The Proton Magnetic Resonance Spectra of Chiral Phosphinate Esters. Chemical Shift Non-equivalence of Enantiomers induced by Optically Active Phosphinothioic Acids[1]

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The ^{1}H n.m.r. spectrum of racemic methyl methylphenylphosphinate [MePhP(O)OMe] recorded in CCl_4 solution in the presence of 1 mol. equiv. of (+)-(*R*)-phenyl-t-butylphosphinothioic acid or (−)-(*S*)-methylphenylphosphinothioic acid contains well separated *P*-methoxy signals ($\Delta\delta$ 7.0 or 5.4 Hz at 100 MHz) for the two enantiomers. For non-racemic samples of the phosphinate ester the enantiomer ratio can be easily and accurately measured. Other phosphinates [*e.g.* RPhP(O)OR′; R = Me, Et, Pr^i, Bu^t, Ph; R′ = Me, Ph] and thiophosphinates [RPhP(O)SR′ but not RPhP(S)OR′] exhibit similar induced chemical shift non-equivalence of enantiomers. The non-equivalence is attributed to the formation of diastereoisomeric complexes in which the optically active acid is hydrogen bonded to the P=O group of the enantiomeric esters.

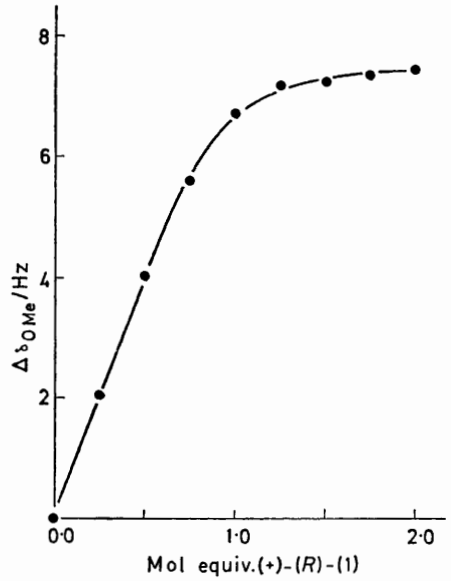
MECHANISTIC and synthetic studies often require a knowledge of the ratio of the enantiomers in a sample of a chiral compound. The enantiomer composition can be deduced from the optical rotation only when the specific rotation of a pure single enantiomer is known. Since the specific rotation is frequently not known, alternative methods of measuring enantiomer ratios are of considerable importance.

Enantiomers generally give rise to identical n.m.r. spectra, but chemical shift non-equivalence can be induced either by including an optically active lanthanide shift reagent in the n.m.r. solution [2] or by using an optically active solvent.[3] Both approaches have been widely reported.[4,5] We now describe a ^{1}H n.m.r. method for measuring the ratios of enantiomers in phosphinate esters that has something in common with both the established techniques but may often be preferable to either.

RESULTS AND DISCUSSION

The 100 MHz ^{1}H n.m.r. spectrum of racemic methyl methylphenylphosphinate, MePhP(O)OMe, in CCl_4 (0.12M solution; 27 °C) includes a doublet (J_{PH} 11.5 Hz) at δ 3.55 due to the *P*-methoxy group. Addition of 0.25 mol. equiv. of optically pure (+)-(*R*)-phenyl-t-butylphosphinothioic acid (1) causes this signal to separate into two doublets of equal intensity 2.1 Hz apart. Continued addition of the optically active acid causes the low field doublet to move progressively downfield and the separation between the two doublets to increase until it reaches 7.0 Hz with 1.0 mol. equiv. of (*R*)-(1). Further addition of the optically active acid has relatively little effect (Figure). The pure (−)-(*S*) enantiomer of MePhP(O)OMe displays only one methoxy signal (δ 3.55) in the presence of (*R*)-(1), whereas other non-racemic samples give two signals of unequal intensity, with that due to the (*S*)-enantiomer being at higher field. For each sample the enantiomer composition implied by the relative intensities (peak heights) of the two methoxy signals agrees well with the ratio estimated from the optical rotation (Table 1).

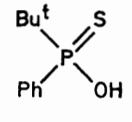
(−)-(*S*)-Methylphenylphosphinothioic acid (2) also induces non-equivalence of the enantiomers of MePhP(O)OMe, but now it is the low field methoxy resonance that is associated with the (*S*)-enantiomer and the



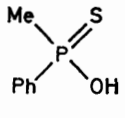
Dependence of the induced non-equivalence of MePhP(O)OMe ($\Delta\delta_{OMe}$/Hz at 100 MHz) on the mol. equivs. of added (+)-(*R*)-Bu^{t}PhP(S)OH (1)

separation between the signals [$\Delta\delta$ 5.4 Hz with 1.0 mol. equiv. (2)] is slightly less than with the acid (1).

Changing the temperature of the n.m.r. sample influences the induced non-equivalence of the enantiomers of MePhP(O)OMe. Thus the values of $\Delta\delta$ (Hz at 100 MHz) using 1.0 mol. equiv. of added (*R*)-(1) in



(1)



(2)

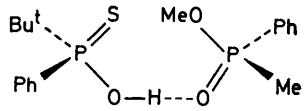
CCl_4 reveal that not only does the separation between the two methoxy signals increase as the sample is cooled, but at lower temperatures the *P*-methyl groups

in the two enantiomers also show significant non-equivalence. Variation of the solvent also has a marked

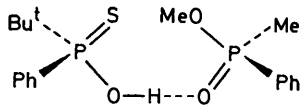
T/°C	+60	+44	+27	+12	−4	−20
$\Delta\delta_{OMe}$/Hz	6.0	6.5	7.0	7.6	8.0	8.5
$\Delta\delta_{PMe}$/Hz	0.0	0.0	0.0	<1.0	1.0	2.0

effect on the induced non-equivalence as the following values of $\Delta\delta_{OMe}$ (in Hz at 100 MHz) for the same mixture of MePhP(O)OMe and (*R*)-(1) (*ca.* 1.0 mol. equiv.) clearly show: 6.6 Hz (CCl_4), 5.1 ($CDCl_3$), 4.9 (CH_2Cl_2), 4.1 (PhH), 1.9 (CD_3COCD_3), 0.0 (CD_3SOCD_3), and 0.0 (CD_3OD).

The induced non-equivalence of the enantiomers of MePhP(O)OMe may be attributed to molecular association. As shown formally in (3) and (4), hydrogen bonding of the ester to an optically active phosphinothioic acid gives rise to diastereoisomeric complexes. The importance of such association is supported by the observed decrease in $\Delta\delta$ when the temperature is raised or the solvent is changed to one more polar than CCl_4. The complete disappearance of induced non-equivalence in methanol and dimethyl sulphoxide is only to be expected in view of the ability of these strongly solvating solvents to suppress hydrogen bonding between solute molecules. As regards the nature of the associates, they must be short lived (rapidly exchanging) on the n.m.r. time scale else separate resonances would be seen for associated and unassociated ester when only small amounts of optically active acid are present. For a given mixture of MePhP(O)OMe and (*R*)-(1) the size of $\Delta\delta_{OMe}$ depends very little on the concentration of the n.m.r. solution ($\Delta\delta_{MeO}$ decreases from 7.0 to 6.5 Hz in going from 0.50 to 0.015M solution), suggesting that the ester and acid are largely associated even in dilute solution. The way in which the magnitude of $\Delta\delta_{OMe}$ increases with the proportion of optically active acid up to 1.0 mol. equiv. but then levels off rather rapidly (Figure) seems consistent with the formation of 1 : 1 complexes.



(3)



(4)

To establish the generality of the n.m.r. phenomena observed for MePhP(O)OMe, 15 chiral phosphinate esters of diverse structure have been examined. Addition of the acid (*R*)-(1) or (*S*)-(2) generally causes substantial changes in the spectra of all these esters (in CCl_4 solution) with signals moving up- or down-field by as much as 0.2 p.p.m. (see Table 3 for details). Non-equivalence is induced when signals from the two enantiomers are displaced by different amounts or in opposite directions. Table 2 contains a summary of the principal results obtained using 1.0 mol. equiv. of optically active acid. Where no value of $\Delta\delta$ is given, the relevant part of the spectrum could not be analysed with confidence. Induced non-equivalence of enantiomers is seen not only with alkylphenylphosphinates, but also with dialkyl (9) and (12) and diaryl (13) and (14) phosphinates and a variety of phosphinothioates. In general both alkyl groups attached to phosphorus and those present in the alkoxy (alkylthio) moiety of the enantiomeric esters give rise to clearly separated n.m.r. signals. It is interesting to note that for (17), but not for (7), only one of the diastereotopic methyl groups in the *P*-iso-

TABLE 1

Enantiomer composition of samples of MePhP(O)OMe measured by optical rotation and by ^{1}H n.m.r. spectroscopy with (+)-(*R*)-Bu^{t}PhP(S)OH

$[\alpha]_D$ (°) (C_6H_6)	%(−)-Enantiomer [a]	% High field enantiomer [b]
−57.8	99.8	⩾99.4
−51.7	94.6	93.9
−37.3	82.2	82.3
−25.8	72.2	72.4
−13.4	61.6	61.9
0.0	50.0	50.3
+11.2	40.3	41.1

[a] Based on $[\alpha]_D$ −58.0° (C_6H_6) for optically pure (−)-MePhP(O)OMe. This value is marginally greater than previous estimates (ref. 23; see also ref. 9). [b] ^{1}H N.m.r. spectra recorded with [MePhP(O)OMe] 0.20M and [Bu^{t}PhP(S)OH] 0.16M; $\Delta\delta_{OMe}$ 6.0 Hz at 100 MHz.

TABLE 2

100 MHz ^{1}H N.m.r. spectra of phosphinyl esters. Chemical shift non-equivalence ($\Delta\delta$) of enantiomers induced by adding 1.0 mol. equiv. of an optically active phosphinothioic acid in CCl_4 at 27 °C [a]

	*Me*PhP(O)O*Me* (5)		*Me*CH$_2$PhP(O)O*Me* (6)		*Me*$_2$CHPhP(O)O*Me* (7)		*Me*$_2$CPhP(O)O*Me* (8)		*Me*$_2$C(*Me*)P(O)O*Me* (9)		
Added (*R*)-(1) $\Delta\delta$/Hz	0.0	7.0 [b]		5.8	~5	3.7	1.8	0.0 [d]	4.0	11.0	18.0
Added (*S*)-(2) $\Delta\delta$/Hz	0.0	5.4 [c]	0.0	4.6	4.0	2.0	1.0	1.1	3.4	8.1	13.6
	*Me*PhP(O)OC*Me*$_3$ (10)		*Me*PhP(O)OPh (11)		*Me*$_2$C(*Me*)P(O)OPh (12)		Ph(*p*-MeOC$_6$H$_4$)P(O)O*Me* (13)		Ph(1-C$_{10}$H$_7$)P(O)O*Me* (14)		
Added (*R*)-(1) $\Delta\delta$/Hz	0.5	5.8	6.9		9.5	7.2		1.8		2.4	
Added (*S*)-(2) $\Delta\delta$/Hz	1.2	4.2	5.1		7.0	4.2		1.3		1.2	
	*Me*PhP(O)S*Me* (15)		*Me*CH$_2$PhP(O)S*Me* (16)		*Me*$_2$CHPhP(O)S*Me* (17)		*Me*$_2$CPhP(O)S*Me* (18)		*Me*PhP(O)SPh (19)		
Added (*R*)-(1) $\Delta\delta$/Hz	2.9 [b]	6.0 [b]	1.6 [b]	4.0 [b]	7.0 [b,c]	0.0	5.0 [b]	4.4 [c]	6.3		
Added (*S*)-(2) $\Delta\delta$/Hz	2.4 [c]	5.2 [c]	1.0 [c]	3.6 [c]	6.5 [c,e]	0.0	3.6 [c]	4.8 [b]	4.0		

[a] [ester] = [acid] = 0.12M. [b] Relative intensity of the high field signal increased by addition of the (*S*)-enantiomer of the ester. [c] Relative intensity of the high field signal increased by addition of the (*R*)-enantiomer of the ester. [d] $\Delta\delta$ 0.4 Hz with 2.0 mol. equiv. of (+)-(R)-(1). [e] Only one of the methyl groups in the *P*-isopropyl substituent exhibited enantiomer non-equivalence.

propyl substituent exhibits enantiomer non-equivalence. For the most part the acid (*R*)-(1) induces greater separation (Δδ) than does (*S*)-(2) but there are exceptions, notably the methoxy group in (8) and the *P*-methyl group in (10). In every case the values of Δδ were reduced to *ca.* half those in Table 2 when only 0.5 mol. equiv. of acid was used, but with 2.0 mol. equiv. the values of Δδ were usually only *ca.* 10% greater than those shown.

Several thiophosphinyl esters such as (20)—(22) were examined, but none of them exhibited induced non-equivalence of enantiomers, or even appreciable changes in chemical shift, with (*R*)-(1). It therefore seems that the P=O group plays a crucial role in the association of a phosphinate ester with a phosphinothioic acid. The oxygen (or sulphur) atom of the alkoxy (or alkylthio) group may also assist in complexing with the acid, but a second interaction of this type is apparently not essential: in the presence of 1.0 mol. equiv. of (*R*)-(1) or (*S*)-(2), t-butylmethylphenylphosphine oxide (23) displays enantiomer non-equivalence in both the methyl (Δδ 6.1 and 3.1 Hz) and the t-butyl (Δδ 4.8 and 3.4 Hz) signals.

TABLE 3

100 MHz ^{1}H N.m.r. spectra of compounds (5)—(27) in CCl_4 without added phosphinothioic acid and with 1.0 mol. equiv. of added (*R*)-(1) or (*S*)-(2) [a]

Compound	Without added acid δ (*J*/Hz)	Added (*R*)-(1) δ			Added (*S*)-(2) δ		
(5)	1.56 (3 H, d, *J* 15)		1.65			1.67	
	3.55 (3 H, d, *J* 11.5) [b]	3.61		3.54	3.62		3.57
(6)	1.08 (3 H, dt, *J* 18, 7)		1.01			1.02	
	2.0—1.6 (2 H, m)						
	3.57 (3 H, d, *J* 11) [b]	3.63		3.57	3.64		3.59
(7)	1.00 (3 H, dd, *J* 17, 7)				1.02		0.98
	1.16 (3 H, dd, *J* 17, 7)				1.12		1.08
	1.95 (1 H, m)		2.13			2.11	
	3.58 (3 H, d, *J* 11) [b]	3.63		3.59	3.64		3.62
(8)	1.08 (9 H, d, *J* 16)	1.07		1.05	1.08		1.07
	3.63 (3 H, d, *J*, 11) [b]		3.65		3.67		3.66
(9)	1.12 (9 H, d, *J*, 15.5)	1.12		1.08	1.13		1.09
	1.29 (3 H, d, *J* 13)	1.47		1.36	1.49		1.41
	3.69 (3 H, d, *J* 10)	3.77		3.59	3.79		3.65
(10)	1.40 (9 H, s)	1.41		1.35	1.40		1.36
	1.50 (3 H, d, *J* 15) [b]	1.61		1.60	1.62		1.61
(11)	1.73 (3 H, d, *J* 15) [b]	1.86		1.79	1.86		1.81
(12)	1.25 (9 H, d, *J* 16.5)	1.26		1.17	1.28		1.21
	1.40 (3 H, d, *J* 13) [b]	1.52		1.45	1.54		1.50
(13)	3.70 (3 H, d, *J* 11)	3.72		3.70	3.72		3.71
	3.84 (3 H, s) [b]		3.81			3.81	
(14)	3.82 (3 H, d, *J* 11) [b]	3.79		3.77	3.82		3.81
(15)	1.87 (3 H, d, *J* 14)	1.98		1.95	1.99		1.97
	2.14 (3 H, d, *J* 12) [b]	2.17		2.11	2.17		2.12
(16)	1.18 (3 H, dt, *J* 20, 8)	1.11		1.09	1.12		1.11
	2.3—1.9 (2 H, m)						
	2.15 (3 H, d, *J* 12) [b]	2.20		2.16	2.17		2.13
(17)	1.08 (3 H, dd, *J* 18, 7)	1.12		1.05	1.12		1.05
	1.26 (3 H, dd, *J* 18, 7)		1.20			1.19	
	2.35—1.95 (1 H, m)						
	2.14 (3 H, d, *J* 11.5) [b]		2.13			2.13	
(18)	1.15 (9 H, d, *J* 17)	1.16		1.11	1.15		1.11
	2.12 (3 H, d, *J* 11.5) [b]	2.13		2.09	2.13		2.08
(19)	1.87 (3 H, d, *J* 13.5) [b]	1.99		1.93	1.99		1.95
(20)	1.94 (3 H, d, *J* 14)		1.94			1.95	
	3.54 (3 H, d, *J* 13.5) [b]		3.55			3.54	
(21)	2.13 (3 H, d, *J* 14) [b]		2.12			*c*	
(22)	1.11 (9 H, d, *J* 17)		1.11			*c*	
	3.64 (3 H, d, *J* 13) [b]		3.64			*c*	
(23)	1.08 (9 H, d, *J* 14.5)	1.07		1.02	1.08		1.05
	1.61 (3 H, d, *J* 12) [b]	1.78		1.72	1.76		1.73
(24)	1.39 (6 H, d, *J* 15)	1.51		1.45		*c*	
	3.67 (3 H, d, *J* 11)		3.66			*c*	
(25)	1.59 (6 H, d, *J* 14) [b]	1.72		1.56		*c*	
(26)	1.38 (3 H, d, *J* 18.5)		1.45			*c*	
	3.73 (6 H, d, *J* 11)	3.73		3.71		*c*	
(27)	3.75 (6 H, d, *J* 10.5) [b]	3.79		3.72		*c*	

[a] *T* 27 °C; [ester] 0.12M. Where no value is shown the relevant part of the spectrum of the ester was too complex to analyse and/or was masked by the added phosphinothioic acid. [b] Additional signals in the aromatic region (*ca.* δ 8—7) were consistent with the proposed structure. [c] Not examined.

Our results show that optically active phosphinothioic acids offer an attractive alternative to optically active solvents [5] and lanthanide shift reagents [6] for measuring ratios of enantiomers in phosphoryl compounds by ^{1}H n.m.r. spectroscopy. Inevitably the resonances caused by groups in the added acid will sometimes overlap with signals from the compound

under investigation. However, except for the aromatic region (which is not usually important in this context), the acids (*R*)-(1) and (*S*)-(2) mask rather little since they both give rise to just one doublet. In fact these acids are complementary since the *P*-t-butyl group in (*R*)-(1)

MePhP(S)OMe (20) MePhP(S)OPh (21)

$Bu^tPhP(S)OMe$ (22) $Bu^tMePhP{=}O$ (23)

(δ 1.13—1.16) * and the *P*-methyl group in (*S*)-(2) (δ 1.84—1.88) * have quite different chemical shifts. To their advantage, phosphinothioic acids can be obtained quite easily in high optical purity, they do not cause broadening of the signals in the spectrum of the compound being examined, only small amounts (5—16 mg) are required, and samples can easily be recovered.

As well as chiral esters, we have looked briefly at the effect of added optically active phosphinothioic acids on the n.m.r. spectra of some achiral phosphoryl compounds. The two *P*-methyl groups in methyl dimethylphosphinate (24) are enantiotopic and normally give rise to just one signal [δ 1.39 (CCl_4) (d, J_{PH} 15 Hz)]. However, if the molecule becomes complexed to an optically active acid these two groups will become diastereotopic. In fact in the presence of 1.0 mol. equiv. of (*R*)-(1) the two *P*-methyl groups in (24) appear

$Me_2P(O)OMe$ (24) $Me_2P(O)OPh$ (25)

$MeP(O)(OMe)_2$ (26) $PhP(O)(OMe)_2$ (27)

as distinct signals (δ 1.51 and 1.45) separated by 5.7 Hz (at 100 MHz). Similarly the *P*-methyl groups in phenyl dimethylphosphinate (25) (Δδ 15.6 Hz) and the methoxy groups in dimethyl methylphosphonate (26) (Δδ 2.4 Hz) and dimethyl phenylphosphonate (27) (Δδ 6.5 Hz) give rise to separate signals in the presence of (*R*)-(1) (1.0 mol. equiv.).

The complete description of a sample of a chiral ester demands not only that the ratio of the enantiomers be known, but also whether the major enantioner has the (*R*)- or (*S*)-configuration. For some of the esters in Table 2 we have been able to prepare optically active samples of known configuration † and use them to establish which n.m.r. signals (high or low field) are associated with which enantiomer (*R* or *S*) under conditions of induced non-equivalence. Thus for the esters (5) and (15)—(17) it is the enantiomer with the same configuration (*R* or *S*) as the added optically active acid that gives rise to the low field signal (or signals when both alkyl groups in the molecule display enantiomer non-equivalence). Although these results show a welcome consistency many more compounds of known configuration will have to be examined before an empirical rule can be firmly established. Then it should be possible to deduce the absolute configuration of a chiral phosphoryl ester simply by examining its n.m.r. spectrum in the presence of (*R*)-(1) and (*S*)-(2). However, the need for caution is underlined by considering *S*-methyl phenyl-t-butylphosphinothioate (18); here the enantiomer having the same configuration as the added optically active acid gives rise to the low field *P*-t-butyl signal but, unusually, the high field *S*-methyl signal.‡ In some respects this anomalous behaviour of the *S*-methyl group was predictable. In the series of methyl alkylphenylphosphinates (5)—(8) the value of $\Delta\delta_{OMe}$ decreases as the size of the *P*-alkyl group increases, Me ⟶ Et ⟶ Pr^i ⟶ Bu^t. Similarly with the methyl alkylphenylphosphinothioates (15)—(17), $\Delta\delta_{SMe}$ decreases as the *P*-alkyl group changes, Me ⟶ Et ⟶ Pr^i. Since $\Delta\delta_{SMe}$ is already zero for the *P*-isopropyl compound (17), it might be predicted that a further increase in size, to the *P*-t-butyl group in (18), would reverse the sense of the induced non-equivalence.

The need for an empirical rule for phosphinate esters relating n.m.r. behaviour and configuration contrasts with the situation for phosphinic amides. We have previously shown that the acids (*R*)-(1) and (*S*)-(2) induce chemical shift non-equivalence of enantiomers in the ^1H n.m.r. spectra of chiral phosphinic amides such as MePhP(O)NHPh and $Bu^tPhP(O)NH_2$.[7] Because these amides contain both donor (N–H) and acceptor (P=O) sites for hydrogen bonding it is comparatively easy to envisage the likely structures of the diastereoisomeric complexes they form with optically active phosphinothioic acids.[7] We can then predict, for a particular combination of amide and acid, the relationship between the n.m.r. behaviour of the amide and its absolute configuration.[7] In contrast to the amides, phosphinate esters contain only a hydrogen bond acceptor group (P=O). We are unable to suggest probable structures for their complexes with phosphinothioic acids beyond purely formal representations such as (3) and (4).

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. Optical rotations were measured at 589 nm (Na D line) and 20 ± 2 °C in a cell of path length 100 mm (capacity *ca.* 0.9 ml) using a Perkin-Elmer 141 polarimeter. ^1H N.m.r. spectra were recorded at 100 MHz (tetramethylsilane inter-

* This is the chemical shift (in CCl_4) when the acid is mixed with a phosphinate ester.

† $Pr^iPhP(S)OH$ and its *S*-methyl ester (17) have not previously been reported. Our optically active samples have (+)-rotations. They are assigned (*R*)-configurations because the (+)-enantiomers of the related esters (15), (16), and (18), as well as the acids from which they are derived, have (*R*) configurations. Proof of the configuration of (+)-(17) is not available.

‡ Comparable behaviour is exhibited by the phosphine oxide (23); the enantiomer having the same configuration as the added acid gives rise to the low field *P*-t-butyl signal but the high field *P*-methyl signal.

nal standard) with a JEOL JNM-PS-100 spectrometer. The results presented in Tables 2 and 3 were obtained by recording the spectrum of the appropriate compound (0.054 mmol) in dry (molecular sieve) CCl_4 (0.45 ml) and then repeating the spectrum after addition of the required amount of the solid optically active phosphinothioic acid (*R*)-(1) or (*S*)-(2). For each compound spectra were thus obtained for solutions containing 0.5, 1.0, and 2.0 mol. equiv. of (*R*)-(1) and 0.5 and 1.0 mol. equiv. of (*S*)-(2). The proportion of (*R*)-(1) or (*S*)-(2) in each sample was confirmed (where possible) by integration of the peaks in the spectrum. The absolute values of the chemical shift δ (Table 3) are estimated to be correct to ±0.005 p.p.m., and the separation between two signals Δδ (Table 2) correct to ±0.002 p.p.m.

The compounds investigated were obtained as described below. Many were hygroscopic and could not be obtained entirely free of water (as shown by i.r. spectroscopy and, in some cases, elemental analysis) even by vacuum distillation. Petroleum refers to the fraction of b.p. 60—80 °C.

(+)-(*R*)-Phenyl-t-butylphosphinothioic acid (1), $[\alpha]_D$ +28.1° (*c* 2.4 MeOH), and (−)-(*S*)-methylphenylphosphinothioic acid (2), $[\alpha]_D$ −22.3° (*c* 1.95 MeOH), were both >99% one enantiomer by n.m.r. spectroscopy.[7] They were prepared as previously described.[7]

Methyl Methylphenylphosphinate (5).—The racemic ester, b.p. 106—110 °C at 0.6 mmHg, was prepared by a literature method.[8] Optically active samples of various composition were available from earlier work.[9]

Phenyl Methylphenylphosphinate (11).—Methylphenylphosphinic chloride [8] (0.70 g, 4.0 mmol) in benzene (3 ml) was added over 15 min to a stirred solution of phenol (0.47 g, 5.0 mmol) and triethylamine (0.61 g, 6.0 mmol) in benzene (6 ml). After heating at reflux for 1 h the mixture was filtered. The filtrate was diluted with ether, washed with 0.5M aqueous sodium hydroxide and water, and dried (Na_2SO_4). Distillation afforded the ester (0.86 g, 3.7 mmol, 93%), b.p. 140—150 °C (oven temperature) at 0.5 mmHg (lit.,[10] 140 °C at 0.1 mmHg) which solidified on cooling.

t-Butyl Methylphenylphosphinate (10).—t-Butyl alcohol (1.0 ml) in benzene (2 ml) was added dropwise to a stirred suspension of sodium hydride (5 mmol) in benzene (2 ml). After 0.5 h, methylphenylphosphinic chloride [8] (0.52 g, 3.0 mmol) in benzene (2 ml) was added dropwise. The mixture was boiled for 1 h and filtered. The filtrate was diluted with ether, washed with water to which sodium hydroxide was added to keep it just alkaline, and dried (Na_2SO_4). Distillation afforded *t-butyl methylphenylphosphinate* (0.077 g, 0.36 mmol, 12%), b.p. 70 °C (oven temperature) at 0.3 mmHg (Found: C, 62.0; H, 8.2. $C_{11}H_{17}O_2P$ requires C, 62.55; H, 8.1%).

S-*Phenyl Methylphenylphosphinothioate* (19).—Methylphenylphosphinic chloride [8] (0.70 g, 4.0 mmol) in benzene (4 ml) was added dropwise to a solution of thiophenol (0.46 g, 4.2 mmol) and triethylamine (0.42 g, 4.2 mmol) in benzene (8 ml). The mixture was heated at 60 °C for 1.5 h and filtered. The filtrate was washed with 5% aqueous sodium carbonate and water, and dried (Na_2SO_4). Distillation gave the ester (0.77 g, 3.1 mmol, 78%), b.p. 160 °C (oven temperature) at 0.5 mmHg (Found: C, 61.9; H, 5.5. Calc. for $C_{13}H_{13}OPS,0.2H_2O$: C, 62.0; H, 5.4%). (This compound has previously been reported [11] but no details are available.)

O-*Phenyl Methylphenylphosphinothioate* (21).—(a) Following published procedures, dimethyl methylphosphonate was sequentially converted into methylphosphonic dichloride,[12] methylphosphonothioic dichloride,[13] and methylphenylphosphinothioic chloride [14] (for which dichloromethane was used in place of benzene in the extraction).

(b) Phenol (0.41 g, 4.4 mmol) in toluene (3 ml) was added dropwise to a stirred suspension of sodium hydride (4.2 mmol) in toluene (5 ml). The temperature was raised to 60 °C and after 10 min methylphenylphosphinothioic chloride (0.76 g, 4.0 mmol) in toluene (2.5 ml) was added dropwise. The mixture was heated at 75—80 °C for 3 h and was then filtered, washed with 3% aqueous sodium carbonate and water, and dried (Na_2SO_4). Distillation afforded O-*phenyl methylphenylphosphinothioate* (0.70 g, 2.8 mmol, 73%), b.p. 135—140 °C (oven temperature) at 0.3 mmHg (Found: C, 63.0; H, 5.45. $C_{13}H_{13}OPS$ requires C, 62.9; H, 5.3%).

O-*Methyl Methylphenylphosphinothioate* (20).—This ester was prepared from methylphenylphosphinothioic chloride [see (a) above] and methanolic benzyltrimethylammonium methoxide; it had b.p. 80—100 °C (oven temperature) at 0.1 mmHg (lit.,[15] 80—85 °C at 0.4 mmHg).

Methyl ethylphenylphosphinate (6) (93%), b.p. 135 °C (oven temperature) at 5 mmHg (lit.,[16] 106—107 °C at 0.8 mmHg), was prepared by treating the phosphinic acid [17] with an excess of diazomethane in ether. Methyl isopropylphenylphosphinate (7) (92%), b.p. 95—100 °C (oven temperature) at 1.5 mmHg (lit.,[18] no b.p. stated), was likewise obtained from the appropriate phosphinic acid.[17]

Methyl t-Butylmethylphosphinate (9).—t-Butylmethylphosphinic chloride [19] (0.42 g, 2.7 mmol) in methanol (2 ml) was added to a stirred solution of sodium methoxide (6 mmol) in methanol (4 ml). After 13.5 h the mixture was filtered and the filtrate carefully concentrated. The residue was dissolved in dichloromethane, washed with water, and dried (Na_2SO_4 then $CaSO_4$). Distillation gave (hydrated) *methyl t-butylmethylphosphinate* (0.25 g, 1.7 mmol, 62%), b.p. 140 °C (oven temperature) at 125 mmHg, *m/e* 150 (15%, M^+), 135 (6), 94 (100), 93 (10), 79 (61), and 57 (55) (Found: C, 42.6; H, 10.15. $C_6H_{15}O_2P,H_2O$ requires C, 42.85; H, 10.2%).

Phenyl t-Butylmethylphosphinate (12).—Phenol (0.23 g, 2.4 mmol) was added to a stirred, ice-cooled suspension of sodium hydride (2.2 mmol) in dimethylformamide (1 ml) under nitrogen. The mixture was warmed to 16 °C for 12 min (to give a clear solution) and then cooled in ice while t-butylmethylphosphinic chloride (0.22 g, 1.4 mmol) in benzene (0.5 ml) was added. The temperature was held at 70—75 °C for 6 h and *ca.* 16 °C for 15 h. The mixture was poured into water (8 ml), made just alkaline with sodium hydroxide, and extracted with benzene (4 then 2 × 2 ml). The combined extracts were washed with water (3 × 3 ml) and dried (Na_2SO_4). Distillation afforded *phenyl t-butylmethylphosphinate* (0.28 g, 1.3 mmol, 93%), b.p. 120 °C (oven temperature) at 8 mmHg, *m/e* 212 (M^+) (Found: C, 60.95; H, 8.1. $C_{11}H_{17}O_2P,0.25H_2O$ requires C, 60.95; H, 8.1%).

Methyl Phenyl-(1-naphthyl)phosphinate (14).—The phosphinic acid, m.p. 185—188 °C (lit.,[20] 185—187 °C), in dichloromethane was treated with an excess of diazomethane in ether. Evaporation of the solvent and crystallisation of the residue from benzene–petroleum–ether (1 : 4 : 0.5) afforded *methyl phenyl-(1-naphthyl)phosphinate* (82%), m.p. 108—109 °C, *m/e* 282 (50%, M^+) and 281 (100) (Found: C, 72.7; H, 5.4. $C_{17}H_{15}O_2P$ requires C, 72.35; H, 5.3%).

Methyl Phenyl-(p-methoxyphenyl)phosphinate (13).—Reaction of the phosphinic acid, m.p. 182—183 °C (lit.,[21] 184 °C), with diazomethane and distillation of the product gave *methyl phenyl-(p-methoxyphenyl)phosphinate*, b.p. 170 °C (oven temperature) at 0.4 mmHg, *m/e* 262 (100%, M^+) and 261 (90) (Found: C, 63.3; H, 5.85. $C_{14}H_{15}O_3P$ requires C, 63.25; H, 5.85%).

S-*Methyl Methylphenylphosphinothioate* (15).—(a) Methyl iodide (1.5 g, 10.5 mmol) and racemic dicyclohexylammonium methylphenylphosphinothioate[7] (0.55 g, 1.56 mmol) were stirred in benzene (18 ml) for 20 h. The mixture was filtered and the filtrate concentrated and distilled to give the racemic ester (0.27 g, 1.42 mmol, 92%), b.p. 100 °C (oven temperature) at 0.1 mmHg (lit.,[22] 115 °C at 0.3 mmHg).

(b) By the same method, dicyclohexylammonium (−)-(*S*)-methylphenylphosphinothioate,[7] $[\alpha]_D$ −8.68° (*c* 3.3 MeOH), afforded the ester (15) having $[\alpha]_D$ −159.1° (*c* 2.2 C_6H_6) {lit.,[23] $[\alpha]_D$ +158° for pure (*R*)-enantiomer}.

S-*Methyl Isopropylphenylphosphinothioate* (17).–(a) A solution of sodium hydrogensulphide (25 mmol) in ethanol (12.5 ml) saturated with hydrogen sulphide was prepared by passing hydrogen sulphide through a solution of sodium ethoxide (25 mmol) in ethanol at 0 °C. The solution was cooled to −20 °C and stirred while isopropylphenyl phosphinic chloride[17] (*ca.* 10 mmol) in benzene (6 ml) was added during 15 min. The mixture was allowed to warm to room temperature. After 0.5 h volatile material was evaporated off and the residue dissolved in water (15 ml). The solution was acidified (concentrated HCl) and extracted with chloroform (15 then 3 × 10 ml). The combined extracts were dried (Na_2SO_4) and evaporated to give crude isopropylphenylphosphinothioic acid (2.1 g, *ca.* 100%) which solidified when cooled, δ($CDCl_3$) 7.95—7.35 (5 H, m), 6.12 (1 H, s), 2.24 (1 H, m), 1.20 (3 H, dd, J_{PH} 19, J_{HH} 7 Hz), and 1.03 (3 H, dd, J_{PH} 20, J_{HH} 7 Hz).

(b) Dicyclohexylamine (0.54 g, 3.0 mmol) in dichloromethane (2 ml) was added to the crude acid (*ca.* 3 mmol) in dichloromethane (3 ml). Dilution with ether precipitated racemic *dicyclohexylammonium isopropylphenylphosphinothioate* (0.97 g, 2.54 mmol, *ca.* 81%), m.p. 160—162 °C after crystallisation from dichloromethane–ether (Found: C, 66.1; H, 9.6; N, 3.7. $C_{21}H_{36}NOPS$ requires C, 66.1; H, 9.5; N, 3.7%).

(c) A solution of the racemic salt (0.57 g, 1.5 mmol) and methyl iodide (1.1 g, 7.5 mmol) in benzene (7 ml) was stirred and boiled gently for 1.5 h. Filtration and distillation of the filtrate gave (hydrated) racemic S-*methyl isopropylphenylphosphinothioate* (0.30 g, 1.39 mmol, 93%), b.p. 120—125 °C (oven temperature) at 0.3 mmHg (Found: C, 55.05; H, 7.25. $C_{10}H_{15}OPS,H_2O$ requires C, 55.1; H, 7.1%).

(d) A solution of (−)-1-phenylethylamine (0.79 g, 6.5 mmol) in dichloromethane (2 ml) was added to a solution of the crude acid (*ca.* 7 mmol) from (a) above in dichloromethane (7 ml). The mixture was concentrated to *ca.* 4 ml and diluted with benzene (4 ml) and ether (15 ml). The material (0.83 g) which deposited during 0.75 h was recrystallised from benzene–petroleum (1 : 1; 8 ml) and the product (0.53 g) was mixed with 0.5M aqueous sodium hydroxide (4 ml). The liberated (−)-1-phenylethylamine was extracted with dichloromethane (3 × 1.5 ml) and the aqueous portion acidified with 12M-hydrochloric acid. The liberated (optically active) phosphinothioic acid was extracted with dichloromethane (4 × 4 ml) and dicyclohexylamine (0.30 g, 1.65 mmol) added. After 10 min the bulk of the solvent was evaporated off and ether (5 ml) added to precipitate dicyclohexylammonium (+)-isopropylphenylphosphinothioate (0.52 g, 1.36 mmol, 39% of theory), $[\alpha]_D$ +11.96° (*c* 2.2 MeOH).

(e) The (+)-salt was treated with methyl iodide as in (c) above to give (+)-S-methyl isopropylphenylphosphinothioate, $[\alpha]_D$ +141.4° (*c* 1.91 C_6H_6).

S-*Methyl Ethylphenylphosphinothioate* (16).—Diethyl phenylphosphonite (prepared from dichlorophenylphosphine, ethanol, and pyridine) was converted into ethyl ethylphenylphosphinate and thence into ethylphenylphosphinic chloride, b.p. 101—104 °C at 0.3 mmHg (lit.,[16] 101 °C at 0.3 mmHg) by published procedures.[16] Reactions analogous to those described above for the isopropyl compounds afforded crude ethylphenylphosphinothioic acid (97%), racemic dicyclohexylammonium ethylphenylphosphinothioate (51%), m.p. 156—157 °C from acetone (lit.,[16] 158 °C), racemic *S*-methyl ethylphenylphosphinothioate (55%), b.p. 122 °C (oven temperature) at 0.3 mmHg (lit.,[16] 120 °C at 0.3 mmHg), dicyclohexylammonium (−)-(*S*)-ethylphenylphosphinothioate, $[\alpha]_D$ −9.8° (*c* 2.4 MeOH) (lit., $[\alpha]_D$ −6.6°,[16] +11.44°[15]), and (−)-(*S*)-S-methyl ethylphenylphosphinothioate,[24] $[\alpha]_D$ −104.4° (*c* 2.93 C_6H_6) (lit.,[16] $[\alpha]_D$ +10.4°).

S-*Methyl Phenyl-t-butylphosphinothioate* (18).—(+)-(*R*)-Phenyl-t-butylphosphinothioic acid (0.075 g, 0.35 mmol), $[\alpha]_D$ +28.1° (*c* 2.4 MeOH), was stirred with triethylamine (0.038 g, 0.38 mmol) and methyl iodide (0.25 g, 2.0 mmol) in benzene (2.5 ml) for 33 h. Filtration and distillation gave (+)-ester (0.075 g, 0.33 mmol, 94%), b.p. 90 °C (oven temperature) at 0.1 mmHg, m.p. *ca.* 69—73° (lit.,[25] b.p. and m.p. not reported), $[\alpha]_D$ +153.1° (*c* 2.3 C_6H_6) (lit.,[25] $[\alpha]_D$ −106.9°). The racemic ester (18) (available from other work[26]) was obtained as a low melting solid after chromatography (alumina; elution with ether) and distillation, b.p. 105 °C (oven temperature) at 0.2 mmHg (lit.,[26] 118—122 °C at 0.6—0.7 mmHg).

O-Methyl phenyl-t-butylphosphinothioate (22)[26] was purified by crystallisation from petroleum and had m.p. 75—75.5 °C (lit.,[26] 71—72 °C); methyl phenyl-t-butylphosphinate (8)[26] was purified by distillation, b.p. 110 °C (oven temperature) at 1.4 mmHg (lit.,[26] 106—108 °C at 1.5 mmHg), and solidified (m.p. *ca.* 40—45 °C) when cold.

Methyl and *Phenyl Dimethylphosphinates*.—Dimethylphosphinic chloride[27] was converted by published methods[28,29] into the phenyl ester (25), b.p. 110 °C (oven temperature) at 1.0 mmHg (lit.,[28] 164—166 °C at 27 mmHg) and the methyl ester (24), b.p. 90 °C (oven temperature) at *ca.* 15 mmHg (lit.,[30] 65—66 °C at 10 mmHg).

Methyl-t-butylphenylphosphine Oxide (23).—A solution of benzylmethyl-t-butylphenylphosphonium bromide (0.60 g, 1.71 mmol) in ethanol (30 ml) containing 5M aqueous sodium hydroxide (5 ml) was boiled gently for 18 h. Most of the ethanol was removed under reduced pressure, water (10 ml) added, and the mixture extracted with dichloromethane (15 then 10 ml). The combined extracts were washed with water, dried (Na_2SO_4), and evaporated. The residue was crystallised twice from petroleum and dried (P_2O_5) at 45 °C and 0.1 mmHg (some loss by sublimination) to give the racemic oxide (0.155 g, 0.79 mmol, 46%), m.p. 76—77 °C (lit.,[31] 76—80 °C for a partially resolved sample). A sample of optically active oxide (23), $[\alpha]_D$ −2.0° (*c* 2.1 MeOH) {lit.,[5a] $[\alpha]_D$ +14.9° for 71% optically pure (*R*)-enantiomer} was available from other work.[26]

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