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An easy synthesis of robust polymer-supported chiral 1,1′-bi-(2-naphthol)s (BINOLs): application to the catalysis of the oxidation of prochiral thioethers to chiral sulfoxides

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Abstract—Polystyrene beads bearing chiral 1,1′-bi-(2-naphthol) (BINOL) moieties are readily prepared by Suzuki couplings between chiral 6-bromo-1,1′-bi-(2-naphthol)s and crosslinked polystyrene beads containing phenylboronic acid residues. With this method, no protecting groups for the phenolic residues are required; any boronic acid groups that do not take part in the Suzuki coupling are removed from the support by in situ hydrolysis, and the BINOL moieties are bound to the support via strong C–C bonds. To test the performance of the new polymer-supported (PS) BINOLs, they were reacted with titanium tetraisopropoxide to give catalysts for the oxidation of aryl methyl thioethers using *t*-butyl hydroperoxide in tetrahydrofuran at 0 °C. The expected sulfoxides were obtained in up to 91% ee. The results obtained with the present catalysts are comparable to those obtained with PS catalysts prepared using more elaborate syntheses, and that have the catalyst moieties bound to the support by potentially labile linking groups.

1. Introduction

Organic reactions where one reactant is bound to a crosslinked, and therefore insoluble, polymer support have been of great interest ever since Merrifield introduced the technique of 'solid phase' peptide synthesis in 1963.[1] The main advantage of using an insoluble polymer is that at the end of a reaction, the polymer-supported (PS) species can be separated easily from the soluble species, usually by filtration. Innumerable PS reactions have been studied since,[2–5] especially in the context of combinatorial chemistry and high throughput synthesis.[6]

PS catalysts are of particular interest because they can often be reused.[7–13] However, in order to obtain the full benefits from such catalysts, they should be (a) relatively easy to prepare and (b) sufficiently robust to withstand repeated use. Usually, the preparation is best achieved by the chemical modification of preformed polymer beads that already have appropriate physical properties. Robustness includes both physical stability and chemical stability. The former can be a problem when PS catalysts are used in stirred batch reactions, because the beads tend to degrade, although they survive much better in flow reactors and these are currently a topic of growing interest.[14–16] The chemical stability includes not only that of the actual catalytic site but also that of the link binding the catalyst moiety to the support. Clearly linkages such as acid-sensitive acetals, for example, are not ideal. With regards to the stabilities of the catalytic sites, in general, relatively little is known because PS catalysts have rarely been reused to their limits and any degradation processes identified.[17]

1,1′-Bi-(2-naphthol) (BINOL) is one of the simplest C_2-symmetric ligands and its enantiomers have been used extensively in the asymmetric catalysis.[18,19] Several PS BINOLs have already been described. They are either (i) *linear* polymers prepared by condensation polymerization between halogen-, boronic acid-, acetylenic- or aldehyde-substituted BINOLs, and appropriate comonomers,[20–24] (ii) *linear* polymers prepared by free radical polymerization

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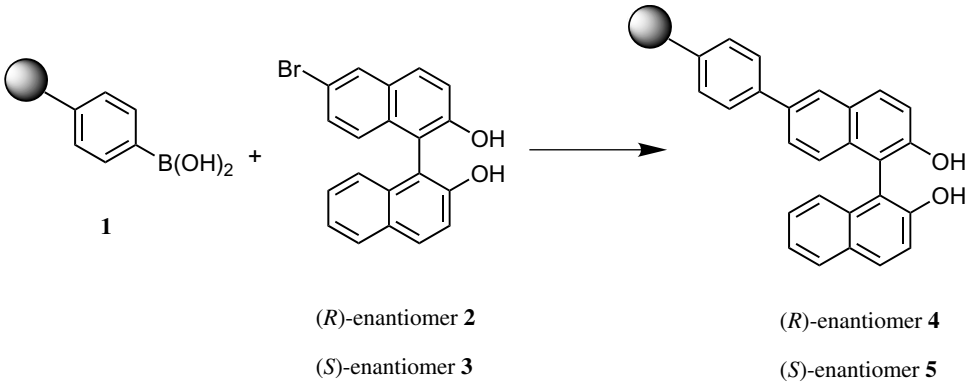


Scheme 1. Reaction used to prepare PS chiral BINOLs.

of BINOL-containing vinyl monomers,[25–27] or (iii) *cross-linked*, and therefore insoluble, polymer beads prepared by attaching BINOL derivatives containing carboxylic acid,[28] hydroxyl,[29,30] or aldehyde groups[31,32] to preformed polymer beads. These latter syntheses give final products in which the BINOL moieties are linked to the support via amide,[28] ether,[29,31,32] or acetal groups.[31,32] One problem with some of these linking groups is that they are sensitive to common reaction conditions and this limits their use. Another problem with this approach (iii) is that any unreacted residues on the beads that remain from the linking reaction might interfere in subsequent applications.

Herein, we report a facile synthesis of crosslinked polymer beads bearing chiral BINOL moieties that are attached to the support via very stable linkages (Scheme 1). The efficacy of these new PS BINOLs has been tested by using them to prepare catalysts for the oxidation of prochiral thioethers to chiral sulfoxides (Scheme 2). These reactions are complex and PS versions have not been studied in detail.[30] This oxidation was selected because chiral sulfoxides have emerged as versatile building blocks and chiral auxiliaries in the synthesis of biologically important compounds.[33]

2. Results and discussion

2.1. Catalyst preparation

In the present work, chiral BINOL moieties were introduced into crosslinked polystyrene beads using the reaction summarized in Scheme 1. First, racemic BINOL was resolved using *N*-benzylcinchonidinium chloride.[34] Each enantiomer was then converted into the corresponding 6-bromo-BINOL following the procedure used by Cai et al. to prepare *racemic* 6-bromo-BINOL (Scheme 3).[35] Thus treatment of (*R*)-BINOL **10** with pivaloyl chloride and pyridine gave monopivalate **11** (74% yield). The latter was then selectively brominated at the 6-position of the phenolic naphthalene moiety by treatment with bromine in a 50:50 v/v mixture of acetonitrile and toluene at 0 °C to give compound **12** (90% yield). The hydrolysis of **12** with sodium hydroxide gave the required (*R*)-6-bromo-BINOL **2** (90%). By an analogous series of reactions, (*S*)-BINOL **13** was converted, via compounds **14** and **15**, into (*S*)-6-bromo-BINOL **3**.

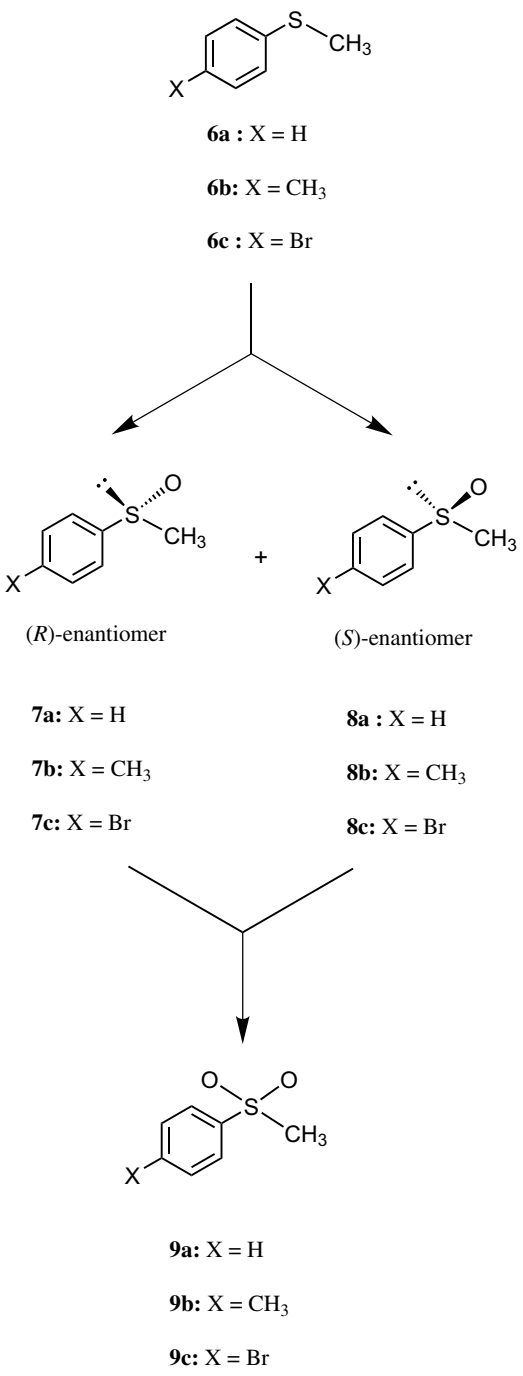
Beads containing boronic acid residues **1** were prepared by treating 1% or 2% crosslinked gel-type polystyrene beads (100–200 mesh) with *n*-butyl-lithium and then trimethyl borate.[36] Direct lithiation of the beads was used because bromination followed by a bromide-lithium exchange might leave some bromo residues on the beads that could react with boronic acid residues **1** to give crosslinks in the subsequent Suzuki couplings. In general, increasing the crosslinking of gel-type polymers, even slightly, decreases swelling and hence restricts access to the reactive sites.[37]

PS chiral BINOLs **4** and **5** were prepared by the Suzuki coupling of bromo compounds **2** and **3** with PS boronic acid **1** (Scheme 1).[38] A relatively long reaction time was used to allow boronic acid residues **1** that did not take part in the Suzuki coupling to hydrolyze.[38] The elemental analysis of the products indicated that <0.1 mmol/g of residues **1** remained. The loadings of residues **4** and **5** were estimated from the gains in the weights of the beads accompanying the Suzuki couplings, and/or by esterifying the OH groups with thiophen-2-carbonyl chloride followed by an elemental analysis for sulfur. The results are summarized in Table 1. It is evident that where loadings were estimated by both methods, the results were similar. As expected,[37] the Suzuki coupling was more efficient with the 1% crosslinked beads than with the 2% crosslinked beads.

The attractive features of this general approach are (i) that the chiral BINOL moiety is linked to the support via an extremely stable aryl–aryl linkage; (ii) the attachment method is a one-pot procedure, (iii) since the Suzuki coupling is tolerant of many functional groups, the phenolic groups of the BINOL moiety do not need protection; (iv) dry reaction conditions are not necessary, and (v) boronic acid residues **1** that do not take part in the coupling are simply removed from the support by hydrolysis. A similar approach has recently been used successfully to synthesize PS (*S*)-α,α-diphenylprolinol[39] and PS (*S*)-α,α-diphenyl-*N*-methylprolinol.[40]

2.2. Catalyzed oxidations

To assess the performance of the new PS BINOLs, PS catalysts were prepared by treatment with titanium tetraisopropoxide. The catalysts were then used for the oxidation of aryl thioethers by *tert*-butyl hydroperoxide.



Scheme 2. Oxidation of aryl methyl thioethers. Note that S–O bonds are shown as single to allow the stereochemistry to be shown clearly.

The oxidation of aryl methyl thioethers to give chiral sulfoxides using *tert*-butyl hydroperoxide in the presence of the catalyst prepared in situ from soluble (*R*)-BINOL and a titanium alkoxide has been studied in detail by Uemura et al.[41,42] The oxidation products generally contained unreacted thioether and sulfone, as well as the desired sulfoxides (Scheme 2).[41,42] Thus a typical oxidation of thioanisole **6a** gave the starting material, sulfoxides **7a**/**8a** and sulfone **9a** in a molar ratio of 24:66:10.[41] Hence, some of the sulfoxide mixture was oxidized further to sulfone **9a**. Clearly this second oxidation is slower than the first, as sulfoxides are usually obtained in good yields. It is well known that with soluble BINOL-derived catalysts, the *minor* sulfoxide enantiomer oxidizes faster than the major enantiomer.[41,42] As a consequence, the % ee of the remaining sulfoxide increases as more sulfone is formed.

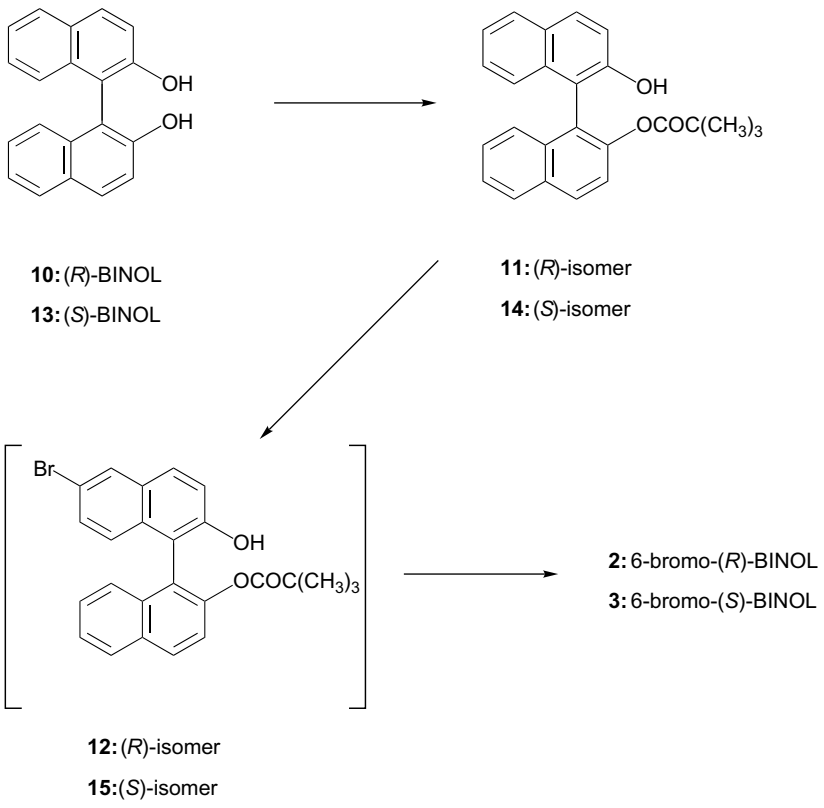
Herein, the oxidation catalysts were prepared in situ by treating the PS BINOLs with titanium tetraisopropoxide in the chosen reaction solvent at its reflux temperature, followed by the addition of a small amount of water at ambient temperature. Oxidations were then carried out by treating the aryl methyl thioether in the same reaction solvent with aqueous *tert*-butyl hydroperoxide (TBHP) in the presence of the catalyst.

Initially, the oxidations of methyl phenyl thioether **6a** were carried out using PS Catalyst I. Uemura et al., in their studies using soluble BINOLs (see above), achieved the best % ees with carbon tetrachloride as the reaction solvent: aromatic solvents and ether solvents gave somewhat lower % ees.[41] In the present work, however, when either carbon tetrachloride or diethyl ether was used as the reaction solvent, the oxidation was extremely slow at 23 °C, probably due to the poor swelling of the polymer beads.[37] Using tetrahydrofuran (THF) or toluene as the reaction solvent gave much better results. The oxidations were monitored by TLC and stopped when sulfone was first detected. To improve the selectivity, the oxidations were carried out at 0 °C: reaction times were generally 36 h. The composition of the final product and the % ee of the sulfoxides were then determined by HPLC over a chiral stationary phase. The results are summarized in Table 2, entries 1–5.

Several conclusions can be drawn from these results.

(i) The use of THF or toluene as the solvent resulted in similar chemical yields and, in each case, sulfoxides **7a**/**8a** were obtained with a 60% excess of the (*R*)-enantiomer **7a**.
(ii) Certain mixtures of THF and toluene gave better stereochemical results than either solvent alone. Thus, the use of these solvents in the ratios 1:1, 2:3 and 3:2 gave ees of 82%, 89% and 84%, respectively: compare entries 1 and 2 with 3–5. These results almost certainly reflect differences in the swelling of the polymer beads.[37]
(iii) Uemura et al. noted that in the preparation of the catalyst by reaction of BINOL with titanium tetraisopropoxide, the moles of water added affected the % ee, and that there was an optimum amount.[41] This was also found to be the case with the present PS reactions. Thus, a repeat of the reaction summarized in entry 3 but with 4.0 mol % of water per mole of thioether gave an ee of 57%, while one with 8.0 mol % gave an ee of 72%.

PS Catalyst II was then used to oxidize thioanisole **6a** in THF at 0 °C, with the aim of this reaction to maximize the yield of the sulfoxides (entry 6). The reaction was monitored by ^{1}H NMR spectroscopy: starting material **6a**, sulfoxides **7a**/**8a** and sulfone **9a** give well-resolved singlets due



Scheme 3. Preparation of 6-bromo-BINOLs **2** and **3** from BINOLs **9** and **13**. As in the procedure of Cai et al.,[35] intermediates **12** and **15** were not isolated.

Table 1. Preparation of PS BINOLs and designations of the derived PS catalysts

Entry	Crosslinking (%) of starting beads	BINOL enantiomer	Loading of residues **4** or **5** (mmol/g)[a]			Degree of substitution[c]	Coupling yield (%)	PS Catalyst prepared[d]
			By weight gain	Via thiophen ester analysis[b]	Average			
1	2[e]	*R*	0.66	—	0.66	0.11	46	I
2	1[f]	*R*	1.16	0.93	1.05	0.13	41	II
3	1[f]	*S*	1.45	1.37	1.41	0.17	53	III

[a] By elemental analysis the final beads contained <0.1 mmol/g of residues **1**.
[b] BINOL residues were esterified using thiophen-2-carbonyl chloride, followed by elemental analysis for sulfur.
[c] Calculated from average loading of residues **4** or **5**.
[d] Designation of final catalyst prepared by treating the PS-BINOL with titanium tetraisopropoxide.
[e] Boronic acid had a loading of 1.66 mmol/g of residues **1**: corresponds to a degree of substitution of 0.24.
[f] Boronic acid had a loading of 2.73 mmol/g of residues **1**: corresponds to a degree of substitution of 0.32.

Table 2. Oxidation of thioethers **6a–6c** Using PS Catalysts I–III[a]

Entry	PS Catalyst	Thioether	Reaction conditions		Composition of product (%)[b]			Major enantiomer	% ee[b]
			Solvent	Time (h)	*S*	SO	SO_2		
1	I	**6a**	THF	36	46	54	Trace	*R*	60
2	I	**6a**	Toluene	36	45	55	Trace	*R*	60
3	I	**6a**	THF/toluene (1:1 v/v)	36	45[c]	55	Trace	*R*	82
4	I	**6a**	THF/toluene (2:3 v/v)	36	40	60	Trace	*R*	89
5	I	**6a**	THF/toluene (3:2 v/v)	36	41	59	Trace	*R*	84
6	II	**6a**	THF	48	30	61	9	*R*	82
7	II	**6a**	THF	24	0	89	11	*R*	9
8	II	**6b**	THF	48	20	51	29	*R*	91
9	III	**6b**	THF	48	18	53	29	*S*	89
10	III	**6c**	THF	48	57	33	10	*S*	73

[a] See Section 4 for typical reaction procedures.
[b] Determined by HPLC.
[c] Using the same reaction conditions but with 111 μL of water added, the chemical yield was 53% and the ee was 57%. With 222 μL of water, the chemical yield was 60% and the ee was 72%.

to the *S*-methyl groups. After a reaction time of 48 h, the reaction gave the corresponding sulfoxides **7a** and **8a** in a combined yield of 61% with an ee of 82% in favour of the (*R*)-enantiomer. The increased % ee compared with the reaction summarized in entry 1 was considered to be due, mainly, to the minor sulfoxide enantiomer **8a** being oxidized more rapidly than the major sulfoxide enantiomer **7a** to the sulfone **9a**. To test this, the racemic sulfoxide of thioanisole was treated with the PS Catalyst II under the usual reaction conditions but for only 24 h. The product was analyzed using HPLC in the usual way (entry 7). As expected the sulfoxide present in the final reaction mixture contained an excess of (*R*)-enantiomer **7a**. Thus, (*S*)-enantiomer **8a** was oxidized to sulfone **9a** faster and the PS reaction behaved analogously to the non-supported reactions discussed above.[41,42]

Several other oxidations similar to that summarized in entry 6 were carried out using Catalysts II and III. The results are summarized in entries 8–10. It is evident (compare entries 8 and 9 with entry 6) that 4-methylthioanisole **6b** is more reactive than thioanisole **6a** (less starting material remaining), while 4-bromothioanisole **6c** is less reactive. This explains, at least in part, the higher % ees in the former case and the lower % ee in the latter. As expected, Catalyst III affords the (*S*)-sulfoxides in excess whilst Catalyst II affords the (*R*)-sulfoxides.

The reuse of the catalysts was also investigated briefly. Comparing the performance of the reused and original catalyst is complicated by the fact the % ees of the sulfoxides depend on how much of each sulfoxide is oxidized to sulfone. Initially Catalyst I recovered from the reaction summarized in entry 4 was, without being retreated with titanium tetraisopropoxide, reused twice under similar reaction conditions. The chemical yields of the sulfoxides and sulfone were almost unchanged but the % ees fell from 89% to 79%. This was considered to be most certainly due to the loss of titanium but not loss or racemization of the BINOL moieties. Consistent with this, when Catalyst II was recovered from the reaction summarized in entry 6, it was retreated with titanium tetraisopropoxide and reused under the previous conditions to give an ee of 81%. The catalyst was again recovered and the procedure repeated twice more. Yields of the sulfoxides and sulfone were similar to before: the ees were 79% and 84%. A more detailed study of the recycling of the catalysts will be made in future using the catalysts for long periods under the more reproducible reaction conditions of a flow system.

3. Conclusions

Polystyrene beads bearing chiral 1,1′-(bi-2-naphthol) (BINOL) moieties **4** or **5** can be prepared readily by a one-pot attachment procedure using Suzuki couplings between the appropriate chiral 6-bromo-1,1′-bi-(2-naphthol) **2** or **3** and polystyrene beads containing phenylboronic acid residues **1**. With this method of synthesis, the BINOL moieties are linked to the support via strong C–C bonds. No protecting groups are needed during the attachment reaction, the reaction conditions need not be dry, and any boronic acid groups that do not take part in the Suzuki coupling are simply removed by in situ hydrolysis.

To assess the performance of the present PS BINOLs, they were reacted in situ with titanium tetraisopropoxide to give catalysts for the oxidation of aryl methyl thioethers with aqueous *tert*-butyl hydroperoxide in THF at 0 °C. The sulfoxides were obtained in chemical yields of 33–61% and ees of 60–91%. These values compare well with those obtained by Uemura et al. who, using soluble BINOL in carbon tetrachloride as the reaction solvent at 0 °C,[40] obtained chemical yields of 39–67% and ees of 80–93%, while those using a PS BINOL employing an acetal linker gave chemical yields of 60–67% and ees of 78–88%.[30] The catalysts containing (*R*)-BINOL moieties predominantly gave the (*R*)-sulfoxides, while that with (*S*)-BINOL residues predominantly gave the (*S*)-sulfoxides.

4. Experimental

4.1. General

Experimental details are as described previously.[39] HPLC was carried out using a Chiralcel OD column; UV detection at λ 254 nm; eluant hexane/*i*-PrOH (9 vol:1 vol), at a flow rate of 1.0 mL/min.

4.2. Preparation of 6-bromo-BINOLs

Racemic BINOL was obtained from Aldrich and resolved using *N*-benzylcinchonidium chloride.[34] This gave (*R*)-BINOL **10**, mp 207–210 °C, $[\alpha]_D^{21} = +29.5$ (*c* 1, THF) {lit.,[34] 206–207 °C; $[\alpha]_D^{21} = +28.6$ (*c* 1, THF)} and (*S*)-BINOL **13**, mp 204–206 °C, $[\alpha]_D^{21} = -29.0$ (*c* 1, THF) {lit.,[34] 205–206 °C; $[\alpha]_D^{21} = -28.5$ (*c* 1, THF)}. By HPLC both enantiomers were 100% of the desired enantiomer.

Each BINOL enantiomer was converted into the corresponding 6-bromo-BINOL using the reaction sequence shown in Scheme 3. The experimental details are as given by Cai et al. for the synthesis of racemic products.[35] As in the procedure of Cai et al.,[35] intermediates **12** and **15** were not isolated.

(*R*)-BINOL monopivalate **11** (74% yield) had a mp of 63–65 °C and $[\alpha]_D^{23} = +58.0$ (*c* 1.0, THF). (*S*)-BINOL monopivalate **14** (50%) had a mp of 63–65 °C and $[\alpha]_D^{20} = -57.1$ (*c* 1.0, THF). Lit.[43] reports for (*S*)-enantiomer $[\alpha]_D^{39} = -56.8$ (*c* 0.51, THF).

(*R*)-6-Bromo-BINOL **2** (90%) had a mp of 82–84 °C and $[\alpha]_D^{20} = -7.5$ (*c* 1.0, THF). It was >99% pure on chiral HPLC analysis. (*S*)-6-Bromo-BINOL **3** (70%) had a mp of 83–85 °C and $[\alpha]_D^{21} = +7.6$ (*c* 1.0, THF). Lit.[43] reports for (*S*)-enantiomer $[\alpha]_D^{25} = +6.3$ (*c* 0.49, THF).

4.3. Synthesis of PS boronic acids

The following is typical of the syntheses used for preparing the catalysts described in Table 1.

4.3.1. Beads used for the experiments summarized in entries 2 and 3. Using the procedures described by Farrall and Frechet,[36] polystyrene beads (11.2 g, 1% crosslinked) were first lithiated by treating a suspension in dry cyclohexane (80 mL) and tetramethylethylenediamine (16 mL) with *n*-butyl-lithium (54 mL; 2.5 M in hexane) for 5 h at 50 °C, then the lithiated product was treated immediately with trimethyl borate (15.2 mL) in dry THF (120 mL) at 20 °C for 68 h. This gave pale orange beads (11.0 g). These had ν_{max} 1360 cm^{-1} (B–O). Found C, 80.45; H, 7.25; B, 2.95. The latter corresponds to a loading of 2.73 mmol of boronic acid groups per gram of beads.

4.4. Synthesis of PS BINOLs

The following synthesis is typical of the reactions summarized in Table 1.[38]

4.4.1. Entry 2. PS boronic acid **1** (2.95 g, 8.1 mmol), (*R*)-6-bromo-BINOL **2** (3.10 g, 8.5 mmol) and THF (20 mL) at 20 °C were introduced in a round-bottomed flask (250 mL). Tetrakis(triphenylphosphine)palladium[0] (0.343 g, 0.30 mmol) dissolved in THF (4 mL) was added via a septum. The flask was screened from light with an aluminium foil. The mixture was stirred for 15 min, then THF (100 mL) and aqueous potassium carbonate (16 mL, 1 M, 16 mmol) were injected. The mixture was stirred and heated at 70 °C for 72 h. A second portion of tetrakis(triphenyl phosphine)palladium[0] (0.11 g, 0.10 mmol) was added and the reaction left at 72 °C for a further 24 h. Bromobenzene (0.5 mL) was then added and the mixture stirred a further 24 h at 72 °C. The beads were filtered off and washed successively with THF, THF–water (1 vol:1 vol), HCl (0.5 M), THF–HCl (1 vol:4 vols), THF–ethyl acetate (4 vols:6 vols), THF–acetone (4 vols:6 vols), THF–methanol (4 vols:6 vols), THF–ether (4 vols:6 vols), methanol and ether. The beads were dried (3.88 g, 56%). The loading calculated by the weight gain was 1.16 mmol of (*R*)-BINOL per gram of beads. The beads had ν_{max} 3519 and 1619 cm^{-1}. Found: C, 88.00; H, 6.36; B, less than 0.1%.

4.4.2. Estimation of the loading of polymer-supported BINOL using thiophen-2-carbonyl chloride (Table 1, entry 2). PS (*R*)-BINOL **4** (0.203 g, 0.55 mmol maximum) was placed in a 50 mL three-neck-round-bottomed flask fitted with a condenser and a gas inlet adaptor. The mixture was left for 1 h under nitrogen prior to the addition of thiophene-2-carbonyl chloride (0.20 mL, 1.87 mmol) and dry pyridine (4 mL). The reaction mixture was stirred for 20 h under nitrogen at 80 °C. The beads were then filtered off and washed with a solution of HCl–H_2O–THF (2 vols:20 vols:10 vols), with water (2 × 25 mL), THF (2 × 25 mL) and finally ether (2 × 25 mL). The product was dried under vacuum overnight to yield orange-yellow beads (0.233 g). They had ν_{max} 1726 cm^{-1}. Found: C, 79.91; H, 5.44; S, 5.17. The latter corresponds to a loading of BINOL ester of 0.81 mmol/g. Allowing for the weight change, the loading of BINOL moieties on the original polymer was 0.93 mmol/g.

4.5. Oxidation reactions

The following procedures are typical for the reactions summarized in Table 2.

4.5.1. Entry 5. A mixture of Catalyst I (0.50 g, 0.33 mmol), THF (4 mL), toluene (6 mL) and titanium tetraisopropoxide (47.87 μL, 0.16 mmol) was heated at reflux under an argon atmosphere for 1 h. After cooling to 20 °C, water (16.7 μL, 0.93 mmol, as a 5% solution in THF) was added and the mixture stirred for 2 h at 20 °C. The mixture was then cooled to 0 °C and thioanisole (183 μL, 1.55 mmol) added. Aqueous *tert*-butyl hydroperoxide (70%, 430 μL, 3.1 mmol) was added dropwise. The reaction was monitored by TLC and stopped at the appearance of the spot due to sulfone. The reaction time was 36 h. The excess of peroxide was quenched by saturated aqueous potassium iodide and the product was extracted with ethyl acetate and washed with saturated aqueous sodium thiosulfate. The organic solution was dried and evaporated to dryness to give the crude product. The amounts of starting material, sulfoxides and sulfone and the ee value were determined by HPLC analysis. The major enantiomer had a retention time of 11.0 min, the minor enantiomer had a retention time of 13.1 min. Column chromatography of the crude product over silica gel (ethyl acetate/hexane: 2 vols to 3 vols) gave a mixture of sulfoxides **7a/8a** with $[\alpha]_D^{20} = +133.7$ (*c* 1.0, acetone) {lit.[44] for pure (*R*)-isomer $[\alpha]_D^{25} = +149$ (*c* 1.0, 95% ethanol)}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.85 (s, 3H), 7.53–7.57 (m, 3H), 7.65–7.68 ppm (m, 2H).

4.5.2. Entry 6. The reaction was carried out using the above procedure except that the reaction was monitored by ^{1}H NMR spectroscopy. Thioether **6a** shows a singlet at δ 2.60 ppm, sulfoxides **7a/8a** show a singlet at δ 2.85 ppm, and sulfone **9a** shows a singlet at δ 3.10 ppm. The reaction was stopped when the percentage of sulfoxide was near maximal. The reaction time was 48 h. The product was analyzed using HPLC. The mixture of sulfoxides isolated by column chromatography was obtained as an oil with $[\alpha]_D^{25} = +121$ (*c* 1.0, 95% ethanol).

4.5.3. Entries 8 and 10. The reactions were carried out using the general procedures given above. After HPLC analysis, samples of sulfoxide were isolated using column chromatography. The mixture of sulfoxides **7b/8b** was obtained as a solid at a mp of 70–73 °C, $[\alpha]_D^{25} = +128$ (*c* 1.0, 95% ethanol) {lit.[45] mp 73–74.5 °C, $[\alpha]_D^{25} = +141$ (*c* 1.0, 95% ethanol)}. The mixture of sulfoxides **7c/8c** was obtained as a solid at a mp of 85–87 °C, $[\alpha]_D^{25} = +76$ (*c* 0.5, chloroform) {lit.[46] for (*S*)-enantiomer $[\alpha]_D^{25} = -105$ (*c* 0.44, chloroform)}.

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