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Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 17 (2006) 1895–1900

Asymmetric borane reduction of prochiral ketones using imidazolium-tagged sulfonamide catalyst

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Received 9 June 2006; accepted 3 July 2006

Abstract—A novel sulfonamide catalyst based on a room temperature ionic liquid (RTIL) has been developed for the enantioselective reduction of ketones in refluxing toluene. The optically active secondary alcohol products were obtained in good enantiomeric excess and excellent yields. The imidazolium-tagged sulfonamide catalyst can be readily recovered and reused four times without any significant loss of catalytic activity.

1. Introduction

The enantioselective reduction of prochiral ketones to the corresponding optically active secondary alcohols plays an important role in asymmetric synthesis.[1] One of the most popular methods using chiral 1,3,2-oxazaborolidines as catalysts was developed by Itsuno et al. and further improved by Corey et al.[2,3] Numerous examples describing the application of this homogeneous catalyst have been reported,[4] but the development of efficient methods of recovering the catalyst is still a challenging target. Over the past 20 years, several groups have reported the preparation and application of heterogeneous catalysts for the enantioselective reduction of ketones.[5] However, only a few of the reducing agents displayed high reactivity and enantioselectivity owing to the diffusion limitations caused by the polymer matrix.[5j,k]

To integrate the advantages of homogeneous and heterogeneous catalysis into one process, a conceptual solution involves the use of 'separation tags', which are chosen such that they dominate over tagged molecules in a complementary separation technique. Ionic liquids, especially task-specific ionic liquids (TSIL), have recently received growing attention and have been introduced as ligands in recoverable catalysts in a series of chemical transformations due to their tunable features for various chemical tasks and their advantages as reusable homogeneous supports,[6,7] such as olefin metathesis,[8] hydrogenation,[9] cyanosilylation of aldehydes,[10] hydroformylation,[11] Negishi cross-coupling reaction,[12] Heck reaction,[13] Suzuki and Stille coupling reactions,[14] Morita–Baylis–Hillman reaction,[15] Friedel–Crafts alkylations or Beckman rearrangements, etc.[16]

Herein, we report the synthesis of an alkyl imidazolium salt-tagged chiral sulfonamide **IL-1** and its application and recycling in the enantioselective reduction of prochiral ketones to optically active secondary alcohols. To compare the sulfonamide **S-1**, catalyst **IL-1** gave the better enantioselectivity (Fig. 1).

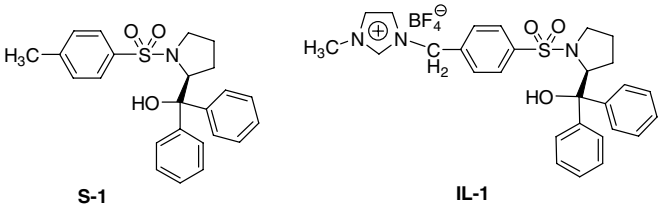

Figure 1.

2. Results and discussion

The route for the synthesis of **IL-1** is illustrated in Scheme 1. In the first step, sulfonylation of the diphenylprolinol

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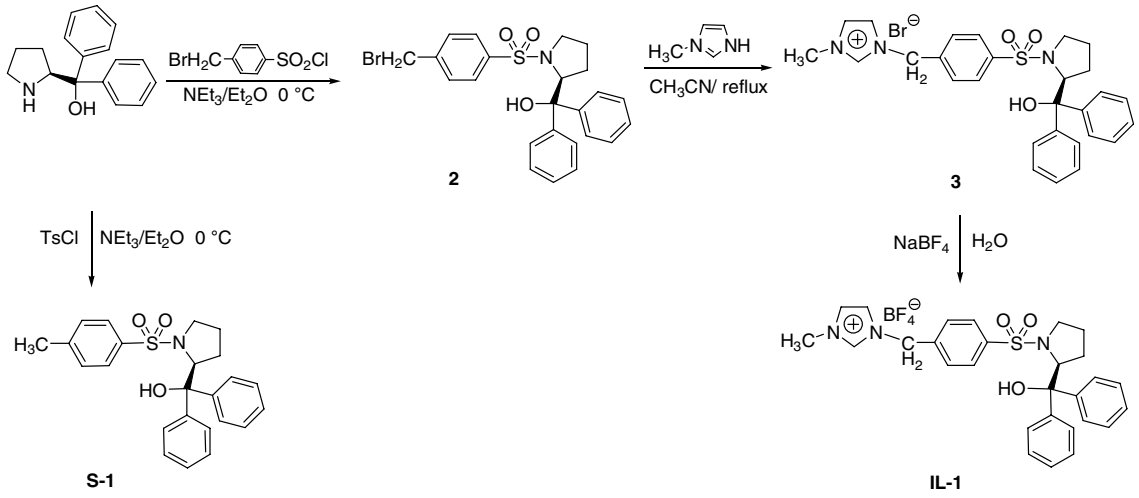
doi:10.1016/j.tetasy.2006.07.003



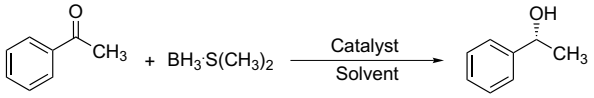
Scheme 1. Synthesis of IL-tagged sulfonamide **IL-1** and sulfonamide **S-1**.

amino group with 4-(bromomethyl)benzene-sulfonyl chloride in the presence of Et_3N at 0 °C over 4 h afforded **2** in 86% yield. In the second step, compound **2** was grafted onto the 1-methylimidazole in refluxing acetonitrile to give **3** in 92% yield. Following anion exchange in water with $NaBF_4$, the desired tetrafluoroborate imidazolium salt **IL-1** was obtained in 98% yield, which was purified by redissolving in a mixture of THF and ethanol, then filtrated to remove the by-product of NaBr and afforded pure ionic liquid (IL)-tagged catalyst **IL-1** as an air-stable colorless and transparent liquid. According to the literature procedures,[17] the sulfonamide catalyst **S-1** was prepared directly from diphenylprolinol and 4-methylbenzene sulfonyl chloride in the presence of Et_3N at 0 °C in 92% yield as the white solid.

It is well known that the stereoselectivity of reduction is affected greatly by solvent, temperature and the amount of catalyst. To find the optimum reaction conditions, we examined the reduction of acetophenone with chiral catalyst **IL-1** under various experimental conditions and compared the catalytic activity and enantioselectivity of catalyst **S-1**. The results are summarized in Table 1.

Firstly, solvent effects were observed. At room temperature (entries 1 and 2), the reduction was completed within 10 h in toluene and 16 h in THF. When the reaction temperature was raised from room temperature to reflux, the reduction was complete in 1.5 h and the ee value was 52% in THF and 65% in toluene (entries 3 and 4), respectively. The results show that toluene is a more effective solvent for the reduction and the level of enantiomeric excess is sensitive to the reaction temperature. The best result could be achieved if the reaction mixture was at reflux.[4d,5,10] Apart from the reaction temperature and solvent, the ratio of the catalysts has an impact on the reduction. When the amount of catalyst was increased from 10 to 15 mol %, the enantiomeric excess increased from 65% to 73% (entries 4 and 5). By increasing further the amount of catalyst to 20 mol %, the ee had only slightly changed (entries 6). We also investigated the effect of catalyst **S-1** on the reduction of acetophenone, and lower enantiomeric excesses

Table 1. Effect of temperature, solvent and catalyst[a,d]



Entry	Solvent	Catalyst	Catalyst (mol %)	Temperature (°C)	Yield[b] (%)	ee[c] (%)
1	THF	**IL-1**	10	rt	94	13
2	Toluene	**IL-1**	10	rt	92	7
3	THF	**IL-1**	10	Reflux	94	52
4	Toluene	**IL-1**	10	Reflux	95	65
5	Toluene	**IL-1**	15	Reflux	95	73
6	Toluene	**IL-1**	20	Reflux	95	75
7	THF	**S-1**	10	Reflux	94	49
8	Toluene	**S-1**	10	Reflux	93	57
9	Toluene	**S-1**	15	Reflux	94	66

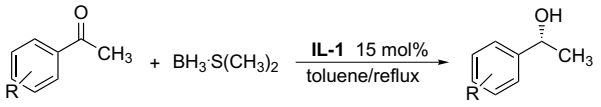
[a] Molar ratio, $PhCOCH_3/BH_3{\cdot}SMe_2$ 1.0:1.1.
[b] Isolated yield after column purification.
[c] Determined by HPLC analysis using Diacel Chiralcel OJ column (eluent: hexane/2-propanol = 9:1).
[d] The absolute configuration was determined by optical rotation.

were observed. It is noted that the ionic liquid not only aids the separation, but also increases the enantioselectivity of the catalyst (entries 4, 5, and 7–9).

Having established the best reaction conditions, the application of catalyst **IL-1** to the reduction of other prochiral ketones was investigated using a catalytic amount (15 mol %) of **IL-1** in refluxing toluene (Table 2). All reductions gave excellent yields and good enantiomeric excesses. The results demonstrate that the steric effects have a significant impact on the enantioselectivity (entries 3, 5, and 6). Comparison of the results obtained from *p*-methoxyacetophenone and *p*-nitroacetophenone indicated that electron-withdrawing groups are relatively beneficial for enantioselectivity.

We also investigated the reduction of α-haloacetophenone under the same conditions. Much higher enantiomeric excesses were observed. Similarly, the results (summarized in Table 3) showed that the enantioselectivity of the reduction was highly dependent on steric effects. The 2,4-disubstituted substrates afforded excellent ees. For example, the reduction of 2,4-dimethyl-α-bromoacetophenone and 2,4-dimethyl-α-chloroacetophenone was obtained in 95% and 96% ee, respectively.

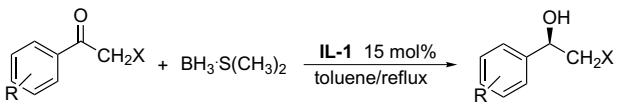
Table 2. Asymmetric reduction of prochiral ketones[a]



Entry	R	Yield[b] (%)	ee[c] (%)	Config.[d]
1	H	94	73	*R*
2	4-Cl	96	75	*R*
3	2-Cl	95	94	*R*
4	4-OCH_3	92	65	*R*
5	2-OCH_3	93	89	*R*
6	2-CH_3	94	91	*R*
7	4-F	95	75	*R*
8	β-Acetonaphthone	96	75	*R*
9	4-NO_2	94	76	*R*

[a] Experiments were performed on a 1.0 mmol scale.
[b] Yields of isolated products after purification by column chromatography.
[c] Determined by using chiral HPLC.
[d] The absolute configurations were determined by optical rotation.

Table 3. Asymmetric reduction of prochiral α-haloacetophenone[a]



Entry	R	X	Yield[b] (%)	ee[c] (%)	Config.[d]
1	H	Br	92	71	*S*
2	H	Cl	93	77	*S*
3[b]	2,4-Dimethyl	Cl	91	96	*S*
4	2,4-Dimethyl	Br	94	95	*S*
5	4-OCH_3	Cl	93	64	*S*
6	4-OCH_3	Br	94	67	*S*

[a] Experiments were performed on a 1.0 mmol scale.
[b] Yields of isolated products after purification by column chromatography.
[c] Determined by using chiral HPLC.
[d] The absolute configurations were determined by optical rotation.

Table 4. Recycling of chiral catalyst **IL-1** (reduction of acetophenone)

	Cycle			
	1	2	3	4
Ligand[a] (%)	98	99	97	98
Yield[a] (%)	96	96	95	96
ee[b] (%)	72.6	72.1	71.4	64.9

[a] Yields of isolated products.
[b] Determined by using chiral HPLC.

The obvious predominance of IL-tagged catalyst **IL-1** can be easily separated and recycled. After the reduction was complete, the reaction was quenched with water and the product isolated by extraction with diethyl ether with the catalyst **IL-1** remaining in the aqueous media. After water was removed at reduced pressure, catalyst **IL-1** was redissolved in ethyl acetate, then washed with water and dried. Ethyl acetate was removed and the catalyst **IL-1** was reused for the next cycle of reduction. Excellent conversions were obtained for four consecutive cycles with little or no loss of performance (Table 4). These results showed the importance of grafting onto an imidazolium ionic liquid pattern to the catalyst to obtain its recycling from the reaction system.

3. Conclusion

In conclusion, we have developed a new catalyst of IL-tagged sulfonamides for the enantioselective borane reduction of prochiral ketones. The catalyst can be recycled four times with minimal loss of catalytic performance.

4. Experimental

All reactions were carried out under an argon atmosphere. THF was dried over sodium and freshly distilled before use. Toluene was distilled over calcium hydride. Acetophenone was dried and distilled over calcium hydride. Other ketones were further purified by recrystallization before use. (*S*)-Diphenylprolinol was prepared according to the literature procedures.[18] Borane–dimethyl sulfide was obtained from Aldrich Chemical Co. The purity of all reagents was checked by NMR spectroscopy.

4.1. General procedure for preparation of IL-sulfonamide catalyst

4.1.1. Synthesis of (*S*)-4-bromomethylbenzene-sulfonyldiphenylprolinol 2. (*S*)-Diphenyprolinol (2.53 g, 10 mmol) and Et_3N (1.55 mL, 11 mmol) were dissolved in Et_2O (30 mL). The solution was stirred at 0 °C and 4-bromomethylbenzene-sulfonyl chloride (2.95 g, 11 mmol) in Et_2O (30 mL) was slowly added. The mixture was stirred for 6 h. The reaction mixture was filtered and the solvent evaporated and purified by flash chromatography on silica gel

(ethyl acetate/hexane = 1:4 as eluent) to give **2** as the white solid (4.17 g, 86% yield), mp 286–288 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76 (d, $J = 8.0$ Hz, 2H), 7.53 (d, $J = 8.0$ Hz, 2H), 7.44–7.26 (m, 10H), 4.92 (t, $J = 11.0$ Hz, 1H), 4.63 (s, 1H), 4.31 (d, $J = 1.2$ Hz, 1H), 3.30 (m, 1H), 2.84 (m, 1H), 1.87 (m, 2H), 1.26 (m, 1H), 0.83 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.4, 143.4, 137.9, 129.7, 128.0, 127.4 (two peaks overlap), 79.9, 67.3, 49.9, 31.5, 29.6, 23.9; IR (neat) 3455, 2969, 1600, 1491, 1336, 1556, 1156, 1091, 1047, 757, 672, 974, 607 cm^{-1}; MS (CI) calcd for $C_{24}H_{25}BrNSO_3$: 486.0, 488.0 (*m*/*z*), found: 468.0, 470.0 (M−18).

4.1.2. Synthesis of IL supported sulfonamide 3. To a solution of **2** (2.42 g, 5.0 mmol) in CH_3CN was added *N*-methylimidazole (0.49 g, 6.0 mmol). The mixture was stirred for 6 h at reflux temperature. After cooling to room temperature, the reaction mixture was concentrated. The residue was purified by flash column chromatography on silica gel (methanol/dichloromethane = 1:10 as eluent) to give the desired product **3** as a colorless transparent liquid (2.60 g, 92% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.53 (s, 1H), 7.52 (d, $J = 8.9$ Hz, 4H), 7.46 (s, 1H), 7.29–7.17 (m, 5H), 7.11–7.05 (m, 6H), 7.03 (s, 1H), 5.47 (s, 2H), 4.68 (s, 1H), 3.74 (s, 2H), 3.21 (s, 3H), 2.76 (br s, 1H), 1.64 (d, $J = 7.8$ Hz, 1H), 1.13 (br s, 1H), 0.88 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.7, 143.2, 138.1, 136.1, 129.2, 127.2 (four peaks overlap), 123.4, 122.0, 79.7, 67.0, 51.3, 49.3 (two peaks overlap), 36.0, 28.5, 23.3; IR (neat) 3365, 3155, 3060, 2977, 2198, 1663, 1569, 1448, 1336, 1158, 1091, 1027, 989, 917, 731, 598, 565 cm^{-1}; MS (CI) calcd for $C_{28}H_{31}BrN_3SO_3$: 488.2, (*m*/*z*), found: 488.2 (*m*/*z*); $[\alpha]_D^{20} = -34.6$ (*c* 1.14, MeOH).

4.1.3. Anion exchange of sulfonamide 3. To a solution of **3** (2.60 g, 4.6 mmol) in H_2O (20 mL) was added $NaBF_4$ (1.0 g, 9.2 mmol). The mixture stirred for 5 h at room temperature. After evaporation of H_2O and purification of the residue, it was redissolved in a mixture of THF and ethanol (1:1), then filtered and the solid thoroughly washed with medley liquids. The filtrate and wash liquids were evaporated at reduced pressure, the residue then redissolved in dichloromethane and again filtrated, to remove the rudimental salt. The sulfonamide catalyst **IL-1** was obtained as a colorless transparent liquid.

4.2. General procedure for asymmetric reduction of prochiral

Under an argon atmosphere, $BH_3{\cdot}SMe_2$ (1.1 mmol) was added to a suspension of IL-tagged sulfonamide catalyst **IL-1** (0.15 mmol) in toluene (5 mL). The suspension was stirred and refluxed for 1 h. Then a toluene (5 mL) solution of ketone (1.0 mmol) was added within 30 min. After the addition was completed, the reaction was quenched with water (2 mL) and extracted with diethyl ether (2 × 5.0 mL). The organic layer was treated with saturated ammonium chloride solution and brine, then dried over anhydrous Mg_2SO_4. After removal of solvent, the residue was purified by flash column chromatography on silica gel to give pure product. The ee value was determined by Chiralcel OJ column (eluent: hexane/2-propanol = 9:1). Catalyst **IL-1** was separated and water removed at reduced pressure. Catalyst **IL-1** was redissolved in ethylacetate, then washed with water and dried. Ethyl acetate was removed and the catalyst **IL-1** was reused for the next cycle of reduction.

4.2.1. (*R*)-1-Phenyl-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 9:1); yield 94%, as colorless oil; $[\alpha]_D^{25} = -38.4$ (*c* 1.32, $CHCl_3$); ee 73%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 (t, $J = 8.9$ Hz, 4H), 7.28 (m, 1H), 4.89 (q, $J = 6.6$ Hz, 1H), 2.04 (s, 1H), 1.49 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.7, 128.4, 125.3, 70.1, 25.1; *m*/*z* (EI) 122 (M+, 12.2%), 107 (62.9%), 79 (100%).

4.2.2. (*R*)-1-(4-Chloro-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 9:1); yield 96%, as colorless oil; $[\alpha]_D^{25} = -39.5$ (*c* 1.21, $CHCl_3$); ee 75%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30 (d, $J = 12$ Hz, 4H), 4.86 (q, $J = 6.4$ Hz, 1H), 1.99 (s, 1H), 1.46 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.2, 128.5, 126.7, 69.6, 25.2; *m*/*z* (EI) 156 (M^+, 13.4%), 141 (56.3%), 113 (26.2%), 77 (100%), 43 (60.8%).

4.2.3. (*R*)-1-(2-Chloro-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 8:1); yield 95%, as colorless oil; $[\alpha]_D^{25} = -49.3$ (*c* 1.12, $CHCl_3$); ee 94%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (d, $J = 8.7$ Hz, 1H), 7.29 (m, 2H), 7.19 (d, $J = 9.3$ Hz, 1H), 5.29 (q, $J = 12$ Hz, 1H), 2.21 (s, 1H), 1.47 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.0, 129.3, 128.3, 127.2, 126.3, 66.9, 23.5; *m*/*z* (EI) 156 (M^+, 9.6%), 141 (54.6%), 113 (22.8%), 77 (100%), 51 (39.3%), 43 (47.5%).

4.2.4. (*R*)-1-(4-Methoxy-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 9:1); yield 92%, as colorless oil; $[\alpha]_D^{25} = -29.3$ (*c* 1.34, MeOH); ee 65%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33 (d, $J = 27$ Hz, 2H), 6.90 (d, $J = 27$ Hz, 2H), 5.10 (br, 1H), 3.85 (s, 3H), 2.88 (s, 1H), 1.49 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.3, 133.4, 128.1, 125.9, 120.6, 66.2, 55.1, 22.8; *m*/*z* (EI) 152 (M+, 14.5%), 137 (60.7%), 107 (100%), 79 (73.5%), 43 (36.6%).

4.2.5. (*R*)-1-(2-Methoxy-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 8:1); yield 93%, as colorless oil; $[\alpha]_D^{25} = -46.8$ (*c* 1.28, $CHCl_3$); ee 89%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 (d, $J = 7.2$ Hz, 1H), 7.28 (q, $J = 15$ Hz, 1H), 6.97 (t, $J = 15$ Hz, 2H), 6.88 (d, $J = 8.4$ Hz, 1H), 5.10 (q, $J = 12$ Hz, 1H), 3.86 (s, 3H), 2.74 (s, 1H), 1.51 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.4, 134.6, 133.3, 128.2, 126.0, 120.7, 110.3, 66.4, 55.2, 22.8; *m*/*z* (EI) 152 (M^+, 25.3%), 137 (100%), 107 (82.3%), 94 (19.2%), 77 (42.9%), 51 (30.3%), 43 (48.4%).

4.2.6. (*R*)-1-(2-Methyl-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 10:1); yield 94%, as colorless oil; $[\alpha]_D^{25} = -47.9$ (*c* 1.03, $CHCl_3$); ee 91%; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 (d, $J = 7.5$ Hz, 1H), 7.24, 7.16 (br, 3H), 5.09 (d, $J = 6.0$ Hz, 1H), 2.34 (s, 3H), 2.27 (s, 1H), 1.45 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.8, 134.1, 130.2, 127.0,

126.2, 124.4, 66.6, 23.8, 18.8; *m*/*z* (EI) 136 (M^+, 18.8%), 121 (70.9%), 91 (98%), 77 (57.8%), 43 (100%).

4.2.7. (*R*)-1-(4-Fluoro-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 10:1); yield 95%, as colorless oil; $[\alpha]_D^{25} = -35.1$ (*c* 1.24, $CHCl_3$); ee 75%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.23 (d, $J = 15$ Hz, 2H), 6.96 (d, $J = 18$ Hz, 2H), 4.74 (q, $J = 18$ Hz, 1H), 3.64 (s, 1H), 1.36 (d, $J = 9.0$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.4, 160.2, 141.5, 126.8, 115.0, 114.7, 69.2, 24.9; *m*/*z* (EI) 140 (M^+, 17.7%), 125 (92.9%), 97 (100%), 77 (34.5%), 43 (66.8%).

4.2.8. (*R*)-1-Naphthalen-2-yl-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 9:1); yield 96%, as colorless oil; $[\alpha]_D^{25} = -38.1$ (*c* 1.05, $CHCl_3$); ee 75%; ^1H NMR (300 MHz, $CDCl_3$): δ 8.10, 7.45 (br, 7H), 7.09 (s, 3H), 5.64 (d, $J = 6.0$ Hz, 1H), 2.44 (s, 1H), 1.65 (d, $J = 6.0$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.2, 133.6, 130.1, 128.8, 127.8, 125.9, 123.1, 121.9, 66.9, 24.3; *m*/*z* (EI) 172 (M^+, 29.6%), 157 (38.2%), 129 (100%), 77 (10%).

4.2.9. (*R*)-1-(4-Nitro-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 6:1); yield 94%, as colorless oil; Mp $[\alpha]_D^{25} = -30.2$ (*c* 1.13, $CHCl_3$); ee 76%; ^1H NMR (300 MHz, $CDCl_3$): δ 8.10 (d, $J = 9$ Hz, 2H), 7.48 (d, $J = 9$ Hz, 2H), 4.97 (q, $J = 21$ Hz, 1H), 2.80 (s, 1H), 1.46 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.4, 146.8, 126.0, 123.6, 69.3, 25.3; *m*/*z* (EI) 167 (M^+, 0.24%), 152 (100%), 107 (82.2%), 77 (60%), 43 (39.9%).

4.2.10. (*S*)-2-Bromo-1-phenyl-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 8:1); yield 92%, as colorless oil; $[\alpha]_D^{25} = +41.5$ (*c* 1.16, $CHCl_3$); ee 71%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.36 (br, 5H), 4.89 (q, $J = 12$ Hz, 1H), 3.60 (m, 2H), 2.87 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.2, 128.4, 125.8, 73.7, 40.0; *m*/*z* (EI) 200 (M^+, 0.22%), 121 (1.5%), 107 (100%), 79 (62.4%).

4.2.11. (*S*)-2-Chloro-1-phenyl-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 8:1); yield 93%, as colorless oil; $[\alpha]_D^{25} = +39.6$ (*c* 1.47, $CHCl_3$); ee (77%); ^1H NMR (300 MHz, $CDCl_3$): δ 7.36 (br, 5H), 4.89 (q, $J = 12$ Hz, 1H), 3.60 (m, 2H), 2.87 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.2, 128.4, 125.8, 73.7, 40.0; *m*/*z* (EI) 156 (M^+, 0.34%), 139 (2.78%), 107 (100%), 79 (80.6%), 51 (31.7%).

4.2.12. (*S*)-2-Chloro-1-(2,4-dimethyl-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 8:1); yield 91%, as colorless oil; $[\alpha]_D^{25} = +41.9$ (*c* 1.29, $CHCl_3$); ee 96%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.40 (d, $J = 9$ Hz, 1H), 7.06 (d, $J = 9$ Hz, 1H), 6.99 (s, 1H), 5.07 (t, $J = 9$ Hz, 1H), 3.63 (m, 2H), 2.31 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.9, 134.9, 131.4, 127.1, 125.4, 70.7, 49.9, 21.0, 19.0; *m*/*z* (EI) 184 (M^+, 2.9%), 135 (100%), 107 (41.8%), 91 (37.7%), 51 (11.9%).

4.2.13. (*S*)-2-Bromo-1-(2,4-dimethyl-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 8:1); yield 94%, as colorless oil; $[\alpha]_D^{25} = +41.5$ (*c* 1.06, $CHCl_3$); ee 95%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.40 (d, $J = 9$ Hz, 1H), 7.06 (d, $J = 9$ Hz, 1H), 6.99 (s, 1H), 5.07 (t, $J = 9$ Hz, 1H), 3.63 (m, 2H), 2.31 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.9, 134.9, 131.4, 127.1, 125.4, 70.7, 49.9, 21.0, 19.0; *m*/*z* (EI) 228 (M^+, 3.9%), 135 (100%), 107 (46.8%), 91 (42%), 51 (10.9%).

4.2.14. (*S*)-2-Chloro-1-(4-methoxy-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 8:1); yield 93%, as colorless oil; $[\alpha]_D^{25} = +18.9$ (*c* 1.19, $CHCl_3$); ee 64%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (d, $J = 6.0$ Hz, 1H), 6.90 (d, $J = 9.0$ Hz, 2H), 4.84 (q, $J = 12$ Hz, 1H), 3.80 (s, 3H), 3.65 (m, 2H), 2.75 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.6, 132.0, 128.6, 127.3, 126.0, 114.0, 73.7, 55.2, 50.8; *m*/*z* (EI) 186 (M^+, 6.0%), 137 (100%), 109 (23.8%), 94 (26.4%), 77 (28.9%).

4.2.15. (*S*)-2-Bromo-1-(4-methoxy-phenyl)-ethanol. Purified by flash chromatography on silica gel (eluent: hexanes/EtOAc = 8:1); yield 94%, as colorless oil; $[\alpha]_D^{25} = +19.6$ (*c* 1.03, $CHCl_3$); ee 67%; ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (d, $J = 6.0$ Hz, 1H), 6.90 (d, $J = 9.0$ Hz, 2H), 4.84 (q, $J = 12$ Hz, 1H), 3.80 (s, 3 H), 3.65 (m, 2H), 2.75 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.6, 132.0, 128.6, 127.3, 126.0, 114.0, 73.7, 55.2, 50.8; *m*/*z* (EI) 232 (M^+, 3.0%), 137 (100%), 109 (15.8%), 94 (16.4%), 77 (21.0%).

Acknowledgements

We thank the NSFC-20021001, NSFC-20572038 and the 'Hundred Scientist Program' from the Chinese Academy of Sciences for the financial support of this work.

References

1. (a) Singh, V. K. *Synthesis* **1992**, *7*, 605; (b) Corey, E. J.; Helal, C. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 1986.
2. (a) Hirao, A.; Itsuno, S.; Nakahama, N.; Yamazaki, N. *J. Chem. Soc., Chem. Commun.* **1981**, 315; (b) Itsuno, S.; Ito, K.; Hirao, A.; Nakahama, S.; Yamazaki, N. *J. Chem. Soc., Chem. Commun.* **1983**, 469; (c) Itsuno, S.; Ito, K. *J. Org. Chem.* **1984**, *49*, 555.
3. (a) Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551; (b) Corey, E. J.; Reichard, G. A. *Tetrahedron Lett.* **1989**, *30*, 5207; (c) Corey, E. J.; Link, J. O. *Tetrahedron Lett.* **1992**, *33*, 3431; (d) Corey, E. J.; Helal, C. J. *Tetrahedron Lett.* **1995**, *36*, 9153; (e) Helal, C. J.; Magriotis, P. A.; Corey, E. J. *J. Am. Chem. Soc.* **1996**, *118*, 10938.
4. (a) Wallbaum, S.; Martens, J. *Tetrahedron: Asymmetry* **1992**, *3*, 1475; (b) Deloux, L.; Srebnik, M. *Chem. Rev.* **1993**, *93*, 763; (c) Mathre, S. A.; Thompson, A. W.; Douglas, K.; Hoogsteen, J. D.; Carroll, E. G.; Corey, E. J.; Grabowski, J. *J. Org. Chem.* **1993**, *58*, 2880; (d) Deninno, M. P.; Perner, R. J.; Morton, H. E.; DiDomenico, S. *J. Org. Chem.* **1992**, *57*, 7115; (e) Bach, J.; Berenger, R.; Gracia, J.; Loscertales, T.; Vilarrasa, J. *J. Org. Chem.* **1996**, *61*, 9021; (f) Quallich, G.

J.; Blake, J. F.; Woodall, T. W. *J. Am. Chem. Soc.* **1994**, *116*, 8516; (g) Yang, G. Sh.; Hu, J. B.; Zhao, G.; Ding, Y.; Tang, M. H. *Tetrahedron: Asymmetry* **1999**, *10*, 4307; (h) Jiang, B.; Feng, Y.; Zheng, J. *Tetrahedron Lett.* **2000**, *41*, 10281.

5. (a) Shuttleworth, S. J.; Allin, S. M.; Sharma, P. K. *Synthesis* **1997**, 1217; (b) Itsuno, S.; Sakurai, Y.; Shimizu, K.; Ito, K. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1859; (c) Itsuno, S.; Ito, K.; Hirao, A.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2887; (d) Itsuno, S.; Nakano, M.; Ito, K.; Hirao, A.; Owa, M.; Kanda, N.; Nakahama, S. *J. Org. Chem.* **1985**, 2615; (e) Caze, C.; El Moualij, N.; Hodge, P.; Lock, C. J.; Ma, J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 345; (f) Franot, C.; Stone, G. B.; Engeli, P.; Spondlin, C.; Waldvogel, E. *Tetrahedron: Asymmetry* **1995**, *6*, 2566; (g) Caze, C.; El Moualij, N.; Hodge, P.; Lock, C. *J. Polym.* **1995**, 621; (h) Felder, M.; Giffels, G.; Wandrey, C. *Tetrahedron: Asymmetry* **1997**, *8*, 1975; (i) Degni, S.; Wilen, C. E.; Leino, R. *Org. Lett.* **2001**, *16*, 2551; (j) Hu, J. B.; Zhao, G.; Yang, G. Sh.; Ding, Z. D. *J. Org. Chem.* **2001**, *66*, 303; (k) Hu, J. B.; Zhao, G.; Yang, G. Sh.; Ding, Z. D. *Angew. Chem., Int. Ed.* **2001**, *40*, 1109; (l) Degni, S.; Wilen, C. E.; Rosling, A. *Tetrahedron: Asymmetry* **2004**, *15*, 1495; (m) Price, M. D.; Sui, J. K.; Kurth, M. J.; Schore, N. E. *J. Org. Chem.* **2002**, *67*, 8086; (n) Seebach, D.; Beck, A. K.; Dahinden, R.; Hoffmann, M.; Kuhnle, F. N. M. *Croat. Chem. Acta* **1996**, *69*(2), 459; (o) Degni, S.; Wilen, C. E.; Leino, R. *Tetrahedron: Asymmetry* **2004**, *15*, 231.
6. (a) Hakkou, H.; Eynde, J. J. V.; Hamelin, J.; Bazureau, J. P. *Tetrahedron* **2004**, *60*, 3745; (b) Hakkou, H.; Vanden Eynde, J. J.; Hamelin, J.; Bazureau, J. P. *Synthesis* **2004**, 1793–1798; (c) Fraga-Dubreuil, J.; Bazureau, J. P. *Tetrahedron* **2003**, *59*, 6121; (d) Fraga-Dubreuil, J.; Bazureau, J. P. *Tetrahedron Lett.* **2001**, *42*, 6097; (e) Handy, S. T.; Okello, M. *Tetrahedron Lett.* **2003**, *44*, 8399.
7. (a) Ikuo, K.; Kazuya, T.; Tomoko, Y.; Hiroki, S. *Chem. Commun.* **2005**, 2134; (b) Herve, C.; Nicolas, A.; Guillemin, J. C.; Marc, M. *J. Organomet. Chem.* **2005**, *690*, 3585; (c) Yanqing, P.; Xueqin, C.; Gonghua, S.; Jing, Ch. *Synlett* **2005**, 2147; (d) Cole, A. C.; Jensen, J. L.; Ntai, I.; Trans, K. L. T.; Weaver, K. J.; Forbes, D. C.; Davis, J. H., Jr. *J. Am. Chem. Soc.* **2002**, *124*, 5962.
8. (a) Yao, Q.; Zhang, Y. *Angew. Chem., Int. Ed.* **2003**, *42*, 3395; (b) Audic, N.; Clavier, H.; Mauduit, M.; Guillemin, J.-C. *J. Am. Chem. Soc.* **2003**, *125*, 9248.
9. (a) Lee, S.; Zhang, Y. J.; Piao, J. Y.; Yoon, H.; Song, C. E.; Choi, J. H.; Hong *J. Chem. Commun.* **2003**, 2624; (b) Geldbach, T. J.; Dyson, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 8114.
10. Baleizão, C.; Gigante, B.; Garcia, H.; Corma, A. *Tetrahedron Lett.* **2003**, *44*, 6813.
11. (a) Brasse, C. C.; Englert, U.; Salzer, A. *Organometallics* **2000**, *19*, 3818; (b) Favre, F.; Olivier-Bourbigou, H.; Commereuc, D.; Saussine, L. *Chem. Commun.* **2001**, 1360; (c) Bronger, R. P. J.; Silva, S. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Chem. Soc., Dalton Trans.* **2004**, 1590.
12. Sirieix, J.; Ossberger, M.; Betzemeier, B.; Knochel, P. *Synlett* **2000**, 1613.
13. (a) Xiao, J.-C.; Twamley, B.; Shreeve, J. M. *Org. Lett.* **2004**, *6*, 3845; (b) Corma, A.; García, H.; Leyva, A. *Tetrahedron* **2004**, *60*, 8553.
14. Zhao, D.; Fei, Z.; Geldbach, T. J.; Scopelliti, R.; Dyson, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 15876.
15. Mi, X.; Luo, S.; Cheng, J.-P. *J. Org. Chem.* **2005**, *70*, 2338.
16. (a) Cole, A. C.; Jensen, J. L.; Ntai, I.; Trans, K. L. T.; Weaver, K. J.; Forbes, D. C.; Davis, J. H., Jr. *J. Am. Chem. Soc.* **2002**, *124*, 5962; (b) Gu, Y.; Shi, F.; Deng, Y. *Catal. Commun.* **2003**, *4*, 597; (c) Qiao, K.; Yokoyama, C. *Chem. Lett.* **2004**, *33*, 472; (d) Gui, J.; Deng, Y.; Hu, Z.; Sun, Z. *Tetrahedron Lett.* **2004**, *45*, 2681.
17. Zhaoqing Xu; Chao Chen; Jiangke Xu; Mingbo Miao; Wenjin Yan; Rui Wang *Org. Lett.* **2004**, *6*, 1193–1195.
18. Mathre, D. J.; Jones, T. K.; Xavier, L. C.; Blacklock, T. J.; Reamre, R. A.; Mohan, J. J.; Jones, E. T.; Hoogsteen, K.; Baum, M. W.; Grabowski, E. J. *J. Org. Chem.* **1991**, *56*, 751.