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# Facile synthesis of chiral isopropyl carbinols with high enantiomeric excess via catalytic enantioselective addition of diisopropylzinc to aldehydes†

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**Abstract**

Highly effective syntheses of chiral alkyl and aryl isopropyl carbinols with high enantiomeric excess (94–98% ee) via catalytic enantioselective addition of diisopropylzinc to aldehydes have been developed.


## 1. Introduction

The introduction of stereogenic isopropyl carbinol groups is a key step in preparing biologically active substances such as cerebresterol,[1] 1α,24(*R*)-dihydroxy-vitamin $D_3$[2] and squalamine.[3] Also, the stereogenic isopropyl carbinol groups play important roles in asymmetric autocatalytic reactions.[4] One of the most convenient methods for introducing such groups is probably the enantioselective isopropylation to aldehydes.[5] Although a number of the catalytic enantioselective additions of dialkylzincs to aldehydes to give secondary alcohols with high enantiomeric excess have been extensively studied,[7] among dialkylzinc reagents employed, diethylzinc has been the most often utilized in the reaction. Only a few examples have been reported on the enantioselective addition of diisopropylzinc.[4,8] Recently, we reported the enantioselective addition of diethylzinc to aldehydes catalyzed by a γ-dialkylamino alcohol, 1,2-*O*-isopropylidene-5-deoxy-5-morpholino-α-D-xylofuranose **1** derived from α-D-xylose.[9] In the course of developing the synthetic usefulness of this catalyst for such reactions, we found that the catalyst is highly effective for the enantioselective isopropylation to both aliphatic and aromatic aldehydes: we describe here these results.

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## 2. Results and discussion

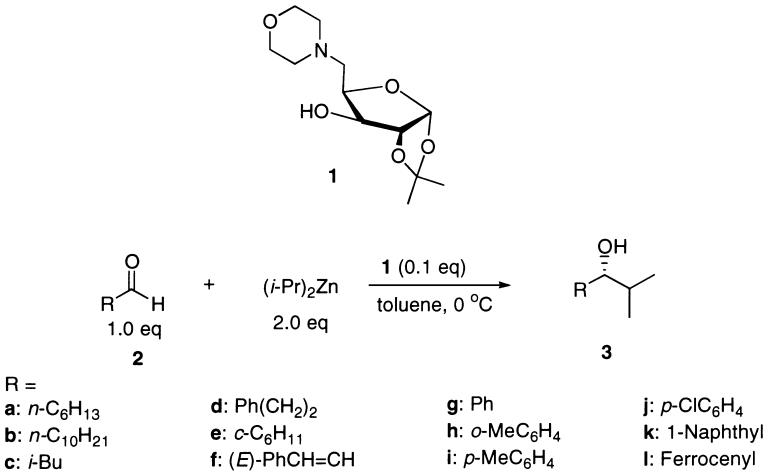
To find the optimum conditions for the catalytic isopropylation to aldehydes, we initially investigated the catalytic, temperature and solvent effects on reactivity and enantioselectivity for the reaction to benzaldehyde. First, we examined the effect of the amount of catalyst. Thus, the reaction was carried out by the addition of 2 equiv. of diisopropylzinc to benzaldehyde in the presence of varying amounts of **1** in toluene at 0°C. As shown in Table 1, the use of 10 mol% of **1** provided the best results, giving 2-methyl-1-phenylpropanol in 96% ee. Increasing the amount of **1** from 2 to 25 mol% did not significantly affect the enantioselectivity, which was 90% ee with 2 mol%, 92% ee with 5 mol%, 96% ee with 10 mol% and 25 mol% of **1**, although the reaction using both 2 and 5 mol% of **1** proceeded more slowly (entries 1–4). Next, we examined temperature effects by carrying out the same reaction with 10 mol% of **1** at various temperatures. When the reaction was performed at 0°C or –25°C, the best enantioselectivity (96% ee) was observed. However, the reaction at –25°C was very slow to give the product alcohol in 64% yield after 35 h (entry 6). Among the solvents examined, the reaction in toluene provided the best result. The same reaction in dichloromethane afforded lower enantioselectivity (entry 7). The catalytic isopropylation of the aldehyde in THF did not occur. This may be attributable to instability of diisopropylzinc reagent in THF. Based on the optimum conditions obtained from Table 1, we carried out the enantioselective addition of diisopropylzinc to other aldehydes **2** in the presence of 10 mol% of **1** in toluene at 0°C (Scheme 1). As shown in Table 2, all the reactions proceeded smoothly to give the corresponding isopropyl carbinols **3** in good yields. The catalyst is found to be highly effective for the isopropylation to both aliphatic and aromatic aldehydes examined with one exception, leading to the corresponding alcohols with very high enantiomeric excesses in the range of 94–98% ee. In the case of an α,β-unsaturated aldehyde, *trans*-cinnamaldehyde, the reaction provided low enantioselectivity (entry 6, Table 2). The steric effect of the *ortho*-substituent of the aromatic ring on asymmetric induction is not significant (entries 8 versus 9). In particular, it is noteworthy that optically active (1-hydroxy-2-methylpropyl)ferrocene **3l** approaching almost 100% ee has been achieved in the reaction of ferrocenecarboxaldehyde

Table 1
Catalytic, temperature and solvent effects on asymmetric induction for enantioselective addition of diisopropylzinc to benzaldehyde using **1** as the catalyst[a]

| Entry | **1** (mol%) | Solvent | Temp (°C) | 1-Phenyl-2-methylpropanol **3g** | | | |
|---|---|---|---|---|---|---|---|
| | | | | Time (h) | Yield (%)[b] | %ee[c] | Confg[d] |
| 1 | 2 | Toluene | 0 | 16 | 62 | 90 | *R* |
| 2 | 5 | Toluene | 0 | 16 | 80 | 92 | *R* |
| 3 | 10 | Toluene | 0 | 4 | 95 | 96 | *R* |
| 4 | 25 | Toluene | 0 | 4 | 95 | 96 | *R* |
| 5 | 10 | Toluene | 25 | 2 | 94 | 91 | *R* |
| 6 | 10 | Toluene | -25 | 35 | 64 | 96 | *R* |
| 7 | 10 | $CH_2Cl_2$ | 0 | 12 | 90 | 47 | *R* |
| 8 | 10 | THF | 0 | | e | | |

[a] [aldehyde] : [*i*-$Pr_2Zn$] : [**1**] = 1 : 2 : 0.1. [aldehyde] = 0.3 M. [b] Isolated yield after column chromatography. [c] Determined by capillary GC analysis using a β-Dex 120 chiral column (Supelco). [d] Assigned by comparison with literature data.[11] [e] No reaction due to instability of diisopropylzinc in THF.

(entry 12), since this chiral alcohol may be used as a synthetic intermediate for the preparation of chiral ligands bearing a ferrocenyl ring.[10] Moreover, the absolute configurations of the product alcohols **3** obtained showed that aldehydes **2** were consistently attacked by diisopropylzinc on their *re* sides in their transition states.[9]




Scheme 1.

Table 2
Enantioselective addition of diisopropylzinc to aldehydes catalyzed by 10 mol% of **1** in toluene at 0°C[a]

| Entry | Aldehydes **2** | Isopropyl carbinols **3** | | | |
|---|---|---|---|---|---|
| | | Time (h) | Yield (%)[b] | %ee | Confg |
| 1 | Heptanal **2a** | 8 | 88 | 96[c] | *S*[h] |
| 2 | Undecanal **2b** | 9 | 84 | 96[c] | *S*[h] |
| 3 | 3-Methylbutanal **2c** | 9 | 82 | 96[c] | *S*[h] |
| 4 | 3-Phenylpropanal **2d** | 6 | 90 | 96[d] (94)[e] | *S*[i] |
| 5 | Cyclohexanecarboxaldehyde **2e** | 8 | 82 | 98[f] | *R*[i] |
| 6 | *trans*-Cinnamaldehyde **2f** | 8 | 80 | 69[d] (41)[e] | *R*[i] |
| 7 | Benzaldehyde **2g** | 4 | 95 | 96[c] (100)[e] | *R*[i] |
| 8 | *o*-Tolualdehyde **2h** | 6 | 87 | 94[c] | *R*[h] |
| 9 | *p*-Tolualdehyde **2i** | 8 | 92 | 94[g] | *R*[h] |
| 10 | *p*-Chlorobenzaldehyde **2j** | 6 | 90 | 95[d] | *R*[h] |
| 11 | 1-Naphthaldehyde **2k** | 12 | 81 | 95[c] | *R*[h] |
| 12 | Ferrocenecarboxaldehyde **2l** | 4 | 93 | 98[d] (100)[e] | *R*[i] |

[a-c] See the corresponding footnotes in Table 1. [d] Determined by HPLC analysis using a Chiralcel OD column (Daicel). [e] Based on the maximum optical rotation values of the corresponding carbinols reported (see experimental section). [f] Determined by capillary GC analysis of its trifluoroacetate using a Chiraldex G-TA chiral column (Astec Inc). [g] Determined by capillary GC analysis using a Chiraldex B-PH chiral column (Astec Inc). [h] By comparison of literature data. [i] Based on comparison of the sign of optical rotations and elution orders of peaks of HPLC or GC analyses of their analogues.

## 3. Conclusion

We have established a highly effective synthesis of optically active alkyl and aryl isopropyl carbinols with 94–98% ee via enantioselective addition of diisopropylzinc to aldehydes using a γ-amino alcohol **1** derived from α-D-xylose as the catalyst. The excellent enantiomeric excess for secondary alcohols bearing similar steric bulk of two groups adjacent to the carbinol group is especially noteworthy, because it is well known that asymmetric reductions of simple ketones with small difference of steric size between two groups attached to the carbonyl using biological or chemical manners generally provide low enantioselectivity.[5,12]

## 4. Experimental

### 4.1. General

All operations with air-sensitive materials were carried out under a nitrogen atmosphere with oven-dried glassware. Liquid materials were transferred with a double-ended needle. The reactions were monitored by TLC using silica gel plates and the products were purified by flash column chromatography on silica gel (Merck; 230–400 mesh). NMR spectra were recorded at 400 MHz for $^{1}H$ and 100 MHz for $^{13}C$ using $Me_4Si$ as the internal standard in $CDCl_3$, and $J$ values are given in hertz. Optical rotations were measured with a high resolution digital polarimeter. Melting points were uncorrected. Enantiomeric excesses (% ees) of the product alcohols were determined by capillary GC analyses using a 20 m Chiraldex G-TA, B-PH and β-Dex 120 chiral column or by an HPLC analysis using a 25 cm Chiralcel OD.

### 4.2. Materials

Most of the organic compounds utilized in this study were commercial products of the highest purity. They were further purified by distillation when necessary. Toluene was distilled over sodium and stored in an ampoule under nitrogen atmosphere. The chiral ligand **1** was synthesized from α-D-xylose by our previous procedure.[9] Diisopropylzinc was prepared according to the literature procedure.[13]

### 4.3. Catalytic enantioselective addition of diisopropylzinc to aldehydes. General procedure

Under a nitrogen atmosphere, a toluene solution (2 ml) of diisopropylzinc (2 mmol) was added to **1** (0.1 mmol) in toluene (1 ml) and stirred at 0°C for 30 min. After aldehyde **2** (1 mmol) was added to this, the mixture was stirred at the same temperature for the appropriate time and then diluted with ether (10 ml). The excess diisopropylzinc was destroyed by addition of 1N HCl and extracted with ether (3×10 ml). The ether extract was dried over anhydrous magnesium sulfate and concentrated in vacuo. The product alcohol **3** was further purified by flash column chromatography on silica gel using an appropriate solvent as eluent.

*4.3.1. (S)-2-Methyl-3-nonanol* ***3a***

Yield, 88%; $R_f$ 0.59 (EtOAc:hexane = 1:4); oil; IR (neat, $cm^{-1}$) 3399, 2930, 1467, 1382, 1030; $^1H$ NMR $\delta$ 0.87–0.93 (m, 9H), 1.26–1.36 (m, 9H), 1.45–1.47 (m, 2H), 1.65 (m, 1H), 3.36 (m, 1H); $^{13}C$ NMR $\delta$ 14.11, 17.06, 18.89, 22.66, 26.03, 29.45, 31.90, 33.47, 34.19, 76.73; $[\alpha]_D^{21}$ –14.1 (0.7, $CHCl_3$); GC analysis using a 30 m β-Dex 120 chiral column showed it to be 96% ee [95°C (isothermal) $t_R(S)$ 50.66 min and $t_R(R)$ 53.14 min].

*4.3.2. (S)-2-Methyl-3-tridecanol* ***3b***

Yield, 84%; $R_f$ 0.72 (EtOAc:hexane = 1:2); oil; IR (neat, $cm^{-1}$) 3365, 2957, 1460; $^1H$ NMR $\delta$ 0.86–0.93 (m, 9H), 1.26–1.35 (m, 17H), 1.44–1.47 (m, 2H), 1.63 (m, 1H), 3.36 (m, 1H); $^{13}C$ NMR $\delta$ 14.13, 17.07, 18.89, 22.70, 26.06, 29.35, 29.64, 29.65, 29.67, 29.78, 31.92, 33.45, 34.19, 76.70; $[\alpha]_D^{21}$ –15.1 (1.07, $CHCl_3$); GC analysis using a 30 m β-Dex 120 chiral column showed it to be 96% ee [130°C (isothermal) $t_R(S)$ 80.71 min and $t_R(R)$ 83.09 min].

*4.3.3. (S)-2,5-Dimethyl-3-hexanol* ***3c***

Yield, 62%; $R_f$ 0.67 (EtOAc:hexane = 1:2); oil; IR (neat, $cm^{-1}$) 3365, 2959, 1468, 1368; $^1H$ NMR $\delta$ 0.89–0.94 (m, 13H), 1.18–1.24 (m, 1H), 1.31–1.37 (m, 2H), 1.63 (m, 1H), 3.45 (m, 1H); $^{13}C$ NMR $\delta$ 17.38, 19.14, 22.15, 24.19, 25.07, 34.28, 43.71, 74.87; $[\alpha]_D^{21}$ –18.8 (0.84, $CHCl_3$); GC analysis using a 30 m β-Dex 120 chiral column showed it to be 96% ee [80°C (isothermal) $t_R(S)$ 23.04 min and $t_R(R)$ 25.19 min].

*4.3.4. (S)-2-Methyl-5-phenyl-3-pentanol* ***3d***

Yield, 90%; $R_f$ 0.62 (EtOAc:hexane = 1:2); oil; IR (neat, $cm^{-1}$) 3390, 3062, 2872, 1485, 1467, 1038, 1011, 745, 697; $^1H$ NMR $\delta$ 0.92 (d, 6H, $J$ = 6.93), 1.40 (br s, 1H), 1.65–1.72 (m, 2H), 1.78–1.80 (m, 1H), 2.65 (m, 1H), 2.84 (m, 1H), 3.40 (m, 1H), 7.16–7.22 (m, 3H), 7.27–7.30 (m, 2H); $^{13}C$ NMR $\delta$ 17.16, 18.77, 32.48, 33.69, 35.96, 76.14, 125.78, 128.39, 128.44, 142.36; $[\alpha]_D^{21}$ –38.2 (3.02, EtOH) {lit.[8] $[\alpha]_D^{26}$ +39.0 (*c* 3.08, EtOH), 96.1% ee *R*}; HPLC analysis using a 25 cm Chiralcel OD column showed it to be 96% ee [*i*-PrOH:hexane = 1:9, flow rate 0.7 mL/min, $t_R(S)$ 9.42 min and $t_R(R)$ 13.98 min].

*4.3.5. (R)-1-Cyclohexyl-2-methylpropanol* ***3e***

Yield, 82%; $R_f$ 0.68 (EtOAc:hexane = 1:2); oil; IR (neat, $cm^{-1}$) 3411, 2829, 1467; $^1H$ NMR $\delta$ 0.90 (d, 3H, $J$ = 6.70), 0.92 (d, 3H, $J$ = 6.80), 0.99–1.28 (m, 6H), 1.40 (m, 1H), 1.57–1.60 (m, 1H), 1.65–1.67 (m, 1H), 1.72–1.87 (m, 3H), 1.85–1.88 (m, 1H), 3.04 (m, 1H); $^{13}C$ NMR $\delta$ 16.53, 19.89, 26.16, 16.44, 26.55, 27.66, 29.76, 29.91, 40.61, 81.06; $[\alpha]_D^{21}$ +4.24 (0.38, $CHCl_3$) {lit.[14] $[\alpha]_D^{25}$ –3.4 (neat), *S*}; GC analysis of its trifluoroacetate using a 20 m Chiraldex G-TA chiral column showed it to be 98% ee [65°C (isothermal) $t_R(S)$ 20.86 min and $t_R(R)$ 22.19 min].

*4.3.6.* trans-*(R)-4-Methyl-1-phenyl-1-penten-3-ol* ***3f***

Yield, 80%; $R_f$ 0.58 (EtOAc:hexane = 1:2); oil; IR (neat, $cm^{-1}$) 3403, 3077, 2962, 1493, 1466, 1023, 988, 746, 691; $^1H$ NMR $\delta$ 0.95 (d, 3H, $J$ = 6.77), 0.99 (d, 3H, $J$ = 6.79), 1.83 (m, 1H), 4.03 (m, 1H), 6.23 (dd, 1H, $J$ = 6.96, 15.92), 6.57 (d, 1H, $J$ = 15.91), 7.24–7.40 (m, 5H); $^{13}C$ NMR $\delta$ 18.06, 18.31, 34.11, 78.16, 126.45, 127.60, 128.57, 130.87, 131.20, 136.82; $[\alpha]_D^{21}$ –8.0 (1.02, EtOH) {lit.[8] $[\alpha]_D^{25}$ +18.1 (*c* 1.07, EtOH), 93.4% ee, *S*}; HPLC analysis using a 25 cm Chiralcel OD column showed it to be 69% ee [*i*-PrOH:hexane = 1:9, flow rate 0.9 mL/min, $t_R(R)$ 8.83 min and $t_R(S)$ 12.83 min].

*4.3.7. (*R*)-2-Methyl-1–phenylpropanol* ***3g***

Yield, 95%; $R_f$ 0.60 (EtOAc:hexane = 1:2); oil; IR (neat, $cm^{-1}$) 3424, 3063, 2934, 1467, 1366, 1021, 757, 699; $^1H$ NMR $\delta$ 0.80 (d, 3H, $J = 6.90$), 1.00 (d, 3H, $J = 6.66$), 1.85 (d, 1H, $J = 2.35$), 1.96 (m, 1H), 4.36 (dd, 1H, $J = 2.09, 6.83$), 7.25–7.36 (m, 5H); $^{13}C$ NMR $\delta$ 18.23, 19.01, 35.27, 80.05, 126.56, 127.42, 128.19, 143.65; $[\alpha]_D^{21}$ +52.1 (1.06, $Et_2O$) {lit.[11] $[\alpha]_D^{20}$ +47.7 (*c* 6.8, $Et_2O$), *S*}; GC analysis using a 30 m β-Dex 120 chiral column showed it to be 96% ee [115°C (isothermal) $t_R(R)$ 56.79 min and $t_R(S)$ 59.07 min].

*4.3.8. (*R*)-2-Methyl-1-(*o*-tolyl)propanol* ***3h***

Yield, 67%; $R_f$ 0.63 (EtOAc:hexane = 1:2); oil; IR (neat, $cm^{-1}$) 3414, 2932, 1486, 1381, 1031, 726; $^1H$ NMR $\delta$ 0.84 (d, 3H, $J = 6.88$), 1.03 (d, 3H, $J = 6.61$), 1.72 (br s, 1H), 1.97 (m, 1H), 2.33 (s, 3H), 4.63 (d, 1H, $J = 6.89$), 7.12–7.85 (m, 3H), 7.41 (d, 1H, $J = 7.48$); $^{13}C$ NMR $\delta$ 17.87, 19.40, 19.44, 34.57, 75.77, 126.06, 127.04, 130.31, 134.96, 142.17; $[\alpha]_D^{21}$ +37.9 (1.12, $CHCl_3$); GC analysis using a 30 m β-Dex 120 chiral column showed it to be 94% ee [130°C (isothermal) $t_R(R)$ 42.33 min and $t_R(S)$ 44.14 min].

*4.3.9. (*R*)-2-Methyl-1-(*p*-tolyl)propanol* ***3i***

Yield, 92%; $R_f$ 0.63 (EtOAc:hexane = 1:2); oil; IR (neat, $cm^{-1}$) 3392, 2960, 1514, 1467, 1397, 1030, 826, 762; $^1H$ NMR $\delta$ 0.78 (d, 3H, $J = 6.83$), 1.00 (d, 3H, $J = 6.64$), 1.80 (d, 1H, $J = 3.23$), 1.94 (m, 1H), 2.34 (s, 3H), 4.31 (dd, 1H, $J = 3.05, 6.97$), 7.14 (d, 2H, $J = 8.02$), 7.20 (d, 2H, $J = 8.02$); $^{13}C$ NMR $\delta$ 18.36, 19.01, 21.11, 35.21, 79.96, 126.50, 128.88, 137.04, 140.70; $[\alpha]_D^{21}$ +44.8 (1.08, $CHCl_3$); GC analysis using a 20 m Chiraldex B-PH chiral column showed it to be 94% ee [110°C (isothermal) $t_R(R)$ 36.04 min and $t_R(S)$ 38.76 min].

*4.3.10. (*R*)-1-(*p*-Chlorophenyl)-2-methylpropanol* ***3j***

Yield, 92%; $R_f$ 0.67 (EtOAc:hexane = 1:2); oil; IR (neat, $cm^{-1}$) 3405, 2985, 1491, 1460, 1083, 1032, 1011, 829, 783; $^1H$ NMR $\delta$ 0.79 (d, 3H, $J = 6.81$), 0.97 (d, 3H, $J = 6.74$), 1.87–1.94 (m, 2H), 2.34 (s, 3H), 4.35 (dd, 1H, $J = 2.47, 6.56$), 7.24 (d, 2H, $J = 8.44$), 7.30 (d, 2H, $J = 8.47$); $^{13}C$ NMR $\delta$ 18.01, 18.84, 35.28, 79.23, 127.91, 128.30, 133.01, 142.03; $[\alpha]_D^{21}$ +38.9 (1.15, $CHCl_3$); HPLC analysis using a 25 cm Chiralcel OD column showed it to be 95% ee [*i*-PrOH:hexane = 1:9, flow rate 0.7 mL/min, $t_R(S)$ 28.23 min and $t_R(R)$ 30.70 min].

*4.3.11. (*R*)-2-Methyl-1-(1′-naphthyl)propanol* ***3k***

Yield, 81%; $R_f$ 0.65 (EtOAc:hexane = 1:2); oil; IR (neat, $cm^{-1}$) 3437, 3055, 2932, 1566, 1511, 1382, 1169, 1035, 995, 793; $^1H$ NMR $\delta$ 0.92 (d, 3H, $J = 6.83$), 1.02 (d, 3H, $J = 6.66$), 1.96 (br s, 1H), 2.25 (m, 1H), 5.18 (d, 1H, $J = 6.16$), 7.44–7.50 (m, 3H), 7.59 (d, 1H, $J = 7.01$), 7.77 (d, 1H, $J = 8.17$), 7.86 (m, 1H), 7.99 (m, 1H); $^{13}C$ NMR $\delta$ 17.50, 20.09, 34.46, 76.51, 123.51, 123.92, 125.25, 125.40, 125.78, 127.83, 128.88, 130.75, 133.83, 139.69; $[\alpha]_D^{21}$ +23.1 (1.00, $CHCl_3$); GC analysis using a 30 m β-Dex 120 chiral column showed it to be 95% ee [175°C (isothermal) $t_R(R)$ 55.58 min and $t_R(S)$ 57.06 min].

*4.3.12. (*R*)-(1-Hydroxy-2-methylpropyl)ferrocene* ***3l***

Yield, 93%; $R_f$ 0.84 ($Et_2O$:$CHCl_3$ = 1:2); mp 32–33°C (lit.[8] mp 33.3–33.5°C); IR (KBr, $cm^{-1}$) 3567, 2963, 1468, 1385, 1042, 1016, 815; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 0.77 (d, 3H, $J = 6.86$), 0.93 (d, 3H, $J = 6.67$), 1.73 (m, 1H), 2.12 (d, 1H, $J = 1.68$), 4.05 (m, 1H), 4.24–4.25 (m, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$), $\delta$ 18.47, 18.69, 34.77, 64.74, 67.50, 67.76, 68.20, 75.11, 93.18; $[\alpha]_D^{21}$

–91.7 (1.01, PhH) {lit.[8] $[\alpha]_D^{24.5}$ +86.1 (*c* 0.99, PhH), 97.7% ee, *S*}; HPLC analysis using a 25 cm Chiralcel OD column showed it to be 98% ee [*i*-PrOH:hexane = 3:97, flow rate 0.35 mL/min, $t_R(R)$ 22.61 min and $t_R(S)$ 24.63 min].

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## References

1. Koch, P.; Nakatani, Y.; Luu, B.; Ourisson, G. *Bull. Soc. Chim. Fr.* **1983**, *7/8* (Part II), 189–194.
2. Okamoto, M.; Tabe, M.; Fujii, T.; Tanaka, T. *Tetrahedron: Asymmetry* **1995**, *6*, 767–778.
3. (a) Moore, K. S.; Wehrli, S.; Roder, H.; Rogers, M.; Forrest Jr., J. N.; McCrimmon, D.; Zasloff, M. *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 1354–1358; (b) Moriarty, R. M.; Enache, L. A.; Kinney, W. A.; Allen, C. S.; Canary, J. W.; Tuladhar, S. M.; Guo, L. *Tetrahedron Lett.* **1995**, *36*, 5139–5142; (c) Rao, M. N.; McGuigan, M. A.; Zhang, X.; Shaked, Z.; Kinney, W. A.; Bulliard, M.; Laboue, B.; Lee, N. *J. Org. Chem.* **1997**, *62*, 4541–4545.
4. (a) Soai, K.; Shibata, T. *J. Synth. Org. Chem. Jpn.* **1997**, *55*, 994–1005, and references cited therein; (b) Shibata, T.; Yonekudo, S.; Soai, K. *Angew. Chem., Int. Ed.* **1999**, *38*, 659–661.
5. In a separate experiment, we carried out the CBS oxazaborolidine-catalyzed borane reduction[6] of *n*-hexyl isopropyl ketone and isobutyrophenone. From the reaction, we obtained the corresponding isopropyl carbinols having 6% ee and 21% ee, respectively.
6. For a review, see: (a) Corey, E. J.; Helal, C. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 1986–2012; (b) Itsuno, S. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. 1, Chapter 6.4, pp. 289–315.
7. For a recent review, see: Soai, K. Shibata, T. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. 2, Chapter 26.1, pp. 911–922; For earlier reviews, see: (a) Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833–856, and references cited therein; (b) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49–69; (c) Noyori, R.; Kitamura, M. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer-Verlag, 1989; pp. 115–198; (d) Knochel, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press, 1991; pp. 211–229; For recent works, see: (e) Reddy, K. S.; Solà, L.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1999**, *64*, 3969–3974; (f) Ding, K.; Ishii, A.; Mikami, K. *Angew. Chem., Int. Ed.* **1999**, *38*, 497–501; (g) Lawrence, C. F.; Nayak, S. K.; Thijs, L.; Zwanenburg, B. *Synlett* **1999**, 1571–1572; (h) Bolm, C.; Muñiz-Fernández, K.; Seger, A.; Raabe, G.; Günther, K. *J. Org. Chem.* **1998**, *63*, 7860–7867; (i) Cho, B. T.; Chun, Y. S. *Tetrahedron: Asymmetry* **1998**, *9*, 1489–1492; (j) Huang, W.-S.; Hu, Q.-S.; Pu, L. *J. Org. Chem.* **1998**, *63*, 1364–1365.
8. Soai, K.; Hayase, T.; Takai, K.; Sugiyama, T. *J. Org. Chem.* **1994**, *59*, 7908–7909.
9. Cho, B. T.; Kim, N. *J. Chem. Soc., Perkin Trans 1.* **1996**, 2901–2907.
10. (a) Matsumoto, Y.; Ohno, A.; Lu, S.; Hayashi, T.; Oguni, N.; Hayashi, M. *Tetrahedron: Asymmetry* **1993**, *4*, 1763–1766. (b) Sawamura, M.; Ito, Y. *Chem. Rev.* **1992**, *92*, 857–871.
11. MacLeod, R.; Welch, F. J.; Mosher, M. S. *J. Am. Chem. Soc.* **1960**, *82*, 876–880.
12. (a) Sih, C. J.; Chen, C.-S. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 570–578. (b) Brown, H. C.; Park, W. S.; Cho, B. T.; Ramachandran, P. V. *J. Org. Chem.* **1987**, *52*, 5406–5412; Erratum: *J. Org. Chem.* **1988**, *53*, 3396, and references cited therein.
13. Rathke, M. W.; Yu, H. *J. Org. Chem.* **1972**, *37*, 1732.
14. *Beilsteins Handbuch Organischen Chemie* **6**, **EIII**, 125.