Proton Magnetic Resonance Non-equivalence of the Enantiomers of Alkylphenylphosphinic Amides [1]

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The ^{1}H n.m.r. spectra of optically active (but optically impure) samples of methylphenylphosphinic amide (3) and its *N*-phenyl (1) and *N*-*p*-nitrophenyl (2) analogues exhibit distinct signals for the *P*-methyl groups in the *R*- and *S*-enantiomers. The two enantiomers in a racemic sample of (1), (2), or (3) give rise to only one *P*-methyl resonance, but this separates into two distinct signals when a foreign optically active phosphinic amide is added. Similar enantiomer non-equivalence can be induced in racemic samples of phenyl-t-butylphosphinic amide (6) and (*N*-phenyl)phenyl-t-butylphosphinic amide (7), while the enantiotopic methyl groups in (*N*-phenyl)dimethylphosphinic amide (8) or dimethylphosphinic amide (9) become non-equivalent in the presence of optically active (1). The observed spectra can all be rationalised in terms of molecular association through hydrogen bonding.

NUCLEAR magnetic resonance spectroscopy can provide valuable information pertaining to the ratio of the enantiomers in a sample of a chiral compound.[2] In early applications the enantiomers were chemically modified with an optically active reagent to give diastereoisomers having different spectroscopic properties.[3] Later it was found that enantiomers may display useful spectroscopic differences when examined in an optically active solvent,[4] or in an achiral solvent containing an optically active additive.[5] The latter approach has increased greatly in importance with the development of optically active lanthanide shift reagents.[6]

In the absence of any foreign optically active substance, the enantiomers present in an ideal dilute solution of a chiral compound have identical n.m.r. spectra. However, as Uskoković and his colleagues [7] discovered in 1969 for the case of dihydroquinine, diastereoisomeric solute–solute interactions can cause non-racemic mixtures of enantiomers to give distinct n.m.r. spectra.† Few subsequent reports of this phenomenon have appeared, although Horeau and Guetté [8] have noted n.m.r. non-equivalence of the enantiomers of some substituted succinic acids and Kabachnik and his co-workers [9] have described their use of ^{31}P n.m.r. spectroscopy to examine some rather complex compounds having both phosphorus and carbon chiral centres.

In the present paper we report a ^{1}H n.m.r. spectroscopic examination of some simple phosphinic amides in which the phosphorus atom is the only chiral centre.

RESULTS AND DISCUSSION

Mixtures of Optically Active and Racemic Phosphinic Amides of Like Structure.—The ^{1}H n.m.r. spectrum of enantiomerically pure (*S*)-(1) [10,11] in $CDCl_3$ (0.23M solution) includes a doublet (J_{PH} 13.6 Hz) at δ 1.74 attributable to the *P*-methyl group. Addition of racemic (1), as a solution (0.23M) in $CDCl_3$, in the amount required to give a mixture of the enantiomers of (1) in the ratio $S:R = 95:5$ results in the appearance of an additional small high field doublet (J_{PH} 13.5—14 Hz) at δ 1.53. Continued addition of racemic (1) causes the small high field doublet progressively to increase in intensity and move downfield while the original doublet moves less dramatically upfield. For each mixture the ratio of the integrated intensities of the two *P*-methyl signals is the same as the ratio of the enantiomers present in the mixture. The two signals coincide in the spectrum of racemic (1) at δ 1.685, a chemical shift substantially different from that of the *P*-methyl group in pure (*S*)-(1). Representative spectra are shown in Figure 1(a)—(d), while the more precise data presented in Table 1 reveal that the separation between the two *P*-methyl signals decreases more or less linearly by *ca.* 0.023 p.p.m. for each 5% increase in the proportion of the minor (*R*) enantiomer in the mixture.

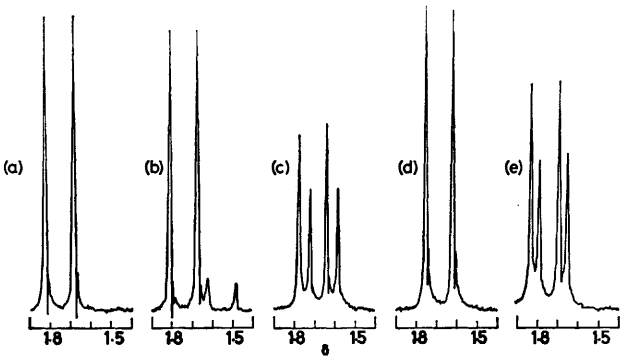

FIGURE 1 ^{1}H N.m.r. spectra (100 MHz) of (1) in $CDCl_3$ showing the *P*-methyl resonance(s) for samples of various enantiomeric composition: (a) 100% *S*; (b) 90% *S*, 10% *R*; (c) 60% *S*, 40% *R*; (d) 50% *S*, 50% *R*; (e) 40% *S*, 60% *R*

I.r. spectroscopic studies have shown that phosphinic amides such as $Ph_2P(O)NHPh$ are associated by means of hydrogen bonds in chloroform solution.[12] Such

† We are grateful to Professor H. Wynberg for bringing this work to our notice.

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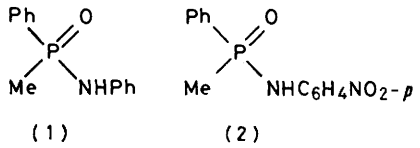
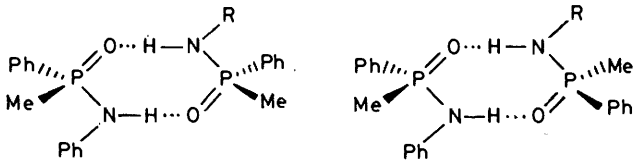
[12] I. Y. Kuramshin, N. R. Safiullina, A. A. Muratova, É. G. Yarkov, and A. N. Pudovik, *J. Gen. Chem.* (*U.S.S.R.*), 1975, **45**, 1177.

association of the chiral phosphinic amide (1) could lead to diastereoisomeric dimers such as (4; R = Ph) and (5; R = Ph) in which the associated molecules have, respectively, the same and opposite configurations at phosphorus. If exchange of partners were slow on the



(1) (2) (3)



(4) (5)

n.m.r. time scale, mixtures of the enantiomers of (1) would in principle show two *P*-methyl signals, one for dimer (4) and its mirror image and the other for dimer (5). The positions of the signals would be independent of the enantiomer ratio and their relative intensities would be equal to the ratio of the diastereoisomeric dimers rather than the ratio of the enantiomers in the mixture.

A situation more in keeping with the likely strength of the hydrogen bonds in the dimeric complexes and more helpful in explaining the observed n.m.r. spectra arises if exchange of partners is a rapid process. Assuming that there is no marked preference for association of molecules of like or opposite configuration * the major enantiomer in a highly unequal mixture will on average be associated mainly with partners of the same configuration whereas the minor enantiomer will for the most part be paired with molecules of opposite configuration. The major and minor enantiomers will therefore be related differently to their time-averaged local environments and will in principle exhibit distinct n.m.r. spectra. As the amounts of the two enantiomers in the mixture become more nearly equal, so molecules of opposite configuration will become increasingly important in the environment of the major enantiomer while molecules of like configuration will increasingly influence the environment of the minor enantiomer. As a result, the extent of the difference in the relationships of the major and minor enantiomers to their local environments will gradually diminish, and with it the differences in the spectra of the enantiomers. Eventually in the racemate both enantiomers will exist in a time-averaged environment made up equally of molecules of like and opposite configuration and their spectroscopic distinction will vanish.

So far we have considered only those mixtures that can be generated from samples of pure (*S*) and racemic (*N*-phenyl)methylphenylphosphinic amide, *i.e.* mixtures in which the *R*-enantiomer is never the major component. However, extension of the argument presented above leads to the prediction that mixtures of equal and opposite composition, *e.g.* 70% *S*, 30% *R* and 30% *S*, 70% *R*, will display identical n.m.r. spectra. In order that we might test this prediction, we prepared (*R*)-(*N*-phenyl)methylphenylphosphinic amide and repeated the original experiment but with the *R*-enantiomer now in excess.

TABLE 1

100 MHz ^{1}H N.m.r. spectra of mixtures of (*S*) and racemic phosphinic amides in $CDCl_3$ at 15 °C: enantiomer ratios and chemical shifts of *P*-methyl resonances [a]

PhMeP(O)NHPh (1)			PhMeP(O)NHC$_6$H$_4$NO$_2$ (2)			PhMeP(O)NH$_2$ (3)		
S/*R* [b]	δ_S	δ_R	*S*/*R* [c]	δ_S	δ_R	*S*/*R* [b]	δ_S	δ_R
100/0	1.740		100/0	1.880		100/0	1.675	
95/5	1.740	1.528	96/4	1.880	1.617	95/5	1.670	1.624
90/10	1.735	1.549	92/8	1.870	1.628	90/10	1.670	1.627
85/15	1.730	1.566	88/12	1.865	1.650	85/15	1.670	1.633
80/20	1.730	1.590	84/16	1.855	1.669	80/20	1.665	1.634
75/25	1.730	1.608	71/29	1.840	1.722	75/25	1.660	1.634
70/30	1.725	1.629	60/40	1.810	1.759	70/30	1.650	1.628
65/35	1.720	1.641	50/50	1.800		65/35	1.650	1.633
60/40	1.710	1.655				60/40	1.650	1.640
55/45	1.695	1.668				55/45	1.650	1.645
50/50	1.685					50/50	1.645	

[a] The total amide concentration was 0.23M for (1), *ca.* 0.12M for (2), and 0.25M for (3). The absolute values of δ_S and δ_R (relative to Me_4Si) are estimated to be correct to ± 0.005 p.p.m.; the separation between the signals ($\delta_S - \delta_R$), measured on a wider expansion, is estimated to be correct to ± 0.002 p.p.m. [b] Enantiomer ratios deduced from the amounts of (*S*) and racemic amide in the mixtures; the ratios of the integrals of the *P*-methyl resonances were the same within experimental error. [c] Enantiomer ratios deduced only from the ratios of the integrals of the *P*-methyl resonances.

R : *S*	100 : 0	90 : 10	80 : 20	70 : 30	60 : 40	50 : 50
δ_R	1.78	1.78	1.775	1.77	1.76	1.73
δ_S		1.64	1.665	1.69	1.72	

The results [see also Figure 1(e)] are as predicted in as much as the minor enantiomer, now that with the *S*-configuration, still gives rise to the higher field signal, and the separation between the two signals decreases as the mixture becomes more nearly racemic. The actual magnitude of the separation between the signals is rather less than was originally observed with the *S*-enantiomer in excess (Table 1) but this and other

* This assumption is made only to simplify the discussion; it is not essential and may not be strictly correct.

discrepancies can doubtless be ascribed to the higher temperature (26 °C) at which the spectra were recorded.

Mixtures of the enantiomers of (*N*-*p*-nitrophenyl)-methylphenylphosphinic amide [11] (2) display behaviour (Table 1) similar to that of the amide (1) except that the n.m.r. non-equivalence of the *P*-methyl groups is even more pronounced,* but of greater significance, in spite of its less impressive appearance, is the enantiomer non-equivalence observed for methylphenylphosphinic amide [11] (3) (Table 1). This establishes that the effect is not dependent on the presence of a substituent at nitrogen, although the relatively small separation of the *P*-methyl signals for the primary amide (3) does suggest that the intrinsic enantiomer non-equivalence of (1) or (2) is amplified by the *N*-aryl group.

TABLE 2

100 MHz ^{1}H N.m.r. spectra of racemic methylphenylphosphinic amides in $CDCl_3$ at 24 °C. Influence of added (*S*)-methylphenylphosphinic amides on the positions of the *P*-methyl resonances [a]

rac-(3) + (*S*)-(1) [b]		*rac*-(1) + (*S*)-(3) [b]		*rac*-(2) + (*S*)-(1) [b]		*rac*-(2) + (*S*)-(3) [b]	
mol ratio *rac* : (*S*)	δ_{Me} of racemate	mol ratio *rac* : (*S*)	δ_{Me} of racemate	mol ratio *rac* : (*S*)	δ_{Me} of racemate	mol ratio *rac* : (*S*)	δ_{Me} of racemate
1 : 0	1.66	1 : 0	1.75	1 : 0	1.835	1 : 0	1.835
1 : 1	1.67, 1.635	1 : 1	1.80, 1.78	1 : 1	1.83, 1.715	1 : 1	1.855, 1.82
1 : 4	1.67,[c] 1.61	1 : 3.5	1.83,[c] 1.80	1 : 4	1.83,[c] 1.67	1 : 4	1.875,[c] 1.83
1 : 14	1.67, 1.595	1 : 14	1.84, 1.80	1 : 8	1.83, 1.66		

[a] In experiments involving only (1) and (3) the total amide concentration was 0.23M. In experiments involving (2), the concentration of (*S*)-(1) or (*S*)-(3) was 0.1M. Values of δ_{Me} (relative to Me_4Si) are estimated to be correct to $\pm$0.005 p.p.m. [b] Anilide (*S*)-(1) was >98% one enantiomer; amide (*S*)-(3) was contaminated with *ca.* 5% of the *R*-enantiomer. [c] Signal intensity increased on addition of the *S*-enantiomer of the racemic component of the mixture.

For all three amides (1)—(3) the less intense *P*-methyl n.m.r. signal, originating from the minor enantiomer, is the one at higher field. A molecule of the minor component in a mixture of enantiomers will, on average, be associated mainly with a molecule of opposite configuration, as in the dimer (5). In this situation its *P*-methyl group may experience long range shielding by the π electrons of the *P*-phenyl group of its partner. The *P*-methyl group of the major component will experience relatively little shielding because its molecules are usually paired as in dimer (4).

Mixtures of Optically Active and Racemic Phosphinic Amides of Unlike Structure.—Further insight into the association of methylphenylphosphinic amides came from examining the n.m.r. spectra of some solutions containing a racemate mixed with a single enantiomer of an amide substituted differently at nitrogen (see Table 2). Thus, for example, addition of the optically active anilide (*S*)-(1) causes the single *P*-methyl resonance exhibited by racemic amide (3) to separate into two equal signals [Figure 2(a); two peaks are superimposed at δ 1.74]: the separation is 0.035 p.p.m. for an equimolar mixture of racemic (3) and (*S*)-(1), but increases to 0.075 p.p.m. when the optically active amide is present in large excess. Clearly the enantiomers of (3) are made magnetically non-equivalent as a result of their association with (*S*)-(1). By careful addition of small amounts of (*S*)-(3) [Figure 2(b)] it was possible to establish that the lower field of the two *P*-methyl resonances is that due to the *S*-enantiomer of the racemate (3). This is consistent with the ideas developed above. In the presence of (*S*)-(1) the molecules of racemic (3) can become cross-associated as in (4; R = H) or (5; R = H) instead of always being associated with other molecules of the same structure. The probability of (*R*)-(3) being associated with a molecule of opposite configuration (albeit perhaps of different structure) is therefore increased by the presence of (*S*)-(1), so that the *P*-methyl group in the *R*-enantiomer will experience enhanced time-averaged shielding by the *P*-phenyl groups of its partners. Conversely, (*S*)-(3) will be associated with a molecule of opposite configuration less often than before and its *P*-methyl group will in consequence feel reduced intermolecular shielding by *P*-phenyl groups. The relative positions of the *P*-methyl resonances can therefore be understood simply in terms of differential shielding of the enantiomers by the *P*-phenyl groups of associated molecules. Support for this view can be found in the behaviour of the other combinations of racemic and optically active methylphenylphosphinic amides shown in Table 2. In every case the enantiomer of the racemate that gives rise to the higher field *P*-methyl resonance is the one liable to suffer increased intermolecular shielding by *P*-phenyl groups, *i.e.* the

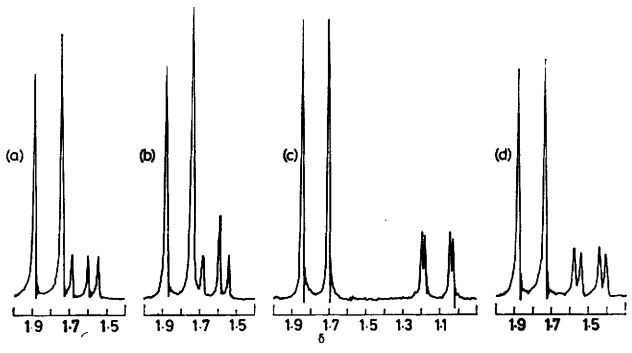


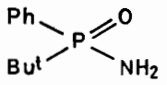
FIGURE 2 ^{1}H N.m.r. spectra (100 MHz) showing the *P*-alkyl resonances for mixtures of phosphinic amides in $CDCl_3$: (a) racemic (3) + (*S*)-(1) (ratio 1 : 4); (b) repeat of (a) after addition of (*S*)-(3); (c) racemic (6) + (*S*)-(1) (ratio 1 : 7); (d) (9) + (*S*)-(1) (ratio 1 : 4)

* Because of the low solubility of the *p*-nitroanilide (2) these spectra were recorded on more dilute solutions. However, it seems most unlikely that higher dilution is of itself the cause of the greater enantiomer non-equivalence.

one having the opposite configuration to that of the added optically active amide.

It is interesting to see that the induced separations of the *P*-methyl resonances of the *R*- and *S*-enantiomers of the racemates in Table 2 arise in three different ways, *viz.* *R* moves upfield while *S* remains essentially unchanged; *S* moves downfield while *R* remains essentially unchanged; and *S* and *R* both move downfield, *S* more so than *R*. To explain these results in detail it is necessary to take into account possible differences in the degrees of association of the two enantiomers of the racemate with the added optically active amide as well as factors (*e.g.* the nature of the substituent on nitrogen in the added amide) which influence the environments of both enantiomers of the racemate in the same way; although such factors do not contribute to the observed enantiomer non-equivalence, they will influence the absolute values of the *P*-methyl chemical shifts. With the information presently available, such explanations are rather speculative and will not be elaborated here.

Having established the ability of the optically active phosphinic amides (*S*)-(1) and (*S*)-(3) to induce n.m.r. non-equivalence in the enantiomers of racemic methylphenylphosphinic amides, we looked briefly at their effects on the spectra of the racemic phenyl-t-butylphosphinic amides (6) and (7). The protons of the



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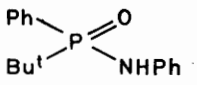
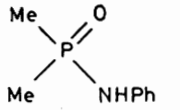


(7)

t-butyl group are separated from the chiral phosphorus atom by three bonds instead of two, and their average position, allowing for rapid rotation about single bonds, is further removed from the *P*-phenyl group of an associated molecule. Nevertheless, addition of (*S*)-(1) to the racemic amide (6) causes the t-butyl resonance (δ 1.098, d, J_{PH} 15 Hz in $CDCl_3$ at 16°) to separate into two signals [δ 1.106 and 1.098 with 1 : 1 molar ratio; δ 1.122 and 1.105 with a 16-fold excess of (*S*)-(1)] of equal intensity [Figure 2(c)]. (*S*)-(3) induces comparable non-equivalence in the enantiomers of the amide (6) [$\Delta\delta_{But}$ 0.012 p.p.m. with a 3.5-fold excess of (*S*)-(3) in $CDCl_3$], but in the case of the racemic anilide (7), no more than a broadening of the t-butyl resonance is seen when either (*S*)-(1) or (*S*)-(3) is added.

Mixtures of Optically Active and Achiral Phosphinic Amides.—The dimethylphosphinic amides (8) and (9)



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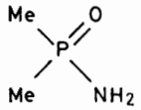

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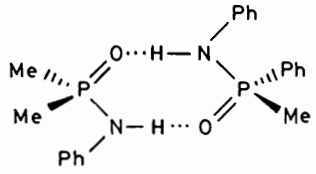

(10)

are achiral, and self-association will not destroy the magnetic equivalence of the enantiotopic methyl groups. On the other hand, association with an optically active phosphinic amide will afford a complex such as (10) in which these same methyl groups are, in principle, magnetically non-equivalent. In practice we find that addition of the optically active anilide (*S*)-(1) does indeed cause the signal due to the *P*-methyl groups in (8) or (9) to separate into two well resolved signals of equal intensity [Table 3 and Figure 2(d)]. In view of the relatively small non-equivalence noted earlier for the enantiomers in non-racemic samples of amide (3) it is not altogether surprising that (*S*)-(3) causes little separation of the *P*-methyl resonances of (8) and (9); indeed, in the case of (8) no clear separation is apparent even with a large excess of (*S*)-(3).

Conclusion.—Alkylphenylphosphinic amides having a *P*-methyl or *P*-t-butyl group are especially well suited for studying enantiomer non-equivalence by ^1H n.m.r. spectroscopy because the protons of the alkyl groups are coupled only to phosphorus. In a number of cases, notably the *p*-nitroanilide (2), non-equivalence is also discernible in the aromatic region of the spectrum; although we have not looked at this closely, it seems inevitable that the multiplicity of the resonances will make difficult any accurate measurement. ^{13}C N.m.r. spectroscopy might well prove useful for examining aryl groups, and also *P*-alkyl groups more complex than methyl or t-butyl. Undoubtedly there is considerable scope for applying n.m.r. spectroscopy to the measurement of enantiomer ratios in samples of chiral phosphinic

TABLE 3

100 MHz ^1H n.m.r. spectra of dimethylphosphinic amides (10) and (11) in $CDCl_3$ at 24 °C. Non-equivalence of the *P*-methyl resonances induced by addition of (*S*)-methylphenylphosphinic amides [a]

(8) + (*S*)-(1) [b]		(8) + (*S*)-(3) [b]		(9) + (*S*)-(1) [b]		(9) + (*S*)-(3) [b]	
mol ratio (8) : (*S*)-(1)	δ_{Me} of (8)	mol ratio (8) : (*S*)-(3)	δ_{Me} of (8)	mol ratio (9) : (*S*)-(1)	δ_{Me} of (9)	mol ratio (9) : (*S*)-(3)	δ_{Me} of (9)
1 : 0	1.62	1 : 0	1.62	1 : 0	1.53	1 : 0	1.53
1 : 1	1.625, 1.59	1 : 1	1.635br	1 : 1	1.51, 1.50	1 : 1	1.525br
1 : 2	1.62, 1.57	1 : 2	1.64br	1 : 2	1.515, 1.49	1 : 2	1.52, 1.51
1 : 8	1.62, 1.545	1 : 8	1.65br	1 : 8	1.51, 1.47	1 : 8	1.525, 1.50

[a] Total amide concentration was *ca.* 0.2M in all experiments. Values of δ_{Me} (relative to Me_4Si) are estimated to be correct to ±0.005 p.p.m. [b] Anilide (*S*)-(1) was >98% one enantiomer; amide (*S*)-(3) was contaminated with *ca.* 5% of the *R*-enantiomer.

amides, determining the configuration at phosphorus, and investigating intramolecular forces.

The observed spectra can be rationalised in terms of molecular association through hydrogen bonds, leading to complexes in which a suitably positioned group in one molecule experiences long range shielding by the *P*-phenyl group of its partner. It is also necessary to suppose that exchange of partners between complexes is fast on the n.m.r. time scale. Our results are all consistent with this picture, but it must remain tentative until independent evidence is found to support it.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were recorded with Perkin-Elmer 237 and 257 instruments and mass spectra with a V.G. Micromass 16B spectrometer. Optical rotations were measured at 589 nm and 20 ± 2 °C in a cell of path length 100 mm (capacity *ca.* 0.9 ml) using a Perkin-Elmer 141 polarimeter. G.l.c. analyses were performed on a Pye 104 flame ionisation chromatograph fitted with a 1.5 m × 4 mm i.d. glass column packed with 3% silicone OV 17 on silanised 100—120 mesh Diatomite C 'Q'.

N.m.r. spectra (tetramethylsilane internal standard) were recorded at 100 MHz with a JEOL JNM-PS-100 spectrometer, using solutions in dry (molecular sieve) $CDCl_3$. 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 compounds, of proven structure and, where applicable, enantiomeric composition and configuration at phosphorus, were available from earlier work: [11] (−)-(*S*)-(*N*-phenyl)methylphenylphosphinic amide (1), $[\alpha]_D$ −28.5° (*c* 2.12 in MeOH) (>98% one enantiomer) and racemic (1); (+)-(*S*)-(*N*-*p*-nitrophenyl)methylphenylphosphinic amide (2), $[\alpha]_D$ +43.6° (*c* 1.7 in MeOH) (≥94% one enantiomer; probably ≥98% one enantiomer based on stereochemistry of methanolysis product) and racemic (2); (+)-(*S*)-methylphenylphosphinic amide (3), $[\alpha]_D$ +9.2° (*c* 2.8 in MeOH) (≥99% one enantiomer) and racemic (3). In some experiments (as indicated) a sample of (*S*)-(3), $[\alpha]_D$ +8.3° (*c* 2.2 in MeOH), contaminated with *ca.* 5% of the *R*-enantiomer, was used; racemic phenyl-t-butylphosphinic amide (6); [13] and racemic (*N*-phenyl)phenyl-t-butylphosphinic amide (7).[14]

(+)-(R)-(N-*Phenyl*)*methylphenylphosphinic Amide* (1).—The reaction of (−)-menthol with methylphenylphosphinic chloride has previously been used to obtain $(S)_P$-menthyl methylphenylphosphinate.[11] The crystallisation mother liquors now served as a source of the R_P-diastereoisomer. They were concentrated to an oil which was dissolved in light petroleum (b.p. 60—80°)–dichloromethane (5 : 1). The solution was cooled at 0° and then at −20° and the resulting solid recrystallised from light petroleum (b.p. 60—80°) at 0°. N.m.r. spectroscopy showed the absence of the S_P-diastereoisomer from the resulting $(R)_P$-menthyl methylphenylphosphinate, m.p. 87—88° (lit.,[15] 89°), $[\alpha]_D$ −16.3° (*c* 2.6 in benzene) (lit.,[15] $[\alpha]_D$ −16° in benzene).

Aniline (1.30 g, 12.5 mmol) in tetrahydrofuran (5 ml) was added slowly to a stirred suspension of potassium hydride (0.5 g, 12.5 mmol) in tetrahydrofuran (25 ml). After 10 min, $(R)_P$-menthyl methylphenylphosphinate (1.18 g, 4.0 mmol) in tetrahydrofuran was added dropwise. After 1 h at room temperature examination by g.l.c. (3% OV 17; 240°) showed that all the phosphinate (R_t 5.2 min) had been consumed; a major product (R_t 10.5 min) and two minor products (R_t 1.85 and 3.3 min) were detected. Solid ammonium chloride (0.7 g, 13 mmol) was added and stirring continued for a further 10 min before water (1 ml) in tetrahydrofuran was cautiously added. The solvent was removed under reduced pressure and chloroform (25 ml) and 1M-hydrochloric acid (16 ml) were added to the residue. The organic layer was separated, the aqueous layer extracted with chloroform (2 × 12 ml), and the total organic extracts were washed with aqueous sodium hydrogen carbonate. The residue remaining after evaporation of the solvent was chromatographed on alumina (50 g). Elution with ether gave a brown liquid (phosphine smell), and with ether–methanol (25 : 1) a solid which on crystallisation from dichloromethane–ether (1 : 1) afforded colourless needles of (*R*)-(*N*-phenyl)methylphenylphosphinic amide (1) (0.085 g, 0.37 mmol, 9%), $[\alpha]_D$ +29.0° (*c* 2.8 in MeOH), identified by comparison of its n.m.r. and i.r. spectra with those of the *S*-enantiomer. A second crop of crystals (0.140 g) was obtained, but this was not a single enantiomer.

(N-*Phenyl*)*dimethylphosphinic Amide* (8) (with R. H. Bowles).—Dimethylphosphinic chloride, b.p. 108—135° (oven temperature) at 56 mmHg, was prepared by the method of Pollart and Harwood [16] from tetramethylbiphosphine disulphide.[17] It was dissolved in dichloromethane and added to an excess of aniline also dissolved in dichloromethane. A solid separated and was collected by filtration. The filtrate, on evaporation, was found by n.m.r. examination to contain little except unchanged aniline. The solid (a mixture of aniline hydrochloride and the required amide) was dissolved in methanol and the solution made just alkaline by addition of methanolic sodium methoxide. Sodium chloride was removed by filtration and the solvent evaporated to leave an oil which crystallised from benzene to give needles of (N-*phenyl*)-*dimethylphosphinic amide* (8), m.p. 121.5—123°, M^+ 169, $\nu_{max.}$ (Nujol) 3 150br (NH), 1 605 (NH deformation), and 1 175, 1 165, and 1 150 cm^{-1} (P=O), $\delta(CDCl_3)$ 7.28—6.80 (5 H, m, Ph), 6.08br (1 H, d, J_{PH} 10 Hz, NH), and 1.62 (6 H, d, J_{PH} 14 Hz, Me) (Found: C, 56.7; H, 7.1; N, 8.3. $C_8H_{12}NOP$ requires C, 56.8; H, 7.15; N, 8.3%). [The above work-up procedure was adopted when it seemed that amide (8) was only very sparingly soluble in dichloromethane and other aprotic solvents. It is now clear that the amide itself, as opposed to the complex it apparently forms with aniline hydrochloride, is reasonably soluble.]

Dimethylphosphinic Amide (9).—Dimethylphosphinic chloride (1.35 g, 12 mmol) in dichloromethane (3 ml) was added dropwise with stirring to a cooled solution of ammonia (*ca.* 2 g) in dichloromethane (30 ml). The precipitate (NH_4Cl) was removed and the filtrate concentrated under reduced pressure. The resulting oil was seen by g.l.c. (3% OV 17; 170°) to contain only one important com-

[13] M. J. P. Harger, *J.C.S. Perkin I*, 1975, 514.
[14] M. J. P. Harger, *J.C.S. Perkin I*, 1977, 605.
[15] O. Korpiun, R. A. Lewis, J. Chikos, and K. Mislow, *J. Amer. Chem. Soc.*, 1968, **90**, 4842.
[16] K. A. Pollart and H. J. Harwood, *J. Org. Chem.*, 1962, **27**, 4444.
[17] G. W. Parshall, *Org. Synth.*, 1973, Coll. Vol. 5, 1016.

ponent (R_t 1.7 min) and had i.r. and n.m.r. spectra consistent with it being the required amide, but repeated attempts at crystallisation failed. Chromatography on alumina (40 g), eluting with ether containing methanol (0—10%), gave material with unchanged spectra and continued resistance to crystallisation. Bulb-tube distillation afforded dimethylphosphinic amide (9), b.p. 80° (oven temperature) at 0.05 mmHg, as a low-melting solid, *m/e* 93 (M^+, 40%) and 78 (100) [impurity *m/e* 170 (10%) and 155 (15)], $\nu_{max.}$ (melt) 3 230 and 3 120 (NH_2), 1 580 (NH_2 deformation), and 1 170 cm^{-1} (P=O), $\delta(CDCl_3)$ 3.1br (2 H, s, NH_2) and 1.53 (6 H, d, J_{PH} 14 Hz, Me) [impurity δ 1.73 (d, J_{PH} 14 Hz) integrating for 0.3H]. Although clearly not pure, this material was used in the n.m.r. investigation for fear that continued attempts to purify it would cause further decomposition. [Dimethylphosphinic amide would be expected to hydrolyse very readily; the mass spectrum suggests the impurity is probably $Me_2P(O)OP(O)Me_2$].

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