Rearrangement of *N*-Phosphinoyl-*O*-sulphonylhydroxylamines and *α*-Bromomethylphosphonamidates: A Stereochemical Study

Thesis submitted for the Degree of
Doctor of Philosophy
at the University of Leicester

by

Ramesh Sreedharan-Menon
Department of Chemistry
University of Leicester

October 1993

ProQuest LLC
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106-1346

To Mum

Acknowledgements

I would like to give special thanks to Martin Harger, whose help and guidance has been invaluable throughout the past four years.

I would like to thank Dr. John Fawcett and Dr. David. R. Russell for performing the X-ray crystallography, and especially for solving those awkward crystal structures.

I would also like to thank everyone in the Organic Labs, especially those who were in my year, for moral support, and the rest of the Academic staff and the technicians in the department for all their help.

Finally I would like to thank the SERC for their funding.

R. Sreedharan-Menon

ABSTRACT

Rearrangement of *N*-Phosphinoyl-*O*-sulphonylhydroxylamines and

α-Bromomethylphosphonamidates: A Stereochemical Study

Part 1

The diastereoisomerically enriched *N*-phosphinoyl-*O*-sulphonylhydroxylamines PhCHMeP(O)(Ph)NHOX [X = methanesulphonyl (Ms) or *p*-nitrobenzenesulphonyl (Ns)] react with $MeNH_2$ and Bu^tNH_2 (neat, 1.0 M, and 0.1 M in CH_2Cl_2) to give the expected diamide rearrangement products PhCHMeP(O)(NHPh)NHR (R = Me or Bu^t). The rearrangement proceeded with high stereospecificity for all concentrations of $MeNH_2$ and for neat Bu^tNH_2. Single crystal X-ray analysis revealed that rearrangement with $MeNH_2$ proceeded largely with retention of configuration at phosphorus. Stereochemical and competition studies on PhCHMeP(O)(Ph)NHOX (X = Ms or Ns) and studies on the enantiomers of $Ph_2P(O)NHOS(O)_2$Camphor have provided strong evidence for phosphonamidic-sulphonic mixed anhydride RP(O)(NHPh)OX (X = Ms or Ns) involvement in the rearrangement. $MeNH_2$ and Bu^tNH_2 also reacted with PhCHMeP(O)(Ph)NHOMs (S_N2 at N) giving the hydrazides PhCHMeP(O)(Ph)NHNHR (R = Me or Bu^t). This was more important for Bu^tNH_2 and competition studies with $(Me\text{-}C_6H_4\text{-}CH_2)_2P(O)NHONs$ using equimolar mixtures of Bu^tNH_2-Bu^tMeNH and Bu^tNH_2-$Pr^i{}_2NH$ showed that Bu^tMeNH was 11.5 times better than Bu^tNH_2 for hydrazide formation while Bu^tNH_2 was only slightly better than $Pr^i{}_2NH$.

Part 2

The diastereoisomers of the α-bromomethylphosphonamidate $BrCH_2P(O)(NHBu^t)$OMenthyl react with $PhCH_2N^+Me_3$ $^-$OMe (QOMe) to give the aminomethylphosphonate $Bu^tNHCH_2P(O)(OMe)$OMenthyl and phosphoramidate Bu^tMeNP(O)(OMe)OMenthyl products resulting from the breakdown of an azaphosphiridine oxide intermediate. Single crystal X-ray analysis revealed that the aminomethylphosphonate was formed with inversion of configuration at phosphorus and that the phosphoramidate was formed very largely with retention of configuration at phosphorus, providing further evidence for azaphosphiridine oxide involvement. The α-bromomethylphosphonamidates $BrCH_2P(O)(NHBu^t)OR$ (R = Me, Cyclohexyl, or Bu^t) react with QOMe and $KOBu^t$ to give the corresponding aminomethylphosphonate and phosphoramidate rearrangement products. It was found that bulky OR groups in the substrate and bulky alkoxides enhance the yield of the aminomethylphosphonate product.

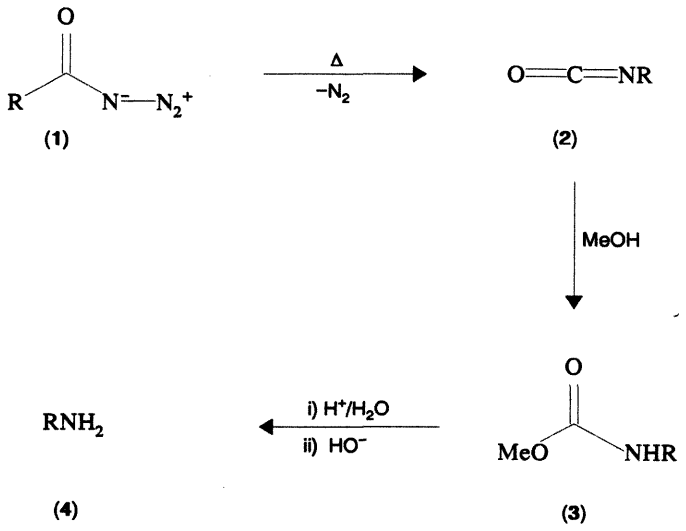
Contents

List of Abbreviations

THF	Tetrahydrofuran
DMF	*N*,*N*-Dimethylformamide
Ms	Methanesulphonyl
Ns	*p*-Nitrobenzenesulphonyl
Cam-SO_3-	Camphor-10-sulphonyl
Men	Menthyl
Me	Methyl
Et	Ethyl
Pr^i	Isopropyl
Bu	Butyl
Bu^t	*tert*-Butyl
Cy	Cyclohexyl
Ar	Aryl
Ph	Phenyl
Q	Benzyltrimethylammonium

Part I; Chapter 1: Introduction

The Curtius, Hofmann, and Lossen Rearrangements

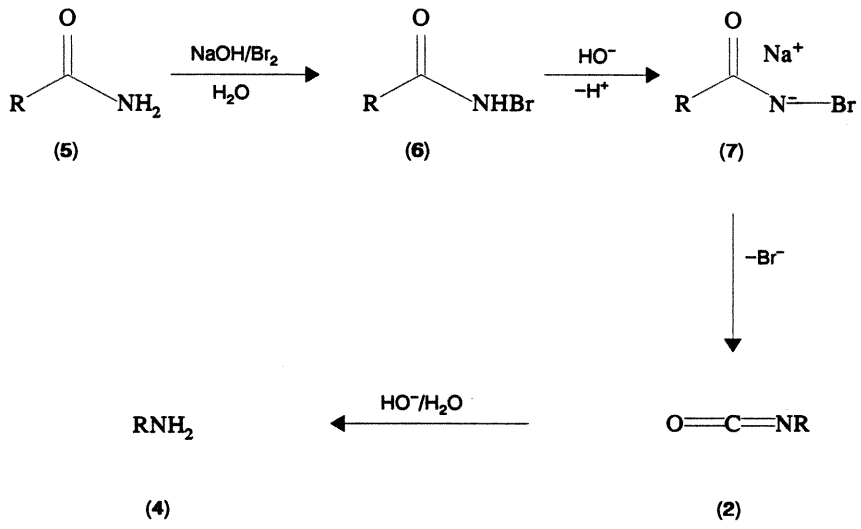


Scheme 1

Acyl azides (1) undergo the Curtius rearrangement on heating.[1,2] The substituent on the carbonyl group migrates to the acyl nitrogen, with concerted elimination of nitrogen, to give the isocyanate (2). The isocyanate may be isolated in high yield[2] and reacted further with a nucleophile such as methanol to give the carbamate (3); the carbamate is normally hydrolysed to the amine (4) (acid hydrolysis followed by treatment with base) (Scheme 1).

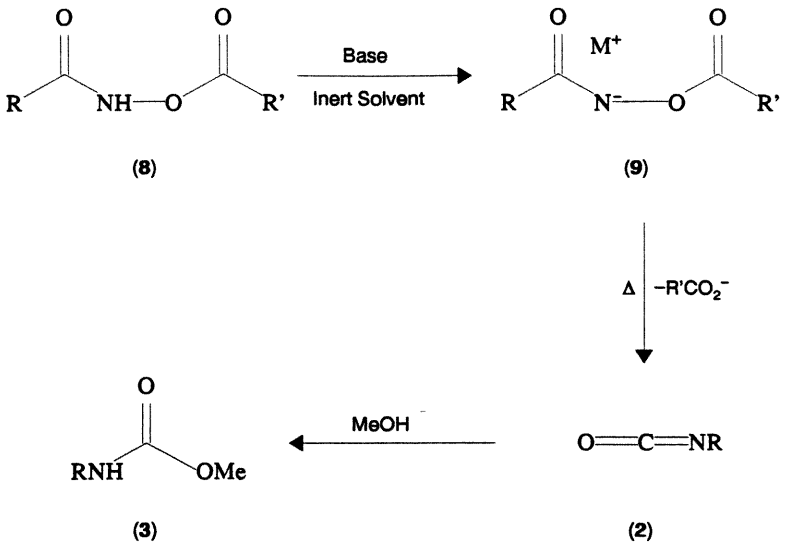
Acyl amides (5) react with aqueous sodium hydroxide and bromine (sodium hypobromite *in situ*) to give *N*-bromocarboxamides (6). Deprotonation of an *N*-bromocarboxamide at nitro-

gen by sodium hydroxide gives the unstable salt (7) which undergoes the Hofmann rearrangement to the isocyanate (2).[3] The isocyanate may be isolated under special conditions but it is normally hydrolysed by excess sodium hydroxide to the amine (4) (Scheme 2).



Scheme 2

O-Acyl derivatives of hydroxamic acids (8) give stable salts (9) when treated with base at low temperatures. On heating, these salts undergo the Lossen rearrangement,[4] eliminating the *O*-acyl group, to give isocyanates (2) (Scheme 3). The isocyanates may be isolated and reacted with a nucleophile of choice, such as methanol to give the carbamate (3), but generally the Curtius rearrangement is preferred for this, since acyl azides are more readily accessible than hydroxamic acid derivatives.



(8) (9) (3) (2)

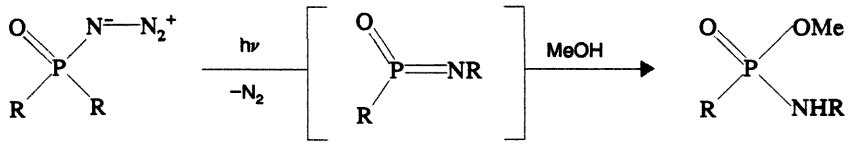
Scheme 3

Phosphinic Azides

(10) (11)

Phosphinic azides (12) undergo a Curtius-like rearrangement on photolysis to give the phosphorus equivalent of the isocyanate, the monomeric metaphosphonimidate (10).[5,6] A monomeric metaphosphonimidate, like monomeric metaphosphate (11),[7] is a planar three-co-ordinate pentavalent species and a powerful electrophile which would polymerise if it were not trapped by a nucleophile, such as methanol to give the phos-

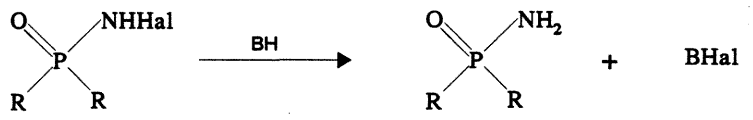
phonamidate (13) (Eq. 1). There is some evidence for thermal rearrangement of phosphinic azides (T > 200 °C),[8] but the metaphosphonimidates have not been trapped. Studies on the thermal rearrangement are of limited value since the azide group is prone to nucleophilic displacement from phosphorus at temperatures much lower than those required to bring about rearrangement.[5]



(12) (10) (13)

Eq. 1

_N_-Halogenophosphinic Amides

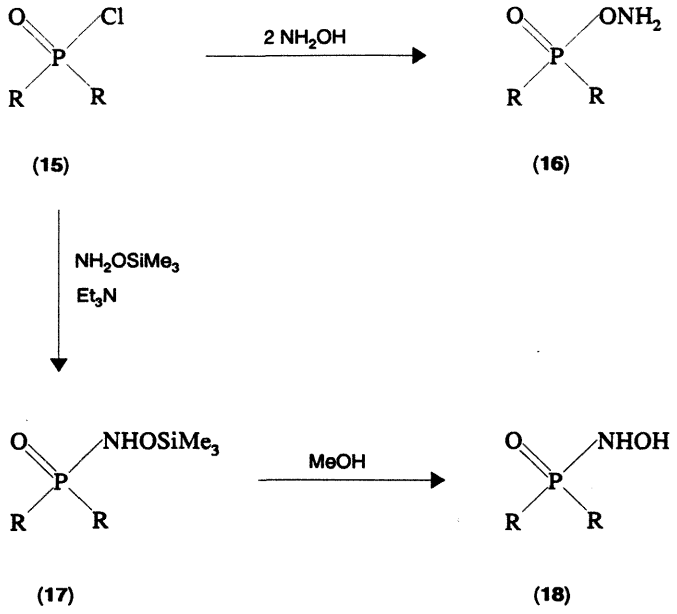


(14)

Eq. 2

_N_-Halogenophosphinic amides (14),[9] unlike their carbon analogues, _N_-halogenocarboxamides, do not rearrange on treatment with base but act as halogenating agents instead (Eq. 2).

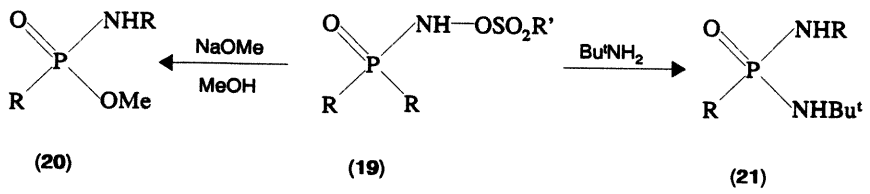
***N*-Phosphinoyl-*O*-sulphonylhydroxylamines**



Scheme 4

The possibility that derivatives of *N*-phosphinoylhydroxylamines (18), the phosphorus analogues of hydroxamic acids, might undergo a Lossen-like rearrangement has been considered. However, the preparation of *N*-phosphinoylhydroxylamines (18) is not as straightforward as might be expected. Unlike the reactions of hydroxylamine with acyl and sulphonyl chlorides,[10,11] which give the *N*-substituted hydroxylamines, the reaction of phosphinic chlorides (15) with hydroxylamine gives the *O*-phosphinoylhydroxylamines (16) (Scheme 4).[12] However, *N*-phosphinoylhydroxylamines (18) can be prepared by treating phosphinic chlorides (15) with *O*-trimethylsilylhydroxylamine and triethylamine,[13] giving *N*-phosphinoyl-

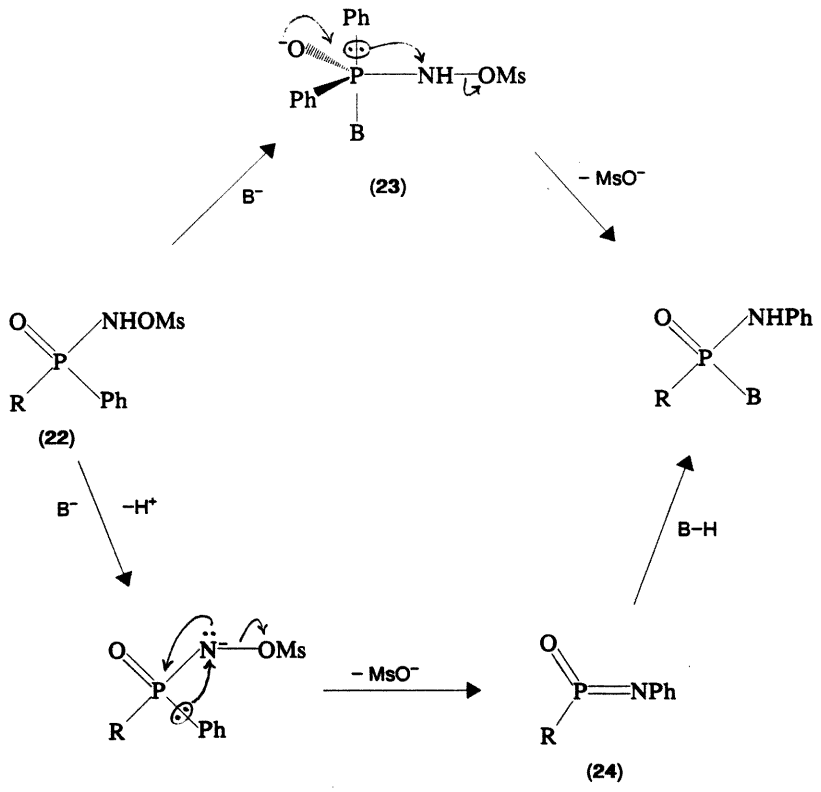
-*O*-trimethylsilylhydroxylamines (17), followed by treatment with methanol to remove the *O*-silyl blocking group (Scheme 4).



Scheme 5

The *O*-acyl derivatives of *N*-phosphinoylhydroxylamines, unlike their carbon counterparts, do not rearrange when treated with base.[14,15] However, the *O*-sulphonyl derivatives (19) do undergo Lossen-like rearrangement;[13] treatment with sodium methoxide in methanol at room temperature gives phosphonamidates (20) (Scheme 5), and rearrangement is seen even with weak bases, such as *tert*-butylamine giving phosphonic diamides (21).

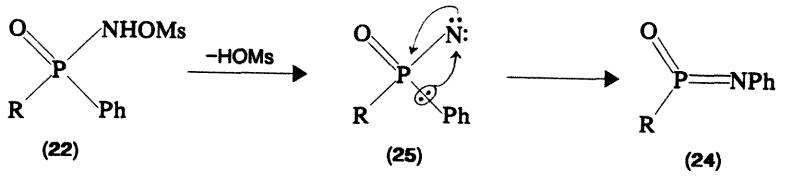
Initial experiments were confined to aryl migration, but rearrangement is not restricted to substrates containing aryl substituents; further study showed that the migratory aptitudes of the groups attached to phosphorus are in the order PhNH, Me_2N >> Ar >> benzyl > alkyl.[16-20] Amino groups migrate exclusively over everything else while aryl groups migrate exclusively over alkyl and benzyl groups; oxygen migration is not seen.[21] Substituents on the phenyl group also affect migration,[14] with electron releasing groups promoting migration and electron withdrawing groups having the reverse effect.



Scheme 6

The reaction of the *N*-phosphinoyl-*O*-sulphonylhydroxylamines (**22**) (R = Me, Et, Pr^i, and Ph) with an equimolar mixture of isopropylamine and *tert*-butylamine (no solvent) under competitive conditions showed little selectivity.[22] By contrast, $Ph_2P(O)Cl$ showed complete selectivity (> 99 %) for the less hindered isopropylamine nucleophile.[22] This clearly suggested that the hydroxylamine derivatives do not react by an associative mechanism like that prevailing for the phosphinic chloride substitution reactions - the rearrangement does not

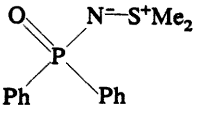
proceed through the phosphorane (23) (Scheme 6; top pathway). Furthermore the *N*-phosphinoyl-*O*-sulphonylhydroxylamines (22; R = Me) and (22; R = Pr^i) reacted at similar rates with methylamine, and with sodium methoxide in methanol.[17] The reactions of the hydroxylamine derivatives are therefore insensitive to steric congestion in the substrate, as well as in the nucleophile, whereas associative nucleophilic substitution at phosphoryl centres is greatly hindered.[23] These observations were thought to point to a mechanism involving the metaphosphonimidate (24). In its rate limiting formation, the reagent would act as a base, not as a nucleophile, and steric effects in the substrate would be of little consequence. In its reactions, because it is both sterically accessible (three-co-ordinate and planar) and a powerful electrophile, it would be unlikely to discriminate between the nucleophiles.



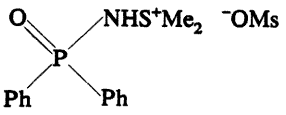
Scheme 7

The metaphosphonimidate might be formed (after initial deprotonation of the substrate at nitrogen by base) either by a group migrating from phosphorus to nitrogen, with displacement of the leaving group (Scheme 6; bottom pathway) or by rearrangement of a singlet nitrene (25) (Scheme 7). The reaction of the methanesulphonate (22; R = Ph) with *tert*-butylamine in dimethyl sulphide (solvent and nitrene trap[24])

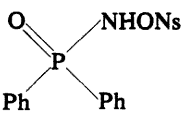
gave some of the sulphilimine (26), the by-product expected for nitrene addition to dimethyl sulphide.[25] However, the methanesulphonate (22; R = Ph), normally stable in solution, reacted with dimethyl sulphide in the absence of base to give the salt (27) (nucleophilic displacement at nitrogen), which, on treatment with *tert*-butylamine, was immediately converted into the sulphilimine (26). This showed that the sulphilimine could be formed by a non-nitrene pathway which might even be competitive with the base induced rearrangement. Furthermore, the nosylate (28), which reacted very much faster with *tert*-butylamine in dimethyl sulphide, gave none of the sulphilimine by-product. Changing the nature of the leaving group should not influence the ability of dimethyl sulphide to trap a nitrene, but for a non-nitrene mechanism the more electronegative nosylate leaving group could enhance deprotonation at nitrogen with respect to nucleophilic attack at nitrogen (salt formation) and rearrangement would proceed much faster, *i.e.* sulphilimine by-product formation would be less competitive. For these reasons the rearrangement is thought not to involve a nitrene mechanism.



(26)



(27)



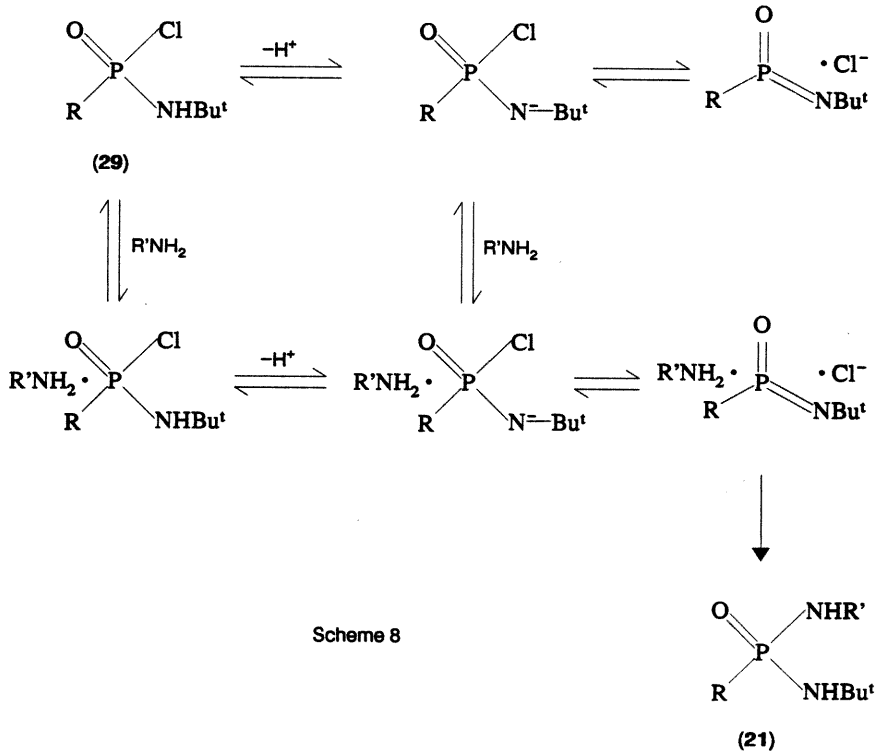
(28)

When the reactions of the *N*-phosphinoyl-*O*-sulphonylhydroxylamines (22; R = Me, Et, Pr^i, and Ph) with an equimolar mixture of isopropylamine and *tert*-butylamine were examined in

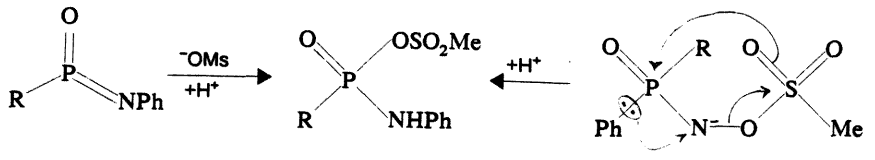
dichloromethane solution they exhibited increasing selectivity for the less hindered nucleophile with increasing dilution.[22] This unexpected behaviour is clearly not consistent with a free metaphosphonimidate as the reaction intermediate. A similar increase in selectivity with dilution was also found for the phosphonamidic chlorides (29; R = Me, Et, Pr^i, Bu^t, Ph, and *o*-tolyl) with the same amine mixture.[26] Kinetic studies on the phosphonamidic chloride (29; R = Ph),[26] with isopropylamine and *tert*-butylamine, showed that reaction was second order in amine at high amine concentrations and first order in amine at low amine concentrations.

If a metaphosphonimidate is generated from the phosphonamidic chloride, and it has an extremely short life span, such that it cannot diffuse into the bulk solvent, it will only be able to react with the nucleophile if it is already in position; otherwise, it will merely revert to starting material (Scheme 8; top pathway). To achieve substitution, preassociation of the nucleophile with the phosphonamidic chloride (or its conjugate base) will therefore be required.[27] Then, since the nucleophile is already present when the metaphosphonimidate is formed, it can react to give the substitution product (21) (Scheme 8; bottom pathway). This preassociation elimination-addition mechanism will be second order in amine (base and nucleophile) and will be important, relative to first order $S_N2(P)$, at high amine concentrations. Since the reactive species in the elimination-addition pathway will be the metaphosphonimidate, the observed low selectivity at high amine concentrations can be understood. At lower concentrations, $S_N2(P)$ will be more important, and

greater selectivity will be observed. If the metaphosphonimidate could exist as the free species, preassociation would not be necessary and elimination-addition would, like $S_N2(P)$, be first order in amine. Then the relative contributions of elimination-addition and $S_N2(P)$ would not depend on the concentration of the amine, and the observed selectivity (or lack of it) would not change on dilution.

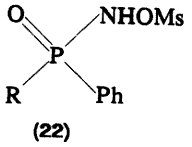


Scheme 8

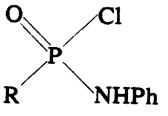


(30)

Scheme 9



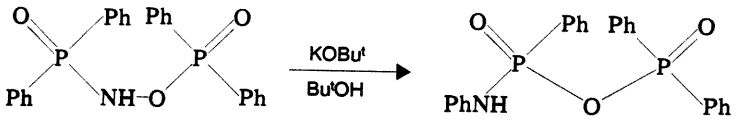
(22)



(31)

Owing to the similarities in the selectivities of the reactions of the phosphonamidic chlorides (29) and the *N*-phosphinoyl-*O*-sulphonylhydroxylamines (22), it was suggested that the reaction intermediate for the latter was the phosphonamidic-sulphonic mixed anhydride (30).[22] This could be formed either by combination of the sulphonate leaving group with the metaphosphonimidate, or directly (after deprotonation at nitrogen) by a concerted rearrangement of the conjugate base of the substrate (Scheme 9). The observed increase in selectivity for the less hindered nucleophile with dilution could then be explained if the mixed anhydride were to behave like the analogous phosphonamidic chloride (31). The postulated phosphonamidic-sulphonic mixed anhydride (30) was not detected spectroscopically, but this could be attributed to it having very high reactivity. The case for its formation was strengthened by a study which showed that the conjugate base of the *N,O*-diphosphinoylhydroxylamine

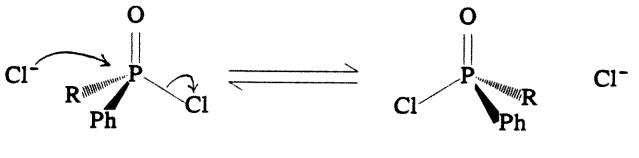
(32), formed from reaction of (32) with potassium *tert*-butoxide in *tert*-butanol, rearranged to the phosphonamidic-phosphinic mixed anhydride (33) (Eq. 3).[28]



(32) (33)

Eq. 3

Knowledge of the stereochemistry of the rearrangement of an *N*-phosphinoyl-*O*-sulphonylhydroxylamine would be useful in determining the nature of the reaction intermediate. To obtain this, we need to observe the change in configuration at a chiral phosphorus centre. Ideally one would study enantiomers, but the precursor to an enantiomer of an *N*-phosphinoylhydroxylamine is an enantiomer of a phosphinic chloride (34). This would be difficult to obtain in an optically pure form and would readily racemise in the presence of chloride ions (Eq. 4). Separation of the enantiomers at the later stages of synthesis would not be feasible and analysis of substrate and product would require the use of chiral chromatography columns and NMR shift reagents.



(34)

Eq. 4

Unlike the Lossen rearrangement, where there is only one group that can migrate, the phosphorus equivalent has two potential migrating groups. If these are different, the phosphorus will be chiral, and if one of the groups is itself chiral, then the compound will exist as diastereoisomers. The advantages of using diastereoisomers would be the relatively easy separation of stereoisomers at the *N*-phosphinoylhydroxylamine stage, or at the final stage of synthesis, and the relatively straightforward analysis of substrates and products by conventional GLC and ^{1}H and ^{31}P NMR spectroscopy. Furthermore, if the chiral group on phosphorus did not migrate, its configuration could not change; it would then be possible to determine any change of configuration at phosphorus relative to this chiral reference group.

It is known that benzyl does not migrate when it is in direct competition with a phenyl group,[19] and it was anticipated that an α-methylbenzyl group would probably behave similarly. Since only the change of configuration at phosphorus is required, relative to the fixed configuration of the reference group, it is not necessary to know the absolute configuration of the α-methylbenzyl reference group. Indeed, the study can be conducted on racemic diastereoisomers.

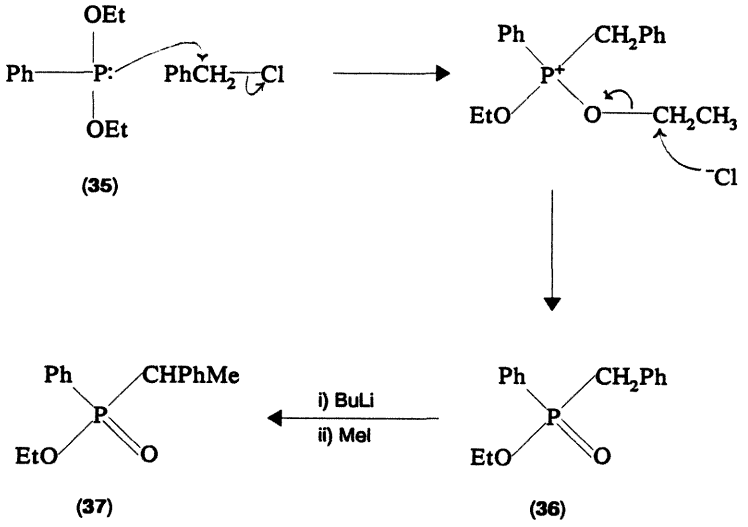
A minor disadvantage of using diastereoisomers is that the outcome of non-stereospecific reaction cannot be (quantitatively) predicted. If the reaction proceeds through a free planar monomeric metaphosphonimidate, both diastereoisomers of substrate will give product having the same stereochemistry (complete non-stereospecificity), but this need not be a 1 : 1 mixture of diastereoisomers; the faces of the meta-

phosphonimidate are diastereotopic, and its reaction may proceed with asymmetric induction (stereoselectivity). Therefore, both diastereoisomers (or enriched mixtures) must be studied, to see if a common diastereoisomer ratio for the product is obtained; this would be the equivalent of racemisation for a reaction performed with enantiomers. Thus, for example, a 3 : 1 mixture and a 1 : 3 mixture of the diastereoisomers of the substrate should both react to give, say, a 45 : 55 mixture of the diastereoisomers of the product if the reaction is completely non-stereospecific but slightly stereoselective. If the reaction proceeds through the phosphonamidic-sulphonic mixed anhydride, there exists the possibility that the rearrangement leading to it could take place with some degree of stereospecificity; reaction of the mixed anhydride with a non-bulky nucleophile at low concentrations [$S_N2(P)$ mechanism] would transfer this stereochemical information to the final product.

A more serious disadvantage of using diastereoisomers is that they may, in principle, behave rather differently. This point will be considered later.

Part I; Chapter 2: The Lossen-Like Rearrangement of *O*-Sulphonyl Derivatives of *N*-[α-Methylbenzyl(phenyl)phosphinoyl]-hydroxylamine

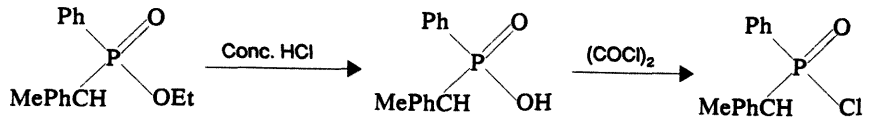
Preparation of the Phosphinic Chloride



Scheme 10

The known ester (36),[29] $\delta_P(CDCl_3)$ 40.1, was prepared cleanly from the Arbuzov reaction of diethyl phenylphosphonite (35) with benzyl chloride (1.2 mol equiv.).[30] Treatment of the ester (36) with *n*-butyllithium (1.0 mol equiv.) in THF-hexane at -70 °C, followed by reaction with iodomethane (2.0 mol equiv.) gave the ester (37), $\delta_P(CDCl_3)$ 44.3 and 43.4, in high yield, as a 47 : 53 mixture of diastereoisomers (Scheme 10). The more direct route to the ester (37), by the Arbuzov reaction of diethyl phenylphosphonite with α-methylbenzyl bromide, was less satisfactory. It gave two additional prod-

ucts, believed to be EtPhP(O)OEt, δ_P 45 (3 %), resulting from reaction of the phosphonite with ethyl chloride (generated in the reaction), and HPhP(O)OEt, δ_P 24 (21 %), resulting from reaction with HBr (believed to be generated by the thermal decomposition of α-methylbenzyl bromide).



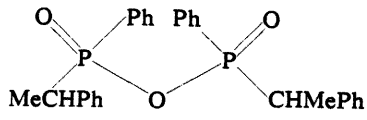
(37) (38) (39)

Eq. 5

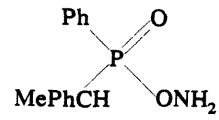
Acid hydrolysis of the ester (37) gave the phosphinic acid (38),[31] $\delta_P(CH_2Cl_2)$ 44.8, and treatment with oxalyl chloride gave the phosphinic chloride (39), $\delta_P(CDCl_3)$ 59.6 and 59.2, as a mixture of comparable amounts of the two diastereoisomers (Eq. 5).

Preparation of the *N*-Phosphinoylhydroxylamine

The reaction of the phosphinic chloride (39) with *O*-trimethylsilylhydroxylamine and triethylamine (1.0 mol equiv.) in dichloromethane gave rise to a series of peaks in the ^{31}P NMR spectrum, δ_P 41.5-40.5 (~ 90 %).[13] These were believed to be due to the phosphinic anhydride (40), but they could conceivably have been the diastereoisomers of the *N*-phosphinoyl-*O*-silylhydroxylamine (42) and their desilylated analogues (43). In the hope that the latter was the case, methanol was added to complete the desilylation process. However, this produced a new compound, δ_P 31.



(40)



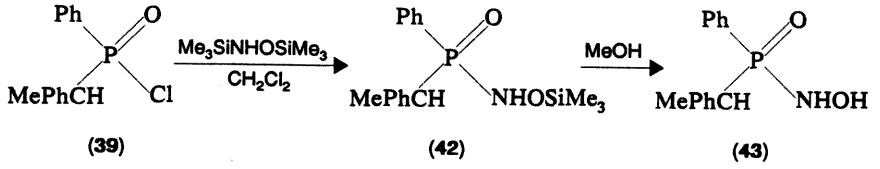
(41)

It seemed possible that the phosphinic chloride (39) was hindered enough to slow down nucleophilic substitution at phosphorus by *O*-trimethylsilylhydroxylamine to the extent that desilylation of the *O*-trimethylsilylhydroxylamine by the phosphoryl group occurred. The liberated hydroxylamine would then compete as a nucleophile with its silylated precursor. This would give the *O*-phosphinoylhydroxylamine (41), which, if unstable under the reaction conditions, could decompose to the salt of the phosphinic acid (38). The salt would react further with the phosphinic chloride to give the phosphinic anhydride (40).

If desilylation of *O*-trimethylsilylhydroxylamine was the problem, then replacing it by *N,O-bis*(trimethylsilyl)hydroxylamine should give better results since the *N*-silyl group, being more reactive, would be expected to be removed first. The reaction of a phosphinic chloride with *N,O-bis*(trimethylsilyl)hydroxylamine has, in fact, recently been reported,[18] and it has been shown that the expected product was formed, along with trimethylsilyl chloride as a volatile by-product.

The reaction of the phosphinic chloride (39) with *N,O-bis*-(trimethylsilyl)hydroxylamine in dichloromethane gave the *N*-phosphinoyl-*O*-silylhydroxylamine (42), $\delta_P(CH_2Cl_2)$ 41.7 and

40.7, as a mixture of comparable amounts of the two diastereoisomers, and a by-product, δ_P 33.7 (*ca.* 10-20 %; variable) (Eq. 6). Fortuitously, the highfield (^{31}P NMR) diastereoisomer of the *N*-phosphinoyl-*O*-silylhydroxylamine (**42**) was less soluble and precipitated from the reaction mixture, to give essentially one diastereoisomer and a mother liquor enriched in the other diastereoisomer. The highfield diastereoisomer (**42**), $\delta_P(CDCl_3)$ 42.0, was completely characterised and showed incorporation of $NHOSiMe_3$: NH, $\delta_H(CDCl_3)$ 5.30 (1 H, s) and $\nu_{max.}$(Nujol) 3130; $OSiMe_3$, $\delta_H(CDCl_3)$ -0.11 (9 H, s); it decomposed at or below its melting point.



(39) (42) (43)

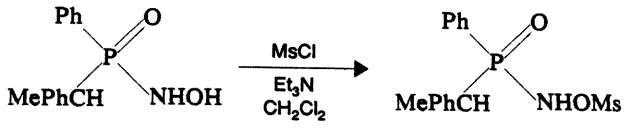
Eq. 6

Desilylation of the enriched mother liquor (see above) with methanol went cleanly and gave the *N*-phosphinoylhydroxylamine (**43**), $\delta_P(CDCl_3)$ 41.9 and 40.1, as a 4.5 : 1 mixture of diastereoisomers (sample **A**) (Eq. 6). Crystallisation of a portion of sample **A** gave an analysis sample that was entirely the lowfield (^{31}P NMR) diastereoisomer. Similar desilylation of the precipitated *N*-phosphinoyl-*O*-silylhydroxylamine (**42**) gave, essentially pure, the highfield (^{31}P NMR) diastereoisomer of the *N*-phosphinoylhydroxylamine (**43**) (sample **B**) (Eq. 6). The ^1H NMR spectra of the two diastereoisomers showed the expected OH signals $\delta_H(CDCl_3)$ 8.5 or 8.1 (samples **A** and **B** respectively) and the NH signals $\delta_H(CDCl_3)$ 6.30 or 5.961 (d;

samples **A** and **B** respectively), the coupling to phosphorus for sample **A** (J_{PH} 11.5) being 30 % larger than that for sample **B** (J_{PH} 8.8). A more striking difference between the diastereoisomers was evident in their IR spectra where, the pure diastereoisomer **A** showed two bands for NH absorption, $\nu_{max.}$(Nujol) 3260 and 3220, instead of one for sample **B**, $\nu_{max.}$(Nujol) 3160.

The preparation of the *N*-phosphinoyl-*O*-trimethylsilylhydroxylamine (**42**) was also performed without separation of the diastereoisomers. Treatment of the mixture with methanol, followed by trituration with ether, gave the *N*-phosphinoylhydroxylamine (**43**) as an *ca.* 1 : 1 mixture of diastereoisomers.

Preparation of the *N*-Phosphinoyl-*O*-sulphonylhydroxylamines



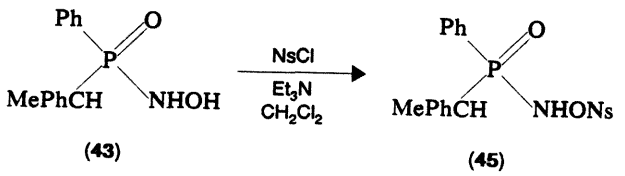
(43) **(44)**

Eq. 7

Samples **A** and **B** of the *N*-phosphinoylhydroxylamine (**43**) were converted into their methanesulphonates (**44**), $\delta_P(CDCl_3)$ 39.6 and 38.4 respectively, in high yield (> 90 %; ~ 60 % after crystallisation), by treatment with methanesulphonyl chloride (1.4 mol equiv.) and triethylamine (1.0 mol equiv.) in dichloromethane (Eq. 7).[18] Crystallisation gave sample **A**, mainly the ^{31}P NMR lowfield diastereoisomer (ratio 80 : 20),

and sample **B**, very largely the sparingly soluble highfield (^{31}P NMR) diastereoisomer (ratio 3 : 97), as determined by ^{31}P and ^{1}H NMR spectroscopy. The ^{1}H NMR spectra of the methanesulphonates showed diastereoisomeric NH signals, $\delta_H(CDCl_3)$ 8.45 and 7.199 (d; samples **A** and **B** respectively), with the coupling to phosphorus for sample **A** (J_{PH} 7) being almost twice that for sample **B** (J_{PH} 3.7). The spectra also showed the characteristic PhP(O) signals, diastereoisomeric α-methyl signals, $\delta_H(CDCl_3)$ 1.70 and 1.550 (dd, J_{PH} 16 or 17.9, J_{HH} 7.5; samples **A** and **B** respectively), showing coupling to the α-hydrogen and phosphorus, and two widely separated diastereoisomeric *S*-methyl singlets, $\delta_H(CDCl_3)$ 3.10 (for sample **A**) and 2.701 (for sample **B**).

The 1 : 1 mixture of diastereoisomers of the *N*-phosphinoylhydroxylamine (**43**) was similarly converted into the methanesulphonate (**44**). Trituration with dichloromethane-ether gave the methanesulphonate as a 39 : 61 mixture of diastereoisomers. To give a 50 : 50 mixture, for use in studies with competing nucleophiles, a calculated amount of the minor diastereoisomer (**A**) was added to the mixture.

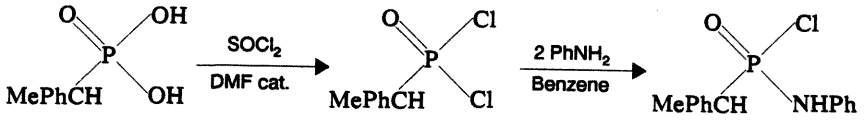


(43) **(45)**

Eq. 8

The reaction of a 1 : 4 mixture of diastereoisomers of the *N*-phosphinoylhydroxylamine (43) (diastereoisomer B in excess) with *p*-nitrobenzenesulphonyl (nosyl) chloride (1.4 mol equiv.) and triethylamine (1 mol equiv.) in dichloromethane (Eq. 8) was almost quantitative, according to the ^{31}P NMR spectrum, but the nosylate (45), $\delta_P(CH_2Cl_2)$ 42.3 and 39.5 (diastereoisomers), was isolated in only about 60 % yield. Crystallisation gave very largely the sparingly soluble highfield (^{31}P NMR) diastereoisomer (3 : 97 mixture of diastereoisomers by ^{31}P NMR spectroscopy). A second preparation gave a similar sample (diastereoisomer ratio 4 : 96) for use in studies with competing nucleophiles.

Preparation of the Phosphonamidic Chloride



(46) (47) (48)

Eq. 9

The phosphonamidic chloride (48) was required for the competition study and the preparation of authentic samples of the expected phenyl-migration rearrangement products. Treatment of the phosphonic acid (46),[32,33] $\delta_P(SOCl_2)$ 34.9, with thionyl chloride and a catalytic quantity of DMF (0.03 mol equiv.) gave the phosphonic dichloride (47), $\delta_P(SOCl_2)$ 54.1. Reaction of this with aniline (2 mol equiv.) in benzene gave the phosphonamidic chloride (48) as a mixture of diastereoisomers (δ_P 41.7 and 41.3) in a ratio *ca.* 1 : 2 (Eq. 9).

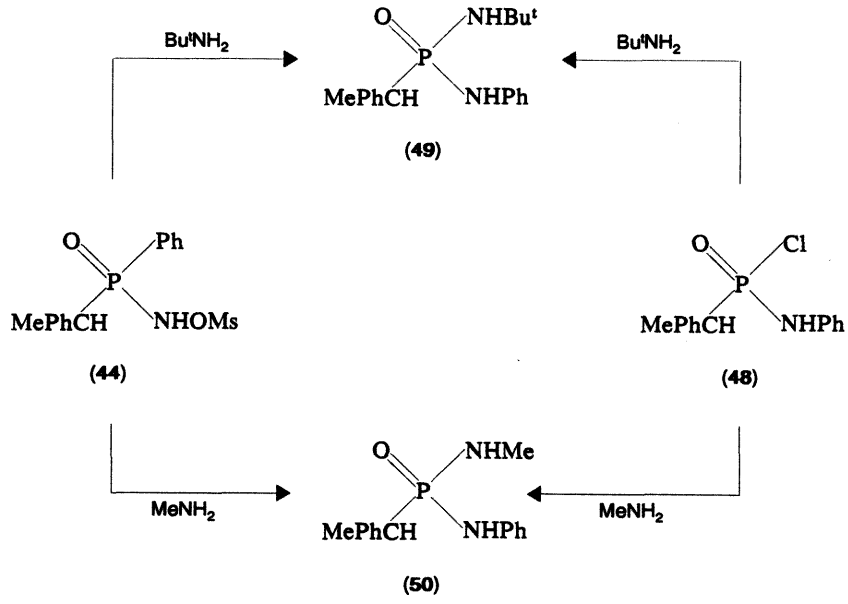
Crystallisation from ether containing benzene gave product having a similar ratio (30 : 70), but crystallisation overnight from a similar solvent mixture gave the pure ^{31}P NMR highfield diastereoisomer.

Reaction of the Methanesulphonate with Amines

The methanesulphonate (44) (samples A and B) was allowed to react with neat *tert*-butylamine and methylamine and also with 1.0 M and 0.1 M solutions in dichloromethane. The products were the diastereoisomeric *N*-*tert*-butylphosphonic diamides (49), δ_P 21.8 and 21.5, or *N*-methylphosphonic diamides (50), δ_P 26.7 and 26.4. The crude products were investigated by ^{31}P NMR spectroscopy in order to obtain their diastereoisomer ratios. The diamides were isolated by partitioning between dichloromethane and water, so that their diastereoisomer ratios could be re-examined by ^{1}H and ^{31}P NMR spectroscopy, and so that their identities could be confirmed.

The ^{1}H NMR spectra of the rearrangement products contained the expected NH and NBu^t or NMe signals, showing incorporation of the amine. They also revealed the absence of the characteristic PhP(O) signals, although the aromatic integrals showed no loss of phenyl, and the α-methyl groups still showed coupling to phosphorus [J_{PH} 17.3 or 17.4 for the diastereoisomers of the *N*-*tert*-butyl-diamide (49), and 17.3 for both diastereoisomers of the *N*-methyl-diamide (50)]. These features indicated phenyl migration to nitrogen (Scheme 11), and further evidence of this was provided by the mass spectra, which showed *m/z* 93 attributable to $PhNH_2^+$. Compar-

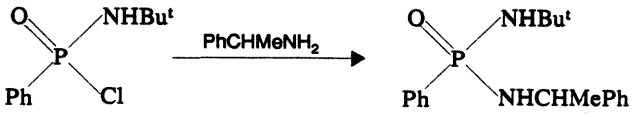
ison of the spectroscopic properties of the products with those of authentic samples, prepared from the phosphonamidic chloride (48) and the appropriate amine (Scheme 11), confirmed their identities.



Scheme 11

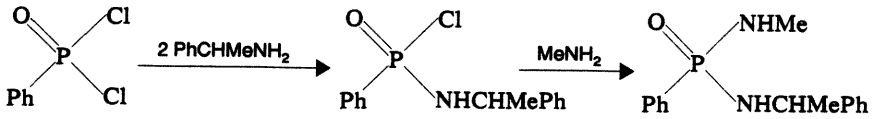
It was clear that the reactions of the methanesulphonate (44) with *tert*-butylamine and methylamine gave largely the products of phenyl migration. To ascertain whether any α-methylbenzyl migration had occurred, authentic samples of these alternative rearrangement products were prepared. Treatment of *N*-*tert*-butyl-*N'*-phenylphosphonamidic chloride (51)[34] with an excess of (±)-α-methylbenzylamine gave an authentic sample of the diamide (52), $\delta_P(CDCl_3)$ 17.3 and 16.5

(diastereoisomers), the products that would result from α-methylbenzyl migration in the with *N-tert*-butylamine (Eq. 10). The diamide (53), $\delta_P(CH_2Cl_2)$ 20.2 and 19.8 (diastereoisomers), that would result from α-methylbenzyl migration in the reaction with methylamine was prepared from phenylphosphonic dichloride and (±)-α-methylbenzylamine (2 mol equiv.), followed by an excess of methylamine (Eq. 11). The ^1H NMR spectra of these compounds showed the characteristic PhP(O) signals, and the α-methyl signals were simply doublets, showing coupling to the α-hydrogen but not to phosphorus. Spectroscopic comparison of the rearrangement reaction mixtures with these authentic α-methylbenzyl-migration products showed that they had not been formed in the reaction (1 % would have been detected).



(51) (52)

Eq. 10

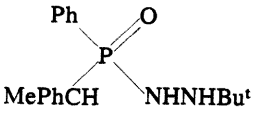


(53)

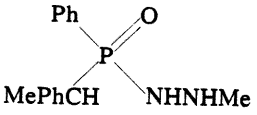
Eq. 11

The reaction of the methanesulphonate (44) with *tert*-butylamine gave a by-product (23 % for 0.1 M Bu^tNH_2), δ_P 33.6. This could be isolated by extraction into aqueous acid (δ_P 41.5),

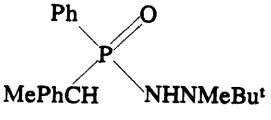
neutralisation, and back-extraction into dichloromethane; it was identified as the hydrazide (54). The identity was confirmed by comparison with an authentic sample prepared from the phosphinic chloride (39) and an excess of *tert*-butylhydrazine in dichloromethane. This hydrazide by-product was presumably formed by nucleophilic displacement of the sulphonate group from nitrogen by the amine, and its formation was seen to be more prominent in the rearrangement reactions using the lower concentrations of amine. The reaction with methylamine also gave a by-product, δ_P 33.8 - presumably the hydrazide (55) - but in lower yield. This seemed surprising, since competition to the base-induced rearrangement from nucleophilic attack at nitrogen might be expected to be more extensive for the less hindered (more nucleophilic) amine. It therefore seemed worthwhile to look briefly at the reaction of the methanesulphonate (44) with *N*-methyl-*tert*-butylamine. This secondary amine is more hindered than either methylamine or *tert*-butylamine, yet it formed substantially more hydrazide (56), $\delta_P(CDCl_3)$ 31.1 (40 % with 1.0 M amine in CH_2Cl_2); the expected diamide rearrangement product (57), δ_P 28.2 and 25.9 (diastereoisomer ratio 42 : 58), was also formed (50 %). Perhaps nucleophilic attack at nitrogen is not susceptible to steric effects in the nucleophile, and larger or more numerous groups in the amine serve only to enhance its nucleophilicity (+I effect).



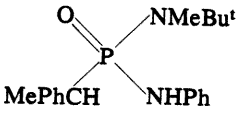
(54)



(55)



(56)

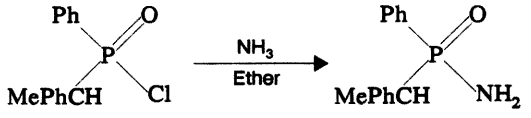


(57)

Hydrazide formation was generally important for the high-field diastereoisomer of the methanesulphonate (**44**) (sample **B**), but was only significant for the lowfield diastereoisomer **A** at low amine concentrations (0.1 M). This demonstrates a potential pitfall of using diastereoisomers, namely their ability to undergo reactions and side-reactions at different rates. This will not be a problem when working with pure diastereoisomers or mixtures of diastereoisomers if there are no side reactions. If, however, one of the diastereoisomers in the mixture is consumed relatively quickly by side reactions, the diastereoisomer composition of the substrate that is converted into product will not be precisely the same as the diastereoisomer composition of the substrate used for doing the experiment.

Other minor by-products having ^{31}P NMR chemical shifts similar to those of the hydrazides were also evident; they were tentatively identified as the diastereoisomers of the phos-

phinic amide (58) by comparison with (^{31}P NMR) an authentic sample of (58) prepared from the phosphinic chloride (39) and an excess of ethereal ammonia (Eq. 12).



(39) (58)

Eq. 12

Stereochemistry of the Rearrangement

The diastereoisomer ratios of the products from the reactions of the methanesulphonates (44) (samples A and B) with *tert*-butylamine and methylamine (neat, 1.0 M, or 0.1 M in dichloromethane) were determined by ^{1}H and ^{31}P NMR spectroscopy. The observed ratios will be affected to some extent by the side reactions that diastereoisomer B preferentially undergoes, since the diastereoisomer composition of the substrate that is converted to product will differ somewhat from the initial ratio in the substrate. The side reactions became more extensive on dilution, so the product diastereoisomer ratios observed at lower concentrations of amine must be interpreted with particular care.

Table 1; Reaction of the methanesulphonate (**44**) with *tert*-butylamine: diastereoisomer ratios of substrate (**A** : **B**) and rearrangement product (**A'** : **B'**).

A : **B**	Bu^tNH_2	**A'** : **B'**
3 : 97	neat[a]	10 : 90
80 : 20		75 : 25
3 : 97	1.0 M[b]	30 : 70
80 : 20	in CH_2Cl_2	67 : 33
3 : 97	0.1 M[b]	41 : 59
80 : 20	in CH_2Cl_2	57 : 43

[a] Neat amine (> 20-fold excess) added to substrate.
[b] Diastereoisomer **B** undergoes extensive side reaction.

The reaction of the methanesulphonate with neat *tert*-butylamine was quite stereospecific; as the concentration of amine was reduced it became less stereospecific, though it still showed appreciable stereospecificity even with 0.1 M *tert*-butylamine (Table 1). The reaction with methylamine differed dramatically, in that it proceeded with near constant stereospecificity at all three concentrations of amine (Table 2). If we are to understand the mechanistic significance of the stereospecificity, we must know whether it corresponds to inversion or retention of configuration at phosphorus.

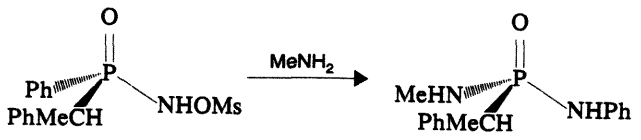
Table 2; Reaction of the methanesulphonate (**44**) with methylamine: diastereoisomer ratios of substrate (**A** : **B**) and rearrangement product (**A'** : **B'**).

A : B	$MeNH_2$	**A' : B'**
3 : 97	neat[a]	7 : 93
80 : 20		79 : 21
3 : 97	1.0 M[b]	8 : 92
80 : 20	in CH_2Cl_2	82 : 18
3 : 97	0.1 M[c]	8 : 92
80 : 20	in CH_2Cl_2	83 : 17

[a] 150 μl neat amine added to substrate at -6 to -10 °C.
[b] Diastereoisomer **B** undergoes some side reaction.
[c] Diastereoisomer **B** undergoes extensive side reaction.

A portion of the 3 : 97 methanesulphonate (sample **B**) was crystallised from dichloromethane to give a crystal of the major diastereoisomer for single crystal X-ray analysis (Fig. 1). That this crystal was indeed the major diastereoisomer was checked, after the X-ray study, by reduction to the phosphinic amide with sodium tetrahydridoborate, and comparison of this (GLC) with the phosphinic amides obtained by reduction of both diastereoisomers of the methanesulphonate. The product formed from the methanesulphonate sample **B** with neat methylamine was crystallised to give pure diastereoisomer **B'** (determined by ^1H NMR spectroscopy) and then recrystallised from toluene gave a crystal suitable for single crystal X-ray analysis (Fig. 2). TLC examination of the crystal after X-ray analysis confirmed that it was indeed the diastereoisomer **B'** of the product. By comparison of the two

stereostructures it can be seen that, in the case of methylamine, the major diastereoisomer of the product was formed from the methanesulphonate with **retention of configuration at phosphorus** (Eq. 13).[35]



Eq. 13

For the reaction with *tert*-butylamine, the sense of the stereospecificity was determined indirectly. The phosphonamidic chloride (**48**) (^{31}P NMR highfield diastereoisomer) reacted with neat methylamine and neat *tert*-butylamine to give the lowfield diastereoisomers of the diamides (**49**) and (**50**) respectively. Assuming that both reactions proceed with the same stereochemistry at phosphorus, then the lowfield diastereoisomers of the two diamides must have the same configuration. The rearrangement reactions of the methanesulphonate sample **B** with the two (neat) amines both gave largely the highfield diastereoisomer; by implication, these have the same configuration, so the rearrangement with *tert*-butylamine must also proceed with **retention of configuration at phosphorus**.

Fig. 1; The structure of *P*-[α-methylbenzyl(phenyl)phosphinoyl]--*O*-methanesulphonylhydroxylamine (**44**) (diastereoisomer **B**) as determined by single crystal X-ray analysis; relative configuration at phosphorus and carbon. Selected bond lengths (Å) and bond angles (°): P-C(1) 1.824(3), P-C(21) 1.786(2), P-N 1.690(2), N-O(2) 1.459(3), C(1)-P-C(21) 109.8(1), C(21)-P-N 109.4(1), N-P-C(1) 98.6(1), C(1)-P-O(1) 115.0(1), C(21)-P-O(1) 111.4(1), N-P-O(1) 111.9(1), P-N-O(2) 111.3(2).

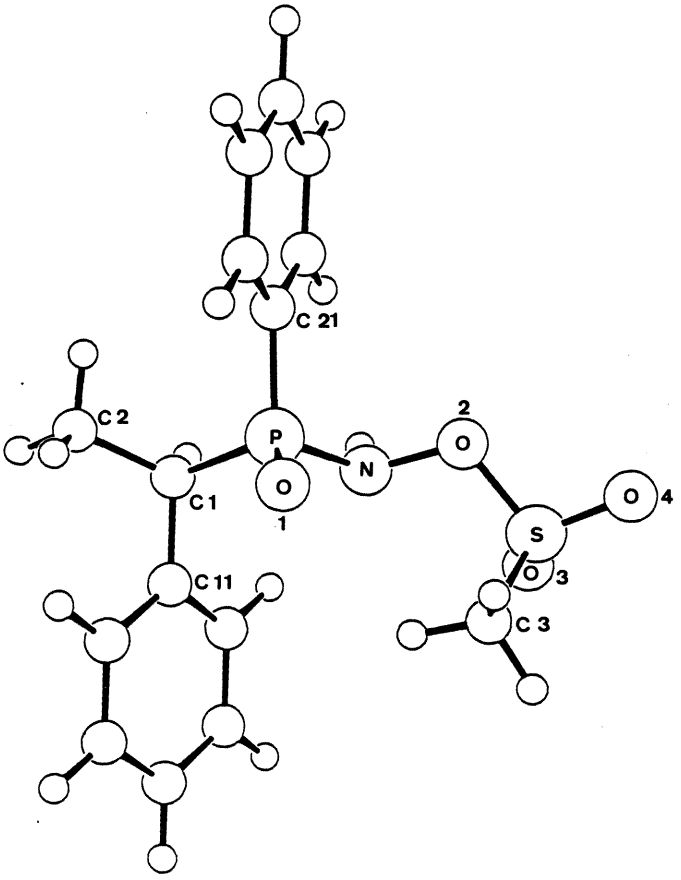
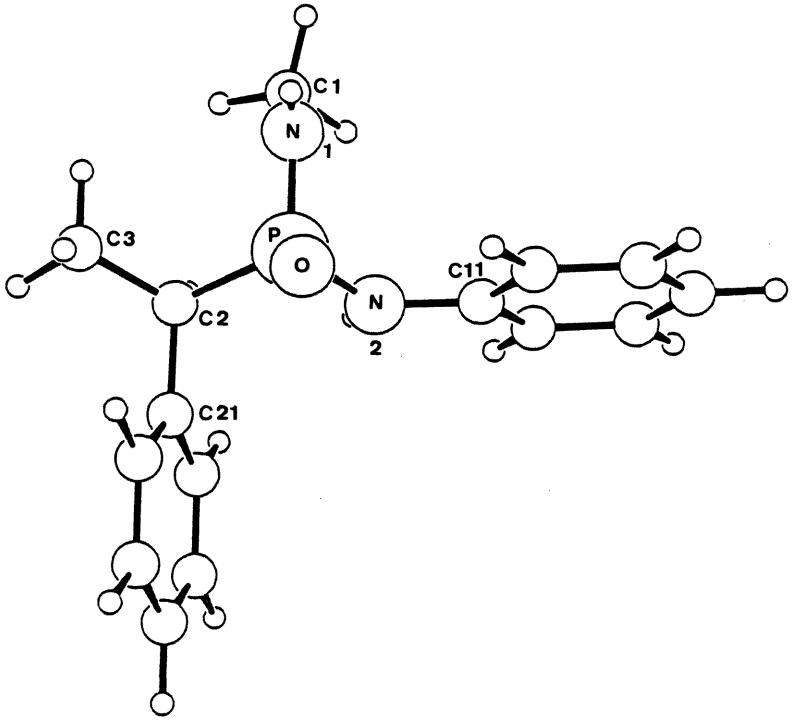


Fig. 2; The structure of *N*-methyl-*N'*-phenyl-*P*-α-methylbenzylphosphonamidate (50) (major diastereoisomer) as determined by single crystal X-ray analysis; relative configuration at phosphorus and carbon. Selected bond lengths (Å) and bond angles (°): P-C(2) 1.825(5), P-N(1) 1.624(6), P-N(2) 1.653(5), N(1)-C(1) 1.477(8), N(2)-C(11) 1.414(5), C(2)-P-N(1) 108.8(3), N(1)-P-N(2) 108.4(3), N(2)-P-C(2) 100.0(2), C(2)-P-O 114.4(2), N(1)-P-O 109.1(3), N(2)-P-O 115.6(2), P-N(1)-C(1) 124.4(5), P-N(2)-C-(11) 128.6(4).

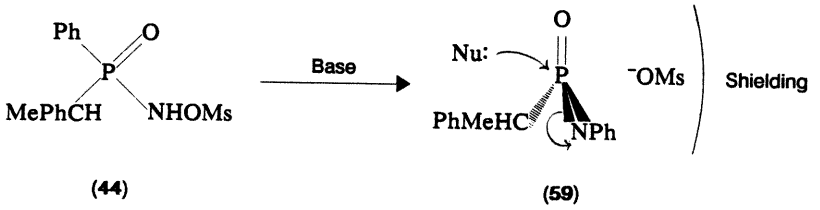


The reaction of the nosylate (45) with methylamine was cleaner than the corresponding reaction of the methanesulphonate (44), with only a small quantity of the hydrazide being formed even at lowest amine concentration (0.1 M). The rearrangement products were again formed largely with **retention of configuration at phosphorus**, for all three amine concentrations, but the reaction was not as stereospecific as for the methanesulphonate. Curiously, the stereospecificity increased (marginally) at lower concentrations (Table 3).

Table 3; Reaction of the nosylate (45) with methylamine: diastereoisomer ratios of substrate (A : B) and rearrangement product (A' : B').

A : B	$MeNH_2$	A' : B'
3 : 97	neat[a]	14 : 86
3 : 97	1.0 M in CH_2Cl_2	12 : 88
3 : 97	0.1 M in CH_2Cl_2	10 : 90

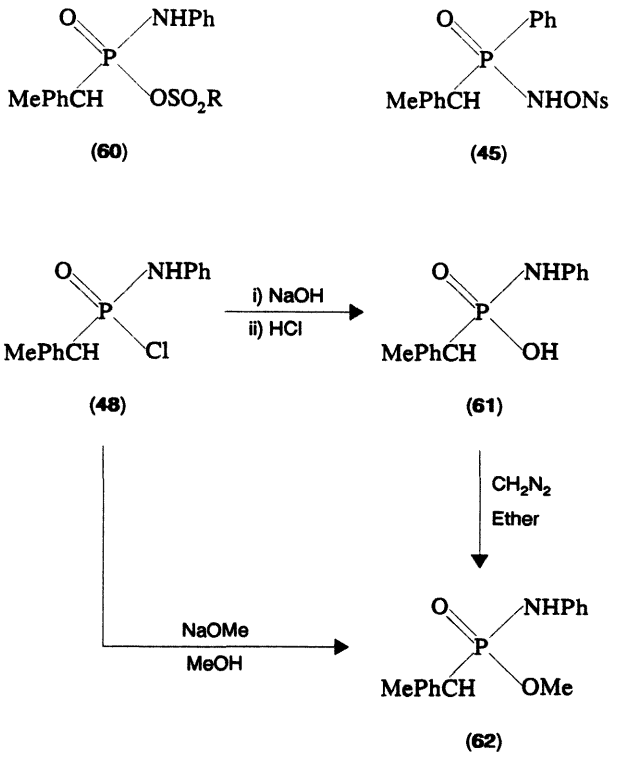
[a] Neat amine added to substrate at -4 °C.



(44) (59)

Scheme 12

If the rearrangement proceeds through a free monomeric metaphosphonimidate (59), a planar species, both diastereoisomers of the substrate will give the same mixture of diastereoisomers of the product. The stereospecificity observed for the rearrangements is therefore not consistent with a free metaphosphonimidate intermediate. If the metaphosphonimidate reacts with the amine before it diffuses away from the leaving group, then the leaving group may shield one face and impose some stereospecificity - presumably with retention of configuration at phosphorus (Scheme 12). At lower amine (nucleophile) concentrations the metaphosphonimidate would have more time to diffuse away from the leaving group before reacting, thus reducing the stereospecificity of product formation. This was indeed observed for the reaction with *tert*-butylamine, but not with methylamine. This mechanism is therefore not consistent with the stereochemical results either. However, it should be recalled that this type of stereochemical behaviour was previously observed for the phosphonamidic chloride $PhP(O)NHBu^tCl$;[26] at lower amine concentrations, substitution showed increasing stereospecificity with isopropylamine as the nucleophile, but loss of stereospecificity with the more hindered *tert*-pentylamine. The behaviour of the methanesulphonate (44) and the nosylate (45) would therefore be consistent with the formation of a phosphonamidic-sulphonic mixed anhydride (60) - analogous to the phosphonamidic chloride (48) - as long as the mixed anhydride were formed with high stereospecificity, and its behaviour resembled that of a phosphonamidic chloride.

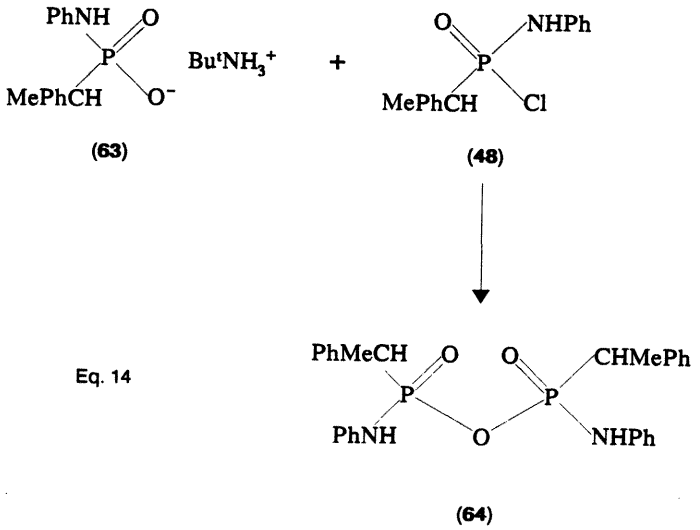


Scheme 13

Evidence for phosphonamidic-sulphonic mixed anhydride involvement came from two minor rearrangement products that were formed in the reactions of the methanesulphonate (**44**) with amine [these products were also seen, in much lower yield, in the reaction of the nosylate (**45**) with 0.1 M methylamine]. The first minor product, δ_P 18, isolated after protonation by extraction in dichloromethane, was identified as the salt of the phosphonamidic acid (**61**) by comparison of the ^1H and ^{31}P NMR spectra of the isolated free acid with those of an authentic sample. The authentic sample was prepared from the phosphonamidic chloride (**48**) by treatment

with aqueous sodium hydroxide, then hydrochloric acid (Scheme 13). Further evidence of the identity of this product was obtained by comparison of the GLC retention time of the methyl ester formed on treatment of the isolated acid with diazomethane, with that of an authentic sample of (**62**), prepared either from the phosphonamidic chloride (**48**) and sodium methoxide, or from the phosphonamidic acid (**61**) and diazomethane (Scheme 13).

The second minor product displayed a series of very close peaks in the ^{31}P NMR spectrum, δ_P 24.4-23.5. It was apparently the phosphonamidic anhydride (**64**), as on prolonged standing in the reaction mixture it was slowly converted into the phosphonamidate salt (**63**). Moreover, the ^{31}P NMR spectrum compared well with that of an authentic sample of the phosphonamidic anhydride (**64**), prepared from the phosphonamidic chloride (**48**) and the *tert*-butylammonium phosphonamidate (**63**) (Eq. 14).



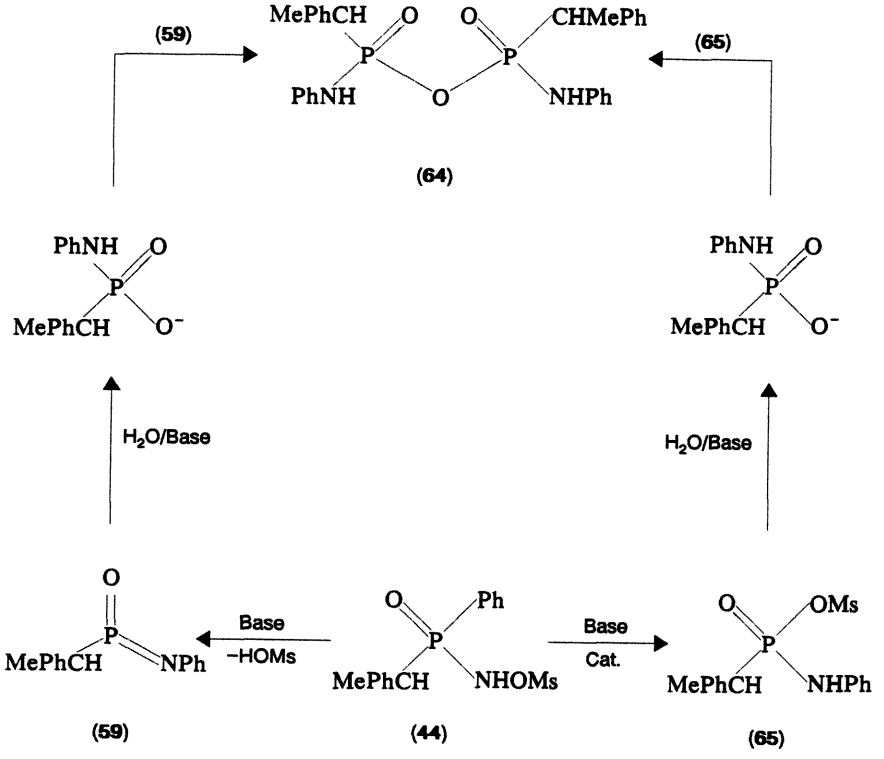
(**63**) (**48**)

(**64**)

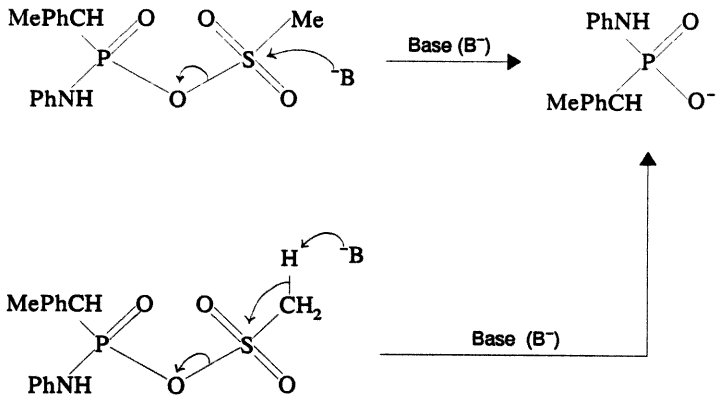
Eq. 14

The conversion of the phosphonamidic anhydride (64) into the phosphonamidate salt was slow, and most occurred only on standing in the reaction mixture, long after the rearrangement was complete. However, some of the salt was already present at the end of the rearrangement [accompanied by much more of the anhydride (64)]. This suggests that the salt is probably formed first, and is converted into the anhydride during the reaction, but the anhydride is subsequently hydrolysed by adventitious water on standing. The phosphonamidate is formally the result of addition of water to the metaphosphonimidate, and in accord with this, it (or the derived phosphonamidic anhydride) became more prominent on dilution, when moisture would be more likely to compete with amine for the metaphosphonimidate (Scheme 14). However, with 1.0 M Bu^tNH_2 in dichloromethane the amount of water relative to amine is expected to be small, yet the phosphonamidate (or the phosphonamidic anhydride) seemed to be disproportionately large. If the reactive species were the metaphosphonimidate, the amount of product due to water would be expected to reflect its proportion in the reaction medium. If, on the other hand, the substrate rearranges to the phosphonamidic--sulphonic mixed anhydride, a reasonable explanation can be found. Now the phosphonamidate ion can be formed from the mixed anhydride not only by reaction with water at phosphorus [$S_N2(P)$; increasing selectivity at lower amine concentrations (*cf.* behaviour of phosphonamidic chlorides)], but also by reaction of the amine at sulphur [$S_N2(S)$ or sulphene mechanism] (Scheme 15). In either case, the phosphonamidic anhyd-

ride (64) would be the result of the phosphonamidate ion reacting further with the mixed anhydride by nucleophilic attack at phosphorus (Scheme 14).



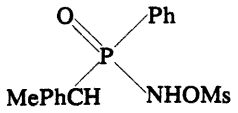
Scheme 14


MePhCH
O
O
Me
P
S
PhNH
O
O
B
Base (B⁻)
PhNH
O
P
MePhCH
O⁻
H
B
MePhCH
O
O
CH2
P
S
PhNH
O
O
Base (B⁻)

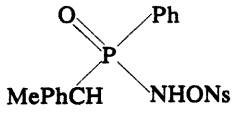
Scheme 15

Part I; Chapter 3: Further Studies on *N*-Phosphinoyl-*O*-sulphonylhydroxylamines

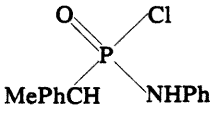
Competition Studies



(44)



(45)



(48)

If phosphonamidic-sulphonic mixed anhydrides are formed in the rearrangements of *N*-phosphinoyl-*O*-sulphonylhydroxylamines it would be interesting to compare their behaviour with that of a suitable model, such as the phosphonamidic chloride (**48**). With this in mind the methanesulphonate (**44**) (a 50 : 50 mixture of diastereoisomers), the nosylate (**45**) (diastereoisomer ratio 4 : 96; **B** in excess), and the phosphonamidic chloride (**48**) (ratio 30 : 70; ^{31}P NMR highfield diastereoisomer in excess) were allowed to react with an equimolar mixture of methylamine and *tert*-butylamine at three concentrations (neat, 1.0 M, and 0.1 M; total amine concentration in dichloromethane). The *N*-methyl/*N*-*tert*-butyl product ratios were determined by ^{31}P NMR spectroscopy (Table 4). This showed that for all three substrates the selectivity of the reaction increased on dilution. The reactions of the methanesulphonate and the phosphonamidic chloride were remarkably similar, reinforcing the argument for the mixed anhydride. The nosylate was substantially less selective than the methanesulphonate, in agreement with previous work where

a nosylate was found to exhibit lower selectivity than the corresponding methanesulphonate.[22] This may also be considered as further evidence of mixed anhydride formation, since changing the leaving group in the substrate should not influence the selectivity of the reaction if all it does is just leave.

Table 4; Reaction of different substrates with 1 : 1 methylamine--*tert*-butylamine under competitive conditions: product ratios as determined by ^{31}P NMR spectroscopy.

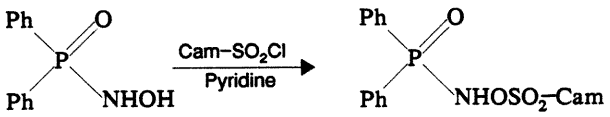
Substrate M = methanesulphonate (44)[a]
P = phosphonamidic chloride (48)[b]
N = nosylate (45)[c]

Substrate	[$MeNH_2$ + Bu^tNH_2]	*N*-Me : *N*-Bu^t
M	neat[d]	86 : 14
P		90 : 10
N		75 : 25
M	1.0 M in CH_2Cl_2	95 : 5
P		94 : 6
N		75 : 25
M	0.1 M in CH_2Cl_2	≥ 99 : 1
P		≥ 99 : 1
N		89 : 11

[a] 50 : 50 mixture of diastereoisomers
[b] 30 : 70 mixture of diastereoisomers
[c] 4 : 96 mixture of diastereoisomers
[d] Neat amine added to substrate at 0 °C.

Stereochemical Studies on Optically Active *N*-Diphenylphosphinoyl-*O*-camphor-10-sulphonylhydroxylamine

If the reaction intermediate is a phosphonamidic-sulphonic mixed anhydride, then an *N*-phosphinoyl-*O*-sulphonylhydroxylamine achiral at phosphorus but with a chiral leaving group will, on rearrangement, give the mixed anhydride as a mixture of diastereoisomers. These diastereoisomers will be formed via diastereoisomeric transition states, so there should be the possibility of asymmetric induction.

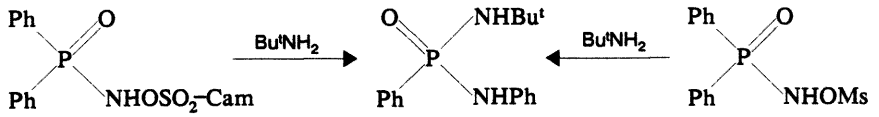


(66) (67)

Eq. 15

To test this idea the enantiomeric camphor-10-sulphonates (67), $\delta_P(CDCl_3)$ 29.6, were prepared, in high yield, by reaction of *N*-(diphenylphosphinoyl)hydroxylamine (66)[13] with (+)- or (-)-camphor-10-sulphonyl chloride (1.35 mol equiv.) in pyridine (Eq. 15).[13]

The (-)-camphor-10-sulphonate (66) was allowed to react with *tert*-butylamine (neat, 3.0 M, 1.0 M, 0.3 M, and 0.05 M in dichloromethane) (Scheme 16). The enantiomer ratios of the known diamide (68),[13] δ_P 11.2, were determined by ^1H NMR spectroscopy with the aid of (-)-methylphenylphosphinothioic acid (70)[36,37] (1 mol equiv.) as a chiral shift reagent. In all cases some asymmetric induction was seen (Table 5).



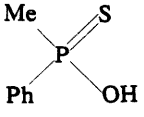
(67) (68) (69)

Scheme 16

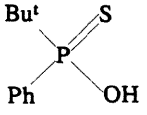
Table 5; Reaction of the (-)-camphor-10-sulphonate (67) with *tert*-butylamine: enantiomer ratios L : H [lowfield : highfield ratio of the *N*Bu^t peaks in the presence of the ^{1}H NMR shift reagent (70)] of the rearrangement product.

Bu^tNH_2	L : H
Neat[a]	53 : 47
3.0 M in CH_2Cl_2	53 : 47
1.0 M in CH_2Cl_2	55 : 45
0.3 M in CH_2Cl_2	56 : 44
0.05 M in CH_2Cl_2	55 : 45

[a] Neat amine (> 20-fold excess) added to the substrate



(70)



(71)

The (+)-camphor-10-sulphonate (67) and the achiral methanesulphonate (69)[13] were also allowed to react with 1.0 M *tert*-butylamine in dichloromethane (Scheme 16). Examination of the resulting diamide (68) revealed asymmetric induction, in the opposite sense, for the former, but no asymmetric induction in the latter (Table 6 and Fig. 3).

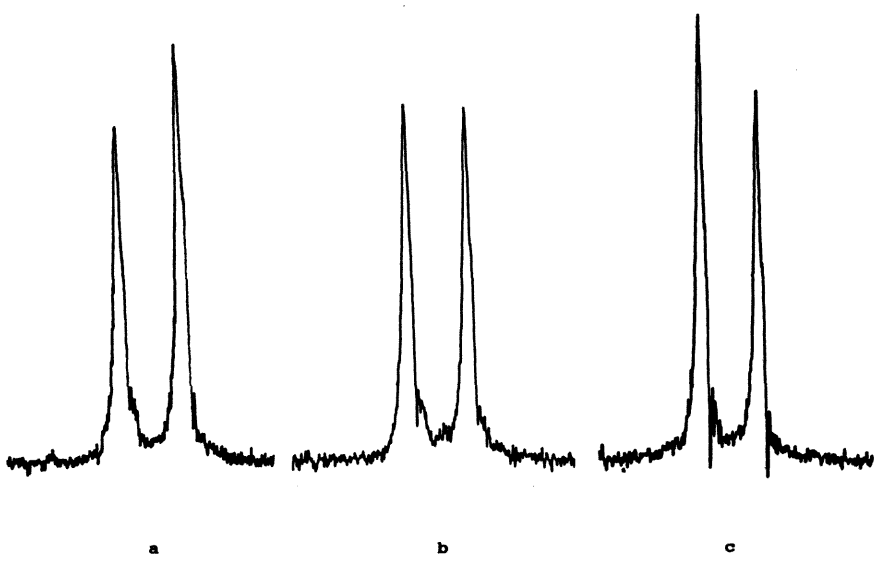
Table 6; Reaction of various sulphonates with 1.0 M *tert*-butylamine or 1.0 M methylamine in dichloromethane: enantiomer ratios L : H [lowfield : highfield ratio in the presence of the ^{1}H NMR shift reagent (70) or (71)] of the rearrangement products.

Substrate: (+)-Camphor = (+)-Camphor-10-sulphonate (67)
Mesylate = Methanesulphonate (69)
(-)-Camphor = (-)-Camphor-10-sulphonate (67)

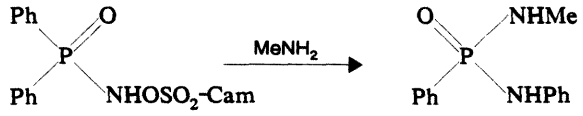
	L : H[a]	
Substrate	With Bu^tNH_2	With $MeNH_2$
(+)-Camphor	46 : 54[b]	52 : 48
Mesylate	50 : 50	-
(-)-Camphor	55 : 45	47 : 53

[a] This is the ratio of the *N*Bu^t or *N*Me peaks for rearrangement with Bu^tNH_2 or $MeNH_2$ respectively.
[b] This value was also obtained in a similar reaction with 1 mol equiv. of tert-butylammonium (-)-camphor-10-sulphonate present in the Bu^tNH_2 solution before the addition of the substrate.

Fig. 3; ^{1}H NMR spectra (NBu^t peaks) showing asymmetric induction in the rearrangement of the camphor-10-sulphonate (**67**) and its absence in the rearrangement of the methanesulphonate (**69**) with 1.0 M *tert*-butylamine in dichloromethane [**a** and **c** are product peaks derived from the (+) and (-) enantiomers of (**67**) respectively, while **b** is for the product from (**69**)].



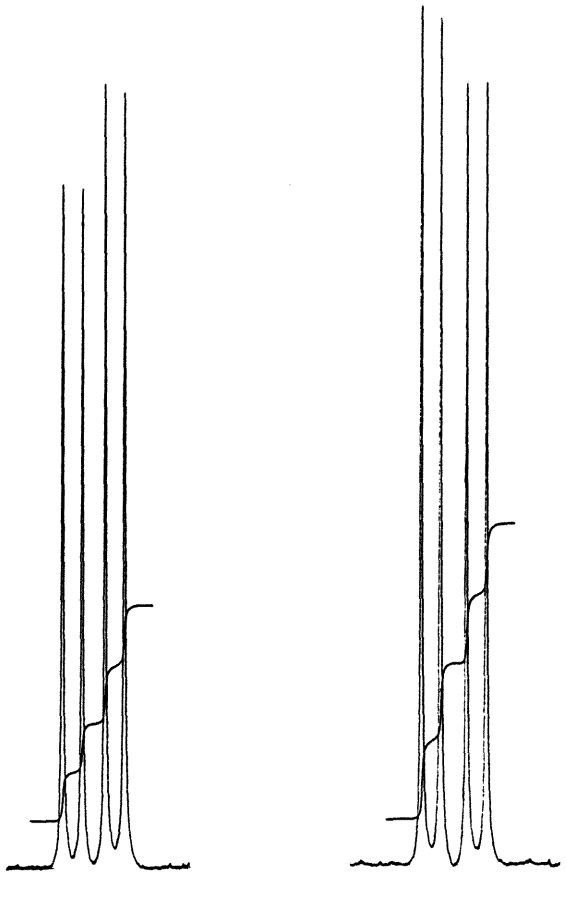
The reactions of both enantiomers of the camphor-10-sulphonate (**67**) with 1.0 M methylamine in dichloromethane gave the diamide (**72**),[22] δ_P 16.4, (Eq. 16). Investigation of the enantiomer ratios of the product by ^{1}H NMR spectroscopy, with the aid of (+)-*tert*-butylphenylphosphinothioic acid (**71**) (1.3 mol equiv.) as a chiral shift reagent,[37,37] again showed some asymmetric induction (Table 6 and Fig. 4).



(67) (72)

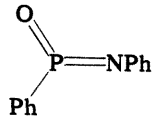
Eq. 16

Fig. 4; ^{1}H NMR spectra (*N*Me peaks) showing asymmetric induction in the rearrangement of the camphor-10-sulphonate (67) with 1.0 M methylamine in dichloromethane [**a** and **b** are the product peaks derived from the (-) and (+) enantiomers of (67) respectively].



a **b**

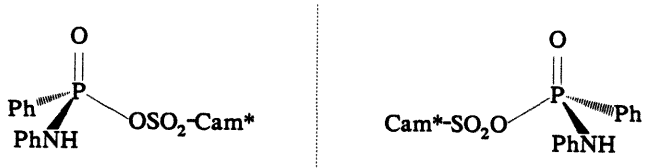
If the rearrangement of the camphor-10-sulphonate (67) proceeded through a free metaphosphonimidate intermediate there would be no asymmetric induction, since the two faces of the metaphosphonimidate (73) are enantiotopic and the nucleophile is achiral. The source of asymmetry in the reaction is the chiral sulphonate, and asymmetric induction will occur if it was involved in some way in product formation. In principle, the chiral leaving group could influence product formation by merely being present in the reaction medium, but this was not the case since the product ratios remained unaltered when the reaction was repeated with the (-)-camphor-10-sulphonate ion (1.0 mol equiv.) already present in the reaction medium.



(73)

The chiral leaving group could influence product formation if it remained close to phosphorus when the nucleophile attacks (the two faces of the metaphosphonimidate will then be diastereotopic). Rearrangement through the metaphosphonimidate involves migration of phenyl to nitrogen with the expulsion of the leaving group. If the line of departure of the leaving group places it close to phosphorus the faces of the metaphosphonimidate would be diastereotopic. There is no reason why this should occur unless the sulphonate leaving group is interacting in some specific way with phosphorus, *i*.e. bonding. This being the case, the most reasonable ex-

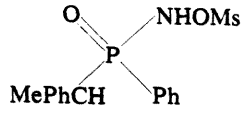
planation is that rearrangement not only involves the migration of phenyl from phosphorus to nitrogen but also involves the transfer of the sulphonate group from nitrogen to phosphorus to give the phosphonamidic-sulphonic mixed anhydride (**74**) as a mixture of diastereoisomers. Whether this transfer is synchronous with phenyl migration will be discussed later. Since the mixed anhydride is diastereoisomeric, the diastereoisomers may, in principle, be formed in unequal amounts, and if they reacted stereospecifically with the nucleophile their configurational inequality would be transferred to the product, *i.e.* an unequal quantity of enantiomers.



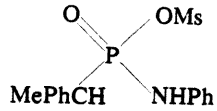
Diastereoisomers of (**74**)

The observed asymmetric induction was small but only a small difference in the energies of the transition states leading to the mixed anhydride can be reasonably be expected. The very fact of asymmetric induction provides further useful support for the formation of the phosphonamidic-sulphonic mixed anhydride.

Spectroscopic Evidence for the Mixed Anhydride



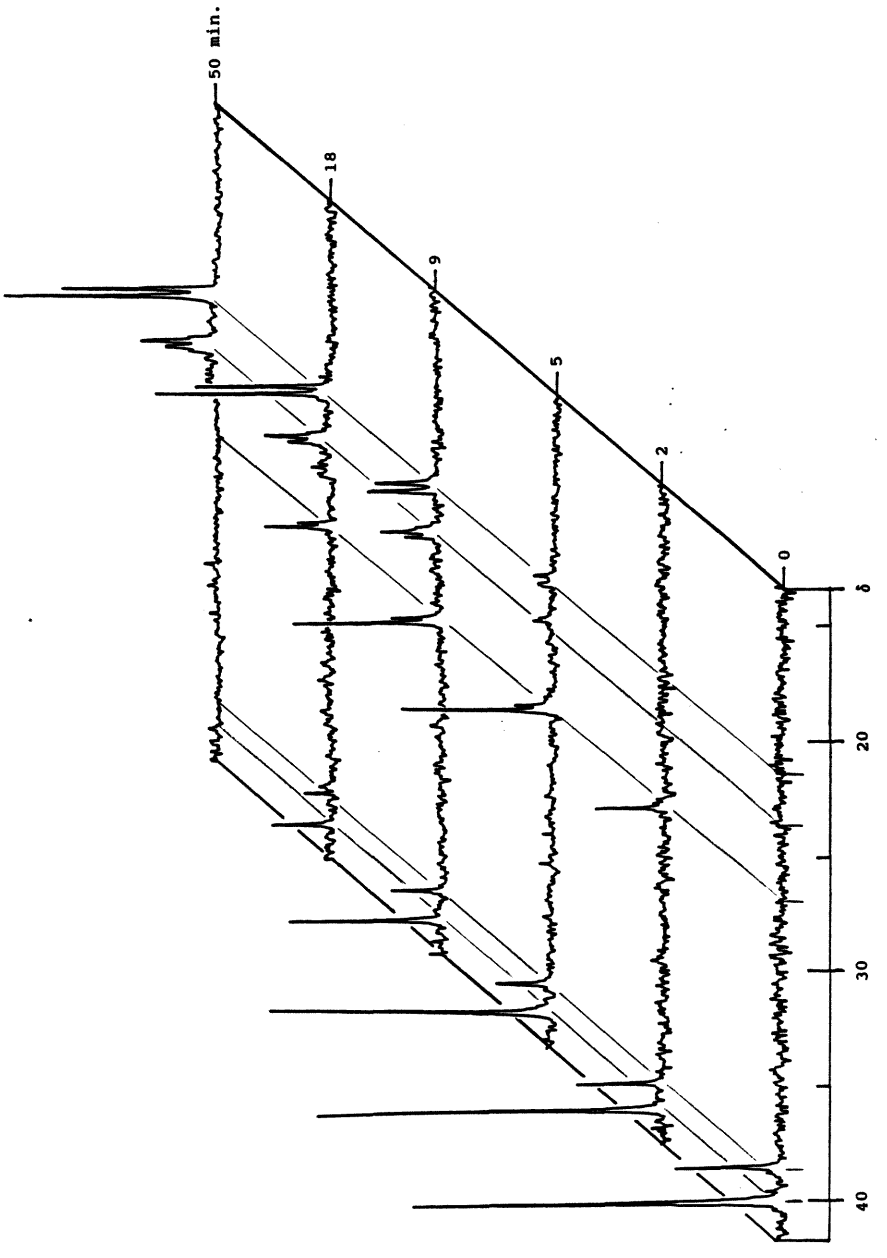
(44)



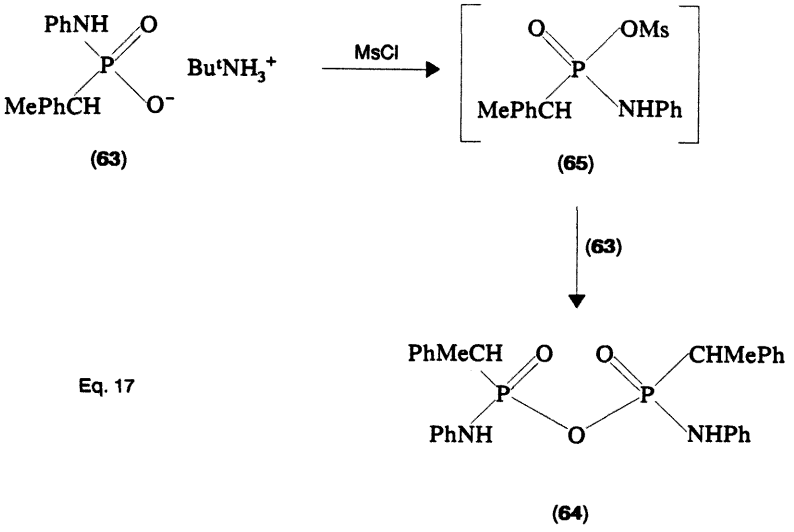
(65)

A ^{31}P NMR investigation of the reaction of the methanesulphonate (44) (sample A; diastereoisomer ratio 80 : 20) with 0.21 M *tert*-butylamine in dichloromethane showed that the substrate was initially converted into a species with a chemical shift in the region expected for rearrangement, δ_P 27.7 and 27.5 (~ 80 : 20 mixture of diastereoisomers) (Fig. 5). This species was not the final product but a short-lived reaction intermediate; the expected phosphonic diamide rearrangement product was formed at its expense. This reaction intermediate is believed to be the phosphonamidic-sulphonic mixed anhydride (65), and the ~ 80 : 20 ratio of its diastereoisomers implies that it is formed with a high degree of stereospecificity. A similar investigation of sample B of the methanesulphonate (diastereoisomer ratio 3 : 97), but with 0.1 M *tert*-butylamine in dichloromethane showed that formation of the hydrazide by-product competed with mixed anhydride (65) formation.

Fig. 5; Detection of a reaction intermediate (^{31}P NMR spectroscopy) in the rearrangement of the methanesulphonate (**44**) with 0.21 M *tert*-butylamine in dichloromethane.

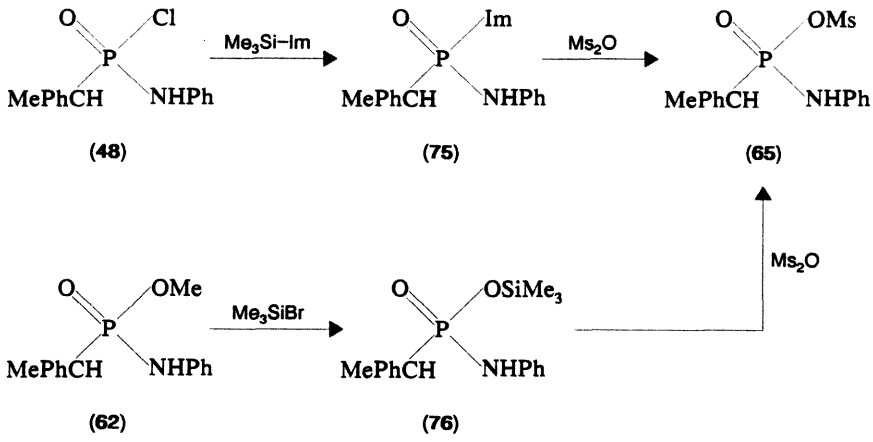


In an attempt to recreate the reaction intermediate, the *tert*-butylammonium phosphonamidate (63) was treated with methanesulphonyl chloride. The reaction was followed by ^{31}P NMR spectroscopy, which showed the salt being converted into the pyrophosphate (64) (Eq. 17). The phosphonamidic-sulphonic mixed anhydride was not detected, presumably because it reacts too quickly with the phosphonamidate anion.



Eq. 17

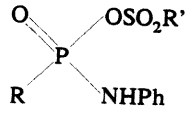
Attempts to synthesise the mixed anhydride with methanesulphonic anhydride and either from the imidazolide (75), prepared from the phosphonamidic chloride and trimethylsilylimidazole,[38] or the *O*-silyl ester (76) of the phosphonamidate, prepared from the methyl phosphonamidate (62) and trimethylsilylbromide,[39] were unsuccessful (Scheme 17).[40]



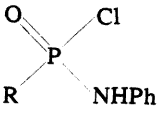
Scheme 17

The Rearrangement

It is clear that rearrangement of the *N*-phosphinoyl-*O*-sulphonylhydroxylamine directly to the monomeric metaphosphonimidate is not a major reaction pathway, since, contrary to the observed results, both diastereoisomers of the methanesulphonate (44) would be expected to give the same ratio of diastereoisomeric products. The evidence for phosphonamidic--sulphonic mixed anhydride (77) formation, however, is strong. The existence of asymmetric induction in the reactions of the camphor-10-sulphonates (67) practically demands mixed anhydride formation, while the persistence of asymmetric induction with all concentrations of *tert*-butylamine (Table 5), and the high stereospecificity of the reactions of the methanesulphonate (44) and the nosylate (45) with methylamine shows that mixed anhydride formation occurred at all concentrations.



(77)



(31)

If the *N*-phosphinoyl-*O*-sulphonylhydroxylamine, on treatment with base, rearranged to the phosphonamidic-sulphonic mixed anhydride (77), it is the way that this then reacts with the nucleophile that will determine the outcome of the reaction. It is reasonable to expect the mixed anhydride (77) to behave like the phosphonamidic chloride (31). Phosphonamidic chlorides have been shown to react with amines by three mechanisms namely,[26] i) $S_N2(P)$, being stereospecific and first order in amine and showing high selectivity for the less bulky nucleophile, ii) preassociation elimination-addition,[27] being second order in amine and showing low selectivity, though its stereospecificity can vary, the reaction being anything from completely stereospecific to non-stereospecific, and finally iii) limiting elimination-addition, which is first order in amine and completely non-stereospecific and non-selective. The reaction can therefore be influenced by the nucleophile, in that bulky nucleophiles will disfavour $S_N2(P)$, and high nucleophile concentrations will favour preassociation elimination-addition; for competing nucleophiles, the phosphonamidic chloride will show increasing selectivity for the less hindered nucleophile as the nucleophile concentration is lowered.

In order to understand the behaviour of the substrates it is necessary to examine the competition and stereochemical studies more closely. Consider the competition study (Table 4). If the phosphonamidic-sulphonic mixed anhydride was formed, there will be a preference for methylamine over *tert*-butylamine for a reaction proceeding by an $S_N2(P)$ pathway. The reaction of $Ph_2P(O)Cl$, by an $S_N2(P)$ mechanism (it cannot react by an elimination-addition mechanism), with an equimolar mixture of isopropylamine and *tert*-butylamine gives an NPr^i/NBu^t product ratio of > 99 : 1.[22] For methylamine this ratio would be much greater, and *tert*-butylamine will not compete with methylamine for the mixed anhydride by an $S_N2(P)$ pathway. If any NBu^t product was formed under competitive conditions it would be due elimination-addition. For the reaction of the methanesulphonate (44) with neat amine the ratio was 86 : 14 (Table 4), the 14 % NBu^t product must be due to elimination-addition. At least a further 14 % of the substrate must have also reacted with methylamine by a similar mechanism, since methylamine could hardly be a less efficient trap than *tert*-butylamine; the $S_N2(P)$ component for methylamine would be 72 % (100 - 14 - 14 = 72). However, an elimination-addition mechanism need not be truly non-selective. Consider, for example, $Pr^iP(O)NHBu^tCl$ reacting by an elimination-addition mechanism with an equimolar mixture of isopropylamine and *tert*-butylamine in dichloromethane, non-selectivity is 1.4 : 1 favouring isopropylamine,[41] showing that bulk on the nucleophile does affect its trapping ability to some degree. For $Ph_2P(O)NHONs$ with 1 : 1 methylamine and *tert*-butylamine non-selectivity is around 2.5 : 1 favouring methylamine,[22] and for the reaction of nosylate (45) with the

neat amine mixture, assuming the reaction proceeds entirely by an elimination-addition mechanism, it cannot be more than 3 : 1 (Table 4). Taking non-selectivity as 2.5 : 1, and applying this to our 86 : 14 ratio we get the elimination--addition contribution by methylamine as 35 % (2.5 x 14 = 35) and $S_N2(P)$ for methylamine as 51 % (100 - 35 - 14 = 51). The other values in Table 4 were similarly manipulated and the results are shown in Table 7.

Table 7; Derived from Table 4: reaction of different substrates with 1 : 1 methylamine/*tert*-butylamine under competitive conditions showing the % contribution of $S_N2(P)$ and elimination-addition (assuming non-selectivity is 2.5 : 1 favouring $MeNH_2$).

Substrate M = methanesulphonate (44)
P = phosphonamidic chloride (48)
N = nosylate (45)

Substrate	$MeNH_2$ + Bu^tNH_2	% $S_N2(P)$	% EA	
		$MeNH_2$	$MeNH_2$	Bu^tNH_2
M	neat	51	35	14
P		65	25	10
N		12.5	62.5	25
M	1.0 M in CH_2Cl_2	82.5	12.5	5
P		79	15	6
N		12.5	62.5	25
M	0.1 M in CH_2Cl_2	> 96.5	< 2.5	< 1
P		> 96.5	< 2.5	< 1
N		61.5	27.5	11

For the stereochemical study it would be useful to know how each diastereoisomer behaved. The stereochemical study was conducted on enriched mixtures of both diastereoisomers, but the behaviour of each diastereoisomer can easily be determined by solving the two following simultaneous equations:

$$3\mathbf{A} + 97\mathbf{B} \longrightarrow a\mathbf{A}' + b\mathbf{B}'$$
$$80\mathbf{A} + 20\mathbf{B} \longrightarrow \alpha\mathbf{A}' + \beta\mathbf{B}'$$

The solutions being:

$$100\mathbf{A} \longrightarrow (1/77)(97\alpha - 20a)\mathbf{A}' + (1/77)(97\beta - 20b)\mathbf{B}'$$
$$100\mathbf{B} \longrightarrow (1/77)(80a - 3\alpha)\mathbf{A}' + (1/77)(80b - 3\beta)\mathbf{B}'$$

The solutions to these simultaneous equations are displayed in Tables 8 and 9, where **A** and **B** are the substrate diastereoisomers, **A'** and **B'** are the product diastereoisomers, and the values (taken from Tables 1 and 2) a and b are the coefficients of **A'** and **B'** respectively, for sample **B**, and α and β are the corresponding coefficients for sample **A**.

Table 8; Reaction of the methanesulphonate (**44**) with *tert*-butylamine: calculated product diastereoisomer ratios (**A'** : **B'**) from substrate (**X** = diastereoisomer **A** or **B**).

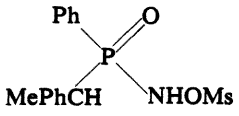
A : **B**	Bu^tNH_2	100 % **X** ⟶ **A'** : **B'**	d.e.
3 : 97	neat	**B** ⟶ 7.5 : 92.5	85.0
80 : 20		**A** ⟶ 91.9 : 8.1	83.8
3 : 97	1.0 M	**B** ⟶ 28.6 : 71.4	42.8
80 : 20	in CH_2Cl_2	**A** ⟶ 76.6 : 23.4	53.2
3 : 97	0.1 M	**B** ⟶ 40.4 : 59.6	19.2
80 : 20	in CH_2Cl_2	**A** ⟶ 61.2 : 38.8	22.4

Table 9; Reaction of the methanesulphonate (**44**) with methylamine: calculated product diastereoisomer ratios (**A'** : **B'**) from substrate (**X** = diastereoisomer **A** or **B**).

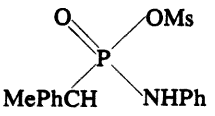
A : **B**	$MeNH_2$	100 % **X** ⟶ **A'** : **B'**	d.e.
3 : 97	neat	**B** ⟶ 4.2 : 95.8	91.6
80 : 20		**A** ⟶ 97.7 : 2.3	95.4
3 : 97	1.0 M	**B** ⟶ 5.1 : 94.9	89.8
80 : 20	in CH_2Cl_2	**A** ⟶ 97[a] : 3[a]	94
3 : 97	0.1 M	**B** ⟶ 5.1 : 94.9	89.8
80 : 20	in CH_2Cl_2	**A** ⟶ 97[a] : 3[a]	94

[a] No sensible solution was obtained from the simultaneous equations for this diastereoisomer at this concentration. This value was obtained by extrapolation, assuming that there is no significant difference between the diastereoisomers, then **A'** = (97.7/95.8) x 94.9 = 96.8, and **B'** = 100 - **A'** = 3.2.

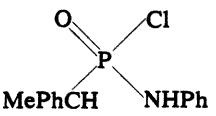
Examination of Table 7 clearly shows that in all cases selectivity for the less hindered nucleophile (methylamine) increased with dilution. This behaviour is exactly what is expected for a phosphonamidic chloride, indicating that the substrates are behaving like phosphonamidic chlorides. Furthermore, the behaviour of the methanesulphonate (**44**) reinforced this view by closely paralleling the behaviour of the phosphonamidic chloride (**48**). The reactions of the phosphonamidic-sulphonic mixed anhydrides may be rationalised as detailed below.



(44)



(65)



(48)

The mixed anhydride (**65**), once formed, could react further at high amine concentrations by a preassociation elimination-addition mechanism.[27] This pathway would not discriminate much between competing nucleophiles, since the product forming species would be the metaphosphonimidate (planar and highly reactive); it may be responsible for the reduced selectivity seen in the competition study (Tables 4 and 7). Both diastereoisomers of the methanesulphonate (**44**) reacted with *tert*-butylamine with high stereospecificity at high amine concentration but with low stereospecificity at low amine concentrations (Table 8). In this case preassociation elimination-addition for the phosphonamidic-sulphonic mixed anhydride (**65**) seems to go with a fairly high degree of

stereospecificity, and it could be that the leaving group blocked one face of the metaphosphonimidate. At lower amine concentrations preassociation elimination-addition becomes less important (proportional to [amine]^2); $S_N2(P)$ and, if the metaphosphonimidate could exist as a free species, limiting elimination-addition can compete more ably. From the competition study we saw that *tert*-butylamine competed with methylamine by an elimination-addition mechanism. Since $S_N2(P)$ is very much faster for methylamine than for *tert*-butylamine, and since elimination-addition for *tert*-butylamine could compete with $S_N2(P)$ for methylamine, it follows, as expected, that elimination-addition is very much greater than $S_N2(P)$ for *tert*-butylamine. The reaction of the mixed anhydride with low concentrations of *tert*-butylamine would proceed through a non-stereospecific elimination-addition pathway involving the free metaphosphonimidate, explaining the loss of stereospecificity seen in the reaction (Table 8). The reaction of the methanesulphonate (44) with *tert*-butylamine, however, was not completely non-stereospecific, even for the 0.1 M amine, but the remaining stereospecificity could be due to a residual preassociation elimination-addition pathway with, perhaps, an $S_N2(P)$ contribution.

The reaction of the diastereoisomers of the methanesulphonate (44) with methylamine, in contrast with their reaction with *tert*-butylamine, showed only a small reduction in stereospecificity on dilution (Table 9). The stereospecificity of the reaction with neat methylamine would be due to contributions by both the fairly highly stereospecific preassociation elimination-addition pathway and the stereospec-

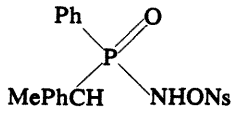
ific $S_N2(P)$ pathway, which accounted for roughly half of product formation (Table 7). At lower methylamine concentrations the preassociation elimination-addition mechanism would be expected to be replaced by a stereospecific $S_N2(P)$ mechanism, resulting in continued high stereospecificity. The observed small decrease in stereospecificity could be due to competition from the non-stereospecific limiting elimination-addition mechanism.

Table 10; Reaction of the nosylate (45) with methylamine: calculated product diastereoisomer ratios (A' : B') from substrate B. The values were calculated assuming that the 3 % of substrate diastereoisomer A made no contribution to product diastereoisomer B', then B' = (B' from Table 3)/97 and A' = 100 - B'.

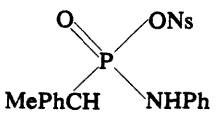
$MeNH_2$	100 % B ⟶ A' : B'	d.e.
neat	11.3 : 88.7	77.4
1.0 M in CH_2Cl_2	9.3 : 90.7	81.4
0.1 M in CH_2Cl_2	7.2 : 92.8	85.6

When compared to the methanesulphonate (44), the nosylate (45) showed a marked reduction in the preference for methylamine over *tert*-butylamine at all concentrations (Table 7), showing that preassociation elimination-addition was much more dominant for the nosylate-containing mixed anhydride (78). This is perhaps due to the more electronegative nosylate leaving group enhancing the acidity of the *N*-hydrogen,[42] encouraging elimination-addition. The rearrangement with

methylamine also proceeded with lower stereospecificity than the methanesulphonate but this could simply be due to the lower $S_N2(P)$ contribution; the stereospecificity of the pre-association elimination-addition pathway for the mixed anhydride (78) is presumably similar to that of the mixed anhydride (65). On the whole, though, the nosylate (45) showed increasing selectivity and, interestingly, increasing stereospecificity on dilution.



(45)

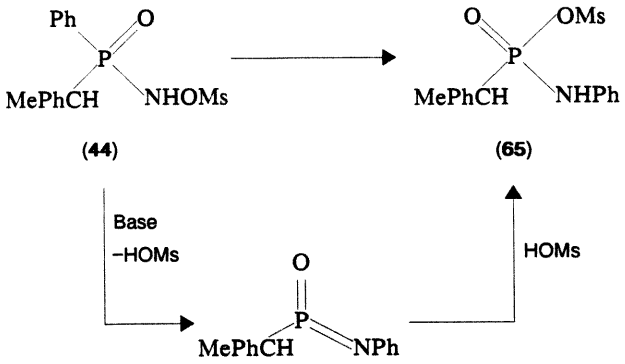


(78)

A curious feature of the reaction of the nosylate (45), under competitive conditions, was that the selectivity with neat and 1.0 M amine mixture was the same. However, the elimination-addition contribution at the two concentrations must be different, but indistinguishable within experimental error, since the stereochemical study showed a slight increase in stereospecificity, due to a greater $S_N2(P)$ contribution. The small increase in stereospecificity for the nosylate with methylamine could simply be due the increasing importance of the $S_N2(P)$ reaction pathway on dilution.

The behaviour of the *N*-phosphinoyl-*O*-sulphonylhydroxylamines is consistent with rearrangement to the phosphonamidic--sulphonic mixed anhydride at all concentrations, but there remains the possibility that rearrangement directly to the

metaphosphonimidate (59) may have a small role. For the methanesulphonate (44) with 0.1 M amine in the competition study elimination-addition accounts for ~ 4 % of the reaction (Table 7). If all the elimination-addition was attributable to rearrangement proceeding directly through the metaphosphonimidate (59) then this mechanism will account for no more than 4 % of the rearrangement with 0.1 M amine. Since the metaphosphonimidate (59) and the phosphonamidic-sulphonic mixed anhydride (65) are both formed from the conjugate base of the methanesulphonate (44) it might be reasonable to expect that the ratio of the two rearrangement pathways will remain roughly constant at all concentrations of amine, so the metaphosphonimidate could account for 4 % of reaction at all concentrations. However, in the reaction of the phosphonamidic chloride (48) under the same conditions, elimination-addition also accounts for 4 % of the reaction. Since the phosphonamidic chloride (48) is already a 'rearranged' species, and bearing in mind the striking similarity in the behaviours of the methanesulphonate (44) and the phosphonamidic chloride (48) under competitive conditions, we would expect the mixed anhydride (65) to also show ~ 4 % elimination-addition; this must mean that rearrangement directly through the metaphosphonimidate (if any) occurs in even less than 4 %, and suggests that rearrangement to the mixed anhydride is probably the only pathway.



Scheme 18

The rearrangement of the substrates to the mixed anhydrides could proceed either by i) a two step process in which a metaphosphonimidate recombines with the sulphonate leaving group or, ii) a concerted mechanism (Scheme 18). If the metaphosphonimidate had a very short lifetime (such that it could not diffuse into the bulk solvent) and the nucleophile was not already present we would expect it to recombine immediately with the sulphonate (with inversion of configuration at phosphorus). The short life time of the metaphosphonimidate would enforce a preassociation elimination--addition mechanism at all concentrations and the stereochemistry of the methanesulphonate (**44**) with *tert*-butylamine would be constant. This was not the case, and, in fact, the loss of stereochemistry, on dilution, suggested that the metaphosphonimidate could exist as a free species.

If the metaphosphonimidate could exist as a free species, it would be more able to diffuse into the bulk solvent at lower amine concentrations. However, the metaphosphonimidate would be less likely to recombine with the sulphonate leaving group, to give the mixed anhydride, and more likely to react directly with amine to give the product (the concentration of amine ≥ 20 times that of sulphonate). Since the metaphosphonimidate would be the reactive species, low stereospecificity and low selectivity would be expected for the reaction of the methanesulphonate with methylamine, but the opposite was observed and this suggested that mixed anhydride formation was not a two-step process.

The stereochemical results (and the ^{31}P NMR study) of the rearrangement imply that the mixed anhydride was formed directly (after deprotonation) from the substrate by a concerted mechanism, with a high degree of (if not complete) stereospecificity. The optically active study also suggested that the mixed anhydride was formed directly from the substrate. The reaction of the (+)-camphor-10-sulphonate (67) with 1.0 M *tert*-butylamine in dichloromethane, containing *tert*-butylammonium (-)-camphor-10-sulphonate (1 mol equiv.), showed no change in the enantiomer ratio of the product, when compared with the reaction without added salt (Table 6). This showed that no inter-molecular exchange of the sulphonate occurred and suggested that the mixed anhydride was formed by an intra-molecular rearrangement (Fig. 6).

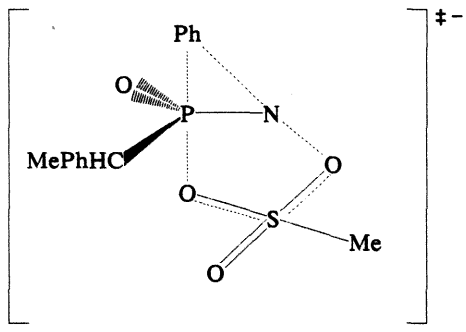
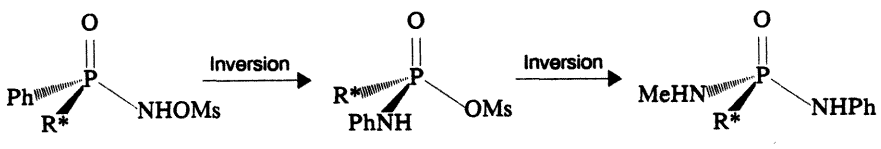


Fig. 6

The rearrangement of the methanesulphonate (44) with methylamine was shown to go with retention of configuration at phosphorus. This result could be explained as rearrangement to the mixed anhydride proceeding largely (or completely) with inversion of configuration at phosphorus, perhaps by a intra-molecular process (Fig. 6), followed by stereospecific displacement of the leaving group by methylamine with inversion of configuration at phosphorus [$S_N2(P)$ at low concentrations or stereospecific preassociation elimination--addition at high concentrations]. The overall retention of configuration at phosphorus, seen in the final product, would then be the result of two inversions (Eq. 18).



R* = PhMeCH

Overall Retention

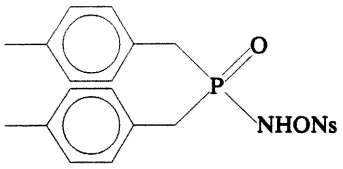
Eq. 18

A Brief Investigation of Hydrazide Formation

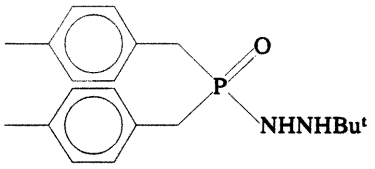
Hydrazide formation occurred to some extent in the reactions of the methanesulphonate (44) with amines. This became more prominent at lower amine concentrations, suggesting that rearrangement to the mixed anhydride (65) may proceed by a mechanism that is of a higher order in amine than is the conversion to hydrazide. More curious, as noted earlier, was that hydrazide formation was more prominent for more hindered amines. If the hydrazide is formed by S_N2 attack at nitrogen, then this behaviour is contrary to what is normally encountered for S_N2 (at carbon), namely that less hindered nucleophiles are more able nucleophiles. It is conceivable that hydrazide formation is enhanced with hindered amines, relative to rearrangement, simply because the bulk of the amine affects the rearrangement process more than it affects nucleophilic substitution at nitrogen (hydrazide formation). This seems unlikely, however, if the rearrangement to the mixed anhydride only requires the amine to act as a base in the rate limiting formation of the phosphonamidic-sulphonic mixed anhydride.

To explore hydrazide formation more closely, the nosylate (79)[43] was allowed to react with a range of amines (0.5 M) in dichloromethane. Both the low concentration of amine and the relatively small migratory aptitude of the benzyl group in the substrate should encourage hydrazide formation.[44] The reaction of the nosylate (79) with methylamine gave several products and, as a result, methylamine was excluded from the

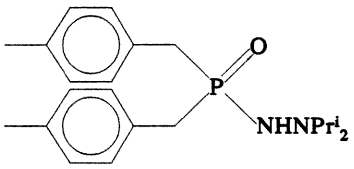
study. The reactions with *tert*-butylamine, diisopropylamine, and *N*-methyl-*tert*-butylamine gave mainly the hydrazides (80), (81), and (82) respectively.



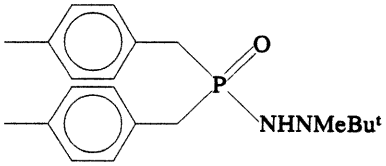
(79)



(80)



(81)



(82)

The nosylate (79) was then subjected to a competition study, by using an equimolar mixture of either *tert*-butylamine and diisopropylamine or *tert*-butylamine and *N*-methyl-*tert*-butylamine in dichloromethane (0.5 M total amine) (Table 11).

Table 11; Reaction of the nosylate (79) with 0.5 M amine mixtures in dichloromethane under competitive conditions: hydrazide product ratios.

Amine: A = 1 : 1 *tert*-butylamine-*N*-methyl-*tert*-butylamine
B = 1 : 1 *tert*-butylamine-diisopropylamine

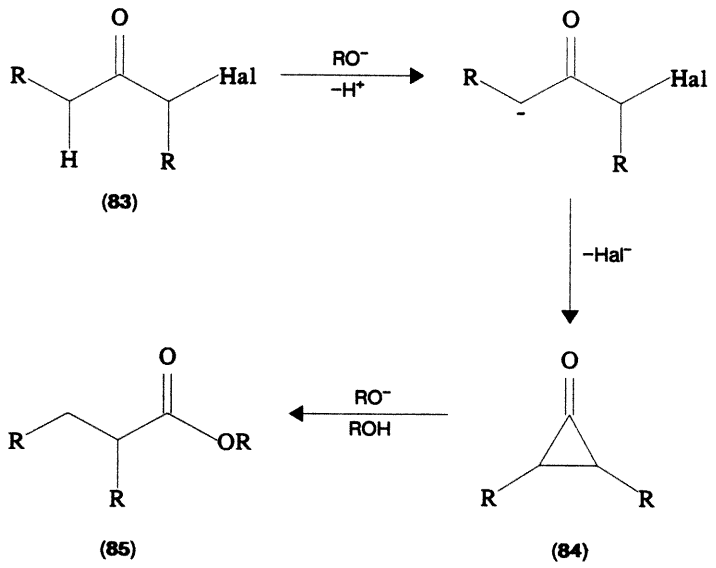
Amine	$-NBu^t$: $-NR^1R^2$
A	8 : 92
B	55 : 45

Some previous work on nucleophilic substitution at nitrogen has shown that steric hindrance is not very important,[45] but a (loose) correlation of reduced nucleophilicity with increased steric hindrance was found in protic solvents.[45] In the competition study with the nosylate (79), a mixed result was obtained; the reaction with the *tert*-butylamine-*N*-methyl--*tert*-butylamine mixture gave the opposite of what might be expected (*i.e.* the more hindered amine was the more effective nucleophile), while the reaction with the *tert*-butylamine--diisopropylamine mixture gave a normal result (*i.e.* the less hindered amine was the more effective nucleophile), albeit that diisopropylamine competed remarkably well.

Normally, progressive alkylation of an amine should reduce its efficiency as a nucleophile (steric hindrance), but where steric factors are unimportant, as would appear to be the case for nitrogen, this same alkylation may serve to enhance the nucleophilicity of the amine (+I effect), thus making the

more alkylated amine the more efficient nucleophile. If this was indeed the case *N*-methyl-*tert*-butylamine would be expected to be a better nucleophile than *tert*-butylamine and would be responsible for the major product, as seen. Similarly one would expect diisopropylamine to be the more efficient nucleophile, but here *tert*-butylamine proved to be marginally better. It could be then that steric effects are now sufficiently important for diisopropylamine so as to moderate its overall nucleophilicity, such that *tert*-butylamine is now the (slightly) more efficient nucleophile.

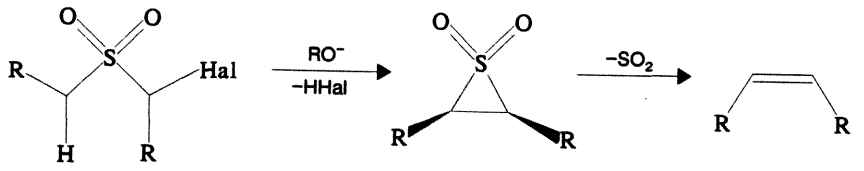
α-Halogenoketones and α-Halogenosulphones



Scheme 19

α-Halogenoketones (83) when treated with base undergo a reaction known as the Favorskii rearrangement giving esters (85).[46] The first step is deprotonation at the α-carbon, followed by ring closure giving the cyclopropanone (84) as an intermediate;[47] nucleophilic addition to the carbonyl group by alkoxide followed by the displacement of the most stable carbanion (and protonation) completes the rearrangement (Scheme 19). α-Halogenosulphones (86) undergo the Ramberg--Backlund rearrangement when treated with base,[48] forming episulphones (87) which are analogous to the cyclopropanones in the Favorskii rearrangement. An episulphone, however, does

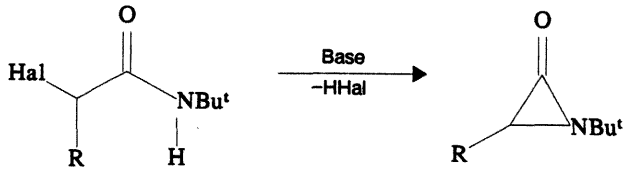
not undergo simple ring opening but breaks down by cheleotropic elimination of sulphur dioxide to give an alkene (88) predominantly as the *cis*-isomer (Eq. 19).



(86) (87) (88)

Eq. 19

α-Halogenocarboxamides



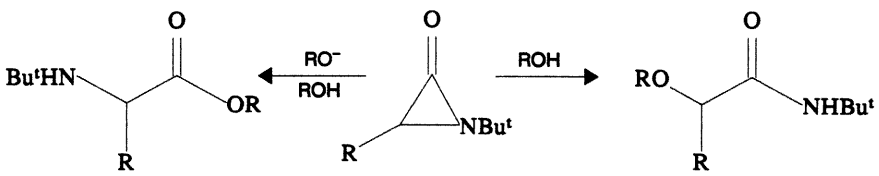
(89) (90)

Eq. 20

α-Halogenocarboxamides (89) eliminate hydrogen halide in the presence of base to give α-lactams (90),[49] analogues of the cyclopropanones in the Favorskii rearrangement (Eq. 20). α-Lactams are relatively stable species and may be prepared optically pure from α-amino acids.[50]

Treatment of α-lactams with protic reagents gives products unlike those from the Favorskii rearrangement, since nucleophilic displacement of nitrogen from the α-carbon occurs, giving α-substituted amides (92) (Scheme 20). However treat-

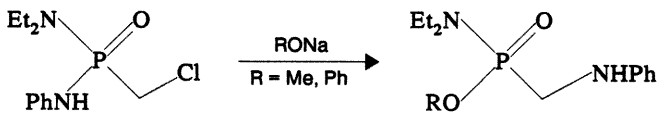
ment with anionic nucleophiles effects substitution at the carbonyl centre, with displacement of the most stable anion, usually nitrogen, giving the α-amino acid derivatives (**91**) (Scheme 20); products derived from C-C bond scission have been observed when the α-carbon bears two phenyl groups.



(**91**) (**90**) (**92**)

Scheme 20

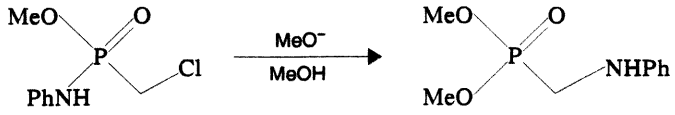
α-Halogenophosphonic Amides



(**93**) (**94**)

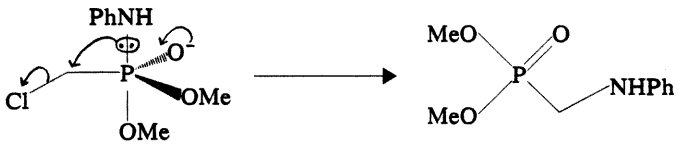
Eq. 21

In 1977 Petrov et al[51] observed that when the α-chlorophosphonic diamide (**93**) was treated with base it underwent a reaction that was superficially similar to the Favorskii rearrangement, giving the α-aminophosphonamidate (**94**) as the product (Eq. 21). Subsequently, other workers[52] found that α-halogenophosphonamidates (**95**) behaved similarly, to give α-aminophosphonamidates (**96**) (Eq. 22).



(95) (96)

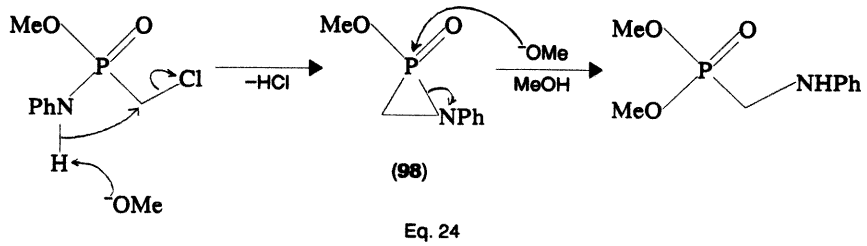
Eq. 22



(97)

Eq. 23

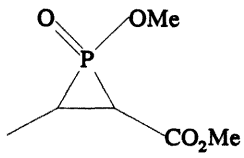
This rearrangement could proceed through a phosphorane (97), with addition of the nucleophile to phosphorus, followed by expulsion of halide as the amino group migrates to the α-carbon (Eq. 23). Comparable phosphorane rearrangements, with migration of an alkyl or aryl group, have been reported.[53] Alternatively, deprotonation at nitrogen and ring closure may give an azaphosphiridine oxide (98) (originally proposed by Petrov et al[51]) which then experiences nucleophilic displacement of nitrogen from the phosphorus centre (Eq. 24).



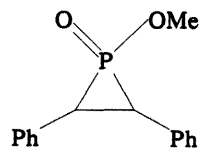
(98)

Eq. 24

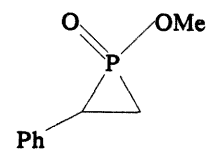
An azaphosphiridine oxide is an example of a three membered ring containing the P=O group. Related species, such as the phosphirane oxides (99), (100), and (101)[54] have been suggested as short-lived intermediates in reactions, and in certain cases, such as the diazaphosphiridine oxide (102)[55] and the phosphirane oxides (103)[56] and (104)[57], they have been isolated. However, azaphosphiridine oxides have not yet been detected, let alone isolated, and must be expected to react rapidly with nucleophiles.



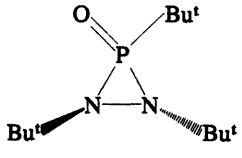
(99)



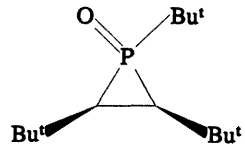
(100)



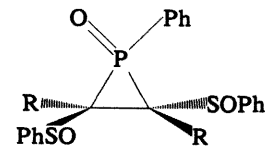
(101)



(102)



(103)

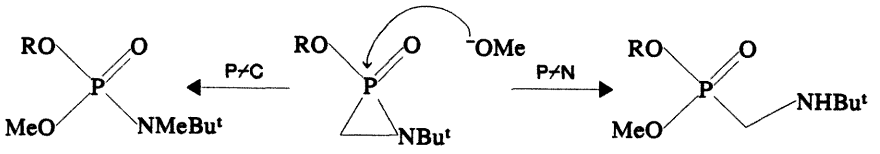


(104)

R = H, OAc

Recent evidence favours the azaphosphiridine oxide pathway, since i) alkyl substituents at the α-carbon enhance the rate of reaction,[52] which is not consistent with rate-limiting associative nucleophilic attack at phosphorus, and ii) more important, when the *N*-substituent is an alkyl group, phosphoramidate products (106) may be formed as well as α-aminomethylphosphonates (107).[58] Phosphoramidate formation is not easily accounted for with the phosphorane mechanism

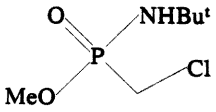
but is easily explained by nucleophilic displacement of the α-carbon from phosphorus in an azaphosphiridine oxide (105) (Scheme 21). As would be expected, alkyl substituents on the α-carbon discourage P-C bond cleavage and phosphoramidate formation.[58,52]



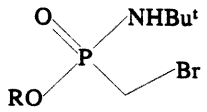
(106) (105) (107)

Scheme 21

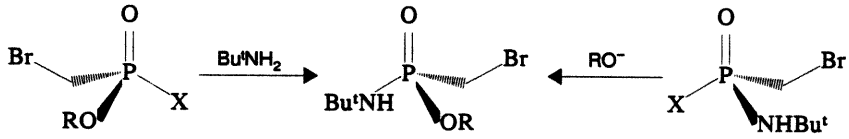
An important difference between the α-halogenophosphonamidate reaction and the Favorskii rearrangement is that, whereas the carbonyl group is trigonal, a phosphoryl group is tetrahedral; rearrangement may, therefore, have stereochemical consequences that can furnish further mechanistic details. In order to study the stereochemistry it would be necessary to establish the relative configuration at phosphorus for the substrate and the products. Ideally the substrate should be one that gives both types of product (P≠N and P≠C bond scission) and since, in this case, the stereochemistry of rearrangement would be determined by single crystal X-ray analysis the chosen substrate and its products (or their derivatives) must be crystalline. The methyl α-chloromethylphosphonamidate (108)[58] could be a useful starting point for the study, and replacing the α-chlorine with bromine should allow the reaction to proceed under milder conditions, thereby reducing the risk of unwanted stereoisomerisation.



(108)



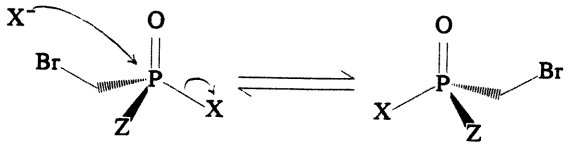
(109)



(109)

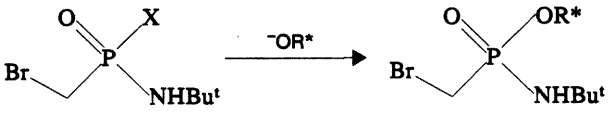
Scheme 22

One approach would be to prepare a single enantiomer of the alkyl α-bromomethylphosphonamidate (109), and study its rearrangement. Preparation from the appropriate optically active phosphonic halide or phosphonamidic halide (Scheme 22) would almost certainly be hampered by racemisation, resulting from halide exchange (Eq. 25), and in any case, preparation of optically active acid halides would be difficult. Preparation of the racemic alkyl α-bromomethylphosphonamidate should be straightforward but subsequent resolution would be required, and it is not obvious how that could be achieved.



Eq. 25

An alternative approach would be to prepare a substrate (110) that exists as diastereoisomers, by incorporating a chiral, non-migrating, alkyl group (Eq. 26), and establishing the configuration at phosphorus relative to this chiral group. The chiral group need not be optically pure, as the study could be conducted on a pair of racemic diastereoisomers. With an ideal alkyl group the diastereoisomers would be easily separable and the reaction could be readily monitored by GLC and ^{1}H and ^{31}P NMR spectroscopy. In this work the alkyl group derived from menthol was chosen, and owing to its cheapness and availability in optically pure form, the study was conducted on single enantiomers of the pair of diastereoisomers. A disadvantage of using diastereoisomers is that they may, in principle, behave differently, and the reaction must therefore be performed on both diastereoisomers (or enriched mixtures of both).

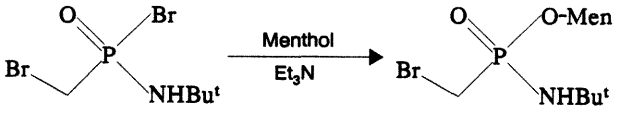


(110)

Eq. 26

Part II; Chapter 2: The Base Induced Rearrangement Of (-)-Menthyl *P*-(Bromomethyl)-*N*-*tert*-butylphosphonamidate

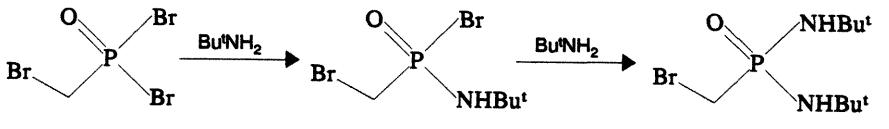
Preparation of the Bromomethylphosphonamidate



(111) (112)

Eq. 27

In principle the bromomethylphosphonamidate (112) could be prepared from the phosphonamidic bromide (111) and (-)-menthol in the presence of base (Eq. 27). However, the phosphonamidic bromide approach was not pursued because of evidence that during its attempted synthesis, from the bromomethylphosphonic dibromide (113)[59] and *tert*-butylamine, it underwent further reaction with *tert*-butylamine,[60] probably by an elimination-addition mechanism,[41] to give the diamide (114) (Eq. 28).

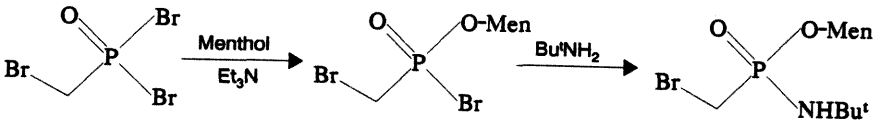


(113) (111) (114)

Eq. 28

Instead, the bromomethylphosphonamidate (112) was prepared by first reacting the bromomethylphosphonic dibromide (113) with (-)-menthol (1.05 mol equiv.) and triethylamine (1.0 mol

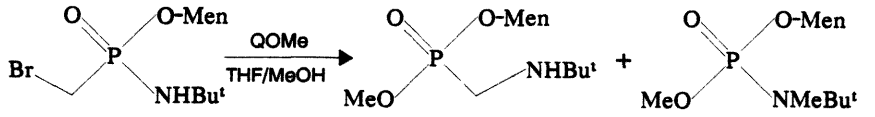
equiv.). This gave the menthyl phosphonobromidate (115), δ_P 19.0 and 17.0 (diastereoisomers) [accompanied by a small quantity of the dimenthyl phosphonate (δ_P 15.7; *ca.* 15 %)] which was then treated with an excess of *tert*-butylamine (Eq. 29). The crystalline product was formed as a 54 : 46 mixture of diastereoisomers with the ^{31}P NMR lowfield diastereoisomer dominant. Careful crystallisation from aqueous ethanol and then light petroleum gave sample **A**, the pure highfield ^{31}P NMR diastereoisomer $\delta_P(CH_2Cl_2)$ 18.0 (determined by GLC and ^{31}P NMR spectroscopy) and crystallisation of one of the mother liquors from light petroleum gave sample **B**, a 60 : 40 mixture of diastereoisomers (determined by ^{31}P NMR spectroscopy) with the lowfield ^{31}P NMR diastereoisomer, $\delta_P(CH_2Cl_2)$ 18.3, in excess.



(113) (115) (112)

Eq. 29

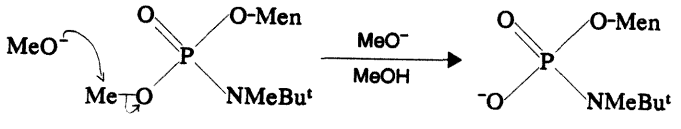
Reaction of the Bromomethylphosphonamidate with Methoxide



(112) (116) (117)

Eq. 30

Each sample of the bromomethylphosphonamidate was treated with 0.2 M benzyltrimethylammonium methoxide (QOMe) in THF-methanol (9 : 1 v/v) at room temperature and the progress of the reaction was followed by ^{31}P NMR spectroscopy. This showed that the substrate (δ_P 18.8; for **A** and 18.7 for **B**) was gradually converted into the aminomethylphosphonate (**116**), δ_P 27.1 and 26.8, and the *N*-methylphosphoramidate (**117**), δ_P 10.4 and 9.3 (Eq. 30); both products were formed as mixtures of diastereoisomers, but the diastereoisomer ratios were very different for the reactions of the two samples of substrate. As the reaction neared completion some demethylation of the *P*-methoxy group of the aminomethylphosphonate was apparent (δ_P 17.2; *ca.* 3 %) (Eq. 31);[61] the substrate was completely consumed in 4.5 h.



Eq. 31

The two types of product were separated by treatment of the mixture with dilute hydrochloric acid (the aminomethylphosphonate passes into the acidic aqueous portion); the products were isolated as oils and were completely characterised (the aminomethylphosphonate was further characterised as the picrate). The phosphoramidate structure was confirmed by ^1H NMR spectroscopy, which showed incorporation of methoxide, diastereoisomeric POMe signals ($\Delta\delta$ 0.016, d, J_{PH} 11.3 or 11.4), and P-C bond scission, indicated by the diastereoisomeric PNMe signals ($\Delta\delta$ 0.004, d, J_{PH} 9.7 or 9.5), while the IR spectrum showed no NH absorption. Confirmation of the aminomethylphosphonate structure was also achieved by ^1H NMR spectroscopy which showed diastereoisomeric POMe signals ($\Delta\delta$ 0.026, d, J_{PH} 10.6 or 10.8) resulting from incorporation of methoxide. The signals for the PCH_2N structure, indicative of P-N bond cleavage, were quite different for the two diastereoisomers; for the major product from sample A, $\delta_H(CDCl_3)$ 2.922 (2 H, ABP, J_{AB} 13.9, J_{AP} 14.9, and J_{BP} 15.7), and for the major product for sample B, $\delta_H(CDCl_3)$ 2.920 (2 H, d, J_{PH} 15.2). The expected NH signals were hidden under the menthyl residue but they were evident in the IR spectrum.

Table 12; Reaction of menthyl *P*-(bromomethyl)-*N*-*tert*-butylphosphonamidate (**112**) with benzyltrimethylammonium methoxide: diastereoisomer ratio of substrate (**B** : **A**) and ratio of aminomethylphosphonate (P⌿N) and phosphoramidate (P⌿C) rearrangement products as determined by ^{31}P NMR spectroscopy.

B : **A** (Substrate)	P⌿N : P⌿C
60 : 40 (Sample **B**)	83 : 17
0 : 100 (Sample **A**)	84 : 16

In principle the two diastereoisomers of the substrate could react with different rates and give different product ratios, but examination of the reaction of sample **B** at 86 % completion (^{31}P NMR spectroscopy) showed that the remaining substrate was still in ~ 3 : 2 diastereoisomer ratio, implying that there is no appreciable difference in the rates of reaction of the diastereoisomers. Also, both samples of substrate gave the two types rearrangement product in a ratio of about 5 : 1 (Table 12), implying no significant difference in their product-forming behaviour.

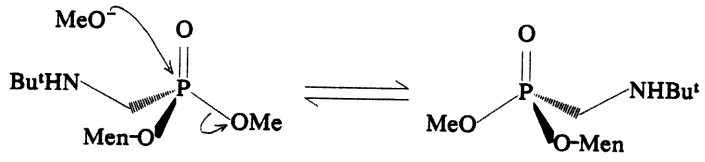
Table 13; Reaction of menthyl *P*-(bromomethyl)-*N*-*tert*-butylphosphonamidate (**112**) with benzyltrimethylammonium methoxide: diastereoisomer ratios of substrate (**B** : **A**) and rearrangement products (P⁄N, **A′** : **B′**; P⁄C, **A″** : **B″**) as determined by ^{31}P NMR spectroscopy.

B : A	A′ : B′ (P⁄N)	A″ : B″ (P⁄C)	Reaction Time[a]
60 : 40 (Sample B)	45 : 55	41 : 59	4.5 h
0 : 100 (Sample A)	96 : 4[b]	95 : 5[c]	4.5 h
	99 : 1[b]	95 : 5[c]	16 min
	88 : 12[b]	95 : 5[d]	6 h

[a] This is the time that the substrate spent in the reaction mixture before quenching with ammonium chloride.
[b] This ratio became evident only after the reaction mixture was worked up, and was determined by ^{1}H NMR spectroscopy after isolation.
[c] Confirmed by ^{1}H NMR spectroscopy.
[d] Determined by ^{1}H NMR spectroscopy after isolation.

The ratio of the diastereoisomers of the *N*-methylphosphoramidate (**117**) (**A″** : **B″**) reflected closely the ratio in the substrate for the reaction of sample **B** (Table 13), but the diastereoisomer ratio of the aminomethylphosphonate (**116**) (**A′** : **B′**) was slightly less than the 60 : 40 of the substrate (sample **B**), possibly because the major diastereoisomer experienced more demethylation. For sample **A** a small difference was evident in the diastereoisomer ratio of both products, suggesting that reaction is not completely stereospecific. To check whether the lack of complete stereospec-

ificity of the rearrangement for sample **A** was inherent or due to stereochemical equilibration of the products, the reaction with sample **A** was repeated; in one case reaction was quenched before it reached completion (93 % complete in 16 min), in another it was allowed to continue for 6 h before quenching. This established that the diastereoisomer ratio of the *N*-methylphosphoramidate (**117**) remained constant for all three experiments (95 : 5), but the ratio of the diastereoisomers of the aminomethylphosphonate (**116**) was greater (99 : 1) than originally observed (96 : 4) for the shorter reaction time, and less (88 : 12) for the longer time (Table 13). This implies that the aminomethylphosphonate (but not the phosphoramidate) experiences some stereochemical equilibration by methoxide exchange (Eq. 32), and suggests that the deviation from the expected ratio of 3 : 2 for sample **B** is also due to this, rather than to demethylation.



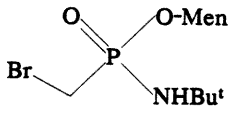
Eq. 32

Stereochemistry of the Rearrangement

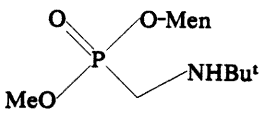
A portion of sample **A** of the bromomethylphosphonate (**112**) was recrystallised from dichloromethane-light petroleum and then aqueous ethanol to produce a crystal suitable for single

crystal X-ray analysis (Fig. 7).[62] Comparison of this stereostructure with those of the rearrangement products would give the stereochemistry of the reaction.

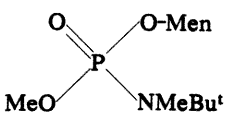
The aminomethylphosphonate from the rearrangement of substrate sample **A** was easily converted into its picrate salt, $\delta_P(CDCl_3)$ 16.4. Crystallisation from ether-light petroleum removed the small amount of the minor diastereoisomer, leaving just the major diastereoisomer (^1H and ^{31}P NMR) and recrystallisation of this sample from ether-light petroleum afforded a crystal suitable for single crystal X-ray analysis (Fig. 8).[62] Comparison of this stereostructure with that of the substrate revealed that the aminomethylphosphonate (**116**) was formed by cleavage of the P-N bond with inversion of configuration at phosphorus.



(112)



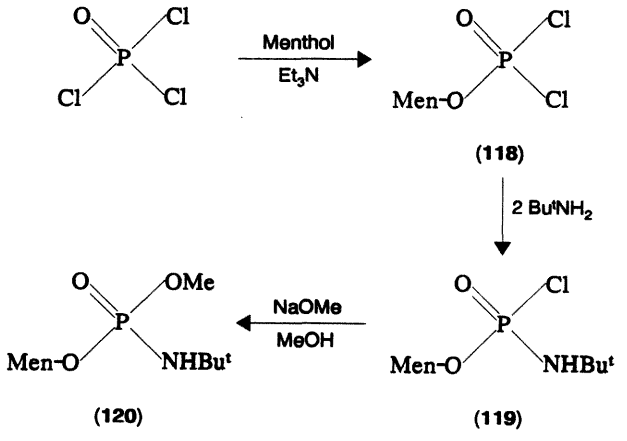
(116)



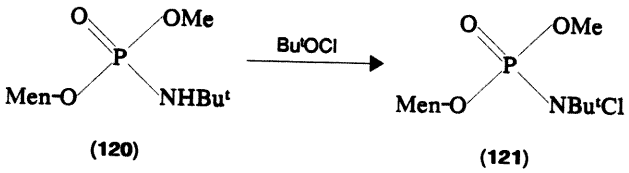
(117)

The *N*-methylphosphoramidate (**117**), being an oil but also being unamenable to derivatisation, presented more of a problem. The first approach was to synthesise one diastereoisomer of the *N*-hydrogen analogue (**120**) of the *N*-methylphosphoramidate, with a view to determining its X-ray structure, and relating it to the *N*-methyl rearrangement product (**117**). The phosphoramidate (**120**) was prepared by first treating phosphoryl chloride with (-)-menthol and triethylamine (1 mol

equiv.). This gave the phosphorodichloridate (**118**) which was treated with *tert*-butylamine (2 mol equiv.), giving the chloramidate (**119**), and then an excess of sodium methoxide (Scheme 23). The phosphoramidate (**120**) was formed as a 60 : 40 mixture of diastereoisomers, $\delta_P(CH_2Cl_2)$ 7.2 and 6.7. Crystallisation from light petroleum (b.p. 40-60 °C) at -40 °C failed to give crystals further enriched in one diastereoisomer; it gave crystals that were a 53 : 47 mixture of diastereoisomers and an enriched mother liquor instead. However, repeated chromatography of the 60 : 40 mixture eventually gave a sample that was > 96 % the lowfield (^{31}P NMR) diastereoisomer. Unfortunately, owing to its high solubility and its tendency to form clumps, a crystal suitable for X-ray study could not be obtained. It was therefore necessary to consider derivatisation of the phosphoramidate (**120**).

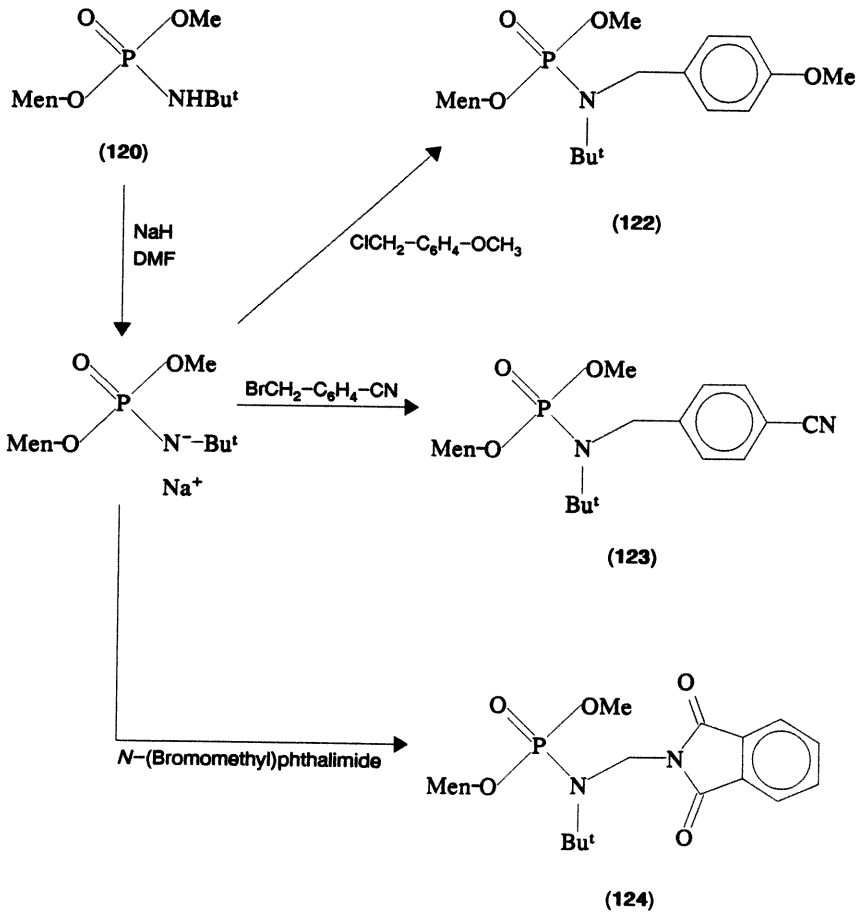


Scheme 23



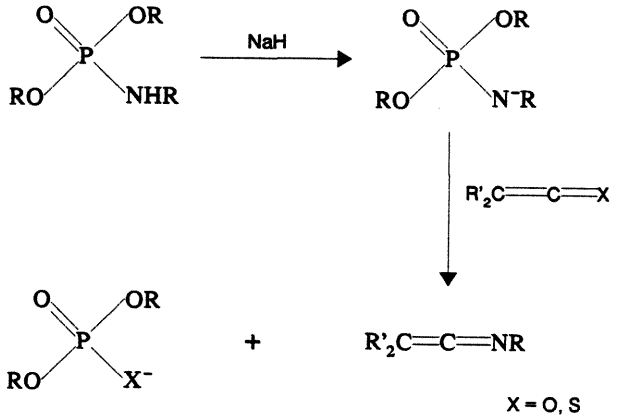
(120) **(121)**

Eq. 33



Scheme 24

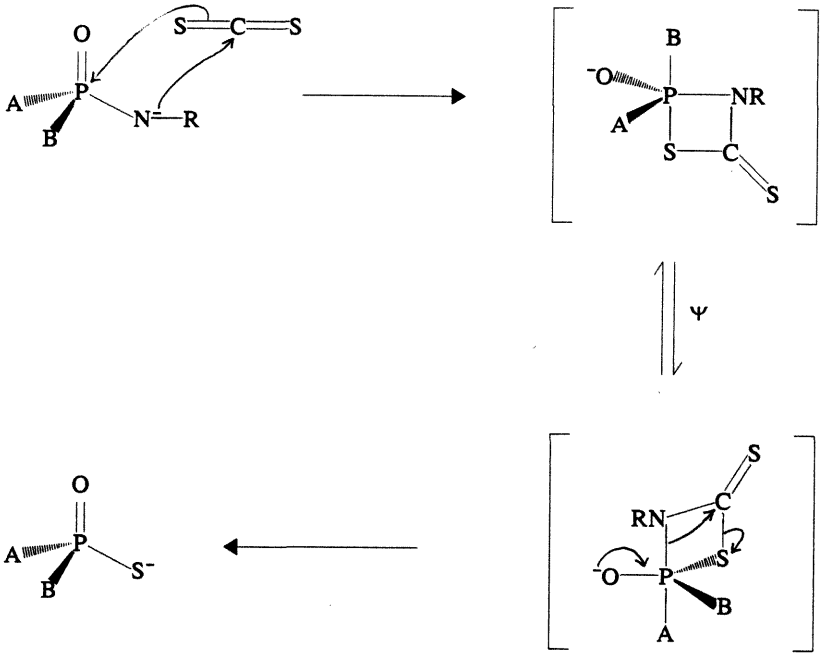
Treatment of the phosphoramidate (120) with *tert*-butyl hypochlorite gave the *N*-chloro analogue (121) which was,[63,9] unfortunately, an oil (Eq. 33). Treatment with sodium hydride in DMF gave the nitrogen anion[64] which was allowed to react with *p*-methoxybenzyl chloride, *p*-cyanobenzyl bromide,[65] and *N*-bromomethylphthalimide[66] to give the *N*-substituted phosphoramidates (122), (123), and (124) (Scheme 24), but these were a semisolid, a glass, and an oil respectively, and in the last two cases the yield was low (competing electron addition reactions[67]). It was clear that straightforward *N*-substitution was unpromising, and that a more radical approach would be required.



Scheme 25

The Wadsworth-Emmons reaction[68] is widely used in organic chemistry to prepare imines from carbonyl compounds. In the reaction, the anion of a phosphorus amide reacts with the carbonyl (or C=S) group, exchanging the amido group for oxygen (or sulphur), forming the imine and a phosphorus by-

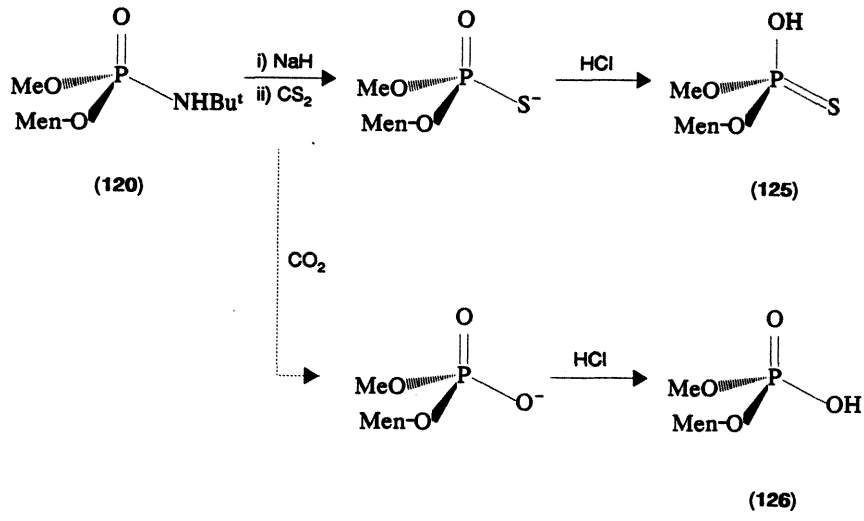
-product (Scheme 25). Of particular importance, this reaction has been shown to proceed with complete retention of configuration at phosphorus,[69,70] the mechanism probably being similar to that of the Wittig reaction (Scheme 26), and it has recently been used to synthesise optically pure phosphorothioates from phosphoramidates.[71]



Scheme 26

The phosphoramidate (120) (60 : 40 mixture of diastereoisomers) was treated with sodium hydride in DMF, giving the nitrogen anion, and then with carbon disulphide to give the phosphorothioate sodium salt as a mixture of diastereoisomers. Treatment with hydrochloric acid gave the crude phosphorothioic acid (125) as a solid (Scheme 27). Owing to the high solubility of the acid, it was purified as the

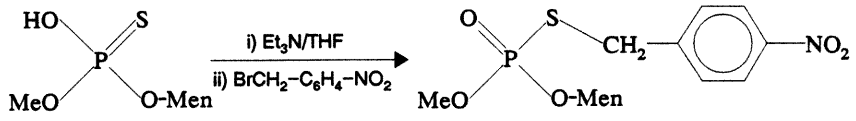
ammonium salt (the *tert*-butylammonium and anilinium salts were also prepared, but were oils), either by precipitating the salt (gelatinous) from dichloromethane by addition of light petroleum (b.p. 40-60 °C), or by washing an aqueous solution of the salt with ether (non-ionic impurities pass into ether).



Scheme 27

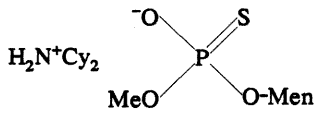
The conversion of the phosphorothioic acid into its ammonium salt, $\delta_P(CH_2Cl_2)$ 58.3 and 58.0 (diastereoisomers), revealed the presence of a phosphorus containing by-product (~ 15 %), $\delta_P(CH_2Cl_2)$ 0.3. This is believed to be the salt of phosphoric acid (126) resulting from reaction of the amidate anion with CO_2 instead of CS_2 (Scheme 27). The by-product could be removed by washing a solution of the triethylammonium salts in dichloromethane with water, the salt of the phosphorothioic acid remaining in the organic phase. The phosphorothioic acid, $\delta_P(CDCl_3)$ 61.0 and 60.6 (diastereoisomers), could be crystallised from light petroleum (b.p. 40-60 °C) at

-20 °C, but this gave clumps of crystals of poor quality, not suitable for X-ray studies. In the hope of obtaining a crystalline derivative, a portion of the acid was treated with *p*-nitrobenzyl bromide and triethylamine in THF to give the *S*-alkylated derivative (127) (Eq. 34), $\delta_P(CDCl_3)$ 26.5 and 26.1 (diastereoisomers); this, unfortunately, could not be crystallised.



(125) (127)

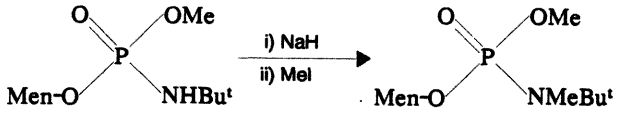
Eq. 34



(128)

Finally, treatment of the phosphorothioic acid with dicyclohexylamine afforded the corresponding salt (128), $\delta_P(CDCl_3)$ 56.7 and 56.0 (diastereoisomers), which gave well formed crystals from light petroleum (b.p. 40-60 °C). Encouraged by this, the enriched phosphoramidate (120) (> 96 % one diastereoisomer; see p. 87) was converted, as above, into the sodium phosphorothioate (some unreacted phosphoramidate was recovered for use later), then into the free acid, and then into the dicyclohexylammonium salt. This was crystallised to give a sample that was ≥ 99.5 % one diastereoisomer $\delta_P(CDCl_3)$

55.9, and this was recrystallised from a mixture of ether, dichloromethane, and light petroleum to give a sample for single crystal X-ray analysis (Fig. 9).[62]

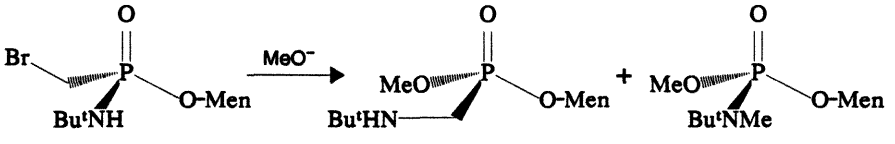


(120) (117)

Eq. 35

The unreacted phosphoramidate (120) recovered above, being the same material that was converted into the phosphorothioate salt for X-ray analysis, was treated with sodium hydride in DMF and then methyl iodide to give a sample of the *N*-methylphosphoramidate (117) that was found to be the lowfield ^{31}P NMR diastereoisomer (98 %) (Eq. 35). To confirm that this was indeed the lowfield diastereoisomer (and not the highfield diastereoisomer, with an even more highfield impurity) a sample was treated with a small portion of a mixture of both diastereoisomers [^{31}P NMR lowfield diastereoisomer in excess; prepared as above from a 60 : 40 mixture of diastereoisomers of the phosphoramidate (117)] and the mixture was re-examined. This showed, as it should, an enhancement of the highfield signal (from 2 % to 15 %), and confirmed that the phosphoramidate (120) had indeed been transformed into the ^{31}P NMR lowfield diastereoisomer of the *N*-methylphosphoramidate (117). This diastereoisomer was also the dominant one formed in the rearrangement of sample **A** of the bromomethylphosphonamidate. Since the phosphorothioate salt will have been formed from the phosphoramidate (120)

with retention of configuration at phosphorus, and conversion of the phosphoramidate (120) into the *N*-methylphosphoramidate (117) does not affect the configuration at phosphorus, it follows, that the configuration of the lowfield *N*-methylphosphoramidate formed in the rearrangement is the same as that of the phosphorothioate salt examined by X-ray crystallography. The *N*-methylphosphoramidate rearrangement product must therefore be formed with **retention of configuration at phosphorus** (Eq. 36).



(112) **(116)** **(117)**

Inversion Retention

Eq. 36

Fig. 7; The structure of menthyl *P*-(bromomethyl)-*N*-*tert*-butylphosphonamidate (**112**) as determined by single crystal X-ray analysis; configuration at phosphorus. Selected bond lengths (Å) and bond angles (°): P-C(1) 1.837(20), P-N 1.618(16), P-O(1) 1.424(14), P-O(2) 1.573(13), C(1)-P-N 105.8(9), C(1)-P-O(1) 112.5(9), C(1)-P-O(2) 98.7(9), N-P-O(1) 115.5(9), N-P-O(2) 104.8(8), O(1)-P-O(2) 117.7(8).

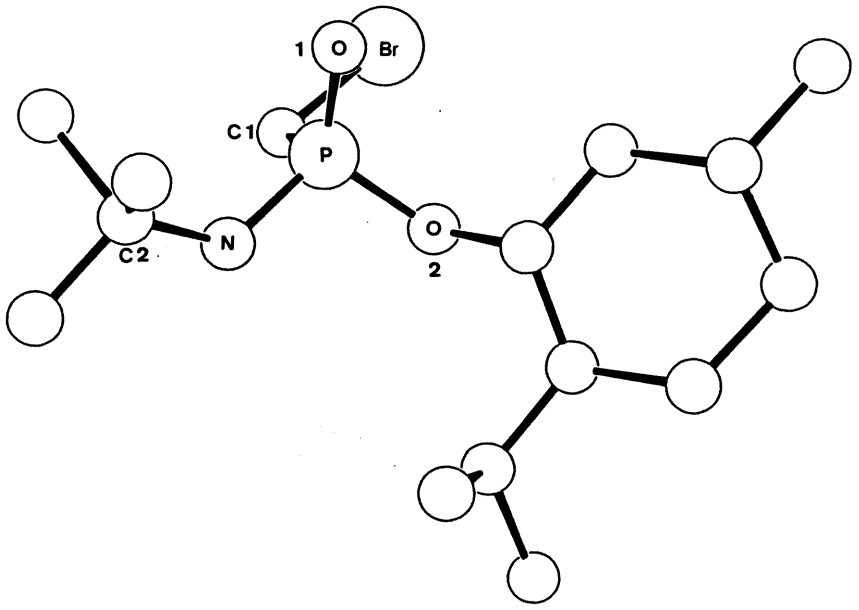


Fig. 8; The structure of menthyl methyl (*tert*-butylamino)methylphosphonate (116) as determined by single crystal X-ray analysis of its picrate salt (picrate anion not shown); configuration at phosphorus. One of four unique formula units, each having different conformations but all having the same configuration at phosphorus. Selected bond lengths (Å) and bond angles (°) for this particular formula unit: P-C(1) 1.836(20), P-O(1) 1.500(13), P-O(2) 1.502(13), P-O(3) 1.559(15), C(1)-P-O(1) 119.3(8), C(1)-P-O(2) 100.2(8), C(1)-P-O(3) 100.1(8), O(1)-P-O(2) 116.7(7), O(1)-P-O(3) 110.9(7), O(2)-P-O(3) 107.8(8).

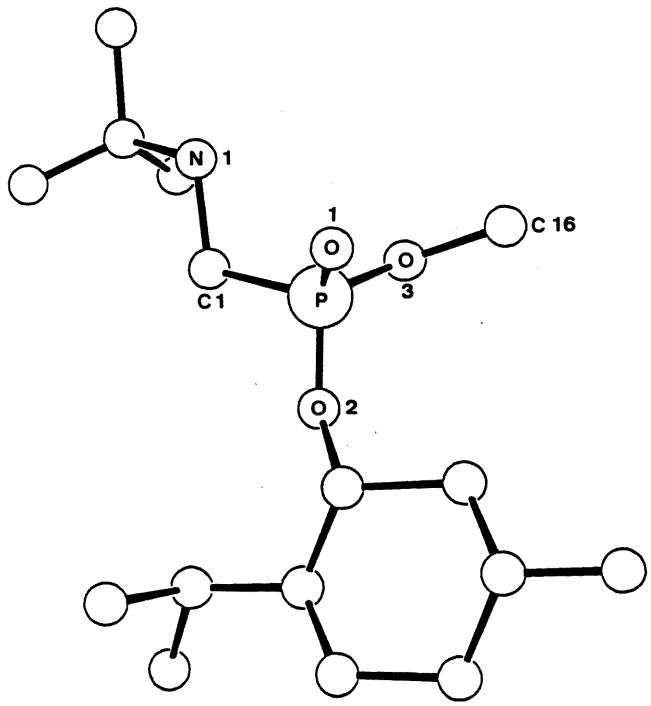
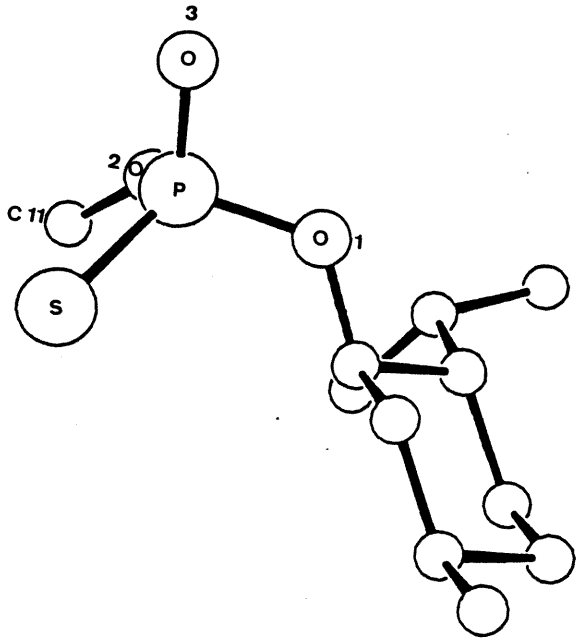
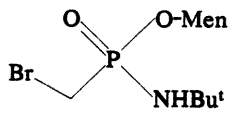


Fig. 9; The structure of dicyclohexylammonium *O*-menthyl *O*-methyl phosphorothioate (**128**) as determined by single crystal X-ray analysis (dicyclohexylammonium cation and diethyl ether of crystallisation not shown); configuration at phosphorus. Selected bond lengths (Å) and bond angles (°): P-O(1) 1.577(7), P-O(2) 1.543(9), P-O(3) 1.483(8), P-S 1.932(3), O(1)-P-O(2) 99.1(6), O(1)-P-O(3) 105.6(4), O(2)-P-O(3) 109.2(6), O(1)-P-S 113.2(3), O(2)-P-S 111.4(4), O(3)-P-S 116.8(3).

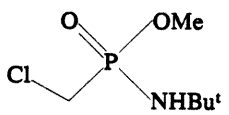


Part II; Chapter 3: The Base Induced Rearrangement Of Alkyl *P*-(Bromomethyl)-*N*-*tert*-butylphosphonamidates

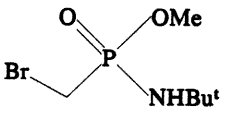
Preparation of Alkyl Bromomethylphosphonamidates



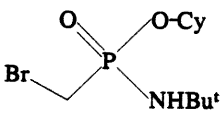
(112)



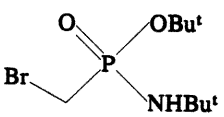
(108)



(129)



(130)

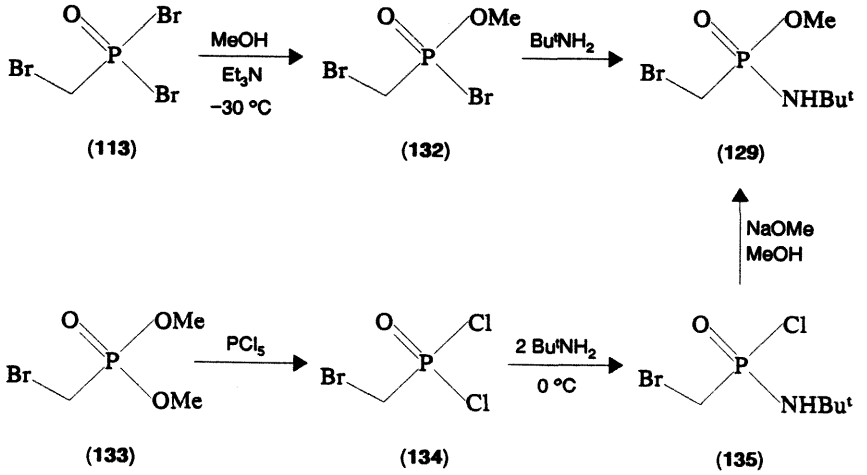


(131)

The 5 : 1 aminomethylphosphonate : phosphoramidate product ratio seen for the reaction of the menthyl bromomethylphosphonamidate (112) is very different to that previously observed for the methyl chloromethylphosphonamidate (108) (*ca.* 2 : 3),[58] also with QOMe in THF-methanol. Such a difference was not expected, and must result from either changing the leaving group from chlorine to bromine, or, more plausibly, changing the *O*-methyl group to *O*-menthyl. To clarify the picture, and in particular to assess the importance of steric factors, the investigation of the menthyl bromometh-

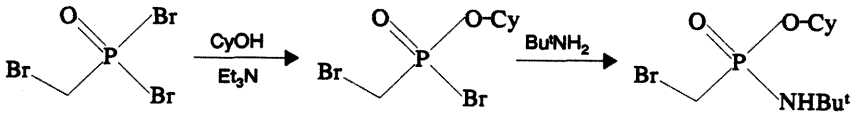
ylphosphonamidate (112) was extended to include its *O*-methyl, *O*-cyclohexyl, and *O*-*tert*-butyl analogues (129), (130), and (131).

The *O*-methyl bromomethylphosphonamidate (129), $\delta_P(CDCl_3)$ 22.6, was prepared by first treating the corresponding phosphonic dibromide with methanol and triethylamine (1 mol equiv.) at -30 °C. This gave the methyl phosphonobromidate (132), δ_P 22.1 [accompanied by a small quantity of the dimethyl phosphonate (δ_P 20.3; *ca.* 10 %)], which was then allowed to react with an excess of *tert*-butylamine (Scheme 28). The product, which was crystalline, was also prepared by first treating the bromomethylphosphonic dichloride (134), prepared from the dimethyl ester (133) and PCl_5 (Scheme 28),[72] with *tert*-butylamine (2 mol equiv.). This gave the phosphonamidic chloride (135), $\delta_P(CDCl_3)$ 29.5, which was then treated with sodium methoxide (Scheme 28).



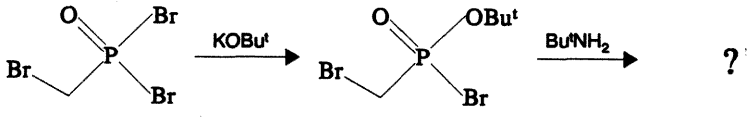
Scheme 28

The *O*-cyclohexyl analogue (**130**), $\delta_P(CDCl_3)$ 19.9, was prepared at room temperature from the phosphonic dibromide (**113**) and cyclohexanol and triethylamine (1 mol equiv.); this gave a mixture containing the cyclohexyl phosphonobromidate (**136**) and the dicyclohexyl phosphonate (δ_P 17.8 and 16.9; ratio *ca.* 2 : 1) [and several anhydrides (*ca.* 50 %), probably due to inadequate drying of the cyclohexanol] which was treated with an excess of *tert*-butylamine (Eq. 37). The product was purified by chromatography followed by crystallisation.



(**113**) (**136**) (**130**)

Eq. 37

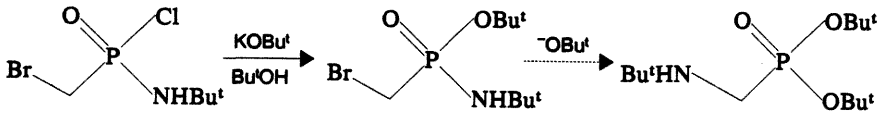


(**113**) (**137**)

Eq. 38

The *O*-*tert*-butyl analogue (**131**) could, in principle, be prepared from the phosphonic dibromide (**113**) with potassium *tert*-butoxide, then *tert*-butylamine (Eq. 38). However, the phosphonobromidate (**137**) would be unlikely to react with *tert*-butylamine because of steric hindrance at phosphorus,[23] so this approach was not adopted. Instead, the *N*-*tert*-butylphosphonamidic chloride (**135**) (see Scheme 28) was treated with potassium *tert*-butoxide (1.0 mol equiv.) in *tert*-butan-

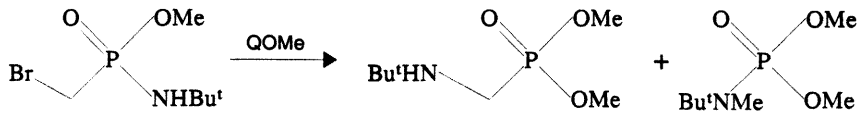
ol. This gave a mixture consisting of the starting material, δ_P 28.8, the required product, δ_P 15.1, and a by-product, δ_P 18.6. The by-product resulted from further reaction of the required product with potassium *tert*-butoxide, and was believed to be the aminomethylphosphonate (138) rearrangement product (Eq. 39). To achieve complete consumption of the starting material, more potassium *tert*-butoxide (0.8 mol equiv.) was added gradually, in small portions; this appeared to limit by-product formation (*ca.* 40 % at completion). The by-product was removed by careful extraction into dilute hydrochloric acid and the *O-tert*-butyl bromomethylphosphonamidate, $\delta_P(CDCl_3)$ 16.4, was purified by crystallisation.



(135) (131) (138)

Eq. 39

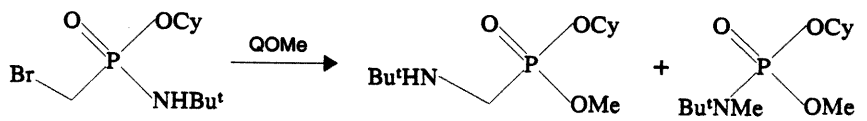
Reaction of Alkyl Bromomethylphosphonamidates



(129) **(139)** **(140)**

Eq. 40

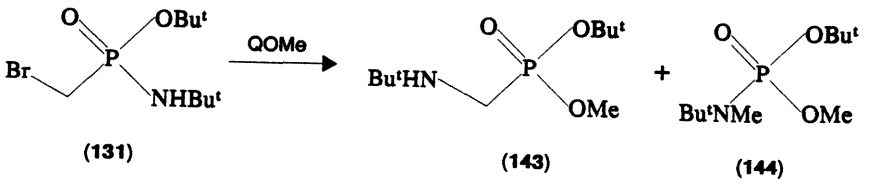
The *O*-methyl compound (129) was treated with 0.2 M QOMe in THF-methanol (9 : 1 v/v) at room temperature and the progress of the reaction was monitored by ^{31}P NMR spectroscopy. This showed that the substrate, δ_P 21.5, was converted into the aminomethylphosphonate (139), δ_P 28.8, and the phosphoramidate (140), δ_P 11.8, in a ratio of *ca.* 1 : 1.3 over a period of 2 h (see Table 14 and Eq. 40). Demethylation of the aminomethylphosphonate (139) appeared early on in the reaction and was more prominent (δ_P 20.0; *ca.* 9 % after 40 min) than in the reaction of the *O*-menthyl substrate (112). The products were separated by extraction of the aminomethylphosphonate into dilute hydrochloric acid, and they were characterised by comparison of their spectroscopic data with that already published.[58]



(130) **(141)** **(142)**

Eq. 41

The *O*-cyclohexyl analogue (130), δ_P 19.0, reacted with QOMe over a period of 2 h to give the aminomethylphosphonate (141), δ_P 26.9, and the phosphoramidate (142), δ_P 9.6, in a ratio of *ca.* 1.3 : 1 (see Table 14 and Eq. 41), with not more than 2 % demethylation of the aminomethylphosphonate. The products were isolated and characterised, and the aminomethylphosphonate was further characterised as the salt with picric acid, $\delta_P(CH_3OH)$ 17.3. Likewise, the *O*-*tert*-butyl substrate (131), δ_P 15.5, was transformed over 2.5 h into the aminomethylphosphonate (143), δ_P 24.1, and the phosphoramidate (144), δ_P 5.9, in a ratio of *ca.* 2 : 1 (Table 14), with virtually no demethylation of the aminomethylphosphonate (Eq. 42). These products were also formed in the reaction of the *O*-methyl substrate (129) with potassium *tert*-butoxide, and were isolated later (see below).

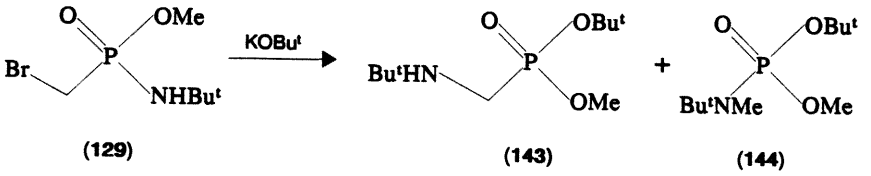


(131) (143) (144)

Eq. 42

The alkyl bromomethylphosphonamidates were also allowed to react with 0.2 M potassium *tert*-butoxide in THF-*tert*-butanol (9 : 1 v/v), the 10 % alcohol (*tert*-butanol) being included for the sake of consistency with the previous experiments which used THF-methanol. For the *O*-methyl analogue (129), $\delta_P(CDCl_3)$ 22.6, on treatment with 0.2 M KOBu^t in THF-Bu^{t}OH, reaction appeared to be instantaneous, with KBr precipitating on mixing; the reaction was certainly complete within 5 min.

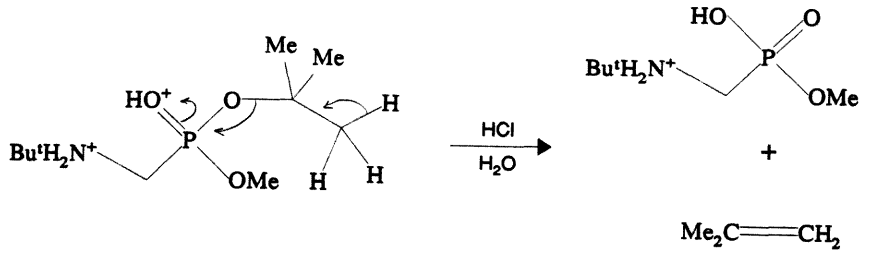
The aminomethylphosphonate (143), δ_P 23.8, and the phosphoramidate (144), δ_P 5.9, were formed in a ratio of *ca.* 3 : 1 (Table 14), the products being the same as those from the reaction of the *O-tert*-butyl compound (131) with QOMe (Eq. 43 *cf.* Eq. 42).



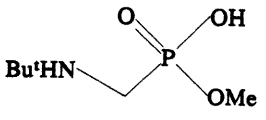
(129) (143) (144)

Eq. 43

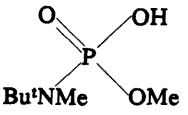
The two rearrangement products had to be separated by chromatography and not by extraction with dilute hydrochloric acid, as was used earlier, as even slight acidity was found to decompose the aminomethylphosphonate (143). Thus, the aqueous acid extract, when basified with sodium hydroxide, yielded no product on attempted back-extraction into organic solvents. The ^{1}H NMR spectrum (CD_3OD) of the material in aqueous solution revealed the absence of an OBu^t group, but showed NCH_2P (d, J_{PH} 15), POMe (d, J_{PH} 10.5), and Bu^{t}N signals. Clearly acidification had removed the *tert*-butyl group from oxygen, giving the parent amino-acid (145), perhaps by loss of butene (Eq. 44). A similar acid-catalysed debutylation of $RP(O)(OBu^t)_2$ has been reported using CF_3CO_2H.[73] Because of their sensitivity to acid all products containing the POBu^t group were isolated by chromatography.



Eq. 44

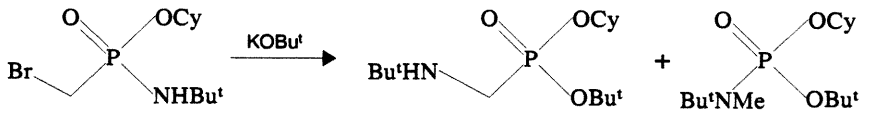


(145)



(146)

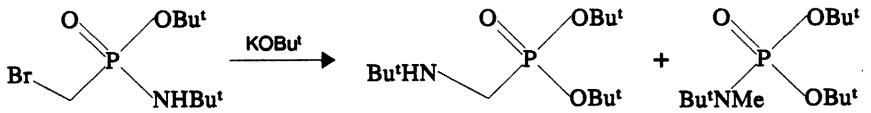
When the above reaction was performed using $KOBu^t$ that had not been freshly sublimed, two further products were formed, δ_P 20.4 and δ_P 7.7 (ratio *ca.* 1 : 3). These were believed to be the potassium salts of the aminomethylphosphonate (145) and the phosphoramidate (146), formed by reaction with hydroxide impurity instead of *tert*-butoxide. Hydroxide, being very much more nucleophilic than *tert*-butoxide, will inevitably give rise to a disproportionately large amount of the total product if there are traces of hydroxide in the potassium *tert*-butoxide or water in the *tert*-butanol. To confirm that water was responsible for these two additional products the reaction was repeated with a little added water (0.3 mol equiv.); examination of the reaction mixture showed that the two additional products were indeed formed in enhanced yield.



(130) **(147)** **(148)**

Eq. 45

The reaction of the *O*-cyclohexyl analogue (**130**), $\delta_P(CDCl_3)$ 19.9, with KOBu^t was almost instantaneous and produced the aminomethylphosphonate (**147**), δ_P 21.9, and the phosphoramidate (**148**), δ_P 3.6, in a ratio of *ca.* 11.5 : 1 (see Table 14 and Eq. 45). The products were separated and fully characterised.



(131) **(138)** **(149)**

Eq. 46

The reaction of the *O*-*tert*-butyl analogue (**131**), $\delta_P(CDCl_3)$ 16.4, with KOBu^t was also almost instantaneous and gave predominantly the aminomethylphosphonate (**138**), δ_P 18.98, the phosphoramidate (**149**), δ_P ($CDCl_3$) 0.9, being detected only after work up of the reaction (ratio *ca.* 32 : 1; see Table 14 and Eq. 46). The ease of this reaction, the chemical shift of its major product, and the almost complete absence of the phosphoramidate (**149**) reinforced the view that the major product here was also the by-product formed in the preparation of the substrate (**131**) (see p. 101).

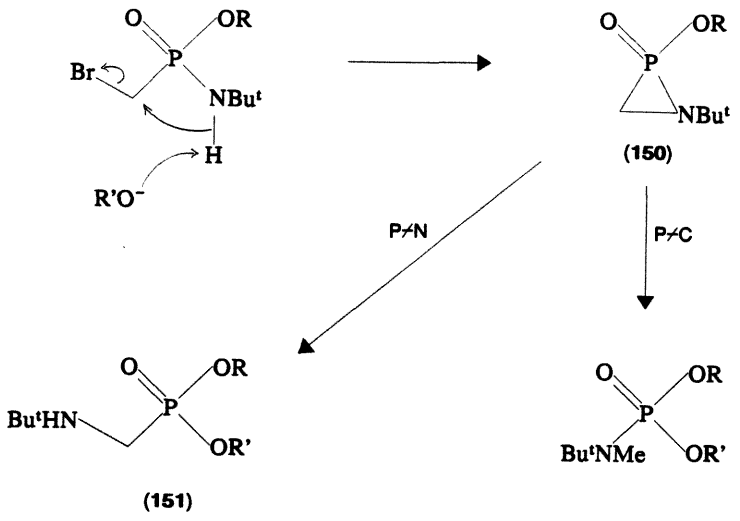
Table 14; Reaction of the alkyl *P*-(bromomethyl)-*N*-*tert*-butylphosphonamidate (**129**), (**130**), or (**131**) with benzyltrimethylammonium methoxide or potassium *tert*-butoxide: product ratios (P⁄N : P⁄C) as determined by ^{31}P NMR spectroscopy.

	Alkoxide P⁄N : P⁄C		
Alkyl group	^-OMe	$^-OBu^t$	$^-OBu^t$ & H_2O
Methyl	43 : 57	77 : 23	24 : 76
Cyclohexyl	57 : 43	92 : 8	
tert-Butyl	68 : 32	97 : 3[a]	
Menthyl	84 : 16[b]		

[a] Determined by ^1H NMR spectroscopy.
[b] This ratio is for sample **A** (100 %).

The reactions of the three substrates and the two alkoxide reagents show that steric effects are important as far as product ratios are concerned. In particular, it seems that hindered substrates favour formation of the aminomethylphosphonate (P⁄N), and hindered nucleophiles also favour formation of the aminomethylphosphonate (Table 14). The fact that the *O*-menthyl substrate (**112**), bearing a secondary alkyl group, behaves as though it is sterically more encumbered than the *O*-*tert*-butyl substrate (**131**) is noteworthy (Table 14). This is unlikely to be due to the effect of the ring in the menthyl group - the *O*-cyclohexyl compound (**130**) shows the

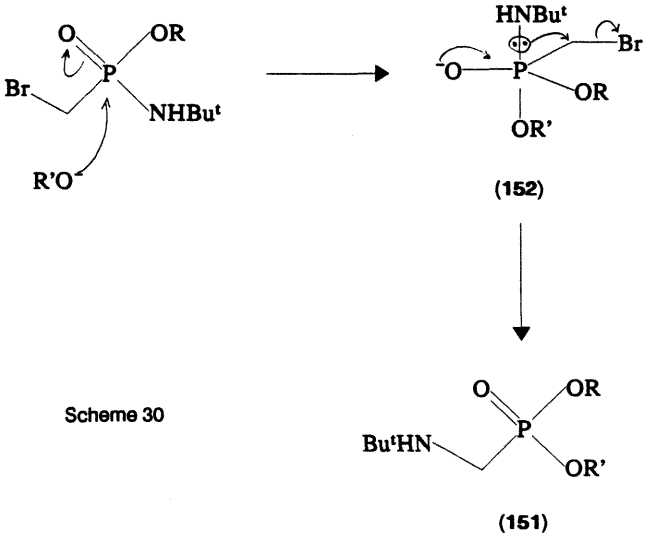
expected behaviour, intermediate between the *O*-methyl and *O*-*tert*-butyl compounds - but is most probably due to the 2-isopropyl group; this will increase the steric impact of the *O*-menthyl group at the phosphorus centre, making menthyl, in effect, more bulky than *tert*-butyl.



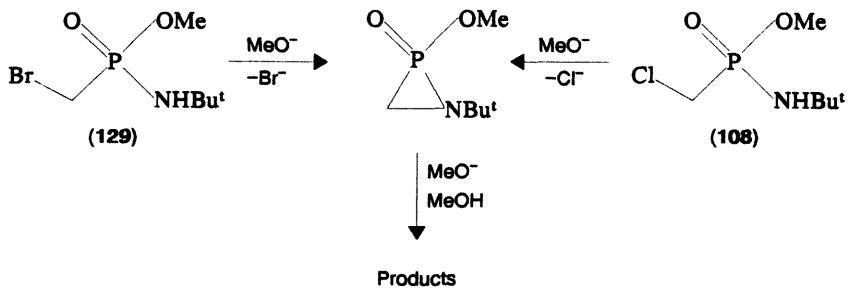
Scheme 29

The alkyl bromomethylphosphonamidates (112), (129), (130), and (131) reacted with alkoxides to give aminomethylphosphonate and phosphoramidate rearrangement products. The products are probably formed through the azaphosphiridine oxide (150) (Scheme 29) but it is also possible that the aminomethylphosphonate (151) could be formed from the phosphorane (152) (Scheme 30). Since nucleophilic substitution at 4-co-ordinate phosphorus is highly sensitive to steric hindrance we would expect a bulky substrate to react with a bulky nucleophile only with some difficulty,[23] so some relative enhancement of the product arising from P-C bond scission could be expected if the phosphorane (152) does contribute to formation of the aminomethylphosphonate (P≠N scission). However, the *O-tert*-butyl compound (131) reacted with potassium

tert-butoxide much faster than it did with benzyltrimethylammonium methoxide and gave almost entirely the aminomethylphosphonate (**138**), the product that would be formed by the phosphorane pathway (Scheme 30; R = R′ = Bu^t). This, in spite of the fact that phosphorane formation must be particularly difficult for such a hindered system. It therefore seems more likely that both products are formed from the azaphosphiridine oxide. Also, the product ratios for the *O*-methyl compound (**129**) (*ca.* 1 : 1.3) and the corresponding chloromethylphosphonamidate (**108**) (*ca.* 1 : 1.6)[58] with methoxide are very similar, and possibly the same within experimental error, and this could be considered evidence of a common intermediate, *i.e.* an azaphosphiridine oxide quenched, in both cases, by methoxide (Scheme 31).



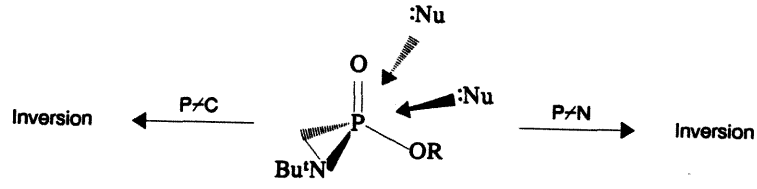
Scheme 30



(129) (108)

Scheme 31

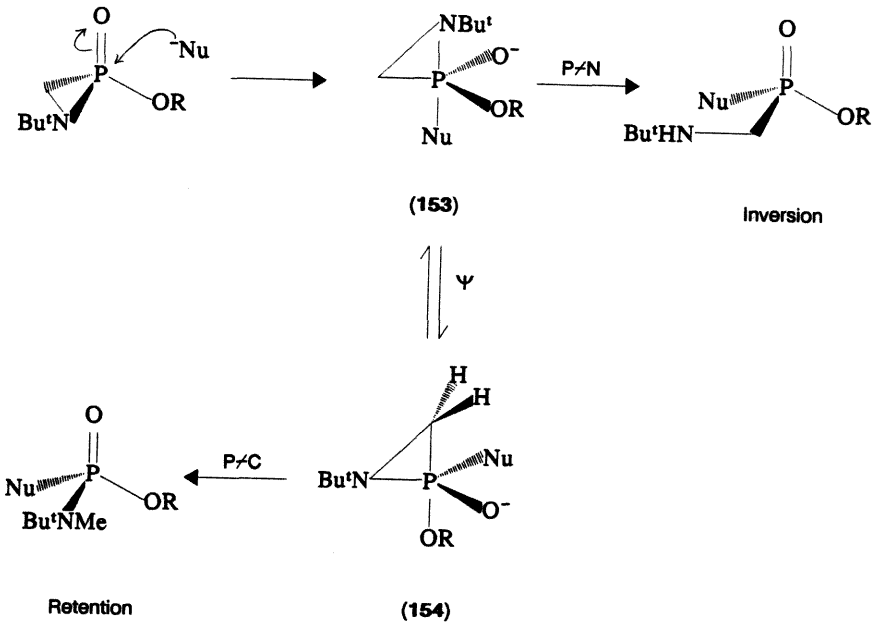
Once the azaphosphiridine oxide has been formed the nucleophile could react with it in two different ways; i) it could directly displace the nitrogen or carbon moiety from phosphorus by an S_N2 mechanism, resulting in inversion of the configuration at phosphorus for both products (Scheme 32), or ii) it could add to the phosphoryl group to give a phosphorane (Scheme 33), with less obvious stereochemical consequences for the products.



Scheme 32

For nucleophilic substitution proceeding through a phosphorane intermediate, the nucleophile will add to the phosphoryl group to form a phosphorane in which the nucleophile occupies an apical position, and the leaving group will depart from an apical position to give the product.[74] The nucleophile need not attack opposite the leaving group, but if the nucleophile did add opposite the leaving group, sub-

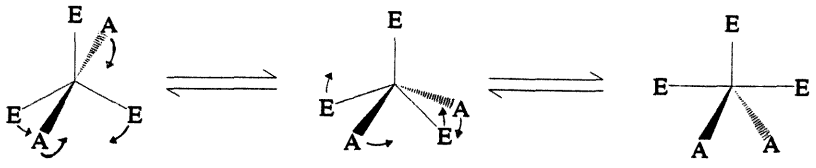
stitution would occur with inversion of configuration at phosphorus; if the phosphorane was a transition state, instead of an intermediate, the substitution would be equivalent to an S_N2 displacement. There are, however, certain rules that govern phosphoranes, a) that the most electronegative group - oxygen in this case - prefers to be apical,[75] and b) that a small ring involving phosphorus will span the apical-equatorial positions.[76] The second of these generally over-rules the first. If rule 'a)' applied, the three-membered ring would have to occupy the equatorial plane with an ideal bond angle of about 120° at phosphorus - twice the preferred value for a three-membered ring. If the ring spanned apical-equatorial positions it would have an ideal bond angle of 90° at phosphorus, and furthermore, going from a tetrahedral azaphosphiridine oxide, bond angle ~ 109° at phosphorus, to the phosphorane would lead to a reduction in ring strain; addition of the nucleophile would in this case be expected to proceed rapidly.[77] Thus, the nucleophile would be expected to add to the azaphosphiridine oxide opposite nitrogen, the more electronegative of the ring elements, to give the phosphorane (153) (apical nitrogen). Cleavage of the P-N bond would then give the aminomethylphosphonate product with inversion of configuration at phosphorus (Scheme 33), as observed for the *O*-menthyl compound (112).



Scheme 33

Once the phosphorane (153) has been formed it can pseudorotate,[76,78] whereby an equatorial bond assumes the role of a 'pivot'. The two remaining equatorial bonds and the apical bonds deform, by converging on their counterparts, to give a tetragonal structure in which the 'pivot' is apical and the other four bonds are positionally equivalent. This structure may return to the original phosphorane by reversing the above process, or may generate a new phosphorane by placing the two formerly apical bonds in equatorial positions (Scheme 34). If the phosphorane (153) underwent a pseudorotation, to make a new phosphorane (154) with carbon apical (the nucleophile would now occupy an equatorial position), rupture of the P-C

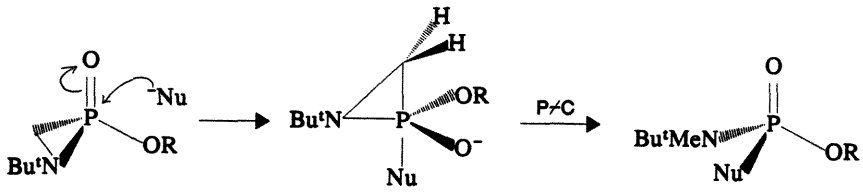
bond would then result in a phosphoramidate being formed with retention of configuration at phosphorus (Scheme 33); this was observed for the *O*-menthyl compound (112).



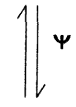
Scheme 34

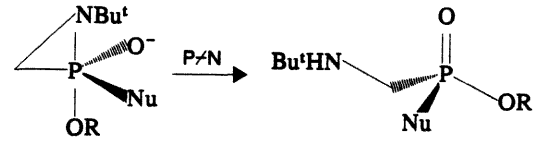
Phosphoranes prefer electronegative elements to be apical but there is evidence that the preference of nitrogen over carbon is not great,[74,79] so attack opposite the P-C bond could be possible. If this was the case we would expect to see some of the phosphoramidate formed with inversion of configuration at phosphorus. For the *O*-menthyl compound (112) some of the phosphoramidate (117) was formed with inversion of configuration (5 %; ~ 1 % of total products). This could occur by direct nucleophilic displacement of carbon from phosphorus (Scheme 32), or by the breakdown of the phosphorane (155) (apical carbon) formed by addition of the nucleophile to the azaphosphiridine oxide opposite the P-C bond (Scheme 35). If the latter occurred, the phosphorane (155) could undergo pseudorotation to (156), and then break down to give the aminomethylphosphonate with retention of configuration at phosphorus (Scheme 36). Although some of the menthyl aminomethylphosphonate (116) was apparently formed with retention of configuration, it was found that when the reaction of the menthyl compound (112) with methoxide was quenched early (16 min) it was in the region of 1 %, and for

reaction quenched after 6 h it was about 12 %. This is most probably due to stereochemical equilibration of the product, by methoxide exchange in the reaction mixture (Eq. 47); it is, therefore, not possible to say whether there is any genuine retention of configuration in the formation of the aminomethylphosphonate.



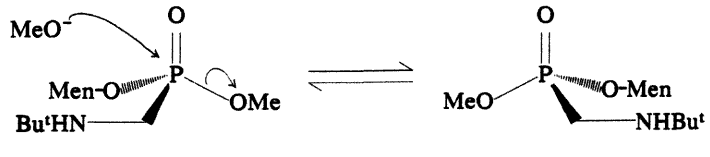
(155) Inversion





(156) Retention

Scheme 35



(116)

Eq. 47

Further experiments revealed a definite trend in the reaction, namely that hindered nucleophiles and hindered substrates both favour formation of the aminomethylphosphonate. Owing to the absence of stereochemical information for the reactions of the alkyl bromomethylphosphonamidates (129), (130), and (131) it is not known whether the phosphoramidate products were formed largely with retention of configuration, as in the case of the *O*-menthyl analogue (112), or with inversion, due to nucleophilic attack opposite the P-C bond. If the course of nucleophilic attack is dependent on the apicophilicities of carbon versus nitrogen,[74,79] and the steric interactions in the two competing phosphoranes (Schemes 33 and 35),[79] it becomes apparent that attack opposite the P-C bond is favoured on steric grounds as the NBu^t group would then be placed equatorial where it would have two nearest neighbours instead of three. However, the hydrogens on the apical carbon will eclipse two equatorial bonds and may also project into the equatorial alkoxy group, if it is large, causing severe interactions. These interactions could remove any steric benefit gained by placing the NBu^t group equatorial, and the small preference for apical nitrogen could then prevail, *i.e.* a large *O*-alkyl group in the substrate disfavours the phosphorane (155) (apical carbon).

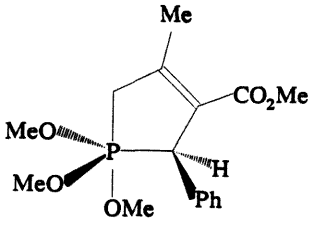
We know that the phosphorane (155), formed by the addition of the nucleophile opposite the P-C bond, accounted for at least 0.8 % of the reaction for the *O*-menthyl substrate (112) (as the phosphoramidate formed with inversion of configuration accounted for 0.8 % of the total products), and we would expect that as the *O*-alkyl group decreases in size, from

O-menthyl to *O*-methyl, this phosphorane would become more important due to less severe interactions between the equatorial *O*-alkyl group and the hydrogens on the apical carbon, *i.e.* the yields of the phosphoramidate formed with inversion of configuration should increase as the size of the *O*-alkyl group in the substrate decreases.

It could be, then, that attack opposite the P-N bond is the first step, but pseudorotation gives rise to a more open structure which is favoured on steric grounds if the *O*-alkyl group (now apical) and the nucleophile (now equatorial) are small (Scheme 33). Although carbon is now apical, and perhaps not as preferred as nitrogen, it could be that the difference in the apicophilicities of carbon and nitrogen is small and that lower steric interactions outweigh the preference for apical nitrogen. If the OR group is large it will be reluctant to occupy an apical position, as this will increase steric interactions (three, instead of two nearest neighbours), and the phosphorane (153) (apical nitrogen) will be favoured. Also, if the nucleophile is large, the interactions with the hydrogens on the apical carbon could offset any benefit obtained by pseudorotation, and the preference for apical nitrogen would be expected to prevail.

The relative apicophilicities of the competing groups on phosphorus affect pseudorotation. In the case of Me_2PF_3 the preference for apical fluorine is large and pseudorotation, putting one methyl group apical, is not seen at room temperature.[75,76] However, with the phosphorane (157),[76] the preference for oxygen over carbon is not as large and pseudorotation is fast on the NMR time scale at room temperature.

The difference in the apicophilicities of nitrogen and carbon is smaller still, and inter-conversion of the two phosphoranes (153) and (154) could be sufficiently rapid that they equilibrate before they collapse to product.



(157)

A factor that must surely influence the product ratio is the leaving ability of nitrogen relative to carbon. If pK_a values of amines and alkanes are taken as a measure of leaving ability we would expect nitrogen to be the better leaving group (*cf.* NH_3, pK_a = 38, and CH_4, pK_a = 48[80]) and the transition state leading to P-N bond cleavage to be more accessible than that leading to P-C bond cleavage. It could be that for the phosphorane with apical carbon (resulting either from pseudorotation or addition opposite the P-C bond) the energy required to cleave the P-C bond is lower than the total energy required to pseudorotate and cleave the P-N bond (Fig. 10); if the two phosphoranes have equilibrated, the product ratios may reflect the thermodynamic ratio of the two phosphoranes.

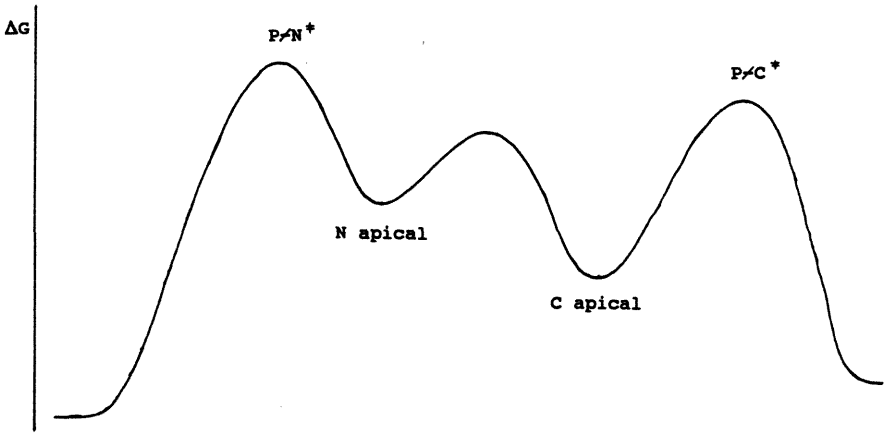


Fig. 10

It is interesting to note that the phosphorane (**155**), from nucleophilic addition of the alkoxide to the azaphosphiridine oxide opposite the P-C bond, and the phosphorane (**154**), derived from pseudorotation of the phosphorane (**153**) (apical nitrogen), are the same in the case of the *O*-methyl compound (**129**) with methoxide, and in the case of the *O*-*tert*-butyl compound (**131**) with *tert*-butoxide (Schemes 33 and 35; OR = Nu = OMe or OBu^t). In the former, if the phosphorane (**154**), derived from pseudorotation of the phosphorane (**153**) is favoured, then it is conceivable that nucleophilic attack opposite the P-C bond may be significant, perhaps even more important than attack opposite the P-N bond, and the phosphoramidate (**140**) may be substantially formed with inversion of configuration at phosphorus. In the latter, where the phosphorane (**153**) (apical nitrogen) is expected to be favoured, the phosphoramidate (**149**) would be formed largely with retention of configuration.

Experimental

M.p.s. were determined using a Kofler hot-stage apparatus, IR spectra were recorded with a Perkin-Elmer 298 instrument, ^{1}H NMR spectra were recorded at 90 MHz with a Varian EM390 or a JEOL JNM-FX90Q spectrometer, and, where specified, at 300 MHz with a Bruker AM 300 spectrometer. ^{31}P NMR spectra (^{1}H-decoupled) were recorded at 24 MHz or 36 MHz with a JEOL JNM-FX60 or a JEOL JNM-FX90Q spectrometer respectively; positive chemical shifts were measured downfield from external 85 % H_3PO_4. For NMR data where the solvent is not specified the reaction medium was used. Where product ratios were determined by ^{31}P NMR the peak heights or integrals were used unless otherwise specified. Routine mass spectra (EI at 70 eV) were obtained with a V. G. Micromass 16B spectrometer or a Kratos Concept and high resolution mass spectra were recorded by the SERC Mass Spectrometry Service at Swansea. GLC analyses were recorded on a Pye Unicam PU4500 chromatograph (column; OV 1701 1μ film, 15 m x 0.53 mm) or capillary chromatograph (column; BP 5 0.25μ film, 25 m x 0.22 mm; equivalent to SE 54), in both cases helium was used as the carrier gas, TLC was performed on silica gel 60 F_{254}, 0.2 mm film on aluminium foil (Merck), and optical rotations were obtained from a Perkin-Elmer 141 polarimeter.

Methanol and ethanol were purified by distillation from their magnesium salts, cyclohexanol and tert-butanol were dried over powdered 3A molecular sieves. Tetrahydrofuran (THF) was distilled from sodium/benzophenone and was stored over 3A/4A molecular sieves and under nitrogen. It was redistilled immediately prior to use. *N,N*-Dimethylformamide

(DMF) was distilled from P_2O_5 under reduced pressure and stored over molecular sieves and under nitrogen, amines were dried over potassium hydroxide unless otherwise specified, potassium *tert*-butoxide was sublimed before use and light petroleum refers to the fraction b.p. 60-80 °C unless otherwise indicated. *O*-Trimethylsilylhydroxylamine was prepared by a published procedure.[13]

N,O-*Bis(trimethylsilyl)hydroxylamine*.- Based on the method of Bottaro[01] et al, finely ground and dried hydroxylamine hydrochloride (11.57 g, 0.167 mol) was added to a stirred solution (powerful magnet) of dry ethylenediamine (15.03 g, 0.25 mol) in dichloromethane (130 ml). The flask was stoppered and left stirring until two distinct liquid phases were present (~ 8 h). A long reflux condenser was fitted and chlorotrimethylsilane (38.52 g, 0.35 mol) was added dropwise over 30 min. When spontaneous reflux had ceased the reaction mixture was stoppered and left stirring for 24 h. Unexpectedly, the reaction stopped at the monosilyl product ($H_2NOSiMe_3$), R_t 2.6 min (10 % E 30, 80 °C); an authentic sample of the bis-silyl product had R_t 7.8 min and refluxing for a further 3 h produced no change. However, when triethylamine (16.87 g, 0.167 mol) in ether (30 ml) was dripped in over 30 min, the reaction was mildly exothermic and much solid was formed. More chlorotrimethylsilane (*ca*. 4 ml, 3.42 g, 31 mmol) was added and the mixture was refluxed for a further 2 h to give the desired product (R_t 7.8 min). The reaction mixture was filtered under nitrogen and the solid (amine hydrochloride) was washed with light petroleum spirit (b.p. 40-60 °C) (70 ml). Solvents were removed from the

filtrate by fractional distillation and the residue was distilled in a Spaltrohr apparatus giving *N,O*-bis(trimethylsilyl)hydroxylamine, 13.9 g (47 %); b.p. 92–93 °C at 150 mmHg (lit.,[81] 131–140 °C at 700 mmHg); $\nu_{max.}$(film) 3280 cm^{-1} (NH).

Diethyl Phenylphosphonite (35)[82].– A mixture of dichlorophenylphosphine (26.9 g, 0.15 mol), anhydrous pyridine (24.5 g, 0.31 mol), and light petroleum (70 ml) was stirred under nitrogen and cooled in ice. A mixture of anhydrous ethanol (13.8 g, 0.30 mol) and light petroleum (5 ml) was added dropwise, and the reaction was left stirring at room temperature overnight. The precipitated pyridine hydrochloride was filtered off under nitrogen and washed with a small quantity of light petroleum. The filtrate was concentrated and distillation afforded diethyl phenylphosphonite (35) (12.7 g, 43 %); b.p. 60–62 °C at 0.05 mmHg (lit.,[83] 99–100 °C at 4 mmHg); $\delta_P(CH_2Cl_2)$ 156.1.

Ethyl Benzyl(phenyl)phosphinate (36)[29].– Diethyl phenylphosphonite (3) (12.0 g, 60.5 mmol) was stirred under nitrogen and heated to 100 °C (bath temperature). Benzyl chloride (9.2 g, 72.7 mmol) was added dropwise, then the bath temperature was raised to 200 °C and the reaction mixture was allowed to stir for a further 3 h. Distillation at *ca.* 150 °C at 0.4 mmHg (lit.,[84] b.p. 198–202 °C at 6 mmHg) gave ethyl benzyl(phenyl)phosphinate (36) (11.8 g, 75 %), $\delta_P(CDCl_3)$ 40.1; $\delta_H(CDCl_3)$ 7.7–7.0 (10 H, m), 3.94 (2 H, m), 3.25 (2 H, d, J_{PH} 18), and 1.25 (3 H, t, J_{HH} 7).

Ethyl α-Methylbenzyl(phenyl)phosphinate (37).- *(a)*[33] A mixture of diethyl phenylphosphonite (35) (496 mg, 2.5 mmol) and 1-bromoethylbenzene (463 mg, 2.5 mmol) was stirred in a gentle stream of nitrogen, and the flask (fitted with an air condenser) was placed in an oil bath, pre-heated to 155 °C, for 75 min. The resulting mixture contained not only the required phosphinate (35), δ_P 43.3 and 42.6 (diastereoisomers) (~ 75 %) but also two other products, δ_P 45.0 (4 %) and δ_P 24.0 (21 %), probably PhEtP(O)OEt and PhHP(O)OEt respectively. Because this reaction was not clean an alternative approach (see below) was adopted.

(b) A solution of ethyl benzyl(phenyl)phosphinate (36) (7.6 g, 29.1 mmol) in THF (50 ml) was stirred at -70 °C (bath temperature) while a solution of *n*-butyllithium in hexane (2.5 M; 12 ml, 30 mmol) was added dropwise over a period of 20 min. After a further 30 min at -70 °C, iodomethane (8.3 g, 60 mmol) in THF (10 ml) was added dropwise and the mixture was allowed to warm slowly to room temperature. All solvent was removed and the residue was dissolved in ether (70 ml). The resulting solution was washed twice with water (50 ml, then 20 ml), dried, and concentrated to yield crude *ethyl α-methylbenzyl(phenyl)phosphinate* (37) (7.2 g, 90 %) as a mixture of diastereoisomers, $\delta_P(CH_2Cl_2)$ 43.0 and 42.4. A small portion was distilled, b.p. 130 °C (oven) at 0.3 mmHg; $\delta_P(CDCl_3)$ 44.3 and 43.4 (major) in a 47 : 53 ratio (impurity at 47.1 *ca.* 5 %); $\delta_H(CDCl_3$, 300 MHz) 7.61-7.04 (10 H, m), 4.19-3.76 (2 H, m), 3.288 and 3.230 (major) (total 1 H; both dq, J_{PH} 18.2 or 16.9, J_{HH} 7.4, PC*H*Me), 1.594 and 1.502 (major) (total 3 H; both dd, J_{PH} 16.9 or 17.5, J_{HH} 7.4, PCH*Me*), and

1.308 and 1.201 (major) (total 3 H; both t, J_{HH} 7.0); *m/z* 274 (M^+, 40 %), 170 (M^+ - $PhCH{=}CH_2$, 40), 169 (M^+ - PhCHMe, 30), 142 (M^+ - $PhCH{=}CH_2$ - $H_2C{=}CH_2$, 20), 141 (M^+ - PhCHMe - $H_2C{=}CH_2$, 100), and 105 ($PhCHMe^+$, 50); $\nu_{max.}$(film) 1220 cm^{-1} (P=O) (Found: M^+, 274.1123. $C_{16}H_{19}O_2P$ requires *M*, 274.1123). The bulk of the product was used without further purification.

α-Methylbenzyl(phenyl)phosphinic Acid (38).- The ester (37) (7.0 g, 25.7 mmol) was stirred and heated under reflux (bath temperature 140 °C) in concentrated hydrochloric acid (25 ml) for 14 h. The mixture was diluted and the product was extracted into dichloromethane and dried. Evaporation of the solvent gave a syrup, which on trituration with ether followed by crystallisation from dichloromethane-ether yielded α-methylbenzyl(phenyl)phosphinic acid (38) (4.1 g, 65 %), m.p. 136-137 °C (from ethyl acetate) (lit.,[31] 133-135 °C); $\delta_P(CH_2Cl_2)$ 44.8; $\delta_H(CDCl_3)$ 12.90 (s, OH), 7.6-7.0 (5 H, m), 7.08 (5 H, br s), 3.10 (1 H, dq, J_{PH} 18, J_{HH} 7), and 1.42 (3 H, dd, J_{PH} 17, J_{HH} 7); $\nu_{max.}$(Nujol) 2650, 2250, 1660 (all br OH), 1170 (P=O), and 950 cm^{-1} (Found: C, 68.0; H, 5.9. Calc. for $C_{14}H_{15}O_2P$: C,68.3; H, 6.1 %).

α-Methylbenzyl(phenyl)phosphinic Chloride (39).- The phosphinic acid (38) was stirred in dichloromethane (*ca.* 2 ml per mmol) and to it oxalyl chloride (2 mol equiv.) was added. When the reaction was complete (δ_P 58.8 and 58.5, diastereoisomers) volatile material was removed, and remaining traces of oxalyl chloride were removed by addition and evaporation of solvent several times, followed by pumping at 0.4 mmHg (> 2 hours). The crude *α-methylbenzyl(phenyl)phosphinic chloride* (39) was obtained as a mixture of diastereoisomers (47 : 53),

$\delta_P(CDCl_3)$ 59.6 and 59.2; $\delta_H(CDCl_3$, 300 MHz) 7.7–6.9 (10 H, m), 3.577 and 3.566 (total 1 H; both dq, J_{PH} 14.5, J_{HH} 7.3), and 1.798 (major) and 1.626 (total 3 H; both dd, J_{PH} 20.1 or 20.9, J_{HH} 7.3); $\nu_{max.}$(Nujol) 1225 (P=O). A portion was crystallised from ether–light petroleum to give a sample (b.p. 40–60 °C) (90 % the diastereoisomer δ_P 59.6; highfield resonance) having m.p. 108–111 °C; *m/z* 266, 264 (M^+, 25 %, ratio 1 : 3), 162, 160 (M^+ – $PhCH{=}CH_2$, 12, ratio 1 : 3), and 105 ($PhCHMe^+$, 100) (Found: M^+, 264.0471. $C_{14}H_{14}ClOP$ requires *M*, 264.0471). The bulk of the material was used without purification.

N-[α-Methylbenzyl(phenyl)phosphinoyl]-O-trimethylsilylhydroxylamine (42).– *(a) N,O*-Bis(trimethylsilyl)hydroxylamine (1.95 g, 11 mmol) was added[10] to a stirred solution of α-methylbenzyl(phenyl)phosphinic chloride (39) (2.26 g, 8.6 mmol) in dichloromethane (7.7 ml) (slight effervescence). The vessel was stoppered in such a way that any excess pressure would be released, and the temperature was maintained at *ca.* 35 °C for 24 h. Some solid was precipitated (see below) but was not removed. All volatile material was evaporated (no heat), and (to remove the last traces of Me_3SiCl) light petroleum was added to, and evaporated from, the residue. Washing with ether afforded the solid *N-[α-methylbenzyl-(phenyl)phosphinoyl]-O-trimethylsilylhydroxylamine* (42) (1.63 g, 57 %) as a comparable mixture of the two diastereoisomers, $\delta_H(CH_2Cl_2)$ 41.7 and 40.7.

(b) In a similar experiment the precipitated solid was filtered off and washed with ether; it was found to be essentially a single diastereoisomer of the *N*-phosphinoyl-*O*-silylhydroxylamine (42) (18 %). A portion crystallised from di-

chloromethane–light petroleum (b.p. 40–60 °C) had m.p. 140–142 °C (decomp.); $\delta_P(CDCl_3)$ 42.0; $\delta_H(CDCl_3$, 300 MHz) 7.96–7.88 (2 H, m), 7.61–7.26 (8 H, m), 5.30 (1 H, s, N*H*), 3.72 (1 H, dq, J_{PH} 11.8, J_{HH} 7.5), 1.45 (3 H, dd, J_{PH} 17.0, J_{HH} 7.5), and −0.11 (9 H, s); *m/z* 333 (M^+, 30 %), 318 (M^+ − Me, 15), 245 [PhCHMe(Ph)P(O)NH_2^+, 15], 120 (80), and 105 ($PhCHMe^+$, 100); $\nu_{max.}$(Nujol) 3130 (NH), 1185 (P=O), and 850 (several maxima) cm^{-1} (Found: C, 60.85; H, 7.4; N, 4.05. $C_{17}H_{24}NO_2PSi$ requires C, 61.2; H, 7.25; N, 4.2 %). The filtrate contained both this diastereoisomer (δ_P 41.0) and the other (δ_P 42.0) in a 1 : 2.5 ratio, together with a by-product (δ_P 34.0, *ca.* 20 %); removal of volatile material (rotary evaporator) and washing of the residue with ether–light petroleum gave a solid that was desilylated as described below.

N-[α-Methylbenzyl(phenyl)phosphinoyl]hydroxylamine (43).– *(a)* The *N*-phosphinoyl-*O*-silylhydroxylamine (42) (1.63 g, 4.9 mmol) from (a) in the above experiment was dissolved in dichloromethane (24 ml) and methanol (1.2 ml, 6 mol equiv.) was added. The reaction was monitored by ^{31}P NMR spectroscopy [δ_P 43.7, 42.5 (diastereoisomers) ---> 42.1, 40.2]. After 86 h all volatile material was removed (rotary evaporator) and the residue was triturated with ether to give the *N*-phosphinoylhydroxylamine (43) (1.24 g, 97 %) as a mixture (*ca.* 1 : 1) of diastereoisomers, $\delta_P(CDCl_3)$ 41.9 and 40.1.

(b) The silylated materials from (b) above were similarly desilylated (complete in *ca.* 24 h), and the residues triturated and washed with ether to give two samples of *N-[α-methylbenzyl(phenyl)phosphinoyl]hydroxylamine* (43): sample B (derived from the precipitated material), essentially one

diastereoisomer, m.p. 130–132 °C (decomp.) after crystallisation from chloroform–light petroleum; $\delta_P(CDCl_3)$ 40.1; $\delta_H(CDCl_3$, 300 MHz) 8.1 (br, O*H*), 7.73–7.37 (5 H, m), 7.20 (5 H, m), 5.961 (1 H, d, J_{PH} 8.8, N*H*), 3.407 (1 H, dq, J_{PH} 15, J_{HH} 7.5), and 1.432 (3 H, dd, J_{PH} 16.9, J_{HH} 7.5); *m/z* 261 (M^+, 5 %), 245 [$PhCHMe(Ph)P(O)NH_2^+$, 40], 141 [$PhCHMe(Ph)P(O)NH_2^+$ – $PhCH{=}CH_2$, 45), 140 [$PhCHMe(Ph)P(O)NH_2^+$ – $PhCHMe^+$, 100), 120 (10), and 105 ($PhCHMe^+$, 65); $\nu_{max.}$(Nujol) 3160 (NH), 1155 (P=O), and 1115 cm^{-1}; sample A (derived from the filtrate), a mixture of diastereoisomers, $\delta_P(CDCl_3)$ 41.9 and 40.1 (ratio *ca.* 4.5 : 1). A small sample of the major diastereoisomer of sample A was obtained by crystallisation from dichloromethane, m.p. 142.5–144.5 °C (decomp.); $\delta_H(CDCl_3)$ 8.50 (1 H, br s, O*H*), 7.55–7.0 (10 H, m), 6.30 (1 H, d, J_{PH} 11.5, N*H*), 3.72 (1 H, dq, J_{PH} 19.5, J_{HH} 7.5), and 1.57 (3 H, dd, J_{PH} 16.5, J_{HH} 7.5); *m/z* 261 (M^+, 6 %); $\nu_{max.}$(Nujol) 3260, 3220 (NH), 1170 (P=O), and 1120 cm^{-1} (Found: C, 64.4; H, 6.3; N, 5.55. $C_{14}H_{16}NO_2P$ requires C, 64.4; H, 6.2; N, 5.4 %).

N-[α-Methylbenzyl(phenyl)phosphinoyl]-O-methanesulphonylhydroxylamine (44).– A suspension of the *N*-phosphinoylhydroxylamine (43) (sample B) (496 mg, 1.90 mmol) in dichloromethane (8 ml) was stirred and cooled in ice. Triethylamine (192 mg, 1.90 mmol) was added, followed immediately by methanesulphonyl chloride (300 mg, 2.60 mmol).[10,65] After 20 min, the mixture was allowed to warm to room temperature. It was diluted with dichloromethane (12 ml) and washed with water (2 × 4 ml), some solid that separated being redissolved by addition of more solvent and warming. The warm solution was dried ($MgSO_4$) and concentrated. Crystallisation from

dichloromethane–light petroleum afforded *N*-[*α*-*Methylbenzyl(phenyl)phosphinoyl*]-*O*-*methanesulphonylhydroxylamine* (44) (sample B) (395 mg, 61 %; 97 % one diastereoisomer), $\delta_P(CDCl_3)$ 38.1; $\delta_H(CDCl_3$, 300 MHz) 7.92–7.85 (2 H, m), 7.69–7.52 (3 H, m), 7.45–7.30 (5 H, m), 7.199 (1 H, d, J_{PH} 3.7, N*H*), 3.627 (1 H, dq, J_{PH} 11.8, J_{HH} 7.5), 2.701 (3 H, s), and 1.550 (3 H, dd, J_{PH} 17.9, J_{HH} 7.5) [small peaks at 3.136 (s) and 1.725 (dd) due to the other diastereoisomer (3 %)]; *m/z* 339 (M^+, 2 %), 324 (M^+ – Me, 2), 245 [$PhCHMe(Ph)P(O)NH_2^+$, 25], 141 [$PhCHMe(Ph)P(O)NH_2^+$ – $PhCH{=}CH_2$, 40], 140 [$PhCHMe(Ph)P(O)NH_2^+$ – $PhCHMe^+$, 95], and 105 ($PhCHMe^+$, 100); *m/z* (CI) 340 ($M{+}H^+$, 40) and 246 ($M{+}H^+$ – $MeSO_3H$, 100); $\nu_{max.}$(Nujol) 3060 (NH) and 1185 cm^{-1} (P=O). A sample further purified by recrystallisation from dichloromethane–light petroleum had m.p. 177–179 °C (decomp.) (Found: C, 53.1; H, 5.3; N, 4.1. $C_{15}H_{18}NO_4PS$ requires C, 53.1; H, 5.35; N, 4.1 %). Crystallisation from dichloromethane afforded a sample (major diastereoisomer, B) for single crystal X-ray analysis. The crystal was glued to a glass filament. Data were measured on a Stöe STADI-2 Weissenberg diffractometer with graphite monochromated Mo-K_α radiation (λ 0.7107 Å) using an *ω*-scan technique. The data were corrected for Lorentz and polarisation effects.

Crystal data for (44) (racemate): $C_{15}H_{18}NO_4PS$, M = 339.35. Monoclinic, space group *I2/a*, a = 20.132(16), b = 10.396(2), c = 17.814(14) Å, β = 117.8(1)°, U = 3299(5) Å^3, Z = 8, μ = 2.62 cm^{-1}, $F(000)$ = 1424, D_c = 1.37 g cm^{-3}, T = 293 K. The structure was solved by direct methods. The phenyl and methyl hydrogen atoms were included in calculated positions with

isotropic thermal parameters refined as groups. The remaining hydrogen atoms were refined as isotropic atoms and all other atoms were refined with anisotropic thermal parameters. Full-matrix least squares refinement of 187 parameters gave R = 0.047 and R_w = 0.049 for 2324 unique reflexions with $I > 3\sigma(I)$. For complete details see Appendix 1.

Samples of the *N*-phosphinoylhydroxylamine (43) having other diastereoisomer compositions were similarly converted into the methanesulphonates. In particular, sample A gave the methanesulphonate (44) (sample A) as a 4 : 1 mixture of diastereoisomers, m.p. 154-157.5 °C; $\delta_P(CDCl_3)$ 39.6 (major) and 38.4; $\delta_H(CDCl_3)$ 8.45 (1 H, d, J_{PH} 7, NH), 7.63-6.85 (5 H, m), 7.12 (5 H, br s), 3.66 (1 H, dq, J_{PH} 15, J_{HH} 7.5), 3.10 (major) and 2.73 (total 3 H; both s), and 1.70 (3 H, dd, J_{PH} 16, J_{HH} 7.5); *m/z* (CI) 340 ($M+H^+$, 35 %) and 246 (100); $\nu_{max.}$(Nujol) 3020 (NH) and 1180 cm^{-1} (P=O). Also, a 1 : 1 mixture of diastereoisomers of the *N*-phosphinoylhydroxylamine (43) was similarly converted into the methanesulphonate (44). Trituration with dichloromethane-ether gave a 39 : 61 mixture of diastereoisomers, but treatment with a calculated amount of the minor diastereoisomer (A) gave a 50 : 50 mixture of diatereoisomers for use in the competition study.

N-[α-Methylbenzyl(phenyl)phosphinoyl]-O-p-nitrobenzenesulphonylhydroxylamine (45).- A suspension of the *N*-phosphinoylhydroxylamine (43) (107 mg, 0.41 mmol) [20 : 80 mixture of

diastereoisomers, $\delta_P(CDCl_3)$ 40.1 in excess*] in dichloromethane (2 ml) was stirred and cooled in ice. Triethylamine (41 mg, 0.41 mmol) was added, followed by *p*-nitrobenzenesulphonyl (nosyl) chloride (128 mg, 0.58 mmol; 1.4 mol equiv.).[18] Cooling was continued for a further 2 min and the mixture was then allowed to warm to room temperature. All volatile material was removed (rotary evaporator) and the residue was washed with ether. The resulting solid was mixed thoroughly with iced water (5 ml) and the crude product was collected by filtration. Further washing with water and then ether gave *N-[α-methylbenzyl(phenyl)phosphinoyl]-O-p-nitrobenzenesulphonylhydroxylamine* (45) (112 mg, 61 %), which crystallised from chloroform as a 3 : 97 mixture of diastereoisomers, $\delta_P(CH_2Cl_2)$ 42.3 and 39.5 (major). A small sample was further purified (crystallisation from chloroform–light petroleum), m.p. 162–163 °C (decomp.); $\delta_P(CDCl_3)$ 40.9; $\delta_H(CDCl_3$, 300 MHz) 8.1–7.7 (4 H, AA'BB'; δ_A 8.07, δ_B 7.76, J_{AB} 8.9), 7.65–7.3 (10 H, m), 7.08 (1 H, d, J_{PH} 0.7, N*H*; exchanges with D_2O), 3.520 (1 H, dq, J_{PH} 10.3, J_{HH} 7.5), and 1.392 (3 H, dd, J_{PH} 18.0, J_{HH} 7.5); *m/z* 446 (M^+, 1 %), 245 [$PhCHMe(Ph)P(O)NH_2^+$, 30], 243 (M^+ – $ArSO_3H$, 25), 141 [$PhCHMe(Ph)P(O)NH_2^+$ – $PhCH{=}CH_2$, 40], 140 [$PhCHMe(Ph)P(O)NH_2^+$ – PhCHMe, 100], and 105 ($PhMeCH^+$, 55); *m/z* (FAB; NOBA matrix)

* The ^{31}P NMR lowfield diastereoisomer of the *N*-phosphinoylhydroxylamine (43) was found to be sparingly soluble in ethyl acetate. Crystallisation of a 1 : 1 mixture of diastereoisomers of (43) from hot ethyl acetate gave a sample that was highly enriched in the ^{31}P NMR lowfield diastereoisomer and a 20 : 80 mixture of diastereoisomers (^{31}P NMR highfield diastereoisomer in excess) in the mother liquor. Recrystallisation of the mother did not improve the diastereoisomer ratio and this material was used in the preparation of the nosylate (45). Recrystallisation of the sample enriched in the ^{31}P NMR lowfield diastereoisomer from ethyl acetate gave the pure lowfield diastereoisomer of (43).

447 ($M+H^+$, 80 %), 289 (100), and 246 [$PhCHMe(Ph)P(O)NH_2+H^+$, 80); $\nu_{max.}$(Nujol) 3200-2500 (NH), and 1190 (P=O) cm^{-1}. The analysis sample was not obtained entirely free of chloroform [Found: C, 51.4; H, 4.1; N, 5.5 (m.p. 159-161 °C). $C_{20}H_{19}N_2O_6PS.0.2CHCl_3$ requires C, 51.6; H, 4.1; N, 6.0 %. Found: C, 48.0; H, 3.7; N, 5.25 (m.p. 162-163 °C). $C_{20}H_{19}N_2O_6PS.0.6CHCl_3$ requires C, 47.8; H, 3.8; N, 5.4 %]. A second preparation of the nosylate (45) gave a 4 : 96 mixture of diastereoisomers (^{31}P NMR highfield diastereoisomer in excess) for use in the competition study.

α-Methylbenzylphosphonic Dichloride (47).- The phosphonic acid (46)[32,33], $\delta_P(CDCl_3)$ 34.6 (broad), prepared from the Arbuzov reaction of $P(OEt)_3$ with 1-bromoethylbenzene, followed by acid hydrolysis of the resulting ester, was stirred in thionyl chloride (20 mol equiv.) with a catalytic quantity of dimethylformamide (0.03 mol equiv.) at 90 °C (bath temp.) until the ^{31}P NMR spectrum contained only one important peak, $\delta_P(SOCl_2)$ 54.1 (*ca.* 3 h). All volatile material was removed and the residue was maintained at ≤ 0.2 mmHg for 1.5 h. The resulting α-methylbenzylphosphonic dichloride (47)[86] was used without further purification.

N-*Phenyl*-P-*(α-methylbenzyl)phosphonamidic Chloride* (48).- α-Methylbenzylphosphonic dichloride (47) (2.27 g, 10.2 mmol) was stirred (powerful magnet) with aniline (1.90 g, 20.4 mmol) in benzene (6 ml) at 25 °C for 24 hours (δ_P 41.7 and 41.3, diastereoisomers; ratio *ca.* 1 : 2). Much solid was precipitated. The mixture was diluted with benzene (10 ml) and the insoluble material ($PhNH_3Cl$) was removed by filtration. The filtrate was reduced in volume and ether was

added. On standing (overnight), crystals of one of the diastereoisomers of N-*phenyl*-P-*(α-methylbenzyl)phosphonamidic chloride* (48) (0.98 g, 34 %) were obtained, m.p. 146–148 °C [from dichloromethane–light petroleum (b.p. 40–60 °C)]; $\delta_P(CDCl_3)$ 42.3; $\delta_H(CDCl_3$, 300 MHz) 7.27 (5 H, br s), 7.3–7.15 (2 H, m), 7.07–6.98 (3 H, m), 5.747 (1 H, br d, J_{PH} 9.4, N*H*), 3.650 (1 H, dq, J_{PH} 17.0, J_{HH} 7.4), and 1.778 (3 H, dd, J_{PH} 22.5, J_{HH} 7.4); *m/z* 281, 279 (M^+, 25 %; ratio 1 : 3), 177, 175 ($M^+ - PhCH{=}CH_2$, 15; ratio 1 : 3), and 105 ($PhCHMe^+$, 100); $\nu_{max.}$(Nujol) 3170 (NH) and 1210 cm^{-1} (P=O) (Found: C, 60.0; H, 5.3; N, 4.7. $C_{14}H_{15}ClNOP$ requires C, 60.1; H, 5.4; N, 5.0 %). A similar preparation,[87] but with most of the benzene being removed from the filtrate prior to the addition of ether, gave the phosphonamidic chloride (83 %) as a mixture of diastereoisomers [in a 30 : 70 ratio, $\delta_P(CDCl_3)$ 43.3 and 42.7 (major)].

N-*Phenyl*-P-*(α-methylbenzyl)phosphonamidic Acid* (61).– The phosphonamidic chloride (48) (110 mg, 0.39 mmol) was heated with 1 M aqueous sodium hydroxide (1 ml) on a steam bath for 1 h. The cooled solution was filtered and acidified to pH 1 by addition, with stirring, of 2 M hydrochloric acid. The mixture was extracted with dichloromethane and the dried extract was concentrated. Trituration with ether gave N-*phenyl*-P-*(α-methylbenzyl)phosphonamidic acid* (61) (79 mg, 77 %); m.p. 125.5–127 °C (from dichloromethane–light petroleum); $\delta_P(CDCl_3)$ 30.3; $\delta_H(CDCl_3)$ 8.5 (2 H, very broad, O*H* and N*H*), 7.4–6.6 (5 H, m), 7.10 (5 H, br s), 3.23 (1 H, dq, J_{PH} 19.5, J_{HH} 7.5), and 1.49 (3 H, dd, J_{PH} 18, J_{HH} 7.5); $\nu_{max.}$(Nujol) 3235 (NH), 2700, 2360, 1650 br (OH), and 1155 cm^{-1}

(P=O) (Found: C, 64.2; H, 6.2; N, 5.5. $C_{14}H_{16}NO_2P$ requires C, 64.4; H, 6.2; N, 5.4 %). This material was used to assist identification of the tert-*butylammonium* N-*phenyl*-P-*(α-methylbenzyl)phosphonamidate* (63), δ_P 18.0, formed in the reaction of the methanesulphonate (44) (sample A) with 0.1 M *tert*-butylamine in dichloromethane. [The salt was extracted into water, the extract acidified (pH ≤ 1), and the free acid back-extracted into dichloromethane: $\delta_P(CDCl_3)$ 30.6; $\delta_H(CDCl_3)$ 7.4-6.8 (5 H, m), 7.18 (5 H, br s), 6.6-5.8 (> 1 H, very broad, N*H* and O*H*), 3.27 (1 H, dq, J_{PH} 20, J_{HH} 7.5), and 1.50 (3 H, dd, J_{PH} 18, J_{HH} 7.5)].

Methyl N-*Phenyl*-P-*(α-methylbenzyl)phosphonamidate* (62).- The phosphonamidic chloride (48) (73 mg, 0.26 mmol; a mixture of diastereoisomers), was added to sodium methoxide (0.4 mmol) in methanol (1.0 ml) and the mixture was stirred for 20 min. The excess methoxide was quenched with ammonium chloride and methanol was removed in vacuo. The residue was partitioned between ether and water and the organic portion was dried ($MgSO_4$) and concentrated. Crystallisation from light petroleum containing a very small quantity of dichloromethane afforded *methyl* N-*phenyl*-P-*(α-methylbenzyl)phosphonamidate* (62) (50 mg, 69 %) (a mixture of diastereoisomers), m.p. 101.5-103 °C; $\delta_P(CDCl_3)$ 31.0 and 30.8 (major); $\delta_H(CDCl_3$, 300 MHz) 7.43-6.81 (10 H, m), 6.184 (major) and 5.800 (total 1 H; both d, J_{PH} 5.3 or 5.0, N*H*), 3.757 and 3.605 (major) (total 3 H; both d, J_{PH} 11.0, O*Me*), 3.417 and 3.353 (major) (total 1 H; both dq, J_{PH} 19.2 or 19.3, J_{HH} 7.4), and 1.646 and 1.515 (major) (total 3 H; both dd, J_{PH} 18.1 or 18.9, J_{HH} 7.4, C*Me*); *m/z* 275 (M^+, 100 %), 171 (M^+ - $PhCH{=}CH_2$, 18), 170 (M^+ -

PhCHMe, 23), 105 ($PhCHMe^+$, 72), and 93 ($PhNH_2^+$, 43); $\nu_{max.}$(Nujol) 3140, 3080 (NH), and 1210 cm^{-1} (P=O); R_t 5.7 and 6.4 (major) min (OV 1701, 230 °C), (Found: M^+, 275.1073. $C_{15}H_{18}NO_2P$ requires *M*, 275.1075). This material was used for identification of the *tert*-Butylammonium *N*-phenyl-*P*-(α-methylbenzyl)phosphonamidate (**63**), δ_P 17.2, formed in the reaction of the methanesulphonate (**44**) (sample B) with 0.1 M *tert*-butylamine in dichloromethane. [The salt was extracted into water, the extract acidified (pH ≤ 1), and the free acid back-extracted into dichloromethane; treatment with diazomethane then gave the methyl phosphonamidate (**62**) as a 1 : 1 mixture of diastereoisomers, R_t 5.7 and 6.4 min (conditions as above)].

N-*Phenyl*-P-*(α-methylbenzyl)phosphonamidic Anhydride* (**64**).- A solution of the phosphonamidic acid (**61**) in the minimum quantity of ether was treated with *tert*-butylamine to give a precipitate of the *tert*-butylammonium salt (**63**), $\delta_P(CH_2Cl_2)$ 18.2. The salt was added to a solution of the phosphonamidic chloride (**48**) in dichloromethane to give N-*phenyl*-P-*(α-methylbenzyl)phosphonamidic anhydride* (**64**) as a mixture of diastereoisomers, $\delta_P(CH_2Cl_2)$ 23-24 (several peaks); crystallised from dichloromethane-light petroleum, m.p. 155-161 °C; $\delta_P(CDCl_3)$ 25.5, 25.0 and 24.6; $\delta_H(CDCl_3$, 300 MHz) 7.4-6.7 (20 H, m), 6.25-5.35 (total 2 H; a series of 7 multiplets, exchangeable with D_2O, N*H*), 3.6-3.15 (2 H, m, PhMeC*H*), and 1.74-1.22 (6 H, m, Ph*Me*CH); *m/z* 504 (M^+, 20 %), 489 (M^+ - Me, 5) 412 (M^+ - NHPh, 15) 105 ($PhCHMe^+$, 100), and 93 ($PhNH_2^+$,

60); $\nu_{max.}$(Nujol) 3170 br (NH), 1240 (P=O), and 950 cm^{-1} (several maxima) (P-O-P) (Found: C, 66.4; H, 6.05; N, 5.7. $C_{28}H_{30}N_2O_3P_2$ requires C, 66.7; H, 6.0; N, 5.55 %).

α-Methylbenzyl(phenyl)phosphinic Amide (58).- A solution of the phosphinic chloride (39) (146 mg, 0.55 mmol) in dichloromethane was added to an excess of anhydrous ammonia dissolved in ether. Volatile material was evaporated and the residue was partitioned between dichloromethane and water. The organic layer was separated, dried, and concentrated. Crystallisation from dichloromethane-light petroleum afforded *α-methylbenzyl(phenyl)phosphinic amide* (58) (66 mg, 49 %) as a mixture of diastereoisomers, m.p. 140-142 °C (resolidifies and melts again at 151-153 °C); $\delta_P(CDCl_3)$ 35.1 and 32.9 (major); $\delta_H(CDCl_3)$ 8.0-6.9 (10 H, m), 3.5-2.9 (1 H, m, PhMeC*H*), 2.80 (2 H, br s, NH_2; exchanges with D_2O), and 1.48 and 1.40 (total 3 H; both dd, J_{PH} 17, J_{HH} 7); *m/z* 245 (M^+, 55 %), 141 (M^+ - $PhCH{=}CH_2$, 45), 140 (M^+ - PhCHMe, 100), and 105 ($PhCHMe^+$, 60); $\nu_{max.}$(Nujol) 3330, 3240, 3130 (NH), and 1175 cm^{-1} (P=O) (Found: C, 68.4; H, 6.8; N, 5.7. $C_{14}H_{16}NOP$ requires C, 68.6; H, 6.6; N, 5.7 %).

N-tert-*Butyl*-N'-*[α-methylbenzyl(phenyl)phosphinoyl]hydrazine* (54).- A solution of the phosphinic chloride (39) (455 mg, 1.85 mmol) in dichloromethane (1 ml) was mixed with a solution of *tert*-butylhydrazine (*ca.* 6 mmol) in dichloromethane (6 ml). After 30 min all volatile material was evaporated and the residue was partitioned between ether and water. The organic portion was extracted with 0.5 M hydrochloric acid, the aqueous extract was basified (pH ≥ 11), and the liberated phosphinoylhydrazide was back-extracted into dichloromethane.

The crude product (310 mg, 55 %) was crystallised from dichloromethane–light petroleum to give N-tert-*butyl*-N'-*-[α-methylbenzyl(phenyl)phosphinoyl]hydrazine* (54) as a mixture of diastereoisomers, m.p. 170–171 °C; $\delta_P(CDCl_3)$ 36.9 (major) and 35.3 (*ca.* 2 : 1); $\delta_H(CDCl_3$, 300 MHz) 7.93–7.06 (10 H, m), 4.134 and 3.912 (total 1 H; both d, J_{PH} 14.5 or 13.3, N*H*), 3.604 and 3.446 (total 1 H; both dq, J_{PH} 16.6 or 13.2, J_{HH} 7.4), 3.061 and 2.936 (total 1 H; both br s, N*H*), 1.661 and 1.408 (total 3 H; both dd, J_{PH} 16.0 or 16.8, J_{HH} 7.4), and 1.073 and 0.870 (total 9H; both s); *m/z* 316 (M^+, 25 %), 301 (M^+ – Me, 30), and 105 ($PhCHMe^+$, 100); *m/z* (CI) 317 ($M+H^+$, 100 %); $\nu_{max.}$(Nujol) 3150 (NH) and 1185 cm^{-1} (P=O) (Found: C, 67.7; H, 7.9; N, 8.75; M^+, 316.1705. $C_{18}H_{25}N_2OP$ requires C, 68.3; H, 8.0; N, 8.85 %; *M*, 316.1705). This compound was also formed in the reaction of the methanesulphonate (44) (sample B) with 0.1 M *tert*-butylamine in dichloromethane. The isolated material (acid extraction of the product, δ_P 41.5) was not pure, but was seen to be a single diastereoisomer, [$\delta_P(CDCl_3)$ 35.3; $\delta_H(CDCl_3$, 300 MHz) 7.96–7.85 (2 H, m), 7.60–7.24 (8 H, m), 3.918 (1 H, d, J_{PH} 13.4 N*H*), 3.445 (1 H, dq, J_{PH} 13.3, J_{HH} 7.4), 1.408 (3 H, dd, J_{PH} 16.8, J_{HH} 7.4), and 0.869 (9 H, s); *m/z* as above].

In the reaction of the methanesulphonate (44) (sample B) (24 mg, 0.07 mmol) with 1.0 M solution of *N*-methyl-*tert*-butylamine (1.4 mmol, a 20-fold excess) in dichloromethane at 20 °C, ^{31}P NMR spectroscopy revealed an important by-product (δ_P 29.6; 40 %) in addition to the expected rearrangement products (57) {diastereoisomers, δ_P 28.2 and 25.9, ratio 42 : 58, 50 % [peaks assigned by comparison with a mixture, δ_P

28.4 and 26.0, resulting from the reaction of the phosphonamidic chloride (48) (mixture of diastereoisomers) with *N*-methyl-*tert*-butylamine]}. The by-product was extracted into 1 M hydrochloric acid (δ_P 39.1), and was back-extracted into dichloromethane after basification (2 M NaOH). It was identified as N-tert-*butyl*-N-*methyl*-N'-*[α-methylbenzyl(phenyl)phosphinoyl]hydrazine* (56) (a single diastereoisomer), and crystallised from ethyl acetate–light petroleum, no clear m.p. (changes without melting above 160 °C; gradually liquifies above 180 °C); $\delta_P(CDCl_3)$ 31.1; $\delta_H(CDCl_3$, 300 MHz) 7.95–7.85 (2 H, m), 7.60–7.25 (8 H, m), 3.323 (1 H, dq, J_{PH} 11.7, J_{HH} 7.4), 3.280 (1 H, d, J_{PH} 17.2, *NH*; exchanges with D_2O), 2.331 (3 H, s), 1.366 (3 H, dd, J_{PH} 16.8, J_{HH} 7.4), and 0.794 (9 H, s); *m/z* 330 (M^+, 25 %), 315 (M^+ – Me, 15), 245 (M^+ – $H_2C{=}NBu^t$, 15), 244 (20), and 105 ($PhCHMe^+$, 100); $\nu_{max.}$(Nujol) 3200 (NH) and 1190 cm^{-1} (P=O) (Found: M^+, 330.1861. $C_{19}H_{27}N_2OP$ requires *M*, 330.1861).

N-*Alkyl*-N'-*phenyl*-P-*(α-methylbenzyl)phosphonic Diamides*.– These compounds were produced in the reactions of the methanesulphonate (44) with methylamine or *tert*-butylamine.

N-*Methyl*-N'-*phenyl*-P-*(α-methylbenzyl)phosphonic diamide* (50). *(a)* A pure sample of one diastereoisomer (product B) of the phosphonic diamide (50) was obtained by crystallisation of the product from the reaction of the methanesulphonate (44) (sample B) with methylamine (neat or 1.0 M solution in dichloromethane): m.p. 132–133 °C (unusual softening at 120–122 °C) (from dichloromethane–light petroleum); $\delta_P(CH_2Cl_2)$ 25.7; $\delta_H(CDCl_3$, 300 MHz) 7.45–6.85 (10 H, m), 4.660 (1 H, d, J_{PH} 10.1, *NH*Ph; exchanges with D_2O), 3.247 (1 H, dq, J_{PH} 17.3,

J_{HH} 7.4, CHMePh), 2.698 (1 H, dq, J_{PH} ~ 12, J_{HH} ~ 6, NHMe; exchanges with D_2O), 2.589 (3 H, dd, J_{PH} 11.4, J_{HH} 5.6, NHMe; simplifies to d when treated with D_2O), and 1.616 (3 H, dd, J_{PH} 17.3, J_{HH} 7.4, CHMePh); *m/z* 274 (M^+, 35 %), 169 (M^+ - CHMePh, 100), 105 ($PhMeCH^+$, 35), and 93 ($PhNH_2^+$, 40 %); $\nu_{max.}$(Nujol) 3220, 3190 (NH), and 1170 cm^{-1} (P=O) [Found: C, 65.2; H, 6.5; N, 10.0 (approx; very small sample); $C_{15}H_{19}N_2OP$ requires C, 65.7; H, 7.0; N, 10.2 %]. A sample recrystallised from toluene was used for single crystal X-ray analysis. The crystal was glued to a glass filament. Data were measured on a Stöe STADI-2 Weissenberg diffractometer with graphite monochromated Mo-K_α radiation (λ 0.7107 Å) using an ω-scan technique. The data were corrected for Lorentz and polarisation effects.

Crystal data for (**50**) (racemate): $C_{15}H_{19}N_2OP$, M = 274.3. Monoclinic, space group $P2_1/a$, a = 10.450(2), b = 13.204(14), c = 10.755(11) Å, β = 97.17(6)°, U = 1472(3) Å^3, Z = 4, μ = 1.41 cm^{-1}, $F(000)$ = 584, D_c = 1.24 g cm^{-3}, T = 293 K. The structure was solved by direct methods. The phenyl and methyl hydrogen atoms were included in calculated positions with a single fixed thermal parameter. The remaining hydrogen atoms were refined as isotropic atoms and all other atoms were refined with anisotropic thermal parameters. Full-matrix least squares refinement of 166 parameters gave R = 0.056 and R_w = 0.059 for 1221 unique reflexions with $I > 3\sigma(I)$. For complete details see Appendix 1.

(b) A sample of the phosphonic diamide (**50**) having a predominance of the other diastereoisomer (product A) (diastereoisomer ratio *ca.* 5 : 1 ratio) was obtained by

distillation of the product from the reaction of the methanesulphonate (44) (sample A) with methylamine (neat or 1.0 M solution in dichloromethane): b.p. 150 °C (oven temp.) at 0.03 mmHg; $\delta_P(CH_2Cl_2)$ 26.2 (major component); $\delta_H(CDCl_3$, 300 MHz) 7.45-6.85 (10 H, m), 5.697 (1 H, d, J_{PH} 6.3, N*H*Ph; exchanges with D_2O), 3.290 (1 H, dq, J_{PH} 16.4, J_{HH} 7.4, C*H*MePh), 2.512 (3 H, dd, J_{PH} 11.6, J_{HH} 5.8, NH*Me*; simplifies to d with D_2O), 2.281 (1 H, dq, J_{PH} ~ 12, J_{HH} ~ 5.5, N*H*Me; exchanges with D_2O), and 1.558 (3 H, dd, J_{PH} 17.3, J_{HH} 7.3, CH*Me*Ph) (smaller signals for diastereoisomer B also present); *m/z* 274 (M^+, 40 %), 169 (100), 105 (60), and 93 (50) (Found: M^+, 274.1235. $C_{15}H_{19}N_2OP$ require *M*, 274.1235).

(c) An authentic sample of the phosphonic diamide (50) was obtained as a mixture of diastereoisomers (by ^1H and ^{31}P NMR; A : B ~ 2 : 1) by treatment of *N*-phenyl-*P*-(α-methylbenzyl)-phosphonamidic chloride (48) with methylamine: m.p. 126-130 °C (from benzene-light petroleum). The two diastereoisomers could not be separated GLC but were separable by TLC (silica; elute with ethyl acetate).

N-tert-*Butyl*-N'-*phenyl*-P-*(α-methylbenzyl)phosphonic diamide* (49). *(a)* A sample of the phosphonamidic diamide (49) (product B dominant in 9 : 1 ratio before recrystallisation) was obtained from the reaction of the methanesulphonate (44) (sample B) with neat *tert*-butylamine: m.p. 120-124 °C (from dichloromethane-light petroleum) (diastereoisomers in *ca.* 1 : 1 ratio after recrystallisation), for product B (major) $\delta_P(CDCl_3)$ 22.5; $\delta_H(CDCl_3$ 300 MHz) 7.40-6.85 (10 H, m), 4.71 (1 H, d, J_{PH} 8, N*H*Ph), 3.246 (1 H, dq, J_{PH} ~ 18, J_{PH} ~ 7.5, C*H*MePh), 2.46 (1 H, d, J_{PH} 14, N*H*Bu^t), 1.622 (3 H, dd, J_{PH}

17.4, J_{HH} 7.4, CHMePh), and 1.304 (9 H, s); for product A (minor) $\delta_P(CDCl_3)$ 22.75; $\delta_H(CDCl_3$, 300 MHz) 7.40–6.85 (10 H, m), 5.11 (1 H, d, J_{PH} 6, NHPh), 3.227 (1 H, dq, J_{PH} ~ 17, J_{HH} ~ 7.5, CHMePh), 2.12 (1 H, d, J_{PH} 13, NHBu^t), 1.529 (3 H, dd, J_{PH} 17.3, J_{HH} 7.3, CHMePh), and 1.190 (9 H, s); *m/z* 316 (M^+, 25 %), 301 (M^+ – Me, 5), 260 (M^+ – C_4H_8, 10), 211 (M^+ – CHMePh, 45), 155 (M^+ – C_4H_8 – CHMePh, 100), 105 ($PhMeCH^+$, 45), and 93 ($PhNH_2^+$, 50); $\nu_{max.}$(Nujol) 3390 (free NH), 3210 (NH), and 1190 cm^{-1} (P=O); R_t 8.3 and 9.5 (major) min (OV 1701, 230 °C). [The data from the 300 MHz ^1H NMR spectrum belongs to the 1 : 1 mixture of diastereoisomers obtained after crystallisation. The assignments were made using the 90 MHz spectra of the 9 : 1 mixture and of a 3 : 1 mixture (product A dominant) obtained from the reaction of sample A with *tert*-butylamine. The N-H data are from the 90 MHz spectra.]

(b) Samples of the phosphonamidic diamide (49) in which diastereoisomer B was less dominant were obtained from other reactions of the methanesulphonate (44) with *tert*-butylamine.

(c) An authentic sample of the phosphonic diamide (49) was obtained as a mixture of diastereoisomers (A : B ~ 3 : 2) by treatment of *N*-phenyl-*P*-(α-methylbenzyl)phosphonamidic chloride (48) with *tert*-butylamine: m.p. 122–123.5 °C (from ether–light petroleum) (Found: C, 68.1; H, 8.1; N, 8.85. $C_{18}H_{25}N_2OP$ requires C, 68.3; H, 8.0; N, 8.85 %).

N-*Alkyl*-N′-(*α*-*methylbenzyl*)-P-*phenylphosphonic Diamides*.- Authentic samples of these compounds were required to confirm that they were not formed in the reactions of the methanesulphonate (44) with methylamine and *tert*-butylamine. They were prepared as detailed below.

N-*Methyl*-N′-(*α*-*methylbenzyl*)-P-*phenylphosphonic diamide* (53). (±)-*α*-Methylbenzylamine in benzene (1 mmol per ml; 2 mol equiv.) was added to a stirred (powerful magnet) solution of phenylphosphonic dichloride in benzene (0.5 mmol per ml) over 20 min in a nitrogen atmosphere. After 2.5 h the mixture was diluted with ether and insoluble material (amine hydrochloride) was removed by filtration under nitrogen. The filtrate containing N-(*α*-*methylbenzyl*)-P-*phenylphosphonamidic chloride*, δ_P 32.9 and 31.3 (diastereoisomers), was treated with an excess of methylamine (4-5 mol equiv.); much solid (amine hydrochloride) precipitated. Solvent was removed (rotary evaporator) and the residue was partitioned between dichloromethane and water. The organic portion was dried ($MgSO_4$) and concentrated to give N-*methyl*-N′-(*α*-*methylbenzyl*)-P-*phenylphosphonic diamide* (53), $\delta_P(CH_2Cl_2)$ 20.2 (major) and 19.8, diastereoisomer ratio ~ 55 : 45. Crystallisation from chloroform-light petroleum gave an almost pure (97 %) sample of the major diastereoisomer, m.p. 133-136 °C; $\delta_H(CDCl_3$, 300 MHz) 7.82-7.71 (2 H, m), 7.52-7.36 (3 H, m), 7.34-7.17 (5 H, m), 4.339 (1 H, ddq, J_{PH} ~ 9, J_{HH} ~ 9 and 6.8, NHC*H*MePh; simplifies to dq with D_2O), 2.866 (1 H, br dd, J_{PH} ~ J_{HH} ~ 9, N*H*CHMePh; exchanged with D_2O), 2.522 (3 H, dd, J_{PH} 12.1, J_{HH} 5.8, NH*Me*; simplified to d with D_2O), 2.38 (1 H, br m, N*H*Me; exchanged with D_2O), and 1.440 (3 H, d, J_{HH} 6.8,

CH*Me*Ph) [small signals for the minor diastereoisomer at 2.633 (dd, J_{PH} 11.8, J_{HH} 5.8, NH*Me*) and 1.480 (d, J_{HH} 6.8, CH*Me*Ph)]; *m/z* 274 (M^+, 12 %), 259 (M^+ - Me, 25), 154 (M^+ - NHCHMePh, 35), and 120 ($PhCHMeNH^+$, 100); $\nu_{max.}$(Nujol) 3290, 3240 (NH), and 1180 cm^{-1} (P=O) (Found: C, 65.3; H, 7.0; N, 10.25. $C_{15}H_{19}N_2OP$ requires C, 65.7; H, 7.0; N, 10.2 %).

N-tert-*Butyl*-N'-*(α-methylbenzyl)*-P-*phenylphosphonic diamide* (52). (±)-α-Methylbenzylamine (363 mg, 0.39 ml, 3.0 mmol) was added to a stirred solution of *N-tert*-butyl-*P*-phenylphosphonamidic chloride (51)[34] (231 mg, 1.0 mmol) in dichloromethane (3 ml). After 30 min the mixture was diluted with dichloromethane and washed first with dilute aqueous sodium hydroxide (to remove any anhydride), then with dilute hydrochloric acid (HCl added until pH just less than 7) to remove the excess amine, and finally with water. The organic portion was dried ($MgSO_4$) and concentrated to give N-tert-*butyl*-N'-*(α-methylbenzyl)*-P-*phenylphosphonic diamide* (52), b.p. 128 °C (oven temp.) at 0.02 mmHg; $\delta_P(CDCl_3)$ 17.3 and 16.5 (diastereoisomers; ratio *ca.* 1 : 1); $\delta_H(CDCl_3$, 300 MHz) 7.90-7.15 (10 H, m), 4.62 and 4.29 (total 1 H; both ddq, J_{PH}, J_{HH}, J_{HH} all ~ 7-9, NHC*H*MePh), 2.81 and 2.71 br (total 1 H; both dd, J_{PH} ~ 9, J_{HH} ~ 7.5, N*H*CHMePh), 2.42 and 2.24 (total 1 H; both d, J_{PH} 7 or 8.5, N*H*Bu^t), 1.47 and 1.41 (total 3 H; both d, J_{HH} 6.8, CH*Me*Ph), and 1.23 and 1.13 (total 9 H; both s); *m/z* 316 (M^+, 20 %), 301 (M^+ - Me, 85), 197 (M^+ - Me - H_2C=CHPh, 45), 140 (M^+ - C_4H_8 - NHCHMePh, 60), 120 ($PhCHMeNH^+$, 100), and 105 ($PhCHMe^+$, 70); $\nu_{max.}(CH_2Cl_2)$ 3400 (NH), 1225, 1200, and 1120 cm^{-1} (Found: M^+ 316.1704. $C_{18}H_{25}N_2OP$ requires *M*, 316.1705).

Stereochemical Studies.- In general the methanesulphonate (44) (sample A or sample B) (27 mg, 0.08 mmol) was added to a large excess of the amine (≥ 20 mol equiv.), neat or as a solution in dichloromethane (1.0 or 0.1 M), at room temperature (Bu^tNH_2) or below ($MeNH_2$; 0 °C). In the case of neat methylamine, the amine was added to the methanesulphonate at -5 to -10 °C. Similar experiments were carried out using the nosylate (45) [3 : 97 ratio, highfield diastereoisomer (^{31}P NMR) in excess] with methylamine.

After a preliminary examination of the reaction mixture by ^{31}P NMR spectroscopy, volatile material was evaporated and the residue was partitioned between dichloromethane and water (to remove RNH_3^+ ^-OMs). The organic layer was dried ($MgSO_4$), and the diastereoisomer ratio of the phosphonic diamide rearrangement product (49) or (50) was determined by ^{31}P NMR spectroscopy (Tables 1 and 2, and Table 3 for the nosylate) and confirmed by ^1H NMR spectroscopy. In some cases the rearrangement product was purified by distillation and/or crystallisation and further characterised. In one case, using the methanesulphonate (sample A) with 0.21 M *tert*-butylamine, the reaction was followed by ^{31}P NMR spectroscopy which revealed the presence of a reaction intermediate δ_P 27.7 (major) and 27.5 (diastereoisomers) (see Fig. 5).

The phosphonic diamide (49) or (50) was formed cleanly in the reaction with neat amine, but side reactions were significant with 1.0 M solutions (3-20 %) and extensive with 0.1 M solutions (15-50 %). The side reactions were more pronounced with *tert*-butylamine than with methylamine, and for diastereoisomer B of the substrate than for diastereoisomer

A. In one case (substrate sample B with 0.1 M Bu^tNH_2) a by--product was isolated by extraction from dichloromethane into aqueous acid and back-extraction into dichloromethane after basification: it was characterised as *N-tert*-butyl-*N'*--[α-methylbenzyl(phenyl)phosphinoyl]hydrazine (54) by comparison with the authentic sample (see p. 135). The phosphonamidic acid salt $PhMeCHP(O)(NHPh)O^- {}^+NH_3Bu^t$ (63) (δ_P ~ 17-18; variable) present in the water wash from a worked-up reaction mixture (substrate sample A or B with 0.1 M Bu^tNH_2) was isolated as the free acid (61) or its methyl ester (62) and compared with authentic samples (see pp. 132 and 133). Other by-products were tentatively identified only by comparison of their ^{31}P NMR chemical shifts in the reaction mixture with those of authentic samples (pp. 134 and 135), *i.e.* α-methylbenzyl(phenyl)phosphinic amide (58) (δ_P ~ 33, two diastereoisomers; signals very close to those of the phosphinoyl hydrazine) and the phosphonamidic anhydride $[PhMeCHP(O)NHPh]_2O$ (64) (δ_P 24.4-23.5, several diastereoisomers). The by-product believed to be (64) was converted into the phosphonamidate salt (63) on prolonged standing (96 h) in the reaction medium, strengthening the evidence for its identity as the phosphonamidic anhydride (64).

No attempt was made to correct the observed diastereoisomer ratios of the phosphonic diamide rearrangement product (Tables 1 to 3) to allow for the fact that the non--rearrangement side reactions consumed diastereoisomer B more quickly than diastereoisomer A (*i.e.* the rearrangement product was formed from a substrate that became slightly more enriched in diastereoisomer A as reaction proceeded), or for

the possibility that side reactions involving rearrangement (*e.g.* reaction with traces of water rather than with RNH_2) could, in principal, have diminished the formation of one of the diastereoisomers of the phosphonic diamide more than the other.

Competition Experiments.- The methanesulphonate (44) (1 : 1 mixture of diastereoisomers) (0.07 mmol) was allowed to react with a large excess (≥ 20 mol equiv.) of an equimolar mixture of methylamine and *tert*-butylamine, neat (at 0 °C) or in dichloromethane (1.0 or 0.1 M total amine, at 12 °C). The relative amounts of the *N*-methyl phosphonic diamide (50) (two diastereoisomers) and the *N*-*tert*-butyl phosphonic diamide (49) (two diastereoisomers) were determined from the ^{31}P NMR spectra of the reaction mixtures (relative peak areas; Table 4).

Similar experiments were carried out using the nosylate (45) (ratio 4 : 96; ^{31}P NMR highfield diastereoisomer in excess) and the phosphonamidic chloride (48) (30 : 70 mixture of diastereoisomers) (Table 4). In the latter case both the *N*-methyl and *N*-*tert*-butyl phosphonic diamides were formed as mixtures of diastereoisomers in which the lowfield (^{31}P NMR) diastereoisomer was in excess.

(-)-N-Diphenylphosphinoyl-O-(camphor-10-sulphonyl)hydroxylamine (67).- Powdered *N*-diphenylphosphinoylhydroxylamine (66)[13,87] (144 mg, 0.62 mmol) was stirred in an ice bath at 5 °C (bath temperature) and pyridine (0.6 ml) was added,[13] followed immediately by (-)-camphor-10-sulphonyl chloride[88] (209 mg, 0.83 mmol, 1.35 mol equiv.). The resulting paste was

stirred for 10 min at 5-10 °C, during which time it became much more mobile. The reaction was quenched with ice water (8 ml) and the precipitated solid was filtered off and was washed first with water and then with light petroleum. Crystallisation from aqueous ethanol afforded *(-)-N-Diphenylphosphinoyl-O-(camphor-10-sulphonyl)hydroxylamine* (67) (196 mg, 71 %), m.p. 153-155 °C (decomp.); $[\alpha]_D$ -11.3° (*c* 8.5 x 10^{-3} in methanol; limited solubility); $\delta_P(CDCl_3)$ 29.6; $\delta_H(CDCl_3$, 300 MHz) 8.836 (1 H, d, J_{PH} 3.9, N*H*; exchanges with D_2O), 8.03-7.89 (4 H, m), 7.64-7.46 (6 H, m), 3.38 (2 H, AB, δ_A 3.698, δ_B 3.064, J_{AB} 15.3, SCH_2), 2.44-2.26 (2 H, m), 2.15-1.91 (3 H, m), 1.78-1.65 (1 H, m), 1.49-1.39 (1 H, m), 1.037 (3 H, s, *Me*), and 0.833 (3 H, s, *Me*); *m/z* (FAB; NOBA matrix) 470 ($M+Na^+$, 12 %) and 448 ($M+H^+$, 100); $\nu_{max.}$(Nujol) 3050 (NH), 1750 (C=O), 1220, 1210, 1200, and 1180 cm^{-1} (P=O). The analysis sample, recrystallised from aqueous ethanol had m.p. 150-152 °C (decomp.) (Found: C, 59.5; H, 5.95; N, 3.2. $C_{22}H_{26}NO_5PS$ requires C, 59.05; H, 5.9; N, 3.1 %). The other enantiomer (67), $[\alpha]_D$ +11.2° (*c* 8.5 x 10^{-3} in methanol), was prepared as above but using (+)-camphor-10-sulphonyl chloride.

N',P-*Diphenyl*-N-tert-*butylphosphonic Diamide* (68).- The combined products from the reactions of *tert*-butylamine with the (-)-camphor-10-sulphonate (67) (see stereochemical studies below) were dissolved in dichloromethane and the solution was washed with dilute aqueous sodium hydroxide (to remove the NMR chiral shift reagent) and water. The organic portion was dried ($MgSO_4$) and concentrated and the residue was crystallised from dichloromethane-light petroleum (b.p. 40-60 °C)

to give the phosphonic diamide (68), m.p. 176–179 °C (lit.,[13] m.p. 176–178 °C); $[\alpha]_D$ −0.66° (*c* 0.035 in chloroform); $\delta_P(CDCl_3)$ 12.7; $\delta_H(CDCl_3)$ 8.03–7.35 (5 H, m), 7.25–6.78 (5 H, m), 5.12 (1 H, d, J_{PH} 7.5, N*H*Ph), 2.80 (1 H, d, J_{PH} 10, N*H*Bu^t), and 1.33 (9 H, s); *m/z* 288 (M^+, 100 %); $\nu_{max.}$(Nujol) 3380, 3240 (NH), and 1200 cm^{-1} (P=O).

N′,P-*Diphenyl*-N-*methylphosphonic Diamide* (72).– The combined products from the reaction of methylamine with the camphor-10-sulphonate (67) (both enantiomers) were dissolved in dichloromethane and the solution was washed with dilute aqueous sodium hydroxide (to remove the NMR chiral shift reagent) and water. The organic portion was dried ($MgSO_4$) and concentrated. Trituration with ether–light petroleum gave the phosphonic diamide (72), m.p. 156–160 °C (lit.,[22] m.p. 156–158 °C); $\delta_P(CDCl_3)$ 17.4; $\delta_H(CDCl_3)$ 8.08–7.34 (5 H, m), 7.21–6.74 (5 H, m), 5.29 (1 H, br, N*H*), 3.03–2.33 (1 H, br), and 2.64 (3 H, dd, J_{PH} 12, J_{HH} 5); *m/z* 246 (M^+, 83 %); $\nu_{max.}$(Nujol) 3220 (NH) and 1175 cm^{-1} (P=O).

Stereochemical Studies.– *(a)* The (−)-camphor-10-sulphonate (67) (31 mg, 0.07 mmol) was added to a solution of *tert*-butylamine (20 mol equiv.) in dichloromethane (0.05, 0.3, 1.0, or 3.0 M) at room temperature. Also neat *tert*-butylamine (> 20 mol equiv.) was added to the substrate at room temperature. When reaction was complete all volatile material was removed and the residue was partitioned between dichloromethane and water. The organic portion was dried ($MgSO_4$) and all of the solvent removed. The crude product was dissolved in $CDCl_3$ and investigated by ^1H NMR spectroscopy using (−)-methylphenylphosphinothioic acid (70)[36] (1 mol equiv.) as

a chiral shift reagent, to determine the enantiomer composition of the phosphonic diamide rearrangement product (Table 5).

(b) The (+)-camphor-10-sulphonate (67) (31 mg, 0.07 mmol) was added in one case to a 1.0 M solution of *tert*-butylamine (20 mol equiv.) in dichloromethane at room temperature and in the other to 1.0 M solution of *tert*-butylamine (20 mol equiv.) in dichloromethane containing *tert*-butylammonium (-)-camphor-10-sulphonate (1 mol equiv.) at room temperature. When reaction was complete, the mixtures were treated as described in *(a)* above (Table 6).

(c) The methanesulphonate (69)[13,87] (22 mg, 0.07 mmol) was added to a 1.0 M solution of *tert*-butylamine (20 mol equiv.) in dichloromethane at room temperature. When the reaction was complete, the mixture was treated as described in *(a)* (Table 6).

(d) For both enantiomers, the camphor-10-sulphonate (67) (31 mg, 0.07 mmol) was added to a 1.0 M solution of methylamine (20 mol equiv.) in dichloromethane at 0 °C. When the reaction had gone to completion, the mixture was treated as described in *(a)* except that (+)-phenyl-*tert*-butylphosphinothioic acid (71)[36,87] (1.3 mol equiv.) was used as the NMR chiral shift reagent (Table 6).

The Reaction of N-*[Bis(4-methylbenzyl)phosphinoyl]*-O-p-*nitrobenzenesulphonylhydroxylamine* (79) *with Amines*.- The nosylate (79)[43] (33 mg, 0.07 mmol) was added to a 0.5 M solution of the appropriate amine (10 mol equiv.; *tert*-butylamine, *N*-methyl-*tert*-butylamine, or diisopropylamine) in dichloro-

methane at room temperature. When the reaction had gone to completion all volatile material was removed and the residue was partitioned between dichloromethane and water. The organic portion was dried ($MgSO_4$) and then concentrated to give the crude hydrazide, which was purified and concentrated as detailed below.

Hydrazide (**80**).- The crude hydrazide was dissolved in ether and extracted into dilute hydrochloric acid. The acidic solution was treated with dilute aqueous sodium hydroxide and the regenerated free hydrazide was back-extracted into dichloromethane. The solution was dried ($MgSO_4$) and concentrated, and the residue was triturated with light petroleum (b.p. 40-60 °C) to give *N*-[bis(4-methylbenzyl)phosphinoyl]--*N'*-*tert*-butylhydrazine (**80**), m.p. 80-85 °C (lit.,[19] m.p. 88-90 °C); $\delta_P(CDCl_3)$ 42.5; $\delta_H(CDCl_3)$ 7.08 (8 H, br s), 3.83 (1 H, d, J_{PH} 13, N*H*), 3.07 (4 H, d, J_{PH} 15; slight non-equivalence of diastereotopic hydrogens apparent), 2.29 (~ 6 H, s, p-*Me* and ~ 2 H, br, N*H* and water), and 1.03 (9 H, s).

Hydrazide (**82**).- Trituration of the crude hydrazide with light petroleum (b.p. 40-60 °C) gave N-*[bis(4-methylbenzyl)-phosphinoyl]*-N'-*methyl*-N'-tert-*butylhydrazine* (**82**), m.p. 46-50 °C (decomp.); $\delta_P(CDCl_3)$ 36.2; $\delta_H(CDCl_3$, 300 MHz) 7.20-7.07 (8 H, m), 3.284 (1 H, d, J_{PH} ~ 15, N*H*), 3.248 (2 H, dd, J_{PH} ~ J_{HH} ~ 15, PC*H*HAr), 2.946 (2 H, dd, J_{PH} ~ J_{HH} ~ 15, PCH*H*Ar), 2.498 (3 H, s, N*Me*), 2.320 (6 H, s, p-*Me*), and 1.003 (9 H, s); *m/z* 358 (M^+, 30 %), 343 (M^+ - Me, 10), 273 [$(MeC_6H_4CH_2)_2P(O)NH_2^+$, 55], and 105 ($MeC_6H_4CH_2^+$, 100); $\nu_{max.}$(Nujol) 3155 (NH) and 1150 cm^{-1} (P=O) (Found: M^+, 358.2168. $C_{21}H_{31}N_2OP$ requires *M*, 358.2174).

Hydrazide (81).- The crude product was triturated, then crystallised from light petroleum (b.p. 40-60 °C) giving N-*[bis(4-methylbenzyl)phosphinoyl]*-N',N'-*diisopropylhydrazine* (81), m.p. 50-52 °C; $\delta_P(CDCl_3)$ 35.4; $\delta_H(CDCl_3$, 300 MHz) 7.23-7.08 (8 H, m), 3.544 (1 H, d, J_{PH} 20.4, N*H*), 3.225 (2 H, dd, J_{PH} 17.6 J_{HH} 14.7, ArC*H*HP), 3.049 (2H, sept, J_{HH} 6.5, Me_2CH), 2.999 (2 H, dd, J_{PH} ~ 15, J_{HH} 14.7, ArCH*H*P), 2.319 (6 H, s, p-*Me*), and 0.982 (12 H, d, J_{HH} 6.5, *Me*$_2$CH); *m/z* 372 (M^+, 100 %), 357(M^+ - Me, 20), 315 (M^+ - Me - CH_2=CHMe, 70), and 105 ($MeC_6H_4CH_2^+$, 75); $\nu_{max.}$(Nujol) 3190 (NH) and 1170 cm^{-1} (P=O) (Found: M^+, 372.2365. $C_{22}H_{33}N_2OP$ requires *M*, 372.2331).

Competitive Reactions of the N-*[Bis(4-methylbenzyl)phosphinoyl]*-O-p-*nitrobenzenesulphonylhydroxylamine* (79) *with Amines*.- The nosylate (79) (33 mg, 0.07 mmol) was added to a solution of the two amines (0.5 M total amine) in dichloromethane at room temperature. The two amines were in a 1 : 1 ratio (5 mol equiv. each) and were either *tert*-butylamine and *N*-methyl-*tert*-butylamine or *tert*-butylamine and diisopropylamine. When reaction was complete the ratio of the two hydrazide products was determined by ^{31}P spectroscopy (Table 11).

Menthyl P-*(Bromomethyl)*-N-tert-*butylphosphonamidate* (112).- A mixture of dried (-)-menthol (2.55 g, 16.3 mmol; 1.05 mol equiv.) and triethylamine (1.58 g, 15.6 mmol) in dichloromethane (15 ml) was added dropwise at room temperature, over 10 min, to a stirred (powerful magnet) solution of bromomethylphosphonic dibromide (113)[59], $\delta_P(CH_2Cl_2)$ 0.5, (4.68g, 15.6 mmol) in dichloromethane (15 ml), with moisture excluded. After 20 min more (-)-menthol (0.12 g, 0.78 mmol, 5 mol %) and triethylamine (79 mg, 0.78 mmol, 5 mol %) were added and the mixture was left stirring for a further 30 min. *tert*-Butylamine (4.66 g, 63.9 mmol; 4.1 mol equiv.) was added dropwise (exothermic) and when the reaction mixture had cooled (*ca.* 20 min) [δ_P 18.4 (major) and 18.1 (mixture of diastereoisomers, ratio 54 : 46); yield ~ 62 % (calc. 3.56 g) (several by-products)] all volatile material was removed and the residue was partitioned between toluene and water. The organic portion was dried ($MgSO_4$) and concentrated; crystallisation from 90 % aqueous ethanol (20 ml) gave a mixture of diastereoisomers [1.53 g, yield 27 %; 46 : 54 ratio, highfield ^{31}P NMR resonance now in excess]. Recrystallisation from 92 % aqueous ethanol (10 ml; overnight refrigeration) gave some material (374 mg) with a diastereoisomer ratio of 3 : 97 which was recrystallised from light petroleum (20 ml) to give the pure highfield (^{31}P NMR) diastereoisomer of *menthyl* P-*(bromomethyl)*-N-tert-*butylphosphonamidate* (112) (sample A) m.p. 155-155.5 °C; $\delta_P(CH_2Cl_2)$ 18.0; $\delta_H(CDCl_3$, 300 MHz) 4.225 (1 H, ddt, J_{PH} 8.0, J_{HH} 4.5 and 10.6), 3.278 (2 H, ABP, δ_A 3.341, δ_B 3.211, J_{AB} 13.0, J_{AP} 10.3, J_{BP} 7.1, PCH_2Br), 2.646 (1 H, d, J_{PH} 6.9, N*H*; exchanges with D_2O), 2.287 (1 H, m), 2.077 (1 H, d sept., J_{HH} 2.5 and 7.0), 1.663 (2 H, m), 1.55-0.75 (14 H),

and 1.355 (9 H, d, J_{PH} 0.6, NBu^t); *m/z* (no M^+) 354, 352 (M^+ - Me, 7 %; ratio 1 : 1), 232, 230, (33; ratio 1 : 1), and 216, 214 (M^+ - Me - $C_{10}H_{18}$, 100; ratio 1 : 1); *m/z* (CI) 387, 385 ($M+NH_4^+$, 1 %; ratio 1 : 1), 370, 368 ($M+H^+$, 5; ratio 1 : 1), 290 (30), and 74 (100); $\nu_{max.}$(Nujol) 3220 (NH) and 1245 cm^{-1} (P=O); R_t 14.7 min (BP 5, 210 °C) (Found: C, 48.85; H, 8.1; N, 3.8. $C_{15}H_{31}BrNO_2P$ requires C, 48.9; H, 8.5; N, 3.8 %). A portion of this diastereoisomer (100 % by GLC) was recrystallised from dichloromethane-light petroleum and then slowly from aqueous ethanol to produce a sample for single crystal X-ray analysis. The crystal was glued to a glass filament. Data were measured on a Stöe STADI-2 Weissenberg diffractometer. All data were collected using graphite monochromated Mo-K_α radiation (λ 0.7107 Å) at 293 K using an ω-scan technique. The data were corrected for Lorentz and polarisation effects.

Crystal data for (112): $C_{15}H_{31}BrNO_2P$, M = 368.3. Hexagonal, space group $P6_1$, a = 10.581(2), c = 30.345(25) Å, U = 2942(3) $Å^3$, Z = 6, μ = 2.18 mm^{-1}, $F(000)$ = 1164, D_c = 1.248 g cm^{-3}. An absorption correction was applied to the data, maximum and minimum transmission factors 0.757 and 0.250 respectively. 1732 Unique reflexions were measured with 687 having $I > 3\sigma(I)$ regarded as observed. The structure was solved by direct methods and difference Fourier techniques. The bromine and phosphorus were refined as anisotropic, all other non-hydrogen atoms were refined with isotropic thermal parameters. The hydrogen atoms were included in calculated

positions. The final R and R_w values are 0.085 and 0.065 respectively for 90 variables, $(\Delta/\sigma)_{max.}$ = 0.001. See Appendix 2 for complete details.

The material from one of the mother liquors of the bromomethylphosphonamidate (112) was crystallised from light petroleum to give a mixture of the diastereoisomers of (112) (sample B), m.p. 113–115 °C; $\delta_P(CH_2Cl_2)$ 18.3 (major) and 18.0, ratio 60 : 40; $\delta_H(CDCl_3$, 300 MHz) 4.34–4.17 (1 H, m), 3.39–3.17 (2 H, m), 2.731 (major) and 2.650 (total 1 H; both d, J_{PH} 7.2 or 7.5, NH), 2.34–2.03 (2 H, m), 1.72–1.62 (2 H, m), 1.55–0.75 (14 H), and 1.355 and 1.351 (major) (total 9 H; both d, J_{PH} 0.7); *m/z* as above; $\nu_{max.}$(Nujol) 3300, 3260 (NH), and 1235 cm^{-1} (P=O); R_t 14.3 (major) and 14.7 min (BP 5, 210 °C).

Menthyl Phosphorodichloridate (118)[89].– A mixture of (–)-menthol (3.13 g, 20 mmol) and triethylamine (2.02 g, 20 mmol) in light petroleum (25 ml) was added dropwise over 20 min to a cooled (ice bath) and stirred solution of phosphoryl chloride (3.07 g, 20 mmol) in light petroleum (15 ml), with moisture excluded. After addition, the mixture was stirred at room temperature for 3.5 h and the precipitated amine hydrochloride was removed by filtration under nitrogen. The filtrate was concentrated to give menthyl phosphorodichloridate (118) (5.06 g, 93 %) $\delta_P(CH_2Cl_2)$ 5.5; $\nu_{max.}$(film) 1290 (P=O), 990, and 970 cm^{-1} (P–O–C); this was used without further purification. (*N.B.* An ampouled sample blackened within two weeks at room temperature.)

Menthyl N-tert-*Butylphosphorochloramidate* (119).- *tert*-Butylamine (2.66 g, 36.4 mmol) in benzene (5 ml) was added dropwise over 5 min to a cooled (ice bath) and stirred solution of the phosphorodichloridate (118) (4.97 g, 18.2 mmol) in benzene (20 ml), with moisture excluded. After 10 min the mixture was warmed to room temperature and stirred for a further 2 h. The precipitated amine hydrochloride was removed by filtration and the filtrate was concentrated to give *menthyl* N-tert-*butylphosphorochloramidate* (119) (5.35 g, 95 %) as an oil (slowly solidified), $\delta_P(CDCl_3)$ 10.5 (major) and 9.8 (diastereoisomers; ratio 65 : 35) and an impurity (~ 9 %); $\delta_H(CDCl_3)$ 4.63-4.13 (1 H, m), 3.23 (1 H, br, N*H*), 2.43-0.70 (18 H), and 1.33 (9 H, s). This material was used without any further purification.

Menthyl Methyl N-tert-*Butylphosphoramidate* (120).- To a cooled (ice bath), stirred solution of the phosphorochloramidate (119) (4.3 g, 14 mmol) in light petroleum (b.p. 40-60 °C) (8 ml), 2 M sodium methoxide (14 ml, 28 mmol; 2 mol equiv.) in methanol was added. After 10 min the excess methoxide was quenched with ammonium chloride (1.5 g, 28 mmol) and volatile material was removed. The residue was partitioned between light petroleum and water, and the organic portion was dried ($MgSO_4$) and concentrated to give the crude product (3.6 g, 85 %), $\delta_P(CH_2Cl_2)$ 7.2 (major) and 6.7 (diastereoisomers; ratio 60 : 40). Crystallisation from light petroleum (b.p. 40-60 °C) at -40 °C gave *menthyl methyl* N-tert-*butylphosphoramidate* (120), m.p. 73-76 °C (diastereoisomer ratio now 53 : 47, lowfield ^{31}P NMR resonance still dominant); $\delta_H(CDCl_3$, 300 MHz) 4.22-4.09 (1H, m), 3.683 and

3.670 (major) (total 3 H; both d, J_{PH} 11.3 or 11.4, OMe), 2.483 and 2.436 (major) (total 1 H; both d, J_{HH} 7.3 or 7.1, NH; exchanges with D_2O), 2.39-2.08 (2 H, m), 1.72-1.59 (2 H, m), 1.54-0.77 (14 H), and 1.275 (major) and 1.271 (total 9 H, both d, J_{PH} 0.7 or 0.8); *m/z* 305 (M^+, 1 %), 290 (M^+ - Me, 8), 168 (M^+ - $C_{10}H_{17}$, 50), 152 (M^+ - Me - $C_{10}H_{18}$, 100), and 112 (M^+ - $C_{10}H_{17}$ - $H_2C{=}CMe_2$, 60); $\nu_{max.}$(Nujol) 3220 (NH) and 1240 cm^{-1} (P=O) (Found: C, 58.9; H, 10.3; N, 4.4; M^+, 305.2127. $C_{15}H_{32}NO_3P$ requires C, 59.0; H, 10.6; N, 4.6 %; *M*, 305.2120). Chromatography of a 60 : 40 mixture of diastereoisomers [rotating silica layer (chromatatron), eluent 1 : 1 ethyl acetate-light petroleum (b.p. 40-60 °C)] followed by the repeated chromatography of enriched fractions afforded a small sample that was > 96 % the lowfield (^{31}P NMR) diastereoisomer (3 % yield).

Derivatives of Menthyl Methyl N-tert-*Butylphosphoramidate* (120).- Although the phosphoramidate (120) was crystalline, all attempts to grow crystals suitable X-ray studies were unsuccessful. Several derivatives were prepared as summarised below, but none of these were obtained in a crystalline form. *(a) tert*-Butyl hypochlorite[90] (87 mg, 0.8 mmol) in $CDCl_3$ (1 ml) was added to a cooled (ice bath) and stirred solution of the phosphoramidate (120) (mixture of diastereoisomers) (197 mg, 0.65 mmol) in $CDCl_3$ (1.9 ml).[9,63] After 3 h at room temperature, removal of volatile material afforded *menthyl methyl* N-tert-*butyl*-N-*chlorophosphoramidate* (121) as an oil, $\delta_P(CDCl_3)$ 6.6 (major) and 6.5 (diastereoisomers; ratio 53 : 47); $\delta_H(CDCl_3)$ 4.43-3.90 (1 H, m), 3.72 (3 H, d, J_{PH} 10, OMe), 2.60-0.67 (18 H, m), and 1.40 (9 H, s).

(b) The phosphoramidate (**120**) (mixture of diastereoisomers) (153 mg, 0.5 mmol) was stirred with sodium hydride (31 mg, 1.3 mmol; 2.6 mol equiv.) in DMF (1 ml) at room temperature. After 1.3 h, *p*-methoxybenzyl chloride (235 mg, 1.5 mmol, 3 mol equiv.) was added and the mixture was stirred for a further 30 min. The excess sodium hydride was quenched with methanol (60 μl) and all solvent was removed. The residue was partitioned between ether and water and the organic portion was dried (Na_2SO_4) and concentrated. Chromatography [silica layer; 1 : 3 ethyl acetate–light petroleum (40–60 °C); R_f 0.21] to remove any remaining *p*-methoxybenzyl chloride, afforded *menthyl methyl* N-p-*methoxybenzyl*-N-tert-*butylphosphoramidate* (**122**) (171 mg, 79 %) as a semi-solid (completely molten above 50 °C); $\delta_P(CH_2Cl_2)$ 11.9 (major) and 10.8 (diastereoisomer; ratio 60 : 40); $\delta_H(CDCl_3)$ 7.07 (4 H, AA′BB′; $\delta_{AA'}$ 7.32, $\delta_{BB'}$ 6.82, J_{AB} 9), 4.5–3.9 (1 H, m), 4.20 (2 H, br d, J_{PH} 13, PNCH_2Ar), 3.76 (3 H, s, *p*-O*Me*), 3.63 (3 H, d, J_{PH} 11, PO*Me*), 2.5–0.8 (18 H), and 1.30 (major) and 1.28 (total 9 H; both s, NBu^t); *m/z* 425 (M^+, 1 %), 369 ($M^+ - H_2C{=}CMe_2$, 5), and 230 (100); *m/z* (CI) 426 ($M{+}H^+$, 11 %), 288 ($M{+}H^+ - C_{10}H_{18}$, 17), and 230 (100); $\nu_{max.}$(Nujol) 1240 cm^{-1} (P=O). (*N.B.* *p*-Methoxybenzyl chloride was used without drying; a portion left over molecular sieves for 24 h decomposed.).

(c) Similar alkylation of the phosphoramidate (**120**) (mixture of diastereoisomers) (153 mg, 0.5 mmol) with *p*-cyanobenzyl bromide[65] (196 mg, 1 mmol; 2 mol equiv.) gave, after chromatography, *menthyl methyl* N-p-*cyanobenzyl*-N-tert-*butylphosphoramidate* (**123**) (17 % yield by ^{31}P NMR spectroscopy) as a glass, $\delta_P(CH_2Cl_2)$ 11.4 and 10.4 (diastereoisomers; 1 : 1 mix-

ture); $\delta_H(CDCl_3)$ 7.51 (4 H, br s), 4.42 and 4.40 (total 2 H; both d, J_{PH} 12 or 13, PNCH_2Ar), 4.10 (1 H, m), 3.66 (3 H, d, J_{PH} 11, POMe), 2.45-0.65 (18 H), and 1.29 and 1.27 (total 9 H, both s); *m/z* 420 (M^+, 1 %), 405 (M^+ - Me, 9), 283 (M^+ - $C_{10}H_{17}$, 14), 267 (M^+ - Me - $C_{10}H_{18}$, 100), and 227 (M^+ - $H_2C{=}CMe_2$ - $C_{10}H_{17}$, 15); *m/z* (CI) 421 ($M{+}H^+$, 80 %), 405 (M^+ - Me, 17), 365 ($M{+}H^+$ - $H_2C{=}CMe_2$, 10), 306 (36), 283 ($M{+}H^+$ - $C_{10}H_{18}$, 100), 267 (M^+ - Me - $C_{10}H_{18}$, 75), 244 (21), and 227 ($M{+}H^+$ - $H_2C{=}CMe_2$ - $C_{10}H_{18}$, 24); $\nu_{max.}$(film) 2220 (C≡N) and 1240 cm^{-1} (P=O).

(d) Similar alkylation of the phosphoramidate (120) (mixture of diastereoisomers) (99 mg, 0.32 mmol) with *N*-(bromomethyl)phthalimide[66] (259 mg, 1.08 mmol; 3.4 mol equiv.) (reaction proceeded overnight) gave, after chromatography, (silica layer; ethyl acetate; R_f 0.52), *menthyl methyl N-tert-butyl-N-(phthalimidomethyl)phosphoramidate* (124) (59 mg, 39 %) as an oil; $\delta_P(CDCl_3)$ 10.8 (major) and 9.9 (diastereoisomers; ratio 63 : 37); $\delta_H(CDCl_3)$ 7.78 (4 H, m), 5.34-5.10 (2 H, m, NCH_2N), 4.22 (1 H, m), 3.74 (3 H, d, J_{PH} 12, POMe), 2.47-0.55 (18 H), and 1.42 (major) and 1.40 (total 9 H; both s); *m/z* (CI) 465 ($M{+}H^+$, 65 %), 449 (M^+ - Me, 20), 409 ($M{+}H^+$ - $H_2C{=}CMe_2$, 8), 327 ($M{+}H^+$ - $C_{10}H_{18}$, 69), 311 (M^+ - Me - $C_{10}H_{18}$, 100), and 271 ($M{+}H^+$ - $H_2C{=}CMe_2$ - $C_{10}H_{18}$, 55); $\nu_{max.}$(film) 1770, 1710 (C=O), and 1250 cm^{-1} (P=O).

O-*Menthyl* O-*Methyl Phosphorothioate* (125).- The phosphoramidate (120) (mixture of diastereoisomers) (765 mg, 2.5 mmol) was stirred with sodium hydride (103 mg, 4.28 mmol; 1.7 mol equiv.) in DMF (4.6 ml) at room temperature. After 1.7 h, carbon disulphide (0.76g, 10 mmol; 4 mol equiv.) was added (deep red colour) and the mixture was left overnight.[69] The

excess sodium hydride was quenched with methanol (100 μl). All solvent was removed and the residue was partitioned between water and ether. The aqueous portion was acidified (HCl) to pH ≤ 1 and the liberated free acid was extracted into light petroleum. The crude acid (125) was purified by crystallisation of its ammonium salt from dichloromethane--light petroleum (b.p. 40-60 °C) and then regenerated. The required acid was accompanied by an impurity [the impurity (~ 15 %), $\delta_P(CH_2Cl_2)$ 0.3 (triethylammonium salt), was evident in the salt of (125),* $\delta_P(CH_2Cl_2)$ 58.3 and 58.0 (diastereoisomers; triethylammonium salt), and was probably the dialkyl phosphate salt of (126) resulting from reaction with CO_2 instead of CS_2] which was removed by partitioning the triethylammonium salt of the impure product between dichloromethane and water (1 : 1; impurity passes into water). The required acid (125) (545 mg, 82 %) was recovered from the organic portion and crystallised from light petroleum (b.p. 40-60 °C) at -20 °C to give O-*menthyl* O-*methyl phosphorothioate* (125) m.p. 65-75 °C; $\delta_P(CDCl_3)$ 61.0 and 60.6 (diastereoisomers; 1 : 1 mixture); $\delta_H(CDCl_3)$ 7.57 (1 H, br s, O*H*), 4.53-4.05 (1 H, m), 3.73 (3 H, d, J_{PH} 13, O*Me*), and 2.40-0.67 (18 H); $\nu_{max.}$(Nujol) 3600-1800 (several maxima; OH) and 820 cm^{-1} (P=S).

A portion of the phosphoramidate (120) having > 96 % the lowfield diastereoisomer (^{31}P NMR) (52 mg, 0.17 mmol) was treated as above to give the acid (125) [> 96 % of the diastereoisomer $\delta_P(CDCl_3)$ 61.2] and some unreacted substrate (12 mg) which was used later (see p. 162).

* The sodium salt, δ_P 1.3, was evident in the reaction mixture.

O-*Menthyl* O-*Methyl* S-p-*Nitrobenzyl Phosphorothioate* (127).- A mixture of the phosphorothioic acid (125) (48 mg, 0.18 mmol), *p*-nitrobenzyl bromide (53 mg, 0.25 mmol; 1.4 mol equiv.) and triethylamine (25 mg, 0.25 mmol; 1.4 mol equiv.) in THF (2 ml) was stirred at 50 °C.[91] After 1 h the solvent was removed and the residue was partitioned between ether and water and the organic portion was dried ($MgSO_4$) and concentrated. Chromatography afforded O-*menthyl* O-*methyl* S-p-*nitrobenzyl phosphorothioate* (127) (51 mg, 71 %) as an oil; $\delta_P(CDCl_3)$ 26.5 and 26.1 (diastereoisomers; ~ 1 : 1 mixture); $\delta_H(CDCl_3)$ 7.84 (4 H, AA'BB', $\delta_{AA'}$ 8.15, $\delta_{BB'}$ 7.54, J_{AB} 9), 4.45-3.88 (1 H, m), 4.11 (2 H, d, J_{PH} 16, SCH_2Ar), 3.62 (3 H, d, J_{PH} 12, O*Me*), and 2.38-0.65 (18 H); *m/z* (CI) 419 ($M+NH_4^+$, 30 %), 402 ($M+H^+$, 15), 281 ($M+NH_4^+ - C_{10}H_{18}$, 100), and 264 ($M+H^+ - C_{10}H_{18}$, 10); $\nu_{max.}$(film) 1525 (NO_2), 1360 (NO_2), and 1270 cm^{-1} (P=O). A crystalline sample could not be obtained.

Dicyclohexylammonium O-*Menthyl* O-*Methyl Phosphorothioate* (128).- The phosphorothioic acid (125) was treated with dicyclohexylamine in light petroleum (b.p. 40-60 °C) to give its salt. Crystallisation from light petroleum (b.p. 40-60 °C) gave *dicyclohexylammonium* O-*menthyl* O-*methyl phosphorothioate* (128), m.p. 151-154 °C; $\delta_P(CDCl_3)$ 56.7 and 56.0 (diastereoisomers; 1 : 1 mixture); $\delta_H(CDCl_3$, 300 MHz) 8.85 (2 H, br s, NH_2^+), 4.144 (1 H, m), 3.612 and 3.600 (total 3 H; both d, J_{PH} 13.2 or 13.0, O*Me*), 3.12-2.93 (2 H, m), and 2.47-0.77 (38 H); *m/z* [Negative ion FAB (NOBA matrix); M = X^+ Y^-] 265 (Y^-, 100 %); $\nu_{max.}$(Nujol) 3200-2140 (NH) cm^{-1} (Found: C, 61.6; H, 10.1; N, 3.0. $C_{23}H_{46}NO_3PS$ requires C, 61.7; H, 10.4; N, 3.1 %).

The phosphorothioic acid (125) [> 96 % the diastereoisomer $\delta_P(CDCl_3)$ 61.2] was similarly converted into the dicyclohexylammonium salt and crystallisation from light petroleum (b.p. 40–60 °C) afforded a sample that was at least 99.5 % one diastereoisomer, $\delta_P(CDCl_3)$ 55.9; $\delta_H(CDCl_3$, 300 MHz) 8.82 (very broad, NH_2^+), 4.117 (1H, dddd, J_{PH} ~ 10, J_{HH} ~ 10, 10, and 4.3), 3.612 (3 H, d, J_{PH} 13.3, OMe), 3.11–2.95 (2 H, m), 2.49–2.38 (1 H, m), 2.256 (1 H, m), 2.17–2.04 (4 H, m), 1.89–1.76 (3 H, m), and 1.75–0.79 (29 H). This sample was allowed to crystallise slowly from a mixture of ether, dichloromethane, and light petroleum to give a crystal suitable for single crystal X-ray analysis. The crystal was glued to a glass filament. Data were measured on a Siemens P4 diffractometer. All data were collected using graphite monochromated Mo-K_α radiation (λ 0.7107 Å) at 293 K using an ω-scan technique. The data were corrected for Lorentz and polarisation effects.

Crystal data for (128): $C_{11}H_{22}O_3PS^-$ $C_{12}H_{24}N^+ \cdot {}^1/_2C_4H_{10}O$, M = 484.7. Monoclinic, space group $C2$, a = 18.218(10), b = 9.892(6), c = 15.851(9) Å, β = 90.27(3)°, U = 2856(3) Å^3, Z = 4, μ = 0.20 mm^{-1}, $F(000)$ = 1068, D_c = 1.127 g cm^{-3}. 1478 Unique reflexions were measured with 1274 having $I > 2\sigma(I)$ regarded as observed. The structure was solved by direct methods and difference Fourier techniques. All non-hydrogen atoms except those of the solvent molecule were refined as anisotropic. The hydrogen atoms bonded to nitrogen were located from difference Fourier maps and the positional parameters refined; all other hydrogen atoms were included in

calculated positions. The final R and R_w values are 0.0583 and 0.0629 respectively for 277 variables, $(\Delta/\sigma)_{max.}$ = 0.52. See Appendix 2 for complete details.

Menthyl Methyl N-tert-*Butyl*-N-*methylphosphoramidate* (117).- The phosphoramidate (117) was isolated from the reaction of the bromomethylphosphonamidate (112) (sample B) with benzyltrimethylammonium methoxide: b.p. 74 °C (oven temp.) at 0.2 mmHg; $\delta_P(CDCl_3)$ 11.5 and 10.5 (major) (diastereoisomers; ratio 41 : 59); $\delta_H(CDCl_3$, 300 MHz) 4.20-4.08 (1 H, m), 3.628 (major) and 3.612 (total 3H; both d, J_{PH} 11.3 or 11.4, O*Me*), 2.665 (major) and 2.661 (total 3 H; both d, J_{PH} 9.7 and 9.5, N*Me*), 2.34-2.10 (2 H, m), 1.71-1.58 (2 H, m), 1.54-0.74 (14 H), and 1.315 (9 H, s); *m/z* 319 (M^+, 1 %), 304 (M^+ - Me, 3), 182 ($M^+ - C_{10}H_{17}$, 12), 166 (M^+ - Me - $C_{10}H_{18}$, 68), and 95 (100); *m/z* (CI) 320 ($M+H^+$, 48 %), 264 ($M+H^+ - H_2C=CMe_2$, 13), 182 ($M+H^+ - C_{10}H_{18}$, 100), 166 (M^+ - Me - $C_{10}H_{18}$, 59), and 126 ($M+H^+ - C_{10}H_{18} - H_2C=CMe_2$, 68); $\nu_{max.}$(film) 1250 cm^{-1} (P=O) (Found: C, 59.4; H, 10.4; N, 4.4; $M+H^+$, 320.2355. $C_{16}H_{34}NO_3P$ requires C, 60.2; H, 10.7; N, 4.4 %; *M*+H, 320.2355).

A sample of the phosphoramidate (117) was also isolated from the reaction of the bromomethylphosphonamidate (112) (sample A) with benzyltrimethylammonium methoxide: $\delta_P(CDCl_3)$ 11.5 (major) and 10.5 (diastereoisomers; ratio 95 : 5); $\delta_H(CDCl_3$, 300 MHz) for major component: 4.137 (1 H, dddd, J_{PH} 7.5, J_{HH} ~ 11, 10.6, 4.5), 3.614 (3 H, d, J_{PH} 11.4, O*Me*), 2.663 (3 H, d, J_{PH} 9.6, N*Me*), 2.31-2.11 (2 H, m), 1.70-1.60 (2 H, m), 1.53-1.23 (3 H, m), 1.314 (9 H, s), and 1.15-0.79 (11 H, m); $\nu_{max.}$(film) 1250 cm^{-1} (P=O).

An authentic sample of the *N*-methylphosphoramidate (117) was prepared as follows: the phosphoramidate (120) (mixture of diastereoisomers) (98 mg, 0.32 mmol) was stirred with sodium hydride (18 mg, 0.75 mmol) in DMF (0.75 ml) for 2.7 h. Methyl iodide (136 mg, 60 μl, 0.96 mmol, 3 mol equiv.) was then added. After 1 h, volatile material was removed and the residue was partitioned between light petroleum and water. The organic portion was dried ($MgSO_4$) and concentrated to give the product [mixture of diastereoisomers; ratio 58 : 42, lowfield (^{31}P NMR) diastereoisomer dominant]. The phosphoramidate (120) (12 mg, 0.04 mmol) [> 96 % the lowfield (^{31}P) diastereoisomer] that was recovered unchanged from the preparation of the dialkyl phosphorothioate (125) (p. 158) was similarly treated, giving the phosphoramidate (117) having a diastereoisomer ratio 98 : 2 with the lowfield (^{31}P NMR) diastereoisomer dominant.

*Menthyl Methyl (*tert*-Butylamino)methylphosphonate* (116).- The (*tert*-butylamino)methylphosphonate (116) was isolated from the reaction of the bromomethylphosphonamidate (112) (sample B) with benzyltrimethylammonium methoxide: $\delta_P(CDCl_3)$ 28.4 and 28.1 (major) (diastereoisomers; ratio 1 : 1.3); $\delta_H(CDCl_3$, 300 MHz) 4.33-4.21 (1 H, m), 3.791 (major) and 3.765 (total 3 H; both d, J_{PH} 10.6 and 10.8, O*Me*), 2.922 and 2.920 (major) [total 2 H; ABP or d, J_{PH} 15.2, PCH_2N], 2.22-2.07 (2 H, m), 1.72-1.61 (2 H, m), 1.51-1.28 (2 H, m), 1.26-0.68 (13 H; includes N*H*), and 1.085 (major) and 1.078 (total 9 H, both s); *m/z* 319 (M^+, 13 %), 304 (M^+ - Me, 39), 182 (M^+ - $C_{10}H_{17}$, 18), and 166 (M^+ - Me - $C_{10}H_{18}$, 100); $\nu_{max.}$(film) 3280 (NH) and 1245 cm^{-1} (P=O). Treatment with

picric acid in benzene and crystallisation from dichloromethane-ether-light petroleum afforded the picrate, m.p. 158-163 °C; $\delta_P(CDCl_3)$ 17.0 (major) and 16.2 (diastereoisomers); $\delta_H(CDCl_3$, 300 MHz) 8.886 (2 H, s), 4.37-4.16 (1 H, m), 3.676 (major) and 3.649 (total 3 H; both d, J_{PH} 11.3 or 11.4, OMe), 3.50-3.30 (2 H, m), 2.12-1.84 (2 H, m), 1.70-0.69 (16 H), and 1.475 (9 H, s); $\nu_{max.}$(Nujol) 3200-2300 cm^{-1} (NH) (Found: C, 48.3; H, 6.7; N, 10.1. $C_{22}H_{37}N_4O_{10}P$ requires C, 48.2; H, 6.8; N, 10.2 %).

A sample of the aminomethylphosphonate (116) was also isolated from the reaction of the bromomethylphosphonamidate (112) (sample A) with benzyltrimethylammonium methoxide: $\delta_P(CDCl_3)$ 28.4 (major) and 28.1 (diastereoisomers; ratio 19 : 1); $\delta_H(CDCl_3$, 300 MHz) major diastereoisomer: 4.273 (1 H, dddd, J_{PH} 6.9, J_{HH} ~ 11, 10.7, and 4.5), 3.765 (3 H, d, J_{PH} 10.8, OMe), 2.922 (2 H, ABP, δ_A 2.941, δ_B 2.903, J_{AB} 13.9, J_{AP} 14.9, J_{BP} 15.7, PCH_2N), 2.26-2.06 (2 H, m), 1.73-1.60 (2 H, m), 1.58-0.75 (15 H; includes NH), and 1.076 (9 H, s); $\nu_{max.}$(film) 3290 (NH) and 1245 cm^{-1} (P=O). Treatment with picric acid in benzene afforded one diastereoisomer of the picrate after crystallisation from ether-light petroleum, m.p. 118.5-120.5 °C; $\delta_P(CDCl_3)$ 16.4; $\delta_H(CDCl_3$, 300 MHz) 8.889 (2 H, s), 4.259 (1 H, dddd, J_{PH} 6.8, J_{HH} ~ 11, ~ 11, and ~ 5), 3.692 (3 H, d, J_{PH} 11.3, OMe), 3.360 (2 H, ABP, δ_A 3.391, δ_B 3.329, J_{AB} ~ J_{AP} ~ J_{BP} ~ 15), 2.13-2.02 (1 H, m), 1.916 (1 H, m), 1.72-1.58 (2 H, m), 1.30-0.70 (14 H), and 1.470 (9 H, s); $\nu_{max.}$(Nujol) 3140-2300 cm^{-1} (NH). A portion of this diastereoisomer was allowed to crystallise slowly from from ether-light petroleum to give a sample suitable for single crystal

X-ray analysis. All crystals examined were found to be non--single. A relatively simple twin with the *c* axes of both components aligned and the *a** and *b** axes of one crystal component aligned with *-a** and *-b** of the other component was glued to glass filament and used for data collection. The relative intensities of the two components were measured and the coincident *hk*0 reflexions scaled accordingly. Data were measured on a Stöe STADI-2 Weissenberg diffractometer. All data were collected using graphite monochromated Mo-K_α radiation (λ 0.7107 Å) at 293 K using an ω-scan technique. The data were corrected for Lorentz and polarisation effects.

Crystal data for the picrate of (116): $C_{16}H_{35}NO_3P^+$ $C_6H_2N_3O_7^-$, M = 548.5. Triclinic, space group $P1$, a = 20.935(20), b = 13.210(13), c = 10.618(3) Å, α = 91.80(6), β = 95.2(1), γ = 94.5(1)°, U = 2913(4) Å^3, Z = 4, μ = 0.15 mm^{-1}, $F(000)$ = 1168, D_c = 1.25 g cm^{-3}. 7415 Unique reflexions were measured with 4703 having $I > 2\sigma(I)$ regarded as observed. The structure was solved by direct methods and difference Fourier techniques; it consists of four unique formula units. No hydrogen atoms were located and all atoms were refined as isotropic. The final R and R_w values are 0.132 and 0.142 respectively for 543 variables, $(\Delta/\sigma)_{max.}$ = 0.53. Although the final R factor is high due to problems of possible overlap of reflexions and lack of sufficient data for full refinement, the essential details of the structure are unambiguous. See Appendix 2 for complete details.

Stereochemical Studies.- A solution of the diastereoisomerically enriched bromomethylphosphonamidate (112) (sample A or B) (48 mg, 0.13 mmol) in THF (0.45 ml) was added to a mixture

of methanolic benzyltrimethylammonium methoxide (40 % w/w) (0.1 ml, 0.2 mmol) and THF (0.45 ml) (reaction medium 0.2 M methoxide in 9 : 1 THF-methanol). After 4.5 h at room temperature the reaction was quenched with ammonium chloride. The mixture was then examined by ^{31}P NMR spectroscopy (peak areas) to determine the ratio of the two rearrangement products (Table 12) and for each, the ratio of the diastereoisomers (Table 13). Volatile material was removed and the residue was partitioned between ether and water. To separate the crude products, the ether layer was washed with 1 M sodium hydroxide solution, water, 1 M hydrochloric acid (acid wash retained), and finally water (final water wash retained). The organic portion was dried ($MgSO_4$) and concentrated to give the phosphoramidate (117). The acid wash and the final water wash were combined and basified with 2 M sodium hydroxide; the liberated (*tert*-butylamino)methylphosphonate (116) was then extracted into ether, dried ($MgSO_4$), and isolated by evaporation of the solvent. The isolated products were further investigated by ^{31}P and ^{1}H NMR spectroscopy (Table 13).

Similar experiments were also performed (sample A only) in which *(a)* the reaction was quenched before completion (16 min; 93 % completion), and *(b)* the reaction was allowed to continue for 6 h before quenching (Table 13).

Bromomethylphosphonic Dichloride (134)[92].- Phosphorus pentachloride (6.36 g, 30.5 mmol) was added[72] to dimethyl bromomethylphosphonate (133)[93], $\delta_P(CDCl_3)$ 21.3, (2.62 g, 12.9 mmol) at room temperature over 10 min with stirring. After 30 min the mixture was heated at 90 °C for 3.5 h. Additional

phosphorus pentachloride (546 mg, 2.6 mmol) was added and heating was continued for a further 30 min. Volatile material ($POCl_3$) was removed (rotary evaporator) and the residue was distilled to give *bromomethylphosphonic dichloride* (134) (1.54 g, 56 %; some product lost during manipulation), b.p. 68 °C (oven temp.) at 0.2 mmHg; $\delta_P(CDCl_3)$ 35.1; $\delta_H(CDCl_3)$ 3.95 (d, J_{PH} 6, CH_2).

P-*(Bromomethyl)*-N-tert-*butylphosphonamidic Chloride* (135).- *tert*-Butylamine (876 mg, 12.0 mmol; 2 mol equiv.) in dichloromethane (6 ml) was added to a stirred solution of bromomethylphosphonic dichloride (134) (1.27 g, 6.0 mmol) in dichloromethane (7 ml) at 0 °C over 5 min. The mixture was then allowed to warm to room temperature. After 30 min it was diluted with light petroleum (5 ml) and the precipitated amine hydrochloride was removed by filtration. The solvent was evaporated to give P-*(bromomethyl)*-N-tert-*butylphosphonamidic chloride* (135) (1.39 g, 93 %), $\delta_P(CDCl_3)$ 29.5; $\delta_H(CDCl_3)$ 3.45 (1 H, br, *NH*), 3.55 (2 H, d, J_{PH} 7.5, PCH_2Br) and 1.41 (9 H, s).

Methyl P-*(Bromomethyl)*-N-tert-*butylphosphonamidate* (129).- A mixture of methanol (55 mg, 1.73 mmol) and triethylamine (174 mg, 1.73 mmol) in dichloromethane (3.5 ml) was added[52] dropwise over 20 min to a stirred solution of bromomethylphosphonic dibromide (113) (509 mg, 1.69 mmol) in dichloromethane (4 ml) at -30 to -20 °C under a nitrogen atmosphere. The mixture was allowed to warm to room temperature. After 40 min, it was cooled to 0 °C and *tert*-butylamine (273 mg, 3.7 mmol; 2.2 mol equiv.) in dichloromethane (2 ml) was added over 2 min. After 50 min at

room temperature, volatile material was removed and the residue was partitioned between ether and water. The organic portion was dried ($MgSO_4$) and concentrated to give the crude product (273 mg, 66 %). Chromatography [silica layer; 70 : 30 ethyl acetate–light petroleum (b.p. 40–60 °C), R_f 0.16] followed by crystallisation from ether–light petroleum (40–60 °C) gave *methyl* P-*(bromomethyl)*-N-tert-*butylphosphonamidate* (**129**), m.p. 71.5–73 °C; $\delta_P(CDCl_3)$ 22.6; $\delta_H(CDCl_3$, 300 MHz) 3.738 (3 H, d, J_{PH} 11.1, OMe), 3.306 (2 H, ABP, δ_A 3.346, δ_B 3.264, J_{AB} 13.2, J_{AP} 9.6, J_{BP} 8.1, PCH_2Br), 2.78 (1 H, br d, J_{PH} 6, NH), and 1.352 (9 H, d, J_{PH} 0.7, NBu^t); *m/z* (no M^+), 230, 228 (M^+ – Me, 100 %); *m/z* (CI) 263, 261 ($M+NH_4^+$, 20 %, ratio 1 : 1), 246, 244 ($M+H^+$, 49, ratio 1 : 1), 230, 228 (M^+ – Me, 18, ratio 1 : 1), 183 (15), 166 (100), and 150 (26); $\nu_{max.}$(Nujol) 3220 (NH), 1240, and 1215 cm^{-1} (P=O) (Found: C, 29.5; H, 6.0; N, 5.7. $C_6H_{15}BrNO_2P$ requires C, 29.5; H, 6.2; N, 5.7 %).

The bromomethylphosphonamidate (**129**) was also prepared (almost quantitatively by ^{31}P NMR spectroscopy) by treating bromomethylphosphonic dichloride (**134**) in dichloromethane (1 ml per mmol) with *tert*-butylamine (2 mol equiv.) in dichloromethane (0.5 ml per mmol) at 0 °C (amine added over 5 min) followed by sodium methoxide in methanol.

tert-*Butyl* P-*(Bromomethyl)*-N-tert-*butylphosphonamidate* (**131**).– Potassium *tert*-butoxide (263 mg, 2.35 mmol; 1.1 mol equiv.) was added (gradually, in small portions) to a stirred solution of the bromomethylphosphonamidic chloride (**135**) (545 mg, 2.2 mmol) in *tert*-butanol (4 ml). Examination of the reaction mixture by ^{31}P NMR spectroscopy revealed the

presence of starting material, δ_P 28.8 (26 %), and two products, δ_P 15.1 (the desired product; 42 %) and δ_P 18.6 (32 %; believed to be the product of *tert*-butoxide-induced rearrangement of the desired product). More potassium *tert*-butoxide (77 mg, 0.7 mmol) was added in small portions, giving the desired product and the by-product in a 3 : 2 ratio. After quenching with ammonium chloride volatile material was removed. The residue was dissolved in ether and was washed with water, very dilute hydrochloric acid (to remove the by-product), and with water again. The organic portion was dried ($MgSO_4$) and concentrated to give the crude product (290 mg, 46 %). Chromatography [silica layer; 1 : 1 ethyl acetate–light petroleum (b.p. 40–60 °C), R_f 0.18; possibly some decomposition during chromatography] and crystallisation from light petroleum (b.p. 40–60 °C) afforded *tert-butyl P-(bromomethyl)-N-tert-butylphosphonamidate* (131) (181 mg, 29 %), m.p. 94–95 °C; $\delta_P(CDCl_3)$ 16.4; $\delta_H(CDCl_3$, 300 MHz) 3.236 (2 H, ABP, δ_A 3.273, δ_A 3.197, J_{AB} 12.9, J_{AP} 9.5, J_{BP} 7.5, PCH_2Br), 2.687 (1 H, br d, J_{PH} 5.7, *NH*; exchanges with D_2O), 1.532 (9 H, s, OBu^t), and 1.336 (9 H, d, J_{PH} 0.6, NBu^t); *m/z* (no M^+) 272, 270 (M^+ – Me, 30 %, ratio 1 : 1) and 216, 214 (M^+ – Me – $H_2C{=}CMe_2$, 100, ratio 1 : 1); *m/z* (CI) 305, 303 ($M{+}NH_4^+$, 14 %, ratio 1 : 1), 288, 286 ($M{+}H^+$, 38, ratio 1 : 1), 249, 247 ($M{+}NH_4^+$ – $H_2C{=}CMe_2$, 38, ratio 1 : 1), and 208 (100); $\nu_{max.}$(Nujol) 3220 (NH), 1235, and 1210 cm^{-1} (P=O) (Found: C, 37.8; H, 7.3; N, 4.9. $C_9H_{21}BrNO_2P$ requires C, 37.8; H, 7.4; N, 4.9 %).

Cyclohexyl P-(Bromomethyl)-N-tert-butylphosphonamidate (130).- A mixture of cyclohexanol (335 mg, 3.34 mmol; 1.1 mol equiv.) and triethylamine (304 mg, 3 mmol) in dichloromethane (3 ml) was added to a stirred solution of bromomethylphosphonic dibromide (113) (903 mg, 3 mmol) in dichloromethane (3 ml) at room temperature. After 1 h, *tert*-butylamine (866 mg, 12 mmol; 4 mol equiv.) was added and the mixture was stirred for 10 min. All volatile material was removed and the residue was partitioned between ether and water. Chromatography of the organic portion [silica layer; 1 : 1 ethyl acetate-light petroleum (b.p. 40-60 °C), R_f 0.20] followed by crystallisation from light petroleum (b.p. 40-60 °C) afforded *cyclohexyl P-(bromomethyl)-N-tert-butylphosphonamidate* (130) (336 mg, 36 %), m.p. 77-79 °C; $\delta_P(CDCl_3)$ 19.9; $\delta_H(CDCl_3$, 300 MHz) 4.498 (1 H, dtt, J_{PH} ~ 9, J_{HH} ~ 9 and 4.3, POC*H*), 3.327 (2 H, ABP, δ_A 3.363, δ_B 3.290, J_{AB} 13.1, J_{AP} 9.5, J_{BP} 7.7, PCH_2Br), 2.77 (1 H, br d, J_{PH} 7, N*H*), 2.08-1.93 (2 H, m), 1.87-1.73 (2 H, m), 1.68-1.51 (2 H, m), 1.49-1.22 (4 H, m), and 1.392 (9 H, d, J_{PH} 0.6, NBu^t); *m/z* (no M^+) 298, 296 (M^+ - Me, 30 %, ratio 1 : 1) and 216, 214 (M^+ - Me - C_6H_{10}, 100, ratio 1 : 1); *m/z* (CI) 314, 312 ($M+H^+$, 11 %, ratio 1 : 1), 234 (58), and 74 ($Bu^tNH_3^+$, 100); $\nu_{max.}$(Nujol) 3210 (NH), 1235, and 1215 cm^{-1} (P=O) (Found: C, 42.4; H, 7.2; N, 4.6. $C_{11}H_{23}BrNO_2P$ requires C, 42.3; H, 7.4; N, 4.5 %).

Reactions of Alkyl Bromomethylphosphonamidates with Alkoxides.- The alkyl bromomethylphosphonamidate (129) to (131) (0.13 mmol) was dissolved in THF (0.45 ml) and treated with either methanolic benzyltrimethylammonium methoxide (0.2 mmol, 0.1 ml) in THF (0.45 ml) or potassium *tert*-butoxide

(22.5 mg, 0.2 mmol) in *tert*-butanol (0.1 ml) and THF (0.45 ml) at room temperature (reaction medium 0.2 M alkoxide 9 : 1 THF-alcohol). When the reaction was complete (2-3 h with methoxide; within 5 min for *tert*-butoxide) the excess alkoxide was quenched with ammonium chloride and the ratio of the rearrangement products was determined by ^{31}P NMR spectroscopy (peak areas) (Table 14). Volatile material was removed and the residue was dissolved in dichloromethane and washed with water. In general, the aminomethylphosphonate product (139) and (141) was then extracted from the dichloromethane solution with aqueous hydrochloric acid (pH just less than 7), leaving the phosphoramidate product (140) and (142) in the organic solution; the aminomethylphosphonate was recovered by basification of the aqueous solution and back-extraction into dichloromethane. The organic portions were dried ($MgSO_4$) and evaporation of solvent gave the two separated products.

In the case where a P-OBu^t group (acid labile) was present, the products (138), (143), (144), (147), (148), and (149) were separated by chromatography [rotating silica disc (chromatatron); ethyl acetate, diluted initially with light petroleum; phosphoramidate eluted first]. The following were obtained:

From (129) with methoxide: *dimethyl (tert-butylamino)methylphosphonate* (139)[58], $\delta_P(CDCl_3)$ 30.2; $\delta_H(CDCl_3)$ 3.80 (6 H, d, J_{PH} 11, OMe), 2.96 (2 H, d, J_{PH} 15, PCH_2N), and 1.09 (10 H; s, NBu^t and br s, NH); $\nu_{max.}$(film) 3300 (NH) and 1235 cm^{-1} (P=O); and *dimethyl* N-tert-*butyl*-N-*methylphosphoramidate* (140)[58],

$\delta_P(CDCl_3)$ 13.1; $\delta_H(CDCl_3)$ 3.66 (6 H, d, J_{PH} 11, OMe), 2.72 (3 H, d, J_{PH} 10, NMe), and 1.31 (9 H, s, NBu^t); $\nu_{max.}$(film) 1240 cm^{-1} (P=O).

From (129) with *tert*-butoxide: tert-*butyl methyl (*tert-*butylamino)methylphosphonate* (143), $\delta_P(CDCl_3)$ 25.3; $\delta_H(CDCl_3)$ 3.76 (3 H, d, J_{PH} 11, OMe), 2.88 (2 H, d, J_{PH} 15.5 PCH_2N), 1.63 (~ 2 H, br s, NH and water), 1.52 (9 H, s, OBu^t), and 1.08 (9H, s, NBu^t); *m/z* (CI) 238 ($M+H^+$, 48 %), 182 ($M+H^+ - H_2C=CMe_2$, 100), 166 ($M^+ - H_2C=CMe_2 - Me$, 11), and 86 (58); $\nu_{max.}$(film) 3300 (NH) and 1255 cm^{-1} (P=O) (Found: $M+H^+$, 238.1572. $C_{10}H_{24}NO_3P$ requires *M*+H, 238.1572); and tert-*butyl methyl* N-tert-*butyl*-N-*methylphosphoramidate* (144), $\delta_P(CDCl_3)$ 7.2; $\delta_H(CDCl_3$, 300 MHz) 3.599 (3 H, d, J_{PH} 11.5, OMe), 2.686 (3 H, d, J_{PH} 9.8, NMe), 1.472 (9 H, d, J_{PH} 0.3, OBu^t), and 1.298 (9 H, s, NBu^t); *m/z* (CI) 238 ($M+H^+$, 18), 222 ($M^+ - Me$, 4), 199 ($M+NH_4^+ - H_2C=CMe_2$, 8), 182 ($M+H^+ - H_2C=CMe_2$, 100), 166 ($M^+ - Me - H_2C=CMe_2$, 71), 143 ($M+NH_4^+ - 2\ H_2C=CMe_2$, 10), and 126 ($M+H^+ - 2\ H_2C=CMe_2$, 35); $\nu_{max.}$(film) 1260 cm^{-1} (P=O) (Found: $M+H^+$, 238.157. $C_{10}H_{24}NO_3P$ requires *M*+H, 238.157). A mixture of these two products was also obtained from the reaction of (131) with methoxide. [All attempts to isolate the (amino-methyl)phosphonate by extraction into aqueous hydrochloric acid were unsuccessful; after basification the product could not be back-extract into dichloromethane and had $\delta_P(CD_3OD)$ 20.8; $\delta_H(CD_3OD)$ 3.58 (3 H, d, J_{PH} 10.5, OMe), 2.74 (2 H, d, J_{PH} 15, PCH_2N), and 1.13 (9 H, s, NBu^t). The absence of an OBu^t signal suggested instability in acid ($-OBu^t$ ---> $-OH + H_2C=CMe_2$), and prompted the use of chromatography to separate the products.] [The reaction of (129) with $KOBu^t$ that was not

freshly sublimed gave two additional products, δ_P 20.4 and 7.7, believed to be the salts of the phosphonic acid (145) and the phosphoramidic acid (146) respectively, formed from hydroxide competition. This was confirmed by repeating the reaction with an added quantity of water (0.7 μl; 0.3 mol equiv.) which showed great enhancement in the yields of these products.]

From (131) with *tert*-butoxide: a mixture (separation not attempted) dominated by *di*-tert-*butyl (tert-butylamino)methylphosphonate* (138), $\delta_P(CDCl_3)$ 20.1; $\delta_H(CDCl_3$, 300 MHz) 2.794 (2 H, d, J_{PH} 15.3, PCH_2N), 1.515 (19 H; s, OBu^t and br NH), and 1.072 (9 H, s, NBu^t); *m/z* 279 (M^+, 10 %), 264 (M^+ - Me, 12), 208 (M^+ - Me - $H_2C{=}CMe_2$, 25), 166 (M^+ - Bu^t - $H_2C{=}CMe_2$, 24), and 152 (M^+ - Me - 2 $H_2C{=}CMe_2$, 100); $\nu_{max.}$(film) 3280 (NH) and 1250 cm^{-1} (P=O) (Found: M^+, 279.196. $C_{13}H_{30}NO_3P$ requires *M*, 279.196), with *di*-tert-*butyl* N-tert-*butyl*-N-*methylphosphoramidate* (147), $\delta_P(CDCl_3)$ 0.9; $\delta_H(CDCl_3$, 300 MHz) 2.631 (3 H, d, J_{PH} 10.0, NMe), 1.456 (18 H, s, OBu^t), and 1.290 (9 H, s, NBu^t), as the minor component.

From (130) with methoxide: *cyclohexyl methyl (tert-butylamino)methylphosphonate* (141), $\delta_P(CDCl_3)$ 28.2; $\delta_H(CDCl_3$, 300 MHz) 4.463 (1 H, dtt, J_{PH} ~ 9, J_{HH} ~ 9 and 5, POCH), 3.766 (3 H, d, J_{PH} 10.7, OMe), 2.922 (2 H, d, J_{PH} 15.1, PCH_2N), 2.03-1.88 (2 H, m), 1.83-1.68 (2 H, m), 1.61-1.45 (3 H, m), 1.43-1.01 (4 H, m; includes NH), and 1.080 (9 H, s, NBu^t); *m/z* 263 (M^+, 6 %), 248 (M^+ - Me, 38), and 166 (M^+ - Me - C_6H_{10}, 100); $\nu_{max.}$(film) 3300 (NH) and 1240 cm^{-1} (P=O); picrate, m.p. 200-201.5 °C (decomp.) (from methanol); $\delta_P(CH_3OH)$ 17.3 (Found: C, 43.7; H, 5.8; N, 11.4. $C_{18}H_{29}N_4O_{10}P$ requires C,

43.9; H, 5.9; N, 11.4 %); and *cyclohexyl methyl* N-tert-*butyl*-N-*methylphosphoramidate* (142), b.p 99 °C (oven temp.) at 0.1 mmHg; $\delta_P(CDCl_3)$ 10.8; $\delta_H(CDCl_3$, 300 MHz) 4.315 (1 H, dtt, J_{PH} ~ 8, J_{HH} ~ 8 and 4, POC*H*), 3.626 (3 H, d, J_{PH} 11.3, O*Me*), 2.705 (3 H, d, J_{PH} 9.6, N*Me*), 2.02-1.87 (2 H, m), 1.81-1.67 (2 H, m), 1.61-1.44 (3 H, m), 1.42-1.16 (3 H, m), and 1.312 (9 H, s, N*Bu*^{t}); *m/z* 263 (M^+, 3%), 248 (M^+ - Me, 17), and 166 (M^+ - Me - C_6H_{10}, 100); $\nu_{max.}$(film) 1255 cm^{-1} (P=O) (Found: M^+, 263.165. $C_{12}H_{26}NO_3P$ requires *M*, 263.165).

From (130) with *tert*-butoxide: tert-*butyl cyclohexyl (*tert-*butylamino)methylphosphonate* (147), $\delta_P(CDCl_3)$ 23.2; $\delta_H(CDCl_3$, 300 MHz) 4.440 (1 H, dtt, J_{PH} ~ 9, J_{HH} ~ 9 and 5, POC*H*), 2.826 (2 H, ABP, δ_A 2.841, δ_B 2.814, J_{AB} 13.8, J_{AP} 14.8, J_{BP} 15.8, PCH_2N), 2.05-1.91 (2 H, m), 1.82-1.68 (2 H, m), 1.62-0.99 (7 H, m; includes N*H*), 1.513 (9 H, s, O*Bu*^{t}), and 1.067 (9 H, s, N*Bu*^{t}); *m/z* 305 (M^+, 5 %), 290 (M^+ - Me, 26), 234 (M^+ - Me - H_2C=CMe_2, 62), and 152 (M^+ - Me - H_2C=CMe_2 - C_6H_{10}, 100); $\nu_{max.}$(film) 3280 (NH) and 1245 cm^{-1} (P=O) (Found: M^+, 305.2120. $C_{15}H_{32}NO_3P$ requires *M*, 305.2120); and tert-*butyl cyclohexyl* N-tert-*butyl*-N-*methylphosphoramidate* (148), $\delta_P(CDCl_3)$ 4.9; $\delta_H(CDCl_3$, 300 MHz) 4.258 (1 H, dtt, J_{PH} ~ 8, J_{HH} ~ 8 and 4, POC*H*), 2.657 (3 H, d, J_{PH} 10.0, N*Me*), 2.01-1.85 (2 H, m), 1.79-1.64 (2 H, m), 1.60-1.16 (6 H, m), 1.459 (9 H, s, O*Bu*^{t}), and 1.299 (9 H, s, N*Bu*^{t}); *m/z* 305 (M^+, 2 %), 290 (M^+ - Me, 7), 234 (M^+ - Me - H_2C=CMe_2, 31), and 152 (M^+ - Me - H_2C=CMe_2 - C_6H_{10}, 100); $\nu_{max.}$(film) 1250 cm^{-1} (P=O) (Found: M^+, 305.212. $C_{15}H_{32}NO_3P$ requires *M*, 305.212).

Appendix 1

X-ray crystallography. Unit cell parameters were determined by least squares refinement of ω measurements for different layers.[94] A Stöe STADI-2 Weissenberg diffractometer was employed, with monochromated Mo-K_α radiation using an ω-scan technique. Structures were solved using the TREF option of SHELXS86.[95] All subsequent calculations were carried out using the computer programme SHELX76.[96]

Crystal data for *N*-[α-methylbenzyl(phenyl)phosphinoyl]--*O*-methanesulphonylhydroxylamine (44) (racemate) (Fig. 11): $C_{15}H_{18}NO_4PS$, M = 339.35. Monoclinic, space group $I2/a$, a = 20.132(16), b = 10.396(2), c = 17.814(14) Å, β = 117.8(1)°, U = 3299(5) Å^3, Z = 8, μ = 2.62 cm^{-1}, λ(Mo-K_α) = 0.7107 Å, F(000) = 1424, D_c = 1.37 g cm^{-3}, T = 293 K. The intensities of 3379 unique reflexions with $2\theta < 54°$ and ($\pm h$, $+k$, $+l$) were measured and the data corrected for Lorentz and polarisation effects to yield 2324 reflexions with $I > 3\sigma(I)$. The phenyl and methyl hydrogen atoms were included in calculated positions (C-H = 1.08 Å) with isotropic thermal parameters refined as groups. The remaining hydrogen atoms were located on a difference Fourier map and were refined as isotropic atoms. All other atoms were refined with anisotropic thermal parameters. Final cycles of refinement employed a weighting parameter g (0.0004) {$w = 1/[\sigma^2F + gF^2]$} and gave the final residual indices R {$= \Sigma\,(|F_o| - |F_c|)/\Sigma|F_o|$} 0.047 and R_w {$= [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$} 0.049. The final difference Fourier was featureless and an analysis of the weighting scheme over $|F_o|$ and $\sin\theta/\lambda$ was satisfactory.

Crystal data for the *N*-methyl-*N'*-phenyl-*P*-(α-methylbenzyl)-phosphonic diamide (**50**) (racemate) (Fig. 12): $C_{15}H_{19}N_2OP$, M = 274.3. Monoclinic, space group $P2_1/a$, a = 10.450(2), b = 13.204(14), c = 10.755(11) Å, β = 97.17(6)°, U = 1472(3) Å^3, Z = 4, μ = 1.41 cm^{-1}, λ(Mo-K$_\alpha$) = 0.7107 Å, F(000) = 584, D_c = 1.24 g cm^{-3}, T = 293 K. The intensities of 2498 unique reflexions with $2\theta < 52°$ and ($+h$, $+k$, $\pm l$) were measured and the data were corrected for Lorentz and polarisation effects to yield 1221 reflexions with $I > 3\sigma(I)$. Although hydrogen atoms were located on the difference Fourier map, the hydrogen atoms of the methyl and phenyl groups were included in calculated positions (C-H = 108 Å) and employed a single fixed thermal parameter. The positional and isotropic thermal parameters of the remaining hydrogen atoms were refined. All other atoms were refined with anisotropic thermal parameters. Final cycles of refinement employed a weighting parameter g (0.0007) {$w = 1/[\sigma^2F + gF^2]$} and gave the final residual indices R {$= \Sigma (|F_o| - |F_c|)/\Sigma|F_o|$} 0.056 and R_w {$= [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$} 0.059. The final difference Fourier was featureless and an analysis of the weighting scheme over $|F_o|$ and $\sin\theta/\lambda$ was satisfactory.

FIG.11

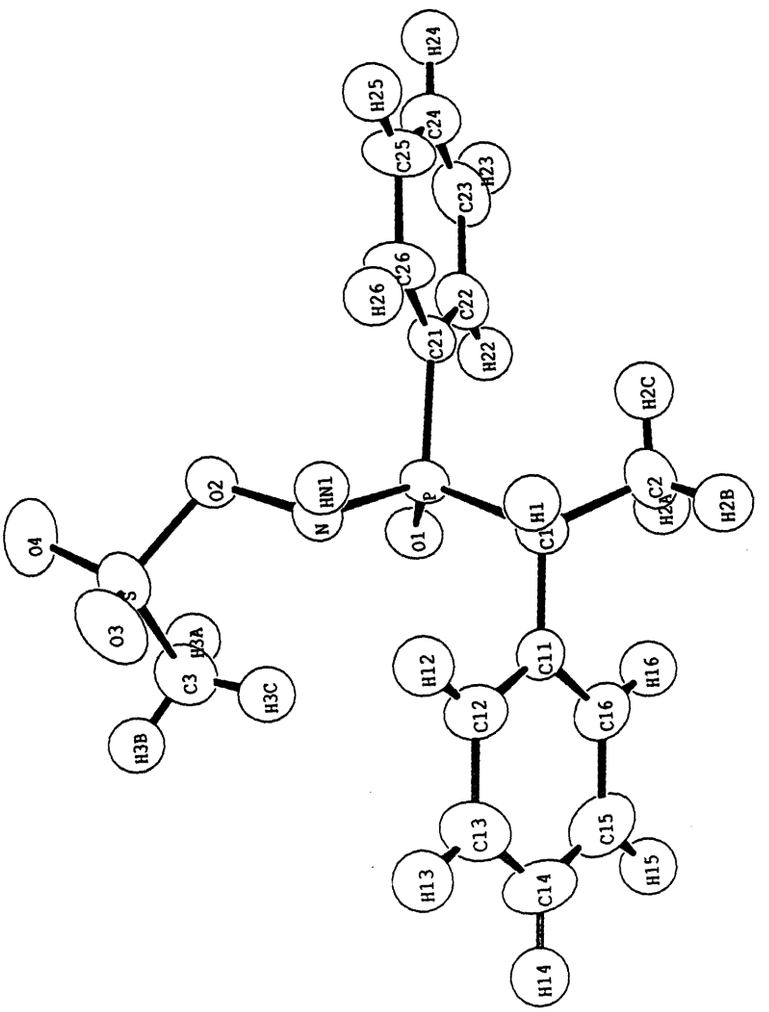

H24
H25
C24
C25
C23
H23
C26
H26
C22
C21
H22
H2C
C2
H2A
H2B
HN1
O2
N
P
O1
C1
H1
O4
S
O3
H3A
C3
H3C
H3B
C11
H12
H16
C12
C16
C13
C15
H13
H15
C14
H14

Table1 Selected Bond lengths (Å)
for N-(-1methylbenzyl)phenylphosphinyl-O-methanesulphonyl hydroxylamine

O(1)-P	1.484(2)	N-P	1.690(2)
C(1)-P	1.824(3)	C(21)-P	1.786(2)
O(2)-S	1.614(2)	O(3)-S	1.414(2)
O(4)-S	1.422(3)	C(3)-S	1.747(4)
N-O(2)	1.459(3)	Hn(1)-N	0.91(3)
H(1)-C(1)	0.93(3)	C(2)-C(1)	1.538(4)
C(11)-C(1)	1.521(3)		

The methyl and phenyl groups were reined as rigid groups with C-H=1.08Å and C-C=1.38Å.

Table2 Selected Bond Angles (°)
for N-(-1methylbenzyl)phenylphosphinyl-O-methanesulphonyl hydroxylamine

N-P-O(1)	111.9(1)	C(1)-P-O(1)	115.0(1)
C(1)-P-N	98.6(1)	C(21)-P-O(1)	111.4(1)
C(21)-P-N	109.4(1)	C(21)-P-C(1)	109.8(1)
O(3)-S-O(2)	109.3(1)	O(4)-S-O(2)	102.6(1)
O(4)-S-O(3)	119.6(2)	C(3)-S-O(2)	103.3(1)
C(3)-S-O(3)	110.2(2)	C(3)-S-O(4)	110.5(2)
N-O(2)-S	109.7(2)	O(2)-N-P	111.3(2)
Hn(1)-N-P	114.7(19)	Hn(1)-N-O(2)	107.9(19)
H(1)-C(1)-P	106.5(19)	C(2)-C(1)-P	109.9(2)
C(2)-C(1)-H(1)	108.5(18)	C(11)-C(1)-P	109.8(2)
C(11)-C(1)-H(1)	107.2(17)	C(11)-C(1)-C(2)	114.6(3)

Table3 Fractional atomic co-ordinates of refined atoms for N-(-1methylbenzyl)phenylphosphinyl-O-methanesulphonyl hydroxylamine

Atom	x	y	z
P	0.47635(4)	0.15954(6)	0.73491(4)
S	0.67941(4)	0.07945(8)	0.78421(6)
O(1)	0.50247(11)	0.29506(17)	0.74884(12)
O(2)	0.59073(11)	0.07410(19)	0.71916(13)
O(3)	0.69958(14)	-0.02973(23)	0.83768(17)
O(4)	0.71171(14)	0.09781(26)	0.72902(18)
N	0.54857(13)	0.05472(23)	0.76624(15)
Hn(1)	0.5350(17)	-0.030(3)	0.7615(18)
C(1)	0.43681(16)	0.1035(3)	0.80272(19)
H(1)	0.4349(16)	0.014(3)	0.7987(18)
C(2)	0.35640(18)	0.1549(5)	0.76958(23)
C(3)	0.68849(21)	0.2188(4)	0.84302(25)
C(11)	0.48958(10)	0.13712(19)	0.89468(10)
C(21)	0.41144(11)	0.13053(17)	0.62621(10)

The methyl and phenyl groups were refined as rigid groups with C-H=1.08Å and C-C=1.38Å. The positional parameters of the methyl carbons C(2) and C(3) were refined as were the first phenyl carbon atoms C(11) and C(21)

Table4 Atomic thermal parameters (x10**4) of refined atoms for N-(-1methylbenzyl)phenylphosphinyl-O-methanesulphonyl hydroxylamine

Atom	U or U11	U22	U33	U23	U13	U12
P	322(4)	286(4)	332(4)	-12(3)	114(3)	-21(3)
S	367(4)	494(5)	589(6)	29(4)	205(4)	7(3)
O(1)	470(12)	279(10)	507(13)	-28(9)	183(10)	-43(8)
O(2)	376(11)	480(12)	403(12)	38(9)	175(10)	14(9)
O(3)	491(15)	675(16)	807(18)	277(14)	157(13)	127(11)
O(4)	623(16)	817(19)	969(21)	30(15)	554(16)	-6(13)
N	356(13)	329(13)	412(14)	33(10)	177(11)	-2(10)
Hn(1)	450(86)					
C(1)	378(17)	457(18)	402(18)	-23(14)	162(14)	-62(13)
H(1)	453(85)					
C(2)	365(19)	1205(36)	550(23)	74(22)	205(17)	-1(19)
C(3)	544(22)	721(24)	770(26)	-272(21)	253(20)	-189(18)
C(11)	390(16)	493(17)	398(16)	-36(13)	222(14)	-65(12)
C(12)	554(21)	693(24)	408(19)	53(16)	199(16)	57(16)
C(13)	574(24)	1165(37)	452(22)	145(22)	186(19)	-58(22)
C(14)	808(31)	1251(40)	463(22)	-216(25)	331(22)	-424(27)
C(15)	866(30)	884(30)	669(27)	-307(23)	480(24)	-272(24)
C(16)	593(21)	631(23)	582(22)	-117(17)	356(18)	-80(17)
C(21)	297(14)	418(16)	368(16)	5(12)	122(12)	25(11)
C(22)	406(17)	572(20)	489(19)	151(15)	180(15)	55(14)
C(23)	422(20)	1071(32)	482(21)	282(21)	150(17)	133(19)
C(24)	467(22)	1369(42)	398(21)	-95(24)	82(17)	163(24)
C(25)	529(24)	1034(32)	636(26)	-409(24)	-18(20)	137(21)
C(26)	517(21)	588(21)	486(20)	-157(17)	9(17)	102(16)

The methyl and phenyl hydrogen atoms were refined with common group isotropic thermal parameters

Table 5 Bond lengths (Å)
for N-(-1methylbenzyl)phenylphosphinyl-O-methanesulphonyl hydroxylamine

O(1)-P	1.484(2)	N-P	1.690(2)
C(1)-P	1.824(3)	C(21)-P	1.786(2)
O(2)-S	1.614(2)	O(3)-S	1.414(2)
O(4)-S	1.422(3)	C(3)-S	1.747(4)
N-O(2)	1.459(3)	Hn(1)-N	0.91(3)
H(1)-C(1)	0.93(3)	C(2)-C(1)	1.538(4)
C(11)-C(1)	1.521(3)	H(2)A-C(2)	1.080(0)
H(2)B-C(2)	1.080(0)	H(2)C-C(2)	1.080(0)
H(3)A-C(3)	1.080(0)	H(3)B-C(3)	1.080(0)
H(3)C-C(3)	1.080(0)	C(12)-C(11)	1.400(0)
C(16)-C(11)	1.402(0)	C(13)-C(12)	1.398(0)
H(12)-C(12)	1.085(0)	C(14)-C(13)	1.402(0)
H(13)-C(13)	1.084(0)	C(15)-C(14)	1.400(0)
H(14)-C(14)	1.083(0)	C(16)-C(15)	1.398(0)
H(15)-C(15)	1.085(0)	H(16)-C(16)	1.084(0)
C(22)-C(21)	1.401(0)	C(26)-C(21)	1.403(0)
C(23)-C(22)	1.398(0)	H(22)-C(22)	1.086(0)
C(24)-C(23)	1.403(0)	H(23)-C(23)	1.085(0)
C(25)-C(24)	1.401(0)	H(24)-C(24)	1.082(0)
C(26)-C(25)	1.398(0)	H(25)-C(25)	1.086(0)
H(26)-C(26)	1.085(0)		

Table 6 Bond Angles (°)
for N-(-1methylbenzyl)phenylphosphinyl-O-methanesulphonyl hydroxylamine

N-P-O(1)	111.9(1)	C(1)-P-O(1)	115.0(1)
C(1)-P-N	98.6(1)	C(21)-P-O(1)	111.4(1)
C(21)-P-N	109.4(1)	C(21)-P-C(1)	109.8(1)
O(3)-S-O(2)	109.3(1)	O(4)-S-O(2)	102.6(1)
O(4)-S-O(3)	119.6(2)	C(3)-S-O(2)	103.3(1)
C(3)-S-O(3)	110.2(2)	C(3)-S-O(4)	110.5(2)
N-O(2)-S	109.7(2)	O(2)-N-P	111.3(2)
Hn(1)-N-P	114.7(19)	Hn(1)-N-O(2)	107.9(19)
H(1)-C(1)-P	106.5(19)	C(2)-C(1)-P	109.9(2)
C(2)-C(1)-H(1)	108.5(18)	C(11)-C(1)-P	109.8(2)
C(11)-C(1)-H(1)	107.2(17)	C(11)-C(1)-C(2)	114.6(3)
H(2)A-C(2)-C(1)	109.5(2)	H(2)B-C(2)-C(1)	109.5(2)
H(2)B-C(2)-H(2)A	109.5(0)	H(2)C-C(2)-C(1)	109.5(2)
H(2)C-C(2)-H(2)A	109.5(0)	H(2)C-C(2)-H(2)B	109.5(0)
H(3)A-C(3)-S	109.5(1)	H(3)B-C(3)-S	109.5(1)
H(3)B-C(3)-H(3)A	109.5(0)	H(3)C-C(3)-S	109.5(1)
H(3)C-C(3)-H(3)A	109.5(0)	H(3)C-C(3)-H(3)B	109.5(0)
C(12)-C(11)-C(1)	118.7(1)	C(16)-C(11)-C(1)	121.2(1)
C(16)-C(11)-C(12)	120.1(0)	C(13)-C(12)-C(11)	119.9(0)
H(12)-C(12)-C(11)	120.1(0)	H(12)-C(12)-C(13)	120.0(0)
C(14)-C(13)-C(12)	120.0(0)	H(13)-C(13)-C(12)	119.9(0)
H(13)-C(13)-C(14)	120.1(0)	C(15)-C(14)-C(13)	120.1(0)
H(14)-C(14)-C(13)	120.0(0)	H(14)-C(14)-C(15)	119.9(0)
C(16)-C(15)-C(14)	119.9(0)	H(15)-C(15)-C(14)	120.1(0)
H(15)-C(15)-C(16)	120.0(0)	C(15)-C(16)-C(11)	120.0(0)
H(16)-C(16)-C(11)	120.1(0)	H(16)-C(16)-C(15)	119.9(0)
C(22)-C(21)-P	118.8(1)	C(26)-C(21)-P	120.9(1)
C(26)-C(21)-C(22)	120.2(0)	C(23)-C(22)-C(21)	119.9(0)
H(22)-C(22)-C(21)	120.2(0)	H(22)-C(22)-C(23)	120.0(0)
C(24)-C(23)-C(22)	120.0(0)	H(23)-C(23)-C(22)	119.9(0)
H(23)-C(23)-C(24)	120.2(0)	C(25)-C(24)-C(23)	120.2(0)
H(24)-C(24)-C(23)	120.0(0)	H(24)-C(24)-C(25)	119.9(0)
C(26)-C(25)-C(24)	119.9(0)	H(25)-C(25)-C(24)	120.2(0)
H(25)-C(25)-C(26)	120.0(0)	C(25)-C(26)-C(21)	120.0(0)
H(26)-C(26)-C(21)	120.2(0)	H(26)-C(26)-C(25)	119.9(0)

Table 7 Non-bonded Contacts
for N-(-1methylbenzyl)phenylphosphinyl-O-methanesulphonyl hydroxylamine

O(2)...P	2.602	Hn(1)...P	2.232
H(1)...P	2.270	C(2)...P	2.757
C(11)...P	2.742	C(22)...P	2.751
C(26)...P	2.781	N...S	2.514
H(3)A...S	2.340	H(3)B...S	2.340
H(3)C...S	2.340	N...O(1)	2.633
C(1)...O(1)	2.796	C(21)...O(1)	2.707
Hn(1)...O(1)	1.945	2, 1.0000, -1.0000,	1.0000
H(26)...O(1)	2.348	2, 1.0000, -1.0000,	1.0000
O(3)...O(2)	2.473	O(4)...O(2)	2.372
Hn(1)...O(2)	1.945	C(3)...O(2)	2.638
O(4)...O(3)	2.451	C(3)...O(3)	2.599
C(3)...O(4)	2.609	C(1)...N	2.665
C(21)...N	2.837	H(2)A...C(1)	2.153
H(2)B...C(1)	2.154	H(2)C...C(1)	2.153
C(12)...C(1)	2.513	C(16)...C(1)	2.547
C(2)...H(1)	2.035	C(11)...H(1)	2.003
C(11)...C(2)	2.573	H(2)B...H(2)A	1.763
H(2)C...H(2)A	1.763	H(2)C...H(2)B	1.764
H(24)...H(2)C	2.006	2, 0.5000, -0.5000,	0.5000
H(3)B...H(3)A	1.764	H(3)C...H(3)A	1.764
H(3)C...H(3)B	1.764	C(13)...C(11)	2.422
C(14)...C(11)	2.796	C(15)...C(11)	2.425
H(12)...C(11)	2.159	H(16)...C(11)	2.159
C(14)...C(12)	2.425	C(15)...C(12)	2.803
C(16)...C(12)	2.427	H(13)...C(12)	2.154
C(15)...C(13)	2.428	C(16)...C(13)	2.800
H(12)...C(13)	2.156	H(14)...C(13)	2.157
C(16)...C(14)	2.422	H(13)...C(14)	2.159
H(15)...C(14)	2.159	H(14)...C(15)	2.155
H(16)...C(15)	2.154	H(15)...C(16)	2.156
H(22)...H(12)	1.995	2, 1.0000, 0.0000,	1.0000
C(23)...C(21)	2.423	C(24)...C(21)	2.797
C(25)...C(21)	2.425	H(22)...C(21)	2.162
H(26)...C(21)	2.162	C(24)...C(22)	2.425
C(25)...C(22)	2.805	C(26)...C(22)	2.430
H(23)...C(22)	2.155	C(25)...C(23)	2.430
C(26)...C(23)	2.803	H(22)...C(23)	2.157
H(24)...C(23)	2.158	C(26)...C(24)	2.423
H(23)...C(24)	2.162	H(25)...C(24)	2.162
H(24)...C(25)	2.155	H(26)...C(25)	2.155
H(25)...C(26)	2.157		

Table 8 Fractional atomic co-ordinates for N-(-1methylbenzyl)phenylphosphinyl-O-methanesulphonyl hydroxylamine

Atom	x	y	z
P	0.47635(4)	0.15954(6)	0.73491(4)
S	0.67941(4)	0.07945(8)	0.78421(6)
O(1)	0.50247(11)	0.29506(17)	0.74884(12)
O(2)	0.59073(11)	0.07410(19)	0.71916(13)
O(3)	0.69958(14)	-0.02973(23)	0.83768(17)
O(4)	0.71171(14)	0.09781(26)	0.72902(18)
N	0.54857(13)	0.05472(23)	0.76624(15)
Hn(1)	0.5350(17)	-0.030(3)	0.7615(18)
C(1)	0.43681(16)	0.1035(3)	0.80272(19)
H(1)	0.4349(16)	0.014(3)	0.7987(18)
C(2)	0.35640(18)	0.1549(5)	0.76958(23)
H(2)A	0.35769(18)	0.2586(5)	0.77388(23)
H(2)B	0.33200(18)	0.1159(5)	0.80735(23)
H(2)C	0.32304(18)	0.1264(5)	0.70423(23)
C(3)	0.68849(21)	0.2188(4)	0.84302(25)
H(3)A	0.67295(21)	0.3014(4)	0.80156(25)
H(3)B	0.74598(21)	0.2287(4)	0.89161(25)
H(3)C	0.65213(21)	0.2124(4)	0.87226(25)
C(11)	0.48958(10)	0.13712(19)	0.89468(10)
C(12)	0.54773(10)	0.05172(19)	0.94286(10)
C(13)	0.59605(10)	0.07879(19)	1.02810(10)
C(14)	0.58619(10)	0.19126(19)	1.06516(10)
C(15)	0.52802(10)	0.27667(19)	1.01699(10)
C(16)	0.47971(10)	0.24958(19)	0.93175(10)
H(12)	0.55537(10)	-0.03535(19)	0.91417(10)
H(13)	0.64108(10)	0.01269(19)	1.06541(10)
H(14)	0.62360(10)	0.21224(19)	1.13117(10)
H(15)	0.52041(10)	0.36374(19)	1.04567(10)
H(16)	0.43470(10)	0.31569(19)	0.89443(10)
C(21)	0.41144(11)	0.13053(17)	0.62621(10)
C(22)	0.37348(11)	0.23527(17)	0.57444(10)
C(23)	0.32597(11)	0.21618(17)	0.48796(10)
C(24)	0.31641(11)	0.09231(17)	0.45323(10)
C(25)	0.35437(11)	-0.01245(17)	0.50497(10)
C(26)	0.40188(11)	0.00666(17)	0.59146(10)
H(22)	0.38087(11)	0.33118(17)	0.60135(10)
H(23)	0.29659(11)	0.29728(17)	0.44790(10)
H(24)	0.27963(11)	0.07752(17)	0.38628(10)
H(25)	0.34696(11)	-0.10836(17)	0.47808(10)
H(26)	0.43129(11)	-0.07445(17)	0.63150(10)

Table 9 Atomic thermal parameters (x10**4)
for N-(-1methylbenzyl)phenylphosphinyl-O-methanesulphonyl hydroxylamine

Atom	U or U11	U22	U33	U23	U13	U12
P	322(4)	286(4)	332(4)	-12(3)	114(3)	-21(3)
S	367(4)	494(5)	589(6)	29(4)	205(4)	7(3)
O(1)	470(12)	279(10)	507(13)	-28(9)	183(10)	-43(8)
O(2)	376(11)	480(12)	403(12)	38(9)	175(10)	14(9)
O(3)	491(15)	675(16)	807(18)	277(14)	157(13)	127(11)
O(4)	623(16)	817(19)	969(21)	30(15)	554(16)	-6(13)
N	356(13)	329(13)	412(14)	33(10)	177(11)	-2(10)
Hn(1)	450(86)					
C(1)	378(17)	457(18)	402(18)	-23(14)	162(14)	-62(13)
H(1)	453(85)					
C(2)	365(19)	1205(36)	550(23)	74(22)	205(17)	-1(19)
H(2)A	1149(91)					
H(2)B	1149(91)					
H(2)C	1149(91)					
C(3)	544(22)	721(24)	770(26)	-272(21)	253(20)	-189(18)
H(3)A	1173(93)					
H(3)B	1173(93)					
H(3)C	1173(93)					
C(11)	390(16)	493(17)	398(16)	-36(13)	222(14)	-65(12)
C(12)	554(21)	693(24)	408(19)	53(16)	199(16)	57(16)
C(13)	574(24)	1165(37)	452(22)	145(22)	186(19)	-58(22)
C(14)	808(31)	1251(40)	463(22)	-216(25)	331(22)	-424(27)
C(15)	866(30)	884(30)	669(27)	-307(23)	480(24)	-272(24)
C(16)	593(21)	631(23)	582(22)	-117(17)	356(18)	-80(17)
H(12)	1045(65)					
H(13)	1045(65)					
H(14)	1045(65)					
H(15)	1045(65)					
H(16)	1045(65)					
C(21)	297(14)	418(16)	368(16)	5(12)	122(12)	25(11)
C(22)	406(17)	572(20)	489(19)	151(15)	180(15)	55(14)
C(23)	422(20)	1071(32)	482(21)	282(21)	150(17)	133(19)
C(24)	467(22)	1369(42)	398(21)	-95(24)	82(17)	163(24)
C(25)	529(24)	1034(32)	636(26)	-409(24)	-18(20)	137(21)
C(26)	517(21)	588(21)	486(20)	-157(17)	9(17)	102(16)
H(22)	1030(64)					
H(23)	1030(64)					
H(24)	1030(64)					
H(25)	1030(64)					
H(26)	1030(64)					

FIG. 12

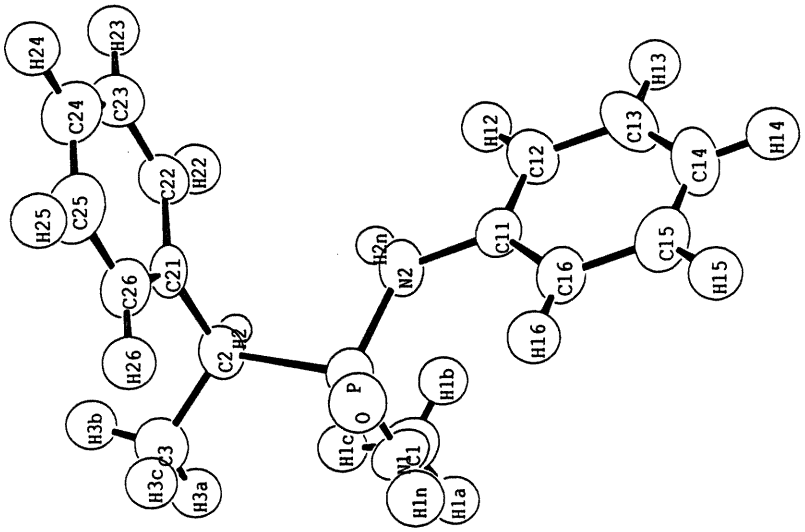

H24
C24
H23
C23
C22
H22
H25
C25
C26
C21
H26
C2
H2
H3b
C3
H3c
H3a
O
P
H1c
H1b
N1
H1n
H1a
H2n
N2
C11
C12
H12
C13
H13
C14
H14
C15
H15
C16
H16

Table1 Fractional atomic co-ordinates of refined atoms for N-methyl-N-(1-methylbenzyl)-P-Phenylphosphondiamide ($C_{15}H_{19}N_2OP$)

Atom	x	y	z
P	0.18279(13)	0.70910(11)	0.93152(12)
O	0.0427(3)	0.72247(28)	0.9371(3)
N(1)	0.2235(6)	0.5940(5)	0.9724(5)
H(1)n	0.183(6)	0.555(5)	0.981(6)
N(2)	0.2785(4)	0.7880(4)	1.0189(4)
H(2)n	0.343(5)	0.798(4)	0.992(4)
C(1)	0.3566(6)	0.5545(5)	0.9840(6)
C(2)	0.2334(6)	0.7347(4)	0.7782(5)
H(2)	0.322(4)	0.730(3)	0.796(4)
C(3)	0.1796(7)	0.6546(5)	0.6815(5)
C(11)	0.2791(3)	0.81185(25)	1.14715(23)
C(12)	0.3880(3)	0.85825(25)	1.21080(23)
C(13)	0.3925(3)	0.88063(25)	1.33804(23)
C(14)	0.2881(3)	0.85659(25)	1.40162(23)
C(15)	0.1791(3)	0.81019(25)	1.33797(23)
C(16)	0.1746(3)	0.78782(25)	1.21072(23)
C(21)	0.2001(4)	0.84316(23)	0.7373(3)
C(22)	0.2967(4)	0.91673(23)	0.7492(3)
C(23)	0.2672(4)	1.01656(23)	0.7141(3)
C(24)	0.1411(4)	1.04283(23)	0.6671(3)
C(25)	0.0445(4)	0.96927(23)	0.6552(3)
C(26)	0.0740(4)	0.86944(23)	0.6902(3)

Table 2 Atomic thermal parameters (x10**4) of refined atoms for N-methyl-N-(1-methylbenzyl)-P-Phenylphosphondiamide ($C_{15}H_{19}N_2OP$)

Atom	U or U11	U22	U33	U23	U13	U12
P	321(8)	506(9)	408(8)	21(8)	92(6)	12(8)
O	335(21)	709(27)	567(23)	-3(20)	141(17)	38(19)
N(1)	510(35)	494(37)	690(38)	123(28)	154(26)	-21(29)
H(1)n	641(252)					
N(2)	338(28)	692(34)	373(25)	-1(25)	144(21)	-3(27)
H(2)n	287(147)					
C(1)	526(40)	604(41)	793(44)	98(35)	140(33)	141(33)
C(2)	362(36)	626(42)	375(30)	-20(27)	106(25)	-4(29)
H(2)	205(119)					
C(3)	889(50)	649(42)	514(39)	-79(33)	191(35)	-36(37)
C(11)	459(34)	398(34)	427(30)	31(25)	129(25)	68(26)
C(12)	477(36)	602(39)	517(36)	-82(30)	91(28)	51(30)
C(13)	743(47)	767(46)	542(39)	-203(33)	-27(34)	34(36)
C(14)	910(55)	801(48)	422(35)	-31(35)	152(36)	155(42)
C(15)	733(47)	677(47)	603(40)	62(34)	291(35)	105(36)
C(16)	523(35)	608(37)	456(31)	16(31)	170(26)	-2(32)
C(21)	483(35)	554(37)	249(27)	20(26)	156(24)	-6(30)
C(22)	452(34)	556(39)	461(32)	-60(30)	63(25)	-64(31)
C(23)	708(48)	604(45)	556(39)	-49(31)	107(33)	-149(34)
C(24)	774(50)	605(43)	678(43)	94(35)	89(36)	88(40)
C(25)	538(41)	804(49)	658(41)	173(37)	29(32)	122(38)
C(26)	488(39)	692(45)	466(35)	82(31)	90(28)	-56(31)

Table3 Selected Bond lengths (Å)
for N-methyl-N-(1-methylbenzyl)-P-Phenylphosphondiamide
($C_{15}H_{19}N_2OP$)

O-P	1.483(3)	N(1)-P	1.624(6)
N(2)-P	1.653(5)	C(2)-P	1.825(5)
H(1)n-N(1)	0.67(6)	C(1)-N(1)	1.477(8)
H(2)n-N(2)	0.78(5)	C(11)-N(2)	1.414(5)
H(2)-C(2)	0.93(4)		
C(3)-C(2)	1.540(7)	C(21)-C(2)	1.525(6)
C(12)-C(11)	1.395(0)		

Phenyl and methyl groups refined as rigid groups
(C-C=1.395Å and C-H =1.08Å)

Table4 Selected Bond Angles (°)
for N-methyl-N-(1-methylbenzyl)-P-Phenylphosphondiamide
($C_{15}H_{19}N_2OP$)

N(1)-P-O	109.1(3)	N(2)-P-O	115.6(2)
N(2)-P-N(1)	108.4(3)	C(2)-P-O	114.4(2)
C(2)-P-N(1)	108.8(3)	C(2)-P-N(2)	100.0(2)
H(1)n-N(1)-P	127(6)	C(1)-N(1)-P	124.4(5)
C(1)-N(1)-H(1)n	108(6)	H(2)n-N(2)-P	113(4)
C(11)-N(2)-P	128.6(4)	C(11)-N(2)-H(2)n	115(4)
H(1)a-C(1)-N(1)	108.7(3)	H(1)b-C(1)-N(1)	103.7(3)
H(1)b-C(1)-H(1)a	109.5(0)	H(1)c-C(1)-N(1)	115.8(3)
H(1)c-C(1)-H(1)a	109.5(0)	H(1)c-C(1)-H(1)b	109.5(0)
H(2)-C(2)-P	101.0(25)	C(3)-C(2)-P	111.1(4)
C(3)-C(2)-H(2)	111.3(25)	C(21)-C(2)-P	110.7(3)
C(21)-C(2)-H(2)	108.4(26)	C(21)-C(2)-C(3)	113.5(4)
H(3)a-C(3)-C(2)	110.2(3)	H(3)b-C(3)-C(2)	104.4(3)
H(3)b-C(3)-H(3)a	109.5(0)	H(3)c-C(3)-C(2)	113.7(3)
H(3)c-C(3)-H(3)a	109.5(0)	H(3)c-C(3)-H(3)b	109.5(0)
C(12)-C(11)-N(2)	118.7(2)	C(16)-C(11)-N(2)	121.2(2)
C(22)-C(21)-C(2)	119.4(3)	C(26)-C(21)-C(2)	120.6(3)

Table5 Fractional atomic co-ordinates
for N-methyl-N-(1-methylbenzyl)-P-Phenylphosphondiamide ($C_{15}H_{19}N_2OP$)

Atom	x	y	z
P	0.18279(13)	0.70910(11)	0.93152(12)
O	0.0427(3)	0.72247(28)	0.9371(3)
N(1)	0.2235(6)	0.5940(5)	0.9724(5)
H(1)n	0.183(6)	0.555(5)	0.981(6)
N(2)	0.2785(4)	0.7880(4)	1.0189(4)
H(2)n	0.343(5)	0.798(4)	0.992(4)
C(1)	0.3566(6)	0.5545(5)	0.9840(6)
H(1)a	0.3590(6)	0.4816(5)	1.0300(6)
H(1)b	0.4111(6)	0.6086(5)	1.0446(6)
H(1)c	0.3986(6)	0.5479(5)	0.8976(6)
C(2)	0.2334(6)	0.7347(4)	0.7782(5)
H(2)	0.322(4)	0.730(3)	0.796(4)
C(3)	0.1796(7)	0.6546(5)	0.6815(5)
H(3)a	0.2185(7)	0.5809(5)	0.7083(5)
H(3)b	0.2141(7)	0.6782(5)	0.5955(5)
H(3)c	0.0756(7)	0.6508(5)	0.6677(5)
C(11)	0.2791(3)	0.81185(25)	1.14715(23)
C(12)	0.3880(3)	0.85825(25)	1.21080(23)
C(13)	0.3925(3)	0.88063(25)	1.33804(23)
C(14)	0.2881(3)	0.85659(25)	1.40162(23)
C(15)	0.1791(3)	0.81019(25)	1.33797(23)
C(16)	0.1746(3)	0.78782(25)	1.21072(23)
H(12)	0.4689(3)	0.87686(25)	1.16158(23)
H(13)	0.4769(3)	0.91656(25)	1.38733(23)
H(14)	0.2916(3)	0.87391(25)	1.50012(23)
H(15)	0.0983(3)	0.79158(25)	1.38718(23)
H(16)	0.0903(3)	0.75189(25)	1.16144(23)
C(21)	0.2001(4)	0.84316(23)	0.7373(3)
C(22)	0.2967(4)	0.91673(23)	0.7492(3)
C(23)	0.2672(4)	1.01656(23)	0.7141(3)
C(24)	0.1411(4)	1.04283(23)	0.6671(3)
C(25)	0.0445(4)	0.96927(23)	0.6552(3)
C(26)	0.0740(4)	0.86944(23)	0.6902(3)
H(22)	0.3943(4)	0.89639(23)	0.7856(3)
H(23)	0.3419(4)	1.07350(23)	0.7234(3)
H(24)	0.1182(4)	1.12012(23)	0.6399(3)
H(25)	-0.0531(4)	0.98960(23)	0.6188(3)
H(26)	-0.0007(4)	0.81248(23)	0.6810(3)

Table6 Atomic thermal parameters (x10**4)
for N-methyl-N-(1-methylbenzyl)-P-Phenylphosphondiamide ($C_{15}H_{19}N_2OP$)

Atom	U or U11	U22	U33	U23	U13	U12
P	321(8)	506(9)	408(8)	21(8)	92(6)	12(8)
O	335(21)	709(27)	567(23)	-3(20)	141(17)	38(19)
N(1)	510(35)	494(37)	690(38)	123(28)	154(26)	-21(29)
H(1)n	641(252)					
N(2)	338(28)	692(34)	373(25)	-1(25)	144(21)	-3(27)
H(2)n	287(147)					
C(1)	526(40)	604(41)	793(44)	98(35)	140(33)	141(33)
H(1)a	500(0)					
H(1)b	500(0)					
H(1)c	500(0)					
C(2)	362(36)	626(42)	375(30)	-20(27)	106(25)	-4(29)
H(2)	205(119)					
C(3)	889(50)	649(42)	514(39)	-79(33)	191(35)	-36(37)
H(3)a	500(0)					
H(3)b	500(0)					
H(3)c	500(0)					
C(11)	459(34)	398(34)	427(30)	31(25)	129(25)	68(26)
C(12)	477(36)	602(39)	517(36)	-82(30)	91(28)	51(30)
C(13)	743(47)	767(46)	542(39)	-203(33)	-27(34)	34(36)
C(14)	910(55)	801(48)	422(35)	-31(35)	152(36)	155(42)
C(15)	733(47)	677(47)	603(40)	62(34)	291(35)	105(36)
C(16)	523(35)	608(37)	456(31)	16(31)	170(26)	-2(32)
H(12)	500(0)					
H(13)	500(0)					
H(14)	500(0)					
H(15)	500(0)					
H(16)	500(0)					
C(21)	483(35)	554(37)	249(27)	20(26)	156(24)	-6(30)
C(22)	452(34)	556(39)	461(32)	-60(30)	63(25)	-64(31)
C(23)	708(48)	604(45)	556(39)	-49(31)	107(33)	-149(34)
C(24)	774(50)	605(43)	678(43)	94(35)	89(36)	88(40)
C(25)	538(41)	804(49)	658(41)	173(37)	29(32)	122(38)
C(26)	488(39)	692(45)	466(35)	82(31)	90(28)	-56(31)
H(22)	500(0)					
H(23)	500(0)					
H(24)	500(0)					
H(25)	500(0)					
H(26)	500(0)					

Table7 Bond lengths (Å)
for N-methyl-N-(1-methylbenzyl)-P-Phenylphosphondiamide
($C_{15}H_{19}N_2OP$)

O-P	1.483(3)	N(1)-P	1.624(6)
N(2)-P	1.653(5)	C(2)-P	1.825(5)
H(1)n-N(1)	0.67(6)	C(1)-N(1)	1.477(8)
H(2)n-N(2)	0.78(5)	C(11)-N(2)	1.414(5)
H(1)a-C(1)	1.080(0)	H(1)b-C(1)	1.080(0)
H(1)c-C(1)	1.080(0)	H(2)-C(2)	0.93(4)
C(3)-C(2)	1.540(7)	C(21)-C(2)	1.525(6)
H(3)a-C(3)	1.080(0)	H(3)b-C(3)	1.080(0)
H(3)c-C(3)	1.080(0)	C(12)-C(11)	1.395(0)
C(16)-C(11)	1.395(0)	C(13)-C(12)	1.395(0)
H(12)-C(12)	1.080(0)	C(14)-C(13)	1.395(0)
H(13)-C(13)	1.080(0)	C(15)-C(14)	1.395(0)
H(14)-C(14)	1.080(0)	C(16)-C(15)	1.395(0)
H(15)-C(15)	1.080(0)	H(16)-C(16)	1.080(0)
C(22)-C(21)	1.395(0)	C(26)-C(21)	1.395(0)
C(23)-C(22)	1.395(0)	H(22)-C(22)	1.080(0)
C(24)-C(23)	1.395(0)	H(23)-C(23)	1.080(0)
C(25)-C(24)	1.395(0)	H(24)-C(24)	1.080(0)
C(26)-C(25)	1.395(0)	H(25)-C(25)	1.080(0)
H(26)-C(26)	1.080(0)		

Table8 Bond Angles (°)
for N-methyl-N-(1-methylbenzyl)-P-Phenylphosphondiamide
($C_{15}H_{19}N_2OP$)

N(1)-P-O	109.1(3)	N(2)-P-O	115.6(2)
N(2)-P-N(1)	108.4(3)	C(2)-P-O	114.4(2)
C(2)-P-N(1)	108.8(3)	C(2)-P-N(2)	100.0(2)
H(1)n-N(1)-P	127(6)	C(1)-N(1)-P	124.4(5)
C(1)-N(1)-H(1)n	108(6)	H(2)n-N(2)-P	113(4)
C(11)-N(2)-P	128.6(4)	C(11)-N(2)-H(2)n	115(4)
H(1)a-C(1)-N(1)	108.7(3)	H(1)b-C(1)-N(1)	103.7(3)
H(1)b-C(1)-H(1)a	109.5(0)	H(1)c-C(1)-N(1)	115.8(3)
H(1)c-C(1)-H(1)a	109.5(0)	H(1)c-C(1)-H(1)b	109.5(0)
H(2)-C(2)-P	101.0(25)	C(3)-C(2)-P	111.1(4)
C(3)-C(2)-H(2)	111.3(25)	C(21)-C(2)-P	110.7(3)
C(21)-C(2)-H(2)	108.4(26)	C(21)-C(2)-C(3)	113.5(4)
H(3)a-C(3)-C(2)	110.2(3)	H(3)b-C(3)-C(2)	104.4(3)
H(3)b-C(3)-H(3)a	109.5(0)	H(3)c-C(3)-C(2)	113.7(3)
H(3)c-C(3)-H(3)a	109.5(0)	H(3)c-C(3)-H(3)b	109.5(0)
C(12)-C(11)-N(2)	118.7(2)	C(16)-C(11)-N(2)	121.2(2)
C(16)-C(11)-C(12)	120.0(0)	C(13)-C(12)-C(11)	120.0(0)
H(12)-C(12)-C(11)	120.0(0)	H(12)-C(12)-C(13)	120.0(0)
C(14)-C(13)-C(12)	120.0(0)	H(13)-C(13)-C(12)	120.0(0)
H(13)-C(13)-C(14)	120.0(0)	C(15)-C(14)-C(13)	120.0(0)
H(14)-C(14)-C(13)	120.0(0)	H(14)-C(14)-C(15)	120.0(0)
C(16)-C(15)-C(14)	120.0(0)	H(15)-C(15)-C(14)	120.0(0)
H(15)-C(15)-C(16)	120.0(0)	C(15)-C(16)-C(11)	120.0(0)
H(16)-C(16)-C(11)	120.0(0)	H(16)-C(16)-C(15)	120.0(0)
C(22)-C(21)-C(2)	119.4(3)	C(26)-C(21)-C(2)	120.6(3)
C(26)-C(21)-C(22)	120.0(0)	C(23)-C(22)-C(21)	120.0(0)
H(22)-C(22)-C(21)	120.0(0)	H(22)-C(22)-C(23)	120.0(0)
C(24)-C(23)-C(22)	120.0(0)	H(23)-C(23)-C(22)	120.0(0)
H(23)-C(23)-C(24)	120.0(0)	C(25)-C(24)-C(23)	120.0(0)
H(24)-C(24)-C(23)	120.0(0)	H(24)-C(24)-C(25)	120.0(0)
C(26)-C(25)-C(24)	120.0(0)	H(25)-C(25)-C(24)	120.0(0)
H(25)-C(25)-C(26)	120.0(0)	C(25)-C(26)-C(21)	120.0(0)
H(26)-C(26)-C(21)	120.0(0)	H(26)-C(26)-C(25)	120.0(0)

Table9 Non-bonded Contacts (Å)
for N-methyl-N-(1-methylbenzyl)-P-Phenylphosphondiamide

($C_{15}H_{19}N_2OP$)

H(1)n...P	2.099	H(2)n...P	2.080
C(1)...P	2.744	H(2)...P	2.200
C(3)...P	2.779	C(11)...P	2.766
C(16)...P	3.189	C(21)...P	2.761
N(1)...O	2.532	N(2)...O	2.655
H(2)n...O	2.256	-2, 1.0000, 2.0000, 0.0000	
C(2)...O	2.787	N(2)...N(1)	2.658
H(1)a...N(1)	2.090	H(1)b...N(1)	2.026
H(1)c...N(1)	2.176	C(2)...N(1)	2.807
C(1)...H(1)n	1.806	C(2)...N(2)	2.666
C(12)...N(2)	2.417	C(16)...N(2)	2.448
C(11)...H(2)n	1.881	C(12)...H(2)n	2.473
H(1)b...H(1)a	1.764	H(1)c...H(1)a	1.764
H(1)c...H(1)b	1.764	H(3)a...C(2)	2.165
H(3)b...C(2)	2.089	H(3)c...C(2)	2.207
C(22)...C(2)	2.522	C(26)...C(2)	2.537
C(3)...H(2)	2.067	C(21)...H(2)	2.021
C(21)...C(3)	2.563	H(3)b...H(3)a	1.764
H(3)c...H(3)a	1.764	H(3)c...H(3)b	1.764
C(13)...C(11)	2.416	C(14)...C(11)	2.790
C(15)...C(11)	2.416	H(12)...C(11)	2.149
H(16)...C(11)	2.149	C(14)...C(12)	2.416
C(15)...C(12)	2.790	C(16)...C(12)	2.416
H(13)...C(12)	2.149	C(15)...C(13)	2.416
C(16)...C(13)	2.790	H(12)...C(13)	2.149
H(14)...C(13)	2.149	C(16)...C(14)	2.416
H(13)...C(14)	2.149	H(15)...C(14)	2.149
H(14)...C(15)	2.149	H(16)...C(15)	2.149
H(15)...C(16)	2.149	C(23)...C(21)	2.416
C(24)...C(21)	2.790	C(25)...C(21)	2.416
H(22)...C(21)	2.149	H(26)...C(21)	2.149
C(24)...C(22)	2.416	C(25)...C(22)	2.790
C(26)...C(22)	2.416	H(23)...C(22)	2.149
C(25)...C(23)	2.416	C(26)...C(23)	2.790
H(22)...C(23)	2.149	H(24)...C(23)	2.149
C(26)...C(24)	2.416	H(23)...C(24)	2.149
H(25)...C(24)	2.149	H(24)...C(25)	2.149
H(26)...C(25)	2.149	H(25)...C(26)	2.149

Appendix 2

X-Ray experimental data for menthyl *P*-(bromomethyl)-*N*-*tert*-butylphosphonamidate (112): The crystals were colourless needles. The crystal used for data collection had the dimensions 0.83 x 0.16 x 0.16 mm. The crystal was glued to glass filament. Accurate unit cell parameters were determined using the optimised setting angles of 338 zero and upper layer reflexions. The intensities of 1732 unique reflexions were collected at 293 K on a Stöe STADI-2 Weissenberg diffractometer with graphite monochromated Mo-K_α radiation (λ = 0.7107 Å) using an omega scan technique (range $7 \leq 2\theta \leq 50^\circ$; $-10 \leq h \leq 10$, $0 \leq k \leq 11$, $0 \leq l \leq 36$; scan width [1.4 + 0.7sin(mu)/tan(ups)]°}; check reflexions monitored every 50 reflexions indicated no crystal decay. The data were corrected for Lorentz and polarisation effects to yield 687 reflexions with $I > 3\sigma(I)$. An absorption correction was applied to the data, maximum and minimum transmission factors 0.757 and 0.250 respectively.

Crystal data for the α-bromomethylphosphonamidate (112) (Fig. 13): $C_{15}H_{31}BrNO_2P$, M = 368.3. Hexagonal, space group $P6_1$, a = 10.581(2), c = 30.345(25) Å, U = 2942(3) Å^3, Z = 6, μ(Mo-K_α) = 2.18 mm^{-1}, F(000) = 1164, D_c = 1.248 g cm^{-3}.

The structure was partially solved by direct methods using the TREF option of SHELXS86;[95] the positions of the bromine, phosphorus, and a carbon atom was found. Including these atoms in cycles of least squares gave an R factor of 0.28 and located the positions of remaining atoms on a difference Fourier map. All refinement used the programme SHELX76.[96] The

hydrogen atom on the nitrogen atom was not located or included in the refinement. Although some of the other hydrogen atoms were located on difference Fourier maps, all hydrogen atoms were included in the refinement cycles in calculated positions (C-H = 0.95 Å). The bromine and phosphorus atoms were refined as anisotropic; all other non--hydrogen atoms were refined with isotropic thermal parameters. The final R and R_w values are 0.085 and 0.065 respectively, [where $w = 1/\sigma^2F + 0.00013F^2$] for 90 variables, $(\Delta/\sigma)_{max.} = 0.001$. The final Fourier map was featureless and an analysis of the weighting scheme over $|F_o|$ and $(\sin\theta)/\lambda$ was satisfactory.

X-Ray experimental data for the picrate salt of menthyl methyl (*tert*-butylamino)methylphosphonate (116): The crystals were yellow needles. All crystal of the compound selected for X-ray examination were found by oscillation and Weissenberg photographs to be non-single. A relatively simple twin crystal (dimensions 0.88 x 0.32 x 0.18 mm) in which the c axes of the two components were aligned and the a^* and b^* axes of one crystal component were aligned with $-a^*$ and $-b^*$ of the other component was glued to a glass filament and used for data collection. The $hk0$ reflexions of the two components were coincident, but Weissenberg photographs of the higher l layers showed sufficient resolution of the two diffraction patterns to allow data to be collected from the major crystal component. The relative intensities of the two components were measured to be approximately 2 : 1 and the overlapping data were scaled accordingly. The setting angles of the upper layer reflexions from the two components were calculated and

compared in order to identify possible pairs of overlapping reflexions. However, examination of the data set collected from the major component indicated no consistent evidence of interference from the minor component in these regions and no action was taken.

Accurate unit cell parameters were determined from the optimised setting angles of 352 zero and upper layer reflexions. Data were collected at 293 K on a Stöe STADI-2 Weissenberg diffractometer with graphite monochromated Mo-K_α radiation (λ 0.7107 Å) using an omega scan technique (range $7 \leq 2\theta \leq 46^\circ$; $-23 \leq h \leq 23$, $-14 \leq k \leq 14$, $0 \leq l \leq 14$; scan width [1.8 + 0.7sin(mu)/tan(ups)]°). Check reflexions every 50 reflexions indicated no crystal decay. The intensities of 7415 unique reflexions were measured. The data were corrected for Lorentz and polarisation effects to yield 4703 reflexions with $I > 2\sigma(I)$. No absorption correction was applied to the data.

Crystal data for the picrate of (116) (Figs. 14 to 19): $C_{16}H_{35}NO_3P^+$ $C_6H_2N_3O_7^-$, M = 548.5. Triclinic, space group $P1$, a = 20.935(20), b = 13.210(13), c = 10.618(3) Å, α = 91.80(6), β = 95.2(1), γ = 94.5(1)°, U = 2913(4) Å^3, Z = 4, μ(Mo-K_α) = 0.15 mm^{-1}, $F(000)$ = 1168, D_c = 1.25 g cm^{-3}. The crystal was found to be triclinic and as the compound is optically active the non-centric space group $P1$ is unambiguous. From the unit cell volume a Z value of 4 was indicated and the structure solution therefore required the location of 144 non-hydrogen atoms. The structure was solved by direct methods using the TREF option of SHELXS86, and by difference Fourier methods using SHELX76. The direct methods tangent refinement

programme gave several possible solutions of approximately equal figure of merit. All of these possible solutions gave partially recognised fragments and were investigated by cycles of least squares refinement and difference Fourier maps. One of the possible solutions located further acceptable atom positions and was pursued as the correct solution. With 85 atoms included in refinement cycles an *R* factor of 0.28 was obtained and most of the remaining atoms located. No hydrogen atoms were included in the refinement and all atoms were refined with isotropic thermal parameters. The final *R* and R_w values are 0.132 and 0.142 respectively [$w = 1/\sigma^2F + 0.0168F^2$] for 543 variables, $(\Delta/\sigma)_{max.} = 0.53$. The final Fourier map was featureless (largest peaks +0.72, -0.82 eÅ^{-3}) and the weighting scheme over $|F_o|$ and $\sin\theta/\lambda$ was satisfactory. The *R* factor is high due to possible overlap of reflexions and lack of sufficient data to allow anisotropic thermal parameters and inclusion of hydrogen atoms; however, the essential details of the four unique formula units are unambiguous.

X-Ray experimental data for dicyclohexylammonium *O*-menthyl *O*-methyl phosphorothioate (**128**): The crystals were pale yellow hexagonal plates. The crystal used for data collection measured 0.41 x 0.34 x 0.14 mm and was glued to a glass filament. Accurate unit cell parameters were determined by least squares refinement of the optimised setting angles of 25 reflexions in the range $10^\circ \leq 2\theta \leq 25^\circ$. The intensities of 1478 unique reflexions were collected at 293 K on a Siemens P4 diffractometer with graphite monochromated Mo-K_α radiation (λ 0.7107 Å) using an omega scan technique (range

$4 \leq 2\theta \leq 42^{\circ}$; $0 \leq h \leq 16$, $0 \leq k \leq 9$, $-15 \leq l \leq 15$). Three standard check reflexions monitored every 100 reflexions indicated no crystal decay. The data were corrected for Lorentz and polarisation effects to yield 1274 data having $I > 2\sigma(I)$ regarded as observed. No absorption correction was applied to the data.

Crystal data for the phosphorothioate (128) (Fig. 20): $C_{11}H_{22}O_3PS^-$ $C_{12}H_{24}N^+ \cdot {}^1/_2C_4H_{10}O$, M = 484.7. Monoclinic, space group $C2$, a = 18.218(10), b = 9.892(6), c = 15.851(9) Å, β = 90.27(3)°, U = 2856(3) Å^3, Z = 4, μ(Mo-K$_\alpha$) = 0.20 mm^{-1}, F(000) = 1068, D_c = 1.127 g cm^{-3}.

The structure was solved by direct methods using the TREF option of SHELXTL,[97] and refined by full-matrix least squares using the programme SHELX76. Refinement of all non-hydrogen atoms with isotropic thermal parameters gave an R factor of 0.17. The hydrogen atoms bonded to nitrogen were located and refined as normal atoms. The hydrogen atoms of the solvent molecule were not located or included in refinement cycles. All other hydrogen atoms were included in calculated positions (C-H = 0.95 Å). With the exception of solvent atoms all non-hydrogen atoms were refined with anisotropic thermal parameters. The final R and R_w values are 0.0583 and 0.0629 respectively [where $w = 1/\sigma^2F + 0.0089F^2$] for 277 variables, $(\Delta/\sigma)_{max.}$ = 0.52. The final Fourier map was featureless (largest peaks +0.34, -0.26 eÅ^{-3}) and an analysis of the weighting scheme over $|F_o|$ and $(\sin\theta)/\lambda$ was satisfactory.

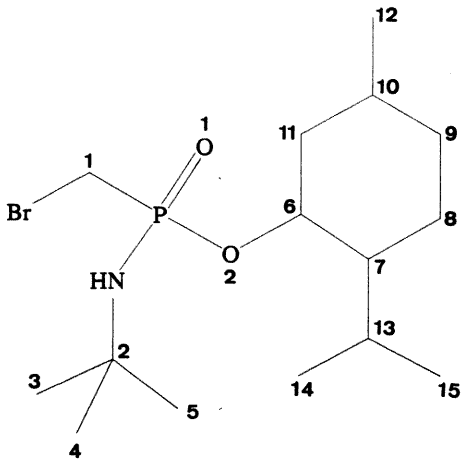


Fig. 13

$(S)_P$ (1*R*, 2*S*, 5*R*)-Menthyl *P*-(bromomethyl)-N-t-butylphosphonamidate

Table 1. Fractional atomic co-ordinates and thermal parameters

Atom	x	y	z	Ueq	
Ueq = 1/3 trace of the orthogonalised U					
Br	0.19828(29)	0.0318(3)	0.07900(0)	0.1074(19)	
N	-0.1987(18)	-0.0260(19)	0.1526(5)	0.062(5)	*
O(1)	-0.1386(14)	0.0145(14)	0.0698(5)	0.060(4)	*
O(2)	-0.1494(14)	-0.2031(14)	0.1106(3)	0.049(4)	*
P(1)	-0.1150(7)	-0.0403(6)	0.10995(22)	0.052(3)	
C(1)	0.0789(22)	0.0495(26)	0.1252(7)	0.075(8)	*
C(2)	-0.2619(26)	0.0697(28)	0.1572(8)	0.080(8)	*
C(3)	-0.143(3)	0.231(4)	0.1488(9)	0.158(13)	*
C(4)	-0.388(4)	0.051(4)	0.1315(11)	0.210(18)	*
C(5)	-0.302(4)	0.076(4)	0.2034(10)	0.194(17)	*
C(6)	-0.2777(19)	-0.3174(19)	0.0890(6)	0.038(5)	*
C(7)	-0.3369(21)	-0.4532(21)	0.1156(6)	0.049(6)	*
C(8)	-0.4519(21)	-0.5843(22)	0.0892(7)	0.067(7)	*
C(9)	-0.4192(26)	-0.5981(27)	0.0401(8)	0.091(8)	*
C(10)	-0.3699(27)	-0.4579(25)	0.0162(6)	0.066(7)	*
C(11)	-0.2361(22)	-0.3246(22)	0.0425(7)	0.057(6)	*
C(12)	-0.3171(28)	-0.466(3)	-0.0300(8)	0.116(11)	*
C(13)	-0.3698(23)	-0.4483(20)	0.1639(6)	0.046(6)	*
C(14)	-0.3917(24)	-0.5784(24)	0.1916(7)	0.077(8)	*
C(15)	-0.5077(27)	-0.4330(28)	0.1663(7)	0.106(10)	*
H(6)	-0.3644(19)	-0.3117(19)	0.0880(6)	0.0500(0)	*
H(7)	-0.2732(21)	-0.4912(21)	0.1195(6)	0.0500(0)	*
H(10)	-0.4176(27)	-0.4021(25)	0.0150(6)	0.0600(0)	*
H(13)	-0.2871(23)	-0.3883(20)	0.1817(6)	0.0500(0)	*
H(1)a	0.1090(22)	0.1504(26)	0.1261(7)	0.0700(0)	*
H(1)b	0.0409(22)	0.0068(26)	0.1531(7)	0.0700(0)	*
H(3)a	-0.070(3)	0.247(4)	0.1701(9)	0.1100(0)	*
H(3)b	-0.188(3)	0.286(4)	0.1566(9)	0.1100(0)	*
H(3)c	-0.098(3)	0.261(4)	0.1207(9)	0.1100(0)	*
H(4)a	-0.343(4)	0.094(4)	0.1043(11)	0.1200(0)	*
H(4)b	-0.466(4)	0.070(4)	0.1369(11)	0.1200(0)	*
H(4)c	-0.426(4)	-0.051(4)	0.1303(11)	0.1200(0)	*
H(5)a	-0.226(4)	0.064(4)	0.2152(10)	0.1200(0)	*
H(5)b	-0.394(4)	-0.007(4)	0.2104(10)	0.1200(0)	*
H(5)c	-0.297(4)	0.161(4)	0.2157(10)	0.1200(0)	*
H(8)a	-0.5260(21)	-0.5657(22)	0.0791(7)	0.0600(0)	*
H(8)b	-0.4939(21)	-0.6675(22)	0.1079(7)	0.0600(0)	*
H(9)a	-0.3241(26)	-0.5787(27)	0.0478(8)	0.0900(0)	*
H(9)b	-0.4643(26)	-0.6812(27)	0.0214(8)	0.0900(0)	*
H(11)a	-0.2071(22)	-0.2665(22)	0.0166(7)	0.0600(0)	*
H(11)b	-0.1789(22)	-0.3703(22)	0.0458(7)	0.0600(0)	*
H(12)a	-0.4174(28)	-0.499(3)	-0.0354(8)	0.0900(0)	*
H(12)b	-0.2977(28)	-0.543(3)	-0.0354(8)	0.0900(0)	*
H(12)c	-0.2590(28)	-0.386(3)	-0.0491(8)	0.0900(0)	*
H(14)a	-0.3930(24)	-0.5701(24)	0.2228(7)	0.0900(0)	*
H(14)b	-0.3250(24)	-0.6098(24)	0.1837(7)	0.0900(0)	*
H(14)c	-0.4866(24)	-0.6475(24)	0.1816(7)	0.0900(0)	*
H(15)a	-0.5038(27)	-0.3971(28)	0.1952(7)	0.0900(0)	*
H(15)b	-0.5692(27)	-0.5360(28)	0.1660(7)	0.0900(0)	*
H(15)c	-0.5456(27)	-0.3900(28)	0.1467(7)	0.0900(0)	*

* Isotropic thermal parameter

Table 1. Fractional atomic co-ordinates and thermal parameters
for menthyl-N-tbutyl bromomethylphosphonamidate

Atom	x	y	z	Ueq	
Ueq = 1/3 trace of the orthogonalised U					
Br	0.19828(29)	0.0318(3)	0.07900(0)	0.1074(19)	
N	-0.1987(18)	-0.0260(19)	0.1526(5)	0.062(5)	*
O(1)	-0.1386(14)	0.0145(14)	0.0698(5)	0.060(4)	*
O(2)	-0.1494(14)	-0.2031(14)	0.1106(3)	0.049(4)	*
P(1)	-0.1150(7)	-0.0403(6)	0.10995(22)	0.052(3)	
C(1)	0.0789(22)	0.0495(26)	0.1252(7)	0.075(8)	*
C(2)	-0.2619(26)	0.0697(28)	0.1572(8)	0.080(8)	*
C(3)	-0.143(3)	0.231(4)	0.1488(9)	0.158(13)	*
C(4)	-0.388(4)	0.051(4)	0.1315(11)	0.210(18)	*
C(5)	-0.302(4)	0.076(4)	0.2034(10)	0.194(17)	*
C(6)	-0.2777(19)	-0.3174(19)	0.0890(6)	0.038(5)	*
C(7)	-0.3369(21)	-0.4532(21)	0.1156(6)	0.049(6)	*
C(8)	-0.4519(21)	-0.5843(22)	0.0892(7)	0.067(7)	*
C(9)	-0.4192(26)	-0.5981(27)	0.0401(8)	0.091(8)	*
C(10)	-0.3699(27)	-0.4579(25)	0.0162(6)	0.066(7)	*
C(11)	-0.2361(22)	-0.3246(22)	0.0425(7)	0.057(6)	*
C(12)	-0.3171(28)	-0.466(3)	-0.0300(8)	0.116(11)	*
C(13)	-0.3698(23)	-0.4483(20)	0.1639(6)	0.046(6)	*
C(14)	-0.3917(24)	-0.5784(24)	0.1916(7)	0.077(8)	*
C(15)	-0.5077(27)	-0.4330(28)	0.1663(7)	0.106(10)	*

* Isotropic thermal parameter
Hydrogen atoms were included in calculated positions with C-H 0.95Å and with fixed isotropic thermal parameters

Table 2. Bond Lengths (Å)
for menthyl-N-tbutyl bromomethylphosphonamidate

C(1)-Br	1.957(20)	C(7)-C(6)	1.485(23)
N-P(1)	1.618(16)	C(11)-C(6)	1.492(22)
O(2)-P(1)	1.573(13)	C(8)-C(7)	1.536(22)
O(1)-P(1)	1.424(14)	C(13)-C(7)	1.515(22)
C(1)-P(1)	1.837(20)	C(9)-C(8)	1.552(25)
C(2)-N	1.473(25)	C(10)-C(9)	1.492(28)
C(6)-O(2)	1.446(19)	C(11)-C(10)	1.623(26)
C(3)-C(2)	1.56(3)	C(12)-C(10)	1.526(26)
C(4)-C(2)	1.47(3)	C(14)-C(13)	1.529(25)
C(5)-C(2)	1.48(3)	C(15)-C(13)	1.549(27)

Bond Angles (°) for
menthyl-N-tbutyl
bromomethylphosphonamidate

O(2)-P(1)-N	104.8(8)	H(5)a-C(5)-C(2)	94.0(17)
O(1)-P(1)-N	115.5(9)	H(5)b-C(5)-C(2)	110.7(17)
O(1)-P(1)-O(2)	117.7(8)	H(5)c-C(5)-C(2)	122.3(17)
C(1)-P(1)-N	105.8(9)	H(6)-C(6)-O(2)	119.6(9)
C(1)-P(1)-O(2)	98.7(9)	C(7)-C(6)-H(6)	97.1(10)
C(1)-P(1)-O(1)	112.5(9)	C(11)-C(6)-H(6)	107.0(10)
C(2)-N-P(1)	126.7(14)	H(7)-C(7)-C(6)	115.6(10)
C(6)-O(2)-P(1)	121.1(11)	C(8)-C(7)-H(7)	95.3(11)
P(1)-C(1)-Br	112.2(10)	C(13)-C(7)-H(7)	96.8(10)
C(3)-C(2)-N	109.9(21)	H(8)a-C(8)-C(7)	110.2(11)
C(4)-C(2)-N	123.5(25)	H(8)b-C(8)-C(7)	108.6(11)
C(4)-C(2)-C(3)	104.2(25)	C(9)-C(8)-H(8)a	87.4(12)
C(5)-C(2)-N	111.1(22)	C(9)-C(8)-H(8)b	120.6(12)
C(5)-C(2)-C(3)	101.5(23)	H(9)a-C(9)-C(8)	90.4(12)
C(5)-C(2)-C(4)	104.2(26)	H(9)b-C(9)-C(8)	128.8(12)
C(7)-C(6)-O(2)	109.2(14)	C(10)-C(9)-H(9)a	95.6(14)
C(11)-C(6)-O(2)	107.1(14)	C(10)-C(9)-H(9)b	113.2(12)
C(11)-C(6)-C(7)	117.2(15)	H(10)-C(10)-C(9)	127.2(13)
C(8)-C(7)-C(6)	110.6(16)	C(11)-C(10)-H(10)	89.0(11)
C(13)-C(7)-C(6)	119.1(16)	C(12)-C(10)-H(10)	108.9(15)
C(13)-C(7)-C(8)	116.4(16)	H(11)a-C(11)-C(6)	139.4(10)
C(9)-C(8)-C(7)	118.2(18)	H(11)a-C(11)-C(10)	90.8(11)
C(10)-C(9)-C(8)	110.9(19)	H(11)b-C(11)-C(6)	101.9(11)
C(11)-C(10)-C(9)	110.1(18)	H(11)b-C(11)-C(10)	96.3(11)
C(12)-C(10)-C(9)	110.4(20)	H(12)a-C(12)-C(10)	78.8(13)
C(12)-C(10)-C(11)	108.4(18)	H(12)b-C(12)-C(10)	116.5(15)
C(10)-C(11)-C(6)	111.0(16)	H(12)c-C(12)-C(10)	127.1(14)
C(14)-C(13)-C(7)	115.9(16)	C(14)-C(13)-H(13)	88.0(12)
C(15)-C(13)-C(7)	107.0(16)	C(15)-C(13)-H(13)	120.3(12)
C(15)-C(13)-C(14)	110.0(17)	H(14)a-C(14)-C(13)	117.8(11)
H(1)a-C(1)-P(1)	104.4(7)	H(14)b-C(14)-C(13)	111.7(11)
H(1)b-C(1)-Br	137.1(7)	H(14)c-C(14)-C(13)	98.1(12)
H(1)b-C(1)-P(1)	83.1(6)	H(15)a-C(15)-C(13)	103.2(11)
H(3)a-C(3)-C(2)	103.1(15)	H(15)b-C(15)-C(13)	91.1(12)
H(3)b-C(3)-C(2)	104.4(16)	H(15)c-C(15)-C(13)	131.8(11)
H(3)c-C(3)-C(2)	120.5(14)		
H(4)a-C(4)-C(2)	100.7(18)		
H(4)b-C(4)-C(2)	134.6(18)		
H(4)c-C(4)-C(2)	90.5(19)		

Table 4. Anisotropic thermal parameters (x10**4)

Atom	U11	U22	U33	U23	U13	U12
Br	562(20)	954(25)	1394(24)	59(23)	37(19)	145(20)
P(1)	654(47)	282(37)	515(36)	57(33)	-21(37)	149(38)

The anisotropic displacement parameter has the form:
exp[-2pi^2(U11h^2a*^2+ ... +2U12hka*b*)]

Table 1. hydrogen atom Fractional atomic co-ordinates for menthyl-N-tbutyl bromomethylphosphonamidate

Atom	x	y	z	Ueq	
H(6)	-0.3644(19)	-0.3117(19)	0.0880(6)	0.0500(0)	*
H(7)	-0.2732(21)	-0.4912(21)	0.1195(6)	0.0500(0)	*
H(10)	-0.4176(27)	-0.4021(25)	0.0150(6)	0.0600(0)	*
H(13)	-0.2871(23)	-0.3883(20)	0.1817(6)	0.0500(0)	*
H(1)a	0.1090(22)	0.1504(26)	0.1261(7)	0.0700(0)	*
H(1)b	0.0409(22)	0.0068(26)	0.1531(7)	0.0700(0)	*
H(3)a	-0.070(3)	0.247(4)	0.1701(9)	0.1100(0)	*
H(3)b	-0.188(3)	0.286(4)	0.1566(9)	0.1100(0)	*
H(3)c	-0.098(3)	0.261(4)	0.1207(9)	0.1100(0)	*
H(4)a	-0.343(4)	0.094(4)	0.1043(11)	0.1200(0)	*
H(4)b	-0.466(4)	0.070(4)	0.1369(11)	0.1200(0)	*
H(4)c	-0.426(4)	-0.051(4)	0.1303(11)	0.1200(0)	*
H(5)a	-0.226(4)	0.064(4)	0.2152(10)	0.1200(0)	*
H(5)b	-0.394(4)	-0.007(4)	0.2104(10)	0.1200(0)	*
H(5)c	-0.297(4)	0.161(4)	0.2157(10)	0.1200(0)	*
H(8)a	-0.5260(21)	-0.5657(22)	0.0791(7)	0.0600(0)	*
H(8)b	-0.4939(21)	-0.6675(22)	0.1079(7)	0.0600(0)	*
H(9)a	-0.3241(26)	-0.5787(27)	0.0478(8)	0.0900(0)	*
H(9)b	-0.4643(26)	-0.6812(27)	0.0214(8)	0.0900(0)	*
H(11)a	-0.2071(22)	-0.2665(22)	0.0166(7)	0.0600(0)	*
H(11)b	-0.1789(22)	-0.3703(22)	0.0458(7)	0.0600(0)	*
H(12)a	-0.4174(28)	-0.499(3)	-0.0354(8)	0.0900(0)	*
H(12)b	-0.2977(28)	-0.543(3)	-0.0354(8)	0.0900(0)	*
H(12)c	-0.2590(28)	-0.386(3)	-0.0491(8)	0.0900(0)	*
H(14)a	-0.3930(24)	-0.5701(24)	0.2228(7)	0.0900(0)	*
H(14)b	-0.3250(24)	-0.6098(24)	0.1837(7)	0.0900(0)	*
H(14)c	-0.4866(24)	-0.6475(24)	0.1816(7)	0.0900(0)	*
H(15)a	-0.5038(27)	-0.3971(28)	0.1952(7)	0.0900(0)	*
H(15)b	-0.5692(27)	-0.5360(28)	0.1660(7)	0.0900(0)	*
H(15)c	-0.5456(27)	-0.3900(28)	0.1467(7)	0.0900(0)	*

FIG.14

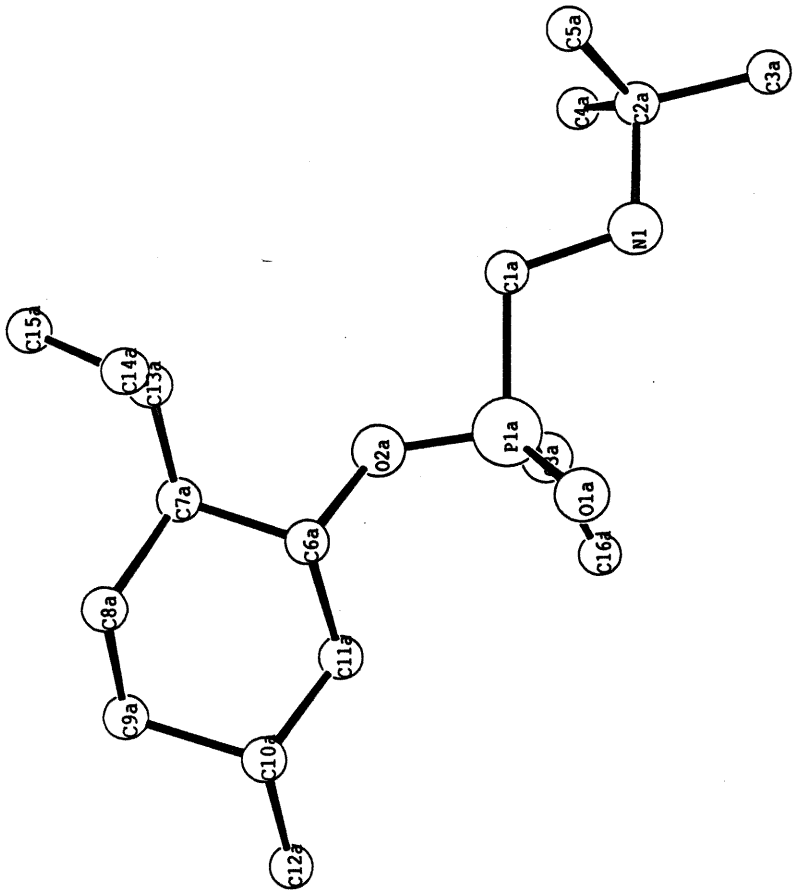

C5a
C4a
C2a
C3a
N1
C1a
C15a
C14a
C13a
P1a
O2a
O1a
C16a
C7a
C6a
C8a
C11a
C9a
C10a
C12a

FIG.15

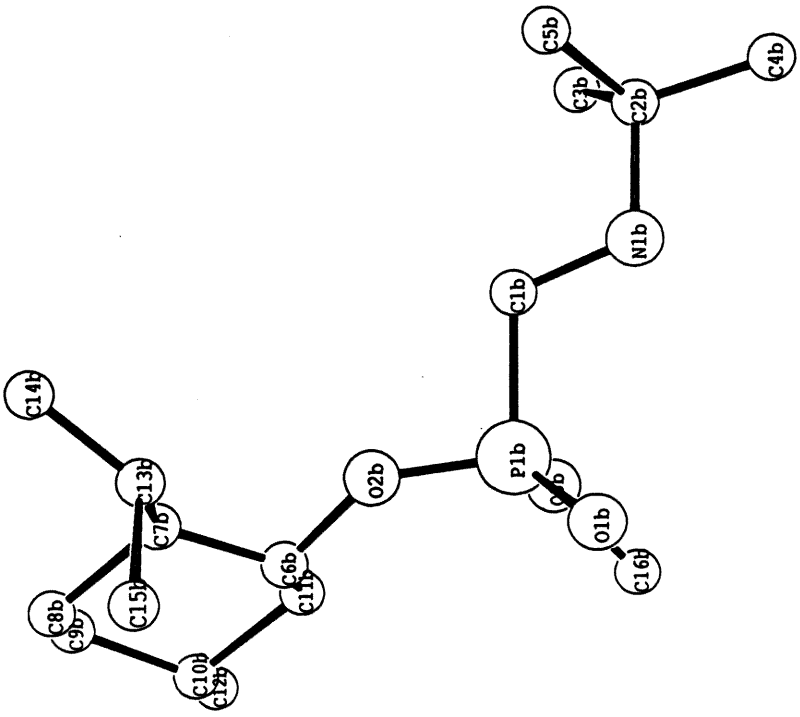

C5b
C4b
C3b
C2b
N1b
C1b
C14b
C13b
O2b
P1b
C7b
O1b
C6b
C16b
C15b
C11b
C8b
C9b
C10b
C12b

FIG.16

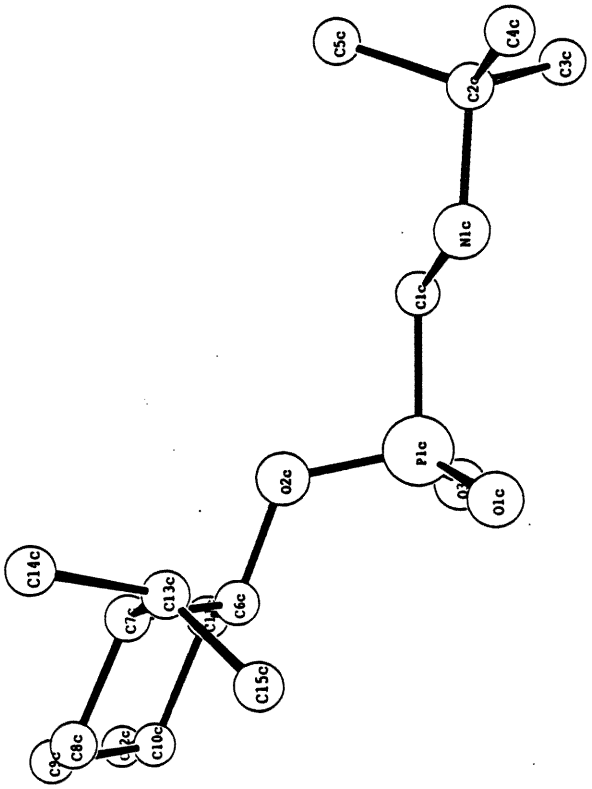

C5c
C4c
C3c
C2c
N1c
C1c
P1c
O2c
O1c
C14c
C13c
C7c
C6c
C15c
C8c
C10c

FIG.17

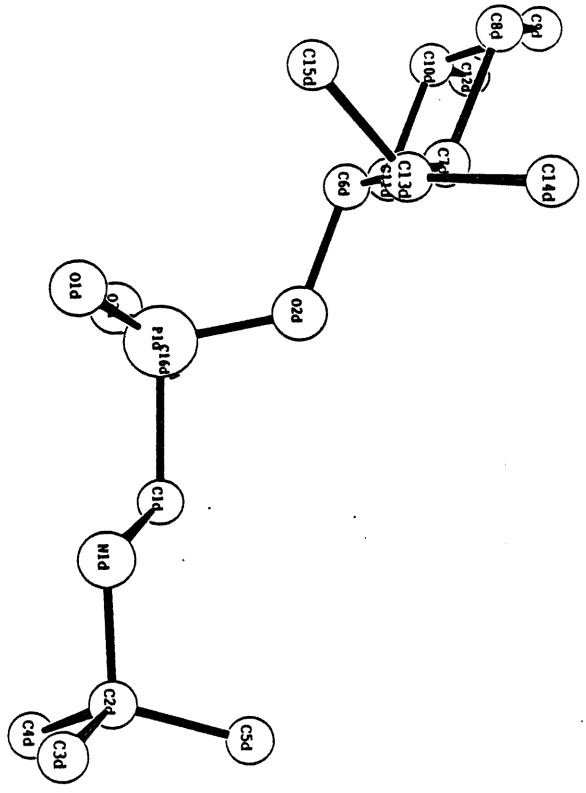
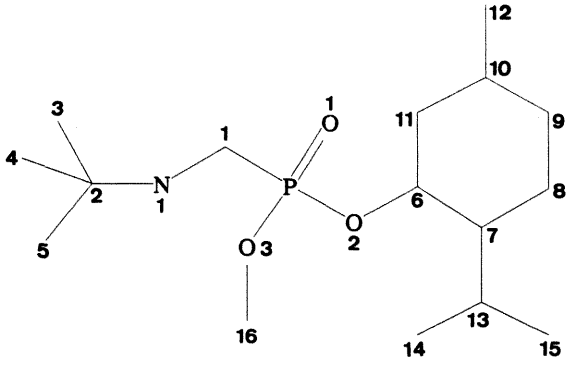
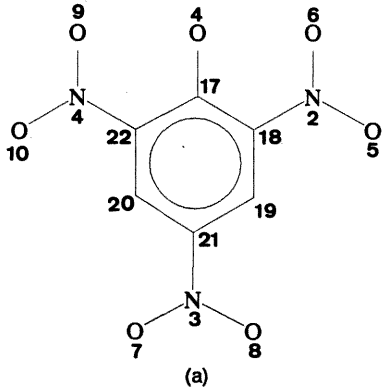
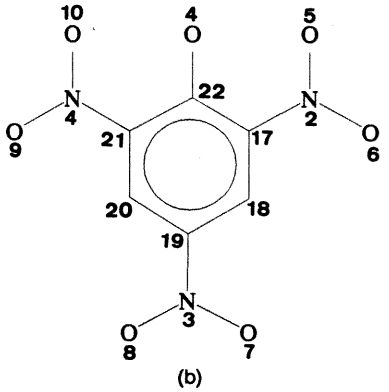

C8d
C9d
C15d
C10d
C12d
C13d
C11d
C6d
C14d
O1d
O2d
P1d
C1d
N1d
C2d
C4d
C3d
C5d

Fig. 18

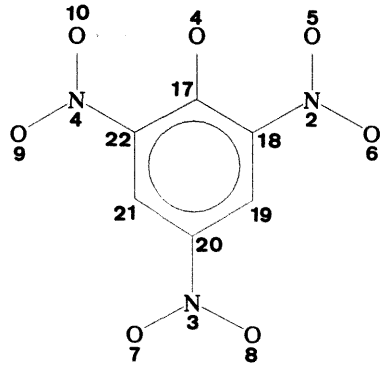

12
10
3
1
O
11
9
4
1
N
P
2
6
8
O
2
5
O 3
7
16
13
14
15


9
O
4
O
6
O
N
4
17
N
2
O
10
22
18
O
5
20
19
21
N
3
O
7
O
8

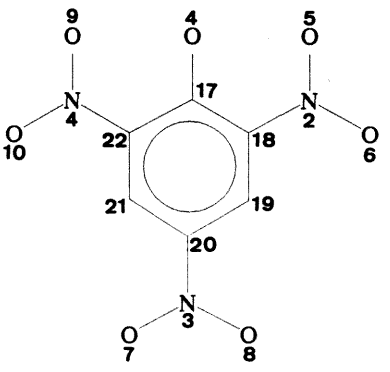
(a)


10
O
4
O
5
O
N
4
22
N
2
O
9
21
17
O
6
20
18
19
N
3
O
8
O
7

(b)

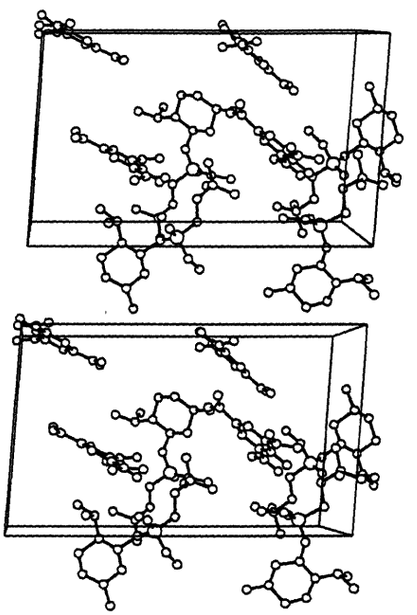

10
O
4
O
5
O
N
4
17
N
2
O
9
22
18
O
6
21
19
20
N
3
O
7
O
8

(c)


9
O
4
O
5
O
N
4
17
N
2
O
10
22
18
O
6
21
19
20
N
3
O
7
O
8

(d)

FIG. 19



$(S)_P$ (1*R*, 2*S*, 5*R*)-Menthyl methyl (t-butylamino)methylphosphonate, picric acid salt

Table 1. Fractional atomic co-ordinates and thermal parameters for $C_{22}H_{37}N_4O_{10}P$

Atom	x	y	z	Ueq	
Ueq = 1/3 trace of the orthogonalised U					
P(1)a	0.87010(0)	0.93830(0)	0.32170(0)	0.0332(11)	*
O(1)a	0.8480(6)	0.9213(9)	0.4504(12)	0.044(3)	*
O(2)a	0.8917(6)	1.0456(10)	0.2932(13)	0.054(3)	*
O(3)a	0.8169(8)	0.8980(12)	0.2158(15)	0.074(4)	*
N(1)a	0.9271(6)	0.7578(10)	0.2870(13)	0.034(3)	*
C(1)a	0.9382(9)	0.8721(14)	0.2727(18)	0.046(5)	*
C(2)a	0.9750(9)	0.6999(14)	0.2215(18)	0.045(5)	*
C(3)a	0.9583(10)	0.5881(16)	0.2548(21)	0.060(6)	*
C(4)a	0.9581(12)	0.7159(20)	0.0747(25)	0.076(7)	*
C(5)a	1.0415(11)	0.7378(17)	0.2702(22)	0.063(6)	*
C(6)a	0.8857(10)	1.1415(15)	0.3649(20)	0.055(5)	*
C(7)a	0.9302(10)	1.2217(15)	0.3078(20)	0.055(5)	*
C(8)a	0.9184(12)	1.3215(19)	0.3752(26)	0.076(7)	*
C(9)a	0.8483(14)	1.3469(21)	0.3631(29)	0.090(8)	*
C(10)a	0.8039(12)	1.2636(19)	0.4170(26)	0.078(7)	*
C(11)a	0.8136(12)	1.1610(19)	0.3591(25)	0.074(7)	*
C(12)a	0.7355(15)	1.2832(24)	0.410(3)	0.106(9)	*
C(13)a	0.9983(12)	1.1991(19)	0.3138(24)	0.076(7)	*
C(14)a	1.0409(17)	1.2166(27)	0.446(4)	0.116(11)	*
C(15)a	1.0356(18)	1.2608(29)	0.205(4)	0.129(12)	*
C(16)a	0.7494(16)	0.8882(25)	0.226(3)	0.107(10)	*
P(1)b	0.50397(24)	0.7202(4)	0.9345(5)	0.0437(12)	*
O(1)b	0.5259(7)	0.7461(11)	1.0698(14)	0.059(4)	*
O(2)b	0.4730(9)	0.6111(15)	0.8944(20)	0.097(5)	*
O(3)b	0.5588(7)	0.7414(11)	0.8469(14)	0.064(4)	*
N(1)b	0.4472(7)	0.8994(11)	0.8931(14)	0.042(4)	*
C(1)b	0.4385(10)	0.7911(16)	0.8639(20)	0.055(5)	*
C(2)b	0.3999(10)	0.9583(16)	0.8098(20)	0.054(5)	*
C(3)b	0.4074(12)	0.9378(19)	0.6706(25)	0.074(7)	*
C(4)b	0.4138(12)	1.0703(19)	0.8570(25)	0.077(7)	*
C(5)b	0.3281(12)	0.9160(18)	0.8369(24)	0.072(6)	*
C(6)b	0.4914(11)	0.5146(18)	0.8776(23)	0.066(6)	*
C(7)b	0.4345(18)	0.4421(29)	0.856(4)	0.120(11)	*
C(8)b	0.4527(22)	0.334(3)	0.837(5)	0.146(14)	*
C(9)b	0.4939(16)	0.3269(26)	0.719(4)	0.109(10)	*
C(10)b	0.5529(16)	0.4040(25)	0.748(3)	0.106(9)	*
C(11)b	0.5400(13)	0.5070(22)	0.7730(29)	0.090(8)	*
C(12)b	0.6027(23)	0.395(4)	0.646(5)	0.160(16)	*
C(13)b	0.3852(22)	0.453(3)	0.968(5)	0.143(14)	*
C(14)b	0.321(4)	0.422(6)	0.917(9)	0.26(3)	*
C(15)b	0.4036(28)	0.414(5)	1.090(7)	0.201(22)	*
C(16)b	0.6221(13)	0.7668(21)	0.8900(27)	0.085(7)	*

(continued)

Atom	x	y	z	Ueq	
P(1)c	0.92382(23)	0.6658(4)	-0.3578(5)	0.0392(12)	*
O(1)c	0.9517(6)	0.7166(9)	-0.4559(12)	0.045(3)	*
O(2)c	0.9697(6)	0.6372(9)	-0.2447(11)	0.0419(29)	*
O(3)c	0.8827(6)	0.5686(10)	-0.4089(12)	0.052(3)	*
N(1)c	0.8783(7)	0.8504(11)	-0.3036(14)	0.060(4)	*
C(1)c	0.8695(9)	0.7383(14)	-0.2804(18)	0.045(5)	*
C(2)c	0.8305(9)	0.9200(14)	-0.2427(18)	0.043(5)	*
C(3)c	0.7625(13)	0.8842(20)	-0.3097(26)	0.080(7)	*
C(4)c	0.8523(11)	1.0291(18)	-0.2652(23)	0.069(6)	*
C(5)c	0.8331(11)	0.9000(18)	-0.0966(23)	0.070(6)	*
C(6)c	1.0234(10)	0.5689(16)	-0.2613(21)	0.058(5)	*
C(7)c	1.0846(10)	0.6188(15)	-0.1757(20)	0.053(5)	*
C(8)c	1.1375(12)	0.5493(19)	-0.1857(26)	0.079(7)	*
C(9)c	1.1165(13)	0.4357(20)	-0.1509(27)	0.084(7)	*
C(10)c	1.0621(13)	0.3946(21)	-0.2345(27)	0.087(8)	*
C(11)c	1.0026(11)	0.4697(17)	-0.2267(22)	0.065(6)	*
C(12)c	1.0381(18)	0.2835(29)	-0.194(4)	0.126(12)	*
C(13)c	1.1022(12)	0.7239(19)	-0.2120(24)	0.076(7)	*
C(14)c	1.1529(14)	0.7770(22)	-0.1045(29)	0.091(8)	*
C(15)c	1.1299(14)	0.7389(22)	-0.3418(29)	0.093(8)	*
C(16)c	0.8430(11)	0.5024(18)	-0.3278(23)	0.069(6)	*
P(1)d	0.43989(24)	0.9896(4)	1.2485(5)	0.0418(12)	*
O(1)d	0.4121(7)	0.9325(10)	1.1372(14)	0.059(4)	*
O(2)d	0.3947(5)	1.0178(8)	1.3492(11)	0.0360(27)	*
O(3)d	0.4765(8)	1.0891(12)	1.2109(16)	0.077(4)	*
N(1)d	0.4933(7)	0.8098(12)	1.3067(15)	0.049(4)	*
C(1)d	0.5011(9)	0.9256(14)	1.3433(19)	0.047(5)	*
C(2)d	0.5401(9)	0.7469(14)	1.3903(18)	0.043(5)	*
C(3)d	0.5220(13)	0.6387(21)	1.3466(27)	0.084(7)	*
C(4)d	0.6081(11)	0.7892(17)	1.3591(22)	0.063(6)	*
C(5)d	0.5300(11)	0.7685(18)	1.5261(23)	0.066(6)	*
C(6)d	0.3360(10)	1.0796(15)	1.3160(20)	0.053(5)	*
C(7)d	0.2817(10)	1.0322(15)	1.3688(20)	0.054(5)	*
C(8)d	0.2220(10)	1.1007(17)	1.3394(22)	0.063(6)	*
C(9)d	0.2408(13)	1.2055(21)	1.4046(28)	0.087(8)	*
C(10)d	0.3015(14)	1.2550(22)	1.3464(29)	0.091(8)	*
C(11)d	0.3593(13)	1.1855(20)	1.3781(27)	0.082(7)	*
C(12)d	0.3281(23)	1.361(4)	1.417(5)	0.163(17)	*
C(13)d	0.2605(12)	0.9178(18)	1.3175(24)	0.072(6)	*
C(14)d	0.2119(12)	0.8666(20)	1.4044(26)	0.079(7)	*
C(15)d	0.2329(15)	0.9084(23)	1.178(3)	0.099(9)	*
C(16)d	0.5151(13)	1.1523(21)	1.3072(27)	0.084(7)	*

(continued)

Atom	x	y	z	Ueq	
O(4)a	0.8116(8)	0.6693(12)	0.1722(16)	0.077(4)	*
O(5)a	0.7288(8)	0.6301(13)	0.5031(17)	0.081(5)	*
O(6)a	0.8069(8)	0.7048(12)	0.4198(16)	0.078(5)	*
O(7)a	0.5844(10)	0.3387(17)	0.1007(23)	0.112(6)	*
O(8)a	0.5728(9)	0.3898(14)	0.2940(19)	0.095(5)	*
O(9)a	0.8214(15)	0.5814(22)	-0.046(3)	0.155(10)	*
O(10)a	0.7278(16)	0.5272(25)	-0.142(4)	0.177(12)	*
N(2)a	0.7588(8)	0.6456(13)	0.4142(17)	0.056(4)	*
N(3)a	0.5992(11)	0.3945(18)	0.1941(24)	0.088(6)	*
N(4)a	0.7561(15)	0.5715(21)	-0.056(3)	0.114(8)	*
C(17)a	0.7599(5)	0.6076(9)	0.1814(11)	0.045(5)	*
C(18)a	0.7335(5)	0.5920(9)	0.2959(11)	0.044(4)	*
C(19)a	0.6802(5)	0.5224(9)	0.3007(11)	0.056(5)	*
C(21)a	0.6532(5)	0.4686(9)	0.1911(11)	0.060(6)	*
C(20)a	0.6796(5)	0.4842(9)	0.0766(11)	0.055(5)	*
C(22)a	0.7330(5)	0.5537(9)	0.0718(11)	0.056(5)	*
O(4)b	0.5630(7)	0.9876(11)	0.8193(15)	0.068(4)	*
O(5)b	0.5703(10)	0.9691(16)	1.0669(21)	0.107(6)	*
O(6)b	0.6451(10)	1.0668(16)	1.1818(22)	0.109(6)	*
O(7)b	0.7849(16)	1.3021(26)	1.012(4)	0.183(12)	*
O(8)b	0.7970(14)	1.3001(22)	0.805(3)	0.156(10)	*
O(9)b	0.6496(14)	1.0503(20)	0.5359(29)	0.142(9)	*
O(10)b	0.5503(15)	1.0744(22)	0.587(3)	0.152(9)	*
N(2)b	0.6143(11)	1.0339(16)	1.0806(22)	0.083(6)	*
N(3)b	0.7676(16)	1.2740(24)	0.903(4)	0.133(10)	*
N(4)b	0.6119(11)	1.0679(17)	0.6120(22)	0.086(6)	*
C(17)b	0.6372(7)	1.0845(11)	0.9683(11)	0.063(6)	*
C(18)b	0.6891(7)	1.1578(11)	0.9886(11)	0.077(7)	*
C(19)b	0.7160(7)	1.2018(11)	0.8857(11)	0.052(5)	*
C(20)b	0.6909(7)	1.1725(11)	0.7626(11)	0.075(7)	*
C(21)b	0.6389(7)	1.0992(11)	0.7424(11)	0.055(5)	*
C(22)b	0.6120(7)	1.0552(11)	0.8452(11)	0.065(6)	*

(continued)

Atom	x	y	z	Ueq	
O(4)c	0.9893(6)	0.9187(9)	0.8211(12)	0.045(3)	*
O(5)c	0.9859(8)	0.9715(12)	0.5685(16)	0.075(4)	*
O(6)c	1.0783(10)	0.9601(15)	0.5028(20)	0.102(6)	*
O(7)c	1.2541(10)	1.1578(16)	0.9579(22)	0.107(6)	*
O(8)c	1.2539(9)	1.1485(14)	0.7564(20)	0.096(6)	*
O(9)c	1.0757(9)	0.9994(13)	1.1513(18)	0.087(5)	*
O(10)c	0.9816(8)	1.0217(13)	1.0512(16)	0.077(4)	*
N(2)c	1.0429(8)	0.9728(12)	0.5883(16)	0.049(4)	*
N(3)c	1.2287(9)	1.1365(14)	0.8529(20)	0.071(5)	*
N(4)c	1.0410(8)	1.0138(12)	1.0572(17)	0.055(4)	*
C(17)c	1.0434(4)	0.9843(9)	0.8228(11)	0.045(5)	*
C(18)c	1.0752(4)	0.9988(9)	0.7141(11)	0.044(5)	*
C(19)c	1.1362(4)	1.0507(9)	0.7227(11)	0.050(5)	*
C(20)c	1.1654(4)	1.0880(9)	0.8400(11)	0.052(5)	*
C(21)c	1.1336(4)	1.0734(9)	0.9488(11)	0.049(5)	*
C(22)c	1.0726(4)	1.0216(9)	0.9402(11)	0.038(4)	*
O(4)d	0.3801(7)	0.7334(11)	1.3932(14)	0.064(4)	*
O(5)d	0.3876(8)	0.6919(12)	1.1423(15)	0.071(4)	*
O(6)d	0.2973(8)	0.6927(13)	1.0322(17)	0.085(5)	*
O(7)d	0.1164(10)	0.4855(16)	1.3987(22)	0.107(6)	*
O8d	0.1161(9)	0.5018(15)	1.2038(20)	0.098(6)	*
O(9)d	0.3843(9)	0.6357(14)	1.6116(18)	0.087(5)	*
O(10)d	0.2917(13)	0.6529(20)	1.6836(28)	0.140(9)	*
N(2)d	0.3318(10)	0.6803(14)	1.1334(19)	0.068(5)	*
N(3)d	0.1420(10)	0.5156(15)	1.3089(22)	0.076(5)	*
N(4)d	0.3303(12)	0.6419(16)	1.5940(21)	0.081(6)	*
C(17)d	0.3275(4)	0.6702(9)	1.3675(11)	0.035(4)	*
C(18)d	0.2971(4)	0.6532(9)	1.2454(11)	0.047(5)	*
C(19)d	0.2363(4)	0.6009(9)	1.2267(11)	0.063(6)	*
C(20)d	0.2058(4)	0.5656(9)	1.3302(11)	0.051(5)	*
C(21)d	0.2361(4)	0.5827(9)	1.4524(11)	0.050(5)	*
C(22)d	0.2970(4)	0.6349(9)	1.4710(11)	0.043(4)	*

* Isotropic thermal parameter

Table 2. Bond Lengths (Å) for $C_{22}H_{37}N_4O_{10}P$

O(1)a-P(1)a	1.500(13)	O(1)c-P(1)c	1.404(13)
O(2)a-P(1)a	1.502(13)	O(2)c-P(1)c	1.544(12)
O(3)a-P(1)a	1.559(15)	O(3)c-P(1)c	1.543(13)
C(1)a-P(1)a	1.836(20)	C(1)c-P(1)c	1.784(20)
C(6)a-O(2)a	1.477(24)	C(6)c-O(2)c	1.515(25)
C(16)a-O(3)a	1.42(4)	C(16)c-O(3)c	1.504(27)
C(1)a-N(1)a	1.524(23)	C(1)c-N(1)c	1.509(23)
C(2)a-N(1)a	1.513(24)	C(2)c-N(1)c	1.577(24)
C(3)a-C(2)a	1.549(28)	C(3)c-C(2)c	1.56(3)
C(4)a-C(2)a	1.59(3)	C(4)c-C(2)c	1.509(29)
C(5)a-C(2)a	1.484(27)	C(5)c-C(2)c	1.58(3)
C(7)a-C(6)a	1.531(29)	C(7)c-C(6)c	1.587(27)
C(11)a-C(6)a	1.55(3)	C(11)c-C(6)c	1.42(3)
C(8)a-C(7)a	1.53(3)	C(8)c-C(7)c	1.50(3)
C(13)a-C(7)a	1.48(3)	C(13)c-C(7)c	1.48(3)
C(9)a-C(8)a	1.52(4)	C(9)c-C(8)c	1.59(4)
C(10)a-C(9)a	1.54(4)	C(10)c-C(9)c	1.44(4)
C(11)a-C(10)a	1.51(4)	C(11)c-C(10)c	1.66(4)
C(12)a-C(10)a	1.47(4)	C(12)c-C(10)c	1.60(5)
C(14)a-C(13)a	1.59(4)	C(14)c-C(13)c	1.59(4)
C(15)a-C(13)a	1.65(5)	C(15)c-C(13)c	1.55(4)
O(1)b-P(1)b	1.488(15)	O(1)d-P(1)d	1.434(14)
O(2)b-P(1)b	1.563(19)	O(2)d-P(1)d	1.546(13)
O(3)b-P(1)b	1.557(16)	O(3)d-P(1)d	1.550(17)
C(1)b-P(1)b	1.837(22)	C(1)d-P(1)d	1.834(20)
C(6)b-O(2)b	1.37(3)	C(6)d-O(2)d	1.549(23)
C(16)b-O(3)b	1.38(3)	C(16)d-O(3)d	1.44(3)
C(1)b-N(1)b	1.448(25)	C(1)d-N(1)d	1.558(24)
C(2)b-N(1)b	1.540(26)	C(2)d-N(1)d	1.566(24)
C(3)b-C(2)b	1.52(3)	C(3)d-C(2)d	1.50(3)
C(4)b-C(2)b	1.54(3)	C(4)d-C(2)d	1.556(29)
C(5)b-C(2)b	1.62(3)	C(5)d-C(2)d	1.50(3)
C(7)b-C(6)b	1.47(4)	C(7)d-C(6)d	1.423(29)
C(11)b-C(6)b	1.58(4)	C(11)d-C(6)d	1.55(3)
C(8)b-C(7)b	1.51(6)	C(8)d-C(7)d	1.61(3)
C(13)b-C(7)b	1.65(6)	C(13)d-C(7)d	1.61(3)
C(9)b-C(8)b	1.59(6)	C(9)d-C(8)d	1.53(4)
C(10)b-C(9)b	1.54(5)	C(10)d-C(9)d	1.57(4)
C(11)b-C(10)b	1.43(5)	C(11)d-C(10)d	1.59(4)
C(12)b-C(10)b	1.57(6)	C(12)d-C(10)d	1.61(6)
C(14)b-C(13)b	1.42(9)	C(14)d-C(13)d	1.56(4)
C(15)b-C(13)b	1.44(8)	C(15)d-C(13)d	1.54(4)

(continued)

Table 2. Bond Lengths (Å) for $C_{22}H_{37}N_4O_{10}P$

C(17)a-O(4)a	1.315(19)	C(17)c-O(4)c	1.368(15)
N(2)a-O(5)a	1.195(26)	N(2)c-O(5)c	1.191(23)
N(2)a-O(6)a	1.221(23)	N(2)c-O(6)c	1.239(28)
N(3)a-O(7)a	1.22(3)	N(3)c-O(7)c	1.21(3)
N(3)a-O(8)a	1.24(3)	N(3)c-O(8)c	1.20(3)
N(4)a-O(9)a	1.36(4)	N(4)c-O(9)c	1.210(25)
N(4)a-O(10)a	1.15(5)	N(4)c-O(10)c	1.251(24)
C(18)a-N(2)a	1.457(20)	C(18)c-N(2)c	1.459(19)
C(21)a-N(3)a	1.439(25)	C(20)c-N(3)c	1.418(21)
C(22)a-N(4)a	1.50(3)	C(22)c-N(4)c	1.462(21)
C(18)a-C(17)a	1.395(17)	C(18)c-C(17)c	1.395(16)
C(22)a-C(17)a	1.395(16)	C(22)c-C(17)c	1.395(15)
C(19)a-C(18)a	1.395(15)	C(19)c-C(18)c	1.395(13)
C(21)a-C(19)a	1.395(16)	C(20)c-C(19)c	1.395(15)
C(20)a-C(21)a	1.395(17)	C(21)c-C(20)c	1.395(16)
C(22)a-C(20)a	1.395(15)	C(22)c-C(21)c	1.395(13)
C(22)b-O(4)b	1.311(20)	C(17)d-O(4)d	1.332(17)
N(2)b-O(5)b	1.20(3)	N(2)d-O(5)d	1.161(26)
N(2)b-O(6)b	1.25(3)	N(2)d-O(6)d	1.262(26)
N(3)b-O(7)b	1.22(6)	N(3)d-O(7)d	1.20(3)
N(3)b-O(8)b	1.30(5)	N(3)d-O8d	1.20(3)
N(4)b-O(9)b	1.21(4)	N(4)d-O(9)d	1.14(3)
N(4)b-O(10)b	1.30(4)	N(4)d-O(10)d	1.32(4)
C(17)b-N(2)b	1.484(27)	C(18)d-N(2)d	1.486(24)
C(19)b-N(3)b	1.38(3)	C(20)d-N(3)d	1.438(21)
C(21)b-N(4)b	1.481(26)	C(22)d-N(4)d	1.420(24)
C(18)b-C(17)b	1.395(20)	C(18)d-C(17)d	1.395(15)
C(22)b-C(17)b	1.395(17)	C(22)d-C(17)d	1.395(16)
C(19)b-C(18)b	1.395(19)	C(19)d-C(18)d	1.395(13)
C(20)b-C(19)b	1.395(17)	C(20)d-C(19)d	1.395(16)
C(21)b-C(20)b	1.395(20)	C(21)d-C(20)d	1.395(15)
C(22)b-C(21)b	1.395(19)	C(22)d-C(21)d	1.395(13)

(continued)

Table 3. Bond Angles (°) for $C_{22}H_{37}N_4O_{10}P$

O(2)a-P(1)a-O(1)a	116.7(7)	O(2)c-P(1)c-O(1)c	117.1(7)
O(3)a-P(1)a-O(1)a	110.9(7)	O(3)c-P(1)c-O(1)c	111.1(8)
O(3)a-P(1)a-O(2)a	107.8(8)	O(3)c-P(1)c-O(2)c	108.1(7)
C(1)a-P(1)a-O(1)a	119.3(8)	C(1)c-P(1)c-O(1)c	113.5(8)
C(1)a-P(1)a-O(2)a	100.2(8)	C(1)c-P(1)c-O(2)c	101.5(8)
C(1)a-P(1)a-O(3)a	100.1(8)	C(1)c-P(1)c-O(3)c	104.5(8)
C(6)a-O(2)a-P(1)a	129.8(13)	C(6)c-O(2)c-P(1)c	121.9(11)
C(16)a-O(3)a-P(1)a	126.4(18)	C(16)c-O(3)c-P(1)c	123.3(12)
C(2)a-N(1)a-C(1)a	112.0(13)	C(2)c-N(1)c-C(1)c	116.6(13)
N(1)a-C(1)a-P(1)a	111.2(12)	N(1)c-C(1)c-P(1)c	113.1(13)
C(3)a-C(2)a-N(1)a	103.6(15)	C(3)c-C(2)c-N(1)c	105.1(15)
C(4)a-C(2)a-N(1)a	104.9(16)	C(4)c-C(2)c-N(1)c	107.7(16)
C(4)a-C(2)a-C(3)a	111.1(16)	C(4)c-C(2)c-C(3)c	113.8(18)
C(5)a-C(2)a-N(1)a	109.9(15)	C(5)c-C(2)c-N(1)c	108.3(15)
C(5)a-C(2)a-C(3)a	112.4(17)	C(5)c-C(2)c-C(3)c	110.4(17)
C(5)a-C(2)a-C(4)a	114.1(18)	C(5)c-C(2)c-C(4)c	111.1(17)
C(7)a-C(6)a-O(2)a	105.6(16)	C(7)c-C(6)c-O(2)c	106.3(15)
C(11)a-C(6)a-O(2)a	108.4(16)	C(11)c-C(6)c-O(2)c	108.2(17)
C(11)a-C(6)a-C(7)a	116.6(18)	C(11)c-C(6)c-C(7)c	113.9(18)
C(8)a-C(7)a-C(6)a	104.4(18)	C(8)c-C(7)c-C(6)c	107.1(17)
C(13)a-C(7)a-C(6)a	114.6(18)	C(13)c-C(7)c-C(6)c	111.5(18)
C(13)a-C(7)a-C(8)a	114.7(18)	C(13)c-C(7)c-C(8)c	113.4(19)
C(9)a-C(8)a-C(7)a	114.4(20)	C(9)c-C(8)c-C(7)c	112.4(20)
C(10)a-C(9)a-C(8)a	111.9(23)	C(10)c-C(9)c-C(8)c	110.5(23)
C(11)a-C(10)a-C(9)a	110.3(23)	C(11)c-C(10)c-C(9)c	109.0(22)
C(12)a-C(10)a-C(9)a	115.0(24)	C(12)c-C(10)c-C(9)c	110.6(25)
C(12)a-C(10)a-C(11)a	112.0(22)	C(12)c-C(10)c-C(11)c	108.9(23)
C(10)a-C(11)a-C(6)a	111.8(19)	C(10)c-C(11)c-C(6)c	109.5(19)
C(14)a-C(13)a-C(7)a	118.3(23)	C(14)c-C(13)c-C(7)c	108.5(20)
C(15)a-C(13)a-C(7)a	110.5(22)	C(15)c-C(13)c-C(7)c	117.9(21)
C(15)a-C(13)a-C(14)a	108.6(23)	C(15)c-C(13)c-C(14)c	108.1(21)

(continued)

Table 3. Bond angles (°) for $C_{22}H_{37}N_4O_{10}P$

O(2)b-P(1)b-O(1)b	119.9(10)	O(2)d-P(1)d-O(1)d	118.0(8)
O(3)b-P(1)b-O(1)b	112.0(8)	O(3)d-P(1)d-O(1)d	110.0(9)
O(3)b-P(1)b-O(2)b	105.7(10)	O(3)d-P(1)d-O(2)d	107.9(8)
C(1)b-P(1)b-O(1)b	116.2(9)	C(1)d-P(1)d-O(1)d	114.2(9)
C(1)b-P(1)b-O(2)b	97.4(10)	C(1)d-P(1)d-O(2)d	101.7(8)
C(1)b-P(1)b-O(3)b	103.6(9)	C(1)d-P(1)d-O(3)d	104.0(9)
C(6)b-O(2)b-P(1)b	139.2(17)	C(6)d-O(2)d-P(1)d	121.5(11)
C(16)b-O(3)b-P(1)b	124.1(16)	C(16)d-O(3)d-P(1)d	119.5(16)
C(2)b-N(1)b-C(1)b	112.0(14)	C(2)d-N(1)d-C(1)d	113.0(13)
N(1)b-C(1)b-P(1)b	113.8(13)	N(1)d-C(1)d-P(1)d	109.1(12)
C(3)b-C(2)b-N(1)b	110.5(18)	C(3)d-C(2)d-N(1)d	104.6(16)
C(4)b-C(2)b-N(1)b	105.0(16)	C(4)d-C(2)d-N(1)d	103.7(15)
C(4)b-C(2)b-C(3)b	115.4(19)	C(4)d-C(2)d-C(3)d	114.4(18)
C(5)b-C(2)b-N(1)b	107.0(16)	C(5)d-C(2)d-N(1)d	107.9(16)
C(5)b-C(2)b-C(3)b	108.1(17)	C(5)d-C(2)d-C(3)d	113.7(19)
C(5)b-C(2)b-C(4)b	110.5(19)	C(5)d-C(2)d-C(4)d	111.6(16)
C(7)b-C(6)b-O(2)b	110.0(23)	C(7)d-C(6)d-O(2)d	108.6(16)
C(11)b-C(6)b-O(2)b	112.6(21)	C(11)d-C(6)d-O(2)d	102.0(15)
C(11)b-C(6)b-C(7)b	113.6(24)	C(11)d-C(6)d-C(7)d	113.5(19)
C(8)b-C(7)b-C(6)b	112(3)	C(8)d-C(7)d-C(6)d	107.9(17)
C(13)b-C(7)b-C(6)b	111.6(29)	C(13)d-C(7)d-C(6)d	115.2(19)
C(13)b-C(7)b-C(8)b	113(3)	C(13)d-C(7)d-C(8)d	108.7(16)
C(9)b-C(8)b-C(7)b	110(4)	C(9)d-C(8)d-C(7)d	107.3(17)
C(10)b-C(9)b-C(8)b	106.0(29)	C(10)d-C(9)d-C(8)d	108.8(23)
C(11)b-C(10)b-C(9)b	116.4(28)	C(11)d-C(10)d-C(9)d	107.8(22)
C(12)b-C(10)b-C(9)b	112(3)	C(12)d-C(10)d-C(9)d	112.1(28)
C(12)b-C(10)b-C(11)b	112(3)	C(12)d-C(10)d-C(11)d	102.5(25)
C(10)b-C(11)b-C(6)b	111.4(25)	C(10)d-C(11)d-C(6)d	105.3(19)
C(14)b-C(13)b-C(7)b	109(5)	C(14)d-C(13)d-C(7)d	109.7(20)
C(15)b-C(13)b-C(7)b	118(4)	C(15)d-C(13)d-C(7)d	114.4(20)
C(15)b-C(13)b-C(14)b	115(5)	C(15)d-C(13)d-C(14)d	110.7(20)

(continued)

Table 3. Bond Angles (°) for $C_{22}H_{37}N_4O_{10}P$

O(6)a-N(2)a-O(5)a 122.7(18)	O(6)c-N(2)c-O(5)c 122.4(18)
C(18)a-N(2)a-O(5)a 116.1(15)	C(18)c-N(2)c-O(5)c 121.2(16)
C(18)a-N(2)a-O(6)a 121.2(17)	C(18)c-N(2)c-O(6)c 116.2(15)
O(8)a-N(3)a-O(7)a 124.9(23)	O(8)c-N(3)c-O(7)c 125.1(21)
C(21)a-N(3)a-O(7)a 117.9(22)	C(20)c-N(3)c-O(7)c 118.6(20)
C(21)a-N(3)a-O(8)a 117.2(20)	C(20)c-N(3)c-O(8)c 116.2(18)
O(10)a-N(4)a-O(9)a 120(3)	O(10)c-N(4)c-O(9)c 126.4(19)
C(22)a-N(4)a-O(9)a 109.4(24)	C(22)c-N(4)c-O(9)c 115.6(16)
C(22)a-N(4)a-O(10)a 117.3(29)	C(22)c-N(4)c-O(10)c 118.1(15)
C(18)a-C(17)a-O(4)a 122.6(12)	C(18)c-C(17)c-O(4)c 121.1(10)
C(22)a-C(17)a-O(4)a 117.3(12)	C(22)c-C(17)c-O(4)c 117.9(10)
C(22)a-C(17)a-C(18)a 120.0(10)	C(22)c-C(17)c-C(18)c 120.0(9)
C(17)a-C(18)a-N(2)a 123.2(11)	C(17)c-C(18)c-N(2)c 121.4(10)
C(19)a-C(18)a-N(2)a 116.8(12)	C(19)c-C(18)c-N(2)c 118.1(11)
C(19)a-C(18)a-C(17)a 120.0(10)	C(19)c-C(18)c-C(17)c 120.0(10)
C(21)a-C(19)a-C(18)a 120.0(11)	C(20)c-C(19)c-C(18)c 120.0(10)
C(19)a-C(21)a-N(3)a 121.1(14)	C(19)c-C(20)c-N(3)c 121.4(12)
C(20)a-C(21)a-N(3)a 118.9(14)	C(21)c-C(20)c-N(3)c 118.5(12)
C(20)a-C(21)a-C(19)a 120.0(10)	C(21)c-C(20)c-C(19)c 120.0(9)
C(22)a-C(20)a-C(21)a 120.0(10)	C(22)c-C(21)c-C(20)c 120.0(10)
C(17)a-C(22)a-N(4)a 123.0(14)	C(17)c-C(22)c-N(4)c 123.0(10)
C(20)a-C(22)a-N(4)a 116.9(14)	C(21)c-C(22)c-N(4)c 116.9(11)
C(20)a-C(22)a-C(17)a 120.0(11)	C(21)c-C(22)c-C(17)c 120.0(10)
O(6)b-N(2)b-O(5)b 127.6(25)	O(6)d-N(2)d-O(5)d 123.1(21)
C(17)b-N(2)b-O(5)b 119.7(20)	C(18)d-N(2)d-O(5)d 120.4(17)
C(17)b-N(2)b-O(6)b 112.7(19)	C(18)d-N(2)d-O(6)d 116.5(17)
O(8)b-N(3)b-O(7)b 125(3)	O8d-N(3)d-O(7)d 121.2(21)
C(19)b-N(3)b-O(7)b 116(3)	C(20)d-N(3)d-O(7)d 118.2(19)
C(19)b-N(3)b-O(8)b 118(3)	C(20)d-N(3)d-O8d 120.6(20)
O(10)b-N(4)b-O(9)b 126.2(27)	O(10)d-N(4)d-O(9)d 124.5(24)
C(21)b-N(4)b-O(9)b 117.3(22)	C(22)d-N(4)d-O(9)d 122.9(22)
C(21)b-N(4)b-O(10)b 115.9(23)	C(22)d-N(4)d-O(10)d 112.5(21)
C(18)b-C(17)b-N(2)b 117.6(12)	C(18)d-C(17)d-O(4)d 122.5(11)
C(22)b-C(17)b-N(2)b 122.2(14)	C(22)d-C(17)d-O(4)d 116.6(11)
C(22)b-C(17)b-C(18)b 120.0(12)	C(22)d-C(17)d-C(18)d 120.0(9)
C(19)b-C(18)b-C(17)b 120.0(11)	C(17)d-C(18)d-N(2)d 120.6(10)
C(18)b-C(19)b-N(3)b 121.1(20)	C(19)d-C(18)d-N(2)d 119.1(11)
C(20)b-C(19)b-N(3)b 118.9(21)	C(19)d-C(18)d-C(17)d 120.0(10)
C(20)b-C(19)b-C(18)b 120.0(13)	C(20)d-C(19)d-C(18)d 120.0(10)
C(21)b-C(20)b-C(19)b 120.0(12)	C(19)d-C(20)d-N(3)d 118.9(12)
C(20)b-C(21)b-N(4)b 120.3(14)	C(21)d-C(20)d-N(3)d 121.0(13)
C(22)b-C(21)b-N(4)b 119.7(14)	C(21)d-C(20)d-C(19)d 120.0(9)
C(22)b-C(21)b-C(20)b 120.0(11)	C(22)d-C(21)d-C(20)d 120.0(10)
C(17)b-C(22)b-O(4)b 123.3(14)	C(17)d-C(22)d-N(4)d 120.3(12)
C(21)b-C(22)b-O(4)b 116.8(12)	C(21)d-C(22)d-N(4)d 119.4(13)
C(21)b-C(22)b-C(17)b 120.0(13)	C(21)d-C(22)d-C(17)d 120.0(10)

Table 4. Non-bonded Contacts (Å) for $C_{22}H_{37}N_4O_{10}P$

N(1)a...P(1)a	2.778
C(6)a...P(1)a	2.698
C(16)a...P(1)a	2.663
O(2)a...O(1)a	2.556
O(3)a...O(1)a	2.521
O(3)a...O(2)a	2.473
C(1)a...O(2)a	2.570
C(7)a...O(2)a	2.396
C(11)a...O(2)a	2.454
C(1)a...O(3)a	2.608
C(3)a...N(1)a	2.406
C(4)a...N(1)a	2.461
C(5)a...N(1)a	2.452
O(4)a...N(1)a	2.761
C(2)a...C(1)a	2.517
C(4)a...C(3)a	2.590
C(5)a...C(3)a	2.521
C(5)a...C(4)a	2.581
C(8)a...C(6)a	2.418
C(9)a...C(6)a	2.882
C(10)a...C(6)a	2.529
C(13)a...C(6)a	2.531
C(9)a...C(7)a	2.567
C(11)a...C(7)a	2.619
C(14)a...C(7)a	2.632
C(15)a...C(7)a	2.572
C(10)a...C(8)a	2.541
C(13)a...C(8)a	2.530
C(11)a...C(9)a	2.503
C(12)a...C(9)a	2.540
C(12)a...C(11)a	2.467
C(15)a...C(14)a	2.633
N(1)b...P(1)b	2.761
C(6)b...P(1)b	2.751
C(16)b...P(1)b	2.591
O(2)b...O(1)b	2.642
O(3)b...O(1)b	2.525
O(3)b...O(2)b	2.486
C(1)b...O(2)b	2.561
C(7)b...O(2)b	2.324
C(11)b...O(2)b	2.458
C(1)b...O(3)b	2.672
C(3)b...N(1)b	2.513
C(4)b...N(1)b	2.446
C(5)b...N(1)b	2.538
C(2)b...C(1)b	2.478
C(4)b...C(3)b	2.587
C(5)b...C(3)b	2.538
C(5)b...C(4)b	2.596
C(8)b...C(6)b	2.464
C(10)b...C(6)b	2.489
C(13)b...C(6)b	2.582
C(9)b...C(7)b	2.543
C(10)b...C(7)b	2.898
C(11)b...C(7)b	2.549
C(14)b...C(7)b	2.508
C(15)b...C(7)b	2.653
C(10)b...C(8)b	2.503
C(13)b...C(8)b	2.635
C(11)b...C(9)b	2.525

C(12)b...C(9)b	2.575
C(12)b...C(11)b	2.494
C(15)b...C(14)b	2.406
N(1)c...P(1)c	2.751
C(6)c...P(1)c	2.674
C(16)c...P(1)c	2.682
O(2)c...O(1)c	2.516
O(3)c...O(1)c	2.431
C(1)c...O(1)c	2.674
O(3)c...O(2)c	2.499
C(1)c...O(2)c	2.581
C(7)c...O(2)c	2.482
C(11)c...O(2)c	2.376
C(1)c...O(3)c	2.634
C(3)c...N(1)c	2.494
C(4)c...N(1)c	2.493
C(5)c...N(1)c	2.558
O(4)c...N(1)c	2.647

1, 0.0000, 0.0000, 1.0000

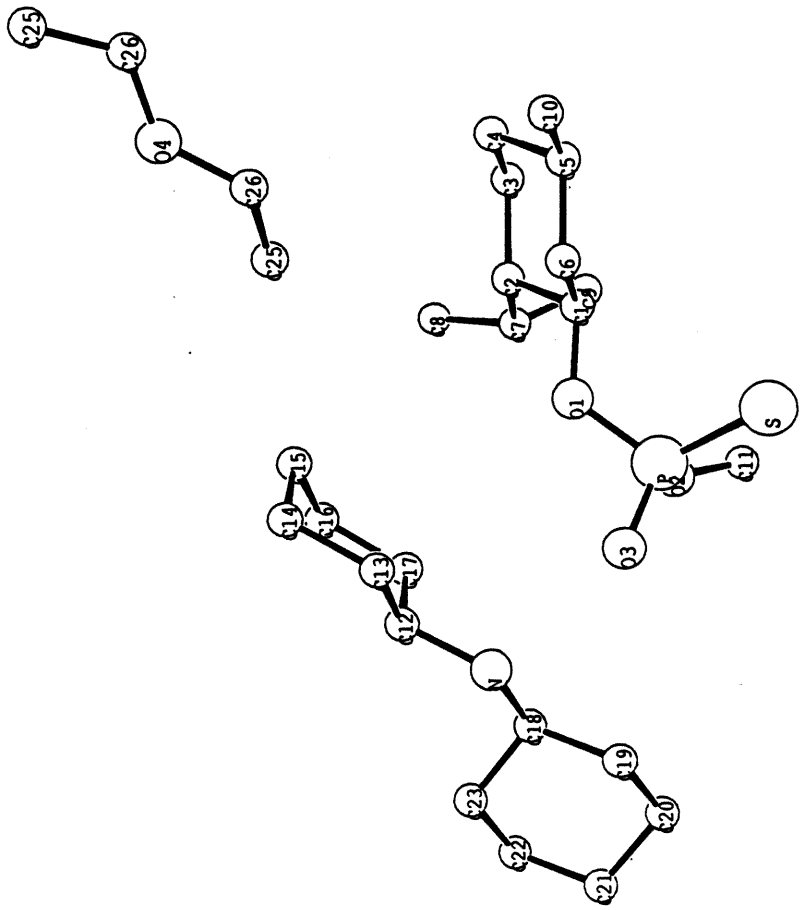
C(2)c...C(1)c	2.625
C(4)c...C(3)c	2.576
C(5)c...C(3)c	2.580
C(5)c...C(4)c	2.547
C(8)c...C(6)c	2.486
C(10)c...C(6)c	2.516
C(13)c...C(6)c	2.536
C(9)c...C(7)c	2.575
C(11)c...C(7)c	2.520
C(14)c...C(7)c	2.494
C(15)c...C(7)c	2.601
C(10)c...C(8)c	2.494
C(13)c...C(8)c	2.494
C(11)c...C(9)c	2.525
C(12)c...C(9)c	2.497
C(12)c...C(11)c	2.649
C(15)c...C(14)c	2.549
N(1)d...P(1)d	2.768
C(6)d...P(1)d	2.701
C(16)d...P(1)d	2.587
O(2)d...O(1)d	2.555
O(3)d...O(1)d	2.445
C(1)d...O(1)d	2.752
O(3)d...O(2)d	2.503
C(1)d...O(2)d	2.627
C(7)d...O(2)d	2.415
C(11)d...O(2)d	2.410
C(1)d...O(3)d	2.673
C(3)d...N(1)d	2.424
C(4)d...N(1)d	2.455
C(5)d...N(1)d	2.476
O(4)d...N(1)d	2.748
C(2)d...C(1)d	2.604
C(4)d...C(3)d	2.567
C(5)d...C(3)d	2.508
C(5)d...C(4)d	2.526
C(8)d...C(6)d	2.457
C(9)d...C(6)d	2.896
C(10)d...C(6)d	2.501
C(13)d...C(6)d	2.558
C(9)d...C(7)d	2.536
C(11)d...C(7)d	2.489
C(14)d...C(7)d	2.591

C(15)d...C(7)d	2.640
C(10)d...C(8)d	2.523
C(13)d...C(8)d	2.617
C(11)d...C(9)d	2.555
C(12)d...C(9)d	2.636
C(12)d...C(11)d	2.496
C(15)d...C(14)d	2.550
O(6)a...O(4)a	2.668
O(9)a...O(4)a	2.589
C(18)a...O(4)a	2.378
C(22)a...O(4)a	2.315
O(6)a...O(5)a	2.119
C(18)a...O(5)a	2.254
C(19)a...O(5)a	2.619
C(18)a...O(6)a	2.337
O(8)a...O(7)a	2.181
C(21)a...O(7)a	2.279
C(20)a...O(7)a	2.693
C(19)a...O(8)a	2.733
C(21)a...O(8)a	2.290
O(10)a...O(9)a	2.183
C(22)a...O(9)a	2.336
C(20)a...O(10)a	2.672
C(22)a...O(10)a	2.276
C(17)a...N(2)a	2.509
C(19)a...N(2)a	2.430
C(19)a...N(3)a	2.468
C(20)a...N(3)a	2.441
C(17)a...N(4)a	2.546
C(20)a...N(4)a	2.470
C(19)a...C(17)a	2.416
C(21)a...C(17)a	2.790
C(20)a...C(17)a	2.416
C(21)a...C(18)a	2.416
C(20)a...C(18)a	2.790
C(22)a...C(18)a	2.416
C(20)a...C(19)a	2.416
C(22)a...C(19)a	2.790
C(22)a...C(21)a	2.416
O(5)b...O(4)b	2.640
N(4)b...O(4)b	2.721
C(17)b...O(4)b	2.381
C(21)b...O(4)b	2.304
O(6)b...O(5)b	2.199
C(17)b...O(5)b	2.326
C(17)b...O(6)b	2.278
C(18)b...O(6)b	2.613
O(8)b...O(7)b	2.239
C(18)b...O(7)b	2.644
C(19)b...O(7)b	2.209
C(19)b...O(8)b	2.299
C(20)b...O(8)b	2.676
O(10)b...O(9)b	2.239
C(21)b...O(9)b	2.301
C(21)b...O(10)b	2.361
C(18)b...N(2)b	2.463
C(22)b...N(2)b	2.520
C(18)b...N(3)b	2.415
C(20)b...N(3)b	2.389
C(20)b...N(4)b	2.494
C(22)b...N(4)b	2.487
C(19)b...C(17)b	2.416

C(20)b...C(17)b	2.790
C(21)b...C(17)b	2.416
C(20)b...C(18)b	2.416
C(21)b...C(18)b	2.790
C(22)b...C(18)b	2.416
C(21)b...C(19)b	2.416
C(22)b...C(19)b	2.790
C(22)b...C(20)b	2.416
C(18)c...O(4)c	2.406
C(22)c...O(4)c	2.368
O(6)c...O(5)c	2.130
C(18)c...O(5)c	2.312
C(18)c...O(6)c	2.294
C(19)c...O(6)c	2.727
O(8)c...O(7)c	2.139
C(20)c...O(7)c	2.259
C(21)c...O(7)c	2.668
C(19)c...O(8)c	2.680
C(20)c...O(8)c	2.230
O(10)c...O(9)c	2.197
C(21)c...O(9)c	2.733
C(22)c...O(9)c	2.265
C(22)c...O(10)c	2.330
C(17)c...N(2)c	2.489
C(19)c...N(2)c	2.448
C(19)c...N(3)c	2.453
C(21)c...N(3)c	2.418
C(17)c...N(4)c	2.512
C(21)c...N(4)c	2.435
C(19)c...C(17)c	2.417
C(20)c...C(17)c	2.790
C(21)c...C(17)c	2.416
C(20)c...C(18)c	2.416
C(21)c...C(18)c	2.790
C(22)c...C(18)c	2.416
C(21)c...C(19)c	2.416
C(22)c...C(19)c	2.790
C(22)c...C(20)c	2.416
O(5)d...O(4)d	2.724
O(9)d...O(4)d	2.688
N(4)d...O(4)d	2.733
C(18)d...O(4)d	2.391
C(22)d...O(4)d	2.320
O(6)d...O(5)d	2.131
C(17)d...O(5)d	2.815
C(18)d...O(5)d	2.304
C(18)d...O(6)d	2.339
C(19)d...O(6)d	2.786
O8d...O(7)d	2.088
C(20)d...O(7)d	2.267
C(21)d...O(7)d	2.728
C(19)d...O8d	2.729
C(20)d...O8d	2.293
O(10)d...O(9)d	2.172
C(17)d...O(9)d	2.817
C(22)d...O(9)d	2.251
C(21)d...O(10)d	2.722
C(22)d...O(10)d	2.276
C(17)d...N(2)d	2.503
C(19)d...N(2)d	2.485
C(19)d...N(3)d	2.440
C(21)d...N(3)d	2.467

C(17)d...N(4)d	2.441
C(21)d...N(4)d	2.430
C(19)d...C(17)d	2.416
C(20)d...C(17)d	2.790
C(21)d...C(17)d	2.416
C(20)d...C(18)d	2.417
C(21)d...C(18)d	2.790
C(22)d...C(18)d	2.416
C(21)d...C(19)d	2.416
C(22)d...C(19)d	2.790
C(22)d...C(20)d	2.416

FIG. 20


C25
C26
O4
O26
C25
C4
C10
C5
C3
C6
C2
C9
C8
C7
O1
S
O2
C11
O3
C15
C14
C16
C13
C17
C12
N
C18
C19
C23
C20
C22
C21

Dicyclohexylammonium $(R)_P$-*O*-[(1*R*, 2*S*, 5*R*)-menthyl]-*O*-methylphosphorothioate

Table 1. Fractional atomic co-ordinates and thermal parameters for $C_{23}H_{46}NO_3PS$

Atom	x	y	z	Ueq	
Ueq = 1/3 trace of the orthogonalised U					
P	0.13982(13)	0.22440(0)	0.11725(15)	0.0398(9)	
S	0.15288(17)	0.0319(3)	0.10300(18)	0.0583(10)	
N	0.1996(5)	0.5751(9)	0.0203(5)	0.0401(28)	
O(1)	0.1639(4)	0.2764(7)	0.2073(4)	0.0541(26)	
O(2)	0.0578(5)	0.2628(11)	0.1202(9)	0.132(6)	
O(3)	0.1778(5)	0.3134(8)	0.0561(5)	0.071(3)	
C(1)	0.1596(5)	0.2003(11)	0.2825(6)	0.046(4)	
C(2)	0.1356(5)	0.2901(12)	0.3527(6)	0.051(4)	
C(3)	0.1376(6)	0.2113(13)	0.4358(5)	0.058(4)	
C(4)	0.2123(6)	0.1554(15)	0.4530(8)	0.076(5)	
C(5)	0.2374(7)	0.0636(15)	0.3814(7)	0.077(5)	
C(6)	0.2337(6)	0.1424(14)	0.3016(7)	0.060(4)	
C(7)	0.0620(7)	0.3621(13)	0.3363(7)	0.065(5)	
C(8)	0.0502(8)	0.4842(16)	0.3920(8)	0.092(6)	
C(9)	-0.0034(7)	0.2689(17)	0.3465(9)	0.094(6)	
C(10)	0.3134(8)	0.0110(19)	0.3972(10)	0.113(7)	
C(11)	-0.0011(7)	0.1899(21)	0.1112(10)	0.115(8)	
C(12)	0.2164(5)	0.6541(11)	0.0986(6)	0.045(4)	
C(13)	0.2850(5)	0.5954(12)	0.1356(6)	0.055(4)	
C(14)	0.3055(7)	0.6679(15)	0.2169(7)	0.079(5)	
C(15)	0.2436(7)	0.6628(12)	0.2780(7)	0.066(5)	
C(16)	0.1756(7)	0.7195(15)	0.2401(7)	0.074(5)	
C(17)	0.1553(6)	0.6545(11)	0.1603(6)	0.053(4)	
C(18)	0.1320(5)	0.6115(11)	-0.0301(6)	0.044(4)	
C(19)	0.1258(6)	0.5163(12)	-0.1024(6)	0.050(4)	
C(20)	0.0598(6)	0.5443(16)	-0.1547(8)	0.075(5)	
C(21)	0.0602(7)	0.6876(15)	-0.1851(7)	0.073(5)	
C(22)	0.0673(7)	0.7825(15)	-0.1150(9)	0.081(6)	
C(23)	0.1350(7)	0.7545(11)	-0.0615(8)	0.067(5)	
O(4)	0.50000(0)	0.409(3)	0.50000(0)	0.207(10)	*
C(25)	0.4036(18)	0.420(4)	0.3937(19)	0.200(11)	*
C(26)	0.4586(26)	0.355(6)	0.4357(28)	0.283(19)	*
Hn(1)	0.247(6)	0.574(11)	-0.013(7)	0.0700(0)	*
Hn(2)	0.198(6)	0.487(14)	0.034(7)	0.0700(0)	*

the hydrogen atoms on the nitrogen were located and refined all other hydrogen atoms were included in calculated positions with C-H = 0.95Å . fixed isotropic thermal parameters were empoyed for all hydrogen atoms.

Table 1A. hydrogen atom co-ordinates for $C_{23}H_{46}NO_3PS$

Atom	x	y	z	Ueq	
Hn(1)	0.247(6)	0.574(11)	-0.013(7)	0.0700(0)	*
Hn(2)	0.198(6)	0.487(14)	0.034(7)	0.0700(0)	*
H(1)	0.1242(5)	0.1304(11)	0.2763(6)	0.0600(0)	*
H(2)	0.1709(5)	0.3603(12)	0.3582(6)	0.0600(0)	*
H(5)	0.2043(7)	-0.0106(15)	0.3791(7)	0.0600(0)	*
H(7)	0.0619(7)	0.3901(13)	0.2790(7)	0.0600(0)	*
H(12)	0.2248(5)	0.7460(11)	0.0842(6)	0.0600(0)	*
H(18)	0.0918(5)	0.6020(11)	0.0074(6)	0.0600(0)	*
H(3)a	0.1040(6)	0.1381(13)	0.4317(5)	0.0600(0)	*
H(3)b	0.1230(6)	0.2698(13)	0.4803(5)	0.0600(0)	*
H(4)a	0.2458(6)	0.2286(15)	0.4581(8)	0.0600(0)	*
H(4)b	0.2117(6)	0.1056(15)	0.5043(8)	0.0600(0)	*
H(6)a	0.2673(6)	0.2156(14)	0.3052(7)	0.0600(0)	*
H(6)b	0.2476(6)	0.0840(14)	0.2569(7)	0.0600(0)	*
H(8)a	0.0913(8)	0.5427(16)	0.3868(8)	0.0600(0)	*
H(8)b	0.0468(8)	0.4532(16)	0.4485(8)	0.0600(0)	*
H(8)c	0.0067(8)	0.5319(16)	0.3773(8)	0.0600(0)	*
H(9)a	0.0036(7)	0.1948(17)	0.3093(9)	0.0600(0)	*
H(9)b	-0.0473(7)	0.3153(17)	0.3316(9)	0.0600(0)	*
H(9)c	-0.0072(7)	0.2366(17)	0.4028(9)	0.0600(0)	*
H(10)a	0.3150(8)	-0.0382(19)	0.4486(10)	0.0600(0)	*
H(10)b	0.3469(8)	0.0844(19)	0.4001(10)	0.0600(0)	*
H(10)c	0.3264(8)	-0.0469(19)	0.3519(10)	0.0600(0)	*
H(11)a	-0.0429(7)	0.2462(21)	0.1178(10)	0.0600(0)	*
H(11)b	-0.0034(7)	0.1172(21)	0.1502(10)	0.0600(0)	*
H(11)c	-0.0002(7)	0.1550(21)	0.0554(10)	0.0600(0)	*
H(13)a	0.3240(5)	0.6021(12)	0.0962(6)	0.0600(0)	*
H(13)b	0.2769(5)	0.5030(12)	0.1492(6)	0.0600(0)	*
H(14)a	0.3480(7)	0.6277(15)	0.2411(7)	0.0600(0)	*
H(14)b	0.3155(7)	0.7595(15)	0.2033(7)	0.0600(0)	*
H(15)a	0.2565(7)	0.7132(12)	0.3269(7)	0.0600(0)	*
H(15)b	0.2347(7)	0.5714(12)	0.2933(7)	0.0600(0)	*
H(16)a	0.1841(7)	0.8124(15)	0.2284(7)	0.0600(0)	*
H(16)b	0.1365(7)	0.7115(15)	0.2792(7)	0.0600(0)	*
H(17)a	0.1410(6)	0.5642(11)	0.1725(6)	0.0600(0)	*
H(17)b	0.1152(6)	0.7016(11)	0.1356(6)	0.0600(0)	*
H(19)a	0.1674(6)	0.5325(12)	-0.1369(6)	0.0600(0)	*
H(19)b	0.1254(6)	0.4243(12)	-0.0853(6)	0.0600(0)	*
H(20)a	0.0185(6)	0.5325(16)	-0.1191(8)	0.0600(0)	*
H(20)b	0.0570(6)	0.4823(16)	-0.2004(8)	0.0600(0)	*
H(21)a	0.0152(7)	0.7021(15)	-0.2143(7)	0.0600(0)	*
H(21)b	0.1000(7)	0.6993(15)	-0.2229(7)	0.0600(0)	*
H(22)a	0.0705(7)	0.8713(15)	-0.1374(9)	0.0600(0)	*
H(22)b	0.0255(7)	0.7760(15)	-0.0798(9)	0.0600(0)	*
H(23)a	0.1396(7)	0.8180(11)	-0.0168(8)	0.0600(0)	*
H(23)b	0.1768(7)	0.7602(11)	-0.0969(8)	0.0600(0)	*

* Isotropic thermal parameter

Table 2. Bond Lengths (Å) for $C_{23}H_{46}NO_3PS$

O(1)-P	1.577(7)	C(8)-C(7)	1.512(17)
O(2)-P	1.543(9)	C(9)-C(7)	1.516(18)
O(3)-P	1.483(8)	C(13)-C(12)	1.494(14)
Hn(1)-N	1.01(12)	C(17)-C(12)	1.485(14)
Hn(2)-N	0.89(14)	C(14)-C(13)	1.520(14)
C(12)-N	1.498(12)	C(15)-C(14)	1.490(16)
C(18)-N	1.509(12)	C(16)-C(15)	1.486(16)
C(1)-O(1)	1.413(11)	C(17)-C(16)	1.464(16)
C(11)-O(2)	1.299(17)	C(19)-C(18)	1.487(14)
C(2)-C(1)	1.491(14)	C(23)-C(18)	1.501(15)
C(6)-C(1)	1.497(14)	C(20)-C(19)	1.482(15)
C(3)-C(2)	1.531(14)	C(21)-C(20)	1.497(19)
C(7)-C(2)	1.539(16)	C(22)-C(21)	1.459(17)
C(4)-C(3)	1.494(15)	C(23)-C(22)	1.520(16)
C(5)-C(4)	1.526(18)	C(26)-O(4)	1.37(5)
C(6)-C(5)	1.486(16)	C(26)-C(25)	1.36(5)
C(10)-C(5)	1.499(18)	S-P	1.932(3)

Table 3. Bond Angles (°) for $C_{23}H_{46}NO_3PS$

O(2)-P-O(1)	99.1(6)	C(17)-C(12)-N	113.3(8)
O(3)-P-O(1)	105.6(4)	C(17)-C(12)-H(12)	106.1(6)
O(3)-P-O(2)	109.2(6)	C(17)-C(12)-C(13)	111.8(8)
Hn(2)-N-Hn(1)	98(10)	H(13)a-C(13)-C(12)	109.9(5)
C(12)-N-Hn(1)	105(6)	H(13)b-C(13)-C(12)	109.5(5)
C(12)-N-Hn(2)	109(8)	C(14)-C(13)-C(12)	110.5(9)
C(18)-N-Hn(1)	115(6)	C(14)-C(13)-H(13)a	110.0(6)
C(18)-N-Hn(2)	110(8)	C(14)-C(13)-H(13)b	107.4(6)
C(18)-N-C(12)	118.5(8)	H(14)a-C(14)-C(13)	110.0(7)
C(1)-O(1)-P	125.0(6)	H(14)b-C(14)-C(13)	107.7(6)
C(11)-O(2)-P	131.3(11)	C(15)-C(14)-C(13)	110.6(9)
H(1)-C(1)-O(1)	109.9(5)	C(15)-C(14)-H(14)a	109.9(6)
C(2)-C(1)-O(1)	109.3(8)	C(15)-C(14)-H(14)b	109.1(7)
C(2)-C(1)-H(1)	108.1(5)	H(15)a-C(15)-C(14)	109.2(6)
C(6)-C(1)-O(1)	108.7(8)	H(15)b-C(15)-C(14)	109.1(7)
C(6)-C(1)-H(1)	110.7(6)	C(16)-C(15)-C(14)	110.9(9)
C(6)-C(1)-C(2)	110.2(8)	C(16)-C(15)-H(15)a	109.5(6)
H(2)-C(2)-C(1)	107.6(5)	C(16)-C(15)-H(15)b	108.7(7)
C(3)-C(2)-C(1)	109.4(9)	H(16)a-C(16)-C(15)	107.9(7)
C(3)-C(2)-H(2)	106.3(5)	H(16)b-C(16)-C(15)	109.3(6)
C(7)-C(2)-C(1)	114.0(8)	C(17)-C(16)-C(15)	112.9(10)
C(7)-C(2)-H(2)	105.5(6)	C(17)-C(16)-H(16)a	107.3(7)
C(7)-C(2)-C(3)	113.5(8)	C(17)-C(16)-H(16)b	109.9(6)
H(3)a-C(3)-C(2)	108.5(5)	C(16)-C(17)-C(12)	112.5(9)
H(3)b-C(3)-C(2)	108.8(6)	H(17)a-C(17)-C(12)	109.8(6)
C(4)-C(3)-C(2)	111.3(8)	H(17)a-C(17)-C(16)	107.8(7)
C(4)-C(3)-H(3)a	108.4(7)	H(17)b-C(17)-C(12)	107.9(6)
C(4)-C(3)-H(3)b	110.3(6)	H(17)b-C(17)-C(16)	109.4(7)
H(4)a-C(4)-C(3)	108.5(7)	H(18)-C(18)-N	105.9(5)
H(4)b-C(4)-C(3)	109.5(6)	C(19)-C(18)-N	108.4(8)
C(5)-C(4)-C(3)	111.1(9)	C(19)-C(18)-H(18)	111.3(5)
C(5)-C(4)-H(4)a	108.8(7)	C(23)-C(18)-N	111.7(8)
C(5)-C(4)-H(4)b	109.5(7)	C(23)-C(18)-H(18)	109.3(7)
H(5)-C(5)-C(4)	107.2(7)	C(23)-C(18)-C(19)	110.1(8)
C(6)-C(5)-C(4)	108.0(11)	H(19)a-C(19)-C(18)	106.2(5)
C(6)-C(5)-H(5)	110.3(7)	H(19)b-C(19)-C(18)	112.7(5)
C(10)-C(5)-C(4)	111.2(10)	C(20)-C(19)-C(18)	111.8(9)
C(10)-C(5)-H(5)	108.8(9)	C(20)-C(19)-H(19)a	107.1(6)
C(10)-C(5)-C(6)	111.3(11)	C(20)-C(19)-H(19)b	109.4(7)
C(5)-C(6)-C(1)	114.2(9)	H(20)a-C(20)-C(19)	106.7(6)
H(6)a-C(6)-C(1)	107.5(6)	H(20)b-C(20)-C(19)	110.2(7)
H(6)a-C(6)-C(5)	108.8(7)	C(21)-C(20)-C(19)	110.6(11)
H(6)b-C(6)-C(1)	109.0(6)	C(21)-C(20)-H(20)a	108.2(7)
H(6)b-C(6)-C(5)	107.8(7)	C(21)-C(20)-H(20)b	111.6(7)
H(7)-C(7)-C(2)	107.1(5)	H(21)a-C(21)-C(20)	107.1(7)
C(8)-C(7)-C(2)	113.3(10)	H(21)b-C(21)-C(20)	108.8(7)
C(8)-C(7)-H(7)	109.0(7)	C(22)-C(21)-C(20)	111.4(10)
C(9)-C(7)-C(2)	112.7(11)	C(22)-C(21)-H(21)a	110.4(7)
C(9)-C(7)-H(7)	106.4(7)	C(22)-C(21)-H(21)b	109.6(7)
C(9)-C(7)-C(8)	108.1(10)	H(22)a-C(22)-C(21)	108.4(7)
H(8)a-C(8)-C(7)	108.8(7)	H(22)b-C(22)-C(21)	109.6(7)
H(8)b-C(8)-C(7)	107.6(7)	C(23)-C(22)-C(21)	112.2(11)
H(8)c-C(8)-C(7)	111.9(7)	C(23)-C(22)-H(22)a	109.0(7)
H(9)a-C(9)-C(7)	107.1(7)	C(23)-C(22)-H(22)b	108.1(8)
H(9)b-C(9)-C(7)	109.9(8)	C(22)-C(23)-C(18)	109.0(10)
H(9)c-C(9)-C(7)	111.4(7)	H(23)a-C(23)-C(18)	112.3(6)
H(10)a-C(10)-C(5)	110.3(8)	H(23)a-C(23)-C(22)	111.3(7)

H(10)b-C(10)-C(5)	109.6(9)	H(23)b-C(23)-C(18)	106.5(7)
H(10)c-C(10)-C(5)	108.5(8)	H(23)b-C(23)-C(22)	108.0(8)
H(11)a-C(11)-O(2)	109.0(9)	C(25)-C(26)-O(4)	126(5)
H(11)b-C(11)-O(2)	112.8(10)	C(26)-O(4)-C(26)	135(6)
H(11)c-C(11)-O(2)	106.6(9)	O(1)-P-S	113.2(3)
H(12)-C(12)-N	109.4(5)	O(2)-P-S	111.4(4)
C(13)-C(12)-N	106.8(8)	O(3)-P-S	116.8(3)
C(13)-C(12)-H(12)	109.4(5)		

Table 4. Anisotropic thermal parameters (x10**4)

Atom	U11	U22	U33	U23	U13	U12
P	389(15)	317(15)	489(15)	40(14)	13(11)	10(13)
S	764(20)	318(15)	668(18)	-24(14)	131(15)	80(14)
N	398(50)	325(44)	480(50)	-12(38)	9(40)	-54(39)
O(1)	968(57)	329(36)	327(39)	-30(31)	168(35)	4(36)
O(2)	352(55)	754(66)	2839(150)	-548(83)	-326(65)	146(45)
O(3)	1169(68)	497(49)	470(43)	43(37)	79(41)	-248(45)
C(1)	482(61)	509(62)	394(59)	107(51)	60(45)	33(54)
C(2)	365(60)	547(63)	615(69)	-66(56)	48(49)	-72(50)
C(3)	759(75)	722(73)	259(52)	44(57)	3(46)	-191(71)
C(4)	600(77)	984(102)	704(81)	187(74)	-177(61)	-27(70)
C(5)	806(89)	873(92)	639(82)	-13(73)	-223(68)	118(73)
C(6)	548(70)	684(75)	575(69)	-71(66)	-6(53)	76(66)
C(7)	784(89)	812(89)	354(59)	-44(61)	127(56)	59(74)
C(8)	881(98)	1042(116)	831(89)	-159(83)	226(76)	128(85)
C(9)	802(93)	1199(132)	827(90)	-205(90)	47(70)	198(97)
C(10)	1163(129)	1011(117)	1217(118)	-50(106)	-450(99)	394(107)
C(11)	626(102)	1584(182)	1241(122)	-283(120)	106(81)	261(106)
C(12)	539(66)	408(63)	389(58)	-18(45)	-26(49)	-53(49)
C(13)	521(65)	624(78)	505(61)	55(54)	1(52)	-132(56)
C(14)	898(94)	931(105)	549(75)	135(64)	-180(68)	-290(75)
C(15)	1132(103)	523(73)	329(63)	33(47)	-255(66)	-185(67)
C(16)	1111(96)	667(78)	455(64)	5(75)	243(65)	7(86)
C(17)	701(75)	404(66)	483(64)	-18(51)	122(55)	104(53)
C(18)	377(55)	539(72)	415(54)	97(57)	49(44)	-92(54)
C(19)	540(68)	469(62)	495(59)	-29(57)	17(50)	49(55)
C(20)	539(74)	1013(109)	700(74)	-29(82)	-100(61)	-167(76)
C(21)	532(70)	1135(117)	531(73)	172(72)	-144(54)	-216(69)
C(22)	766(95)	728(90)	937(103)	223(82)	-286(80)	65(71)
C(23)	752(79)	329(67)	932(87)	-4(61)	-185(65)	79(57)

The anisotropic displacement parameter has the form:
exp[-2pi^2(U11h^2a*^2+ ... +2U12hka*b*)]

Table 5. Non-bonded Contacts (Å)

C(1)...P	2.653				
H(1)...P	2.703				
C(11)...P	2.591				
H(11)b...P	2.866				
H(11)c...P	2.813				
O(1)...S	2.935				
O(2)...S	2.880				
O(3)...S	2.918				
C(1)...S	3.299				
H(1)...S	2.963				
H(6)b...S	3.025				
C(11)...S	3.214				
H(16)a...S	2.997	1,	0.0000,	1.0000,	0.0000
H(23)a...S	2.853	1,	0.0000,	1.0000,	0.0000
N...S	3.357	2,	0.5000,	0.5000,	0.0000
Hn(1)...S	2.359	2,	0.5000,	0.5000,	0.0000
O(3)...N	2.680				
H(12)...N	2.022				
C(13)...N	2.402				
H(13)a...N	2.574				
H(13)b...N	2.577				
C(17)...N	2.493				
H(18)...N	1.992				
C(19)...N	2.431				
H(19)a...N	2.592				
H(19)b...N	2.614				
C(23)...N	2.490				
Hn(2)...Hn(1)	1.437				
C(12)...Hn(1)	2.016				
C(13)...Hn(1)	2.455				
H(13)a...Hn(1)	2.235				
C(18)...Hn(1)	2.146				
O(3)...Hn(2)	1.798				
C(12)...Hn(2)	1.972				
C(13)...Hn(2)	2.495				
C(18)...Hn(2)	1.992				
C(19)...Hn(2)	2.539				
O(2)...O(1)	2.374				
O(3)...O(1)	2.439				
H(1)...O(1)	1.952				
C(2)...O(1)	2.369				
H(2)...O(1)	2.535				
C(6)...O(1)	2.365				
H(6)a...O(1)	2.509				
H(6)b...O(1)	2.560				
C(7)...O(1)	2.895				
H(7)...O(1)	2.455				
O(3)...O(2)	2.467				
H(11)a...O(2)	1.842				
H(11)b...O(2)	1.883				
H(11)c...O(2)	1.815				
H(2)...C(1)	1.996				
C(3)...C(1)	2.467				
H(3)a...C(1)	2.649				
C(4)...C(1)	2.899				
C(5)...C(1)	2.505				
H(6)a...C(1)	2.000				
H(6)b...C(1)	2.017				

C(7)...C(1)	2.542
H(7)...C(1)	2.587
C(2)...H(1)	2.002
C(3)...H(1)	2.663
C(6)...H(1)	2.036
H(3)a...C(2)	2.042
H(3)b...C(2)	2.045
C(4)...C(2)	2.498
H(4)a...C(2)	2.675
C(5)...C(2)	2.943
C(6)...C(2)	2.450
H(6)a...C(2)	2.625
H(7)...C(2)	2.033
C(8)...C(2)	2.549
C(9)...C(2)	2.543
H(9)a...C(2)	2.670
C(3)...H(2)	2.015
C(4)...H(2)	2.632
C(6)...H(2)	2.602
C(7)...H(2)	2.013
C(8)...H(2)	2.576
H(4)a...C(3)	2.008
H(4)b...C(3)	2.020
C(5)...C(3)	2.491
H(5)...C(3)	2.667
C(6)...C(3)	2.845
C(7)...C(3)	2.567
C(9)...C(3)	2.983
H(3)b...H(3)a	1.551
C(4)...H(3)a	2.007
C(5)...H(3)a	2.665
C(4)...H(3)b	2.029
H(5)...C(4)	2.022
C(6)...C(4)	2.437
H(6)a...C(4)	2.621
C(10)...C(4)	2.495
H(10)a...C(4)	2.678
H(4)b...H(4)a	1.551
C(5)...H(4)a	2.041
C(6)...H(4)a	2.631
C(10)...H(4)a	2.663
C(5)...H(4)b	2.049
H(6)a...C(5)	2.005
H(6)b...C(5)	1.993
H(10)a...C(5)	2.033
H(10)b...C(5)	2.026
H(10)c...C(5)	2.012
C(6)...H(5)	2.023
C(10)...H(5)	2.017
C(10)...C(6)	2.464
H(10)b...C(6)	2.644
H(10)c...C(6)	2.642
H(6)b...H(6)a	1.551
C(10)...H(6)a	2.630
C(10)...H(6)b	2.623
H(8)a...C(7)	2.028
H(8)b...C(7)	2.015
H(8)c...C(7)	2.064
H(9)a...C(7)	2.012
H(9)b...C(7)	2.044

H(9)c...C(7)	2.061				
C(8)...H(7)	2.031				
C(9)...H(7)	2.003				
H(9)a...H(7)	2.257				
C(9)...C(8)	2.450				
H(9)b...C(8)	2.617				
H(9)c...C(8)	2.669				
H(8)b...H(8)a	1.551				
H(8)c...H(8)a	1.551				
H(8)c...H(8)b	1.551				
C(9)...H(8)b	2.601				
C(9)...H(8)c	2.653				
H(9)b...H(9)a	1.551				
H(9)c...H(9)a	1.551				
H(9)c...H(9)b	1.551				
H(10)b...H(10)a	1.551				
H(10)c...H(10)a	1.551				
H(10)c...H(10)b	1.551				
H(11)c...C(11)	2.662	2,	0.0000,	0.0000,	0.0000
H(11)b...H(11)a	1.551				
H(11)c...H(11)a	1.551				
H(11)c...H(11)b	1.551				
H(11)c...H(11)c	1.755	2,	0.0000,	0.0000,	0.0000
H(13)a...C(12)	2.026				
H(13)b...C(12)	2.020				
C(14)...C(12)	2.476				
H(14)b...C(12)	2.658				
C(15)...C(12)	2.885				
C(16)...C(12)	2.453				
H(16)a...C(12)	2.653				
H(17)a...C(12)	2.016				
H(17)b...C(12)	1.993				
C(18)...C(12)	2.584				
C(23)...C(12)	3.097				
C(13)...H(12)	2.020				
C(14)...H(12)	2.675				
C(16)...H(12)	2.646				
C(17)...H(12)	1.973				
H(17)b...H(12)	2.203				
H(14)a...C(13)	2.050				
H(14)b...C(13)	2.023				
C(15)...C(13)	2.475				
H(15)b...C(13)	2.676				
C(16)...C(13)	2.874				
C(17)...C(13)	2.467				
H(13)b...H(13)a	1.551				
C(14)...H(13)a	2.050				
C(14)...H(13)b	2.019				
C(15)...H(13)b	2.654				
H(15)a...C(14)	2.014				
H(15)b...C(14)	2.013				
C(16)...C(14)	2.450				
H(16)a...C(14)	2.639				
C(17)...C(14)	2.877				
H(14)b...H(14)a	1.551				
C(15)...H(14)a	2.021				
C(15)...H(14)b	2.012				
C(16)...H(14)b	2.648				
H(16)a...C(15)	1.994				
H(16)b...C(15)	2.011				

C(17)...C(15)	2.459
H(15)b...H(15)a	1.551
C(16)...H(15)a	2.013
C(16)...H(15)b	2.003
C(17)...H(15)b	2.680
H(17)a...C(16)	1.974
H(17)b...C(16)	1.992
H(16)b...H(16)a	1.551
C(17)...H(16)a	1.968
H(17)b...H(16)a	2.220
C(17)...H(16)b	1.998
H(17)a...H(16)b	2.234
C(18)...C(17)	3.076
H(17)b...H(17)a	1.551
H(19)a...C(18)	1.976
H(19)b...C(18)	2.051
C(20)...C(18)	2.459
H(20)a...C(18)	2.616
C(21)...C(18)	2.878
C(22)...C(18)	2.459
H(22)b...C(18)	2.650
H(23)a...C(18)	2.059
H(23)b...C(18)	1.991
C(19)...H(18)	2.035
C(22)...H(18)	2.673
C(23)...H(18)	2.024
H(20)a...C(19)	1.977
H(20)b...C(19)	2.018
C(21)...C(19)	2.450
H(21)b...C(19)	2.671
C(22)...C(19)	2.847
C(23)...C(19)	2.449
H(23)b...C(19)	2.587
H(19)b...H(19)a	1.551
C(20)...H(19)a	1.982
C(21)...H(19)a	2.596
C(23)...H(19)a	2.570
C(20)...H(19)b	2.008
H(21)a...C(20)	1.995
H(21)b...C(20)	2.015
C(22)...C(20)	2.442
H(22)b...C(20)	2.658
C(23)...C(20)	2.892
H(20)b...H(20)a	1.551
C(21)...H(20)a	2.008
H(21)a...H(20)a	2.257
C(22)...H(20)a	2.628
C(21)...H(20)b	2.047
H(22)a...C(21)	1.977
H(22)b...C(21)	1.990
C(23)...C(21)	2.472
H(23)b...C(21)	2.638
H(21)b...H(21)a	1.551
C(22)...H(21)a	1.999
C(22)...H(21)b	1.990
H(22)a...H(21)b	2.241
H(23)a...C(22)	2.064
H(23)b...C(22)	2.027
H(22)b...H(22)a	1.551
C(23)...H(22)a	2.038

C(23)...H(22)b	2.027				
H(23)b...H(23)a	1.551				
C(25)...O(4)	2.430				
C(26)...C(26)	2.528	2,	1.0000,	0.0000,	1.0000

References

1) D. V. Banthorpe in Patai, *The Chemistry of the Azido Group*, 1971, Interscience, London, p. 397.

2) P. A. S. Smith, *Org. Reactions*, 1946, 3, 337.

3) E. S. Wallis and J. F. Lane, *Org. Reactions*, 1946, 3, 267.

4) L. Bauer and O. Exner, *Angew. Chem. Internat. Edit.*, 1974, 13, 376.

5) M. J. P. Harger and M. A. Stephen, *J. Chem. Soc., Perkin Trans. 1*, 1981, 736; M. J. P. Harger and S. Westlake, *Tetrahedron*, 1982, 38, 1511.

6) G. Bertrand, J.-P. Majoral, and A. Baceiredo, *Tetrahedron Lett.*, 1980, 21, 5015.

7) F. H. Westheimer, *Chem. Rev.*, 1981, 81, 313; M. Regitz and G. Maas, *Top. Curr. Chem.*, 1981, 97, 71.

8) F. Weissbach and W. Jugelt, *J. Prakt. Chem.*, 1975, 317, 394; W. T. Reichte, *Inorg. Chem.*, 1964, 3, 402.

9) M. J. P. Harger and M. A. Stephen, *J. Chem. Soc., Perkin Trans. 1*, 1980, 705.

10) H. L. Yale, *Chem. Rev.*, 1943, 33, 209.

11) K. Brink, W. Gombler, and C. Bliefert, *Z. Anorg. Allg. Chem.*, 1977, 429, 255; U. Hermann, M. Yaktapour, and C. Bliefert, *Naturforsch Teil B*, 1978, **33**, 574; H. Metzger in Houben-Weyl, *'Methoden der Organischen Chemie'*, G. Thieme Verlag, Stuttgart, 1968, Band 10/4, p. 215.

12) M. J. P. Harger, *J. Chem. Soc., Perkin Trans 1*, 1981, 3284.

13) M. J. P. Harger, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2699.

14) M. J. P. Harger and A. Smith, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1787.

15) M. J. P. Harger, *J. Chem. Soc., Chem. Commun.*, 1979, 930.

16) M. J. P. Harger and A. Smith, *J. Chem. Soc., Perkin Trans 1*, 1986, 2169.

17) M. J. P. Harger and A. Smith, *J. Chem. Soc., Perkin Trans 1*, 1987, 683.

18) M. J. P. Harger and A. Shimmin, *Tetrahedron*, 1992, **48**, 7539.

19) M. J. P. Harger and A. Smith, *J. Chem. Soc., Perkin Trans 1*, 1990, 1447.

20) M. J. P. Harger, *J. Chem. Res. (S)*, 1993, 176.

21) M. J. P. Harger and A. Smith, *J. Chem. Soc., Perkin Trans 1*, 1985, 2651.

22) M. J. P. Harger and A. Smith, *J. Chem. Soc., Perkin Trans 1*, 1990, 2507.

23) R. F. Hudson, *Structure and Mechanism in Organophosphorus Chemistry*, Academic Press, London, 1965, p. 259.

24) L. Horner and A. Christmann, *Chem. Ber.*, 1963, 96, 388; W. Ando, N. Ogino, T. Migita, *Bull. Chem. Soc. Jpn.*, 1971, 44, 2278; Y. Hayashi and D. Swern, *Tetrahedron Lett.*, 1972, 1921; D. C. Appleton, D. C. Bull, J. McKenna, and A. R. Walley, *J. Chem. Soc., Perkin Trans 2*, 1980, 385; T. L. Gilchrist and C. J. Moody, *Chem Rev.*, 1977, 77, 409.

25) M. J. P. Harger and A. Smith, *J. Chem. Soc., Perkin Trans. 1*, 1986, 377.

26) S. Freeman and M. J. P. Harger, *J. Chem. Soc., Perkin Trans 2*, 1988, 81.

27) W. P. Jencks, *Acc. Chem. Res.*, 1980, 13, 161; *Chem. Soc. Rev.*, 1981, 10, 345.

28) M. J. P. Harger, *Tetrahedron Lett.*, 1990, 31, 1451.

29) L. Horner, H. Hoffmann, W. Klink, H. Ertel, and V. G. Toscano, *Chem. Ber.*, 1962, 95, 581.

30) Arbuzov, *Pure Appl. Chem.*, 1964, 9, 307; A. K. Bhattacharya and G. Thyagarajan, *Chem. Rev.*, 1981, 81, 415.

31) M. Epstein and S. Buckler, *Tetrahedron*, 1962, 18, 1231.

32) Prepared by M. J. P. Harger essentially as E. Kagan, R. D. Birkenmeyer, and R. E. Strube, *J. Am. Chem. Soc.*, 1959, 81, 3026.

33) G. M. Kosolapoff, *J. Am. Chem. Soc.*, 1945, 67, 2259.

34) Prepared by S. Freeman; see S. Freeman and M. J. P. Harger, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1399.

35) Preliminary communication; J. Fawcett, M. J. P. Harger, and R. Sreedharan-Menon, *J. Chem. Soc., Chem. Commun.*, 1992, 227.

36) M. J. P. Harger, *J. Chem. Soc., Perkin Trans 2*, 1978, 326.

37) M. J. P. Harger, *J. Chem. Soc., Perkin Trans 2*, 1980, 1505.

38) W. Dabkowski, J. Michalski, C. Radziejewski, and Z. Skrzypczynski, *Chem. Ber.*, 1982, 115, 1636.

39) L. Wozniak and J. Chojnowski, *Tetrahedron*, 1989, 45, 2465.

40) W. Dabkowski, J. Michalski, and Z. Skrzypczynski, *Chem. Ber.*, 1985, 118, 1809.

41) M. J. P. Harger, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2127.

42) J. March, *Advanced Organic Chemistry*, 4th edition, 1992, John Wiley and Sons Inc., New York, p. 263-264.

43) Prepared by M. J. P. Harger; unpublished results.

44) A. Shimmin; unpublished results.

45) F. Yamamoto and S. Oae, *Bull. Chem. Soc. Jap.*, 1975, 48, 77.

46) A. S. Kende, *Organic Reactions*, 1960, 11, 261; P. J. Chenier, *J. Chem. Educ.*, 1978, 55, 286.

47) R. B. Loftfield, *J. Am. Chem. Soc.*, 1950, 72, 632; 1951, 73, 4707.

48) L. A. Paquette, *Organic Reactions*, 1977, 25, 1.

49) I. Lengyel and J. C. Sheehan, *Angew. Chem., Int. Ed. Engl.*, 1968, 7, 25; G. L'abbe, *Angew. Chem., Int. Ed. Engl.*, 1980, 19, 276.

50) H. Quast and H. Leybach, *Chem. Ber.*, 1991, 124, 849.

51) K. A. Petrov, V. A. Chauzov, T. S. Erokhina, and I. V. Pastukhova, *J. Gen. Chem. USSR (Engl. Trans.)*, 1977, 47, 2501.

52) M. J. P. Harger and A. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1681.

53) S. E. Fishwick, J. Flint, W. Hawes, and S.Trippett, *J. Chem. Soc., Chem. Commun.*, 1967, 1113; H. Hellman and J. Bader, *Tetrahedron Lett.*, 1961, 724.

54) P. Burns, G. Capozzi, and P. Haake, *Tetrahedron Lett.*, 1972, 925; A. J. Fry and L.-L. Chung, *Tet. Lett*, 1976, 645; K. A. Petrov, V. A. Chauzov, T. S. Erokhina, and I. V. Pastukhova, *J. Gen. Chem. USSR (Engl. Trans.)*, 1976, 46, 2387.

55) H. Quast, M. Heuschmann, and M. O. Abdel-Rahman, *Angew. Chem., Int. Ed. Engl.*, 1975, 14, 486.

56) H. Quast and M. Heuschmann, *Angew. Chem., Int. Ed. Engl.*, 1978, 17, 867.

57) T. Oshikawa and M. Yamashita, *Bull. Chem. Soc. Jpn.*, 1986, 59(10), 3293.

58) M. J. P. Harger and A. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1989, 563.

59) Prepared by M. J. P. Harger and J. Trafford; see J. A. Cade, *J. Chem. Soc.*, 1959, 2266.

60) J. Trafford, undergraduate research project, University of Leicester, 1990.

61) M. D. M. Gray and D. J. H. Smith, *Tetrahedron Lett.*, 1980, 21, 859; P. Sutter and C. D. Weis, *Phosphorus Sulphur*, 1978, 4, 335.

62) J. Fawcett, M. J. P. Harger, D. R. Russell, and R. Sreedharan-Menon, *J. Chem. Soc., Chem. Commun.*, 1993, in the press (3/04762/ccc).

63) B. Altenkirk and S. S. Israelstam, *J. Org. Chem.*, 1962, 27, 4532.

64) *Cf.* S. Coulton, G. A. Moore, and R. Ramage, *Tetrahedron Lett.*, 1976, 4005.

65) F. H. Case, *J. Am. Chem. Soc.*, 1925, 47, 1143. Prepared by H. Silkowski (undergraduate research project, University of Leicester, 1992), method adapted from L. M. Harwood and C. J. Moody, *Experimental Organic Chemistry*, Blackwell Scientific Publications, Oxford, 1989, p. 482.

66) Prepared by M. J. P. Harger; see O. Mancera and O. Lemberger, *J. Org. Chem*, 1950, 15, 1253.

67) See J. March, *Advanced Organic Chemistry*, 4th edition, 1992, John Wiley and Sons Inc., New York, p. 307; E. C. Ashby, *Acc. Chem. Res.*, 1988, 21, 414.

68) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Org. Chem.*, 1964, 29, 2816; W. S. Wadsworth, Jr., *Organic Reactions*, 1977, 25, 73.

69) W. J. Stec, *Acc. Chem. Res.*, 1983, 16, 411.

70) D. Bouchu, F. Tardy, M. Moreau, J. Dreux, A. Skowronska, and J. Michalski, *Tetrahedron Lett.*, 1985, 26, 443.

71) B. Krzyzanowska and W. J. Stec, *Heteroatom Chem.*, 1991, 2, 123.

72) R. C. Grabiak, J. A. Miles, and G. M. Schwenzer, *Phosphorus Sulphur*, 1980, 9, 197.

73) J. W. Perich and R. B. Johns, *Aust. J. Chem.*, 1991, 44, 503.

74) G. R. J. Thatcher and R. Kluger, *Adv. Phys. Org. Chem.*, 1989, 25, 99.

75) E. L. Muerrerties, W. Mahler, and R. Schmutzler, *Inorg. Chem.*, 1963, 2, 613.

76) F. H. Westheimer, *Acc. Chem. Res.*, 1968, 1, 70.

77) R. F. Hudson and C. Brown, *Acc. Chem. Res.*, 1972, 5, 204; C. R. Hall and T. D. Inch, *Tetrahedron*, 1980, 36, 2059.

78) R. S. Berry, *J. Chem. Phys.*, 1960, 32, 933; I. Ugi, D. Marquarding, H. Kluscek, G. Gokel, and P. Gillespie, *Angew. Chem., Int. Ed. Engl.*, 1970, 9, 705;

79) S. Trippett, *Phosphorus Sulphur*, 1976, 1, 89.

80) J.March, *Advanced Organic Chemistry*, 3rd edition, 1985, John Wiley and Sons, New York, p. 222.

81) J. C. Bottaro, C. D. Bedford, and A. Dodge, *Synth. Commun.*, 1985, 15, 1333.

82) N. Thomas, undergraduate research project, University of Leicester, 1978.

83) E. A. Chernyshev, E. F. Bugerenko, N. A. Nikolaeva and A. D. Petrov, *Dokl. Akad. Nauk SSSR*, 1962, 147, 117.

84) H. G. Henning, *J. Prakt. Chem.* 1965, 29, 93; *Chem. Abstra.*, 1965, 63, 7036.

85) R. K. Crossland and K. L. Servis, *J. Org. Chem.*, 1970, **35(9)**, 3195; G. Opitz, *Angew. Chem., Int. Ed. Engl.*, 1967, **6**, 107.

86) R. S. Edmundson and E. W. Mitchell, *J. Chem. Soc.* (C) 1968, **16**, 2091; this describes a different method of preparation.

87) Prepared by M. J. P. Harger.

88) Prep M. J. P. Harger as *Organic Synthesis Collective Volume V*, John Wiley and Sons Inc., London, p. 878.

89) R. J. W. Cremlyn, R. M. Ellam and N. Akhtar, *Phosphorus Sulphur*, 1978, 5, 1.

90) *Organic Syntheses Collective Volume IV*, John Wiley and Sons Inc., London, p. 125.

91) Method gleaned from J.March, *Advanced Organic Chemistry*, 3rd edition, 1985, John Wiley and Sons, New York, p. 360; E. E. Reid, *Organic Chemistry of Bivalent Sulphur*, Vol. 2, 1960, Chemical Publishing Co., Inc., New York, p. 24.

92) CAS N° [66167-74-6]; see *Chem. Abstra.*, 1978, **88**, P153546z.

93) Prepared by M. J. P. Harger; see W. R. Griffiths and J. C. Tebby, *Phosphorus Sulphur*, 1978, 5, 101-6.

94) W. Clegg and G. M. Sheldrick, *Z. Kristallogr.*, 1984, **167**, 23.

95) G. M. Sheldrick, SHELXS86 Programme for Crystal Structure Solution, University of Göttingen, Germany, 1986.

96) G. M. Sheldrick, SHELX76 Programme for Crystal Structure Determination, University of Cambridge, 1976.

97) SHELXTL, PC version 4.2, Programme package for structure solution and refinement, Siemens Analytical Instruments Inc., Madison, WI, 1990.