Supporting Information

Highly Enantioselective Cyanosilylation of Aldehydes Catalyzed by Novel β–Amino Alcohol-Titanium Complexes

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Contents of the supporting information:

Experimental Section

General Methods. ^1H NMR spectra were recorded in $CDCl_3$ at 300, 400 or 600 MHz. Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR data were collected at 75 or 100 MHz with complete proton decoupling. Chemical shifts are reported in ppm from the TMS with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0). Enantiomeric excesses were determined by chiral GC analysis on Chirasil DEX CB or by chiral HPLC analysis on Chiralcel OD in comparison with the authentic racemates. All aldehydes, TMSCN and substituted salicylaldehydes were purchased and used directly without further purification. Solvents were purified by usual method. CH_2Cl_2 was distilled over CaH_2. Other solvents were dried over Na.

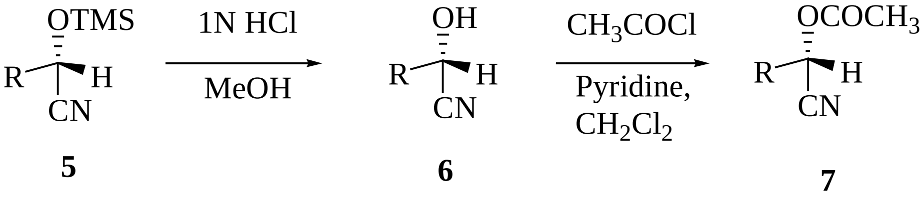
General procedure for preparation of chiral amino-alcohol ligands (1a-j and 2a-c).

A mixture of salicylaldehyde or its derivative (1 mmol) and chiral amino-alcohol (1 mmol) in absolute EtOH was stirred for 36 hours. Then $NaBH_4$ (114 mg, 3 mmol) was directly added in it. After the mixture was stirred for additional several hours, it was quenched by water. The resulting mixture was extracted with CH_2Cl_2, and the organic layer was washed with brine. After drying over anhydrous sodium sulfate. The solvent was removed and the residue was purfied by silica gel column chromatography to afford the title compounds **1a-j** and **2a-c**.

General procedure for asymmetric cyanosilylation of aldehydes.

To a solution of **1b** (4.2 mg, 0.0125 mmol) in CH_2Cl_2 (0.2 mL), Ti(O*i*-Pr)$_4$ (1 M in toluene, 12.5 µL, 0.0125 mmol) was added at room temperature, and then the mixture was stirred at 30˚C for 1 hour under N_2 atmosphere. To this solution, aldehyde (0.25 mmol) was added under –20˚C, followed by the addition of TMSCN (60 µL, 0.5 mmol) and CH_2Cl_2 (0.3 mL). The reaction was monitored by TLC, after the reaction time given in Table 2, the mixture was concentrated and then purified by flash silica gel chromatography to obtain the isolated yield of the corresponding cyanohydrin trimethylsilyl ether.

Derivation of cyanohydrins



The corresponding cyanohydrin trimethylsilyl ether was dissolved in MeOH (2 mL) and then 1N HCl (2 mL) was dropped to the mixture. The mixture was stirred vigorously at room temperature for 4 hours. The aqueous solution was then extracted with CH_2Cl_2, and the combined organic layer was dried with anhydrous sodium sulfate. After evaporating the solvent, the corresponding cyanohydrin was obtained. After measuring the optical rotation, the pure cyanohydrin (10 μL) was converted directly into the corresponding acetate by reaction with two equivalents of acetyl chloride (0.2 mL) and pyridine (0.1 mL) in CH_2Cl_2 (2 mL) at room temperature for 1 hour. The reaction was quenched by water and extracted with CH_2Cl_2, The organic extracts were washed with brine and dried over anhydrous sodium sulfate. Evaporation of solvents and purification of the residue by silica gel chromatography gave the corresponding acetate, which was used for the determination of enantiomeric excess.

Data of Ligands.

(1*R*, 2*S*)-2-(*N*-2'-hydroxyl-benzyl) amino-1, 2-diphenyl-1-ethanol (1a): mp 95-97 ^{o}C; $[\alpha]^{25}_{D}$ +12.7 (*c* 0.40 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.37 (m, 6H), 7.18-7.24 (m, 4H), 7.13 (m, 1H), 6.80 (m, 2H), 6.70 (m, 1H), 4.90 (d, J = 6.4 Hz, 1H), 3.89 (d, J = 6.4 Hz, 1H), 3.81 (d, J = 13.6 Hz, 1H), 3.56 (d, J = 13.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 140.3, 137.6, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 126.8, 122.5, 119.1, 116.4, 68.2, 50.2. HRMS: calculated [M+H] for $C_{21}H_{21}NO_2$ 320.1645, found 320.1642.

(1*R*, 2*S*)-2-(*N*-2'-hydroxyl-3'-methyl-benzyl) amino-1, 2-diphenyl-1-ethanol (1b): mp 72-74 °C; $[\alpha]^{25}_{D}$ +13.6 (*c* 0.40 $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.20-7.38 (m, 10H), 6.70 (m, 1H), 6.60-6.66 (m, 2H), 4.92 (d, *J* = 6.0 Hz, 1H), 4.89 (d, *J* = 6.4 Hz, 1H), 3.80 (d, *J* = 13.6 Hz, 1H), 3.54 (d, *J* = 13.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 140.3, 137.7, 129.9, 128.7, 128.5, 128.4, 128.4, 128.2, 126.8, 126.0, 125.2, 121.9, 118.6, 68.4, 50.3, 15.7. HRMS: calculated [M+H] for $C_{22}H_{23}NO_2$ 334.1802, found 334.1807.

(1*R*, 2*S*)-2-(*N*-2'-hydroxyl-3'-*tert*butyl-benzyl) amino-1, 2-diphenyl-1-ethanol (1c): mp 36-38 °C; $[\alpha]^{25}_{D}$ +6.34 (*c* 4.00 $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.36 (m, 6H), 7.18-7.22 (m, 5H), 6.67 (m, 2H), 6.60-6.66 (m, 2H), 4.94 (d, *J* = 6.0 Hz, 1H), 3.89 (d, *J* = 5.6 Hz, 1H), 3.83 (d, *J* = 13.2 Hz, 1H), 3.57 (d, *J* = 13.6 Hz, 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 140.4, 137.5, 136.8, 128.6, 128.4, 128.4, 128.2, 128.1, 126.7, 126.6, 126.0, 122.8, 118.3, 109.7, 67.9, 50.5, 34.7, 29.5. HRMS: calculated [M+H] for $C_{25}H_{29}NO_2$ 376.2271, found 376.2268.

(1*R*, 2*S*)-2-(*N*-2'-hydroxyl-5'-methoxy-benzyl) amino-1, 2-diphenyl-1-ethanol (1d): mp 144-145°C; $[\alpha]^{25}_{D}$ +10.4 (*c* 0.40 $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.21-7.38 (m, 10H), 6.75 (m, 1H), 6.69-6.71 (m, 2H), 6.38 (m, 1H), 4.93 (d, *J* = 6.2 Hz, 1H), 3.90 (d, *J* = 6.2 Hz, 1H), 3.81 (d, *J* = 13.8 Hz, 1H), 3.68 (s, 3H), 3.54 (d, *J* = 13.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 151.6, 140.4, 137.7, 128.7, 128.5, 128.4, 128.3, 128.2, 126.8, 123.3, 116.8, 114.2, 113.7, 77.7, 68.3, 55.8, 50.4. HRMS: calculated [M+H] for $C_{22}H_{23}NO_3$ 350.1751, found 350.1745.

(1*R*, 2*S*)-2-(*N*-2'-hydroxyl-5'-chloro-benzyl) amino-1, 2-diphenyl-1-ethanol (1e): mp 114-116 °C; $[\alpha]^{25}_{D}$ +14.5 (*c* 0.40 $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 5H), 7.17 (m, 4H), 7.06 (m, 2H), 7.73 (m, 2H), 4.91 (d, *J* = 5.2 Hz, 1H), 3.87 (d, *J* = 4.8 Hz, 1H), 3.77 (d, *J* = 13.6 Hz, 1H), 3.52 (d, *J* = 13.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 140.1, 137.2, 128.7, 128.5, 128.4, 128.4, 128.3, 128.0, 126.7, 123.9, 123.6, 117.7, 68.1, 49.8. HRMS: calculated [M+H] for $C_{21}H_{20}ClNO_2$ 354.1255, found 354.1256.

(1*R*, 2*S*)-2-(*N*-2’-hydroxyl-5’-bromo-benzyl) amino-1, 2-diphenyl-1-ethanol (1f): mp 136-138 ^{o}C; $[\alpha]^{25}_{D}$ +14.8 (*c* 0.40 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 5H), 7.19 (m, 4H), 6.89 (d, 2H), 6.68 (d, 2H), 4.91 (d, *J* = 6.0 Hz, 1H), 3.87 (d, *J* = 6.0 Hz, 1H), 3.78 (d, *J* = 14.0 Hz, 1H), 3.52 (d, *J* = 14.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 140.1, 137.2, 131.3, 130.9, 128.7, 128.5, 128.4, 128.3, 126.8, 124.5, 118.2, 110.8, 68.1, 49.7. HRMS: calculated [M+H] for $C_{21}H_{20}BrNO_2$ 398.0750, found 398.0756.

(1*R*, 2*S*)-2-(*N*-2’-hydroxyl-5’nitro-benzyl) amino-1, 2-diphenyl-1-ethanol (1g): mp 193-194 ^{o}C; $[\alpha]^{25}_{D}$ +1.0 (*c* 0.1 DMSO); ^{1}H NMR (400 MHz, D_6-DMSO) δ 7.91-7.98 (m, 2H), 7.14-7.26 (m, 10H), 6.74 (m, 1H), 4.85 (d, *J* = 5.64 Hz, 1H), 3.86 (d, *J* = 5.64 Hz, 1H), 3.66 (d, *J* = 14.88 Hz, 1H), 3.55 (d, *J* = 14.88 Hz, 1H); ^{13}C NMR (100 MHz, D_6-DMSO) δ 143.2, 139.5, 138.5, 129.2, 128.0, 128.0, 127.5, 127.4, 127.2, 126.0, 125.0, 116.2, 75.8, 67.8, 47.2. HRMS: calculated [M+H] for $C_{21}H_{20}N_2O_4$ 365.1496, found 365.1501.

(1*R*, 2*S*)-2-(*N*-2’-hydroxyl-3’, 5’-di-*tert*butyl-benzyl) amino-1, 2-diphenyl-1-ethanol (1h): mp 52-54 ^{o}C; $[\alpha]^{25}_{D}$ –2.0 (*c* 0.20 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18-7.36 (m, 11H), 6.65 (s, 1H), 4.92 (d, *J* = 6.0 Hz, 1H), 3.88 (d, *J* = 6.4 Hz, 1H), 3.78 (d, *J* = 13.2 Hz, 1H), 3.56 (d, *J* = 13.2 Hz, 1H), 1.41 (s, 9H), 1.21 (s, 9H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 140.5, 137.8, 135.9, 128.6, 128.4, 128.2, 128.1, 126.8, 123.3, 122.9, 122.0, 68.3, 51.1, 34.9, 34.1, 31.6, 29.6. HRMS: calculated [M+H] for $C_{29}H_{37}NO_2$ 432.2897, found 432.2887.

(1*R*, 2*S*)-2-(*N*-2’-hydroxyl-3’, 5’-dibromo-benzyl) amino-1, 2-diphenyl-1-ethanol (1i): mp 55-57 ^{o}C; $[\alpha]^{25}_{D}$ +21.3 (*c* 0.40 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.31 (m, 7H), 7.19 (m, 4H), 6.86 (s, 1H), 4.96 (d, *J* = 6.0 Hz, 1H), 4.85 (d, *J* = 6.0 Hz, 1H), 3.81 (d, *J* = 14.0 Hz, 1H), 3.54 (d, *J* = 14.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 139.9, 136.7, 134.0, 130.1, 128.8, 128.6, 128.5, 128.5, 126.7, 125.2, 111.2, 110.6, 68.2, 49.8. HRMS: calculated [M+H] for $C_{21}H_{19}Br_2NO_2$ 475.9855, found 475.9850.

(1*R*, 2*S*)-2-(*N*-2'-hydroxyl-3'-adamantanyl-5'-*tert*butyl-benzyl) amino-1, 2-diphenyl-1-ethanol (1j): mp 44-46 °C; $[\alpha]^{25}_D$ –6.4 (*c* 0.40 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11-7.36 (m, 11H), 6.65 (s, 1H), 4.92 (d, *J* = 6.4 Hz, 1H), 3.87 (d, *J* = 6.0 Hz, 1H), 3.76 (d, *J* = 13.2 Hz, 1H), 3.54 (d, *J* = 13.2 Hz, 1H), 2.14 (m, 15H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 140.6, 137.8, 136.3, 128.6, 128.5, 128.4, 128.2, 128.1, 126.8, 123.2, 122.8, 122.0, 68.2, 51.1, 40.4, 37.2, 37.0, 34.1, 31.6, 29.2. HRMS: calculated [M+H] for $C_{35}H_{43}NO_2$ 510.3327, found 510.3452.

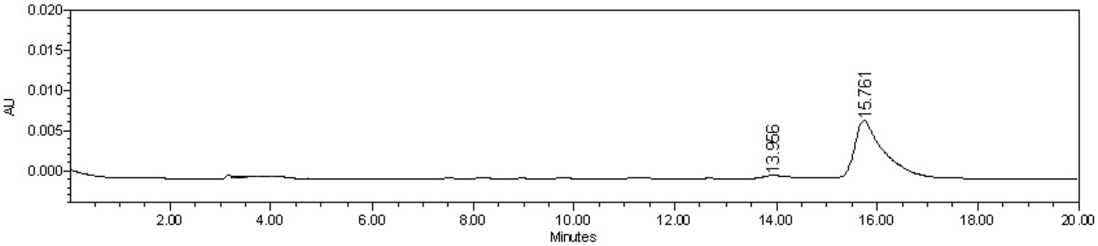
(*S*)-2-(*N*-2'-hydroxyl-3'-methyl-benzyl) amino-2-methyl-1-ethanol (2a): mp 33-35 °C; $[\alpha]^{25}_D$ +47.5 (*c* 0.40 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03-7.04 (d, *J* = 7.2 Hz, 1H), 6.83-6.85 (d, *J* = 7.6 Hz, 1H), 6.69 (t, 1H), 4.04 (d, *J* = 13.6 Hz, 1H), 3.92 (d, *J* = 13.6 Hz, 1H), 3.70 (m, 1H), 3.48 (m, 1H), 2.86 (m, 1H), 2.22 (s, 3H), 1.13 (d, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 129.8, 125.7, 125.2, 122.2, 118.6, 65.8, 53.8, 50.0, 16.4, 15.7. HRMS: calculated [M+H] for $C_{11}H_{17}NO_2$ 196.1332, found 196.1330.

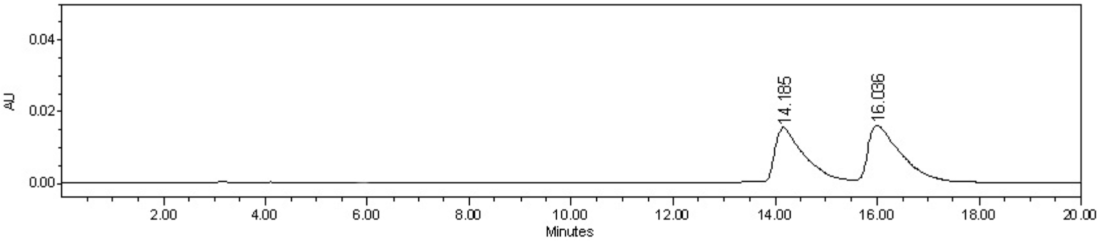
(*S*)-2-(*N*-2'-hydroxyl-3'-methyl-benzyl) amino-2-*iso*-butyl-1-ethanol (2b): mp 71-72 °C; $[\alpha]^{25}_D$ +12.8 (*c* 0.40 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.69 (t, 1H), 3.82 (d, *J* = 3.6 Hz, 1H), 3.79 (d, *J* = 3.2 Hz, 1H), 3.54 (d, *J* = 5.6 Hz, 1H), 3.52 (d, *J* = 5.2 Hz, 1H), 2.76 (m, 1H), 2.23 (s, 3H), 1.71 (m, 1H), 1.45 (m, 1H), 1.30 (m, 1H), 0.93 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 129.9, 125.8, 125.3, 122.2, 118.6, 63.4, 56.1, 49.9, 40.4, 24.9, 22.8, 22.7, 15.7. HRMS: calculated [M+H] for $C_{14}H_{23}NO_2$ 238.1802, found 238.1804.

(S)-2-(N-2’-hydroxyl-3’-methyl-benzyl) amino-2-benzyl-1-ethanol (2c): mp 87-88 °C; $[\alpha]^{25}_{D}$ –19.0 (c 0.50 $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, 1H), 7.17-7.25 (m, 4H), 7.04 (d, J = 7.2 Hz, 1H), 6.82 (d, J = 7.2 Hz, 1H), 6.69 (t, J = 7.6 Hz, 1H), 3.73 (d, J = 3.6 Hz, 1H), 3.71 (d, J = 4.0 Hz, 1H), 3.54 (d, J = 5.2 Hz, 1H), 3.52 (d, J = 4.8 Hz, 1H), 2.98 (m, 1H), 2.78-2.94 (m, 2H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 138.0, 129.9, 129.2, 128.7, 126.6, 125.8, 125.3, 122.0, 118.7, 62.6, 59.6, 50.3, 37.3, 15.7. HRMS: calculated [M+H] for $C_{17}H_{21}NO_2$ 272.1645, found 272.1648.

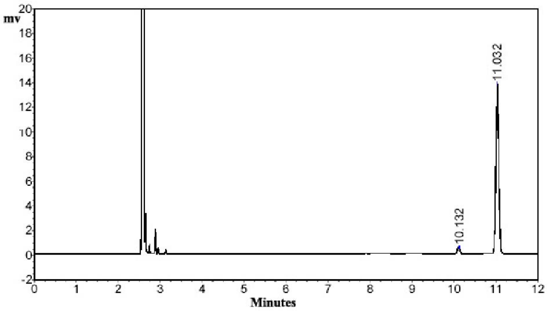
Data of Product:

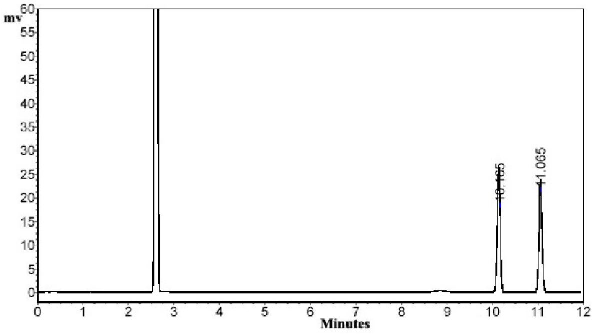
2-Hydroxy-2-phenylacetonitrile (6a): $[\alpha]^{25}_{D}$ –45.7 (c 1.38 $CHCl_3$) for S-enantiomer in 94%ee [lit.[1] $[\alpha]^{24}_{D}$ +36.8 (c 2.0 $CHCl_3$) for R-enantiomer in 85%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 7.40-7.60 (m, 5H), 5.55 (s, 1H), 2.91 (br s, 1H). Enantiomeric excess was determined by HPLC on a Chiralcel OD column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, t_{R1} = 13.966 min (minor), t_{R2} = 15.761 min (major).



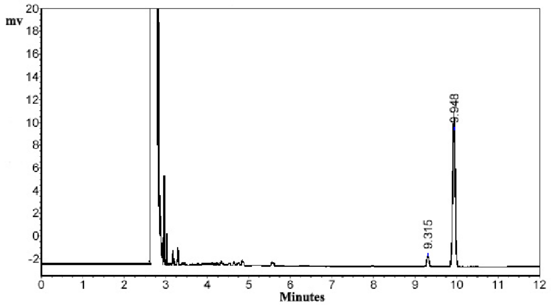


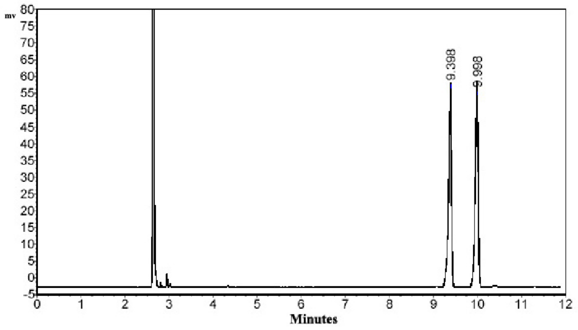
2-Hydroxy-2-(4-methylphenyl) acetonitrile (6b): $[\alpha]^{25}_{D}$ –42.1 (*c* 2.04 $CHCl_3$) for *S*-enantiomer in 93%ee [lit.[1] $[\alpha]^{24}_{D}$ +36.4 (*c* 2.0 $CHCl_3$) for *R*-enantiomer in 71%ee]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25-7.42 (m, 4H), 5.50 (s, 1H), 3.10 (br s, 1H), 1.98 (s, 3 H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 158 °C (isothermal), inject temperature = 200 °C, detector temperature = 250 °C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 10.132 min (minor), t_{R2} = 11.032 min (major).



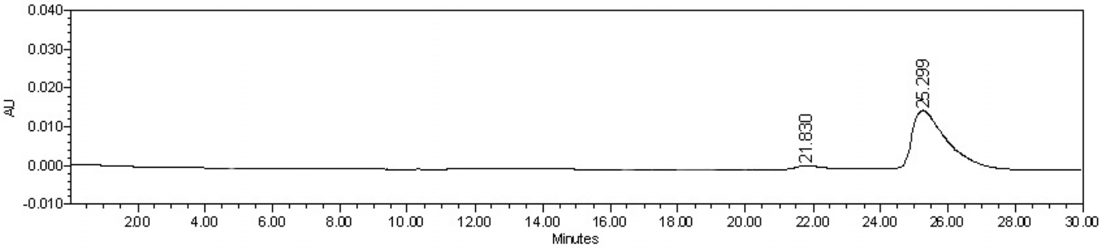


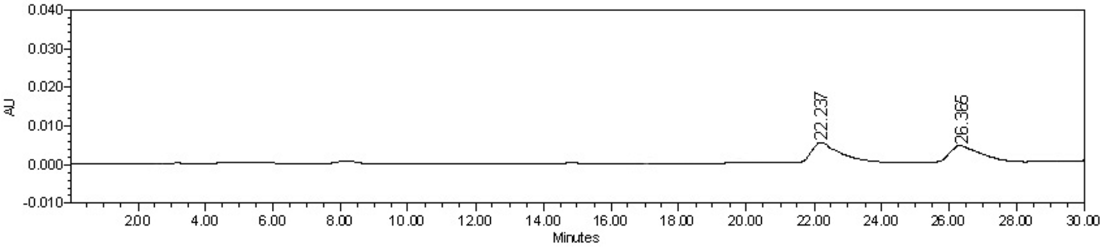
2-Hydroxy-2-(3-methylphenyl) acetonitrile (6c): $[\alpha]^{25}_{D}$ –36.1 (*c* 2.00 $CHCl_3$) for *S*-enantiomer in 88%ee; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22-7.69 (m, 4H), 5.48 (s, 1H), 2.43 (br s, 1H), 2.39 (s, 3 H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 158 °C (isothermal), inject temperature = 200 °C, detector temperature = 250 °C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 9.315 min (minor), t_{R2} = 9.948 min (major).



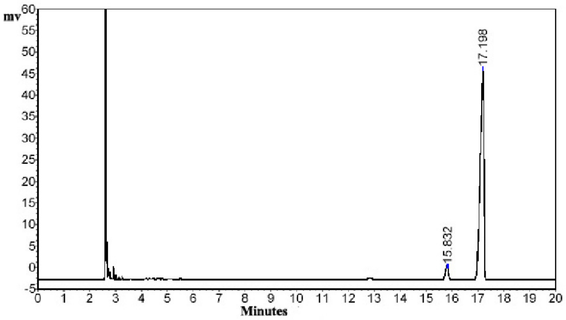


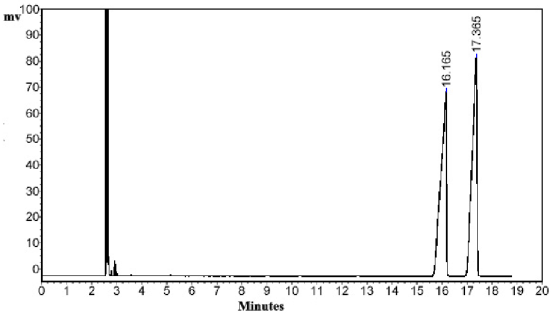
2-Hydroxy-2-(4-methoxyphenyl) acetonitrile (6d): $[\alpha]^{25}_{D}$ –44.8 (*c* 1.30 $CHCl_3$) for *S*-enantiomer in 93%ee [lit.[1] $[\alpha]^{24}_{D}$ +41.7 (*c* 1.4 $CHCl_3$) for *R*-enantiomer in 91%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 6.96-7.46 (m, 4H), 5.49 (s, 1H), 3.84 (s, 3H), 2.7 (br s, 1 H). Enantiomeric excess was determined by HPLC on a Chiralcel OD column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, t_{R1} = 21.830 min (minor), t_{R2} = 25.229 min (major).



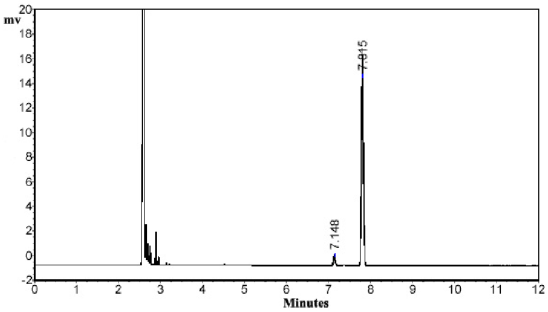


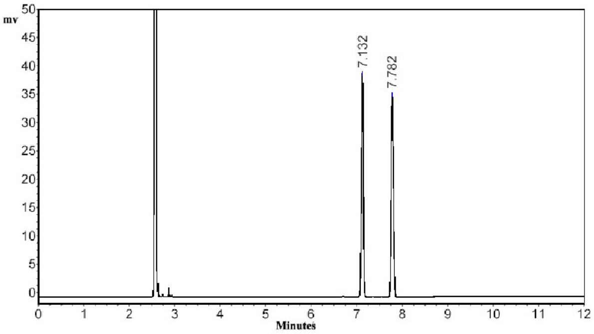
2-Hydroxy-2-(3-methoxyphenyl) acetonitrile (6e): $[\alpha]^{25}_{D}$ –37.2 (*c* 2.36 $CHCl_3$) for *S*-enantiomer in 90%ee [lit.[1] $[\alpha]^{24}_{D}$ +22.8 (*c* 1.5 $CHCl_3$) for *R*-enantiomer in 56%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 6.93-7.47 (m, 4H), 5.50 (s, 1H), 3.82 (s, 3 H), 3.10 (br s, 1H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 158 ^oC (isothermal), inject temperature = 200 ^oC, detector temperature = 250 ^oC, inlet pressure = 5.516×10^4 Pa, t_{R1} = 15.832 min (minor), t_{R2} = 17.198 min (major).



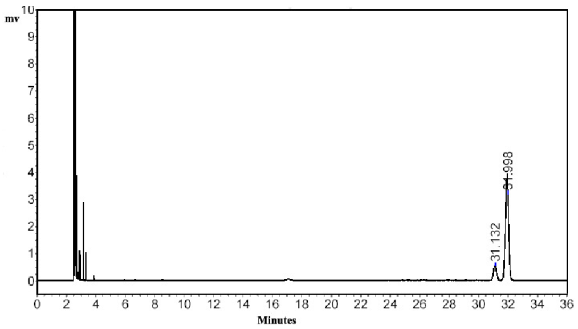


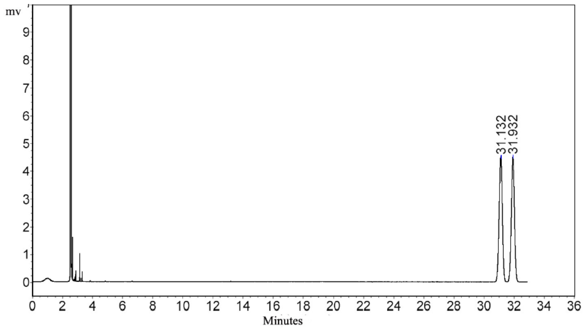
2-Hydroxy-2-(4-fluorophenyl) acetonitrile (6f): $[\alpha]^{25}_{D}$ –33.6 (*c* 1.62 $CHCl_3$) for *S*-enantiomer in 92%ee [lit.[2] $[\alpha]^{20}_{D}$ +36.4 (*c* 6.4 $CHCl_3$) for *R*-enantiomer in 94%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 7.18-7.92 (m, 4H), 5.52 (s, 1H), 4.48 (br s, 1H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 158 °C (isothermal), inject temperature = 200 °C, detector temperature = 250 °C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 7.148 min (minor), t_{R2} = 7.815 min (major).



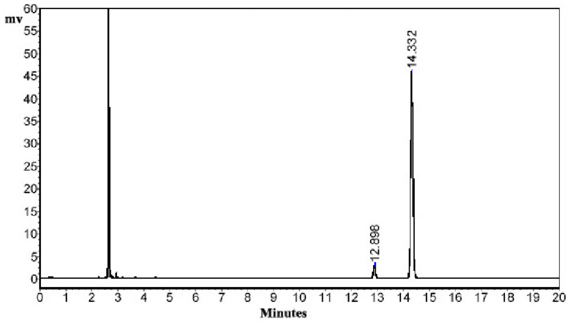


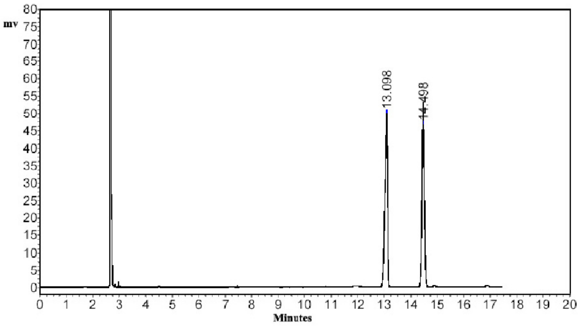
2-Hydroxy-2-(2-chlorophenyl) acetonitrile (6g): $[\alpha]^{25}_{D}$ –2.2 (*c* 2.72 $CHCl_3$) for *S*-enantiomer in 76%ee; ^1H NMR (600 MHz, $CDCl_3$) δ 7.27-7.93 (m, 4H), 5.89 (s, 1H), 3.41 (br s, 1H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 130 °C (isothermal), inject temperature = 200 °C, detector temperature = 250 °C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 31.132 min (minor), t_{R2} = 31.998 min (major).



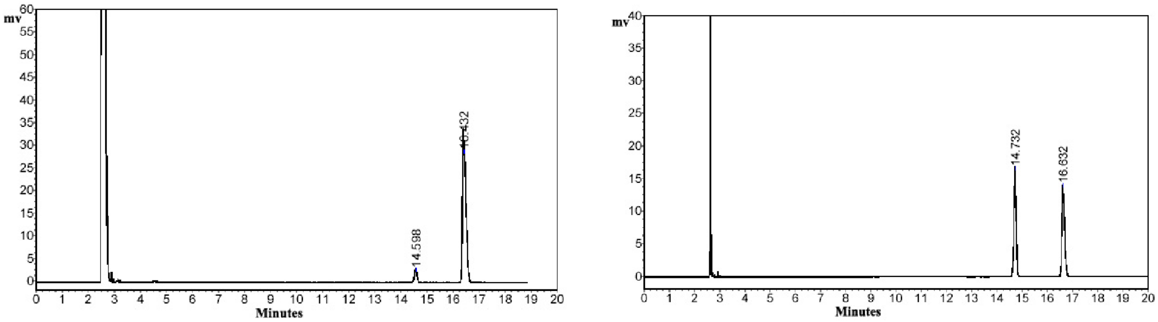


2-Hydroxy-2-(3-chlorophenyl) acetonitrile (6h): $[\alpha]^{25}_{D}$ –41.3 (*c* 1.90 $CHCl_3$) for *S*-enantiomer in 90%ee; ^1H NMR (600 MHz, $CDCl_3$) δ 7.27-7.86 (m, 4H), 5.54 (s, 1H), 3.94 (br s, 1H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 158 °C (isothermal), inject temperature = 200 °C, detector temperature = 250 °C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 12.898 min (minor), t_{R2} = 14.332 min (major).

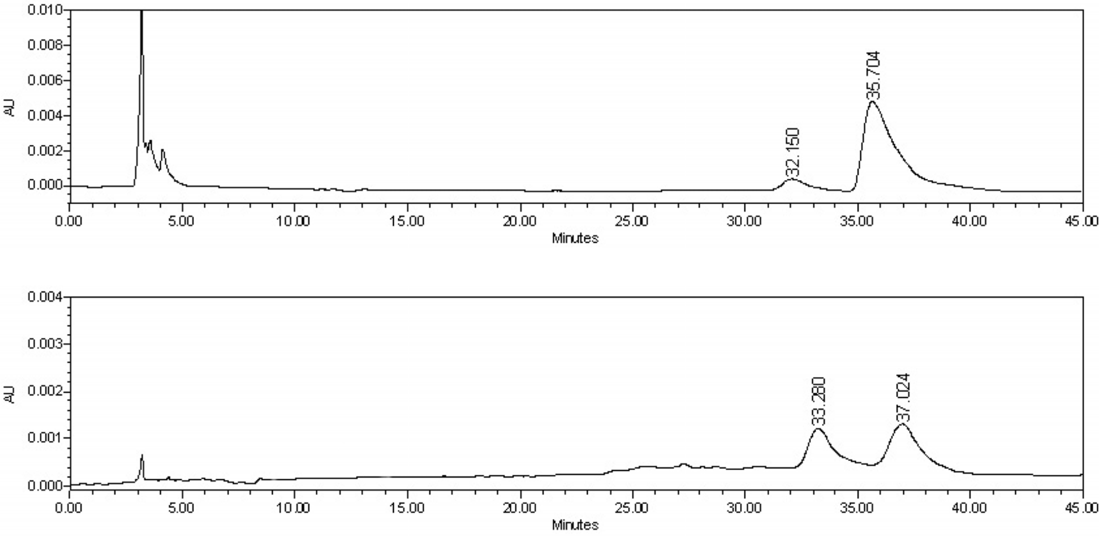




2-Hydroxy-2-(4-chlorophenyl) acetonitrile (6i): $[\alpha]^{25}_{D}$ –34.5 (*c* 1.70 $CHCl_3$) for *S*-enantiomer in 87%ee [lit.[3] $[\alpha]^{25}_{D}$ +27.2 (*c* 1.487 $CHCl_3$) for *R*-enantiomer in 66%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 7.39-7.82 (m, 4H), 5.52 (s, 1H), 4.28 (br s, 1H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 158 °C (isothermal), inject temperature = 200 °C, detector temperature = 250 °C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 14.598 min (minor), t_{R2} = 16.432 min (major).

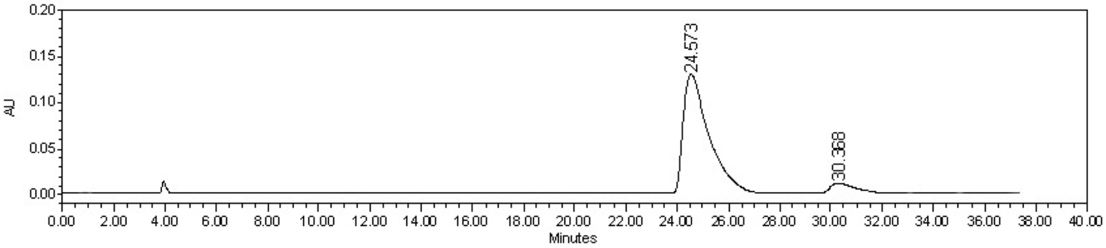


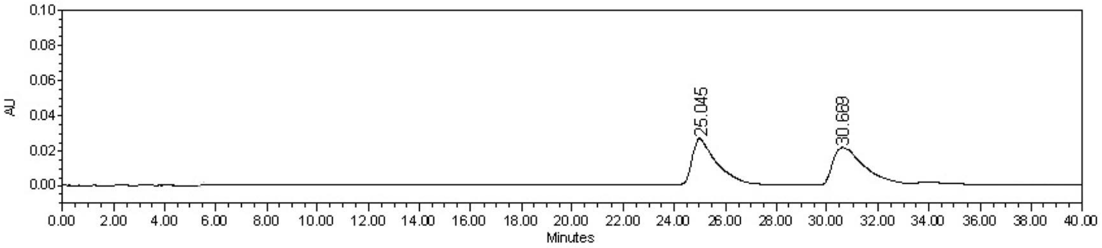
2-Hydroxy-2-(4-cyanophenyl) acetonitrile (6j): $[\alpha]^{25}_{D}$ –20.1 (*c* 2.30 $CHCl_3$) for *S*-enantiomer in 80%ee [lit.[1] $[\alpha]^{24}_{D}$ +6.5 (*c* 1.5 $CHCl_3$) for *R*-enantiomer in 20%ee]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68-8.02 (m, 4H), 5.65 (s, 1H), 3.88 (br s, 1 H). Enantiomeric excess was determined by HPLC on a Chiralcel OD column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, t_{R1} = 33.150 min (minor), t_{R2} = 35.704 min (major).



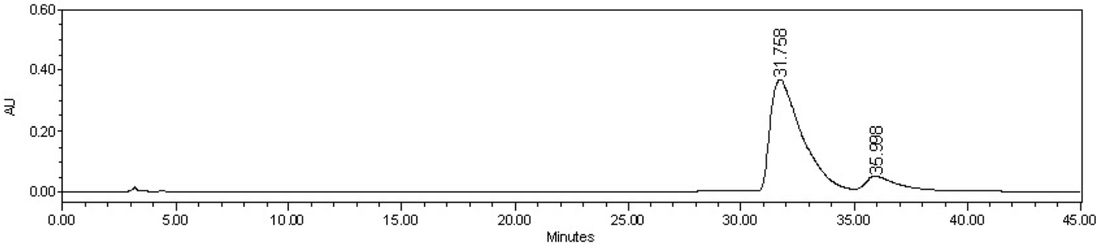
2-Hydroxy-2-(1'-naphthyl) acetonitrile (6k): $[\alpha]^{25}_{D}$ –67.4 (*c* 1.00 $CHCl_3$) for *S*-enantiomer in 82%ee [lit.[4] $[\alpha]^{24}_{D}$ –62.6 (*c* 1.4 $CHCl_3$) for *S*-enantiomer in 76%ee]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50-8.16 (m, 7H), 6.18 (s, 1H), 3.20 (br s, 1 H). Enantiomeric excess was determined by HPLC on a

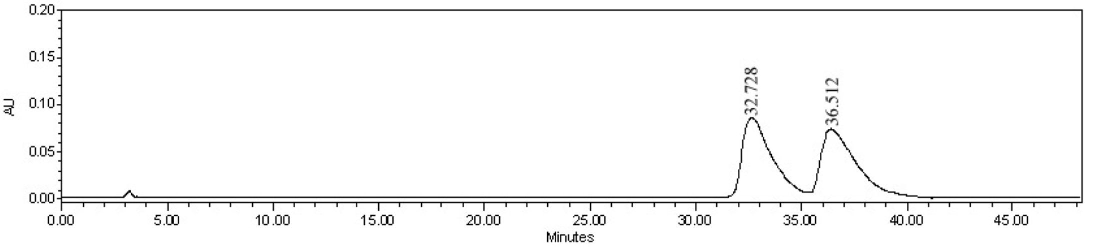
Chiralcel OD column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, t_{R1} = 24.573 min (major), t_{R2} = 30.368 min (minor).



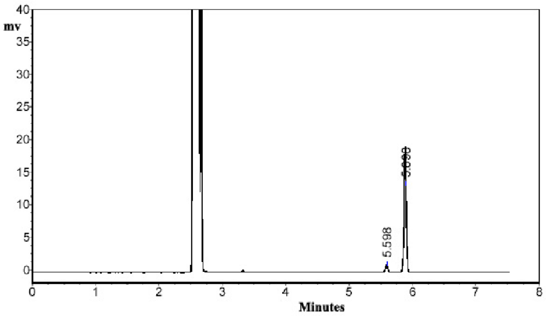


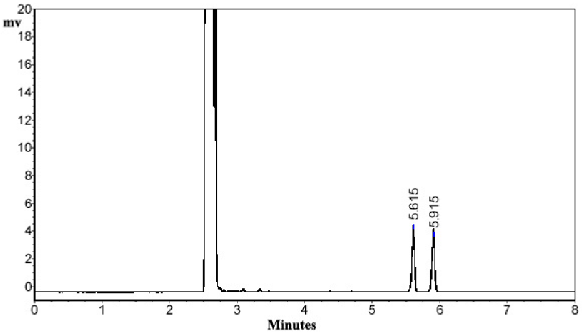
2-Hydroxy-2-(2'-naphthyl) acetonitrile (6l): $[\alpha]^{25}_{D}$ –29.1 (*c* 1.00 $CHCl_3$) for *S*-enantiomer in 75%ee [lit.[3] $[\alpha]^{24}_{D}$ +26.4 (*c* 0.522 $CHCl_3$) for *R*-enantiomer in 86%ee]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28-8.03 (m, 7H), 5.72 (s, 1H), 3.16 (br s, 1 H). Enantiomeric excess was determined by HPLC on a Chiralcel OD column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, t_{R1} = 31.758 min (major), t_{R2} = 35.998 min (minor).



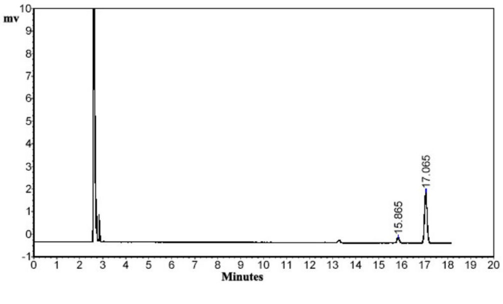


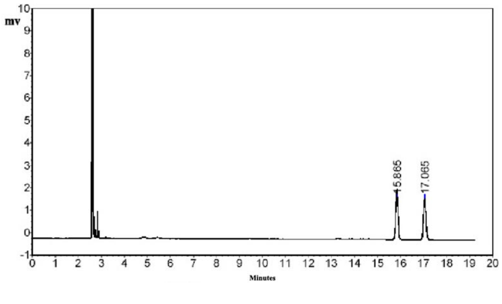
2-Hydroxy-2-(2’-furyl) acetonitrile (6m): $[\alpha]^{25}_{D}$ –18.7 (*c* 0.52 $CHCl_3$) for *S*-enantiomer in 89%ee [lit.[5] $[\alpha]^{31}_{D}$ +23.30 (*c* 0.92 $CHCl_3$) for *R*-enantiomer in 61%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 7.27-7.71 (m, 3H), 5.57 (s, 1H), 4.31 (br s, 1H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 145 °C (isothermal), inject temperature = 200 °C, detector temperature = 250 °C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 5.598 min (minor), t_{R2} = 5.898 min (major).



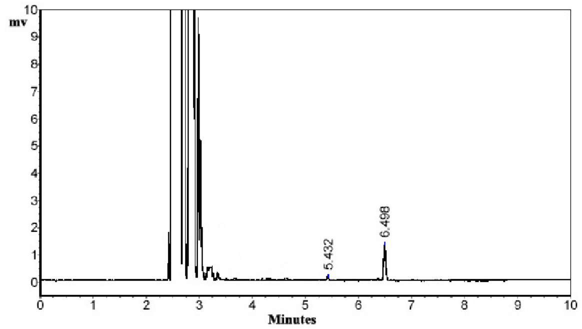


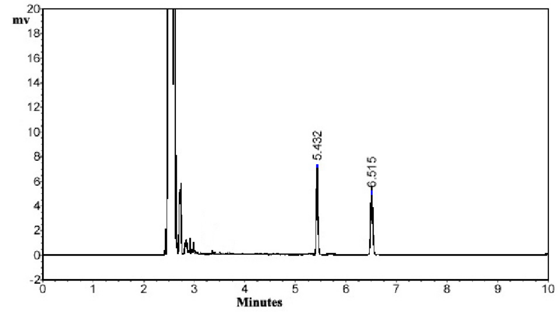
(*E*)-2-Hydroxy-4-phenyl-3-butenenitrile (6n): $[\alpha]^{25}_{D}$ –27.3 (*c* 2.68 $CHCl_3$) for *S*-enantiomer in 82%ee [lit.[1] $[\alpha]^{24}_{D}$ +19.2 (*c* 1.9 $CHCl_3$) for *R*-enantiomer in 72%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 7.32-7.49 (m, 5H), 6.75 (dd, *J* = 15.8 Hz, 1.1 Hz, 1H), 6.28 (dd, *J* = 15.8 Hz, 5.7 Hz, 1H), 5.19 (dd, *J* = 5.7 Hz, 1.1 Hz, 1H), 2.71 (br s, 1H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 168 °C (isothermal), inject temperature = 200 °C, detector temperature = 250 °C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 15.865 min (minor), t_{R2} = 17.065 min (major).



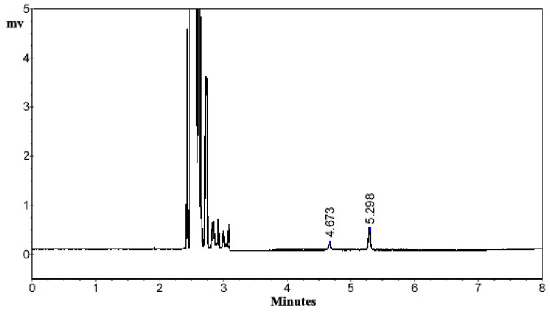


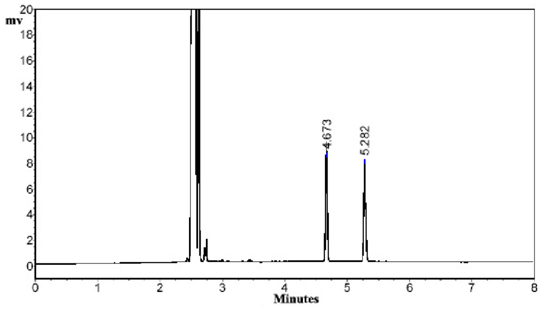
(*E*)-2-Hydroxy-3-pentenenitrile (6o): $[\alpha]^{25}_{D}$ –31.3 (*c* 0.50 $CHCl_3$) for *S*-enantiomer in 82%ee [lit.[1] $[\alpha]^{24}_{D}$ –35.7 (*c* 0.3 $CHCl_3$) for *S*-enantiomer in 89%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 6.10 (m, 1H), 5.64 (m, 1H), 4.93 (dd, *J* = 1.2 Hz, 6.1 Hz, 1H), 3.70 (br s, 1H), 1.80 (dd, *J* = 6.1 Hz, 1.2 Hz, 1H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 117 ^{o}C (isothermal), inject temperature = 200 ^{o}C, detector temperature = 250 ^{o}C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 5.432 min (minor), t_{R2} = 6.498 min (major).



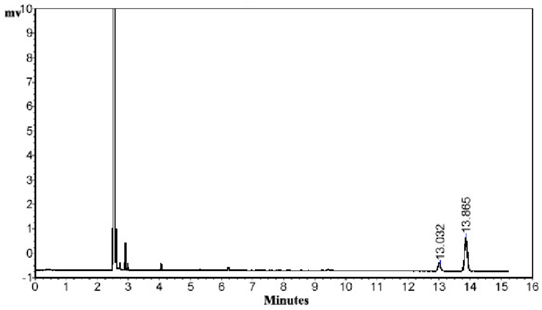


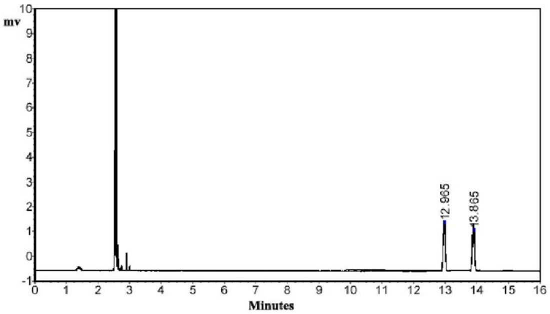
2-Hydroxyheptanenitrile (6p): $[\alpha]^{25}_{D}$ –13.2 (*c* 0.40 $CHCl_3$) for *S*-enantiomer in 57%ee [lit.[4] $[\alpha]^{24}_{D}$ –11.5 (*c* 1.1 $CHCl_3$) for *S*-enantiomer in 89%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 4.48 (m, 1H), 2.83 (br s, 1H), 1.23-1.87 (m, 11H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 140 ^{o}C (isothermal), inject temperature = 200 ^{o}C, detector temperature = 250 ^{o}C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 5.932 min (minor), t_{R2} = 6.515 min (major).



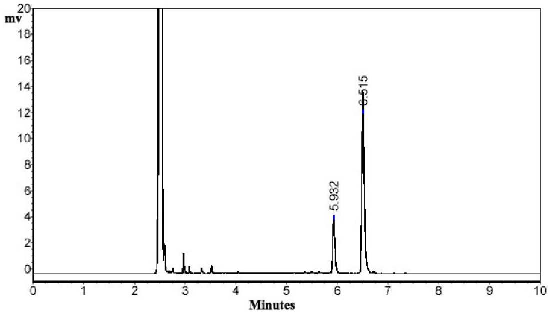


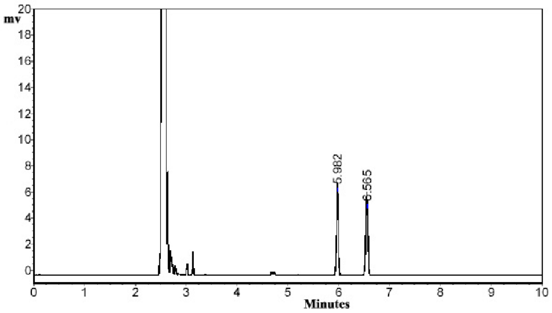
2-Hydroxy-3-phenylpropionenitrile (6q): $[\alpha]^{25}_{D}$ –8.6 (*c* 1.00 $CHCl_3$) for *S*-enantiomer in 72%ee [lit.[5] $[\alpha]^{30}_{D}$ +6.36 (*c* 0.94 $CHCl_3$) for *R*-enantiomer in 59%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 7.19-7.46 (m, 5H), 4.68 (s, 1H), 3.14 (m, 2H), 2.28 (br s, 1H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 140 °C (isothermal), inject temperature = 200 °C, detector temperature = 250 °C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 13.032 min (minor), t_{R2} = 13.865 min (major).





2-Hydroxy-3-methylbutanenitrile (6r): $[\alpha]^{25}_{D}$ –7.9 (*c* 0.70 $CHCl_3$) for *S*-enantiomer in 60%ee [lit.[1] $[\alpha]^{24}_{D}$ +4.2 (*c* 1.3 $CHCl_3$) for *R*-enantiomer in 34%ee]; ^1H NMR (600 MHz, $CDCl_3$) δ 4.28 (s, 1H), 3.38 (br s, 1H), 2.05 (m, 1H), 1.08 (m, 6H). Enantiomeric excess was determined by GC on Varian, CP-Chirasil DEX CB (0.25 mm × 25 m), column temperature = 117 °C (isothermal), inject temperature = 200 °C, detector temperature = 250 °C, inlet pressure = 5.516×10^4 Pa, t_{R1} = 4.673 min (minor), t_{R2} = 5.298 min (major).





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