Chemical Shift Non-equivalence of Enantiomers in the Proton Magnetic Resonance Spectra of Partly Resolved Phosphinothioic Acids

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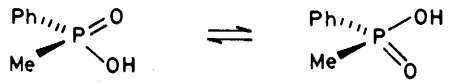
Optically active samples of methylphenylphosphinothioic acid (2) and phenyl-t-butylphosphinothioic acid (3) give rise to distinct ^{1}H n.m.r. spectra for the two enantiomers, with the separation between the two *P*-alkyl resonances depending on the enantiomer composition of the sample, the concentration and temperature of the n.m.r. solution, and the nature of the solvent. These optically active acids induce magnetic non-equivalence of enantiomers in racemic samples of other compounds, including *O*-methyl *O*-hydrogen phenylphosphonothioate (6), methyl-*NP*-diphenylphosphinic amide (8),† and phenyl-t-butylphosphinic amide (9). The potential value of the optically active acids (2) and (3) as reagents for determining enantiomer ratios and configurations by n.m.r. spectroscopy is demonstrated using methylphenylphosphinic amide (7). The behaviour of all the systems examined can be understood in terms of molecular association arising from hydrogen bonding.

We have recently described the ^{1}H n.m.r. spectra of methylphenylphosphinic amide and related chiral amides, with particular reference to the magnetic non-equivalence of the enantiomers in optically active (but not optically pure) samples, and the induction of non-equivalence in racemic modifications of other phosphinic

† In previous papers (refs. 1 and 9) compound (8) has been named as (*N*-phenyl)methylphenylphosphine amide.

amides.[1] The observed spectra were rationalised in terms of molecular association leading to short-lived diastereoisomeric complexes.

In principle it should be possible to observe comparable behaviour with other compounds containing hydrogen-bonding donor and acceptor groups attached to a chiral phosphorus atom. Conceptually the simplest of these are the phosphinic acids, but compounds such as (1) cannot be resolved because their anions are achiral, and the salts they form with optically active bases are not therefore diastereoisomeric.[2,3] In any case, the enantiomers of a phosphinic acid are in tautomeric equilibrium and will rapidly interconvert.



(*R*)-(1) (*S*)-(1)

When one of the oxygen atoms in a chiral phosphinic acid is replaced by sulphur the tautomeric forms are no longer enantiomers and resolution becomes feasible.[3,4] We have therefore made use of optically active phosphinothioic acids to test and extend the ideas previously advanced[1] to account for the behaviour of phosphinic amides. This seemed especially worthwhile because the comparative ease of preparation and resolution of phosphinothioic acids, as well as their solubility in solvents of low polarity, would make them attractive for use as reagents for determining enantiomer ratios and configurations by means of n.m.r. spectroscopy.

RESULTS AND DISCUSSION

Crystalline (—)-methylphenylphosphinothioic acid (2) was obtained from the racemic acid by resolution using quinine.[5] With dicyclohexylamine it formed a salt having a specific rotation ($[\alpha]_{578}$ —9.35°, $[\alpha]_D$ —8.68°, in methanol) in agreement with the value recorded by Benschop and van den Berg [5] ($[\alpha]_{578}$ —9.22° in methanol). Although larger rotations have sometimes been reported for dicyclohexylamine salts of (2),[6] the n.m.r. spectrum of our free acid (see below and Experimental section) proved beyond reasonable doubt that it was >99% one enantiomer. The (—)-enantiomer of (2) is known to have the (*S*)-configuration.[7] By mixing it with the racemate it was possible to examine the n.m.r. spectra of samples of (2) containing between 50 and 100% of the (*S*)-enantiomer. The chemical shifts of the *P*-methyl groups (d, J_{PH} 14 Hz) in representative mixtures are shown in Table 1.

Resolution of phenyl-t-butylphosphinothioic acid (3) with (—)-1-phenylethylamine afforded not only the pure (+)-enantiomer [having the (*R*)-configuration [8]], $[\alpha]_D$ +28.1° (in methanol), but also a sample $[\alpha]_D$ —24.9° consisting of *ca.* 94.5% of the (—)-enantiomer. The chemical shift of the *P*-t-butyl group (d, J_{PH} 18 Hz) in (3) could therefore be determined for a wide range of mixtures of the (*R*)- and (*S*)-enantiomers (Table 1).

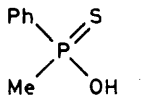
TABLE 1

100 MHz ^{1}H N.m.r. spectra of alkylphenylphosphinothioic acids in $CDCl_3$. Enantiomer ratios and chemical shifts of *P*-alkyl resonances [a]

PhMeP(S)OH (2)			PhBu^{t}P(S)OH (3)					
S/*R* [b]	δ_S	δ_R	*R*/*S* [b]	δ_R	δ_S	*S*/*R* [b]	δ_S	δ_R
100/0	2.055		100/0	1.135		94/6	1.130	1.070
90/10	2.042	1.984	90/10	1.125	1.069	90/10	1.125	1.071
80/20	2.035	1.994	80/20	1.120	1.080	80/20	1.120	1.082
70/30	2.025	1.996	70/30	1.120	1.094	70/30	1.115	1.091
60/40	2.019	2.003	60/40	1.110	1.098	60/40	1.105	1.095
50/50	2.016		50/50	1.110		50/50	1.110	

[a] For all spectra the concentration of acid was 0.23M; the temperature was 14.5 for (2) and 20 °C for (3). [b] Ratio of enantiomers in the sample; the ratio of the integrals of the *P*-alkyl resonances was in agreement for every spectrum in which the separation of the signals was sufficient to allow accurate integration.

The most significant points that emerge from examination of the data in Table 1 are as follows. (i) A single enantiomer of (2) or (3) gives rise to only one *P*-alkyl resonance. (ii) The racemic modification of (2) or (3) also gives only one *P*-alkyl signal, but at a chemical shift which differs from that of the single enantiomer. (iii) Mixtures of the enantiomers of (2) or (3) display two



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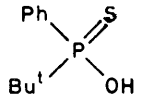

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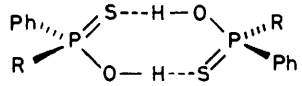

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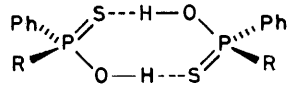


(5)

P-alkyl resonances having a separation that decreases as the amounts of the two enantiomers in the mixture become more nearly equal. (iv) For each spectrum the integrated intensity ratio of the two signals is the same as the ratio of the two enantiomers present in the mixture. (v) The minor enantiomer in a mixture always gives rise to the highfield of the two *P*-alkyl resonances, irrespective of its configuration at phosphorus. All

[1] M. J. P. Harger, *J.C.S. Perkin II*, 1977, 1882; *J.C.S. Chem. Comm.*, 1976, 555.
[2] F. Ephraim, *Ber.*, 1911, **44**, 631.
[3] H. S. Aaron, T. M. Shryne, and J. I. Miller, *J. Amer. Chem. Soc.*, 1958, **80**, 107.
[4] M. Mikołajczyk and M. Leitloff, *Russ. Chem. Rev.*, 1975, **44**, 670.
[5] H. P. Benschop and G. R. van den Berg, *Rec. Trav. chim.*, 1968, **87**, 362.
[6] N. J. De'ath, K. Ellis, D. J. H. Smith, and S. Trippett, *Chem. Comm.*, 1971, 714; see also K. E. DeBruin and D. M. Johnson, *J. Amer. Chem. Soc.*, 1973, **95**, 4675.
[7] H. P. Benschop, G. R. van den Berg, and H. L. Boter, *Rec. Trav. chim.*, 1968, **87**, 387.
[8] J. Michalski and Z. Skrzypzynski, *J. Organometallic Chem.*, 1975, **97**, C31.

these points can be explained if it is supposed that phosphinothoic acids are associated in solution as short-lived (rapidly exchanging) diastereoisomeric dimers such as (4) and (5). The minor component in a mixture of enantiomers will on average be associated mostly with a *molecule* of opposite configuration, as in (4), and its *P*-alkyl group will be liable to long-range shielding by the *P*-phenyl group of its partner, whereas the major enantiomer will generally be paired with a molecule of like configuration, as in (5).

Other features also point to molecular association as the cause of enantiomer non-equivalence. For example, the separation between the two t-butyl signals in the spectrum of a sample of (3; $R/S = 90/10$) increases with the concentration of the substrate ($CDCl_3$ solution; 15 °C) and decreases when the temperature is raised

[(3)]/M	0.025	0.100	0.375	1.50
Δδ/p.p.m.	0.039	0.049	0.057	0.061

(chlorobenzene solution; [(3)] 0.23M). In less polar solvents such as benzene and carbon tetrachloride the

T/°C	−35	−10	17	39	66	90	115
Δδ/p.p.m.	0.076	0.072	0.068	0.060	0.054	0.049	0.039

signals from the two enantiomers of (3) are separated rather more widely than in $CDCl_3$. On the other hand, strongly solvating solvents such as methanol and dimethyl sulphoxide completely destroy the observed magnetic non-equivalence of the enantiomers, presumably because they suppress self-association of the substrate.

Molecular association can also explain the effect that an optically active phosphinothioic acid has on the spectrum of a racemic and structurally distinct acid. Consider, for example, a solution of racemic methylphenylphosphinothioic acid (2). Because there are equal amounts of the two enantiomers, (*R*)-(2) and (*S*)-(2) will have the same probability of being associated with a molecule of like (or opposite) configuration. The *P*-alkyl groups in the two enantiomers will therefore experience the same average shielding and will have the same chemical shift. If the optically active acid (*R*)-(3) is added, the probability of (*R*)-(2) being associated with a molecule of like configuration, whether (2) or (3), will increase, as will the probability of (*S*)-(2) being associated with a molecule of opposite configuration. Following the above suggestion that a *P*-alkyl group experiences greater shielding from the *P*-phenyl group of its partner when that partner has the opposite configuration [*cf.* the complex (4)], we would now predict that addition of (*R*)-(3) to racemic (2) will induce non-equivalence of the enantiomers with (*S*)-(2) being the more strongly shielded. Were (*S*)-(3) to be added instead of (*R*)-(3), the spectrum of racemic (2) should be identical except that the signals due to the (*R*)- and (*S*)-enantiomers would be interchanged. These predictions are fully borne out by the relevant results shown in Table 2. Not surprisingly, the difference in chemical shift of the *P*-methyl group in the enantiomers of (2) increases as the proportion of optically active (3) in the n.m.r. sample increases, and with it the probability of (2) being associated with (3) rather than with itself, while the apparently lesser ability of (*S*)-(3), relative to (*R*)-(3), to induce non-equivalence is only to be expected in view of its lower enantiomeric purity. The remaining results in Table 2 make clear that observation of induced non-equivalence is not restricted to racemic acids having a *P*-methyl group. Thus non-equivalence is clearly seen for the *P*-t-butyl group in racemic (3) and is even more pronounced for the *P*-methoxy-group in racemic *O*-methyl *O*-hydrogen phenylphosphonothioate (6). Moreover, the results in Table 3 show that the optically active phosphinothioic acids (2) and (3) can also induce enantiomer non-equivalence in the racemic phosphinic amides (7)—(9). For this to be so, the acid and the amide must, to some extent, cross-associate when mixed, at the expense of self-association, to form complexes such as (10) and (11). In contrast to the situation with a racemic phosphinothioic acid (Table 2), the separation between the n.m.r. signals of the enantiomers in a racemic phosphinic amide does not increase with the proportion of added optically active phosphinothioic acid beyond the point of a 1 : 1 mixture. It may be that cross-association between amide and acid is so favourable, relative to acid–acid and amide–amide association, that almost all the amide is associated with acid in a 1 : 1 mixture. In accord with our previous postulates, the non-equivalence of the enantiomers of (7) or (8) induced by the acid (*R*)-(3) is in the opposite sense to that induced by (*S*)-(2), and in both cases the enantiomer which experiences the greater shielding is the

TABLE 2

100 MHz ^1H N.m.r. spectra of racemic acids in $CDCl_3$ at 14.5 °C. Non-equivalence induced by added optically active phosphinothioic acids [a]

Mol. ratio racemic : optically active	Racemic (2) + (*R*)-(3) δ_{Me} of racemate		Racemic (2) + (*S*)-(3)[b] δ_{Me} of racemate		Racemic (3) + (*S*)-(2) δ_{But} of racemate		Racemic (6) + (*R*)-(3) δ_{MeO} of racemate		Racemic (6) + (*S*)-(2) δ_{MeO} of racemate	
1 : 0	2.006		2.006		1.103		3.803		3.803	
1 : 1	2.023	1.958[c]	2.019[c]	1.964	1.136	1.110	3.790	3.683	3.801	3.740
1 : 2	2.023	1.935	2.018	1.941	1.147	1.115	3.802	3.650	3.808	3.710
1 : 4	2.028	1.920	2.015	1.922	1.156[c]	1.117	3.799	3.617	3.816	3.694
1 : 8	2.030	1.915	2.015	1.912	1.163	1.121	3.803	3.604	3.808	3.675

[a] Total acid concentration was 0.23M for all spectra. For each mixture the two signals from the racemic acid were of equal intensity. These signals were doublets with J_{PH} 14 for (2), 18 for (3), and 14 Hz for (6). [b] (*S*)-(3) was contaminated with *ca.* 5.5% of the (*R*)-enantiomer. [c] Relative intensity of signal increased by addition of the (*S*)-enantiomer of the racemic component of the mixture.

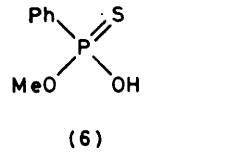
one having the configuration that places its *P*-alkyl group syn [as, for example, in (10)] rather than anti [as in (11)] to the *P*-phenyl group of the associated acid. For all three racemic amides (7)—(9), as well as for the racemic acid (6), the non-equivalence induced by optically active (3) exceeds that induced by (2). Perhaps the bulk of the *P*-t-butyl group in (3) restricts rotation about the Ph–P bond and increases the population of those conformations in which the plane of the benzene ring is more or less perpendicular to the But–P bond: this would result in the π electrons exerting greater shielding on a molecule with which (3) is associated.

TABLE 3

100 MHz ^{1}H N.m.r. spectra of racemic phosphinic amides in $CDCl_3$ at 14.5 °C. Non-equivalence induced by added optically active phosphinothioic acids [a]

Mol. ratio racemic: optically active	Racemic (7) + (*S*)-(2) δ_{Me} of racemate		Racemic (8) + (*S*)-(2) δ_{Me} of racemate		Racemic (9) + (*S*)-(2) δ_{But} of racemate	
1 : 0	1.670		1.746		1.121	
1 : 1	1.780 [b]	1.672	1.896 [b]	1.825	1.132	1.068
1 : 2	1.792	1.688	1.928	1.858	1.124	1.061
1 : 4	1.787	1.690	1.935	1.878	1.128	1.066
1 : 8	1.792	1.698	1.951	1.886	1.121	1.061
	Racemic (7) + (*R*)-(3) δ_{Me} of racemate		Racemic (8) + (*R*)-(3) δ_{Me} of racemate		Racemic (9) + (*R*)-(3) δ_{But} of racemate	
1 : 0	1.670		1.746		1.121	
1 : 1	1.790	1.597 [b]	1.908	1.797 [b]	1.122	1.018
1 : 2	1.803	1.603	1.936	1.824	1.116	1.009
1 : 4	1.807	1.619	1.945	1.837	1.103	0.994
1 : 8	1.802	1.612	1.953	1.849	1.109	1.002

[a] Total solute concentration was 0.23M for all spectra. For each mixture the two signals from the racemic amide were of equal intensity. These signals were doublets with J_{PH} 14.5 for (7) and (8) and 16 Hz for (9). [b] Relative intensity of signal increased by addition of the (*S*)-enantiomer of the amide.



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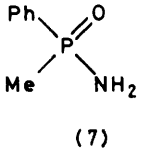

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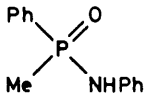

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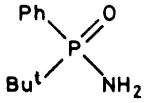

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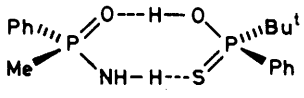

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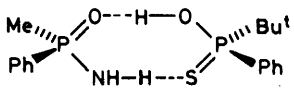
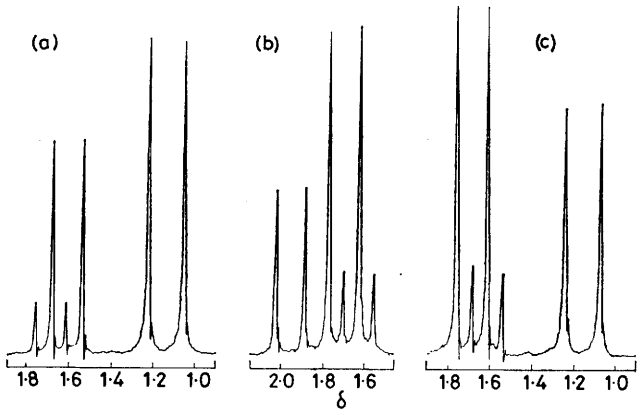


(11)

From the foregoing results it seems probable that optically active phosphinothioic acids can be generally useful in determining the enantiomeric purity and the configuration of compounds of the type XYP(S)OH or XYP(O)NHR provided that one of the groups X or Y gives a suitable n.m.r. signal. To illustrate this, small amounts of the acid (*R*)-(3) were added to a sample of methylphenylphosphinic amide (7), $[\alpha]_D$ +5.42° (*c* 3.5 in methanol), dissolved in $CDCl_3$ until the *P*-methyl doublets (J_{PH} 14.5 Hz) arising from the two enantiomers of (7) had about the optimal separation ($\Delta\delta$ *ca.* 0.5 J_{PH}) for accurate integration of all four spectral lines (Figure).



100 MHz ^{1}H N.m.r. spectra of $MePhP(O)NH_2$ (7), $[\alpha]_D$ +5.42, in $CDCl_3$ at 13.5 °C: (a) with added (+)-(*R*)-But^{t}PhP(S)OH (3) (0.48 molar equiv.); (b) with added (−)-(*S*)-MePhP(S)OH (2) (0.40 molar equiv.); (c) with added (−)-(*S*)-But^{t}PhP(S)OH (3) (0.24 molar equiv.)

From the relative intensities of the two *P*-methyl doublets the sample of (7) was estimated to be an 80 : 20 mixture of enantiomers. Also, since association with (*R*)-(3) resulted in the major enantiomer of (7) being shielded more than the minor enantiomer, the major enantiomer was assigned the (*S*)-configuration, shown in (10), rather than the (*R*)-configuration shown in (11). When (*S*)-(2) or (*S*)-(3) was used as the optically active phosphinothioic acid in place of (*R*)-(3) (Figure) the same conclusion was reached as regards the composition [80—81% (*S*)-enantiomer] of the sample of (7). To appreciate the validity of these results, they should be seen in the light of our earlier work [9] with the amide (7) in which the (+)-enantiomer was shown to have the (*S*)-configuration (by chemical correlation) and a specific rotation $[\alpha]_D$ +9.2° when enantiomerically pure (as evidenced by the rotation of the product of solvolysis in dilute methanolic hydrochloric acid): that being so, the present sample of (7) must actually be a 79.5 : 20.5 mixture of the (*S*)- and (*R*)-enantiomers. For the present purposes it is, perhaps, unfortunate that even without an optically active additive the sample of amide (7) gives distinct *P*-methyl resonances (δ 1.66 and 1.62) for the major and minor enantiomers.[1] However, such intrinsic non-equivalence is probably dependent on the presence of an aromatic substituent on phosphorus whereas induced non-equivalence should not be. In any case, an optically active additive is necessary for determining configuration, and also for clear separation of

[9] M. J. P. Harger, *J.C.S. Perkin I*, 1977, 2507.

the signals when the spectrum of (7) is recorded at 60 MHz or when the sample contains other than a large excess (*ca.* 80%) of one enantiomer. The marked difference in the amounts of (*S*)-(3) and (*R*)-(3) that had to be added to the sample of (7) to achieve the same separation (Figure) is doubtless a consequence of intrinsic non-equivalence: whereas (*S*)-(3) merely enhances the existing separation between the enantiomers of (7), (*R*)-(3) opposes and reverses the sense of their non-equivalence.

Throughout this paper we have accepted the established view that a phosphinothioic acid exists in solution in the thione [>P(S)OH] rather than the thiol [>P(O)SH] form.[10] In fact, the discussion of non-equivalence arising from self-association would not be materially different if the thiol form were dominant. The same is not true, however, as regards the non-equivalence induced in a phosphinic amide. For example, if (*R*)-(3) existed in the thiol form it would (according to our ideas) associate with the amide (7) in such a way that the (*R*)-enantiomer, rather than the (*S*), would be the more shielded. Clearly, then, any determination of configuration can be valid only if the basic premise of a thione structure is correct. There seems no doubt that (2) and (3) are thione, but it would be imprudent to discount the possibility that some phosphinothioic acids may in some circumstances prefer a thiol structure.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. Optical rotations were measured at 589 (Na D line) or 578 nm and 20 ± 2 °C in a cell of path length 100 mm (capacity *ca.* 0.9 ml) using a Perkin-Elmer 141 polarimeter. N.m.r. spectra were recorded at 100 MHz with a JEOL JNM-PS-100 spectrometer, using solutions in dry (molecular sieve) $CDCl_3$. The absolute values of the chemical shift δ (relative to internal tetramethylsilane) are estimated to be correct to ±0.005 p.p.m., and the separation between two signals in a single spectrum correct to ±0.002 p.p.m. Experiments involving mixtures of compounds or isomers were generally carried out by mixing appropriate volumes of equally concentrated solutions of the individual compounds; in this way the *total* molar concentration of substrate remained constant throughout a series of spectra.

Phosphinic Amides.—The following were available from previous work: racemic and (+)-(*S*)-methylphenylphosphinic amide (7),[9] racemic and (−)-(*S*)-methyl-*NP*-diphenylphosphinic amide (8),[9] and racemic phenyl-t-butylphosphinic amide (9).[11]

Methylphenylphosphinothioic Acid (2).[12,13]—A solution of sodium hydrogen sulphide (0.5 mol) in ethanol (250 ml) saturated with hydrogen sulphide was prepared by passing hydrogen sulphide through a solution of sodium ethoxide (0.5 mol) in ethanol. The solution was stirred and cooled (*ca.* −20°) while methylphenylphosphinic chloride (35 g, 0.20 mol),[14] b.p. 96—102° at 0.3 mmHg, in dry benzene (100 ml) was added dropwise during 40 min. The mixture was allowed to warm to room temperature and the solvent was removed under reduced pressure. The residue was dissolved in water (300 ml) and the solution was acidified with 12M-hydrochloric acid and extracted with chloroform (150 ml, 3 × 50 ml). The extracts were dried (Na_2SO_4) and dicyclohexylamine (39.8 g, 0.22 mol) in benzene (60 ml) was added in portions. Volatile material was removed under reduced pressure and the residue was triturated with ether to give the dicyclohexylamine salt of methylphenylphosphinothioic acid (59 g, 0.167 mol, 84%).

A portion of the salt was recrystallised twice from acetone and this material (1.6 g, 4.5 mmol) was dissolved in chloroform (25 ml). The solution was extracted with 0.4M-sodium hydroxide (25 ml) and the aqueous extract was washed with chloroform (15 ml) and ether (15 ml) and then acidified with concentrated sulphuric acid (0.8 ml). Extraction with chloroform (20 ml, 3 × 10 ml) gave an oil which on bulb-tube distillation afforded racemic methylphenylphosphinothioic acid (2), b.p. 115—125° (oven temp.) at 0.1 mmHg (lit.,[12] 82—85° at 0.05 mmHg), which solidified on standing, m.p. 43—46°, δ($CDCl_3$) 8.1—7.3 (5 H, m, Ph), 7.3br (1 H, s, OH), and 2.016 (3 H, d, J_{PH} 14 Hz, Me).

The bulk of the dicyclohexylamine salt (53 g, 0.15 mol) was dissolved in 1.7M-sodium hydroxide (150 ml) and the liberated amine was extracted with benzene (40 ml, 20 ml). The aqueous solution was acidified with concentrated sulphuric acid (17 ml) and extracted with dichloromethane (60 ml, 3 × 30 ml). The extracts were concentrated to an oil which was dissolved in acetone (50 ml) and added slowly (exothermic) to a solution of dried quinine (0.15 mol) in acetone (900 ml). After boiling for 1 h the hot mixture was filtered and allowed to stand at *ca.* 28° overnight when fine crystals (17.6 g) were deposited. Successive recrystallisations from acetone–methanol (8 : 1 and 4 : 1) afforded the quinine salt of one enantiomer of (2) (5.6 g, 11.3 mmol, 15% of theory); from this the free acid was isolated as described above for the isolation of racemic (2) from its dicyclohexylamine salt, but without distillation. Crystallisation from ether–petroleum gave (−)-(*S*)-methylphenylphosphinothioic acid (2), m.p. 91—93.5°, $[\alpha]_D$ −22.3°, $[\alpha]_{578}$ −23.6° (*c* 1.95 MeOH), δ($CDCl_3$) 8.05—7.3 (5 H, m, Ph), 7.25br (1 H, s, OH), and 2.055 (3 H, d, J_{PH} 14 Hz); no signal was visible at δ 1.98 (<1% would have been detected), but one did appear when a small amount of racemic (2) was added. The dicyclohexylamine salt of this acid had $[\alpha]_D$ −8.68°, $[\alpha]_{578}$ −9.35° (*c* 3.3 MeOH), m.p. 148—150° (lit.,[5] $[\alpha]_{578}^{25}$ −9.22°, MeOH, m.p. 152°).

Resolution of Phenyl-t-butylphosphinothioic Acid (3).—Racemic phenyl-t-butylphosphinothioic acid, m.p. 124—125° (lit.,[15] 126—127°), δ($CDCl_3$) 7.99—7.21 (6 H, m, Ph and OH) and 1.103 (9 H, d, J_{PH} 18 Hz, Bu^t) was available.[16] A portion (21.4 g, 0.10 mol) was dissolved in chloroform (100 ml) and a solution of (−)-1-phenylethylamine (12.1 g, 0.10 mol) in chloroform (40 ml) was added. Traces of

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[11] M. J. P. Harger, *J.C.S. Perkin I*, 1975, 514.

[12] A. Ratajczak, *Roczniki Chem.*, 1962, **36**, 175 (*Chem. Abs.*, 1962, **57**, 15,147f).

[13] H. S. Aaron, R. T. Uyeda, H. F. Frack, and J. I. Miller, *J. Amer. Chem. Soc.*, 1962, **84**, 617.

[14] O. Korpiun, R. A. Lewis, J. Chikos, and K. Mislow, *J. Amer. Chem. Soc.*, 1968, **90**, 4842.

[15] H. Hoffmann and P. Schellenbeck, *Chem. Ber.*, 1966, **99**, 1134.

[16] N. J. De'ath, Ph.D. Thesis, University of Leicester, 1970.

insoluble material were removed by filtration and the resulting solution (δ includes 0.99 and 0.92, both d, J_{PH} 17 Hz) was diluted initially with benzene (80 ml) and subsequently with petroleum (b.p. 60—80°) (in excess). The salt (A) which precipitated consisted of *ca.* 90% of the diastereoisomer having δ 0.99 while the mother liquor (B) was 80—85% the diastereoisomer having δ 0.92.

The precipitate (A) was dissolved in hot chloroform (80 ml) and ether (80 ml) was added to give the (−)-1-phenylethylamine salt of one enantiomer of (3) (8.95 g, 26.7 mmol, 53% of theory), $[\alpha]_D$ +24.3° (*c* 2.4 MeOH), δ($CDCl_3$) includes 0.99 (9 H, d, J_{PH} 17 Hz) and no detectable signal at 0.92. This was mixed with a slight excess of 0.5M-sodium hydroxide (55 ml), the liberated (−)-1-phenylethylamine was extracted with dichloromethane (3 × 15 ml), and the aqueous solution was acidified with 6M-hydrochloric acid. The solid which separated was extracted with dichloromethane (30 ml, 3 × 20 ml) and crystallised from petroleum (b.p. 60—80°) to give (+)-(*R*)-phenyl-t-butylphosphinothioic acid (3) (5.1 g, 23.7 mmol), m.p. 103—106° (softens at 96°) (lit.,[8] 96°), $[\alpha]_D$ +28.1° (*c* 2.4 MeOH) (lit.,[6,8] $[\alpha]_D$ 21.5° MeOH), δ($CDCl_3$) 7.83—7.19 (6 H, m, Ph and OH) and 1.135 (9 H, d, J_{PH} 18 Hz), containing only a trace (<1%) of the (−)-enantiomer, δ 1.065 (d, J_{PH} 18 Hz).

The mother liquor (B) was concentrated and ether (100 ml) was added. Chloroform was then added until most of the solid had dissolved and the remaining undissolved material (85—90% of the diastereoisomer with δ 0.92) was worked up as before. The resulting acid (3) was dissolved in hot petroleum (b.p. 40—60°)–ether (10 : 1, 30 ml) and the crystals which formed on cooling [enriched in (+)-(3)] were discarded; the mother liquor was concentrated and twice crystallised from petroleum (b.p. 60—80°) to give (−)-(*S*)-phenyl-t-butylphosphinothioic acid (3) (1.53 g, 7.2 mmol), m.p. 96—98°, $[\alpha]_D$ −24.9° (*c* 2.2 MeOH), δ($CDCl_3$) 7.84—7.19 (6 H, m, Ph and OH) and 1.13 and 1.07 (total 9 H, ratio *ca.* 19 : 1, both d, J_{PH} 18 Hz).

O-*Methyl* O-*Hydrogen Phenylphosphonothioate* (6).—The tetramethylammonium salt of *O*-methyl phenylphosphonothioate, m.p. 131—132° (lit.,[17] 135°), was prepared from *OO*-dimethyl phenylphosphonothioate and trimethylamine as described by Thuong and Chabrier.[17] To this was added an excess of 1M-sulphuric acid, and the mixture was extracted with ether. Removal of the solvent under reduced pressure afforded *O*-methyl *O*-hydrogen phenylphosphonothioate (6) as an oil, δ($CDCl_3$) 8.15—7.36 (5 H, m, Ph), 7.22br (1 H, s, OH), and 3.803 (3 H, d, J_{PH} 14 Hz, MeO) contaminated with a trace of ether. Because of the danger of decomposition [18] this material was used without distillation.

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[17] N. T. Thuong and J.-P. Chabrier, *Bull. Soc. chim. France*, 1970, 780.

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