Supporting Information

Chiral Amplification Based on Enantioselective Dual Phase Distribution of a Scalemic Bisoxazolidine Catalyst

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1. Synthetic Procedures

Alkylation products were purified by column chromatography on silica gel (particle size 32-63 μm) as indicated below. Liquid aldehydes were treated with K_2CO_3 and purified by distillation. Solid aldehydes were purified by chromatography on silica column and freeze-dried prior to use. ^1H and ^{13}C NMR spectra were collected on a 300 MHz NMR spectrometer.

Synthesis and Characterization of Bisoxazolidine **1**¹

A mixture of (1*R*,2*S*)-*cis*-1-aminoindan-2-ol (5 g, 33.6 mmol) and 1,2-cyclohexanedione (1.83 g, 16.3 mmol) was refluxed in toluene using a Dean-Stark trap in the presence of catalytic amounts of formic acid until formation of water was completed. After cooling to room temperature, the solvent was removed under reduced pressure. Crystallization of the crude residue from acetonitrile and methylene chloride gave 5.5 g of (+)-**1** as a white powder (14.5 mmol, 90%). ^1H NMR (300 MHz, CDCl_3) δ = 0.87 (d, J = 12.0 Hz, 2H), 1.26-1.46 (m, 6H), 2.83 (bs, 2H), 3.13 (d, J = 2.9 Hz, 4H), 4.69-4.74 (m, 2H), 5.01 (d, J = 5.3 Hz, 2H), 7.17-7.26 (m, 6H), 7.37-7.43 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ = 23.9, 37.2, 39.6, 69.9, 81.9, 102.1, 125.9, 126.0, 127.7, 128.6, 141.8, 144.6. Anal. Calcd $\text{C}_{24}\text{H}_{26}\text{N}_2\text{O}_2$: C, 76.98; H, 7.00; N, 7.48; Found: C, 76.66; H, 6.86; N, 7.40. The specific rotation of the enantiomers of bisoxazolidine **1** was determined by polarimetry as $[\alpha]_{589}^{26.5} = +65.2$ for (1*R*,2*S*)-aminoindanol-derived **1**, c = 1.0 g/100 mL anhydrous CHCl_3 and $[\alpha]_{589}^{26.5} = -65.7$ in the case of (1*S*,2*R*)-aminoindanol-derived **1**, c = 1.0 g/100 mL anhydrous CHCl_3 .

A crystal was obtained by slow evaporation of a solution containing scalemic bisoxazolidine in toluene and hexanes (1:4 v/v). Crystal data for the racemic single crystal: $C_{24}H_{26}N_2O_2$, $M = 374.47$, $0.50 \times 0.50 \times 0.50 \text{ mm}^3$, monoclinic, space group $P2_1/c$, $a = 5.6854(3) \text{ \AA}$, $b = 27.5579(17) \text{ \AA}$, $c = 12.2702(7) \text{ \AA}$, $\beta = 101.4130(10)^\circ$, $V = 1884.45(19) \text{ \AA}^3$, $Z = 4$, $D_c = 1.320 \text{ g/cm}^3$, $F_{000} = 1600$, SMART platform CCD, Siemens/Bruker, MoK α radiation, $\lambda = 0.71073 \text{ \AA}$, $T = 173(2) \text{ K}$, $2\theta_{\text{max}} = 56.7^\circ$, 17221 reflections collected, 4561 unique ($R_{\text{int}} = 0.0285$). Final $GooF = 1.026$, $R_I = 0.0388$, $wR2 = 0.0954$, R indices based on 3615 reflections with $I > 2\sigma(I)$ (refinement on F^2), 261 parameters, 0 restraints. Lp and absorption corrections applied, $\mu = 0.084 \text{ mm}^{-1}$. Data were integrated with the Siemens SAINT program and corrected for the affects of absorption using SADABS. The structures were solved by direct methods and refined with full-matrix least-square analysis using SHELX-97-2 software. Non-hydrogen atoms were refined with anisotropic displacement parameters and all hydrogen atoms were placed in calculated positions and refined with a riding model.

Procedure for Enantioselective Addition of Diethylzinc to Aldehydes

To a solution of the catalyst (7.0 mg, 0.019 mmol) in 0.5 mL of anhydrous toluene was added Et_2Zn (2.8 mmol, 1 M in hexanes) at room temperature. After stirring for 30 minutes, the aldehyde (0.94 mmol) was added at once. Upon completion of the reaction, the mixture was treated with saturated NH_4Cl solution and extracted with CH_2Cl_2 . The combined organic layers were dried over anhydrous MgSO_4 and solvents were removed

under reduced pressure. Flash chromatography (SiO₂, 5-15% EtOAc in hexanes) gave pure secondary alcohols. The enantiomeric excess was determined by chiral GC and HPLC as indicated below. The purity of aldehydes proved important to yield and enantioselectivity. For example, when freshly distilled benzaldehyde **2a** was employed in the reaction, 1-phenylpropanol, **3a**, was obtained in 99% yield and 95% ee. However, **3a** was obtained in 91% yield and 78% when nondistilled **2a** was used.

Procedure for Enantioselective Addition of Dimethylzinc to Aldehydes

To a solution of the catalyst (17.5 mg, 0.047 mmol) in 0.5 mL of anhydrous toluene was added Me₂Zn (2.8 mmol, 1 M in heptane) at room temperature. After stirring for 30 minutes, the aldehyde (0.94 mmol) was added at once. Upon completion of the reaction, the mixture was treated with saturated NH₄Cl solution and extracted with CH₂Cl₂. The combined organic layers were dried over anhydrous MgSO₄ and removed under reduced pressure. 1-Arylethanol were isolated by flash chromatography (SiO₂, 5-15% EtOAc in hexanes) and the enantiomeric excess was determined by chiral HPLC, vide infra.

2. Analysis of Nonlinear Effects and Mechanistic Studies

a) Ethylation

To a solution of scalemic **1** (7.0 mg, 0.019 mmol, (+)-**1** in excess) in anhydrous toluene was added Et₂Zn (2.8 mmol, 1 M in hexanes) at room temperature. After stirring for 30 minutes, formation of a white precipitate was observed and benzaldehyde, **2** (100 mg, 0.94 mmol) was added at once. Upon completion of the reaction, the mixture was treated with saturated NH₄Cl solution and extracted with CH₂Cl₂. The combined organic layers were dried over anhydrous MgSO₄ and removed under reduced pressure. Flash chromatography (SiO₂, 5% EtOAc in hexanes) gave 1-phenylpropanol, **3**. The enantiomeric excess was determined by chiral HPLC on Chiralcel OD, hexanes:EtOH = 97:3, t₁ = 7.9 min, t₂ = 9.2 min, α = 1.27.

entry	%ee of 1	%ee of 3	yield of 3 (%)
1	25	58	92
2	50	84	96
3	75	92	94
4	100	96	99

The reaction was carried out as described above and no precipitation was observed. The enantiomeric excess was determined by chiral HPLC on Chiralcel OD, hexanes:EtOH = 97:3.

entry	%ee of 1	%ee of 3	yield of 3 (%)
1	25	14	94
2	50	35	98
3	75	55	98
4	100	80	99

b) Methylation

To a solution of scalemic **1** (17.5 mg, 0.047 mmol, (+)-**1** in excess) in anhydrous toluene was added Me₂Zn (2.8 mmol, 1 M in hexanes) at room temperature. After stirring for 30 minutes, formation of a white precipitate was observed and benzaldehyde, **2** (100 mg, 0.94 mmol) was added at once. Upon completion of the reaction, the mixture was treated with saturated NH₄Cl solution and extracted with CH₂Cl₂. The combined organic layers were dried over anhydrous MgSO₄ and removed under reduced pressure. 1-Phenylethanol, **4**, was isolated by flash chromatography (SiO₂, 5% EtOAc in hexanes). The enantiomeric excess was determined by chiral GC on octakis(6-*O*-methyl-2,3-di-*O*-pentyl)- γ -cyclodextrin, 70-120 °C, 5 °C/min, t₁ = 17.6 min, t₂ = 17.9 min.

entry	%ee of 1	%ee of 4	yield of 4 (%)
1	25	32	77
2	50	57	82
3	75	78	88
4	100	88	92

c) Alkynylation

Phenylacetylene (2.8 mmol) was added to a mixture of scalemic **1** (35 mg, 0.094 mmol, 10 mol%, (+)-**1** in excess) and Me₂Zn (2.8 mmol, 1 M in heptane) in a solution of 2.8 mL of heptane and 0.5 mL of toluene at -4.0 °C. After 10 minutes, 100 mg (0.94 mmol) of aldehyde **2** was added. Upon completion of the reaction, the heterogeneous mixture was treated with saturated NH₄Cl solution and extracted with CH₂Cl₂. The combined organic

layers were dried over anhydrous MgSO₄ and solvents were removed under reduced pressure. Flash chromatography (SiO₂, 10% ethyl acetate in hexanes) afforded the pure propargylic alcohol **5**. The enantiomeric excess was determined by chiral HPLC on Chiralcel OD, hexanes:EtOH = 92:8, t₁ = 10.2 min, t₂ = 12.4 min, α = 2.14.

entry	%ee of 1	%ee of 5	yield of 5 (%)
1	25	37	60
2	50	69	72
3	75	84	87
4	100	93	89

d) Analysis of the Precipitate Formed From a Solution of Scalemic **1 in Toluene and Hexanes (1:4 v/v)**

Bisoxazolidine (+)-**1** (100 mg, 50% ee) was added to 10 mL of a solution consisting of toluene and hexanes (1:4 v/v). The mixture was stirred at room temperature for 12 hours. The precipitate formed was isolated by filtration and washed 3 times with small portions of hexanes. After the solid was dried under vacuum, gravimetric analysis revealed that 47 mg (47%) of **1** was recovered. Removal of the solvents from the filtrate gave 53 mg of **1** (53%). Each residue was hydrolyzed, converted to carbamate **7**, and analyzed by chiral HPLC using the method described below. The ee of the crystalline material corresponding to 47% of the originally employed bisoxazolidine was determined as 6% and chromatographic analysis of the catalyst recovered from the supernatant (the remaining 53% yield) revealed 89% ee.

To prove that the observed NLE's result from the low solubility of the racemic ligand and is not affected by the solubility of a ligand/organozinc adduct, we prepared two solutions containing either enantiopure (+)-**1** or (-)-**1** and 150 times excess of diethylzinc in toluene and hexanes (1:4 v/v):

Solution A: (+)-**1** (120 mg, 0.33 mmol) and Et₂Zn (48 mmol).

Solution B: (-)-**1** (40 mg, 0.11 mmol) and Et₂Zn (16 mmol).

Upon mixing of the clear solutions, thus generating a 3:1 ratio of the enantiomers, formation of a precipitate was observed within 5 minutes. After 30 minutes, 54 mg of a white precipitate was collected and analyzed by NMR spectroscopy. We found that the precipitate did only contain **1** and there was not trace of Et₂Zn. The ligand was then hydrolyzed and derivatized for HPLC analysis as shown below. As expected, the HPLC enantioseparation of *N*-(*tert*-butoxycarbonyl)-1-aminoindan-2-ol, **7**, showed that the sample was nearly racemic (4.5% ee).

e) Derivatization of **1 for HPLC Analysis**

The recovered catalyst (100 mg, 0.27 mmol) was stirred in 3 M HCl for 24 h. Then, the mixture was treated with 10% Na₂CO₃ until it was slightly basic. The aqueous layer was extracted several times with CH₂Cl₂ and the combined organic layers were dried over anhydrous MgSO₄. Solvents were removed *in vacuo* and the residue was dissolved in THF:methanol (6:1). To this solution, NaHCO₃ (27 mg, 0.27 mmol) and di-*tert*-butyl

dicarbonate (59 mg, 0.27 mmol) were added. The mixture was stirred at 25 °C for 12 hours until deionized water was added and the mixture was extracted with CHCl₃. The combined organic layers were dried over anhydrous MgSO₄ and solvents were removed under reduced pressure. Flash column chromatography (10% EtOAc in hexanes) furnished *N*-(*tert*-butoxycarbonyl)-1-aminoindan-2-ol, **7**, as a white solid (65 mg, 0.26 mmol, 96%). ¹H NMR δ = 1.51 (s, 9H), 2.24 (d, *J* = 5.0 Hz, 1H), 2.91 (dd, *J* = 16.5 Hz, 2.2 Hz, 1H), 3.12 (dd, *J* = 16.5 Hz, 5.2 Hz, 1H), 4.58 (m, 1H), 5.06 (bs, 1H), 5.14 (bs, 1H), 7.20-7.31 (m, 4H), ¹³C NMR: 29.5, 40.1, 59.6, 74.3, 80.6, 125.1, 125.9, 127.7, 128.7, 140.4, 141.4, 156.8. The enantiomers of **7** were resolved by HPLC on Chiralcel AD, hexanes:*i*-PrOH = 92:8, *t*₁ = 10.6 min, *t*₂ = 13.8 min, α = 1.42.

f) Mechanistic Studies

To prove that the bisoxazolidine is the actual catalyst and not a precatalyst, the alkylation of benzaldehyde was conducted with stoichiometric amounts of **1** and diethylzinc. It is well known that amino alcohols undergo deprotonation with Et₂Zn to form a catalytically active species. Accordingly, no reaction occurs when these precatalysts are used in the presence of one equivalent of Et₂Zn (precatalyst:Et₂Zn = 1:1), that is, amino alcohol-catalyzed reactions require the use of excess of organozinc reagent. Employing **1**, Et₂Zn and benzaldehyde in a ratio of 1:1:1 and 0.5:1:1 (to afford an equimolar ratio based on each *N,O*-ketal group of **1**), we observed formation of alcohol **3a** in 95-97% yield and 96-97% ee, see below. Importantly, no conversion would have occurred in the presence of amino alcohols under these conditions (or if **1** was a precatalyst that required deprotonation to generate a catalytically active species) because the whole amount of Et₂Zn would have been consumed to form the actual catalyst.

A) To a solution of **1** (175.0 mg, 0.47 mmol) in 1.0 mL of anhydrous toluene was added Et₂Zn (0.94 mmol, 1 M in hexanes) at room temperature. After stirring for 30 minutes, **2a** (100 mg, 0.94 mmol) was added at once and the reaction was continued for 2 hours. The mixture was treated with saturated NH₄Cl solution and extracted with CH₂Cl₂. The combined organic layers were dried over anhydrous MgSO₄ and solvents were removed

under reduced pressure. Flash chromatography (SiO₂, 5% EtOAc in hexanes) gave pure **3a** (97%, 96%ee).

B) To a solution of **1** (350.0 mg, 0.94 mmol) in 1.0 mL of anhydrous toluene was added Et₂Zn (0.94 mmol, 1 M in hexanes) at room temperature. After stirring for 30 minutes, **2a** (100 mg, 0.94 mmol) was added at once and the reaction was continued for 2 hours. The mixture was treated with saturated NH₄Cl solution and extracted with CH₂Cl₂. The combined organic layers were dried over anhydrous MgSO₄ and solvents were removed under reduced pressure. Flash chromatography (SiO₂, 5% EtOAc in hexanes) gave pure **3a** (95%, 97%ee).

These results clearly show that **1** is not a precatalyst but catalyzes the alkylation of aldehydes in its free form. Accordingly, NMR analysis of a mixture of **1** and Me₂Zn, which was used due the well-known lower fluxionality of dimethylzinc adducts compared to diethylzinc analogues, revealed that complexation occurs rapidly but without deprotonation. The significant line-broadening observed reveals formation of an organozinc species and integration shows that this occurs without deprotonation. Despite the use of Me₂Zn, only averaged signals (even when NMR analysis was performed in less than 30 minutes after formation of a mixture of **1** and Me₂Zn) were detected which prevented further equilibration studies. The chemical shift of free Me₂Zn is -0.50 ppm which changes to -0.55 ppm in the presence of **1**.

NMR Spectrum of (+)-**1** and 2 equivalents of ZnMe₂ after 30 minutes in CDCl₃ using toluene as internal standard.

NMR Spectrum of (+)-1 and 2 equivalents of ZnMe₂ after 90 minutes in CDCl₃ using toluene as internal standard.

3. NMR Spectroscopic and Chromatographic Characterization of Alkylation Products

1-Phenylpropanol (**3a**)²

Chromatographic purification (hexanes:ethyl acetate = 95: 5) gave 126 mg (0.93 mmol, 99%, 96% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.83 (t, J = 7.6 Hz, 3H), 1.57-1.89 (m, 2H), 2.88 (bs, 1H), 4.43 (t, J = 6.6 Hz, 1H), 7.20-7.27 (m, 5H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.7, 32.3, 76.3, 126.6, 127.8, 128.8, 145.2.

The ee was determined by HPLC on Chiralcel OD, hexanes:EtOH = 97:3, t_1 = 7.9 min, t_2 = 9.2 min, α = 1.27.

1-(4-Methoxyphenyl)propanol (**3b**)²

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 154 mg (0.93 mmol, 99%, 96% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.81 (t, J = 7.3 Hz, 3H), 1.56-1.90 (m, 2H), 1.96 (bs, 1H), 3.71 (s, 3H), 4.44 (t, J = 6.8 Hz, 1H), 6.79 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 8.8 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ = 9.2, 30.7, 54.2, 74.6, 112.7, 126.2, 135.8, 157.9.

The ee was determined by GC on octakis(6-*O*-methyl-2,3-di-*O*-pentyl)- γ -cyclodextrin, 90-110 °C, 7 °C/min, t_1 = 59.1 min, t_2 = 61.2 min, α = 1.04.

1-(3-Methoxyphenyl)propanol (**3c**)⁴

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 144 mg (0.86 mmol, 92%, 91% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.87 (t, J = 7.3 Hz, 3H), 1.61-1.79 (m, 2H), 2.58 (bs, 1H), 3.75 (s, 3H), 4.50 (t, J = 6.6 Hz, 1H), 6.76 (ddd, J = 8.3 Hz, 2.4 Hz, 1.0 Hz, 1H), 6.85-6.87 (m, 2H), 7.21 (dd, J = 8.3 Hz, 8.3 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.4, 32.1, 55.4, 76.0, 111.7, 113.1, 118.7, 129.6, 146.7, 159.9.

The ee was determined by HPLC on Chiralpak AD, hexanes:*i*-PrOH = 97:3, t_1 = 20.9 min, t_2 = 22.3 min, α = 1.08.

1-(4-Cyanophenyl)propanol (**3d**)⁴

Chromatographic purification (hexanes:ethyl acetate = 85:15) gave 137 mg (0.86 mmol, 91%, 90% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.92 (t, J = 7.3 Hz, 3H), 1.70-1.79 (m, 2H), 2.55 (d, J = 3.4 Hz, 1H), 4.82 (m, 1H), 7.44 (d, J = 8.3 Hz, 2H), 7.61 (d, J = 8.3 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.1, 32.5, 75.2, 111.1, 119.2, 126.9, 132.4, 150.4.

The ee was determined by HPLC on Chiralpak AD, hexanes:*i*-PrOH = 97:3, t_1 = 32.2 min, t_2 = 34.6 min, α = 1.08.

1-(3-Cyanophenyl)propanol (3e)⁴

Chromatographic purification (hexanes:ethyl acetate = 85:15) gave 145 mg (0.90 mmol, 96%, 92% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.91 (t, J = 7.3 Hz, 3H), 1.69-1.78 (m, 2H), 2.80 (d, J = 3.4 Hz, 1H), 4.63 (m, 1H), 7.41-7.63 (m, 4H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.1, 32.3, 74.9, 112.4, 119.2, 129.4, 129.9, 130.8, 131.2, 146.5.

The ee was determined by HPLC on Chiralpak AD, hexanes:*i*-PrOH = 95:5, t_1 = 17.4 min, t_2 = 18.9 min, α = 1.10.

1-(1-Naphthyl)propanol (3f)²

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 149 mg (0.82 mmol, 87%, 78% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.94 (t, J = 7.3 Hz, 3H), 1.78-2.01 (m, 2H), 2.17 (bs, 1H), 5.12 (dd, J = 5.1 Hz, 7.6 Hz, 1H), 7.39-7.45 (m, 3H), 7.53 (d, J = 6.6 Hz, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.67-7.82 (m, 1H), 7.95-8.02 (m, 1H). ¹³C NMR (75 MHz, CDCl₃) δ = 11.1, 31.7, 73.1, 123.5, 123.9, 126.0, 126.1, 126.5, 128.4, 129.5, 131.1, 134.4, 140.8.

The ee was determined by HPLC on Chiralcel OD, hexanes:EtOH = 90:10, t_1 = 7.0 min, t_2 = 11.0 min, α = 2.00.

1-(2-Naphthyl)propanol (3g)³

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 157 mg (0.86 mmol, 92%, 91% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.86 (t, J = 7.3 Hz, 3H), 1.62-1.95 (m, 2H), 2.47 (bs, 1H), 4.62 (t, J = 6.6 Hz, 1H), 7.36-7.43 (m, 3H), 7.66 (s, 1H), 7.73-7.78 (m, 3H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.7, 32.3, 76.6, 124.8, 125.3, 126.3, 126.6, 128.3, 128.5, 128.7, 133.5, 133.8, 142.5.

The ee was determined by HPLC on Chiralcel OD, hexanes:EtOH = 95:5, t_1 = 12.0 min, t_2 = 14.0 min, α = 1.22.

1-(4-Tolyl)propanol (**3h**)²

Chromatographic purification (hexanes:ethyl acetate = 95:5) gave 140 mg (0.93 mmol, 99%, 86% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.85 (t, J = 7.3 Hz, 3H), 1.60-1.92 (m, 2H), 2.31 (s, 3H), 2.46 (bs, 1H), 4.45 (t, J = 6.8 Hz, 1H), 7.10 (d, J = 8.6 Hz, 2H), 7.16 (d, J = 8.6 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.7, 21.7, 32.3, 76.3, 126.5, 129.6, 137.5, 142.3.

The ee was determined by GC on octakis(6-*O*-methyl-2,3-di-*O*-pentyl)- γ -cyclodextrin, 70-110 °C, 7 °C/min, t_1 = 22.1 min, t_2 = 23.7 min, α = 1.06.

1-(4-Chlorophenyl)propanol (**3i**)²

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 155 mg (0.91 mmol, 97%, 86% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.87 (t, J = 7.3 Hz, 3H), 1.60-1.92 (m, 2H), 2.35 (d, J = 2.6 Hz, 1H), 4.47 (dt, J = 2.6 Hz, 6.6 Hz, 1H), 7.21-7.30 (m, 4H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.6, 32.5, 75.8, 128.0, 129.1, 133.6, 143.6.

The ee was determined by HPLC on Chiralcel OB-H, hexanes:EtOH = 98:2, t_1 = 5.1 min, t_2 = 6.8 min, α = 1.62.

1-(4-Fluorophenyl)propanol (**3j**)²

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 138 mg (0.89 mmol, 95%, 94% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.84 (t, J = 7.6 Hz, 3H), 1.59-1.79 (m, 2H), 2.76 (bs, 1H), 4.48 (t, J = 6.6 Hz, 1H), 6.98 (dd, J = 8.8 Hz, $J_{H,F}$ = 8.8 Hz, 2H), 7.24 (dd, J = 8.8 Hz, $J_{H,F}$ = 5.1 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.3, 32.2, 75.5, 115.3 (d, $J_{C,F}$ = 21.2 Hz), 127.8 (d, $J_{C,F}$ = 8.1, Hz), 140.5 (d, $J_{C,F}$ = 3.0 Hz), 162.3 (d, $J_{C,F}$ = 244.8 Hz).

The ee was determined by HPLC on Chiralpak AD, hexanes:*i*-PrOH = 97:3, t_1 = 8.1 min, t_2 = 9.0 min, α = 1.18.

1-(3-Thienyl)propanol (**3k**)⁵

Chromatographic purification (hexanes:ethyl acetate = 85:15) gave 132 mg (0.93 mmol, 99%, 71% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.88 (t, J = 7.3 Hz, 3H), 1.70-1.79 (m, 2H), 2.62 (bs, 1H), 4.60 (t, J = 6.6 Hz, 1H), 7.01 (d, J = 5.4 Hz, 1H), 7.11 (m, 1H), 7.25 (m, 1H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.3, 31.4, 72.2, 121.0, 126.0, 126.2, 146.4.

The ee was determined by HPLC on Chiralpak AD, hexanes:EtOH = 98:2, t_1 = 14.3 min, t_2 = 15.5 min, α = 1.11.

1-Cyclohexylpropanol (**3l**)²

Chromatographic purification (hexanes:ethyl acetate = 95:5) gave 123 mg (0.86 mmol, 92%, 90% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.92-1.80 (m, 16H), 3.24 (m, 1H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.8, 26.8, 26.9, 27.1, 27.3, 28.4, 29.8, 43.7, 78.0.

The ee was determined by GC on octakis(6-*O*-methyl-2,3-di-*O*-pentyl)- γ -cyclodextrin, 80-90 °C, 1 °C/min, t_1 = 19.8 min, t_2 = 20.3 min, α = 1.03.

1-Phenyl-3-pentanol (**3m**)⁶

Chromatographic purification (hexanes:ethyl acetate = 85:15) gave 128 mg (0.78 mmol, 83%, 35% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 1.03 (t, J = 7.6 Hz, 3H), 1.43-1.62 (m, 2H), 1.68-1.94 (m, 2H), 2.26 (bs, 1H), 2.62-2.98 (m, 2H), 3.61 (m, 1H), 7.27-7.40 (m, 5H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.5, 30.8, 32.6, 39.1, 73.1, 126.3, 128.9, 129.0, 142.9.

The ee was determined by HPLC on Chiralcel OD, hexanes:2-propanol = 95:5, t_1 = 10.5 min, t_2 = 15.0 min, α = 1.53.

1-Phenyl-pent-1-en-3-ol (**3n**)⁷

Chromatographic purification (hexanes:ethyl acetate = 85:15) gave 148 mg (0.91 mmol, 97%, 40% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.94 (t, J = 7.3 Hz, 3H), 1.52-1.65 (m, 2H), 2.28 (bs, 1H), 4.16 (m, 1H), 6.18 (dd, J = 6.8 Hz, 16.4 Hz, 1H), 6.53 (d, J = 16.4 Hz, 1H), 7.18-7.36 (m, 5H). ¹³C NMR (75 MHz, CDCl₃) δ = 10.4, 30.8, 74.9, 127.0, 128.1, 129.1, 130.9, 132.9, 137.4.

The ee was determined by HPLC on Chiralcel OD, hexanes:2-propanol = 85:15, t_1 = 11.2 min, t_2 = 14.9 min, α = 1.40.

1-Phenylethanol (**4a**)¹⁰

Chromatographic purification (hexanes:ethyl acetate = 95:5) gave 106 mg (0.86 mmol, 92%, 88% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 1.42 (d, J = 6.3 Hz, 3H), 2.84 (bs, 1H), 4.77 (q, J = 6.3 Hz, 1H), 7.23-7.31 (m, 5H). ¹³C NMR (75 MHz, CDCl₃) δ = 25.7, 70.7, 126.0, 127.9, 129.0, 146.4.

The ee was determined by HPLC on Chiralpak AD, hexanes:EtOH = 98:2, t_1 = 9.7 min, t_2 = 10.7 min, α = 1.15.

1-(3-Methoxyphenyl)ethanol (**4b**)¹⁰

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 124 mg (0.82 mmol, 87%, 82% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 1.42 (d, J = 6.4 Hz, 3H), 2.78 (bs, 1H), 3.75 (s, 3H), 4.77 (q, J = 6.4 Hz, 1H), 6.77 (ddd, J = 8.1 Hz, 2.7 Hz, 1.0 Hz, 1H), 6.88-6.90 (m, 2H), 7.22 (dd, J = 8.1 Hz, 8.1 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ = 25.7, 55.7, 70.7, 111.5, 113.3, 118.3, 130.0, 148.3, 160.2.

The ee was determined by HPLC on Chiralpak AD, hexanes:EtOH = 94:6, t_1 = 9.9 min, t_2 = 10.6 min, α = 1.10.

1-(4-Cyanophenyl)ethanol (**4c**)¹²

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 113 mg (0.77 mmol, 82%, 90% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 1.47 (d, J = 6.6 Hz, 3H), 2.84 (bs, 1H), 4.93 (q, J = 6.6 Hz, 1H), 7.47 (d, J = 8.1 Hz, 2H), 7.58 (d, J = 8.1 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ = 25.9, 70.0, 111.3, 119.5, 126.7, 132.8, 151.9.

The ee was determined by HPLC on Chiralpak AD, hexanes:*i*-PrOH = 95:5, t_1 = 25.7 min, t_2 = 28.2 min, α = 1.11.

1-(1-Naphthyl)ethanol (**4d**)¹¹

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 142 mg (0.83 mmol, 86%, 92% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 1.57 (d, J = 6.3 Hz, 3H), 2.42 (bs, 1H), 5.52 (q, J = 6.3 Hz, 1H), 7.37-7.48 (m, 3H), 7.58 (d, J = 7.1 Hz, 1H), 7.71 (d, J = 8.3 Hz, 1H), 7.82 (m, 1H), 8.01 (m, 1H). ¹³C NMR (75 MHz, CDCl₃) δ = 24.9, 67.5, 122.6, 123.8, 126.1, 126.6, 128.4, 129.5, 130.8, 133.4, 134.4, 142.0.

The ee was determined by HPLC on Chiralpak AD, hexanes:EtOH = 97:3, t_1 = 10.9 min, t_2 = 11.7 min, α = 1.26.

1-(2-Naphthyl)ethanol (**4e**)⁸

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 155 mg (0.90 mmol, 96%, 91% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 1.50 (d, J = 6.4 Hz, 3H), 2.46 (bs, 1H), 4.94 (q, J = 6.4 Hz, 1H), 7.39-7.45 (m, 3H), 7.71-7.79 (m, 4H). ¹³C NMR (75 MHz, CDCl₃) δ = 24.0, 69.3, 122.7, 122.8, 124.7, 125.0, 126.6, 126.9, 127.2, 131.8, 132.2, 143.8.

The ee was determined by HPLC on Chiralpak AD, hexanes:*i*-PrOH = 96:4, t_1 = 13.5 min, t_2 = 14.6 min, α = 1.10.

1-(4-Fluorophenyl)ethanol (**4f**)⁹

Chromatographic purification (hexanes:ethyl acetate = 85:15) gave 125 mg (0.89 mmol, 95%, 92% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 1.42 (d, J = 6.4 Hz, 3H), 2.75 (bs, 1H), 4.80 (q, J = 6.4 Hz, 1H), 7.00 (dd, J = 8.8 Hz, $J_{\text{H,F}}$ = 8.8 Hz, 2H), 7.28 (dd, J = 8.8 Hz, $J_{\text{H,F}}$ = 5.5 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ = 25.8, 70.2, 115.8 (d, $J_{\text{C,F}}$ = 21.2 Hz), 127.7 (d, $J_{\text{C,F}}$ = 7.6 Hz), 142.2 (d, $J_{\text{C,F}}$ = 3.0 Hz), 162.7 (d, $J_{\text{C,F}}$ = 244.7 Hz).

The ee was determined by HPLC on Chiralpak AD, hexanes:*i*-PrOH = 97.5:2.5, t_1 = 19.0 min, t_2 = 20.1 min, α = 1.07.

1-(4-Bromophenyl)ethanol (**4g**)¹³

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 174 mg (0.87 mmol, 93%, 89% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 1.42 (d, J = 6.6 Hz, 3H), 2.39 (bs, 1H), 4.80 (q, J = 6.6 Hz, 1H), 7.47 (d, J = 8.5 Hz, 2H), 7.58 (d, J = 8.5 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ = 25.5, 69.9, 121.4, 127.4, 131.8, 145.0.

The ee was determined by HPLC on Chiralpak AD, hexanes:*i*-PrOH = 98:2, t_1 = 18.7 min, t_2 = 20.1 min, α = 1.09.

1-Cyclohexylethanol (**4h**)¹⁴

Chromatographic purification (hexanes:ethyl acetate = 90:10) gave 106 mg (0.83 mmol, 88%, 81% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 0.82-1.27 (m, 10H), 1.60-1.87 (m, 4H), 2.61 (bs, 1H), 3.48 (m, 1H). ¹³C NMR (75 MHz, CDCl₃) δ = 20.7, 26.7, 26.8, 27.0, 29.0, 29.1, 45.6, 72.4.

The ee was determined by GC on octakis(6-*O*-methyl-2,3-di-*O*-pentyl)- γ -cyclodextrin, 55 °C, t_1 = 35.2 min, t_2 = 38.4 min, α = 1.09.

4-Phenyl-2-butanol (**4i**)¹⁵

Chromatographic purification (hexanes:ethyl acetate = 85:15) gave 125 mg (0.84 mmol, 89%, 33% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 1.19 (d, J = 6.1 Hz, 3H), 1.62-1.86 (m, 2H), 2.43 (bs, 1H), 2.60-2.89 (m, 2H), 3.77 (m, 1H), 7.13-7.29 (m, 5H). ¹³C NMR (75 MHz, CDCl₃) δ = 24.1, 32.7, 41.4, 67.9, 126.4, 128.9, 129.0, 142.7.

The ee was determined by HPLC on Chiralcel OD, hexanes:EtOH = 95:5, t_1 = 10.8 min, t_2 = 13.5 min, α = 1.31.

4-Phenyl-but-3-en-2-ol (**4j**)¹⁶

Chromatographic purification (hexanes:ethyl acetate = 85:15) gave 115 mg (0.88 mmol, 94%, 41% ee) of a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ = 1.33 (d, J = 6.1 Hz, 3H), 2.81 (bs, 1H), 4.42 (m, 1H), 6.20 (dd, J = 6.3 Hz, 15.1 Hz, 1H), 6.53 (d, J = 15.1 Hz, 1H), 7.18-7.36 (m, 5H). ¹³C NMR (75 MHz, CDCl₃) δ = 24.0, 69.4, 127.0, 128.4, 129.1, 129.8, 134.2, 137.3.

The ee was determined by HPLC on Chiralcel OD, hexanes:2-propanol = 85:15, t_1 = 7.8 min, t_2 = 10.5 min, α = 1.47.

4. NMR Spectra of Secondary Alcohols

1-Phenylpropanol (3a)

1-(4-Methoxyphenyl)propanol (**3b**)

1-(3-Methoxyphenyl)propanol (**3c**)

1-(4-Cyanophenyl)propanol (**3d**)

1-(3-Cyanophenyl)propanol (**3e**)

1-(1-Naphthyl)propanol (**3f**)

1-(2-Naphthyl)propanol (**3g**)

1-(4-Tolyl)propanol (**3h**)

1-(4-Chlorophenyl)propanol (**3i**)

1-(4-Fluorophenyl)propanol (**3j**)

1-(3-Thienyl)propanol (**3k**)

1-Cyclohexylpropanol (**3I**)

1-Phenyl-3-pentanol (**3m**)

1-Phenyl-pent-1-en-3-ol (**3n**)

1-Phenylethanol (**4a**)

1-(3-Methoxyphenyl)ethanol (**4b**)

1-(4-Cyanophenyl)ethanol (**4c**)

1-(1-Naphthyl)ethanol (**4d**)

1-(2-Naphthyl)ethanol (**4e**)

1-(4-Fluorophenyl)ethanol (**4f**)

1-(4-Bromophenyl)ethanol (**4g**)

1-Cyclohexylethanol (**4h**)

4-Phenyl-2-butanol (**4i**)

4-Phenyl-but-3-en-2-ol (**4j**)

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