The Synthesis of Optically Active *P*-Phenyl-*P*-(2,4,6-trimethylphenyl)-phosphinamide and an X-Ray Structure of (−)-(1*R*)-*N*-(1-Phenylethyl)-(S_P)-*P*-phenyl-*P*-(2,4,6-trimethylphenyl)phosphinamide

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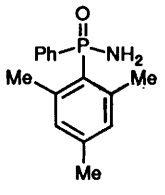
The primary phosphinic amide *P*-phenyl-*P*-(2,4,6-trimethylphenyl)phosphinamide has been prepared in optically active form (75% enantiomeric excess) in six steps from dichlorophenylphosphine. The configuration of the intermediate *N*-(1-phenylethyl)-*P*-phenyl-*P*-(2,4,6-trimethylphenyl)phosphinamide has been established by an X-ray crystal structure determination of the minor diastereoisomer. This compound exhibits in the solid state two independent rotameric conformations about the P–N bond. Geometry optimisation by MNDO MO calculations refined these to the same rotamer having the nitrogen lone pair *anticlinal* to the P–O bond.

In connection with another project we required a synthetic method for the preparation of optically active *P*-phenyl-*P*-(2,4,6-trimethylphenyl)phosphinamide (**1**). There is a paucity of work in the literature on primary phosphinic amides and at the commencement of this work to our knowledge there was only one reported preparation of an optically active primary phosphinamide.[1] Harger obtained (−)-(*S*)-*P*-methyl-*P*-phenylphosphinamide **3** by treatment of the menthyl phosphinate **2** with potassium amide.[1] Certain aspects of this procedure led us to seek an alternative route for the preparation of optically active **1**. Thus the method relies on the separation of a 1:1 mixture of diastereoisomeric phosphinates by fractional crystallisation which even if successful can be tedious and low yielding. The phosphinates prepared from mesitylphenylphosphinic chloride (**7**) and menthol were obtained as an oil that failed to crystallise from a variety of solvents. Furthermore the diastereoisomers were not easily separated by chromatography. Similarly the analogous diastereoisomeric phosphinate mixture derived from borneol could not be separated.

We now report an alternative route which was successful for the preparation of optically active mesitylphenylphospinamide (**1**) in quite good optical yield.



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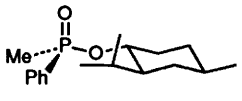

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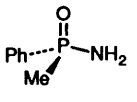

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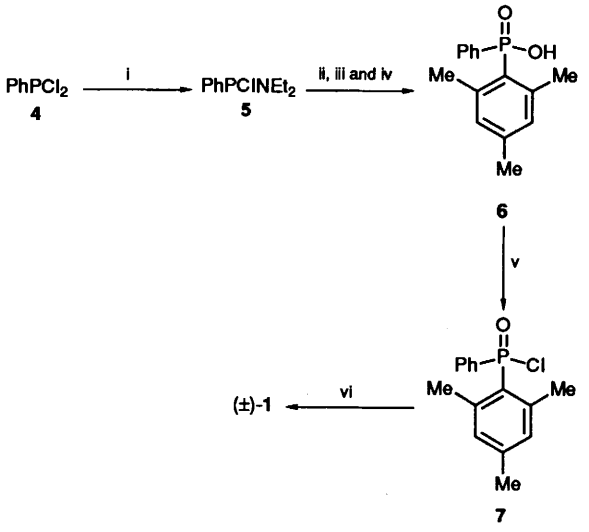
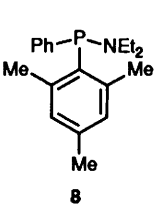
Results and Discussion

Synthesis.—Using a synthetic route analogous to that reported by Mislow *et al.*,[2] *P*-phenyl-*P*-(2,4,6-trimethylphenyl)-phosphinic acid **6** was prepared in 42% yield (Scheme 1).

Treatment of dichlorophenylphosphine **4** with diethylamine in ether gave, after distillation, the aminophosphine **5**, which was then reacted with mesitylmagnesium bromide to give compound **8**. Oxidation of **8** with hydrogen peroxide in acetone and then hydrolysis of the tertiary phosphinamide **9** gave the phosphinic acid **6**. The hydrolysis of the intermediate phosphinamide **9** proved to be particularly sluggish, requiring stirring at room temperature for six days. Possibly the access of water molecules to the phosphorus atom in **9** is sterically hindered by the mesityl group, though poor solubility of **9** in the aqueous medium might also contribute to the slow hydrolysis.



Scheme 1 *Reagents and conditions:* i, $HNEt_2$, Et_2O, 0 °C, 2 h, RT overnight, 76%; ii, 2,4,6-$Me_3C_6H_2MgBr$, Et_2O; iii, H_2O_2, acetone, reflux, 4 h; iv, conc. HCl, 6 days, 42%; v, $SOCl_2$, reflux, 2 h; vi, EtOH, NH_3, CH_2Cl_2, 0 °C, 2 h, RT, weekend, 83%



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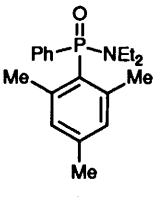

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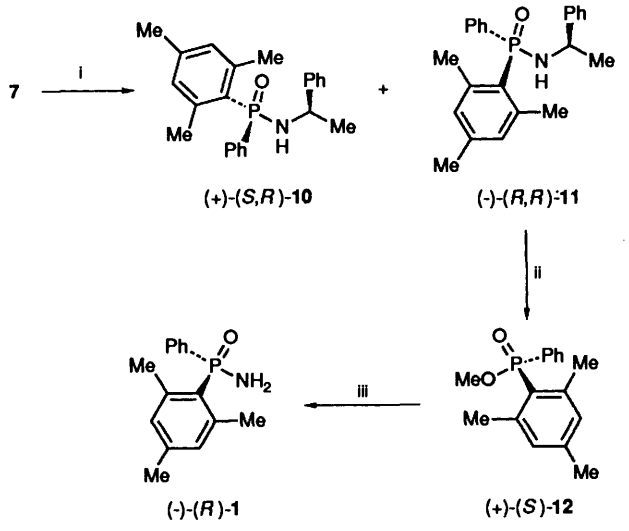
Racemic **1** can be prepared in two steps from **6**. Treatment of **6** with thionyl chloride followed by reaction of the resultant phosphinic chloride **7** with a saturated ethanolic ammonia solution, gave the previously unreported phosphinamide (±)-**1** in 83% yield.

Compounds **1**, **6** and **7** demonstrated several features in their ^1H NMR spectra which confirmed that a mesityl group had been incorporated into these compounds. At δ 2.27–2.35 there was a sharp singlet corresponding to the 4-methyl group and at δ 2.48–2.49 there was either a singlet or doublet with a small (*ca.* 1 Hz) coupling to phosphorus; this signal was assigned to the 2- and 6-methyl groups. These signals integrated at 1:2 protons respectively as expected. The two mesityl ring protons (3- and 5-H) appeared at δ 6.83–6.95 as a doublet resonance,

with an associated four-bond coupling to phosphorus of 3.7–5.3 Hz.

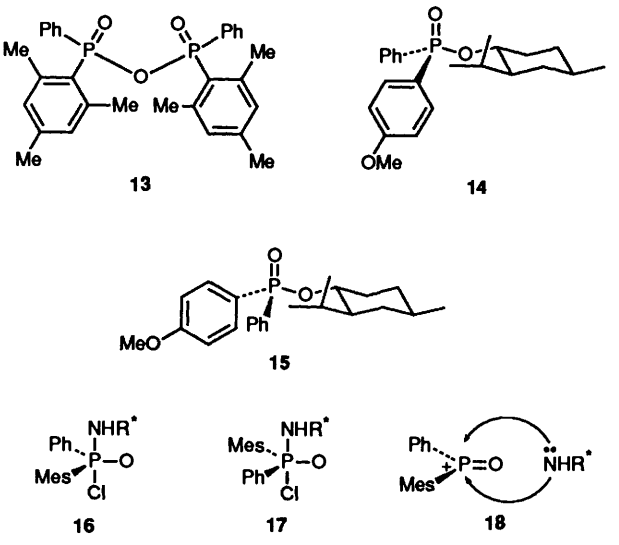
As phosphinic acid **6** was in hand, attention was directed towards attempting to resolve the phosphorus chiral centre. Addition of an ethereal solution of the phosphinic chloride **7** to a mixture of (+)-(*R*)-1-phenylethylamine and triethylamine in ether gave a 1.0:2.2:6.5 mixture of products (determined by ^{31}P NMR spectroscopy) after stirring overnight and aqueous work-up (Scheme 2). Each of the three components was isolated by flash column chromatography. Analysis of their NMR spectra (^1H and ^{31}P) indicated that the products were the pyrophosphinate **13** (11%), (+)-(*S,R*)-**10** (18%), and (−)-(*R,R*)-**11** (61%). The stereochemical assignments were made on the basis of a crystal structure determination of the minor diastereoisomer, (+)-(*S,R*)-**10** (see later). The pyrophosphinate **13** presumably results from the reaction of **7** with unreacted **6** during the preparation of **7**. NMR spectroscopy (^1H and ^{31}P) indicated that both (+)-(*S,R*)-**10** and (−)-(*R,R*)-**11** were diastereoisomerically pure.



Scheme 2 *Reagents and conditions:* i, (+)-(*R*)-1-phenylethylamine, Et_3N, Et_2O, 0 °C, 2 h, RT overnight, 78% combined; ii, MeOH, HCl, reflux, 5 h, 89%; iii, NH_3, $NaNH_2$, THF, −33 °C, 6 h, 87%

It is evident that such an imbalance of diastereoisomers (+)-(*S,R*)-**10** and (−)-(*R,R*)-**11** should not obtain in a classical resolution. Indeed it is more reminiscent of a kinetic resolution, but it is clearly not that straightforward since more than 50% of the major diastereoisomer, (−)-(*R,R*)-**11** was obtained. Similar effects have been noticed previously; thus Knowles,[3] in the preparation of menthyl phosphinates **14** and **15** reported a 4:1 imbalance of diastereoisomers in favour of **14**. A rapid equilibration by chloride exchange of the enantiomeric phosphinic chloride precursors, one enantiomer of which reacted preferentially with menthol, was forwarded as an explanation. A similar explanation probably accounts for the predominance of (−)-(*R,R*)-**11** though alternative rationales could be advanced. Ligand rearrangement in a pentacoordinate intermediate **16** to give **17** seems unlikely. Unimolecular dissociation of **7** to give a phosphinylinium cation **18** and chloride ion also seems improbable. In this case the phosphinylium ion is prochiral and when reacted with a chiral reagent such as the amine could conceivably exhibit asymmetric induction. The stereomutation phenomenon is welcomed as it improves the economy of the procedure.

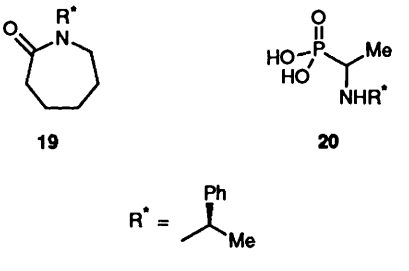
Compounds (+)-(*S,R*)-**10** and (−)-(*R,R*)-**11** are protected versions of the desired products and it was hoped that reductive demethylbenzylation would yield homochiral phosphinamide **1**. To our knowledge this reaction has not been performed on this



Mes = 2,4,6-$Me_3C_6H_2$

type of system before. However, 1-phenylethyl groups have been removed reductively from amides **19**[4] and α-aminophosphonic acids **20**,[5] in the former case with a dissolving metal reduction (NH_3/Na),[4] and in the latter case with catalytic hydrogenation (Pearlman's catalyst).[5] It was found in the case of compounds (+)-(*S,R*)-**10** and (−)-(*R,R*)-**11** that despite various attempts under different conditions, neither of these methods was effective in removing the 1-phenylethyl group. This may be a reflection of steric hindrance or the phosphorus atom altering the nature of the directly bonded nitrogen by π-bonding. Thus the original plan to remove the 1-phenylethyl group in one step without affecting the stereochemistry at phosphorus was thwarted. However, it was found that when (−)-(*R,R*)-**11** was heated to reflux in acidic methanol for 5 h (Scheme 2) the phosphinamide was cleanly converted in 89% yield to (+)-*S*-**12** (88% ee). It was found that the addition of Pirkle's reagent (−)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol as a chiral auxiliary to a dilute solution of **12** in deuteriochloroform resulted in chemical shift nonequivalence of the enantiomeric methoxy doublet signals in the 270 MHz ^1H NMR spectrum. A 4 Hz separation was achieved with a three-fold excess of the chiral auxiliary [minor (−)-enantiomer signal downfield], enabling the enantiomeric excess to be determined by integration as 88%. Presumably the polar P–O bond in **12** interacts with the OH group in Pirkle's reagent. Other groups have used acidic solvolysis to improve the nucleofugicity of other leaving groups on phosphorus atoms.[6,7]

Reaction of the methyl phosphinate (+)-(*S*)-**12** in THF with sodamide in liquid ammonia at −33 °C for 6 h gave an 87% yield of (−)-(*R*)-**1** (75% ee). The addition of Pirkle's chiral 9-anthryl auxiliary to a dilute solution of **1** in deuteriochloroform resulted in a good splitting (11 Hz at 270 MHz) of the mesityl ring, *meta* proton doublet signal [minor (+)-enantiomer upfield] enabling the enantiomeric excess to be measured (75%) by integration.



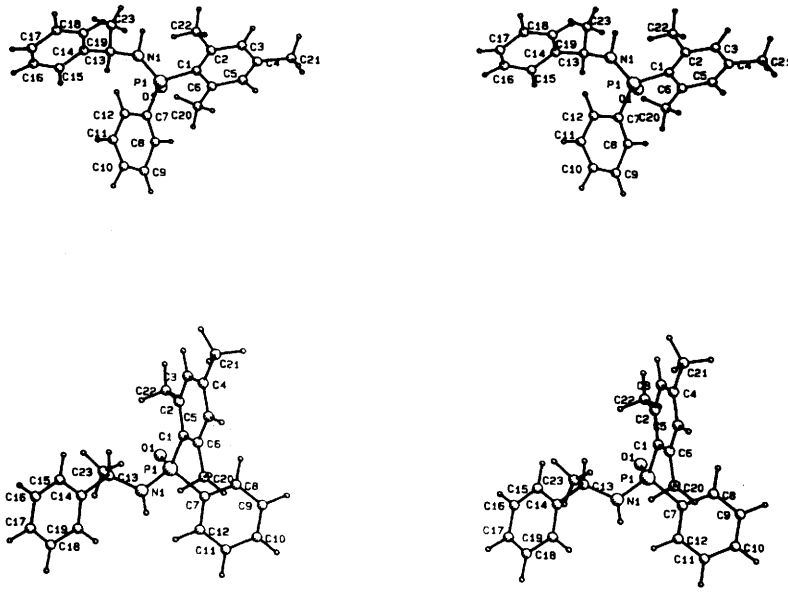


Fig. 1 Stereoscopic view of the two independent molecules of **10**. Upper diagram molecule 1, lower diagram molecule 2.

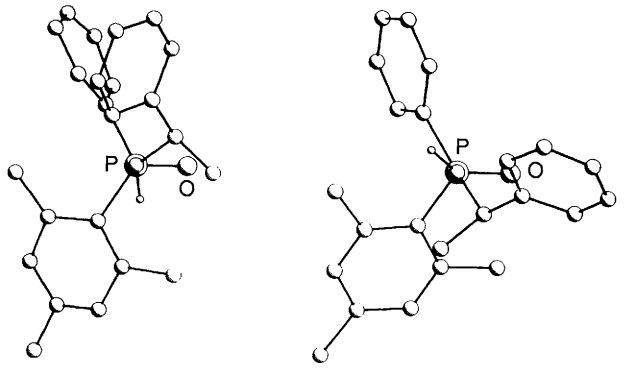


Fig. 2 The two independent molecules of **10** viewed along the N–P bond direction with the P–O bond projection horizontal. Left-hand diagram molecule 1, right-hand diagram molecule 2.

In Scheme 2 both the methanolysis of (−)-(*R*,*R*)-**10** and the reaction of sodamide with (+)-(*S*)-**12** have been depicted as proceeding with inversion of stereochemistry at phosphorus.* Although this has not been confirmed experimentally, there is precedence in the literature that phosphinamides undergo acid-catalysed methanolysis with inversion of the stereochemistry at phosphorus[1,6,7] as do methyl phosphinates with Grignard reagents[6,7] and menthyl phosphinates with potassium amide.[1]

X-Ray Crystal Structure.—The minor diastereoisomer of the *N*-(1-phenylethyl)phosphinic amide was deemed to have the better crystals for X-ray analysis. The structure, which exhibited two independent molecules in the unit cell, is depicted in Fig. 1. Since the 1-phenylethylamine used in the synthesis had the *R*-configuration, the configuration at phosphorus in this minor diastereoisomer **10** is shown to be *S*. Accordingly the other (major) diastereoisomer must have the R_C R_P-configuration.

Atomic coordinates and selected geometrical parameters for the two independent molecules of the minor diastereoisomer **10** are listed in Tables 1 and 2, respectively. The atom labelling is indicated in Fig. 1. Bond lengths and angles generally agree to within the limits of experimental accuracy, which are, however, rather wide in this structure due to the paucity of X-ray intensity data (see Experimental section). Larger differences occur in the conformations of the two molecules (Table 2). The overall conformation of the molecule is determined by the rotations about the five bonds [C(1)–P, C(7)–P, C(14)–C(13), C(13)–N and P–N]. The differences in torsion angles about these bonds are *ca.* −45, +46, +8, 0 and −97°, respectively. The most significant difference is the conformation about the P–N bond (see Fig. 2).

To account for the shortening of the P–N bond in compounds of type $Ph_2P(O)NRR'$ (R,R′ = alkyl or H) from the standard length of 1.80 Å to the observed[8–11] values of 1.62–1.68 Å, and the generally flattened bonding geometry at the nitrogen atom, it has been suggested[12] that there is strong π-bonding between nitrogen and phosphorus. It was further suggested[12] that this π-bonding may involve a non-classical n–σ* bond and that the lone pair of electrons on nitrogen would, in consequence, tend to be oriented essentially *antiperiplanar* to the polar P–O bond. This is approximately the case in molecule **1**, where the pertinent torsion angle is 160°, but not in molecule **2** (torsion angle 48°) (see Table 2 and Fig. 2). The P–N bond lengths are, however, virtually identical at 1.613 and 1.622 Å. It would seem that the orientation of the lone pair of electrons on the nitrogen atom relative to the P–O bond is not highly energy sensitive and that packing considerations may play an important role in determining the actual conformation about the P–N bond. A similar conclusion is reached from consideration of the P–N conformation in the crystal structures of the analogous molecules[$Ph_2P(O)NMe_2$],[8][$Ph_2P(O)NH_2$],[9][$Ph_2P(O)N(H)CH_2CH_2Cl$],[10][$Ph_2P(O)N(Me)CH_2CH_2Ph$][11] and[$Ph_2P(O)N(H)CH_2CH_2Ph$].[11] In three cases the lone pair –N–P–O conformations are probably *antiperiplanar*, but in the other two cases the lone pair appears to be oriented *synclinal* to the P–O bond.

MNDO molecular orbital calculations[13] on **10**, in which, starting from the X-ray structures, all the parameters were refined, resulted in essentially the *same* geometry and heat of formation from each of the two independent molecules. Considering the key parameters listed in Table 2, bond lengths are identical to four significant figures, bond angles differ by a maximum of 0.2° (mean difference 0.06°) and torsion angles differ by a maximum of 1.0° (mean difference 0.4°). Averaged

* Even in the unlikely event that both nucleophilic displacements at phosphorus in Scheme 2 proceeded with retention, the stereochemical assignment of the phosphinic amide would stand.

Table 1 Fractional atomic coordinates ($\times 10^4$) with esds in parentheses

	x	*y*	*z*
Molecule 1			
P(1)	−626(4)	0	−355(2)
O(1)	−76(13)	1332(13)	−262(6)
N(1)	−478(12)	−929(13)	364(6)
C(1)	12(15)	−970(15)	−1051(8)
C(2)	1206(15)	−966(16)	−1015(9)
C(3)	1738(16)	−1467(19)	−1624(12)
C(4)	1102(16)	−1805(17)	−2238(10)
C(5)	−85(16)	−1944(18)	−2262(9)
C(6)	−700(16)	−1501(17)	−1697(9)
C(7)	−2212(17)	316(16)	−594(9)
C(8)	−2595(28)	1338(23)	−1037(16)
C(9)	−3837(41)	1752(31)	−1240(23)
C(10)	−4488(41)	921(46)	−878(20)
C(11)	−4277(24)	−236(45)	−436(15)
C(12)	−3033(19)	−487(27)	−263(10)
C(13)	−521(15)	−372(17)	1090(8)
C(14)	−1423(14)	−1061(21)	1504(8)
C(15)	−2203(19)	−242(19)	1847(12)
C(16)	−2916(23)	−897(29)	2300(14)
C(17)	−3017(19)	−2213(31)	2331(12)
C(18)	−2235(21)	−3018(21)	2010(11)
C(19)	−1508(17)	−2458(21)	1557(9)
C(20)	−1973(16)	−1681(23)	−1764(12)
C(21)	1669(16)	−2219(28)	−2913(9)
C(22)	2039(19)	−515(29)	−331(12)
C(23)	667(20)	−365(25)	1531(10)
Molecule 2			
P(1)	−4664(4)	−2516(6)	−4383(2)
O(1)	−4873(10)	−1065(10)	−4495(6)
N(1)	−5656(12)	−3429(15)	−4859(7)
C(1)	−4583(12)	−2934(15)	−3425(8)
C(2)	−4856(13)	−2005(16)	−2891(9)
C(3)	−4843(14)	−2369(20)	−2173(8)
C(4)	−4510(15)	−3663(23)	−1937(9)
C(5)	−4217(16)	−4568(19)	−2449(9)
C(6)	−4285(14)	−4234(17)	−3172(8)
C(7)	−3281(15)	−3023(16)	−4682(9)
C(8)	−2255(16)	−2837(29)	−4236(10)
C(9)	−1186(22)	−3059(32)	−4485(15)
C(10)	−1147(19)	−3424(27)	−5194(13)
C(11)	−2155(21)	−3568(28)	−5659(12)
C(12)	−3219(15)	−3352(18)	−5404(9)
C(13)	−6897(13)	−3278(15)	−4765(8)
C(14)	−7683(18)	−3068(22)	−5470(12)
C(15)	−8394(21)	−1904(25)	−5547(16)
C(16)	−9114(30)	−1693(44)	−6138(26)
C(17)	−9188(31)	−2603(56)	−6689(24)
C(18)	−8474(37)	−3703(57)	−6665(20)
C(19)	−7675(21)	−3954(27)	−6037(12)
C(20)	−3982(17)	−5345(20)	−3666(10)
C(21)	−4434(25)	−4122(31)	−1137(10)
C(22)	−5183(19)	−568(21)	−3037(11)
C(23)	−7330(16)	−4521(22)	−4374(9)

values are listed in Table 2 and Fig. 3 depicts the MNDO-refined molecule 1 viewed in the same direction as the X-ray structures shown in Fig. 2. MNDO-refined molecule 2 is indistinguishable from molecule 1. It is clear that, as far as the P–N bond is concerned, both molecules have refined to a geometry quite similar to that of the X-ray structure of molecule 1, with the nitrogen lone-pair electrons probably *anticlinal* to the P–O bond (Table 2). Detailed comparison of the conformations about the P–N bond is, however, not possible due to the uncertainties in the location of the hydrogen atom bonded to nitrogen from the X-ray studies, and the resulting uncertainties in the calculation of the orientation of the nitrogen lone pair. A short intramolecular contact distance of 2.98(3) Å between methyl carbon atom C(20) and C(7) of the neighbouring phenyl ring in the X-ray structure of molecule 1 becomes 3.21 Å in the MNDO-refined molecule.

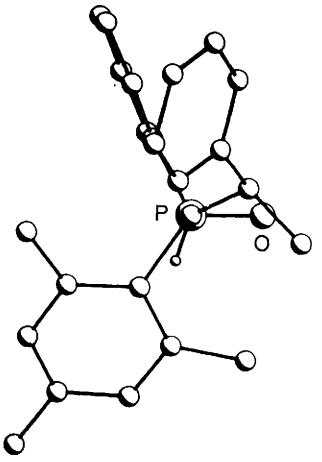


Fig. 3 MNDO refined molecule. View direction as for Fig. 2.

Experimental

^{1}H NMR spectra were recorded in $CDCl_3$ (TMS reference) on either a JEOL FX90Q (89.6 MHz) or a JEOL GX270 (270 MHz) spectrometer; *J* values are in Hz. ^{31}P NMR spectra were recorded in $CDCl_3$ (85% H_3PO_4 reference) on a JEOL FX90Q spectrometer at 36.2 MHz. IR spectra were recorded on a Pye-Unicam SP3-100 instrument in the phase indicated in the text. Melting points were determined on a Gallenkamp hot-stage apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter in chloroform at 25 ± 1 °C and are in 10^{-1} deg cm^2 g^{-1}. Mass spectra were recorded on a Kratos MS 80 instrument. All solvents were dried according to literature procedures. The amines were dried by heating at reflux for 1 h over KOH, and were then distilled and then stored over KOH. All other reagents were used as received. Flash chromatography was carried out using silica gel (230–400 mesh). All manipulations involving potentially toxic phosphorus compounds were performed wearing protective gloves and in an efficient fume hood.

Syntheses.—P-*Phenyl*-P-2,4,6-*trimethylphenylphosphinic acid* (**6**). Dry magnesium turnings (17.2 g, 0.70 mol) and ether* (50 cm^3) were placed in a 1 litre three-necked flask fitted with a mechanical stirrer, a reflux condenser, a self-equalising dropping funnel and a nitrogen inlet and outlet. A small portion (*ca.* 10 cm^3) of a solution of 1-bromomesitylene (91.3 g, 0.46 mol) in ether (100 cm^3) was allowed into the reaction flask and 1,2-dibromoethane (1.5 cm^3) was added. The reaction vessel was warmed gently until reflux commenced and became self-sustaining. The remainder of the 1-bromomesitylene solution was added dropwise at a rate such that the reflux was maintained. On completion of the addition the reflux was continued for a further 3 h. The Grignard solution was cooled in an ice-bath and to it was added dropwise with stirring chloro(diethylamino)phenylphosphine (**5**)[14] (98.9 g, 0.46 mol) in dry ether (100 cm^3). On completion of the addition the cooling bath was removed and stirring was continued for 5 h. The reaction was allowed to stand at room temperature overnight and the solids were removed by suction filtration. Concentration of the filtrate gave a yellow oil which was dissolved in acetone (150 cm^3) and then 15% H_2O_2 (82 cm^3) was added at such a rate to maintain a strong reflux. When all

* 'Ether' refers to diethyl ether throughout.

Table 2 Selected bond lengths (Å), bond angles and torsion angles (°). Values in parentheses are esds. Esds for torsion angles are *ca.* 1.5°.

	X-ray structure		MNDO-refined
	Molecule 1	Molecule 2	
P–O	1.476(13)	1.485(11)	1.511
P–N	1.613(13)	1.622(14)	1.702
P–C(1)	1.837(17)	1.811(15)	1.794
P–C(7)	1.834(19)	1.811(16)	1.773
N–C(13)	1.461(18)	1.457(18)	1.471
N–H(N)	1.14	1.04	1.003
O–P–N	115.4(8)	112.9(7)	110.3
O–P–C(1)	111.1(7)	110.4(7)	115.7
N–P–C(1)	105.2(6)	110.0(7)	105.0
O–P–C(7)	105.3(8)	111.3(7)	107.3
N–P–C(7)	107.0(8)	104.6(7)	109.7
C(1)–P–C(7)	113.0(8)	107.3(7)	108.9
P–N–C(13)	121.6(10)	119.9(10)	122.2
P–N–H(N)	127	124	109.7
C(13)–N–H(N)	91	114	111.3
C(2)–C(1)–P–N	−79.7	−117.1	−108.8
C(6)–C(1)–P–N	112.4	60.4	74.2
C(8)–C(7)–P–N	161.6	−156.3	−178.3
C(12)–C(7)–P–N	−14.3	36.5	7.1
C(15)–C(14)–C(13)–N	−132.2	−122.9	−122.8
C(19)–C(14)–C(13)–N	47.8	54.4	58.1
C(23)–C(13)–N–P	−108.1	−109.4	−93.4
C(14)–C(13)–N–P	126.2	128.2	141.2
C(13)–N–P–O	37.2	−58.3	24.6
C(13)–N–P–C(1)	160.0	65.6	149.7
C(13)–N–P–C(7)	−79.5	−179.4	−93.4
H(N)–N–P–O	−83	141	−108.3
H(N)–N–P–C(1)	39	−95	16.9
H(N)–N–P–C(17)	160	20	133.7
ee[a]–N–P–O	160	48	131.2
ee[a]–N–P–C(1)	−77	172	−103.6
ee[a]–N–P–C(7)	44	−73	13.2

[a] ee denotes the probable position of the nitrogen lone pair.

the peroxide had been added the reaction mixture was heated at reflux for 4 h. The reaction mixture was allowed to cool slightly and concentrated hydrochloric acid (150 cm^3) was added slowly. The mixture was stirred vigorously for 6 days. A semi-solid was isolated by suction filtration which upon trituration with ether (100 cm^3) gave **6** (55.4 g) as a colourless powder. The crude acid was recrystallised from ethanol–water to afford colourless crystals of **6** (50.2 g, 42%), m.p. 163–165 °C (Found: C, 69.4; H, 6.7. $C_{15}H_{17}PO_2$ requires C, 69.22; H, 6.58%); ν_{max}(Nujol)/cm^{-1} 2470–2130 br. (P–OH), 1155 (P=O); δ_H 2.27 (3 H, s, 4-Me), 2.48 (6 H, d, $^4J_{PH}$ 1.2, 2- and 6-Me), 6.83 (2 H, d, $^4J_{PH}$ 3.7, 3- and 5-H), 7.24–7.65 (5 H, m, aromatic), 13.08 (1 H, s, OH); δ_P 38.1.

P-*Phenyl*-P-(2,4,6-*trimethylphenyl*)*phosphinamide* [(±)-**1**]. The acid **6** (20.0 g, 76.9 mmol) was heated to reflux with freshly distilled thionyl chloride (50 cm^3) for 2 h. The reaction mixture was allowed to cool and the thionyl chloride was removed on a rotary evaporator. Any residual thionyl chloride was removed by azeotropic distillation with toluene (2 × 20 cm^3) to afford crude **7** as a very pale yellow oil (21.4 g), which was used in the next step without any further purification. ν_{max}(neat)/cm^{-1} 1230 (P=O); δ_H 2.33 (3 H, s, 4-Me), 2.46 (6 H, d, $^4J_{PH}$ 1.8, 2- and 6-Me), 6.95 (2 H, d, $^4J_{PH}$ 5.3, 3- and 5-H), 7.32–7.93 (5 H, m, aromatic); δ_P 46.9. The ^1H NMR spectrum of crude **7** indicated the presence of *ca.* 5.5 mol% of the pyrophosphinate **13**. The phosphinic chloride **7** was dissolved in dichloromethane (60 cm^3) and was added dropwise to a stirred, saturated ethanolic ammonia solution (160 cm^3) and dichloromethane (120 cm^3), cooled to −10 to −15 °C. On completion of the addition the mixture was stirred at −10 to −15 °C for 1 h and then ammonia gas was bubbled through the solution for 15 min. The reaction mixture was warmed to room temperature and stirring was continued over the weekend. The reaction mixture was transferred to a separating funnel with chloroform (300 cm^3), and washed successively with aqueous 5% K_2CO_3 (2 × 100 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated to dryness to yield the crude amide (±)-**1** (18.5 g). Recrystallisation from toluene gave pure (±)-**1** (16.6 g, 83%) as a colourless powder, m.p. 210.5–212.5 °C (Found: C, 69.6; H, 7.0; N, 5.7. $C_{15}H_{18}NOP$ requires C, 69.48; H, 7.00; N, 5.4%); ν_{max}(Nujol)/cm^{-1} 3322, 3236 and 3134 (NH_2), 1178 (P=O); δ_H 2.31 (3 H, s, 4-Me), 2.49 (6 H, s, 2- and 6-Me), 3.12–3.57 br. (2 H, s, NH_2), 6.87 (2 H, d, $^4J_{PH}$ 4.5, 3- and 5-H), 7.22–7.86 (5 H, m, aromatic); δ_P 28.2.

(1R)-N-(1-*Phenylethyl*)-(S_P/R_P)-P-*phenyl*-P-(2,4,6-*trimethylphenyl*)*phosphinamides* (+)-(S,R)-**10** *and* (−)-(R,R)-**11**. The crude phosphinic chloride **7** (prepared from 10.0 g, 38.5 mmol of **6** as described above) in ether (25 cm^3) was added dropwise with stirring (mechanical stirrer) to a solution of (+)-(*R*)-1-phenylethylamine (5.13 g, 42.4 mmol) and triethylamine (4.28 g, 42.4 mmol) in ether (125 cm^3) cooled in an ice-bath. On completion of the addition the reaction mixture was stirred at 0 °C for 2 h and then for a further 5 h at room temperature. The reaction mixture was allowed to stand overnight and the triethylamine hydrochloride was removed by suction filtration. Rotary evaporation of the ether gave a residue which was dissolved in chloroform (500 cm^3) and was washed with water (2 × 200 cm^3), *ca.* 0.25 mol dm^{-3} HCl (2 × 100 cm^3), saturated aqueous K_2CO_3 (2 × 100 cm^3) and brine (1 × 200 cm^3). The chloroform solution was dried ($MgSO_4$) and evaporated to afford a white semi-solid (14.7 g). The ^{31}P NMR spectrum indicated that the crude product was a mixture of three

components which integrated in the ratio 1.0:2.2:6.5. The crude product was purified by flash column chromatography using ether–dichloromethane (1:1) as eluent yielding three compounds eluted in the following order: bis[phenyl(2,4,6-trimethylphenyl)]pyrophosphinate **13** (1.02 g, 11%), which was recrystallised from diisopropyl ether–acetone to afford colourless crystals (0.60 g, 6%), m.p. 182–184 °C (decomp.) (Found: C, 71.4; H, 6.2. $C_{30}H_{32}P_2O_3$ requires C, 71.70; H, 6.42%); ν_{max}(Nujol)/cm^{-1} 1225 (P=O); δ_H 2.28 (6 H, s, 4-Me), 2.37 (12 H, s, 2- and 6-Me), 6.85 (4 H, s br, 3- and 5-Me), 7.32–7.52 (6 H, m, aromatic), 7.67–7.80 (4 H, m, aromatic); δ_P 30.4; (+)-(*S*,*R*)-**10** (2.58 g, 18%), which was recrystallised from toluene–hexane to afford a colourless waxy solid (1.81 g, 13%), m.p. 134–136 °C (Found: C, 76.3; H, 7.4; N, 3.8. $C_{23}H_{26}NOP$ requires C, 76.01; H, 7.21; N, 3.85%), $[\alpha]_D$ +42.7° (*c* 0.01), ν_{max}(Nujol)/cm^{-1} 3170 and 3230 (NH), 1185 (P=O); δ_H 1.53 (3 H, d, $^3J_{HH}$ 6.7, PhCH*Me*), 2.29 (3 H, s, 4-Me), 2.46 (6 H, s, 2- and 6-Me), 3.08 (1 H, t, $^3J_{HH}$ 9.1, $^2J_{PH}$ 9.1, NH), 4.67 (1 H, m, PhC*H*Me), 6.88 (2 H, d, $^4J_{PH}$ 3.7, 3- and 5-H), 7.2–7.4 (8 H, m, phenyl), 7.55 (2 H, m, phenyl); δ_P 27.4; (−)-(*R*,*R*)-**11** (8.46 g, 61%), which was recrystallised from toluene to afford colourless needles (6.85 g, 49%), m.p. 161–162 °C (Found: C, 75.8; H, 7.4; N, 3.9. $C_{23}H_{26}NOP$ requires C, 76.01; H, 7.21; N, 3.85%), $[\alpha]_D$ −10.5° (*c* 0.01); ν_{max}(Nujol)/cm^{-1} 3200 (NH), 1184 (P=O); δ_H 1.63 (3 H, d, $^3J_{HH}$ 6.8, PhCH*Me*), 2.27 (3 H, s, 4-Me), 2.34 (6 H, s, 2- and 4-Me), 3.16 (1 H, t, $^3J_{HH}$ 9.0, $^2J_{PH}$ 9.0, NH), 4.50 (1 H, m, PhC*H*Me), 6.82 (2 H, d, $^4J_{PH}$ 3.5, 3- and 5-H), 7.22 (5 H, s, Ph), 7.41 (3 H, m, phenyl), 7.68 (2 H, m, phenyl); δ_P 27.0.

(+)-(*S*)-*Methyl phenyl*(2,4,6-*trimethylphenyl*)*phosphinate* (+)-(S)-**12**. The major diastereoisomer (−)-(*R*,*R*)-**11** (6.61 g, 18.2 mmol), methanol (85 cm^3) and 98% H_2SO_4 (1.6 cm^3) were heated at reflux for 5 h with monitoring by TLC. The reaction mixture was allowed to cool, chloroform (200 cm^3) was added and then the solution was washed with aqueous 10% $NaHCO_3$ (3 × 50 cm^3) and water (2 × 50 cm^3). The chloroform solution was dried ($MgSO_4$) and concentrated on a rotary evaporator to afford a colourless liquid (6.17 g). The crude product was purified by flash column chromatography on silica gel through a short column (3 cm) to afford a colourless liquid (4.14 g, 89%); $[\alpha]_D$ +22.8° (*c* 0.33) (Found: C, 69.4; H, 6.9. $C_{16}H_{19}O_2P$ requires C, 70.06; H, 6.98%); ν_{max}(neat)/cm^{-1} 1225 (P=O), 1035 (P–OMe); δ_H 2.29 (3 H, s, 4-Me), 2.49 (6 H, d, $^4J_{PH}$ 1.2, 2- and 6-Me), 3.74 (3 H, d, $^3J_{PH}$ 11.1, OMe), 6.91 (2 H, d, $^4J_{PH}$, 4.2, 3- and 5-H), 7.45 (3 H, m, phenyl), 7.66 (2 H, m, phenyl); δ_P 37.2. The enantiomeric excess in this phosphinate (5.4 mg) was determined to be 88% by ^{1}H NMR analysis (270 MHz) in $CDCl_3$ of the externally diastereotopic methoxy doublet signals [δ 3.506 and 3.522, (+) and (−)-**12** respectively] observed in the presence of (−)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol (15.2 mg) as a chiral auxiliary.

(−)-(R)-P-*Phenyl*-P-(2,4,6-*trimethylphenyl*)*phosphinamide* (−)-(R)-**1**. A 250 cm^3 three-necked flask was placed in a bath of vermiculite and was fitted with a mechanical stirrer and a dry-cold condenser with a $CaCl_2$ guard tube. Ammonia gas was passed through a tube of KOH pellets and then condensed into the above apparatus (*ca.* 150 cm^3). Sodium metal (1.00 g, 43.5 mmol) was cut into small pieces and added slowly. After the addition of the first piece of sodium, iron(III) nitrate (0.08 g) was also added. The mixture was then stirred for 30 min. The apparatus was fitted with a self-equalising dropping funnel and (+)-(*S*)-**12** (4.00 g, 14.6 mmol) in THF (freshly distilled from $LiAlH_4$, 40 cm^3) was added dropwise. The temperature in the reaction vessel was maintained just at the reflux point of liquid ammonia for 6 h with monitoring by TLC. The reaction mixture was then allowed to warm up to room temperature overnight. NH_4Cl (4.00 g) was added cautiously and then the mixture was stirred for 15 min. Water (40 cm^3) in THF (20 cm^3) was added slowly and the mixture was stirred for a further 30 min, once the addition was complete. The contents of the reaction flask were poured into a round bottom flask and concentrated on a rotary evaporator. The residue was dissolved in chloroform (200 cm^3) and separated. The aqueous residue was extracted with chloroform (2 × 100 cm^3). The combined chloroform extracts were washed with aqueous 10% $KHCO_3$ (2 × 100 cm^3) and water (2 × 100 cm^3), dried ($MgSO_4$) and evaporated to dryness to afford a cream solid (3.54 g). The solid was placed on the top of a dry, short (3 cm) flash column, the flask was washed out with ether–dichloromethane (1:1) and then the column was eluted under pressure with this solvent (500 cm^3). The column was then eluted with methanol (500 cm^3). On evaporation of the appropriate fractions the pure (−)-(*R*)-**1** (3.30 g, 87%) was obtained, m.p. 191–193 °C; $[\alpha]_D$ −43.0° (*c* 0.03). The NMR and IR spectra of this compound were identical to those obtained for the racemic compound. The enantiomeric excess in this phosphinic amide (5.8 mg) was determined to be 75% by ^{1}H NMR analysis (270 MHz) in $CDCl_3$ of the externally diastereotopic mesityl ring proton signals [δ 6.73 and 6.77 for (+)- and (−)-**1** respectively] observed in the presence of (−)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol (25.4 mg) as a chiral auxiliary.

Crystallographic Studies.—*Crystal data.* $C_{23}H_{26}NOP$, M_r = 363.4, monoclinic, space group $P2_1$, a = 11.412(3), b = 10.023(9), c = 18.475(6) Å, β = 97.48(2)°, V = 2095 Å^3, Z = 4, D_c = 1.15 g cm^{-3}, $F(000)$ = 776, μ(Mo-Kα) = 0.137 mm^{-1}, λ = 0.710 69 Å.

A crystal (0.5 × 0.2 × 0.2 mm) was mounted on an Enraf-Nonius CAD-4 diffractometer; cell dimensions and intensities were measured by $\omega/2\theta$ scans with graphite-monochromated Mo-Kα radiation. 3896 reflections were scanned in the range $2 < \theta < 25°$, and of these, 1608, having $F > 5\sigma(F)$ were considered observed and used in the analysis. Three standard reflections measured every 2 h showed no significant variation in intensity.

The structure was determined by Patterson and Fourier methods and refined by least-squares using anisotropic thermal parameters for the non-hydrogen atoms. Hydrogen atoms bonded to carbon were placed in calculated positions (C–H = 1.08 Å) riding on their respective bonded atoms. In each of the two independent molecules, the approximate position of the hydrogen atom bonded to the nitrogen was located from a difference map. For the methyl groups, in each case, one of the hydrogen atoms could be located from a difference map with some degree of certainty and the approximate positions of the other two could then be calculated. All H atoms were assigned a fixed isotropic thermal parameter, U = 0.1 Å^2. Weights, $w = 1/[\sigma^2(F) + 0.005F^2]$, were used in the least-squares refinement. The calculations were terminated when all shift/esd ratios were <0.1 and R = 0.0650, R_w = 0.0958 for 1608 observed reflections. The residual electron density in a final difference map was within the range ±0.35 e Å^{-3}. The absolute configuration depicted in Fig. 1 is established through the known configuration (*R*) at C(13). The inverse structure gave slightly higher values of R and R_w, 0.0651 and 0.0960, respectively.

Complex neutral-atom scattering factors were employed. Computations were carried out on the University of Birmingham IBM 3090 computer and on the Amdahl 5890 at the Manchester Computing Centre with the SHELXS 86[15] and SHELX 76[16] packages. The molecular diagrams were drawn using PLUTO.[17]

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and the full set of bond lengths and angles.*

* For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1992, issue 1.

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