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A Soluble-Polymer System for the Asymmetric Transfer Hydrogenation of Ketones

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The appropriate combination of methacrylate polymers permits the synthesis of a soluble polymer for use in ruthenium(II)-catalyzed asymmetric transfer hydrogenation reactions. Using a 7:3 copolymer of a poly(ethylene glycol) ester and a hydroxyethyl ester, a derived ruthenium(II)/norephedrine complex catalyses reduction of acetophenone in up to 95% yield and 81% ee.

Introduction

Recent years have seen significant advances in the development of supported homogeneous catalysts for use in asymmetric catalysis.[1] These provide a significant potential advantage by providing a means for the separation of the catalyst from the mixture after the reaction is complete; the purification of the reaction product is greatly facilitated, and the recovered catalyst may be reused. Some supported systems depend on the use of insoluble resin beads which may be removed from the reaction by a simple filtration. Applications[2−5] include asymmetric epoxidation, the asymmetric catalysis of the reduction of ketones with borane,[2] dialkylzinc additions to aldehydes,[3] and asymmetric Diels−Alder reactions.[4] A drawback of this approach, however, is that under certain circumstances, i.e., if the bead is not compatible with the required solvent, many of the potential active catalyst sites may be inaccessible to the solution-borne reagents.[1] In addition, it may be difficult to assess the level of catalyst loading on the polymer bead with accuracy.

To circumvent these limitations, attention has recently turned to the development of small soluble-polymer and dendrimer supports.[6−9] This class of supported system is based on the use of a polymer or dendrimer with a molecular weight typically in the order of 5−10 000 Da, i.e., small by comparison with resin beads but large by comparison with the attached catalyst. Such catalysts have the advantage of total solubility and unhindered active sites and may be analyzed without difficulty with routine spectroscopic techniques. The removal of these supported catalysts from the reaction mixture may be achieved using membrane-separation methods[9] or by selective precipitation under specific conditions. Dendrimer and soluble-polymer modifications have been

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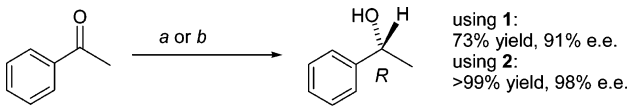
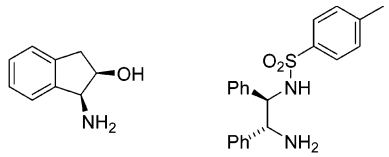
SCHEME 1[a]



[a] Reagents and conditions: (a) 0.25 mol % [Ru(*p*-cymene)Cl_2]$_2$, 1 mol % ligand **1**, 2.5 mol % KOH, *i*-PrOH; (b) 0.25 mol % [Ru(*p*-cymene)Cl_2]$_2$, 0.5 mol % ligand **2**, HCO_2H/Et_3N.

made to catalysts for the addition of dialkylzinc reagents to aldehydes[7] and the Sharpless dihydroxylation.[8]

In previous work in our laboratories, we have investigated the ruthenium(II)- and rhodium(III)-catalyzed asymmetric reduction of ketones to alcohols using transfer hydrogenation.[10−12] In our studies, we have focused on the use of β-amino alcohols such as *cis*-aminoindanol **1** and monotosylated 1,2-diamines such as TsDPEN **2** as ligands for this process (Scheme 1).[10] Both of these ligand systems were introduced by Noyori, who has also reported extensively on the applications and mechanism of the new catalysts.[11] Amino alcohols afford the greatest rate enhancements but are limited to the reduction of C═O bonds, while the monotosylated diamines are more versatile and may be used in the asymmetric reduction of C═O and C═N bonds.



(1*S*,2*R*)-*cis*-aminoindanol: **1** (*R*,*R*)-TsDPEN: **2**

In a parallel research program, we have investigated the potential of copolymers of methacrylates (Figure 1) to operate as supporting systems for asymmetric catalysis.[9h,13,14] Such polymers are relatively simple to prepare, in predictable molecular weights, using established radical polymerization chemistry with the chain-transfer catalyst CoBF **3**.[15] Since the reaction is highly versatile, with a high degree of substrate-tolerance, it is possible to employ it in copolymerization of two or more monomers. In our work, we have examined the combination of two monomers to create such a copolymer, in which one provides the required solubility properties and the other provides a point of attachment for a catalyst in the post-polymerization modification of the system. The ratio of each monomer, and also the overall polymer weight, may potentially be selectively modified for use under any prescribed reaction solvent and conditions.

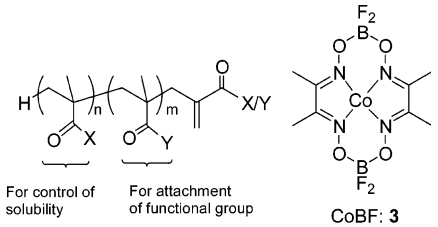


FIGURE 1. Copolymers of methacrylates.

In our work on the asymmetric catalysis of diethylzinc addition to aldehydes, for example, a soluble polymer **4** containing a combination of methacrylate and hydroxyethyl methacrylate (7:3 ratio) provided the foundation for a suitable support.[13] This was elaborated to the ephedrine-functionalized derivative **5** using a Suzuki aryl−aryl bond-forming reaction in a key step (Scheme 2).[16−18]

Since this work had been successful, we theorized that the extension of this class of methacrylate copolymer to asymmetric transfer hydrogenation reactions might provide a valuable tool for asymmetric catalysis. Previous investigations into supported systems for this class of reaction have led to the development of bead-based systems containing TsDPEN-type ligands[19] and several classes of soluble polymer-supported variants.[20] One of these new systems was a polymer bead supported system

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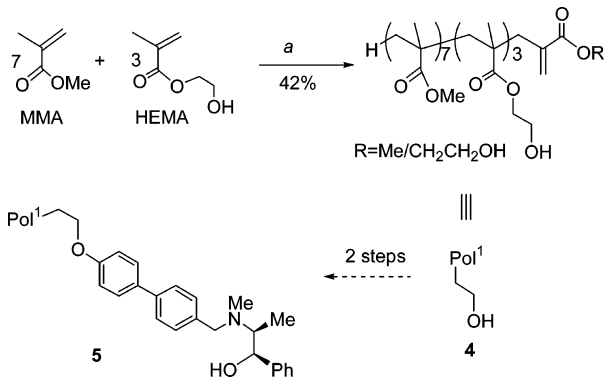
SCHEME 2[a]



[a] Reagents and conditions: (a) cat. AIBN, sodium bis (2-ethylhexyl)sulfosuccinate, 0.06 mol % CoBF, 4 h, rt.

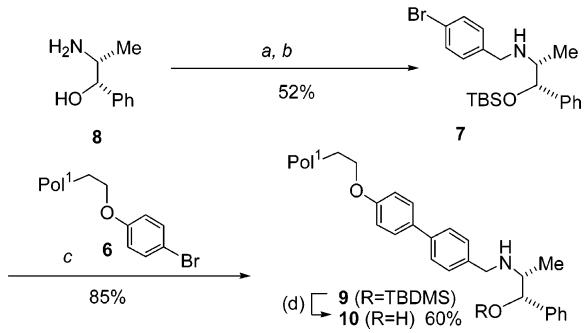
developed at EvotecOAI.[19a] Other supported systems feature a silica support for use in continuous reactions[19b] and the direct incorporation of TsDPEN into a polystyrene polymer during the polymerization step.[19c] The reported soluble polymers include a methacrylate/ethylene copolymer bearing a chiral amino acid,[20a] poly(acrylic acid) supports,[20b] polyamide-linked DPEN derivatives,[20c] and dendrimer-supported TsDPEN ligands.[20e,f] Many of these have given excellent results in the ketone reduction in terms of both conversion and enantioselectivity.

Results and Discussion

Our starting point for this investigation was the polymer that had been employed in our dialkylzinc addition work, i.e., **4**, which was derived from a 7:3 copolymer of methyl methacrylate and hydroxyethyl methacrylate. Polymer **4** is soluble in a range of organic solvents and may be conveniently analyzed using ^{1}H NMR spectrometry in order to verify both its molecular weight and composition. Polymer **4** was first converted via a tosylate derivative to the *p*-bromophenol derivative **6** following a procedure already reported by this group.[13] Polymer **6** was then coupled to the TBDMS-protected *N*-(*p*-bromobenzyl) derivative **7** of (1*S*,2*R*)-norephedrine **8** using an aryl−aryl coupling reaction[17] which we had previously developed in the group (Scheme 3). Treatment of the resulting polymer **9** with TBAF resulted in deprotection to give **10** in 60% yield.

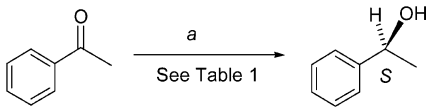
Norephedrine was selected as an appropriate amino alcohol for this application because its secondary amine derivatives have been demonstrated to be excellent ligands for asymmetric transfer hydrogenation of ketones when used in complexes with Ru(II).[11,12] The modified Suzuki reaction was based on a previously reported procedure[17] in which a boronic acid is first generated in

SCHEME 3[a]



[a] Reagents and conditions: (a) TBDMSCl, imidazole, THF, reflux, o/n, 79%; (b) *p*-Br$C_6H_4CH_2$Br, Et_3N, THF, 63%; (c) **7**, Pd(dppf)Cl_2·DCM, THF, 3 equiv of KOAc, 1.1 equiv of bis (pinacolato)diboron, 80 °C, 2 h; then **6**, Na_2CO_3, Pd(dppf)Cl_2, THF, 80 °C, o/n; (d) TBAF, THF, 4 h, rt.

SCHEME 4[a]

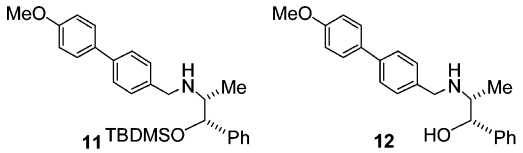


[a] Reagents and conditions: (a) [Ru(*p*-cymene)Cl_2]$_2$ (0.4 equiv with respect to amino alcohol), mol % catalyst indicated in Table 1, KOH (2.5 equiv with respect to Ru(II), *i*-PrOH.

TABLE 1. Asymmetric Reduction of Acetophenone Using (1*S*,2*R*)-Norephedrine Ligand on Soluble Polymer Supports

entry	ligand	mol %	time (h)	cosolvent	yield/%	ee/%
1	(1*S*,2*R*)-norephedrine	1	o/n	DCM	82	73
2	**12**	1	4	none	70	82
3	**10**	0.71	o/n	none	9	77
4	**10**	0.44	o/n	DCM	20	77
5	**10**	0.44	o/n	none	13	51
6	**10**	1.42	o/n	none	11	73
7	**10**	1.42	o/n	$CHCl_3$	7	71
8	**10**	0.88	o/n	MeCN	14	8
9	**15**	0.56	o/n	DCM	44	81
10	**19**	2.62	o/n	none	52	81

situ and then coupled directly to an aryl bromide through the use of essentially identical conditions but a stronger base. To provide a nonpolymer-bound ligand for comparison, this reaction was also used for the coupling of **7** with 4-bromoanisole, resulting in successful formation of **11** in 76% yield, which was subsequently deprotected with TBAF to give amino alcohol **12** in 54% yield.



With ligands **10** and **12** in hand, some asymmetric transfer hydrogenations were investigated (Scheme 4, Table 1) use acetophenone as the test substrate. Both (1*S*,2*R*)-norephedrine and **12** gave good results (entries 1 and 2); however, the performance of polymer-bound ligand **10** was restricted by the very poor solubility which it exhibited in the reaction solvent, 2-propanol (Table 1, entries 3−8). In the first reaction the yield of product,

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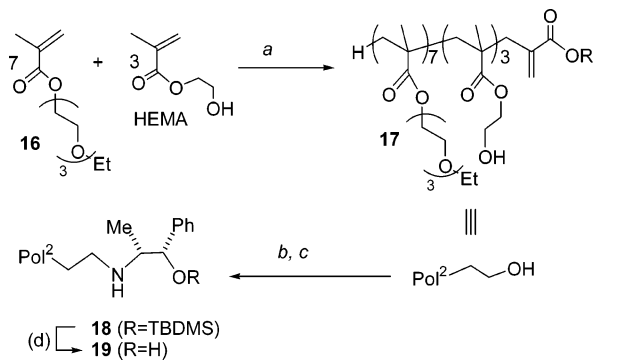
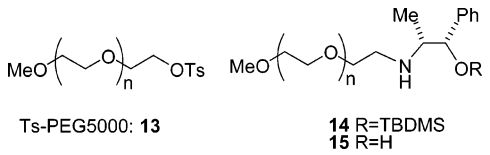
SCHEME 5[a]



[a] Reagents and conditions: (a) cat. AIBN, 10 ppm CoBF, 48 h, 60 °C; (b) TsCl, Et_3N, DCM, rt, 2 d, 45%; (c) TBDMS-(1*S*,2*R*)-norephedrine, K_2CO_3, MeCN, reflux, 2 d, 62%; (d) TBAF, THF, o/n, rt, 65%.

despite an extended reaction time, was only 9%, although the ee was encouraging at 77% and in the direction expected for this ligand (*S*). The use of a cosolvent and/or sonication had no significant beneficial effect.

In view of this result, we sought alternative copolymers which would exhibit improved solubility, yet retain the catalytic properties of the ephedrine component. A poly(ethylene glycol) (PEG) chain seemed an attractive choice because such groups have been employed in soluble polymers for a number of asymmetric reactions.[8] To determine whether the PEG group would be compatible with our solvent system, a reaction between tosylated PEG5000 **13** and TBDMS-protected (1*S*,2*R*)-norephedrine was completed in order to furnish **14**, which was then deprotected with TBAF to give **15**. This compound proved to be quite effective in ketone reduction (Scheme 4, Table 1, entry 9), and afforded a product of 81% e.e. in 44% yield without the need for a cosolvent.



With this promising result in hand, we sought an appropriate copolymer containing PEG groups for improved solubility (Scheme 5). This was prepared from the appropriate monomers HEMA and **16**; we selected a PEG monomer with a low molecular weight as we did not want to increase the polymer bulk disproportionately relative to the mass of the catalyst. The resulting copolymer **17** was tosylated without difficulty. Rather than employing the palladium-catalyzed coupling route, however, we instead carried out the direct reaction of TBDMS-protected (1*S*,2*R*)-norephedrine with tosylated polymer **17** under the same conditions as employed for the synthesis of **15**. This proceeded well and delivered product **18** in 62% yield, reducing the reaction sequence by two steps. The subsequent desilylation completed the synthesis of **19** in 65% yield.

In the first test as a ligand for transfer hydrogenation, polymer **19** delivered a product of 81% ee in 52% isolated yield (Table 1, entry 10) following an overnight reaction time and represented the best result to date for this class of supported catalyst. This was gratifying as we had been anxious that the shorter separation of the ligand from the backbone relative to earlier generations might reduce its capacity to bind to the ruthenium. More encouragingly, no cosolvent was required to maintain solubility, suggesting that the short PEG chains provided the required solubility for maximum reactivity. Further studies revealed that the minimal catalyst loading for the reaction was ca. 2 mol %, above; lower catalyst loadings gave significantly lower conversions. A short study of the extent of reaction with time was completed (Table 2). This revealed that the reaction was some 75% complete after 6 h when 2 mol % catalyst was used. However, an overnight reaction period only raised this to 85%, suggesting that a significant leveling-off of conversion was taking place.

TABLE 2. Use of Ligand 19 in Transfer Hydrogenation of Acetophenone

entry	catalyst (mol %)	time (h)	Yield/%	ee (%) (*R*/*S*)[b]
1	0.5[a]	o/n	16	80 (*S*)
2	0.5	o/n	30	77 (*S*)
3	1	o/n	46	79 (*S*)
4	2	1	26	79 (*S*)
5	2	2	50	79 (*S*)
6	2	4	66	81 (*S*)
7	2	6	75	81 (*S*)
8	2	20	85	81 (*S*)

[a] 1.7 equiv of ligand/Ru atom; ratio is 2.7 equiv of ligand/Ru atom in other cases. [b] ee's were determined by chiral HPLC.

TABLE 3. Repeated Reduction of Acetophenone Catalyzed by 19/Ru(II)

catalyst (mol %)	time (h)	conversion (%)
4	1	55
4	2	82
4	4	95
	substrate reloaded[a]	
4	1	58
4	2	74
4	4	85
	substrate reloaded[a]	
4	14	77

[a] A quantity of substrate equal to that initially employed was added at this point.

With the use of 4 mol % of ligand **19**, the conversion was raised sharply to 95% after 4 h. More interestingly, the catalyst was still active; addition of a further quantity of acetophenone (equal to the initial loading) revealed that the catalyst continued to reduce the ketone (Table 3). This result suggests that the supported catalyst may be compatible with membrane-separation systems in which a reactor is repeatedly dosed with quantities of substrates. There was, however, a deterioration of activity after the third addition of ketone substrate. This may be a result of slow catalyst decomposition and will be addressed in future studies of these reagents.

Finally, a short series of ketones was subjected to asymmetric transfer hydrogenation using ligand **19**, and an interesting set of results was achieved (Figure 2). The reduction of aryl/alkyl ketones gave consistently good results, as would be expected from literature precedent. In all cases, the ee values observed were similar to those reported for the untethered reagents.

In the case of unsubstituted aromatic ketones, the yields and ee's were generally good; however, the intro-

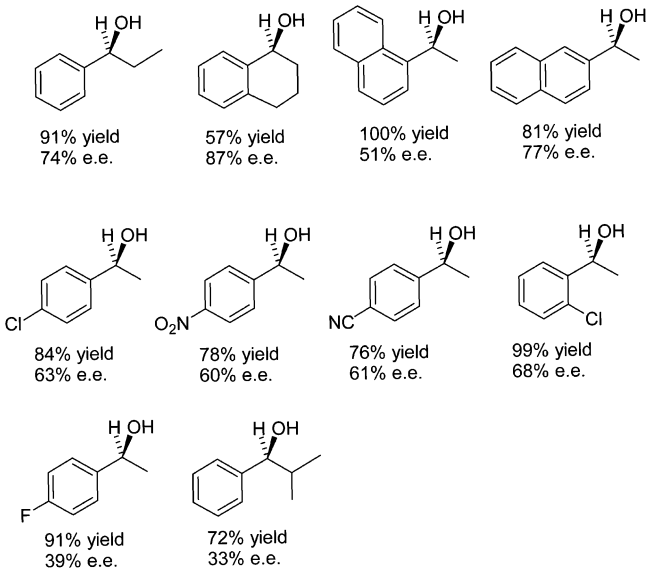


FIGURE 2. 2. Alcohols formed by ketone reduction using**19**/Ru(II).

duction of substitutents had a marked effect. *p*-Fluoroacetophenone, in particular, gave a product of very low ee. In the last example, the introduction of a larger group (than methyl) on the side of the ketone opposite the aromatic ring also appears to reduce the enantioselectivity. This is in agreement with literature precedent for the reduction of such substrates using amino alcohol/Ru(II) systems[10b] and suggests that a steric effect is also involved in the reduction process, in addition to the known electronic effects.[11f] The slightly lower selectivity observed for the ortho-substituted substrates also has literature precedent.[11a]

Conclusion

In conclusion, we have demonstrated that, through the appropriate selection of monomers, methacryate copolymers have the potential to act as competent soluble-polymer supports for asymmetric catalysts. The polymers may be prepared in large quantity through the use of well-established radical polymerization chemistry with the assistance of chain transfer catalysts and attached to chiral ligands using routine organic transformations and reagents. The materials may be conveniently analyzed using ^{1}H NMR spectroscopy. More significantly, the versatile and tolerant nature of the polymerization methodology provides a means for the rapid preparation and use of a "fine-tuned" reagent toward particular applications through judicious selection of monomer substitution. The polymer-supported reagents described in this paper have the potential for use in a membrane-separation reactor. This is currently the subject of ongoing studies and our results will be reported in due course.

Experimental Section

For general experimental details, see the Supporting Information.

(1*S*,2*R*)-(+)-2-Amino-1-[(*tert*-butyldimethylsilyl)oxy]-propane. *tert*-Butyldimethylsilyl chloride (4.79 g, 31.8 mmol) and imidazole (4.51 g, 66.3 mmol) were added to a solution of (1*S*,2*R*)-(+)-norephedrine **8** (4.0 g, 26.5 mmol) dissolved in THF (20 mL). The white cloudy reaction mixture was heated at reflux overnight. The resulting yellow reaction mixture was allowed to cool before dilution with ethyl acetate (200 mL) and washed with 1 M HCl solution (100 mL). The aqueous layer was extracted using ethyl acetate (100 mL), and the combined organic extracts were dried using magnesium sulfate, filtered, and concentrated in vacuo to give the crude product as a yellow oil. The crude product was purified using column chromatography (SiO_2, EtOAc/hexane gradient) to give the pure product as a white solid (5.57 g, 79% yield): mp 218−220 °C; $[\alpha]^{22}_D$ = +84.5 (*c* 1, $CHCl_3$), lit[21] $[\alpha]^{22}_D$ = −44.1 (*c* 1, $CHCl_3$, for 1*R*, 2*S* isomer); IR (Nujol) 3240, 1581, 1499, 1377 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.04 (br s, 2H), 7.38−7.25 (m, 5H), 5.01 (d, 1H, *J* = 3.7 Hz), 3.40 (qd, 1H, *J* = 3.7, 6.7 Hz), 1.27 (d, 3H, *J* = 6.7 Hz), 0.95 (s, 9H), 0.22 (s, 3H); −0.21 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 140.2, 128.6, 128.5, 127.1, 75.2, 54.2, 26.4, 18.5, 13.2, −4.5; MS (CI) *m*/*z* 266 (MH^+); CI HRMS calcd for ($C_{15}H_{27}NOSi)^+$ 266.1940, found 266.1941.

(1*S*,2*R*)-2-(4-Bromobenzylamino)-1-phenyl-1-[(*tert*-butyldimethylsilyl)oxy]propane 7. Triethylamine (1.76 g, 2.42 mL, 18.5 mmol) was added to a solution consisting of (1*S*,2*R*)-(+)-2-amino-1-[(*tert*-butyldimethylsilyl)oxy]propane, (4.63 g, 17.4 mmol) dissolved in THF (30 mL) and stirred for 30 min. *p*-Bromobenzyl bromide (4.37 g, 17.5 mmol) was added to the reaction mixture and heated at reflux overnight. The resulting thick, white reaction mixture was allowed to cool before dilution with EtOAc (200 mL). The reaction solution was then washed with 1 M HCl solution (100 mL) and the sodium hydrogen carbonate solution extracted with EtOAc (100 mL). The combined organic extracts were dried using magnesium sulfate, filtered, and concentrated in vacuo to give the crude product as a yellow oil. The crude product was purified using column chromatography to give the product **7** as a pale yellow oil (4.81 g, 63% yield): $[\alpha]^{22}_D$ = +26 (*c* 1, chloroform); IR (liquid film) 3322, 2956, 2857, 2709, 2362, 1948, 1896, 1740, 1647, 1592, 1488, 1452, 1255, 1106, 1070 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, 2H, *J* = 8.5 Hz), 7.33−7.22 (m, 5H), 7.07 (d, 2H, *J* = 8.5 Hz), 4.61 (d, 1H, *J* = 5.0 Hz), 3.77 (d, 1H, *J* = 13.8 Hz), 3.64 (d, 1H, *J* = 13.8 Hz), 2.73 (m, 1H), 1.40 (brs, 1H), 1.02 (d, 3H, *J* = 6.0 Hz), 0.88 (s, 9H), 0.03 (s, 3H), −0.20 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 144.0, 138.5, 130.9, 129.9, 127.5, 127.3, 127.0, 120.1, 77.3, 59.7, 53.3, 25.6, 17.8, 9.0, −4.6; MS (CI) *m*/*z* 436 (MH^+ Br^{81}), 434 (MH^+ Br^{79}), 356 (MH^+ − Br), 214, 212; CI HRMS calcd for ($C_{22}H_{32}Br^{79}NOSi)^+$ 434.1515 found 434.1512.

(1*S*,2*R*)-2-(4′-Anisylbenzylamino)-1-phenyl-1-[(*tert*-butyldimethylsilyl)oxy]propane 11. (1*S*,2*R*)-2-(Bromobenzylamino)-1-phenyl-1-[(*tert*-butyldimethylsilyl)oxy]propane, **7** (0.70 g, 1.61 mmol), was dissolved in THF (15 mL). To the stirred solution was added dichloro[1,1-bisdiphenylphosphinoferrocene]-palladium(II)·DCM (0.04 g, 0.05 mmol), bis(pinacolato)diboron (0.45 g, 1.77 mmol), and potassium acetate (0.47 g, 4.78 mmol). The orange reaction mixture was heated at 80 °C for 2 h. The resulting black reaction mixture was allowed to cool before the addition of bromoanisole (0.6 g, 0.4 mL, 3.22 mmol), dichloro-[1,1-bisdiphenylphosphinoferrocene]palladium(II)·DCM (0.04 g, 0.05 mmol), and sodium carbonate (2 M, 4 mL). The reaction mixture was then reheated at 80 °C overnight. The black reaction mixture was allowed to cool before the product was extracted with ethyl acetate (150 mL). The organic layer was then washed with water (100 mL) and a brine solution (100 mL). The organic layer was dried using magnesium sulfate, filtered, and concentrated in vacuo to give the crude product as a yellow oil. This was purified by column chromatography (SiO_2, EtOAc/hexane gradient) to give the pure product, **11**, as a pale yellow oil (0.56 g, 76% yield): $[\alpha]^{22}_D$ = +24 (*c* = 1, chloroform); IR (Nujol) 3300, 3028, 1883, 1646, 1610, 1583, 1526, 1500, 1291, 1181 cm^{-1}; ^{1}H NMR(300 MHz, $CDCl_3$) δ 7.51

(21) Brussee, J.; van Benthem, R. A. T. M.; Kruse, C. G.; Gen, A. *Tetrahedron: Asymmetry* **1990**, *1*, 163−166.

(d, 2H J = 8.4 Hz), 7.46 (d, 2H J = 8.1 Hz), 7.31−7.22 (m, 7H), 6.96 (d, 2H, J = 8.8 Hz), 4.65 (d, 1H, J = 5.0 Hz), 3.85 (d, 1H, J = 13.5 Hz), 3.84 (s, 3H), 3.72 (d, 1H, J = 13.5 Hz), 2.82 (m, 1H), 1.53 (brs, 1H), 1.06 (d, 3H, J = 6.2 Hz), 0.89 (s, 9H), 0.07 (s, 3H), −0.19 (s, 3H); ^{13}C NMR(75.5 MHz, $CDCl_3$) δ 159.0, 142.9, 139.2, 139.1, 133.6, 128.2, 128.0, 127.9, 127.2, 126.9, 126.6, 114.2, 77.8, 58.7, 55.3, 50.7, 25.9, 18.2, 15.4, −4.5, −4.1; m/z 462 (MH^+), 266, 240, 197, 134; CI HRMS calcd for $C_{29}H_{39}NO_2Si$ 462.2828, found 462.2826.

(1*S*,2*R*)-2-(4′-Anisylbenzylamino)-1-phenyl-1-propanol 12. TBAF (0.51 g, 1.95 mmol) was added to a solution consisting of (1*S*,2*R*)-2-(bromobenzylamino)-1-phenyl-[(*tert*-butyldimethylsilyl)oxy]propane **11** (0.25 g, 0.54 mmol) dissolved in THF (10 mL). The reaction mixture was allowed to stir at room temperature overnight. The yellow reaction mixture was diluted with EtOAc (150 mL) and washed with water (200 mL). The water layer was extracted using EtOAc (100 mL), and the combined organic extracts were dried using magnesium sulfate, filtered, and concentrated in vacuo to give the crude product as a green oil. The crude product was purified by column chromatography (SiO_2, EtOAc/hexane gradient) to give the pure product **12** as a white solid (0.10 g, 54% yield): mp 110−112 °C; $[\alpha]^{22}_D$ = +32 (c = 1, chloroform); IR (Nujol) 3373, 3312, 1887, 1737, 1604, 1463, 1377 cm^{-1}; ^{1}H NMR(300 MHz, $CDCl_3$) δ 7.54−7.50 (m, 4H), 7.39−7.22 (m, 7H), 6.98 (d, 2H, J = 8.8 Hz), 4.83 (d, 1H, J = 3.8 Hz), 3.92 (s, 2H), 3.85 (s, 3H), 3.03 (qd, 1H, J = 6.6, 3.8 Hz), 2.67 (brs, 2H), 0.88 (d, 3H, J = 6.6 Hz); ^{13}C NMR(75.5 MHz, $CDCl_3$) δ 159.1, 141.2, 139.8, 138.8, 138.1, 133.3, 128.5, 128.1, 128.0, 127.0, 126.8, 126.0, 114.2, 73.0, 57.7, 55.3, 50.8, 14.5; CI m/z 348, 330, 240, 197; CI HRMS calcd for $C_{23}H_{26}NO_2$ (M + H) 348.1964, found 348.1960.

Initial HEMA/MMA (3:7 Ratio) Soluble Copolymer 4. Sodium bis(2-ethylhexyl) sulfosuccinate (2.0 g) was added to a 1 L flange flask glass reactor under a nitrogen atmosphere. Water (450 mL) was added to the reactor, and the mixture was heated to 80 °C and stirred using a turbine impeller at 150 rpm 4,4′-Azobis(4-cyanovaleric acid) (2.0 g) was added to the reaction mixture immediately prior to the monomer/catalyst feed. A solution of catalytic chain transfer agent (CoBF) (0.024 g) in MMA (135 mL) and HEMA (65 mL) was fed from a Schlenk tube via a FMI pump set at a rate of 3.33 mL min^{-1}. The polymerization was left for 4 h, at which time 100% conversion was reached. The solvent was removed from the polymer using an oven set at 150 °C to give the polymer, **4**, as a yellow solid which when ground appeared as a white powder (70.0 g): IR (Nujol) 3434, 1727, 1277, 1152, 1075 cm^{-1}; ^{1}H (250 MHz, $CDCl_3$) δ 6.30−6.20 (m), 5.60−5.50 (m), 4.20−4.05 (m), 3.90−3.80 (m), 3.60 (brs), 2.10−1.80 (brm), 1.20−0.80 (brm); ^{13}C (75.5 MHz, $CDCl_3$) δ 178.0, 176.8, 66.7, 60.2, 54.2, 51.7, 44.7, 44.4, 18.4, 16.5; m/z (GPC) M_n = 2940, Pdi = 1.78; T_g = 59 °C (Inflection point), 49 °C (Onset), heated from 0 to 160 °C at 20 °C/min.

Tosylated HEMA/MMA (3:7 Ratio) Soluble Copolymer. Triethylamine (4.85 g, 6.74 mL, 48 mmol) was added to HEMA/MMA copolymer, **4** (10.0 g, 3.4 mmol), which was dissolved in DCM (70 mL). Tosyl chloride (9.17 g, 48 mmol) and DMAP (0.50 g, catalytic) were added to the reaction mixture, and the reaction was allowed to stir for 2 days. The orange/red solution was concentrated in vacuo to give a yellow solid. The yellow solid was transferred to a sinter funnel and washed with diethyl ether (200 mL) and hexane (100 mL). The pale yellow solid was redissolved in DCM (100 mL) and washed with water (300 mL), dried using magnesium sulfate, and concentrated in vacuo to give a pale yellow solid. This was ground using a pestle/mortar, transferred to a sinter funnel, and washed further with diethyl ether (200 mL), methanol (200 mL), and hexane (100 mL) to give the product as a white powder (10.60 g, 78% yield): IR (Nujol) 1730, 1598, 1275, 1244, 1177, 1150, 923, 815 and 748 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.85−7.80 (m), 7.39 (brd, J = 14.0 Hz), 6.25−6.20 (m), 5.55−5.50 (m), 4.30−4.20 (m), 4.20−4.10 (m), 3.60 (brs), 2.47 (brs), 2.05−1.80 (brm), 1.05−0.70 (brm); ^{13}C (75.5 MHz, $CDCl_3$) δ 177.8, 176.9, 145.1, 132.8, 130.0, 127.9, 67.2, 66.8, 62.2, 62.0, 54.2, 51.8, 44.9, 44.5, 21.7, 18.7, 16.7; m/z (GPC) M_n = 4116, Pdi = 1.56; T_g T_g = 51 °C (inflection point), 40 °C (Onset), heated from 0 to 160 °C at 20 °C/min.

Bromophenyl-Derivatized HEMA/MMA Soluble Copolymer 6. Sodium hydride (0.45 g, 18.79 mmol) was added to THF (30 mL) and allowed to stir for 20 min before the addition of bromophenol (1.63 g, 9.39 mmol). Tosylated HEMA/MMA tosylated copolymer (1.60 g, 0.40 mmol) was added to the reaction mixture, and the mixture was allowed to reflux for 48 h. The reaction mixture was allowed to cool before being filtered through a sinter funnel and the filtrate concentrated in vacuo to give a pale brown solid. The pale brown solid was redissolved in EtOAc (100 mL) and washed with water (100 mL). The organic layer was dried using magnesium sulfate and concentrated in vacuo to give the crude product as a brown solid. This was triturated using diethyl ether (60 mL) to give the product **6** as a pale brown solid (0.95 g, 60% yield): IR (Nujol) 2400−1800, 1729, 1591, 1489, 1273, 1245, 1150, 1066, 824 cm^{-1}; ^{1}H (250 MHz, $CDCl_3$) δ 7.40−7.30 (m), 6.90−6.80 (m), 4.35−4.25 (m), 4.25−4.10 (brm), 3.60 (brs), 2.05−1.80 (brm), 1.10−1.00 (brm), 1.00−0.80 (brm); ^{13}C (75.5 MHz, $CDCl_3$) δ 177.7, 176.8, 176.4, 157.4, 132.2, 117.2, 116.3, 113.2, 65.6, 65.4, 63.1, 54.3, 51.7, 44.8, 44.4, 18.6, 16.3; m/z (GPC) refractive index detector M_n = 5192, Pdi = 1.36; UV detector M_n = 4205, Pdi = 1.48; T_g = 76 °C (inflection point), 63 °C (onset), heated from 0 °C to 160 °C at 20 °C/min.

Suzuki Coupling between Bromophenyl-Derivatized HEMA/MMA 6 and (1*S*,2*R*)-2-(Bromobenzylamino)-1-phenyl-[(*tert*-butyldimethylsilyl)oxy]propane 7 To Give Polymer 9. (1*S*,2*R*)-2-(Bromobenzylamino)-1-phenyl-[(*tert*-butyldimethylsilyl)oxy]propane (0.25 g, 0.57 mmol), **7**, and dichloro[1,1-bis diphenylphosphinoferrocene]palladium(II)·DCM (0.012 g, 0.015 mmol) were dissolved in THF (10 mL). Potassium acetate (0.17 g, 1.72 mmol) and bis(pinacolato)-diboron (0.16 g, 0.63 mmol) were added to the reaction mixture and heated at 80 °C for 2 h. The black reaction mixture was allowed to cool before the addition of bromo-derivatized HEMA/MMA copolymer **7** (0.13 g), sodium carbonate solution (2 M, 1.44 mL), and dichloro[1,1-bisdiphenylphosphinoferrocene]-palladium(II)·DCM (0.012 g, 0.017 mmol). The reaction mixture was then heated at 80 °C overnight. The black reaction mixture was allowed to cool before being concentrated in vacuo to give the crude product as a black/gray solid. This was redissolved in EtOAc (200 mL) and washed with water (100 mL). The organic layer was dried using magnesium sulfate, filtered, and concentrated in vacuo to give the crude product as a black oil. Methanol (2 × 50 mL) was added to the crude product and stirred vigorously. The methanol extract was then carefully removed to leave the purified product, **9**, as a black solid (0.11 g): IR (solid state) 2952, 1725, 1607, 1498, 1448, 1387, 1244, 1145, 1062; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−6.80 (brm), 4.65−4.60 (m), 4.35−4.10 (brm), 3.55 (brs), 2.85−2.80 (m), 2.05−1.80 (brm), 1.20−0.90 (brm), 1.00 (brs), 0.04 (brs), −0.20 (brs); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 178.0, 176.9, 176.1, 132.3, 134.1, 129.1, 128.2, 127.9, 127.2, 126.8, 126.6, 116.4−114.8, 113.2, 65.2, 63.2, 54.3, 51.8, 44.8, 44.5, 25.8, 24.8, 18.7, 18.1, 16.4, 15.2, −4.6, −5.0; GPC refractive index detector M_n = 5516, Pdi = 2.23, UV detector M_n = 3983, Pdi = 2.50; T_g onset 93 °C, inflection point 123 °C.

Removal of the TBDMS Group from the HEMA/MMA-Supported Chiral Norephedrine Derivative 9 To Give 10. The HEMA/MMA-supported TBDMS protected chiral norephedrine derivative, **9** (0.26 g), was dissolved in THF (10 mL) before the addition of tetrabutylammonium fluoride (0.31 g, 1.19 mmol). The reaction mixture was allowed to stir for 4 h at room temperature. The black reaction mixture was concentrated in vacuo to give the crude product as a black solid. The crude product was redissolved in EtOAc (150 mL) and washed with water (100 mL). The organic layer was dried using magnesium sulfate, filtered, and concentrated in vacuo

to give the crude product as a black solid. Methanol (2 × 50 mL) was added to the crude product and vigorously stirred. The methanol extract was then carefully removed from the sample to leave the pure product, **10**, as a black solid (0.17 g): IR 3100, 2949, 1723, 1598, 1592, 1489, 1436, 1387, 1240, 1146, 1067; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.25 (m), 6.90−6.80 (m), 5.30−5.25 (m), 4.35−4.25 (brm), 4.25−4.05 (brm), 3.70−3.50 (brs), 2.10−1.60 (brm), 1.40−0.85 (m); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 176.9, 176.5, 175.9, 164.6, 157.4, 156.8, 156.5, 131.3, 127.3, 127.0, 126.8, 115.4, 114.0, 113.9, 112.3, 72.1, 64.5, 62.2, 60.8, 53.5, 53.3, 50.1, 43.8, 43.5, 29.3, 28.7, 17.8, 16.7, 15.5, 13.1; GPC refractive index detector M_n = 4335, PDi = 1.94, UV detector M_n = 3270, PDi = 1.96; T_g Onset 82 °C, inflection point 96 °C.

Tosylated MeO-PEG5000 13. Poly(ethylene glycol) (PEG) methyl ester 5000 (10.0 g, 2.0 mmol) was dissolved in DCM (anhydrous, 40 mL) before the addition of tosyl chloride (0.76 g, 4.0 mmol) and triethylamine (0.49 g, 0.68 mL, 5.2 mmol). DMAP (0.10 g, 0.82 mmol) was added to the reaction mixture and stirred overnight. The reaction mixture was concentrated in vacuo to give the crude product as a white solid. The crude product was washed with MeOH (200 mL), which was then carefully removed to give the pure product, **13**, as a white solid (9.27 g): IR (solid state) 2876, 1963, 1466, 1341, 1279, 1240, 1176, 1146, 1097 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, 2H, J = 8.5 Hz), 7.35 (d, 2H, J = 8.5 Hz), 4.17−4.14 (2H, m), 3.65−3.60 (m, satellite), 3.63−3.53 (brs, ca. 450H), 3.40−3.35 (m, satellite), 2.45 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 145.1, 130.2, 128.4, 92.4, 72.3, 71.5, 70.8, 69.6, 69.0, 59.4, 22.0; GPC M_n = 7319, PDi = 1.05.

TBDMS-Protected Norephedrine MeOPEG5000 14. TBDMS-protected (1*S*,2*R*)-(+)-norephedrine (0.21 g, 0.79 mmol) was dissolved in MeCN (40 mL, distilled) before the addition of tosylated MeO-PEG5000, **13** (2.0 g, ca. 0.4 mmol), and potassium carbonate (0.12 g, 0.88 mmol). The reaction mixture was heated at reflux for 2 days. After 2 days of reflux, the reaction mixture was allowed to cool before dilution with EtOAc (150 mL). The reaction mixture was then filtered to remove the insoluble material. The reaction mixture was concentrated in vacuo to give the crude product as an oil. The crude product was washed with diethyl ether (250 mL) and the diethyl ether removed carefully. The crude product was dissolved in DCM (60 mL) and precipitated using diethyl ether (100 mL) to give the product, **14**, as a white solid (1.96 g): IR (solid state) 2877, 1466, 1341, 1359, 1279, 1241, 1146, 1094, 1059 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67−7.60 (m, 3H), 7.33−7.09 (m, 2H), 4.89 (m, 1H), 4.60 (m, 2H), 4.10−3.55 (brm, ca. 450H), 2.75−2.70 (m, 1H), 2.60 (brs, 2H), 1.01 (brd, 3H, J = 6.0 Hz), 0.91 (brs, 9H), 0.04 (brs, 3H), −0.20 (brs, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 127.7, 126.6, 125.9, 91.8, 71.7, 70.9, 70.6, 65.6, 58.8, 48.9, 42.5, 25.7, 15.1, 0.8, −3.9, −4.7; GPC M_n = 7366, PDi = 1.062.

Norephedrine-Functionalized MeO-PEG5000 15. TBDMS (1*S*,2*R*)-(+)-norephedrine-functionalized PEG polymer, **14** (0.7 g), was dissolved in THF (20 mL) before the addition of TBAF (0.7 g, 2.22 mmol). The reaction mixture was stirred at room temperature overnight. The reaction mixture was concentrated in vacuo before being redissolved in MeOH (50 mL) and precipitated out of solution using diethyl ether (100 mL). The crude product was redissolved in DCM (250 mL) and washed with brine solution (70 mL). The organic layer was dried using $MgSO_4$, filtered, and concentrated in vacuo to give the pure product, **15**, as a white solid (0.56 g): IR (solid state) 2877, 1466, 1455, 1341, 1278, 1240, 1146, 1094 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.35−7.30 (brm, 5H), 4.78 (d, 1H J = 4.0 Hz), 4.00−3.95 (m, 2H), 3.65−3.55 (brm, ca. 350h), 2.95−2.90 (m, 1H), 2.33 (brs, 2H), 0.81 (d, 3H, J = 6.0 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 128.3, 127.3, 126.3, 72.2−63.5, 59.3, 49.4, 21.6; GPC M_n = 4476, PDi = 1.36.

Synthesis of Ethyl PEG Ester Methacrylate/HEMA Copolymer (7:3 Ratio) 17. 2-Hydroxyethyl methacrylate (2.26 g, 1.56 mL, 17.4 mmol) and PEG ethyl ether methacrylate **16** (20.0 g, 18.6 mL, 40.7 mmol) were purged with N_2 while keeping the mixture at 0 °C. In a predried Schlenk tube was weighed COBF (0.004 g, 0.009 mmol) and placed under vacuum for 30 min before being dissolved in butanone (10 mL). This Schlenk tube was then immersed in liquid nitrogen until the solution had become a solid. The Schlenk tube was then placed under vacuum and carefully immersed in a beaker containing cold water ensuring that the total solid volume was immersed in the water. The Schlenk tube was kept under vacuum until the solution had just become liquid again and then placed under nitrogen. This freeze/thaw process was repeated three times to give the stock solution of COBF. COBF stock solution (1 mL) was removed and further diluted with 9 mL of butanone (0.09 M). This was degassed using the same freeze/thaw process a total of three times. Various volumes of the diluted COBF solution were then used in the copolymerization. The reaction mixture was then cooled to 0 °C for 30 min and diluted with butanone (10 mL). COBF solution (2.5 mL, 0.22 mmol) was added to the reaction mixture and allowed to cool to 0 °C for 30 min. AIBN (0.048 g, 0.30 mmol) was then added to the cooled reaction mixture. The reaction mixture was then heated at 60 °C for 2 days. The reaction mixture was cooled before removal of the solvent in vacuo to give the crude product as an oil. The crude product was dissolved in MeOH (50 mL) and precipitated out of solution using diethyl ether (150 mL) to give a polymer layer at the base; the top liquid layer was carefully removed. This process was repeated to give the pure product (after drying), **17**, as a white semisolid (3.99 g): IR (solid state) 3473, 2929, 2868, 1722, 1485, 1449, 1386, 1350, 1273, 1245, 1105 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.25−6.20 (m), 5.55−5.50 (m), 4.15−4.05 (m), 3.85−3.80 (m), 3.75−3.60 (m), 3.55 (q, J = 7.0 Hz), 1.95−1.80 (m), 1.19 (t, J = 7.0 Hz), 1.10−1.00 (brm), 1.00−0.90 (brm); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 177.6, 176.7, 70.5, 70.4, 69.6, 68.4, 66.5, 63.9, 59.9, 54.2, 44.9, 44.6, 19.0, 16.8, 10.0; GPC M_n = 4473, PDi = 1.59, T_g onset 61 °C.

Synthesis of Tosylated PEG Ethyl Ester/HEMA Copolymer. PEG ethyl ester MMA/HEMA copolymer, **17**, (3.92 g) was dissolved in DCM (anhydrous, 30 mL) before the addition of triethylamine (2.09 g, 2.9 mL, 20.68 mmol). Tosyl chloride (3.95 g, 20.7 mmol) and DMAP (0.2 g, 1.6 mmol) were added to the reaction mixture and stirred at room temperature for 2 days. The orange/red solution was concentrated in vacuo to give a yellow solid. The yellow solid was transferred to a sinter funnel and washed with diethyl ether. The pale yellow solid was redissolved in DCM (200 mL) and washed with water (100 mL), dried using magnesium sulfate, and concentrated in vacuo to give a pale yellow solid. This was ground using a pestle/mortar, transferred to a sinter funnel, and washed further with diethyl ether (200 mL) to give the product as a pale yellow semisolid (2.21 g): IR (solid state) 2971, 2867, 1725, 1647, 1597, 1448, 1357, 1271, 1149 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80−7.70 (m), 7.40−7.30 (m), 6.25−6.20 (weak m), 5.35−5.30 (weak m), 4.25−4.15 (m), 4.15−4.05 (m), 3.70−3.50 (brm), 3.45 (q, J = 7.0 Hz), 2.45 (brs), 1.22 (t, J = 7.0 Hz), 1.10−1.00 (brm), 1.00−0.85 (brm); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 177.2, 176.0, 145.0, 132.6, 130.3, 128.2, 70.6, 70.5, 69.7, 68.4, 66.5, 63.9, 62.2, 54.2, 45.0, 44.6, 21.7, 18.5, 16.6; used directly in next step.

Reaction between TBDMS-Protected Norephedrine and Tosylated PEG/HEMA Copolymer. Tosylated PEG ethyl ester/HEMA copolymer (7.35 g) was placed under vacuum for 30 min before being dissolved in MeCN (70 mL, distilled and stored over molecular sieves). (1*S*,2*R*)-(+)-2-Amino-1-[(*tert*-butyldimethylsilyl)oxy]propane (6.36 g, 23.9 mmol) and potassium carbonate (4.27 g, 30.89 mmol) were added to the reaction vessel and heated at reflux for 2 days. After 2 days of reflux, the cloudy reaction mixture was allowed to cool before being diluted with EtOAc (150 mL). The reaction mixture was filtered to remove insoluble material and washed with water (3 × 50 mL). The organic layer was dried over $MgSO_4$ and the solvent removed in vacuo to give the crude

product as a pale yellow oil. The crude product was dissolved in a minimum amount of diethyl ether and precipitated with hexane to give the product **18** as an oil (5.1 g, 62% yield): IR 3601, 2929, 2859, 2359, 2342, 1725, 1456, 1248 and 1107 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.30−7.20 (m), 4.55−4.50 (m), 4.25−4.15 (m), 4.15−4.05 (m), 3.70−3.60 (brm), 3.55 (q, J = 7.0 Hz), 2.80−2.70 (m), 1.95−1.75 (brm), 1.21 (t, J = 7.0 Hz), 1.10−1.00 (m), 1.00−0.85 (brm), 0.95 (brs), 0.05 (brs), −0.20 (brs); ^{13}C (75.5 MHz, $CDCl_3$) 128.5, 127.5, 71.1, 71.0, 70.2, 67.0, 59.1, 56.8, 56.1, 55.9, 55.7, 45.1, 45.0, 44.7, 44.6, 26.3, 15.6, −4.1, −6.2; GPC M_n = 7500, PDi = 1.93, T_g onset 130 °C.

Removal of the TBDMS Group from the PEG/HEMA-Supported TBDMS-Protected Norephedrine 18. The PEG/HEMA-supported TBDMS-protected chiral norephedrine derivative **18** (4.95 g) was dissolved in THF (70 mL) before the addition of tetrabutylammonium fluoride (3.0 g). The reaction mixture was allowed to stir overnight at room temperature. The reaction mixture was concentrated in vacuo to give the crude product as an oil. The crude product was redissolved in EtOAc (150 mL) and washed with water (2 × 100 mL). The organic layer was dried over magnesium sulfate, filtered, and concentrated in vacuo to give the crude product **19** as a yellow oil (2.82 g, 65% yield): IR 3424, 2973, 2868, 1724, 1449, 1244, 1103 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35−7.25 (m), 6.25−6.20 (weak m), 5.55−5.50 (weak m), 4.85−4.80 (m), 4.15−4.00 (brm), 3.70−3.50 (brm), 3.55 (q, J = 7 Hz), 2.95−2.90 (m), 2.00−1.80 (brm), 1.18 (brt, J = 7 Hz), 1.15−1.00 (m), 1.00−0.85 (m); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 177.5, 176.5, 128.5, 128.0, 127.9, 127.0, 126.1, 70.5, 70.5, 70.3, 69.7, 68.3, 66.4, 63.8, 53.6, 44.5, 18.5, 15.0, 14.0; GPC M_n = 5262, DPi = 1.66, Tg onset 103 °C.

General Procedure for Transfer Hydrogenation of Ketones. Ligand (1 mol % or level indicated in relevant table) and (*p*-cymene)ruthenium(II) dichloride dimer (0.0077 g, 0.125 mmol) were dissolved in dry IPA (5 mL). The reaction mixture was then heated at 80 °C for 60 min. At this stage, a cosolvent (10 mL) was used to help solubilization of the polymer ligand. The reaction mixture was then transferred via cannula to a solution of acetophenone (0.6 g, 5 mmol) dissolved in IPA (45 mL). KOH/IPA (0.1 M, 1.25 mL) was then added to the reaction mixture and allowed to stir for 3 h or overnight in the case of the polymer ligands. The reaction mixture was passed through a thin plug of silica before removal of the solvent in vacuo to furnish the crude product as a brown oil. The crude product was purified using column chromatography using a solvent gradient of EtOAc in hexane to give the pure product. Enantiomeric excesses were determined by chiral GC or HPLC against racemic standards prepared by reduction with $NaBH_4$. Absolute configurations were confirmed by comparison of the GC or HPLC data with that previously reported for each compound. It should be noted that the mol % of ligand was, in each case, calculated by inspection of the relevant ^1H NMR spectrum for the polymer used. The integral of the peaks characteristic of the ephedrine unit (e.g., methines adjacent to OH or N) compared to that of the methyl groups on the polymer backbone provides a useful quantitative measurement process. The relative number of moles of ephedrine per gram of polymer, and hence the loading, is relatively easy to calculate using this method.

(*S*)-1-Phenylethanol:[10a] 79% ee (*S*) by HPLC (Chiracel OD, ethanol/hexane = 5:95 (1 mL/min), *S* isomer 9.0 min, *R* isomer 7.9 min; 46% yield; ^1H NMR (300 MHz, $CDCl_3$) 7.37−7.25 (m, 5H), 4.86 (q, 1H, J = 6.4 Hz), 1.92 (br s, 1H), 1.48 (d, 3H, J = 6.4 Hz).

(*S*)-1-(2′-Naphthyl)ethanol:[10a] 77% ee (*S*) by HPLC (Chiracel OD, ethanol/hexane = 5:95 (1 mL/min), *S* isomer 13.5 min, *R* isomer 15.2 min; 81% yield; ^1H NMR (300 MHz, $CDCl_3$) 7.86−7.81 (m, 4H), 7.53−7.42 (m, 3H), 5.07 (dq, 1H J = 3.20, 6.39 Hz), 1.94 (d, 1H, J = 3.20 Hz), 1.59 (d, 3H, J = 6.68 Hz).

(*S*)-1-(1′-Naphthyl)ethanol:[10a] 51% ee (*S*) by HPLC (Chiracel OD, ethanol:hexane = 5:95 (1 mL/min), *S* isomer 14.1 min, *R* isomer 21.9 min; 100% yield; ^1H NMR (300 MHz, $CDCl_3$) 8.16−8.09 (m, 1H), 7.91−7.84 (m, 1H), 7.80−7.77 (d, 1H, J = 8.14 Hz), 7.70−7.67 (d, 1H, J = 7.3 Hz), 7.56−7.45 (m, 3H), 5.68 (q, 1H, J = 6.4 Hz), 1.91 (br s, 1H), 1.68 (d, 3H, J = 6.4 Hz).

(*S*)-1-Phenylpropanol:[10a] 74% ee (*S*) by HPLC (Chiracel OD, ethanol/hexane = 5:95 (1 mL/min), *S* isomer 9.3 min, *R* isomer 8.2 min; 91% yield; ^1H NMR (300 MHz, $CDCl_3$) 7.36−7.23 (m, 5H), 4.60 (t, 1H, J = 6.6 Hz), 1.91−1.69 (m, 2H), 1.88 (br s, 1H), 0.92 (t, 3H, J = 7.5 Hz).

(*S*)-1-Tetralol:[10a] 87% ee (*S*) by HPLC (Chiracel OD, ethanol/hexane = 3:97 (1 mL/min), *S* isomer 8.9 min, *R* isomer 9.6 min; 57% yield; ^1H NMR(300 MHz, $CDCl_3$) 7.46−7.41 (m, 1H), 7.23−7.17 (m, 2H), 7.12−7.09 (m, 1H), 4.79 (br s, 1H), 2.87−2.69 (m, 2H), 1.99−1.60 (m, 5H).

(*S*)-1-(4-Nitrophenyl)ethanol:[22] 60% ee (*S*) by GC (oven 170 °C), (*R*) isomer 18.06 min, (*S*) isomer 18.75 min; 78% yield; ^1H (400 MHz, $CDCl_3$) 8.20 (dd, 2H, J = 9, 2 Hz), 7.55 (dd, 2H, J = 9, 2 Hz), 5.03 (quartet, 1H, J = 7 Hz), 2.02 (brs, 1H), 1.53 (dd, 3H, J = 7, 2 Hz).

4-((*S*)-1-Hydroxyethyl)benzonitrile:[11b] 61% ee (*S*) by GC (oven 160 °C) (*R*) isomer 16.70 min, (*S*) isomer 17.64 min; 76% yield; ^1H (400 MHz, $CDCl_3$) 7.64 (d, 2H, J = 9 Hz), 7.49 (d, 2H, J = 9 Hz), 4.96 (quartet, 1H, J = 6 Hz), 1.94 (brm, 1H), 1.50 (dd, 3H, J = 6, 2 Hz).

(*S*)-1-(2-Chlorophenyl)ethanol:[23] 68% ee (*S*) by GC (oven 140 °C) (*R*) isomer 8.71 min, (*S*) isomer 9.74 min; 99% yield; ^1H (400 MHz, $CDCl_3$) 7.59 (dd, 1H, J = 8, 2 Hz), 7.32−7.28 (m, 2H), 7.22 (dd, 1H, J = 8, 2 Hz), 5.29 (dq, 1H, J = 6.5, 3.8 Hz), 1.99 (d, 1H, J = 3.8 Hz), 1.49 (d, 3H, J = 6.5 Hz).

(*S*)-1-(4-Fluorophenyl)ethanol:[22] 39% ee (*S*) by GC (oven 115 °C) (*R*) isomer 9.26 min, (*S*) isomer 9.93 min; 91% yield; ^1H (400 MHz, $CDCl_3$) 7.36−7.32 (m, 2H), 7.03 (dt, 2H, J = 8.8, 2.0 Hz), 4.89 (dq, 1H, J = 6.5, 3.0 Hz), 1.83 (t, 1H, J = 3.0 Hz), 1.49 (d, 3H, J = 6.5 Hz)

(*S*)-2-Methyl-1-phenylpropan-1-ol:[10a] 33% ee (*S*) by GC (oven 115 °C) (*R*) isomer 18.77 min, (*S*) isomer 19.35 min; 72% yield; ^1H (400 MHz, $CDCl_3$) 7.36−7.25 (m, 5H), 4.37 (dd, 1H, J = 6.8, 3.0 Hz), 1.96 (heptet, 1H, J = 6.8 Hz), 1.80 (d, 1H, J = 3.0 Hz), 1.00 (d, 3H, J = 6.8 Hz), 0.80 (d, 3H, J = 6.8 Hz).

(*S*)-1-(4-Chlorophenyl)ethanol:[10j,23] 63% ee (*S*) by GC (oven 140 °C) (*R*) isomer 10.56 min, (*S*) isomer 11.06 min; 84% yield; ^1H (400 MHz, $CDCl_3$) 7.35−7.25 (m, 4H), 4.89 (dq, 1H, J = 6.3, 2.8 Hz), 1.79 (t, 1H, J = 2.8 Hz), 1.48 (d, 3H, J = 6.3 Hz).

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Supporting Information Available: ^1H NMR spectra of all polymer-supported reagents and ^1H and ^{13}C NMR of all new compounds lacking elemental analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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