Asymmetric Induction. Part 3.[1,2] Asymmetric Reduction of Ketones with Amine-boranes in the Presence of Acids

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Asymmetric reductions of a series of ketones with (+)-1-phenylethylamine–borane and boron trifluoride–diethyl ether are described; solvent and temperature effects have been studied, and the use of other acidic components has been explored. Asymmetric reductions have also been effected with α-amino-ester–boranes (14—23% optical yields) and with diastereoisomeric amine–boranes containing chiral nitrogen atams. 2-Aminoethanols were prepared in high yield by reaction of α-amino-ester–boranes with boron trifluoride.

In earlier parts of this series [1,2] the use of alkyl(hydro)-dipinan-3α-yl borates for asymmetric reduction of ketones and imines (4—46% optical yields) was described. We have now studied other reagents containing four-co-ordinate boron atoms and report our initial results with amine–boranes.

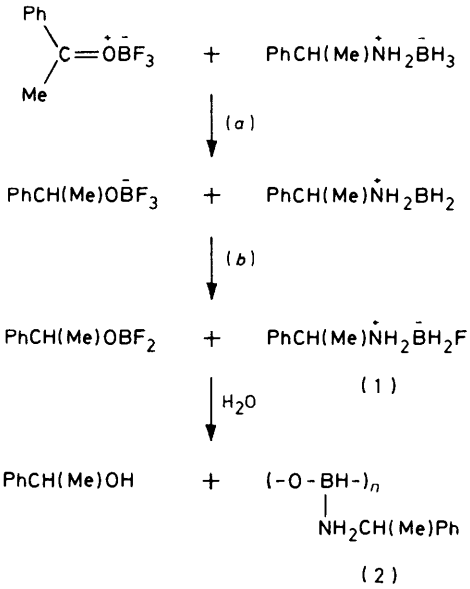
Reduction of ketones with chiral amine–boranes has not received much attention. Fiand and Kagan [3] prepared amine–boranes from (*S*)-1-methyl-2-phenylethylamine and its *N*-methyl and *NN*-dimethyl derivatives, and showed that acetophenone was reduced to optically active 1-phenylethanol with these reagents, but the optical yields (3.6—5%) were disappointingly low. Borch and Levitan [4] studied the asymmetric reduction of acetophenone with (+)-(*R*)-1-phenylethylamine–borane and the reduction of heptan-2-one with the enantiomeric amine–borane in various solvents. Reduction was incomplete after reaction periods of 4 h and the optical yields of the resultant alcohols were only 1.5—3.3%. The absolute configuration of heptan-2-ol was 'opposite' to that of the amine–borane used in polar and non-polar solvents, whereas reaction of the (*R*)-amine–borane with acetophenone gave (*R*)-1-phenylethanol in benzene or carbon tetrachloride and the (*S*)-alcohol in methanol. The incomplete reduction is consistent with the reactions of amine–boranes not containing *N*-aryl groups, but the observation of optical induction is not in accord with the proposed mechanism involving dissociation of the amine–borane followed by reduction of the ketone by borane.

The acid-catalysed reaction, however, leads to much faster reaction; in the reduction of 4-t-butylcyclohexanone with trimethylamine–borane, for example, an equimolecular quantity of boron trifluoride was required, and mechanistic evidence indicated that the amine–borane remained intact in the course of reduction.[5] This reaction appeared to be more promising for asymmetric synthesis than the unpredictable uncatalysed process and we decided to study the reduction of ketones with (+)-(*R*)-1-phenylethylamine–borane in the presence of Lewis acids.

RESULTS AND DISCUSSION

The amine-borane was prepared by adding (+)-1-phenylethylamine to a solution of diborane in tetrahydrofuran. Asymmetric reduction of acetophenone was carried out with equimolecular quantities of the amine–borane and boron trifluoride–diethyl ether in tetrahydrofuran at 0 °C. G.l.c. analysis indicated that reduction was complete after 0.5 h to give (+)-(*R*)-1-phenylethanol (13.5% optical purity). Checks on the optical purity of the product were carried out (see Experimental section), including preparation of the hydrogenphthalate.

The mechanism suggested for the reduction of ketones with amine–boranes and boron trifluoride [5] applied to acetophenonone and 1-phenylethylamine–borane



Scheme

(Scheme) implied that hydrogen transfer, reaction (*a*), is followed by fluorine transfer, reaction (*b*); work-up then gives 1-phenylethanol.

During the isolation of the alcohol, a solid by-product was obtained; it was stable to aqueous acid but was rapidly hydrolysed by base to give 2-methylbenzylamine and hydrogen. The i.r. spectrum showed absorption at 2 340, 2 410, and 2 440 cm^{-1} (B–H) but indicated the absence of OH groups. Apart from resonances due to a 2-methylbenzyl group, there was a broad singlet at

τ 3.87 (2 H, NH_2) in the ^1H n.m.r. spectrum; the ^{19}F n.m.r. spectrum of the compound and of the aqueous solution obtained by base hydrolysis showed no fluorine resonances. Although the structure is not known with certainty, the spectroscopic data and the elemental analysis suggest that the compound is a polymer (2) formed by hydrolysis of the expected by-product (1) of the reduction reaction; its isolation is consistent with the proposed mechanism.

The reaction was also applied to heptan-2-one, methyl t-butyl ketone, and ethyl isopropyl ketone (Table 1).

TABLE 1

Reduction of ketones at 0 °C with (+)-(*R*)-1-phenylethylamine–borane and boron trifluoride–diethyl ether in molar ratio of 1 : 1 : 1

Entry	Reactant	Solvent	$[\alpha]_D^{25}$ (neat) of alcohol	Induction (%) [a]
1	PhCOMe	THF	+5.81 ± 0.20	13.5 ± 0.5 *R*
2		CH_2Cl_2	+3.40 ± 0.16	8.0 ± 0.4 *R*
3		Et_2O	+8.90 ± 0.17	20.7 ± 0.4 *R*
4		n-C_5H_{12}	+3.26 ± 0.04	7.2 ± 0.1 *R*
5	EtCOPr^i	THF	+0.19 ± 0.01	2.0 ± 0.1 *R*
6	$MeCOC_5H_{11}$	THF	−0.23 ± 0.03 [b]	2.5 ± 0.1 *R*
7	MeCOBu^t	THF	−0.40 ± 0.01	4.9 ± 0.1 *R*

[a] Based on values quoted in ref. 1*a*. [b] Determined in MeOH (*c* 5.0).

Reduction again occurred rapidly and quantitatively to give the corresponding alcohols containing excess of the (*R*)-enantiomer, but the optical induction was much less than with acetophenone. 2-Acetylferrocene was reduced to 2-ethylferrocene with the amine–borane, as observed previously for reaction with mixed hydride reagents.[6]

In an attempt to optimise optical induction, further experiments with acetophenone, 1-phenylethylamine–borane, and boron trifluoride in a molar ratio of 1 : 1 : 1 were carried out. Lowering the reaction temperature to −78 °C produced a small increase in optical purity of (*R*)-1-phenylethanol (Table 2). A study of solvent

TABLE 2

Reduction of acetophenone in tetrahydrofuran with (+)-(*R*)-1-phenylethylamine and various acids

Acid	Molar ratio of ketone : amine–borane : acid	Temperature (°C)	$[\alpha]_D^{25}$ (neat) of alcohol	Induction (%)
$AlCl_3$	1 : 1 : 1	0	+3.81 ± 0.26	8.6 ± 0.3 *R*
HCl	1 : 1 : 1	0	+2.07 ± 0.03 [a]	4.5 ± 0.1 *R*
BF_3	1 : 1 : 1	−78	[+6.37]	14.8 *R*
BF_3	2 : 1 : 2	0	+4.02 ± 0.20	9.5 ± 0.5 *R*
BF_3	2 : 1 : 2	−78	+5.5 ± 0.27	12.8 ± 0.6 *R*

[a] Determined in MeOH (*c* 5.0).

effects showed that diethyl ether (21% optical induction) was more effective than tetrahydrofuran, whereas optical purity was less with dichloromethane and with pentane (Table 1). With a molar ratio of acetophenone, amine–borane, and boron trifluoride of 2 : 1 : 2 there was a drop in optical induction at 0 °C, but at −78 °C induction was similar to that obtained with a 1 : 1 : 1 ratio (Table 2). When hydrogen chloride was used instead of boron trifluoride, reduction was only 80% complete after 0.5 h and the optical purity of the product was 5%. Aluminium chloride was a less effective Lewis acid than boron trifluoride; although quantitative reduction occurred, optical induction was only 9% (Table 2).

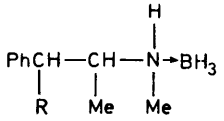
Since the acid-catalysed asymmetric reduction of ketones with the amine–borane rapidly goes to completion and results in consistent induced chirality, we were encouraged to study the use of other amine–boranes including α-amino-ester–boranes.

The advantages of using L-amino-acid esters is that the acids from which the esters are readily prepared are available in high optical purity and the esters are soluble in organic solvents.

Mixing stoicheiometric quantities of leucine methyl ester and diborane in tetrahydrofuran gave a stable solution; addition of 1 equiv. acetophenone resulted in the formation of 1-phenylethanol in only 48% yield after 5 h at ambient temperature; since ketones are reduced rapidly by diborane, it appears that the initial solution contains the amine–borane (3), which is respon-

$Me_2CHCH_2CH(CO_2Me)NH_2 \rightarrow BH_3$

(3)



(4) R = H
(5) R = OH
(6) R = Cl

sible for the slow reduction of acetophenone. When the reaction mixture at 0 °C was treated with 1 equiv. boron trifluoride–ether immediately after the addition of acetophenone, reduction was complete after 30 min and optically active 1-phenylethanol was isolated in almost quantitative yield. L-Leucine methyl ester–borane reacted similarly with 3,3-dimethylbutan-2-one and with heptan-2-one, and the asymmetric reduction of acetophenone was also carried out with the amine–boranes derived from L-phenylalanine methyl ester and L-valine methyl ester. The results (Table 3) show that the *S*-enantiomers of the alcohols are present in excess, with optical purities of 14—22%.

As in the case of the reaction of ketones with 1-phenylethylamine–borane, we propose that activation of the ketone carbonyl group by the Lewis acid is followed by hydrogen transfer from the amino-acid ester–borane and then by fluorine transfer. The two sets of reactions are also parallel in that configurations are retained; the amine–borane derived from (*R*)-1-phenylethylamine gives alcohols in which the (*R*)-enantiomer predominates, while (*S*)-alcohols result from the amine–boranes formed from (*S*)-amino-acid esters. In discussing the asym-

metric reduction of cyclic imines with lithium butyl(hydro)dipinan-3α-yl borate, in which the chiral centres are α to the boron atom, a preferred transition state was proposed which resulted in a product of correct stereochemistry.[1b] Although the observation of asymmetric reduction of ketones with chiral amine–boranes is presumably due to the formation of preferred transition states in which there are minimum interactions between the substituents of the chiral centre and those attached to the carbon of the ketone carbonyl group, the fact that the chiral centre is β to the boron atom makes the interpretation of the stereochemical result less certain.

Induction, however, is significantly greater with amino-acid ester–boranes than with the phenylethylamine–borane under comparable condition, *cf.* entries 6 and 7 (Table 1) and entries 4 and 5 (Table 3); this may be due to the formation of a more restricted cyclic transition state involving the carbonyl group of an amino-acid ester–borane.

In the reactions of amino-acid ester–boranes with ketones (Table 3) the ester and ketone carbonyl groups both appear to be available for reaction and the quantitative reduction of the latter implies that the Lewis acid co-ordinates preferentially with the ketone. In order to clarify the mechanism it was of interest to study the reactions in the absence of ketones. We found that addition of 1 equiv. of boron trifluoride–ether to solutions of amine–boranes derived from the methyl esters of L-leucine, L-phenylalanine, and L-tryptophan in tetrahydrofuran resulted in complete reduction after 1 h at 20 °C; the corresponding optically active amino-alcohols were isolated in almost quantitative yield and characterised as their acid oxalates. These amino-alcohols have been prepared previously by refluxing the amino-acid ethyl ester hydrochlorides with lithium aluminium hydride in tetrahydrofuran for 4—6 h (80—90% yield) [7] or with a four-fold excess of sodium borohydride in aqueous ethanol for 4—9 h; [8] reaction of substituted phenylalanines with a large excess of diborane in tetrahydrofuran for 15—30 h is required to produce the corresponding amino-alcohols.[9] Our mild procedure may prove to be generally useful for the preparation of 2-aminoethanols.

We were also interested in studying the asymmetric reduction of ketones with amine–boranes containing a chiral nitrogen atom. Fiand and Kagan [3] prepared the amine–borane (4) from (*S*)-1,*N*-dimethyl-2-phenylethylamine and separated the diastereoisomers. We obtained the related amine–borane (5) from 1,*N*-dimethyl-2-hydroxy-2-phenylethylamine (L-ephedrine) and diborane; reaction of the compound with acetophenone in the presence of boron trifluoride gave a quantitative yield of 1-phenylethanol containing a preponderance of the (*R*)-enantiomer (Table 4), but the amine–borane was a viscous liquid unsuitable for the preparation of diastereoisomers. Treatment of 1,*N*-dimethyl-2-chloro-2-phenylethylamine, derived from L-ephedrine, with borohydride gave the crystalline amine–borane (6). The ^{1}H N.m.r. spectrum of this compound showed pairs of doublets at τ 4.70 and 5.2 [PhC*H*(Cl)], at 7.3 and 7.5 (NH*Me*), and at 9.00 and 9.05 [CH*Me*NH] attributed to diastereoisomers; integration indicated that the isomers were present in equal amounts. Fractional crystallisation of the amine–borane gave a single diastereoisomer (6A), τ 4.70, 7.35, and 9.05. A sample of the amine–borane enriched in the second isomer (6B) (ratio of 6A : 6B *ca.* 1 : 2) was also obtained. Reduction of acetophenone in the presence of boron trifluoride was carried out with isomer (6A), with a mixture of (6A) and (6B) (1 : 1), and with the amine–borane enriched in isomer (6B) (Table 4), and in each case 1-phenylethanol was obtained almost quantitatively. Isomer (6A) gave the alcohol containing a small excess of the (−)-(*S*)-enantiomer (0.6% induction) and isomer (6B) produced a much larger excess of the (+)-(*R*)-enantiomer; from a knowledge of the composition of the amine–borane enriched in isomer (6B) (n.m.r.), optical induction in the latter case is approximately 16%. Although it is clear that the differences observed for the two diastereoisomers are due to the opposite chirality of the quaternary nitrogen atoms, an interpretation of the results based on preferred transition states must await determination of configurations in these amine–boranes, and extension to a range of related amine–boranes and a variety of substrates.

TABLE 3

Reduction of ketones in THF at 0 °C with amino-ester–boranes and boron trifluoride–diethyl ether in the molar ratio 1 : 1 : 1

Entry	Ketone	Amino-ester	$[\alpha]_D^{25}$ (neat) of alcohol	Induction (%)
1	PhCOMe	$MeO_2CCH(NH_2)CH_2CHMe_2$	−7.29 ± 0.05	17.0 ± 0.1 *S*
2		$MeO_2CCH(NH_2)CH_2Ph$	−7.71 ± 0.12	18.0 ± 0.3 *S*
3		$MeO_2CCH(NH_2)CHMe_2$	−8.55 ± 0.06	19.9 ± 0.1 *S*
4	$MeCOC_5H_{11}$	$MeO_2CCH(NH_2)CH_2CHMe_2$	+1.53 ± 0.05	14.7 ± 0.5 *S*
5	$MeCOBu^t$		+1.82 ± 0.64	22.5 ± 0.5 *S*

TABLE 4

Reduction of acetophenone at 0 °C with 1,*N*-dimethyl-2-phenylethylamine derivatives and boron trifluoride–diethyl ether in the molar ratio 1 : 1 : 1

Amine–borane	$[\alpha]_D^{25}$ (neat) of 1-phenylethanol	Induction (%)
(5)	+3.62 ± 0.18	8.5 ± 0.5 *R*
(6A)	−0.27 ± 0.02	0.6 ± 0.05 *S*
(6A + 6B) (1 : 1)	+3.52 ± 0.12	8.2 ± 0.2 *R*
(6A + 6B) (1 : 2)	+4.55 ± 0.05	10.6 ± 0.1 *R*

EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer 457 grating spectrometer, and n.m.r. spectra on Perkin-Elmer 60-MHz R12 (^{1}H) and 90-MHz R32 (^{19}F) spectrometers. Analytical g.l.c. was performed on a Perkin-Elmer F11 instrument fitted with either a 50-m or a 2-m Carbowax column; peak areas were compared with those from authentic samples of known composition. Optical rotations were measured on a Perkin-Elmer 141 digital polarimeter at 25 ± 1 °C. Solvents and reagents were purified as already described.[1a]

(+)-(*R*)-1-Phenylethylamine–borane was obtained as a white solid, m.p. 119—120 °C, $[\alpha]_D$ +76.3° (benzene) {lit.,[4] m.p. 119—120 °C, $[\alpha]_D$ +77.3° (benzene)} from (*R*)-1-phenylethylamine, $[\alpha]_D$ +38.5° (98.3% optically purity).[4]

Asymmetric Reduction of Acetophenone with (+)-1-Phenylethylamine–Borane in the Presence of Acids.—(*a*) A solution of acetophenone (4.80 g, 0.04 mol) in tetrahydrofuran (25 ml) was added to a solution of (+)-1-phenylethylamine–borane (5.35 g, 0.04 mol) in tetrahydrofuran (50 ml) at 0 °C. Boron trifluoride–diethyl ether (5 ml, 0.04 mol) was added, and the solution was stirred at 0 °C for 0.5 h. After removal of solvent, water (2 ml) was added cautiously and the precipitate was removed by filtration. 3N-Sodium hydroxide was added, the solution was extracted with ether (4 × 25 ml), the ether solution was washed with 3N-hydrochloric acid (4 × 25 ml), and then with water; g.l.c. analysis indicated that reduction had occurred quantitatively. Evaporation of the ether and distillation of the residue gave 1-phenylethanol, b.p. 44—47 °C at 0.8 mmHg, $[\alpha]_D^{25}$ +5.61° (neat) {lit.,[10] $[\alpha]_D^{19}$ 42.9° (neat)}.

To ensure that the product was not contaminated with 1-phenylethylamine, an equimolecular mixture of the optically active amine and the racemic alcohol was submitted to the above separation procedure; the alcohol was optically inactive.

Several samples of 1-phenylethanol (8.3—13.1% optical purity) were converted into the hydrogenphthalate esters by heating with phthalic anhydride–pyridine at 100 °C for 3 h; in a typical example, 1-phenylethanol, $[\alpha]_D$ +5.61° (13.1% optical purity) gave the hydrogenphthalate, m.p. 105—106 °C, $[\alpha]_D$ −4.9° (EtOH) (12.3% optical purity) {lit.,[11] m.p. 81—82 °C, $[\alpha]_D$ −40.7° (EtOH) for hydrogenphthalate of (+)-1-phenylethanol alcohol and m.p. 108 °C for the racemate]}.

The reactions in various solvents (Table 1), at −78 °C (Table 2) and with acetophenone–[(+)-1-phenylethylamine–borane]–[boron trifluoride–diethyl ether] in the molar ratio 2 : 1 : 2 (Table 2) were carried out as described above.

The white solid, decomp. 160—180 °C, analysed as follows; Found: C, 64.2; H, 8.1; N, 9.4. $(C_8H_{12}BNO)_n$ requires C, 64.5; H, 8.1; N, 9.2%.

(*b*) A solution of aluminium chloride (6 g) in tetrahydrofuran (50 ml) (freshly prepared by adding tetrahydrofuran during 0.5 h to sublimed aluminium chloride in a liquid nitrogen bath under a rapid stream of dry nitrogen) was added to (+)-1-phenylethylamine–borane (0.03 mol) and acetophenone (0.03 mol) at 0 °C. After 0.5 h, the reaction mixture was worked up as in (*a*) to give 1-phenylethanol, $[\alpha]_D$ +3.55°; g.l.c. analysis indicated that complete reduction had occurred.

(*c*) A freshly prepared solution of dry hydrogen chloride in tetrahydrofuran (26.3 ml of 0.95M solution) was added to (+)-1-phenylethylamine–borane (0.025 mol) and acetophenone (0.025 mol) in tetrahydrofuran. After 0.5 h at 0°, the precipitate was removed by filtration and the solution was worked up as in (*a*); g.l.c. analysis indicated that 82% reduction had occurred. 1-Phenylethanol, $[\alpha]_D$ +2.0° (MeOH) {lit.,[12] $[\alpha]_D$ 45.6° (MeOH)}, was isolated by preparative g.l.c. with a Perkin-Elmer F21 instrument through columns (5 × 2 m) of Versamide 930 at 160 °C and with a nitrogen flow rate of 300 ml min^{-1}.

Reduction of other Ketones with (+)-1-Phenylethylamine–Borane in the Presence of Boron Trifluoride–Diethyl Ether.—Asymmetric reductions of t-butyl methyl ketone, ethyl isopropyl ketone, and heptan-2-one were carried out as described for acetophenone (*a*). The results are given in Table 1.

Acetylferrocene (0.05 mol) was reduced as described for acetophenone in (*a*). After treatment of the reaction mixture with base, the product was recovered with pentane and chromatographed on alumina. Elution with light petroleum (b.p. 40—60 °C) gave an orange liquid (92%), shown to be ethylferrocene by comparison of the n.m.r. spectrum and t.l.c. behaviour with an authentic sample.[6]

Methyl Esters of L-Amino-acids.—Methyl ester hydrochlorides were prepared from L-leucine, L-valine, L-phenylalanine, and L-tryptophan.[9] Solutions of the hydrochlorides in the minimum quantity of water were made basic with 30% aqueous potassium carbonate; extraction with ether, refluxing the resultant oil in benzene in a Dean–Stark apparatus for 5 h, and removal of the solvent gave anhydrous L-amino-acid methyl esters.

Asymmetric Reduction of Ketones with L-Amino-acid Methyl Ester–Boranes and Boron Trifluoride Diethyl Ether.—A solution of diborane in tetrahydrofuran (1.23M, 32.4 ml, 40 mmol) was added to a solution of L-leucine methyl ester (5.8 g, 40 mmol) in tetrahydrofuran (25 ml). Acetophenone (4.8 g, 40 mmol) in tetrahydrofuran (25 ml) was added and then boron trifluoride–diethyl ether (5 ml). After evaporation of the solvent and addition of 30% aqueous sodium hydroxide, the product was extracted into ether; g.l.c. analysis on a 50-m Carbowax column at 130 °C showed that the only product was 1-phenylethanol (retention time, 2 min). Distillation gave the alcohol, b.p. 44—47 °C/1.0 mmHg, $[\alpha]_D^{24}$ −7.35° (neat), almost quantitatively. The same procedure was applied to the reduction of t-butyl methyl ketone and heptan-2-one with the L-leucine derivative and to the reduction of acetophenone with L-phenylalanine methyl ester–borane and with L-valine methyl ester–borane; the results of duplicate experiments in each case are given in Table 3.

Reaction of L-leucine methyl ester–borane and acetophenone (without boron trifluoride–diethyl ether), for 5 h, work-up in the usual way, and g.l.c. analysis showed that the product contained 1-phenylethanol (48%) and acetophenone (52%).

Reduction of L-Amino-acid Methyl Esters with Diborane and Boron Trifluoride–Diethyl Ether.—L-Leucine methyl ester (5.8 g, 40 mmol) was treated with diborane and boron trifluoride–diethyl ether as described above; after 1 h at 20 °C, the usual work-up (except that ethyl acetate was used for extraction) gave 2-amino-4-methylpentanol as an oil (4.43 g, 95%), characterised as its acid oxalate, m.p. 179—182 °C, $[\alpha]_D$ +6.3° (H_2O) {lit.,[13] m.p. 186—187 °C, $[\alpha]_D$ +6.34° (H_2O)}. Similarly were prepared 2-amino-3-phenylpropanol acid oxalate (100 ± 1%), m.p. 171—173 °C, $[\alpha]_D$ −10.3° (H_2O) {lit.,[13a] m.p. 161—163 °C, $[\alpha]_D$ −11.9° (H_2O)} from L-phenylalanine methyl ester, and 2-amino-3-indol-3-ylpropanol acid oxalate (94 ± 3%), m.p.

203—204 °C, $[\alpha]_D$ −23.0° (H_2O) {lit.,[13b] m.p. 204—205 °C, $[\alpha]_D$ +25.3° (H_2O)} from L-tryptophan methyl ester.

2-Hydroxy-1,N-dimethyl-2-phenylethylamine–Borane.— A diborane–tetrahydrofuran solution (95 ml, 125 mmol) was added during 1 h to a solution of (+)-2-hydroxy-1,*N*-dimethylphenylethylamine (L-ephedrine) (16.7 g, 100 mmol) in tetrahydrofuran (100 ml). When hydrogen evolution had ceased, water (5.4 ml) was added and after 12 h, the solution was evaporated and ether (120 ml) was added. Filtration and evaporation of the solvent gave the amine–borane as a viscous liquid which failed to crystallise.

2-Chloro-1,N-dimethyl-2-phenylethylamine–Borane.— A solution of sodium borohydride (6 g) in 1,2-dimethoxyethane (200 ml) was added during 1 h to a suspension of 2-chloro-1,*N*-dimethyl-2-phenylethylamine, m.p. 197—198 °C, $[\alpha]_D$ +119° (H_2O) {lit.,[14] m.p. 196—197 °C, $[\alpha]_D$ +119° (H_2O)}, in 1.2-dimethoxyethane (75 ml) at 0—5 °C. After stirring for 2 h, the mixture was filtered and the solvent was evaporated to give the *amine–borane* as a white solid, m.p. 134—135 °C, $[\alpha]_D$ +89° (*c* 1.0 in C_6H_6); τ($CDCl_3$) 2.65 (5 H, s, aromatic), 4.70 (d) and 5.2 (d) [PhC*H*(Cl)], 7.3 (d) and 7.5 (d) (NH*Me*) and 9.00 (d) and 9.05 (d) (CH*Me*NH) (Found: C, 60.7; H, 8.9; Cl, 17.9; N, 7.1 $C_{10}H_{17}BClN$ requires C, 60.8; H, 8.7; Cl, 18.0; B, 5.5; N, 7.1%).

A solution of the amine–borane (10 g) in the minimum quantity of boiling benzene was filtered and hexane was added to the boiling solution until a faint turbity appeared; the solid obtained on cooling was recrystallised to give one diastereoisomer (3.6 g), m.p. 146—147.5 °C, $[\alpha]_D$ +51.5 (*c* 1.0 in C_6H_6); τ($CDCl_3$) 2.65 (5 H, s, aromatic), 4.70 [1 H, d, PhC*H*(Cl)], 7.35 (3 H, d, NH*Me*), and 9.05 [3 H, d, CH*Me*NH]. The mother-liquors from the fractional crystallisation gave the amine–borane, $[\alpha]_D$ +100.2 (*c* 1.0 in C_6H_6), enriched in the other diastereoisomer.

Reduction of Acetophenone with 1,N-Dimethyl-2-phenylethylamine–Borane Derivatives.—Reductions of acetophenone with equimolecular amounts of amine–boranes and boron trifluoride–diethyl etherate in tetrahydrofuran at 0 °C were carried out as described previously for (+)-1-phenylethylamine–borane, and gave 1-phenylethanol almost quantitatively; duplicate experiments gave the results summarised in Table 4.

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