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Polymer supported *trans*-1-phenylsulfonylamino-2-isoborneolsulfonylaminocyclohexane ligand for the titanium catalyzed organozinc addition to ketones

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Dedicated to Professor José Antonio Abad on occasion of his retirement

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Abstract—The catalytic enantioselective addition of different organozinc reagents, such as diethylzinc, or in situ generated phenylzinc derivatives to simple ketones was accomplished using titanium tetraisopropoxide and supported chiral ligands derived from *trans*-1-phenylsulfonylamino-2-isoborneolsulfonylamidocyclohexane, to give the corresponding tertiary alcohols with enantioselectivities up to >99%. A simple and efficient procedure for the synthesis of the disulfonamide monomeric ligand and the corresponding polymerization is described.

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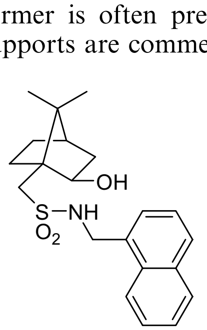
1. Introduction

Nowadays, the catalytic enantioselective generation of compounds with stereogenic tertiary carbon atoms can be easily achieved in most cases.[1] However, the related approach to compounds bearing quaternary stereocenters is still an enormous challenge for synthetic organic chemistry. Thus, every novel enantioselective procedure for the construction of a fully substituted carbon center is of great value,[2] the simplest approach for the preparation of chiral tertiary alcohols being the enantioselective 1,2-addition of organometallic reagents[3] to ketones.[4]

Recently, we have introduced isoborneolsulfonamide[5] **1** as the first chiral ligand[6] able to promote the catalytic enantioselective addition of dialkylzinc reagents to simple ketones[7] in the presence of titanium tetraisopropoxide,[8] other bisisoborneolsulfonamides improve the previous results.[9] Among all ligands tested, *trans*-1-arylsulfonylamino-2-(isobornylsulfonylamino)cyclohexane derivatives **2** gave the best results,[10] not only for the alkylation but also for the arylation process.[11] Although isoborneolsulfonamide ligands can be isolated from the crude reaction by flash chromatography, its recovery still remains difficult. In order to facilitate the separation of homogeneous ligands or catalysts from the reaction mixture, they are usually immobilized on solid supports.[12] There are two main methods to immobilize a chiral ligand on a support: (a) grafting of the desired ligand onto a preformed support containing reactive groups and (b) co-polymerization of a suitable functionalized ligand with polymerizable monomers and cross-linkers. While the latter offers many possibilities for generating and controlling a specific environment around the ligand within the polymer matrix (needing more synthetic efforts), the former is often preferred since many suitable polymeric supports are commercially available.



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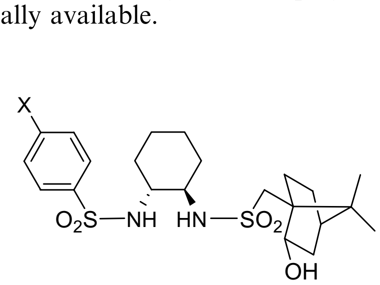

2a: X = Me
2b: X = MeO

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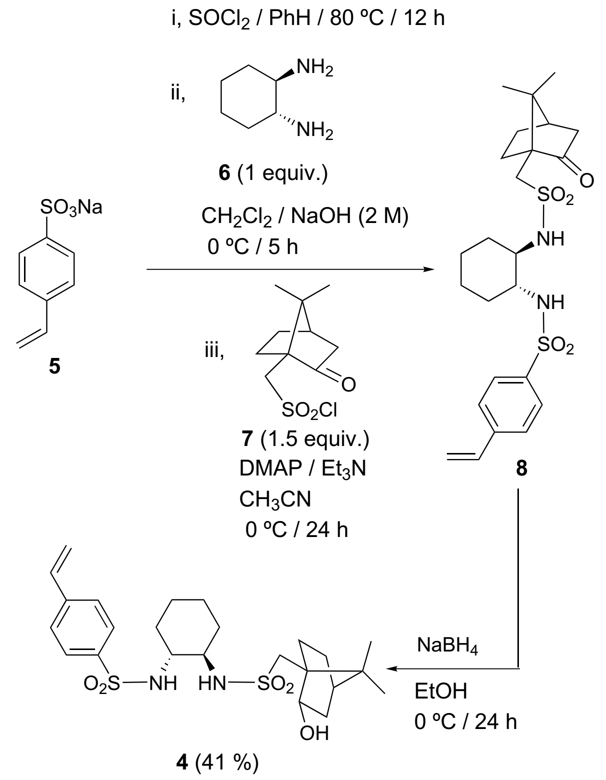
Herein, we report for the first time the preparation and use of heterogeneous chiral ligands of different polymers **3** supporting *trans*-1-(phenylsulfanylamino)-2-(isobornylsulfonylamino)cyclohexane moieties. We have chosen a styrene co-polymerization strategy to immobilize our chiral ligand, since this strategy has been used fruitfully in the heterogenization of typical chiral ligands, among other, BINOL,[13] NOBIN,[14] TADDOL,[15] bis(oxazolines),[16] salens,[17] 1,2-diamines,[18] 1,2-disulfonamides,[19] and 1,2-hydr-oxysulfonamides.[20]

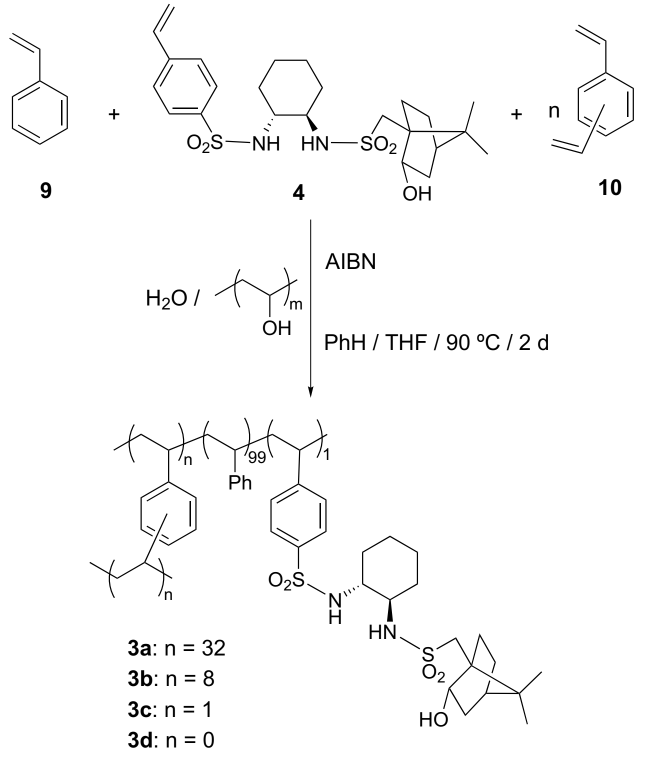
2. Results and discussion

In order to follow this strategy, the styryl derivative **4** had to be prepared (Scheme 1). Thus, the reaction of commercially available sodium 4-vinylbenzenesulfonate **5** with thionyl chloride under standard conditions[21] gave the expected sulfonyl chloride derivative, which was trapped by reaction with (1*R*,2*R*)-*trans*-1,2-diaminocyclohexane **6** under classical biphasic conditions for amino acid protection.[22] The final standard coupling reaction[23] of the in situ prepared amine with (1*S*)-(+)-10-camphorsulfonyl chloride **7** yielded the corresponding ketone **8**, which was diastereoselectively reduced to monomer **4** with good chemical yields and diastereoselectivities (de >80%). Monomer **4** could be easily isolated in its pure form (>99%) by column chromatography with a moderate overall yield.



Scheme 1.

Once monomer **4** was obtained, the following step was the co-polymerization with styrene **9** and divinylbenzene **10**, using a typical radical polymerization protocol in a suspension of polyvinyl alcohol (average molecular weights 85,000–146,000).[24] In this way, we prepared four different polymers changing only the amount of the cross-linker and therefore their swelling properties (Scheme 2). All polymers could be easily isolated from the reaction media just by filtration and were purified by successive washes with methanol and hexane. The chemical yield was practically quantitative and microanalysis showed the total incorporation of monomer **4** to the formed polymer.[25]

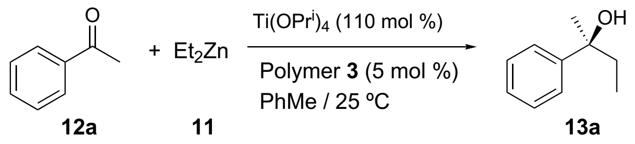


Scheme 2.

Polymeric ligands **3** were tested first in the enantioselective addition of commercially available diethylzinc **11** to acetophenone **12a** in the presence of $Ti(OPr^i)_4$. The reaction gave the expected tertiary alcohol **13a** at room temperature. Although the reaction rate was very slow, the enantioselectivity was excellent in all cases tested, minor (*R*)-enantiomer could not be detected by chiral column GC-analysis (Table 1, entries 1–4), independent of the polymer used.

The reuse of polymer **3c** was studied by filtering and washing it with dry toluene under an argon atmosphere. We found that after three uses, its activity decreased to nil (compare entries 2, 5, and 6 in Table 1). In order to accelerate the reaction, we focused on the possibility of using some faster alkoxide scavenger,[26] and for that purpose, the reaction was performed in the presence of an excess amount of Et_3B (Table 1, entry 7). Although the reaction under these new conditions took place in only 9 days, it is still far from the reaction times using the homogenous ligands **2**.[10]

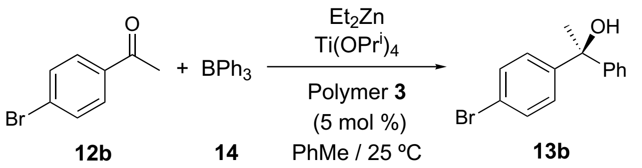
Table 1.



Entry	Polymer	Time (d)	Yield[a] (%)	ee[b] (%)
1	**3a**	17	16	>99
2	**3b**	17	23 (17)[c]	>99 (>99)[c]
3	**3c**	17	56	>99
4	**3d**	17	36	>99
5	**3c**	17[d]	17	>99
6	**3c**	17[e]	<5	—
7	**3c**	9[f]	36	>99

[a] Isolated yields after bulb-to-bulb distillation.
[b] Determined by GLC using a β-CD column.
[c] In parentheses are results obtained without stirring.
[d] Reaction performed after one use of polymer.
[e] Reaction performed after two uses of polymer.
[f] Reaction performed in the presence of 1.6 equiv of Et_3B.

Table 2.



Entry	Polymer	Time (d)	Yield[a] (%)	ee[b] (%)
1	**3a**	6	47	71 (+)
2	**3b**	6	70	73 (+)
3	**3c**	6	70	83 (+)
4	**3d**	0.75	83	86 (+)
5	**3c**[c]	6	55	82 (+)
6	**3c**[d]	6	<5	—

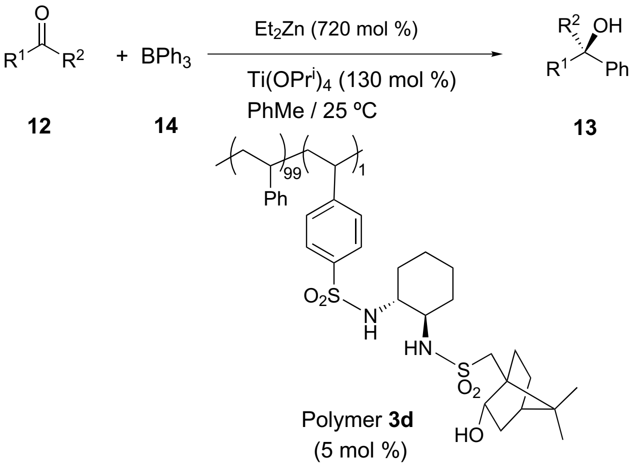
[a] Isolated yields after column chromatography.
[b] Determined by HPLC using a Chiralcel-ODH column; the sign of the predominant enantiomer is indicated in parentheses.
[c] Reaction performed after one use of polymer.
[d] Reaction performed after two uses of polymer.

After this partial success found for the enantioselective ethylation of acetophenone, we turned our attention to the zinc reagent reactivity. The idea was to improve the reactivity of the zinc reagent in order to diminish the reaction time. Recently, the preparation of ethyl phenyl zinc reagent by transmetalation of diethylzinc with triphenylboron has been described.[27] This intermediate showed a higher reactivity and enantioselectivity compared with the related diethyl or diphenylzinc reagents.[28] The corresponding ethyl phenyl zinc intermediate was obtained starting from commercially available triphenyl boron **14** and diethylzinc **11** by heating in toluene at 70 °C. This intermediate was reacted in situ with *para*-bromoacetophenone **12b** in the presence of substoichiometric amounts of polymeric ligands **3** and a small excess of titanium tetraisopropoxide to give the expected diaryl ethanol derivative **13b** with good enantioselectivities (Table 2).

In the reaction shown in Table 2, we observed a different behavior, depending on the solubility of polymeric ligand. Thus, a decrease of the amount of the cross-linker improved the chemical yield and enantioselectivity, with the best results being obtained with the soluble polymer **3d** in only 18 h (entry 4). As in the previous case, the possible reuse of ligand **3c** was studied, we found a similar behavior as in the case of using diethylzinc (compare entries 3, 5, and 6).

Finally, we studied the catalytic enantioselective phenylation of different ketones using the soluble polymer **3d** (Table 3).[29] The reaction gave good enantioselectivities for methyl aryl ketones, practically independently of the electronic character of the aryl substituents (entries 1–6). These results are in the range of those obtained using ligands **2**,[10] not only concerning the enantioselectivity or yield, but also the reaction times. Increasing the size of the substituents of ketone **12** (i.e., from methyl to ethyl) led to longer reaction times with slightly worse enantioselectivities (entry 7). The reaction with 2-hexanone gave a modest 38% ee (entry 8).

Table 3.



Entry	R^1	R^2	Time (d)	No	Yield[a] (%)	ee[b] (%)
1	4-BrC_6H_4	Me	0.75	**13b**	83	86 (+)
2	4-FC_6H_4	Me	0.75	**13c**	98	87 (+)
3	4-ClC_6H_4	Me	0.75	**13d**	99	88 (+)
4	$4\text{-F}_3CC_6H_4$	Me	0.5	**13e**	86	90 (+)
5	3-MeC_6H_4	Me	0.75	**13f**	98	88 (−)
6	4-MeC_6H_4	Me	1	**13g**	80	84 (−)
7	4-BrC_6H_4	Et	6	**13h**	54	71 (+)
8	Bu^n	Me	2	**13i**	98	38 (*R*)
9	$4\text{-F}_3CC_6H_4$	Me	0.75[c]	**13e**	97	80 (+)
10	$4\text{-F}_3CC_6H_4$	Me	3[d]	**13e**	87	71 (+)
11	$4\text{-F}_3CC_6H_4$	Me	5[e]	**13e**	<5	—
12	4-MeC_6H_4	Me	1.5[c]	**13g**	74	80 (−)
13	4-MeC_6H_4	Me	3[d]	**13g**	84	42 (−)
14	4-MeC_6H_4	Me	5[e]	**13g**	<5	—

[a] Isolated yields after column chromatography.
[b] Determined by HPLC using Chiralcel columns; the absolute configuration or the sign of the predominant enantiomer is indicated in parentheses.
[c] Reaction performed after one use of polymer.
[d] Reaction performed after two uses of polymer.
[e] Reaction performed after three uses of polymer.

The last part of this study was focused on the possible recovery and reuse of the soluble polymer **3d**. In this case, the crude reaction mixture, obtained after typical aqueous work-up, extraction and solvent elimination, was treated with methanol and filtered in order to isolate polymer **3d** as an amorphous solid, from the methanolic phase containing the tertiary alcohol. The yield of recovered polymer **3d** was in the range of 75–90%. Unfortunately, the activity of the polymer decreased rapidly after a few reuses (compare entries 4 and 9–11, as well as 6 and 12–14). The reason for this decrease is still unclear since transmission electron microscopy experiments of twofold recovered polymer **3d** did not show the expected presence of titanium occluded in the polymer.[30]

3. Conclusion

In conclusion, we have described an easy and simple synthesis of polymers bearing chiral *trans*-1-phenylsulfonylamino-2-isoborneolsulfonylaminocyclo-hexane moiety. These ligands have been shown to be good promoters for the heterogeneous and homogenous catalytic enantioselective alkylation and arylation of ketones. Work is currently in progress in order to anchor the above chiral moiety to other polymeric materials, improving the possible recovery and reuse.

Acknowledgements

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References

1. (a) *Stereoselective Synthesis (Houben-Weyl)*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1996; Vols. 1–10; (b) *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vols. 1–3.
2. (a) Fuji, K. *Chem. Rev.* **1993**, *93*, 2037–2066; (b) Corey, E. J.; Guzmán-Pérez, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 388–401; (c) Ramón, D. J.; Yus, M. *Curr. Org. Chem.* **2004**, *8*, 149–183; (d) *Quaternary Stereocenters—Challenges and Solutions for Organic Synthesis*; Christoffers, J., Baro, A., Eds.; Wiley-VCH: Weinheim, 2005.
3. Yus, M.; Ramón, D. J. *Recent Res. Dev. Org. Chem.* **2002**, *6*, 297–378.
4. Ramón, D. J.; Yus, M. In Ref. 2d, pp 207–241.
5. (a) Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **1997**, *8*, 2479–2496; For a review, see: (b) Yus, M.; Ramón, D. J. *Pure Appl. Chem.* **2005**, *77*, 2111–2119.
6. (a) Ramón, D. J.; Yus, M. *Tetrahedron Lett.* **1998**, *39*, 1239–1242; (b) Ramón, D. J.; Yus, M. *Tetrahedron* **1998**, *54*, 5651–5666.
7. For an overview, see: Ramón, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2004**, *116*, 286–289.
8. For reviews on enantioselective reactions promoted by titanium derivatives, see: (a) Ramón, D. J.; Yus, M. *Recent Res. Devel. Org. Chem.* **1998**, *2*, 489–523; (b) Ramón, D. J.; Yus, M. *Chem. Rev.* **2006**, *106*, 2126–2208.
9. For recent results from our group, see: (a) Yus, M.; Ramón, D. J.; Prieto, O. *Tetrahedron: Asymmetry* **2002**, *13*, 2291–2293; (b) Yus, M.; Ramón, D. J.; Prieto, O. *Tetrahedron: Asymmetry* **2003**, *14*, 1103–1114; (c) Prieto, O.; Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2003**, *14*, 1955–1957; (d) Yus, M.; Ramón, D. J.; Prieto, O. *Eur. J. Org. Chem.* **2003**, 2745–2748.
10. (a) Forrat, V. J.; Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2005**, *16*, 3341–3344; (b) Forrat, V. J.; Prieto, O.; Ramón, D. J.; Yus, M. *Chem. Eur. J.* **2006**, *12*, 4431–4445.
11. For reviews on asymmetric arylation processes, see: (a) Bolm, C.; Hildebrand, J. P.; Muñiz, K.; Hermanns, N. *Angew. Chem., Int. Ed.* **2001**, *40*, 3284–3308; (b) Schmidt, F.; Stemmler, R. T.; Rudolph, J.; Bolm, C. *Chem. Soc. Rev.* **2006**, *35*, 454–470.
12. For reviews, see: (a) Gladysz, J. A. *Chem. Rev.* **2002**, *102*, 3215–3216, thematic issue on recoverable catalysts and reagents; (b) Corma, A.; García, H. *Chem. Rev.* **2003**, *103*, 4307–4365; (c) Dai, L.-X. *Angew. Chem., Int. Ed.* **2004**, *43*, 5726–5729; (d) Itsuno, S.; Haraguchi, N.; Arakawa, Y. *Recent Res. Devel. Org. Chem.* **2005**, *9*, 27–47.
13. See for instance: (a) Sellner, H.; Faber, C.; Rheiner, P. B.; Seebach, D. *Chem. Eur. J.* **2000**, *6*, 3692–3705; (b) Sasai, H.; Jayaprakash, D. *Tetrahedron Lett.* **2001**, *12*, 2589–2595; (c) Herres, S.; Hesemann, P.; Moreau, J. J. E. *Eur. J. Org. Chem.* **2003**, 99–105; (d) Hesemann, P.; Moreau, J. J. E. *C. R. Chim.* **2003**, *6*, 199–207; (e) Sekiguti, T.; Iizuka, Y.; Takizawa, S.; Jayaprakash, D.; Arai, T.; Sasai, H. *Org. Lett.* **2003**, *5*, 2647–2650.
14. Mandoli, A.; Pini, D.; Orlandi, S.; Mazzini, F.; Salvadori, P. *Tetrahedron: Asymmetry* **1998**, *9*, 1479–1482.
15. See for instance: (a) Seebach, D.; Marti, R. E.; Hintermann, T. *Helv. Chim. Acta* **1996**, *79*, 1710–1740; (b) Rheiner, P. B.; Sellner, H.; Seebach, D. *Helv. Chim. Acta* **1997**, *80*, 2027–2032; (c) Sellner, H.; Seebach, D. *Angew. Chem., Int. Ed.* **1999**, *38*, 1918–1920; (d) Altava, B.; Burguete, I.; Fraile, J. M.; García, J. I.; Luis, S. V.; Mayoral, J. A.; Vicent, M. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 1503–1506; (e) Degni, S.; Wilén, C.-E.; Leino, R. *Org. Lett.* **2001**, *3*, 2551–2554; (f) Sellner, H.; Rheiner, P. B.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 352–387.
16. (a) Diéz-Barra, E.; Fraile, J. M.; García, J. I.; García-Verdugo, E.; Herrerías, C. I.; Luis, S. V.; Mayoral, J. A.; Sánchez-Verdú, P.; Tolosa, J. *Tetrahedron: Asymmetry* **2003**, *14*, 773–778; (b) Mandoli, A.; Orlandi, S.; Pini, D.; Salvadori, P. *Tetrahedron: Asymmetry* **2004**, *15*, 3233–3244.
17. See for instance: (a) Canali, L.; Sherrington, D. C.; Deleuze, H. *React. Funct. Polym.* **1999**, *40*, 155–168; (b) Heckel, A.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 913–926; (c) Sellner, H.; Hametner, K.; Günther, D.; Seebach, D. *J. Catal.* **2003**, *215*, 87–93.
18. Itsuno, S.; Tsuji, A.; Takahashi, M. *J. Polym. Sci. Part A: Polym. Chem.* **2004**, *42*, 4556–4562.
19. Halm, C.; Kurth, M. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 510–512.
20. See for instance: (a) Itsuno, S.; Watanabe, K.; Ito, K.; El-Shehawy, A. A.; Sarhan, A. A. *Angew. Chem., Int. Ed.* **1997**, *36*, 109–110; (b) El-Shehawy, A. A.; Abdelaal, M. Y.; Watanabe, K.; Ito, K.; Itsuno, S. *Tetrahedron: Asymmetry* **1997**, *8*, 1731–1734; (c) Itsuno, S.; El-Shehawy, A. A.; Sarhan, A. A. *React. Funct. Polym.* **1998**, *37*, 283–287; (d) Itsuno, S.; Watanabe, K.; Watanabe, K.; Matsumoto, T.; Kuroda, S.; Yokoi, A.; El-Shehawy, A. A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2011–2016; (e) Itsuno, S.; Watanabe, K.; El-Shehawy, A. A. *Adv. Synth. Catal.* **2001**, *343*, 89–94.

21. Yus, M.; Ramón, D. J.; Prieto, O. *Tetrahedron: Asymmetry* **2002**, *13*, 1573–1579.
22. See for instance: (a) Fischer, E.; Lifschitz, W. *Chem. Ber.* **1915**, *48*, 360–378; (b) McChesney, E. W.; Swann, W. K. *J. Am. Chem. Soc.* **1937**, *59*, 116–118; (c) Baganz, H.; Baganz, H. *Arch. Pharm.* **1957**, *290*, 567–571; (d) Greene, T. W.; Wuts, P. G. M. In *Protective Groups in Organic Synthesis*, 3rd ed.; John Wiley and Sons: New York, 1999; pp 603–607.
23. Prieto, O.; Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2000**, *11*, 1629–1644.
24. (a) Gómez, C.; Ruiz, S.; Yus, M. *Tetrahedron Lett.* **1998**, *39*, 1397–1400; (b) Gómez, C.; Ruiz, S.; Yus, M. *Tetrahedron* **1999**, *55*, 7017–7026; (c) Yus, M.; Gómez, C.; Candela, P. *Tetrahedron Lett.* **2001**, *42*, 3977–3979; (d) Alonso, F.; Candela, P.; Gómez, C.; Yus, M. *Adv. Synth. Catal.* **2003**, *345*, 275–279; (e) Candela, P.; Gómez, C.; Yus, M. *Russ. J. Org. Chem.* **2004**, *40*, 795–801.
25. General procedure for the synthesis of polymers **3**: To a solution of sodium 4-vinylbenzenesulfonate **5** (2.47 g, 12 mmol) in benzene (80 mmol) were added $SOCl_2$ (5.2 mL, 72 mmol) and a few drops of DMF. The resulting solution was refluxed for 12 h and all the volatiles were removed under reduced pressure (0.1 Torr) to yield the corresponding sulfonyl chloride derivative. This compound was soluble in CH_2Cl_2 (32 mL) and this solution was slowly added (20 min) to a mixture of (1*R*,2*R*)-1,2-diaminocyclohexane **6** (1.37 g, 12 mmol) in CH_2Cl_2 and aqueous NaOH solution (2 M, 16 mL) at 0 °C. After 4 h, allowing the temperature to rise to 25 °C, the mixture was treated with HCl (2 M, 3 × 60 mL). The resulting acidic aqueous phase was basified with NaOH (6 M) and extracted with CH_2Cl_2 (3 × 60 mL). The organic layers were dried over Na_2SO_4, filtered, and the solvents were removed under reduced pressure (15 Torr). The resulting crude product was dissolved in CH_3CN (50 mL) at 0 °C, and to this new solution were added subsequently Et_3N (7.6 mL, 54 mmol), 4-dimethylaminopyridine (0.73 g, 6 mmol) and (1*S*)-(+)-10-camphorsulfonyl chloride **7** (4.52 g, 18 mmol). The resulting mixture was stirred for 24 h allowing the temperature to rise to 25 °C. The reaction was quenched by the addition of NaOH (3 M, 30 mL) and extracted with ethyl acetate (4 × 30 mL). The resulting organic layer was dried over Na_2SO_4, filtered, and the solvents were removed under reduced pressure (15 Torr). The resulting crude product **8** was dissolved in ethanol (50 mL) at 0 °C and treated with $NaBH_4$ (1.82 g, 4.8 mmol). After 24 h, allowing the temperature to rise to 25 °C, ethanol was removed under reduced pressure (15 Torr) and the residue was treated with HCl (2 M, 25 mL) and extracted with ethyl acetate (4 × 30 mL). The resulting organic layer was dried over Na_2SO_4, filtered, and the solvents were removed under reduced pressure (15 Torr). The residue was purified by column chromatography using silica gel and mixtures of hexane/ethyl acetate with decreasing ratios, yielding the monomer **4**. This monomer **4** (0.496 g, 1 mmol) was dissolved in benzene (12 mL) and THF (4 mL) at 25 °C under an argon atmosphere. To this solution was successively added styrene **9** (11.35 mL, 99 mmol), AIBN (0.128 g, 0.78 mmol), divinylbenzene (for amounts see Scheme 2). This solution was slowly added over an aqueous solution at 0 °C, obtained in turn by heating polyvinyl alcohol (0.2 g) in water (50 mL) at 40 °C for 30 min and final filtration. The resulting mixture was heated at 90 °C for 2 days. Polymers **3** were obtained just after filtration, washing with portions of water, methanol and hexane, and final drying over reduced pressure (0.1 Torr) during 24 h {**3d**: $[\alpha]_D^{25} = +1.9$ (*c* 1.4, PhMe)}.
26. For recent uses of boron compounds as alkoxide scavengers, see: (a) Yu, C.-M.; Kim, J.-M.; Shin, M.-S.; Cho, D. *Tetrahedron Lett.* **2003**, *44*, 5487–5490; (b) Xia, G.; Shibatomi, K.; Yamamoto, H. *Synlett* **2004**, 2437–2439.
27. For examples on the enantioselective phenylation of aldehydes after boron/zinc transmetalation, see: (a) Rudolph, J.; Schmidt, F.; Bolm, C. *Adv. Synth. Catal.* **2004**, *346*, 867–872; (b) Rudolph, J.; Hermanns, N.; Bolm, C. *J. Org. Chem.* **2004**, *69*, 3997–4000; (c) Bolm, C.; Zani, L.; Rudolph, J.; Schiffers, I. *Synthesis* **2004**, 2173–2180; (d) Bolm, C.; Schmidt, F.; Zani, L. *Tetrahedron: Asymmetry* **2005**, *16*, 1367–1376; (e) Özçubukçu, S.; Schmidt, F.; Bolm, C. *Org. Lett.* **2005**, *7*, 1407–1409; (f) Rudolph, R.; Lormann, M.; Bolm, C.; Dahmen, S. *Adv. Synth. Catal.* **2005**, *347*, 1361–1368; (g) Dahmen, S.; Lormann, M. *Org. Lett.* **2005**, *7*, 4597–4600.
28. (a) Rudolph, J.; Rasmussen, T.; Bolm, C.; Norrby, P.-O. *Angew. Chem. Int. Ed.* **2003**, *42*, 3002–3005; (b) Fontes, M.; Verdaguer, X.; Solà, L.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **2004**, *69*, 2532–2543; (c) Rudolph, J.; Bolm, C.; Norrby, P.-O. *J. Am. Chem. Soc.* **2005**, *127*, 1548–1552.
29. General procedure for the enantioselective phenylation of ketones: A solution of Et_2Zn (1.1 M in toluene, 6.5 mL, 7.2 mmol) was slowly added to a pressure tube charged with triphenylborane **14** (0.39 g, 1.6 mmol) at 0 °C under an argon atmosphere. The resulting solution was warmed to 70 °C for 16 h. Then, the mixture was cooled to 0 °C and transferred to a Schlenk tube. To this mixture were added the corresponding polymer **3** (0.5 g, 0.05 equiv of isobornyl structure), $Ti(OPr^i)_4$ (0.39 mL, 1.3 mmol) and ketone **12** (1 mmol). The reaction mixture was stirred at 25 °C (see Table 3) and quenched by successive addition of methanol (1 mL) and a saturated solution of NH_4Cl (15 mL). The mixture was filtered through Celite and the resulting mixture was extracted with ethyl acetate (3 × 10 mL). The resulting organic layer was dried over Na_2SO_4, filtered, and the solvent removed under reduced pressure (15 Torr). The residue was purified by column chromatography using silica gel and mixtures of hexane/ethyl acetate with decreasing ratios, to yield the corresponding alcohol **13**.
30. We thank a referee for calling our attention to this possibility.