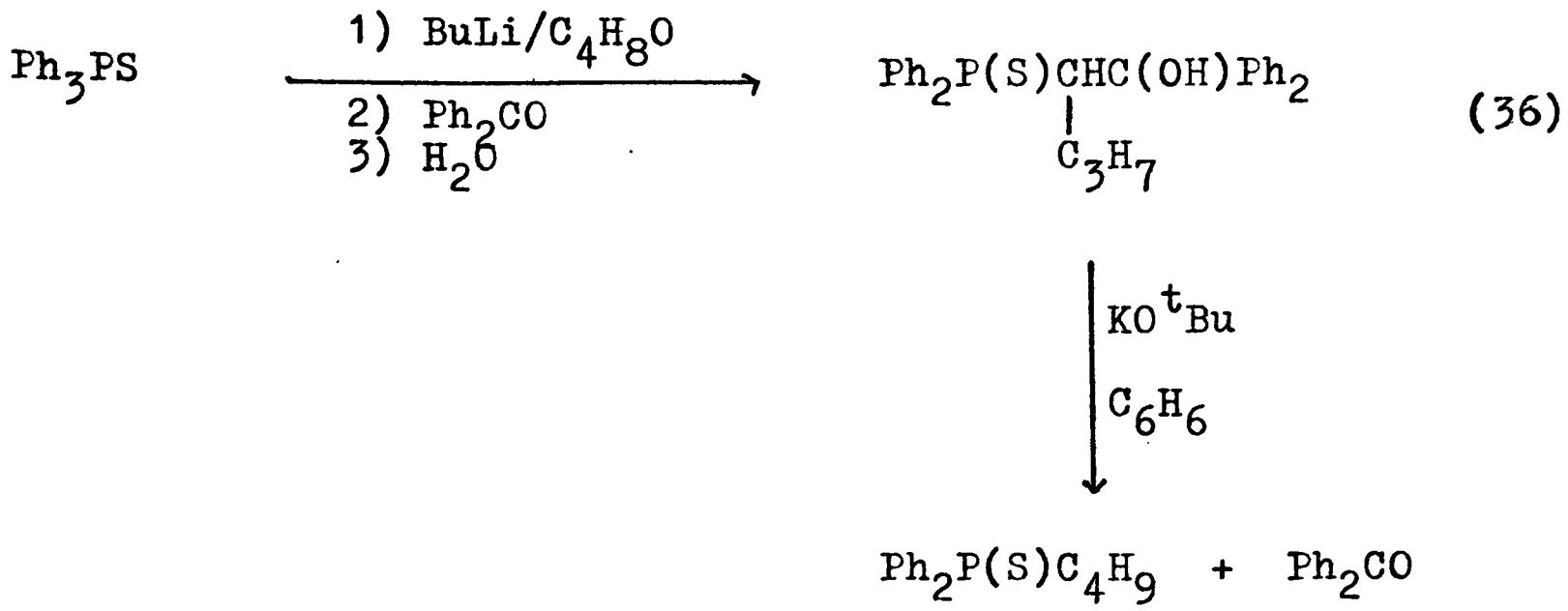
* It has recently been found that trans-2-hydroxy-2-diphenylphosphinylcycloheptane can be fragmented to trans-cycloheptene in 15% yield, by treatment with sodium hydride/dimethylsulphoxide/25° [100].

tert-butoxide in refluxing benzene.

At this stage, two theories may be postulated as to why phosphine sulphides (30) and (32) behave differently to phosphine sulphides (23), (25), and (26) upon treatment with base. Firstly, the difference may be solely due to entropy effects: sulphides (23), (25), and (26) each fragment to two molecules upon treatment with base, but, were (30) and (32) to follow an analogous mode of cleavage, the entropy gain would be less. Secondly, in the cleavage of phosphine sulphides (23) and (26), the ylid produced is a formal primary carbanion (or, metallated carbanion), and the ylid produced by cleavage of (26), although formally a secondary carbanion, is further stabilised by the phenyl substituent on the carbanion. Were phosphine sulphide (30) to fragment to aldehyde and ylid, the carbanion so produced would be secondary, and, therefore, destabilised relative to metallomethyldiphenylphosphine sulphide. Such a factor might make the activation energy for such a mode of cleavage too high relative to another mode of reaction viz. dehydration. Phosphine sulphide (32) would, if it underwent cleavage to ketone and ylid, produce a formally tertiary carbanion, and thus be even further inhibited from such a mode of reaction.

To test the second of these two theories, a 1-alkyl substituted 2-hydroxyalkyldiphenylphosphine sulphide was prepared, in which C_1-C_2 was not part of a ring system. (1-Hydroxydiphenylmethyl)butyldiphenylphosphine sulphide (36) was prepared (Scheme 60). Considerable difficulty was experienced in obtaining good yields of this compound, and much longer reaction times for each of the two steps were required to give a yield of 80% than for, say, the preparation of phosphine

sulphide(23).



(36)

Scheme 60.

Furthermore, the species 1-lithiobutyldiphenylphosphine sulphide did not attack cyclohexanone at carbonyl, but apparently deprotonated it to the enolate anion; on addition of cyclohexanone to an ethereal solution of 1-lithiobutyldiphenylphosphine sulphide, the deep red-black colour was discharged rapidly, but only butyldiphenylphosphine sulphide could be recovered from the mixture. Such observations suggest that the 1-lithiohutyldiphenylphosphine sulphide 'anion' is quite hindered as a nucleophilic species: as this carbanion is only secondary, the result is perhaps noteworthy.

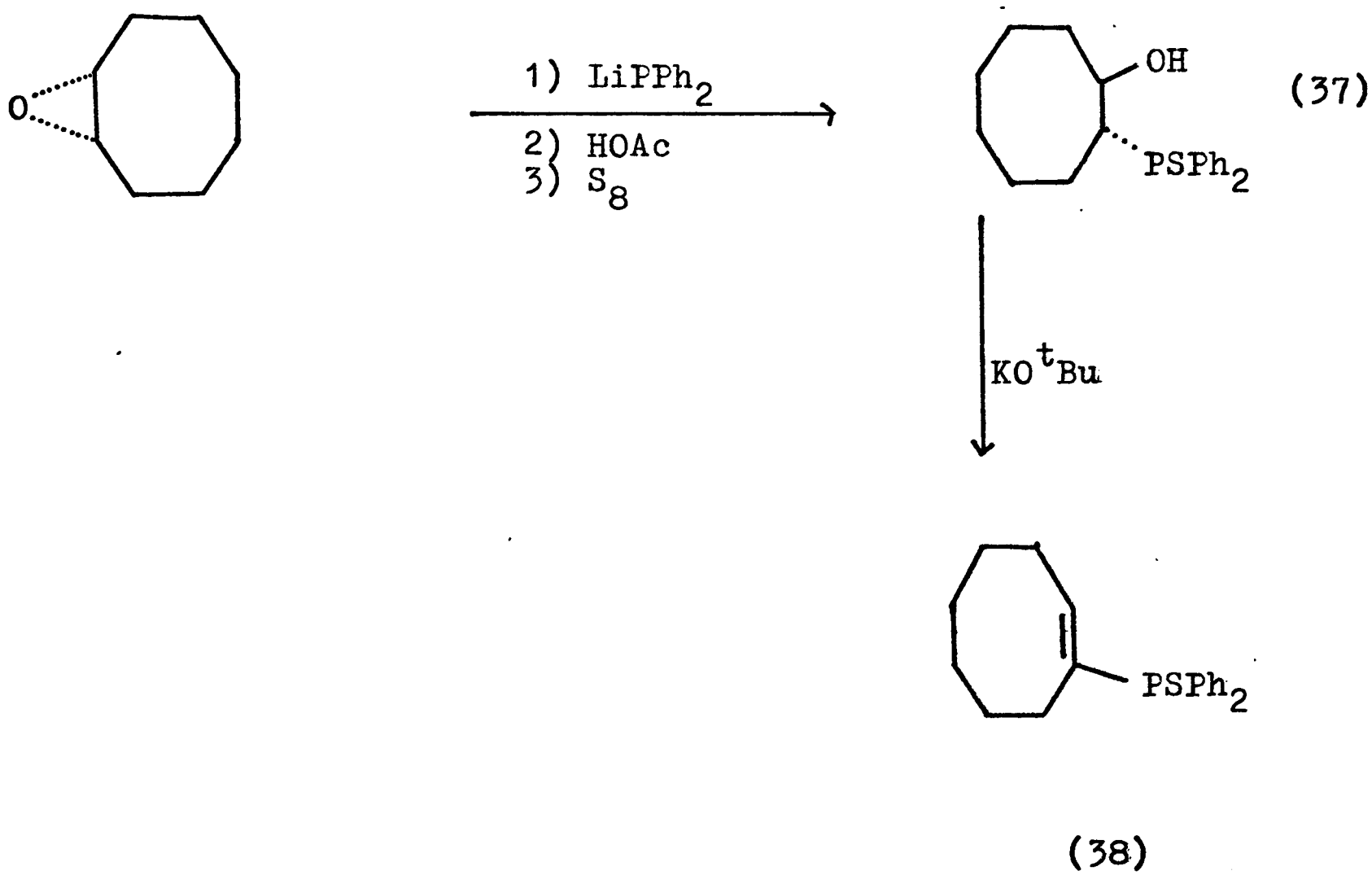
Treatment of phosphine sulphide (36) with potassium t-butoxide in refluxing benzene effected cleavage to butyldiphenylphosphine sulphide and benzophenone (Scheme 60).

From this result, it might appear that the nature of the thiophosphinyl ylid produced, were C_1 - C_2 cleavage to occur, has less to do with the pathway of cleavage of the anion of a 2-hydroxyalkyldiphenylphosphine sulphide than do entropy considerations. It is, however, just possible that the mode of cleavage of sulphides (30) and (32) with base is influenced by stereochemical factors (for example, the alkoxide anion of (30) might only fragment about the C_1 - C_2 bond in a highly disfavoured axial-axial conformation). Such factors would not be expected to be so dominant in a larger ring system. Accordingly, a study was made of the base-induced fragmentation of trans-2-diphenylphosphinthioyl-cyclooctanol (37).

The analogous phosphine oxide (22) fragments with sodium hydride at 20° to yield trans-cyclooctene[72,94] (Scheme 47). Phosphine sulphide (37) was prepared in overall 46% yield (Scheme 61).

Considerable difficulty was experienced in its purification: the product after repeated chromatography was a viscous oil, which deposited crystals only after standing for sixteen months. Eventually, a moderate yield of crystals was obtained by repeated evaporation of ethyl acetate from the oil, with seeding.

Upon treatment with potassium t-butoxide in refluxing benzene, (37) yielded 1-diphenylphosphinthioylcyclooctene (38) (Scheme 61).



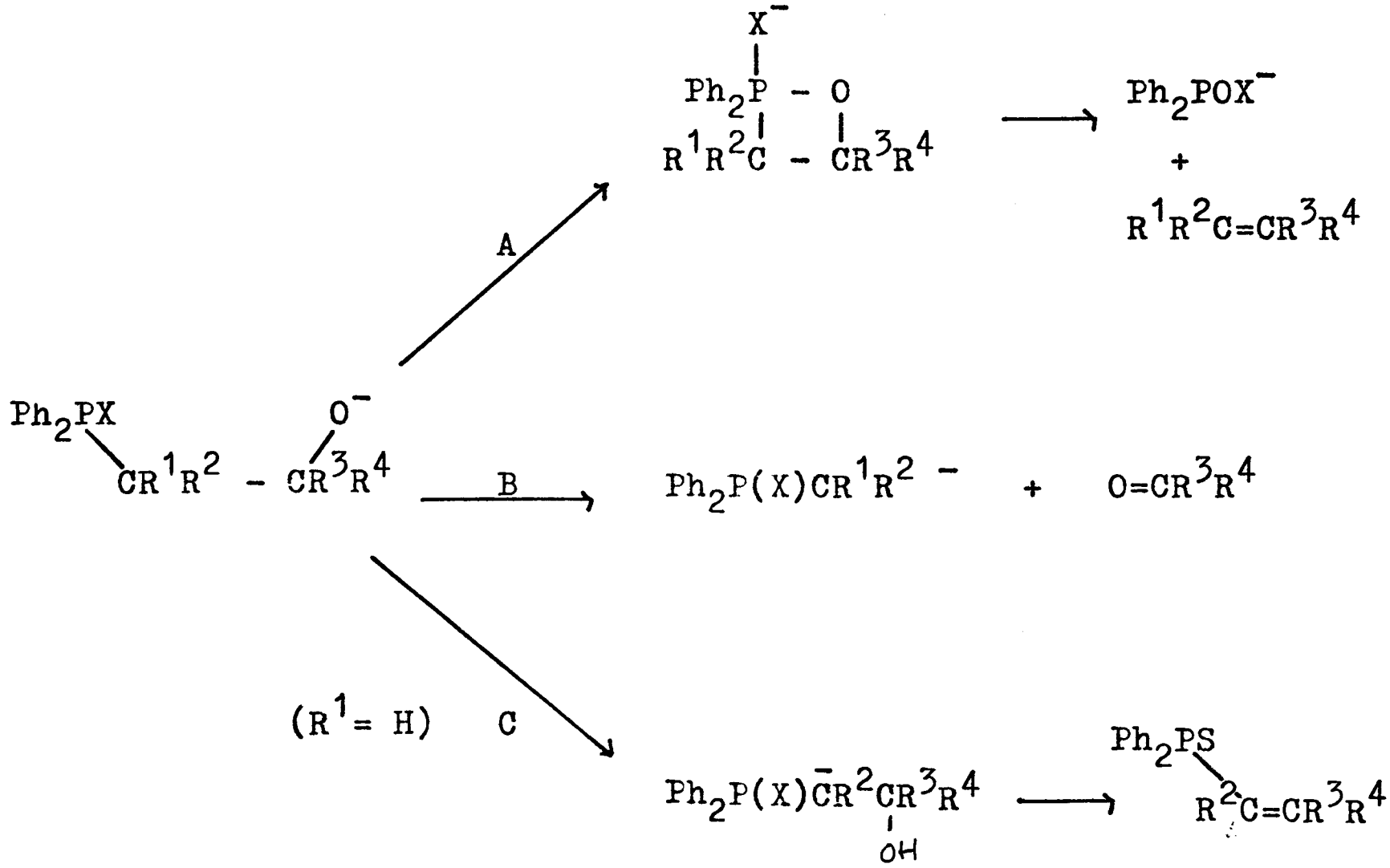
Scheme 61.

(38) was obtained as a non-crystallisable oil, but the assignment of structure was confirmed by satisfactory analytical data, the presence of the molecular ion in the mass spectrum (326), bands at 3045 and 1618 cm^{-1} in the infra-red spectrum, and the presence of a doublet of triplets at 3.66τ in the n.m.r. spectrum. The magnitude of J_{P-H} (24Hz) makes the assignment of <u>cis</u> arrangement of alkyl groups about the double bond likely: phosphine sulphide (34) has a ^1H n.m.r. signal at 3.73τ (J_{P-H} = 23 Hz). Phosphine sulphide (38) was obtained in 75% yield.

To summarise: the characteristic reaction of a 2-hydroxyalkyldiphenylphosphine sulphide, in which C_1 -C_2 is not part of a ring system, with strong base and under suitable conditions of solvent and temperature (varying from phosphine sulphide to phosphine sulphide) is cleavage of the C_1 -C_2 bond to yield a thiophosphinyl ylid and a ketone. The reaction depends upon the cation associated with the base: amongst Group Ia metals, potassium favours cleavage and lithium hinders it altogether. 2-Hydroxyalkyldiphenylphosphine oxides under similar conditions react in Horner fashion to yield olefins and diphenylphosphinate anion. 2-Hydroxyalkyldiphenylphosphine sulphides, in which C_1 -C_2 is part of a ring system, undergo dehydration about C_1 -C_2 if this is possible (i.e. if there is a hydrogen on the carbon α to phosphorus), and are otherwise stable to base. The choice of pathways between dehydration and C_1 -C_2 bond cleavage has been rationalised in terms of predominant entropy effects. No example has been found in this work of a 2-hydroxyalkyldiphenylphosphine sulphide fragmenting in Horner fashion to an olefin and diphenylphosphinthioate anion: the only known example is shown in Scheme 23: in this example, dehydration about C_1 -C_2 is not possible, and cleavage of the C_1 -C_2

bond would lead to a thiophosphinyl ylid where the charge resided upon an sp^2 hybridised carbon; such ylids are not easily formed[74,75] (This argument does not, however, explain why the phosphine sulphide in Scheme 23 is not stable to the reaction conditions).

The overall difference in behaviour of 2-hydroxyalkyldiphenylphosphine sulphides and the corresponding oxides towards strong base may perhaps be linked to the relative ease of nucleo-philic attack at thiophosphinyl and phosphinyl groups. In general, such attack is 5 - 50 times faster at phosphinyl (in, say, phosphonates and phosphates) than at the corresponding thiophosphinyl compound[101]. In Scheme 62, there are three competing paths open to the anion of a 2-hydroxyalkyldiphenyl-phosphine chalconide: oxaphosphetan formation, leading to completion of the Horner reaction (path A); C_1 -C_2 cleavage (path B); and dehydration about C_1 -C_2 (path C). Alternatively, the anion may be stable to further reaction (such as when lithium is the counter-ion).

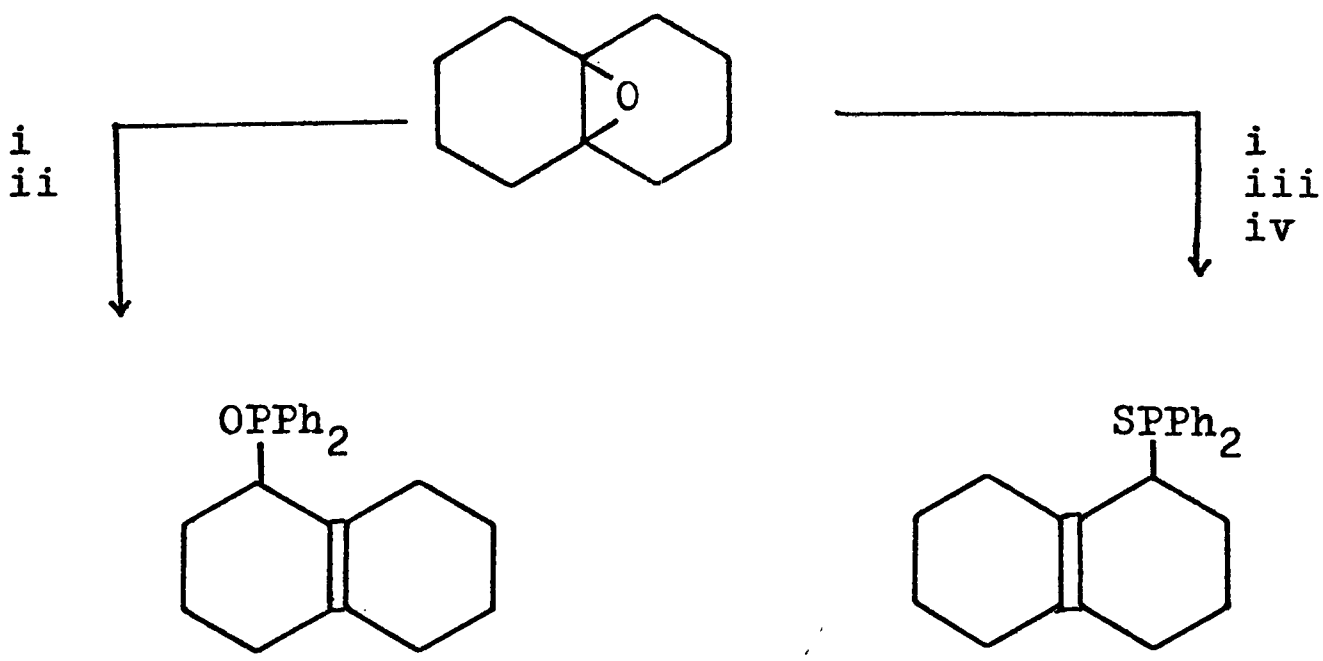


(X = O, S)

Scheme 62.

If, in path A, nucleophilic attack at phosphorus is made less favourable, then path B may become <u>relatively</u> more favoured as a fate for the phosphine chalconide anion, even though the stability of the departing ylid may be decreased analogously. Path C will be favoured in those cases where path B does not proceed (for example, where X = O and R_{1-4} are hydrogen or alkyl[94]), and chalcaphosphetan formation is impossible on steric grounds (for example, where Ph_2PX and O^- are <u>trans</u> in a small ring, as in phosphine oxide (31)). Path B may be reversible, and co-existent with path A (as for example, where X = O and $R_1 = R_3 = H$, $R_2 = R_4 = Ph$[94]): here the more stable isomer of the olefin $CR_1R_2{=}CR_2R_4$ will be produced. Where path A is disfavoured on steric grounds, and path B on entropy or ylid stability grounds, and $R_1 \neq H$, then the phosphine chalconide anion may be stable to further reaction (as with the anions of phosphine oxide (33) and phosphine sulphide (32)).

At a stage in the investigation when base-induced cleavage of 2-hydroxyalkyldiphenylphosphine sulphides to ketones and thiophosphinyl ylids appeared to be a general reaction, the reaction of lithium diphenylphosphide with 11-oxa tricyclo [4.4.1.$0^{1,6}$] undecane (Δ^9-octalin epoxide) was studied. The products isolated after work-up with hydrogen peroxide or sulphur were not a hydroxyalkylphosphine oxide or sulphide, but the allylphosphine oxide and sulphide shown in Scheme 63.



(39) (40)

i = PPh_2Li/C_4H_8O ii = H_2O_2/HOAc iii = MeOH iv = S_8

1-Diphenylphosphinthioylbicyclo [4.4.0] dec-9-ene (40) was obtained in 88% yield and the corresponding oxide (39) in 90% yield. The evidence for the structures of (39) and (40) may be summarised as follows:

a) There is no peak in the i.r. or n.m.r. spectra corresponding to -OH.

b) The n.m.r. spectrum of (40) contains a signal at 6.75τ (dt, J_{P-H} = 6, J_{H-H} = 15Hz: 1H). For comparison, the α- protons in allyldiphenylphosphine sulphide resonate at 6.71τ.

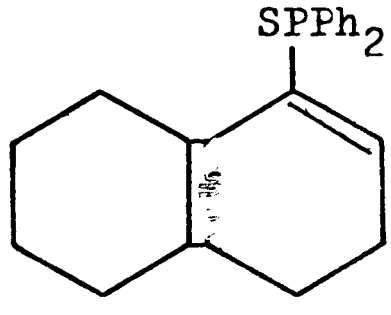
c) The ^{13}C n.m.r. of (39) and (40) contains signals in the region ascribed to olefinic carbons, in addition to the four pairs of signals attributable to the carbons of the phenyl groups. No bands ascribable to C=C are visible in the i.r. spectrum, though.

d) The molecular ions (336 for the oxide and 352 for the sulphide) are present in the mass spectra.

e) Satisfactory analyses were obtained.

To aid in the identification of (39) and (40), the ^{13}C n.m.r. spectra of triphenylphosphine oxide, triphenylphosphine sulphide, methyldiphenylphosphine sulphide[42], and allyldiphenylphosphine sulphide[102] were recorded. These are given and discussed in a separate chapter.

Treatment of phosphine sulphide (40) with potassium t-butoxide in refluxing benzene gave an oil, which was tentatively assigned as an approximately 1:2 mixture of (40) and its $\Delta^{1,2}$ isomer (41), on the basis of its ^{1}H n.m.r. spectrum.

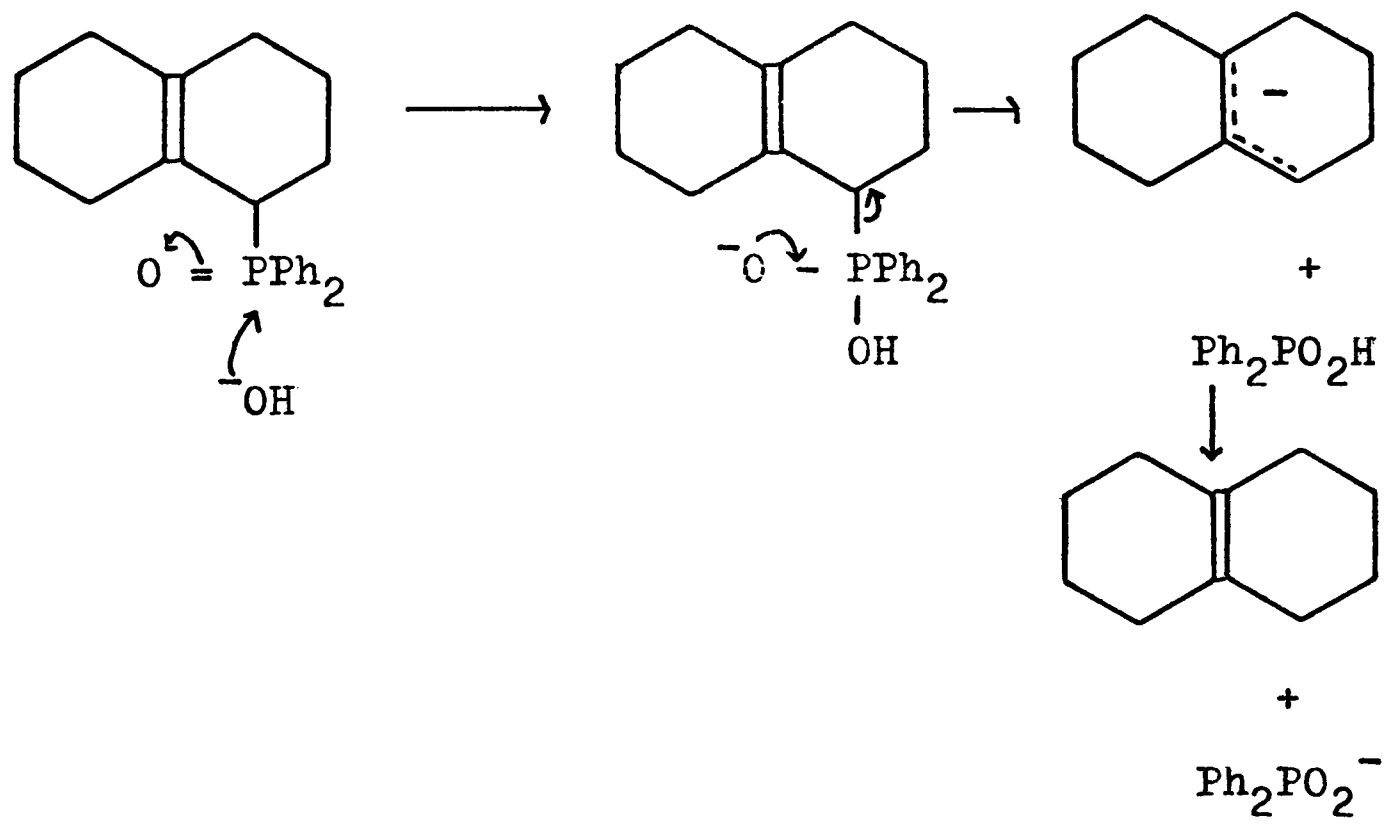


(41)

Sulphide (41) shows a broad doublet at 4.44τ (J_{P-H} = 30 Hz). Estimation of the percentage composition of the mixture was made upon the ratio of signals due to the ortho protons; these being exceptionally low (1.85 - 2.25τ) in (41). Although t.l.c. analysis of the oil showed only two spots, (41) could not be isolated and properly characterised, and further comment upon its mode of formation and stereochemistry seems premature.

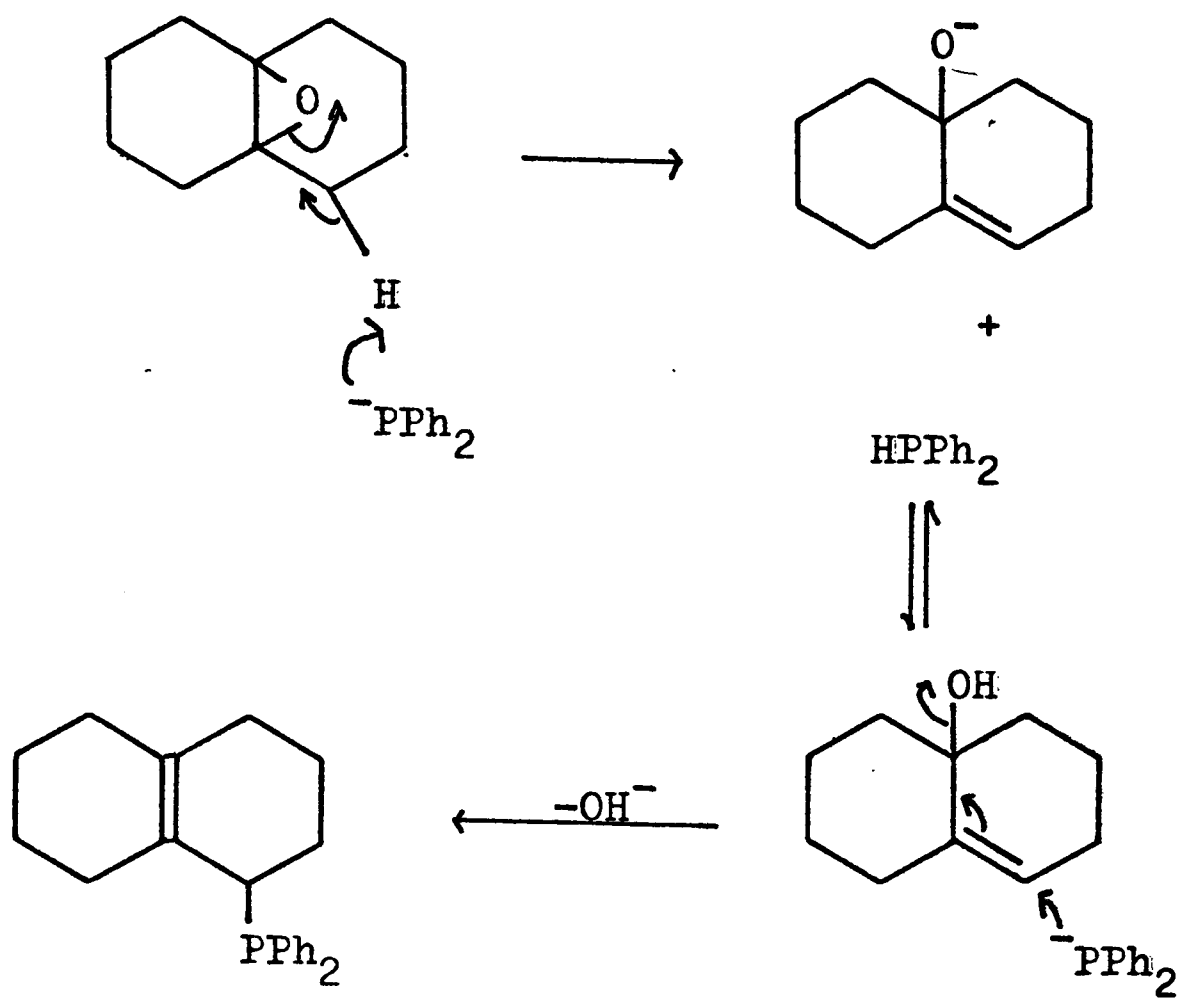
Phosphine oxide (39) was, on the other hand, unaffected by treatment with potassium t-butoxide in refluxing benzene. This result has been commented upon in Chapter 1. The difference in behaviour between (39) and (40) is not easily rationalised.

Phosphine oxide (39), upon fusion with sodium hydroxide[103] at 280° gave a distillate, indicated by n.m.r. to be an approximately 13:2 mixture of benzene and Δ^9 -octalin. G.l.c. revealed also that small amounts of tetralin and napthalene had been produced, but that no other isomer of octalin had been formed. This result may be interpreted as evidence that in (39) the double bond is located in the 9,10 position. Cleavage, as outlined in Scheme 64, would involve an allyl anion as leaving group.



Scheme 64.

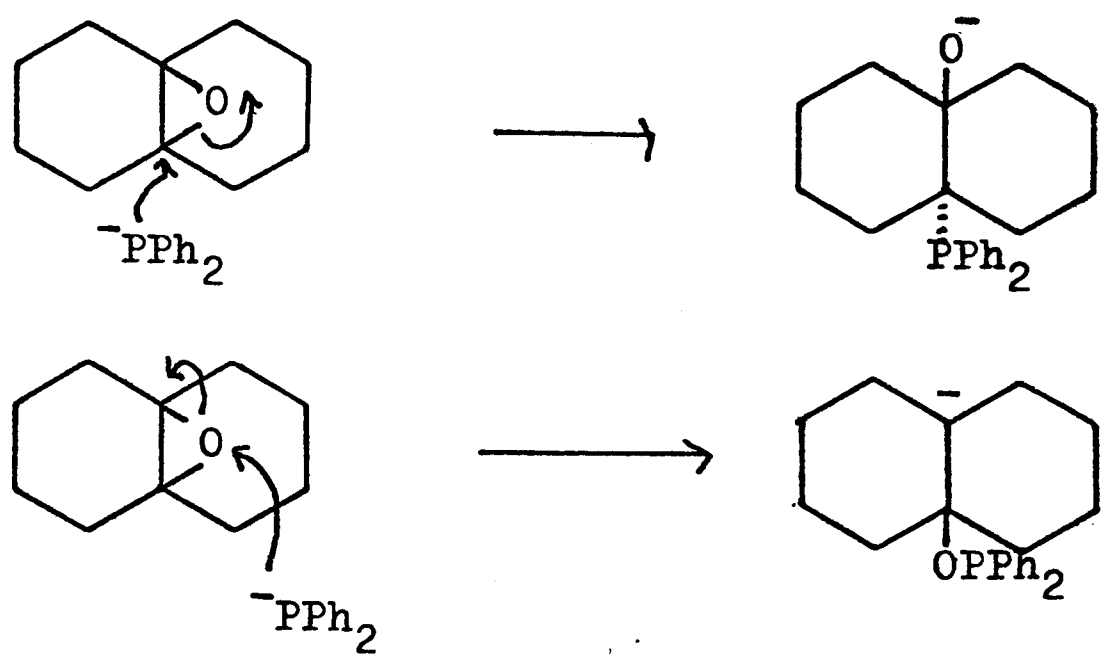
A suggested mechanism for the production of phosphine (42), the precursor of (39) and (40) is shown in Scheme 65.



(42)

Scheme 65.

An alternative initial step involving attack at either oxygen or the carbon α- to oxygen would produce intermediates from which it is difficult to envisage a route to phosphine (42)(Scheme 66.)



Scheme 66.

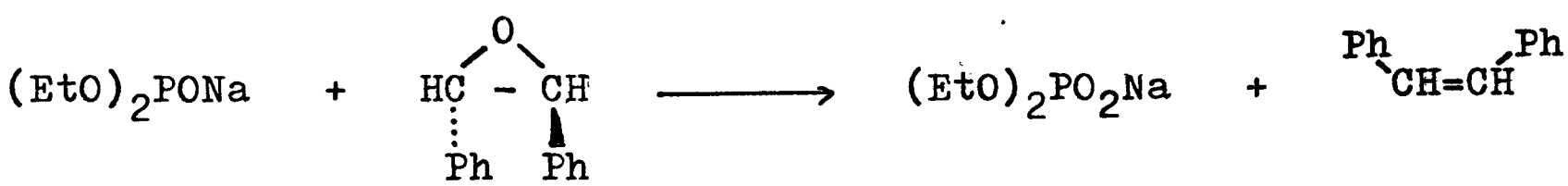
Attempts were made to provide support for the proposed mechanism. Lithium diphenylphosphide was treated with allyl alcohol and with 1-methylcyclohex-2-enol. In neither case were products derived from nucleophilic attack by diphenylphosphide upon the alcohol isolated. This does not, however, discount the mechanism proposed in Scheme 65. Of the allyl cations derived by loss of hydroxide ion from allyl alcohol, 1-methylcyclohex-2-eneol, and alcohol (43), the latter would be expected to be more stable than the rest. If, in the S_N2' displacement proposed in Scheme 65, there were an element of S_N1 character, then alcohol (43) would be the most likely of the three alcohols under discussion to react with diphenylphosphide ion in this fashion.

An attempt to prepare 10-hydroxybicyclo [4.4.0]dec-1-ene (43) by rearrangement of Δ9-octalin epoxide in the presence of lithium diethylamide[104] was not successful: at least six products were obtained, and these were not separable by distillation.

Δ^9-octalin epoxide was also treated with lithium thiophenoxide in tetrahydrofuran. Distillation of the crude product, after quenching, gave three fractions, each consisting of more than one component. Thus no clean cleavage of the epoxide to one product was observed. The epoxide was unaffected by treatment with sodium thiophenoxide in tetrahydrofuran. Allyl bromide, upon treatment with lithium diphenylphosphide, and subsequent treatment with sulphur, gave allyldiphenylphosphine sulphide, albeit contaminated with some propenyldiphenylphosphine sulphide. Such a route could not be extended to an independent synthesis of phosphine sulphide (40). Attempted allylic bromination of Δ^9-octalin with N-bromosuccinimide in refluxing carbon tetrachloride with or without a trace of benzoyl peroxide, gave tetralin as sole product, even with a reaction time of less than five minutes. Production of the phosphine (42) from the treatment of Δ^9-octalin epoxide with lithium diphenylphosphide must thus stand as a curio of

organophosphorus chemistry. Both tetramethyloxirane[94] and 1,2-dimethyl-cyclohexene epoxide (see above) react with lithium diphenylphosphide by cleavage of the oxirane ring to give 2-hydroxyalkylphosphines (isolated as the oxides or sulphides), as does the very hindered epoxide, 1-methyl cis-cyclooctene epoxide[94]. No other nucleophile was found to open Δ^9-octalin epoxide to a product analogous to (42). A fine interplay of nucleophilicity, basicity, and steric hindrance is indicated.

In the book 'Organophosphorus Chemistry' by B.J.Walker, the transformation outlined in Scheme 67 is stated as a problem question[105].



Scheme 67

This reaction would be an alternative route to the alkoxide intermediates in the Horner-Emmons reaction[17,18]. No literature reference to such a reaction could, however, be found, and an attempt was made to see if such a reaction was feasible.

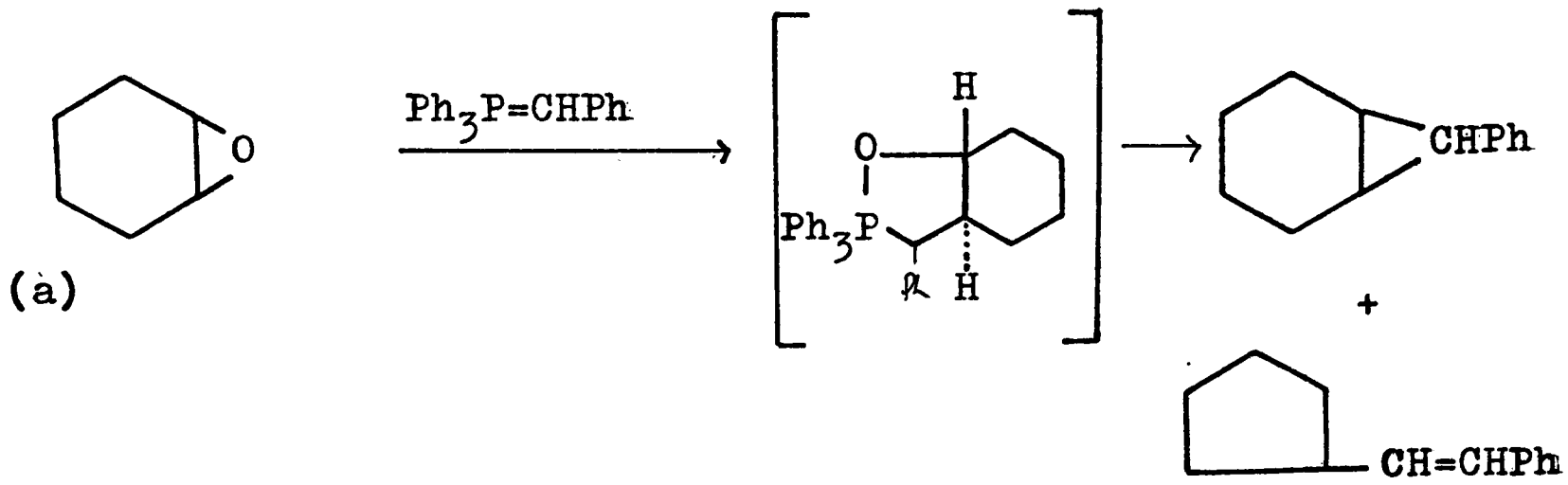
Diethylphosphite was treated with sodium hydride in 1,2-dimethoxyethane, and subsequently with trans-stilbene epoxide. Even after prolonged refluxing of the reaction mixture, the epoxide was recovered in good yield, and no cis- or trans-stilbene was detected. Without further information or experimentation, the status of the reaction designated in Scheme 67 remains uncertain.

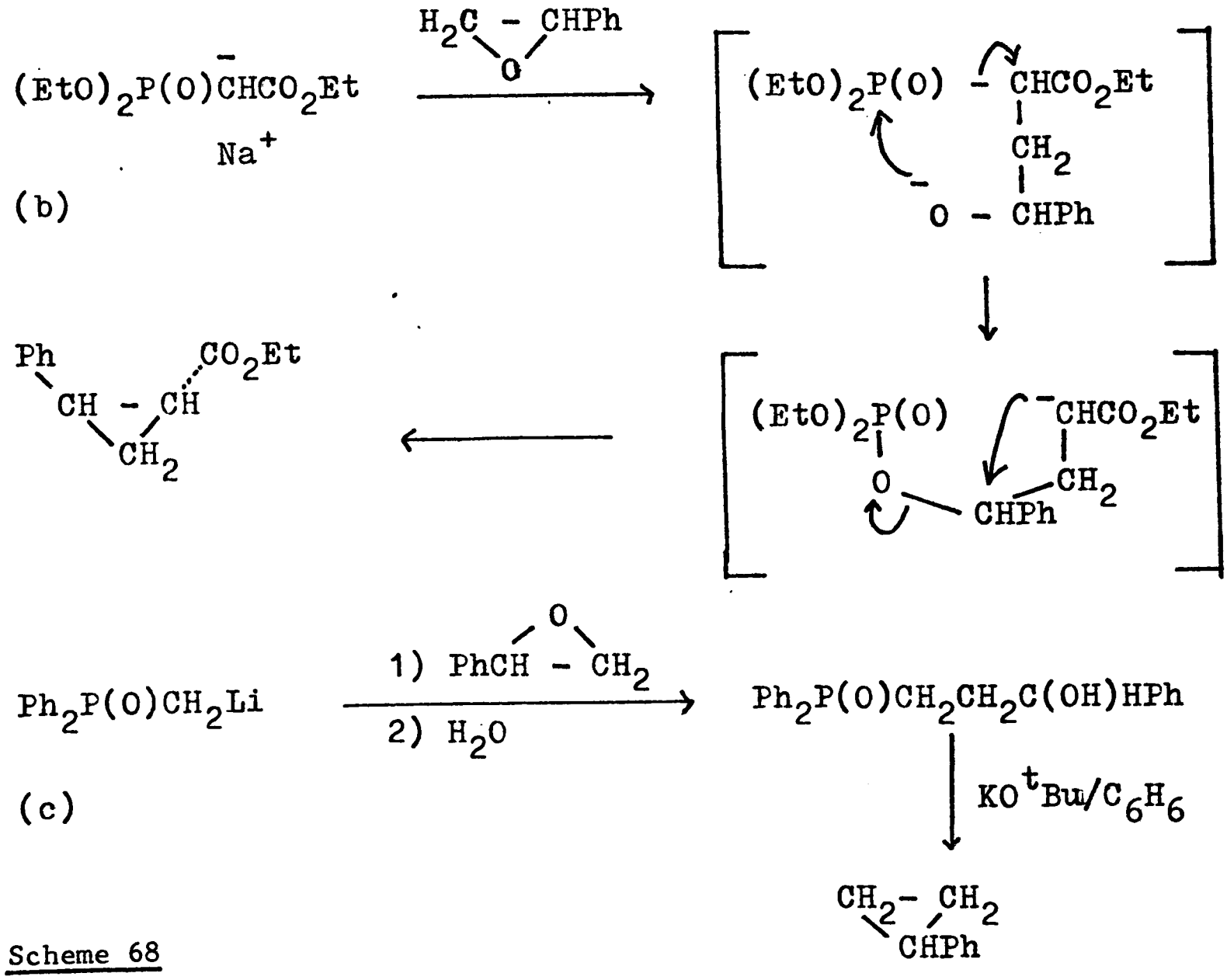
Chapter 4.

A POSSIBLE ROUTE TO CYCLOBUTANES VIA A MODIFIED HORNER REACTION.

Introduction

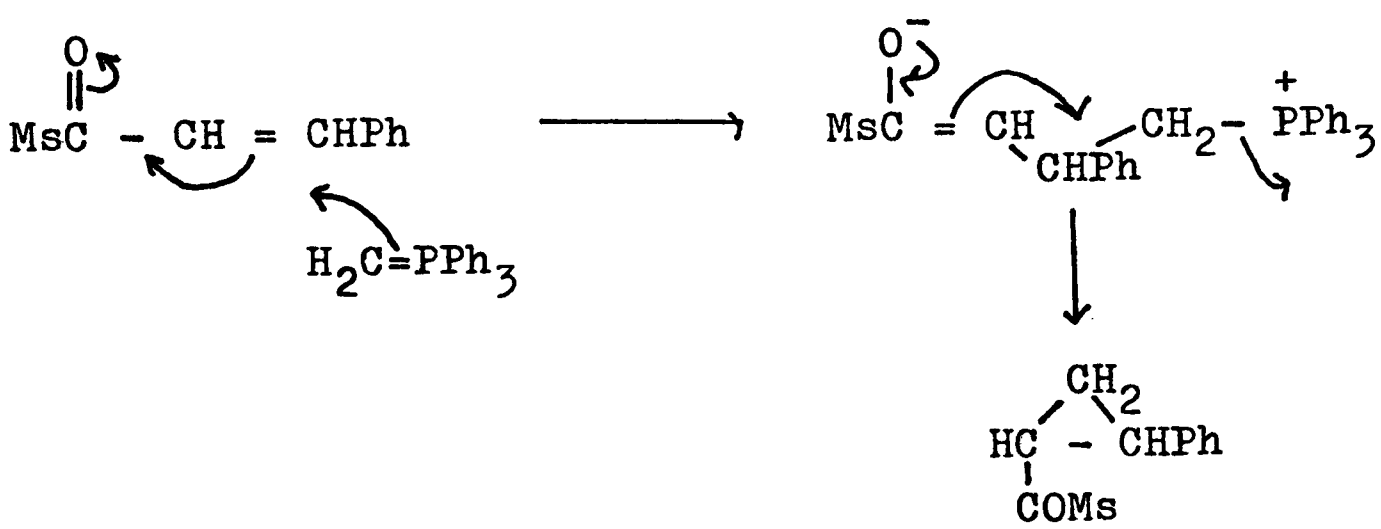
The Wittig and Horner reactions have been extended to the synthesis of cyclopropanes[106,107,108]. Scheme 68 shows some examples of this, with indications as to the proposed mechanisms.





Scheme 68

These reactions may involve, as an intermediate or transition state, a 1,2-oxaphospholan (Scheme 68a). There is evidence, though, that the reaction pathway in Scheme 68b is involved, in this case at least. The stereochemistry about the carbon atom α - to the phenyl group is inverted, indicating an S_N2 displacement at this centre[109]. Phosphoranes have also given cyclopropanes with some hindered α,β -unsaturated ketones[110] (Scheme 69). It is perhaps worthy of note that no cyclobutene is formed in this reaction (i.e. <u>via</u> a 5,6 dihydro-1,2-oxaphosphorinan) (This is, of course, a different class of reaction to those shown in Scheme 68).

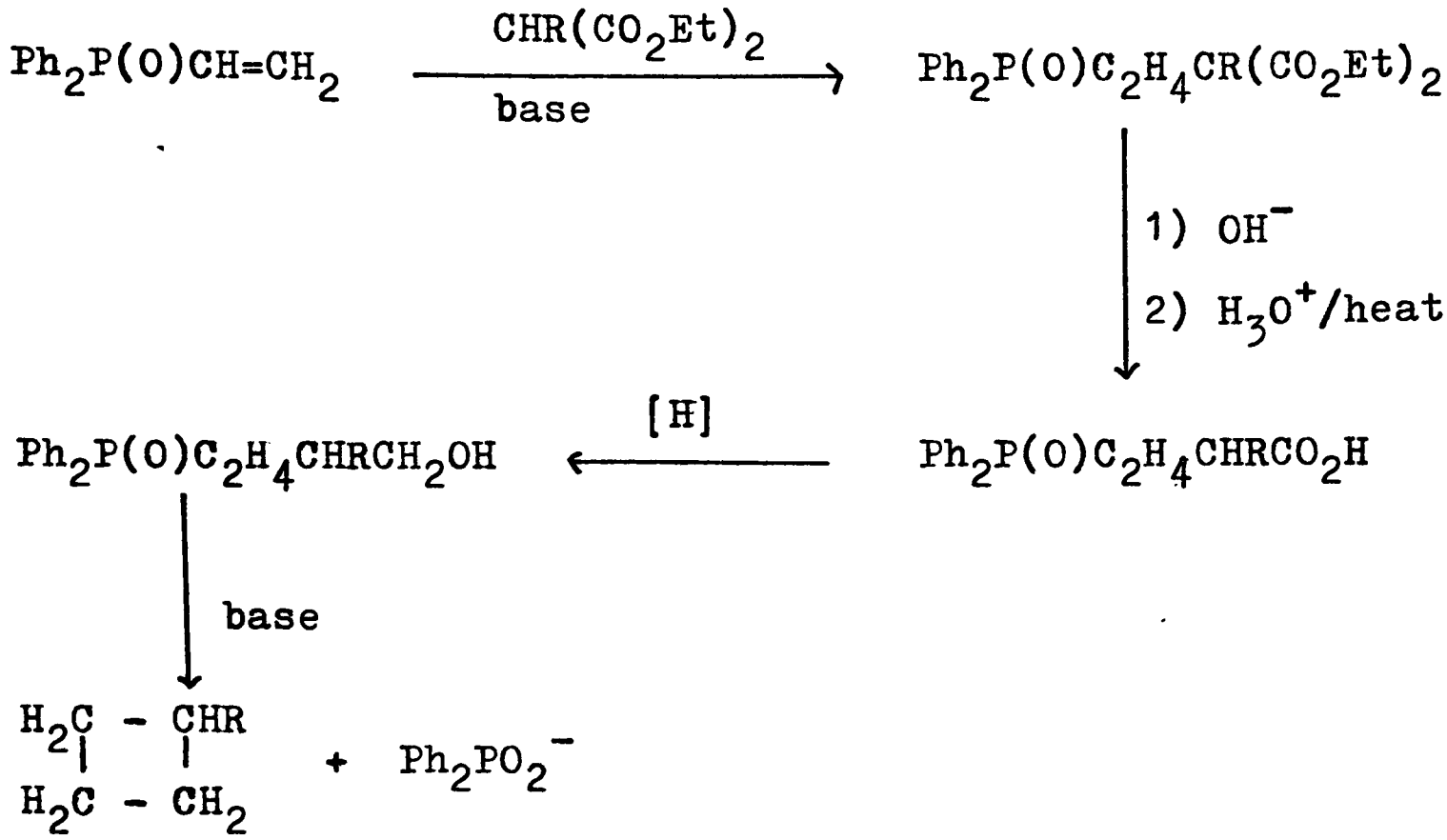


(Ms = 2,4,6-trimethylphenyl)

<u>Scheme 69</u>

It was considered that the sequence outlined in Scheme 70 might be a possible way of synthesising cyclobutanes. The route is formally analogous to Horner's cyclopropane synthesis[110] (Scheme 68c). Michael-type additions to diphenylvinylphosphine oxide (1) have already been considered (Chapter 1). The rest of the steps outlined in Scheme 70

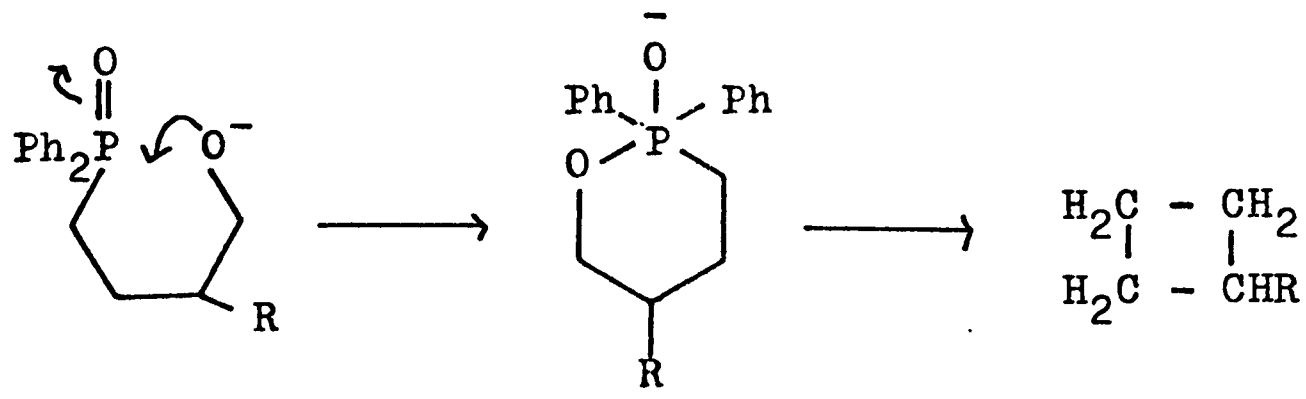
are simple manipulative chemistry. The route would offer some scope in that the R-group could be introduced, in principle, prior to or following the Michael-type addition step.



(R = H, alkyl, aryl, etc).

Scheme 70

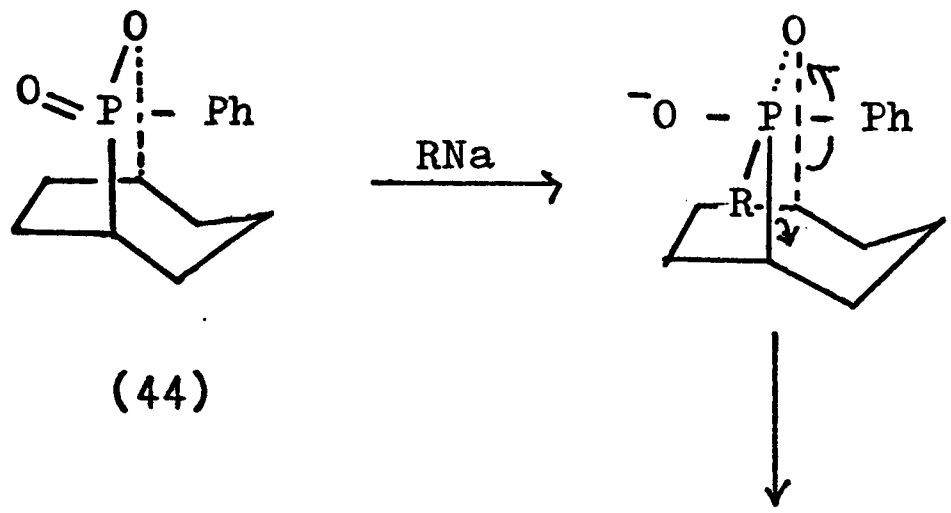
The final step in Scheme 70 might then proceed as outlined in Scheme 71.



Scheme 71

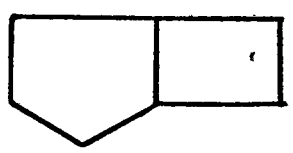
An alternative pathway to the kind of intermediate shown in Scheme 71 was also considered. The phosphinate (44) has recently been prepared[111],

and treatment of this with, say, an alkylsodium could lead to an intermediate which might again collapse to a cyclobutane (Scheme 72).



(44)

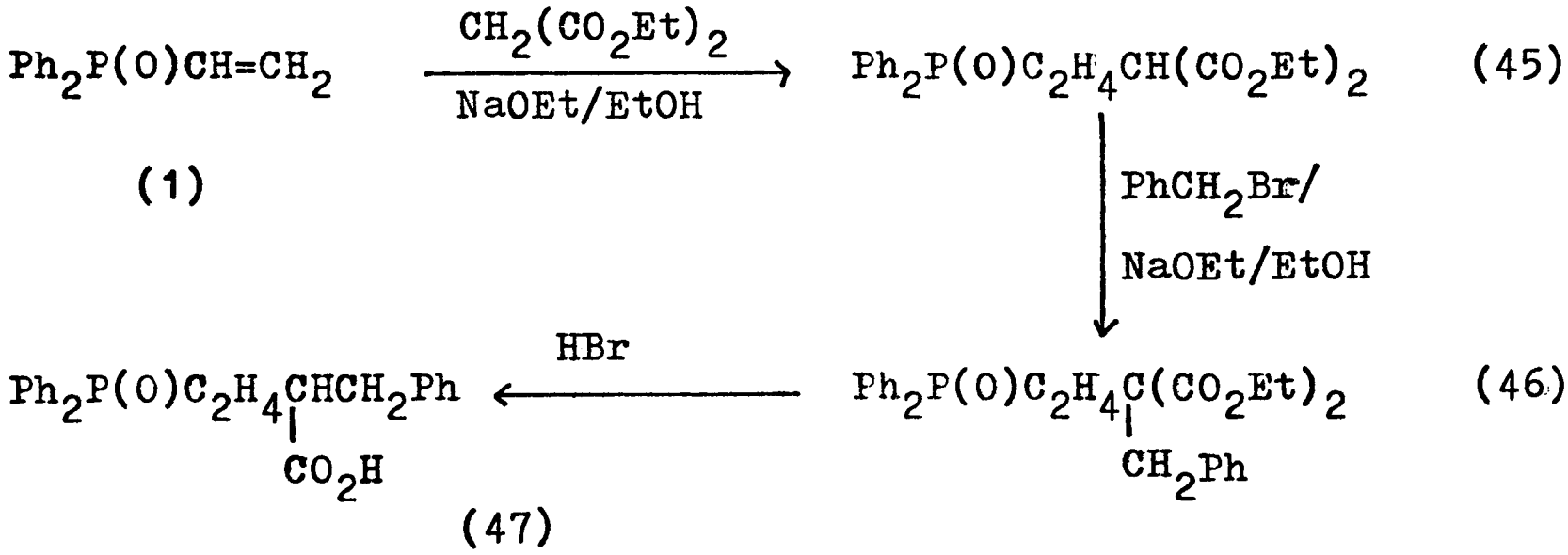
(R = alkyl, aryl)



Scheme 72

Results and Discussion.

The synthesis shown in Scheme 73 was attempted.



Scheme 73.

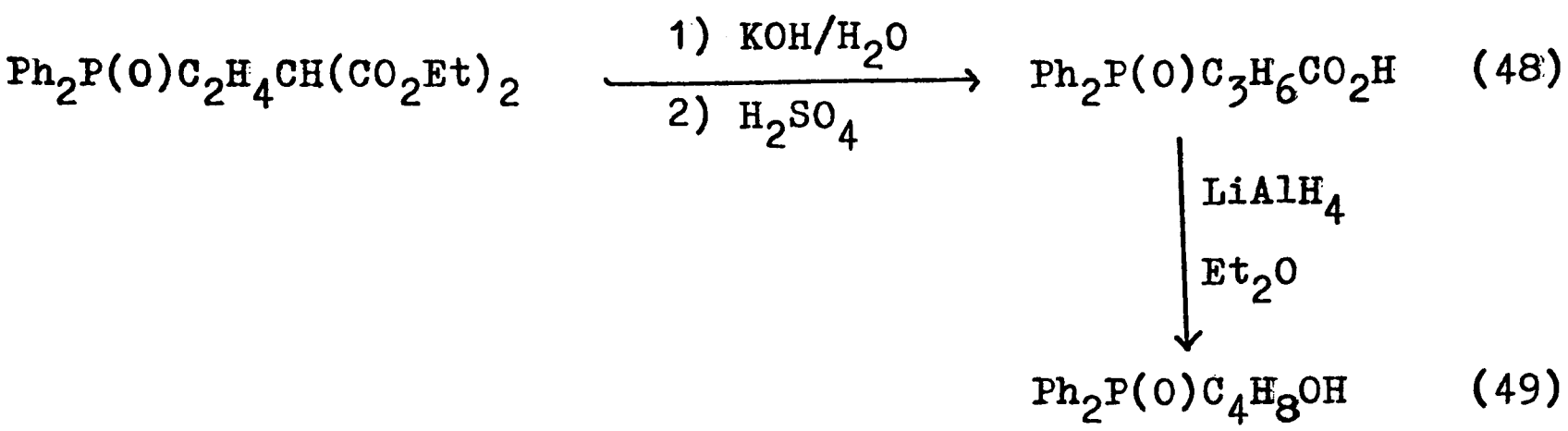
Phosphine oxide (1) underwent addition of malonic ester, in the presence of sodium ethoxide in ethanol at reflux, to give diphenyl-3,3 bis-(carboxyethyl)propylphosphine oxide (45) in 87% yield. Adduct (45) was obtained as an oil, even after chromatography. Its n.m.r. spectrum showed, however, that it was pure enough to use in the next step. Treatment of (45) with sodium ethoxide in refluxing ethanol and

benzyl bromide gave 3,3-bis-(carboxyethyl)4-phenylbutyldiphenylphosphine oxide (46), which was isolated in 50% yield as oily yellow crystals. These could not, however, be purified. Oxide (46) was treated with concentrated hydrobromic acid under reflux[112]. The acid fraction of the product, after work-up, was obtained only in about 14% yield as a hard gum. The rest of the organic material was an intransigent black mass. The route shown in Scheme 73, was then abandoned, without examining the gum to see if it was phosphine oxide (47).

In an attempt to carry out a 'one-pot' addition of malonic ester to phosphine oxide (1) and subsequent benzylation of the adduct, a multiplicity of products was obtained. These were separated by chromatography and are listed in order of increasing polarity. Phosphine oxide (46) was obtained pure in 5.5% yield, phosphine oxide (45) pure in 58% yield, and phosphine oxide (2) (Scheme 7) in 27% yield. In addition, an unidentified product D (see experimental) was obtained: its n.m.r. spectrum was similar to these of the three other products, with, in addition, a hydroxyl group at 5.4 τ. It was obtained in very low yield.

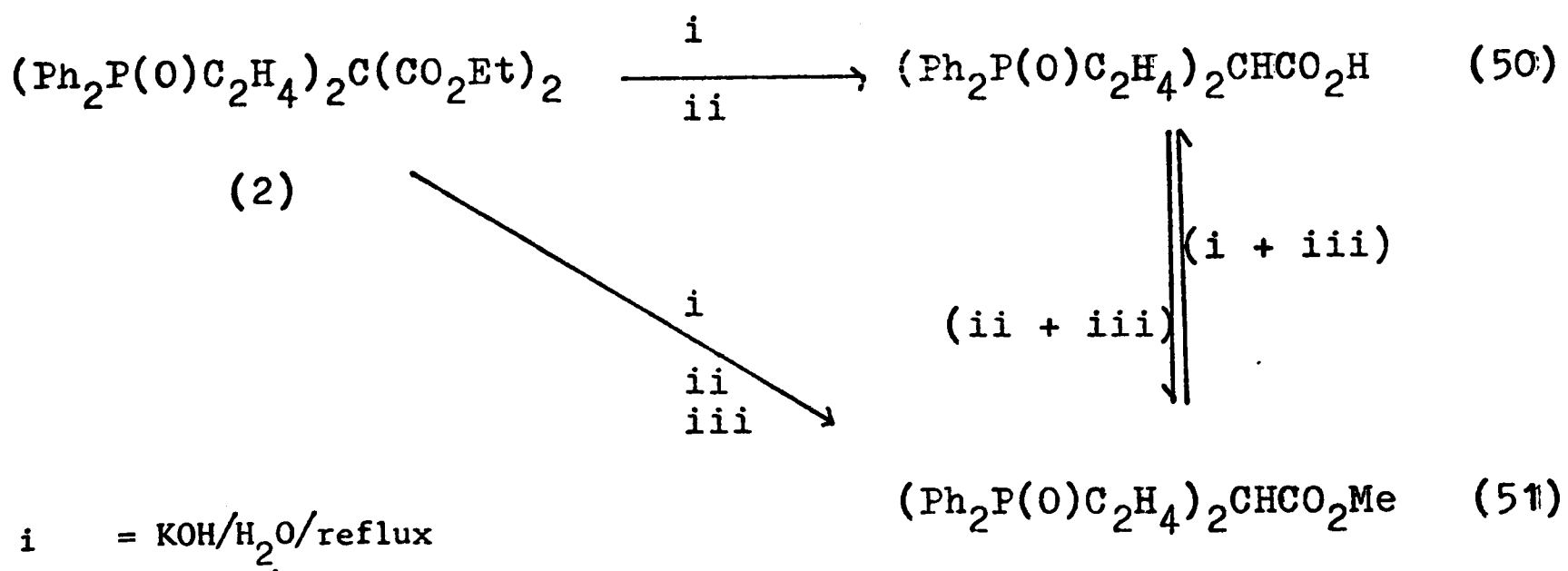
In view of the latter result, an attempt was made to prepare oxide (46) by the addition of benzylmalonic ester to oxide (1). Adduct (46) was thus obtained as an impure brown oil; it was treated with strong aqueous potassium hydroxide at reflux, followed by acidification with concentrated sulphuric acid, and heating to decarboxylate the diacid[112]. The product, about a 22% yield of oily yellow solid, was not fully characterised. At this point, there seemed little justification in proceeding with a series of compounds which were difficult to purify, and were obtained in only low to moderate yields. Accordingly, efforts to complete the synthesis of benzylcyclobutane were abandoned.

Phosphine oxide (45) was itself subjected to hydrolytic decarboxylation sequence, followed by reduction (Scheme 74).



Scheme 74

4-Diphenylphosphinylbutanoic acid (48) was obtained in 74% yield. Reduction of (48) to the alcohol (49) was accomplished with an excess of lithium aluminium hydride in refluxing ether, but only a 25% yield was obtained. The reasons for the low yield are discussed later. Diphenylphosphine oxides are, in general, readily crystallisable. Thus, in place of R = benzyl in Scheme 70, an approach with R = (2-diphenylphosphinylethyl) was attempted (Scheme 75). Bis-(2-diphenylphosphinylethyl)diethyl malonate (2) was obtained (Scheme 18) in 83% yield: an improvement upon the literature yield (45%)[47].



i = KOH/H_2O/reflux
ii = H_2SO_4/heat
iii = MeOH/reflux

Scheme 75.

Phosphine oxide (2) was hydrolysed and decarboxylated to bis-(2-diphenylphosphinylethyl)ethanoic acid (50) in 79% yield. This was isolated as a non-crystallisable foam. The structure of (50) was confirmed by n.m.r. (τ 1.00 (br.s.:1H), 2.20 - 70 (10H), 7.40 - 8.40 (9H)). For analytical purposes, (50) was converted to its methyl ester (51) by treatment with acidic methanol at reflux, in 73% yield.

The reduction of acid (50) to the corresponding alcohol proved to be very difficult. Thus (50) was unaffected by lithium aluminium hydride under a variety of conditions in ethereal solvents, including 1,2-dimethoxyethane at reflux for six hours. It was considered that the methyl ester (51) might be more easily reduced by lithium aluminium hydride. Ester (51) was prepared directly from phosphine oxide (2) in a 'one-pot' procedure in 57% yield (τ 2.20 - 70 (10H), 6.39 (s,3H), 7.35 - 8.40 (9H)). However, this ester, too, was substantially unaffected by lithium aluminium hydride under a variety of conditions.

There must by considerable steric hindrance about the carbonyl group in both ester (51) and acid (50). Newman's 'rule of six' states, empirically, that carboxylic esters containing substituents on the γ-carbon atom (of the acid fragment) are hydrolysed much less rapidly under basic conditions than are other esters. A similar situation is present in acid (50) and methyl ester (51), where two γ- carbon atoms are present, each bearing a bulky diphenylphosphinyl substituent, and nucleophilic attack by AlH_4^- may thus be very hindered. Such an argument might also explain why acid (48) is reduced by lithium aluminium hydride to alcohol (49) in such poor yield. Additionally, it might explain why ester (51) is hydrolysed only slowly by alkali (see Experimental).

Diborane is a classic reducing agent for carboxylic acids[113]. The reaction of boron trifluoride/sodium borohydride with acid (50),

however, gave only a 9.5% yield of 2,2-bis-(2-diphenylphosphinylethyl) ethanol (52), along with much unchanged acid (50). Seemingly, diborane, generated <u>in situ</u>, is still subject to steric effects about carbonyl groups.

Finally, acid (50) was reduced to alcohol (52) in satisfactory yield by the new reagent, boranedimethylsulphide (BMS)[114]. BMS has recently been shown to reduce aliphatic and aromatic carboxylic acids in excellent yield. With 1.2 molar equivalents of BMS alcohol (52) was obtained in 88% yield (a twelve molar equivalent of BMS resulted in only a marginal increase in yield to 92%) (Scheme 76).

$$(Ph_2P(O)C_2H_4)_2CHCO_2H \xrightarrow[C_4H_8O]{BH_3SMe_2} (Ph_2P(O)C_2H_4)_2CHCH_2OH$$

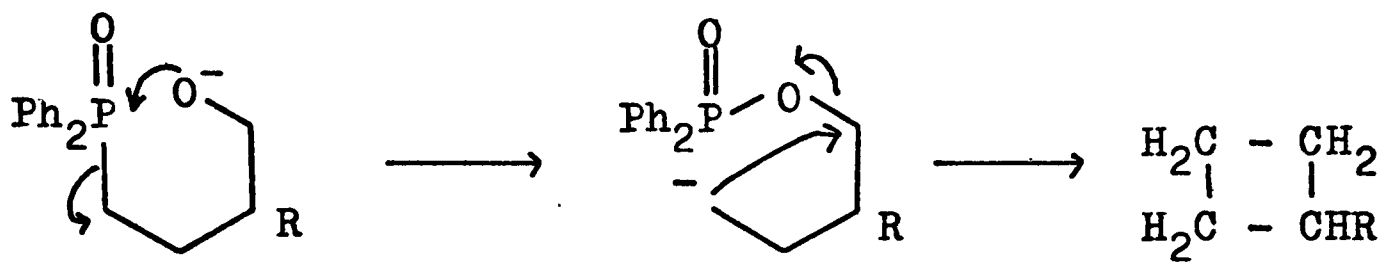
(52)

Scheme 76.

Alcohol (52) had τ 2.25 - 70 (10H), 6.08 (br.s., 1H: -O<u>H</u>), 6.45 (br.s., 2H: -C<u>H</u>$_2$ -O), 7.60 - 90(m,5H) and 8.20 - 50 (m,4H: alkyl H). Attempts were made to fragment alcohol (52) to a cyclobutane (Scheme 70, R = $Ph_2POCH_2CH_2$). With potassium <u>t</u> - butoxide in refluxing benzene or toluene, (52) was recovered in good yield after an aqueous quench. Similarly, alcohol (52) failed to fragment with sodium hydride as base, in tetrahydrofuran at reflux, or in dimethylsulphoxide at 100°. There was, however, a visible sign of proton abstraction from (52) when sodium hydride was the base.

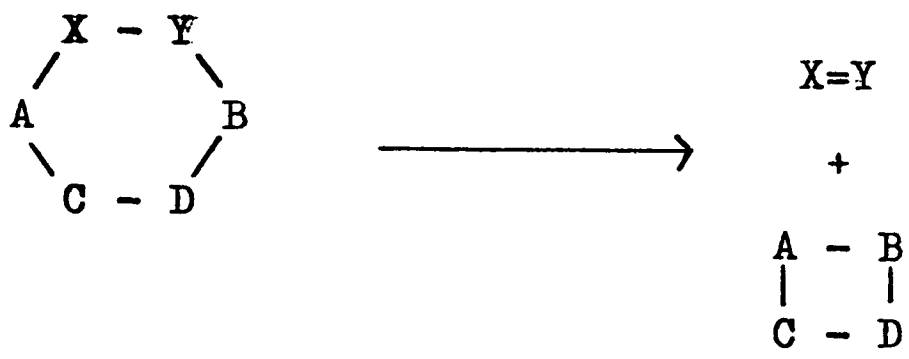
Two explanations may be offered as to why alcohol (52) failed to fragment to a cyclobutane upon treatment with strong base. Firstly, it is possible (but unlikely) that the entropy loss associated with

a six-membered transition state/intermediate (Scheme 71) would be too great to allow reaction to proceed. Secondly, if the reaction pathway for successful cyclobutane production were to be as outlined in Scheme 77 (by analogy with Scheme 68b), then fragmentation would be disfavoured as carbanion (54) is destabilised greatly with respect to alkoxide (53).



Scheme 77.

If, however, the latter argument is true, then it is difficult to see why the example of Horner's cyclopropane synthesis given in Scheme 68c succeeds, unless the phenyl group present in that example offers 'general' assistance in stabilising a carbanion-like transition-state. Perhaps the real reason as to why alcohol (52) failed to fragment to a cyclobutane lies in the relative inaccessibility of the transition-state for a process as outlined in Scheme 78a, actual examples of which are scarce, compared with the transition-state for a process such as shown in Scheme 78b, of which many examples exist in phosphorus chemistry.



Scheme 78.

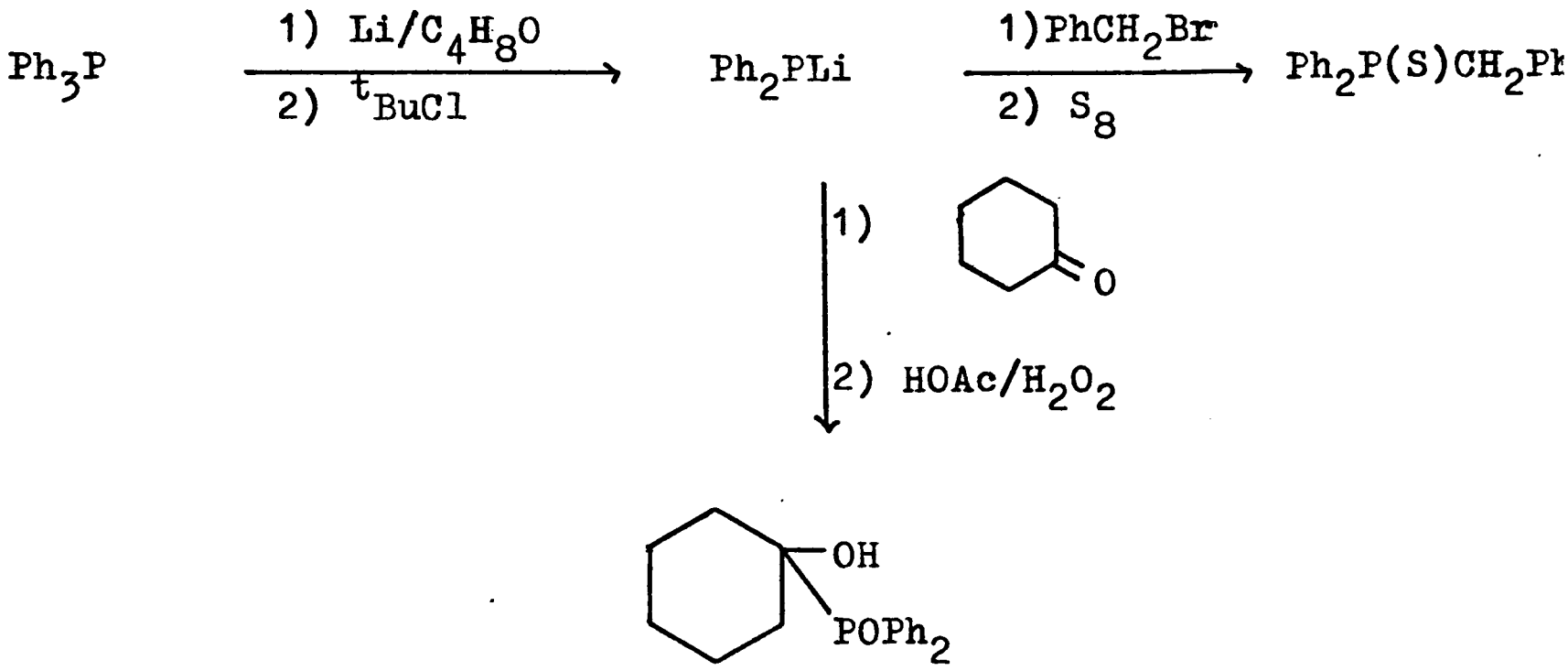
A route to cyclobutanes along the lines of Scheme 72 was not greatly examined: cycloocta-1,3-diene heated with chlorodiphenylphosphine at 100° for 28 days and subsequently treated with water gave no 9-phosphabicyclo [4.2.1.] non-5-ene 9-oxide.

Chapter 5.

REPEATED LITHIATIONS AT PHOSPHORUS (III)

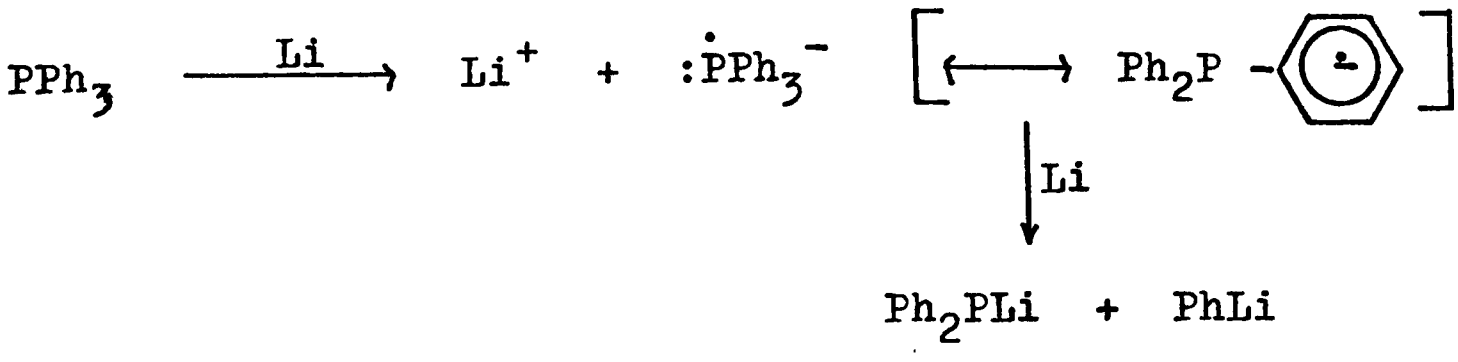
Introduction.

The cleavage of triaryl derivatives of the Group Vb elements by Group 1a metals in ethereal solvents is well known[115], but such reactions were not put to synthetic use until Aguiar prepared lithium diphenylphosphide[116] and studied its reactions with electrophiles[116,117] (Scheme 79).



Scheme 79.

More recently, lithium diphenylphosphide has been used in the production of 2-hydroxyalkyldiphenylphosphine oxides [72,94] (See chapter 3). The mechanism of the P-Ph bond cleavage has not been discussed. Presumably, the initial step involves electron transfer from the metal to the ring or a phosphorus 3d orbital, and the addition of a second electron effects fission of the bond in question (Scheme 80).



Scheme 80

There would appear to be no reason why any aryl phosphine (arsine, etc) should not undergo cleavage by alkali metals. Accordingly, as a 'one-pot' reaction, the sequential lithiation and alkylation of triphenylphosphine to benzylmethylphenylphosphine was attempted.

Results and Discussion.

Triphenylphosphine, stirred in tetrahydrofuran, was treated with 2.2 mole equivalents of lithium, followed by 2-chloro 2-methylpropane (one mole equivalent: to destroy the phenyllithium produced). At this point, the reaction mixture was a clear cherry-red colour. One mole equivalent of iodomethane was then added, to yield a nearly colourless solution. Again, this was treated with lithium (2.2 mole equivalents) and 2-chloro 2-methylpropane, to give a bright orange solution. Benzyl bromide (0.6 mole equivalents, by titration to near-colourlessness of the solution) was then added. Aqueous methanol was quickly added, followed by hydrogen peroxide. The n.m.r. of the crude product showed that it contained, *inter alia*, methyldiphenylphosphine oxide[118], benzyldiphenylphosphine oxide[118], as well as benzylmethylphenylphosphine oxide. Repeated recrystallisations, with reworking of the mother liquors, gave, as isolated and characterised products, benzyldiphenylphosphine oxide (5.4%) and benzylmethylphenylphosphine oxide (9%). Yields were not optimised, and, perhaps, could have been improved by chromatographic separation of the products.

It was considered that by separating excess lithium from the lithium phosphide at each stage of the reaction, and by carefully titrating each alkylation step, the yield of benzylmethylphosphine oxide could be increased. Furthermore, in the standard preparation of lithium diphenylphosphide[72,118], use is made of *three* mole equivalents of lithium. Such an excess of lithium would now be practicable in the modified experimental procedure. Accordingly, each lithium phosphide, when produced, was blown over into a clean vessel *via* a steel tube,

under nitrogen, and then titrated with the appropriate haloalkane. Unfortunately, the yield of the desired product was not increased by such a procedure.

One possibility is that the alkylation of a lithium phosphide is not a high yield process: lithium diphenylphosphide may be benzylated in about 60% yield[116] (epoxides, however, alkylate lithium diphenylphosphide in high yield[41,69]). Consider, however, the second lithiation step of the attempted reaction (Scheme 81a). The phenyl-lithium produced could then attack methyldiphenyl phosphine by an S_NP process[119], and also act as a base, thus leading to a complexity of products (Scheme 81b)

a) $Ph_2PMe \xrightarrow{2Li} PhPMeLi + PhLi$

b) $Ph_2PMe \xrightarrow{PhLi} \xrightarrow{"S_NP"} Ph_3P + MeLi$

$\downarrow$

$Ph_2PCH_2Li + PhH$

Scheme 81

Since the completion of this work, it has been shown[120] that both di-t-butylphenylphosphine and diethylphenylphosphine may be cleaved by lithium in tetrahydrofuran (to, respectively, lithium di-t-butylphosphide and lithium diethylphosphide).

EXPERIMENTAL SECTION

General

'dried' refers to the removal of traces of water from a liquid system by standing over anhydrous sodium sulphate.

'evaporated' refers to the removal of solvent(s) under reduced pressure on a Buchi apparatus.

'm' refers to the melting point of a compound, in ^{o}C, taken on a Kofler block. It is corrected.

'b' refers to the boiling point of a compound in ^{o}C. It is recorded at atmospheric pressure unless otherwise stated.

'saturated sodium bicarbonate', '2N sodium hydroxide', and the like, refer to aqueous solutions.

Bases

Sodium hydride was supplied as a 60% w/w admixture with heavy oil. Before use, it was washed thoroughly with light petrol, under nitrogen. Weights of this material given in parentheses in the experimental section refer to the 60% w/w material; molar quantities to the actual amount of NaH present.

Methyllithium was supplied as a solution in ether.

Butyllithium was supplied as a solution in n-hexane.

Triethylamine, N-2-propylcyclohexylamine, and 2,2,6,6-tetramethylpiperidine were redistilled from potassium hydroxide before use.

Solvents

'petrol' is redistilled light petroleum spirit, b.60 - 80°.

'light petrol' is redistilled petroleum spirit, b.30 - 40°.

'THF' is tetrahydrofuran, redistilled from sodiobenzophenone and stored over BDH Type 4A molecular sieves under nitrogen.

'DME' is 1,2-dimethoxyethane, purified and stored as for THF.

1,4-dioxan was distilled from sodium, then from sodiobenzophenone.

Ethanol (dry) was redistilled from magnesium ethoxide.

Benzene, toluene, xylene, and diethyl ether were all stored over bright sodium wire.

Di-n-butyl ether was passed down an alumina column before use.

'DMF' is N,N-dimethylformamide, dried by passage down an alumina column before use.

'DMSO' is dimethylsulphoxide, redistilled at reduced pressure from calcium hydride.

Acetone was redistilled from potassium carbonate.

1,2-dichloroethane 'AR' was passed down an alumina column before use.

Dichloromethane was purified by shaking with small portions of concentrated sulphuric acid until the latter remained colourless, then washed with water and saturated sodium bicarbonate, and distilled from phosphorus pentoxide.

Chromatography

Column chromatography was carried out using either 'silica' (M60 silica gel) or 'alumina' (CAMAG neutral alumina, Activity 1).

Thin layer chromatography - 't.l.c.' - was carried out using 0.3mm thick plates, either of Merck unbaked Hf254 silica gel or of unbaked aluminium oxide.

Spectroscopy

Infra-red spectra were recorded on a Perkin - Elmer 257 spectrophotometer.

'ν' refers to the i.r. spectrum, quoted in cm^{-1}.

^{1}H nuclear magnetic resonance spectra were recorded either on a Perkin-Elmer R14 instrument (operating at 100MHz) or a Perkin-Elmer R32 instrument (operating at 90MHz), using ^{2}H-chloroform as solvent (unless otherwise stated) and tetramethylsilane as internal standard.

'τ' refers to the n.m.r. spectrum, and 'J' is the coupling constant,

in Hertz.

Mass spectra were obtained with a Varian CH7 instrument, of ionising voltage 70 e.v., with direct insertion. Where present, only the molecular ion (M^+) is recorded.

Microanalyses

These were carried out under the supervision of Dr. F. Strauss, of this department.

Reaction Temperatures

-78° was maintained by an acetone/dry ice bath.

-63° was maintained by a chloroform/dry ice slush bath.

-40° was maintained by a carbon tetrachloride/chloroform/dry ice slush bath.

-10° was maintained by an ice/salt bath.

0° and 10° were maintained by an ice bath.

'20°' refers to the ambient temperature.

100° was maintained by a boiling water-bath.

Other temperatures were achieved with an oil bath.

General Method of Preparation of an approximately 1M Solution of Lithium diphenylphosphide in THF.

Triphenylphosphine (39.9g; 1.5×10^{-1} mol.) was stirred in THF (150 ml) under nitrogen, and to it was added small pieces of freshly-cut lithium (3.14g; 4.5×10^{-1} mol.). A pale yellow colour developed at the metal surfaces immediately, and, within 15 min., the solution had become deep red. It was stirred at 20° for 2h, and 2-chloro 2-methylpropane (16.5ml; 1.5×10^{-1} mol.) added so as to maintain a gentle reflux. When all the 2-chloro 2-methylpropane had been added, the colour of the solution changed from a deep cloudy red to a bright cherry colour: this sometimes occured before all the 2-chloro 2-methylpropane had been added, in which case addition was immediately stopped. The solution was refluxed for a further 5 min. then cooled to 0°. It was transferred by syringe or steel tube to another reaction vessel.

If too much 2-chloro 2-methylpropane had been added, then the products of the reaction would inevitably contain t-butyldiphenylphosphine oxide (or sulphide). which was not easily separated from other phosphine oxides (or sulphides). $C_4H_9POPh_2$ has τ8.76 (d,J_{P-H} = 16, 9H) and $C_4H_9PSPh_2$ has τ8.67 (d,J = 16).

2-Hydroxyethyltriphenylphosphonium chloride. -

Triphenylphosphine (131g; 5×10^{-1} mol) and 2-chloroethanol (40.3g; 5×10^{-1} mol.) were refluxed overnight in xylene (150ml). On cooling the mixture, a white crystalline mass separated, which was collected at the pump and washed with 1 :1 mixture of ether and light petrol. The yield of 2-hydroxyethyltriphenylphosphonium chloride was 171g (100%) m.233° (lit.[121] 233°).

2-Hydroxyethyldiphenylphosphine oxide. -

a)[121] 2-Hydroxyethyltriphenylphosphonium chloride (165g; 4.8×10^{-1}mol) and potassium hydroxide (54.0g; 9.6×10^{-1} mol.) were refluxed

together in 50% aqueous ethanol (450ml) for 1h. ca 300ml of liquid was then distilled off, and the residue, after cooling, was extracted with dichloromethane (2 x 100ml), having adjusted the aqueous phase to ca. pH7. The organic extracts were dried and evaporated to give a yellow oil (138.7g) which could not easily be further purified, and was used directly in the next stage.

b)[72] Lithium diphenylphosphide (5×10^{-1} mol.) was added dropwise over 30 min to oxirane (25ml; 5.5×10^{-1} mol), stirred under nitrogen at -10°. Stirring was continued another 30 min to give a nearly colourless solution. Acetic acid (40ml; 6.7×10^{-1} mol.) was added slowly with vigorous stirring. The mixture was cooled to 0° and 30% hydrogen peroxide (200ml) added dropwise over 20 min. Stirring was continued for another 45 min, then water (1000ml) was added, and the mixture extracted with dichloromethane (2 x 500ml). The organic extracts were washed with saturated sodium bicarbonate (500ml), dried, and evaporated to give a yellow oil which solidified upon standing (104.7g). Recrystallisation from benzene gave 2 - hydroxy-ethyldiphenylphosphine oxide (90.0g; 74%). m.87-8° (lit.[72] 88.5-91.5^{o}). τ 2.15 - 60 (10H), 5.70 (br.s., 1H), 6.02 (dt, $J_{P-H} = 15$, $J_{H-H} = 8$, 2H), 7.40 (dt. $J_{P-H} = 10$, 2H). ^{13}C n.m.r. - see separate section.

2-Chloroethyldiphenylphosphine oxide[73]-

2-Hydroxyethyldiphenylphosphine oxide (68g; 2.7×10^{-1} mol.) was stirred in benzene (250ml) at 0°, and to it was added phosphorus pentachloride (58.0g; 2.7×10^{-1} mol.). The mixture was then cautiously refluxed for 20 min., cooled to 0°, and water (50ml) added slowly. Three layers separated: the top two were washed together with saturated ice-cold sodium bicarbonate (3 x 100ml), after which only one organic layer remained. This was dried and evaporated to yield an oil which solidified to give crystals (59.6g; 90%) of 2-chloroethyldiphenylphosphine oxide. τ 2.20 - 45 (4H), 2.55 - 80 (6H), 6.25 (dt, $J_{P-H} = 11$, $J_{H-H} = 7$, 2H), 7.20 (dtm $J_{P-H} = 10$, 2H).

Diphenylvinylphosphine oxide. -

2-Chloroethyldiphenylphosphine oxide (59.5g; 2.25×10^{-1} mol.) was refluxed with triethylamine (38ml; 2.8×10^{-1} mol.) in benzene (220ml), with stirring, for 1.25h. Filtration of the cooled solution and evaporation gave an oil (35.4g) which deposited crystals on standing. No satisfactory solvent for a one-step recrystallisation was found: the normal procedure adopted was to employ ethyl acetate, and re-work the mother liquors a further two or three times. In this way, diphenylvinylphosphine oxide was obtained as a powder (33.8g; 66%). The analytical sample had m.117° (lit[54] 117°). (Found: C,73.55; H,5.8. Calcd. for $C_{14}H_{13}OP$: C,73.7; H,5.75%)
τ 2.15 - 80 (11H), 2.90 - 4.00 (2H).
If the triethylamine were not redistilled, then reaction times of 5 - 6 h were necessary for complete dehydrohalogenation of the starting material. Samples of diphenylvinylphosphine oxide containing starting material were not easily purified, as the two tend to co-crystallise from benzene or ethyl acetate.

Reaction of Lithium diphenylphosphide with 1,2-Dibromoethane.-

Lithium diphenylphosphide (5×10^{-1} mol.) was added to 1,2-dibromoethane (64.5ml; 7.5×10^{-1} mol.) under nitrogen, with stirring, at 0°. Stirring was continued for a further 1h, then, over 30 min, was added 30% hydrogen peroxide (200ml), with cooling of the mixture at 0°. Stirring was maintained for a further 1h, then water (1000ml) was added, and the (lower) organic layer separated. The aqueous layer was extracted with dichloromethane (2 x 300ml), and the combined organic phases washed with saturated sodium bicarbonate (500ml), dried, and evaporated on a boiling water bath to give sticky crystals (105.4g), shown by n.m.r. and m.p. to consist essentially of diphenylphosphinic acid.

Reaction of Benzoin with Diphenylvinylphosphine oxide.-

To sodium hydride (0.48g; 1.2 x 10^{-2} mol.), stirred under nitrogen, was added, dropwise, benzoin (2.12g; 10^{-2} mol.) in DMF (20ml). To the resulting deep red solution was added diphenylvinylphosphine oxide (2.28g 10^{-2} mol.) in DMF (35ml). The mixture was heated to 100° and held there for 75h. To the deep yellow solution was then added water (20ml), and the mixture shaken between water (150ml) and ether (3 x 50ml). The ethereal layers were washed with water (25ml) dried, and evaporated to give a brown oil (3.14g). T.l.c. of this showed many products more polar than the starting materials, and the oil was discarded.

Reaction of Salicylaldehyde with Diphenylvinylphosphine oxide.-

To sodium hydride (0.48g; 1.2 x 10^{-2} mol.), stirred under nitrogen, was added salicylaldehyde (1.22g; 10^{-2} mol.) in ether (5ml). A pale yellow solid formed, and the ether was removed with the aid of a warm water bath and a fast stream of nitrogen. Then diphenylvinylphosphine oxide (2.28g; 10^{-2} mol.) in acetonitrile (20ml) was added, and the mixture refluxed for 24h. Water (20ml) was added, and the mixture extracted with ether (5 x 50ml). The extracts were washed with water (200ml), dried, and evaporated to give a yellow oil (1.57g) Distillation of this afforded only salicylaldehyde.

Attempted Reaction of N-bromoacetamide with Diphenylvinylphosphine oxide.-

N-bromoacetamide (4.14g; 3 x 10^{-2} mol.) sodium acetate trihydrate (3.75g), and diphenylvinylphosphine oxide (1.37g; 6 x 10^{-3} mol.) were stirred in acetone (240ml) and water (120ml) for 18h. The mixture was concentrated to ca. 100ml by evaporation, and extracted with dichloromethane (3 x 40ml). Drying and evaporation of the organic extracts gave a solid (1.72g) shown to consist mainly of starting material, by n.m.r. and t.l.c. comparison.

Attempted Reaction of Iodine and Potassium hydroxide with Diphenylvinylphosphine oxide. -

Powdered potassium hudroxide (0.56g; 10^{-2} mol.) and diphenylvinylphosphine oxide (1.14g; 5×10^{-3} mol.) were stirred in DME (15ml) and to this was added iodine (1.27g; 5×10^{-3} mol.) in DME (15ml) over 15 min. The mixture was stirred for 24h, then saturated sodium sulphite (50ml) added The mixture was extracted with dichloromethane (2 x 15ml), the extracts washed with brine (20ml), dried, and evaporated to give an off-white solid (0.88g) shown to be starting material by t.l.c. and n.m.r. comparison.

Attempted Reaction of t-Butylhydroperoxide with Diphenylvinylphosphine oxide. -

To a stirred solution of diphenylvinylphosphine oxide (2.28g; 10^{-2} mol.) and t- butylhydroperoxide (as a 70:30 mixture with di-t-butylperoxide)(1.80g; 1.4×10^{-2} mol.) in benzene (10ml), was added Triton B (N-benzyltrimethylammonium hydroxide, 40% w/v in methanol)(0.11g; 2×10^{-4} mol.) such that $t \leq 10^{o}$. The mixture was stirred at 20° for24h, and water (10ml) added. The benzene layer was separated, and the aqueous layer extracted with benzene (20ml). The combined benzene fractions were washed with brine (10ml), dried, and evaporated to yield an oil, shown to be a mixture of starting materials by t.l.c. and n.m.r.

Attempted Reaction of Sodium 3-chloroperoxybenzoate with Diphenylvinylphosphine oxide. -

a) Diphenylvinylphosphine oxide (2.28g; 10^{-2} mol.) and sodium hydride (0.06g; 1.5×10^{-3} mol.) were stirred under nitrogen in THF (15ml) and 3-chloroperoxybenzoic acid (1.80g; 1.1×10^{-2} mol.) in THF (15ml) added over 10 min. The mixture was stirred for 24h, and water (20ml) added. The ethereal layer was separated, and the aqueous portion extracted with dichloromethane (2 x 20ml). The combined

organic portions were washed with saturated sodium sulphite (2 x 20ml) 2M sodium hydroxide (10ml), and brine (20ml), dried and evaporated to give a solid (2.12g) identified as diphenylvinylphosphine oxide.

b) Diphenylvinylphosphine oxide (2.28g 10^{-2} mol.) and 3 - chloroperoxybenzoic acid (1.74g; 10^{-2} mol.) were stirred, in the dark, in methanol (25ml), and 2.5M sodium hydroxide (4.0ml; 10^{-2} mol.) was added slowly, such that $t \lesssim 20^{o}$. Stirring was continued for 24h and water (100ml) added. The mixture was extracted with dichloromethane (3 x 25ml), and the organic extracts washed with saturated sodium carbonate (50ml), saturated sodium sulphate (50ml), dried, and evaporated to give a solid (2.35g), identified as diphenylvinylphosphine oxide.

Attempted Reaction of 3-Chloroperoxybenzoic acid with Diphenylvinylphosphine oxide.-

3-chloroperoxybenzoic acid (1.08g; 6.3×10^{-3} mol.) and diphenylvinylphosphine oxide (1.14g; 5×10^{-3} mol.) were refluxed in 1,2-dichloroethane (15ml) for 24h. The mixture was cooled, washed with saturated aqueous sodium carbonate (50ml), saturated sodium sulphite (50ml), dried, and evaporated to give a solid (1.08g), shown by t.l.c. and n.m.r. to be diphenylvinylphosphine oxide.

Attempted Reaction of Trifluorperoxyacetic acid with Diphenylvinylphosphine oxide.-

Diphenylvinylphosphine oxide (5.70g; 2.25×10^{-2} mol.) was refluxed in dichloromethane (30ml) and to this, over 45 min. was added a mixture of trifluoracetic acid (5.5ml; 7.5×10^{-2} mol.) and 85% hydrogen peroxide (1.7ml; 5×10^{-2} mol.) in dichloromethane (20ml). Refluxing was maintained for 25h. The mixture was cooled to 0° and saturated sodium sulphite (50ml) added with caution. The organic

layer was separated, and the aqueous portion extracted with dichloromethane (50ml). The combined organic phases were washed with saturated sodium bicarbonate (3 x 50ml), dried, and evaporated to give a solid (4.76g), identified as starting material.

Reaction of Lithium diphenylphosphide with Ethyl formate.- Lithium diphenylphosphide (10^{-1} mol.) was added, with stirring under nitrogen, to ethyl formate (7.2g; 10^{-1} mol.) and the milky yellow mixture left for 20h. Acetic acid (7.5ml; 1.25×10^{-1} mol.) was added, and the mixture stirred vigorously, then cooled to 0°. 30% hydrogen peroxide (40ml) was added over 45 min., and the mixture stirred for a further 15 min. Water (100ml) was added, and the organic layer separated. The aqueous phase was extracted with dichloromethane (100ml) and the organic layers combined, washed with saturated sodium bicarbonate, dried, and evaporated to give a yellow oil (19.4g). Chromatography of this (ethyl acetate/silica) gave diphenylphosphinic acid as the only product.

Reaction of Methyldiphenylphosphine sulphide with Bromine,- Triphenylphosphine sulphide (2.94g; 10^{-2} mol.) was stirred in THF (20ml) under nitrogen, and methyllithium (1.0M; 10ml; 10^{-2} mol.) added slowly. The solution was stirred for 2h, and bromine (0.52ml; 10^{-2} mol) added all at once, with vigorous reaction. Stirring was continued for 30 min, then water (10ml) added, and the ethereal layer separated. The aqueous phase was extracted with dichloromethane (20ml). The organic layers were combined, washed with saturated sodium sulphite (20ml), dried, and evaporated to yield a red oil (5.30g). Chromatography of this (ethyl acetate/alumina) gave diphenylphosphindithioic acid as the only mobile product. m.95-6° (lit[95] 95 - 7°).

Reaction of Chlorodiphenylphosphine with Paraformaldehyde.[79]- Chlorodiphenylphosphine (22g; 10^{-1} mol.) and paraformaldehyde (3g; 10^{-1} mol.) were refluxed in decalin (70ml) for 17h. The decalin was removed by distillation, and the cooled residue treated with water (100ml) and chloroform (100ml). The mixture was boiled, and the hot chloroform layer separated and filtered through a cotton wool plug. Petrol was added to the chloroform extract, depositing brown crystals. The aqueous phase was once more extracted in this fashion, to yield a total of 6.75g of crystals. These were shown to be diphenylphosphinic acid m.192° (lit.[122] 190°). τ -0.87 (br.s.,1H), 2.15 - 45 (4H), 2.55 - 75 (6H).

Reaction of Butyllithium and Bromine with 2-Hydroxyethyldiphenylphosphine oxide.-

2-Hydroxyethyldiphenylphosphine oxide (2.46g; 10^{-2} mol.) was stirred in THF (30ml) at -63°, under nitrogen and to it was added, over 20min, butyllithium (2.0M; 10ml; 2 x 10^{-2} mol.). The mixture was stirred a further 40min to a deep red colour[72], then, still at -63°, bromine (0.76ml; 1.5 x 10^{-2} mol.) was added. The mixture was warmed slowly to 20° and stirred there for 20h. Saturated sodium sulphite (25ml) was added and the ethereal layer separated. The aqueous portion was extracted with dichloromethane (2 x 20ml) and the organic portions combined, washed with brine (25ml), dried, and evaporated, yielding an orange oil (2.48g). T.l.c. of this (ethyl acetate/alumina) revealed a complex mixture of products. The oil was covered with ethyl acetate and, in time, deposited crystals (0.41g). These were recrystallised twice from ethyl acetate to give needles of 1,2-bis(diphenylphosphinyl)ethane m.268-9° (lit.[54] 268-70°). M^+ 430. τ2.15 - 60 (10H), 7.48 (m,2H).

Attempted Reaction of Mesityl oxide with Trimethylamine N-oxide.- Mesityl oxide (4.9g; 5 x 10^{-2} mol.) and trimethylamine N-oxide (3.75g; 5 x 10^{-2} mol.) were refluxed together for 6H in DMF (20ml). The mixture was cooled, diluted with dichloromethane (50ml) and washed with water (2 x 200ml). The solution was dried, and evaporated to yield a pale yellow liquid, shown by t.l.c. and i.r. comparison to be mesityl oxide.

Reaction of Hydrogen peroxide with Diphenylvinylphosphine oxide.- Diphenylvinylphosphine oxide (3.42g; 1.5 x 10^{-2} mol.) was stirred at 0° in methanol (25ml) and 30% hydrogen peroxide (4ml) was added, followed by 2.5M sodium hydroxide (6.0ml; 1.5 x 10^{-2} mol.), at such a rate that $t \leqslant 10^{o}$. The mixture was stirred in the dark for 24h, then water (150ml) was added. The mixture was extracted with dichloromethane (3.4 ml), and the organic extracts washed with saturated sodium sulphite (100ml), dried, and evaporated to yield a white oil, which furnished crystals on standing (3.04g). Recrystallisation from ethyl acetate/petrol gave bis(2-di-phenylphosphinylethyl) peroxide (2.89g; 79%) m.267 - 8°. Satisfactory analytical data were not obtained (Found: C,65.2; H,6.35. $C_{28}H_{28}O_4P_2$ requires C,70.9; H,5.95. $C_{28}H_{28}O_4P_2.2H_2O$ requires C,65.9; H,6.3%). The material decomposed to a red oil upon attempted recrystallisation from di-n-butyl ether. The structure was assigned on the basis of the following data: τ 2.15 - 65 (10H), 3.75 (dt, J_{P-H} = 12, J_{H-H} = 8, 2H), 7.27 (dt, J_{P-H} = 14, 2H). ν(nujol) 3130 (m), 1440 (s, obscured), 1230 (w), 3360 (w), 1155 (s), 1115 (w), 1095 (w), 1070 (w), 1030 (m), 1015 (sh), 994 (w), 827 (w), 795 (w), 746 (m), 726 (m), 694 (m), m/e: 215 (100%). 201 (97), 216 (91), 77 (75), 202 (65), 217 (15), 243 (10), 244 (13), 245 (4), 246 (1). ^{13}C n.m.r. - see separate section.

The material (0.200g) was dissolved in acetic acid (5ml), and treated with a solution of potassium iodide (0.2g) in acetic acid (10ml). The liberated iodine was titrated against sodium thiosulphate (aqueous; 0.05M). The titres of two concurrent runs were 1.50 and 1.55ml.

$$\text{mmoles } I_2 \text{ liberated} = 0.5 \times \frac{(1.50 + 1.55)}{2} \times 0.05$$

$$= \text{mmoles peroxide present}$$

$$\text{mol. wt. peroxide} = \frac{0.200}{0.5 \times 1.525 \times 0.05}$$

$$= 525 \text{ (to 3.s.f.)}$$

This corresponds closely to the molecular weight of the putative dihydrate (526). The error in this experiment may be estimated at (1.55 - 1.50)/1.525 i.e. about 3%: the difference in molecular weights between the anhydrous and dihydrated peroxide is about 7%.

Reaction of bis-(2-Diphenylphosphinylethyl)peroxide with Potassium t-butoxide.-

bis-(2-Diphenylphosphinylethyl)peroxide (1.23g; 5×10^{-2} mol.) and potassium t-butoxide (0.50g; 5×10^{-3} mol.) were stirred in DMSO (15ml) for 24h. Water (200ml) was added and the mixture extracted with dichloromethane (5 x 25ml). The organic extracts were washed with water (200ml), dried, and evaporated to yield a brown oil (0.61g). Purification of this via chromatography (ethyl acetate/alumina) gave an oil (0.51g). The n.m.r. of this was consistent with a 1:1 mixture of 2-hydroxyethyldiphenylphosphine oxide and another component having resonances in the region of 2.2 - 2.6 τ

and a complex multiplet at 2.7 - 3.5 τ . No further separation was possible.

Reaction of bis-(2-Diphenylphosphinylethyl) ether with Lithium aluminium hydride.-

Bis-(2-Diphenylphosphinylethyl)ether (0.368g; 7.5×10^{-4} mol.) and lithium aluminium hydride (0.019g; 5×10^{-4} mol.) were stirred under nitrogen in THF at 20° for 30 min. Water (10ml), containing acetic acid (0.1ml) was added, and the mixture extracted with dichloromethane (2 x 10ml). The organic extracts were dried and evaporated to give an oil (0.342g), which was crystallised from ethyl acetate to give needles of 2-hydroxyethyldiphenylphosphine oxide (0.310g; 84%), identified by m.p. and n.m.r. comparison.

Reaction of 2-Hydroxyethyldiphenylphosphine oxide with Diphenyl-vinylphosphine oxide.-

2-Hydroxyethyldiphenylphosphine oxide (2.46g; 10^{-2} mol.) was stirred under nitrogen in THF (20ml) at -78°, and butyllithium (1.5M; 6.7ml; 10^{-2} mol.) was added over 15 min. Stirring was continued for another 30 min to give a pale orange solution. Diphenylvinylphosphine oxide (2.28g; 10^{-2} mol.) in THF (20ml) was added over 30 min to give a thick white precipitate. The mixture was stirred for 22h at 20°, then water (25ml) added. The ethereal layer was separated, and the aqueous phase extracted with dichloromethane (2 x 25ml). The organic layers were combined, washed with brine (25ml), dried, and evaporated to give an oil (4.22g). T.l.c. (methanol/alumina) and n.m.r. revealed this to be a complex mixture, and it was abandoned.

bis-2-(Diphenylphosphonylethyl)ether.-

Lithium diphenylphosphide (1.5×10^{-2} mol.) was added to digol ditosylate (2.07g; 5×10^{-3} mol.) and the mixture stirred under nitrogen overnight. Methanol (10ml) was added, followed by 30% hydrogen peroxide (10ml) and methanol (10ml), over 15min., at 0°. Stirring was continued for a further 1h, then water (50ml) was added,

and the mixture extracted with dichloromethane (3 x 50ml). The extracts were washed with 2M sodium hydroxide (50ml), and brine (50ml), dried, and evaporated to yield a yellow oil (3.15g). Chromatography of this (methanol/alumina) gave an oil, the n.m.r. of which showed it to contain some tert-butyldiphenylphosphine oxide. Further chromatography (ethyl acetate/alumina) gave a yellow oil (2.68g) which solidified upon standing. Recrystallisation from ethyl acetate afforded crystals of bis-(2-diphenylphosphinylethyl) ether (2.23g; 94%) m.81-2°. The analytical sample was recrystallised once more (Found: C, 68.5; H, 6.3 $C_{28}H_{28}O_3P_2$. H_2O requires C, 68.3; H,6.15%). τ 2.15 - 60 (10H), 6.33 (dt, J_{P-H} = 12, J_{H-H} = 10, 2H), 7.54 (dt, J_{P-H} = 13, 2H). m/e 228 (100%) 201 (100%), 227 (68), 77 (66), 202 (60), 245 (15), 18 (15). ^{13}C n.m.r. - see separate section.

Reaction of Sodium Hydroxide with Diphenylvinylphosphine oxide. - Diphenylvinylphosphine oxide (1g) was stirred with 2M sodium hydroxide (20ml) and methanol (20ml) for 24h. The mixture was evaporated to dryness, and the oily residue shaken between brine (40ml) and dichloromethane (2 x 50ml). The organic layers were dried and evaporated to furnish an oily solid (1.12g). Two recrystallisations from benzene gave feathery crystals of bis-1,2-(diphenylphosphinyl) ethane (0.92g; 96%) m. 268-9° (lit.[54] 268-70°); mixed m.267-8°.

Dimethylmethylphosphonate. -

Trimethylphosphite (124g; 1 mol.) and methyl iodide (7.1g; 5×10^{-2} mol.) were refluxed under an efficient condenser for 10 min. until the vigorous reaction subsided. Distillation afforded dimethylmethylphosphonate b.82-3°/20mmHg (lit.[123] 60°/10mmHg) 118.8g; 96%).

Methylphosphonyl chloride.[124]

Dimethylmethylphosphonate (49.6g; 4×10^{-1} mol.) was refluxed overnight with concentrated hydrochloric acid (50ml). The mixture was

dried by azeotroping off the aqueous phase with benzene on a Dean and Stark apparatus over 6h. To the solid residue of methylphosphonic acid was added phosphorus pentachloride (208.2g; 1 mol), and the mixture refluxed for 2.5h. The mixture was fractionally distilled, and the fraction b.101°/300mmHg (lit.[124] 50-55°/20mmHg) collected (52.5g; 99%). The product solidified slowly, and was kept in a flask with a well-greased stopper.

Di-(2-bromoethyl)methylphosphonate.-

Triethylamine (41.5ml; 3×10^{-1} mol.) was stirred in DME (100ml), and to this added methylphosphonyl chloride (19.95g; 1.5×10^{-1} mol.) in DME (200ml), so that $t \leq 10°$, Then 2-bromoethanol (37.5g; 3×10^{-1} mol) in DME (25ml) was added, again such that $t \leq 10°$. The mixture was stirred at 20° for 2h, then refluxed for 30 min (care!). After cooling and filtering, the mixture was evaporated and distilled. The fraction b.151-4°/2.0 mmHg was collected to yield di-2-bromoethylmethylphosphonate (29.1g; 63%). The analytical sample was distilled once more b.138°/0.4 mmHg (Found: C,19.4; H, 3.85. $C_5H_{11}O_3PBr_2$ requires C,19.35; H,3.6%), τ 5.67 (dt, J_{P-H} = 8 J_{H-H} = 6, 4H), 6.47 (t,4H), 8.43 (d, J_{P-H} = 18, 3H).

Reaction of Base with Di-(2-bromoethylmethylphosphonate.-

Butyllithium (2.0M; 15ml; 3×10^{-2} mol.) was stirred under nitrogen in THF (400ml) at -78°, and to it was added, over 1.25h, di-(2-bromoethyl)methylphosphonate (3.1g; 10^{-2} mol.) in THF (75ml). The mixture was stirred a further 28h at -78°, then acetic acid (1.8ml; 3×10^{-2} mol.) was added, and the whole evaporated to dryness. The residue was extracted with chloroform (75ml), which was dried and evaporated to yield a yellow oil (2.48g). Distillation of this gave only starting material.

A similar result pertained when using lithium N-2-propylcyclohexylamide or lithium triphenylmethide as base, or when adding

the butyllithium in two equal portions. When the reaction was performed at t $>$ - 78°, oils were obtained on distillation, the n.m.r's of which showed them to contain n-butyl groups.

Reaction of Dimethylmethylphosphonate with Lithium-N-2-propylcyclohexylamide and 1-Bromobutane. -

N-2-Propylcyclohexylamine (4.23g; 3×10^{-2} mol.) was stirred in THF (80ml) at -78° under nitrogen, and to it was added butyllityium (2.0N; 15ml; 3×10^{-2}mol.) and the whole stirred for 1h. Then, over 30 min, dimethylmethylphosphonate (3.72g; 3×10^{-2} mol.) in THF (20ml) was added. Stirring was continued at -78° for 5h. 1-Bromobutane (4.01g; 3×10^{-2} mol.) in THF (20ml) was added, and the whole stirred overnight. 2M hydrochloric acid (50ml) was added, and the organic layer separated, washed with 2M hydrochloric acid (50ml) and brine (50ml), dried, and evaporated to give a liquid (1.49g). The n.m.r. of this showed it to be a mixture of starting material, mono-, di-, and tri-alkylated material, by comparison with the n.m.r. spectra of authentic material[57].

If the reaction was performed instead at room temperature, the major product isolated was a white, highly water-soluble solid, the n.m.r. of which was consistent with it being a mixture of phosphonamides.

Attempted Reaction of Oxirane with Dimethylmethylphosphonate.-

Dimethylmethylphosphonate (6.2g; 5×10^{-2} mol.) was stirred in THF (50ml) under nitrogen at -78°, and to it was added butyllithium (2.5M; 20ml; 5×10^{-2} mol.) Stirring was continued for 15 min, then oxirane (2.5ml; 5×10^{-2} mol.) was added, and stirring continued for 5h. Again, butyllithium (20ml) was added, followed, after 15min by oxirane (2.5ml), and the mixture stirred for a further 9h at -78° and 40h at 20°. The THF was removed by

evaporation, and the residue treated with water (40ml) and acetic acid (6ml). The mixture was extracted with chloroform (2 x 20ml), and the organic extracts were dried and evaporated to yield a yellow oil (2.15g). Distillation of this gave, as the only volatile product, hexan-1-ol, identified by b.p., i.r., and n.m.r. comparison with an authentic sample.

tris-(2-Chloroethyl)phosphite.-

Triethylamine (84ml; 6×10^{-1} mol.) was stirred in THF (200ml) at 0°, and over 10 min phosphorus trichloride (17.6ml; 2×10^{-1} mol.) was added, followed by 2-chloroethanol (44.5ml; 6.6×10^{-1} mol.) over 30 min. The mixture was refluxed gently for 2h, cooled, filtered, and evaporated to yield a yellow liquid (46.5g). Rapid distillation of this afforded a fraction b.132°/2.0mmHg (30.8g; 57%), identified as tris-(2-Chloroethyl)phosphite. τ 5.35 (dt, $J_{P-H} = 7$, $J_{H-H} = 6$), 5.81 (t). The i.r. spectrum did not contain a band at ca. 1250cm^{-1}.

The slower the distillation, the lower the yield of product, and the larger the amount of an orange, involatile, water-soluble oil produced.

Di(2-chloroethyl)(carboxyethyl)methylphosphonate.-

Ethylbromoacetate (8.55g; 5×10^{-2} mol.) and tris-(2-chloroethyl) phosphite (13.48g; 5×10^{-2}mol.) were heated together at 100° for 3h. Distillation gave di(2-chloroethyl)(carboxyethyl)methyl-phosphonate (11.7g; 80%) b. 180-202°/1.5mmHg. The analytical sample was purified by chromatography (ethyl acetate/alumina) and redistilled b.155/0.2mmHg (found: C,32.85; H,5.15, $C_8H_{15}Cl_2O_5P$ requires C,32.8; H,5.15%). τ 5.35 - 90 (m,6H), 6.28(t,$J_{H-H} = 7$, 4H), 6.93 (d,$J_{P-H} = 22$, 2H), 8.72 (t,$J_{H-H} = 8$, 3H).

Attempted Reactions of Di(2-chloroethyl)(carboxyethyl)methyl-phosphonate with Base.-

a) Di(2-chloroethyl)(carboxyethyl)methylphosphonate (3.65g; 1.25×10^{-2} mol.) in DME (20ml) was added over 10 min to sodium hydride (0.12g; 3×10^{-2} mol.) in DME (10ml), under nitrogen, at 0°. Stirring was continued for 15min, by which time hydrogen evolution was adjudged to have ceased. The mixture was refluxed for 6h, and water added (20ml). The mixture was extracted with di-chloromethane (2 x 20ml), the organic extracts washed with brine (10ml), dried, and evaporated to yield a yellow oil (3.10g). Distillation of this afforded only starting material.

b) Di(2-chloroethyl)(carboxyethyl)methylphosphonate (5.86g; 2×10^{-2} mol.) was refluxed with potassium tert-butoxide (3.36g; 3×10^{-2} mol.) in benzene (100ml) for 16h. Water (25ml) was added, and the organic layer separated, dried, and evaporated to give a pale oil (4.05g). Distillation of this afforded only starting material. T.l.c. of the crude product showed that little else was present.

Di-(3-bromopropyl)methylphosphonate.-

To triethylamine (20.7ml; 1.5×10^{-1} mol.) stirred in THF (50ml) was added methylphosphonyl chloride (9.98g; 7.5×10^{-2}mol.) in THF (100ml), such that $t \leq 10^{o}$. Then, still keeping $t \leq 10^{o}$, 3-bromopropanol (20.8g; 1.5×10^{-1} mol.) in THF (20ml) was added. The mixture was stirred overnight in a cold water bath, then filtered and evaporated, completing the evaporation at 1mmHg on a boiling water bath. There remained a clear brown oil (20.1g; 79%) of di-(3-bromopropyl)methylphosphonate. Upon attempted distillation (b.ca. 120°/0.1mmHg) or chromatography (ethyl acetate/

alumina or silica), the main product obtained was 2-keto 2-methyl 1,3,2,-dioxaphosphorinan, a soft solid: τ , as lit.[86], 5.22 - 86 (m, 4H), 7.89 (m, 2H), 8.49(d,J_{P-H} = 18, 3H).

An analytically pure sample of di-(3-bromopropyl)methylphosphonate could not thus be obtained. The n.m.r. of the crude material looked 'clean' however: τ , as lit.[86], 5.82(pseudo q., J_{P-H} = J_{H-H} = 7, 4H), 6.50 (t, J_{H-H} = 7, 4H), 7.80 (psuedo t., J_{H-H} ave. = 7, 4H), 8.48 (d, J_{P-H} = 18, 3H).

Attempted Reactions of di-(3-bromopropyl)methylphosphonate with base:-

a) Butylithium (1.9M; 16.0ml; 3 x 10^{-2} mol.) was stirred under nitrogen in THF (450ml) at -78°, and to it was added di-(3-bromopropyl)methylphosphonate (3.38g; 10^{-2}mol.) over 4h. The mixture was stirred a further 27h, then brought to room temperature and 2M hydrochloric acid (15ml) added. The mixture was evaporated to dryness, and the residue extracted with chloroform (50ml), and this filtered through a cotton wool plug. The filtrate was dried and evaporated to yield a yellow oil (2.80g). Distillation of this afforded starting material, 2-keto 2-methyl 1,3,2,- dioxaphosphorinan, and an oil b.140-5°/0.4mmHg, shown by n.m.r. to contain n-butyl group(s). It was not further examined.

b) To 2,2,6,6,-tetramethylpiperidene (4,23g; 3 x 10^{-2}mol.) in THF (250ml) was added butyllithium (1.9M; 15.8ml; 3 x 10^{-2}mol) and the mixture stirred for 30min. Then it was warmed to 60° and, over 1h, di-(3-bromopropyl)methylphosphonate (3.38g; 10^{-2} mol.) added, in THF (50ml). Stirring was continued for 24h, then the mixture was cooled, treated with 2M hydrochloric acid (40ml) and the whole evaporated to dryness. Extraction of the mixture with ether, followed by evaporation and distillation, gave a yellow oil b.143-5°/1.0mmHg, of complex n.m.r. It was not further examined.

tris-(3-Chloropropyl)phosphite.-

Triethylamine (28ml; 2 x 10^{-1} mol.) was stirred at 0° in THF (75ml) and, over 5min, there was added trichlorophosphine (5.9ml; 6.7 x 10^{-2} mol.) in THF (10ml). Then 3-chloropropanol (16.7ml; 2.x 10^{-2}mol.) was added over 20 min., ensuring that t $\lesssim 10^{o}$. After addition was complete, the mixture was refluxed gently for 2.5h, cooled, filtered, evaporated, and distilled to give a fraction b $170\text{-}80^{o}$/2.0mmHg (8.95g; 45%). τ 5.65 - 90 (m,6H), 6.32 (t,$J_{H\text{-}H}$ = 7, 6H), 7.75 - 8.05 (m,6H). There was no infra-red band corresponding to P = 0.

Attempted reaction of tris-(3-chloropropyl)phosphite with methyl bromoacetate.-

Tris-(3-chloropropyl)phosphite (8.90g; 2.85 x 10^{-2} mol.) and methyl bromoacetate (4.73g; 2.85 x 10^{-2} mol.) were heated under reflux for 4h. Distillation of the mixture gave only starting materials.

Triphenylphosphine sulphide.[125]-

Triphenylphosphine (52.4g; 2 x 10^{-1} mol.) and sulphur (7.04g 2.2 x 10^{-1} mol.) were dissolved in carbon disulphide (250ml), and the solvent distilled off at atmospheric pressure; the last traces being removed under reduced pressure. The solid residue was recrystallised from ethanol, thus: ethanol (500ml) was boiled with the solid, and filtered. The filtrate was chilled at -78°, and the crystals filtered off and washed with chilled ethanol. The filtrate was boiled again with the residue from the first filtration, rechilled, and more crystals collected. The process was repeated once more to yield triphenylphosphine sulphide (45.2g; 79%) m.159-61° (lit.[95] $161\text{-}2^{o}$).

2.2-Diphenyl 2-hydroxyethyl)diphenylphosphine sulphide.[95]-

Triphenylphosphine sulphide (2.94g; 10^{-2} mol.) was stirred in THF (15ml) under nitrogen, and to it was added methyllithium (1.0M 10ml; 10^{-2} mol.). The mixture was stirred 2h to a deep red solution, and benzophenone (1.82g; 10^{-2} mol.) in THF (15ml) added. The mixture

refluxed for 3h, cooled and water (20ml) added. The ethereal layer was separated, dried, and evaporated to give a pale yellow solid (4.43g). Recrystallisation of this (with re-working of the mother liquors) from ethyl acetate gave (2,2-diphenyl 2-hydroxyethyl)diphenylphosphine sulphide (3.20g; 80%) m.116°. The analytical sample was recrystallised once more m.147-8° (lit.[97] 148-50°) (Found: C,75.4; H,5.55. Calcd. for $C_{26}H_{23}OPS$; C,75.4; H,5.55%). τ 2.15 - 3.00 (20H), 3.38 (br.s., 1H), 6.34 (d, J_{P-H} = 10, 2H) (lit.[56] τ 2.65, 3.42 (s), 6.42 (d,J = 10.2)).

Thermal Decomposition of (2,2-Diphenyl 2-hydroxyethyl)diphenylphosphine sulphide.

(2,2-Diphenyl-2-hydroxyethyl)diphenylphosphine sulphide (0.6g) was heated at 220°/0.1mmHg over 1h. A distillate was collected (0.045g) and identified as a mixture of benzophenone and methyldiphenylphosphine sulphide by t.l.c., i.r., and n.m.r.

Reactions of (2,2-Diphenyl 2-hydroxyethyl)diphenylphosphine sulphide with Base.

a) To sodium hydride (0.24g; 6 x 10^{-3} mol.) stirred under nitrogen was added (2,2-diphenyl 2-hydroxyethyl)diphenylphosphine sulphide (2.07g; 5 x 10^{-3} mol.) in THF (20ml). The mixture effervesced, and was stirred at 20° for 24h. A yellow precipitate slowly formed. Water (40ml) was added, and the ethereal layer separated, dried, and evaporated to yield a yellow oil (1.39g). Distillation of this gave methyldiphenylphosphine sulphide b.160-3°/0.15 mmHg (lit[95] 162-3°/0.4mmHg) (0.69g; 60%) and benzophenone b.183-5°/0.15mmHg (0.60g; 66%) which solidified upon standing. Both products were identified by i.r., and n.m.r. comparisons with authentic material. Both had Rf ca. 0.5 (light petrol/silica). No 1,1-diphenylethene was detected by t.l.c.

b) (2,2-Diphenyl 2-hydroxyethyl)diphenyl phosphine sulphide (2.07g; 5 x 10^{-3} mol.) was refluxed with potassium t-butoxide

(0.70g; 7.5×10^{-3} mol.) in benzene (20ml) for 12h. Water (20ml) was added, and the benzene separated, dried, and evaporated to yield a yellow oil (1.48g). Distillation of this gave methyldiphenylphosphine sulphide (0.79g; 68%) and benzophenone (0.62g; 67%)

(2,2-Diphenyl 2-hydroxyethyl)diphenylphosphine oxide.[126]

Triphenylphosphine oxide (5.56g; 2×10^{-2} mol.) was stirred as a slurry in ether (20ml) under nitrogen, and to it was added methyllithium (1.0M; 20ml; 2×10^{-2} mol.). The mixture was stirred 1.5h to a pale orange solution, then benzophenone (3.64g; 2×10^{-2} mol.) in ether (20ml) was added, and the mixture stirred a further 1h. A white gum separated, which became solid upon stirring. It was filtered off, whashed with much water, and dried over phosphorus pentoxide, giving a solid (13.0g) Solution of this in benzene revealed that much water was still present. Accordingly, the material was taken up in benzene (50ml), dried, and evaporated to yield crystals (6.0g; 75%) of (2,2-di-phenyl 2-hydroxyethyl) diphenylphosphine oxide. Recrystallisation from ethyl acetate gave crystals m.192-3° (lit[126] 192-3°). τ 2.40 - 75, 2.85 - 3.00 (20H), 3.20 (s,1H), 6.60 (d, J_{P-H} = 11, 2H) (lit[74] τ 2.7, 6.65 (d, J=9.6), 4.5 (m)).

Reaction of (2,2-Diphenyl 2-hydroxyethyl)diphenylphosphine oxide with Sodium hydride. -

To sodium hydride (0.48g; 1.2×10^{-2} mol.) stirred under nitrogen was added (2,2-diphenyl 2-hydroxethyl)diphenylphosphine oxide (3.98g; 10^{-2} mol.) in THF (50ml). Hydrogen was briskly evolved, to give a colourless solution. This became cloudy after ca. 30min and progressively more yellow. Stirring was continued for 24h, and water (30ml) added. The ethereal layer was separated, the aqueous layer extracted with ether (30ml), and the organic layers combined, dried, and evaporated to yield a yellow oil (2.17g).

T.l.c. (ether/light petrol/silica) showed that the main component of the product had Rf ca, 0.6, faster-running than benzophenone or methyldiphenylphosphine oxide. Distillation afforded a fraction b.122-38°/1.5mmHg, which was redistilled to give 1,1-diphenylethene b.122°/1.2mmHg (1.20g; 67%)(lit.[84] 140 - 1°/14mmHg). τ 2.20 - 70 (10H), 4.47 (s,2H).

Benzyldiphenylphosphine sulphide,-

Lithium diphenylphosphide (1.3×10^{-1} mol.) was added to benzyl chloride (1.3×10^{-1} mol. 16.05g). Water was then added (100ml) the organic layer separated, washed with water (100ml), dried, and evaporated to give a yellow oil (36.4g) This was mixed with sulphur (4.7g; 1.5×10^{-1} mol.) and benzene (30ml), and the whole refluxed 1h. Upon cooling, crystals separated. These were collected at the pump, washed with ice-cold benzene, and dried in vacuo to yield benzyldiphenylphosphine sulphide m. 162 - 3° (lit.[116] 162-3°). τ 2.10 - 3.00 (15H), 6.16 (d, J_{P-H} = 13, 2H). (21.0g; 53%).

(2-Hydroxy 1,2,2-triphenylethyl)diphenylphosphine sulphide,-

Benzyldiphenylphosphine sulphide (3.08g; 10^{-2} mol.) was stirred as a slurry in ether (20ml) under nitrogen, and to it was added butyllithium (1.9M; 5.25ml; 10^{-2} mol.) over 15min, to give a deep red solution. Benzophenone (1.82g; 10^{-2} mol.) in ether (15ml) was then added, and immediately a white precipitate was thrown down. Stirring was continued for 1h, and water (20ml) added. The mixture was shaken between dichloromethane (125ml) and water (250ml). The organic layer was separated, dried, and evaporated to yield a pale yellow solid., which was recrystallised from ethyl acetate (with re-working of the mother liquors) to yield crystals of (2- hydroxyl,2,2-triphenyl ethyl)diphenylphosphine sulphide (4.75g: 97%)m.154-6°. The analytical sample was recrystallised twice more (Found:C,76.1; H,5.85. $C_{32}H_{27}OPS$ requires C,75.55; H,5.75%). τ 2.10 - 3.25 (26H), 6.21 (d, J_{P-H} = 15, 2H).

Reaction of 2-Hydroxy-1,2,2-triphenylyethyl)diphenylphosphine sulphide with Potassium t-butoxide.-

(2-Hydroxy 1,2,2-triphenylethyl)diphenylphosphine sulphide (2.45g; 5×10^{-3} mol.) and potassium t-butoxide (0.70g; 7.5×10^{-3} mol.) were refluxed together in benzene (25ml) for 9h. Water (20ml) was added, and the benzene layer separated. The aqueous portion was extracted with benzene (20ml), and the benzene layers dried and evaporated to yield a white oil (2.38g). Upon chromatography (benzene/silica), this yielded benzophenone (0.84g; 92%) and benzyldiphenylphosphine sulphide (1.40g; 97%) and benzyldiphenylphosphine sulphide (1.40g; 97%), identified by n.m.r. and m.p.

cis-4-t-Butyl 1-(diphenylphosphinthioylmethyl)cyclohexanol.-

Triphenylphosphine sulphide (5.85g; 2×10^{-2} mol.) was stirred under nitrogen in THF (20ml), and to it was added methyllithium (1.0M; 20ml; 2×10^{-2} mol.). Stirring was continued for 1h, then 4-t-butylcyclohexanone (3.08g; 10^{-2} mol.) in ether (5ml) was added, and the whole stirred for 5 min to a yellow solution. Water (25ml) was added, and the mixture shaken between water (200ml) and dichloromethane (125ml). The organic layer was separated, dried, and evaporated to yield a solid (7.85g). This was recrystallised from ethyl acetate (with re-working of the mother liquors) to give crystals of cis-4-t-butyl 1-(diphenylphosphinthioylmethyl) cyclohexanol (6.23g; 80%). The analytical sample was recrystallised once more m.174° (Found: C,72.0; H,7.7 $C_{23}H_{31}OPS$ requires C,71.7; H,8.1%). τ 2,00 - 65 (10H), 4.84 (br.s., 1H), 7.16 (d, J_{P-H} = 11, 2H), 7.95 - 8.80 (m, 9H), 9.33 (s, 9H).

trans-4-t-Butyl 1-(diphenylphosphinthioylmethyl)cyclohexanol.-

Lithium diphenylphosphide (1.5×10^{-2} mol.) was added to cis-4-tert-butyl methylenecyclohexanone epoxide (1.60g; 10^{-2} mol.) in THF (10ml), and the mixture stirred overnight under nitrogen. Acetic

acid (1ml) was added, followed by water (20ml) and the ethereal layer separated. The aqueous portion was extracted with dichloromethane (10ml), and the organic extracts combined, washed with saturated sodium carbonate (30ml), brine (30ml), dried and evaporated to yield white crystals (3.43g), assumed to be trans-4-t-butyl 1-(diphenylphosphinomethyl)cyclohexanone.

1.71g of this solid was treated with sulphur (0.16g; 5×10^{-3} mol.) and benzene (10ml). The benzene was removed at 350mmHg/100° and the yellow solid residue was treated with dichloromethane (25ml). This solution was washed with saturated sodium carbonate (25ml), brine, (25ml), dried, and evaporated to yield a yellow solid (1.45g). This was recrystallised twice from ethyl acetate to give large crystals of trans-4-t-butyl 1-(diphenylphosphinthioylmethyl)cyclohexanol m.161-3°. The n.m.r. spectrum shows that it is contaminated with the analogous phosphine oxide. τ 2.00 - 35, 2.45 - 60 (10H), 5.40 (br.s., 1H) 7.24 (d, J_{P-H} = 10,2H), 7.90 - 8.15, 8.35 - 8.95 (m,9H), 9.18 (s, 9H). (1.20g; 63%).

cis/trans-4-t-Butyl 1-(diphenylphosphinylmethyl)cyclohexanol.- To triphenylphosphine oxide (5.56g; 2×10^{-2} mol.) stirred as a slurry in ether, under nitrogen, was added methyllithium (1.0M; 20ml; 2×10^{-2} mol.), and the mixture stirred 1.5h to a pale orange solution. 4-tert-butylcyclohexanone (3.08g; 2×10^{-2} mol.) in THF (20ml) was added, and the whole stirred 2h. Water (20ml) was added and the organic layer separated. The aqueous portion was extracted with dichloromethane (20ml), and the organic extracts combined, washed with brine (20ml), dried, and evaporated to give an orange oily crystalline mass (6.98g). Recrystallisation of this from benzene/petrol gave crystals of 4-t-butyl 1-(diphenylphosphinylmethyl)cyclohexanol (5.41g; 75%). The n.m.r. spectrum shows the

presence of cis and trans isomers in approximately 1:2 ratio (the n.m.r. spectrum of the orange product showed approximately the same ratio). τ2.00 - 40, (10H), 4.77 (br.s., ½H), 5.38 (br.s., ½H), 7.36 (d, J_{P-H} = 10, ⅔H), 7.46 (d, J_{P-H} = 11, 1⅓H), 7.90 - 8.80 (m, 9H), 9.18 (s, 6H), 9.24 (s, 3H). Recrystallisation from ethyl acetate gave the trans isomer (vide infra).

trans-4-t-Butyl 1-(diphenylphosphinylmethyl)cyclohexanol.- The white solid assumed to be trans-4-tert-butyl 1-(diphenylphosphinomethyl)cyclohexanol (vide supra)(1.71g) was dissolved in methanol (15ml) and cooled to 0°. Hydrogen peroxide (30%; 10ml) was added, with stirring, over 5 min, and the mixture left for 1.5h. Ice-cold saturated sodium sulphite (150ml) was added with care, and the mixture extracted with dichloromethane (3 x 25ml). The organic extracts were washed with sodium carbonate (50ml), brine (50ml), dried, and evaporated to give a solid (1.41g). Recrystallisation from ethyl acetate gave crystals of trans-4-t-butyl 1-(diphenylphosphinylmethyl)cyclohexanol (1.18g; 64%) m.222-3° (Found: c,74.65; H,8.25. $C_{23}H_{31}O_2P$ requires C,74.6; H, 8.45%). τ 2.10 - 55 (10H), 5.97 (br.s., 1H), 7.46 (d, J_{P-H} = 11, 2H), 7.95 - 8.80 (m, 9H), 9.18 (s, 9H).

Reaction of cis-4-t-Butyl 1-(diphenylphosphinthioylmethyl)cyclohexanol with Potassium t-butoxide:- 4-t-Butyl 1-diphenylthiophosphinylmethylcyclohexanol (3.09g; 8×10^{-3} mol.) was refluxed with potassium t-butoxide (1.12g; 1.2×10^{-2} mol.) in benzene (30ml) for 9h. Water (20ml) was added, and the benzene layer separated, dried, and evaporated to give a yellow oil (3.00g). T.l.c. (light petrol/silica) indicated the main components to be 4-t-butylcyclohexanone and methyldiphenyl-

phosphine sulphide. Distillation of the oil afforded 4-t-butyl-cyclohexanone b.104-6°/16mmHg (lit[127] 106-8°/18mmHg)(1.20g; 97%) identified by i.r. comparison with authentic material.

Reaction of cis/trans-4-t-Butyl 1-(diphenylphosphinylmethyl) cyclohexanol with Sodium hydride.-

4-t-Butyl 1-diphenylphosphinylmethylcyclohexanol (3.70g; 10^{-2} mol) was stirred with sodium hydride (0.48g; 1.2×10^{-2} mol.) in HF (50ml) under nitrogen for 24h. The solution became yellow and cloudy after evolution of hydrogen had ceased. Water (30ml) was added, and the organic layer separated. The aqueous portion was extracted with ether (30ml) and the organic extracts dried and evaporated to give a liquid. This was distilled to give 4-t-butylmethylenecyclohexane (1.17g; 84%) b.138-40/300mmHg (lit[128] 78 - 80°/18mmHg). $\tau(CCl_4)$ 5.38 (s,2H), 7.80 - 9.00 (9H), 9.15 (s, 9H). ν(neat) 3070, 1660 (lit[129] 3082, 1658 cm^{-1}).

trans-2-Diphenylphosphinthioylcyclohexanol.-

Lithium diphenylphosphide (1.5×10^{-1} mol.) was added to cyclohexene epoxide (9.8g; 10^{-1} mol.), and the mixture stirred under nitrogen overnight. Acetic acid (10ml) was added, and the mixture stirred vigorously. Water (250ml) was added, and the ethereal layer separated. The aqueous portion was extracted with dichloromethane (2 x 125ml), and the organic portions combined, washed with 2M sodium hydroxide (100ml), brine (200ml), dried, and evaporated to give a pale yellow liquid. This was taken up in benzene (500ml) and treated with sulphur (6.4g; 2×10^{-1} mol.). The benzene was removed at 100°/300mmHg. The residue was treated with dichloromethane (100ml) and excess sulphur filtered off. Evaporation of the filtrate gave off-white crystals (30.2g), which were recrystallised from benzene/petrol to give trans - 2-diphenylphosphinthioylcyclohexanol (28.2g; 90%) m.173° (lit[130] 178°). The analytical

sample had m.173-4° (Found: C,68.45; H,6.55. Calcd. for $C_{18}H_{21}OPS$ C,68.35; H,6.7%). τ 1.85 - 2.20 (4H), 2.55 - 2.65 (6H), 5.37 (s, 1H), 5.91 (m,1H), 7.23 (m,1H), 7.90 - 8.85 (m,8H).

Reaction of trans-2-Diphenylphosphinthioylcyclohexanol with Potassium t-butoxide.-

trans-2-Diphenylphosphonylcyclohexanol (2.53g; 8 x 10^{-3} mol.) and potassium t-butoxide (1.68g; 1.5 x 10^{-2} mol.) were refluxed together in benzene (25ml) for 9h. Water (20ml) was then added, and the benzene layer separated. The aqueous phase was extracted with benzene (10ml), and the combined organic portions washed with brine (20ml), dried, and evaporated to yield an oil (2.53g), of which the i.r. spectrum showed no bands assignable to -OH and a new band at 1630 cm^{-1} (s). On standing, the oil deposited large crystals, which were recrystallised from petrol(4)/benzene (1) to give 1-diphenylphosphinthioylcyclohexene (2.27g; 96%) m.79-81°. The analytical sample had m.82° (Found: C,72.7; H,6.45. $C_{18}H_{19}PS$ requires C,72.45; H,6.4%) τ 2.10 - 2.35 (4H), 2.65 - 2.75 (6H) 3.73 (br.d., J_{P-H} = 23, 1H), 7.82 (br.s., 4H) 8.38 (br.s., 4H).

trans-2-Diphenylphosphinylcyclohexanol;

Lithium diphenylphosphide (2.25 x 10^{-2} mol.) was added under nitrogen to cyclohexene epoxide (1.47g; 1.5 x 10^{-2} mol.), and the whole stirred overnight. Acetic acid (3ml) was added, and the mixture stirred vigorously, then cooled to 0°, and 30% hydrogen peroxide (15ml) added over 30min. The mixture was stirred at 20° for a further 1h, and water (30ml) added. The mixture was extracted with dichloromethane (2 x 30ml), and the organic extracts washed with saturated sodium carbonate (30ml), saturated sodium sulphite (30ml), dried, and evaporated to yield an oil (6.42g). Two recrystallisations from ethyl acetate/petrol gave crystals of trans-2-diphenylphosphinylcyclohexanol (4.56g; 91%) m.152° (lit[131] 151-2°) τ 2.10 - 60 (10H), 5.00 (br.s., 1H), 6.18 (m,1H), 7.35 - 8.90 (m,8H).

Reaction of trans-2-Diphenylphosphinylcyclohexanol with Potassium t-butoxide.-

Potassium t-butoxide (0.42g; 3.75×10^{-3} mol.) and trans-2-diphenylphosphinylcyclohexanol (0.75g; 2.5×10^{-3} mol.) were refluxed together in benzene (10ml) for 12h. Water was added (10ml), and the benzene layer separated. The aqueous phase was extracted with dichloromethane (10ml) and the combined organic phases washed with brine (10ml), dried, and evaporated to give a solid (0.56g; 80%) identified as 1-diphenylphosphinylcyclohexene monohydrate. The analytical sample was recrystallised from ethyl acetate m.124-5° (depositing liquid on the cooler parts of the Kofler block before melting) (Found: C,72.5; H, 6.85. $C_{18}H_{19}OP.H_2O$ requires C,72.0; H,7.05%). τ 2.25 - 65 (10H), 3.65 (br.d., J_{P-H} = 21, 1H), 7.44 (s,2H, exchanges with ^2H_2O), 7.82 (m,4H), 8.34 (m,4H).

1,2-Dimethylcyclohexene.[137]-

Iodomethane (33.1g; 2.33×10^{-1} mol.) was added, with stirring, to magnesium (5.6g; 2.33×10^{-1} mol.) in ether (100ml), over 15 min. The mixture was then refluxed for 15min, and cooled to -10°. Then, ensuring that $t \leq 5°$, over 2h was added 2-methylcyclohexanone (22.4g; 2×10^{-1} mol.) in ether (25ml). Then (care!) 2M hydrochloric acid (50ml) and crushed ice (50g) was added, and the ether layer separated, washed with saturated sodium bisulphite (100ml), water (2 x 100ml), dried, and evaporated to give a minty-smelling liquid. ν (neat) shows 3420cm^{-1}, and scarcely any absorption due to C = O. The liquid was distilled slowly from iodine (0.05g), keeping the bath temperature at 160°, and the distillate was collected over saturated sodium sulphite (50ml). The organic layer was separated, dried, and redistilled from a chip of sodium (to remove any secondary alcohols present), yielding 12.6g (57%) of 1,2-dimethylcyclohexene b.137-9° (lit[132] 136°). N.m.r. and i.r. spectra showed that little, if any, isomeric alkenes were present.

1,2-Dimethylcyclohexene epoxide.-

1.2-dimethylcyclohexene (12.4g; 1.13 x 10^{-1}mol.) was stirred in dichloromethane (250ml) with anhydrous sodium carbonate (20g) and a mixture of 40% peroxyacetic acid (11.0g; 27.5ml; 1.4 x 10^{-1}mol.) and sodium acetate trihydrate (9g), added such that $t \leqslant 25^{\circ}$. Stirring was continued for 1h after addition, then saturated sodium sulphite (250ml) was added, and the organic layer separated, washed with saturated sodium carbonate (250ml), dried, and evaporated to give a minty oil, which was distilled through a 10" Vigreux column to give a 1,2-dimethylcyclohexene epoxide (9.1g; 65%) b.155-7° (lit.[133] 150-1°). τ 6.20 - 8.35, including 7.58 (strong s)).

1,2-Dimethyl trans-2-diphenylphosphinthionylcyclohexanol.-

Lithium diphenylphosphide (2.25 x 10^{-2} mol.) was added, under nitrogen, to 1,2-dimethyl cyclohexene epoxide (1.89g; 1.5 x 10^{-2} mol.) and stirred overnight. Water (50ml) was added, and the mixture extracted with dichloromethane (2 x 50ml). The organic extracts were washed with brine (50ml), dried, and evaporated to yield a yellow oil, which was taken up in benzene (50ml) and treated with sulphur (0.96g; 3 x 10^{-2} mol.) and left overnight. The mixture was evaporated to dryness, and the residue treated with dichloromethane (50ml), filtered, and the filtrate evaporated to give a yellow oil (6.50g). Recrystallisation from ethyl acetate furnished crystals of 1,2-dimethyltrans-2-diphenylphosphinthioylcyclohexanol (3.08g; 60%) m.206-9°. The analytical sample was purified *via* chromatography (benzene (1)/chloroform (8)/silica) and recrystallised from ethyl acetate to give needles m.212° (Found: C,70.0; H,7.55. $C_{20}H_{25}OPS$ requires C,69.75; H,7.3%). τ 1.50 - 1.93 (4H), 2.45 - 65 (6H), 4.51 (s, 1H), 7.80 - 8.85 (14H, including 8.68 (s), 8.56 (d, J_{P-H} = 22)).

1,2-Dimethyl trans-2-Diphenylphosphinylcyclohexanol.-

Lithium diphenylphosphide (2.25 x 10^{-2} mol.) was added with stirring, under nitrogen, to 1,2-dimethylcyclohexene epoxide (1.89g; 1.5 x 10^{-2} mol.) and left overnight. Acetic acid (3ml) was added, and the mixture stirred

vigourously, and cooled to -10°. 30% hydrogen peroxide (15ml) was added over 30 min., and stirring continued for another 1h. Water (30ml) was added, and the mixture extracted with dichloromethane (2 x 30ml). The organic extracts were washed with saturated sodium carbonate (30ml), saturated sodium sulphite (30ml), dried, and evaporated to give a solid (6.70g). Recrystallisation from chloroform/light petrol gave crystals of 1,2-dimethyl trans-2-diphenylphosphinylcyclohexanol (2.94g; 60%) The analytical sample had m.199° (Found: C,73.4; H,7.7. $C_{20}H_{25}O_2P$ requires C,73.15; H,7.65%). τ 1.85 - 2.20 (4H), 2.50 - 65 (6H), 4.87 (s, 1H), 7.95 - 8.85 (14H, including 8.68 (s), 8.71 (d, J_{P-H} = 18).

Reaction of 1-Lithiobutyldiphenylphosphine sulphide with Cyclohexanone.- Triphenylphosphine sulphide (5.86g; 2 x 10^{-2} mol.) was stirred in THF (20ml) under nitrogen, and butyllithium (2.4M; 8.3ml; 2 x 10^{-2}mol.) added. Stirring was continued for 3h to give a black solution, then cyclohexane (1.96g; 2 x 10^{-2} mol.) in ether (10ml) added, immediately discharging the colour, and the mixture was stirred a further 1.5h. Water (20ml) was added, and the organic layer separated, dried, and evaporated to give crystals (4.64g), which were recrystallised from ethyl acetate/petrol, and identified as butyldiphenylphosphine sulphide (4.20g; 77%)m.46° (lit[134] 45°). τ 2.15 - 70 (10H), 7.55 - 7.75 (m,2H), 8.35 - 75 (m,4H), 9.13 (t, J_{H-H} = 7, 3H).

1-Hydroxydiphenylmethyl)butyldiphenylphosphine sulphide:- Triphenylphosphine sulphide (5.86g; 2 x 10^{-2} mol) was stirred in THF (20ml) under nitrogen), and butyllithium (2.4M; 8.3ml; 2 x 10^{-2} mol) added. Stirring was continued for 4h, then benzophenone (3.64g; 2 x 10^{-1} mol.) in ether (20ml) added, and the mixture stirred a further 6h under reflux. Water (20ml) was added, and the organic layer separated, dried, and evaporated to give a solid (8.80g). Recrystallisation from ethyl

acetate gave 4.81g of crystals. A further 3.80g of white precipitate was collected by filtration of the aqueous phase of the work-up; this was recrystallised to give 3.50g of solid. Both solids had m. and mixed m. 197 - 8°. The material was thus identified as 1-(hydroxydiphenylmethyl) butyldiphenylphosphine sulphide (7.31g; 80%) The analytical sample had m.199° (Found: C,76.35; H,6.3. $C_{29}H_{29}OPS$ requires C,76.3; H,6.4%). τ 1.85 - 3.05 (20H), 3.34 (m, 1H), 6.28 (m,1H), 7.95 - 8.50 (m,2H), 8.95 - 9.50 (m,2H), 9.71 (t, J_{H-H} = 8, 3H).

Reaction of 1-(Hydroxydiphenylmethyl)diphenylbutylphosphine sulphide with Potassium t-butoxide.-

Potassium t-butoxide (0.59g; 7.5×10^{-3} mol.) and 1-(hydroxydiphenyl-methyl)butyldiphenylphosphine sulphide (1.60g; 2.5×10^{-3} mol.) were refluxed together in benzene (20ml) for 18h. Water (10ml) was added, and the organic phase separated, washed with brine (10ml), dried, and evaporated to give a yellow oil (1.37g). This was purified by chroma-tography, twice, (ethyl acetate/alumina) to give an oil (0.90g; 94%) identified by n.m.r. as butyldiphenylphosphine sulphide.

trans-2-Diphenylphosphinthioylcyclooctanol.-

Lithium diphenylphosphide (1.5×10^{-1}mol.) was added dropwise to a solution of cis-cyclooctene epoxide (12.6g; 10^{-1} mol.) in THF (15ml). The mixture was stirred overnight, and acetic acid (10ml) added dropwise, with vigorous stirring. The mixture was washed with water (100ml), and 2M sodium hydroxide solution (50ml), dried, and evaporated to yield a yellow oil, which was treated with sulphur (3.2g; 10^{-1} mol.) and benzene (100ml). The mixture was evaporated to dryness at 100°/450mmHg to yield a yellow oil (33.2g). Purification via chromatography (chloroform (2)/benzene(1)/ alumina) gave, as a single spot on t.l.c., a yellow oil (22.4g). After standing for 1.33 years, the oil had partially crystallised. These were separated by decanting off the oil, and recrystallised from ethyl acetate/petrol to give trans-2-diphenylphosphinthioylcyclooctanol. The analytical sample was recrystallised twice more from ethyl acetate m.105-6°. (Found: C,69.65; H,7.25. $C_{20}H_{25}OPS$ requires C,69.75;H,7.3%). τ 1.95-

- 2.25 (4H), 2.50 - 65 (6H), 5.70 (br.s., 1H) 6.95 (m, 1H), 8.10 - 8.70 (m, 14H). M^+ 344.

Further crops of crystals were obtained from the oil by covering it with ethyl acetate, seeding, and allowing the solvent to evaporate. In this way, after recrystallisation, a total of 15.7g (46%) of crystals were obtained.

Reaction of trans-2-Diphenylphosphinthioylcyclooctanol with Potassium t-butoxide-

trans-2-Diphenylphosphinthioylcyclooctanol (2.75g; 8 x 10^{-3}mol.) and potassium t-butoxide (1.68g; 1.5 x 10^{-2} mol) were refluxed together in benzene (25ml), for 9h. The solution was cooled, washed with water (20ml), brine (20ml), and dried. G.l.c. tests (silver tetrafluorborate/50°) did not reveal the presence of any trans-cyclooctene in this solution. The solution was evaporated to yield a yellow oil, which was purified via chromatography(benzene/alumina) to give a thick pale yellow oil, identified as 1-diphenylphosphinthionylcyclooctene (1.97g; 75%). The oil was heated at 90°/0.2mmHg, and analysed (Found: C,73.3; H,7.3. $C_{20}H_{23}PS$ requires C,73.6; H,7.1%). ν(neat) 3045 (s), 1618 (m). τ 2.10 - 35 (4H), 2.55 - 60 (6H), 3.66 (dt, J_{P-H} = 24, J_{H-H} = 8, 1H), 7.35 - 7.75 (m, 4H), 8.35 - 8.65 (m,8H). M^+ 326.

Bicyclo [4.4.0] dec-9-ene.-

(1)[135] To 1,2-diaminoethane (distilled directly from KOH into the reaction vessel)(475ml) was added tetralin (66.1g; 5 x 10^{-1} mol.) and the whole stirred vigorously whilst small lithium pieces (21g; 3 mol.) were added; about 6g at first, then, when reaction had commenced (colour changes through red to ultramarine), the rest was added over 45min. The mixture was heated at 100° for 2h, then stirred at 20° overnight, to a grey-purple solution. Again, the mixture was heated to 100° for 15min, initiating a vigorous reaction. When reaction had subsided, the mixture was heated a further 15min to give a liver-

coloured mixture This was cooled to 0°, and a mixture of ethanol (200ml) and crushed ice (100g) added over 20 min, with vigorous stirring, as solid developed. Ice-water (700ml) and benzene (500ml) were added, and the organic layer removed. The aqueous phase was extracted with benzene (500ml), and the benzene extracts washed with 2M hydrochloric acid (1000ml), brine (500ml), dried, and evaporated. The liquid product was distilled through a 14" Vigreux column, and the fraction b.197-9° (lit.[135] 198-200°) collected. The yield of crude bicyclo [4.4.0] dec-9-ene was 52.5g (77%).

(2) [136]The bicyclo [4.4.0] dec-9-ene was added at -10° to a stirred mixture of iso-amyl nitrite (50ml; 3.75 x 10^{-1}m.) and concentrated hydrochloric acid (31ml; 3.75 x 10^{-1}mol. of 'HCl'), such that t $\leq -7^{o}$. Stirring was continued for a further 1.5h at -10°, then the mixture was filtered at the pump, the blue residue washed with ice-cold methanol (100ml), and the filtrate and washings combined and cooled with a small piece of solid carbon dioxide to yield a further crop of blue solid. The blue residues were dried at 50°/16mmHg to give a bright blue solid (23.9g; 32%)m.89-91°, which was recrystallised from acetone/ether to give tourquoise needles of trans-9-chloro 10-nitroso bicyclo [4.4.0] decane (19.5g; 26%) m.92° (lit[136] 91-2°).

(3) [136]The trans-9-chloro 10-nitroso bicyclo [4.4.0] decane (19.0g; 9.4 x 10^{-2} mol.) was warmed slowly with stirring in N,N-diethylaniline (30ml) to 70°. Gas evolution commenced, and the bath temperature was gradually raised to 90°, and held there for 2.5h. The black mixture was treated with 2M hydrochloric acid (250ml) and extracted with light petrol (3 x 75ml). The petrol extracts were washed with 2M hydrochloric acid (100ml), brine (100ml), dried and evaporated to yield a pale brown liquid (11.5g), which was distilled, the fraction b.120°/100mmHg being collected (lit.[136] 77.5^{o}/14mmHg). The yield of bicyclo [4.4.0] dec-9-ene was 9.7g (76%).

11-Oxa tricyclo [4.4.1.$0^{1,6}$] undecane.-

Bicyclo [4.4.0] dec-9-ene (6.8g; 5 x 10^{-2} mol.) was stirred with anhydrous sodium carbonate (7.5g) in dichloromethant (10ml) at -10°, and peroxy-acetic acid (30% w/w in acetic acid) (12.4ml; 5.25 x 10^{-2} mol.) was dropped in over 3.25 h, such that $5^{o} \leq t \leq 10^{o}$. Stirring was continued for a further 1h, then water (25ml) added, and the organic layer separated. The aqueous phase was extracted with dichloromethane (2 x 15ml), and the combined organic portions were washed with saturated ferrous sulphate (2 x 25ml), dried, and evaporated to give a pale yellow liquid (7.2g). Distillation of this afforded a fraction b.88-90°/16mmHg, identified as 11-oxa tricyclo [4.4.1.$0^{1,6}$] undecane (5.60g; 74%). The analytical sample had b.89.5°/15mmHg (Found: C,79.05; H, 10.5. $C_{10}H_{16}O$ requires C,78.9; H,10.6%). ν(neat) 2935 (s), 2855 (s), 2835 (m), 1445 (m), 1435 (m), 1415 (w), 1365 (w), 1345 (w), 1195 (m), 990 (w), 985 (w), 970 (m), 875 (m), 860 (m), 845 (s), 830 (m), 800 (w), 680 (w). τ 7.95 - 8.40 (m, 8H), 8.40 - 8.90 (m,8H).

1-Diphenylphosphinthioyl bicyclo [4.4.0] dec-9-ene-,

Lithium diphenylphosphide (3 x 10^{-2} mol.) was added, under nitrogen, to tricyclo [4.4.1.$0^{1,6}$] 11-oxa undecane (3.04g; 2 x 10^{-2} mol.) and the mixture stirred overnight. Vigorously stirred, the mixture was treated with acetic acid (2ml), followed by water (50ml). The micture was extracted with dichloromethane (2 x 50ml), and the organic extracts washed with 2M sodium hydroxide (25ml) and brine (50ml), dried, and evaporated to give a yellow oil. This was treated with benzene (50ml) and sulphur (1.28g; 4 x 10^{-2} mol.) and left overnight. The mixture was evaporated to dryness, and the oily residue taken up in dichloromethane (50ml), filtered, and the filtrate evaporated to yield a yellow solid (6.67g). Two recrystallisations from dichloromethane gave lemon crystals m. 152-3° (d), identified as 1-diphenylphosphinthio-bicyclo [4.4.0.] dec-9-ene (6.20g; 80%) The analytical sample was

purified by chromatography (benzene/alumina), and recrystallised twice more from dichloromethane, m. 156-8° (d) (Found: C,75.2; H,7.2. $C_{22}H_{25}PS$ requires C,74.95; H,7.15%). τ 1.55 - 75 (4H), 2.50 - 60 (6H), 6.75 (dt, J_{P-H} = 6, J_{H-H} = 15, 1H), 7.80 - 9.15 (m, 14H). M^+ 352. ν ($CHCl_3$) 3050 (w), 2975 (m), 2930 (s), 2855 (m), 1475 (m), 1450 (m), 1435 (s), 1180 (m), 1160 (sh), 1085 (s), 955(s), 895 (w), 835 (w), 695 (m), 655 (m). ^{13}C n.m.r. - see separate section.

1-Diphenylphosphinyl bicyclo [4.4.0.] dec-9-ene.-

Lithium diphenylphosphide (2.25×10^{-2} mol.) was added, under nitrogen to 11-oxa tricyclo [4.4.1.0^{1,6}] undecane (2.28g; 1.5×10^{-2} mol.), and the mixture stirred overnight. Acetic acid (3ml) was added, and the mixture stirred vigorously at 0°. 30% hydrogen peroxide (15ml) was added with caution over 30min, and the mixture stirred at 20° for a further 1h. Water (30ml) was added, and the mixture extracted with dichloromethane (2 x 30ml). The organic extracts were washed with saturated sodium carbonate (30ml), saturated sodium sulphite (30ml) dried, and evaporated to give a solid (7.30g). This was recrystallised from benzene to give 1-diphenylphosphinylbicyclo [4.4.0.] dec-9-ene (4.56g; 90%). The analytical sample was recrystallised once more from benzene as needles m.215-8° (evolving liquid above 170°) (Found: C,75.1; H,7.75. $C_{22}H_{25}OP.H_2O$ requires C,74.6; H, 7.7%). τ 1.90-2.15 (4H), 2.50 - 70 (6H), 7.30 (dt, J_{P-H} = 5, J_{H-H} = 13. 1H), 7.75 - 8.95 (m,14H): τ(6^2H-DMSO) had, in addition, 6.08 (br.s, 2H, exchangable with ^2H_2O). M^+336; $(M + 18)^+$ 354.

Reaction of 1-Diphenylphosphinthioyl bicyclo [4.4.0] dec-9-ene with Potassium t-butoxide.-

1-Diphenylthiophosphinyl bicyclo [4.4.0.] dec-9-ene (0.106g; 3×10^{-4} mol.) and potassium tert-butoxide (0.062g; 5.4×10^{-4} mol.) were

refluxed together in benzene (5ml) for 24h. Water (5ml) was added, and the benzene layer separated. The aqueous portion was extracted with benzene (5ml), and the combined benzene layers were dried and evaporated to give a brown oil (0.100g). T.l.c. (benzene/silica) showed that starting material was still present, along with another, slightly less polar substance. N.m.r. showed that starting material was still present, but that the sextet at 6.75 τ was greatly diminished in intensity. Furthermore, the aromatic signal was more complex, there being another signal due to ortho (?) hydrogens at 1.85 - 2.25τ, of approximately twice the intensity of the 1.55 - 75 τ signal. A doublet (J_{P-H} = 30) had appeared at 4.44 τ, both lines being broadened. It was tentatively concluded that the reaction product was a 2:1 mixture of 1-diphenylphophinthioyl bicyclo[4.4.0] dec-1-ene and starting material.

Reaction of 1-diphenylphosphinyl bicyclo [4.4.0] dec-9-ene with Sodium Hydroxide[79].-

1-Diphenylphosphinyl bicyclo[4.4.0] dec-9-ene (2.18g; 6 x 10^{-3} mol.) and finely-powdered sodium hydroxide (0.48g; 1.2 x 10^{-2} mol.) were heated together on a Wood's metal bath at 280°. A liquid (b.ca. 80°) distilled over immediately, and was collected over 20 min. The yield was 0.315g. N.m.r. (CCl_4) showed that the major components were benzene and bicyclo[4.4.0] dec-9-ene in a 13:2 ratio. A small percentage of tetralin was also detected, but no olefinic peak corresponding to bicyclo[4.4.0] dec-1-ene was detected. G.l.c. (15% carbowax/150°) confirmed the presence of bicyclo [4.4.0] dec-9-ene and of tetralin, and also showed the presence of napthalene in the distillate.

Attempted allylic bromination of bicyclo [4.4.0] dec-9-ene.- Bicyclo [4.4.0] dec-9-ene (8.9g; 5 x 10^{-2} mol.), N-bromosuccinimide (6.8g; 5 x 10^{-2} mol.), and a crystal of dried

benzoyl peroxide were brought to reflux in carbon tetrachloride (25ml). After 10min, no yellow crystals remained at the bottom of the reaction mixture, and reaction was judged to have been completed. The mixture was filtered and evaporated to yield a brown liquid. Distillation of this gave a colourless liquid b.102-117°/1.0mmHg (5.1g). N.m.r. and g.l.c. indicated that this was a mixture of tetralin and bicyclo [4.4.0] dec-9-ene[137].

Reaction of lithium N-2-propylcyclohexylamide with 11-oxa tricyclo [4.4.1.0^{4}] undecane.[104]-

To butyllithium (2.5M; 10ml; 2.5 x 10^{-2} mol.) was added, dropwise, N-2-propylcyclohexylamine (4.1ml; 2.5 x 10^{-2} mol.) in ether (10ml) over 20 min. The mixture was stirred for a further 10 min, then dropwise, over 30 min, was added 11-oxa tricyclo [4.4.1.0^{4}] undecane (1.52g; 10^{-2} mol.) in ether (10ml). The mixture was stirred for 24h then water (20ml) added, and the ethereal layer separated. The aqueous portion was extracted with ether (3 x 20ml), and the organic portions combined and washed with 2M hydrochloric acid (2 x 20ml), saturated sodium bicarbonate (20ml) and water (20ml). After drying and evaporating there remained a yellow liquid, which was shown by t.l.c. to contain at least six components. Distillation afforded fractions b.113-4°, 119-26°, 126-30°, and 130-42°, all of which still produced at least six spots on t.l.c. (ether/light petrol 1:1/silica). ν(neat) of each had 3640cm^{-1} (br.m) but no absorption in the region of 1670cm^{-1}.

Reaction of Lithium diphenylphosphide with Propen-3-ol.-

Lithium diphenylphosphide (7.5 x 10^{-2} mol.) was added under nitrogen, to propen-3-ol (2.90g; 5 x 10^{-2} mol.) and the mixture stirred overnight. Acetic acid (6ml) was added, and the thick mass stirred vigorously at 0° whilst 30% hydrogen peroxide (30ml) was added over 30 min.

Stirring was continued for a further 30min., and water (80ml) added. The organic layer was separated, and the aqueous portion extracted with dichloromethane (40ml). The combined organic layers were washed with saturated sodium bicarbonate (40ml), dried, and evaporated to give an oil (7.09g). Purification of this via chromatography (ethyl acetate/silica) gave diphenylphospinic acid m.191-3° (lit.[122] 190°).

Reaction of lithium thiophenoxide with 11-oxatricyclo [4.4.1.0^{1,6}] undecane:-

To thiophenol (1.10g; 10^{-2} mol.), stirred under nitrogen in THF (40ml) at 0°, was added butyllithium (2.0M; 5.0ml; 10^{-2} mol.) over 15min. The mixture was stirred a further 15 min, then 11-oxatricyclo [4.4.1.0^{1,6}] undecane (1.21g; 8 x 10^{-3} mol.) in THF (10ml) was added, and the whole stirred overnight. Water (10ml) was added, and the mixture extracted with dichloromethane (2 x 20ml.). The extracts were washed with 2M sodium hydroxide (2 x 10ml), brine (10ml), dried, and evaporated to yield a brown liquid (1.65g). Distillation gave 11-oxa tricyclo [4.4.1.0^{1,6}] undecane (0.52g) b.65°/0.25 mmHg, and fractions b.75-125°/0.25 mmHg (0.42g) and 125-60°/0.25mmHg (0.62g). These latter two contained at least three components each (by t.l.c. ether/silica); i.r. and n.m.r. indicated the presence of n-butyl and hydroxyl functions, and they were not further examined.

Methyldiphenylphosphine sulphide.[95]-

Triphenylphosphine sulphide (2.94g; 10^{-2} mol.) was stirred in THF (20ml) under nitrogen, and to it was added methyllithium (1.0M; 10ml; 10^{-2} mol.) The mixture was stirred for 2h to a deep red solution. Water (10ml) was added, and the ethereal layer separated, dried, and evaporated to give a yellow oil. This was distilled to yield methyldiphenylphosphine sulphide (1.74g; 75%) b.192°/1.0mmHg (lit.[95] 155-7°/0.2mmHg). ^{13}C n.m.r. - see separate section.

Allyldiphenylphosphine sulphide:-

a) Lithium diphenylphosphide (5×10^{-2} mol.) was added to allyl bromide (6.04g; 5×10^{-2} mol.), under nitrogen, and the mixture stirred overnight. Water (40ml) was added, and the ethereal layer separated, dried, and evaporated to yield a yellow oil. This was taken up in benzene (30ml) and treated with sulphur (1.60g; 5×10^{-2} mol.), and left overnight. The mixture was then filtered, and directly chromatographed (benzene/alumina) to yield an oil (4.20g). Distillation of this affordedallyldiphenylphosphine sulphide (3.50g; 27%) b.198°/0.3mmHg (lit.[102] 172-6°/0.01 mmHg). N.m.r. showed that the material was still contaminated with tert-butyldiphenylphosphine sulphide and propenyldiphenylphosphine sulphide (τ 3.0 - 4.9 (m), 8.00 (dm, J_{P-H} = 7Hz)). The sample was considered too impure for ^{13}C n.m.r. work.

b) (i)[102] potassium ethylxanthate (8.0g; 5×10^{02} mol.) was stirred in acetone (100ml) and, over 45min, allyl bromide (4.75ml; 5×10^{-2}mol.) in acetone (10ml) added. Stirring was continued for a further 1.25h and the mixture filtered, evaporated, and distilled to yield allyl ethylxanthate b.65-6°/0.3mmHg (6.55g; 81%) as a pale yellow liquid of novel odour (lit.[102] b.92-105°/12mmHg).

τ 3.97 - 4.37 (m, 1H), 4.76 (d, $J_{H-H_{trans}}$ = 16, 1H), 4.89 (d, $J_{H-H_{cis}}$ = 10, 1H), 5.40 (q, J_{H-H} = 7, 2H), 6.26 (d, J_{H-H} = 6, 2H), 8.61 (t,3H).

ii) [102] Chlorodiphenylphosphine (8.85g; 4×10^{-2} mol.) and allyl ethylxanthate (6.45g; 4×10^{-2} mol.) were heated together at 210° for 10 min Distillation of the black tar gave allyldiphenylphosphine sulphide (3.11g; 30%) as a viscous oil b.202-3°/0.5mmHg (lit.[102] 172-6°/0.01mmHg).

τ 2.10 - 35 (4H), 2.55 - 65 (6H), 3.97 - 4.43 (m, 1H), 4.78 - 5.04 (m, 2H) 6.71 (dd, J_{H-H} = 14, J_{P-H} = 7,2H).

trans-Stilbene epoxide.-

trans - stilbene (18.0g 10^{-1} mol.) was stirred vigorously in dichloro-

methane (100ml) at 20°, and to it was added, over 5 min, peroxoacetic acid (43%; 50ml), buffered by the pre-addition of anhydrous sodium acetate (3.0g). The mixture was stirred for 24h, then poured into water (200ml). The organic phase was separated, and the aqueous portion extracted with dichloromethane (50ml). The organic phases were washed with saturated sodium bicarbonate (2 x 100ml), dried, and evaporated to yield a solid (19.1g). Recrystallisation from methanol furnished trans-stilbene expoxide (17.1g; 87%) m.67° (lit.[72] 66°) τ 2.7 - 80 (5H), 6.33 (1H).

Reaction of trans-stilbene epoxide with sodium diethylphosphonate.- To sodium hydride (1.20g; 2 x 10^{-2} mol.) stirred under nitrogen, was added, with caution, diethylphosphonate (2.72g; 2 x 10^{-2} mol.) in DME (10ml). After hydrogen evolution had ceased, trans-stilbene epoxide (3.92g; 2 x 10^{-2} mol.) in DME (20ml) was added, to give a yellow solution. This was refluxed for 24h, cooled, and water (50ml) added. The ethereal layer was separated, dried, and evaporated to yield a yellow oil (3.74g), which solidified upon standing. It was identified as starting material by t.l.c. (benzene/petrol/alumina) and n.m.r.

Diphenyl3,3-bis(Carboxyethyl)propylphosphine oxide.-[138] To dry ethanol (25ml) was added sodium chips (0.46g; 2 x 10^{-2} mol.) After solution, malonic ester (3.2g; 2 x 10^{-2} mol.) in ethanol (5ml) was added dropwise, with stirring. The mixture was brought to reflux, and diphenylvinylphosphine oxide (4.56g; 2 x 10^{-2} mol.) in ethanol (25ml) added dropwise over 1h. The mixture was refluxed a further 15min cooled, and 2M hydrochloric acid (10ml) added. The mixture was filtered and evaporated to dryness to give a cloudy green oil. This was taken up in chloroform, dried, and evaporated to give a green oil (7.80g). Purification via chromatography (ethanol/silica) gave 6.74g (87%) of a green oil assigned as diphenyl3,3-bis (carboxyethyl)propylphosphine

oxide τ2.15 - 65 (10H), 5.82 (q, J_{H-H} = 7, 4H), 6.60 (t, J_{H-H} = 7,1H) 7.40 - 7.95 (m, 4H), 8.79 (t, 6H).

Reaction of diphenyl 3,3-bis (Carboxyethyl)propylphosphine oxide with Benzyl bromide.-

Sodium chips (0.39g; 1.7×10^{-2} mol.) were dissolved in ethanol (20ml) and to this was added diphenyl 3,3-bis (carboxyethyl)propylphosphine oxide (6.6g; 1.7×10^{-2} mol.) in ethanol (25ml). The mixture was refluxed for 15min, to give a lemon solution, then, dropwise, benzyl bromide (2.0ml; 1.7×10^{-2} mol.) in ethanol (5ml) was added, and the whole refluxed for 2h. The mixture was then cooled, adjusted to pH 6 with concentrated hydrochloric acid, and filtered. The filtrate was evaporated to yield a brown oil, which was purified via chromatography (benzene/silica) to give 4.1g (50%) of a sticky yellow solid, which could not be further purified by chromatography or recrystallisation. It was assigned as 3,3-bis (carboxyethyl)4-phenylbutyldiphenylphosphine oxide. τ 2.20 - 3.10 (15H), 5.86 (q, J_{H-H} = 7, 4H), 6.78 (s, 2H), 7.60 - 7.95 (m, 4H), 8.33 (t, 6H).

The yellow solid was refluxed in concentrated hydrobromic acid (25ml) for 24h. Water (50ml) was added and the mixture extracted with chloroform (5 x 50ml). Evaporation of the chloroform layers gave a brown oil, which was dissolved in 2M sodium hydroxide (40ml). This was washed with dichloromethane (25ml), then adjusted to pH 1 with concentrated hydrochloric acid, and extracted with chloroform (3 x 50ml). The chloroform extracts were dried and evaporated to give a hard gum (0.51g) which could not be purified.

Reaction of Malonic ester, Benzyl bromide and Diphenylvinylphosphine oxide. -

Sodium pieces (0.46g; 2×10^{-2} mol.) were dissolved in ethanol (25ml)

and to this was added malonic ester (3.2g; 2×10^{-2} mol.) in dry ethanol. This was followed by the addition of diphenylvinylphosphine oxide (4.56g; 2×10^{-2} mol.) in ethanol (25ml) to the mixture, at reflux. After 30min, benzyl bromide (3.42g; 2×10^{-2} mol.) in ethanol (5ml) was added dropwise. The whole was refluxed overnight, and evaporated to dryness. Water (25ml) and dichloromethane (50ml) were added to the residue, and the organic layer separated, dried, and evaporated to yield a pale yellow liquid (9.00g). Chromatography (ethyl acetate/silica) gave, in increasing order of polarity, benzyl bromide, malonic ester, A, an oil (0.50g), and B, an oil (3.40g.) The eluant was changed to ethyl acetate (1)/ethanol (9), and C, a yellow oil (1.65g) obtained. Changing the eluant to ethanol gave D (0.11g) as crystals. A solidified on standing, and was recrystallised (benzene/petrol) to give 3,3-bis (carboxyethyl)4-phenylbutyldiphenylphosphine oxide m.102° (Found: C,70.45; H, 6.6, $C_{28}H_{31}O_5P$ requires C,70.3; H,6.55%). B also solidified upon standing, and was recrystallised (benzene/petrol) to give diphenyl 3,3-bis (carboxyethyl)propylphosphine oxide m.80-5°. The analytical sample had m.87-9° (Found: C,67.05; H,6.4. $C_{21}H_{25}O_5P$ requires C,66.95; H,6.5%) C was solidified by slow evaporation from benzene, to give off-white prisms m.123°. Recrystallisation from benzene gave crystals m.183-4° and mixed m. 183-5°, which were assigned as bis(2-diphenylphinylethyl) diethyl malonate (lit[47] 184-5°). The n.m.r. spectrum of D showed that it contained an -OH group. It was not further examined.

Benzylmalonic ester-

Sodium (2.3g; 10^{-1} mol.) was dissolved in ethanol (20ml), and malonic ester (16.1g; 10^{-1} mol.) added to this. Then, cautiously with stirring, benzyl bromide (11.9ml; 10^{-1} mol.) was added, in ethanol (10ml) and the whole refluxed for 1.25h. The ethanol was evaporated off, and the residue treated with water (30ml). The ester (upper)

layer was separated, and the aqueous phase extracted with ether (30ml) The organic layers were combined, dried, and evaporated to give a yellow liquid (21.3g). Distillation of this afforded benzylmalonic ester b.230°/85mmHg (15.1g; 60%) (lit.[139] 145-55°/5mmHg). τ 2.83 (s,5H), 5.88 (q, J_{H-H} = 8, 4H), 6.36 (t, J_{H-H} = 8, 1H), 6.80 (d, 2H) 8.84 (t, 6H).

Reaction of Benzylmalonic ester with diphenylvinylphosphine oxide.- Sodium (0.69g; 3 x 10^{-2} mol.) was dissolved in ethanol (40ml) and to this was added benzylmalonic ester (7.50g; 3 x 10^{-2} mol.) in ethanol (10ml), dropwise. The mixture was brought to reflux, and diphenylvinylphosphine oxide (6.84g; 3 x 10^{-2} mol.) in ethanol (30ml) added over 40min. The whole was refluxed a further 2h, then cooled and 2M hydrochloric acid (15ml) added. The mixture was evaporated to dryness and extracted with chloroform (100ml). Drying and evaporation of this gave a brown oil (13.5g). T.l.c. (ethyl acetate/silica) showed, by comparison, that the material was mainly 3,3-bis (carboxyethyl)4-phenylbutyldiphenylphosphine oxide, but the oil could not be purified by recrystallisation even with seeding.

3.0g of this oil was refluxed with potassium hydroxide (1.07g; 1.9 x 10^{-2} mol.) in water (5ml) for 2h. The mixture was evaporated to dryness and cooled. Sulphuric acid (1ml) and water (2ml) were added, and the mixture refluxed for 3h. The mixture was cooled and made alkaline with 2M sodium hydroxide (ca. 50ml). The mixture was washed with dichloromethane (20ml), separated from an oily layer that dissolved neither in the dichloromethane nor the alkali, and adjusted to pH 1 with concentrated hydrochloric acid. The mixture was then extracted with dichloromethane (3 x 20ml). The extracts were dried and evaporated to give a yellow oil (0.51g) which was solidified by slow evaporation from ethanol, to give sticky yellow crystals, which could not be further purified.

4-Diphenylphosphinylbutanoic acid.-

3,3-bis(carboxyethyl)propyldiphenylphosphine oxide (2.5g; 6.45×10^{-3} mol.) was refluxed with potassium hydroxide (1.07g; 1.9×10^{-2} mol.) in water (8ml) for 2h, with stirring. The mixture was evaporated to dryness, by removal of the condenser, and, after cooling, sulphuric acid (1ml; 1.9×10^{-2} mol.) added. The mixture was refluxed 3h, cooled, and made alkaline with 2M sodium hydroxide (ca. 50ml). The mixture was washed with ether (25ml), made acidic with concentrated hydrochloric acid, and extracted with dichloromethane (3 x 40ml). The extracts were dried and evaporated to give 4-diphenylphospinylbutanoic acid m.152° (1.37g; 74%) (Found: C,67.1; H,6.3 $C_{16}H_{19}O_3P$ requires C,66.7; 5.95%. τ -0.55 (br.s., 1H), 2.25 - 65 (10H), 7.45 - 75 (m, 4H), 7.95 - 8.25 (m,2H).

4-Diphenylphosphinylbutan-1-ol.-

4-Diphenylphosphinylbutanoic acid (0.189g; 5×10^{-4} mol.) was refluxed with lithium aluminium hydride (0.033g; 9×10^{-4} mol.) in ether (5ml) for 3.25h. The mixture was cooled, and treated with 2M hydrochloric acid (5ml). The mixture was then shaken between dichloromethane (20ml) and 50% sodium hydroxide (10ml). The organic portion was separated and the aqueous layer extracted with dichloromethane (10ml). The organic phases were washed with saturated sodium bicarbonate (20ml), dried and evaporated (using benzene to azeotrope off traces of water) to give a solid (0.046g; 25%) assigned as 4-diphenylphosphinylbutan-1-ol τ 2.20 - 75 (10H), 5.05 (br.s., 1H) 6.42 (br.t., J_{H-H} = 7, 2H), 7.55 - 7.95 (m) and 8.05 - 50 (m) (6H). The aqueous portions were combined and made acidic with concentrated hydrochloric acid and extracted with dichloromethane (2 x 30ml). Drying and evaporation gave starting material (0.135g).

bis-(2-Diphenylphosphinylethyl)diethylmalonate[47].-

Sodium pieces (1.73g; 7.5×10^{-2} mol.) were dissolved in ethanol (30ml) with stirring, and malonic ester (6.0g; 3.75×10^{-2} mol.) in benzene (10ml) added. The mixture was brought to reflux, and vinyldiphenylphosphine oxide (17.1g; 7.5×10^{-2} mol.) in benzene (100ml) added. Refluxing was continued for 6h, then the mixture cooled, and water (40ml) added. The benzene layer was separated, and the aqueous layer extracted with benzene (40ml). The benzene fractions were washed with brine (100ml) dried, and evaporated to give a yellow semicrystalline mass (19.2g). Recrystallisation from benzene furnished bis-(2-diphenylphosphinylethyl) diethyl malonate (17.2g; 83%) m. 183-4°. A further recrystallisation from benzene gave needles m.184-5° (lit.[47] 184-5°). τ 2.15 - 65 (10h) 5.87 (q, J_{H-H} = 8, 4H), 7.80 (br.s., 8H), 8.63 (t,6H).

bis-(2-Diphenylphosphinylethyl)ethanoic acid.-

bis-(2-diphenylphosphinylethyl)diethyl malonate (9.40g; 1.53×10^{-2} mol.) was refluxed with potassium hydroxide (4.12g; 7.35×10^{-2} mol.) in water (25ml) for 2.5h. The mixture was evaporated to dryness, cooled, and treated with sulphuric acid (4.0ml; 7.5×10^{-2} mol.) and water (10ml) then refluxed for 3h. The mixture was again cooled and treated with 2M sodium hydroxide to pH ca.14. The mixture was washed with dichloro-methane (50ml), and made pH ca. 1 with concentrated dichlorene acid and then extracted with dichloro methane (3 x 50ml), and the organic extracts dried and evaporated to give a foam (6.28g; 79%), assigned as bis-(diphenylphosphinylethyl)ethanoic acid. The foam olefied on a Kofler block, and could not be purified. τ 1.00 (br.s., 1H), 2.20 - 70 (10h), 7.40 - 90 (m) and 7.90 - 8.40 (m) (9m). For analytical purposes, the acid was converted to its methyl ester, thus:

The acid (0.516g; 10^{-3} mol.) was refluxed with sulphuric acid (0.1ml) in methanol (10ml) for 24h. The cooled mixture was made alkaline with

2M sodium hydroxide and evaporated. The residue was treated with water (10ml) and dichloromethane (20ml), and the organic layer separated, dried, and evaporated to yield methyl bis-(2-diphenylphosphinylethyl)-ethanoate (0.387g; 73%). m. 145-7°. The analytical sample had m.148-50° (Found: C,70.35; H, 5.95. $C_{31}H_{32}O_4P_2$ requires C,70.2; H, 6.1%). τ 2.20 - 70 (10H), 6.39 (s, 3H), 7.35 - 8.40 (m, 9H).

Methyl bis-(2-diphenylphosphinylethyl)ethanoate.-

Bis-(2-diphenylphosphinylethyl)diethyl malonate (10.5g; 1.68×10^{-2} mol.) was refluxed with potassium hydroxide (3.75g; 6.7×10^{-2} mol.) in water (30ml) for 2.5h. The mixture was evaporated to dryness, cooled, and sulphuric acid (4.0ml; 7.6×10^{-2} mol.) added. The mixture was refluxed for a further 3h, then evaporated to dryness, and methanol (25ml) added. The mixture was refluxed for 4h, cooled, and evaporated to dryness. The residue was shaken between 1M sodium hydroxide (200ml) and dichlorometane (3 x 50ml). The organic portions were dried and evaporated to give a foam (5.78g). This was purified by chromatography (methanol/alumnia) to give an oil (5.60g) which deposited crystals upon standing. Recrystallisation from benzene furnished methyl bis-(2-diphenylphosphinylethyl) ethanoate m.145-7°.

Attempted Reduction of bis-(2-Diphenylphosphinylethyl)ethanoic acid with Lithium aluminium hydride.-

Bis-(2-diphenylphosphinylethyl)ethanoic acid (1.03g; 2×10^{-3} mol.) was refluxed with lithium aluminium hydride (0.076g; 2×10^{-3} mol.) in DME (20ml) under nitrogen for 6h. The mixture was cooled and treated with water (100ml) and 2M hydrochloric acid (10ml), and extracted with dichloromethane (3 x 50ml). The organic portions were washed with 2M sodium hydroxide (50ml), dried, and evaporated to give a solid (0.67g) The n.m.r. spectrum of this material indicated that it was nearly all starting material.

Attempted Reduction of Methyl bis-(2-diphenylphosphinylethyl)ethanoate with lithium aluminium hydride.-

Methyl bis-(2-diphenylphosphinylethyl)ethanoate (0.53g; 10^{-3} mol.) was refluxed with lithium aluminium hydride (0.114g; 3×10^{-3} mol.) in DME under nitrogen for 6h. The mixture was cooled to 0°, and 1M hydrpchloric acid (20ml) added, with care, followed by a mixture of 30% hydrogen peroxide (2ml) and methanol (8ml). The mixture was stirred for 1h at 20°, then evaporated, and shaken between saturated sodium sulphite (50ml) and dichloromethane (3 x 20ml). The organic phases were dried and evaporated to give crystals (0.36g), which were identified as starting material by n.m.r. and t.l.c.

Hydrolysis of Methyl bis-(2-diphenylphosphinylethyl)ethanoate.-

Methyl bis-(2-diphenylphosphinylethyl)ethanoate (5.30g; 10^{-2} mol.) was refluxed with potassium hydroxide (2.24g; 4×10^{-2} mol.) in 50% aqueous methanol (50ml) for 33h. The reaction was monitored with t.l.c. (methanol/alumina). The reaction mixture was evaporated to small volume, and washed with dichloromethane (2 x 50ml). The aqueous phase was acidified with concentrated hydrochloric acid (10ml) and extracted with dichloromethane (3 x 100ml). The organic extracts were washed with brine (50ml) and dried and evaporated to give a foam (3.35g; 65%) of bis-(2-diphenylphosphinylethyl)ethanoic acid.

Reduction of bis-(2-Diphenylphosphinylethyl)ethanoic acid by Diborane (generated in situ)[113].-

To a mixture of sodium borohydride (0.102g; 2.7×10^{-3} mol.) and bis-(2-diphenylphosphinylethyl)ethanoic acid (1.55g; 3×10^{-3} mol.) was added diglyme (15ml) with stirring under nitrogen. Hydrogen was evolved over 20min, and then a solution of boron trifluoride etherate (redistilled from calcium hydride: 0.512g; 3.6×10^{-3} mol.) in diglyme was added over 20min. The mixture was stirred at 20° for 3h, then

treated with ice-water (20ml). The mixture was poured into more ice-water (180ml), and extracted with dichloromethane (3 x 40ml). The organic extracts were washed with ice-water ((200ml), dried, and evaporated to yield an oil (1.54g). T.l.c. (methanol/alumina) indicated that starting material was still present, so the material was taken up in dichloromethane (20ml) and washed with 2M sodium hydroxide (50ml). Drying and evaporation of the organic portion gave a foam (0.95g). The foam was purified via chromatography (methanol/alumina) to give a yellow oil (0.14g), which furnished crystals upon treatment with ethyl acetate, of 2,2-bis-(2-diphenylphosphinylethyl)ethanol (9.5%). Two recrystallisations from ethyl acetate gave crystals m.167-8° (Found: C,71.55; H,6.8 $C_{30}H_{32}O_3P_2$ requires C,71.7; H,6.4%). τ 2.25 - 70 (10H), 6.08 (br.s 1H), 6.45 (br.s., 2H), 7.60 - 7.90 (m, 5H), 8.20 - 50 (m, 4H). M^+ 502.

2,2-bis-(2-Diphenylphosphinylethyl)ethanol.-

Bis-(2-diphenylphosphinylethyl)ethanoic acid (2.83g; 5.5×10^{-3} mol.) was stirred under nitrogen in THF, and, over 30min there was added borane-dimethylsulphide[114] (0.66ml; ca, 6.6×10^{-3} mol.) The mixture was stirred a further 15min, until all hydrogen evolution had ceased, then refluxed for 4h. The mixture was cooled, and dry methanol (2ml) added over 15min. There was a vigorous evolution of hydrogen, and the mixture was stirred a further 30min, then evaporated to dryness and the residue taken up in dichloromethane (25ml), washed with water (10ml) saturated sodium carbonate (20ml), and brine (10ml). The solution was dried and evaporated to give 2,2-bis-(2-diphenylphosphinylethyl)ethanol (2.47g; 88%) m.164-5°.

Attempted Reactions of 2,2-bis-(2-diphenylphosphinylethyl)ethanol with Base.-

a) Sodium hydride (0.12g; 3×10^{-3} mol.) was stirred under nitrogen, and to it was added 2,2-bis-(2-diphenylphosphinylethyl)ethanol (1.00g;

2×10^{-3} mol.) in THF (25ml). The mixture was stirred for 5 min after hydrogen evolution had ceased, and, when no white precipitate appeared, refluxed for 35min. The mixture became cloudy; it was cooled and treated with water (10ml). The organic layer was separated, and the aqueous portion was extracted with dichloromethane (10ml). The organic phases were washed with brine (10ml), dried, and evaporated to give a foam (1.01g), shown by t.l.c. and n.m.r. to be starting material.

b). To sodium hydride (0.06g; $1,5 \times 10^{-3}$ mol.) stirred under nitrogen, was added 2,2-bis-(2-diphenylphosphinylethyl)ethanol (0.50; 10^{-3} mol.) in DMSO (10ml). After 2.5h, the solution remained clear, and was warmed to 100° over 15 min, and held there for 5 min., when a white precipitate formed. The mixture was cooled, and quenched with water (150ml). The mixture was extracted with dichloromethane (3 x 25ml), and the organic extracts washed with water (2 x 100ml), dired, and evaporated to yield an oil (0.202g), which deposited crystals on standing. Recrystallisation from ethyl acetate gave starting material m.164-5°.

c) 2,2-bis-(2-diphenylphosphinylethyl)ethanol (1.00g; 2×10^{-3} mol.) and potassium t-butoxide (0.25g; 2.25×10^{-3} mol.) were refluxed together in toluene (15ml) for 12h. The cooled mixture was treated with water (10ml), the organic phase separated, and the aqueous layer extracted with dichloromethane (10ml). The organic portions were washed with brine (10ml), dried, and evaporated to yield a pale orange solid (0.89g), identified as starting material.

Attempted Reaction of Dichlorophenylphosphine with Cycloocta-1,3-diene.-

Dichlorophenylphosphine (35.8g; 2×10^{-1} mol.) and cycloocta-1,3-diene (19.2g; 2×10^{-1} mol.) were heated together at 100-110° for 28 days. The mixture was cooled, washed with petrol (3 x 50ml), mixed

with dichloromethane (100ml). and poured onto crushed ice (100g). The organic layer was separated, washed with saturated sodium bicarbonate (2 x 250ml), and water (250ml), dried, and evaporated to give a brown oil (10.3g). T.l.c. and n.m.r. showed that this consisted essentially of cycloocta-1,3-diene.

Benzylmethylphenylphosphine oxide.-

To triphenylphosphine (13.1g; 5×10^{-2} mol.) in THF (60ml) under nitrogen, was added lithium (in small freshly-cut strips) (0.77g; 1.1×10^{-1} mol.) and the mixture stirred 2h in a deep red colour. Tert-butyl chloride (5.5ml; 5×10^{-2} mol.) was added so as to maintain a gentle reflux, and the mixture refluxed a further 5 min., then cooled to 0°, and iodomethane (3.1ml; 5×10^{-2} mol.) added. The cherry-red colour vanished immediately, and the mixture was stirred at 20° for 2h, the lithium pieces (0.77g; 1.1×10^{-1} mol.) added, and the mixture stirred 2h to a bright orange-yellow colour. 2-Chloro 2-methyl propane (5.5ml; 5×10^{-2} mol.) was added, and the mixture refluxed a further 5 min, and cooled to 0°. The colour was titrated with benzyl bromide (3.2ml; 2.7×10^{-2} mol.) and 50% aqueous methanol (50ml) was quickly added. The mixture was stirred 15 min, to allow excess lithium to be destroyed, then 30% hydrogen peroxide (50ml) added over 30 min, at 0°. A vigorous reaction ensued, and the mixture was stirred a further 30 min. Water (100ml) was added, and the organic (upper) layer separated. The aqueoud phase was extracted with dichloromethane (3 x 50ml), and the combined organic portions washed with 2M sodium hydroxide (100ml) and brine (100ml), dried, and evaporated to give a yellow semicrystalline mass (10.0g.) Recrystallisation from petrol/benzene gave benzyldiphenylphosphine oxide (0.79g) m.160-1° (lit.[116] 192-3°). τ 2.25 - 70 (10H), 2.88 (s, 5H), 6.38 (d, J_{P-H} = 15,2H). The mother liquors were evaporated, and the residue recrystallised four times from

ethyl acetate to give crystals of benzylmethylphenylphosphine oxide (1.05g) m.141-2°. (Found: C,73.35; H,6.5. $C_{14}H_{15}OP$ requires C,73.05; H,6.55%). τ 2.25 - 3.05 (10H), 6.72 (d, J_{P-H} = 16, 2H), 8.35 (d, J_{P-H} = 12, 3H). M^+ 230.

The n.m.r. spectrum of the crude product indicated also that methyldiphenylphosphine oxide (τ 8.85 (d, J_{P-H} = 14)) (lit.[118] τ 8.90 (d, J_{P-H} = 13.3)) may have been one of the other products.

APPENDIX I

^{13}C Nuclear Magnetic Resonance Data.

^{13}C n.m.r. spectra were recorded on a Brucker WH90 instrument, operating at 22.63MHz, using ^{2}H-chloroform as solvent and locking signal. Signals are recorded here in p.p.m. (δ) downfield from tetramethylsilane. Coupling constants (J) are expressed in Hz, and are corrected to one decimal place. Assignments are based upon the ^{1}H decoupled spectrum, unless otherwise stated.

Methyldiphenylphosphine sulphide.

In this and all other compounds discussed here, the four carbons of the phenyl group are labelled thus: C_1 is α- to phosphorus, C_2 is the ortho, C_3 the meta, and C_4 the para carbon. The assignment of C_1 and the coupling constants of C_2 - C_4 are based upon peak heights.

C_{methyl} 21.7 (d, J = 58.5); C_1 132.8 (d, J = 127.5); C_2 - C_4 128.8 (d, J = 12.5), 130.8 (d, J = 9.7), 131.5 (d, J = 1.9).

Triphenylphosphine sulphide.

C_1 132.9 (d, J = 85.5); C_2 - C_4 128.5 (d, J = 12.2), 131.6 (d, J = 3.6), 132.2 (d, J = 5.0). (as lit.[151]).

Triphenylphosphine oxide.

C_1 132.6 (d, J = 103.0); C_2 - C_4 128.5 (d, J = 12.2), 131.8 (d, J = 1.5), 132.1 (d, J = 5.0) (lit.[140] C_4 134.6 (Me_2CO); and as lit.[151] (^{2}H - $CHCl_3$)).

Allyldiphenylphosphine sulphide.

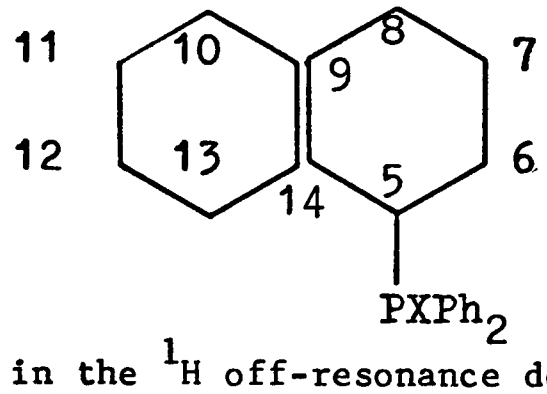
$$\underset{\qquad}{Ph_2P(S) - CH_2 - CH = CH_2}$$
$$\qquad\qquad C_5 \quad C_6 \quad C_7$$

Assignments of C_6 and C_7 are based upon the ^{1}H off-resonance decoupled spectrum; C_6 appears as a doublet of doublets and C_7 as a doublet of triplets.

C_5 39.0 (d, J = 52.5), C_7 121.2 (d, J = 13.4), C_6 127.3 (d, J = 8.6), C_1 131.8 (d, J = 102.6), C_2 - C_4 128.6 (d, J = 10.9), 130.8 (d, J = 10.8), 131.5 (d, J = 3.4).

1-diphenylphosphinyl bicyclo [4.4.0] dec-9-ene and

1-diphenylphosphinthioyl bicyclo [4.4.0] dec-9-ene.



The signals in the ^1H off-resonance decoupled spectrum of each compound due to C_2, C_3, C_4, C_9 and C_{14} have not been assigned; they are given in p.p.m. with relative peak integrals in parentheses.

X = O: C_6, C_7, C_{11}, C_{12} 19.8, 20.2; C_8, C_{10}, C_{13}, 31.9, 35.5; C_5 47.7 (d, J = 62.2); C_1 135.9 (d, J = 88.2); C_2, C_3, C_4, C_9, C_{14}, 126.9 (30), 128.0 (482), 128.5 (798), 130.9 (393), 131.0 (213), 131.9 (497), 132.2 (395).

X = S: C_6, C_7, C_{11}, C_{12} 19.4, 19.6, 20.1; C_8, C_{10}, C_{13} 31.7, 33.4, 34.7, 35.5; C_5 51.3 (d, J = 38.9); C_1 136.5 (d, J = 54.3); C_2, C_3, C_4, C_9, C_{14}, 127.7 (506), 128.0 (325), 128.3 (511), 130.9 (1000), 131.9 (568), 132.2 (469), 133.4 (564), 133.7 (502).

2-Hydroxyethyldiphenylphosphine oxide.

Only the data for aliphatic carbons are given in this and the next two compounds. C_5 is α- to phosphorus. C_5 32.9 (d, J = 69.7), C_6 56.0 (s).

bis-(2-Diphenylphosphinylethyl)ether.

C_5 30.5 (d, J = 70.8), C_6 64.1 (s).

bis-(2-Diphenylphosphinylethyl)peroxide.

C_5 29.1 (d, J = 70.7), C_6 69.7 (s).

A few general remarks may be made. Assignments of C_2 - C_4, in general, can only be made when deuterated derivatives are available. Whilst it is tempting to assign them in descending order of coupling constants, it should be noted that, in allydiphenylphosphine sulphide (see above), $J_{P-C_7} > J_{P-C_6}$, and, in the last three compounds, all containing the $PH_2POCH_2CH_2$ unit, $J_{P-C_6} = 0$. In addition, it has been noted that, in general, in the ^1H n.m.r. spectra of P (IV) compounds, $J_{P-H_\beta} > J_{P-H_\alpha}$[118].

APPENDIX II

Further Properties of Diphenylvinylphosphine Oxide - A Discussion of the Nature of the P=O Bond.

Theoretical calculations upon the molecules phosphine oxide and trimethylphosphine oxide indicate that the phosphorus d orbitals of π symmetry contribute significantly to the bonding in the phosphinyl linkage[9,144]. That is to say, there is reason to formulate this bond as 'P=O' rather than as '$P^{+} - O^{-}$'. It might therefore be fruitful to make a comparison between the phosphinyl and carbonyl linkages. In Tables 10 and 11, the carbonyl and phosphinyl stretching vibrations in the infra-red region are tabulated for, respectively, related phosphonates and esters, and phosphine oxides and ketones.

Infra-red frequencies of some phosphonates and esters[a]

Compound	$\nu_{P=O}$[b]	$\nu_{C=O}$[b]	$\nu_{C=C}$[b]
$CH_2=CHPO(OEt)_2$	1249		1618
$CH_2=CHCO_2Et$		1706	1623
$CH_2=CH-CH_2PO(OEt)_2$	1253		1642
$CH_2=CH-CH_2CO_2Et$		1739	1645

[a] reference 145

[b] in cm^{-1}

Table 10

Infra-red frequencies of some phosphine oxides and aryl ketones[a]

Compound	$\nu_{P=O}$[b]	$\nu_{C=O}$[b]	$\nu_{C=C}$[b]
$CH_2=CHPOPh_2$	1173		1608
$CH_2=CH-CH_2POPh_2$	1175		1640
$CH_3CH_2POPh_2$	1175		
$CH_2=CHCOPh$		1678	
CH_3CH_2COPh		1692	
$(CH_3CH_2)_3PO$	1176		
$(CH_3CH_2)_2CO$		1717	

[a] all recorded in $HCCl_3$ solution

[b] in cm^{-1}

Table 11

From tables 10 and 11 it can be seen that the P=O stretching frequency is remarkably unaffected by the nature of the substituents on phosphorus, in the series of compounds examined, whereas the frequency of the C=O stretch is very much influenced by the presence of a conjugated π system. On the other hand, the C=C stretching frequency is very much lowered on passing from β,γ-unsaturated phosphinyl compounds to their α,β-unsaturated isomers, and in this respect the phosphinyl compounds mirror the behaviour of the corresponding carbonyl compounds.
These results indicate the inability of phosphorus in such systems to permit π-electron delocalisation through itself, and they are perhaps more consistent with a description of the phosphinyl linkage as a co-ordinate bond (i.e. $P^+ - O^-$) rather than a 'true' double bond (i.e. P=O). Actual conjugation between a phosphinyl group and an olefinic bond would be expected to lower the i.r. stretching frequencies of both components (as is the case in analogous α,β -unsaturated ketones) relative to a non-conjugated example. The variation in C=C stretching

frequency between α,β-and β,γ-unsaturated phosphinyl compounds can be explained by the electron-withdrawing properties of the diphenylphosphinyl and diethoxyphosphinyl groups (see also Introduction)**. A description of the phosphinyl linkage as a co-ordinate bond is in full agreement with the facility of Michael-type additions to diphenylvinylphosphine oxide (1) (see Chapter 1) and with the unwillingness of 1-diphenylphosphinyl-bicyclo[4.4.0] dec-9-ene (39) to isomerise to an α,β-unsaturated isomer upon treatment with potassium t-butoxide (see Chapter 3).
The ^{13}C n.m.r. spectra of triphenylvinylphosphonium bromide (4) and related vinylphosphonium salts show marked deshielding of the β-carbon, similar to that observed for other olefins bearing an electron-withdrawing group (see Table 12)[147].

^{13}C n.m.r. shifts of $X\text{-}C^5H{=}C^6H_2$ [a,b]

X	C^5	C^6
H-	122.8	122.8
Me-	133.1	115.0
NC-	107.7	137.8
Ph_3P^+-	119.2	145.2
Me_3N^+	142.7	112.1

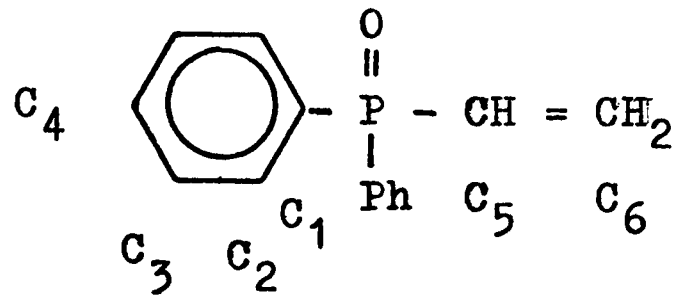
[a] reference [147]

[b] in p.p.m. downfield from tetramethylsilane

Table 12

** In view of the seeming inertness of the P=O stretching frequency in phosphine oxides to the nature of the substituents, the frequency of 1215 cm^{-1} recorded for the complex $Fe(CO)_4.CH_2{=}CHPOPh_2$ is worthy of note.[146].

It was of interest to see whether the β-carbon in diphenylvinylphosphine oxide was also greatly deshielded with respect to ethane.



Assignment is based upon the off-resonance decoupled spectrum and upon coupling constants**.

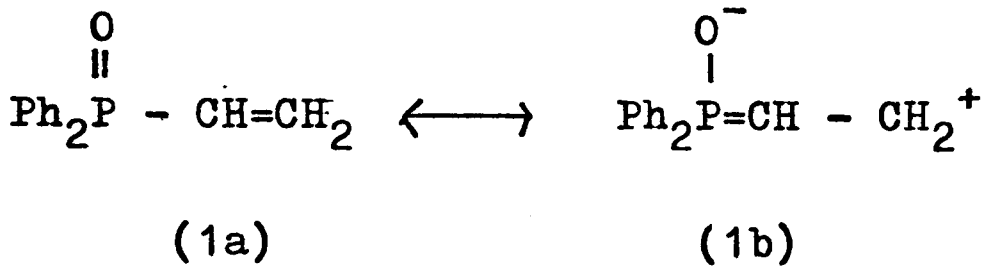
C_1	132.4 (J_{P-C} =105.0)
C_{2-4}	128.5 (J = 11.8); 131.3 (J = 9.8); 131.8 (J = 2.8)
C_5	131.5 (J = 96.4)
C_6	134.4 (J = 11.8)

Clearly, the large deshielding of the β-carbon atom in phosphonium salt (4) is not found in the corresponding phosphine oxide (1), where <u>both</u> the α- and β-carbon atoms are deshielded relative to ethane, and the β-carbon deshielded more. It is also worth noting that, whilst the coupling constants between the phosphorus and C_1 are nearly the same in the two compounds (J = 96.0 in phosphine oxide (1); J = 90.3 in phosphonium salt (4)), the coupling constants between phosphorus and C_5 are more different (J = 96.4 in phosphine oxide (1); J = 80.0 in phosphonium salt (4))[147].

It would appear therefore, that there is much less withdrawl of electron density from the olefinic carbons in phosphine oxide (1) than in

** The spectrum was recorded on a Varian XL-100 instrument, in $^2HCCl_3$ Quoted signals are in p.p.m. downfield from T.M.S. and coupling constants in Hertz. This work has recently been confirmed by Schweizer[151].

phosphonium salt (4) The canonical form (4b) is a much more important contributer to the ground state of phosphonium salt (4) than is (1b) to phosphine oxide (1), as judged by ^{13}C n.m.r. shifts: (Scheme 83).



Scheme 83

Such a description of the ground state of phosphine oxide (1) also correlates with the infra-red data.

Three further attempts have been made to prepare epoxyvinyldiphenylphosphine oxide (6). Phosphine oxide (1) was recovered unchanged after treatment with N-bromoacetamide in t-butanol/water[148] or dimethylsulphoxide/water[149] at 20° for 24h. The reaction of 2-chloromethyldiphenylphosphine oxide with paraformaldehyde and sodium hydride in tetrahydrofuran at reflux or in dimethylsulphoxide at 20° gave diphenylphosphinic acid as the only phosphorus-containing product, after aqueous quench. In one experiment employing dimethylsulphoxide as solvent, volatile products were distilled out of the reaction mixture by application of a slight vacuum, before the aqueous quench. In this way, a 36% yield of vinyl chloride was obtained.

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Abstract.

Chapter 1.

This chapter is concerned with some reactions of diphenylvinylphosphine oxide (1). Phosphine oxide (1) is known to undergo nucleophilic additions analogous to the Michael reaction[1]. Triphenylvinylphosphonium bromide also undergoes a number of nucleophilic additions, including the Schweizer reaction[2]. Thus, triphenylvinylphosphonium bromide, upon treatment with the sodium salts of benzoin or salicylaldehyde, yields 2,3-diphenyl 2,5-dihydrofuran[3] and 3,4-chromene[4], respectively. An attempt to extend the Schweizer reaction to phosphine oxide (1) was not successful.

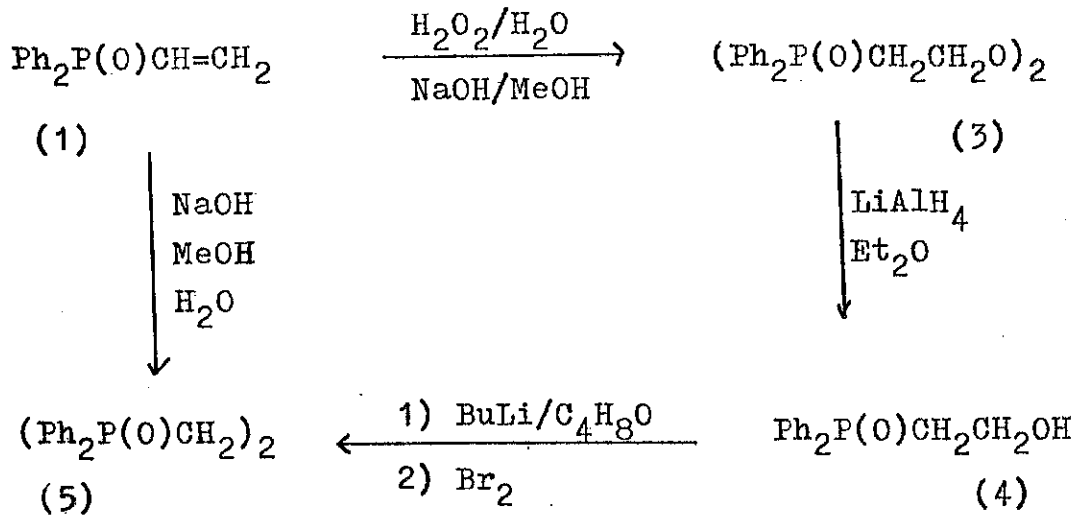
Several possible synthetic routes to epoxyvinyldiphenylphosphine oxide (2) have been explored.

$$Ph_2P(O) - CH - CH_2 \qquad (2)$$

Phosphine oxide (1) was found to be inert to several epoxidising conditions, for example, unbuffered trifluorperoxyacetic acid in refluxing dichloromethane[5], and t-butylhydroperoxide/Triton B in methanol[6]. Phosphine oxide (1) was converted to bis-(2-diphenylphosphinyl-ethyl)peroxide (3) in 79% yield, by treatment with alkaline hydrogen peroxide. Peroxide (3) is unusually stable. Reaction of (3) with lithium aluminium hydride gave 2-hydroxyethyl diphenylphosphine oxide (4) in 84% yield.

Phosphine oxide (1) was converted to 1,2-bis-(diphenylphosphinyl)ethane (5) upon treatment with aqueous methanolic sodium hydroxide, in 96% yield. Phosphine oxide (5) had also previously been obtained by the reaction of triphenylvinylphosphonium bromide with sodium hydroxide[7]. Phosphine oxide (5) was also isolated in 19% yield from the treatment

of phosphine oxide (4) with two mole equivalents of butyllithium, and subsequent treatment with bromine (Scheme 1).



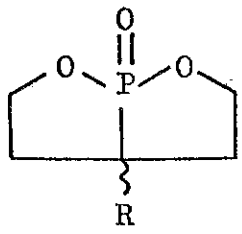
Scheme 1

On the basis of the spectroscopic properties of phosphine oxide (1), it is considered that there is little congugation between the C=C and the P=O groups.

Chapter 2

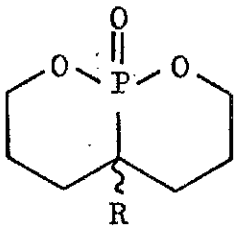
This chapter deals with the synthesis and stereochemical properties of bicyclic phosphonates. Attempts were made to prepare bicyclic phosphonates (6) and (7).

Alkylphosphonates can be lithiated, and subsequently alkylated, by treatment with butyllithium in tetrahydrofuran at -40°[8] or -78°[9]. Di-(2-bromoethyl)methylphosphonate failed, however, to cyclise to phosphonate (6) after treatment with a range of bases under varying conditions. Similarly, although 'stabilised' alkylphosphonates can be metallated by treatment with sodium hydride in dimethoxyethane, and subsequently alkylated[10], di(2-chloroethyl)(carboxyethyl)methylphosphonate (11) failed to cyclise to phosphonate (8) under a variety of conditions.



(6) R = H

(8) R = CO_2Et



(7) R = H

(9) R = CO_2Me

(10) R = CN

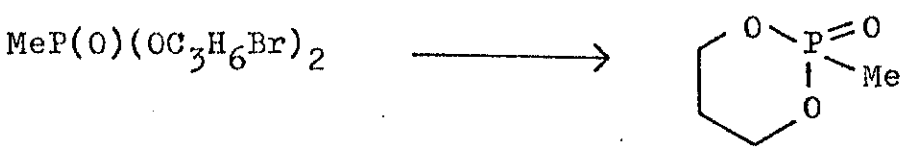
$(EtO_2C)CH_2P(O)(OC_2H_4Cl)_2$

(11)

Although di-(3-bromopropyl)methylphosphonate (12) has been cyclised to phosphonate (7) upon treatment with butyllithium in tetrahydrofuran at -78° [11], this reaction could not be repeated. Furthermore, phosphonate (12) decomposed upon attempted distillation (ca. 120°/0. 1mmHg) to 2-keto 2-methyl 1,3,2-dioxaphosphorinan (13) (Scheme 2).

Though tris-(2-chloroethyl)phosphite underwent an Arbusov reaction with ethyl bromoacetate at 100° to yield phosphonate (11) in 80% yield, tris-(3-chloropropyl)phosphite did not, under reflux, react in such fashion with either methyl bromoacetate or chloroacetonitrile, to yield possible precursors for phosphonates (9) and (10).

Amide bases, such as lithium N-2-propylcyclohexylamide, have been found to be capable of generating the lithioanion of dimethylmethylphosphonate, in tetrahydrofuran at -78°. At 20°, however, phosphonamides were the major products.



(12) (13)

Scheme 2

Chapter 3.

This chapter is concerned with an investigation of the reactions of 2-hydroxyalkyldiphenylphosphine sulphides with base. The analogous 2-hydroxyalkyldiphenylphosphine oxides, upon treatment with suitable base, fragment in Horner fashion[12] to olefin and diphenylphosphinate[13]. A number of structural types of the phosphine sulphides have been examined, and two different pathways of decomposition, upon treatment with suitable base, have been found:

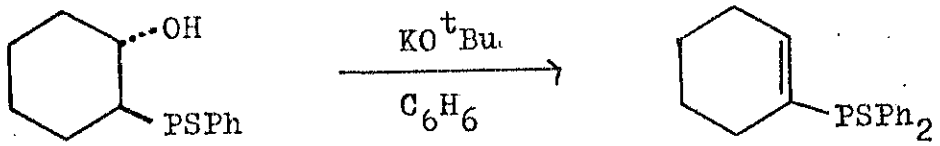
a) Cleavage of the C_1 - C_2 bond (e.g. Scheme 3)

b) Dehydration (e.g. Scheme 4)

Decomposition in mode b) has so far only been observed where C_1 - C_2 is part of a ring system. The choice between a) and b) for a given phosphine sulphide is considered to be due to entropy effects.

$$Ph_2P(S)CH_2\text{-}\ C(OH)Ph_2 \xrightarrow[2)\ H_2O]{1)\ NaH/C_4H_8O} Ph_2P(S)CH_3 + Ph_2CO$$

Scheme 3.

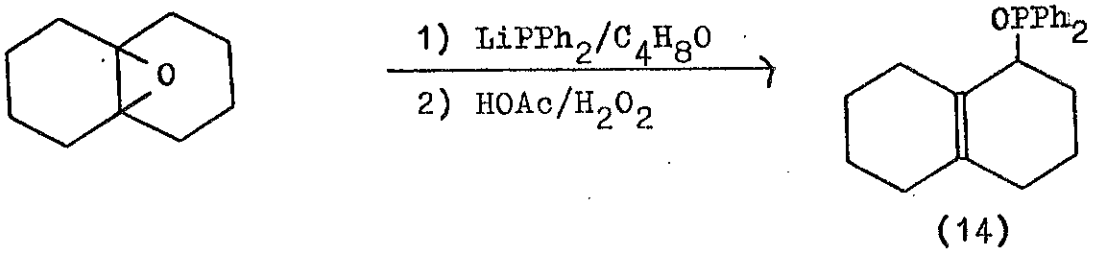


Scheme 4.

The lithium alkoxides of 2-hydroxyalkyldiphenylphosphine sulphides are stable, in all cases examined. This behaviour is analogous to the

corresponding alkoxides of the phosphine oxides[14].

Lithium diphenylphosphide was treated with a number of epoxides to yield (after suitable work-up) 2-hydroxyalkyldiphenylphosphine oxides and sulphides. In contrast, treatment of 11-oxa tricyclo [4.4.1.0 ^{1,6}] undecane with lithium diphenylphosphide led to the isolation of the allylphosphine oxide (14) (and of the corresponding sulphide) in 90% yield (Scheme 5).

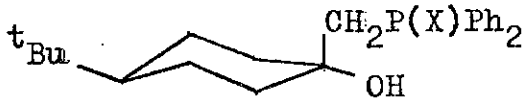


(14)

Scheme 5.

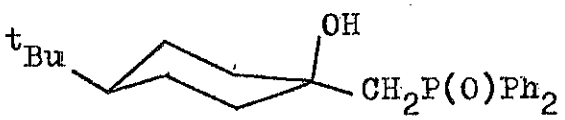
Fusion of (14) with sodium hydroxide at 280° gave a mixture of benzene and bicyclo[4.4.0] dec-9-ene. (14) was unaffected by treatment with potassium tert-butoxide in refluxing benzene. In contrase, the corresponding phosphine sulphide gave an oil tentatively assigned as a 1:2 mixture of starting material and the $\Delta^{1,2}$ isomer.

Lithiomethyldiphenylphosphine sulphide underwent addition to 4-t-butylcyclohexanone to give the axial phosphine sulphide (15), whilst lithiomethyldiphenylphosphine oxide gave a 2:1 mixture of the equatorial (16) and axial (17) phosphine oxides. The mixture of (16) and (17), upon treatment with potassium t-butoxide in refluxing benzene, gave 4-t-butylmethylenecyclohexane in 84% yield, by a Horner reaction.



(15) X = S

(17) X = O

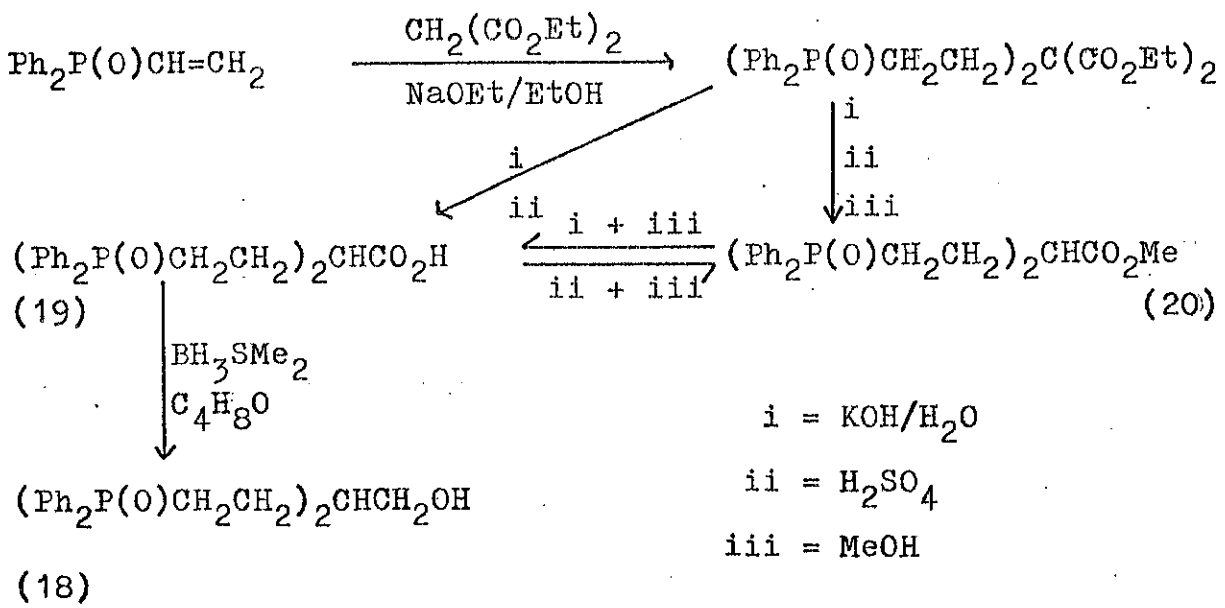


(16)

Chapter 4

A possible route to cyclobutanes via a modification of the Horner reaction analogous to the fragmentation with base of 3-hydroxyalkyldiphenylphosphine oxides to cyclopropanes[15] is described in this chapter. A route to the possible precursor 2,2-bis-(2-diphenylphosphinylethyl) ethanol (18) is shown in Scheme 6.

Acid (19) and the methyl ester (20) were not reduced to alcohol (18) by treatment with lithium aluminium hydride under a variety of conditions. In addition, methyl ester (20) was hydrolysed only slowly to acid (19) by treatment with refluxing aqueous methanolic potassium hydroxide. These results are rationalised by an extension of Newman's 'rule of six'[16].



Scheme 6

Alcohol (18) was unaffected by treatment with a range of base systems. Possible reasons for the failure of such 4-hydroxyalkyldiphenylphosphine oxides to act as cyclobutane precursors are discussed. An analogous abortive route to benzylcyclobutane was attempted.

Chapter 5.

This chapter is concerned with a 'one-pot' conversion of triphenylphosphine to benzylmethylphenylphosphine oxide. Treatment of triphenylphosphine with lithium in tetrahydrofuran results in cleavage of a P - Ph bond to yield phenyllithium and lithium diphenylphosphide[17]. Treatment of the lithium diphenylphosphide with iodomethane, followed by treatment with lithium, benzyl bromide, and hydrogen peroxide yielded benzylmethylphenylphosphine oxide in 9% yield, after fractional crystallisation. Benzyldiphenylphosphine oxide (5.4%) was another isolated product.

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