Some Enantioselective Borane Reductions of Prochiral Ketones Catalysed by Polymer-supported Oxazaborolidines Bound *via* the Boron Atom

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Polystyrenes containing arylboronic acid residues were prepared and treated with (1R,2S)-(−)-norephedrine to give polymer-supported (PS) chiral oxazaborolidines. The latter were investigated as catalysts for the reductions of acetophenone and/or propiophenone by the borane–dimethyl sulfide complex. A variety of reaction conditions was used. The results were compared with those obtained using the non-polymeric analogue of the catalysts prepared by reaction of (1R,2S)-(−)-norephedrine with phenylboronic acid. When used under the best reaction conditions of those investigated (30 mol% of catalyst in tetrahydrofuran at 20 °C) the percentage ees obtained with the better PS catalyst were almost the same as those obtained using the non-polymeric analogue under similar reaction conditions. It was shown that the PS reaction with propiophenone was >95% complete in 20 min. The PS catalyst could be recycled successfully at least three times.

Several organic reactions have been developed in recent years that achieve highly enantioselective asymmetric syntheses.[1] Some of the most attractive of these reactions are those which achieve asymmetric synthesis by means of a chiral catalyst, because with such systems a relatively small amount of the initial chiral species can be used to prepare a relatively large amount of the chiral product. One reaction of this general type is the reduction of aryl alkyl ketones by borane [reaction (1)] catalysed by chiral oxazaborolidines[2,3] such as compounds 1,[4] 2,[5] 3[6,·] and 4.[8] The catalyst may be prepared *in situ*, for example by reaction of an appropriate β-amino alcohol with borane,[4,9] or in a separate step, for example by removal of water from an equimolar mixture of an appropriate β-amino alcohol and a boronic acid.[6–8]

1

2 R = H
3 R = Me
4 R = Ph
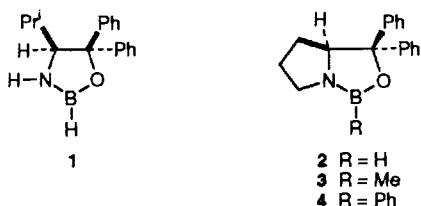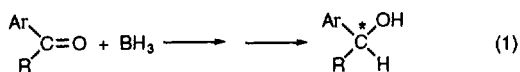
Attachment of chiral catalysts to insoluble polymer supports is currently of considerable interest[10] because at the end of reactions using polymer-supported (PS) catalysts the catalyst can be removed efficiently and easily from the chiral products and it is then available for re-use. Several chiral β-amino alcohols have been bound to crosslinked polystyrenes and then converted into PS oxazaborolidines.[11–14] The latter have been used either as reagents[11,12] or as catalysts.[13,14] A major objective in the field of PS asymmetric synthesis[10] is to be able to design rationally a suitable support system for any particular PS asymmetric synthesis, such that carrying out the reaction using the polymer support does not have a deleterious effect on the enantiomeric excesses (ees) achieved. As part of a programme designed to investigate the effect of various polymer supports on the stereochemical course of asymmetric syntheses,[15–19] we have studied examples of reaction (1) catalysed by PS chiral oxazaborolidines in which the catalytic groups are bound to the polymer *via* the boron atom.[19]

Reaction (1) was selected for study because the reaction proceeds quite rapidly in the absence of added catalyst to give the racemic alcohol. For example, under typical reaction conditions the reduction of propiophenone is >40% complete after 1 h at ambient temperature (see below). As a consequence of this the PS catalysts are operating in a competitive situation and if, for example, access to the chiral catalytic sites in the polymer beads is significantly restricted by diffusion and/or the bound functionalities interfere with each other in any way, the ees obtained will be expected to be less than those obtained using an analogous non-polymeric catalyst under otherwise similar reaction conditions. The competitive situation therefore makes such studies a very sensitive test of the performance of the PS chiral catalysts and it also provides a valuable means to probe the various ways in which a polymer support can influence the outcome of a PS reaction.
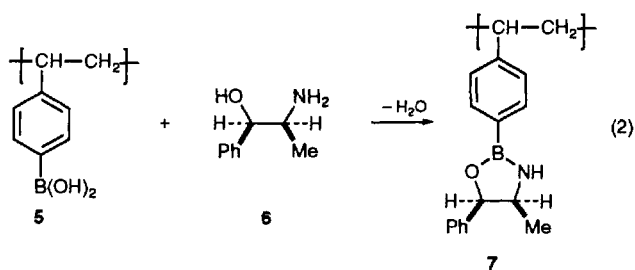
B-Aryl- or *B*-alkyl-oxazaborolidines are of particular interest because these catalysts are more stable on storage than the B–H analogues,[2,6] yet they normally give similar ees;[9,20,21] occasionally the ees are higher.[6] The present type of PS catalysts are, therefore, likely to be particularly suitable for recycling.

We now report the results obtained using as catalysts PS oxazaborolidines prepared by the reaction of crosslinked polystyrenes containing phenylboronic acid residues 5 with (1R,2S)-(−)-norephedrine 6. The latter was selected because whilst its use leads to substantial ees, the ees obtained are not so high that it is not possible for the PS catalysts to show increases as well as decreases in ees in comparison with non-supported systems. We have recently reported a similar study using crosslinked styrene–2-vinylthiophene copolymers.[19] Although these latter supports are lithiated more easily than the present supports, they display significant diffusion limitations which result in ees lower than those obtained in the present study.

Results and Discussion

Synthesis of Catalysts.—Catalyst A, a crosslinked polystyrene containing residues 7, was prepared as follows. A mixture of 4-bromostyrene (49 mol%), styrene (49%) and

commercial divinylbenzene (2%) was copolymerised using a free radical initiator to give brominated gel-type[22] crosslinked polystyrene beads. The beads were treated with butyllithium to bring about a bromine–lithium exchange.[23] Then, without isolation, the lithiated polymer was treated successively with trimethyl borate and hydrochloric acid. This gave polymer beads containing arylboronic acid residues 5. Elemental analyses indicated that the bromo groups were transformed into boronic acid groups with an overall efficiency of ca. 50%. Treatment of this polymer with (1R,2S)-(−)-norephedrine 6 and removal of the water formed as a result of reaction (2) gave catalyst A. Elemental analysis indicated that this last reaction took place in only 63% yield. Accordingly the final polymer contained 1.2 mmol g⁻¹ of the catalytic oxazaborolidine residues 7 and 0.7 mmol g⁻¹ of arylboronic acid residues 5.

$$\text{CH—CH}_2 \quad + \quad \overset{HO}{\underset{Ph}{\text{H--}}}\overset{NH_2}{\underset{Me}{\text{--H}}} \quad \xrightarrow{-H_2O} \quad \text{CH—CH}_2 \tag{2}$$

5   B(OH)₂   6   7

Catalyst B was intended to be a linear, and therefore soluble, polymer analogue of catalyst A, but crosslinking occurred during the synthesis. Copolymerisation of 4-bromostyrene and styrene gave a soluble brominated polystyrene. Lithiation, as before, followed by treatment with borane[24] then aqueous acid gave an insoluble polymer containing residues 5. Since the polymer would not dissolve in any of a wide range of solvents, the insolubility was almost certainly a result of crosslinking, probably due to the formation of a small amount of diarylborane residues 8 during the borane treatment. The subsequent acid treatment would convert these into diaryl-boronic acid residues 9. Treatment of the crosslinked polymer with the norephedrine 6 gave, via reaction (2), catalyst B containing 0.8 mmol g⁻¹ of oxazaborolidine residues 7 and 0.3 mmol g⁻¹ of arylboronic acid residues 5.

8 X = H
9 X = OH

10
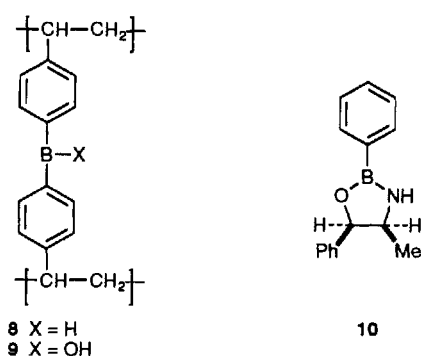
The third catalyst used was compound 10, the non-polymeric analogue of catalysts A and B. It was synthesised by the treatment of commercial phenylboronic acid with the norephedrine 6.

Since all the catalysts were likely to be sensitive to moisture, they were stored in a desiccator.

Catalysis of Reaction (1).—The reactions selected for the present study were the reductions of acetophenone and propiophenone, i.e. reaction (1) where Ar = phenyl and R = Me and Et, respectively, using the borane–dimethyl sulfide

complex. Except where indicated otherwise each reaction was carried out using procedure I. This involved adding a solution of the ketone over 5 min to a stirred mixture of the PS catalyst, the reaction solvent and the borane complex. The borane complex and ketone were used in equimolar amounts. With the PS reactions the mixture was then left to react at 20 °C for 24 h; with the non-supported reactions for 30 min. Because of these extended reaction times, the reductions were essentially complete and this facilitated isolation of the alcohol products. The ees were determined for the isolated products by measurement of the optical rotation and, in most cases, by gas chromatography using a chiral stationary phase. The results from the two methods were in close agreement. All reactions produced predominantly the (R)-alcohol. The reductions were generally carried out in duplicate. A variety of reactions were carried out in order to determine the effect of various parameters on the stereochemical course of the reactions. Most of the results are summarised in Table 1 and the effects of the choice of various parameters are discussed in the following sections.

Choice of reaction solvent. In reactions where one of the reactants is bound to a gel-type crosslinked polymer, the choice of reaction solvent is crucial because in addition to meeting the usual requirements of a successful reaction solvent, the solvent must also swell the crosslinked polymer beads sufficiently for the bound species, more than 99% of which are within the beads, to become accessible to the other reactants. Three solvents were tried in the present work: tetrahydrofuran (THF), a solvent widely used for borane reactions, dichloromethane and toluene. It is evident from comparison of the results summarised in entries 2–4, 5 and 8 of Table 1 that THF was much the more effective solvent for the present PS reactions. Accordingly it was used for all the subsequent reactions in this work.

Mole percentage of catalyst used. In order to determine the optimum mol% of catalyst to use, a series of reductions of propiophenone were carried out at various mol% of catalyst A. The results, summarised in Table 1 entries 6–11, indicate that the % ees increase up to the use of ca. 30 mol% of catalyst, after which there is no further significant increase. The results obtained for the other reactions in Table 1 using 10 and 30 mol% of catalyst A show a similar trend. To a smaller extent, so do the results obtained using compound 10 as the catalyst. These observations can be rationalised on the basis that a certain minimum amount of accessible catalyst is required to ensure that essentially all the reduction takes place under the influence of the chiral catalyst.

Role of the polymer support. Comparison of entries 6 and 12 in Table 1 indicates that catalyst B gives a lower %ee than catalyst A under similar reaction conditions. This suggests that catalyst B is more highly crosslinked than catalyst A. Higher crosslinking would result in reduced swelling and hence reduced accessibility to the catalytic sites. This would allow the uncatalysed reduction to play a bigger role in the overall reaction.

When catalyst A was used at 30 mol% in THF the ees obtained in both reductions were only slightly smaller than when compound 10 was used as the catalyst, viz. 74 vs. 78% ee for the reduction of acetophenone and 75 vs. 76% ee for the reduction of propiophenone. Two effects would be expected to result in the supported reactions giving lower ees. The first effect is diffusion. Evidently the beads swell adequately in THF and there are a sufficiently large number of readily accessible chiral catalytic sites for diffusion not to be a major problem in the present system. The second effect arises from the fact that in addition to the catalytic sites 7, catalyst A contains arylboronic acid residues 5. The deleterious effect of having methylboronic acid present in reductions catalysed by B-methyloxazaboro-lidines has been reported before,[2,25,26] and we have

Table 1 Catalysis of reductions of acetophenone and propiophenone under various conditions[a]

Entry	Catalyst	Mol% of catalyst	Solvent[b]	Reaction procedure[c]	Ketone PhCOR R	Chemical yield (%)[d]	ee (%)[e]
1	A	10	THF	I	Me	75	58
2	A	30	THF	I	Me	89	74
3	A	30	DCM	I	Me	96[f]	60
4	A	30	Tol	I	Me	70	51
5	A	30	Tol	I	Et	74	56
6	A	3	THF	I	Et	85	38
7	A	10	THF	I	Et	67	53
8	A	30	THF	I	Et	72	75
9	A	40	THF	I	Et	80	76
10	A	50	THF	I	Et	83	78
11	A	100	THF	I	Et	80	77
12	B	3	THF	I	Et	84	24
13	A[g]	30	THF	I	Me	85	72
14	A[h]	30	THF	I	Me	88	68
15	A[h]	30	THF	I	Me	86	71
16	A	30	THF	II	Et	98[f]	89
17	A	30	THF	III	Et	96[f]	60
18	(10)	30	DCM	I	Me	100[f]	71
19	(10)	10	THF	I	Me	>95[f]	74
20	(10)	30	THF	I	Me	>95[f]	78
21	(10)	10	THF	I	Et	>95[f]	73
22	(10)	30	THF	I	Et	>95[f]	76
23	(10)	30	THF	II	Me	100[f]	86
24	(10)	30	THF	II	Et	100[f]	84
25	(10)	30	THF	III	Et	100[f]	56

[a] All reactions were carried out at 20 °C using equimolar amounts of ketone and BH_3Me_2S. [b] Tol = toluene; THF = tetrahydrofuran; DMC = dichloromethane. [c] See text for details of procedures I to III. [d] Yields of isolated product. [e] Determined by optical rotation of isolated product. All reactions produced predominantly the (R)-alcohol. [f] Yield determined by GLC. [g] Using the catalyst recovered from the reaction summarised in entry 2. [h] Using the catalyst recovered from the reaction summarised in the preceding entry.

demonstrated the presence of such an effect with phenylboronic acid. Thus, the reduction of propiophenone catalysed by 30 mol% of compound **10**, in the presence of 1.2 mmol of phenylboronic acid per mmol of compound **10** gave an ee of 70%, i.e. 6% lower than in the absence of the boronic acid. Perhaps with the polymer this effect is reduced. Thus, in catalyst A most of the catalytic sites **7** may have been formed in the more accessible parts of the beads whilst most of the unchanged arylboronic acid sites **5** are in the less accessible parts.

Recycling of PS catalyst. The recycling of catalyst A was investigated. The catalyst from the reaction presented in entry 2 of Table 1 was recovered and then re-used three times. The results are given in entries 13–15. It is evident that catalyst A recycles with little or no loss of performances at least three times. It is interesting to note that with the PS catalyst the oxazaborolidine unit can be recycled intact.

Procedures II and III. Thus far the reductions were carried out using procedure I, i.e. by adding the ketone over 5 min to a stirred mixture containing the catalyst and all the borane–dimethyl sulfide complex. This general procedure is widely used by other workers. However, it exposes a significant fraction of the ketone to a substantial excess of the reducing agent for up to 5 min thus favouring a contribution from the uncatalysed reduction. This is especially the case in the early stages of the addition of the ketone. This prompted us to investigate briefly alternative addition sequences.[2,6]

In procedure II the catalyst (30 mol%) and an equimolar amount of the borane complex were mixed, then after 30 min the rest of the reducing agent and all of the ketone were added gradually over 10 min. Comparison of entries 8 and 16, 20 and 23, and 22 and 24 in Table 1 indicates that this procedure does result in significantly higher ees: for the particular reaction investigated the ee was 14% higher when catalyst A was used and 8% higher when catalyst **10** was used.

In procedure III the catalyst and all the ketone were mixed and the mixture left for 10 min before the borane complex was added gradually over 10 min. The objective was to try to ensure

there was never an excess of the borane complex present. Comparison of Table 1 entries 8 and 17, and 22 and 25 indicates that compared with procedure I this procedure results in a substantial drop in the ees achieved, both with the polymeric and non-polymeric catalysts. It may well be that with this procedure the rate of addition of the borane complex is crucial and that if it is too slow the alkoxyborane formed as the initial reduction product then itself serves as the reducing agent and is less enantioselective. Similar suggestions have been made by others.[7]

It is clear then that these reduction systems are complex[7] and that the ees achieved are significantly dependent on the experimental procedures used. A detailed investigation lay outside the scope of the present work but it is interesting to note that the reactions both with the polymeric and non-polymeric catalysts display similar trends.

Conversion vs. time curves. So far the PS reactions had been carried out for 24 h at 20 °C to ensure that the reaction was complete thereby simplifying product isolation and analysis. To estimate the time required for high yields in typical reactions, propiophenone was reduced using procedures I and II and the reactions were monitored by GC. The results obtained using procedure I are summarised in Fig. 1. The results obtained using procedure II were very similar. An uncatalysed reduction was also monitored. It is evident that the reactions using PS catalyst A and catalyst **10** were >95% complete after 20 and 5 min, respectively, whereas in the absence of added catalyst the reduction was only 22% complete after 20 min and (not shown in Fig. 1) 84% complete after 10 h.

Conclusion

Catalyst A, 2% crosslinked polystyrene beads containing 1.2 mmol g^{-1} of chiral oxazaborolidine residues **7**, catalyses the reductions of acetophenone and propiophenone by the borane–dimethyl sulfide complex. The enantiomeric excesses obtained when the catalyst is used at 30 mol% in THF are almost as high
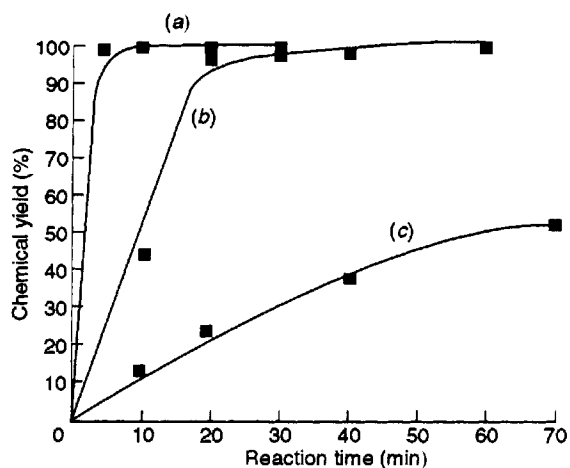
Fig. 1 Progress curves for the reduction of propiophenone in THF at 20 °C using the borane, dimethyl sulfide complex. (a) Using 30 mol% of catalyst 10 and procedure I. (b) Using 30 mol% of PS catalyst A and procedure I. (c) No catalyst added.

as those obtained using compound 10, the non-polymeric analogue of catalyst A, under similar conditions. This is despite the fact that in this reaction system the PS catalyst had to compete with the uncatalysed reaction which gives racemic product. Catalyst A can be re-used with little or no loss of performance at least three times.

Experimental

Acetophenone and propiophenone were distilled under reduced pressure from calcium hydride. The $(1R,2S)$-$(-)$-norephedrine was $> 99\%$ pure. The borane–dimethyl sulfide complex in THF solution was purchased from Aldrich and used as received. THF for use as a solvent was distilled from sodium prior to use. All reactions were carried out under dry nitrogen.

Optical rotations were measured in a 0.25 dm cell on a Polartronic (Haensh-Schmidt) polarimeter for the sodium D line and are given in units of 10^{-1} deg cm^2 g^{-1}. GC was performed on a Chrompak CP9000 instrument (injection temperature 250 °C, FID detector temperature 260 °C, column temperature 115 °C) using a WCOT Fus sil column (50 m × 0.25 mm) containing CP cyclodextrin-β-2,3,6-M-19. The ratios of R- and S-alcohols were determined from their peak areas. The NMR spectrum was obtained on a Gemini 200 (200 MHz) instrument as a solution in deuteriochloroform; J values are given in Hz. Infrared spectra were measured on either Perkin-Elmer 882 or 1710 instruments. Gel permeation chromatography (GPC) was carried out using a Waters μ-Styragel 4-column set with THF as the eluent.

Preparation of Catalyst A.—(a) *Brominated crosslinked polystyrene.* A mixture of styrene (10.4 g, 100 mmol), 4-bromostyrene (18.4 g, 100 mmol) and commercial divinyl-benzene (0.52 g, 2 mmol of divinylbenzenes, 2 mmol of ethylstyrenes) was copolymerised to give a crosslinked gel-type polymer using the procedure described by Jacobelli *et al.*[27] but without a diluent; v_{max}(Nujol mull)/cm^{-1} 1020 (C–Br); Br, 27.7% corresponding to 3.45 mmol g^{-1} and a degree of substitution of 50%.

(b) *Conversion of bromo groups into boronic acid groups* 5. The above polymer (10.0 g, 35 mmol of bromo groups) in toluene (50 cm^3) was allowed to swell for 30 min before butyllithium (2.5 mol dm^{-3} in hexane; 25 cm^3, 6.25 mmol) was added to it. The mixture was then stirred at 65 °C for 3.5 h. At the end of this period the suspension was allowed to settle and then most of the solvent was removed using a syringe. The

polymer was washed three times with dry toluene, again using a syringe. THF (80 cm^3) was then added and the mixture was stirred and trimethyl borate (11.36 cm^3, 100 mmol) added to it. After being stirred at ambient temperature for 18 h the mixture was allowed to settle and, using a syringe, most of the solvent was removed and the beads washed with THF. The polymer was then stirred with a mixture of dioxane, water and concentrated hydrochloric acid (100 cm^3, 10 : 1 : 4 v/v) at 60 °C for 2 h. The mixture was cooled and the polymer filtered off. The polymer was transferred to a Soxhlet apparatus and washed for 24 h each first with a mixture of dioxane and water (3 : 1 v/v) and then with dioxane. The washed beads were dried to constant weight (8.4 g); v_{max}/cm^{-1} 3400br (H) and 1340 (B–O); B, 2.2% corresponding to 2.2 mmol g^{-1} of boronic acid residues 5 and a degree of substitution of *ca.* 25%.

(c) *Oxazaborolidine synthesis.* A mixture of the above polymer (7.20 g, 16 mmol of boronic acid residues) and $(1R,2S)$-$(-)$-norephedrine (2.95 g, 19 mmol) was stirred and heated in a flask fitted with a Dean–Stark trap containing 4 Å molecular sieves and a condenser. The mixture was heated under reflux for 24 h. The mixture was then cooled and the polymer beads filtered off and washed in a Soxhlet apparatus first with toluene then with THF. The product was dried to constant weight to give white beads (8.4 g); v_{max}(Nujoll mull)/cm^{-1} 3400 and 3200 (O–H and N–H), 1340 (B–O and B–N) and 1050 (B–C); B, 1.9; N, 1.7% corresponding to the presence of 1.2 mmol g^{-1} of oxazaboro-lidine residues 7, 0.7 mmol g^{-1} of unchanged boronic acid residues 5 and a reaction yield of 63%.

Preparation of Catalyst B.—(a) *Brominated linear polystyrene.* A mixture of 4-bromostyrene (1.0 g, 5.4 mmol), styrene (4.0 g, 38 mmol) and azoisobutyronitrile (350 mg, 2.2 mmol) was degassed and then the reaction vessel was sealed and heated in an oil bath at 90 °C. After 14 h the reaction was cooled and the crude product dissolved in chloroform. Precipitation into methanol gave the product as a white powder, which was collected and dried (4.50 g); Br, 10.8% corresponding to a bromo content of 1.35 mmol g^{-1} and a degree of substitution of 16%. By GPC relative to polystyrene standards it had $\bar{M}_n$ = 6600 and $\bar{M}_w$ = 40 800.

(b) *Conversion of bromo groups into boronic acid groups* 5. The above polymer (1.00 g, 1.35 mmol of bromo groups) in THF (100 cm^3) was added dropwise to a vigorously stirred solution of butyllithium (2.06 mol dm^{-3} in hexane; 26.2 cm^3, 54 mmol) in THF (100 cm^3) at -77 °C over a period of 5 h. After 45 min a solution of borane in THF (1 mol dm^{-3}; 20 cm^3, 20 mmol) was added and the solution was then stirred at ambient temperature overnight. Most of the solvent was evaporated off and the crude material was stirred with methylene dichloride and hydrochloric acid (2 mol dm^{-3}) for 2 h. The product was filtered off, washed with THF, and dried to give a white solid (480 mg); v_{max}/cm^{-1} 3400br (O–H) and 1340 (B–O); 1.35% corresponding to 1.35 mmol g^{-1} of boronic acid residues 5 and a degree of substitution of 14%.

(c) *Oxazaborolidine synthesis.* The above polymer (300 mg, 0.4 mmol of boronic acid residues) was treated with $(1R,2S)$-$(-)$-norephedrine (300 mg, 2.0 mmol) using the procedure described above to give the oxazaborolidine-containing polymer, which was obtained as a white powder (330 mg); v_{max}(Nujol mull)/cm^{-1} 3400 and 3200 (O–H and N–H), 1340 (B–O and B–N) and 1050 (B–C); B, 1.1; N, 1.1% corresponding to the presence of 0.8 mmol g^{-1} of oxazaborolidine residues 7 and 0.3 mmol g^{-1} of unchanged boronic acid residues 5 and a reaction yield of 73%.

4-*Methyl*-2,5-*diphenyl*-1,3,2-*oxazaborolidine* 10.—A mixture of phenylboronic acid (0.89 g, 7.3 mmol) and $(1R,2S)$-$(-)$-norephedrine (1.00 g, 6.6 mmol) in toluene were stirred together

for 2.5 h using the procedure described above. After cooling the reaction mixture the solvent was evaporated off and the residue distilled from bulb-to-bulb at 200 °C/0.5 mmHg. The distillate (1.43 g) was a colourless glassy solid; v_{max}(liquid film)/cm^{-1} 3458 (N–H); δ_H(200 MHz; CDCl$_3$) 0.74 (3 H, d, J 6.5, CH$_3$), 3.90 (1 H, br s, NH); 4.20 (1 H, m, 4-H), 5.70 (1 H, d, J 8.2, 5-H) and 7.3–7.8 (10 H, m, 2 × C$_6$H$_5$) (Found: M$^+$, 237.1330. C$_{15}$H$_{16}$BNO requires M, 237.1325); [α]$_D$ +172 (c 5 in CHCl$_3$).

Asymmetric Reductions Using Polymer-supported Oxazaboro- lidines.—The following procedures are typical.

(a) *Procedure I.* A mixture of the polymer-supported catalyst (0.33–3.3 mmol depending on the particular experiment: see Table 1) and THF (20 cm^3) was stirred for 1 h at 20 °C prior to the addition of the borane–dimethyl sulfide complex (2.0 mol dm^{-3} in THF; 5.5 cm^3, 11.1 mmol). After 30 min a solution of the ketone (11.1 mmol) in THF (2 cm^3) was added dropwise over 5 min. The mixture was then stirred at 20 °C for 24 h. Using a syringe the reaction solvent was removed and the polymer beads washed several times with THF. The combined organic solutions were quenched with hydrochloric acid (2 mol dm^{-3}; 100 cm^3) and the reaction product extracted with ethyl acetate (3 × 25 cm^3). The combined extracts were washed with brine (2 × 10 cm^3), dried (MgSO$_4$) and then the solvent removed under reduced pressure. The residue was distilled bulb-to-bulb at ca. 100 °C/5 mmHg. The purity of the product was monitored by ^{1}H NMR spectroscopy. Optical rotations were determined for solutions in dichloromethane or chloroform and compared with the following literature values: (S)-1-phenylethanol [α]$_D^{23}$ 52.5 (c 2.27, CH$_2$Cl$_2$)^{28} and (R)-1-phenylpropanol [α]$_D^{23}$ +45.45 (c 5.15, CHCl$_3$).^{28} Typical GC retention times for (R)- and (S)-1-phenylethanols were 26.7 and 28.3 min, respectively; (R)- and (S)-1-phenylpropanols 30.8 and 32.0 min, respectively.

(b) *Procedure II.* PS catalyst A (2.50 g, 3.00 mmol) was allowed to swell in THF (15 cm^3) for 18 h. Borane–dimethyl sulfide complex (2 mol dm^{-3} in THF; 1.5 cm^3, 3.00 mmol) was added dropwise and the mixture left for 30 min. A solution of propiophenone (1.34 g, 10.00 mmol) in THF (350 cm^3) and the rest of the borane–dimethyl sulfide complex in THF (3.50 cm^3, 7.00 mmol) were then simultaneously added dropwise at the rate of 0.35 cm^3 min^{-1} using two separate syringes driven by a Harvard Apparatus 22. The rest of the reaction procedure was as described in procedure I above.

(c) *Procedure III.* PS catalyst A (2.50 g, 3.00 mmol) was allowed to swell in THF (15 cm^3) for 18 h. Propiophenone (1.34 g, 10.00 mmol) was added and the mixture stored at 20 °C for 10 min. A solution of the borane–dimethyl sulfide complex in THF (2 mol dm^{-3}; 5 cm^3; 10.00 mmol) was then added by syringe at the rate of 0.5 cm^3 min^{-1}. The rest of the reaction procedure is as described in procedure I above.

Asymmetric Reductions Catalysed by Compound 10.—The following procedure is typical.

Procedure I. The borane–dimethyl sulfide complex (1 mol dm^{-3} in THF; 8.2 cm^3, 8.2 mmol) was added dropwise over 10 min to a stirred solution of compound 10 (0.63 mmol or 1.89 mmol depending on the particular experiment: see Table 1) and the ketone (8.2 mmol) in THF (9 cm^3) at 20 °C. After 30 min the reaction mixture was quenched with hydrochloric acid (2 mol dm^{-3}). The product was then extracted and the reaction yield estimated using a Perkin-Elmer 8320 capillary gas chromatography. The solution was distilled and the ee determined as described above.

Progress Curves.—Reactions were carried out using Proce- dures I and II as described above, but from time to time samples (0.2 cm^3 each) were taken, transferred to test tubes and immediately quenched with hydrochloric acid (2 mol dm^{-3}; 1.0

cm^3). The mixture was extracted with ethyl acetate (2 × 2 cm^3), the extracts washed with brine then dried over magnesium sulfate. The organic solution was analysed using a Perkin-Elmer 8320 capillary gas chromatograph.

References

1 S. G. Davies, J. M. Brown, A. J. Pratt and G. Fleet, *Chemistry in Britain*, 1989, 259–292; R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, 1994.
2 For an excellent recent review of this field see: S. Wallabaum and J. Martens, *Tetrahedron: Asymmetry*, 1992, 3, 1475.
3 D. K. Jones, D. C. Liotta, I. Shinkai and D. J. Mathre, *J. Org. Chem.*, 1993, 58, 799.
4 S. Itsuno, Y. Sakurai, K. Ito, A. Hirao and S. Nakahama, *Bull. Chem. Soc. Jpn.*, 1987, 60, 395.
5 E. J. Corey, R. K. Bakshi and S. Shibata, *J. Am. Chem. Soc.*, 1987, 109, 5551.
6 E. J. Corey, R. K. Bakshi, S. Shibata, C.-P. Chen and V. K. Singh, *J. Am. Chem. Soc.*, 1987, 107, 7925.
7 D. J. Mathre, A. S. Thompson, A. W. Douglas, K. Hoogsteen, J. D. Carroll, E. G. Corley and E. J. J. Grabowski, *J. Org. Chem.*, 1993, 58, 2880.
8 M. P. DeNinno, R. P. Perner and L. Lijewski, *Tetrahedron Lett.*, 1990, 31, 7415.
9 G. J. Quallich and T. M. Woodall, *Synlett.*, 1993, 929.
10 P. Hodge, in *Innovation and Perspectives in Solid Phase Synthesis*, ed. R. Epton, SPCC (UK) Ltd., Birmingham, 1990, pp. 273–292.
11 S. Itsuno, M. Nakano, K. Ito, A. Hirao, M. Owa, N. Kanda and S. Nakahama, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2615.
12 S. Itsuno, Y. Sakurai, K. Ito, A. Hirao and S. Nakahama, *Polymer*, 1987, 28, 1005.
13 S. Itsuno, K. Ito, T. Maruyama, N. Kanda, A. Hirao and S. Nakahama, *Bull. Chem. Soc. Jpn.*, 1986, 59, 3329.
14 M. Watanabe and K. Soai, *J. Chem. Soc., Perkin Trans. 1*, 1994, 837.
15 J. C. Briggs and P. Hodge, *J. Chem. Soc., Chem. Commun.*, 1988, 310.
16 J. C. Briggs, P. Hodge and Zhang Zhengpu, *Reactive Polymers*, 1993, 19, 73.
17 P. Hodge, A. Ibbotson, P. W. Stratford and D. Sung, in *Macromolecules 1992*, ed. J. Kahovec, VSP, Utrecht, 1993, pp. 441–448.
18 P. Hodge, E. Khoshdel, J. Waterhouse and J. M. J. Fréchet, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2327.
19 N. El Moualij, PhD Thesis, Université des Sciences et Technologies de Lille, 1993; C. Caze, N. El Moualij, P. Hodge and C. J. Lock, *Polymer*, 1995, in the press.
20 E. J. Corey and J. O. Link, *Tetrahedron Lett.*, 1989, 30, 6275.
21 G. J. Quallich and T. M. Woodall, *Tetrahedron Lett.*, 1993, 34, 4145.
22 D. C. Sherrington, in *Polymer-supported Reactions in Organic Synthesis*, eds. P. Hodge and D. C. Sherrington, Wiley, Chichester, 1980, ch. 1.
23 M. J. Farrall and J. M. J. Fréchet, *J. Org. Chem.*, 1976, 41, 3877.
24 A. A. H. Al-Kadhumi, P. Hodge and F. G. Thorpe, *Polymer*, 1985, 26, 1695.
25 D. J. Mathre, T. K. Jones, L. C. Xavier, T. J. Blacklock, R. A. Reamer, J. J. Mohan, E. T. T. Jones, K. Hoogsteen, M. W. Baun and E. J. J. Grabowski, *J. Org. Chem.*, 1991, 56, 751.
26 T. K. Jones, J. J. Mohan, L. C. Xavier, T. J. Blacklock, D. J. Mathre, P. Sohar, E. E. T. Jones, R. A. Reamer, F. E. Roberts and E. J. J. Grabowski, *J. Org. Chem.*, 1991, 56, 763.
27 H. Jacobelli, M. Bartholin and A. Guyot, *J. Appl. Polym. Sci.*, 1979, 23, 927.
28 U. Nagai and T. Shishido, *Tetrahedron*, 1965, 21, 1701.